European Molecular Liquids Group (EMLG)
and
Japanese Molecular Liquids Group (JMLG)
Annual Meeting 2026

University of Strathclyde, Glasgow
31st August – 3rd September

EMLG/JMLG 2026 is kindly sponsored by:

CCP5
Collaborative
Computational Project
Computer Simulation of Condensed Phases

Molecular Simulation
Taylor & Francis
by informa

TRIPLE DISTILLED
ESTD 1823
AUCHENTOSHAN
AUCHENTOSHAN
SINGLE MALT SCOTCH WHISKY

Glasgow
CITY COUNCIL

RSC
Applied Interfaces

molecules
an Open Access Journal by MDPI

Contents

Right-click and update field

Oral Contributions

Session 1

Surfactant Assembly and Disassembly far from Equilibrium — Colin Bain

Surfactant Assembly and Disassembly far from Equilibrium

Colin D. Bain

Department of Chemistry, Durham University, Durham, UK
e-mail: c.d.bain@durham.ac.uk

The assembly of surfactants in aqueous solution to form micelles was postulated by McBain more than a century ago [1] and ninety years have passed since the canonical structure of a spherical micelle was first proposed by Hartley [2]. The mechanism by which surfactant micelles form and break-up was addressed in 1974 in an elegant paper by Aniansson and Wall [3], who proposed a stepwise mechanism with two relaxation times, one characteristic of the entry or exit of a single surfactant molecule from a micelle and the other, slower, time with the complete disassembly of a micelle into surfactant monomers. The Aniansson and Wall model is limited to small deviations from equilibrium and, for some systems, gives poor predictions of the concentration dependence of relaxation times. In the intervening years, a consensus has begun to emerge that there are actually two distinct mechanisms by which micelles can break down (or form) [4]: one is via a stepwise loss of monomers from a micelle until it disappears [3], and the other is the collision of two micelles to form a 'supermicelle' that can then shed monomers to form a single micelle of normal size [5] [6]. Which mechanism dominates depends not only on the nature of the surfactant but also on the total concentration of surfactant and – critically – the monomer concentration. The rates of both mechanisms are strong functions of the deviation from equilibrium, for different reasons.

This talk will describe our current understanding of the assembly and disassembly of surfactant micelles, explain why the 'rate constants' of these processes vary strongly with the perturbation from equilibrium and discuss the implications of these observations for the many practical processes where surfactant solutions are far from equilibrium. The extent to which experimental evidence is consistent with these models will be discussed.

References

[1] J. W. McBain, *Trans. Faraday Soc.*, **9,** 99 (1913).
[2] G. S. Hartley, *Kolloid Z.*, **88**, 2 (1939).
[3] E. A. G. Aniansson and S. N. Wall, *J. Phys. Chem.* **78**, 1024 (1974).
[4] For a clear recent exposition, see J. Mysona, A. McCormick and D. Morse, *Phys. Rev. E*, **105**, 034602 (2022).
[5] M. Kahlweit and M. Teubner, *Adv. Colloid Interface Sci*. **13**, 1 (1980).
[6] I. M. Griffiths, C. J. W. Breward, D. M. Colegate, P. J. Dellar, P. D. Howell, and C. D. Bain, *Soft Matter*, **9**, 853 (2013).

Computer simulations of complex self-assembly – and obstinate agglomeration

A. Dastan[1], J. Earnshaw[1] and D.J. Cleaver[1]

[1]Materials and Engineering Research Institute, Sheffield Hallam University
e-mail: d.j.cleaver@shu.ac.uk

Most of the twisted fibres and threads found in natural systems are formed through spontaneous self-assembly of small molecules, such as peptides, and stabilised by hydrogen bonds rather than covalent cross-links [1]. This can lead to amazing structures, since the inherent flexibility of hydrogen bonds allows for morphological change within a self-assembly pathway. However, it also imposes a considerable restriction - for a given object type to exist it needs not only to be stable (to changes in mechanical environment, temperature, pH, ...), but also to be a reproducible end-point of a full aggregation process [2]. This requires it to have a complete, kinetically accessible pathway, potentially involving several generations of aggregate [3].

Here, we use molecular dynamics simulation to examine bipartite particle-based systems which combine the thread-packing of chromonics and the frustrations of amphiphilicity to yield a range of self-assembled structures with emergent supramolecular chirality. Through this, we find a veritable zoo of hierarchical, chiral self-assembled structures, the supramolecular morphologies of which emerge from choices of particle-level parameters [3]. As well as directly observing how structures such as fibres, bundles and tubules nucleate and grow, often via intermediate states with super-extensive growth modes.

We then contrast this with the behaviour of functionalised Polyhedral Oligomeric Silsesquioxanes (POSS) systems which, for most choices of ligand, lock into disordered, immobile glasses at high temperatures. When appropriately blended within an organic matrix material, however, even these POSS systems can be effectively dispersed to achieve target composite behaviours [4].

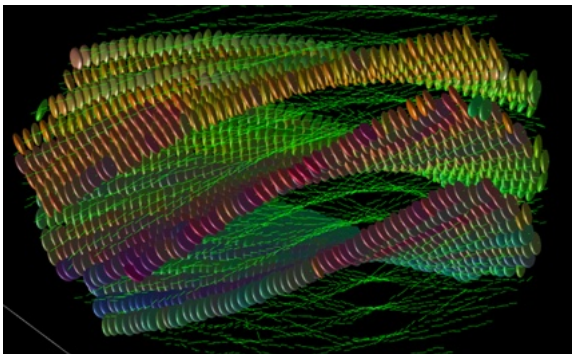

Figure 1 *– Side view of a twisted, multi-sheet bundle self-assembled by a mixture of discotic and spherical particles. For clarity, the spheres are not shown, and the discs are shown in full for three layers but as short, axial lines for all others.*

References

[1] I.W. Hamley, *Chemie Angew*, **46**, 8128 (2007).
[2] A. Dastan, W.J. Frith and D.J. Cleaver, *J Phys Chem B*, **121**, 9920 (2017).
[3] A. Dastan, E.A. Matsumoto, W.J. Frith and D.J. Cleaver, *Mol Phys*, **116**, 2823 (2018).
[4] J. Earnshaw, Molecular Dynamics simulation of polyhedral oligomeric silsesquioxanes (POSS) and their polymeric nanocomposites, PhD Thesis, Sheffield Hallam University (2022).

Integral Equations and Density Functional Theory for the cluster fluid phase of fluids with competing interactions

Martin B. Sweatman

School of Engineering, University of Edinburgh, Mayfield Road, Edinburgh, EH9 3FB.
e-mail: martin.sweatman@ed.ac.uk

Fluids with short-ranged attractive (SA) interactions and long-ranged repulsive (LR) interactions, often called SALR fluids, are known to form clusters of particles at low concentrations for suitable combinations of SALR parameters. These clusters can appear to behave like a stable dispersion of liquid-like droplets. SALR fluids are, therefore, often considered a reasonable model for some biological molecules, such as proteins, and other large molecules that are also known to form large stable clusters in solution.

Due to their strong concentration fluctuations over multiple length scales, these cluster fluids have proved quite challenging to model theoretically using standard methods, such as integral equations and density functional theory. Here, some recent progress in this area towards obtaining an accurate density functional theory (DFT) for the cluster fluid phase is presented [1,2].

In the first part of this presentation, some issues with published DFT approaches are described and a weighted DFT that can potentially overcome these issues is suggested [1]. A key input into this weighted DFT is accurate knowledge of the pair direct correlation function at a specific density for the cluster fluid. This can be generated using integral equation methods, although standard integral equation closures and/or Picard iteration solution methods for these clustered states often fail. However, ChatGPT 5 has been used to help design a suitable algorithm that can overcome such “stiffness” problems for some closures [2]. This progress is described in the second part of this presentation, although more work is needed to fully demonstrate the utility of this approach.

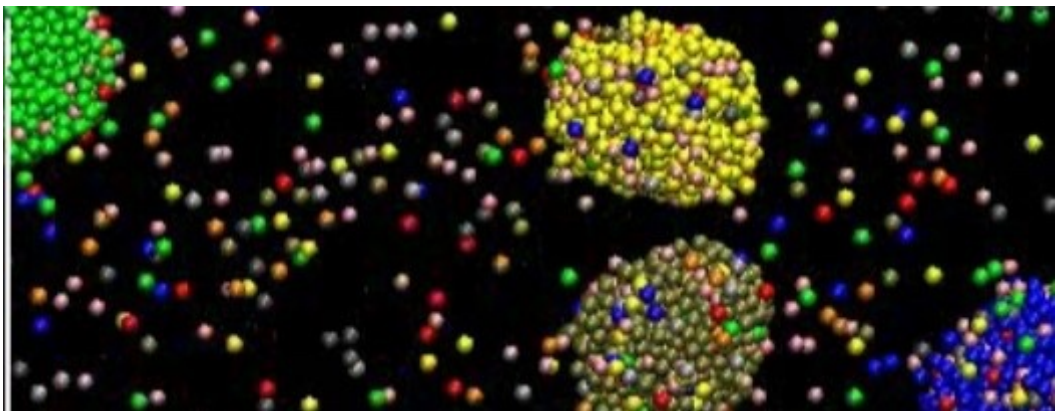

Figure 1 *– Example of the cluster fluid phase of the hard sphere double Yukawa SALR fluid*

Acknowledgements: I am grateful for insightful conversations with Leo Lue and the hard work of Jiazheng Tan on aspects of this study.

References

[1] M.B. Sweatman, submitted to Molecular Physics, 2026.
[2] M.B. Sweatman and J. Tan, submitted to Molecular Physics, 2026.

Comprehensive Theoretical Approaches to the Self-Assembly Process at the Molecular Level

H. Sato[1,2]
[1]Department of Molecular Engineering, Kyoto University
[2]Fukui Institute for Fundamental Chemistry, Kyoto University
e-mail: hirofumi@moleng.kyoto-u.ac.jp

Self-assembly, in which highly ordered structures form spontaneously, has attracted the attention of many researchers. Whilst it is often described as a quantitative conversion that yields a unique product from a macroscopic perspective, the process involves many intermediates that connect to form a complex network of numerous elementary steps at the molecular level. To gain insight into the process, a comprehensive approach is vital, and we have been developing a variety of theoretical approaches, including statistical mechanics for liquids, quantum chemistry, dynamical theory and so on. Prof Hiraoka (U Tokyo) developed an experimental protocol utilising NMR, called QASAP. As the theoretical counterpart, we developed NASAP (numerical analysis of the self-assembly process), providing more detailed information. In this treatment, the process is simulated on the network of possible intermediates using the Gillespie algorithm to be consistent with QASAP. The analysis has been successfully applied to various systems [1], especially in drawing a new perspective on a chemical reaction network [2]. Figure 1 illustrates an example of NASAP, in which a caged dinuclear palladium complex $[Pd_2L_4]^{4+}$ is analysed as a time evolution of the self-assembly [3].

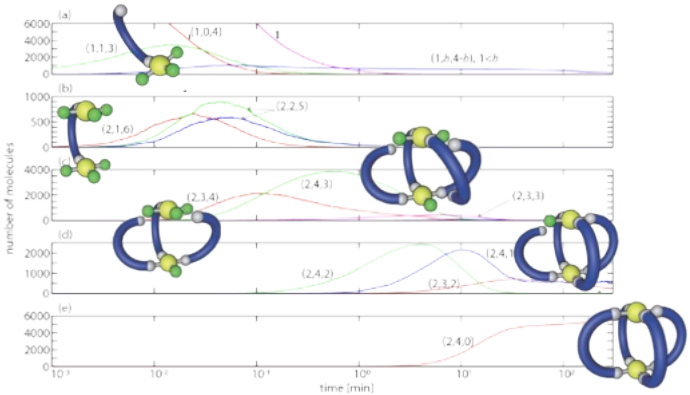

Figure 1 *– Analysis by NASAP allows the long-term changes in all intermediates to be tracked. Reproduced from [3] with permission from the Royal Society of Chemistry.*

In addition, a coarse-grained analysis is proposed for this cage-formation system to extract interactions among constituent units during assembly [4]. Recent developments in a quantum-statistical mechanical hybrid theory for solvated molecules, RISM-SCF-cSED, will be addressed if time permits [5].

Acknowledgements
The author thanks Prof Shuichi Hiraoka, Dr Satoshi Takahashi, Dr Satoru Iuchi and all the collaborators, including the students.

References
[1] S. Takahashi, S. Iuchi, S. Hiraoka, and H. Sato, *Phys. Chem. Chem. Phys.*, **25**, 14659 (2023).
[2] S. Takahashi, T. Abe, H. Sato, and S. Hiraoka, *Chem.*, **9**, 2971 (2023). T. Abe, K. Takeuchi, M. Higashi, H. Sato, and S. Hiraoka, *Nature Chem.*, **15**, 7630 (2024).
[3] S. Takahashi, Y. Sasaki, S. Hiraoka, and H. Sato, *Phys. Chem. Chem. Phys.*, **21**, 6341 (2019).
[4] Y. Ichikawa, K. Sugiyama, M. Higashi, S. Hiraoka, and H. Sato, *Chem. Lett.*, **53**, upae099 (2024).
[5] K. Imamura, D. Yokogawa, and H. Sato, *J. Chem. Phys.*, **160**, 050901 (2024).

2D Network of PDMS and PEO-PPO-PEO at the air-water interface

B. Kővágó[1,2], A. Araminthe[3], A. El Haitami[3], S. Cantin[3], E. H. G. Backus[1,2]
[1]Institute of Physical Chemistry, Faculty of Chemistry, University of Vienna, Währinger Str. 42, 1090 Vienna, Austria
[2]University of Vienna, Vienna Doctoral School in Chemistry (DoSChem), Währinger Str. 42, 1090 Vienna, Austria
[3]CY Cergy Paris Université, LPPI FP95000 Cergy, France
e-mail: ellen.backus@univie.ac.at

Thin polymer films based on polymer blends can be used as coatings with tunable properties. Such films can be created with the Langmuir film method: polymers are deposited on water controlling their density by compression, potentially cross-linked to obtain networks, and subsequently transferred onto a solid substrate resulting in stable thin films. As a first step to design such films, the miscibility properties of non-cross-linked polymer blends must be understood. In this work, we focus on understanding the miscibility properties of amphiphilic poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) triblock copolymer and predominantly hydrophobic poly(dimethylsiloxane) (PDMS). We analyzed surface pressure-area isotherms to determine the phase transitions of the blends and used Brewster angle microscopy (BAM) to understand the mixing behavior at the interface. We combined these results to build a surface pressure-composition phase diagram and identified a miscibility region independent of composition at low surface pressure. To connect the phase diagram with molecular level information, sum frequency generation (SFG) spectroscopy has been performed. With this method basically the vibrational spectrum of the interface can be obtained. From peak amplitudes in the CH-OH and CO spectral region, we conclude that polymers change their orientation after the phase transition. To make a stable network, as a second step towards coatings, light induced cross linking of the end groups of the PDMS in the miscibility region on the water surface has successfully been conducted.

Structure and Single Particle Dynamics at the Free Surface of Imidazolium-Based Ionic Liquids

H. Tóth Ugyonka[1], Gy. Hantal[2], I. Szilágyi[3], A. Idrissi[4], M. Jorge[5], P. Jedlovszky[1]

[1]Department of Chemistry, Eszterházy Károly Katholic University, H-3300 Eger, Leányka u. 12, Hungary
[2]Department of Polymer Engineering, BUTE University, H-1111 Budapest, Hungary
[3]Department of Physical Chemistry and Materials Science, University of Szeged, H-6720 Szeged, Hungary
[4]Laboratory LASIR, University of Lille, F-59000 Villeneuve d'Ascq, France
[5]Department of Chemical and Process Engineering, University of Strathclyde, G1 1XJ Glasgow, UK
e-mail: jedlovszky.pal@uni-eszterhazy.hu

We present results of a systematic investigation of the structural and single particle dynamical properties at the free surface of imidazolium-based room temperature ionic liquids by applying intrinsic analysis methods both at the molecular and atomic levels. Besides assessing the effect of the potential model and temperature, we focus in particular on the effect of changing the anion type, and, hence, their shape and size. In doing so, we try to elucidate the relative roles of electrostatic interactions, hydrophobic (or, strictly speaking, apolar) effects and steric restrictions on the properties of the interface. Further, we also address the role of the length of the cation alkyl chains, known to protrude into the vapor phase, on the surface dynamics of the ions.

Concerning the surface structure, we see no evidence for the existence of a double-layer-type arrangement of the ions, nor for their self-association at the surface of the liquid. Instead, our results show that cation chains associate into apolar domains that protrude into the vapor phase, while charged groups form domain that are embedded in this apolar environment at the surface. However, the apolar chains largely obscure the cation groups to which they are bound, while the smaller and more mobile anions can more easily access the free surface, leading to a somewhat counterintuitive net excess of negative charge at the interface. Importantly, this excess charge could only be identified by applying intrinsic analysis. [1] Our results also show that this surface can be viewed as a superposition of two "interfaces", one between a hydrophobic layer of cation alkyl chains and the vapor phase, and another between that hydrophobic layer and an ionic fluid composed of polar groups of the cations and anions. Remarkably, the properties of this ionic surface are practically independent of the cation alkyl chain length, suggesting they are a universal feature of imidazolium-based RTILs. [2]

Further, we observe that the surface dynamics of ionic liquids, being dominated by strong electrostatic interactions, are about two orders of magnitude slower than that for common molecular liquids. Furthermore, the free energy driving force for exposing apolar chains to the vapor phase "pins" the cations at the surface layer for much longer than anions, allowing them to perform noticeable lateral diffusion at the liquid surface during their stay there. On the other hand, anions, accumulated in the second layer beneath the liquid surface, stay considerably longer here than in the surface layer. The ratio of the mean surface residence time of the cations and anions depends on the relative size of the two ions: larger size asymmetry typically corresponds to larger values of this ratio. We also find, in a clear contrast with the bulk liquid phase behavior, that anions typically diffuse faster at the liquid surface than cations. Finally, our results show that the surface dynamics of the ions is largely determined by the apolar layer of the cation alkyl chains at the liquid surface, as in the absence of such a layer, cations and anions are found to behave similarly with respect to their single particle dynamics. [3]

References

[1] H. Tóth Ugyonka, Gy. Hantal, I. Szilágyi, A. Idrissi, M. Jorge, P. Jedlovszky, *J. Coll. Interface Sci.*, **676**, 989 (2024)
[2] H. Tóth Ugyonka, Gy. Hantal, I. Szilágyi, A. Idrissi, M. Jorge, P. Jedlovszky, *J. Phys. Chem. Letters* **16,** 1873 (2025)
[3] H. Tóth Ugyonka, Gy. Hantal, I. Szilágyi, A. Idrissi, M. Jorge, P. Jedlovszky, *J. Phys. Chem. B* **129,** 579 (2025).

Flow-enhanced self-assembly of amyloid-β peptides studied by nonequilibrium molecular dynamics simulations

M. Otawa[1,2], S. G. Itoh[1,2,3], H. Okumura[1,2,3]
[1]The Graduate University for Advanced Studies
[2]Institute for Molecular Science
[3]Exploratory Research Center on Life and Living Systems
e-mail: hokumura@ims.ac.jp

Alzheimer's disease is associated with aggregates of amyloid-β (Aβ) peptides. Aβ peptides exist in extracellular fluids, whose fluidity is higher than that of intracellular environments, suggesting that flow effects should be considered in the aggregation process. Recently, it was experimentally reported that flow on extracellular membrane surfaces enhances the aggregation of Aβ peptides. However, the molecular mechanism underlying this phenomenon remains unclear.

To investigate this problem, we developed a new nonequilibrium molecular dynamics (NEMD) simulation method suitable for generating flow on biological membrane surfaces [1]. In this method, the centre of mass of the lipid bilayer is constrained using Lagrange multipliers to prevent drift of lipid molecules, while external lateral forces are applied to water molecules to induce flow. In addition, the temperature of the system is controlled using the Nosé–Hoover thermostat.

Application of this method to membrane‐water systems successfully reproduced parabolic velocity profiles similar to Poiseuille flow, as shown in Fig. 1. Using this approach, we further performed NEMD simulations of systems containing multiple amyloid-β fragments on membrane surfaces and investigated their aggregation processes under flow conditions. The simulations revealed that peptide aggregation is enhanced in the presence of flow compared with quiescent conditions. We will also discuss the molecular mechanism by which flow promotes peptide aggregation.

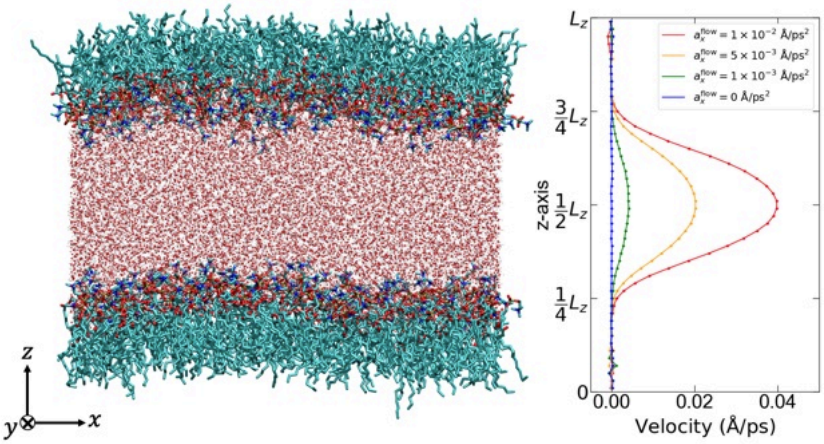

Figure 1 *–Poiseuille-like flow generated between lipid bilayers.*

References

[1] M. Otawa, S. G. Itoh, and H. Okumura, *J. Chem. Theory Comput.* **20**, 10199 (2024).

Molecular Structure and Lipid Ordering at Vesicle–Gold Nanoparticle Interfaces Revealed by SEIRS Spectroscopy

T. Bebesi Farkasné[1], M. Pálmai[1], I.Cs. Szigyártó[1], A. Bóta[1], Z. Varga[1,2], J. Mihály[1,3]

[1]HUN-REN Research Centre for Natural Sciences, Institute of Materials and Environmental Chemistry, H-1117 Budapest, Magyar tudósok körútja 2

[2]Budapest University of Technology and Economics, Department of Physical Chemistry and Materials Science, H-1111 Budapest, Műegyetem rakpart 3

[3]Eszterházy Károly Catholic University, Department of Chemistry, H-3300 Eger, Leányka út 12

e-mail: mihaly.judith@ttk.hu

We investigated the molecular structure of lipid-based colloidal dispersions in aqueous media using plasmon-enhanced infrared spectroscopy (SEIRA or SEIRS). Lipid vesicles, representing soft self-assembled nanostructures in liquid phase, serve as model interfaces for studying molecular ordering at curved lipid–water boundaries. By coupling these systems with plasmonic nanostructures like gold nanoparticles (AuNPs) and employing surface-enhanced infrared spectroscopy, we probed vibrational signatures sensitive to interfacial hydration, lipid chain ordering, and local dielectric environment.
Shifts in CH_2 stretching vibrations indicate changes in the packing of phospholipid acyl chains, while variations in phosphate and carbonyl vibrational bands reveal electrostatic interactions and modifications in hydrogen-bonding environments at the membrane interface. Furthermore, cooperative aggregation of AuNPs on phospholipid vesicle surfaces leads to localized nanoparticle clustering driven by membrane-mediated interactions, resulting in structural rearrangements. The plasmonic behaviour of aggregated AuNPs plays a critical role in enhancing local electromagnetic fields near the membrane surface, significantly amplifying infrared absorption signals in SEIRS measurements. This enhancement enables highly sensitive detection of subtle conformational and dynamic changes in lipid membranes and interfacial biomolecular interactions that are difficult to observe using conventional IR spectroscopy alone.

The project was supported by the National Research, Development, and Innovation Office of Hungary under grants (K_131657; Advanced_25_152698; Advanced_24_150077; Starting_24_150629).

References

[1] T. Bebesi, M. Pálmai, I.Cs. Szigyártó, A. Gaál, A. Wacha, A. Bóta, Z. Varga, J. Mihály, *Colloids and Surfaces B: Biointerfaces*, **246**, 114366 (2025).

Session 3

A metastable phase of amorphous aggregates governs solution structure — Klaas Wynne

A metastable phase of amorphous aggregates governs solution structure

Zhiyu Liao,[1] Ankita Das,[1] Ben A. Russell,[1] Ikhlas M.M. Ahmed,[2] Immacolata Abate,[2] Ian MacLaren,[3] Rebecca Beveridge,[2] and Klaas Wynne[1]

[1]School of Chemistry, University of Glasgow, G12 8QQ, UK

[2]Dept. of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, UK

[3]School of Physics and Astronomy, University of Glasgow, Glasgow, G12 8QQ UK

e-mail: klaas.wynne@glasgow.ac.uk

The structure of solutions is traditionally assumed to consist of individual solvated solute molecules, occasionally forming transient dimers or small clusters. Here we show that this textbook view is fundamentally incomplete: concentrated aqueous electrolyte solutions contain a previously unrecognised metastable amorphous phase composed of amorphous aggregates (AAs), into which the majority of solute molecules spontaneously assemble, even under undersaturated conditions.[1] Using a range of experimental techniques, we reveal a hierarchical population extending from molecular oligomers to micrometre-scale amorphous fractal solids and millimetre-scale assemblies. AAs form by a barrierless diffusion-limited process, rationalised by a modification of classical nucleation theory that accounts for their reduced free-energy barrier and fractal structure. These findings demonstrate that a metastable amorphous aggregate phase is intrinsic to concentrated solutions, revising the classical description of solubility, supersaturation and nucleation kinetics.

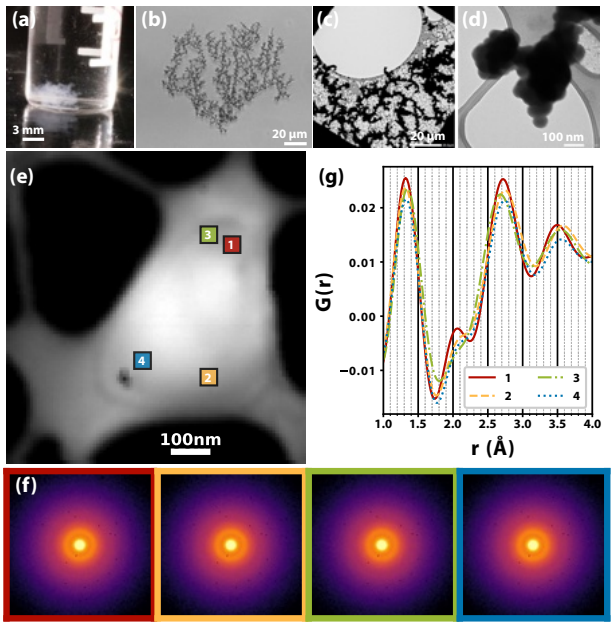

Figure 1 – Microscopic imaging of the solid forms of amorphous aggregates (AAs) in undersaturated solution*. (**a**) After several days of aging, millimetre-sized fluffy macroscopic objects can be observed by eye in undersaturated solution. (**b**) Visible light microscopic imaging shows that the fluffy macroscopic aggregates consist of 10–100 µm AA fractals. (**c**) TEM image of AA fractals on carbon film/copper grid (scale bar, 20 µm). (**d**) Idem, showing that the AA fractals consist of ~1-µm nodular aggregates of ~100-nm spheres positioned on a lacey carbon film. (**e**) Annular dark field image calculated from the 4D-STEM imaging dataset showing a typical nodular aggregate (10-nm scan step size). (**f**) Four exemplar electron-diffraction patterns from the from the selected areas 1-4 shown in (e). (**g**) Four pair distribution functions (PDFs) extracted from selected areas in (e), showing 3 clear near-neighbour distances.*

References

(1) Liao, Z.; Das, A.; Russell, B.; Ahmed, I.; Abate, I.; MacLaren, I.; Beveridge, R.; Wynne, K. A Metastable Phase of Amorphous Aggregates Governs Solution Structure. *ChemRxiv* **2026**. https://doi.org/10.26434/chemrxiv-2025-x4kh4/v2.

Protein sequestration into biomolecular condensates and hydration water.

G. Franzese[1,2]
Please underline the presenting author
[1]Departament de Física de la Matèria Condensada, Facutat de Física, Universitat de Barcelona, Martí i Franquès 1, Barcelona 08028, Spain
[2]Institut de Nanociencia i Nanotecnologia de la Universitat de Barcelona (IN2UB)
e-mail: gfranzese@ub.edu

Biological processes such as the sequestration of superoxide dismutase 1 (SOD1) into biomolecular condensates, including fused in sarcoma (FUS) and stress granules, are vital for understanding disease mechanisms, including amyotrophic lateral sclerosis (ALS). Moreover, protein–crowder interactions within these condensates are recognized as fundamental to cellular phase separation and disease-related processes. However, the specific role of the hydration environment in governing SOD1's behavior and transition dynamics within these condensates remains poorly understood, limiting our ability to accurately model these critical biological systems [1]. We incorporate explicit water into an implicit solvent model (OPEP) to investigate how water influences SOD1's behavior, residence times, and transition rates among associative states. We employ the advanced CVF water model, which accurately captures hydrogen-bond networks at the molecular level [3, 4]. While the OPEP model indicates that bovine serum albumin (BSA) crowders reduce SOD1's partition coefficient (PC) into FUS condensates primarily through non-specific interactions, our explicit-water approach points to hydration entropy in BSA as a key contributor to the observed PC reduction (**Fig. 1**). This result offers a new perspective on the system's free-energy landscape, complementing those obtained from OPEP alone. Our research supports the notion that explicitly modeling water can enhance our understanding of protein–crowder interactions and their biological implications, further emphasizing the potential role of water in cellular phase separation and disease-related processes [5].

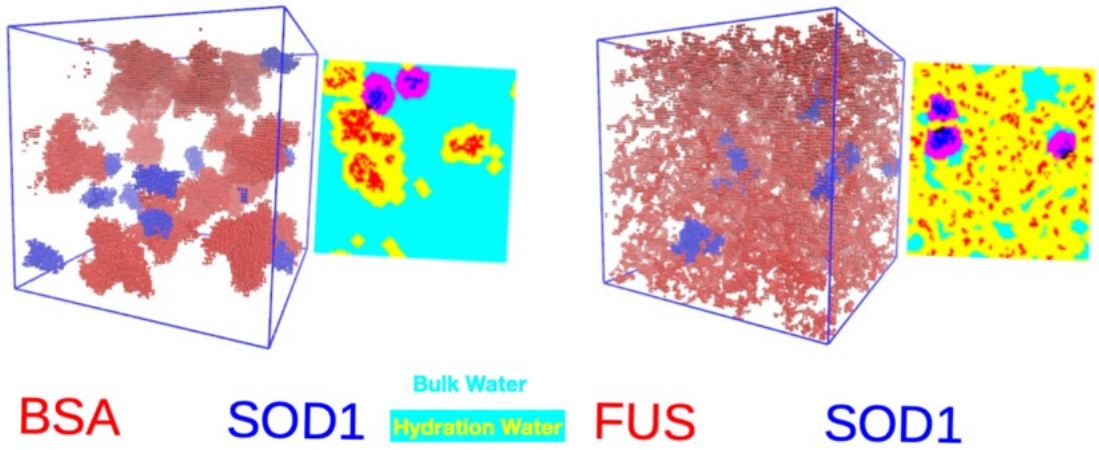

Figure 1 *– Simulation snapshots of SOD1 in contact with BSA (left) and FUS (right) are shown in their 3D implicit-water representation (with SOD1 in blue and the other protein in red) or as 2D sections with water (turquoise for bulk and yellow or purple for hydration water).*

References

[1] N. Samanta, S. S. Ribeiro, M. Becker, E. Laborie, R. Pollak, S. Timr, F. Sterpone, and S. Ebbinghaus, J. Am. Chem. Soc. **143**, 19909 (2021).
[3] L. E. Coronas and G. Franzese, J. Chem. Phys. **161**, 164502 (2024).
[4] L. E. Coronas, O. Vilanova, and G. Franzese, J. Mol. Liq. **434**, 128032 (2025).
[5] L. E. Coronas, S. Timr, F. Sterpone, and G. Franzese, J. Chem. Phys. **164**, 094910 (2026).

Structure-Making Solvation of Ferulic Acid in Protic and Aprotic Solvents: Experiments, Molecular Simulations, and Perspectives on Viscosity

Martina Požar[1]
[1]University of Split, Faculty of Science, Ruđera Boškovića 33, 21000 Split, Croatia
e-mail: marpoz@pmfst.hr

Solvent structure-making is an important feature of molecular organization in liquids as it shapes thermodynamic, dynamic and reactive properties. In this contribution, we present experimental and computational results on the solvation of ferulic acid in a series of solvents: the protic alcohols methanol, ethanol, and 2-propanol, and the aprotic solvents tetrahydrofuran (THF) and dimethyl sulfoxide (DMSO) [1]. Precise viscometric measurements over a broad temperature range reveal that ferulic acid acts as a structure-making solute across all investigated systems, while molecular dynamics simulations provide a molecular-level interpretation of these observations. The simulations reveal pronounced cross-species correlations and mixed clustering in protic solvents, which is further underlined by the analysis of hydrogen-bond dynamics and the long lifetimes of solute-solvent interactions, reflecting the dual donor-acceptor character of ferulic acid.

Building on these results, we will also briefly discuss ongoing computational work aimed at further examining viscosity in these systems. In particular, preliminary results from molecular dynamics simulations will be presented, including a comparison of different approaches for estimating viscosity.

References

[1] R. Tomaš, O. Politeo, M. Vraneš, M. Guettari, S. Herenda and M. Požar. *Phys. Chem. Chem. Phys.*, **28**, 7136-7147 (2026)

Characterizing the electrolyte/graphene interface: an integrated approach with modelling and experiments

P. Carbone[1]
[1]Department of Chemistry, University of Manchester, Oxford Road, M13 9PL, Manchester (U.K.)
e-mail: paola.carbone@manchester.ac.uk

The physical-chemistry of the graphene/aqueous–electrolyte interface underpins the operational conditions of a wide range of devices. Despite its importance, this interface is poorly understood due to the challenges faced in its experimental characterization and the difficulty of developing models that encompass its full physics. [1]
In this talk I'll show how combining molecular simulations with experiments, it is possible to investigate the relationship between wetting, double layer structure, friction coefficient and interfacial dynamics and understand how these properties are related to the capacitive properties of the interface. I'll initially introduce the new multiscale modelling techniques we developed to capture the ions-induced polarization of graphite modelling simultaneously the coupled motion of the surface electrons and ions in the solution.[2, 3] Then I'll show some applications of the methods to electrified bulk interfaces and under confinement [4, 5] and show how the simulation results can be an invaluable tool to understand experimental data.[6, 7, 8]

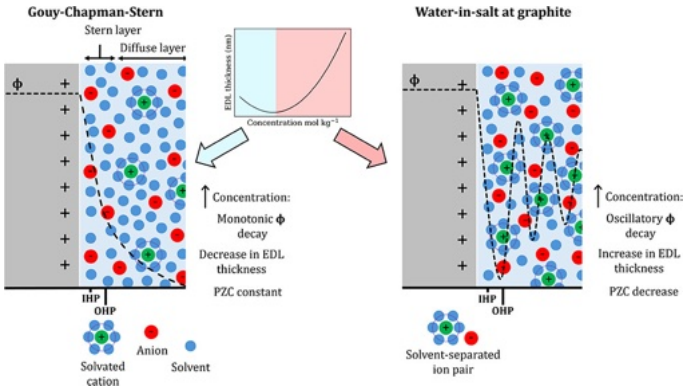

Figure 1 *– Sketch of the structure of the double layer in dilute and water-in-salt electrolytes [1]*

References

[1] J. D. Elliott, et al., *J. Mater. Chem. C*, **10**, 15225 (2022).
[2] J. D. Elliott, A. Troisi, P. Carbone, *J. Comp. Theory Sim.*, **16**, (2020), 5253.
[3] N. DiPasquale, et al., *J. Comp. Theory Sim.*, **17**, (2021), 4477.
[4] Z. Wei, et al., *Carbon*, **198**, (2022), 132.
[5] L. Smith et al., *ACS Appl. Mater. Interface*, **16,** (2024), 56316.
[6] J. D. Elliott, et al., *Carbon*, **292** (2023), 292.
[7] Z. Wei, et al., *J. Am. Chem. Soc.*, **146**, (2023), 760.
[8] H. O. Wood, et al. *J. Phys. Chem. C*, **130**, (2026). 5965.

What can UV Resonance Raman tell us about molecular liquids? From solutions to self-assembly

B. Rossi[1]
[1]Elettra Sincrotrone Trieste, Strada Statale 14 - km 163,5 in AREA Science Park
34149 Basovizza, Trieste ITALY
e-mail: barbara.rossi@elettra.eu

Raman spectroscopy is a well-established inelastic scattering technique that is widely used in laboratories for the detection and molecular characterization of various types of matter, including liquids, solutions, and gels. Raman spectra contain unique information about molecular vibrations, providing spectroscopic fingerprints that are highly sensitive to molecular reorganization, conformational changes, and intermolecular interactions. UV Resonance Raman (UVRR) spectroscopy is a variant of the standard Raman technique that exploits the tuning of the incident light into an electronic absorption band of the sample, thereby enhancing selected vibrational modes. Thanks to this resonance effect, UVRR offers several advantages compared to conventional off-resonance Raman spectroscopy, such as: (i) a significant increase in detection sensitivity, (ii) selective, label-free probing of specific functional groups in the sample, and (iii) suppression of the interfering fluorescence background, which often limits Raman signal detection. These features make UVRR spectroscopy a highly sensitive and selective label-free probe for investigating the structure and dynamics of molecular liquids. Through resonant enhancement of selected vibrational modes, UVRR provides insights into intermolecular interactions, solvation processes, and structural fluctuations in the liquid phase.
In this contribution, we present an overview of the basic principles of UVRR spectroscopy and its applications for the molecular characterization of liquids. Selected case studies will be discussed to demonstrate the usefulness of the UVRR method for the investigation of molecular liquids [1], aqueous solutions [2], biomacromolecules [3], and self-assembling systems [4]. Finally, we highlight the opportunities offered by the multi-wavelength UVRR spectroscopy facility recently implemented in the new IUVS laser laboratory at Elettra Sincrotrone Trieste.

References

[1] C. Bottari, L. Almasy, B. Rossi, B. Bracco, M. Paolantoni and A. Mele, *J. Phys. Chem. B* **126(23)**, 4299 (2022).
[2] B. Rossi, M. Tommasini, P.M. Ossi, M. Paolantoni A. Author, *Phys. Chem. Chem Phys*, **26**, 22023 (2024).
[3] S. Venturi, B. Rossi, M. Tortora, R. Torre, A. Lapini, P. Foggi, M. Paolantoni, S. Catalini, *Int. J. Biol. Macromol*, **242**, 124421 (2023).
[4] W. Heard, L.Pesce, P. T. Gierth, S. Adorinni, T.K. Ronson, B. Rossi, J.D. Thoburn, T. D147, 30842 (2025).

When Theory Meets Experiment: What Does it Take to Accurately Predict ^{1}H NMR Dipolar Relaxation Rates in Neat Liquid Water from Theory?

D. Paschek[1], N. Stolte[2], A.M.C. Tony[1], J. Busch[1], A. Strate[1], R. Ludwig[1], D. Marx[2]
[1]Institut für Chemie, Universität Rostock, 18059 Rostock, Germany
[2]Lehrstuhl für Theoretische Chemie, Ruhr-Universität Bochum, 44780 Bochum, Germany
e-mail: dietmar.paschek@uni-rostock.de

In this contribution, we compute the ^{1}H nuclear magnetic resonance (NMR) relaxation rate of liquid water at ambient conditions. We are using structural and dynamical information from Coupled Cluster Molecular Dynamics (CCMD) trajectories generated at CCSD(T) electronic structure accuracy while also considering nuclear quantum effects in addition to consulting information from x-ray and neutron scattering experiments. Our analysis is based on a recently presented computational framework for determining the frequency-dependent NMR dipole–dipole relaxation rate of spin 1/2 nuclei from Molecular Dynamics (MD) simulations [1-2], which allows for an effective disentanglement of its structural and dynamical contributions and includes a correction for finite-size effects inherent to MD simulations with periodic boundary conditions. A close to perfect agreement with experimental relaxation data is achieved if structural and dynamical information from CCMD trajectories is considered, leading to a re-balancing of the rotational and translational dynamics, which can also be expressed by the product of the self-diffusion coefficient and the reorientational correlation time of the H–H vector $D_0 \times \tau_{HH}$. The simulations show that this balance is significantly altered when nuclear quantum effects are taken into account.[3] Our analysis suggests that the intermolecular and intramolecular contributions to the ^{1}H NMR relaxation rate of liquid water are almost similar in magnitude, unlike what was predicted earlier from fully classical MD simulations.

- .

References

[1] D. Paschek, J. Busch, E. Mock, R. Ludwig, A. Strate*, J. Chem. Phys.*, **160**, 074102 (2024).
[2] D. Paschek, J. Busch, E. Mock, R. Ludwig, A. Strate*, J. Chem. Phys.*, **161**, 139902 (2024).
[3] D. Paschek, J. Busch, A.M.C. Tony, R. Ludwig, A. Strate, N. Stolte, H. Forbert, D. Marx*, J. Chem. Phys.*, **162**, 054501 (2025).

Generalised Langevin Data Analysis for Phonon Dynamics in Liquid Water

Shinya Hosokawa[1]

[1]Faculty of Materials for Energy, Shimane University, Matsue 690-8504, Japan
e-mail: s_hosokawa@mat.shimane-u.ac.jp

To investigate the phonon dynamics on molecular liquids with different intermolecular interactions, we have carried out a series of inelastic x-ray scattering (IXS) experiments at BL35XU [1] of the SPring-8, such as acetone with dipole interaction [2], CCl_4 with van der Waals one [3], and benzene with π-π stacking one [4]. The obtained spectra were analysed using a generalised Langevin formalism (GLF) with a memory function including thermal and two viscoelastic damping factors [5]. The fast sound was observed in any of molecular liquids [2-4] of about 50% beyond the corresponding hydrodynamic value, independent of the types of intermolecular interactions. However, we found that the viscoelastic relaxation times well coincide with the vibrational or rotational relaxation times obtained by Raman scattering and infrared spectra. Accordingly, we concluded that the terahertz sounds observed by IXS require extra energies of these excitations for the propagations. Then, we recall liquid water with hydrogen bonding intermolecular interaction. As is well-known, liquid water has the fastest terahertz sound velocity of about 110% [6] among molecular liquids. We used our experimental IXS data shown in Fig. 1(a) [7] for the GLF analysis, and the solid curves indicate the best GLF fits, from which the fast sound in good agreement with the previous result [6] was obtained. Figure 1(b) shows the Q dependence of slow (circles) and fast (triangles) viscoelastic relaxation times in the memory function obtained from the GLF analysis. In the presentation, we discuss the origin of the fast sound in liquid water by comparing these viscoelastic relaxation times in the memory function with Raman scattering and infrared data showing the vibrational and rotational relaxation times in water molecules. Moreover, we will encompass these analyses to the supercritical fluid water state.

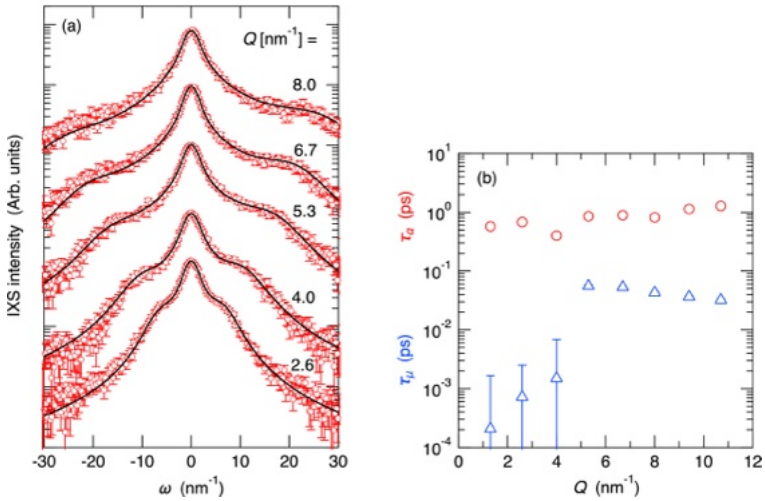

Figure 1 *– (Left) Logarithmic plots of S(Q,ω) spectra of liquid water. (Right) Viscoelastic parameters obtained from GLF analysis.*

References

[1] A. Q. R. Baron et al., *J. Phys. Chem. Solids*, **61**, 461-465 (2000).
[2] S. Hosokawa et al., *J. Mol. Liq.*, **332**, 115825-1-9 (2021).
[3] S. Hosokawa and K. Yoshida, *J. Mol. Liq.*, **395**, 123828-1-8 (2024).
[4] S. Hosokawa and K. Yoshida, *J. Mol. Liq.*, **339**, 123063-1-9 (2023).
[5] J. P. Boon and S. Yip, *Molecular Hydrodynamics*, 1980, McGraw-Hill, New York.
[6] F. Sette, et al., *Phys. Rev. Lett.*, **75**, 850-853 (1995).
[7] T. Yamaguchi et al., *J. Phys. Chem. Solids*, **66**, 2246-2249 (2005).

Structural transitions in liquid water at high temperatures and pressures: A molecular dynamics approach.

I. Skarmoutsos[1], F. Martelli[2,3], E. Guardia[4]

[1] Laboratory of Physical Chemistry, Department of Chemistry, University of Ioannina, 45110 Ioannina, Greece
[2] Dipartimento di Fisica, Università degli Studi di Roma La Sapienza, Piazzale Aldo Moro 5, Rome 00185, Italy
[3] CNR-Istituto dei Sistemi Complessi, Piazzale Aldo Moro 5, Rome 00185, Italy
[4] Departament de Física, Universitat Politècnica de Catalunya, Campus Nord-Edifici B4-B5, Jordi Girona 1-3, Barcelona E-08034, Spain

e-mail: iskarmoutsos@uoi.gr

Molecular dynamics simulations of liquid water were performed using the TIP4P-2005 model at elevated pressures, spanning temperatures from ambient to near-critical conditions. Analysis of local structural, dynamical, and entropic properties reveals two distinct structural transitions occurring in intermediate and high-temperature regimes. These are marked by extrema and crossovers in multiple descriptors, along with significant rearrangements of the hydrogen-bond network. The structural changes are further reflected in intermolecular vibrational and librational dynamics, as evidenced by modifications in velocity correlation spectral densities and in translational and rotational densities of states.

References

[1] I. Skarmoutsos, F. Martelli, and E. Guardia*, J. Chem. Phys.*, **164**, 054503 (2026).
[2] I. Skarmoutsos, and E. Guardia*, Chem. - Eur. J.*, **31***,* e202500423 (2025).

OrthoBoXY: A Simpler Way to Compute True Self-Diffusion Coefficients and Viscosities from MD Simulations

M. Brandt[1], D. Paschek[1], R. Ludwig[1,2]
[1]University of Rostock, Albert-Einstein-Str. 27, 18059 Rostock, Germany
[2]Leibniz Institute of Catalysis, Albert-Einstein-Str. 29A, 18059 Rostock, Germany
e-mail: marcel.brandt@uni-rostock.de

Self-diffusion coefficients calculated from molecular dynamics (MD) simulations with periodic boundary conditions are known to exhibit a system size-dependence. The deviation from the "true" system size-independent self-diffusion coefficient can be calculated via a correction term to the simulated self-diffusion coefficient. This correction, known as the Yeh-Hummer correction, requires the knowledge of the viscosity and shows a $1/L$ dependency, where L is the length of a cubic simulation box. [1]

When stretching the box along the *z*-axis, we obtain an orthorhombic system where the self-diffusion coefficient becomes direction-dependent. By employing a hydrodynamic model, it is possible to exactly determine the difference between the simulated and the "true" self-diffusion coefficient for varying box size ratios. Interestingly, at a so-called "magic" ratio the hydrodynamic effects cancel each other out and the correction vanishes in the *x*- and *y*-direction. The OrthoBoXY method now uses simulation boxes with this "magic" box size ratio of $L_z/L_x = L_z/L_y = 2.793\ldots$ in order to obtain the "true" system size-independent self-diffusion coefficients in the *x*- and *y*-direction. Moreover, the still system size-dependent self-diffusion coefficient in the *z*-direction can be used to determine the viscosity. [2,3]

MD simulations of a variety of molecular liquids, ionic liquids and liquid mixtures have demonstrated the accuracy of this approach for systems where the Yeh-Hummer correction holds true. However, there are some systems known to not be described properly by this correction. For example, electrolyte solutions show a smaller deviation from the "true" self-diffusion coefficient than predicted by the Yeh-Hummer correction, i.e. the self-diffusion coefficient is overcorrected. In our recent work, we use the OrthoBoXY method to investigate the system size-dependence of these systems.

References

[1] I.-C. Yeh, G. Hummer, *J. Phys. Chem. B*, **108**, 15873–15879 (2004).
[2] J. Busch, D. Paschek, *J. Phys. Chem. B*, **127**, 7983–7987 (2023).
[3] J. Busch, D. Paschek, *J. Phys. Chem. B*, **128**, 1040–1052 (2024).

A Multifidelity Monte Carlo Approach for Simulating the Diffusion Coefficient of Water

T. Frömbgen[1], A. Kuhn[2], J. Dölz[2], B. Kirchner[1]
[1]Mulliken Center for Theoretical Chemistry, University of Bonn, Beringstraße 4, 53115 Bonn, Germany
[2]Institute for Numerical Simulation, University of Bonn, Friedrich-Hirzebruch-Allee 7, 53115 Bonn, Germany
e-mail: tomfroe@uni-bonn.de, bkirch@uni-bonn.de

Self-diffusion coefficients computed from molecular dynamics simulations are known to suffer from systematic finite-size effects. To mitigate this dependence, additive correction terms have been proposed. [1,2] More recently, the OrthoBoXY approach [3] introduced tetragonal simulation boxes with specific aspect ratios for which the correction term vanishes.

In this contribution, we present an alternative strategy: a multifidelity Monte Carlo framework for the computation of diffusion coefficients of water that explicitly exploits, rather than corrects for, the size dependence. [4] Multifidelity methods, originally developed in the field of uncertainty quantification, combine computational models that evaluate the same quantity of interest—in this case the diffusion coefficient—at different levels of accuracy and computational cost. [5] In our framework, the model hierarchy is defined by the size of the simulation boxes. Water is represented by a rigid three-point model, and uncertainties in the non-bonded force-field parameters, namely the Lennard-Jones parameters and partial charges, are propagated through the simulations.

To assess the capabilities of the proposed framework, we conduct a large-scale study involving six computational models, three parameter calibrations, cubic and tetragonal simulation box geometries, and two sets of perturbed force-field parameters. Our results demonstrate that computational speed-ups of up to one order of magnitude can be achieved when successive models exhibit only small differences in their correlations with the high-fidelity model. Furthermore, nearly all combinations of high- and low-fidelity models outperform simulations relying exclusively on a single high-fidelity model, highlighting the robustness and efficiency of the multifidelity approach.

References

[1] B. Dünweg and K. Kremer, *J. Chem. Phys.*, **99**, 6983–6997 (1993).
[2] I.-C. Yeh and G. Hummer, *J. Phys. Chem. B*, **108**, 15873–15879 (2004).
[3] J. Busch and D. Paschek, *J. Phys. Chem. B*, 127, 7983–7987 (2023).
[4] T. Frömbgen, A. Kuhn, J. Dölz, and B. Kirchner, *J. Chem. Phys.*, **164**, 024504 (2026).
[5] B. Peherstorfer, K. Willcox, and M. Gunzburger, *SIAM Rev.*, **60**, 550–59 (2018).

Session 5

On the Aggregation of Amphiphiles in Water: Hydrotropy as the missing link between salts and surfactants — João Coutinho

On The Aggregation of Amphiphiles in Water: Hydrotropy as the missing link between salts and surfactants

Dinis O. Abranches[1], João A. P. Coutinho[1]

[1]CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193, Aveiro, Portugal

e-mail: jcoutinho@ua.pt

Hydrotropes and surfactants are commonly employed to enhance the aqueous solubility of hydrophobic compounds, and they are traditionally regarded as distinct classes based on the assumption that surfactants solubilize via micelle formation whereas hydrotropes do not. In the first part of this communication this distinction is critically examined by systematically investigating the solubilization of carbamazepine in aqueous solutions of two homologous families: sodium sulfates and sodium sulfonates, spanning species from inorganic salts to classical surfactants. Across these families, solubility enhancement increases monotonically with the apolar volume of the anion,[1] as shown in Figure 1, with densely charged ions inducing salting-out and amphiphilic compounds promoting salting-in. Analysis of the dilute concentration regime using Setschenow constants reveals a continuous trend encompassing hydrotropes and surfactants, with no separation between them.

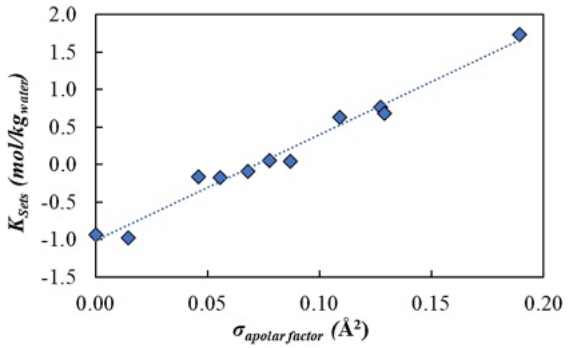

Figure 1 *– Correlation between apolar factor and Setschenow constants for the sodium alkyl sulfate salts.*

At higher amphiphile concentrations, deviations from linear behavior define critical aggregation concentrations that correlate systematically with anion apolarity among hydrotropes and surfactants, and align closely with reported critical micelle concentrations. These results establish a unified framework in which hydrotropes and surfactants follow the same structural and thermodynamic principles, supporting a continuum view of solubilizing agents rather than two fundamentally distinct classes.

The mechanisms of enhanced solubility on these systems are highlighted by molecular dynamic simulations, and, in the final part of this communication, it will be shown how other phenomena, apparently unrelated, such as the impact of dissolved gases on the transport properties of electrolytes, [2] or the solubility of gases in aqueous solutions of ionic liquids, can be understood under the light of the aggregation of amphiphiles in water around an apolar compound.

Acknowledgment: The authors are grateful to FCT, Portugal, for financial support through national funds FCT/MCTES (PIDDAC) to CICECO from projects UID/50011/2025 and LA/P/0006/2020.

References

[1] B. P. Soares, D. O. Abranches, T. E. Sintra, A. Leal-Duaso, J. I. García, E. Pires, S. Shimizu, S. P. Pinho, and J. A. P. Coutinho, *ACS Sustain. Chem. Eng.*, **8**, 5742 (2020)

[2] E. E. Fileti, D. O. Abranches, J. A. P. Coutinho*, J. Phys Chem B*, **130**, 5059 (2026)

How Much Water Is Too Much? Structural and Dynamical Transitions in Solvate Ionic Liquid Electrolytes

J. K. Philipp-Taube[1], A. Strate[1], D. Paschek[1], R. Ludwig[1]
[1]University of Rostock, Albert-Einstein-Str. 27, 18059 Rostock, Germany
e-mail: jule.philipp@uni-rostock.de

The controlled dilution of highly coordinated electrolyte systems with molecular solvents offers a promising route to tune transport and stability properties in advanced energy materials.[1] Here, we investigate the structural and dynamical evolution of solvate ionic liquid (SIL) electrolytes upon gradual water addition, with particular focus on the transition from a coordination-driven system, the water-in-solvate-ionic-liquid (WISIL) regime, to its breakdown at higher water contents.

Using a combined experimental and molecular dynamics simulation approach, we resolve how water is incorporated into the SIL formed by the equimolar mixture of [Li][NTf_2] and triglyme (G3). At low water content, water remains highly dispersed and preferentially inserts into the cationic chelate complex $[Li(G3)]^+$ coordination shell, forming long-lived $[Li(H_2O)(G3)]^+$ motifs that preserve the coordination-dominated local structure of the SIL. In this regime, the addition of water substantially lowers viscosity and enhances ionic conductivity while largely maintaining the wide electrochemical stability window (ESW) characteristic of the neat SIL.[2]

Upon further dilution, a distinct structural transition occurs: the coordinated complexes progressively disintegrate and extended water–water hydrogen-bond networks emerge[3], accompanied by increased molecular mobility and increasingly bulk-like water behavior. This transition is further characterized by predominantly hydrated lithium cations and a substantially narrowed ESW, approaching that of conventional aqueous electrolytes.

Our results identify a narrow compositional window in which water addition is beneficial and reveal the molecular mechanisms governing the crossover from dispersed mixing to hydrogen-bond network formation in complex electrolyte solutions. The findings connect microscopic mixing behavior with macroscopic transport and electrochemical properties, providing insights into solvent-driven structural transitions in highly concentrated electrolyte mixtures.

References

[1] K. Ueno, J. Murai, H. Moon, K. Dokko and M. Watanabe*, J. Electrochem. Soc.*, **164**, A6088 (2016).
[2] J. K. Philipp, D. Paschek, L. Kruse, A.-E. Surkus, B. Austrup, M. Schönhoff, R. Ludwig, *ChemPhysChem*, e70353 (2026, in print).
[3] J. K. Philipp, A. Strate, F. M. Januszewski, L. Möhring, L. Kruse, M. Bühl, D. Paschek, R. Ludwig, *J. Phys. Chem. B* (2026, submitted).

Stability and affinity of *Plasmodium falciparum* proteins in ionic liquids

P. C. C.da Silva[1,2], L. Martínez[1,2]
[1]Institute of Chemistry, Universidade Estadual de Campinas, Campinas, Brazil.
[2]Center for Computing in Engineering and Sciences
e-mail: p234849@dac.unicamp.br

The effects of ionic liquids (ILs) on proteins are well known and widely studied for various applications [1]. Compared to conventional solvents, ILs exhibit several advantageous properties, including negligible volatility, moderate conductivity and viscosity, liquid state over a wide temperature range, excellent solvation ability, and high thermal stability. A diverse range of interactions promotes the self-organization of ILs into complex structures. Biocompatible ionic liquids retain these properties while maintaining manageable toxicity levels, making them attractive for pharmaceutical applications, such as reducing the need for additives in vaccine formulations and simplifying handling logistics [2]. In this work, Hamiltonian Replica Exchange Molecular Dynamics simulations were employed to investigate the effect of concentration changes in choline-derived ionic liquids on the stability and structure of *Plasmodium falciparum* proteins. Additionally, solvation structures were characterized using Kirkwood–Buff solution theory [3]. The proteins analyzed—AMA1, MSP1, and MSP2, associated with *P. falciparum*, the primary causative agent of malaria—were studied in aqueous solutions of choline geranate (CAGE), choline lactate (CAL), and choline chloride (CACL) at concentrations of 0.125 M, 0.250 M, 0.5 M, 1.0 M, and 2.0 M. Kirkwood–Buff integrals (KBIs) revealed distinct behaviors among the three ionic liquids. Choline chloride behaves similarly to a conventional salt, showing minimal variation in solvation effects with concentration and acting as a preferentially excluded, protein-stabilizing cosolvent. In contrast, CAGE and CAL exhibit behavior typical of biocompatible ionic liquids: their affinities, as quantified by KBIs, vary with concentration. Although they are not completely excluded from the protein surface, their electrostatic interactions—modulated by the nature of both cations and anions—contribute to protein stabilization at optimal concentrations. Furthermore, the KBIs of the ions forming CAGE converge to different values, indicating distinct local structuring. The choline cation also exhibits complex behavior, with variations in accumulation at different distances from the protein surface. Structural analyses based on RMSD and RMSF indicate that lower IL concentrations are sufficient to maintain protein structures in their functional conformations. This suggests the existence of an optimal concentration range in which epitope structures remain preserved in the presence of cosolvents. In AMA1, key residues in disordered regions—K489, R503, K508, and R512—were stabilized. The spatial distributions of relevant functional groups of each cosolvent were further characterized using Minimum Distance Distribution Functions and KBIs. These approaches enabled a molecular-level understanding of protein–cosolvent interactions and their impact on protein stability.

References

[1] V. Piccoli, L. Martínez*, J Phys Chem B*, **129**, 6765-6776 (2025).
[2] Y-L. Wang, et al, *Chem Rev,* **120,** 5798–5877 (2020).
[3] IL. Shulgin, E. Ruckenstein, *J Phys Chem B,* **110**, 12707–12713 (2006).

Relationship between ion pair formation in aqueous solutions and anomalous decrease in NMR signal intensity of solvent

H. Maki[1], R. Matsuda[2], Y. KOH[1]

[1] Graduate School of Engineering, Kobe University, 1-1 Rokkodai-cho, Nada-ku, Kobe, Japan
[2] Faculty of Engineering, Kobe University, 1-1 Rokkodai-cho, Nada-ku, Kobe, Japan
e-mail: maki@kobe-u.ac.jp

The formation behavior of various ion pairs in high-concentration electrolyte aqueous solutions was analyzed using quantitative ^{1}H NMR for water molecule and multinuclear NMR for ions. While the signal intensity of multinuclear NMR showed a linear relationship with electrolyte concentration, the quantitative ^{1}H NMR showed a significantly lower signal intensity than expected due to the reduced physical properties of the solution resulting from the low mobility of water molecules in the hydration structure, and the decrease in the activity of water molecules due to reduced mobility. Furthermore, it was confirmed that the undetectable amount of water by quantitative ^{1}H NMR tended to decrease due to the release of hydrated water into free water as a result of the destabilization of the ionic hydration structure by ion pair formation. The electrolyte concentration dependence of the chemical shifts of ^{1}H NMR and multinuclear NMR, and the undetectable amount of water by quantitative ^{1}H NMR, both changed characteristically at the electrolyte concentrations at which SSIP and CIP formation began.

The electrolytes XCl, XBr, XNO_3, $XClO_4$, and X_2SO_4 (X=Li, Na) were dissolved in pure water to near-saturation concentrations. Based on these stock solutions, 25 solutions of different concentrations were prepared. Ion pair formation behavior and solvation structure were estimated by performing ^{1}H, ^{7}Li, and ^{23}Na qNMR measurements on the prepared solvents. The amount of H_2O determined by ^{1}H qNMR was determined based on the signal area of the ^{1}H qNMR of pure water.

Fig. 1 shows the electrolyte concentration dependence of the detected water molecules by ^{1}H qNMR measurement of concentrated aqueous solutions. The × marks in the figure represent the difference between the actual amount of H_2O present (○) calculated from density measurement of the sample solution and the amount of H_2O detected by ^{1}H qNMR (●) (= amount of undetected water, A_{un}). The A_{un} initially increases with increasing ion concentration due to the formation of hydration structures, but this increasing trend slows down. This is due to dehydration occurring due to the formation of solvent-separated ion pairs (SSIP), which increases the amount of detected water. At even higher concentrations, except for LiCl aqueous solutions, dehydration becomes more pronounced due to the formation of contact ion pairs (CIP), further increasing the amount of detected water and causing A_{un} to decrease. In both Li-based and Na-based solutions, the amount of A_{un} is greater when the anion is NO_3^- (×) than when it is Cl^- (×). This is because the ionic interaction between NO_3^-, which has a large ionic radius, and the cation is small, making it difficult to form an ion pair. Furthermore, in both the Li and Na systems, when the anion was ClO_4^- or especially SO_4^{2-}, the A_{un} value was small. This suggests that these anions have extremely weak electrostatic interactions with cations, do not form ion pairs such as SSIP, and that the structural disruption of the hydrogen bond network by the anions does not significantly reduce the mobility or activity of water molecules near the cations.

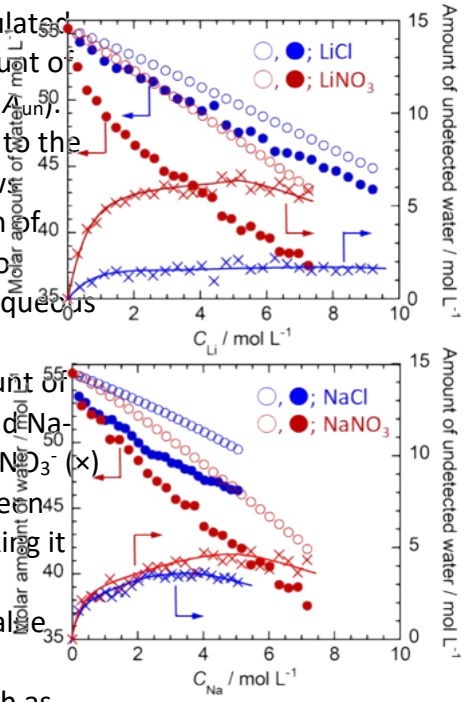

Fig. 1 Detected H_2O ratios by ^{1}H qNMR in XCl and XNO_3 aq. Open symbols; calculated H_2O amount from the sample solution density (y axis). Close symbols; detected H_2O amount by ^{1}H qNMR (y axis). Cross symbols; differential value between ○ and ● (i.e., A_{un}; y2 axis).

Structural and Spectroscopic Evidence of Hydrogen Bonded Anionic Wires in Protic Ionic Liquids

Maham Azhar[1], Loai Al-Sheakh[1], Lasse Hunger[1], Andreas Appelhagen[1], Lennart Kruse[1] and Ralf Ludwig[1,2]*

[1]Institut für Chemie, Abteilung Physikalische Chemie Universität Rostock, Albert-Einstein-Straße 27, 18059 Rostock, Germany
[2]Leibniz Institut für Katalyse an der Universität Rostock e.V. Albert-Einstein-Straße 29a, 18059 Rostock, Germany
ralf.ludwig@uni-rostock.de

Hydrogen Bonding between ions of like charge challenges the fundamental principle of electrostatics that opposite charges attract and like charges repel. We used triethylamine ($(CH_3CH_2)_3N$) and two different alkanedicarboxylic acids ($HOOC(CH_2)_nCOOH$) with n = 0,1, namely ethanedionic (oxalic) and propanedionic (malonic) acid in equal ratio.

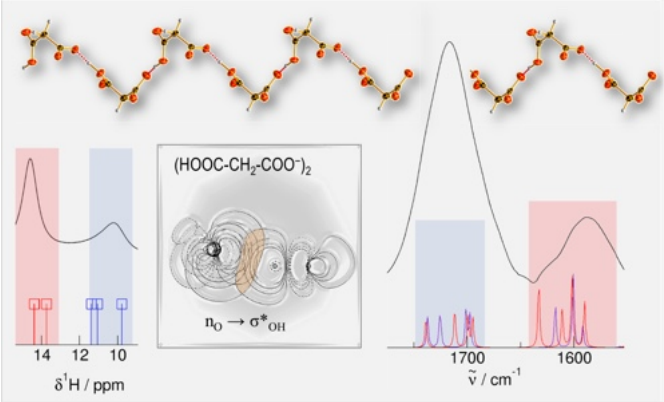

***Figure 1**: Graphical summary of IR, NMR, NBO and anionic wires structure*

H-bonds between cations have been observed in hydroxy-functionalized ionic liquids.[1] More recently, we replaced the hydroxy- by carboxy-functionalized cations in similar ILs. We observed doubly H-bonded cationic dimers in the solid, the liquid and the gas phase.[2]
In this work, we have shown similar structural motifs for anionic clusters in PILs. The anionic wires were identified by X-ray crystallography in the solid state, wherein the anions are linked by the $^-OH\cdots O^-$ type H-bonds. The H-bonds within the anionic wire are significantly stronger than those between cation and anion despite repulsive Coulomb interaction in the first and attractive ones in the latter case. Analysis by NMR and IR spectroscopy suggests that the binding motifs of the solid structure are mainly preserved in the liquid state of the supercooled PILs.
This conclusion is drawn from density functional theory (DFT) calculations of the same structural motifs as observed in the solid state. The calculated ^1H NMR chemical shifts and IR C=O frequencies for these H-bond structures correspond well with the measured spectroscopic signatures. The anionic chains remain intact even when gradually removing the counterions. A fourfold negatively charged chain tetramer still exhibits strong H-bonds that are hardly weaker than those in the neutral species. These findings highlight the fundamental role of hydrogen bonding for the unusual attractive interaction between ions of like charge.

References

[1] A. Knorr, P. Stange, and K. Fumino et al., *ChemPhysChem,* **17**, 458 (2016).
[2] L. Hunger, L. Al-Sheakh and D. H. Zaitsau et al., *Chemistry – A European Journal* **28**, e202200949 (2022).

Hierarchical Self-Assembly and Sound Attenuation in the Audible-Frequency Region in Phenol–AOT Organogels

Katsura Nishiyama,[1] **Kensuke Okamoto**,[2] **Nattasamon Petchsang**,[3]
Rio Kita,[4] **Yukiteru Katsumoto**[5]
[1]Department of Environmental Technology, Meijo University, Nagoya, 468–8502, Japan
[2]Division of Environmental Technology, Meijo University, Nagoya, 468–8502, Japan
[3]Department of Materials Science,Faculty of Science, Kasetsart University, Bangkok 10900, Thailand
[4]Department of Physics, Tokai University, Kanagawa 259–1292, Japan
[5]Department of Chemistry, Faculty of Science, Fukuoka University, Fukuoka 814–0180, Japan
e-mail: knis@meijo-u.ac.jp (KN)

Soft supramolecular materials often exhibit hierarchical organization accompanied by collective fluctuations over broad spatial and temporal scales. In this study, we investigate how solvent-dependent self-assembly governs acoustic energy dissipation in phenol–AOT organogels [1]. Fig. 1 illustrates the present concept schematically.

Phenol and bis(2-ethylhexyl) sulfosuccinate (AOT) spontaneously form organogels in several organic solvents through hydrogen bonding and solvophobic association. We prepare organogels using cyclohexane, hexane, m-xylene, and 2,2,4-trimethylpentane. Scanning electron microscopy (SEM) reveals solvent-dependent interconnected domains comprising lamellar and sheet-like aggregated structures on the micrometer scale. Cyclohexane- and hexane-based systems generate comparatively heterogeneous porous structures, whereas m-xylene produces smoother and more continuous domains.

We measure sound attenuation under Z- and A-weighting conditions in the audible-frequency region. The results suggest that mesoscale organization governs acoustic dissipation in these soft materials. Because acoustic wavelengths greatly exceed the characteristic pore dimensions observed by SEM, direct scattering from individual pores likely plays only a minor role. Instead, collective viscoelastic relaxation and dynamic structural rearrangements within interconnected domains efficiently dissipate acoustic energy. Agarose hydrogels possessing nanoscale network structures also exhibit attenuation profiles similar to those of the organogels, suggesting that hierarchical organization itself essential role in dissipation in soft systems.

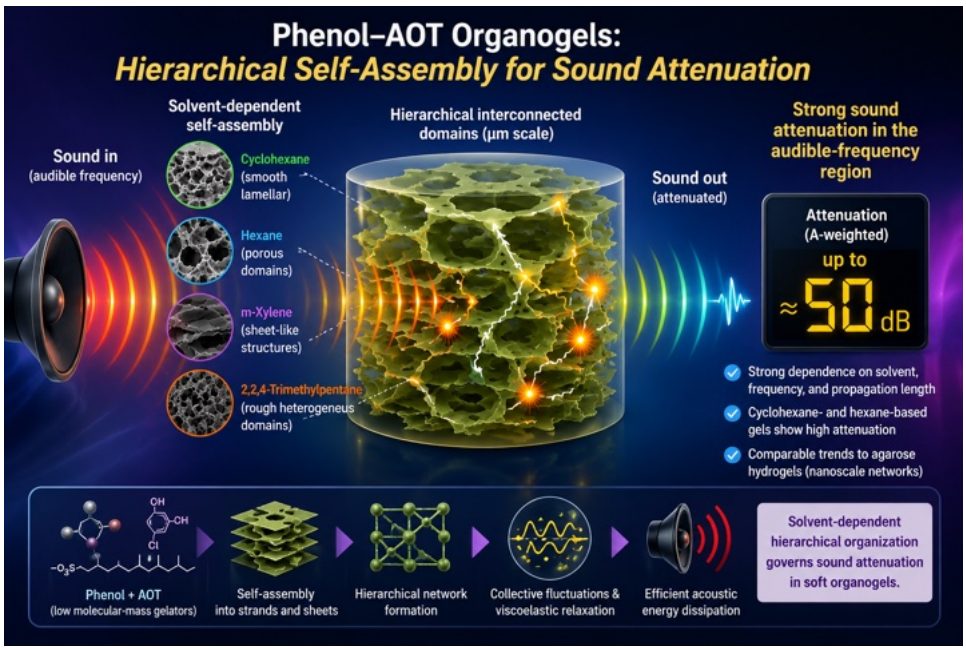

Fig. 1. Schematic concept of organogel structures applied to sound attenuation.

plays an acoustic matter

References
[1] KN. et al., *Phys. Chem. Chem. Phys.* 25 2776–2780. (2023)

Machine learning-based first-principles simulations of nanoconfined water

V. Kapil[1]
[1]Department of Physics & Astronomy
University College London, UK
e-mail: v.kapil@ucl.ac.uk

Water confined at the nanoscale is ubiquitous in geological, biological and technological environments, yet its molecular-scale behaviour remains poorly understood. Here, I will discuss our work combining first-principles electronic structure theory, machine learning and advanced statistical sampling to investigate water under extreme confinement. We find that monolayer water exhibits remarkably rich phase behaviour, including unconventional crystalline ices, a hexatic-like phase intermediate between a solid and a liquid, and a superionic phase with exceptionally high proton conductivity. Nuclear quantum effects strongly enhance proton transport and lower the conditions required to access the superionic regime. More generally, we show that subtle changes in confinement geometry and the surrounding material can strongly modify the hydrogen-bond network and phase behaviour of water. I will conclude by discussing methodological advances that are enabling increasingly realistic first-principles simulations of nanoconfined water and bringing direct comparison with experiment within reach.

LCST-type Phase Separation of Phosphonium-based Ionic Liquid–Water Mixed Solutions

M. Kawano[1], K. Sadakane[2], H. Iwase[3], M. Matsugami[4], T. Takamuku[5]

[1]Graduate School of Science and Engineering, Saga University, Honjo-machi, Saga 840-8502, Japan

[2]Faculty of Life and Medical Sciences, Doshisha University, 1-3 Tatara Miyakodani, Kyotanabe, Kyoto 610-0394, Japan

[3]Comprehensive Research Organization for Science and Society (CROSS), 162-1 Shirakata, Tokai, Ibaraki 319-1106, Japan

[4]Faculty of Liberal Arts, National Institute of Technology (KOSEN), Kumamoto College, 2659-2 Suya, Koshi, Kumamoto 861-1102, Japan

[5]Faculty of Science and Engineering, Saga University, Honjo-machi, Saga 840-8502, Japan

e-mail: takamut@cc.saga-u.ac.jp

Various ionic liquids (ILs) are miscible with not only polar molecular liquids (MLs) like ethanol, but also nonpolar MLs such as benzene, despite electrolytes. However, IL–ML mixed solutions often separate into IL-rich and ML-rich phases with varying temperature. Such phase separation of IL–ML mixed solutions has been applied to a homogeneous liquid–liquid extraction for proteins [1]. For imidazolium-based ILs mixed solutions with several MLs, upper critical solution temperature (UCST)-type phase separation occurs with lowering temperature. In contrast, lower critical solution temperature (LCST)-type phase separation of phosphonium-based IL–water mixed solutions takes place with rising temperature. Microscopic interactions among IL's cation and anion and ML decide the types of phase separation. For application of phase separation of IL–ML mixed solutions with changing temperature to extraction, the mechanism of phase separation should be understood at a molecular level.

In this investigation, we aimed at clarifying the mechanism of LCST-type phase separation for tetrabutylphosphonium trifluoroacetate ($[P_{4444}][CF_3COO]$)–water mixed solutions at both microscopic and mesoscopic scales. Figure 1 shows phase diagram for the solutions. NMR and IR spectroscopic techniques were used to observe the change in microscopic interactions with increasing temperature. Furthermore, the microscopic interactions were simulated by molecular dynamics (MD) calculations. Small-angle neutron scattering (SANS) method was applied to observe the enhancement of concentration fluctuation in the mixed solutions with increasing temperature at the mesoscopic scale. The present results on LCST-type phase separation of $[P_{4444}][CF_3COO]$–water solutions were compared with those on UCST-type phase separation of 1-alkyl-3-methylimidazolium bis(trifluoromethylsulfonyl)amide ($[C_N mim][TFSA]$, N represents the alkyl chain length) mixed solutions with dioxane and formamide previously investigated [2-4].

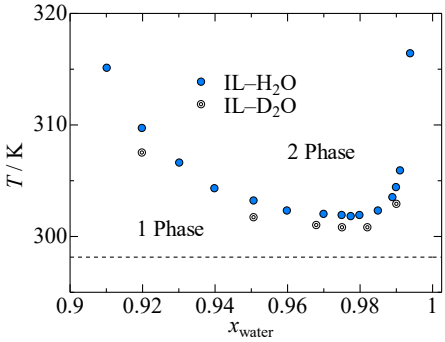

Figure 1 *Phase diagrams of $[P_{4444}][CF_3COO]$–H_2O and –D_2O. The dashed line gives 298 K.*

1,4-

References

[1] Y. Deguchi, N. Nakamura, and H. Ohno, *Sep. Purif. Technol.*, **251**, 117286 (2020).

[2] M. Kawano, K. Sadakane, H. Iwase, M. Matsugami, B. A. Marekha, A. Iddrissi, and T. Takamuku, *Phys. Chem. Chem. Phys.*, **22,** 5332 (2020).

[3] M. Kawano, K. Sadakane, H. Iwase, M. Matsugami, B. A. Marekha, A. Iddrissi, and T. Takamuku, *Phys. Chem. Chem. Phys.*, **23,** 24449 (2021).

[4] M. Kawano, A. Tashiro, Y. Imamura, M. Yamada, K. Sadakane, H. Iwase, M. Matsugami, B. A. Marekha, A. Iddrissi, and T. Takamuku, *Phys. Chem. Chem. Phys.*, **24,** 13698 (2022).

Local Structure of Mixtures of Ionic Liquids with Molecular Solvents: Spectroscopy and Molecular Modeling Analysis.

A. Shagurin[1,2], Patrik Musil[3] Natalia T. Correia[2], Frederic Affouard[2], Milan Předota[3], Pál Jedlovszky[4], Abdenacer Idrissi[1]

[1]University of Lille, CNRS UMR 8516 -LASIRe - Laboratoire Avancé de Spectroscopie pour les Interactions la Réactivité et l'environnement, 59000 Lille, France
[2]Univ. Lille, CNRS, INRAE, Centrale Lille, UMR 8207 - UMET - Unité Matériaux et Transformations, F-59000 Lille, France
[3]University of South Bohemia, Department of Physics, Faculty of Science,Ceske Budejovice, Czech Republic
[4]Department of Chemistry, Eszterházy Károly Catholic University, Eger, Hungary

e-mail: nacer.idrissi@univ-lille.fr

A central difficulty in simulating $BmimBF_4$/water mixtures is that force fields validated separately for the pure ionic liquid and pure water do not necessarily remain thermodynamically consistent when combined. The predicted miscibility may depend strongly on the water model, ionic-liquid parameters, cross-interactions, and charge treatment. For this reason, the free energy of mixing is a more stringent validation criterion than density or transport properties alone, because it directly probes whether the model predicts a thermodynamic tendency toward mixing or demixing.[1]

In this work, the compatibility of the SPC/E[2] water model with the Canongia Lopes[3] force field for $BmimBF_4$ was assessed from the composition dependence of the excess enthalpy and excess free energy of mixing. The latter was obtained using an alchemical thermodynamic-integration approach,[4] in which intermolecular interactions were progressively removed along a λ-path: electrostatic interactions were first switched off, followed by Lennard-Jones interactions using a soft-core potential. The resulting free energies of the mixtures were then compared with the mole-fraction-weighted values of the pure components to obtain the excess free energy as a function of $BmimBF_4$ content.

The calculated excess free energy displays a strongly non-ideal and non-monotonic composition dependence. It is slightly negative on the water-rich side, indicating favorable mixing at low $BmimBF_4$ content, but becomes positive at intermediate ionic-liquid mole fractions, with a pronounced maximum around $\chi_{BmimBF_4} \approx 0.6$-$0.7$. This positive region suggests that, for these compositions, the force-field combination predicts an unfavorable thermodynamic contribution to mixing, consistent with a tendency toward microscopic segregation or reduced miscibility. The return to lower or negative values at higher $BmimBF_4$ content indicates that the balance of ion–ion, water–water, and ion–water interactions changes markedly across composition.

References

(1) Idrissi, A.; Jedlovszky, P. Thermodynamics of Mixing Primary Alkanolamines with Water. *J. Phys. Chem. B* **2018**, *122* (23), 6251–6259. https://doi.org/10.1021/acs.jpcb.8b01052.
(2) Berendsen, H. J. C.; Grigera, J. R.; Straatsma, T. P. The Missing Term in Effective Pair Potentials. *J. Phys. Chem.* **1987**, *91* (24), 6269–6271. https://doi.org/10.1021/j100308a038.
(3) Canongia Lopes, J. N.; Deschamps, J.; Pádua, A. A. H. Modeling Ionic Liquids Using a Systematic All-Atom Force Field. *J. Phys. Chem. B* **2004**, *108* (6), 2038–2047. https://doi.org/10.1021/jp0362133.
(4) Klimovich, P. V.; Shirts, M. R.; Mobley, D. L. Guidelines for the Analysis of Free Energy Calculations. *J Comput Aided Mol Des* **2015**, *29* (5), 397–411. https://doi.org/10.1007/s10822-015-9840-9.

Mixing, De-mixing and Molecular Aggregation in Aqueous Solutions : Molecular Dynamics Simulation and Graph Theoretical Analysis

R. Singh[1], J. Ryu[1], J.-H. Choi[1]

[1]Department of Chemistry, Gwangju Institute of Science and Technology (GIST), Republic of Korea
e-mail: junhochoi@gist.ac.kr

Understanding mixing and de-mixing behavior in various solutions is critical in basic science and industrial fields, but the clarification of operation at molecular level remains a challenge. Recently, we have attempted to elucidate the liquid-liquid and liquid-solid phase separation phenomena in terms of molecular aggregation behavior in diverse aqueous solutions. [1] At the high solute concentrations in solute-water mixtures, the solute molecules exhibit a tendency to self-associate with distinct morphological structure in varying composition of mixture. The topological structure of molecular aggregates was examined by using molecular dynamics (MD) simulation and graph theoretical analysis. The two representative molecular aggregates are shown, that is, closely packed aggregates are formed by less interaction with water, while spatially extended aggregates are formed through significant interaction with water. The relationships between molecular aggregation behavior and mixing, de-mixing process were demonstrated in salt solutions [1], upper critical solution temperature (UCST) [2], lower critical solution temperature [3], loop-behavior systems [4] employing MD simulation studies and graph theory.

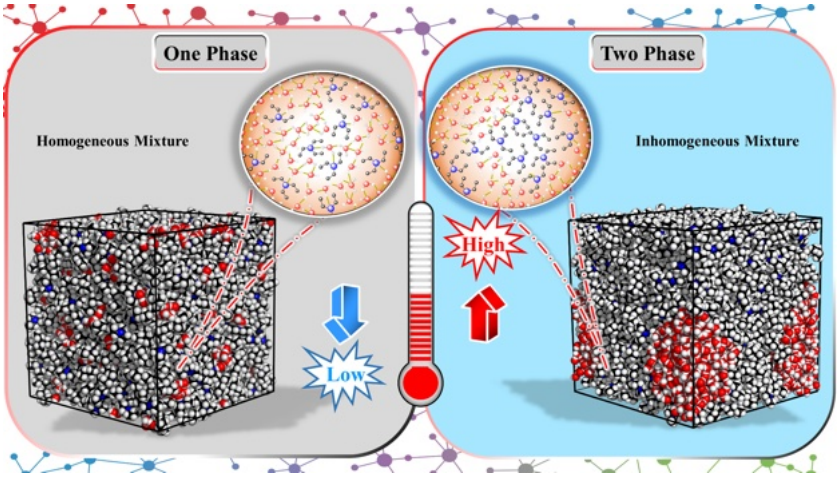

Figure 1 *– Molecular aggregation behavior in triethylamine (TEA)-water mixture. At lower temperature, the small-sized TEA aggregates are compatible with liquid water, but large self-associated aggregates are separated from liquid water at higher temperature in TEA-water mixture.*

References

[1] J.-H. Choi, H. Lee, H. R. Choi, and M. Cho, *Annu. Rev. Phys. Chem.*, **69**, 125, (2018).
[2] S. Parameswaran, S. Choi, and J.-H. Choi, *J. Mol. Liq.*, **347**, 118339 (2022).
[3] R. Singh, J. Seo, J. Ryu, and J.-H. Choi, *Phys. Chem. Chem. Phys.*, **26**, 18970 (2024)
[4] R. Singh, J. Ryu, and J.-H. Choi, *J. Mol. Liq.*, **440**, 128983 (2025).

Revisiting the State of Water in [BMIM][BF4] Aqueous Solutions

Marco Paolantoni[1], Brenda Bracco[1], Barbara Rossi[2], Paola Sassi[1], Andrea Mele[3]

[1]Department of Chemistry, Biology and Biotechnology, University of Perugia,
Via Elce di Sotto 8, 06123 Perugia, Italy
[2]Elettra Sincrotrone Trieste, S.S. 114 km 163.5, Basovizza, 34149 Trieste, Italy
[3]Department of Chemistry, Materials and Chemical Engineering "G. Natta",
Politecnico di Milano, 20133 Milano, Italy
e-mail: marco.paolantoni@unipg.it

Mixtures of water with ionic liquids (ILs) represent promising, tunable systems with potential applications in various areas, ranging from green chemistry to biocatalysis, biopreservation, and energy-related applications [1].
Achieving a molecular-level description of water is crucial for explaining chemical, physicochemical and solvation properties of IL/water systems. However, despite numerous investigations on this subject, a deep understanding of the state of water and its modification in the whole concentration range is still partial controversial and incomplete, even for the prototypical [BMIM][BF4]/water system. Moreover, similarly to other ILs, upon the addition of water, several macroscopic properties of these mixtures exhibit nonlinear trends, with maxima or minima in different hydration domains. As such, the system can be exploited to increase our knowledge on the link between macroscopic properties and microscopic (molecular-level) features.
Here, the hydration features of [BMIM][BF4]/water solutions were investigated across the entire concentration range, by analysing UV-Raman and ATR-FTIR spectra. In particular, inspired by the multivariate curve resolution (MCR) approach [2], a differential method was employed to isolate the so-called solute-correlated (SC) spectrum, which highlights the vibrational contributions of water molecules perturbed by the solute (hydration or interfacial water). We will present this method as a useful way to obtain reliable quantitative information about the hydration features of ILs aqueous mixtures, including hydration numbers and aggregation properties [3,4]. The results will be discussed in connection with molecular dynamics (MD) simulation findings [5] and related approaches.
The primary goal is to gain a consistent picture on the state of water within the [BMIM][BF4]/water system in the different concentration regimes. This information is crucial for achieving a full understanding of this prototypical mixture in relation to its mesoscopic and macroscopic properties.

References

[1] V.A. Azov, K.S. Egorova, M.M. Seitkalieva, A.S. Kashin, and V.P. Ananikov, *Chem. Soc. Rev.,* **47,** 1250 (2018).
[2] D. Ben-Amotz, *J.Am. Chem. Soc.,* **141**, 10565 (2019).
[3] F. Matroodi, C. Bottari, B. Rossi, A. Mannu, M. Paolantoni, A. Mele, *J. Mol. Liq.*, **395** 123881 (2024).
[4] C. Bottari, L. Almásy, B. Rossi, B. Bracco, M. Paolantoni, A. Mele, *J. Phys. Chem. B*, **126** 4299 (2022).
[5] T.-M. Chang, S.E. Billeck, *J. Phys. Chem. B*, **125** 1227 (2021).

Resolving Oligomeric Anions in Carboxylic Acid–Carboxylate Systems: the case of Choline–Geranate

E.Rezabal [2]

[1]Kimika Fakultatea, University of the Basque Country (EHU/UPV) 20018 Donostia, Spain
[2]Donostia International Physics Center, 20018 Donostia, Spain
e-mail: elixabete.rezabal@ehu.eus

Carboxylic acid/carboxylate mixtures in ionic liquids are frequently proposed to form oligomeric anionic species stabilized by hydrogen bonding, although the protonation state within these aggregates—ranging from localized to dynamically exchanging or symmetrically shared protons—often remains difficult to determine experimentally. One prominent example is choline–geranic acid at a 1:2 ratio (CAGE12), which has attracted considerable attention due to its outstanding therapeutic performance in drug delivery and drug activation, particularly in transdermal and anticancer applications [1,2]. In this system, NMR observations [3] indicating proton mobility have led to suggestions that oligomeric anionic motifs may be present; however, whether these correspond to long-lived complex anions or to dynamically fluctuating acid–carboxylate pairs remains unresolved.

Here we combine ATR–FTIR spectroscopy with ab initio and machine-learned force-field molecular dynamics simulations to elucidate the structure and proton dynamics of CAGE12. The simulations reveal a highly fluctuating hydrogen-bond network and provide key dynamical insight: although geranic acid (AGE) and geranate (GE) frequently form hydrogen-bonded contacts, these associations are short-lived and do not stabilize persistent oligomeric anions. Proton transfer between AGE and GE occurs intermittently, consistent with available NMR observations, and requires comparatively sustained hydrogen-bond configurations that are only occasionally achieved.

The proton is thus not symmetrically shared but shuttles between distinct molecular species while preserving carboxylic and carboxylate chemical identities. In agreement with this picture, experimental and theoretical vibrational spectra display coexisting carboxylate and carboxylic acid signatures, with no spectral features characteristic of proton-shared oligomeric anions.

These results reconcile apparently conflicting spectroscopic interpretations and demonstrate that CAGE12 is governed by transient carboxylic/carboxylate pairing rather than long-lived complex anions. More broadly, this work shows how combining vibrational spectroscopy with machine-learned molecular dynamics enables direct resolution of proton dynamics and ion-pairing motifs in complex ionic liquids relevant to functional and biomedical applications.

References

[1] Y. Shi, Z. Zhao, K. Peng, Y. Gao, D. Wu, J. Kim, S. Mitragotri *Adv. Healthcare Mater.* **10**, 2001455 (2021) and references therein

[2] M. C. Verdugo, E. Rezabal et al. *Chemical Communications*, **61**, 12167-12170 (2025).

[3] J. Takeda et al. *ACS Biomaterials Science & Engineering*, **7**, 595-604 (2021).

Intermolecular Vibrational Band of Deep Eutectic Solvents Composed of Lithium Salt and Amide: Composition Dependence

M. Koyakkat[1], H. Shirota[1]

[1] 1-33 Yayoi, Inage-ku, Chiba 263-8522, Department of Chemistry, Chiba University
e-mail: shirota@faculty.chiba-u.jp

The eutectic phenomena are recognized in our surroundings, such as solder and anti-icing agents. When a mixture composed of more than two components shows a huge reduction in melting point compared to the neat components and it becomes the liquid state at ambient temperatures, it is referred to as a deep eutectic solvent (DES). The great advantages of DES include its easy preparation, often just mixing (or sometimes with mild heat), and environmentally friendly nature, when the components are appropriately selected. DES is thus getting more attention recently [1,2].

Typical DESs are composed of a pair of hydrogen-bonding donor and acceptor (often a salt). Because the intermolecular interaction in DES is strong, the viscosity is high. Further, the intermolecular interaction in DESs is complicated because they involve cations, anions, and hydrogen-bonding donors. An effective approach to understand the microscopic intermolecular interaction in liquids/solutions is to examine the intermolecular vibrational band, which is located in the low-frequency region < ~150 cm^{-1} [3,4]. Herein, we report the intermolecular vibrational behaviour of (i) lithium bis(trifluoromethylsulfonyl)amide/organic amide systems [5] and (ii) lithium salt/acetamide systems [6].

In the study of lithium bis(trifluoromethylsulfonyl)amide/organic amide systems [5], we compared five organic amides (acetamide, acetamide, propanamide, *N*-methylacetamide, butyramide, and urea). The line shape and vibrational frequency of the low-frequency spectrum depend on the host amide. The peak frequency and the first moment of the intermolecular vibrational bands of the acetamide- and urea-based DESs were in a higher-frequency region compared to the other three DESs, which indicates stronger microscopic interactions in the former case.

In the study of lithium salt/acetamide systems [6], we investigated the anion dependence of the intermolecular vibrational dynamics of DESs composed of five lithium salts and acetamide. The line shape and first moment of the intermolecular vibrational band strongly depended on the anion species. The order of the first moments indicates that the microscopic intermolecular interactions are stronger in the DESs of lithium salts with nitrate $[NO_3]^-$ and trifluoromethanesulfonate $[OTf]^-$ than in those of lithium salts with perchlorate $[ClO_4]^-$, bis(fluorosulfonyl)amide $[NF_2]^-$, and bis(trifluoromethylsufonyl)amide $[NTf_2]^-$. Like simple aprotic molecular liquids, a correlation of the first moment of the low-frequency band and the bulk parameter (the square root of surface tension divided by density) in the present DES systems is confirmed, except for Li[OTf]/acetamide system. Compared with the lithium bis(trifluoromethylsulfonyl)amide/organic amide systems, the anion of lithium salt is more sensitive to the intermolecular vibration and bulk liquid properties than the host organic amide.

References

[1] E.L. Smith, A.P. Abbott, K.S. Ryder, *Chem. Rev.* **114**, 11060 (2014).
[2] B. B. Hansen, S. Spittle, B. Chen, D. Poe, Y. Zhang, J. M. Klein, A. Horton, L. Adhikari, T. Zelovich, B. W. Doherty, B. Gurkan, E. J. Maginn, A. Ragauskas, M. Dadmun, T. A. Zawodzinski, G. A. Baker, M. E. Tuckerman, R. F. Savinell, and J. R. Sangoro, *Chem. Rev.* **121**, 1232 (2021).
[3] D. McMorrow, W. T. Lotshaw, and G. A. Kenneywallace, *IEEE J. Quantum Electron.* **24**, 443 (1988).
[4] N. A. Smith and S. R. Meech, *Int. Rev. Phys. Chem.* **21**, 75 (2002)
[5] M. Koyakkat and H. Shirota, *J. Phys. Chem. B* **129**, 4023 (2025)
[6] M. Koyakkat and H. Shirota, *J. Chem. Phys.* **164**, 144507 (2026).

Harnessing machine learning for the design and structural classification of periodic mesoporous silica.

A. Mawbey[1], T. Stavert[1], J. Cardona[1], M. Jorge[1]

[1] Department of Chemical and Process Engineering, University of Strathclyde, 75 Montrose Street, Glasgow G1 1XJ, UK

e-mail: a.mawbey@strath.ac.uk

Understanding the self-assembly process involved in producing ordered mesoporous silica (OMS) is vital to both improve control over the molecular structure and guide the design of sustainable manufacturing of these materials. Whilst the use of ammonium surfactants (e.g. cetyltrimethylammonium bromide, CTAB) produces a highly ordered OMS with a variety of potential applications (separations, catalysis, drug delivery, etc.) [1], the economic and environmental limitations of this surfactant impose limits on its large-scale industrial use. Efforts have been made to use more environmentally friendly amine surfactants, such as dodecylamine (DDA), but this invariably has led to a much lower degree of order in the resulting porous structures [2].

This work employs coarse-grained molecular dynamics to investigate a mixed surfactant approach, combining amine surfactants with a small quantity of ammonium surfactant to improve OMS sustainability whilst retaining a high degree of structural order. Initial results, shown in Figure 1, indicate that the addition of ammonium surfactants has a significant impact on silica structure, highlighting the potential for these systems to unlock the sustainability of OMS materials.

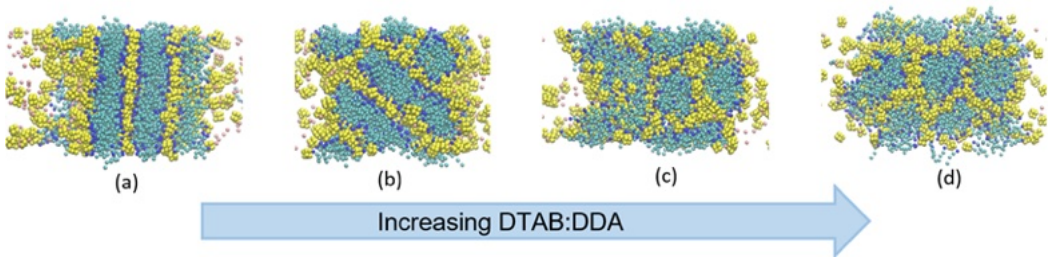

Figure 1 – *Simulated configurations of surfactant (blue) and silica (yellow) at a pH of 10.5. With a surfactant fraction as DDA of* ***(a)*** *1, showing a clear lamellar phase;* ***(b)*** *0.75, showing a disordered lamellar phase;* ***(c)*** *0.5, showing a disordered hexagonal phase;* ***(d)*** *0.25, showing a more ordered hexagonal phase.*

To overcome the limitations of manual structural classification and quantify the simulated materials degree of order, we have developed a machine learning classification model using the PointNet architecture [3]. The model successfully classifies common OMS structures to a high degree of accuracy (up to 99%). Crucially, through use of a dynamic subcloud sampling technique, this model captures the emergence of local order within larger-scale self-assembly trajectories.

These tools work together to promote a quantifiable strategy for greener OMS synthesis through the computational design.

References

[1] J. G. Croissant, Y. Fatieiev, A. Almalik, and N. M. Khashab*, Adv Healthc Mater*, **vol. 7**, Page (2018).

[2] A. Centi, J. R. H. Manning, V. Srivastava, S. van Meurs, S. V. Patwardhan, and M. Jorge, *Mater Horiz*, **vol. 6**, pp. 10277-1033 (2019).

[3] C. R. Qi, H. Su, K. Mo and L. J. Guibas, *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*, July 21-26, Honolulu, USA, 2017, pp. 652–660

A Graph-based approach for the structural characterization of macromolecules and their interactions with the environment

K. Jonas (née Drysch)[1], Y. Dawer[1], P. Zaby[1], K. Buchmüller[1], L. Dick[1], B. Szabó[2], O. Hollóczki[2], B. Kirchner[1]

[1]Mulliken Center for Theoretical Chemistry, University of Bonn, Beringstraße 4, 53115 Bonn, Germany

[2]Department of Physical Chemistry, Faculty of Science and Technology, University of Debrecen, H-4032 Debrecen, Hungary

e-mail: kdrysch@uni-bonn.de

The use of molecular dynamics (MD) simulations to gain molecular-level insights into macromolecular interactions with environmental and physiological systems has become increasingly important. Yet, efforts have remained focused on naturally occurring biomolecules that rely on known monomer motifs. This has raised the need for robust, generalised tools to study chemically relevant macromolecular systems.
In this contribution, we introduce **MakroLyzer** [1], an open-source program that uses a graph-based representation of macromolecules to determine structural descriptors such as the asphericity parameter, the anisotropy factor, the radius of gyration, the order parameter, and local conformational features. We demonstrate the utility of MakroLyzer by examining the aggregation behaviour of nanoplastics such as polyethylene (PE) and nylon 66 (N66) under different simulation protocols [2, 3].
In addition, we present studies on the interactions between nanoplastic particles and their environment, including the adsorption of drug molecules onto nanoplastic surfaces [4].
Finally, we discuss recent projects examining the behaviour of chemically functionalised nanoplastics in complex liquid environments. Particular emphasis is placed on analysing the interaction between the particle surface and the surrounding solvent molecules. One example of this is the detection of hydrogen bonds between the particles and the surrounding solvent molecules, as illustrated in Fig. 1.

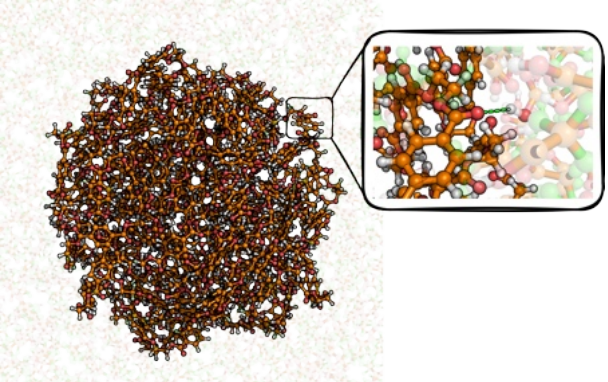

Figure 1 *– Hydrogen bond analysis between a nanoplastic particle and the surrounding solvent.*

References

[1] K. Drysch, Y. Dawer, P. Zaby, K. Buchmüller, L. Dick, P. Mutzel, O. Hollóczki and B. Kirchner *J. Phys. Chem. B*, **129**, 12997–13008 (2025).
[2] B. Szabó, P. Zaby, L. Dick, K. Drysch, Y. Dawer, W. Reckien, A. Udvardy, F. Neese, B. Kirchner and O. Hollóczki, *J. Phys. Chem. B*, **130**, 881-893 (2026)
[3] K. Drysch, B. Kirchner, O. Hollóczki and L. Dick, *ChemRxiv (preprint)* (2026)
[4] L. Dick, P. R. Batista, P. Zaby, G. Manhart, V. Kopatz, L. Kogler, V. Pichler, F. Grebien, V. Bakos, B G. Plósz, N. Zlatkov Kolev, L. Kenner, B. Kirchner and O. Hollóczki, *Sci. Rep.*, **14**, 25853 (2024)

Nanoplastics from theoretical chemistry

Boglárka Szabó, Maxim Varenicja, Oldamur Hollóczki
Department of Physical Chemistry, Faculty of Science and Technology, University of Debrecen, Egyetem tér 1, 4032 Debrecen, Hungary
e-mail: holloczki.oldamur@science.unideb.hu

Nanoplastic particles are at least two orders of magnitude smaller than eukaryotic cells, and therefore their environmental and health effects are likely to stem from their molecular level interplay with living organisms. The underlying interactions with biomolecular systems are, however, difficult to characterize experimentally, due to the complexity of polymer systems and the biological matrix they are embedded in. To overcome these obstacles, we employed molecular modeling, which helped us understanding the changes nanoplastics induce in the molecular structure of biomolecules in solution.

Modeling nanoplastics has its own challenges, in particular creating reasonable starting geometries for these polymer assemblies. We established an involved, rigorous workflow to generate nanoplastic models for molecular simulations through the self-assembly of polymer macromolecules [1]. To avoid such a series of simulations every time before simulating a system that contains nanoplastics, we created an online library, where the best obtained structures are freely available, aiding future modeling studies in the field. The self-assembly of the macromolecules composing the nanoplastics is strongly influenced by the solvent, as we found that the density of these particles varies significantly in different media. A similar protocol was used to predict the adsorption of antibiotics on nanoplastics through the example of tetracycline, and was found that this process can have a severe impact through the known Trojan horse effect, and also via hindering the absorption of drugs into the body during treatment [2].

Furthermore, we investigated examples of proteins, lipids, and nucleic acids in contact with polymer systems. Interactions of polyethylene particles with lipid bilayers showed significant perturbations in the membrane structure. Polystyrene was found prone to crossing membranes that resemble the blood-brain barrier. We found that the molecules adsorbed onto the surface of these plastics, i.e. the corona, have a decisive effect in this process. Interactions of polymers with proteins [3] and DNA [4] both triggered significant changes in the conformation and self-assembly of these biomolecules, which may also have severe biological impact. In future studies molecular modeling will be employed to more complex systems, which will enable us to connect the predictions from our calculations with direct toxic effects induced by these pollutants.

References

[1] B. Szabó et al., *J. Phys. Chem. B.* **130**, 881 (2026).
[2] L. Dick et al., *Sci. Rep.* **14**, 25853 (2024).
[3] O. Hollóczki, S. Gehrke, *Sci. Rep.* **9**, 16013 (2019).
[4] M. Varenicja, O. Hollóczki, Nano Lett. **25**, 15890 (2025).

Machine-learning-tuned classical force fields for refrigerants: transferability across thermophysical properties, state points, and liquid interfaces

B. P. Agbodekhe, E. J. Maginn

Department of Chemical and Biomolecular Engineering,
University of Notre Dame, Notre Dame, IN 46556, USA
e-mail: ed@nd.edu

Hydrofluorocarbon refrigerants used in heating, ventilation, air conditioning, and refrigeration (HVACR) systems have high global warming potential and are being phased out under the Kigali Amendment to the Montreal Protocol. Meeting this challenge requires both the discovery of low-GWP replacement mixtures and the reclamation of legacy refrigerants, the latter requiring separation of azeotropic and near-azeotropic mixtures. Because reliable experimental data for the relevant mixtures and conditions are scarce, molecular simulation is an indispensable predictive tool in this effort, but its fidelity rests on the accuracy and transferability of the underlying force fields (FFs). One promising approach optimizes the non-bonded (Lennard-Jones) parameters of an FF against experimental vapor-liquid equilibria (VLE) data via a machine-learning protocol, while retaining the bonded parameters and partial charges of a standard classical FF such as GAFF [1-3]. Two questions follow: do such VLE-tuned FFs transfer to properties and thermodynamic states absent from the tuning set, and do they extend to mixtures and interfaces?

We address these questions through an extensive, multi-property validation of new FFs we have developed for seven refrigerants spanning three chemical classes [4,5]. For difluoromethane (R-32) and pentafluoroethane (R-125), four near-degenerate VLE-tuned candidate FFs per molecule were evaluated against eleven thermophysical, transport, and structural properties not used in tuning, each at several state points. The VLE-tuned models proved highly transferable, generally outperforming an expert-tuned FF for R-32 and GAFF for R-125. Properties absent from the tuning resolved differences that VLE data alone could not, enabling a robust ranking of otherwise indistinguishable parameter sets. We then test generality across five additional refrigerants (R-50, R-170, R-14, R-134a, and R-143a), adding two new tests: the surface tension and properties at subcooled liquid states far from the VLE manifold. The new FFs capture surface-tension trends well, with quantitative agreement within ~10% for four of the five fluids and retain near-saturation predictive quality at subcooled conditions. Tuning only the Lennard-Jones parameters while preserving the classical physics-based functional form thus yields models that transfer across property types, chemical classes, and thermodynamic conditions, providing a foundation for simulating the mixtures and interfaces central to refrigerant reclamation and a circular HVACR economy.

References

[1] B. J. Befort, R. S. DeFever, G. M. Tow, A. W. Dowling, and E. J. Maginn, *J. Chem. Inf. Model.*, **61**, 4400 (2021).
[2] N. Wang, M. N. Carlozo, E. Marin-Rimoldi, B. J. Befort, A. W. Dowling, and E. J. Maginn, *J. Chem. Theory Comput.*, **19**, 4546 (2023).
[3] M. N. Carlozo, N. Wang, A. W. Dowling, and E. J. Maginn, *Digit. Discov.*, **5**, 1650 (2026).
[4] B. Agbodekhe, E. Marin-Rimoldi, Y. Zhang, A. W. Dowling, and E. J. Maginn, *J. Chem. Eng. Data*, **69**, 427 (2024).
[5] B. Agbodekhe and E. J. Maginn, *in preparation* (2026).

AI-Enabled Discovery of Deep Eutectic Solvents and Their Chemical Space

João P. Santos[1], Filipe H. B. Sosa[1], Dinis O. Abranches[1], João A. P. Coutinho[1]

[1]CICECO—Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal
e-mail: jdinis@ua.pt

Deep eutectic solvents (DESs), binary liquid mixtures noted for their strong intermolecular interactions, have emerged as promising green alternatives to traditional organic solvents. The design of these novel solvents is complex, as their properties do not simply reflect the weighted average of their precursors. Incorporating low molecular weight compounds, such as water, to reduce viscosity or modulate other properties is a common practice. This leads to an overly complex and extensive DES design space, where the number, chemical nature, and relative composition of precursors must be carefully tuned [1]. Machine learning (ML), with its innate ability to correlate variables, presents a promising alternative to trial-and-error approaches in the design of DESs.

In this work, Gaussian processes (GPs) [2] were used to fit and predict several physicochemical properties of DESs, namely density, viscosity, and melting temperature. Experimental data was collected from the literature, including over 400 unique DES combinations and more than 4000 independent data points. Each dataset was carefully split into training, validation, and testing sets to determine the optimal GP architecture and hyperparameters for each physicochemical property. Coefficients of determination exceeding 0.95 were achieved for all studied properties, including viscosity, which spanned values over eight orders of magnitude, and melting temperature, which encompassed a range of nearly 700 K. Using the trained GP models, new DES-based lubricants were designed by exploring the sigma profile space of DESs. The GPs suggested novel combinations of precursors not present in the original database to achieve desired viscosities and melting temperatures. These novel DESs were experimentally prepared and characterized for the first time in this work. Viscosity and tribological properties were also measured, which surpassed common standards in the literature for low and high operational temperatures, effectively leading to DES formulations suitable for lubricant applications.

Acknowledgments
This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UID/50011/2025 (DOI 10.54499/UID/50011/2025) & LA/P/0006/2020 (DOI 10.54499/LA/P/0006/2020), financed by national funds through the FCT/MCTES (PIDDAC). Filipe Sosa acknowledges FCT (CEECIND/07209/2022).

References

[1] D. O. Abranches and J. A. P. Coutinho. Annual Review of Chemical and Biomolecular Engineering **14** (2023): 141-163.
[2] D. O. Abranches, E. J. Maginn, Y. J. Colón, Proc. Natl. Acad. Sci. U.S.A., **vol. 121** (2024), e2404676121.

AI-Driven Discovery of Novel Low-Melting-Point Ionic Liquids

Gaopeng Ren[1], Austin M. Mroz[1,2], Frederik Philippi[1], Tom Welton[1], Kim E. Jelfs[1*]

[1]Department of Chemistry, Imperial College London, White City Campus, London, UK
[2]I-X Centre for AI in Science, Imperial College London, White City Campus, London, UK
e-mail: k.jelfs@imperial.ac.uk

Ionic liquids (ILs) are promising materials with applications in catalysis, energy storage, and separations, but their discovery is limited by the vast chemical space and scarcity of experimental data. These studies present machine learning frameworks using variational autoencoders (VAEs) and conditional variational autoencoders (CVAEs) to generate novel low-melting-point ILs. One approach combines graph-based link prediction with VAEs to expand known IL datasets and generate diverse cation–anion combinations, while another introduces ion-scoring methods and large PubChem ion datasets to improve structural diversity. Both studies incorporate melting point prediction and molecular dynamics validation to identify ILs with melting points below 373 K. The results demonstrate that integrating generative deep learning, graph neural networks, tabular models and physics-informed filtering can efficiently expand IL chemical space and accelerate the discovery of low-melting-point ILs.

References

[1] Gaopeng Ren, Austin M. Mroz, Frederik Philippi, Tom Welton and Kim E. Jelfs*, Digital Discovery*, **5**, 643-652 (2026).
[2] Gaopeng Ren, Austin M. Mroz, Frederik Philippi, Tom Welton and Kim E. Jelfs*, Chemical Science*, **17**, 4621-4631 (2026).

Predicting Partition Coefficients of Biomolecules in Aqueous Biphasic Systems

A. Margarida D. Pinhão[1], B. Emanuel V. Capela[1], C. João A. P. Coutinho[1], D. Mara G. Freire[1], E. Dinis O. Abranches[1]

[1]CICECO-Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Portugal
e-mail: margaridapinhao@ua.pt

Aqueous Biphasic Systems (ABSs) have emerged as a viable approach in the purification of biomolecules without loss of biological activity. Unlike traditional water-organic biphasic systems, ABSs consist of two immiscible aqueous phases and are non-toxic, non-flammable, and biocompatible. Ionic liquids (ILs) are often used as ABS constituents to better control biomolecule-solvent interactions and enhance separation performance. However, given the vast library of ILs, the selection of suitable systems for each target biomolecule relies on laborious trial-and-error campaigns. Machine learning (ML), particularly Gaussian process (GP) models have been shown to be capable of predicting physicochemical properties of materials and emerge as a viable alternative to help design IL- based ABSs.

In this work, GP models were developed to predict the partitioning behaviour of several biomolecules, such as caffeine, nicotine, phenylalanine, gallic acid and levodopa, in different polyethylene glycol-dextran (PEG-DEX) ABSs. Sigma profiles, molecular descriptors derived from quantum chemistry calculations, were employed. The GP models were able to predict the partition coefficients of all biomolecules across several different ABSs. Overall, coefficients of determination of 0.99 and 0.85 were attained for the training and testing sets, respectively. The testing set consisted of novel ABSs never seen before by the model, highlighting its predictive and generalization capability. The methodology developed in this work significantly accelerates the design of separation and purification processes based on ABSs, guiding the experimental design and reducing trial and error screening.

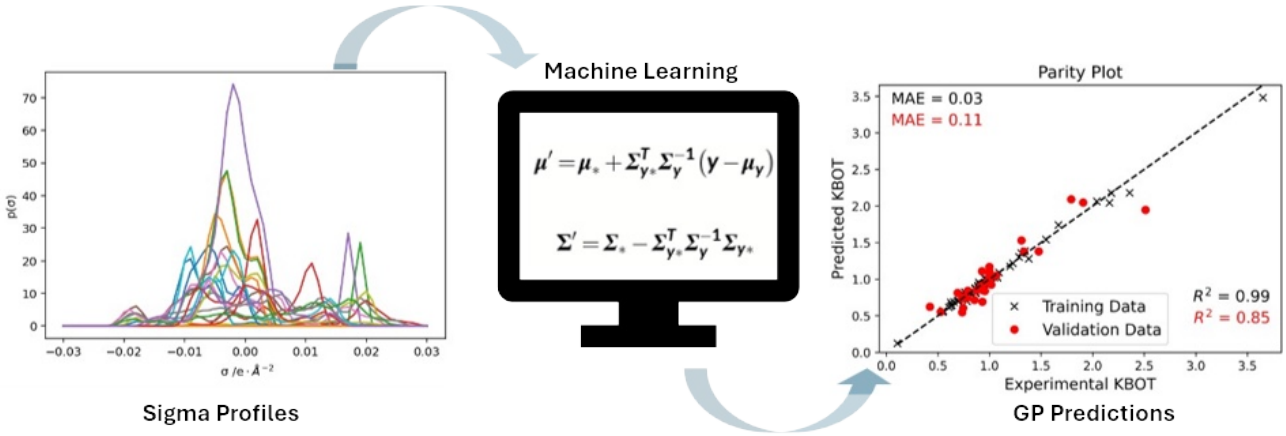

Figure 1 *– Sigma profiles of all the Ionic Liquids added as adjuvants to the Aqueous Biphasic Systems, used as input to the Gaussian Process model to predict the relative Partition Coefficients of the solutes in the DEX-rich, bottom phase, achieving R-Squared values of 0.99 and 0.85 for the training and testing sets, respectively.*

The role of interfacial water in stabilizing biological membranes

F. Martelli[1]
[1]CNR Institute for Complex Systems
[2]Department of Physics, Sapienza University of Rome
e-mail: fausto.martelli@cnr.it

We simulate bacterial- and mammalian-like membranes under tensile stress and show that interfacial water helps membranes respond to mechanical stress. In mammalian-like membranes, the hydrogen-bonded water network remains stable under lateral stress. In bacterial-like membranes, stress smooths the membrane surface and partially separates water from the membrane. This suggests that interfacial water is not merely passive but actively contributes to membrane stability and resilience, with differences among membrane types potentially reflecting biological and evolutionary adaptations.

References

[1] V. Losasso, M. Chiricotto, and F. Martelli*, ACS Applied Materials & Interfaces*, **18**, 12368–12382 (2026).

Cation/anion and monovalent/divalent selectivity in negatively charged nanopores: reduced models versus experiments and molecular dynamics simulations

Eszter Molnárné Lakics[1], Zoltán Ható[1], Salman Shabbir[1,2], Dirk Gillespie[3], Dezső Boda[1], Mónika Valiskó[1]
[1]Center for Natural Sciences, University of Pannonia, Hungary
[2]Department of Engineering, Reykjavik University, Iceland
[3]Department of Physiology and Biophysics, Rush University Medical Center, Chicago, USA
e-mail: valisko.monika@mk.uni-pannon.hu

The anomalous mole fraction effect (AMFE) is widely regarded as a hallmark of calcium versus monovalent ion selectivity in negatively charged pores [1]. In this experiment, a mixture of $CaCl_2$ and monovalent electrolytes (NaCl or KCl) are used and the total conductance versus mole fraction function is computed. We talk about AMFE if this function has a minimum, but in general, this function is nonlinear due to strong correlations of ions with each other and with the charged pore wall. While AMFE is well understood in highly cation-selective narrow ion channels [2], its microscopic origin in wide synthetic nanopores, where anions may also contribute to transport, remains less clear [3].

Here, we use a reduced Nernst-Planck + Local Equilibrium Monte Carlo framework [4,5] to study ionic transport in negatively charged nanopores. Water is implicit in this model. The adjustable parameter is the diffusion coefficient of the ions in the pore. By fitting pore diffusion coefficients to either experimental conductance points [3] or conductance values obtained from molecular dynamics (MD) simulations [6], we reproduce the conductance versus mole fraction curve. We study how the different interactions of monovalent and divalent cations with the pore charges govern the selectivity behavior and how the underlying phenomena explain the behavior observed in experiments and MD simulations.

Our results demonstrate that preferential selectivity between monovalent and divalent cations is modulated by cation versus anion selectivity in wide nanopores, where anion leakage and loss of cation selectivity are observed due to the strong adsorption of divalent cations to pore charges. This effect increases with increasing calcium mole fraction. Our study is a typical example of multiscaling, where our models span the spectrum from simple representations using implicit water to all-atom models (explicit water) used in MD, and experimental reality.

References

[1] W. Almers, E. W. McCleskey, and P. T. Palade. *J. Physiol.*, **353**(1):565–583, (1984).
[2] D. Gillespie and D. Boda. *Biophys. J.*, **95**(6):2658–2672, (2008).
[3] D. Gillespie, D. Boda, Y. He, P. Apel, and Z.S. Siwy. *Biophys. J.* **95**(2):609–619, (2008).
[4] H. Fabian, Zs. Sarkadi, M. Valisko, D. Gillespie, and D. Boda. *J. Mol. Liq.*, **368**:120715, (2022).
[5] E. Molnárné Lakics, M. Valiskó, Z. Ható, D. Gillespie, and D. Boda. *J. Chem. Phys.* in press, (2026).
[6] S. Shabbir, D. Boda, and Z. Ható. *J. Chem. Phys.* in press, (2026).

Toward large-scale coarse-grained dynamics simulations of gas diffusion aided by machine-learning in realistic systems

Tetsuro Nagai[1], Zhiye Tang[2], Yoshitake Sakae[3], Tatsuya Yamada[4], Nobuaki Kikkawa[5], Ryosuke Jinnouchi[5], Kumiko Nomura[6], Masayuki Kimura[6], and Susumu Okazaki[7]

[1]Research Institute for Interdisciplinary Science, Okayama University, Japan
[2]Institute for Molecular Science, Japan
[3]Center for Management of Information Technologies, Kagoshima University, Japan
[4]Research Organization for Information Science and Technology, Japan
[5]Toyota Central R&D Labs., Inc., Japan
[6]Toyota Motor Corporation, Japan
[7] Graduate School of Nanobioscience, Yokohama City University, Japan

e-mail: tnagai@okayama-u.ac.jp

Mass transport within heterogeneous media is a widespread phenomenon observed in various physical, chemical, and biological systems. Examples of such heterogeneous media include gas separation membranes for carbon capture, polymer electrolyte membranes, and the cathode catalyst layers of fuel cells. Molecular diffusion is key to understanding mass transport and molecular dynamics (MD) simulations are a powerful tool for examining the diffusion process in atomistic detail. However, the timescales associated with molecular diffusion in heterogeneous systems often exceed those accessible by conventional all-atom MD simulations, thereby limiting the direct applicability of MD to these problems.

One promising strategy to overcome this limitation is to construct coarse-grained dynamics of the diffusing molecules. For this purpose, we proposed the dynamic Monte Carlo (MC) approach [1], which can effectively generate long-time trajectories of diffusing molecules. The dynamic MC method requires the free energy landscape and position-dependent diffusion constant of a diffusing molecule as input and these input quantities can be obtained from MD simulations. This approach was demonstrated in applications to hydrogen gas diffusion through polymer electrolyte membranes [2,3]. In addition to reproducing gas permeability at various water uptakes, we clarified the molecular-level mechanism of the gas permeation.

However, the evaluation of input quantities for an entire large-scale system, such as a 100 nm-scale cathode catalyst layer model, using MD calculations is computationally prohibitive. To address this issue, we adopted the machine learning (ML) approach. We employed support vector regression (SVR) with the smooth overlap of atomic positions (SOAP) kernel to predict the input quantities from local chemical structures [4]. The ML model can be trained using a small subset of the input quantities or those obtained for smaller or more tractable systems resembling the large-scale system in question. We can thus circumvent the evaluation of the input quantities in the entire system.

In this presentation, we introduce our recent efforts to apply our methodology to oxygen gas transport in the large-scale, realistic all-atom cathode catalyst layer model constructed based on experimental structural information. This work helps establish a common framework for evaluating mass transport in spatially heterogeneous systems.

References

[1] **T. Nagai** et al., *J. Chem. Phys.* **156**, 154506 (2022).

[2] **T. Nagai** and Susumu Okazaki, *J. Chem. Phys.* **157,** 054502 (2022).

[3] **T. Nagai** et al., *J. Chem. Phys.* **156**, 044507 (2022).

[4] **T. Nagai** et al., *J. Chem. Theory Comput.* **21**, 2598–2611 (2025).

Oxygen Diffusion in Water- and Ionomer-filled Carbon Mesopores

N. Kikkawa[1], R. Jinnouchi[1], T. Nagai[2], S. Okazaki[3], M. Kimura[4]
[1]Toyota Central R&D Labs., Inc.
[2]Okayama University
[3]Yokohama City University
[4]Toyota Motor Corporation
e-mail: kikkawa@mosk.tytlabs.co.jp

Mesoporous carbon is a promising cathode catalyst support for polymer electrolyte fuel cells [1], as it can both mitigate catalyst poisoning by ionomer and reduce oxygen transport resistance at the ionomer-catalyst interface. However, oxygen transport resistance is also significantly affected by additional factors, including long diffusion pathways and blockage within pores by liquid water and ionomer. Therefore, optimizing the pore structure is essential to minimize overall transport resistance. To support such optimization, we have conducted molecular dynamics (MD) simulations to analyse oxygen transport within mesopores [2]. Considering the diversity of pore sizes, filing materials, and occupancies in actual fuel cells, we systematically investigated the effects of these factors on oxygen diffusion using an in-house automated tool for generating molecular systems [3, 4]. As a result of the comprehensive analysis, as shown in Figure 1a, the oxygen diffusion coefficient D followed the order: low occupancy > water-filled > ionomer-filled conditions. Interestingly, in the water-filled conditions, the diffusion coefficient was comparable to that in bulk water, whereas under ionomer-filled conditions, it was approximately one order of magnitude lower than that in bulk ionomer. Oxygen diffusion in ionomer-filled pores is extremely slow, making it difficult to analyze by MD simulations alone. To address this limitation, we employed a combined approach of free energy landscape calculation and kinetic Monte Carlo simulations [5, 6] to additionally investigate the long-time dynamics of oxygen diffusion. The analysis revealed that oxygen diffusion is hindered by the trapping of oxygen molecules in voids formed near the pore walls (Figure 1b).

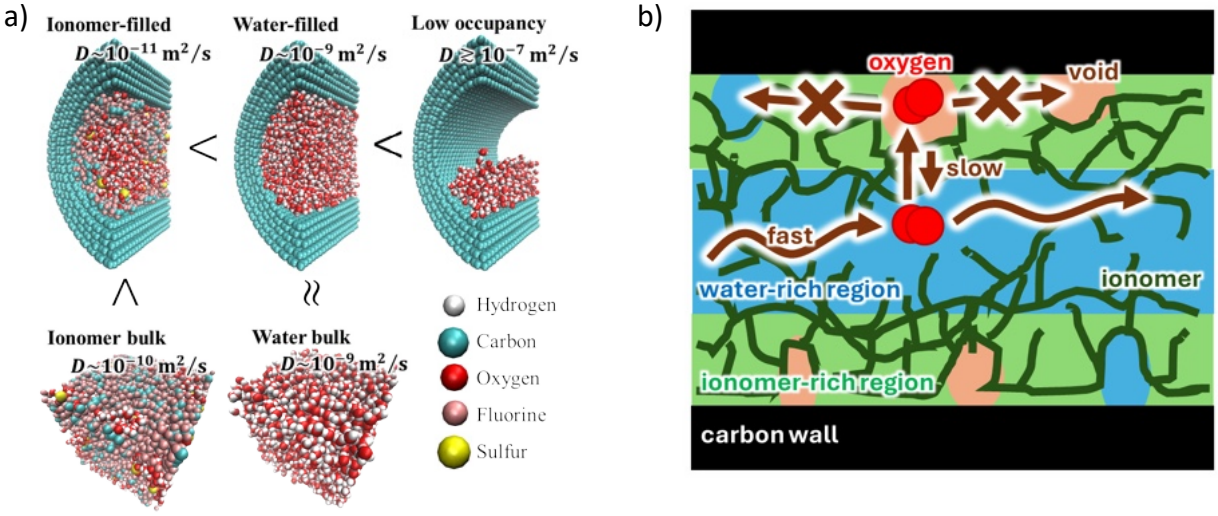

Figure 1 *– a) Snapshots (cross-sectional views are shown for pore systems) and oxygen diffusion coefficients in various conditions. b) Diffusion mechanism in ionomer-filled mesopores.*

References

[1] K. Kodama, *et al.*, *Nat. Nanotechnol.*, **16**, 140 (2021).
[2] N. Kikkawa and M. Kimura, *Langmuir*, **40**, 1674 (2024).
[3] N. Kikkawa and R. Jinnouchi, *J. Phys. Chem. C*, **126**, 11518 (2022).
[4] N. Kikkawa, et al., *ACS Appl. Mater. Interfaces*, **14**, 53744 (2022).
[5] T. Nagai, A. Yoshimori, S. Okazaki, *J. Chem. Phys.*, **156**, 154506 (2022).
[6] T. Nagai and S. Okazaki, *J. Chem. Phys.*, **157**, 054502 (2022).

Water self-dissociation in slit pores displays non-monotonic behavior as a function of water filling

S. Ruiz-Barragan[1],D. Muñoz-Santiburcio[2], S. Körning[3], D. Marx[3]
[1]Universitat Politécnica de Catalunya, Departament de Física, Terrassa 08222, Spain
[2] Instituto Andaluz de Ciencias de la Tierra, Spanish Research Council, Armilla, 18100, Spain
[3] Lehrstuhl für Theoretische Chemie, Ruhr-Universität Bochum, Bochum, 44780, Germany
e-mail: sergio.ruiz.barragan@upc.edu

Although nanofluidics and chemistry in nanoconfined liquids has emerged as an exciting field, the quantitative impact of confinement on fundamental properties remains often unclear [1,2]. Currently, there is not yet consensus on the impact of slit pore confinement on water selfdissociation [1,2] , namely if this ubiquitous elementary reaction is enhanced, unaltered or suppressed by nanoconfinement. We address this question for well-defined water/graphene slit pore systems that allow us to carefully establish the appropriate thermodynamic conditions for different pore fillings, specifically pressure [3,4]. Anticipating our key results, we show that the energetics of the self-dissociation reaction is very sensitive to even subtle changes of the confinement conditions, leading even to non-monotonic behavior depending on water filling.

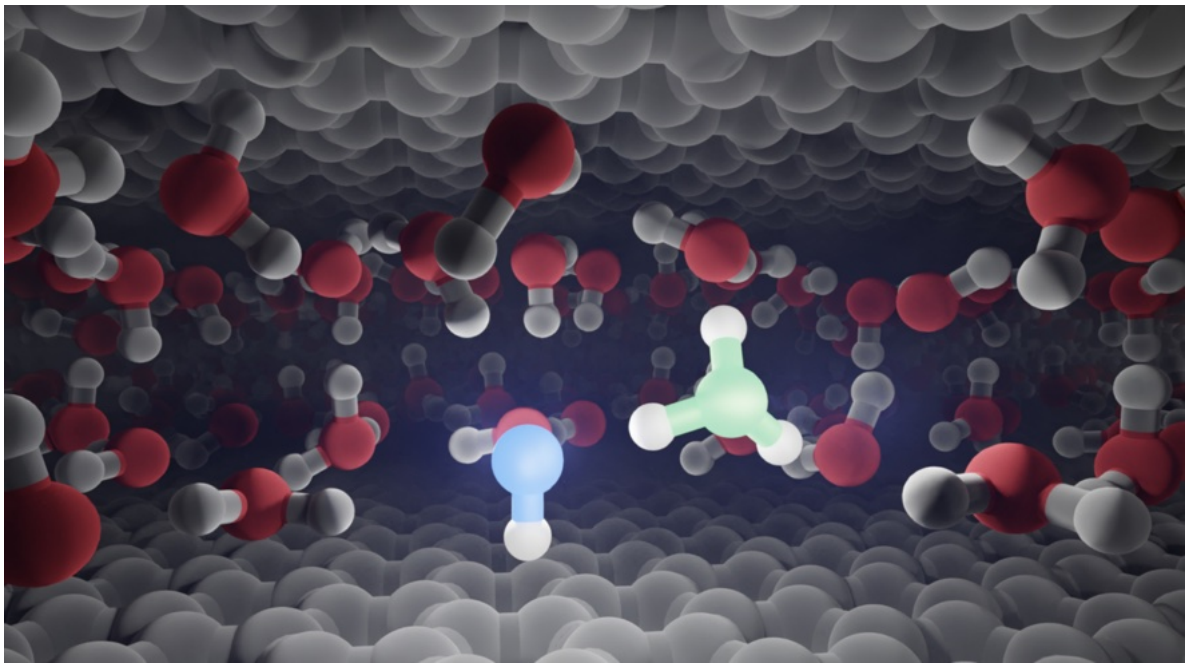

***Figure 1** – Solvated hydronium-hydroxide contact ion pair in nanoconfined water in a graphene slit pore.*

References

[1] D. Muñoz Santiburcio and D. Marx, Phys. Rev. Lett., 119, 056002 (2017)
[2] S. Di Pino, Y. A. Perez Sirkin, U. N. Morzan, V. M. Sanchez, A. Hassanali and D. A. Scherlis, Angew. Chem. Int. Ed., 62, e202306526 (2023)
[3] S. Ruiz-Barragan, D. Muñoz-Santiburcio, S. Körning and D. Marx, Phys. Chem. Chem. Phys., 22,10833 (2020)
[4] S. Ruiz-Barragan, H. Forbert and D. Marx, Phys. Chem. Chem. Phys., 25, 28119 (2023)

Confined Binary Active Brownian Particles: Preferential Wall Accumulation and Correspondence with Equilibrium Fluid Mixtures

K. Šindelka[1], M. Lísal[1,2]

[1]Institute of Chemical Process Fundamentals, Czech Academy of Sciences, Prague, Czech Republic

[2]Department of Physics, Faculty of Science, Jan Evangelista Purkyně University, Ústí nad Labem, Czech Republic

e-mail: sindelka@icpf.cas.cz

Active Brownian particles (ABPs) serve as a generic model for synthetic active matter systems such as active colloids which can self-propel while undergoing Brownian motion. Under confinement, ABPs exhibit propulsion-induced wall accumulation [1], a fundamentally non-equilibrium behaviour with potential for practical applications such as microfluidics or lab-on-chip devices. In multi-component systems, the wall accumulation is further influenced by differences in particle activities which introduce demixing and spatial heterogeneity.

We use overdamped Langevin dynamics to study equimolar binary ABP mixtures confined in slit pores, varying slit width, propulsion strength, and interaction asymmetry. Two mixtures are considered: equal size particles with different softness (B1 mixture), and equal softness ones with different sizes (B2 mixture), at both gas-like and liquid-like densities.

The ratio of slit width to persistence length (related to propulsion strength) governs the wall accumulation behaviour. In B1 mixtures, overlapping wall-density peaks induce strong local crowding at higher activities, driving confined or surface motility-induced phase separation (MIPS). In B2 mixtures, spatially shifted density peaks of smaller and larger particles suppress MIPS in favour of compositionally distinct multi-layer structures, with smaller particles preferentially occupying the innermost wall layer.

Direct comparison with equilibrium Lennard-Jones fluid mixtures shows that ABP wall enrichment requires no attractive particle-wall interactions, is tunable by propulsion, and generates substantially larger wall pressures than those in adsorbed fluids. These results advance understanding of demixing and self-organisation in confined active colloidal systems, with implications for microfluidic particle sorting.

References

[1] K. Šindelka, A. Gadermeteva, M. Lísal, Soft Matter, 21, 7544-7564 (2021).

Cosolvent Effects on Peptide Aggregation Studied with All-Atom MD and a Solvation Theory

Nobuyuki Matubayasi
Graduate School of Engineering Science, Osaka University, Osaka 560-8531 Japan
e-mail: nobuyuki@cheng.es.osaka-u.ac.jp

Solvent affects strongly the structures of biomolecules. The aggregation state of a biomolecule can then be modulated by the solvent environment, and indeed, it is considered that cosolvents act to regulate the structures and aggregation tendencies of proteins in biological systems. This work addresses the molecular mechanism of the effects of ATP (adenosine triphosphate) on peptide aggregation from the energetic standpoint by combining all-atom MD simulation and a solvation theory [1,2]. ATP is present in cells at concentrations much higher than required for its biological reactions as the energy source, and it has been shown experimentally that ATP acts as a cosolvent to inhibit the aggregation of proteins and peptides [3]. The aggregation core of amyloid *b* was employed as a model peptide, and the changes in the equilibria between the dissociated and aggregate states of the peptide induced by addition of ATP as a cosolvent was examined in comparison to the case of urea cosolvent.

The equilibrium of *n*-mer formation from *n* monomers (1-mers) is determined by the excess chemical potential of the *n*-mer μ_n^{ex} (*n* = 1 for 1-mer). The change in the equilibrium constant upon addition of the cosolvent at a concentration of *c* is then given by the corresponding changes in μ_n^{ex} for the species involved. The cosolvent-induced change in μ_n^{ex} is expressed exactly as

$$\mu_n^{\mathrm{ex}}(\text{at cosolvent concentration of } c) - \mu_n^{\mathrm{ex}}(\text{in pure-water solvent}) = \Delta\left\langle \nu^{\mathrm{solv}} \right\rangle + O(c^2)$$

due to the variational theorem, where $\Delta\left\langle \nu^{\mathrm{solv}} \right\rangle$ is the cosolvent-induced change in the solvation free energy averaged over the solute structures sampled in the pure-water solvent. In the contributions are absent from the changes in the structures (configurational entropies) and the peptide-peptide interactions. The force fields were Amber03w and TIP4P/2005.

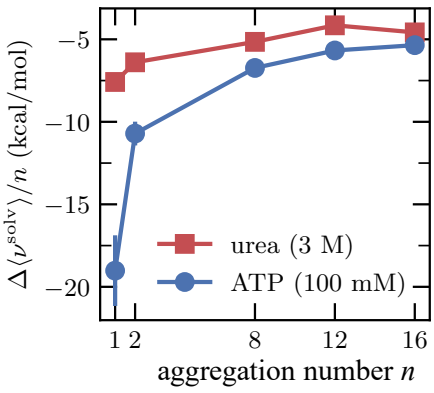

Figure 1. Cosolvent-induced changes in the solvation free energies per monomer averaged over the structures of peptide or its *n*-mer sampled in the pure-water solvent.

Figure 1 shows $\Delta\left\langle \nu^{\mathrm{solv}} \right\rangle$ as a function of the aggregation number *n*. Each *n*-mer is stabilized upon addition of ATP or urea, and the extent of stabilization is stronger at small *n*. This means that ATP is more effective for the inhibition by two orders of magnitude compared with urea at similar concentrations. Through and urea favor the 1-mer, leading to the inhibition of aggregation by virtue of the above equation. It can also be shown the decomposition of free energy, it is revealed that the aggregation is inhibited by the van der Waals interaction both for ATP and urea. Although the electrostatic interaction with the highly charged ATP is strong, it is essentially cancelled by the loss of interactions with water. The observed features of energetics are common between ATP and urea, indicative of the non-specificity of the ATP's (and urea's) effects of aggregate inhibition.

References

[1] T. M. Do, D. Horinek, and N. Matubayasi, *Phys. Chem. Chem. Phys.*, **26**, 11880 (2024).
[2] T. M. Do, N. Matubayasi, and D. Horinek, *Phys. Chem. Chem. Phys.*, **27**, 6325 (2025).
[3] A. Patel, L. Malinovska, S. Saha, J. Wang, S. Alberti, Y. Krishnan, and A. A. Hyman, *Science*, **356**, 753 (2017).

Software development and application for material design based on the statistical mechanics theory of liquids

N. Yoshida[1]
[1]Graduate School of Informatics, Nagoya University
e-mail: noriwo@nagoya-u.ac.jp

Biological environments are composed of complex mixtures of water, electrolytes, proteins, lipids, and various other biomolecules. To design biocompatible materials that function effectively in such environments, it is essential to account for the intricate physicochemical properties of these multi-component solutions. Traditional simulation approaches often face challenges when trying to capture solvent effects at molecular resolution, especially in heterogeneous and biologically relevant conditions. To address this, we have developed software based on the three-dimensional reference interaction site model (3D-RISM), a statistical mechanics theory of molecular solvation, referred as the reference interaction site model integrated calculator (RISMiCal).[1-4] The 3D-RISM theory enables the efficient and accurate prediction of solvation structures and thermodynamic properties by solving integral equations for solvent distribution functions around solutes. Our implementation focuses on biomolecular systems, allowing for the analysis of solvation and interactions of proteins, polymers, and other macromolecules in solution.

This software provides a powerful platform for understanding the structure-function relationship of biomolecules in complex solvents and has applications in material design, drug discovery, and biotechnology. In this presentation, we will introduce the theoretical background and capabilities of the software, highlighting recent advancements in methodology, including improvements in numerical solvers, hybrid approaches with molecular dynamics, and enhanced sampling techniques.

Furthermore, we will discuss recent developments that integrate 3D-RISM theory with machine learning methods. By combining physics-based solvation theory with data-driven models, we aim to accelerate the prediction and screening of material properties, opening new avenues in the design of smart, adaptive, and biocompatible materials.

References

[1] N. Yoshida, IOP Conf. Series: Materials Science and Engineerging, 773 (2020),012062 (DOI: 10.1088/1757-899X/773/1/012062)
[2] N. Yoshida, J. Chem. Info. Model., 57, (2017) 2646-2656 (DOI:10.1021/acs.jcim.7b00389)
[3] Y. Maruyama, N. Yoshida, J. Comput. Chem., (2024) 45, 1470-1482 (DOI: 10.1002/jcc.27340)
[4] K. Kanemaru, T. Yamaguchi, N. Sakumichi, T. Sakai, N. Yoshida J. Phys. Chem. B. (2025) 129, 9769-9780 (DOI: 10.1021/acs.jpcb.5c03519)

Electrical properties of the inner space of infectious bacteriophage MS2

N. Vodolazkaya[1], I. Budzanivska[2], V. Farafonov[1,3], O. Bondarenko[2], V. Bardyk[4], M. Bakumenko[3,4], D. Nerukh[3]

[1]Department of Physical Chemistry and Materials Science, V.N. Karazin Kharkiv National University, Svoboda Sq. 4, Kharkiv, 61022, Ukraine
[2]Virology Department, ESC 'Institute of Biology and Medicine', Taras Shevchenko National University of Kyiv, 64/13, Volodymyrska Str., Kyiv, 01601, Ukraine
[3]Department of Mathematics, Aston University, Birmingham, B4 7ET, UK
[4]Molecular Physics Department, Taras Shevchenko National University of Kyiv, 64/13, Volodymyrska Str., Kyiv, 01601, Ukraine
e-mail: d.nerukh@aston.ac.uk

Using protein complexes as a basis for developing nanoscale materials has drawn increasing interest. In this sense, viral capsids attract particular attention as they provide robust monodisperse structures of varying sizes and shapes. The interior of these particles has been utilized as a template for the synthesis of metal oxide particles in inorganic materials, as the basis of the self-assembling system for recognition and ordering nanocrystals. The structure of virus capsids was adapted as a biological template for the nucleation and orientation of semiconductor nanowires and composites and building blocks for 2D and 3D materials. Bacteriophage MS2 has many advantages in targeted drug delivery, clinical diagnostic tools and for vaccine development. MS2 bacteriophage is used as a model virus to evaluate the effectiveness of antiviral and antiseptic drugs and is an essential instrument for research on water treatment and purification, particularly filtration and disinfection processes [1,2].

Our study is devoted to the de novo synthesis of infectious MS2 bacteriophage in the presence of acid–base molecular probes designed to enable their incorporation during capsid assembly and to probe the internal electrostatic environment of the virus [3,4]. Transmission electron microscopy, dynamic light scattering, ζ-potential measurements, UV–Vis spectroscopy, and the apparent pK_a^a values were combined with molecular dynamics simulations. Neutral Red incorporated into MS2 exhibited a significant increase in pK_a^a value compared to pure water, the so-called medium effect ($\Delta pK_a^a = pK_a^a - pK_a^w \approx 3$), corresponding to an estimated electrostatic potential of approximately −216 ± 8 mV. This behaviour is consistent with the localisation of the probe in a strongly anionic microenvironment associated with the RNA-containing interior rather than the capsid outer surface.

Comparative analysis with anionic micellar systems, liposomes, DNA solutions, and protein-based media showed that similar spectral shifts occur only in highly anionic environments.

Molecular dynamics simulations support these findings and indicate preferential localisation of the probe inside the capsid in proximity to RNA. These results demonstrate that the MS2 interior is characterized by a highly negative electrostatic potential governed by genomic RNA and illustrate the applicability of molecular probes for studying nanoscale electrostatic environments in viral systems.

References

[1] Lin Chen, et.al., Curr. Res. Food Sci., V. 5, Page 175 (2022).
[2] V. Baldasso, et.al., Water Research, V.203, Page 117496 (2021).
[3] N. Vodolazkaya, et.al., The Journal of Physical Chemistry B, V.126, Page 8166 (2022).
[4] N. Vodolazkaya, et.al., International Journal of Biological Macromolecules, V.364, Page 152268 (2026)

Coarse-grained model to study the effects of electric fields on protein interactions

A. Johnson[1], D. Ray[2,4], M. Madani[3], J. K. G. Dhont[2,3], F. Platten[2,3], K. Kang[2], and S. Kantorovich[1]

[1] University of Vienna, Kolingasse 14-16, 1090, Vienna, Austria.
[2] Institute of Biological Information Processing, IBI-4, Forschungszentrum Jülich, 52428 Jülich, Germany.
[3] Faculty of Mathematics and Natural Sciences, Heinrich Heine University Düsseldorf, 40225 Düsseldorf, Germany.
[4] Solid State Physics Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400085, India.

e-mail: agaya.johnson@univie.ac.at

Proteins can transition between a wide range of organisational states, from soluble monomers to disordered phases and ordered structures [1,2]. Experiments have shown that, depending on protein and salt concentration, lysozyme-sodium thiocyanate solutions exhibit homogeneous solution states, coexistence between crystalline and liquid phases, or liquid-liquid phase separation. The corresponding phase boundaries can be shifted by applying an external electric field [3,4]. To gain deeper insight into the mechanisms underlying these phase transformations, we present a coarse-grained model of lysozyme in sodium thiocyanate solution, representing the protein as an ellipsoid decorated with charged and adhesive surface patches. Counterions and monovalent salt are treated explicitly via excluded-volume repulsion and Coulombic interactions. Using the ESPResSo software package [5], we perform molecular dynamics simulations with explicit solvent. We investigate (i) how patch size and salt–patch interactions influence ion distributions around a single protein, with and without an external electric field, and (ii) the resulting effective interactions between two proteins as functions of patch properties, salt concentration, and applied electric field.

References

[1] J. D. Gunton, A. Shiryayev, and D. L. Pagan, *Protein Condensation: Kinetic Pathways to Crystallization and Disease*, Cambridge University Press (2007).
[2] A. Stradner and P. Schurtenberger, *Soft Matter*, 16, 307–323 (2020).
[3] D. Ray, M. Madani, J. K. G. Dhont, F. Platten, and K. Kang, *The Journal of Physical Chemistry Letters*, 15 (31), 8108–8113 (2024).
[4] D. Ray, M. Madani, J. K. G. Dhont, F. Platten, and K. Kang, Electric field-induced control of protein crystal morphology, 21 (16), 3012–3021 (2025).
[5] R. Weeber et al., *Comprehensive Computational Chemistry*, 3, 578–601 (2024).

Tuning the water models to elucidate the effect of ATP to disordered proteins in high ATP concentration

Toshifumi Mori[1], Norio Yoshida[2]
[1]Graduate School of Engineering, Kyoto University
[2]Graduate School of Informatics, Nagoya University
e-mail: toshi_mori@moleng.kyoto-u.ac.jp

ATP plays a fundamental role as an energy currency in biomolecular systems. The concentration of ATP in cells is yet much higher than what is needed for proteins to function. It has recently been realized that ATP in high concentration can dissolve protein aggregates and regulate liquid-liquid phase separations, indicating the role of ATP as a hydrotrope [1]. To understand its underlying molecular mechanism, molecular dynaimics (MD) simulations have been applied to study the ATP-protein interactions. Yet, ATP molecules in MD simulations with classical force fields tend to over-aggregate compared to experimental dissociation constants [2], and aggregation of ATP molecules can negatively affect the protein-ATP interactions. We anticipated that this over-aggregation is partly due to the TIP3P water model, which is widely used but has been known to fail in properly describing protein unfolded state, e.g., shows over-compact character.

To this end, we examined different water models to see how the over-aggregation of ATP molecules can be controlled. In particular, we compared TIP4P-D and OPC against TIP3P, which are designed to improve the behavior of the protein unfolded state. Our MD simulations on the ATP in ~15 mM concentration showed that ATP aggregates to a single cluster in the TIP3P water, whereas dynamic changes in the ATP cluster size were observed in the TIP4P-D and OPC waters. This indicates that ATP over-aggregation can be reduced by changing the water model.

Next, by simulating the ATP-protein interaction for the disordered protein α-Synuclein, we found that water model also has a large impact on the ATP-protein interactions. In particular, ATP bound to the protein was almost fully preserved once formed in the TIP3P water, whereas repeating binding/unbinding from the protein was observed in the TIP4P-D and OPC waters.

These results indicate the importance of water models in describing the ATP-protein interaction in high ATP concentration and also suggests that the interaction can be tuned by choosing the appropriate water model [3].

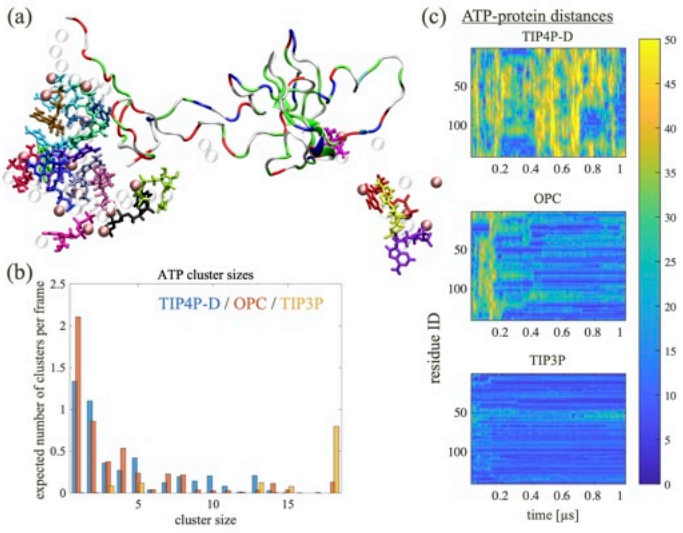

Figure 1 *– Summary of ATP-protein interactions. (a) Characteristic snapshot, (b) distribution of cluster sizes, and (c) distances between ATP and residues in α-Synuclein along the trajectories.*

References

[1] A. Patel *et al.*, *Science*, **356**, 753-756 (2017).

[2] J. Mehringer *et al.*, *Cell Reports Phys. Sci.*, **2**, 100343 (2021).
[3] T. Mori and N. Yoshida, *J. Chem. Phys.* **159**, 035102 (2023).

Application of the modern theory of associated fluids for the description of self-assembly phenomena of surfactant molecules. Solubilization of biomolecules in reverse micelles.

Myroslav Holovko

Yukhnovskii Institute for Condensed Matter Physics of the NAS of Ukraine,
1 Svientsitskii str., Lviv, 79011, Ukraine.

e-mail: holovko@icmp.lviv.ua

We analyse the possibility of the application of the statistical-mechanical approaches developed in the modern theory of associative fluids for the description of self-assembly phenomena of surfactant molecules in aqueous solutions [1]. In developed theoretical formalism, the potentials of intermolecular interactions are split into three parts. One of them is the short-range repulsive part responsible for excluded volume effects by molecules. The second one is the short-range strongly attractive part responsible for different clusterization effects, including self-assembly phenomena. The third part is long-range and responsible for the screening and renormalization phenomena. The specificity of the developed approach are connected with the application of the activity diagram expansions for the description of the short-range attractive part of interactions and the density diagram expansions for the description of the last two parts of interactions. Classification and reduction of the obtained diagrams in such expansions leads to the multidensity formalism, whose specificity strongly depends on types of described clusterization phenomena.

In this report special attention is focused on the application of the developed approach for the description of solubilization of biological molecules in reverse micellar systems and the study of biomolecules' influence on the properties of considered systems. As an example, we consider solubilization of cytochrome-c in water in oil reverse micellar systems. For the explanation and the treatment of cytochrome-c influence on the properties of considered micellar systems, a pairing sticky hard sphere model was introduced [2]. In this approach, the empty micelles are described by the sticky hard sphere model, and the presence of cytochrome-c is represented by an additional attractive potential characterized by an association parameter that leads to the pair formation of micelles. This association parameter was determined by fitting the experimental structure factors obtained by SAXS measurements. From this parameter the decrease in the percolation threshold has been estimated, and the change in the critical parameters of liquid–liquid phase transition, induced by cytochrome-c, was interpreted. As the second example, we consider the solubilization of mRNA in water in reverse wormlike micellar systems with lipid covering. The structure properties of the considered system are described in the framework of the analytical treatment of the fused hard-sphere chain model [3] with a small modification for direct inclusion of micellar resistance length. It is shown that the influence of mRNA leads to an increase in the rigidity of micelles.

References

[1] I. Yukhnovskii, M. Holovko. Statistical Theory of Classical Equilibrium Systems. Kyiv, Akademperiodyka, 2025.
[2] G. Cassin, Yu. Duda, M. Holovko, J. P. Badiali, M. P. Pileni. J. Chem. Phys., 107 (1997), 2683.
[3] Yu. Duda, E. Vakarin, Yu. Kalyuzhnyi, M. Holovko. Physica, A 245 (1997), 393.

Deep Eutectic Solvents for Biocatalysis: Advanced Materials and Enzymatic Modulation

Francisca J. Benítez[1,2], Elena Formoso [1,3], Elixabete Rezabal [1,2]

[1] Donostia International Physics Center, Donostia - Sebastián, Spain
[2] Polymers and Advanced Materials Department, Faculty of Chemistry, University of the Basque Country UPV/EHU, Donostia - San Sebastián, Spain
[3] Kimika Fisikoa, Farmazia Fakultatea, Euskal Herriko Unibertsitatea UPV/EHU, Gasteiz, Spain
e-mail: francisca.benitez@dipc.org

Deep eutectic solvents (DESs) are formed through the association of hydrogen-bond acceptors (HBAs) and hydrogen-bond donors (HBDs), generating eutectic mixtures with melting temperatures lower than those of their individual components. Their tunable composition and hydrogen-bonding interactions enable the design of microenvironments of interest for biocatalytic applications.

An example of DES-based advanced materials is eutectozymes, enzyme-loaded eutectogels designed to enhance enzyme stability, catalytic efficiency, and operational reusability [1]. These soft hybrid materials address the need for sustainable and robust biocatalytic platforms and provide an improvement in enzymatic immobilization [2]. Compared to conventional systems, their gel-like consistency, biocompatible matrix and resilience under operational conditions opens new avenues in biotechnology, bioelectronics, and environmental technologies.

In this talk, we will present computational research on such DES-based biocatalytic systems, by focusing on two areas: understanding the basis of euctectogel stability, and the modulation of enzymatic activity in DES environments. A combined computational and experimental approach is used to uncover structure–property relationship of DES-based materials, supporting their rational design for targeted functions.

References

[1] K. Kumar, M. Calderón, A. Beloqui, and M. L. Picchio, *Chemcatchem*, **16**, 12, e202400204. (2024).
[2] M. E. Martínez Cartagena, L. Suarez, A. Ontoria, F. J. Benítez, E. Rezabal. M. S. Orellano, M. Calderón, C. Huck-Iriart, A. S. Picco, M. L. Picchio, A. Beloqui. *Advanced Materials*, e17014, (2025).

Poster Contributions

Poster 1: Predicting and Understanding Peptide Aggregation using Stochastic Machine Learning

Predicting and Understanding Peptide Aggregation using Stochastic Machine Learning

João P. Santos[1], Pavel Zelenovskii[2], Filipe Figueiredo[2], Dinis O. Abranches[2]

[1]CICECO—Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal
[2]Department of Physics & CICECO–Aveiro Institute of Materials, University of Aveiro, Aveiro, 3810-193, Portugal
e-mail: jdinis@ua.pt

Peptides can self-assemble into ordered nanostructures such as nanofibers, nanotubes, or sheets. They are promising functional elements for energy harvesting and energy storage systems, and are inherently eco-friendly [1]. Unfortunately, the peptide space is too vast to explore using costly and time-consuming experimental or computational (e.g., molecular dynamics) trial-and-error approaches. As such, a method to convert the discrete set of all synthesizable peptides to a continuous mathematical space, navigable through simple optimization procedures, is proposed in this work based on sigma profiles [2].

The aggregation propensity of all possible dipeptides (400) and tripeptides (8000) in water was taken from the literature, estimated using computational simulations. This dataset was split into training and testing sets using stratified sampling. The training data was used to fit a Gaussian process (GP) model, followed by making predictions for peptides never seen before by the model (testing set). The GP model exhibited remarkable performance, attaining testing set coefficients of determination of 0.87 for dipeptides and 0.85 for tripeptides. To minimize model data requirements, GPs were combined with the stochastic frameworks of active learning and Bayesian optimization. This demonstrated that GPs serve as laboratory companions, suggesting amino acid combinations that maximize peptide self-aggregation with only a handful of training examples. All in all, this work establishes a new paradigm on digital molecular spaces for peptides and their efficient navigation by exploiting sigma profiles.

Acknowledgments
This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UID/50011/2025 (DOI 10.54499/UID/50011/2025) & LA/P/0006/2020 (DOI 10.54499/LA/P/0006/2020), financed by national funds through the FCT/MCTES (PIDDAC).

References
[1] P. S. Zelenovskii, K. Romanyuk, M. S. Liberato, P. Brandao, et al., Funct. Mater., **vol. 31** (2021), 2102524.
[2] D. O. Abranches, E. J. Maginn, Y. J. Colón, Proc. Natl. Acad. Sci. U.S.A., **vol. 121** (2024), e2404676121.

Rational Design of Deep Eutectic Electrolytes For Sustainable Energy Storage

Dinis O. Abranches[1], Gabriel L. Camilo[1], Eudes E. Fileti[1,2], João A. P. Coutinho[1]

[1]CICECO—Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal
[2]Institute of Science and Technology, Federal University of São Paulo, São José dos Campos, São Paulo, Brazil
e-mail: jdinis@ua.pt

Deep eutectic solvents (DESs) represent a paradigm in green chemistry, where liquid solvents are prepared by mixing two solid precursors without any chemical reaction [1]. The resulting liquid arises from eutectic-type solid-liquid equilibrium. Recently, this DES framework was extended to the so-called deep eutectic electrolytes (DEEs), which incorporate an electrolyte component as one of the precursors [2]. Instead of dissolving a conventional solid electrolyte in an organic solvent, a solid salt (e.g., LiTFSI) is mixed with a compatible precursor to form a eutectic at room temperature. These DEEs combine the low cost, non-volatility, and environmental benignity of DESs with the high ionic mobility and electrochemical stability required for energy-related applications.

In this work, a combination of computational approaches, namely molecular dynamics and the thermodynamic model COSMO-RS, was employed to investigate the formation of DEEs. The main intermolecular interactions between DEE precursors were studied, enabling the formulation of heuristic rules to readily identify precursor pairs capable of forming liquid DEEs. Moreover, this work demonstrates how negative deviations from ideality can be reliably predicted and achieved, thereby facilitating DEE formation with severe melting point depressions. Finally, based on the developed predictive framework, several new DEEs with high interest for energy-related applications were proposed and experimentally validated.

Acknowledgments
This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UID/50011/2025 (DOI 10.54499/UID/50011/2025) & LA/P/0006/2020 (DOI 10.54499/LA/P/0006/2020), financed by national funds through the FCT/MCTES (PIDDAC).

References

[1] D. O. Abranches and J. A. P. Coutinho. Annual Review of Chemical and Biomolecular Engineering **14** (2023): 141-163.
[2] Rui-Lan Liu, W. Yang, Q. Wang, X. Du, B. Hu, Y. Chen, and Dan-Yang Wang. Ceramics International 50, no. 5 (2024): 8178-8184.

Poster 3: Effects of amphoteric molecules on proton conduction in the [C2HIm][OAc] Pseudo-Protic Ionic Liquid system

Effects of amphoteric molecules on proton conduction in the [C2HIm][OAc] Pseudo-Protic Ionic Liquid system

Yashna Dawer[1], **Prof. Dr. Barbara Kirchner** [1]
[1]Mulliken Center for Theoretical Chemistry, University of Bonn, Beringstr. 4, 53115 Bonn, Germany
e-mail: ydawer@uni-bonn.de

Pseudo-protic ionic liquids have recently become interesting candidates for potential application as proton-conducting electrolytes in fuel cells. These form a unique class of ionic liquids which owing to the low pKa difference between the involved species undergo partial ionization, leading to a complicated mixture inherently consisting of neutral molecules along with the dissociated ions. This affords the formation of extensive hydrogen bonding networks within the ionic liquids allowing for proton shuttling through the system, thus, inducing a Grotthuss diffusion enhanced conductivity.

In previous studies, the rich acid-base equilibrium in the 1-methyimidazolium acetate [C1HIm][OAc] system has been investigated through classical and *ab initio* molecular dynamics simulations to reveal factors influencing the conductivity, including the degree of ionization and introduction of neutral molecules [1, 2]. In this contribution, we are extending the study to the [C2HIm][OAc] ionic liquid – using *ab initio* MD (AIMD) simulations to investigate the effect of the increased side chain length on the hydrogen bond network formation and therefore, on the expected facile proton transport mechanism.

Since conductivity in such systems is sensitive to the introduction of amphoteric molecules, we explore the influence of the simple α-amino acid – L-alanine in its neutral and zwitterionic forms on the ionization and Grotthuss diffusion. Moreover, a similar investigation is performed with the neutral and protonated forms of an interesting non-canonical analogue of alanine, namely, 2-aminopropionamidine (N-alanine). These nitrogen-based analogues of α-amino acids known as α-amino amidines were brought into focus by J.B.S. Haldane's proposition of ammonia as a possible life-supporting solvent and differ from native amino acids solely in the replacement of oxygen-based functionalities by nitrogen-based counterparts. In our previous investigations [3, 4], the solvation behaviours of these compounds in water and ammonia have been studied, contrasting them with those of α-amino acids. Based on findings from these studies, they could be considered potential candidates for aiding proton conduction in ionic liquids – a question that is explored in the present investigation.

References

[1] L. Wylie, M. Kéri, A. Udvardy, O. Hollóczki, and B. Kirchner, *ChemSusChem*, **16**, e202300535 (2023).
[2] J. Ingenmey, S. Gehrke, and B. Kirchner, *ChemSusChem*, **11**, 1900 (2018).
[3] H. Niemöller, J. Blasius, O. Hollóczki, and B. Kirchner, *Journal of Molecular Liquids*, **367**, 120282 (2022).
[4] H. Niemöller, J. Ingenmey, O. Hollóczki, and B. Kirchner, *The Journal of Physical Chemistry B*, **129**, 3007–3017 (2025).

Molecular Origin of Triglyceride Viscosity and Water Transport

Y. Kitamura[1], A. Sunouchi[2], D. Isaka[2], S. Tsujino[2], T. Watanabe[2], K. Fujimoto[3]*

[1] Graduate School of Science and Engineering, Kansai University, 3-3-35 Yamate-cho, Suita, Osaka 564-8680, Japan.
[2] Technical Division, The Nisshin OilliO Group, Ltd., 1 Shinmori-cho, Isogo-ku, Yokohama 235-8558, Japan.
[3] Department of Chemistry and Materials Engineering, Faculty of Chemistry, Materials and Bioengineering, Kansai University, 3-3-35 Yamate-cho, Suita, Osaka 564-8680, Japan
e-mail: k-fuji@kansai-u.ac.jp

Triglycerides (TGs) have nearly identical atomic compositions and similar bulk properties, such as density and cohesive energy. Nevertheless, their viscosities vary widely. Simple empirical rules—that viscosity increases with chain length and decreases with the number of double bonds—cannot explain the order observed in our measurements: triolein (18:1) is by far the most viscous, whereas trioctanoin (8:0) and trilinolenin (18:3) show comparable viscosities despite the much longer chains of 18:3. This indicates that chain length and unsaturation alone do not determine the flow behavior of TGs.

We performed all-atom molecular dynamics (MD) simulations of three TGs—8:0, 18:1, and 18:3. The simulations yielded self-diffusion coefficients and shear viscosities, and the calculated viscosity trend was consistent with the experimental results. To identify the molecular origin of the differences, we systematically examined common descriptors, including cohesive energy density, molecular size represented by the radius of gyration and hydrodynamic radius, single-molecule conformations, and mesoscale aggregate shapes.

None of these descriptors accounted for the viscosity trend. The cohesive energy densities differed by less than 2%. Molecular size, single-molecule conformation, and aggregate morphology also failed to reproduce the observed trend. Instead, the decisive factor was the local parallel alignment of carbon-chain segments. These aligned segments act as junctions that connect through glycerol backbones to form extended network structures. Such networks were abundant in 18:1, less frequent in 8:0, and almost absent in 18:3, matching the measured viscosity order. The junctions were also longer-lived in 18:1. In a star-polymer-like picture, a TG molecule can diffuse only after all three chains have relaxed; therefore, long-lived aligned chains retard molecular motion and increase viscosity. These results demonstrate that fine-scale packing, particularly local ordering of carbon chains, governs TG dynamics more strongly than bulk thermodynamics or molecular size. This insight provides a molecular basis for designing oils and lubricants with tailored flow properties.

Building on this framework, we further examined the distribution and transport of water in these oils. Water molecules were found mainly near the ester carbonyl (C=O) groups of the TGs. Rather than diffusing independently, water motion was coupled to the diffusion of the surrounding TG framework. Thus, the local oil structure controls not only the flow of TG molecules themselves but also the transport of dissolved water.

References

[1] Y. Kitamura, Y. Yasuda, J. Metoki, S. Tsujino, K. Yoshimura, T. Watanabe, and K. Fujimoto, *RSC Adv.*, **15**, 45514 (2025).

Extraction and Speciation of Nickel and Cobalt in Choline Chloride-Based Deep Eutectic Solvents

E. Rezabal[1,2], L. Hernandez-Fernandez[1,2]
[1]Kimika Fakultatea, University of the Basque Country (EHU/UPV) 20018 Donostia, Spain
[2]Donostia International Physics Center, 20018 Donostia, Spain
Presenting author, e-mail: laura.hernandez@ehu.eus

Deep eutectic solvents (DESs) have emerged as promising sustainable media for the recycling of lithium-ion batteries due to their low toxicity, low cost, and strong metal dissolution capabilities. However, a molecular-level understanding of metal dissolution and speciation in these complex media remains limited, hindering the rational optimization of recycling processes.

In this work, theoretical chemistry simulations were employed to investigate the leaching mechanisms of transition metals in choline chloride-based DESs combined with ethylene glycol, lactic acid, and malonic acid. In parallel, the speciation of transition metals in these DES environments was explored both as the thermodynamic outcome of the leaching process and in the context of their potential use as functional electrolytes in electrochemical energy storage devices, such as supercapacitors.

Particular emphasis was placed on nickel and cobalt as representatives of distinct physicochemical behaviors. Literature reports [1] reveal notable differences in their coordination chemistry: while cobalt adopts coordination environments commonly observed for transition metal ions, nickel exhibits markedly different speciation, suggesting unique thermodynamic preferences and coordination motifs.

Elucidating the fundamental reactivity and speciation of nickel and cobalt advances both the optimization of recycling processes and the valorization of the resulting leaching solutions, supporting more sustainable circular economy strategies.

References

[1] J.T.M. Amphlett, M.D. Ogden, W. Yang, and S. Choi, *Journal of Molecular Liquids*, **318** (2020).

Li-ion Transport Related to LiTFSA Cluster Size in Localized High-Concentration Electrolytes Using Molecular Dynamics Simulations

Yuki Ito[1], Taiki Shiba[2], Kaoru Dokko[2], Kazushi Fujimoto[3]

[1] *Department of Chemistry and Materials Engineering, Graduate School of Science and Engineering, Kansai University, 3-3-35 Yamate-cho, Suita, Osaka 564-8680, Japan.*

[2]*Department of Chemistry and Life Science, Yokohama National University, 79-5 Tokiwadai, Hodogaya-ku, Yokohama 240-8501, Japan.*

[3]*Department of Chemistry and Materials Engineering, Faculty of Chemistry, Materials and Bioengineering, Kansai University, 3-3-35 Yamate-cho, Suita, Osaka 564-8680, Japan.*

e-mail: k-fuji@kansai-u.ac.jp

Efficient Li^+ transport is essential for the performance of lithium batteries. Localized high-concentration electrolytes (LHCEs) exhibit heterogeneous salt-rich and diluent-rich regions. Therefore, clarifying how this heterogeneous structure affects Li^+ diffusion is important for understanding Li^+ transport in LHCEs.

In our previous study, we investigated an LHCE composed of FEC (solvent), TTE (diluent), and LiTFSA (salt), and showed that Li^+ species in diluent-rich regions significantly contribute to the overall Li^+ transport [1]. In this study, we examined two LHCEs composed of FEC, LiTFSA, and either nBME or tBME as the diluents, focusing on how differences in LiTFSA cluster structures affect Li^+ transport. The molar ratio was LiTFSA:FEC:BME = 1:6:3.7.

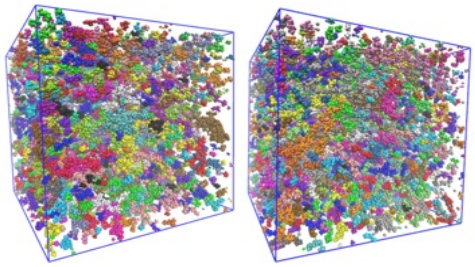

Figure 1 *Cluster-colored snapshots of the nBME system (left) and tBME system (right).*

Cluster analysis revealed that the nBME and tBME systems formed different LiTFSA cluster structures (Figure 1). The cluster volume distribution showed that larger LiTFSA clusters were preferentially formed in the nBME system, whereas many smaller clusters were formed in the tBME system. This difference is likely related to the different coordination abilities of nBME and tBME toward Li^+. tBME coordinates more readily with Li^+ than nBME, which suppresses LiTFSA aggregation. As a result, the tBME system contains smaller LiTFSA clusters and more non-clustered Li^+ species.

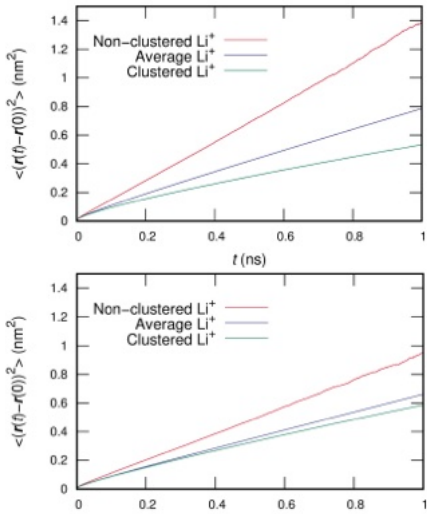

Figure 2 *MSDs of non-clustered Li^+, clustered Li^+, and the average over all Li^+. The upper and lower panels correspond to the nBME and tBME systems,*

MSDs calculated separately for clustered and non-clustered Li^+ showed that non-clustered Li^+ diffused faster than clustered Li^+ (Figure 2), indicating that Li^+ species in diluent-rich clustered regions enhance the overall Li^+ transport. In addition, the center-of-mass MSD of LiTFSA clusters larger than 1 nm^3 revealed that cluster translational motion also contributes to Li^+ transport. By further analyzing the diffusion behavior for different cluster sizes, we discuss size-dependent Li^+ transport involving non-clustered Li^+ species, medium-sized LiTFSA clusters, and large LiTFSA clusters.

These results suggest that suppressing excessive LiTFSA aggregation and forming mobile small-to-medium-sized clusters are important for promoting Li^+ diffusion in LHCEs.

References

[1] Y. Ito, Y. Yasuda, Y. Konishi, T. Shiba, K. Dokko, K. Fujimoto, *J. Phys. Chem. C*, **130**, 1327-1337 (2026).

Accurate computational method for configurational entropy via efficient solvation free energy calculation

R. Kaji[1], S. Hervø-Hansen[1], K. Kasahara[1], N. Matubayasi[1]
[1]Graduate school of Engineering Science, The University of Osaka
e-mail: kaji-ry@cheng.es.osaka-u.ac.jp

Introduction Configurational entropy reflecting the flexibility of molecular structures is a crucial quantity for understanding biological processes such as protein folding and ligand binding. In statistical mechanics, configurational entropy is defined using the probability density function $P(\mathbf{r}^N)$ of molecular coordinates $\mathbf{r}^N$ as

$$S^{conf} = -k_{\mathrm{B}} \int d\mathbf{r}^N P(\mathbf{r}^N) \log P(\mathbf{r}^N) \quad (1)$$

Direct computation of configurational entropy is generally difficult because of the high dimensionality of molecular conformation space, and therefore several approximate computational methods have been proposed [1]. In this study, we propose an accurate computational method to evaluate the change in configurational entropy of molecules in solution from molecular dynamics (MD) simulations based on solvation free energy calculations.

Theory In solution, the configurational-entropy change of a solute molecule can be expressed as

$$T\Delta S^{\mathrm{conf}} = \Delta\langle E(\mathbf{r}^N) + \nu(\mathbf{r}^N)\rangle - \Delta G, \quad (2)$$

where $E(\mathbf{r}^N)$ is the intramolecular potential energy of the solute, $\nu(\mathbf{r}^N)$ is the solvation free energy at a fixed configuration of the solute, and ΔG is the free-energy change. ΔG can be calculated from the free-energy change of the isolated solute and the change in the solvation free energy. Based on this relationship, configurational-entropy changes can be rigorously evaluated by combining MD simulations in solution, vacuum, and solvation free energy calculations. However, as the flexibility of target solute molecules increases, the computation of solvation free energy with solute being flexible ($\Delta\mu$) becomes challenging. In this work, we constructed an efficient scheme based on an error minimization method to realize an accurate estimation of $\Delta\mu$ through the $\nu(\mathbf{r}^N)$ values for a small number of configurations.

Results and Discussion Configurational-entropy changes were calculated for linear alkanes and alkanediols from bent to extended states, and carboxylic acids from *syn* to *anti* conformations in water. Figure 1 shows the configurational-entropy changes together with corresponding free energy and energetic contribution. For linear alkanes and alkanediols, configurational-entropy changes increased with alkyl chain length, destabilizing extended state. In butanoic acid, the *syn* conformation is stabilized mainly by energetic contributions. In contrast, in *o*-anisic acid, the configurational entropy of the *anti* conformation was more than 1 kcal/mol smaller than that of the *syn* conformation because of restricted rotational degrees of freedom induced by intramolecular hydrogen bond formation between the carboxyl and methoxy groups. Comparison with the quasi-harmonic approximation (QHA) showed that configurational entropy changes of linear alkanes and alkanediols are significantly larger with QHA than with the present method, indicating strong anharmonicity in these systems.

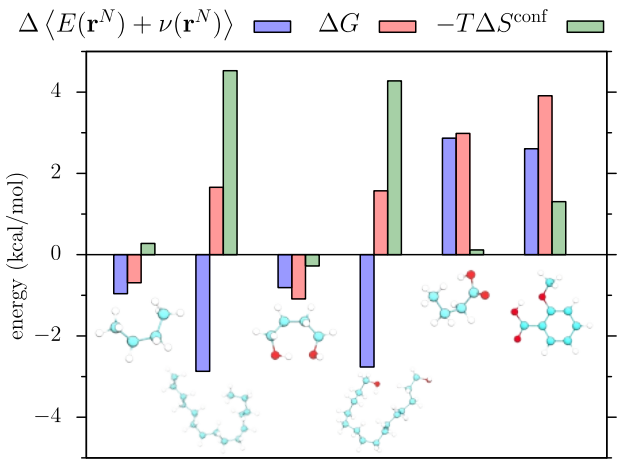

Figure 1 *– The changes in configurational entropy, free-energy, and energetic contribution.*

References

[1] S. Hikiri, T. Yoshidome, and M. Ikeguchi, *J. Chem. Theory Comput.*, **12**, 5990 (2016).
[2] S. Hervø-Hansen, K. Okita, K. Kasahara, and N. Matubayasi, *J. Chem. Theory Comput.*, **21**, 1064 (2025).

Molecular Binding Processes Elucidated by State-to-State Transition Theory and Molecular Dynamics Simulation

K. Kasahara[1], R. Okabe[1], C. A. Chang[2], T. Mori[3], and N. Matubayasi[1]
[1]Graduate School of Engineering Science, The University of Osaka
[2]Department of Chemistry, University of California at Riverside
[3]Graduate School of Engineering, Kyoto University
e-mail: kasahara@cheng.es.osaka-u.ac.jp

The dynamics of proteins, including folding and unfolding as well as ligand binding and unbinding, proceed through a number of intermediate states, which are closely related to biological functions. To elucidate the structural dynamics of biological systems based on molecular dynamics (MD) simulations, the Markov state model (MSM)[1] has been widely utilized. This method enables the description of long-timescale dynamics of the target molecule based on transitions between states that characterize distinct stable structures. A practical limitation is the need to introduce a coarse-grained timescale, namely, a lag time, in computing transition probabilities. It is known that the resulting kinetic properties, such as rate constants, can be sensitive to the choice of the lag time.

To overcome this limitation, we propose the integral-equation formalism of population dynamics (IEPDYN) to describe the population dynamics of distinct configurational states ($j = 1,2,\cdots$)[2]. According to classical reaction dynamics theory, the probability density associated with a given state obeys the Liouville equation, including influx from and efflux to neighbouring states. By introducing a Markov approximation for the crossing of boundaries separating the states, one can derive tractable integral equations governing the state populations at time t, $P_j(t)$, and the population flux from state j to state i at time t, $Q_{ij}(t)$ (**Fig.** 1). The time-dependent quantities appearing in these equations ($P_j^0(t), M_{jk}(t), R_{ij}(t)$, and $K_{ijk}(t)$) are associated with the retention behaviours within a given state and the state-to-state transitions. Because these quantities depend only on a few states in the local neighbourhood of a given state, they can be computed using a set of short-timescale MD simulations. The population dynamics on long timescales can be predicted by solving the set of the integral equations of $P_j(t)$ and $Q_{ij}(t)$. The IEPDYN method is formulated in continuous time and therefore does not rely on a lag time. Consequently, kinetic quantities obtained from IEPDYN are free from lag-time dependence.

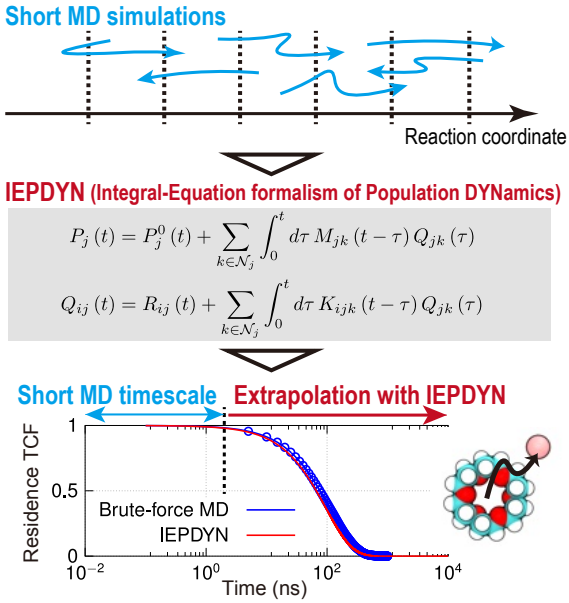

Figure 1 *– Prediction of the time-correlation function (TCF) associated with the state change based on the short-timescale MD and IEPDYN[2] method.*

We apply the IEPDYN method to the binding and unbinding kinetics of CH_4/CH_4, Na^+/Cl^-, and 18-crown-6-ether (crown ether)/K^+ in water. For both kinetics, the time constants estimated from the IEPDYN method are comparable to those obtained from brute-force MD simulations. The required timescale of each MD trajectory in the IEPDYN method is approximately two orders of magnitude shorter than that in the brute-force MD approach in the crown ether/K^+ system.

References

[1] V. S. Pande, K. Beauchamp, and G. R. Bowman, *Methods*, **52**, 99 (2010).
[2] K. Kasahara, R. Okabe, C. A. Chang, T. Mori, and N. Matubayasi, *J. Chem. Phys.*, **164**, 124112 (2026).

Concentration-Dependent Dynamics in Solvate Ionic Liquids via NMR Relaxometry

L. Kruse[1], T. Winter[1], J. K. Philipp-Taube[1], A. Strate[1], D. Paschek[1], R. Ludwig[1,2]
[1]Physical and Theoretical Chemistry, University of Rostock, Albert-Einstein-Str. 27, 18059 Rostock/DE
[2]Department Life, Light & Matter, University of Rostock, Albert-Einstein-Str. 25, 18059 Rostock/DE
[3]Leibniz Institut für Katalyse an der Universität Rostock e.V., Albert-Einstein-Str. 29a, 18059 Rostock/DE
e-mail: lennart.kruse@uni-rostock.de

In contrast to conventional Ionic Liquids (ILs), which consist of organic and/or inorganic ions, the so-called Solvate Ionic Liquids (SILs) are being formed by mixing a salt and a solvent, which form stochiometric chelate complexes. These room-temperature liquids have been studied extensively regarding their electrolyte properties such as conductivity and self-diffusion.[1] To shed more light on the ion- and molecule specific dynamics, fast field cycling (FFC) NMR relaxometry is used to measure the frequency-dependent T_1 spin-lattice relaxation times (Fig. 1). By fitting the relaxation rates ($R_1 = 1/T_1$) to relaxation models the self-diffusion coefficients and rotational correlation times of different species are determined. This method has proven to be well suited to investigate neat ILs.[2] However, literature involving FFC studies on SILs systems is scarce. To address this shortcoming, we investigate the SIL consisting of lithium bis(trifluoromethylsulfonyl)imide ($LiNTf_2$) and triethylenglycoldimethylether (triglyme/G3). In this SIL, the triglyme coordinates the Li^+ cation in a crown-ether like manner and thereby forms complexes like $[Li(G3)_1]^+$, as it has been shown by MD simulations and far-infrared measurements.[3] However, the structure of these complexes highly depends on the concentration of the salt. To address the concentration effect on the dynamics we probed two different lithium salt/triglyme mixtures over a broad temperature range, with salt:solvent ratios of 1:1 and 1:2, yielding structures like $[Li(G3)_1][NTf_2]$ and $[Li(G3)_2][NTf_2]$. By measuring the T_1 spin-lattice relaxation times of ^1H and ^{19}F nuclei using FFC NMR, we obtain dynamic information of the G3 and NTf_2 anions, respectively. Finally, we find good agreement between experimentally obtained values of self-diffusion coefficients and rotational correlation with those derived from MD simulations.

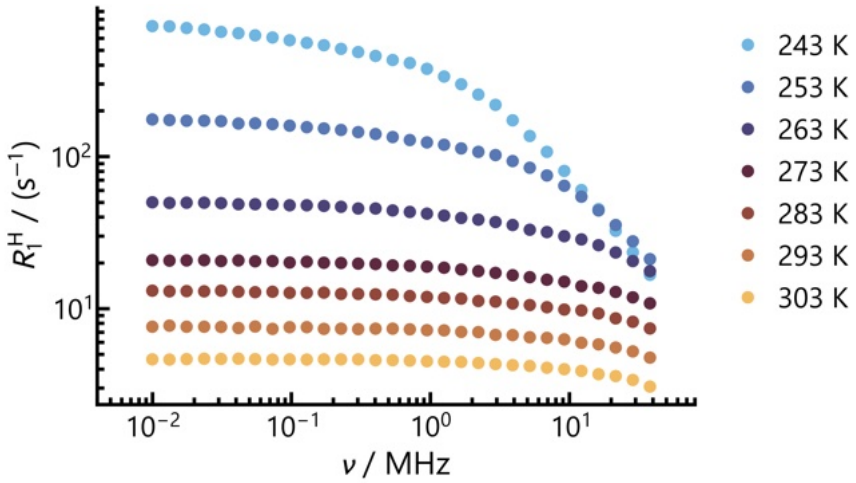

Figure 1 *– Temperature-dependent ^1H NMR dispersion profiles of the SIL $[Li(G3)_2][NTf_2]$ obtained from fast field cycling NMR relaxometry.*

References

[1] T. Tamura et al., *Chemical Letters*, **39**, 753 (2010).
[2] L. Kruse et al., *Journal of Physical Chemistry Letters*, **15**, 10410 (2024).
[3] J. K. Philipp et al., *ChemPhysChem*, **26**, e202400991 (2025).

Automating the Self-Consistent Electrostatic Embedding Model

Z. Macpherson[1], L. Lue[1], M. Jorge[1]
[1]University of Strathclyde, Glasgow, G1 1XJ
e-mail: zoe.macpherson.2018@uni.strath.ac.uk

The ability of molecular simulations to reliably predict thermodynamic and transport properties depends crucially on the quality of underlying force field models, which describe the bonded and non-bonded interactions of molecules. Emulating experimental observations has allowed us to design these models over the past 50 years to study previously inaccessible chemistry. The most widely used force fields are nonpolarisable, and consequently fail to capture polarisation effects, resulting in systematic deviations in properties such as the dielectric constant. This raises questions about model performance in areas relevant to drug discovery, eg predicting solvation, transfer or binding free energies. Such deviations can be mitigated through post facto polarisation corrections;[1] however, knowledge of the liquid phase dipole moment, a quantity related to polarisation, is required.

Our research group developed Self-Consistent Electrostatic Embedding (SCEE): a computationally efficient approach combining classical molecular simulations with ab initio calculations to accurately capture polarisation effects.[2] Previously applied to various polar solvents, we have automated this approach within a new Python workflow, enabling dipole moment calculations at unprecedented accuracy across a wide range of molecules.[3,4] We demonstrate Automated SCEE through two test cases: i) wide exploration of the phase space of water, including liquid, vapour and supercritical states;[5] ii) dipole moment calculation of substituted aromatic molecules in the liquid phase, by far the largest molecules to which this approach has been applied. Our results reveal new connections between the liquid dipole moment and local interactions, particularly hydrogen bonding.

References

[1] M. Jorge and L. Lue, (2019): The Dielectric Constant: Reconciling Simulation and Experiment, *J. Chem. Phys.*, 150,084108
[2] M. Jorge, J. R. B Gomes, and A. W. Milne, (2021): Self Consistent Electrostatic Embedding for Liquid Phase Polarisation, *J. Mol. Liq.,* 114550
[3] M. Jorge, M. C. Barrera, A. W. Milne, C. Ringrose and D. J. Cole, (2023): What Is the Optimal Dipole Moment for Nonpolarisable Models of Liquids?, *J. Chem. Theo. And Comp.*, 1790-1804
[4] M. Jorge, J. R. B. Gomes, and M. C. Barrera, (2022): The Dipole Moment of Alcohols in the Liquid Phase and In Solution, *J. Mol. Liq.*, 356, 119033
[5] Z. Macpherson, J. R.B. Gomes, M. Jorge and L. Lue (2024): The Dipole Moment of Supercritical Water – Local vs Mean-field Polarisation Contributions, *Mol Phys*, e2381574., DOI: 10.1080/00268976.2024.2381574

Understanding the Nature of Hydration of Aqueous Alkali Metal Carbonates Employing Molecular Dynamics Simulations

Pujarini Mahapatra[1], P. Padma Kumar[1]
[1] Department of Physics, Indian Institute of Technology Guwahati, 781039, Assam, India
e-mail: pujarini.mhapatra@iitg.ac.in

Aqueous alkali metal carbonates (M_2CO_3, where M = Li^+, Na^+, and K^+) have attracted significant attention due to their critical role in CO_2 capture, energy storage, and various industrial processes. Despite extensive experimental progress in understanding their macroscopic properties, the molecular-level mechanisms governing solvation and ion-association behaviour in these systems with varying concentrations remain largely unexplored. To address this gap, we present a comprehensive molecular dynamics (MD) investigation of aqueous Li_2CO_3, Na_2CO_3, and K_2CO_3 using a refined force field model, validated against the experimental solubility limits of the respective salts. The study highlights how the local environment of carbonate ions (CO_3^{2-}) evolves with solute concentration, providing fresh insights into the role of alkali metal cations in promoting the self-aggregation of carbonates. The trajectory analysis predicts that the mobility of all the solute and solvent species decreases with concentration, leading to the co-movement of cations and carbonate ions near their solubility limit. Notably, Li^+ exhibits anomalously slow diffusion compared to the larger Na^+ and K^+ ions, owing to its stronger association with carbonate ions, which is consistent with the experimentally observed low solubility of Li_2CO_3 in water. This behaviour is attributed to the size-sensitive "hardness" of the hydration shells of cations, corroborated in terms of the water residence times in their first hydration shells. In addition, enhanced sampling via umbrella sampling is employed to compute the free energy profile of CO_2 transfer across the gas–liquid interface, revealing the thermodynamic preference and solubility of CO_2 in carbonate media. This provides molecular-level insight into the energetics governing CO_2 absorption in carbonate-based capture systems.

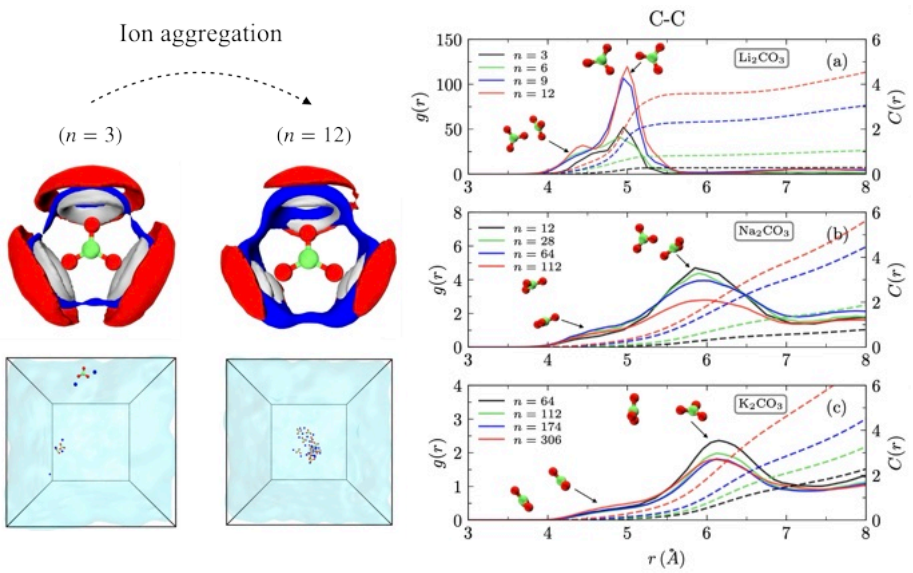

Figure 1 *– Left: Hydration isosurfaces around CO_3^{2-} at low (dilute) and high (beyond solubility) concentrations with corresponding simulation snapshots showing the transition from dispersed ions to aggregates. Right: Carbonate–carbonate RDFs (solid lines) and coordination numbers, RCNs (dashed lines), for C···C correlations in aqueous Li_2CO_3, Na_2CO_3, and K_2CO_3, quantifying enhanced ion aggregation at higher concentrations.*

References

[1] P. Mahapatra and P. P. Kumar, Chemical Engineering Science, 2026, 123914.
[2] P. P. Kumar, A. G. Kalinichev and R. J. Kirkpatrick, The Journal of Physical Chemistry B, 2009, 113, 794–802.

Development of a prediction method of a solvent configuration based on Extended Molecular Ornstein-Zernike theory

Y. Matsui[1], N. Yoshida[1]

[1]Graduate school of informatics Nagoya University Aichi Japan
e-mail: matsui.yusei.h0@s.mail.nagoya-u.ac.jp

Solvent is essential for the structure and function of biomolecules. Determining the solvation structure around biomolecules is crucial for understanding their roles. The Extended Molecular Ornstein-Zernike (XMOZ) theory describes the solvation structure around a complex solute molecule as a six-dimensional distribution function of both position and orientation [1]. While this distribution function is certainly useful for understanding the solvation, determining an explicit molecular configuration identical to that obtained from X-ray or neutron diffraction experiments would also be of substantial value. In this study, we developed a prediction method of a solvent configuration based on XMOZ theory (Figure 1). Since our method is a straightforward extension of the "Placevent method" which is based on three-dimensional reference interaction site model (3D-RISM) theory [2], we refer to it as the "Molecular Placevent" method.

In the Molecular Placevent method, explicit solvent molecules are placed through an iterative procedure. In each iteration, the position and orientation corresponding to the maximum of the distribution function are identified, an explicit solvent molecule is placed at that position and orientation, and the density corresponding to the placed molecule is subtracted from the original distribution function. The density-subtraction region is defined as the positions corresponding to an isotropic region centered at the position of the maximum point and all orientations. The isotropic region is determined such that the integrated three-dimensional population function within the region corresponds to a single solvent molecule.

To demonstrate the performance, the molecular placevent method was applied to some protein systems and predicted solvent configurations were compared to neutron diffraction or joint X-ray/neutron data. The predicted positions and orientations of water molecules directly coordinated to the protein or ligand were in good agreement with the experimental results. A detailed discussion on the performance of the proposed method will be presented at the conference.

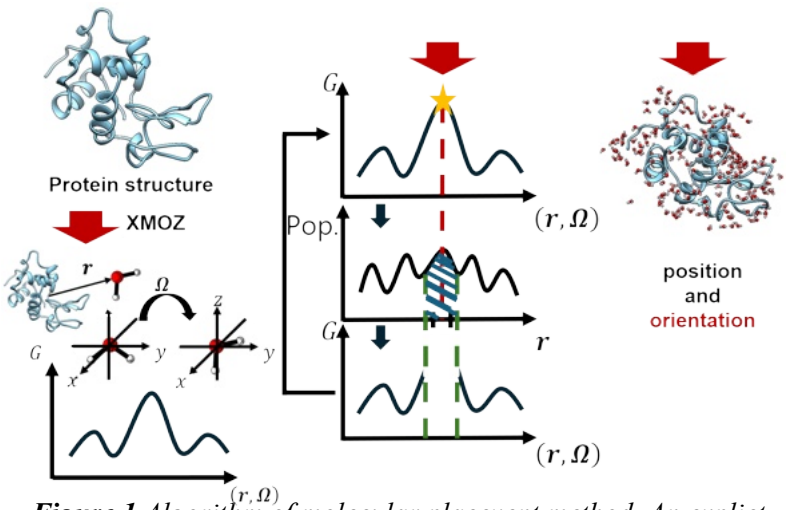

Figure 1 *Algorithm of molecular placevent method. An explict solvent molecular configuration is predicted from a distribution function G obtained by XMOZ theory.*

Since molecular placevent method can determine solvent hydrogen configurations including atoms, it will be highly useful for especially elucidating the role of solvent, water, in biochemical systems where the application of neutron diffraction is challenging.

References

[1] R. Ishizuka, N. Yoshida, *J. Chem. Phys.*, **139**, 084119 (2013).
[2] D. J. Sindhikara, N. Yoshida, F. Hirata, *J. Comput. Chem.*, **33**, 1536 (2012).

Molecular Dynamics Calculations of Fine 3D Free Energy Map for Water Molecule Solved in Polymers and Lipid Bilayers

K. Fujimoto[1], Z. Tang[2], T. Nagai[3], W. Shinoda[3], S. Okazaki[4]
[1]Kansai University, Suita, Osaka 564-8680, Japan
[2]Institute for Molecular Science, Myodaiji, Okazaki 444-8585, Japan
[3]Okayama University, Tsushima-naka, Okayama 700-8530, Japan
[4]Yokohama City University, Kanazawa-ku, Yokohama 236-0027, Japan

e-mail: okazaki.sus.oy@yokohama-cu.ac.jp

We developed an efficient calculation method for free energy of transfer of small molecules from vacuum to inside of the inhomogeneous media such as polymers and lipid bilayers. The method enables us to draw fine three dimensional (3D) free energy map consisting of one million meshes. The calculations adopted three techniques. First, the free energy was calculated according to Widom equation [1] combined with a new importance sampling method. Second, the method samples thousands of test molecules simultaneously, each of which follows single-particle canonical distribution independently of each other. The sampling was also accelerated by high-temperature sampling method. Computational cost of the method is much lower than that of the conventional particle insertion method based on inefficient random samplings.

The position-dependent free energy plays a central role in dynamic Monte Carlo calculations as reported in our previous papers [2-4]. Further, the fine free energy map must present abundant information about microscopic absorption mechanism such as spatial distribution of absorption points together with their stabilization energy. It also presents information about diffusion mechanism such as 3D diffusion path networks formed by spatially distributed free energy saddle points connected by slopes from the minimum points.

Here we applied the method to water molecule in two soft materials, amorphous polylactic acid (PLA) and dipalmitoyl phosphatidyl choline (DPPC) and obtained the fine 3D free energy map with 0.05 nm resolution as shown in Fig. 1. The former is a solid polyester in which water molecule can make hydrogen bonds with the ester groups. The latter forms a bilayer where lipid molecules are ordered though they are still flexible and mobile. Water molecules can diffuse in both media. However, the diffusion mechanism must be very different from each other reflecting the difference in free energy landscape as clearly shown in the figure.

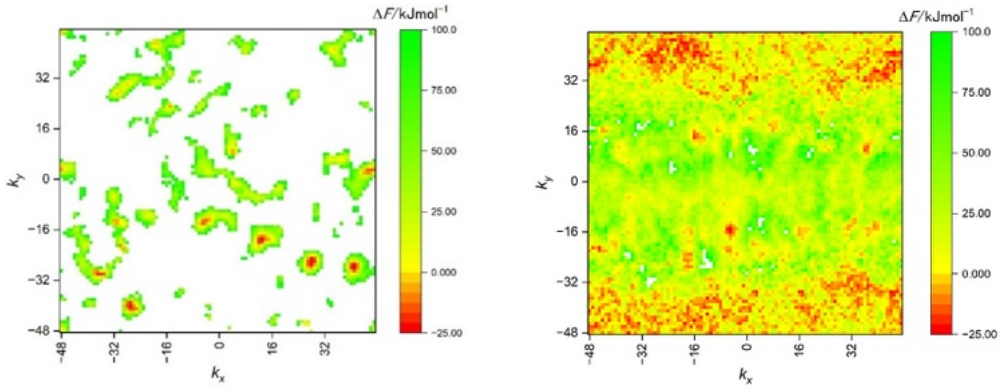

Figure 1 *– Cross sections of the calculated 3D free energy of transfer of water molecule* $\Delta F\left(k_x,k_y,k_z\right)$ *at* k_z=0 *from vacuum to inside of the (left) PLA and (right) DPPC.*

References

[1] B. Widom, *J. Chem. Phys.* **39**, 2808 (1963).
[2] T. Nagai, A. Yoshimori, S. Okazaki, *J. Chem. Phys.*, **156**, 154506 (2022).
[3] T. Nagai, S. Okazaki, *J. Chem. Phys.*, **157**, 054502 (2022).
[4] S. Okazaki, *J. Chem. Phys.*, **160**, 174111 (2024).

Using the Zeno line to assess and refine molecular models

Thomas Paterson[1], Marcus N. Bannerman[2], Leo Lue[1]

[1] Department of Chemical and Process Engineering, University of Strathclyde, James Weir Building, 75 Montrose Street, Glasgow G1 1XJ, United Kingdom

[2] School of Engineering, University of Aberdeen, Aberdeen AB24 3UE, United Kingdom

e-mail: thomaspaterson@strathclyde.ac.uk

The Zeno line is the locus of points on the temperature–density plane where the compressibility factor of the fluid is equal to one. It has been observed to be straight for a broad variety of real fluids, although the underlying reasons for this are still unclear. In this work, a detailed study of the Zeno line and its relation to the vapor–liquid coexistence curve is performed for two simple model pair-potential fluids: attractive square-well fluids with varying well-widths λ and Mie n-6 fluids with different repulsive exponents n. Interestingly, the Zeno lines of these fluids are curved, regardless of the value of λ or n. We find that for square-well fluids, λ ≈ 1.8 presents a Zeno line, which is the most linear over the largest temperature range. For Mie n-6 fluids, we find that the straightest Zeno line occurs for n between 8 and 10. Additionally, the square-well and Mie fluids with the straightest Zeno line showed the closest quantitative agreement with the vapor–liquid coexistence curve for experimental fluids that follow the principle of corresponding states (e.g., argon, xenon, krypton, methane, nitrogen, and oxygen). These results suggest that the Zeno line can provide a useful additional feature, in complement to other properties, such as the phase envelope, to evaluate molecular models [1].

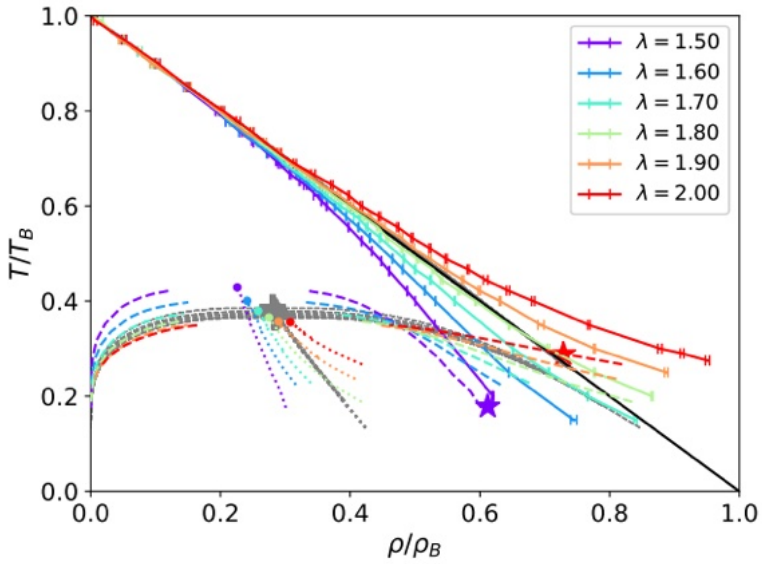

Figure 1 *– The Zeno line (i.e. locus of points with Z = 1) for attractive square-well fluids of varying well width λ (coloured solid lines) and real/corresponding-states fluids (gray solid lines). T_B is the Boyle Temperature, and ρ_B is the Zeno density. The dashed lines denote the boundaries of the vapour-liquid coexistence regions, and the dotted lines are the rectilinear diameters. The filled circles are the critical points for the square-well fluids, while the gray plus is the critical point for the corresponding states fluids. The red star denotes the triple point for the square-well system with λ = 2.*

Acknowledgements

The authors gratefully acknowledge financial support from CCP5.

References

[1] Thomas Paterson, Marcus N. Bannerman, Leo Lue; Using the Zeno line to assess and refine molecular models. *J. Chem. Phys.* 21 April 2024; 160 (15): 154503. https://doi.org/10.1063/5.0192770

Monolayers or Micelles? The Unusual Adsorption of Ionic Surfactants onto Inorganic Surfaces

Samuel P. L. Proctor[1], Tom Robinson[1], Peter J. Dowding[2], Philip J. Camp[1]
[1]School of Chemsitry, University of Edinburgh, David Brewster Road, Edinburgh EH9 3FJ, Scotland
[2]Infineum UK Ltd., Milton Hill Business and Technology Centre, OX13 6BD, UK
e-mail: samuel.proctor@ed.ac.uk

Approximately 20% of the world's energy consumption is spent overcoming friction within mechanical contacts.[1] Therefore, controlling friction and wear is important to sustainability in a wide range of industrial scenarios, with large social, economic and environmental impacts. This field of study, known as tribology, focuses on understanding and reducing friction and wear with lubrication. The first lubricant additives, isolated in the 1920s, were simple fatty acids that adsorbed onto surfaces as monolayers in a "head-up-tails-down" fashion.[2] Since then, more complex additives, such as modern friction modifiers have been capable to self-assemble into reverse micelles. This work focuses on how molecular-dynamics (MD) simulations offer a complementary approach to traditional tribology testing alongside start-of-the-art neutron scattering experiments and accelerate the design of lubricant formulations.

In a proof-of-principle study, the aggregation and interfacial behaviour an anionic aerosol-OT surfactant are investigated. In non-polar solvent with water, the surfactants form reverse-micelles, consistent with small-angle neutron scattering data. At the iron-oxide/oil interface, MD simulations with water show the formation of hemi-micelles and hemi-cylinders, structures that are highly anomalous for such compounds. Strikingly, these unique features are in excellent agreement with neutron reflectometry measurements, strongly validating the simulation results.

The second project focuses on Duomeen TDO, an additive consisting of a doubly charged ammonium cation and two carboxylate anions, used for the lubrication and dispersion of molybdenum disulfide-coated magnetic iron nanoparticles in magnetorheological fluids (MRFs). Results on the self-assembly as a function of water concentration are presented, alongside simulation-derived rheological responses and the interfacial adsorption on iron oxide and molybdenum disulfide, which differs significantly between the two surfaces.

Acknowledgments
This work was supported jointly by Engineering and Physical Sciences Research Council and Infineum UK Ltd. The authors would like to thank Professor Alex Routh (University of Cambridge) and Dr. Alexander Armstrong (ISIS Neutron and Muon Source) for conducting the neutron reflectometry experiments.

References
[1] K. Holmerg and A. Erdemir, *Friction*, **5**, 263-284 (2017).
[2] H. Spikes, *Tribol Lett*, **60**, 5 (2015).

Insights on Liquid-Liquid Equilibria By Application of Flory-Huggins Approach

Wolffram Schröer[1,2], Sabine Wagenfeld[2], and Bernd Rathke[2*]

[1]Institut für Anorganische und Physikalische Chemie, Universität Bremen, Germany

[2]Technische Thermodynamik, Universität Bremen, 28359 Bremen, Germany

(*) e-mail: rathke@uni-bremen.de

Phase behavior is a prerequisite for a basic understanding of thermophysical properties. A number of systematic studies focusing on liquid-liquid equilibria were published during the last decades. As some studies have been focused on specific tasks, e.g., extraction, the avoidance of a demixing (fuel technology) or the optimization of specific formulations (pharmaceutics or cosmetics), scientific driven systematic studies are rare. Experimental results are often described in terms of empirical or semi-empirical or group contribution models, sometimes more sophisticated simulations corroborate the results.
A critical assessment of the experimental and theoretical data is rather tricky, as different components with their different thermophysical properties and their versatile molecular interactions might result in inextricable contributions to (a) uncertainties of the experimental data and (b) the quantitative determination / calculation of molecular interactions.
Therefore, we have performed systematic investigations on the liquid-liquid phase behavior of mixtures of normal alkanes with the molecular solvents ethanol or acetonitrile [1,2]. Both types of mixtures show partial miscibility with upper critical solution temperatures, which are shifted systematically when the chain lengths of one component and, therefore, the molecular interactions are varied gradually. The main objective was to identify systematic trends of the phase behavior. Ethanol as a polar molecule connected with a dipole moment comparable to water is able to form hydrogen bonds. Acetonitrile exhibits a high dipole moment and shows partial miscibility with a couple of common molecular liquids, typically connected with the appearance of upper critical points. Acetonitrile allows for the study of molecular interactions influenced by a dipole moment without the appearance of hydrogen bonds. Recently, in literature experimental LLE of mixtures of acetic acid and alkanes have been reported [3] which exhibit a similar beavior as ACN mixtures. On the molecular level, additionally, hydrogen bonds and dimerization have to be considered.

The different systems show limited miscibility with upper critical solution temperatures (UCSTs), they show variations from a asymmetric shape to an almost symmetrical one. The UCST decreases with decreasing length of the alkyl-chains of the alkane. The systems show the same universal critical behavior. The variations of the parameters are mainly determined by the size of the alkyl-chains. We are discussing the determination of the free enthalpies on basis of a Flory-Huggins like approach, which allows for a description and partially a prediction of UCSTs and critical compositions of the different systems. This approach also gives insights on the molecular interactions.

References

[1] S. Diekmann, E. Dederer, S. Charmeteau, S. Wagenfeld, J. Kiefer, W. Schröer, B. Rathke, *J. Phys. Chem. B*, **124**, 156 (2020).
[2] S. Wagenfeld, W. Schröer, B. Rathke, *J. Chem. Eng. Data*, **69**, 2273 (2024).
[3] H. Matsuda, T. Segawa, T. Tsuji, K. Naito, Y. Kakuta, K. Kurihara, K. Tochigi, *J. Chem. Eng. Data*, **71,** 718 (2026).

Probing Ion Dynamics in Ionic Liquids with Fast Field Cycling NMR Relaxometry

A. Strate[1], L. Kruse[1], A. M. C. Tony[1], D. Paschek[1], R. Ludwig[1]
[1]University of Rostock, Albert-Einstein-Str. 27, 18059 Rostock, Germany
e-mail: anne.strate@uni-rostock.de

Fast field cycling (FFC) NMR relaxometry provides unique insights into molecular dynamics across broad frequency and temperature ranges, making it particularly powerful for the investigation of ionic liquids (ILs). This class of materials exhibits a complex interplay of rotational and translational motions that governs their distinctive macroscopic properties. However, capturing these coupled dynamics across multiple timescales remains challenging. In this contribution, we present a framework that combines FFC NMR relaxometry with molecular dynamics (MD) simulations to disentangle rotational and translational motions in ILs.

In our previous work on translational dynamics [1], we demonstrated that intermolecular heteronuclear ^{1}H-^{19}F interactions play a crucial role in the quantitative analysis of NMR dispersion (NMRD) profiles in ILs where both cations and anions carry NMR-active nuclei. In such systems, intermolecular relaxation is not solely governed by homonuclear ^{1}H-^{1}H and ^{19}F-^{19}F interactions, but also includes significant ^{1}H-^{19}F heteronuclear terms. Neglecting these contributions leads to systematic errors in the evaluation of relaxation data, particularly in the low-frequency regime commonly used to extract translational self-diffusion coefficients. In this regime, application of the low-frequency approach (LFA) to total relaxation rates results in a substantial underestimation of self-diffusion coefficients. To overcome this limitation, we employ an isotopic substitution strategy in which either the cation, the anion, or neither component is selectively deuterated, enabling a controlled comparison between “single-spin” and “two-spin” systems. This approach allows for a reliable determination of translational self-diffusion coefficients, either directly from total relaxation rates in the single-spin case or from properly separated intermolecular contributions in two-spin systems.

With respect to rotational dynamics, our recent studies [2,3] introduces advanced motional models that go beyond the commonly assumed isotropic reorientation. Using the model systems [TEA][NTf_2] and [C_5Py][NTf_2], we demonstrate how ion-specific geometry and internal flexibility govern the relaxation behavior. While nearly spherical cations can be described by classical Bloembergen-Purcell-Pound (BPP) models, elongated ions require anisotropic descriptions, and anions containing CF_3 groups necessitate the inclusion of fast internal rotations. The simultaneous analysis of ^{1}H and ^{19}F relaxation data over a wide temperature range enables a consistent decomposition of relaxation rates, including both homo- and heteronuclear intermolecular contributions. The resulting rotational correlation times and self-diffusion coefficients show excellent agreement with MD simulations, providing strong validation of the proposed framework.

References

[1] L. Kruse, A. M.C. Tony, D. Paschek, P. Stange, R. Ludwig, A. Strate, *J. Phys. Chem. Lett.*, **15**, 1, (2024).
[2] L. Kruse, T. van Alphen, J. Busch, D. Paschek, R. Ludwig, A. Strate, *Phys. Chem. Chem. Phys.*, **27**, 10927-10938, (2025).
[3] L. Kruse, A. M. Chiramel Tony, D. Rauber, R. Ludwig, D. Paschek, A. Strate, *Magn. Reson. Chem.*, **64**, 3, 265‑272, (2026).

Building Nanoplastic Models for Molecular Calculations

B. Szabó[1], P. Zaby[2], L. Dick[2], K. Drysch[2], Y. Dawer[2], W. Reckien[2], B. Kirchner[2], O. Hollóczki[1*]
[1]University of Debrecen
[2]University of Bonn
e-mail: holloczki.oldamur@science.unideb.hu

Molecular simulations of plastic nanoparticles have become increasingly important in uncovering the toxicity of micro- and nanoplastics. Modeling nanoplastics requires realistic starting structures, otherwise the simulations may produce faulty results. Building such structures most often relies on folding multiple polymer chains into a tightly entangled particle, which is a complex task and necessitates careful optimization. Here we present a systematic workflow that employs a simulated annealing approach to generate low-energy nanoplastic models. The resulting structures are further refined through semiempirical quantum chemical geometry optimizations with the GFN2-xTB method, followed by benchmark single-point energy calculations using both GGA and hybrid DFT functionals. We demonstrate the effectiveness of this protocol on six types of plastics: polyethylene, polypropylene, polystyrene, nylon-66 and polyurethane.

The most stable geometries obtained (Figure 1) show notable agreement with previously reported theoretical and experimental structures. Polyethylene, for instance, forms a highly ordered arrangement, with long chain segments predominantly in *trans* conformation, similarly to the crystal structure of this polymer. In contrast, polypropylene and polystyrene exhibit helical chain geometries characterized by alternating *gauche* and *trans* configurations along the backbone. For nylon-66, folding is more complex due to hydrogen bonding between amide groups, leading to parallel chains connected through hydrogen-bond networks within the particle. Finally, all optimized structures are made publicly available in an online repository, with the aim of supporting and advancing future simulation studies, including enabling ensemble-based investigations [1].

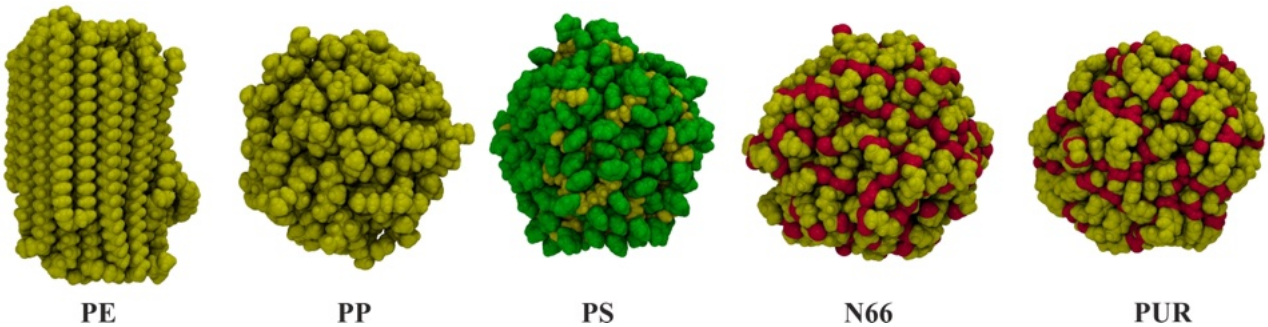

Figure 1 *– 3D structure of the obtained most stable plastic models*

References

[1] B. Szabó, P. Zaby, L. Dick, K. Drysch, Y. Dawer, W. Reckien, A. Udvardy, F. Neese, B. Kirchner, O. Hollóczki*, J. Phys. Chem. B,* **130***,* 2, 881–893 (2026).

Poster 19: Molecular Dynamics Study on the Cosolvency Mechanism of Poly(methyl acrylate) in Ethanol/Water Mixtures

Molecular Dynamics Study on the Cosolvency Mechanism of Poly(methyl acrylate) in Ethanol/Water Mixtures

I. Takahashi[1], Y. Yasuda[2], M. Kato[1,3], and K. Fujimoto[4]

[1]Grad. Sch. of Life Sci., Ritsumeikan Univ., 1-1-1 Nojihigashi, Kusatsu, Shiga 525-8577, Japan

[2]Grad. Sch. of Frontier Sci., The Univ. of Tokyo, 5-1-5 Kashiwanoha, Kashiwa, Chiba 277-8561, Japan

[3]Dept. of Appl. Chem., Coll. of Life Sci., Ritsumeikan Univ., 1-1-1 Nojihigashi, Kusatsu, Shiga 525-8577, Japan

[4]Dept. of Chem. and Mater. Eng., Fac. of Chem., Mater. and Bioeng., Kansai Univ., 3-3-35 Yamate-cho, Suita, Osaka 564-8680, Japan

e-mail: k-fuji@kansai-u.ac.jp

Polymeric materials are widely used in both everyday applications and as advanced functional materials, and solubility is a critical factor governing their properties. When polymers are employed in biomedical applications — such as dentures, bone cement, and contact lenses — dissolution in biological environments may lead to mechanical degradation and leaching of potentially harmful substances. Polymer solubility has conventionally been evaluated using Hansen solubility parameters (HSP) [1], which describe solute–solvent interactions in terms of dispersion forces, polarity, and hydrogen bonding. However, acrylic polymers are known to exhibit an anomalous cosolvency phenomenon: they show low solubility in pure water or pure ethanol individually, yet dissolve readily in ethanol/water mixtures at 80 vol% ethanol [2]. This behavior cannot be explained by conventional solubility indices based on pairwise solute–solvent interactions, and a molecular-level mechanistic understanding is therefore required. In this study, we perform molecular dynamics (MD) simulations of a single polymer chain in ethanol/water mixtures and discuss the molecular origin of polymer dissolution stability based on the solvation structure between the polymer and solvent. Poly(methyl acrylate) (PMA) was used as a structurally simpler analogue of poly(methyl methacrylate), for which cosolvency has been well investigated [2].

A 580-mer single-chain PMA was constructed and mixed into ethanol/water solutions at 0, 20, 40, 60, 70, 80, 90, and 100% (v/v) ethanol using PACKMOL. All MD simulations were performed using GROMACS-2022 [3] (double precision) with OPLS-AA [4] force field for PMA and ethanol, and TIP4P [5] model for water. To generate initial polymer conformations spanning from globule to coil states, NPT simulations were performed at 300 K for solvents and 400 K for PMA, 1 bar for 50 ns, yielding structures with normalized radii of gyration ($\overline{R_g} = R_g/R_g^{\text{polymer state}}$) of 0.4, 0.7, 1.0, and 1.3. Two sets of simulations were then conducted:

(1) Equilibrium conformation analysis.

Polymer chains with $\overline{R_g}$ = 0.4, 0.7, 1.0, and 1.3 were each dissolved in 0, 40, 80, and 100% (v/v) ethanol solution, and simulated at 363.15 K and 1 bar. The equilibrium chain conformations were compared across solvent compositions. The resulting R_g of the polymer increased with increasing alcohol concentration.

(2) Solvation structure analysis.

An extended chain ($\overline{R_g}$ = 1.3) was dissolved in 0, 20, 40, 60, 70, 80, 90, and 100% (v/v) ethanol solution. Simulations were performed at 363.15 K and 1 bar with the polymer backbone restrained, allowing analysis of the solvation structure around the dissolved polymer chain as a function of ethanol content.

References

[1] C. M. Hansen, *The Three Dimensional Solubility Parameter and Solvent Diffusion Coefficient: Their Importance in Surface Coating Formulation.* Copenhagen (1967). [2] J. M. G. Cowie, M. A. Mohsin and I. J. MuCwen, *polymer*, **28**, 1569 (1987). [3] S. Pall *et al*., *J. Chem. Phys.* **153**, 134110 (2020). [4] W. J. Jorgensen, D. S. Maxwell, J. TiradoRives, *J. Am. Chem. Soc.* **118**, 11225 (1996). [5] W. J. Jorgensen *et al.*, *J. Chem. Phys.*, **79**, 926 (1983).

Computer Simulation Study of the Solvation of Inorganic Salts in N,N-Dimethylformamide

Helga Tóth Ugyonka,[1,2] Viktor Szilágyi,[3] Ákos György Juhász,[3,4] Abdenacer Idrissi,[5] Angela Jedlovszky-Hajdú,[3] and Pál Jedlovszky[1*]

[1] Department of Chemistry, Eszterházy Károly Catholic University
[2] Center for Natural Sciences, University of Pannonia
[3]Department of Biophysics and Radiation Biology, Semmelweis University
[4]Unità di Ingegneria Tissutale, ISBReMIT, Fondazione IRCCS Casa Sollievo della Sofferenza
[5]University of Lille, CNRS UMR 8516 -LASIRe - Laboratoire Avancé de Spectroscopie pour les Interactions la Réactivité et l'environnement
e-mail: jedlovszky.pal@uni-eszterhazy.hu

N,N-dimethylformamide (DMF) is one of the most widely used aprotic dipolar solvents in both synthetic chemistry and the chemical industry. It is applied in numerous organic syntheses, the processing of cellulosic biomass, and the production of various plastics, acrylic fibers, resins, adhesives, synthetic leathers, and pesticides, as well as in electrochemistry, nanoparticle synthesis, and electrospinning. The effect of inorganic salts on the local structure of DMF, which is crucial for processes such as electrospinning, is studied using molecular dynamics simulations. Four salts: LiCl, LiBr, $MgCl_2$, and $CaCl_2$ are examined at different concentrations across their full solubility ranges.

The molecular dynamics simulations of solutions of four inorganic salts, along with neat DMF as a reference, were performed in the *N,p,T* ensemble at 298 K and 1 bar. The DMF molecules have been described by the HIJ[1] model. The performance of several interaction models of the salts was assessed. With appropriate charge scaling, all models reasonably reproduced the experimental properties. The only exception in this respect is the solubility of the salts: as only the AMBER model is found to be able to simultaneously reproduce the good solubility of all the four salts considered, this is the model of our choice in this study. Our results revealed that the structure of these solutions is primarily determined by the strong interaction between the cations and the solvation shell DMF molecules. This strong interaction destroys the weak, CH-donated H-bonding structure of neat DMF.

The average lifetime of cation-DMF contacts is found to be in the order of 1 ns for Li^+ and Ca^{2+} while, for $Mg^{2+,}$ it turns out to be several orders of magnitude longer than the entire length of our simulated equilibrium trajectories of 50 ns. Further, the interaction energy of contact Mg^{2+}-DMF pairs falls in the order of covalent chemical bonds, the coordination number is resulted in exactly 6.00 in every case, and the first solvation shell itself is exceptionally well ordered. All these findings strongly suggest (yet do not prove) the formation of the $[Mg(DMF)_6]^{2+}$ hexa-complex by a Mg^{2+} ion and its six first shell DMF neighbors.

References

[1] B. Honti, A. Idrissi, and P. Jedlovszky, *J. Phys. Chem. B,* **125**, 4819–4830 (2021).

Poster 21: Evolution of Equation of State for Molecular Fluids: Reconciling Molecular Rigor with Industrial Engineering Demands

Evolution of Equation of State for Molecular Fluids: Reconciling Molecular Rigor with Industrial Engineering Demands

A. Trokhymchuk

Yukhnovskii Institute for Condensed Matter Physics of the NAS of Ukraine, Lviv 79011, Ukraine

e-mail: adt@icmp.lviv.ua

The quest for a generalized equation of state (EOS) for molecular fluids remains a central challenge bridging fundamental statistical mechanics and applied chemical engineering. The conceptual foundation for understanding fluid non-ideality was established more than a century ago by the van der Waals (vdW) theory, which identified excluded volume and intermolecular cohesion as the principal factors governing fluid phase behavior [1]. Despite well-known theoretical limitations, particularly in the treatment of short-range repulsion, vdW-type cubic equations of state (CEOS), such as the Soave-Redlich-Kwong and Peng-Robinson models, remain the standard industrial tools for process simulation [2,3]. Their continuing success is largely due to their mathematical simplicity, computational robustness, and effective empirical parameterization of attractive interactions [2].

In contrast, modern statistical mechanics seeks to establish a rigorous connection between macroscopic thermodynamic behavior and microscopic intermolecular forces through thermodynamic perturbation theory (TPT). Traditional TPT approaches employ a purely repulsive hard-sphere (HS) reference system and therefore require higher-order perturbation terms to achieve quantitative accuracy. Recent developments, however, demonstrate the advantages of non-HS reference systems, in which the short-range attractive contribution is incorporated directly into the reference state. Such range-based decompositions substantially reduce the perturbation magnitude and restore the viability of highly accurate analytical first-order TPT descriptions [4,5].

At the same time, translating microscopically rigorous EOS models into general engineering practice remains challenging. Advanced non-cubic EOS formulations, including Statistical Associating Fluid Theory (SAFT)-type approaches, provide improved predictive capabilities for complex and associating fluids, but may also exhibit non-physical mathematical artifacts, such as fictitious critical points or anomalous multiple-volume roots, which complicate reliable industrial implementation [6]. In parallel, alternative interpretations of supercritical fluid behavior based on higher-order percolation transitions have recently been proposed, suggesting the existence of a mesophase separating liquid-like and gas-like states [7].

This lecture will review the historical evolution of EOS development and analyze the structural trade-offs between empirical simplicity and theoretical rigor. Particular emphasis will be placed on recent non-HS perturbation approaches developed in our work, which aim to reconcile molecular realism with analytical tractability. By combining modern molecular simulation results, range-separated perturbation schemes, and rigorous analysis of mathematical artifacts, we outline a pathway toward a new generation of microscopically grounded EOS models suitable for both fundamental studies and industrial chemical process design [8].

References

[1] J.O. Valderrama, *J. Supercritical Fluids*, **55**, 415 (2010).
[2] G.M. Kontogeorgis, R. Privat and J.N. Jaubert, *J. Chem. Eng. Data*, **64**, 4619 (2019).
[3] S. Gupta, J.R. Elliott, A. Anderko, J. Crosthwaite, W.G. Chapman and C.T. Lira, *Ind. Eng. Chem. Res.*, **62**, 3394 (2023).
[4] I. Nezbeda, R. Melnyk and A. Trokhymchuk, *J. Supercritical Fluids*, **55**, 448 (2010).
[5] A. Trokhymchuk, V. Hordiichuk, R. Melnyk and I. Nezbeda, *arXiv:2604.25882* (2026).
[6] N.M. Alsaifi and J.R. Elliott, *Ind. Eng. Chem. Res.*, **61**, 15661 (2022).
[7] J.F. Maguire and L.V. Woodcock, *J. Molec. Liq.*, **373**, 121199 (2023).
[8] J.M. Kontogeorgis, R. Dohrn, I.G. Economou, J.C. de Hemptinne, A. ten Kate, S. Kuitunen, M. Mooijer, L.F. Zilnik and V. Vesovic, *Ind. Eng. Chem. Res.*, **60**, 4987 (2021).

Spectroscopic study of intermolecular interactions in mixtures of lithium nitrate with protic ionic liquids

F. Tuteri[1], B. Bracco[1], B. Rossi[2], Y. Morisawa[3], M. Paolantoni[1]
[1]Department of Chemistry, Biology and Biotechnology, University of Perugia,
Via Elce di Sotto 8, 06123 Perugia, Italy
[2]Elettra Sincrotrone Trieste, S.S. 114 km 163.5, Basovizza, 34149 Trieste, Italy
[3]Kindai Univ, Sch Sci & Engn, Osaka 5778502, Japan
federica.tuteri@dottorandi.unipg.it

Protic ionic liquids (PILs) represent a promising class of materials for numerous applications, including electrochemical ones, thanks to their high ionic conductivity, low volatility and tunable physicochemical properties[1].
In recent years, increasing attention has been focused on mixtures of PILs with inorganic salts, since the addition of species such as $LiNO_3$ can significantly alter the microscopic structure and transport properties of these systems, making them potentially attractive candidates as electrolyte for lithium devices[2].
Despite this growing interest, the solvation environment of Li^+ ions and their influence on the intermolecular interactions that determine the structure and properties of PILs are not yet fully understood[3].
In this work, the structural organization and intermolecular interactions in mixtures of lithium nitrate ($LiNO_3$) with ethylammonium nitrate (EAN) and propylammonium nitrate (PAN) at different compositions were investigated.
The characterization of these systems concerned the adoption of an integrated approach based on ATR-FTIR, Raman (532 and 785 nm excitation wavelength), and UV-Raman (213 and 248 nm excitation wavelength) spectroscopy.
The most innovative contribution concerns the application of a differential spectral analysis procedure to extract solute-correlated spectra, providing selective information on the lithium solvation shell in non-aqueous systems[4].
Overall, the results obtained highlight how the addiction of $LiNO_3$ leads to deep reorganization of the local structure of nitrate-based PILs.

References

[1] Gardiner, D. J., Hester, R. E. & Grossman, W. E. L. Infrared and Raman spectra of lithium and ammonium nitrate solutions in liquid ammonia. *J. Chem. Phys.* **59**, 175–184 (1973).
[2] Hu, X. *et al.* Thermal stability of ionic liquids for lithium-ion batteries: A review. *Renew. Sustain. Energy Rev.* **207**, 114949 (2025).
[3] O.Russina, R. Carminiti, T. Méndez-Morales, J. Carrete, O.Cabeza, L.J. Gallego, L.M. Varela, A.Triolo. How does lithium nitrate dissolve in a protic ionic liquid? Journal of Molecular Liquids **205**, (2015)16-21.
[4] Ben-Amotz D. Hydration-Shell Vibrational Spectroscopy. *J Am Chem Soc* 2019;141(27):10569–10580.

Selectivity of Nanopores: Extending the Scalability Framework to Concentration Gradient Conditions Across Membrane Interfaces

Kristóf Tormási, Dezső Boda, Mónika Valiskó
Center for Natural Sciences, University of Pannonia, Hungary
e-mail: valisko.monika@mk.uni-pannon.hu

Nanopores are nanoscale channels embedded in a membrane that enable the controlled transport of ions between the bulk phases located on the two sides of the membrane. Depending on the charge pattern created on the pore wall, the nanopore produces different output functions in response to various input parameters, from which a response function can be constructed. For uniformly charged nanopores, one such response function is selectivity. If the electrolyte concentrations differ on the two sides of the membrane, then, in addition to the electrical potential difference (voltage), the concentration gradient also acts as a driving force for ion transport.

The aim of this research is to investigate the selectivity of nanopores in this asymmetric case. If a parameter can be found that, on the one hand, can be uniquely expressed from the input system parameters through an analytical equation, and, on the other hand, for which selectivity is a unique (though not necessarily analytical) function, then the selectivity of the nanopore can be predicted easily. This phenomenon is referred to as scaling. In the case of nanopores, the input parameters include the pore radius, pore length, applied voltage, surface charge density, concentration, and ionic charges. In a previous publication of our research group [1], a scaling parameter was developed on the basis of linearized Poisson–Boltzmann theory for infinite pores. This parameter is related to the Dukhin number commonly used in the literature, and it works well as a scaling parameter for finite pores in the symmetric case, when the concentration is the same on both sides of the membrane [2,3].

The goal of this work is to extend this scaling theory to the case where the electrolyte concentrations in the bulk phases on the two sides of the membrane are different. Our derivation showed that the scaling parameter of the asymmetric system can be expressed as the harmonic mean of the scaling parameters corresponding to the left and right sides (where the left- and right-side concentrations are used separately). Using the Poisson–Nernst–Planck theory, we performed calculations for different combinations of the input system parameters and demonstrated that the scaling works as well as in the symmetric case; that is, the method has essentially the same limitations. Local Equilibrium Monte Carlo simulations have also been performed to assess the effect of ionic correlations for multivalent electrolytes.

References

[1] Zs. Sarkadi, D. Fertig, M. Valiskó, and D. Boda. *J. Mol. Liq.*, **357**:119072 (2022).
[2] Zs. Sarkadi, Z. Ható, M. Valiskó, D. Boda. *J. Mol. Liq.* **387**:122571, 2023.
[3] Zs. Sarkadi, Z. Ható, M. Valiskó, D. Boda. submitted 2026

On the interactions between nucleic acids and nanoplastics

M. Varenicja[1], O.Hollóczki[1]
[1]University of Debrecen, Faculty of Science and Technology, Institute of Chemistry, Department of Physical Chemistry
e-mail: holloczki.oldamur@science.unideb.hu

Micro- and nanoplastics (MNPs), formed through the degradation of larger plastic waste, can be detected even in remote environments and have been shown to enter the food chain and the human body. Increasing experimental evidence points to their potential epigenetic and mutagenic effects, suggesting direct interactions with DNA. However, the molecular-level mechanisms behind these effects remain unexplored.

In our earlier study [1], we showed that positively charged polystyrene chains can induce a conformational transition in DNA from the canonical B form toward a more A-like structure. In this work, we explore through molecular dynamics simulations how different nanoplastics interact with DNA, through comparing an array of neutral and positively charged polymers. As a model system, we practically relevant DNA sequences, as well as repeating AT- and CG-rich sequences.

To generate DNA–nanoplastic complexes, we employed simulated annealing and high-temperature equilibrium simulations. While simulated annealing worked well for neutral systems, it proved less suitable for positively charged complexes, where short simulations at elevated temperature were more effective. The resulting structures were then simulated in aqueous environment. We found that neutral polystyrene, polyethylene, and nylon-6,6 oligomers tend to dissociate from DNA, indicating weak interactions. In contrast, positively charged polystyrene derivatives form stable complexes and induce pronounced structural changes in the DNA double helix, typically shifting it from B-DNA toward A-like conformations. Increasing the charge density on the polymer further makes these effects even more pronounced. Furthermore, we comparing the interaction energies of B-DNA structures to other conformations reveals that the strongly interacting, charged plastics tend to induce even more severe changes in the DNA conformations.

Thus, our results consistently show that they can significantly change DNA structure. This suggests that nanoplastics, in particular charged polymers, may have a direct impact on DNA-related biological processes.

References

[1] M. Varenicja, O. Hollóczki, *Nano Lett.* ***25*** **(44)**, 15890-15894 (2025)

Investigating phase behaviour of lipid-water-ethanol systems in lipid nanoparticle (LNP) formation

A. Waren[1], Y. Perrie[2], J. Sefcik[3]

[1]CMAC, CEDAR, an EPSRC Centre for Doctoral Training in Cyber-Physical Systems for Medicines Development and Manufacturing, Department of Chemical and Process Engineering, University of Strathclyde, Glasgow, UK
[2]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK
[3]Department of Chemical and Process Engineering, University of Strathclyde, Glasgow, UK

e-mail: alice.waren@strath.ac.uk

Lipid nanoparticles (LNPs) are used as drug delivery systems, attracting much attention after their successful application in nucleic acid therapeutics including mRNA vaccines 1 . LNPs are manufactured through mixing of ethanolic lipid solutions and aqueous solutions containing nucleic acid therapeutic payloads, typically using microfluidic mixers due to their controllable and reproducible mixing conditions. Molecular self-assembly of LNPs results from the complex interplay of constituent material properties and process parameters related to solution composition, temperature, and mixing[2]. However, the process of self-assembly during mixing remains a “black-box” model requiring further research and understanding of this interplay to enable rational process development to enhance scalability and therapeutic advancements.

The aim of this project is to gain insight into the phase behaviour of LNPs by developing phase diagrams for the self-assembly process using a frequently used constituents: SM102, DSPC, Cholesterol, and DMG-PEG2000. Firstly, by establishing lipid constituent solubility in ethanol and binary water-ethanol miscible environments, we map out suitable concentration ranges
LNP manufacturing. Secondly, we investigate their phase behaviour as the environment changes (e.g., water-ethanol ratio, pH, and ionic strength) and its impact on self-assembly. Lastly, we develop a phase diagram that identifies environments for stable LNP formation using widely used lipid constituents.

These findings will aid further development of process models for controlling the manufacturing process to tailor manufacturing to desired outcomes enabling faster production, reduced waste, and better control and scalability. This can be applied to enhance development of LNPs as drug delivery systems in therapeutics.

Acknowledgements
We would like to thank the CMAC EPSRC Centre for Doctoral Training in Cyber-Physical Systems for Medicines Development and Manufacturing (CEDAR0 (Grant Ref. EP/Y035593/1) for funding this work.

References
[1] G. Guerrini, D. Magri, S. Gioria, D. Medaglini, L. Calzolai. Characterization of nanoparticles based vaccines for COVID-19, *Nat Nanotechnol*. **17(6):**570-6 (2022).
[2] V. Nele, V. Campani, S. Alia Moosavian, G. De Rosa. Lipid nanoparticles for RNA delivery: Self-assembling vs driven-assembling strategies. *Adv Drug Deliv Rev*. **208:115291**(2024).

Solution-Phase Co-Oligomer Analysis as a Predictive Tool for Co-Crystal and Co-Amorphous Forms

Zhiyu Liao,[1] Immacolata Abate,[2] Rebecca Beveridge,[2] and Klaas Wynne[1]
[1]School of Chemistry, University of Glasgow, G12 8QQ, UK
[2]Dept. of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, UK
e-mail: klaas.wynne@glasgow.ac.uk

Multicomponent molecular solids underpin technologies ranging from pharmaceuticals to functional materials, including co-amorphous drug delivery systems (CAMS). However, there is no general method to predict whether a mixture of small molecules will form a cocrystal, a homogeneous glass, or separate crystalline phases. Here we show that solution-phase noncovalent oligomers, detected by nanoelectrospray ionization mass spectrometry (nESI-MS), enable direct prediction of the solid-state forms obtained from multicomponent mixtures.[1] By analysing the distribution and stoichiometry of mixed oligomers formed in dilute solution, we find that well-defined complexes with a fixed molar ratio reliably precede the formation of stoichiometric cocrystals, whereas disordered ensembles of mixed aggregates with variable composition lead instead to single-phase amorphous solids. In contrast, the absence of detectable mixed oligomers correlates with macroscopic phase separation into the individual crystalline components. This solution-phase oligomer analysis operates on microliter sample volumes, requires no prior structural information and is compatible with a wide range of molecular systems. Our results establish a mechanistic link between pre-nucleation aggregation in solution and the emergent structure of multicomponent molecular solids, enabling rapid, physically grounded screening of co-formers and co-assemblies across fields from pharmaceutical formulation to materials science.

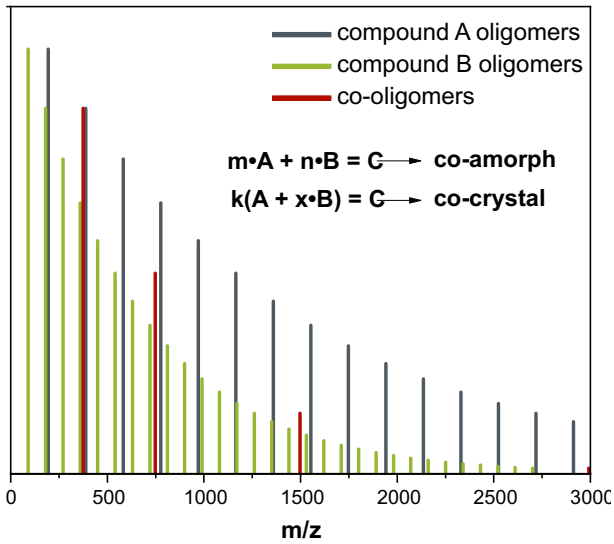

Figure 1 – Schematic representation of a predictive workflow for co-structure formation in drug formulations using solution-phase oligomer analysis. *nESI-MS reveals the detailed distribution and stoichiometry of oligomers and co-oligomers formed in solution. These molecular signatures serve as precursors that indicate the propensity of forming either co-crystals or co-amorphous solids.*

References

(1) Liao, Z.; Abate, I.; Beveridge, R.; Wynne, K. Solution-Phase Co-Oligomer Analysis as a Predictive Tool for Co-Crystal and Co-Amorphous Forms. *ChemRxiv* **2026**. https://doi.org/10.26434/chemrxiv.10001669/v1.