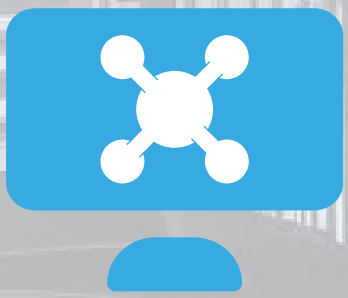


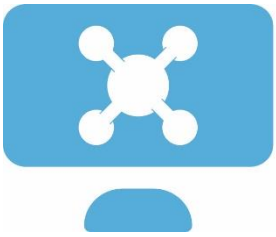
COMPUTATIONAL CHEMISTRY DAY 2025

Book of abstracts

University of Zagreb Faculty of Pharmacy and Biochemistry

June 7th, 2025

Zagreb, Croatia, EU



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Foreword

Welcome to the fifth edition of the *Computational Chemistry Day* (CCD). Last year, we took a break from organizing CCD, as Croatia had the honor of hosting the *19th Central European Symposium on Theoretical Chemistry* (CESTC). Our intention was to encourage integration between our local community and this broader regional event. CESTC is held annually in rotation among several Central European countries — Austria, Croatia, the Czech Republic, Hungary, Poland, and Slovakia. Our vision is for CCD and CESTC to evolve into complementary gatherings, serving local and regional communities, respectively.

At our previous meeting in 2023, CCD took an important step forward by becoming more international — both in terms of its organizing committee and participant base. We are committed to continuing this path, deepening connections with researchers from neighboring countries and fostering a collaborative spirit across borders.

Although this year's program does not include a workshop, we remain dedicated to incorporating such activities in the future. We warmly welcome and encourage your suggestions for workshop topics, as they are vital for keeping CCD dynamic and relevant.

The rapid advancement of artificial intelligence (AI) is one of the defining developments of our time. While its transformative potential is already evident in many fields, its impact on computational chemistry is still emerging. Whether AI will introduce entirely new methods and concepts, enhance existing algorithms, or assist (or even replace) us in routine tasks — such as setting up and managing computations, remains an open question. With great curiosity and anticipation, we look forward to witnessing these developments and hope to hear about the first breakthroughs at future Computational Chemistry Days.

The Organizing Committee

Program of the *Computational Chemistry Day 2025*

Saturday, June 7th, 2025 (Location: Botanical Garden "Fran Kušan", University of Zagreb Faculty of Pharmacy and Biochemistry, Schrottova 37, Zagreb, Croatia, EU).

08:45 – 09:00 **Opening addresses**

1st session (moderator: Tomislav Piteša)

09:00 – 09:30 **Antonija Mravak (FCT, Split), Stefan Vajda, Richard A. J. O'Hair and Vlasta Bonačić-Koutecký**
Translating insights from gas phase catalysts into solid state materials for sustainable future (IL)

09:30 – 10:00 **Robert Vianello (RBI, Zagreb)**
With a little help from computer-aided drug design: new antitumor agents as tubulin polymerization inhibitors (IL)

10:00 – 10:15 **Marina Juribašić Kulcsár and Mario Pajić (RBI, Zagreb)**
Experimental work guided by computational results: reactions of boronic acids and amines give structurally-diverse B←N adducts (CL)

10:15 – 10:30 **Antonio Ljulj (FPB, Zagreb), Lea Malezan, Maria Kolympadi Marković, Dean Marković, Davor Šakić and Valerije Vrček**
Computational methods for predicting the pK_a of terminal alkynes (CL)

10:30 – 10:45 **Tea Frey and Ivan Kodrin (DC-FS, Zagreb)**
Computational investigation of mechanical properties of organic molecular crystals (CL)

10:45 – 11:30 **Coffee break**

2nd session (moderator: Tana Tandarić)

11:30 – 12:00 **Igor Rončević (DC-UM, Manchester)**
Conjugated π-systems and how to describe them (IL)

12:00 – 12:30 **Hanfeng Cai, Zoran Štefanić, Tomica Hrenar, Ayelet Fishman and Aleksandra Maršavelski (DC-FS, Zagreb)**
Allosteric regulation and structural dynamics of thermostable L-lactate dehydrogenase: insights from molecular dynamics simulations and experimental analysis (IL)

12:30 – 12:45 **Vlasta Mohaček Grošev (RBI, Zagreb) and Jože Grdadolnik**
Hyaluronic acid dipeptide gels studied by Raman spectroscopy, atomic force microscopy and DFT calculations (CL)

12:45 – 13:00 **Haseena Sheik, Luca Grisanti and Antonio Prlj (RBI, Zagreb)**
Study of photorelaxation pathways in 7H and 9H tautomers of 2,6-diaminopurine (CL)

13:00 – 13:15 **Nenad Mijić and Emir Imamagić (SRCE)**
Benchmark of linear algebra libraries accelerated on graphical processors (CL)

13:15 – 14:45 **Lunch break**

3rd session (moderator: Antonio Prlj)

14:45 – 15:15 **Jaka Sočan (NCI, Ljubljana)**
The quest for real density-splay coupling constant (IL)

15:15 – 15:45 **Mihael Eraković (RBI, Zagreb)**
Spin-free SC-NEVPT2 method for the quantum embedding of the open-shell systems (IL)

15:45 – 16:15 **Martina Manenica (Hikma Ltd.) and Branimir Bertoša**
Activation mechanism of transcription factor MntR from the bacterium *Halalkalibacterium halodurans* for DNA binding (IL)

16:15 – 16:30 **Gan Wang, Piotr Nowakowski (RBI, Zagreb), Nima Farahmand Bafi, Benjamin Midtvedt, Falko Schmidt, Agnese Callegari, Ruggero Verre, Mikael Käll, Siegfried Dietrich, Svyatoslav Kondrat and Giovanni Volpe**
Monte Carlo study of alignment of microscopic disks by critical Casimir forces (CL)

16:30 – 16:45 **Martina Perić Bakulić (FCT, Split)**
Noble metal nanoclusters: tiny structures, big impact (CL)

16:45 – 16:50 **Concluding remarks**

Poster session with more coffee

17:00 – 21:00 Poster session

(IL): invited lecture, (CL): contributed lecture

Table of contents

Lectures

IL 1. Translating Insights from Gas Phase Catalysts into Solid State Materials for Sustainable Future

Antonija Mravak,[a] Stefan Vajda,[b] Richard A. J. O'Hair[c] and Vlasta Bonačić-Koutecký[d,e]

amravak@ktf-split.hr

[a]Faculty of Chemistry and Technology, University of Split, Ruđera Boškovića 35, 21000 Split, Croatia
[b]J. Heyrovský Institute of Physical Chemistry, Dolejškova 2155/3, 18223 Prague 8, Czech Republic
[c]School of Chemistry, University of Melbourne, Flemington Rd Parkville 30, 3010 Victoria, Australia
[d]Center of Excellence for Science and Technology, University of Split, Poljička cesta 35, 21000 Split, Croatia
[e]Humboldt University of Berlin, Brook – Taylor – Strasse 2, 12489 Berlin, Germany

Development of new catalytic materials plays an important role in the transition to sustainable energy. Systems with metal centers ranging from single atoms to well-defined size-selected clusters show promising catalytic performance. Theoretical and experimental gas phase studies provide information on their structural and electronic properties while allowing investigation of the influence of the size and composition on reactivity.

Transferring these insights into solid state materials facilitates the design of new catalysts with tailored activity and selectivity. In this context, metal-organic frameworks (MOFs) are a promising class of materials with three distinct catalytic sites available for reaction. Specifically, the gas phase system of {CuH} coordinated with bipyridine ligand serves as a model for incorporating catalytic center within the MOF linker. The goal is to propose a catalyst for hydrogen production from formic acid [1]. Similarly, ligated ruthenium clusters provide a basis for the design of zeolite-based catalysts using the "*ship-in-a-bottle"* principle for CO conversion into methane [2]. Another material design approach includes deposition of size-selected copper clusters on metal-oxide supports with the goal of CO_2 mitigation and production of valuable chemicals [3]. By combining DFT theoretical modeling with experiments, the goal is to predict and develop new catalysts with improved properties while gaining a deeper understanding of their structure-function relationships.

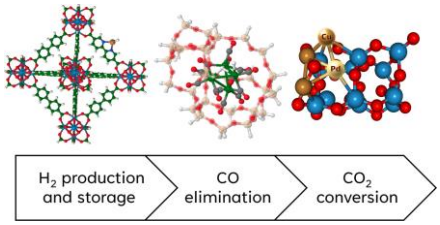

Figure 1. Overview of the designed catalysts.

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[1] R. A. J. O'Hair, A. Mravak, M. Krstić, V. Bonačić-Koutecký, *ChemCatChem* **11** (2019) 2443–2448.

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[3] (a) A. Halder, C. Lenardi, J. Timoshenko, A. Mravak, B. Yang, L. K. Kolipaka, C. Piazzoni, S. Seifert, V. Bonačić-Koutecký, A. I. Frenkel, P. Milani, S. Vajda, *ACS Catal.* **11** (2021) 6210-6224; (b) A. Mravak, S. Vajda, V. Bonačić-Koutecký, *J. Phys Chem. C* **126** (2022) 18306-18312.

IL 2. With a Little Help from Computer-Aided Drug Design: New Antitumor Agents as Tubulin Polymerization Inhibitors

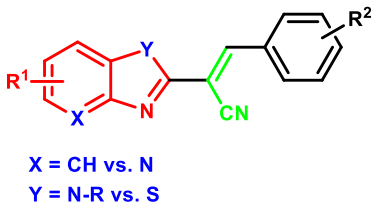
Robert Vianello

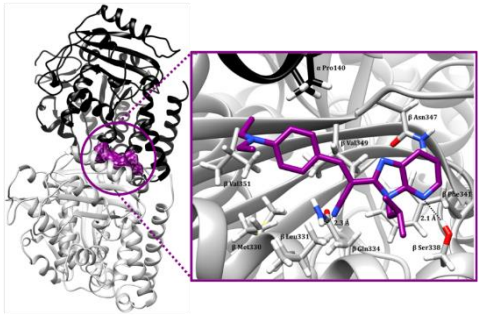
robert.vianello@irb.hr

Laboratory for the Computational Design and Synthesis of Functional Materials, Ruđer Bošković Institute, Zagreb, Croatia

Nitrogen heterocycles, particularly benzazoles, are central to modern medicinal chemistry due to their versatile chemical and biological properties, serving as key scaffolds in designing novel bioactive molecules [1]. The benzimidazole core, resembling natural purines, has been refined to create selective and potent ligands, drawing significant pharmaceutical interest.

This study presents the design, synthesis, and *in vitro* antiproliferative activity of new antitumor agents. Starting with variously substituted benzimidazole-derived acrylonitriles [2], we evaluated their ability to inhibit tubulin polymerization as a possible mechanism of their biological activity. Immunofluorescence staining and tubulin polymerization assays confirmed tubulin as the primary target, with several compounds showing high selectivity, low cytotoxicity, and promising antitumor potential. Computational analysis revealed binding preferences, affinities, and critical protein-ligand interactions governing the binding. The obtained insight underlined a simple idea to replace the benzimidazole phenyl ring with pyridine, leading us to prepare several imidazo[4,5-*b*]pyridine derivatives [3] that exhibited markedly improved tubulin polymerization inhibition compared to the original benzimidazole analogues.





References:

[1] (a) U. Acar Çevik *et al.*, *ChemistrySelect* **9** (2024) e202401566; (b) A Kumar *et al.*, *Pharmaceuticals* **16** (2023) 299; (c) L.-S. Feng *et al.*, *Arch. Pharm.* **355** (2022) 2200051.

[2] (a) N. Perin, L. Hok, A. Beč, L. Persoons, E. Vanstreels, D. Daelemans, R. Vianello, M. Hranjec, *Eur. J. Med. Chem.* **211** (2021) 113003; (b) A Beč, L. Hok, L. Persoons, E. Vanstreels, D. Daelemans, R. Vianello, M. Hranjec, *Pharmaceuticals* **14** (2021) 1052.

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Acknowledgments: *Croatian Science Foundation*, grant number IP-2020-02-8090.

IL 3. Conjugated π-Systems and How to Describe Them

Igor Rončević

igor.roncevic@manchester.ac.uk

Department of Chemistry, University of Manchester, Manchester M13 9GB, United Kingdom

This talk will discuss the electronic structure of various π-conjugated systems in terms of simple (tight-binding) models. We will explore the relationship between aromaticity, coherence, and electronic structure, using cyclocarbons, annulenes, and porphyrin nanorings as examples.

Cyclo[*n*]carbons (Fig. 1a) are loops of *n* carbon atoms. Recent advances in scanning probe microscopy (SPM) have enabled the on-surface synthesis and characterisation of these unusual molecular carbon allotropes, which have long served as a playground for theoretical approaches [1,2]. We will compare SPM resonance images with high-level ab initio calculations, showing that the electronic structure of cyclocarbons can be captured by a particle-on-a-ring model.

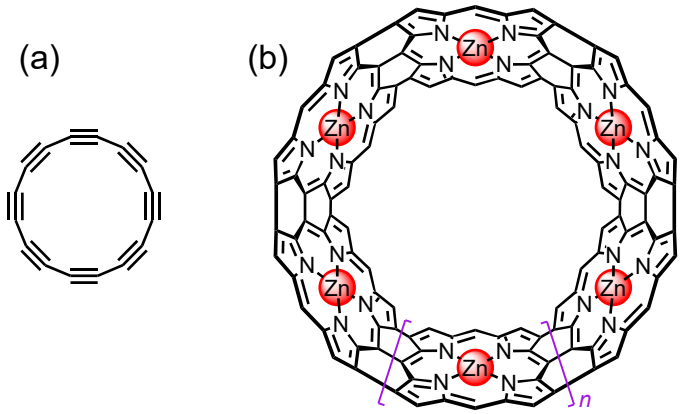

Figure 1. (a) Cyclo[16]carbon. (b) Edge-fused porphyrin nanoring.

Conjugated porphyrin nanostructures (Fig. 1b) display remarkable properties such as quantum interference and length-independent conductance, which make them excellent candidates for molecular electronics [3]. These properties stem from the coherent delocalisation of the wavefunction through the whole molecule, which becomes weaker as the molecule become larger. By analysing the ways in which π-systems can distort, we will estimate the maximum size at which edge-fused porphyrin nanorings (Fig. 1b) can still be expected to exhibit quantum behaviour [4].

References:

[1] I. Rončević, F. J. Leslie, M. Rossmannek, I. Tavernelli, L. Gross, H. L. Anderson, *J. Am. Chem. Soc.* **145** (2023) 26962–26972.

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IL 4. Allosteric Regulation and Structural Dynamics of Thermostable L-Lactate Dehydrogenase: Insights from Molecular Dynamics Simulations and Experimental Analysis

Hanfeng Cai,[a] Zoran Štefanić,[b] Tomica Hrenar,[c] Ayelet Fishman[a] and Aleksandra Maršavelski[c]

amarsavelski.chem@pmf.hr

[a]*Department of Biotechnology and Food Engineering, Technion-Israel Institute of Technology, Haifa 3200003, Israel*

[b]*Ruđer Bošković Institute, Bijenička cesta 54, 10000 Zagreb, Croatia*

[c]*Department of Chemistry, Faculty of Science, University of Zagreb, Horvatovac 102a, 10000 Zagreb, Croatia*

Understanding the allosteric regulation of *Geobacillus stearothermophilus* L-lactate dehydrogenase (GsLDH), a homotetrameric enzyme, is crucial for its application in industrial biocatalysis due to its role in lactate-pyruvate interconversion and NAD^+/NADH cofactor regeneration. In this study, we combined experimental and computational approaches to elucidate the mechanisms underlying the enzyme's allosteric activation by fructose 1,6-bisphosphate (FBP), which stabilizes tetramerization and enhances substrate affinity for pyruvate. We compared the wild-type (wt) enzyme with a triple mutant and a single mutant to assess the contributions of oligomerization and allosteric modulation. Our findings reveal that the triple mutant retains its tetrameric structure and high substrate affinity regardless of FBP. In contrast, the single mutant maintains tetramerization but lacks the enhanced substrate affinity, suggesting that oligomerization alone is insufficient to propagate the allosteric signal. Both oligomerization and allosteric modulator binding are necessary to establish communication pathways that effectively modulate substrate affinity, as demonstrated by significant changes in K_m [1]. To investigate dynamic conformational changes, we employed molecular dynamics (MD) simulations and applied our newly developed tool, MDavocado [2]. This computational tool visualizes MD trajectories using time-resolved Ramachandran plots, effectively aggregating millions of data points into interpretable visualizations. This approach enables rapid identification of flexible regions and global motion patterns across all amino acids. The application of MDavocado highlighted how FBP-induced oligomerization correlates with coordinated backbone dynamics, reinforcing the necessity of dual structural and allosteric inputs for optimal enzyme function. Our findings advance the understanding of structure-allostery relationships in industrially relevant enzymes and underscore the utility of MDavocado in resolving complex protein dynamics.

References:

[1] H. Cai, S. Shulami, Z. Štefanić, T. Hrenar, A. Maršavelski, A. Fishman, *Protein Sci.* submitted.

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IL 5. The Quest for Real Density-Splay Coupling Constant

Jaka Sočan

jaka.socan@ki.si

Laboratory for Molecular Modeling, National Institute of Chemistry,
Hajdrihova 19, SI-1001 Ljubljana, Slovenia

Our aim is to prove the existence of a finite density-splay coupling constant across various real-life polymers. To achieve this, we derive a multiscale continuum field model of a polymer in the isotropic phase [1], using sufficiently decorrelated simulation trajectories as the basis for analysis. By examining long-wavelength fluctuation amplitudes of monomer density and nematic tensor components, we gain quantitative insight into the coupling between density and order. To date, we have characterized density-splay coupling in double-stranded DNA and are currently extending this analysis to other polymer systems

References:

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IL 6. Spin-free SC-NEVPT2 Method for the Quantum Embedding of the Open-Shell Systems

Mihael Eraković[a,b] and Markus Reiher[a,b]

merakov@irb.hr

[a]*Department of Physical Chemistry, Ruđer Bošković Institute, Bijenička cesta 54, 10000 Zagreb, Croatia*
[b]*ETH Zürich, Department of Chemistry and Applied Biosciences, Vladimir-Prelog-Weg 2, 8093 Zürich, Switzerland*

High-level electronic structure models are essential for the correct description of molecular systems. These methods, however, suffer from unfavorable scaling with respect to system size, which limits their applicability. On the other hand, in many cases, such as the molecular recognition problem and the exploration of the chemical reaction mechanisms, only a small region of the large system is important for the process of interest. In those cases, it is usually sufficient to apply the high-level model on the relevant fragment only, while the rest of the system can be described with the low-level mean-field approaches. Quantum embedding methods, such as projection-based embedding [1], density matrix embedding theory [2], and bootstrap embedding [3], exploit this principle and have been successfully used to model large scale systems.

Embedding methods can yield fragments with significant multiconfigurational character, for which adequate electronic structure models, such as active space approaches, must be used. Density matrix renormalization group (DMRG) with the *N*-electron valence state perturbation theory (NEVPT2) has emerged as a go-to method for these cases [4]. In the case of systems with local open-shell regions, embedding methods can yield different effective potentials for the embedded α and β electrons, which is incompatible with the spin-free implementations of NEVPT2. Spin-free variant, however, has a more favorable scaling with respect to the active space size. We therefore developed an extension of the spin-free strongly contracted NEVPT2 method that treats the spin-difference term as a perturbation and works out-of-the-box with the commonly used spin-free DMRG software [5]. We present the results obtained by applying this method to the selected systems of interest to demonstrate its efficiency and accuracy.

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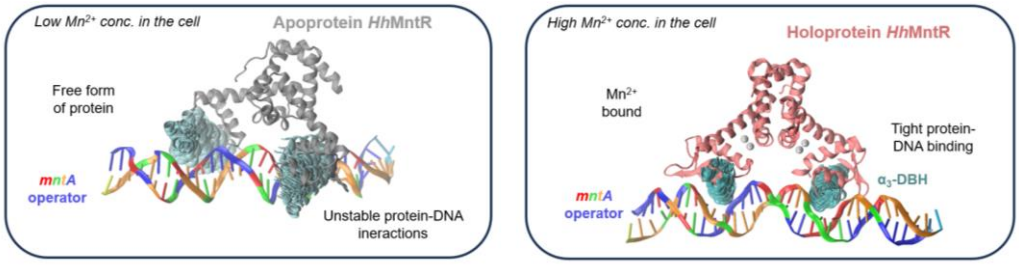
IL 7. Activation Mechanism of Transcription Factor MntR from the Bacterium *Halalkalibacterium halodurans* for DNA Binding

Martina Manenica[a] and Branimir Bertoša[b]

mmanenica@chem.pmf.hr

[a]*Hikma Ltd., Research and Development, Slavonska avenija 24/6, 10 000 Zagreb, Croatia*
[b]*University of Zagreb, Faculty of Science, Horvatovac 102a, 10 000 Zagreb, Croatia*

Transition metals, including iron, zinc and manganese, are essential for the survival of bacteria. The MntR protein (*Hh*MntR) plays a pivotal role in regulating manganese ion (Mn^{2+}) homeostasis in the bacterium *Halalkalibacterium halodurans*. To explore the structural and dynamic properties of various forms of *Hh*MntR upon Mn^{2+} binding, long-range all-atom molecular dynamics (MD) simulations were conducted, ranging from 500 ns to 1.25 µs. These simulations uncovered an allosteric mechanism triggered by Mn^{2+} binding, which modifies the non-covalent interaction network within the protein structure. This alteration results in a conformational change that significantly impacts the positioning of the DNA binding domains, thereby affecting the DNA binding affinity of *Hh*MntR [1]. In the next phase of research, the obtained structures of *Hh*MntR were aligned with DNA sequence corresponding to *mntA* operator by molecular docking. MD simulations of the resulting *Hh*MntR-DNA complexes provided valuable insights into the molecular interactions occurring between *Hh*MntR and DNA. The free *Hh*MntR exhibited highly dynamic behavior, frequently attaching to and detaching from the DNA backbone and inner grooves on a nanosecond timescale. In contrast, *Hh*MntR with Mn^{2+} in the binding site established stable and consistent non-covalent interactions with DNA. Similar behaviors were observed even in simulations that commenced with the protein separated from DNA by additional 10 Å to simulate complex formation. Moreover, key amino acids that contribute to the formation of the *Hh*MntR-DNA complex were identified, leading to the development of a molecular framework that facilitates *Hh*MntR's function as a transcription factor. Overall, the observed behaviors enhance the lateral movement of *Hh*MntR along the DNA sequence, allowing the protein to remain in proximity to the DNA while searching for specific base pairs to bind strongly upon activation by Mn^{2+} [2].



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[2] M. Manenica, B. Bertoša, *Int. J. Biol. Macromol.* **311** (2025) 142937.

CL 1. Experimental Work Guided by Computational Results: Reactions of Boronic Acids and Amines Give Structurally-Diverse B←N Adducts

Marina Juribašić Kulcsár and Mario Pajić

Marina.Juribasic@irb.hr

Ruđer Bošković Institute, Division of Physical Chemistry, Bijenička cesta 54, HR-10000 Zagreb, Croatia

Boronic acids $(RB(OH)_2$, R is aryl or alkyl) are important building blocks employed from organic synthesis, materials science to medicine [1]. Boroxines $(RBO)_3$, cyclotrimeric anhydrides of boronic acids, are formed by a reversible entropically-favorable dehydration of boronic acids [1]. Boron atoms in boroxines are Lewis acidic sites with a high affinity toward amines [2]. Synthesis of stable boroxine-amine adducts proceeds *via* ligand-facilitated trimerization [2]. The boronic acid first gives the corresponding boroxine, which reacts with the ligand (amine) usually forming one dative boron-nitrogen (B←N) bond, *i.e.* an adduct **A31**, Figure 1.

Herein, we describe a computational analysis of the structure, stability and spectra of B←N adducts of the phenylboronic acid (PBA) and a series of amines, Figure 1 [3]. Calculations guided the experimental work toward a successful isolation of adducts **A31**, **A32** and/or **A61** depending on the amine structure. Competitive binding experiments indicated that the exchange of the amines in adducts **A31** follows the computed adduct stabilities that increase with the amine basicity. Following the DFT prediction, the first adduct with two different amines, DMAP and pip, bound to one boroxine moiety was isolated and structurally characterized. The correlation of the calculated stabilities of adducts with pK_a values suggests that amines with pK_a larger than about 8 could form both **A31** and **A32** adducts. Less basic amines with pK_a lower than 8 would form only adducts **A31**. Results show that calculations can be used to predict possible and preferred product(s) and their spectral characteristics.

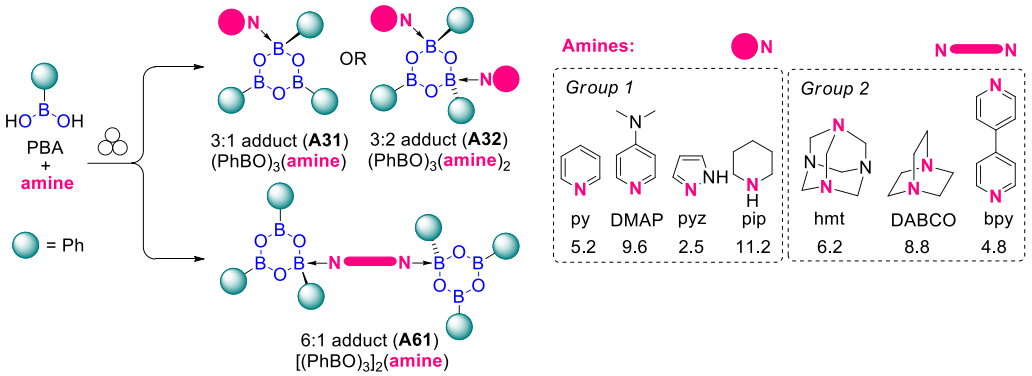

Figure 1. Reaction of phenylboronic acid and a series of amines with pK_a values for their conjugate acids.

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CL 2. Computational Methods for Predicting the pKa of Terminal Alkynes

Antonio Ljulj,[a] Lea Malezan,[a] Maria Kolympadi Marković,[b] Dean Marković,[b] Davor Šakić[a] and Valerije Vrček[a]

aljulj@pharma.hr

[a]*University of Zagreb Faculty of Pharmacy and Biochemistry, Ante Kovačića 1, Zagreb, Croatia*
[b]*Department of Biotechnology, University of Rijeka, Radmile Matejčić 2, Rijeka, Croatia*

The acid dissociation constant (pK_a) is among the most widely used physicochemical properties of molecules, as it is essential for understanding their chemical behavior in various environments. This is particularly true in aqueous solutions, where ionization significantly influences molecular interactions and reactivity. pK_a influences the pharmacokinetic profiles of drugs, including their absorption, distribution, metabolism, and excretion. It is also an important consideration in the design of drug excipients, delivery systems, and formulation vehicles [1]. One of the important chemical processes affected by the pK_a of alkynes is deuterium labelling. This process enables the synthesis of deuterated terminal alkynes, which are valuable intermediates used in a wide range of applications across biotechnology, medicinal chemistry, analytical chemistry, pharmaceutical and the agrochemical industry [2].

Although many experimental techniques exist for determining the pK_a of molecules—such as potentiometric titration, fluorometry, calorimetry, voltammetry and nuclear magnetic resonance—there is little data on computational methods that offer both speed and high accuracy [1b]. In this study, we used density functional theory (DFT) methods in the Gaussian software package, installed on the "Supek" supercomputer, to evaluate and compare several computational strategies for predicting the pK_a of terminal alkynes. These included thermodynamic cycles, isodesmic reaction schemes, GIAO-NMR chemical shifts, and hydrogen exchange barrier calculations.

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CL 3. Computational Investigation of Mechanical Properties of Organic Molecular Crystals

Tea Frey and Ivan Kodrin

tfrey@chem.pmf.hr

University of Zagreb Faculty of Science, Department of Chemistry, Horvatovac 102a, Zagreb, Croatia

The mechanical response of a molecular crystal to an applied force is a core material property closely connected to crystal packing and intermolecular interactions. With the advancements in crystal engineering, many flexible molecular crystals have been discovered which can be applied in the pharmaceutical industry and as nano- and micromechanical devices [1]. Some molecular systems exhibit polymorphism, allowing them to pack into crystalline structures in multiple ways, resulting in different mechanical responses. In this study, *p*-halogenated benzene-based esters are used to computationally explore the correlation between mechanical properties and crystal structure. These esters were selected based on previous experimental research on bromine derivatives that exhibit multiple polymorphs, with one being elastic and another brittle [2]. To predict and rationalize the mechanical response, we use periodic DFT methods implemented in CRYSTAL23 program. All crystal structures are optimized, and calculations of elastic constants are performed. From these calculations, mechanical properties such as Young's moduli are calculated and correlated with other computational tests, such as virtual tensile tests and interaction energies. Computational results are complemented with experimental studies to predict and explain the intermolecular interactions that lead to specific mechanical responses. By varying *para*-substituted halogens (chlorine, bromine and iodine), we investigate how subtle changes in molecular structure impact molecular packing and flexibility of synthesized materials. This work represents a step towards developing a computational methodology for predicting and understanding mechanically responsive crystalline organic materials.

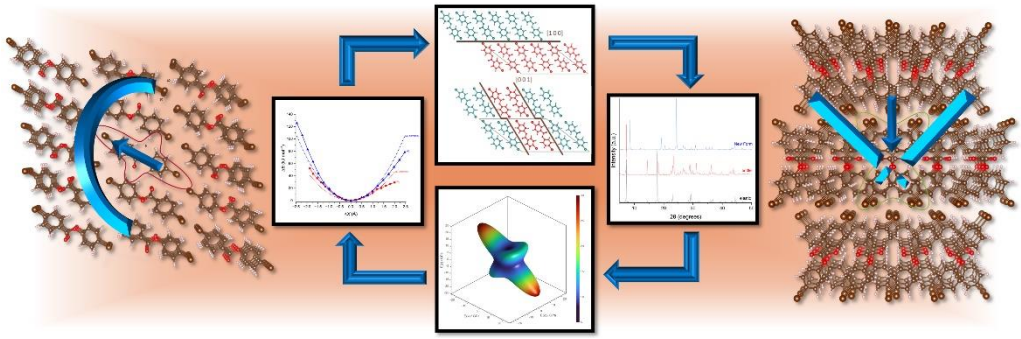

Figure 1. Computational modeling of mechanical properties of organic molecular crystals.

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CL 4. Hyaluronic Acid Dipeptide Gels Studied by Raman Spectroscopy, Atomic Force Microscopy and DFT Calculations

Vlasta Mohaček Grošev[a] and Jože Grdadolnik[b]

mohacek@irb.hr

[a]*Ruđer Bošković Institute, Bijenička 54, 10000 Zagreb, Croatia*
[b]*National Institute of Chemistry, Hajdrihova 19, 1000 Ljubljana, Slovenia*

We studied hyaluronic acid dipeptide gels as a model system for some antibacterial gel. Since one of the requirements for the active pharmaceutical ingredient is that it does not change when applied in formulation, it was important to monitor gels for any changes in vibrational spectra. N-Acetyl-Alanine-Methyl Amide (NAcAlaNHMA) and N-Acetyl-Tyrosine-Methyl Amide (NAcTyrNHMA) display different crystal packing (Fig. 1a and 1b), due to different hydrogen bond networks. Both dipeptides show good solubility in water [1], and form well miscible gels with hyaluronic acid (Fig. 1c and 1d).

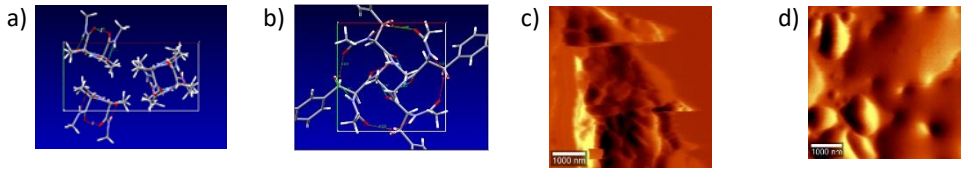

Figure 1. a) crystal structure of NAcAlaNHMA and b) NAcTyrNHMA powder, AFM images of c) NAcAlaNHMA/hyaluronate and d) NAcTyrNHMA/hyaluronate gels.

Phonons of the NAcAlaNHMA crystal were calculated using CRYSTAL09 program [2], while normal modes of NAcTyrNHMA and two basic disaccharide units of hyaluronic acid (HA), N-acetyl-β-D-glucosamine-β-(1→4)-D-glucuronic acid sodium salt, and β-D-glucuronic acid-β-(1→3)-N-acetyl-β-D-glucosamine sodium salt [3] were obtained using Gaussian16. Most of the observed gel bands correspond either to HA or to dipeptides in the crystalline form, while in one particular NAcTyrNHMA gel different spectrum was observed (Fig.2).

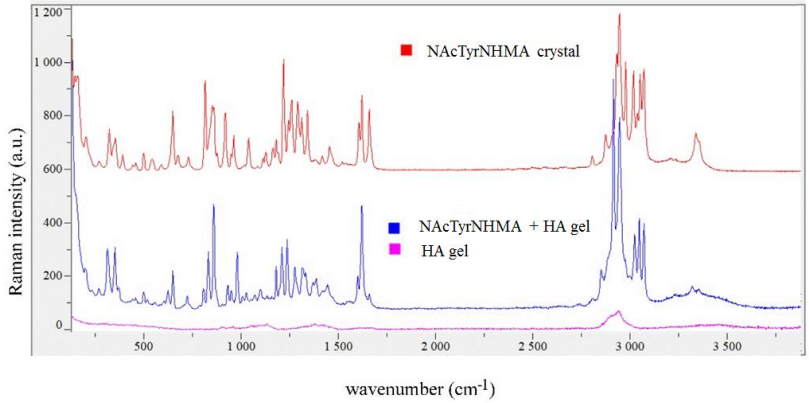

Figure 2. Raman spectra of NAcTyrNHMA powder and mixed with HA gel compared to the spectrum of HA gel.

Gels with a dipeptide-to-disaccharide molar ratio of 2:1 exhibited distinct shift in key vibrational modes most notably in the N–H stretching and C–O–H bending regions of the spectrum suggesting the formation of hydrogen bonds between the dipeptide and the HA matrix. These spectral shifts were consistent with the hypothesis that NAcTyrNHMA engages in specific binding interactions with the carboxyl and hydroxyl groups present on the hyaluronic acid backbone. The data support a model where one dipeptide molecule binds to the glucosamine carboxyl group and another to the glucuronic acid carboxylate group, forming a stabilized complex within the gel network. This behavior was not observed for NAcAlaNHMA, likely due to its simpler, less polar side chain, which lacks the phenolic hydroxyl group of tyrosine that facilitates hydrogen bonding.

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CL 5. Study of Photorelaxation Pathways in 7H and 9H Tautomers of 2,6-Diaminopurine

Haseena Sheik, Luca Grisanti and Antonio Prlj

hsheik@irb.hr

Ruđer Bošković Institute, Bijenička 54, 10000 Zagreb, Croatia

Understanding the ultrafast relaxation mechanisms of photoexcited nucleobase analogs is crucial for elucidating their photostability and potential biological implications. In this study, we employ nonadiabatic molecular dynamics simulations with surface hopping to investigate the ultrafast relaxation mechanisms of 2,6-diaminopurine in both its 7H and 9H tautomeric forms. Simulations are performed in vacuum and aqueous solution (implicit water clusters) using DFT/TDDFT electronic structure. Our results highlight the influence of solvation and on the excited-state dynamics and the role of conical intersections in system relaxation back to the ground state. This study provides deeper insights into the photophysics/photochemistry of purine derivatives and their implications for photostability in biological and biomimetic systems.

CL 6. Benchmark of Linear Algebra Libraries Accelerated on Graphical Processors

Nenad Mijić and Emir Imamagić

nenad.mijic@srce.hr

University of Zagreb, University Computing Centre SRCE, Josipa Marohnica 5, 10000 Zagreb

Computational chemistry increasingly relies on high-performance computing (HPC) to address complex scientific challenges. Graphics Processing Units (GPUs) have become a crucial tool for accelerating a wide range of simulations and calculations, offering new opportunities for efficiency and scalability. In this work, we provide a general overview of how numerical libraries for GPUs are influencing the development of computational chemistry. We discuss the benefits of using GPUs for typical computational tasks and highlight some of the challenges that arise when adapting traditional algorithms to GPU architectures. The use of GPU-accelerated computing enables researchers to study larger systems, perform longer simulations, and explore new areas of chemical research. As GPU hardware and software ecosystems continue to evolve, their impact on computational chemistry is expected to grow even further.

CL 7. Monte Carlo Study of Alignment of Microscopic Disks by Critical Casimir Forces

Gan Wang,[a] Piotr Nowakowski,[b,c,d] Nima Farahmand Bafi,[c,d,e] Benjamin Midtvedt,[a] Falko Schmidt,[f] Agnese Callegari,[a] Ruggero Verre,[g] Mikael Käll,[g] Siegfried Dietrich,[c,d] Svyatoslav Kondrat[c,d,e,h] and Giovanni Volpe[a]

Piotr.Nowakowski@irb.hr

[a]*Department of Physics, University of Gothenburg, SE-41296, Gothenburg, Sweden*
[b]*Division of Physical Chemistry, Ruđer Bošković Institute, Bijenička cesta 54, 10000, Zagreb, Croatia*
[c]*Max Planck Institute for Intelligent Systems, Heisenbergstraße 3, D-70569, Stuttgart, Germany*
[d]*IV th Institute for Theoretical Physics, University of Stuttgart, Pfaffenwaldring 57,D-70569, Stuttgart, Germany*
[e]*Institute of Physical Chemistry, Polish Academy of Sciences, 01-224, Warsaw, Poland*
[f]*Nanophotonic Systems Laboratory, Department of Mechanical and Process Enginnering, ETH Zürich, CH-8092, Zürich, Switzerland*
[g]*Department of Physics, Chalmers University of Technology, SE-41296, Gothenburg, Sweden*
[h]*Institute for Computational Physics, University of Stuttgart, Allmandring 3, D-70569, Stuttgart, Germany*

Critical Casimir forces act between small objects immersed in a liquid that is close to the critical point. In this study [1], colloidal disks of micrometer size were suspended in a water–lutidine binary mixture near its lower critical demixing point. We observed that the critical Casimir attraction caused the disks to align over the circular patches on the substrate in two distinct configurations — parallel or perpendicular — depending on the size of the patch and the thermodynamic distance from the critical point. I will present a theoretical method based on an adapted Monte Carlo simulation to calculate the probabilities of these configurations. The interaction potential between the disk and substrate consists of critical Casimir, screened electrostatic and gravitational interactions, and it is modeled using the Derjaguin approximation. The theoretical predictions are in qualitative agreement with experimental results.

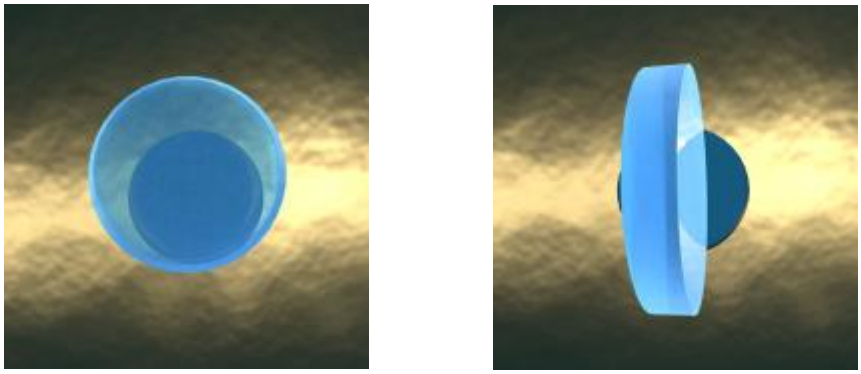

Figure 1. Schematic plot of the disk over the patch on the substrate in parallel (left panel) and perpendicular (right panel) configurations.

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CL 8. Noble Metal Nanoclusters: Tiny Structures, Big Impact

Martina Perić Bakulić

martina.peric-bakulic@ktf-split.hr

Faculty of Chemistry and Technology, University of Split, Ruđera Boškovića 35, 21000, Split, Croatia

Nanoscience, followed closely by computational chemistry, has emerged as a powerful and valuable research avenue in recent decades [1, 2]. This is largely due to the unique physical phenomena observed at the nanoscale between 1 and 100 nm, which aligns with Richard Feynman's visionary idea of manipulating matter at the atomic level, as famously presented in his lecture *"There's Plenty of Room at the Bottom"* [3].

Within this scale, atomically precise noble metal nanoclusters (NCs) have gained significant attention, particularly for biomedical applications. Gold and silver NCs, in particular, stand out due to their ultra-small size, excellent biocompatibility, intense photoluminescence, low toxicity, and photostability. However, their standalone use in bioimaging is limited, as they tend to degrade in biological environments, losing both structural integrity and optical function.

To overcome this, functionalization with biomolecules plays a critical role. Such surface modifications not only stabilize the NCs but also enhance their emission properties, reduce toxicity, and enable specific target recognition - essential for effective biosensing. This presentation focuses on the optical properties of noble metal NCs , aiming to explore their dual potential: enhancing light-harvesting capabilities for solar energy applications, and enabling advanced bioimaging properties. Special emphasis is placed on integrating noble metal NCs with organic dyes and tailored ligands.

Time-dependent density functional theory (TDDFT) serves as a key theoretical approach, providing insight into the origins of optical properties in both liganded NCs and bio-nano hybrids of noble metals, guiding the design of multifunctional nanomaterials [4-7].

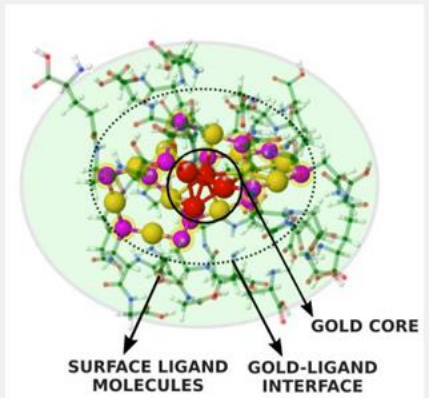

Figure 1. Schematic representation of gold nanocluster as a multishell system [5].

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Posters

P 1. Computational Study of Mechanical Properties of Halogenated Azobenzene Crystals

Stipe Blažević, Tea Frey and Ivan Kodrin

sblazevic.chem@pmf.hr

University of Zagreb Faculty of Science, Department of Chemistry, Horvatovac 102a, Zagreb, Croatia

Traditionally, molecular crystals are considered brittle and inflexible. However, numerous examples have demonstrated elastic or plastic mechanical responses, challenging this assumption. This discovery has led to growing research on flexible molecular crystals positioning them as a promising class of functional materials due to their elasticity or plasticity. Mechanical flexibility opens up many potential applications of flexible molecular crystals in numerous fields, such as pharmaceuticals, mechanical actuators and optoelectronics [1,2]. Studies have shown that azobenzene derivatives exhibit different mechanical properties, such as bending magnitude, due to a trans-cis photoisomerization [3]. This study investigates some of these derivatives, focusing on how subtle modifications in chemical structure and intermolecular interactions influence their mechanical behavior. Some of the researched structures exhibit polymorphism, which is the ability of a compound to crystallize into more than one crystal structure. Mechanical properties of known polymorphs of halogenated azobenzenes were examined in this study. The influence of chemical structure on mechanical properties was explored by varying para-substituted halogens (chlorine and bromine). Periodic DFT methods implemented in the CRYSTAL23 program were used to optimize molecular geometries and to compute properties such as interaction energies and virtual tensile tests. The synthesis of chlorine and bromine derivatives has been successful, of which chlorine's crystal structure has demonstrated elastic behavior in preliminary tests. The findings show that both molecular structure and crystal rearrangements impact interaction energies and tensile tests, which can be directly correlated to the material's mechanical properties. These results highlight the potential of computational modeling in predicting and tailoring the mechanical behavior of organic crystalline materials.

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P 2. Selective Butyrylcholinesterase Inhibition by α-Acylaminobenzamides: A Quantum Chemical Docking Study

Jakov Borovec, Toni Divjak, Alma Ramić, Nika Jakobović, Bruna Bakota, Karla Krstinić, Ines Primožič and Tomica Hrenar

jakov.borovec@student.pmf.hr

Department of Chemistry, , University of Zagreb Faculty of Science, Horvatovac 102a, HR-10000 Zagreb, Croatia

Alzheimer's disease is a devastating neurodegenerative disorder that progressively impairs individuals' cognitive abilities, ultimately leading to severe memory loss and difficulty performing everyday tasks [1,2]. This incurable illness ranks among the leading causes of death worldwide, highlighting its significant impact on global health. The cholinergic hypothesis posits that an acetylcholine deficiency, a crucial neurotransmitter involved in learning, memory, and attention, contributes significantly to the disease's progression. Acetylcholine exerts its effects by binding to specific receptors in the brain. However, enzymes called cholinesterases, primarily acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), break down acetylcholine, effectively terminating its signaling. In individuals with Alzheimer's disease, acetylcholine levels are significantly reduced due to neuronal degeneration and impaired synthesis, leading to the development of cholinesterase inhibitors as the primary treatment strategy.

This study aims to find the best selective inhibitor of BChE by semi-flexible quantum-chemical molecular docking. A newly developed parallelized Monte Carlo algorithm for sampling the huge configurational spaces was used for structure generation [3]. This algorithm considered all translational, rotational, and torsional degrees of freedom. To ensure physically realistic structures, a *smart structure generator* was used to discard any configurations with conflicting atoms. Binding energies within the active site were estimated using single-point quantum chemical calculations with the PM7 hamiltonian [4]. The top 1000 local minima identified through this process underwent geometry optimization for further refinement. Finally, the optimized structures were clustered and ranked based on binding energy. An automated hydrogen bond search module and visual inspection were used to analyze the resulting docked structures.

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P 3. Predicting Fluorescence Efficiency of J-aggregate Squaraine Dyes as (Semi)Transparent Solar Concentrator Luminophores

Margarita Bužančić Milosavljević

margarita@stim.unist.hr

Center of Excellence for Science and Technology-Integration of Mediterranean region (STIM), Faculty of Science, University of Split, Poljička cesta 35, 2100 Split, Croatia

Reliable prediction of fluorescence quantum yield (QY) from first principles is essential for the rational design of high-performance fluorophores [1], particularly for applications in transparent luminescent solar concentrators (TLSCs). In this study, we employ a combination of density functional theory (DFT) and time-dependent DFT (TD-DFT) methods to investigate the electronic, optical, and photophysical properties of squaraine-based J-aggregates in toluene for application as (semi)transparent luminophores.

Radiative and non-radiative rate constants are calculated using Fermi's Golden Rule within the framework of the vertical harmonic approximation (VH) model for both ground and excited states. To evaluate the accuracy of quantum yield predictions, we systematically analyze the effect of different lineshape broadening functions (Gaussian, Lorentzian, and Voigt) on predicted transition rates.

Applying these methods to a series of covalently bound squaraine oligomers—dimers, trimers, and tetramers—we identify the SQA tetramer (or larger) J-aggregate, composed of monomeric subunits with a central squaric acid ring and two oxygen atoms, as a promising NIR-active luminophore. These systems exhibit selective near-infrared (NIR) absorption and emission, along with high predicted fluorescence QY [2]. Their tunable and size-dependent photophysical properties suggest strong potential for further optimization and integration into transparent solar-harvesting systems.

Our findings highlight the importance of accurate vibrational structure modeling in the prediction of QY and demonstrate how theoretical methods can effectively guide the development of new, efficient fluorophores for luminescent solar technologies.

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P 4. Estimating Spectral Bandwidths with the Nuclear Ensemble Approach

Andrea Cocut[a] and Marin Sapunar[b]

andrea.cocut@chem.pmf.hr

[a]*Department of Chemistry, Faculty of Science, University of Zagreb, Horvatovac 102a, 10000 Zagreb, Croatia*
[b]*Ruđer Bošković Institute, Bijenička 54, 10000 Zagreb, Croatia*

The Nuclear Ensemble Approach (NEA) is a widely used method for simulating electronic absorption spectra by computing excitation energies and oscillator strengths of several electronic states across an ensemble of nuclear geometries. The absorption cross-section is then obtained by convolving each sampled point with kernel functions. In practice, Gaussian kernel functions [1] are typically employed, where the bandwidth parameter critically influences the smoothness of the resulting density estimate. A bandwidth that is too small may lead to overfitting, capturing noise rather than the true underlying distribution, while an excessively large bandwidth can cause underfitting. In the present literature [2], the rule-of-thumb bandwidth estimators are mostly used, with Silverman's rule [3] being the most common.

A key challenge in NEA simulations is the computational cost associated with large sample sizes, as each geometry requires expensive single-point electronic structure calculations. In this work, we adopt a more rigorous approach for selecting the bandwidth parameter by employing cross-validation to estimate the optimal value of the bandwidth parameter for a given sample. Our goal is to minimize the required sample size while preserving spectral accuracy, thereby reducing computational costs. To facilitate this, we developed a custom implementation based on the Fast Fourier Transform Kernel Density Estimation (FFTKDE) algorithm from the KDE.py library. We compared our method with Silverman's estimator and experimental data, assessing performance across total spectra as well as spectra decomposed into either adiabatic or diabatic (obtained using wave function overlaps [4]) state contributions. Additionally, we determined the uncertainty estimate with bootstrap resampling and conducted a thorough analysis of how sample size and the number of cross-validation splits impact the bandwidth estimation.

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P 5. Vibrational Self-Consistent Field Theory Based Wigner Distribution for Sampling Initial Conditions for Trajectory Surface Hopping Dynamics

Robert Cvjetinović,[a] Rajko Ćosić,[b] Jovan Odavić,[c] Marin Sapunar[d] and Nađa Došlić[d]

rcvjetinovic.chem@pmf.hr

[a]*Department of Chemistry, Faculty of Science, University of Zagreb, Horvatovac 102a, Zagreb, Croatia*
[b]Department of Physics, *Università degli Studi di Napoli Federico II, Corso Umberto I 40, Naples, Italy*
[c]*IT4Innovations National Supercomputing Center, Technical University of Ostrava, Studentská 6231/1b, Ostrava, Czech Republic*
[d]*Division of Physical Chemistry, Ruđer Bošković Institute, Bijenička 54, Zagreb, Croatia*

For trajectory surface hopping simulations, the choice of initial conditions can have a great impact on obtained photochemical observables [1, 2, 3]. One of the more popular methods for generating initial conditions is sampling from the harmonic Wigner distribution due to the fact that it is simple to use and has a low computational cost, while still taking into account the quantum nature of the nuclei. However, it doesn't take into account the anharmonicity and the coupling between normal modes [2]. This can greatly affect the obtained observables, as was recently demonstrated for methyl hydroperoxide (MHP) [3]. While sampling from a trajectory obtained using a quantum thermostat provides more reliable results for MHP [3], it is significantly more expensive compared to sampling from the harmonic Wigner distribution. The quantum thermostat can also introduce unknown errors, which is why it is advisable to validate the results with even more expensive path-integral molecular dynamics simulations [4].

In this work we will present a novel approach based on anharmonic Wigner distributions generated from the vibrational self-consistent field wavefunctions in the harmonic oscillator or the distributed Gaussian basis. The method takes anharmonicity and normal mode coupling into account in a mean-field manner, and when combined with an adaptive density-guided approach for automatic generation of the potential energy surfaces [5], provides a cheap and easy to use alternative to the above-mentioned methods. The performance of the method is illustrated on MHP and malonaldehyde.

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P 6. *In Silico* Profiling of Physicochemical and ADMET Properties of Boron Compounds

Dea Demeter,[a] Nikola Basarić[b] and Višnja Stepanić[b]

ddemeter@chem.pmf.hr

Department of Chemistry, Faculty of Science, University of Zagreb, Horvatovac 102a, Zagreb, Croatia

Boron-containing compounds constitute a diverse chemical group with a wide range of structures and properties. While medicinal chemistry has traditionally focused on standard carbon-based compounds, interest in boron-containing compounds has grown in recent decades due to their emerging therapeutic potential [1]. Certain classes of boron containing compounds have been gaining more attention as potential drugs [1, 2]. As persistent health challenges demand broader chemical exploration, diversifying the scope of investigated compounds is essential [1].

In the presented research study, various organoboron derivatives from classes recognized in literature for their medical potential, were compared mutually and with known drugs, based on predicted physicochemical and ADMET properties in order to assess their drug-likeness [2]. Data was collected from the open-access databases DrugBank and PubChem. Molecules were represented by physicochemical descriptors estimated by SimulationsPlus and DataWarrior software and structural fingerprints calculated using RDKit. Descriptor selection was performed through multiple analyses and keeping only features most relevant for characterization of (physico)chemical space of organoborons. Additionally, molecules were analyzed using criteria from Lipinski's Rule of Five and Veber's rule.

Compound comparison was performed using unsupervised machine learning methods, including Principal Component Analysis (PCA), t – distributed Stochastic Neighbor Embedding (t – SNE) and Uniform Manifold Approximation and Projection (UMAP). These methods are useful tools for visualizing high-dimensional spaces. Additionally, other methods of data analysis and visualization were also used in order to illustrate variations in key descriptors across compound classes.

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P 7. Computational Investigation of the Novel Diaminoterephthalate-Based Fluorophores

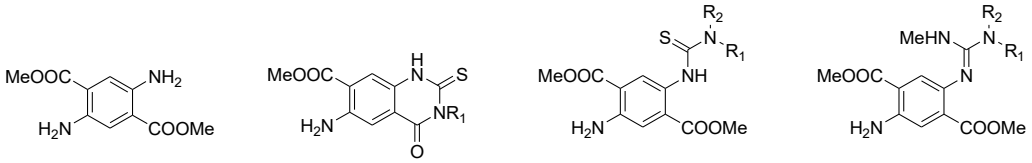
Zoran Glasovac, Ivana Antol and Davor Margetić

glasovac@irb.hr

Division of organic chemistry and biochemistry, Ruđer Bošković Institute, Bijenička cesta 54, HR-10000 Zagreb, Croatia

Diaminoterephthalates are typical representatives of the single-benzene-based fluorophores, and they became important building blocks for devising new organic optoelectronic materials [1,2]. The typical fluorescence band of the simple *N*-alkylated 2,5-diaminoterephthalates (**DATA**, Fig. 1) falls above 500 nm, with the observed Stokes shift larger than 100 nm [1]. This was attributed to the specific arrangement of the electron-donating and the electron-accepting groups, leading to the S_1 with highly pronounced charge-transfer character [3]. Besides that, geometry changes triggered by the antiaromaticity in the S_1(FC) region were also recognized as the mechanism that strongly contributes to the large Stokes shift [3,4].

Recently, we found that the PBE0/6-31G(d)//M06-2X/6-31G(d) model presents a simple but quite accurate computational model for predicting absorption and the emission maxima in the selected terephthalate-based fluorophores [5]. Herein, we are presenting calculated basic photophysical properties (λ_{Em} and λ_{Abs}) for the series of thioureas (**1** and **2**, Fig. 1) and guanidines (**3**), as well as the acid/base properties of the guanidine derivatives and their tendency toward intramolecular proton transfer in the S_1 state.



DATA **1** (R_1 = alkyl or aryl) **2** (R_1, R_2 = alkyl or H) **3** (R_1, R_2 = alkyl or H)

Figure 1. Schematic structures of the investigated groups of compounds.

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P 8. *Optuna* Package in Reactive Force-Field Optimization: the Li/O Case Study

Vjeran Gomzi and Jakov Juvančić

vjeran.gomzi@unizg.fer.hr

University of Zagreb Faculty of Electrical Engineering and Computing, Unska 3, 10 000 Zagreb, Croatia

Reactive force fields are used in molecular dynamics to model reactivity of large structures with reasonable accuracy. Development of the force field comes down to finding the set of parameters for modeling structures consisting of specific atom species. Reactive force field such as the used in ReaxFF package involves optimization of considerable number of parameters, making the optimization process lengthy and laborious, even for the systems of just two atom species. The standard protocol implemented offers single-parameter parabolic minimization, a process which is robust, although does not account for possible parameter dependencies [1]. Here we use a novel *Python* set of routines implemented in the *Optuna* package to gain more control and speed up the optimization. Force-field for lithium and its oxide species, of interest in modeling of lithium-air batteries, has been developed and has been used with considerable success [2]. This force-field, however, is based on electronegativity equilibration method (EEM) used to model atomic charges. A novel method that resolves two major theoretical problems of the previous EEM approach is based on Kohn–Sham density functional theory approximated to the second order (ACKS2) for modeling the charge distribution. This method for Li/O has recently been developed although some shortcomings of the optimized force field are observed [3]. Here we develop protocol for the use of *Optuna* capabilities in the optimization of the ReaxFF force field, and apply it in development of the improved ACKS2 reactive force field for Li/O systems. We validate the force field by the quality of reproduction of the (crystal) structures and DFT charges.

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P 9. Computational Study of Mechanically Flexible Polymorphs of Halogenated Phenyl Benzoates

Igor Kerš, Tea Frey and Ivan Kodrin

igor.kers@student.pmf.hr

University of Zagreb Faculty of Science, Department of Chemistry, Horvatovac 102a, Zagreb, Croatia

For a long time, molecular solids have been used in various fields such as pharmaceuticals, electronics, and materials science. It was shown that molecular solids exhibit electronic and optical properties which could be utilized to make molecular semiconductors and optoelectronics. Despite their potential, molecular solids also possess negative traits that hinder their marketability, leaving room for improvement and motivating scientists to develop new molecular materials [1]. Crystal engineering plays a crucial role in synthesizing new molecular materials with desired properties. One way to accomplish that is by understanding crystal packing, which results from intermolecular interactions [2]. Crystal bending and shearing are physical properties which can be directly tied to the crystal structure. Molecular compounds of the same chemical composition can pack in different ways forming polymorphs. For instance, 4-bromophenyl 4-bromobenzoates form polymorphs with very different physical properties: one is brittle while the other is elastic [3]. This study focused on finding the relationship between intramolecular interactions in molecular crystals and their elastic properties. Various derivatives of *p*-halogenated phenyl benzoates were modeled and their crystal structures were optimized using periodic DFT methods in CRYSTAL23 program. Their elastic behavior was investigated by calculating interaction energies between molecules along specific crystal planes and performing virtual tensile tests. Additionally, different polymorphs and the influence of chemical structure by varying halogens in *para* position were examined to assess how minor structural differences affect mechanical properties. Finally, computational results were compared to experimental studies. A positive correlation between computational and experimental findings could enhance future research in designing molecular crystals with desired physical properties.

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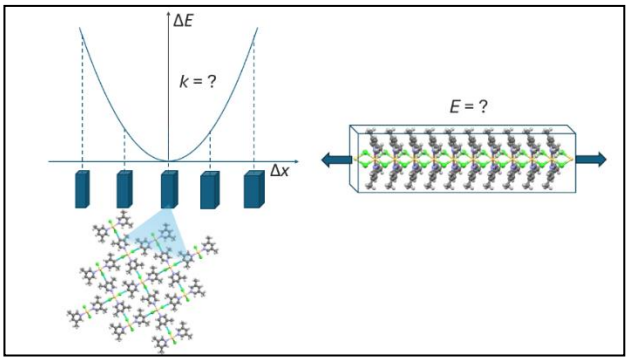
P 10. Computational Studies of Flexible Cadmium(II) and Copper(II) Coordination Polymers

Lea Komočar, Mateja Pisačić, Marijana Đaković and Ivan Kodrin

lea.komocar@chem.pmf.hr

University of Zagreb Faculty of Science, Department of Chemistry, Horvatovac 102a, Zagreb, Croatia

The discovery that crystals can move in response to external light, thermal, or mechanical stimuli has changed the previously held belief that crystals are static systems [1]. When subjected to external mechanical forces, crystals typically bend either elastically or plastically. While numerous organic crystals that dynamically respond to external stimuli have been documented, the number of metal-organic crystal systems with such properties remains limited [2]. Research has shown that one-dimensional coordination polymers are excellent candidates for studying the relationship between mechanical flexibility and structural characteristics [3]. Additionally, it has been established that the explanation for the type of mechanical bending lies in the intermolecular interactions between the building blocks in crystal packing [4]. To gain a deeper understanding of these fascinating crystalline behaviors, we have chosen to study crystals of coordination polymers of cadmium(II) and copper(II) halides with 3,5-dimethylpiridine (**3,5-dmp**): $[CdCl_2(\mathbf{3,5\text{-}dmp})_2]_n$ (**1**), $[CdBr_2(\mathbf{3,5\text{-}dmp})_2]_n$ (**2**), $[CuCl_2(\mathbf{3,5\text{-}dmp})_2]_n$ (**3**), $[CuBr_2(\mathbf{3,5\text{-}dmp})_2]_n$ (**4**). Using computational DFT methods, the deformation of the unit cells along the crystallographic axes was simulated. Comparison of the fitted potential energy curves enabled us to better understand the effect of intermolecular interactions on mechanically induced flexibility.



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P 11. Mechanistic Study of the Conversion of Primary Alcohols and Butadiene to Branched Ketones Using Rhodium Catalyst

Chaiyaporn Lakmuang[a] and Boodsarin Sawatlon[b]

clakmuan@irb.hr

[a]*Division of Physical Chemistry, Ruđer Bošković Institute, Zagreb, Croatia*
[b]*Department of Chemistry, Chulalongkorn University, Bangkok, Thailand*

The direct formation of ketones without premetalation is a key priority in catalysis research as it offers more straightforward reaction process and fewer steps [1]. Here we present our investigation of the mechanism for the conversion 3-methoxybenzyl alcohol and butadiene into branched isobutyl ketone with rhodium (I) complex catalyst under basic condition using density functional theory [2]. The reaction consists of four main steps: (I) oxidation of the alcohol reactant to generating the corresponding aldehyde and rhodium(I) hydride complex as active catalyst, (ii) hydrogenation of butadiene to form the allyl–Rh(I) complex, (iii) carbonyl addition from the allylic carbon to produce rhodium(I) alkoxide intermediate, and (iv) hydrogen transfer processes to generate the desired ketone product, which is released in its enolate form. The rate-determining states are in the carbonyl addition process (both intermediate and transition state) with an energy barrier of +30.4 kcal/mol. The formation of the linear ketone is hindered by steric effects from two PPh_3 ligands bound to the Rh center throughout the reaction. Moreover, the positions of transferred hydrogens in our proposed catalytic cycle are consistent with the results of the deuterium labeling experiment, highlighting the hydrogen (auto)transfer process in this conversion of primary alcohol to branched ketones.

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P 12. Tools for Prediction of pK_a Values of Acetylenes: GIAO-NMR Chemical Shifts and Hydrogen Exchange Barriers

Antonio Ljulj,[a] Lea Malezan,[a] Maria Kolympadi Marković,[b] Dean Marković[b] and Valerije Vrček[a]

lea.malezan@gmail.com

[a]*University of Zagreb Faculty of Pharmacy and Biochemistry, Ante Kovačića 1, Zagreb, Croatia*
[b]*Department of Biotechnology, University of Rijeka, Radmile Matejčić 2, Rijeka, Croatia*

The diversity in acidity among compounds containing a terminal alkyne group indicates that such functional groups can exhibit very different acid-base properties, which can significantly influence a compound's biological activity, chemical stability, and environmental fate [1]. The acidity of terminal alkynes is extremely important in organic chemistry and the pharmaceutical industry. For this reason, we aimed to develop a simple and efficient computational protocol to estimate their pKa values. To this end, we examined various quantum chemical methods by analyzing and testing a collection of compounds with known experimental pKa values. Although standard thermodynamic approaches proved insufficient, we identified two methods we consider reliable: a kinetic approach, based on calculating the proton exchange barriers in terminal alkynes, and a spectroscopic approach, based on the theoretical calculation of ^{1}H NMR chemical shifts. Both methods show a very good correlation with experimental data, confirming their practical value for predicting the acidity of alkynes [2].

Using these approaches, we calculated the pKa values of drugs containing a terminal alkyne group (ethinylestradiol, rasagiline, selegiline, pargyline, 5-ethynyluracil, and erlotinib). The results showed that the predicted pKa values of these compounds vary by as much as 8 to 9 pK_a units.

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P 13. Screening of Commercial Compound Library for Novel Catalytic Inhibitors of DPP3

Luka Petohleb,[a] Antonia Matić[b] and Antonija Tomić[b]

lukapetohleb97@gmail.com

[a]*Faculty of Science, Horvatovac 102A, Zagreb, Croatia*
[b]*Division of organic chemistry and biochemistry Ruđer Bošković Institute, Bijenička cesta 54, Zagreb, Croatia*

Dipeptidyl peptidase III (DPP3) is a zinc-dependent metalloprotease that cleaves dipeptides from the N-terminus of oligopeptide substrates. It is found in almost all human tissues and is thought to contribute to protein degradation, blood pressure regulation [1], protection against oxidative stress, and pain modulation [2]. Although DPP3 is implicated in several physiological and pathological processes, including oxidative stress response and cancer progression [3], only a few strong DPP3 inhibitors are known, and even the most potent ones lack specificity, targeting multiple metallopeptidases [4]. Identifying specific DPP3 inhibitors would provide valuable tools for a more detailed investigation of its role in human health and disease.

In this study, we applied a virtual high-throughput screening (vHTS) approach using the Glide program from Schrödinger to identify novel and more selective inhibitors of DPP3's enzymatic activity from the Enamine compound library. Out of 460 160 compounds in the Hit Locator Library, 12 candidates showing the most favorable docking scores and binding geometries with DPP3's active site were selected for further analysis. These were subjected to molecular dynamics (MD) simulations of at least 400 ns. Compound selected for experimental validation was chosen based on stable binding interactions and favorable binding free energy calculated using the MM-PBSA method.

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P 14. Integrating Computational IR Spectroscopy and Principal Component Analysis for Monitoring Mechanoenzymatic Transformation of Glycolic Acid

Zrinka Pišonić, Jakov Borovec, Tomica Hrenar and Aleksandra Maršavelski

zpisonic@chem.pmf.hr

University of Zagreb Faculty of Science, Department of Chemistry, Horvatovac 102a, Zagreb, Croatia

Poly(glycolic acid) (PGA) is a biodegradable and biocompatible polymer with growing importance in biomedical and environmentally sustainable applications [1]. Its synthetic pathway involves the esterification of glycolic acid to form linear oligomers, which then undergo cyclization to yield glycolide, a six-membered cyclic diester. Subsequently, glycolide is converted into PGA via ring-opening polymerization [2]. Traditional synthesis routes for glycolide and PGA typically require high temperatures, metal catalysts, and solvents. In contrast, mechanoenzymatic synthesis using *Candida antarctica* lipase B (CALB) under solvent-free conditions offers a greener and potentially more scalable alternative. However, real-time monitoring and product identification in such solid-state biocatalytic reactions remain challenging due to limited spectral resolution and overlapping vibrational features.

In this study, we combined attenuated total reflection infrared (ATR-FTIR) spectroscopy with density functional theory calculations and principal component analysis (PCA) to monitor and interpret the transformation of glycolic acid to glycolide under solvent-free conditions using CALB. Theoretical IR spectra of both glycolic acid and glycolide were computed at the B3LYP-D3BJ/6-311++g(d,p) level, showing good agreement with key experimental vibrational bands. PCA was applied to experimental IR data collected across different reaction time points, enabling clear separation of reactant and product phases and aiding in spectral assignment. This approach demonstrates how computational tools coupled with multivariate analysis can significantly improve the interpretation of complex spectral data and provide product identification in complex reaction mixtures.

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P 15. Disruption of Monoamine Oxidase B Enzyme by SARS-CoV-2 Spike Protein: Implications for Neurodegenerative Diseases

Lucija Vrban and Robert Vianello

lvrban@irb.hr

Division of Organic Chemistry and Biochemistry, Ruđer Bošković Institute, Bijenička cesta 54, 10 000 Zagreb, Croatia

COVID-19, caused by the **SARS-CoV-2** virus, is primarily associated with respiratory symptoms, but increasing evidence suggests significant neurological effects, possibly due to the virus's interaction with monoamine oxidase (**MAO**) enzymes [1]. Our research investigates the binding of the SARS-CoV-2 spike protein to the **MAO-B** enzyme, with the hypothesis that this interaction disrupts the delicate balance of the monoaminergic system, potentially leading to neurodegenerative processes [2].

We employed a comprehensive computational approach to investigate the interactions between the **spike protein** and the **MAO-B** enzyme. Flexible molecular docking algorithms were used to predict binding orientations and affinities, followed by **molecular dynamics (MD) simulations** to stabilize and provide insights into the dynamics of the protein complex. High-affinity binding sites for the spike protein on MAO-B were identified, and MD simulations confirmed the stability of these interactions. **MM-GBSA** analysis revealed a high binding affinity of the spike protein to the MAO-B enzyme and consequential significant changes in the free binding energy of inhibitors and endogenous substrates on the complex. To further validate the impact of the spike protein on the catalytic activity of MAO-B and its potential effect on neurotransmitter metabolism and neurodegenerative pathways, **quantum mechanics/molecular mechanics (QM/MM) simulations** will be conducted.

The obtained results suggest a potential mechanism through which COVID-19 could affect the monoaminergic system, contributing to neurological symptoms in patients. The study highlights the need for further experimental validation and the development of therapeutic interventions to mitigate these effects. Understanding the described interactions opens new avenues for treating neurodegenerative consequences associated with COVID-19 [3].

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P 16. Quantum Tunneling in the Low-Lying Water Hexamer Isomers

Nina Tokić and Marko Tomislav Cvitaš

ntokic@phy.hr

Department of Physics, Faculty of Science, Bijenička cesta 32, Zagreb, Croatia

Studying water clusters is of great importance because the behavioral essence of intermolecular forces between the water molecules mimics that of the bulk. The water hexamer is a particularly interesting water cluster to investigate both experimentally and theoretically because it is the smallest one with a 3D structure, often called the smallest water droplet. The energetically lowest structural isomers detected experimentally are prism, cage, and book [1].

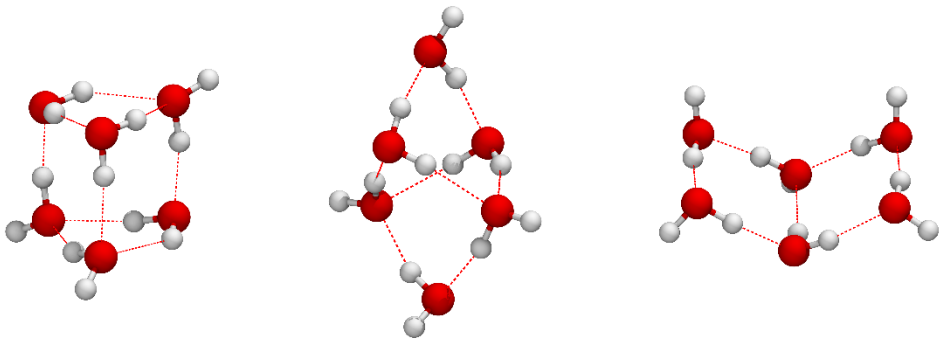

Figure 1. The lowest-energy structural isomers of the water hexamer: prism (left), cage (middle) and book (right).

Tunneling splittings (TSs) of these isomers are calculated using the modified WKB (Wentzel–Kramers–Brillouin), a semiclassical method based on instanton theory [2]. The method starts with finding the minimum action path, along which the semiclassical wavefunction is constructed and inserted into the Herring formula, yielding tunneling matrix elements. Finally, splittings are obtained by diagonalizing the tunneling matrix. TSs in the water hexamer prism are determined for a number of excited low-frequency vibrational modes. Internal rotation of a double-donor water monomer is identified as the mechanism that potentially plays a role in the appearance of the TS pattern in vibrationally excited states in addition to the mechanisms that shape the TS pattern in the ground state. The ground-state TSs of the water hexamer cage were found to form a doublet of doublets. The finer splitting is two orders of magnitude smaller due to a significant difference in the barrier heights for bifurcations of the water monomers at the two opposite vertices of the cage. First estimates of the ground-state TSs in the water hexamer book structure are also calculated. The TS pattern is again a doublet of doublets, caused by the monomer motions on one side of the book isomer. The wider doublet is of similar size to that in the cage and the narrower doublets an order of magnitude larger than that in the cage.

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P 17. Identification of SH2D3C as a Novel Interactor of DPP III

Sanja Tomić, Ana Tomašić Paić, Lucija Horvat and Mihaela Matovina

Sanja.tomic@irb.hr

Institute Ruđer Bošković, Bijenička 54, 10000 Zagreb, Croatia

The zinc dependent exopeptidase DPP III has broad specificity towards naturally occuring peptides four to eight amino acid residues long. In addition to its enzymatic activity DPP III interacts with other proteins and, through these interactions, participates in several pathophysiological processes in humans. One such 'moonlighting' activitiy of DPP III is mediated through its interaction with SH2D3C, one of three members of a protein family known as novel SH2-containing proteins (NSPs), which are characterized by the presence of both an SH2 domain and a Ras GEF-like domain (a domain similar to guanine nucleotide exchange factor domains of Ras family GTPases).

We have shown that SH2D3C binds to DPP III through its C-terminal Ras GEF-like domain using several low-throughput experimental methods, detected the colocalization of the proteins in living cells, and confirmed their direct interaction in the cytosol and membrane ruffles [1]. Computational analysis further supported the binding of the C-terminal domain of SH2D3C to DPP III. This was the first indication that SH2D3C might be an interactor of DPP III, and that their interaction might represent a link between the regulation of the oxidative stress response via the KEAP1–NRF2 pathway and the processes in which SH2D3C is involved, including cell adhesion, migration, and growth. Furthermore, we computationally mutated three Arg residues, Arg125, Arg159 and Arg598, of DPP III that form strong interactions with SH2D3C and whose mutations were detected in cancer cells, and studied the interaction of mutated variants of DPP III with SH2D3C.

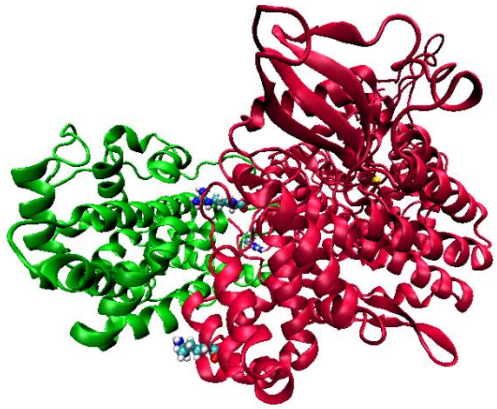

Figure 1. The DPP III - SH2D3C complex used in the computational study. Arginines that have been found to be mutated in cancer cells are shown in ball and stick representation.

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P 18. Stability Indicators of Hydrogenated Fullerenes

Tomislav Došlić,[a] Manuel Martinović[b] and Nađa Došlić[b]

mmartin@irb.hr

[a]*Faculty of Civil Engineering, University of Zagreb, Zagreb, Croatia*
[b]*Institute Ruđer Bošković, Bijenička 54, 10000 Zagreb, Croatia*

In predicting stability of hydrogenated fullerenes, the Isolated Pentagon Rule successfully correlates with stable fullerenes, but fails to differentiate among stable isoforms. Various graph-theory originating descriptors and topological descriptors have been developed over the years to describe fullerene stability, with moderate success and with implementation in a range of software programs [1]. Fullerene stability doesn't correlate with the number of resonant or Kekulé structures either, which is the case in benzenoid hydrocarbons: among the 1812 isomers of C_{60}, the most energetically stable one is 20^{th}, while the most unstable one is 1^{st} in the ranking by number of resonance structures [1]. Certain hydrogenated forms of C_{60} fullerenes, including $C_{60}H_{36}$ and $C_{60}H_{60}$, have been experimentally observed as stable. In the context of Kekulé structures of buckminsterfullerene, hydrogenation of bonds can be thought of as reduction of numbers of resonant structures at certain locations [2]. In our preliminary findings, based on DFT energies of variously hydrogenated buckminsterfullerenes, stability of partially hydrogenated structures surprisingly correlates with the number of resonant structures. The most energetically stable hydrogenation patterns, seem to be when hydrogen atoms are added in pairs. The correlation is present across various level of theory. Current preliminary TDDFT data [3], is the starting point for upcoming calculations that explore excited states of hydrogenated fullerenes at higher levels of theory.

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Notes

Impressum

Name of the conference: *Computational Chemistry Day 2025*
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University of Zagreb Faculty of Science
Croatian Chemical Society
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Date: June 7th, 2025

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