9th Visegrad Symposium on Structural Systems Biology

ABSTRACTS OF ORAL PRESENTATIONS

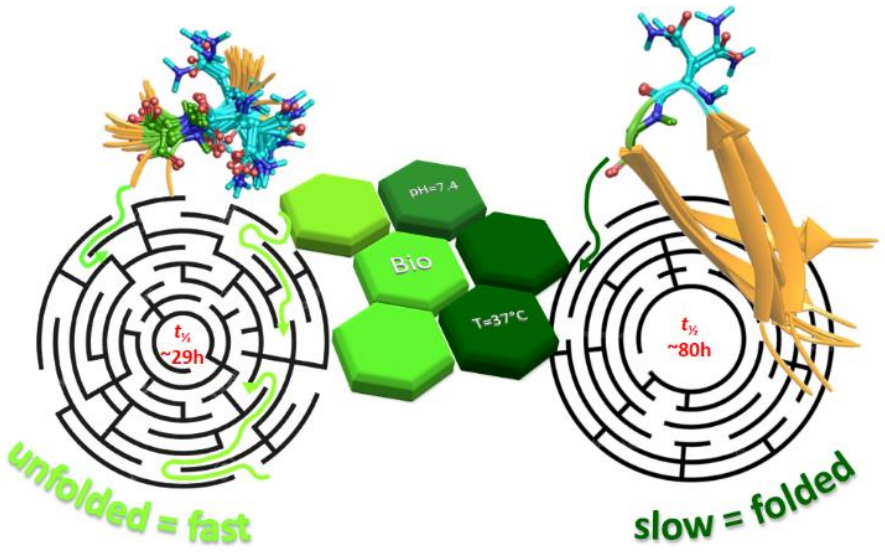
The autors of the abstracts bear the full responsibility for the scientific and linguistic content.

Shielding proteins Achilles heel

András Perczel

Laboratory of Structural Chemistry and Biology & MTA-ELTE Protein Modeling Research Group at the Institute of Chemistry, Eötvös Loránd University, 1117, Pázmány Péter st. 1/A, Budapest, Hungary,

The spontaneous isomerization of amino acids leading to the rearrangement of protein backbone and fold is a topic that challenges the belief that these vital biomolecules, once assembled by nature will last a lifetime unless they suffer grave attacks. That actually isn't so; 3 out of every 1000 residues is a chronometer – signaling the passing of time by inevitably introducing unrepairable changes in the protein backbone without any inducement. We have conducted a systematic analysis of this phenomenon, hoping to provide a better overview of the factors that should be considered when designing protein drugs, antibodies, assessing the severity of mutations or simply when considering the "life expectancy" of protein molecules. There have been, of course, numerous noteworthy efforts to clarify the molecular details of spontaneous isomerization of Asn/Asp residues, but we feel that the emphasis has been a bit misplaced; here we show that electrostatic contribution of the residues at the (*i*-1) and especially (*i*+2) positions, the local conformation and ultimately the flexibility of the backbone determine the isomerization rates, thus nearly pre-formed reaction centers such as on-pathway folds greatly increase the risk of isomerization. All protein drugs (*e.g.* developed as antibodies against cancer cells) expensive to manufacture have to be stored on the shelf and thus, are affected by this isomerization.



Ion Specific Effects on Polymer Interactions

Mikael Lund[1]

[1] Department of Chemistry, Lund University, SE-22100 Lund, POB 124.

Corresponding author: mikael lund at teokem lu se

Through intermolecular and intramolecular interactions, the stability of (bio)polymers in aqueous solution is influenced by the presence of salt. Not only does the salt *concentration* or ionic strength play an important role, but so does the salt *type*. The latter observation can be traced back to early works of Franz Hofmeister and the underlying molecular mechanisms was later studied via a combination of atomistic computer simulations and high resolution experimental techniques.

In this presentation we propose a new model for describing ion specific effects in aqueous solution of polymers and other macromolecules. The model combines macroscopic and microscopic observables from experiment or all-atom MD simulations into a coarse grained model where large length and time scales can be studied. Our model include transfer free energy terms for describing salting out, i.e. when salt is excluded from the solute surface and can cause a polymer collapse and/or induce aggregation. To capture salting in, i.e. when ions bind to the solute surface we use a two-state binding parametrised via NMR experimental data. We demonstrate how the model, based on the Metropolis Monte Carlo algorithm, can be applied to aqueous solutions of PEG, caffeine, and proteins.

Validation of force fields for the study of amyloid-b peptide interactions with membrane gangliosides.

Michael C. Owen[1], Robert Vacha[1]

[1] Central European Institute of Technology, Masaryk University, Kamenice 753/5, Brno 625 00, Czech Republic.

Corresponding author: michaelowen27@gmail.com

The formation of b-sheet-rich toxic oligomers of the amyloid-b (Ab) peptide is mediated by the interaction of the peptide with the GM1 gangliosides[1]. These sugar-containing glycolipids structures introduce a third macromolecule, carbohydrates, to further complicate the interactions between peptide and lipid bilayer. Although atomistic molecular dynamics (MD) simulations is an ideal tool for characterizing this system, the ability of the two most popular force fields, CHARMM and Amber, to model these systems has yet to be compared. Systems comprised of Ab and bilayers comrised of GM1 in DOPC were constructed and represented with four force fields – CHARMM36, CHARMM36m, Amber99SB*-ILDN with Robert Best correction, and Amber14SB. Three (3) x 500 ns simulations were carried out on each system, and the sampling of each were compared to Hamiltonian replica-exchange simulations of equal trajectory length. A detailed analysis of the interactions between peptide, membrane and ganglioside will be presented.

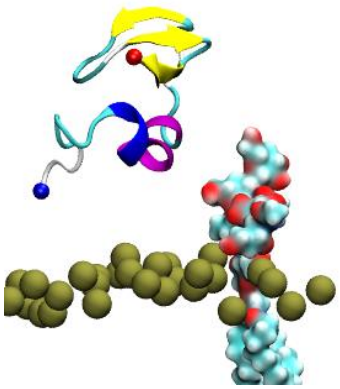


Fig. 1. The interaction between Ab and the GM1 ganglioside.

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Tuning membrane structure-elasticity to improve lung models at the microscale

Lisa D. Muiznieks

Elvesys Microfluidics Innovation Center, 83 avenue Philippe Auguste, 75011 Paris, France

The lung is the main organ of respiration whose function is to facilitate gas exchange across the alveolar-capillary (air-liquid) interface (ALI). Altered tissue stiffness is a hallmark of many diseases and is typically related to concomitant changes in the composition and/ or integrity of fibrous matrix protein networks. Currently, essential contributions from matrix mechanical profiles to cell fate and tissue function are largely overlooked in models of lung health and disease. Elastin is the extracellular matrix protein that provides elasticity to vertebrate tissues, including the lung. The protein is largely conformationally disordered, driving entropic elastic recoil, but also contains regions of local structure. It is becoming clear that a balance of structure, disorder and dynamics combines to modulate elastic mechanical properties such as extensibility, strength and stiffness. Here we present approaches to alter structural features of recombinant elastin in order to modulate mechanical properties of cross-linked elastic membranes. Furthermore, we describe efforts to incorporate elastic membranes with mechanically tuned profiles into a microscale lung-on-chip platform to better model the uptake of toxic nanoparticles from the air or the effect of drugs for lung disease.

Title: Strategies for developing human papillomavirus (HPV) vaccine delivery system for cervical cancer

Nasir Uddin, PhD

Associate Professor, College of Pharmacy

Larkin University, Miami, FL

Cervical cancer, caused by Human Papillomavirus (HPV), is the third most prevalent cancer for women all over the world. According to World Health Organization (WHO), only in 2008, there were an estimated 529,000 new cases and 274,00 deaths due to cervical cancer. It is the leading cause of death from cancer among women in developing countries, where it causes about 190,000 deaths each year. Unlike many cancers, cervical cancer can be prevented. Currently, two prophylactic HPV vaccines, Gardasil (Merck, USA) and Cervarix (GlaxoSmithKline, UK) are available. Both Gardasil and Cervarix vaccines consist of 'virus-like particles' (VLPs) which are multi-protein structures that mimic the organization and conformation of authentic naïve viruses but do not contain any genetic material. The approximate cost for three doses of either vaccine is about $400 to $500. While both Gardasil and Cervarix are the only vaccines against cervical cancer, these vaccines have significant drawbacks that limit their applications in resource poor areas. These vaccines are expensive, require cold chain storage, less patient compliance, involved with painful intramuscular administration, and require trained personnel to administer them by injection. In addition, there is a growing concern regarding their adverse effects which includes but not limited to pain, fatigue, redness, swelling, fever, GI symptoms (diarrhea, nausea, vomiting), headache, dizziness, myalgia and arthralgia. Therefore, it is in high demand to find a new delivery system of HPV vaccine (VLPs) with more patient compliant route of administration to address these issues. One most feasible way is to develop a particulate based vaccine delivery system using a biodegradable and biocompatible polymer. Particulate formulations offer several advantages in vaccine development such as particulate carriers can serve as an effective antigen delivery system that is able to enhance and/or facilitate the uptake of antigens by antigen-presenting cells. Also, particle-based vaccines are easy to prepare and scale up, cost effective, can be preserved in room temperature. Particulate vaccine can be administered in solution form orally, which makes them more patient compliant. In an in vivo rat model, we have evaluated the particulate dosage forms of HVP vaccine for oral administration to prevent cervical cancer. We also have investigated the quickly soluble film dosage form of particulate vaccine or VLPs for buccal administration. Film dosage forms for buccal administration has several advantages. Unlike oral administration buccal administration can avoid first pass effect and can be highly efficient with lower dose. Also, buccal mucosa, compared with the other mucosa, provides better permeability of the drug.

Activation of STIM calcium sensor

Daniel Bonhenry[1], Rüdiger H.Ettrich[1,2]

[1]Center for Nanobiology and Structural Biology, Institute of Microbiology, Academy of Sciences of the Czech Republic, Zámek 136, CZ-373 33, Nové Hrady, Czech Republic. bonhenry@nh.cas.cz

[2]College of Biomedical Sciences, Larkin University, Miami, FL 33169, United States. rettrich@ularkin.org

STIM (Stromal interaction molecule) is a protein located at the level of the membrane from the endoplasmic reticulum or sarcoplasmic reticulum. Its N-terminal is located within the luminal part of the organelle and the longer C-terminal is bathing in the cytosol both connected by a single short transmembrane (TM) α-helix. The N-terminal has the ability to probe the calcium level within the ER thanks to a pair EF-hand like motifs [1]. On the other side of the membrane, the cytosolic part is responsible for activating target calcium-channels in the plasma membrane depending on the calcium level within the storage unit. While some organisms like *Drosophila* are known to have one variant of STIM, two variants (STIM1 & 2) are expressed ubiquitously in the cells of vertebrate [2]. While extensive studies have been performed on STIM1, STIM2 remains more elusive [3].

We focus here on the luminal domain of STIM1 and STIM2. NMR based solution structure revealed their luminal part is a compact structure constituted by 10 small α-helices and 2 β-strands when bound to a calcium ion [4]. Based on these structures, molecular dynamics simulations were performed on reconstructed minimal STIM segments based on the luminal domain. The latter was anchored to a membrane by means of the transmembrane helix reconstructed *in-silico*. Dynamic and stability of these proteins were studied in presence of different ionic environments.

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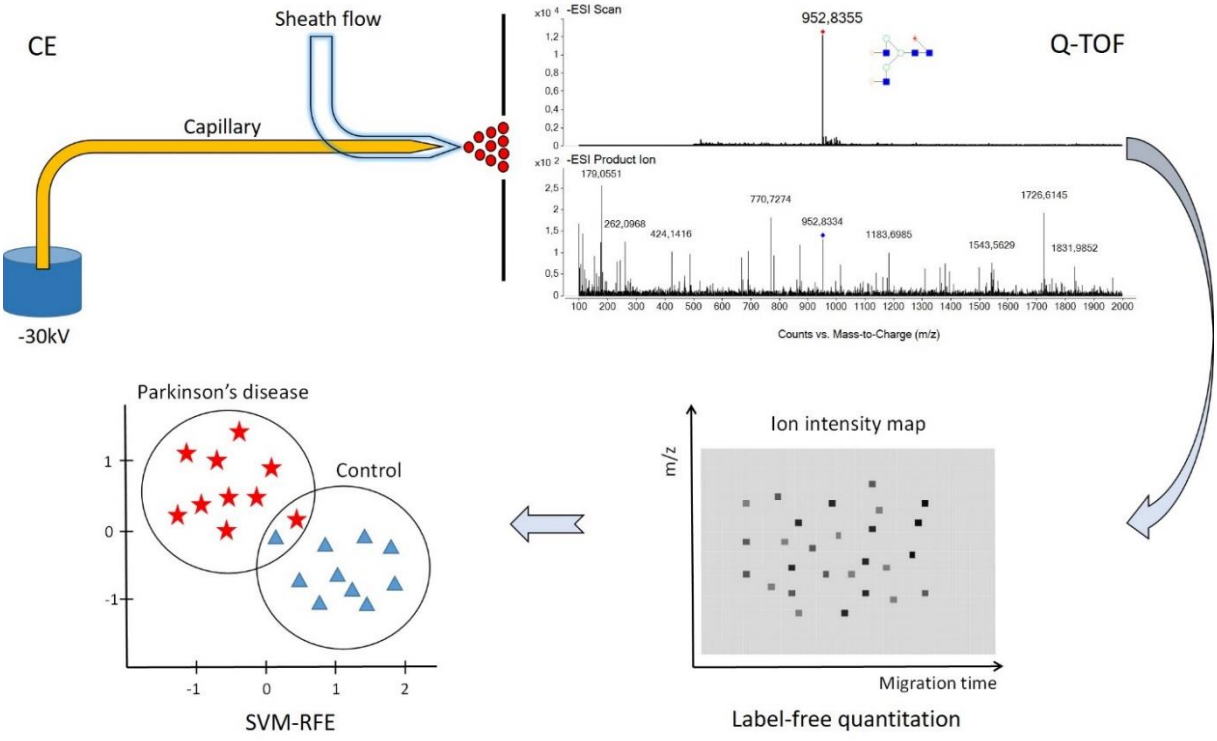
Alterations of human serum glycosylation: The challenge of analytical chemistry

Csaba Váradi

Faculty of Materials Science and Engineering, Institute of Chemistry, University of Miskolc, Hungary

csaba.varadi22@gmail.com

Glycans, linked to proteins as co- and/or post-translational modifications are the results of complicated biochemical processes involving a plethora of enzymes during and after translation. The structural heterogeneity of glycans is based on the actual activity of glycosidases and glycosyl-transferases, which can be altered in pathological conditions. Comprehensive glycosylation analysis offers a new avenue in biomarker discovery as glycans apparently transmit bio-specific information therefore, sensitive indicators of the actual state of the underlying biochemical mechanisms. With the help of validated biomarkers, diseases can be diagnosed at early stages, also saving patients from sometimes complicated and invasive diagnostic procedures. Recent advances in bioseparation sciences enables the identification of glycosylation changes on serum glycoproteins, and helps to reveal potential carbohydrate-specific alterations.



Quinolone derivatives as universal chromophores for standardized dynamic Stokes shift measurements

Stella Schmode, Esther Heid and Christian Schröder

University of Vienna, Faculty of Chemistry, Department of Computational Biological Chemistry, Währingerstraße 17, A-1090 Vienna, Austria.

Corresponding author: stella.schmode@univie.ac.at

Understanding the solute-solvent interactions is an essential part for developing high performance liquid phase reactions. The dynamic Stokes shift is an easily accessible observable to determine such interactions by experimental as well as theoretical work. Therefore, solvation dynamics is deduced from the spectral shift of a sensitive chromophore over time. The crux of the matter is the choice of a suitable probe. Limited solubility inhibits the standardized use of a prototype chromophore. Furthermore, Stokes shifts measured with diverse probes do not necessarily give the same solvent dynamics and results cannot be adjusted by simple linear correlation.

Here, we present a toolbox of chromophores with diverse physico-chemical properties, which are all based on the same quinolone skeleton. In our molecular dynamics approach we utilize the proven dye N-Methyl-6-oxyquinolone and derivatives. To fit the requirements of any molecular and ionic liquid, the dye toolbox i.a. contains ionic quinolones. Solvation dynamics are monitored by non-equilibrium molecular dynamics simulations. We suppose, the similarity in the dye skeleton will allow for quantitative comparability.

Computational study of self-assembly of bacteriochlorophyll in chlorosomes

David Řeha

CNSB, Institute of Microbiology of the Czech Academy of Sciences,
Zamek 136, 37333 Nove Hrady, Czech Republic

Faculty of Sicence, University of South Bohemia in C. Budejovice
Branišovská 164, 37005,Českе Budějovice, Czech Republic

Corresponding author: reha@nh.cas.cz

Chlorosomes are light-harvesting complexes found in photosynthetic bacteria. They are composed of bacteriochlorophylls with minor contributions from proteins, lipids, carotenoids and quinones. Proteins are confined to the surface of the chlorosome while most bacteriochlorophyll molecules are found within the interior where they assemble into aggregates. These aggregates consist of lamellar structures, in which bacteriochlorophylls form curved layers while hydrophobic esterifying alcohols of bacteriochlorophylls from adjacent layers interdigitate and hold the system together. Such an arrangement supports strong excitonic coupling between the pigments within a layer and enables efficient excitation energy transfer.

In this work, the mechanism of the formation of curved layers of bacteriochlorophylls were studied using molecular dynamics (MD) simulations and QM/MM calculations. The MD simulations were performed on several model motifs of bacteriochlorophyll layers [1]. The curvature of the layer has formed shortly after begening of MD simulation. QM/MM cauculation was performed on the curved and flat parts of the leyer in order to specify the most important contributions of curvature formation.

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Prediction of electrostatic parameters for a general polarizable force field

Esther Heid[1,2], Markus Fleck[1], Payal Chatterjee[2], Christian Schröder[1], Alexander D. MacKerell Jr.[2]

[1] Department of Computational Biological Chemistry, University of Vienna, 1090 Vienna, Währingerstrasse 17.

[2] Department of Pharmaceutical Sciences, School of Pharmacy, University of Maryland, Baltimore, Maryland 21201, USA.

Corresponding author: esther.heid@univie.ac.at

Polarizable force fields for molecular dynamics simulations have become increasingly important during the last decades. The inclusion of polarizability improves the accuracy of electrostatic interactions between atoms, and thus the accuracy of calculated observables such as, amongst others, refractive indices, diffusion coefficients, conductivities, dielectric spectra, timescales of the time-dependent Stokes shift, or even protein and DNA folding processes. The electrostatic parameters for polarizable force fields, i. e. the atomic polarizabilities and partial charges, can be obtained quantum-mechanically [1,2] but for an automated assignment of parameters for small organic compounds a more general approach is needed. We thus developed a prediction algorithm for atomic polarizabilities and charges, which is based solely on the structure of a molecule [3]. The algorithm was trained on high quality quantum-mechanical polarizabilities and charges of a large number of molecules. The identity of each atom and its chemical surroundings was described on the basis of CGenFF atom types, and fed either to a linear increment scheme, or a neural net. The predicted polarizabilities and charges recover the quantum-mechanical values very well, with average errors only in the second decimal. The prediction algorithm can be downloaded from Ref. [4], and will, in adapted form, be incorporated in the Drude General Force Field (DGenFF) which will generate polarizable force fields for small drug-like molecules similar to the current fixed charge (nonpolarizable) CGenFF routine.

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Investigation of Methylamine at Aqueous Surfaces by Computer Simulation Methods

Réka Anna Horváth[1], Balázs Fábián[2], György Hantal[3], Sylvain Picaud[4], Milán Szőri[5] and Pál Jedlovszky[6]

[1] Apáczai Csere János School of the ELTE University, H-1053, Budapest, Papnövelde utca 4-6. [2]Department of Inorganic and Analytical Chemistry, Budapest University of Thechnology and Economics, H-111, Budapest, Szent Gellért tér 4. [3]Computational Physics group, University of Vienna, A-1090, Vienna, Boltzmanngasse 5. [4]Institut UNITAM (CNRS UMR 6213), Université Fanche-Comté, F-25030, Besançon, 16 route de Gray [5]Institute of Chemistry, University of Miskolc, H-3515, Miskolc, Egyetemváros A/2 [6]Department of Chemistry, Eszterházy Károly University, H-3300, Eger, Leányka utca 6.

Corresponding author: rekahorvathr@gmail.com

Methylamine is already known for its relative atmospherical and interstellar abundance among amines, therefore many theories assume a special role of it in the prebiotic evolution as well as in several reactions included in the nitrogen cycle of the Earth. According to *ab initio* calculations and experiments, aqueous surfaces have a catalytic effect on these reactions through their interaction with methylamine. For examination of the behaviour of methylamine at icy surfaces and at the liquid-vapour interface of water-methylamine mixtures computer simulations were performed.

Related to the panspermia hypothesis the adsorption equilibrium of methylamine was investigated on the surface of amorphous ice, which is characteristic to the interstellar medium, by grand canonical Monte Carlo simulation method at five different temperatures ranging from 200 K to 20 K. We demonstrated the strong tendency of methylamine molecules for being adsorbed at the surface of amorphous ice, including their ability for multilayer adsorption. Our analyses revealed that the methylamine prefers to be in all the orientations where the carbon-nitrogen bond axis lays parallel with the macroscopic ice surface, and also that at low chemical potential values the methylamine tends to form up three hydrogen bonds with the surface water molecules of the amorphous ice.

The liquid-vapour interface of aqueous methylamine solutions of several different, finite concentrations was also investigated by molecular dynamics simulation method. Our results indicated that methylamine molecules show a tendency to be accumulated in the first molecular layer, however, they do not show considerable self-association at the surface of their aqueous solutions. Surface methylamine molecules strongly prefer the alignment in which the apolar CH_3 group points straight to the vapour phase. The presence of the methylamine accelerates the exchange of methylamine and water molecules between the surface layer and the bulk phase, furthermore, methylamine molecules slow down the lateral diffusion of each other and immobilise the water molecules within the surface layer.

As a consequence, we have seen that methylamine could play indeed a special role in the prebiotic evolution as it is described in the panspermia hypothesis, and based on our results, it is also possible that the methylamine might participate in atmospherical reactions.

Molecular Dynamics and Metadynamics Insights of 1,4-Dioxane Induced Structural Changes of Biomembrane Model

Zsófia Borbála Rózsa1, Lukács J. Németh2, Balázs Jójárt2, Károly Nehéz3, Béla Viskolcz1, Milán Szőri1

1 Institute of Chemistry, University of Miskolc, Egyetemváros A/2, H-3515 Miskolc, Hungary

2 Department of Food Engineering, Faculty of Engineering, University of Szeged, Mars tér 7. H-6724, Szeged, Hungary

3 Department of Information Engineering, University of Miskolc, Miskolc-Egyetemváros Informatics Building, H-3515 Miskolc, Hungary

Corresponding author: kemzsofi@uni-miskolc.hu

1,4-dioxane is a cytotoxic B2 type human carcinogen, a serious water pollutant produced solely by industrial activity. The effect of 1,4-dioxane on phospholipid membrane models composed by DPPC and its branched isomer (IPPC) was investigated using MD simulations. Clear and polluted membranes were compared by membrane parameters such as APL, VPL, compressibility modulus, membrane thickness and orderliness of lipid tails. While neat systems significantly differ from each other, the presence of the pollutant has the same effect on both types of lipid membranes: high density of dioxane appears at the vicinity of ester groups which pushes away lipid headgroups from each other, leading to an overall change in lipid structure: APL and VPL grows, while the orderliness of lipid tails, membrane thickness and compressibility modulus decreases. Orientational preferences of water and dioxane molecules were also investigated and different membrane regions have been specified according to the stance of water molecules. Free energy profile for 1,4-dioxane penetration mechanism into DPPC membranes was carried out using metadynamics for two different concentrations of the pollutant (c_1=7.51, c_2=75.10 g/dm^3), which showed that the higher the concentration is, the lower the free energy of penetration gets. A relatively small free energy barrier was found in the headgroup region and accumulation of dioxane is thermodynamically unfavored in the middle of the bilayer. The penetration mechanism has been described in detail based on the orientational preference of 1,4-dioxane molecules and the free energy profile.

Interaction of Hg(II) Cation with Thyminein dependence on pH; DFT and QM/MM MD Approach

Jaroslav V. Burda, Filip Šebesta

Faculty of Mathematics and Physics, Charles University, Ke Karlovu 3,121 16 Prague 2, Czech Republic.

Corresponding author: burda@karlova.mff.cuni.cz

Double-stranded DNA with thymine mismatches represents an effective target for Hg(II) cations, which bind between mismatched thymine (T) bases and form T-Hg(II)-T metal-mediated base pairs. In addition, T-Hg(II)-T base pairs can be localized next to each other. [1] This ability can be used for construction of electric sensors or charge-transporting materials.

Also a proton transfer from nitrogen N3 to oxygen O2 with respect to possible mutations during DNA replication was explored Transition between keto and enol form of thymine can be catalyzed by hydrated metal cations leading to very low activation barrier. In order to analyze the course of the studied keto-enol transition, the reaction electronic flux [4] is determined along intrinsic reaction coordinates obtained at the same computational level. Also Bader's AIM and ETS-NOCV analyses are carried out at the B3LYP/TZ2P(4f core for Hg) level using ZORA approach.

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Computational spectroscopy of reverse micelles: What can we learn about macromolecular confinement?

Philipp Honegger[1], Michael Schmollngruber, Othmar Steinhauser[1]
[1] Department of Computational Biological Chemistry, University of Vienna, 1090, Vienna, Währingerstraße 17.

Corresponding author: philipp.honegger@univie.ac.at

In contrast to contemporary experiments in diluted buffers, the biomacromolecules forming the machinery of life function encapsulated in a cell, crowded by up to 400 g/L of organic matter in the cytosol. Confined space effects impact the physico-chemical properties of both water and biomolecules [1,2,3,4] and alter the reaction kinetics and equilibria they partake in. Reverse micelles consist of a water nanopool encapsulated by an amphiphilic surfactant, thus providing a cell model simple enough to synthesize or simulate. Computational spectroscopy forms the link between experiment and computational model, allowing for simulation verification and aiding in experiment interpretation.
Water encapsulated in such a cell mimic exhibits a surprisingly low dielectric constant, yet fast collective dynamics. In elucidating these observations, we show that dielectric relaxation spectroscopy (DRS) is an excellent complement to more well-known single-particle methods since it is able to capture important cross-correlations of different molecules as well. [1,2,3]
Biological cell environments are inherently complex and heterogeneous, and so are the spatially resolved hydration dynamics of biomacromolecules. To date, these site-specific hydration dynamics are studied via the solute hydrogen-water nuclear Overhauser effect (NOE) crosspeaks.
We show that in reverse micelles, these cross-peaks do not only reveal biomolecule surface hydration dynamics, but may also serve as a microscope into the cellular situation of the biomolecule itself. Furthermore, we address the long-standing debate about the long-ranged – thus in principle unspecific – nature of the intermolecular NOE. We explain which measureable observables are specific to the biomolecule hydration layer and which are not.[4]

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Modelling Reaction Pathways of Constituents in the Interstellar Medium

Anita Rágyanszki[1], Aristo Kong[2], René Fournier[1]

[1] Department of Chemistry, York University, Toronto, ON, Canada.

2 Department of Chemistry, University of Toronto, Toronto. ON, Canada

Corresponding author: a.ragyanszki@utoronto.ca

Life as we know it is the result of billions of years of evolution, from the very first microorganisms that were able to flourish in the harsh environment of early Earth, to the astounding diversity and complexity of today's lifeforms. Although piecing together the process by which we evolved from our early ancestors is facilitated by records of their existence, understanding how the very first living organisms came into existence is a challenge that is more difficult to solve. These initial building blocks of life, such as nucleotides, which form our DNA, and amino acids, which are the units that come together to form proteins, must have been created very early on and then evolved over time to form complex organisms. One theory of how these organisms came to be is that the molecules that today form the building blocks of life were originally formed in outer space and subsequently transported to Earth, possible via meteorites that landed on its surface.

In the universe, matter is not uniformly distributed. There are regions where matter is concentrated, namely galaxies such as our Milky Way, which occupy only a small portion of the observable, vast space. Between groups of star systems we find the Interstellar Medium (ISM), which possesses special properties that make it ideal for analysing its chemical composition. Chemical species in the ISM contain information about the chemically controlled Universe, secrets of the cosmos, and the origin of the life. Within the ISM we can observe molecular clouds, which are clusters of molecules and particles that have the ability to interact with each other. Plenty of molecules have been detected in molecular clouds, specifically in dense clouds, in interstellar mediums in the last 100 years. Yet, the path that molecules undertake during their formation from smaller component particles in ISM remain unclear.

The goal is to develop a new chemical model to describe all the possible reaction pathways, that can be undertaken by molecules found in the ISM; and investigate what sort of chemistry led specifically to the building blocks of biology. The aim is to introduce a better model to solve astrochemical problems. We hope to also find answers to the possible formation mechanism of the building blocks of the life, as well as the possibility for the existence of biomolecules that have not been detected in ISM.

The Liquid State of Proteins

Régis Pomès

Molecular Structure and Function, Hospital for Sick Children, and Department of Biochemistry, University of Toronto, Ontario, Canada

Although it was long thought that proteins must adopt a well-defined three-dimensional structure to perform their biological function, it is now known that many proteins are at least partly disordered in their functional state. Even more remarkably, certain disordered proteins such as elastin have the capacity to self-assemble and separate into a liquid phase. In the aggregated state, elastin fulfills a vital role by imparting extensibility, elastic recoil, and resilience to diverse tissues including arterial walls, skin, lung alveoli, and the uterus. Understanding the molecular determinants of these properties has the potential to help in the rational design of useful biomimetic materials such as vascular grafts or artificial skin.

Despite the biological importance of elastin and over eighty years of study, there is still no consensus model for its structure. We used massive computing to model the microscopic structure of elastin. Molecular dynamics simulations exceeding 0.2 ms afford insight into the structural ensemble of elastin-like peptides. Results demonstrate that the hydrophobic domains of elastin are structurally disordered even when assembled together, like a bag of snakes or a plate of spaghetti. Consistent with the entropic nature of elastic recoil, the aggregated state is stabilized both by the hydrophobic effect and by an increase in conformational entropy upon self-assembly. This highly-disordered state underlies the two remarkable properties of elastin, its capacity to separate into a liquid phase and to undergo elastic recoil. The structural ensemble of the elastin-like aggregate obtained here provides the first atomistic view into what may be called the liquid state of proteins.

Keywords: protein phase separation, structural disorder, elastin, self-assembled elastomers, polymer melt.

Structural and functional analysis of interactions between subunits of TRK channel by MD

Natalia Kulik[1], Jost Ludwig[1], Claudia Fernanda Pena-Sulantay[2]

[1] Center for Nanobiology and Structural Biology, Institute of Microbiology, Academy of Sciences of the Czech Republic, 37333, Nové Hrady, Czech Republic, Zamek 136

[2] Department of Chemical and Biomolecular Engineering, University of Connecticut, Storrs, Connecticut 06269

Corresponding author: kulik@nh.cas.cz

Potassium ions are known to play crucial role in cell physiology, especially in membrane processes. *Saccharomyces cerevisiae* demonstrate ability to grow in a wide range of K+ concentrations and are used as a model organism for TRK channel study.

The structure of Trk1 is thought to consist of two (or according to other computational data four [1]) identical protomers (M1PM2 element), each of them containing four transmembrane domains (A-D) on one peptide chain. Trk channels cannot only mediate K^+ translocation but are also able to promote the flux of Cl^- and other anions across the plasma membrane [2, 3]. It will require presence of an additional pore and it could have a tetrameric composition in which a central inter-domain pore is formed.

The main goal of our work is to gain fundamental knowledge about the functional structure of this channel, identify role of selected residues in ion translocation by computational methods. MD simulation and modeling were used to build different compositions of TRK multimeters and equilibrate complexes. Systems were simulated in POPC membrane by GROMACS with CHARMM force field [4]. Stability of multimer structures and formation of inter-domain pore was analyzed.

We have found that stable inter domain channels are not fully formed in dimers, but in tetramers C and B. Selected complexes were assumed for further confirmation by experimental BiFC methods. To apply it we need identified water exposed residues for attachment of GFP proteins, predict Gly-tag length. To complete previous model [5] we built lost intracellular loops by *ab initio* modeling and proposed for gene expression.

As far as we didn't observed ion tanslocation through membrane during unrestrained MD we applied additional force to check ability of selected multimers to permit ion translocation.

Additionally effect of choline ions in potassium attraction to the channel has been studied. Choline ions competitively inhibit attraction of potassium ions mainly through the binding close to the pore.

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Simulating Biological Systems Coupling Particles and Fields with Molecular Dynamics

Michele Cascella

Department of Chemistry, and Hylleraas Centre for Quantum Molecular Sciences

University of Oslo, Norway

The hybrid particle-_eld with molecular dynamics (hPF-MD) is a newly-established methodology based on density-functional potentials for the simulations of molecular systems [1]. Thanks to its low computational costs, hPF-MD is capable of treating large-scale soft matter systems using relatively small high-performance architectures [2]. As case examples, I will _rst present the _rst hPF-MD model for peptides, showing how it is able to sculpt the main features of the folding diagram for model hydrophobic-polar sequences [3]. Then, I will introduce advances in the fundamental electrostatic theory for density-_eld in both homogeneous and non-homogeneous dielectric [4]. This is a crucial ingredient to expand the application range of hPF-MD to a large variety of biological systems, which are characterized by a strong polar/ionic character. I will show how they can be e_ectively used to simulate poly-electrolyte systems like charged surfactants or polar-apolar mixtures [5].

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Significance of π-π Interactions in the Phase Separation of Intrinsically Disordered Proteins

Andrea Guljas[1,2], Julie D. Forman-Kay[1,2], Robert M. Vernon[2], Régis Pomès[1,2]

[1] Department of Biochemistry, University of Toronto, 1 King's College Cir, M5S 1A8, Toronto, ON, Canada

[2] Department of Molecular Medicine, Hospital for Sick Children, 686 Bay St, M5G 0A4, Toronto, ON, Canada

Protein liquid-liquid phase separation (LLPS) is an important feature of cellular function that involves the self-association of proteins into biomolecular condensates, including membraneless organelles and biomaterials. Many proteins that undergo LLPS contain low complexity intrinsically disordered regions (IDRs) that are enriched in π-orbital-containing groups. Data mining of high-resolution structures of folded proteins in the protein data bank (PDB) showed that the frequency of occurrence of planar π-π interactions increases for highly solvated regions not involved in regular secondary structure, pointing to the likely importance of π-π interactions in IDRs. This, together with the ability to identify many phase-separating proteins based on predicted long-range π-π contacts, suggests that π-π interactions play a significant role in phase separation [1]. Despite these statistical findings, the structural and energetic properties of π-π interactions of IDRs that enable phase separation are poorly understood. We examine this problem by investigating π-π interactions between amino acid residues, with the goal of better understanding the structural and physico-chemical basis of LLPS of IDRs.

We analyze the PDB to extract statistical information regarding the relative positions and orientations of each pair of amino acids, including the distances between sp2-hybridized planes and their relative orientations. Next, we conduct quantum chemical calculations to characterize the energies of π-π interactions between residues. Linking these calculations to our statistical data will provide insights into the contribution of π-π stacking to intra- and inter-molecular interactions of proteins, enabling more quantitative description of IDRs and their involvement in LLPS.

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Structure and reactivity of aptamers and selected molecular systems in the pathological form of prions

Milan Melicherčík, Ján Urban and Pavel Mach

Faculty of Mathematics, Physics and Informatics, Comenius University in Bratislava, Slovakia

Knowledge of the structure of biologically active substances is tightly connected with knowing their behaviour at molecular level. The same can be stated for prions – proteins whose changed structure causes a change of their biological character [1]. This pathological change is responsible for transmissible spongiform encephalopathies that form a group of fatal degenerative diseases of the *central nervous system of humans and some species of mammals.*

*A*ptamers are single-stranded oligonucleotides whose affinity and selectivity to bind the targets make them very attractive. Their use as molecular recognition elements has motivated many theoretical and experimental papers. Several RNA aptamers have been selected that bind with high affinity to PrPc [2].

Our contribution is oriented to the application of theoretical methods on the study of selected prion sequences with aptamers as well as selected molecules

Molecular dynamics simulations (MD) with as precise as possible description of interactions and quantum chemical calculations have been applied for the study of the structure and interaction model systems. The obtained results are discussed.

Acknowledgements

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Structure, functional characterization and dynamics of a novel domain of the motor subunit of the Type I restriction enzyme EcoR124 involved in complex assembly and DNA binding.

Rudi H. Ettrich

College of Biomedical Sciences, Larkin University, Miami, FL

The Type I restriction-modification enzyme EcoR124 is a pentameric complex consisting of one specificity subunit, two methylation subunits and two motor subunits (HsdR) that can recognize specific DNA sequences and perform double-stranded DNA cleavage and modification. If the complex recognizes invading unmethylated DNA the complex starts to translocate over thousands of bp followed by consequent cleavage of the DNA non-specifically at distant sites. Although EcoR124 is one of the better-studied Type I restriction-modification enzymes, its structural and functional complexity is evident from results of over half a century of research, EcoR124 still presents many challenges including missing structural information. While the structure of motor subunit HsdR, responsible for core functions such as DNA translocation and cleavage, was solved around 10 years ago [1], a large part of the C-terminus remained unresolved in all available crystal structures to date. In all crystals structures so far four domains form a square planar arrangement and the unresolved part of the C-terminal was predicted to be all helical and enhance the fourth domain [2]. The crystal structure of the C-terminus of HsdR, refined to 2.45 Å resolution, is presented and reveals that this part of the protein forms an independent C-terminal domain, which displays a unique α-helical fold. The C-terminal domain structure was resolved applying a crystallographic chaperone approach: by fusion of the C-terminal 152 amino acids of HsdR to the GFP variant pHluorin [3], overexpression, crystallization and phasing by molecular replacement were successfully accomplished. The full-length HsdR model [4], produced by combining an existing wild-type structure and the herein determined C-terminal domain reveals a possible DNA binding groove lined by positively charged residues. *In vivo* and *in vitro* assays with the C-terminus deletion mutant of HsdR support the idea that this domain is involved in DNA binding and assembly of the whole complex. Conserved residues identified though sequence analysis in the C-terminal domain may play a key role in protein-protein and protein-DNA interactions. Hence, the motor subunit of EcoR124 is comprised of five structural and functional domains and the fifth, C-terminal domain reveals a novel fold characterized by four conserved motifs in subfamily IC. Computational modeling including molecular dynamics suggested the possible role of C-terminal domain in binding and positioning of DNA to the catalytic residue during the cleavage activity.

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Biomolecular Interactions in Ionic Liquids

Babak Minofar [1,2]

[1] a Center for Nanobiology and Structural Biology, Institute of Microbiology, Academy of Sciences of the Czech Republic, NovéHrady, Czech Republic b

[2] Faculty of Science, University of South Bohemia, Branišovská 1760, 37005 ČeskéBudějovice, Czech Republice

Ionic liquids due to their special properties became very attractive for many applications such as in separation process, catalysis and biochemistry. Aqueous solution of ionic liquids has strong effect on structure and dynamics of biomolecules and influence folding/unfolding, accelerating/retarding enzymatic catalytic reactions. Understanding the role of hydrated ionic liquids on biomolecules in molecular level is crucial because ionic liquids are considered to be as green solvents. Solvation of biomolecules in aqueous solution of ionic liquids change the structural and dynamical properties of biomolecules by influencing stabilization, aggregation, solubility or folding/unfolding. Also such media has effect on enzymatic reaction by influencing the activation energy barrier which gives molecular picture of enzymatic reactions in non-aqueous media. Rate of many reactions can be altered by addition of solvents by charge delocalization of transition state or hydrogen bonds. In order to rationalize solvation and dynamics of biomolecules in ionic liquids, MD simulations have been used. MD simulations can give static and dynamical picture of biomolecules in hydrated ionic liquids solutions.

We have studied the interaction of ionic liquids with formate dehydrogenases enzyme which revealed that in low concentrations of some ionic liquids the activity of enzyme can be enhanced while some other ionic liquids with anions such as acetate ion due to completion with substrate can decrease the activity of enzyme.[1]

In this contribution the influence of ionic liquids on properties of aqueous solutions and structure and dynamics of biomolecules in ionic liquids will be discussed.

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Glycerol carbonate as a fuel additive for a sustainable future

Milán Szőri[1], Binod Raj Giri[2], Zhandong Wang[2], Alaaeldin E. Dawood[2], Béla Viskolcz[1] and Aamir Farooq[2]

[1]Institute of Chemistry, University of Miskolc, H-3515 Miskolc, Egyetemváros A/4., Hungary.

[2]King Abdullah University of Science and Technology (KAUST), Clean Combustion Research Center, Physical Sciences and Engineering Division, 23955-6900, Thuwal, Saudi Arabia.

Corresponding author: milan.szori@uni-miskolc.hu

Policymakers and researchers have been considering a shift from conventional fossil fuels to renewable sources due to the growing concerns over global warming and diminishing oil reserves. Biodiesel, a renewable bio-driven fuel, can be derived from vegetable oils and animal fats, and is considered to be bio-degradable, non-toxic and environmentally friendly. The cetane number and calorific power of biodiesel are quite similar to those of conventional diesel. Crude glycerol of about 10–20% by volume appears as a byproduct in biodiesel production. The increasing demand for biodiesel has led to a substantial increase of glycerol supply in the global market and a dramatic fall in the price of glycerol which has warranted alternative uses of glycerol. One potential way to deal with the crude glycerol overflow is to convert it to glycerol carbonate (GC) and use GC as a fuel or fuel additive. Prior studies have indicated that carbonate esters can significantly reduce particulate emissions during engine combustion. In this work, we have explored possible reaction pathways in the initial stage of glycerol carbonate pyrolysis. *Ab initio*/RRKM-master equation methods are employed to differentiate various reaction pathways and to obtain the pressure- and temperature-dependence of the major channels. We have found that glycerol carbonate decomposes almost exclusively to produce CO_2 and 3-hydroxypropanal over 800–2000 K and radical forming channels are unimportant. As 3-hydroxypropanal is one of the main products of GC decomposition, and aldehydes are known to have a very high impact on soot reduction, we conclude that GC has great potential for cleaner combustion as a fuel additive.

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Systematic molecular design

Cheikh Wafaa, Christian Orlando Camacho López, Min-Yen Lu, Attila Surányi, Dániel Pecsmány, Enikő Mester, Béla Fiser, Zsolt Fejes, Milán Szőri, Béla Viskolcz

Department of Chemistry, University of Miskolc , H3519, Miskolc, Egyetemváros 1.

Corresponding author: viskolcz@gmail.com

Polyurethane (PUs) are present in many aspects of everyday lives such as the rigid foam insulation panel in construction, seat cushion in automotive and elastomeric materials in medical industries. Conventional PUs are made from petrochemical based starting materials which raised severe health and environmental concerns. The substitution of petro-based polyols with carbohydrate polyols have shown to improve biodegradability and mechanical properties of PUs. Reaction pathways were examined with density functional theory to design novel environmental friendly polyurethanes. Based on the calculated thermodynamic properties, the reactivity of sugars towards isocyanates was compared. Sugars in Deep Euthectict Solvent form were selected to avoid the solvation problems of biomolecules.

Kinetic parameters of phenyl isocyanate–monoalcohol reactions has been studied using a microreactor system. The monoalcohol components were propan-1-ol, butan-1-ol, propan-2-ol and butan-2-ol. The applied technique provides a simple way to study the effects of various factors (e.g. structure of the isocyanate and the alcohol, temperature, solvents, concentration of reagents, catalysis) on the kinetics of the isocyanate–alcohol reactions. We will also demonstrate to understand the experimental results, based on first principle calculations. The systematic molecular design will be discussed.

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ABSTRACTS OF POSTER PRESENTATIONS

The autors of the abstracts bear the full responsibility for the scientific and linguistic content.

Excited state dynamics of conjugated polyenes
Ab-initio and semiempirical calculation of electronic absorption spectra

Jaroslav V. Burda, Filip Šebesta, and Radim Cajzl

Faculty of Mathematics and Physics, Charles University, Ke Karlovu 3,121 16 Prague 2, Czech Republic.

Corresponding author: burda@karlova.mff.cuni.cz

Correct quantum chemical calculation of absorption spectra and excited state dynamics of linear conjugated polyenes has been a challenging task for long decades. Here, we present an extensive computational study describing properties of linear conjugated polyenes from ethane up to polyene with 22 carbon atoms in the main chain. For calculation of the calculation of electronic absorption spectra we use many ab-initio quantum chemical methods, TDDFT approach and semiempirical methods. These static calculations were a prerequisite for excited state dynamics of said polyenes, which were employed using Tully surface hopping combined with the OM1 method.

This calculation allowed subsequent calculation of excited state dynamics. Here, we obtained reliable mean lifetimes of Ag and Bu excited states for ethylene, butadiene, hexatriene and oktatetraene; moreover, we have an initial guess of these lifetimes for polyenes with 20 and 22 carbon atoms. All of these results are in agreement with experimental data. There is ongoing work focused on refining existing lifetimes and obtaining them for remaining polyenes.

Influence of the preparation technique on the properties of MWCNT/ZnO used as additives for BC hybrid membranes

Bilal El Mrabate[1], Mahitha Udayakumar[1,2], Zoltan Nemeth[1,2]

[1]Institute of Chemistry, University of Miskolc, Miskolc-Egyetemváros, H-3515, Hungary [2] Higher Education and Industry Cooperation Center of Advanced Materials and Intelligent Technologies, University of Miskolc, Miskolc-Egyetemváros, H-3515, Hungary

Corresponding author: elmrabatebilal@gmail.com

Ensuring safe drinking water for millions of people who experience water scarcity around the world is one of the main challenges of the 21st century, in spite of the recent efforts in developing new water treatment systems, the problem of water shortage has not been solved.

This work presents the synthesis of MWCNT-ZnO composites which are used as additives for the preparation of photoactive BC membranes. The MWCNT-ZnO additives were prepared following two different techniques, the solvothermal synthesis and the impregnation technique in both cases the MWCNT content was set to 10%. For the membrane preparation the ratio of the additives (MWCNT-ZnO) was varied as follows: 10%, 20%, 50%, 80% and 90% in order to evaluate the effect of the additives on the final membrane.

The fabricated membranes were characterized by scanning electron microscopy, X-ray diffraction, specific surface area measurement, dynamic light scattering, electrical conductivity, contact angle, mechanical test, Raman spectroscopy. The measurements show that by changing the preparation technique in case of additives different morphologies can be obtained. The membranes which contain additives prepared by solvothermal synthesis present higher electrical conductivity and positive zeta potential values compared to the membranes with additives prepared by impregnation technique.

The membranes will be applied in water treatment for removal of viruses and contaminant such as heavy metals, dyes, bacteriophages using three major parameters, first one the adsorption which is strongly connected to the surface area of the nanohybrids, second parameter is the photocatalytic activity of the ZnO nanoparticles and the third one is the electrostatic interactions between the membrane and the species present in contaminated water which is controlled by the surface charges. By doing this we can ensure the creation of a completely new photoactive nanohybrid membrane which can be applied in the removal of widely contaminants present in water.

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Effective recycling of polyurethane wastes with enhanced CO_2 reduction

Mahitha Udayakumar[1, 2*], Bilal El Mrabate[2], Tamás Koós[3], Katalin Szemmelveisz[3], János Lakatos[2], László Vanyorek[1, 2], Zoltán Németh[1, 2]

[1]Higher Education and Industry Cooperation Center of Advanced Materials and Intelligent Technologies, University of Miskolc, Miskolc-Egyetemváros, H-3515, Hungary.
[2]Institute of Chemistry, University of Miskolc, Miskolc-Egyetemváros, H-3515, Hungary.
[3]Department of Combustion Technology and Thermal Energy, University of Miskolc, Miskolc-Egyetemváros, H-3515, Hungary.

Corresponding author: mahiuday1@gmail.com

Non-graphitic (Glassy) carbon foams were made from the waste polyurethane elastomers and semi-flexible foams by crosslinking the structure with acidified sucrose solution followed by pyrolysis and activation in inert atmospheres like N_2 and CO_2. A higher carbon content of about 99% was attained in a single step carbonization and activation process carried out at 1000 °C in CO_2 atmosphere. Extremely high BET surface area (2127 m^2/g and 2013 m^2/g) of carbon foams were achieved during the single step process. Thermogravimetric (TG) analysis revealed the mass loss and the behaviour of impregnated polyurethane foams at different temperatures in N_2, O_2 and CO_2 atmosphere. The amount of fixed carbon content and the CO_2 production during pyrolysis is calculated using TG curves. X-ray diffraction (XRD) and Raman analysis showed that the carbon foams are non-graphitized and glassy or vitreous in nature. The surface morphology of the carbon foams was investigated by Focus Ion Beam Scanning Electron Microscopy (FIB-SEM) and High Resolution Transmission Electron Microscopy (HRTEM). Other parameters such as pore size distribution, density, electrical conductivity, hardness, strength, contact angle and zeta potential have also been measured. Based on the measured properties, these glassy carbon foams could be a promising material for applications in energy storage devices, adsorption and filtration, catalyst support, high temperature crucibles etc.

Water catalysed reduction of CO_2 to methanol in Aqueous-phase (a quantum chemical study of a mechanism)

Rachid Hadjadj[1], Béla Fiser[1,2], Imre G. Csizmadia[1,3], Béla Viskolcz[1]

[1]Institute of Chemistry, University of Miskolc, Miskolc, Hungary
[2]Ferenc Rákóczi II. Transcarpathian Hungarian Institute, Beregszász, Transcarpathia, Ukraine
[3]Department of Chemistry, University of Toronto, Canada

The energy supply processes are widely recognized as the main cause of the carbon dioxide emissions to the atmosphere inducing detrimental effects such as global warming [1].

The possible solution of this problem can be a common solution to the energy storage difficulties of the renewable energies. Turning carbon dioxide to environmentally fine chemicals such as methanol by storing energy in chemical bonds through hydrogenative reductions can be the most convenient way of storage for the renewable energies [2].

After providing a gas-phase uncatalyzed molecular network of CO_2 hydrogenation in a previous work [3]. we aimed in this project to design a water catalysed molecular network in aqueous-phase described by the molecular ratio of the reactants 1:3 (CO_2 + $3H_2$) leading to methanol and using the Gaussian program package, we calculated the thermodynamic properties of the intermediate species and transition states under the W1 composite method considering water as solvent.

All the calculations were carried out in normal conditions.

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Computer Simulation of Formamide-Water Systems

Bálint Kiss[1,2], Balázs Fábián[3], Abdenacer Idrissi[2], Milán Szőri[1] and Pál Jedlovszky[4]

[1] Institute of Chemistry, University of Miskolc, Egyetemváros A/2, H-3515 Miskolc, Hungary

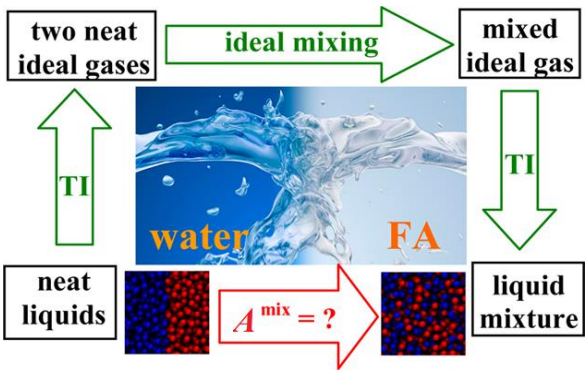
[2] Univ.lille, CNRS, UMR8516 - LASIR- Laboratoire de Spectrochiéie Infrarouge et Raman, F-59000, France

[3] Institute of Organic Chemistry and Biochemistry of the CAS, Flemingovo náměstí 542/2, 166 10 Praha 6, Czech Republic

[4] Department of Chemistry, Eszterházy Károly University, Leányka utca 6, H-3300 Eger, Hungary

kemkissb@uni-miskolc.hu

The combinations of five potential models of formamide and three models of water were tested in Monte Carlo (MC) simulation along an appropriately chosen thermodynamic cycle by using thermodynamic integration.



The mixing of formamide and water is very close to the ideal mixing, since both the energy and entropy of mixing is near to the ideal one in the entire composition range. The Helmholtz free energy of mixing stays always negative in the case of every model combination. Most of the model combinations either show immiscibility, or approach the miscibility limit very closely in certain compositions. Based on the energy of mixing and the miscibility of the model combinations, we selected the CHARMM formamide and SPC/E water models for further simulations of the formamide-water mixtures. Molecular dynamics (MD) simulations were performed in the canonical (N,V,T) ensemble to study the liquid−vapor interface of formamide-water systems. The molecules in the interfacial layer were determined by the ITIM method (Identification of the Truly Interfacial Molecules). The surface molecules indicate the presence of a strong lateral hydrogen-bonding network, in which the water and formamide molecules mix with each other even on the molecular level. The results show no strong adsorption or lateral self-association of the components on the surface. The density profiles indicate only slight surface accumulation of formamide at low formamide concentration. The preferred orientation of the surface molecules is parallel with the liquid surface in the case of both water and formamide molecules. The dynamics of the molecules in the interface layer is also governed by the hydrogen bonds. Thus, the formamide and water molecules stabilizes each other in the interfacial layer, slowing down the lateral diffusion of each other, or even preventing each other from lateral diffusion.

Development of antibacterial additives for polyurethane foams

Emőke Sikora[1,2], Emma Szőri-Dorogházi[1,2], Lilla Varga[1], Béla Viskolcz[1,2], László Vanyorek[1,2]

[1] Institute of Chemistry, University of Miskolc, 3515, Miskolc-Egyetemváros

[2] Higher Education Industry Cooperation Centre, University of Miskolc, 3515, Miskolc-Egyetemváros

Corresponding author: kemsik@uni-miskolc.hu

Polyurethanes (PU) are widely used in everyday life, for example PU are used to make mattresses, car seats, sponges, etc. If antibacterial properties could be given to PU, it could be beneficial in medical, public transport or household fields.

In our experiments, antibacterial Ag nanoparticle-containing PU foams were developed. Different Ag additives were made by chemical reduction techniques. Based on electron microscope images the average diameter of AgNPs was 12,14 nm. The XRD results proved, that elemental silver has been prepared. Escherichia coli DH5α strains were used for antibacterial tests. The following four additives showed antibacterial activity: gum arabic/AgNP, sodium alginate/AgNP, gum arabic/EG/AgNP and PEG/AgNP. In the next step the antibacterial additives were mixed in polyol and MDI to prepare foams. The silver content of the additives and the PU foams was 500 ppm in all cases. The Ag NP-containing additives can be easily dispersed in the polyol phase during the synthesis process, forming homogenous foams. The bacterial testing of the additive-containing PU foams was performed in LB nutrient medium and LB agar plate. As a result, it was found that two foams, gum arabic/AgNP and PEG/AgNP containing foams showed antibacterial effect.

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Synthesis of superparamagnetic iron oxide nanoparticles for DNA purification

Ágnes Mária Ilosvai[1], Emma Szőri-Dorogházi[1,2], Csaba Váradi[1,3], Béla Viskolcz[1,4], László Vanyorek[1,5]

[1] Faculty of Materials Science, Institute of Chemistry, University of Miskolc, 3515, Miskolc, Egyetemváros 1.

[1]E-mail: ilosvaiagnes001@gmail.com [2]E-mail: kemszdoe@uni-miskolc.hu [4]E-mail: bela.viskolcz@uni-miskolc.hu

[5]E-mail: kemvanyi@uni-miskolc.hu

Nowadays DNA purification is still time consuming and sophisticated procedure. Commonly used centrifuge- and column-based protocols require specialised equipment, often use toxic reagents, and are not economically scalable or practical to use in a high-throughput manner. Although it has been known for some time that magnetic beads can provide an elegant answer to these issues. [1]

In order to do this, superparamagnetic iron-oxide nanoparticles were prepared by a combined combustion-sonochemical method in which iron(II)-acetate was used as iron precursor. These iron-containing nanoparticles were first dispersed in polyethylene-glycol (PEG 400) using high-efficient ultrasonic technique. Sonochemical treatment initiated the precipitation of iron hydroxide particles, then the PEG based colloids were burnt to create the iron oxide nanoparticles.

DNA binding capacity of these nanoparticles produced were tested for biological applications such as DNA purification. In this experiments, purified pBAD type vector DNA was used which is a high copy number vector. The plasmid purification from *Escherichia coli* host was performed by a general plasmid purification protocol which combines the conventional alkaline-SDS lysis and a HiBind® technology. In tests of the binding of DNA to the nanoparticles, DNA was detected in the elution fraction, which means that DNA bound reversibly to these nanoparticles. After further improvements, application of such magnetic nanoparticles can provide a method for fast and simple DNA purification from complex samples.

The magnetic nanoparticles were examined by X-ray powder diffractometry (XRD) and high-resolution electron microscopy (HRTEM). In XRD experiment three phases were observed: ferrimagnetic magnetite (Fe_3O_4), antiferromagnetic hematite (α-Fe_2O_3), and ferrimagnetic maghemite (γ-Fe_2O_3). The maghemite phase became the largest in the produced samples (61.8%). Samples were also characterized by Fourier transform infrared spectroscopy (FTIR) and zeta potential measurements, in order to identify functional groups of the surfaces and to examine the surface charge of the nanoparticles. Hydroxyl groups and carbon were identified on the surface of tested nanoparticles. Presence of OH groups on the surface of the magnetic nanoparticles resulted in negative zeta potential due to the deprotonation of hydroxyl groups. This phenomenon gives good dispersibility properties to magnetic nanoparticles in aqueous phase. Between the hydroxyl groups of the nanoparticles and DNA hydrogen bond interaction can be formed, thus magnetic iron oxide based nanoparticles are good candidate for DNA purification applications.

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Development and characterization of biologically active selenium nanoparticles

Ádám Prekob[1*], Viktória Hajdu[1], Béla Viskolcz[1], László Vanyorek[1]

[1] Institute of Chemistry, University of Miskolc, 3515, Miskolc-Egyetemváros

*Corresponding author: kempadam@uni-miskolc.hu

Oxidative stress may cause different diseases in human body such as Alzheimer Disease. The oxidative stress is caused by oxigen-contained free radicals that are neutralized with glutathione peroxidase protein. Selenium is an important element for this mehanism.

In this research, biologically active selenium nanoparticles were synthesised with biocompatible stabilizers. For the synthesis, reductive method was used with sodium-selenite precursor and cystein amino acid as reductive agent. Gum arabic, guar gum, sodium-alginate and polyvinylpyrrolidone were used as non-toxical stabilizers. The stabilizers presence were verified by Fourier Transformation X-ray Spectroscopy (FTIR). Images were made about all the four samples using transmission electronmicroscopy (TEM) for morphology and size characterization. X-ray diffraction (XRD) method was used to evidence the success of the reduction.

The particle size of two samples were under 25 nm, while the other two were under 120 nm. The nanoparticles made colloidical system with the water medium. The particles were in an easy soluble and biocompatible matrix.

Acknowledgments: I would like to thank for István Kocserha and Ferenc Kristály for the XRD measurements, and Tamás Varga for the TEM images. Thank for the help of Béla Viskolcz and László Vanyorek for supporting my work.

Kinetic study of Glycerol Carbonate and OH Radical using Ab initio method

Ravikumar Thangaraj[1], Milan Szori[1]

[1] Institute of Chemistry, University of Miskolc, Miskolc-Egeyetemvaros, H-3515, Hungary

Corresponding author: milan.szori@gmail.com

Global concern on the fossil fuel depletion and enhanced carbon dioxide emission directed towards the search of alternative renewable energy sources. Biodiesel is an efficient substitution for the conventional crude oil derived products. Crude glycerol is one of the major byproducts in biodiesel production and there is an increased stock of glycerol in the global market which reduces its commercial market value. Glycerol carbonate from crude glycerol can be applied as a fuel additive, which can promote cleaner combustion by significantly reducing the production of unburnt carbon, CO and particulate matter. In the past, glycerol carbonate can be used as a fuel additive and analyzed their possible reaction pathways using Ab initio/RRKM-master equation methods [1]. The reaction of hydroxyl radicals with oxygenated fuel for H abstraction is a crucial primary oxidation pathways during combustion [2]. The primary goal of this work is to study the kinetic behavior of Glycerol Carbonate and OH radical using Ab initio method. We have used MP2/cc-pVTZ method to achieve the transition state and CCSD/cc-PVXZ (where X=D,T) methods for Single Point calculations.

On The Comparison of Ab Initio and Classical Polarizable MD Simulations of Ionic Liquids

András Szabadi[1], Christian Schröder[1]

[1] Department of Computational Biological Chemistry, University of Vienna, 1090, Vienna, Währinger Strasse 17, Austria.

Corresponding author: christian.schroeder@univie.ac.at

Ionic liquids (ILs) have received considerable attention in the past two decades, a trend that is likely to continue in the future. Multiple studies investigating the dynamics of these species have been published, using both ab initio [1] and classical molecular dynamics [2] approaches.

In many cases, these two methods can be considered complementary to each other, as the former describes electronic degrees of freedom more accurately, while the latter allows for the investigation of larger systems and longer trajectories at affordable computational costs. Therefore, a combination of the benefits of both strategies would yield a powerful tool for interrogating the dynamics of ILs.

The aim of this study is to reproduce the results of Kirchner *et al*. [1], an ab initio molecular dynamics analysis of 1-butyl-3-methylimidazolium tetrafluoroborate and chloride ([BMIM][BF_4]/[BMIM][Cl]) in an aqueous solution, using a classical polarizable MD force field. Preliminary findings show a considerable crystal field effect, widening the distribution of dipole moments in case of the ab initio trajectories. On the other hand, neglection of polarizability in a classical MD simulation yields unrealistically narrow distributions. Our goal is to arrive at realistic values at low computational costs and large systems, validating our findings via calculating dielectric and IR spectra and comparing them to experiment.

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Computational analysis of conductivity contributions in an ionic liquid mixture

Veronika Zeindlhofer[1], Leopold Zehetner[1,] Werner Paschinger[2,3],

Alexander Bismarck[2], Christian Schröder[1]

[1] Institute of Computational Biological Chemistry, University of Vienna, 1090, Vienna, Währinger Straße 17.

Corresponding author: veronika@mdy.univie.ac.at

[2]Institute of Material Chemistry & Research, University of Vienna, 1090, Vienna, Währinger Straße 42.

[3]Polymer and Composite Engineering (PaCE) Group, Imperial College London, SW7 2AZ, London, South Kensington Campus.

The accurate description of ionic liquid (IL) dynamics using molecular dynamics simulations remains a challenge. ILs are often highly viscous, requiring long simulation times to achieve statistical accuracy. While most nonpolarizable IL force fields can capture the structure of ILs quite well, dynamics are often too slow. Furthermore, an appropriate theoretical framework for the calculation of transport properties is required, since in some ionic liquids classical laws of liquid dynamics such as the Stokes-Einstein relation do not apply. Despite these obstacles, the accurate prediction of IL transport properties is highly desired, considering their popularity for electrochemical applications.

In this work [1], we investigated liquid dynamics in binary IL mixtures of 1-ethyl-3-methylimidazolium tetrafluoroborate and dicyanamide $[C_2mim][BF_4]$/$[C_2mim][N(CN)_2]$ following an experimental study by Hefter *et al.* [2]. We developed a charge-scaled coarse-grained model for the pure ILs that also succeeded at reproducing experimental densities and conductivities of the mixtures. The coarse-graining allowed long enough simulation times to ensure high statistical accuracy of the calculated conductivity. To investigate the interplay of the ion species in the mixture, we calculated self and cross-contributions of the ion species to the total conductivity. Analysis of the ion diffusion also revealed that dynamics in $[C_2mim][BF_4]$/$[C_2mim][N(CN)_2]$ are strongly heterogeneous.

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Elucidating Phospholipid Membrane Binding of DEP domain in the Wnt Signaling Pathway

Francesco L Falginella[1,2], Robert Vácha[1,2,3]

[1] CEITEC – Central European Institute of Technology, Masaryk University, 625 00, Brno, Kamenice 753/5

[2] National Centre for Biomolecular Research, Masaryk University, 625 00, Brno, Kamenice 5

[3] Department of Condensed Matter Physics, Masaryk University, 611 37, Brno, Kotlářská 267/2

Corresponding author: falginella.francesco@gmail.com

Signal transduction represents the mechanism by which cells communicate and interact with the extracellular environment and each other. Wnt signaling pathway is arguably one of the most studied and dissected pathway, due to its high level of conservation among species and involvement in a variety of (patho-)physiological processes [1]. Yet, the molecular events underlying the pathway activation and progression remain mostly elusive. It has been suggested that Dishevelled protein (DVL) plays the key role of a signaling hub for both canonical and non-canonical Wnt signaling branches [2,3]. In particular, a single DVL domain, called DEP (DVL, Egl-10, Pleckstrin), was shown to interact with phospholipid bilayers [4] and Wnt transmembrane receptor, Frizzled [5], triggering DVL recruitment to the plasma membrane (PM) and cytoplasmic signaling activation. By means of all-atom Molecular Dynamics simulations, we elucidated the structural details responsible for DEP-PM interaction and how this event is modulated by membrane lipid composition and the domain post-translational modifications (PTMs). Our results suggest that the recently identified phosphorylation sites on DEP domain [6] do not act as simple electrostatic modulators but rather make the interaction environment dependent.

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Thermal analysis of dimethylsulfoxide action on model biological membranes

Ivan Klbik[1], Igor Maťko[2], Ondrej Šauša[2], Katarína Čechová[2]

[1] *Department of Nuclear Physics and Biophysics, Faculty of Mathematics, Physics and Informatics, Comenius University in Bratislava, 842 48, Bratislava, Slovak Republic*

[2] *Institute of Physics, Slovak Academy of Sciences, 84511, Bratislava, Slovac Republic*

Dimethylsulfoxide is one of the most effective cryoprotective agents used in order to minimalise cryoinjury during cryopreservation [1]. There is no consensus about its molecular action on biological membranes. Certain hypotheses claim dimethylsulfoxide replaces part of water molecules at surface of plasma membrane and form complexes with surounding water layer that shields plasma membrane from impact of ice crystals or stabilise the membrane against osmotical stress during dehydration [1]. Another positive effect could be reduction of dehydration of intracellular membrane systems which may have deleterious consequences on their integrity and function [2].

The aim of this contribution is to examine effect of low concentrated dimethylsulfoxide on thermal behaviour of model systems representing biological membrane using differential scanning calorimetry. Emphasis is put on effect of freeze – thaw cycle upon stability and integrity of model systems. The obtained results are discussed.

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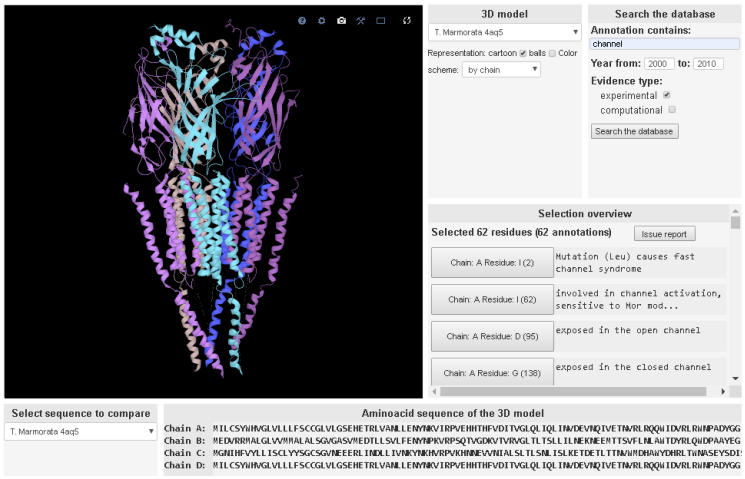
NACHRDB: unraveling the structure-function relationships in nicotinic acetylcholine receptors (nAChRs)

Aliaksei Chareshneu[1,2], Ravi José Tristao Ramos[1,2], Crina-Maria Ionescu[1,2], Jaroslav Koča[1,2]

[1]National Centre for Biomolecular Research, Faculty of Science, Masaryk University, 625 00 Brno, Kamenice 5, Czech Republic, [2]Central European Institute of Technology, Masaryk University, 625 00 Brno, Kamenice 5, Czech Republic,

Corresponding author: 479052@mail.muni.cz

The nicotinic acetylcholine receptor (nAChR) is an evolutionary ancient allosteric membrane protein mediating the synaptic transmission [1]. This prototypic member of the superfamily of pentameric ligand-gated ion-channel is involved in many physiological processes (from learning to motor control), neurological diseases (Alzheimer's and Parkinson's diseases, schizophrenia, epilepsy), and addictions (alcohol, tobacco) [2]. Since its biochemical isolation in 1970 [3], extensive studies generated huge amounts of structural-functional data. However, the cumulative knowledge on nAChRs, spanning ~50 years of research, is not systematically accessible. The wide variety in receptor types, residue numbering schemes, and methods used, together with diverse terminology, the absence of comprehensive structural annotation, and the scattered nature of the existing findings make it harder to summarize the current knowledge and apply it efficiently to promote further discoveries. There is no single resource providing an access to and visualization of such diverse, complex, and extensive information. To fill this gap, we developed NACHRDB



(https://crocodile.ncbr.muni.cz/Apps/NAChRDB/) – a web-accessible manually curated database which not only provides intuitive and fast access to relevant structural-functional data on nAChRs, but also facilitates its interpretation by integrating the residue-level annotations with interactive and highly responsive visualization of sequence and 3D structure. Besides, NACHRDB can provide the users with a prediction of residues potentially relevant for the allosteric regulation of nAChRs, based on the analysis of partial atomic charges profile. We believe that NACHRDB not only can guide the further studies in the field of nAChRs, helping the researchers to detect hitherto unknown association between structure and function of nAChRs, but also serve as a key starting point in unification of the state-of-art knowledge in the broad field of ion channels. NACHRDB is a part of a larger web-based platform of smart bioinformatic tools, called CrocoTools (http://crocodile.ncbr.muni.cz), providing bioinformatics webservers and standalone software to analyze the sequence, structure, and function of the molecules of life. We warmly encourage anyone to try it out and provide suggestions.

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Theoretical study of lincosamide based antibiotics to combat drug resistance

Zeenat Zara[1,2], David Reha[1,2]

[1]*Faculty of Science, University of South Bohemia in Ceske Budejovice, Branišovská 1760, 370 05 České Budějovice, Czech Republic*

[2]*Center for Nanobiology and Structural Biology, Institute of Microbiology of the Czech Academy of Sciences, Zamek 136, 373 33, Nove Hrady, Czech Republic*

Corresponding author: reha@nh.cas.cz

In our project, we have employed tools of computational chemistry to propose new antibiotics which would be effective against drug resistant bacteria. Lincosamide, one of the most prescribed classes of antibiotics, prevents the transpeptidation in the *Staphylococcus aureus [1, 2]* during the peptide chain formation by inhibiting the peptidyltransferase[3]. However, mutations and other rRNA modifications, especially to the base A2085 of the 23S rRNA, have led to a growing resistance problem. **Thus,** we have used molecular dynamics (MD) simulations and quantum mechanics - molecular mechanics (QM/MM) calculations to study the lincosamide and its designed derivative interaction in wild-type A2085, and singly or doubly A2085-methylated mutated *Staphylococcus aureus* ribosomes in order to propose effective drug modifications.

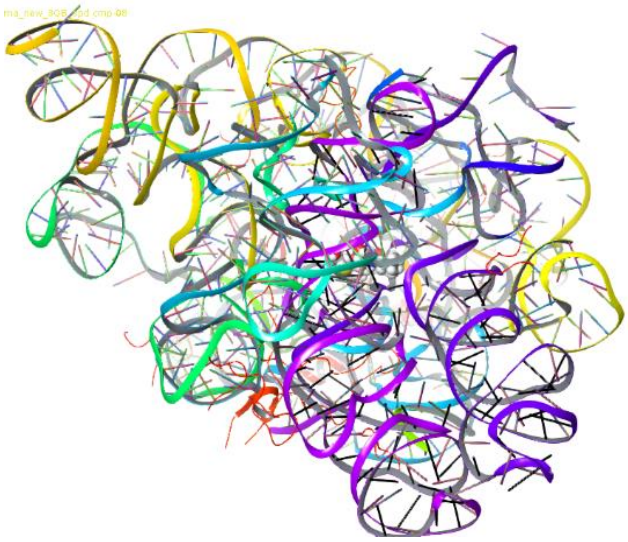

Figure.2 Protein_RNA_SPD and candidate ligand

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Identification of mass-spectrometric ionization of Procainamide labelled glycans by computational chemistry

Atharva Deshpande[1], Andrea Guljas[2,3], Eymann Sheikh[4], Aristo Kong[4], Anita Rágyanszki[4,5], Milán Szőri[6], Csaba Váradi[6], Zsófia Borbála Rózsa[6], Béla Fiser[6,7], Imre G. Csizmadia[4,6], Béla Viskolcz[6]

[1]Department of Chemical and Physical Sciences, University of Toronto, Mississauga, L5L 1C6, Mississauga, 3359 Mississauga Rd

[2] Department of Molecular Medicine, Hospital for Sick Children, 686 Bay St, M5G 0A4, Toronto, ON, Canada

[3] Department of Biochemistry, University of Toronto, 1 King's College Cir, M5S 1A8, Toronto, ON, Canada

[4] Department of Chemistry, University of Toronto St. George, M5S 1A8, Toronto, 27 King's College Cir.

[5] Department of Chemistry, York University, Toronto, ON, Canada.

[6] Institute of Chemistry, University of Miskolc, Miskolc-Egyetemváros, H-3515 Miskolc, Hungary

[7] Ferenc Rákóczi II. Transcarpathian Hungarian Institute, UA-90200 Beregszász, Transcarpathia, Ukraine

Corresponding author: atharva.deshpande@mail.utoronto.ca

N-acetyl-galactoseamine is labelled with Procainamide as a dye. The labeling is done using different catalysts(water and acetic acid) and different solvents(water, DMSO). These different environments are simulated using Computational Chemistry softwares namely Gaussian 09. The level of theory used in Gaussian is B3LYP/6-31G(d). All the calculations are based on this level of theory and the respective graphs of the thermal energies are plotted. It is observed that as the catalyst increases in size, the energy of the reaction pathway decreases and as the solvent medium becomes more polar the energy of the reaction pathway increases for the same catalyst.

After the sugar is labeled using the dye the acetic acid catalysed in DMSO solvent is chosen and ionised for detection with mass spectrometry and fluoroscent detection.

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Performance of 2-Anthranilic Acid (2AA) on Glycan Detection by Mass Spectrometry and Fluorescence Spectroscopy: Computational and Analytical study

Chuanfeng Li[1], Andrea Guljas[2,3], Eymann Sheikh[1], Aristo Kong[1], Anita Rágyanszki[1,4], Milán Szőri[5], Csaba Váradi[5], Zsófia Borbála Rózsa[5], Béla Fiser[5,6], Imre G. Csizmadia[1,5], Béla Viskolcz[5]

[1] Department of Chemistry, University of Toronto St. George, M5S 1A8, Toronto, 27 King's College Cir.

[2] Department of Biochemistry, University of Toronto, 1 King's College Cir, M5S 1A8, Toronto, ON, Canada

[3] Department of Molecular Medicine, Hospital for Sick Children, 686 Bay St, M5G 0A4, Toronto, ON, Canada

[4] Department of Chemistry, York University, Toronto, ON, Canada.

[5] Institute of Chemistry, University of Miskolc, Miskolc-Egyetemváros, H-3515 Miskolc, Hungary

[6] Ferenc Rákóczi II. Transcarpathian Hungarian Institute, UA-90200 Beregszász, Transcarpathia, Ukraine

Corresponding author: chuanfeng.li@mail.utoronto.ca

Mass Spectrometry has become one of the most reliable method in analyzing glycol-components of glycoprotein in replacement of optical methods: liquid chromatography (LC), capillary electrophoresis (CE). Yet the most commonly used fluorescent dye in optical methods, 2-Aminobenzamide, does not perform as well for mass spectrometry due to high ionization energy [1]. Hence, several derivatives were selected and, one of which, 2-Anthranilic Acid, was studied in glycan labelling mechanisms within different solvents (Gas Phase; Water; DMSO)and different catalysts (No catalyst; H2O; AcOH) and, examined the ionization energy and excited state energy using Gaussian 09W to predict it's performance in mass spectrometry. The result showed a decreasing in energy barrier as the size of catalyst increase from H_2O to AcOH, with no significant difference in three different solvents. The ionization energy in DMSO and with AcOH catalyst was calculated. Further researches of comparisons between calculated result and experiment result will be conducted.

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Fine-tuning ionization properties of 2-aminobenzamide through mass spectroscopy in order to generate potential sensitive indicator of glycosylation

Jade Hu[1], Andrea Guljas[2,3], Eymann Sheikh[1], Aristo Kong[1], Anita Rágyanszki[1,4], Milán Szőri[5], Csaba Váradi[5], Zsófia Borbála Rózsa[5], Béla Fiser[5,6], Imre G. Csizmadia[1,5], Béla Viskolcz[5]

[1] Department of Chemistry, University of Toronto St. George, M5S 1A8, Toronto, 27 King's College Cir.

[2] Department of Biochemistry, University of Toronto, 1 King's College Cir, M5S 1A8, Toronto, ON, Canada

[3] Department of Molecular Medicine, Hospital for Sick Children, 686 Bay St, M5G 0A4, Toronto, ON, Canada

[4] Department of Chemistry, York University, Toronto, ON, Canada.

[5] Institute of Chemistry, University of Miskolc, Miskolc-Egyetemváros, H-3515 Miskolc, Hungary

[6] Ferenc Rákóczi II. Transcarpathian Hungarian Institute, UA-90200 Beregszász, Transcarpathia, Ukraine

Corresponding author: jade.hu@mail.utoronto.ca

Glycosylation is a process which produces diverse glycosides through attaching glycans onto biological substances. This is a significant biological process and any defects in it may lead to diseases. Formulating a sensitive indicator which can detect glycosylation would prove ideal in analyzing diseases. One technique in creating an indicator is labelling the glycan with a dye. The following research analyzes the labelling of the glycan proxy ((R)-N-(1-hydroxy-3-oxopropan-2-yl) acetamide) with 2-aminobenzamide through computational methods. The computational method used is Gaussian 09. The labelling mechanism is analyzed using density functional theory under the B3LYP/6-31G(d) level of theory. Further ionization energy was analyzed through using VIP and AIP under the same level of theory. Research goals includes analyzing multiple pathways in different solvents catalyzed by two different compounds in order to determine which pathway is the most energetically favorable. Furthermore, the final compound which is the most energetically stable will be taken into account for mass spectroscopy and ionization in order to further analyze the dyes potential properties of being an indicator for glycosylation.

Acknowledgements

This research was enabled in part by support provided by (name of the regional partner organization) (Web address) and Compute Canada (www.computecanada.ca). The GITDA (Governmental Information-Technology Development Agency, Hungary) is gratefully acknowledged for allocating additional computing resources used in this work. This research was supported by the European Union and the Hungarian State, co-financed by the European Regional Development Fund in the framework of the GINOP-2.3.4-15-2016-00004 project, which aimed to promote the cooperation between the higher education and the industry. BF thanks the financial support by the New National Excellence Programme of the Ministry of Human Capacities (HU) under the ÚNKP-17-4-I-ME/17. Furthermore, the generous support from the Institute of Chemistry, University of Miskolc is gratefully acknowledged.

Growth Mechanism of Benzo(a)pyrene - A Theoretical Study

Edina Reizer[1], Imre G. Csizmadia[1,2], Árpád B. Palotás[3], Károly Nehéz[4], Béla Viskolcz[1] and Béla Fiser[1,5,*]

[1]Institute of Chemistry, University of Miskolc, Miskolc-Egyetemváros, H-3515, Miskolc, Hungary
[2]Department of Chemistry, University of Toronto, Toronto, M5S 1A1, Ontario, Canada
[3]Institute of Energy and Quality Affairs, University of Miskolc, Miskolc-Egyetemváros, H-3515 Miskolc, Hungary
[4]Department of Information Engineering, University of Miskolc, Miskolc-Egyetemváros Informatics Building, H-3515 Miskolc, Hungary
[5]Ferenc Rákóczi II. Transcarpathian Hungarian Institute, Beregszász, 90200 Transcarpathia, Ukraine
* Corresponding author: fiser.bela@gmail.com

In this study, the formation of benzo(a)pyrene was examined which is one of the most toxic polycyclic aromatic hydrocarbon (PAH) formed by incomplete combustion processes. In a total of ten growth pathways were analyzed applying the hydrogen abstraction acetylene addition (HACA) and the Diels-Alder growth mechanisms (Figure 1).

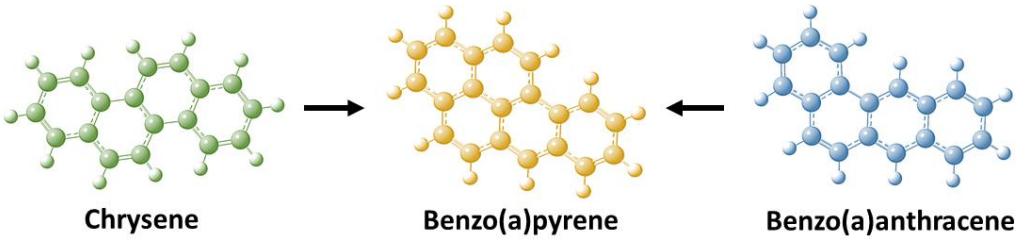

Figure 1: A schematic illustration of the studied reaction mechanism.

The reactions started from chrysene and benzo(a)anthracene, which are less toxic than the final product as they are containing only four aromatic rings. The corresponding thermodynamic properties were determined by hybrid density functional theory [B3LYP/6-31+G(d,p) and M06-2X/6-311++G(d,p)]. The pathways include addition reactions, ring closures, hydrogen abstractions, and intramolecular hydrogen shifts. The obtained results show that energetically the pathways from the two starting materials are very similar to each other, and the benzo(a)pyrene could be reached through the above mentioned steps.

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Polyurethane foam synthesis using sugar-based deep eutectic solvents

Dániel János Pecsmány[1], Enikő Mester[1], Benjámin Jánosi[1], Emma Zhang[1], Koppány Juhász[2], Béla Viskolcz[1], Béla Fiser[1,3]

[1]Institute of Chemistry, University of Miskolc, Miskolc-Egyetemváros, H-3515 Miskolc, Hungary

[2]Department of Industrial Materials Technology, Bay Zoltán Nonprofit Ltd. for Applied Research Engineering Division (BAY-ENG), H-3519 Miskolc, Iglói út 2.

[3]Ferenc Rákóczi II. Transcarpathian Hungarian Institute, UA-90200 Beregszász, Transcarpathia, Ukraine

Corresponding author: pecsmany.daniel@gmail.com

The purpose of this research was to prepare polyurethane foams which are based on ionic liquids (IL or so-called deep eutectic solvents, DES) instead of traditional polyols. To prepare the foams, sugar based ionic liquid was reacted with Ongronat® 2100 (polymeric MDI). IL systems were made by using different sugars (*e.g.* xylitol, fructose) and choline chloride (ChCl). The components were tested with different molar ratios until stable systems were achieved. DMCHA were applied as catalyst in proper percentages. Distilled water was added to the samples which have not contained it already. Different additives such as fillers and chain extenders were also used which can prevent shrinkage of the structure of foams. Some chain extenders can also be useful to promote propagation, because these molecules can increase strength. The foams were more stable within which pentaerythritol has been applied as chain extender. The durability is an issue, but foams with reasonable stability were produced by using sugar based ionic liquids.

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