8TH VISEGRAD SYMPOSIUM ON STRUCTURAL SYSTEMS BIOLOGY

BOOK OF ABSTRACTS & PROGRAM

20TH - 23RD JUNE 2018

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20th - 23rd June 2018
Opatová, Lučenec, Slovakia

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Schedule of Events

Wednesday, 20th June 2018

14:00–18:00 Registraion
18:00–18:10 Conference opening
18:10–18:50 R. Ettrich – Modulation of human ORAI1 channels: modeling and simulations

19:00–20:00 Dinner

20:00–22:00 Poster session

Thursday, 21st June 2018

Chairman: L. Gorb

9:00–9:30 K. V. Venkatechalam – Perspectives on the Evolution of Ligand Binding in Molecular Signaling Versus Enzyme Catalysis: 3'-Phosphoadenosine 5'-Phosphosulfate (PAPS) synthase (PAPSS) Isoforms as an Intermediate Model System
9:30–10:00 N. J. Galant – From Conception to Clinic: Combating Protein Misfolding Diseases Using Conformation-Specific Antibodies
10:00–10:30 J. Ludwig – MIFE and FLISE: Alternative non invasive electro¬physio¬logical methods to analyze ion fluxes across cell membranes

10:30–10:50 Coffee break

Chairman: P. Mach

10:50–11:20 J. Burda – The Description of the Reactions in Solutions with Constant pH
11:20–11:50 L. Gorb – From $(AT)_3$ and $(GC)_3$ DNA mini-helixes to Dickerson dodecamer: results of recent density functional theory calculations
11:50–12:10 Z. Garaiová – Nanoparticles in HIV vaccine development. The interaction with biomimetic membranes.
12:10–12:30 D. Řeha – Computational Study of Interactions of Helicene Derivates with DNA

12:30–14:00 Lunch

14:30–17:00 Sightseeing tour in Lucenec
17:00–20:00 Dinner in brewery restaurant Franz
20:00–22:00 Poster session

Friday, 22nd June 2018

Chaiman: K. V. Venkatechalam

9:00–9:30 I. Jákli – Structure and reactivity properties of asparagine containing motifs in proteins
9:30–10:00 M. Owen – Alzheimer's Lipids: How Amyloid-β Conformation is affected by Lipid Bilayer Composition
10:00–10:30 D. Bonhenry – Simulation of a calcium sensor – STIM

10:30–10:50 Coffee break

Chairman: B. Viskolcz

10:50–11:20 E. Heid – Current advances of atomic polarizability calculations and their relevance for computer simulation
11:20–11:40 A. Rágyanszki – Artificial Neural Networks as a Tool to Describe Conformational Changes
11:40–12:00 A. Guljas – Selection of Candidates for the First Small-Molecule Inhibitor of the Retinoblastoma Binding Protein 4
12:00–12:20 Z. B. Rózsa – Dioxane-induced changes on the interfacial region of phosphatidyl-choline membranes

12:30–14:00 Lunch

Chairman: R. Ettrich

14:00–14:20 B. Fiser – Low-Molecular-Weight Sulphur Containing Biomolecules - A Theoretical Study
14:20–14:40 V. Zayats – Entanglements in transmembrane proteins
14:40–15:00 N. Kulik – Conformational changes in reaction center of PS II upon photochemical reduction of plastoquinones
15:00–15:20 S. K. Pandey – Allosteric activation of Arginine repressor protein by L-arginine
15:20–15:40 F. Šebesta – Interaction of Hydrated Metal Cations with Thymine and Glycylglycine N-methylamide Using DFT and QM/MM MD Approach

18:00– Conference dinner

Saturday, 23rd June 2018

departure

Poster presentations

Poster No.	Author name	Poster title
Wednesday 20:00		
1	M. Aryafard	Molecular dynamic simulation of cellulose dissolution in 1-ethyl-3-methylimidazolium acetate
2	J. Deme	Quantum chemical computations on Diels-Alder reactions
3	R. Deme	N-Protected β-Amino Acid Formation from N-Protected α-Amino Acids via Wolf Rearrangement
4	X. Guo	Multifunctional $C_6H_{14}O$ Chemicals: from Green Energy Storage to Biobased Chemicals
5	D. Kale	Overexpression studies of Saccharomyces cerevisiae K^+ Translocating Membrane Proteins (Trks)
6	R. Kedia	Multifunctional C_4H_8O Bioderived Chemicals: from Green Energy Storage to Biobased Chemicals
7	A. Kong	Sugars in space: quantum chemical study on the formation of glycerone from formaldehyde and hydroxy carbene on interstellar medium dust grains
8	N. Kulik	Computational modeling of efective inhibitors of topoisomerase IA
9	K. Marrs	Bio-based Polyurethanes-A Computational and Experimental Study
10	M. Melicherčík	The Influence of Site Mutations on Activity of XPB Protein
11	M. T. H. Nguyen	Mechanism of the Interaction between Gold (I) Complexes and Tioredoxin reductase (modeled by Cysteine and Selenocysteine)
Thursday 20:00		
12	L. Plačková	Teoretical study of PAPSS1 linkers
13	A. Prekob	Colloid chemical characterization of carbon nano spheres
14	E. Reizer	Computational Study on the Formation of Benzo(a)pyrene
15	A. R. Sampaco III	Building Models for Understanding Peptide Conformations using Artifcial Neural Network
16	E. Sheikh	Quantum Chemical Analysis of the Possible Formation Mechanism of Cyanomethanimine in Dense Molecular Clouds
17	E. Sikora	Chlorate elimination from industrial water, catalyst development and characterization
18	E. Sikora	Development of Bactericidal Polyurethane Additives
19	I. Sukuba	A neural network interface for DL_POLY and its application to liquid water
20	V. Zeindlhofer	A shell-resolved analysis of hydrotropic solvation of cofee ingredients in aqueous mixtures of 1-ethyl-3-methylimidazolium acetate
21	J. Zhang	Amino Acids in Action: Glycine Based Polyurethane
22	B. Zheng	Te Formation of Cyanamide: An Interstellar Prebiotic Molecule

Abstracts of Oral Presentations

Modulation of human ORAI1 channels: modeling and simulations

Daniel Bonhenry[1], Saurabh Kumar Pandey[1], Lydie Plackova[1], David Řeha[1], Irene Frischauf[3], Isabella Derler[3], Rainer Schindl[2], Christoph Romanin[3], Rüdiger H. Ettrich[1]

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Orai1 is a calcium-selective channel located in the plasma membrane, and belongs to the family of calcium release activated channels (CRAC) [1]. Orai1, as component of store-operated calcium entry (SOCE), is activated by the second component of SOCE, STIM1, when intracellular calcium stores are depleted. STIM1, located at the endoplasmatic reticulum (ER), senses levels of calcium in the ER and is activated by calcium store depletion. In turn, calcium influx via Orai1 channel refills calcium levels in the endoplasmic reticulum [2]. Based on the *Drosophila melanogaster* Orai crystal structure [3] a homology model of human Orai1was prepared that includes extracellular and intracellular loops existing only in the human isoform [4]. The sequence and architecture of Orai channels is unique among other ion channels and suggests a novel gating mechanism. The selectivity filter is formed by a ring of six glutamate residues followed by a hydrophobic and consequent basic region further down the pore. The pore extends into cytosol by approximately 20 Å. Using combined experimental and theoretical approaches this study focuses on the central ion pore to investigate the gating mechanism of this unique channel including altered gating of Orai1 mutants occurring in tumor cells [6], the communication between the intracellular loop and the N-terminus [7], or its interaction with STIM1.

References:

[1] M. G. Matias et al "Animal Ca2+ release-Activated Ca2+ (CRAC) Channels Appear to Be Homologous to and Derived from the Ubiquitous Cation Diffusion Facilitators" BMC Research Notes 2010, 3, 158
[2] S. Feske "CRAC channelopathies" Pflugers Archiv : European journal of physiology 2010, 460 (2),417-435
[3] X. Hou et al "Crystal Structure of the Calcium Release-Activated Calcium Channel Orai" Science 2012, 3389 (6112), 1308–1313
[4] I. Frischauf et al "A calcium-accumulating region, CAR, in the channel Orai1 enhances Ca(2+) permeation and SOCE-induced gene transcription" Science Signaling 2015, 8, ra131
[5] S. Feske et al "A mutation in Orai1 causes immune deficiency by abrogating CRAC channel function" Nature 2006, 441, 179-185
[6] Frischauf et al "Transmembrane helix connectivity in Orai1 controls two gates for calcium dependent transcription", Science Signaling 2017, 10 (507): eaao0358..
[7] Fahrner et al "Communication between N-terminus and Loop2 tunes Orai activation" The Journal of Biological Chemistry 2018, 293: 1271-1285.

Perspectives on the Evolution of Ligand Binding in Molecular Signaling Versus Enzyme Catalysis: 3'-Phosphoadenosine 5'-Phosphosulfate (PAPS) synthase (PAPSS) Isoforms as an Intermediate Model System

K.V. Venkatachalam

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3'-Phosphoadenosine 5'-Phosphosulfate (PAPS) synthase (PAPSS) catalyze the formation PAPS in two steps. First inorganic sulfate reacts with alpha-phosphoryl part of ATP to form adenosine 5'-phosphosulfate (APS) and pyrophosphate (PPi) catalyzed by ATP-sulfurylase (ATPS) domain activity of PAPSS. APS released from the ATPS domain is instantaneously bound by APS kinase (APSK) domain of the dimeric PAPSS. The 3'-oxyanion of the APS attacks the gamma-phosphoryl of the new ATP that is now bound to APSK domain. With this nucleophilic attack ATP is cleaved between beta-gamma position to form ADP and PAPS. ATPS being an alpha-beta phosphoryl splitter it has the characteristic HXGH motif and APSK being a beta-gamma splitter has the typical P-loop GXXGXXK motif. There are two isozymes of PAPSS. PAPSS1 located on chromosome 4q25 is predominantly expressed in tissues such as skin and brain. PAPSS2 gene is located on the chromosome 10q23.2-24.3 and is heavily expressed in tissues such as liver, adrenal gland etc. PAPSS2 mRNA is spliced in to two forms 2a and 2b. PAPSS2b differs from 2a in that it has extra pentapeptide sequence GMALP. PAPSS1 and PAPSS2a/b are about 73% identical in amino acid sequences, nevertheless the kinetics of PAPSS formation between these isoforms are distinct. Structural comparisons of PAPSS1 and PAPSS2b would allow to identify the specific features of PAPSS2b. This would then allow to explain the kinetic differences between PAPSS 1 and 2a/b and reveal clues on molecular evolution of binding (Kd/Km) versus catalysis (Kcat). For the sulfurylase half-reaction, previous molecular simulation studies predict that in addition to the characteristic H425NGH428 motif, at least one arginine residue plays a key role in the catalytic reaction. The second oxyanion negative charge is balanced by the positive charge of the arginine nitrogen making it unreactive. Thus, the reactive free oxyanion of the sulfate is facilitated closer to the alpha-phosphoryl for the actual ATPS catalytic reaction to occur. Similarly, with APSK the proposed D1xD2T motif (Venkatachalam et.al. unpublished) and the corresponding molecular details will be resolved. Data from this will allow to elucidate whether the beta-carboxylate anion of D1 or the neighboring D2 would remove the proton from the 3'-OH ribose of APS making it an oxyanion nucleophile which would then react with gamma-phosphate of ATP to form PAPS and ADP. In addition, mutants of H425NGH428 motif are being studied by X-ray crystallography to understand the rationale behind increased activity of N426-K and null backward activity of G427-A. In summary, this talk will focus on some of the perspectives of enzyme binding versus catalysis using PAPSS1 and PAPSS2b as an intermediate between real binding seen with signaling versus molecules/macromolecules that are destined to be involved in catalysis.

From Conception to Clinic: Combating Protein Misfolding Diseases Using Conformation-Specific Antibodies

Natalie J. Galant, Avi Chakrabartty

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Protein misfolding diseases are caused by proteins in the body which can misfold and disrupt organ function. Many of these diseases, such as transthyretin (ATTR) amyloidosis, are nearly impossible to diagnose and patients are only identified at advanced stages when little or no time is left for treatment. We have recently developed conformation-specific antibodies which can potentially treat and/or diagnose ATTR amyloidosis. These antibodies specifically bind to the disease-associated forms of by recognition of a cryptotope (an epitope normally buried and inaccessible in the native protein, but exposed in its altered conformation). From project conception to eventual commercialization and FDA-approved clinical trials, we will discuss the trajectory of this immunotherapeutic drug pipeline.

Acknowledgements: *This work was supported by the Ted Rogers Centre for Heart Research.*

MIFE and FLISE: Alternative non invasive electro-physiological methods to analyze ion fluxes across cell membranes

Jost Ludwig

Center for Nanobiology and Structural Biology, Institute of Microbiology, ASCR, v.v i., Czech Republic

"Classical" electrophysiology like patch- (voltage- and current-) clamp is an invaluable tool to measure ion fluxes across cell membranes and elucidate mechanism and regulation of ion translocating systems. However, patch clamp requires the formation of a "Giga-seal" between membrane and pipette and thus requires (enzymatic) removal of any kind of cell wall if present (like in plant and fungal cells). Another possible disadvantage is in some cases the fact that patch clamp is (mostly) invasive and in many cases the physiological cell interior is more or less replaced with the pipette filling solution. Furthermore, the ion(s) carrying the measured currents can only be determined indirectly by measurements using different pipette- and bath solutions.

MIFE (Microelectrode Flux Estimation) and FLISE (Flux estimation using ion selective electrodes) are two non invasive methods based on measuring the concentration changes of ions that can be used to determine the net fluxes of specific ions through tissues, monolayers of cells (MIFE) or cells in suspension (FLISE) without any treatment [1]. As an example, ion flux measurements across the plasma membrane of yeast cells and their dependence on the function of the S. cerevisiae main K^+-translocation system Trk1 will be given [2].

Acknowledgments: *This work has been funded by Grant Agency of the Czech Republic (1619221S) and C4Sys - Center For Systems Biology In The Czech Republic (LM2015055)*

References:

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The Description of the Reactions in Solutions with Constant pH

Jaroslav V. Burda

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Solutions with constant pH represent from the thermodynamic point necessity of additional Legendre transformation of Gibbs free energy to the new thermodynamic Gibbs-Alberty potential:

$$G' = G - n_C(H)\mu(H^+)$$

Within this description, chemical reactions do not run into the equilibrium concentrations as suppose according to the Guldberg-Waage dynamic principle but to the chosen value of hydrogen chemical potential. In this way modified equilibrium constant K' has to be defined as a function of proton concentration in solution:

$$K' = \frac{(\sum[C])(\sum[D])}{(\sum[A])(\sum[B])}.$$

According to this description, reaction is no longer dependent of concrete molecular forms taken into the equilibrium constant but pH dependent mixture of all relevant forms, which vary by number of active protons.

For the pH dependent rate constants, the formalism of branch reaction need to be considered, e.g. if B and C in the following reactions differ by one active proton:
then the product ratio can be evaluated in the form of effective rate constants:

$$A + B \overset{k_1}{\rightarrow} R \quad \text{and} \quad A + C \overset{k_2}{\rightarrow} S$$

All forms with different number of active protons represent individual reaction channels mutually interconnected via Henderson-Hasselbalch equation of fast acid-base equilibrium:

$$\frac{[R]}{[S]} = \frac{k_1.[B]}{k_2.[C]} = \frac{k_1.[HB]}{k_2.[B^-]} = \frac{k_1}{k_2}.K_a.[H^+] = \frac{x_1.k_1}{x_2.k_2} = \frac{k_1^{eff}}{k_2^{eff}}$$

For this kind of description all dominant forms must be included together with some additional forms in those cases the transition barriers are sufficiently low (with relatively high rate constants) despite of possibly low concentrations of corresponding forms.

$$\mathrm{pK_a} = \mathrm{pH} + \log\left(\frac{[\mathrm{HA}]}{[\mathrm{A^-}]}\right)$$

Several examples will be presented to demonstrate both thermodynamic and kinetic formalisms.

From $(AT)_3$ and $(GC)_3$ DNA mini-helixes to Dickerson dodecamer: results of recent density functional theory calculations

Leonid Gorb

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We present the results of the first comprehensive DFT study of the following DNA mini-helixes: $(AT)_3$, $(GC)_3$, $(AT)_5$, $(GC)_5$ and Dickerson dodecamer immersed in vacuum or in water bulk (CPCM model of continuum type). The results are presented in the form of the analysis of geometrical parameters of such DNA building blocks as DNA-bases, nucleosides and nucleotides, and the type of specific hydration of minor and major DNA groves. Also, the stability of Dickerson dodecamer, that contains 'rare' tautomeric forms, is compared with the stability of a conical dodecamer. The comparison of obtained data with the results related to different DNA building blocks (i.e. DNA bases, nucleotides. DNA mini-helixes, etc.) is presented.

The optimization of the geometry has been performed at DFT/B97-D3 level augmented by def2-SVP basis set.

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[1] Wing, R., Drew, H., Takano, T., Broka, C., Tanaka, S., Itakura, K., Dickerson R.E., Nature 1980, 287, 755 - 758; doi:10.1038/287755a0

Nanoparticles in HIV vaccine development. The interaction with biomimetic membranes.

Zuzana Garaiová[1], Sopio Melikishvili[1], Sylwia Michlewska[2,3], Maksim Ionov[2], Elzbieta Pedziwiatr-Werbicka[2], Iveta Waczulikova[1], Maria Angeles Muñoz-Fernández[4], Rafael Gomez-Ramirez[5], Francisco Javier de la Mata[5], Maria Bryszewska[2], Tibor Hianik[1]

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The vaccine against HIV virus is still not available. Various kinds of strategies are being investigated within this field. We will report the application of nanoparticles as possible adjuvants for improved delivery of antigens towards immune cells. As a novel adjuvants, carbosilane based dendrimers (CBDs) were studied for complexation with peptides derived from HIV virus [1]. Synthetic peptides as antigenic structures represent one of the potential vaccination approaches mainly due to their simple production, precise characterization and relative safety. However, peptides by themselves are often unstable and prone to enzymatic degradation. In addition, they are poorly immunogenic, necessitating the need for an adjuvant and a specialised delivery system. For this reasons HIV-derived peptides were complexed with CBDs nanoparticles followed by the study of their interaction with the model cell membranes. Using various biomimetic membranes such as Langmuir monolayers or lipid vesicles, we have shown that HIV peptides when being complexed with CBDs nanoparticles interact stronger with lipid molecules than the uncomplexed ones. The interaction depends on the type of nanoparticles as well as on the lipid composition [2]. CBDs nanoparticles can be considered as carriers for HIV synthetic peptides, and thus as potential vaccination composite.

Acknowledgements: *This work was supported by Slovak Research and Development Agency, APVV (projects No. APVV-14-0267 and SK-PL-2015-0021), Polish Ministry of Science and Higher Education and VEGA 1/0152/15.*

References:

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[2] Melikishvili S, et al. The effect of polyethylene glycol-modified lipids on the interaction of HIV-1 derived peptide-dendrimer complexes with lipid membranes. Biochim. Biophys. Acta. 2016; 1858(12):3005-3016. Available from: doi:10.1016/j.bbamem.2016.09.005.

Computational Study of Interactions of Helicene Derivates with DNA

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[1]*Center for Nanobiology and Structural Biology, Institute of Microbiology of CAS, Nové Hrady, Czech Republic*
[2]*Faculty of Science, University of South Bohemia in České Budějovice, Czech Republic*

The functioning and structural stability of DNA are strictly regulated and affected by DNA-binding enzymes and variety of low-molecular ligands. The one of the well known examples of DNA binding compounds is DNA intercalators, mainly industrial toxins or frequently used cancerostatic drugs. These planar polyaromatic compounds interact with DNA primarily via intercalation mode, which is principle of their genotoxic effects or curative properties. Helicenes and their derivates ares example of non-planar polyaromatic DNA binding molecules which are helical in opposite to well known planar polyaromatics DNA intercalators. In general, there is a lack of knowledge on DNA interactions with helicenes containing polar substitutions, which are indtroduced in order to increase solulability of helicens in polar solvents.

In this study, we have investigated the interaction of the recently developed water-soluble cationic [6]helicene derivative (1-butyl-3-(2-methyl[6]helicenyl)-imidazolium bromide) with single-stranded and double-stranded DNA (primary sequence of one of the strands AAC CCA GAT GTC CTA CAG GAT AGC TCG CAG) be means of MD simulations and quantum chemistry calculations. This computational study was performed in collaboration with experimental group from Palacky University, Olomouc, CZ. In this study we have focus on investigation of different binding motifs of both enantiomers of our helicene derivate and comparing the results with unsubstituted [6]helicene.

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Structure and reactivity properties of asparagine containing motifs in proteins

András Láng, Imre Jákli and András Perczel

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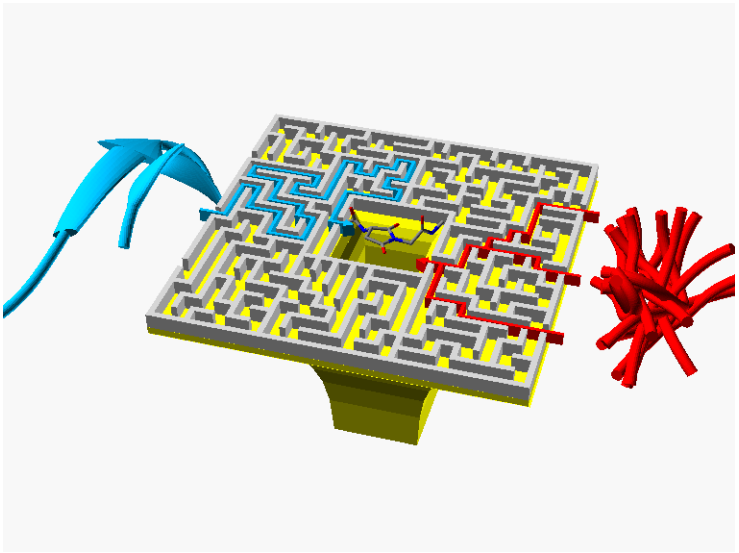
Protein integrity over time is vital for its function. Spontaneous isomerization of Asn or Asp through a succinimide intermediate occurs within days at biological conditions, when –Asn–Gly– or –Asp–Gly– sequence motif present in the protein. Isomerization is ticking as a "time bomb" at a characteristic rate constant threatening protein integrity though remains hidden until changes become prevalent. The ring opening of succinimide intermediate produced a ratio of 4:1 for β-Asp-Gly and α-Asp-Gly. According to our results increase of temperature, pH and backbone mobility makes the isomerization faster. If a positively charged residue is present after the glycine residue, (e.g Arg or Lys), then the speed will increase further. In contrast to that, the larger sidechains or well defined 3D structure, acts as a protective factor by shielding the "Achilles' heel" of proteins, but hardly stops isomerization to occur. Protection of these sites is critical for long-lived proteins such as hemoglobin, crystallin of erythrocytes, eye and neuroglias. Present work attempts to reveal the structural reasons behind this reaction and the possible defense against it using structural databases and computational tools, supported by NMR experimental data of more than 30 polypeptide models.



Alzheimer's Lipids: How Amyloid-β Conformation is affected by Lipid Bilayer Composition

Michael C. Owen[1,2], Waldemar Kulig[3], Chetan Poojari[3,4], Tomasz Rog[3,4], Birgit Strodel[1,5]

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To resolve the contribution of ceramide-containing lipids to the aggregation of the amyloid-β protein into β-sheet rich toxic oligomers, we employed molecular dynamics simulations to study the effect of cholesterol-containing bilayers comprised of POPC (70% POPC, and 30% cholesterol) and physiologically relevant concentrations of sphingomyelin (SM) (30% SM, 40% POPC, and 30% cholesterol), and the GM1 ganglioside (5% GM1, 70% POPC, and 25% cholesterol). The increased bilayer rigidity provided by SM (and to a lesser degree, GM1) reduced the interactions between the SM-enriched bilayer and the N-terminus of Aβ42 (and also residues Ser26, Asn27, and Lys28), which facilitated the formation of a β-sheet in the normally disordered N-terminal region. Aβ42 remained anchored to the SM-enriched bilayer through hydrogen bonds with the side chain of Arg5. With β-sheets in the at the N and C termini, the structure of Aβ42 in the sphingomyelin-enriched bilayer most resembles β-sheet-rich structures found in higher-ordered Aβ fibrils. Conversely, when bound to a bilayer comprised of 5% GM1, the conformation remained similar to that observed in the absence of GM1, with Aβ42 only making contact with one or two GM1 molecules.

Simulation of a calcium sensor – STIM

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The stromal interaction molecule (STIM) is a protein located at the level of the membrane of the cellular calcium stores, namely the endoplasmic reticulum (ER) or sarcoplasmic reticulum (SR). This protein is able to sense the level of calcium ions within the stores and to trigger the activation of calcium channels located in the plasma membrane (PM) upon depletion of calcium [1].

STIM is a single-pass transmembrane protein. Its N-terminal is located within the luminal part of the ER while the C-terminal is bathing in the cytosol. The N-terminal has the ability to probe the calcium level within the ER thanks to EF-hand calcium binding motifs [2]. On the other side of the membrane, the cytosolic part holds the domain able to bind and activate [3] target calcium-channels in the plasma membrane depending on the calcium level within the ER.

In non-excitable cells, such as lymphocytes, mutations impairing the proper function of this protein lead to immunodeficiency, autoimmune disease or myopathy [4].

Molecular dynamics simulations of wild-type phenotype as well as mutants are used to explore how this protein is sensitive to luminal Ca^{2+} levels and initiates a cascade of events leading to the refilling of the calcium stores.

References:

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Current advances of atomic polarizability calculations and their relevance for computer simulation

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Polarizable molecular dynamics simulations of biologically relevant systems have become increasingly important in recent years. Such simulations require atomic polarizabilities as additional force field parameters, but those are somewhat difficult to obtain. Statistically averaged atomic polarizabilities decomposed via regression from the experimental density and refractive index have been used extensively to characterize the electronic properties of organic solvents and ionic liquids [1,2]. Possible applications are the prediction of the density and refractive index of yet unknown ionic liquids [2] and the setup of polarizable force fields. However, the peculiarities of a molecule are disregarded when using averaged polarizabilities and may not be represented well if the molecule differs largely from the training set. Furthermore, the electronic properties of solutes in solution cannot be described, since density and refractive index have only been decomposed for bulk phase so far. Also polarizabilities of excited states are out of reach. Thus, we developed a quantum mechanical, ab-initio method to calculate atomic polarizabilities of arbitrary molecules [3,4]. The method was shown to correctly depict the polarizabilities of common fluorescence chromophores [3] and a variety of ionic liquid [4]. Small to medium sized molecules can thus be characterized in detail using minutes to few hours of computation time at high levels of theory. This new perspective on atomic polarizabilities and its effects on computer simulation and force field development are discussed.

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Artificial Neural Networks as a Tool to Describe Conformational Changes

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The development of advanced computers plays an important role in theoretical and computational chemistry. In the last decade of the 20th century, third generation computers have appeared. This technology presents the opportunity to develop computational artificial intelligence techniques. By harnessing the knowledge machinery that may thus be developed, computational science can be applied to chemistry to aid its progression toward becoming an exact science.

Inspired by biological networks on the brain, Artificial Neural Networks are parallel computing systems consisting of large number of simple processors called neurons that transmit information to each other through their many interconnections. ANN models attempt to use similar "organizational" principles that are believed to be used in the human brain. This system of computation consists the nodes of these networks, which commonly refer to as 'artificial neurons'. ANNs also involve algorithms which are inspired by how neurons interconnect and interact in the brain. They can be used to "teach" computers how to perform complex tasks.

Our research team uses ANNs to discover and understand relationships between molecular geometry and forces acting on the individual atoms. Building on the work of Behler et al. as well as other teams of scientists [1,2], new geometry descriptor variables are searched and analysed for input into the ANN, and a more effective method (e.g., stochastic gradient descent [3]) is implemented for optimizing ANN. The ANN is then used to compute accurate forces at a small computational cost. This method will allow us to simulate conformational changes and to predict the full conformational network for peptides or small proteins.

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Selection of Candidates for the First Small-Molecule Inhibitor of the Retinoblastoma Binding Protein 4

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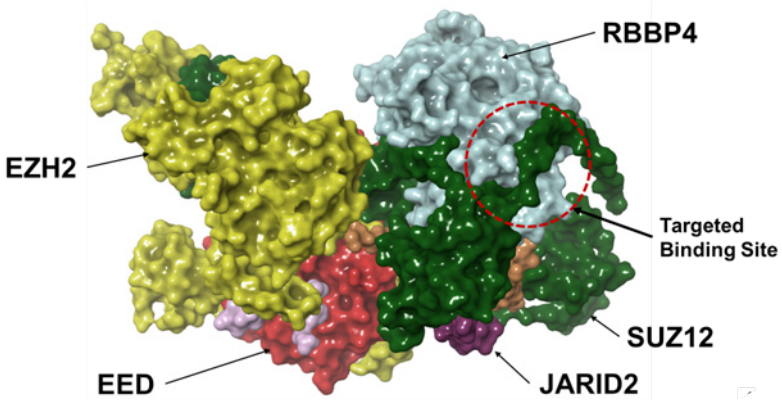
WD40 repeat (WDR) domains are protein-protein interaction scaffolds that represent a new target class in drug discovery [1]. An example WDR protein, the retinoblastoma-binding protein 4 (RBBP4), is part of multiple complexes that are involved in tumour initiation and progression, including the polycomb repressive complex 2 (PRC2), shown below, and the nucleosome remodelling and deacetylation (NuRD) complex [2, 3]. These two complexes have been targeted through other protein subunits to reduce their hyperactivity in cancerous cells, however there is no known inhibitor of RBBP4 to date.



Our aim was to discover the first protein-protein interaction inhibitors targeting the WDR domain of RBBP4. We employed virtual screening methods to screen a database of compounds for their potential interaction with the side pocket of RBBP4, with the intent of inhibiting its interaction with the MTA1 protein within the NuRD complex. Following filtering of the database and separation of the compounds into a drug-like and fragment library, the compounds were docked using three docking softwares: Glide, ICM, and FlexX. We then conducted pairwise RMSD comparisons and normalized score calculations, and selected compounds based in part on the similarity of their docking pose results. Finally, compounds were selected by visual inspection for confirmation by experimental methods: 56 drug-like as well as 23 fragments were selected and remain to be verified experimentally. Potential lead structures will be further optimized and modified to improve their potency for inhibiting RBBP4 protein interactions.

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Dioxane-induced changes on the interfacial region of phosphatidyl-choline membranes

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1,4-dioxane is a highly hydrophilic, water miscible, environmentally nondegradable pollutant. It is generally used as an organic solvent, but also occurs as an industrial by-product. It is proven to cause cancer in animals, and it is classified as "likely to be carcinogenic to humans" [1]. Here, the effects of 1,4-dioxane have been studied on phosphatidyl-choline membranes, using molecular dynamics (MD) simulations. To understand the effects of 1,4-dioxane on phosphatidyl-choline membranes, we have used bilayers built from DPPC and IPPC molecules and MD simulations were carried out in pollutant free and polluted (in the presence of 100 1,4-dioxane molecules) environment. The MD simulations were performed in a biologically relevant fluid-crystalline phase (T = 330 K, p = 1 atm, 50 water molecules/lipid) for 5×125 ns long for each system with CHARMM36 force field using GROMACS 5.1.2. program package. The water-membrane interface has been analyzed based on the orientational order of water and dioxane molecules to shed light on dioxane-induced structural changes.

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Low-Molecular-Weight Sulphur Containing Biomolecules - A Theoretical Study

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Low-molecular-weight Sulphur (LMWS) containing species are important and play a key role in many biochemical processes. They can be found in a wide variety of organisms including prokaryotes, plants, and mammals. These special molecules participate in signal transduction, gene regulation and protect living organisms against free radicals. Databases are essential in Today's research. The main purpose of this study is to create a core dataset, a small molecular library of LMWS structures with >100 entries and organize the available information. It will contain the most important structural and functional properties of LMWS species. For a selected set of molecules, a detailed comparison will be presented based on the calculated properties of the molecules. The database could serve as a starting point for the design of new LMWS containing compounds.

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Entanglements in transmembrane proteins

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It was discovered in 1994 that proteins can fold into complex knotted structures [1]. Since then many protein families with knots were identified and various knot types were described. Along with the knot topology, the slipknot topology was described and distinguished as another type of entanglement in proteins [2]. The knots and slipknots in proteins are recognized based on probabilistic methods to close polypeptide chain and also on a branch of mathematics – knot theory [2]. Up-to-date the role of knots and slipknots in proteins is still not understood. Later it was shown that transmembrane (TM) proteins can also form knots and slipknots [3, 4]. Here we focused on TM proteins with non-trivial topology. We found that there are altogether 11 families of TM proteins with slipknots and one family with knotted topology. Do all of them have unique type of slipknot/knot fingerprint? We identified four distinct types of slipknot and one type of knot fingerprint. Further, we found that all proteins with non-trivial topology belong to the same large class of transmembrane proteins – secondary active transporters. The slip/knot type is highly conserved despite very low (<10%) sequence similarity between these protein families. Taking into account limited structural data of TM proteins in general, this is very likely that more slip/knotted protein families exist in nature, it will be interesting to see whether those proteins have a new fingerprint or preserve already known types of fingerprints.

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Conformational changes in reaction center of PS II upon photochemical reduction of plastoquinones

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Photosystem II is a pigmen--protein complex, which absorbs energy of the light and converts it to the energy, leading to reduction of plastoquinone to plastoquinol and water splitting. Electron separation occur in the reaction center, placed in the thylakoid membrane, consisting mainly of glycolipids (MGDG, DGDG, SQDG) [1]. After charge separation on P680+/Pheo- electron travels through RC to the primary electron acceptor – strongly bound plastoquinone Qa . Than electron is transferred to mobile plastoquinone Qb, which leaving reaction center binding place after second electron transfer and reduction to plastoquinol.

All this changes in the oxidative state of Qa and Qb appear with participation of other non-protein molecules (like bicarbonate ion, waters, Fe) and protein residues. In this study we wanted to analyze dynamics of Qa and Qb during selected steps of electron transfer and analyze role of recently co-crystallized third plastoquinone Qc in plastoquinone pool [2].

The crystal structure of reaction center of PS II from cyanobacteria T.vulcanus [3] was selected for calculation, missed lipids were built manually and added from 4v62 [2]. Parameters for cofactors, small molecules and lipids for classical MD simulation with Amber force field in Gromacs were obtained from [4] and [5]. The missing parameters for lipids were derived with Gaussian 09, Acpype and Antechamber. Parameterized system was embedded in a membrane with InflateGRO methodology [5].

We found out important residues, participating in stabilizing Qa and Qb orientation in the binding cavity. Also observed changes in HB network of Qb in case of different protonation and oxidation state, leading to either cleavage it from the binding pocket or reversible motion inside of channel II [2]. Also our calculation confirmed previously proposed idea that Qc in the binding channel I could not participate in a cytochrome b559 oxidation-reduction die to absence of any specific interaction with P680 or any closeby amino acid was found.

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Allosteric activation of Arginine repressor protein by L-arginine

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Arginine repressor (ArgR) is the master regulator of arginine regulon in various bacteria. It senses the intracellular concentration of L-arginine (L-arg) and provides feedback control of L-arg metabolism [1, 2]. ArgR is a hexameric protein where each monomer consists of N-terminal (DNA binding) domain and a C-terminal (L-arg binding) domain [3, 4]. Despite of wealth of information available about structure of ArgR, the mechanism of L-arg binding to C-terminal domain is largely unknown.

Molecular dynamics (MD) simulation approach was used to study the dynamic behaviour of ArgR in Bacillus subtilis and Escherichia coli. GROMACS-5.0, YASARA and VMD tools were used to perform structural modelling, MD simulations and analysis. AMBER99SB force field was used for MD simulations.

ArgR of E. coli (EcArgR) and B. Subtilis (BsArgR) have different residues at the trimer-trimer interface, e.g. EcArgR has Arg110 residue at the interface which is mainly responsible for trimer-trimer rotation whereas in BsArgR there is no such charged residue at this position. In BsArgR the C-terminal α4-helix contains two charged residues which form saltbridges across trimer-trimer interface. Binding of L-arginine to ArgR in the core domain leads to conformational changes of N-domains. The MD simulations of linker helix mutants (K75A/R78A/D82A) showed that the linker helix residues are crucial for the rotation in BsArgR. Despite of different amino acid residues responsible for trimer-trimer rotation, the rotational behaviour is very similar for ArgR in both bacteria. It suggests that binding of L-arginine allosterically activates the conformational changes via trimer-trimer rotation and this rotational motion are essential and very integral to ArgR function.

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Interaction of Hydrated Metal Cations with Thymine and Glycylglycine N-methylamide Using DFT and QM/MM MD Approach

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Interaction of metal cations with DNA or peptides is of great importance for understanding cell processes, development novel drugs and also new materials. Such reactions are strongly influenced by solution pH and not seldom accompanied by a proton transfer which often represents the rate-determining step for the total reaction. This requires involvement of surroundings at a sufficiently good level in the calculations and dynamics aspects should have an impact on a reaction course.

In our contribution, we initially focus on a transition between the keto and enol form of thymine, i.e. proton transfer from nitrogen N_3 to oxygen O_2. Particularly, an influence of different hydrated metal cations – Hg^{II} and biologically significant Mg^{II}, Zn^{II} cations – on its reaction rate is presented, when differences in the reaction electronic flux [1] and the electronic density in bond critical points are determined along studied intrinsic reaction coordinates (IRC).

Binding of the hydrated Hg^{II} cation to the N_3 position of thymine itself, which is associated with the proton transfer from the N_3 position, plays an important role during formation Hg^{II} bridges between thymine mismatches in a DNA helix. As the thymine-Hg-thymine structures can exist next to each other in the DNA helix [2], such materials are assumed convenient for construction of charge-transporting devices. The process of Hg-N_3(T) bond formation is studied from dynamical point of view using the QM/MM umbrella sampling MD approach when calculated free-energy profiles for interaction of thymine and $[Hg(H_2O)_5(OH)]^+$ or $[Hg(H_2O)_4(OH)_2]$ clusters are shown. The obtained results are finally compared with the previous ONIOM [3] and our DFT-D calculations.

Similarly, a proton transfer is of great significance during Cu^{II} cation binding to the nitrogen of peptide bonds in proteins. In this case, glycylglycine N-methylamide is considered as a model system and an influence of a proton acceptor on the course of the reaction is compared.

The static QM calculations are carried out at the DFT-D level using double-ξ basis set for optimization and triple-ξ basis set for singlepoint calculations. An implicit solvation model and effective core potentials for 3d transition metals are considered at both of the levels.

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Abstracts of Poster Presentations

Molecular dynamic simulation of cellulose dissolution in 1-ethyl-3-methylimidazolium acetate

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The interaction at the surface of biomolecules such as proteins, enzymes, DNA and bio-polymers with materials play a key role in many applications in science and technology for example in bio-inspired nanotechnologies and enzyme engineering. The bimolecular interactions made a huge cross link between biology, physics and chemistry to offer prospect for new technologies such as nano-bio technologies.

Carbohydrates include many important biomolecules that play key roles in the immune system, fertilization, preventing pathogenesis, blood clotting and "etc". One of the novel sources of cellulose is recycling it from wastes such as old cloths and trunks but the major problem is dissolution because cellulose is insoluble in water and many common organic solvents due to its three dimensional hydrogen bond network. It is shown that some imidazolium based ionic liquids are able to dissolve cellulose at rather high concentrations [1]. Thus understanding the biomolecular interactions of ionic liquids with cellulose, glucose and cellobiose can give us important information on biomolecular interactions in bulk solution and surface of biomolecules.

Computer calculation is powerful tool for solving scientific problems. Theoretical modeling and simulations provide complementary approaches for experimental studies and have been applied for exploring biomolecule–surface adsorb mechanisms, determining the binding specificity towards different surfaces, dissolution, as well as the thermodynamics and kinetics of adsorption. Wide variety of interactions happen when a solute has been solvated in different solutions, so that, understanding the interaction forces between solute – solvent, biomolecules – surface, diffusion coefficient and other parameters are important.

Interactions of biomolecules in non-aqueous solutions by dissolution of haloalkane dehalogenase enzymes in organic solvents and effect of solvent on enzymatic activity and enzyme's structure have been studied previously[2]. In this study we would like to investigate biomolecular interactions at the surfaces both in aqueous and non-aqueous media by classical molecular dynamics simulations (MD) by GROMACS package. Thus three saccharides namely glucose, cellobiose and cellulose were chosen and solvated in ethyl methyl imidazolium acetate with different concentrations. By analysis of MD data, the effect of cations and anions on the structure and mechanism of dissolution of cellulose in ionic liquid will be explored.

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Quantum chemical computations on Diels-Alder reactions

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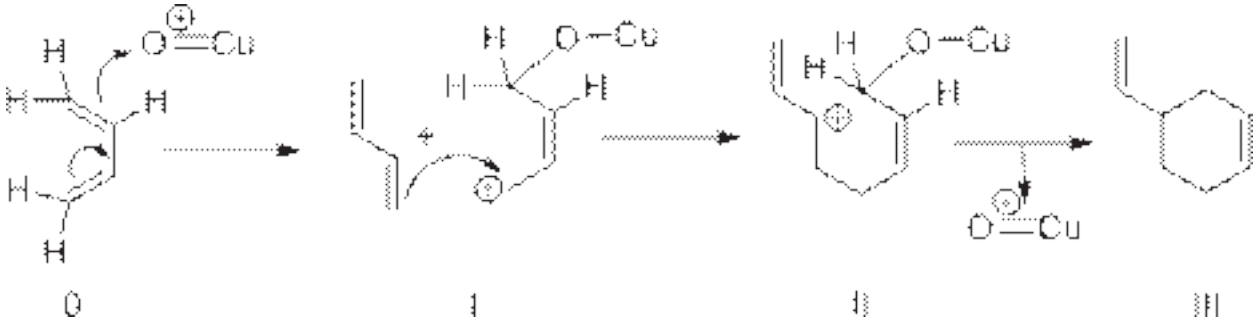
The Diels-Alder reactions are used in organic synthesis reactions involving a conjugated diene and a substituted alkene, to form a substituted cyclohexene derivative. Furthermore, this method is also useful for forming 6-membered systems with good control over regio- and stereochemical properties [1,2].

The reaction kinetics might be affected by different substituents; in addition, catalysts (i.e. CuO) can also modify the reaction mechanism.

Theoretical computations were carried out at the B3LYP/6-31G(d,p) and MP2/6-31G(d,p) levels of theory by our research group to investigate the mechanism of Diels-Alder reactions between cis-butadiene and trans-butadiene or cis-butadiene and ethylene.



The formation of styrene was investigated by catalytic electrochemical oxidation (anodic oxidation) from cis-butadiene in the presence of copper oxide ($^{+}$CuO) as an electrochemical catalyst. Similarly, the cathodic reduction of cis-butadiene to form butane was considered to be catalysed by the anionic catalyst model ($^{-}$CuO). It is hoped that the studied mechanism may be useful to experimentally investigate the electrochemical formation of poly-styrene with reduced waste as a green technology in the future.

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N-Protected β-Amino Acid Formation from N-Protected α-Amino Acids *via* Wolff Rearrangement

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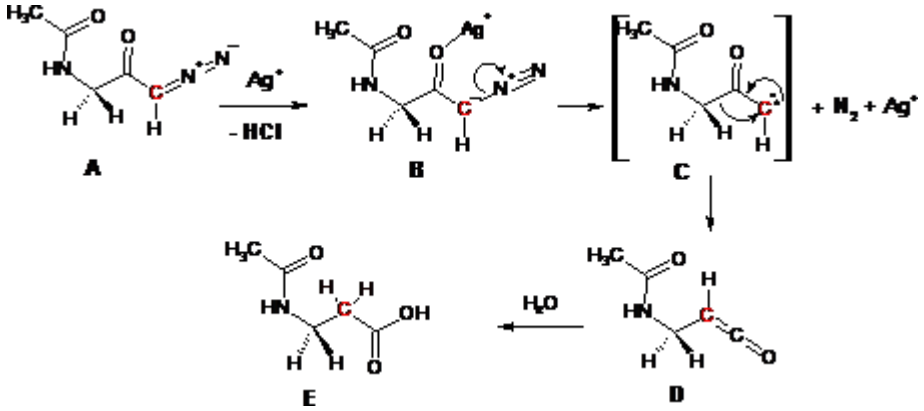
β-Amino acids have found extensive applications as components of biologically active peptides and small molecule pharmaceuticals. Synthetic derivatives of biologically relevant peptides incorporating β-amino acids often display interesting pharmacologically activity, with increased potency and enzymatic stability [1].

Several methods are known for the synthesis of β-amino acids [2], of which the most practical method seems to be the Wolff- rearrangement, hiding some unanswered questions. Therefore, our research group has decided to map the full reaction mechanism of this rearrangement for natural amino acids by theoretical computations at the B3LYP/6-31G(d,p) and MP2/6-31G(d,p) levels of theory; glycine was the starting point for our study, illustrated in the scheme. Solvent effects were also considered, both implicitly and explicitly. Not only the uncatalysed, thermal transformation is involved, but the influence of transition metal catalysts (i.e. Ag^+) is also studied. We considered both the singlet and triplet reaction routes, due to the formation of the carbene intermediate.



Acknowledgements: *Computational Resources provided by the GITDA (Govermental Information-Technology Development Agency, Hungary) are gratefully acknowledged. 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, aimed to promote the cooperation between the higher education and the industry. BF and MSz thanks the financial support by the New National Excellence Program of the Ministry of Human Capacities (HU) under the ÚNKP-17-4-I-ME/17 and ÚNKP-17-4-III-ME/26 project, respectively. Furthermore, the generous support from the Institute of Chemistry, University of Miskolc is gratefully acknowledged.*

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Multifunctional $C_6H_{14}O$ Chemicals: from Green Energy Storage to Biobased Chemicals

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$C_6H_{14}O$ isomers are high-carbon compounds that have a high cetane number and a high lower heating value, which is close to fuels that we currently use [1]. These characteristics make these six-carbon compounds candidates to becoming a biofuel or a fuel additive. Compounds with this empirical formula are either alcohols or ethers. Alcohols are usually blended into fuels due to their higher density than ethers, and because ethers have relatively low densities, they are used as fuel additives [2]. Currently there are many studies investigating fuel properties of simple isomers in this family, such as 1-hexanol. 1-hexanol is attractive due to its high cetane number and high energy density [3]. However, the fuel properties of other isomers are not widely discovered yet, so that 1-hexanol may not be the most optimal choice of biofuel. Therefore, the main purpose of this study is to use computational methods to investigate the fuel properties of 32 isomers with this formula to find the most promising structure to act as a biofuel, and we expect that there should be some isomers that have better fuel properties than 1-hexanol. The computations are conducted using the Gaussian software package with the aid of a super computer located in the University of Miskolc. We will evaluate the energy change over a complete oxidation route of the isomers by carrying out optimizations and single point calculations to obtain isomers' energy density. Also, we will investigate physical properties, toxicity, and industry applications of these isomers to come up with the most suitable compound as a biofuel.

Acknowledgements: *Computational Resources provided by the GITDA (Governmental Information-Technology Development Agency, Hungary) are gratefully acknowledged. 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, aimed to promote the cooperation between the higher education and the industry. BF and MSz thanks the financial support by the New National Excellence Program of the Ministry of Human Capacities (HU) under the ÚNKP-17-4-I-ME/17 and ÚNKP-17-4-X-ME/26 project, respectively.*

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Overexpression studies of Saccharomyces cerevisiae K^+ Translocating Membrane Proteins (Trks)

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In *S. cerevisiae* (*S. c.*) there are two specific K^+ translocation proteins: Trk1 and Trk2, that allows cells to survive and grow under different environments from a few μM to hundreds of mM [K^+] and maintaining internal [K^+] relatively constant [1]. Trks are structurally related to prokaryotic Trk, Ktr and plant HKT proteins [2]. Based on sequence alignments and experimental studies, a structural model for Trk1 was developed. However, this model includes only transmembrane domains without most of the extra- and intracellular parts, viz. the ("Long Hydrophilic Loop" (LHL), C tail (66 a.a.) and N tail (49 a.a) of protein [5]. LHL is not homologous between Trk1 and Trk2 and differs largely in length i.e. 648 aa in Trk1 and 327 aa in Trk2 [1, 3]. The main objective of this work was to overexpress full length Trk, cytosolic parts (LHL, C, N tails) and transmembrane parts (A & D domain) of Trk1 for subsequent structure analysis.

Different GFP fusion constructs of TRK1 and TRK2 with and without LHL, as well as constructs in which GFP was fused to LHL alone, A and D domains were prepared and used to transform *S. c.* BY4741[*Δtrk1,2, tok1*] cells [4]. Fluorescence microscopy of yeast cultures with Trk1/GFP and Trk2/GFP showed even distribution of protein at the cell periphery, Trk1[ΔLHL]/GFP showed a punctuate distribution pattern. TRK1(A)/GFP and TRK1(D)/GFP showed membrane fluorescence. GFP/LHL(Trk1) was found in the cytosol. Western blot analysis of yeast plasma membrane fractions showed bands for GFP labelled Trk-proteins at their approximate expected sizes, indicating full-length expression of the constructs.

Different constructs of TRK1 full length or in parts were generated and overexpression studies were performed in *E. coli*. We observed that TRK1(D)/GFP was expressed but it was in inclusion bodies. C-tail and N-tail was purified as a fusion protein with GFP and attempts were made to crystallize the C-tail.

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Multifunctional C_4H_8O Bioderived Chemicals: from Green Energy Storage to Biobased Chemicals

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The production and use of biofuels has become increasingly important in previous years due to depleting fossil fuel reserves, rising concerns regarding greenhouse gas emissions, and emissions of toxic air pollutants from the combustion of fossil fuels[1]. Oxygenates derived from carbohydrates of lignocellulosic biomass can be tailored to exhibit desired physico-chemical fuel properties[2]. The aim of this project is to identify the best biofuel candidates among all possible 26 constitutional isomers of C_4H_8O using CCSD(T)/cc-pV(T,Q)Z//MP2/aug-cc-pVDZ quantum chemical calculation and relevant data from literature. For each isomer, the standard enthalpy of formation (ΔfH°) and lower heating values (LHV) were computed. Calculated ΔfH° values were compared with literature values to validate the computed LHV results. Molecules with LHVs higher than those of ethanol or biodiesel were picked for further study on toxicity using LD50 and LC50 values from literature and these values were compared with those of ethanol and gasoline mixtures to determine their relative toxicities. Molecules with relatively low toxicity, present in liquid or gaseous states at STP were among the best candidates for biofuel. In addition, molecules with properties desired for use in internal combustion engines such as low viscosity, low boiling temperature and high vapor pressures were preferred[3]. Once a potential fuel candidate exhibiting these properties is identified, further research will be done on the potential biological pathways through which the fuels can be most efficiently produced from various photosynthetic organisms using currently available synthetic biology tools.

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Sugars in space: *quantum chemical* study on the formation of glycerone from formaldehyde and hydroxy carbene on interstellar medium dust grains

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Among many theories on the origin of life, regions between star systems in a galaxy (interstellar medium) is hypothesized to provide prebiotic material on Earth. Simple sugars, including glycerone, are confirmed to exist in interstellar medium (ISM) and can be products of the formose reaction.

In the studied segment of the formose reaction, hydroxy carbene is sequentially added to formaldehyde, forming glycolaldehyde after the first addition and glycerone (aka dihydroxyacetone or DHA) in the second. Each studied step involves the formation of an epoxide intermediate, after which the carbonyl group is restored through a hydrogen shift. The theorised mechanism was validated through quantum chemical calculations. An exothermic and exergonic pathway favourable in ISM conditions was found, suggesting a possible mechanism for glycerone formation.

The products in question participate in energy production (the phosphorylated form of glycerone, DHA-P, participates in glycolysis) and storage (glycerone is the source of the glycerine backbone in lipids). The studied reaction is a segment of the formose reaction—further polymerization can lead to pentose (ribose) and hexose, which take part in the formation of RNA and DNA. Hence, this research investigates the hypothesis of exogenous production and delivery of prebiotic material to Earth, facilitating the formation of life supporting conditions.

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Computational modeling of effective inhibitors of topoisomerase IA

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Eukaryotic topoisomerases I (TOPO 1) are the targets of an increasing number of anti-cancer and anti-tumor drugs that act by inhibition these enzymes. Computational docking of potential active compounds would be appreciated for prediction of potential antimicrobial drugs, potentially lowering the experimental costs and time [1].

In our work we focused on the search of possible binding places for binding of different drugs, select prominent inhibitors and predict possible effects on enzyme action. Several approaches were used for search and analysis inhibitors, including characterization geometry of binding partners (Yasara [2], VMD), calculation of energy parameters such as binding affinity and charge distribution (Schrodinger [3]).

The potential inhibitors of TOPO 1 [1] where downloaded from PubChem database and used for building of pharmacophore. We also made screening of more than 325 mln entries from PubChem Database employing new approach based on filtering under MeSH classification with combination of different docking methods for inhibitor selection (rigid and flexible docking with, induced fit docking, MD simulation).

Based on our study we also proposed optimal work-flow which can be used for further search and selection other biologically active compounds.

Finally we had choose top-10 compounds based on this pharmacophore hypotheses and then we use it for rational manual construction of new compounds, that were not found in PubChem database.

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Bio-based Polyurethanes-A Computational and Experimental Study

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Bio-based (cellubiose & cellulose) polyurethane (PU) foams were studied using experimental and theoretical tools. PU foams (control samples) were synthesized based on commercially available polyol blends (FFP303 and PG19) and polyisocyanate (Ongronat 2100). The effect of cellulose as a filler on the resulting PU foams was investigated by adding it to the polyol and isocyanate mixtures. Control sample heights were compared with the heights of foams containing 1%, 5%, 10%, 15%, 20% and 30% cellulose by mass, respectively.

Furthermore, cellobiose as a potential replacement of the petro-based polyol is investigated. The reactivity of each hydroxyl group of cellobiose towards phenyl isocyanate was calculated and compared using density functional theory. The preliminary results are promising. Our aim is to develop industrial quality PU foams by using cellulose or cellobiose as an inexpensive and environmentally friendly alternative to conventional polyols.

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The influence of Site Mutations on Activity of XPB protein

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The ERCC3/XPB ATP-dependent DNA helicase is one of the ten subunits of the general transcription factor TFIIH. As the TFIIH is involved in transcription, nucleotide excision repair (NER) and cell cycle control, the mutations in its subunits may have pleiotropic effects. There are known only several mutations non fatal for the cells, yet causing serious illnesses. Based on previous experimental work, we have simulated wild type enzymes from archaebacteria and eukaryotes and thier mutants.

All but one ERCC3 mutants are extremely sensitive to UV-irradiation. However, none of them was able to repair CPD or 6-4PP or to recover RNA synthesis after UV-irradiation. We have compared the most sensitive (UV24 cell line; S382P mutation) and most resistant (UV68 cell line; V471F mutations) mutants. We have found that the sensitive cells have more apaptotic cells, form more DSBs, have higher frequency of chromosomal aberations and stronger G1/S block. Molecular dynamcs analysis of the S382P ERCC3 protein has revealed significant fluctuation in protein loop next to DNA binding domain.

Acknowledgements: *Support from APVV-16-0600 is acknowledged.*

Mechanism of the Interaction between Gold (I) Complexes and Thioredoxin reductase (modeled by Cysteine and Selenocysteine)

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Gold(I) complexes have been demonstrating a considerable potential as a promising candidate for new class of anticancer drugs. Among these, the prominent representative is the Au(I) coordinated with N-heterocyclic carben ligands (NHCs) which have attracted a great deal of interest for their strong antiproliferative activities against cancer cells. In order to gain deeper insight to the mechanism biological action of the Au(I) compounds, the binding Au(I) NHC complex to Cysteine (Cys) and Selenocysteine (Sec) have been investigated by QM methods as a model for the binding of the complex to the thioredoxin reductase active sites, which are known as a important target for gold species. Geometries were optimized at the B3LYP-GD3BJ/6-311++G(2df,2dp)/MWB60/C-PCM level. Single points calculations are carried out using the better implicit solvation model – DPCM/scaled-UAKS. Electronic properties of the reduction process are further investigated using NBO, ESP, ALIP, and QTAIM analyses. The calculations show that the complex formations of Au(I) NHC fragment with these two amino acids go through the similar pathways. The replacement of Cl atom belonging to gold complex with either selenoate or thiolate groups is characterized by a low activation barrier energy of ca. 8 kcal.mol^{-1} which corresponds to large rate constant of approximately 107 s^{-1}. In the case of interactions Au(I) NHC compound with thiol and selenol, the products are proposed to be obtained from a two-step procedure consisting of the deprotonation of SeH and SH groups followed by interaction of the intermediates with gold complex.

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Theoretical study of PAPSS1 linkers

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PAPS synthase is a bifunctional enzyme that catalyses the formation of 3´-Phosphoadenosine 5´-Phosphosulfate (PAPS) in two sequential steps. Human 3´-Phosphoadenosine 5´-Phosphosulfate Synthase (PAPSS) consists of N-terminal (1-260 aa) APS kinase domain and a C-terminal ATP sulfurylase domain (20-623 aa). [1] PAPS synthase, using ATP, converts biochemically inert inorganic sulfate to metabolically active PAPS which is the universal sulfuryl donor of the cell in mammals. The second step of this reaction is catalysed by the kinase domain of PAPSS. In this step adenosine 5´-Phosphosulfate (APS) reacts with ATP to form PAPS and ADP. [2] The problems with sulfonation can lead to severe clinical consequences, such as osteochondrodysplasia. [1]

Three forms of PAPSS are now known, namely PAPSS1, PAPSS2a, and PAPSS2b. PAPSS2a and PAPSS2b have different splice variants. [3]

In this study we have focused on PAPSS1 kinase domain and sulfurylase domain linkers, which according to the experiments play a role in the ligand binding, thus influencing the stability of ligand-protein complex. In silico linkers of protein domains were prepared using the YASARA software. The MD simulations of PAPSS1 kinase and sulfurylase domain linkers were performed using GROMACS software with AMBER99SB force field. The ligands were docked to these linkers by the program GLIDE. The results from ligand docking will be presented.

Acknowledgements: *Support from the Grant Agency of the University of South Bohemia is acknowledged.*

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Colloid chemical characterization of carbon nano spheres

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In this research, carbon black spheres were examined to characterize their structure and colloid chemical properties. The carbon black samples were produced by the Columbian Tiszai Carbon Ltd. from Tiszaújváros, Hungary. 95% of the carbon black production is produced by very similar pyrolysis technologies which use high (1400-2000°C) temperatures and quenching water to decompose the starting material (usually quench oil) [1]. The samples were directly taken from the furnaces; thus, no preparation was used in for their delivery. Scanning electron microscopy (SEM) was used to examine the structure of the carbon black samples and to measure the size of the spheres. With the use of the images size-distribution diagrams were made. X-ray diffraction spectoscopy (XRD) was used to detect metal-oxide impurities which could modify the results of different measurements like zeta potential measurement. Fourier transformation infra-red spectroscopy (FTIR) was used in order to identify the functional groups of the spheres. These groups are responsible for the behavior of the spheres in different mediums. Zeta potential measurement was made to characterize the colloid chemical properties like stability in suspensions.

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Refereces:

[1] https://pentacarbon.de/wiki/

Computational Study on the Formation of Benzo(a)pyrene

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In the last few decades the molecular growth of polycyclic aromatic hydrocarbons (PAHs) has become one of the central subjects in combustion chemistry. These aromatic components composed of united aromatic rings are formed during the incomplete combustion of the carbonceous material and they are considered as the precursors of soot. Being ubiquitous pollutants in the environment, the Environmental Protection Agency issued a list of „16 priority PAHs" for being the primary standards for all PAHs. This list also includes chrysene, benzo(a)anthracene and benzo(a)pyrene which have enhanced carcinogenic effects and they are the main focus of this work. In this study the formation of the aforementioned benzo(a)pyrene from chrysene and benzo(a)anthracene is examined (Figure 1) by assuming that the methyl additions/cyclization (MAC) mechanism occurs. In order to determine the possible reaction pathways density functional theory calculations have been perfomed.

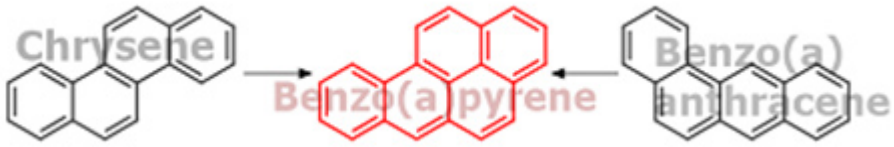

Figure 1. Schematic representation of the studied reactions leading to benzo(a)pyrene.

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Building Models for Understanding Peptide Conformations using Artificial Neural Networks

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The amino acid sequence of a protein is believed to contain all necessary information needed to predict its three-dimensional structure. Prediction of a protein's three-dimensional structure requires a complete understanding of the relationship between the different conformations available to an amino acid sequence and their corresponding energies. However, accurate computations of the energy of most protein structures is currently not possible due to the limitations of current computational resources. To initiate protein folding studies based on quantum chemistry and lay down its foundations, proteins can be gradually built from smaller models like single amino acids and di-/tri-peptides. The data obtained from electronic structure calculations of these molecules are fitted to mathematical models that can accurately describe the relationships between structure and energy but are still less complex than the Schrödinger equation. In this study, we attempt to describe the potential energy surface of selected amino acids and peptides using artificial neural networks. This will serve to augment the current knowledge on functions describing potential energy surfaces and the initial efforts to the bottom-up approach to protein folding, providing a deeper understanding into the energetics of peptide or protein folding.

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Quantum Chemical Analysis of the Possible Formation Mechanism of Cyanomethanimine in Dense Molecular Clouds

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E-Cyanomethanimine, was detected towards Sagittarius B2(N) in 2013 by comparing GBT PRIMOS survey spectra to laboratory rotational spectra from a screening experiment [1]. This detection of E- Cyanomethanimine is of much significance to prebiotic chemistry since it is considered a hydrogen cyanide dimer, which could potentially lead to the synthesis of hydrogen cyanide pentamer - adenine ($C_5H_5N_5$). Adenine as a purine nucleobase is a part of DNA and RNA molecules; as a biomolecule, it takes part in cellular respiration. It also plays a role in protein synthesis reactions as well, thus it is quite integral to life [2]. This is significant due to a central theory regarding the interstellar origins of life due to early Earth being bombarded with meteorites carrying "biomolecules" that "kick-started" life [3].

This study proposes four new reactions for the synthesis of E-cyanomethanimine in gas-phase under dense cloud conditions of temperature 15 K and pressure 0 atm., starting with small and abundantly present molecules in interstellar medium (ISM); namely hydrogen cyanide, carbon monoxide, ammonia, formaldehyde, hydrogen peroxide and carbon dioxide [4]. Since the temperature and pressure in ISM is extremely low, exothermic reactions with low energy barriers are considered feasible in dense clouds.

B3LYP/6-31G(d) level of theory was used to optimize geometries of the minima and IRCs were calculated under dense cloud conditions to obtain the transition states (TS). Single point calculations were also performed using MP2/6-31G(d) level of theory to obtain thermodynamic values. Using the thermodynamic data calculated for the proposed reactants, transition states, and the product, the respective stabilities were examined, and the proposed reactions were compared. Since the proposed reaction is calculated to be exothermic, with low energy barriers under dense cloud conditions, theoretically, the criteria for a reaction to occur in ISM has been fulfilled.

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Chlorate elimination from industrial water, catalyst development and characterization

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During chlor-alkali electrolysis process application to membrane cells, chlorates are produced. The chlorate removal is equally important environmentally and technologically. One option for the removal is hydrogenation by using catalysts [1, 2].

In our work, hydrogenation catalysts were developed and tested for chlorate removal. Nitrogen-doped bamboo-like carbon nanotubes (BCNTs) were grown from butylamine on aluminium oxide and zeolite containing carriers by CCVD (Catalytic Chemical Vapour Deposition) synthesis. Then Pd nanoparticles were created on their surface by wet impregnation using $PdCl_2$ precursor solution. The prepared catalysts carbon-content were checked by thermogravimetry. The morphology of the catalysts was characterized by SEM-EDS. The catalytic activity of the samples was examined in the hydrogenation of butene first. After the satisfying result, a catalytic measuring system was designed and created, which allows continuous monitoring of chlorate content in a flow system. From the result it can be stated that the developed catalysts can be used to reduce the chlorate-content.

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Development of Bactericidal Polyurethane Additives

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In our experiments, we synthetized antibacterial polyurethane additives by using silver nanoparticles, in an industrial framework. The antimicrobial effect of Ag nanoparticles is well exploited in the production of PUR (polyurethane)-based hospital mattresses, car seats, sponges, etc. Three different supported silver-containing additives were prepared using different methods. One of the additives is Ag/PEG 400, a polyol-based silver colloid, while the other two samples are solid additives. The reducing agent in the case of the polyol-based silver colloid was polyethylene-glycol. During the preparation of magnesium-oxide-supported colloidal silver, ethanol was used as the reducing material. Guar-gum-encapsulated silver nanoparticles were synthetized by sodium-borohydride. All additives were examined by electron microscopy; the nanoparticles showed high dispersibility, and small particle diameter. PUR foams were made by using the three additives, and the silver content was 500 ppm in every case. The additives were tested on E. coli and the most efficient additive was found to be the Ag/PEG 400 sample. The additives can easily be dispersed in the polyol phase, the as synthetized foams are homogenous.

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A shell-resolved analysis of hydrotropic solvation of coffee ingredients in aqueous mixtures of 1-ethyl-3-methylimidazolium acetate

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Although aqueous ionic liquids have been successfully applied in biomass extraction for quite a few years, their general ability to enhance the solubility of small organic molecules in water has only been unraveled recently [1]. Co-solvents increasing the solubility of hydrophobic molecules in water are commonly referred to as "Hydrotropes" and have a wide range of possible applications such as in the formulation of drugs, cosmetics and cleaning agents and can be used in crystallization and purification technology.

Despite the increasing popularity of hydrotropic substances, there is still no general consent on the driving force behind hydrotropic solvation, especially when ionic liquids are concerned. To investigate mechanisms of hydrotropy in aqueous ionic liquids, classical Molecular Dynamics simulations are a valuable tool since they allow the analysis of solvent structure around a solute at a molecular level. However, a reliable method for spatial decomposition such as Voronoi tessellation is required in order to obtain meaningful structural information. Voronoi tessellation enables a parameter-free, reliable and fully shell-resolved analysis of preferential solvation, solvent orientation and dielectric properties and thus helps to determine whether classical theories of hydrotropy are applicable in the case of aqueous ionic liquids or if new explanations are required [2].

For this work, we chose a selection of small aromatic compounds present in coffee as model solutes to study their hydrotropic solvation in aqueous mixtures of the ionic liquid 1-ethyl-3-methylimidazolium acetate ([EMIM][OAc]) with classical Molecular Dynamics Simulation. We show that Voronoi tessellation is superior to classical structural analysis methods and test possible hydrotropy mechanisms for [EMIM][OAc].

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Amino Acids in Action: Glycine Based Polyurethane

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The main focus of this project was to produce bio-based polyurethanes using amino acids. 4,4'-methylenebis(cyclohexyl isocyanate) (H12MDI), and glycine was applied as reactants. Fourier-transform infrared spectroscopy was used to characterize the synthesized polyurethanes. The molar ratio of the isocyanate and amino acid was 1:1. The effect of various additives (e.g. catalysts, solvent, blowing agent) and reaction conditions (e.g. homogenization) were studied and compared. The results of the experiments show that homogenization of the samples facilitates the reaction efficiency. The most promising parameters have been selected and glycine-based polyurethanes were synthesized. Further experiments are required to finetune the properties of the samples.

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The Formation of Cyanamide: An Interstellar Prebiotic Molecule

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Cyanamide is a prebiotic molecule in the interstellar medium (ISM) that can be used in the formation of complex organic molecules. As such, it is of heavy interest in astrochemistry. Cyanamide is known to react in interstellar media to form amino acids, polypeptides, nucleotides, as well as isomerize into carbodiimide, a precursor for assembling amino acids [1, 2]. Furthermore, cyanamide is involved in the formation of oligomeric compounds that could potentially serve as catalysts in the ISM [3]. In this way, understanding the mechanisms leading to the formation of this cyanamide in the harsh conditions of the ISM is a crucial step to determining a thorough understanding of the origin of life.

Although previous mechanisms based on laboratory and computational study have been proposed [4], this study utilizes computational methods to determine the most favorable synthesis pathways starting from smaller molecular building blocks known to exist in the ISM. DFT and MP2 calculations under 15 K and 0 atm conditions were conducted using the Gaussian09W software package to determine the energetic and entropic properties of the reactants, products, intermediates, and transition states for reactions leading to cyanamide. Four novel reaction mechanisms resulting in cyanamide formation were investigated. Of the four, the most probable reactions were determined via comparison of the thermodynamic and kinetic properties of the molecules.

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