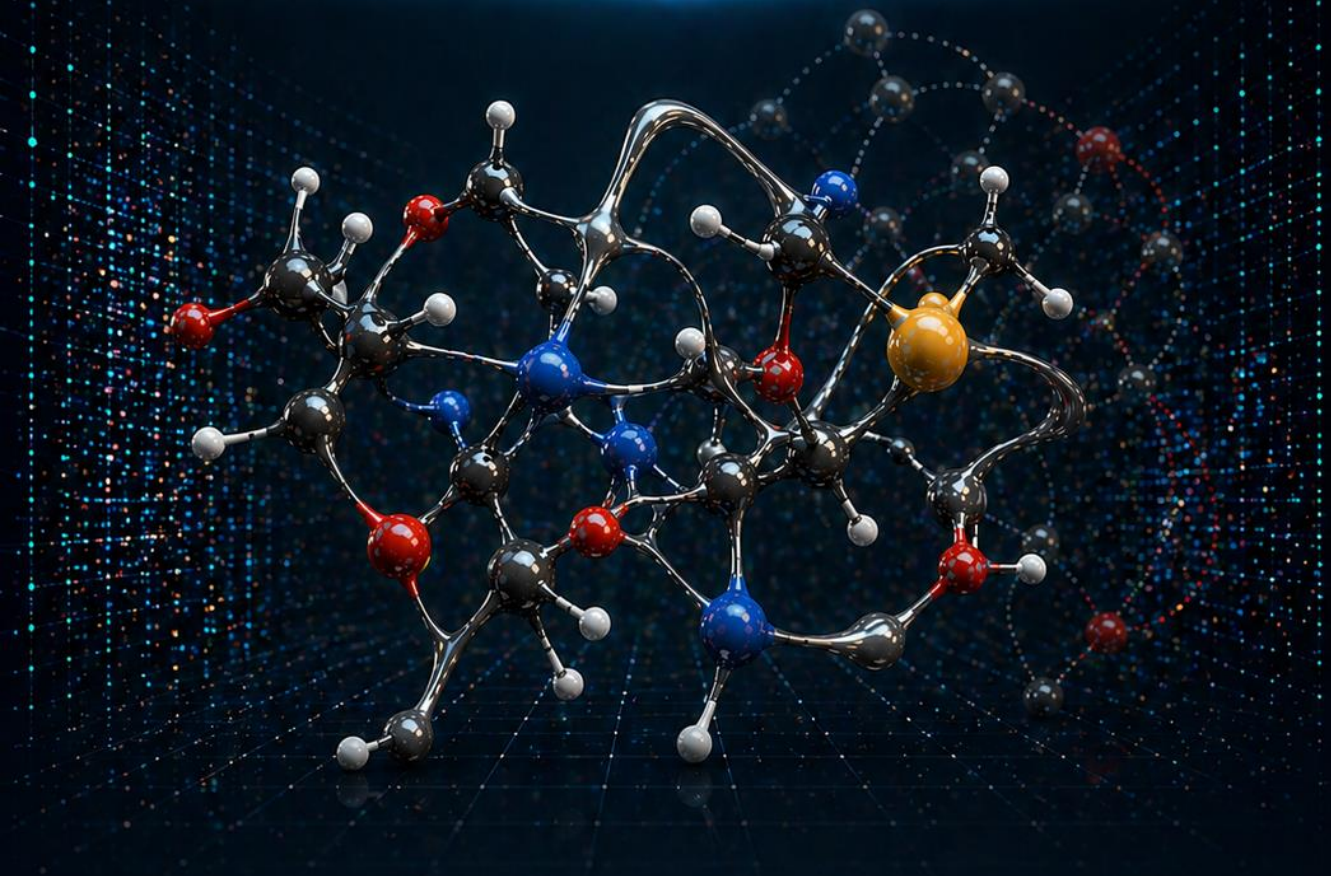
COMPUTATIONAL CHEMISTRY DAY 2026



Book of Abstracts

Ruđer Bošković Institute, Zagreb, Croatia

May 8-9, 2026

Computational Chemistry Day

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Zagreb, Croatia




Foreword

Dear colleagues,

It is our great pleasure to welcome you to the 6th edition of Computational Chemistry Day, CCD2026!

CCD2026 will be held at the Ruđer Bošković Institute on 9 May 2026. The conference is organized by computational chemists and scientists from five Croatian institutions: the Ruđer Bošković Institute, the Faculty of Science and the Faculty of Pharmacy and Biochemistry of the University of Zagreb, the Croatian Chemical Society and the University of Zagreb University Computing Centre SRCE.

CCD2026 brings together more than 90 international computational scientists and experimental researchers, who apply computational chemistry methods in their projects to gain insight into various (bio)chemical reaction mechanisms, as well as molecular and materials properties. Most participants are young researchers and students from various Croatian institutions in Zagreb, Rijeka, and Split.

CCD2026 also has an international character, with half of the lecturers coming from Austria, Finland, Portugal, Serbia and the United Kingdom. The lectures cover hot topics ranging from life sciences and quantum computing to novel nano/materials, chemicals, and chemical reaction mechanisms. A lecture from a start-up perspective is also included, with the aim of introducing us to technology transfer and the commercialization of scientific outputs.

CCD2026 is preceded by an introductory workshop on MD simulations on the Supek supercomputer, supported by courses on using Supek and Linux command-line tools. The workshop will be held on 8 May 2026 at SRCE.

We hope that you will spend a useful and inspiring time with us, gain new perspectives, and be encouraged to develop new projects and discoveries.

The Organizing Committee

Program of the *Computational Chemistry Day 2026*

Pre-conference workshops

Friday, April 8th, 2026 (Location: University of Zagreb, University Computing Centre SRCE, J. Marohnića 5, Zagreb)

10:00 – 11:00 **Kristijan Dekanić (SRCE, Zagreb)**
Introductory workshop on *Linux* command line interface

11:00 – 12:00 **Kristijan Dekanić (SRCE, Zagreb)**
Introductory course on using the *Supek* supercomputer

12:30 – 17:00 **Gordan Horvat (Department of Chemistry, University of Zagreb Faculty of Science, Horvatovac 102a, Zagreb)**
A beginner's guide to GROMACS and best practices on Supek supercomputer

The Conference

Saturday, April 9th, 2026 (Location: Ruđer Bošković Institute, Bijenička 54, Zagreb)

09:00 – 09:15 **Opening addresses**

Dr. sc. David Smith, Director of the Ruđer Bošković Institute
Prof. dr. sc. Ivančica Ternjej, Dean of the University of Zagreb Faculty of Science
Prof. dr. sc. Zrinka Rajić, Dean of the University of Zagreb Faculty of Pharmacy and Biochemistry
Ivan Marić, Director of the University of Zagreb University Computing Centre SRCE
Prof. dr. sc. Ernest Meštrović, President of the Croatian Chemical Society

1st session (moderator: Branimir Bertoša)

09:15 – 09:45 **Pedro Alexandrino Fernandes** (University of Porto, Porto)
Toxins In Motion: Computational Exploration of Snake Venom Protein Mechanisms (IL)

09:45 – 10:15 **Bojan Žagrović** (University of Vienna, Vienna)
The Physicochemical Code of RNA-Protein Biology (IL)

10:15 – 10:45 **Antonija Tomić** (Ruđer Bošković Institute, Zagreb)
A Multidisciplinary Approach to Understanding How DPP3 Catalytic Activity Influences Its Interaction with Keap1 and Vice Versa (IL)

10:45 – 11:00 **Dušan P. Malenov (University of Belgrade, Belgrade), Jelena M. Živković and Snežana D. Zarić**
Are Energies of Hydrogen Bonds of Metal Complexes Predictable? Computational Study in the Gas Phase (CL)

11:00 – 11:15 **Lucija Vrban Đerek and Robert Vianello (Ruđer Bošković Institute, Zagreb)**
Predictive Atomistic Modeling of Antitumor Drug Encapsulation within Supramolecular Hosts (CL)

11:15 – 12:00 **Coffee break**

2nd session (moderator: Marin Sapunar)

12:00 – 12:30 **Ana Sunčana Smith (Friedrich Alexander University Erlangen-Nürnberg, Erlangen / Ruđer Bošković Institute, Zagreb)**
Computational Mechanochemistry (IL)

12:30 – 13:00 **Fabijan Pavošević (Algorithmiq, Helsinki)**
Molecular Excitation Energies Simulated on a Superconducting Quantum Computer (IL)

13:00 – 13:30 **Ivana Nikšić-Franjić (Ruđer Bošković Institute, Zagreb)**
The (Super)Chaotropic Effect: A Computational Chemist's Perspective (IL)

13:30 – 13:45 **Margarita Bužančić Milosavljević (University of Split, Split), Antonija Mravak and Martina Perić Bakulić**
Molecular Engineering of DSSC Sensitizers: A DFT Study (CL)

13:45 – 14:00 **Davor Šakić (University of Zagreb, Zagreb)**
Changing Basis Sets: A Computational Chemist's Journey into Start-up World (CL)

14:00 – 15:30 **Lunch break**

3rd session (moderator: Valerije Vrček)

15:30 – 16:00 **Daniela Kalafatović (University of Rijeka, Rijeka)**
Generative AI in Peptide Discovery (IL)

16:00 – 16:30 **Igor Rončević (University of Manchester, Manchester)**
A Molecule with Half-Möbius Topology (IL)

16:30 – 16:45 **Beren Dempsey, Ashok Keerthi and Igor Rončević (University of Manchester, Manchester)**
Tuning Spin Polarisation in Symmetric Graphene Nanoribbons (CL)

16:45 – 17:00 **Slađana Đorđević and Slavko Radenković (University of Kragujevac, Kragujevac)**
σ-Aromaticity in Dicationic Halogenated Cycloalkanes (CL)

17:00 – 17:15 **Bernhard Kretz and Ivor Lončarić (Ruđer Bošković Institute, Zagreb)**
Machine-learning Based Non-Adiabatic Molecular Dynamics for Nano-porous Graphene (CL)

17:15 – 17:30 **Marina Juribašić Kulcsár and Mario Pajić (Ruđer Bošković Institute, Zagreb)**
Role of Acid Additives in the C–H Bond Activation by Palladium(II) Acetate (CL)

17:30 – 17:35 **Concluding remarks**

17:35 – 22:00 **Poster session (moderator: Marko Tomislav Cvitaš)**

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

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Invited lectures

Toxins in Motion: Computational Exploration of Snake Venom Protein Mechanisms

Pedro Alexandrino Fernandes

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Snakebite envenoming is the most serious neglected tropical disease, causing 81-138 thousand deaths annually [1]. The venom's lethality results, in part, from the action of several highly toxic enzymes secreted in the venom. This talk will focus on some of the most relevant enzymatic toxins and explain how computational chemistry helps understand their mechanism of action [1].

We will analyse the results of rigorous computer simulations of viper enzymatic toxins through molecular dynamics and quantum-mechanical methods. The toxins are simulated in their realistic physiological matrices. In particular, we will analyse their chemical catalytic mechanisms and interaction with vital biological targets, such as the cell membrane [2-4], hyaluronic acid, collagen IV, and coagulation factors [2-5]. We will further propose a molecular mechanism of toxicity of C-terminal peptides derived from snake venom phospholipase A2-like proteins [6].

Finally, we will discuss the possibility and strategies for inhibiting these toxins with small molecules, including making the inhibitors more universal. By providing a microscopic view of the catalytic processes underlying toxicity, computational chemistry highlights the destructive precision of venom enzymes and the opportunities they offer to understand advanced principles of catalysis and specificity.

References:

[1] A. L. Oliveira, M. F. Viegas, S. L. da Silva, M. J. Ramos, P. A. Fernandes, *Nat. Rev. Chem.* **6** (2022) 451–469 (2022).

[2] J. Castro-Amorim, A. V. Pinto, A. K. Mukherjee, M. J. Ramos, P. A. Fernandes, *Chem. Sci.* **16** (2025) 1974-1985.

[3] A. L. Novo de Oliveira, M. T. Lacerda, M. J. Ramos, P. A. Fernandes, *Toxins* **16** (2024) 71.

[4] A. V. Pinto, P. Ferreira, A. V. Cunha, R. W. A. Havenith, A. L. Magalhães, M. J. Ramos, P. A. Fernandes, *Chem. Sci*. **15** (2024) 9793-9805.

[5] J. Castro-Amorim, A. Oliveira, A. K. Mukherjee, M. J. Ramos, P. A. Fernandes, *J. Chem. Inf. Model.* **63** (2023) 4056–4069.

[6] J. T. S. Coimbra, A. Gissler, E. Nitor, K. Rostamipour, A. V. Cunha, M. J. Ramos, P. A. Fernandes, *JACS Au* **4** (2024) 4295-4306.

Generative AI in Peptide Discovery

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In an era increasingly shaped by artificial intelligence, peptide discovery is transitioning from a resource-intensive, trial-and-error process reliant on human intuition toward a data-driven paradigm characterized by high predictive accuracy and scalability. The immense size of peptide sequence space, coupled with a limited understanding of sequence-to-function relationships, makes the identification of new functional peptides inherently challenging [1]. To address this, we integrate machine learning with a genetic algorithm-based exploration strategy to efficiently identify sequences with strong self-assembly propensity [2]. A neural network trained on experimentally validated peptides and coarse-grained molecular dynamics data achieves an accuracy of 81.9%, enabling the discovery of self-assembling peptides in previously unexplored regions of the sequence space with low similarity to the training set. This framework is readily extendable to therapeutic peptide discovery through a multi-objective optimization that balances antimicrobial activity and toxicity. Beyond improving the exploration of unknown peptide spaces, we employ generative AI to accelerate discovery, supporting continued innovation in the field.

References:

[1] E. Dražić, D. Jelušić, P. Janković Bevandić, G. Mauša and D. Kalafatovic, *ACS Nano* **19** (2025) 20295–20320.

[2] M. Njirjak, L. Žužić, M. Babić, P. Janković, E. Otović, D. Kalafatovic, G. Mauša, *Nat. Mach. Intell.* **6** (2024) 1487–1500.

The (Super)Chaotropic Effect: A Computational Chemist's Perspective

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Hydrogen bonding and the hydrophobic effect underpin associative processes in water, while specific-ion effects are described by the Hofmeister concept of kosmotropic and chaotropic ions. The *chaotropic effect*, the pronounced affinity of large, especially superchaotropic anions for hydrophobic and neutral polar environments, represents a distinct assembly motif orthogonal to the hydrophobic effect. It governs molecular recognition and binding phenomena across biomolecular, soft-matter and solid-state systems [1].

Our findings highlight the power of computational chemistry, particularly density functional theory and molecular dynamics simulations in clarifying the (super)chaotropic effect. We introduced molecular descriptors that quantify chaotropicity [2] and distinguish the unique hydration patterns of kosmotropes, chaotropes, and hydrophobes. Computational studies of prominent superchaotropic anions, including boron clusters and polyoxometalates, demonstrate how these species interact with peptides, biological membranes and supramolecular assemblies [3]. The most significant application of these clusters is their function as innovative, broadband membrane carriers. They facilitate the transport of diverse hydrophilic molecules across biological membranes, without depending on conventional amphiphilic design principles [1].

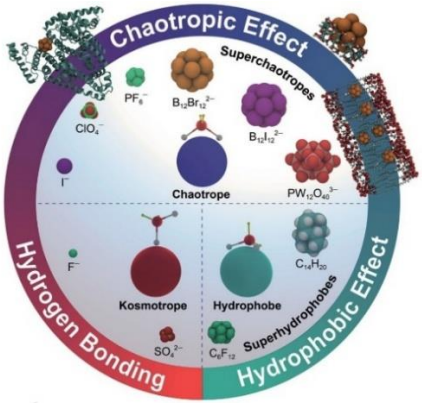

Figure 1. Illustration of the chaotropic effect as a molecular assembly motif in chemistry, shown as a principle distinct from the hydrophobic effect.

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[3] A. Barba-Bon, A. El Haitami, C. Pasquier, I. Nikšić-Franjić, O. Diat, P. Bauduin, S. Cantin, W. M. Nau, *Angew. Chem. - Int. Ed*. **63** (2024) e202412834.

Molecular Excitation Energies Simulated on a Superconducting Quantum Computer

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Exact quantum chemical treatment of electronically excited states exhibits exponential scaling with system size on classical computers. Quantum computing offers a formally more favorable scaling; however, current noisy intermediate-scale quantum (NISQ) devices impose stringent constraints on circuit depth. Practical demonstrations therefore require carefully optimized hybrid quantum–classical workflows that minimize hardware resource demands.

Here, we present a hybrid protocol for computing molecular excitation energies that integrates the ΔADAPT algorithm with optimized circuit preparation, quantum detector tomography, dynamical decoupling, informationally complete measurements, and tensor-network-based QPU postprocessing. Using IBM superconducting quantum hardware, we compute the lowest singlet–singlet ($S_0 \rightarrow S_1$) and singlet–triplet ($S_0 \rightarrow T_1$) excitation energies for representative fluorophores.

The computed results reproduce the correct singlet–triplet ordering and show good agreement with experimental measurements and high-level classical reference calculations. These findings demonstrate that, when combined with advanced error mitigation and postprocessing strategies, current quantum devices can capture essential excited-state energetics relevant to molecular systems used in photodynamic therapy and photocatalysis.

A Molecule with Half-Möbius Topology

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π-Conjugated systems are fascinating because their electrons are highly delocalised, while remaining bound by their orbital basis. In π-conjugated rings a key phenomenon is aromaticity, or the presence of a ring current in a magnetic field, which demonstrates that the electronic wavefunction is coherently delocalised around the whole molecular ring. Topologically trivial π-conjugated rings with ring currents obey Hückel's rule: they are aromatic if they have $4N+2$ π-electrons, and anti-aromatic if they have $4N$ π-electrons, where N is an integer.

In rings that resemble a Möbius strip, which is a body with a single edge, Hückel's rules are reversed [1]. This reversal is a consequence of a 180° twist in their orbital basis upon one circulation of the ring.

This talk will present our recent work on the characterisation of a molecule with half-Möbius topology (Fig. 1), in which the orbital basis twists by 90° upon one circulation of the ring [2].

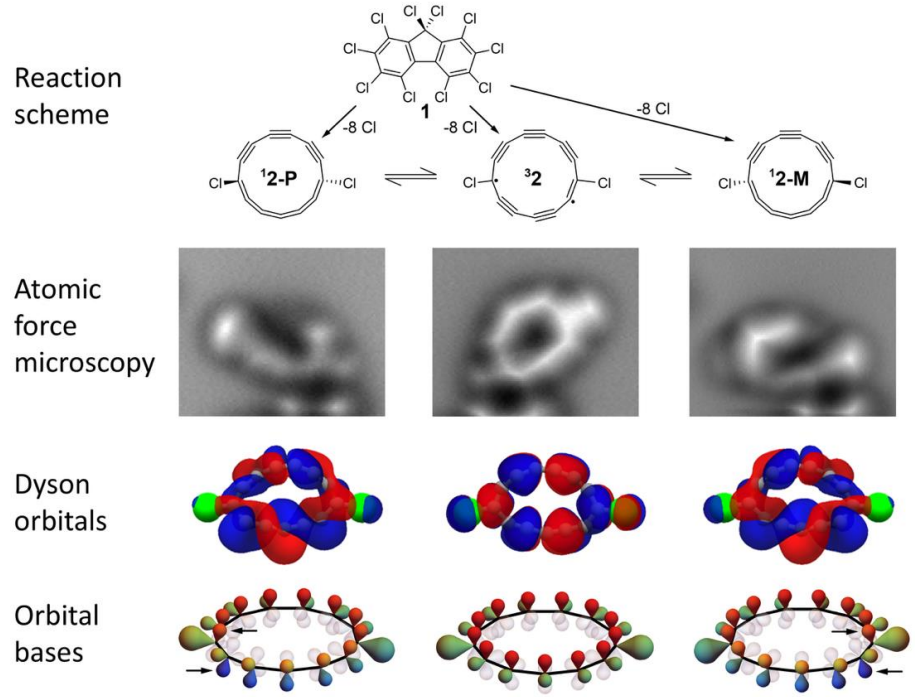

Figure 1. A molecule with half-Möbius topology

References:

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[2] I. Rončević, F. Paschke, Y. Gao, L.-A. Lieske, L. A. Gödde, S. Barison, S. Piccinelli, I. Tavernelli, J. Repp, F. Albrecht, H. L. Anderson, L. Gross, *Science* (2026), in press, DOI: 10.1126/science.aea3321.

Computational Mechanochemistry

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Mechanical force can dictate reaction pathways, reshape energy landscapes, and control bond scission and formation. Molecular-scale mechanochemical transformations can, in turn, drive supramolecular reconfiguration and the emergence of mesoscale material architectures. The intrinsically non-equilibrium and multiscale nature of these processes makes their theoretical description particularly challenging. In this presentation, I will discuss state-of-the-art computational approaches for modeling systems subjected to external forces or generating internal stresses, with examples ranging from molecular switches and polymer networks fracturing under strain to mechanochemical reactions induced by mechanical milling.

A Multidisciplinary Approach to Understanding How DPP3 Catalytic Activity Influences Its Interaction with Keap1 and Vice Versa

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The Keap1–Nrf2 (Kelch-like ECH-associated protein 1 – Nuclear factor erythroid 2-related factor 2) signaling pathway is the main regulator of the oxidative and electrophilic stress response in the cell [1]. More than a decade ago, dipeptidyl peptidase 3 (DPP3), a ubiquitously expressed zinc-dependent exopeptidase, was identified as a component of the Keap1 protein interaction network, suggesting its involvement in cellular responses to oxidative stress [2]. By binding to the Kelch domain of Keap1, DPP3 disrupts the Keap1–Nrf2 regulatory pathway, thereby preventing Keap1-mediated ubiquitination and degradation of Nrf2 and promoting Nrf2-dependent transcription of cytoprotective genes. While Nrf2 activation is protective in normal cells, its constitutive upregulation in cancer cells promotes evasion of oxidative stress, resistance to apoptosis, and increased proliferation, a phenomenon often referred to as the "dark side" of Nrf2 signaling.

Although DPP3 catalytic activity is not required for its interaction with Keap1, the potential impact of peptidase inhibition on this interaction has not yet been investigated. The aim of this study was to examine how enzymatic inactivation of DPP3 influences its interaction with the Kelch domain of Keap1, and vice versa, using a combination of experimental approaches (isothermal titration calorimetry and kinetic analyses) and computational methods (standard and adaptive steered molecular dynamic simulations).

This work was funded by the European Union under the NextGenerationEU Programme and by Croatian Science Foundation under the project IP-2025-02-7100.

References:

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[2] (a) B. E. Hast, D. Goldfarb, K. M. Mulvaney, M. A. Hast, P. F. Siesser, F. Yan, D. N. Hayes, M. B. Major, *Cancer Res.* **73** (2013) 2199–2210; (c) B. E. Hast, E. W. Cloer, D. Goldfarb, H. Li, P. F. Siesser, F. Yan, V. Walter, N. Zheng, D. N. Hayes, M. B. Major, *Cancer Res.* **74** (2014) 808–817.

The Physicochemical Code of RNA-Protein Biology

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The notion of physicochemical complementarity is one of the most important mechanistic paradigms in molecular biology. Recently, we have characterized a robust, statistically significant matching between the nucleobase-density profiles of mRNA coding sequences and the nucleobase-binding profiles of the protein sequences they encode. Overall, our results both support and redefine the stereochemical hypothesis concerning the origin of the genetic code, the idea that the code evolved from direct interaction preferences between amino acids and the appropriate bases. Moreover, our findings support the possibility of direct, complementary, co-aligned interactions between mRNAs and their autogenous proteins even in present-day cells, especially if both are unstructured, with implications extending to different facets of nucleic-acid/protein biology. In this talk, I will focus on different lines of evidence regarding the complementarity hypothesis, with a particular focus on computational and experimental tests as well as functional implications. Finally, I will provide evidence in support of a proposal that proteins may in general interact with RNAs that are compositionally related to their own autogenous mRNA, as a simple, yet powerful organizational principle behind the structure of RNA-protein interaction networks in the cell.

Contributed lectures

Molecular Engineering of DSSC Sensitizers: A DFT Study

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Efficient harvesting of solar energy represents one of the central challenges in the transition toward sustainable energy systems. The solar energy reaching the Earth in one hour exceeds the total annual global energy consumption [1], highlighting the potential of solar technologies. Among various approaches, dye-sensitized solar cells (DSSCs) remain one of the most promising and extensively investigated systems for direct solar energy conversion. Inspired by natural photosynthesis, DSSCs represent a low-cost, structurally versatile, and sustainable alternative to traditional photovoltaic devices [2]. However, despite significant experimental and technological progress, further improvements in efficiency and stability are still required. One of the most important components governing DSSC performance is the sensitizer [3].

Here we present the theoretical design and characterization of DSSC sensitizers, a key component that can be tuned for improved electron injection into the semiconductor band and faster electrolyte regeneration. Different organic, natural, and hybrid (natural dye–noble metal nanocluster) sensitizers, as well as their doped derivatives in combination with various semiconductors and electrolytes, have been investigated in the context of DSSC applications [4].

The prediction of their structural, optical, and photovoltaic properties has been carried out within the framework of density functional theory (DFT) and time-dependent DFT (TD-DFT). These theoretical investigations enable systematic evaluation of electronic structure, absorption characteristics, and energy level alignment relevant for efficient charge injection and regeneration processes. The obtained results contribute to a better understanding of structure–property relationships and support further optimization of sensitizer design. They demonstrate the value of theoretical modeling in guiding the development of improved DSSC materials.

References:

[1] (a) E. Hossain, *The Sun, Energy, and Climate Change*, pp. 1–67, Springer Cham, 2023; (b) M. G. Norton, *A Modern History of Materials. From Stability to Sustainability*, pp. 127-146, Springer Cham, 2023.

[2] R. Sasikumar, S. Thirumalaisamy, B. Kim, B. Hwang, *Renew. Sustain. Energy Rev.* **199** (2024) 114549.

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Tuning Spin Polarisation in Symmetric Graphene Nanoribbons

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Manipulating spin degrees of freedom in low-dimensional materials offers a pathway to low-energy, potentially disruptive technologies [1]. Graphene nanoribbons (GNRs), with their tuneable edge states, provide a versatile platform for exploring ways to manipulate spin [2]. However, the ground state of symmetric GNRs is an equal superposition of two Ising states (Fig. 1a), preventing the realisation of edge-based quantum spin chains. Recently, Janus GNRs (Fig. 1b), which are chemically desymmetrised GNRs, were proposed as a solution for this symmetry-breaking problem [3]. While Janus GNRs do host spin-polarised edges, their chemical asymmetry limits the possibilities of manipulating their spin states.

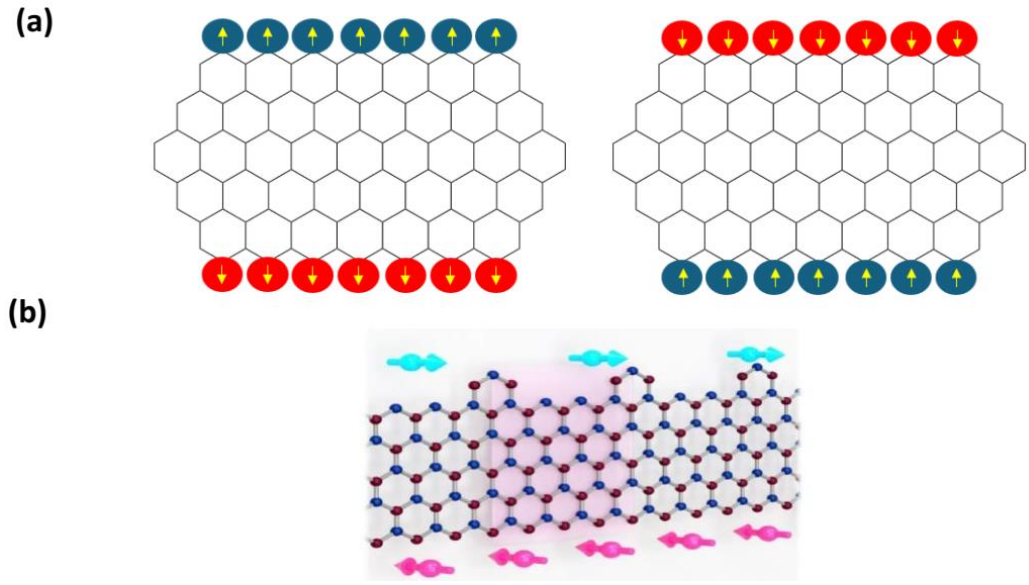

Figure 1. (a) Degenerate Ising ground states of symmetric GNRs. (b) Ground state of Janus GNRs [3].

In this work, we propose an electric field-mediated mechanism for achieving spin-polarised edges in symmetric GNRs, i.e. selecting one of the Ising states in Fig. 1a. The electric field breaks inversion symmetry by polarising the orbitals on the GNR edges [4]. In combination with spin-orbit coupling, this breaks the degeneracy of the Ising states. In contrast to Janus GNRs, using this mechanism the spin polarisation can be turned on and off using the electric field.

Our Heisenberg Hamiltonian calculations suggest that this mechanism may be achievable in symmetric GNRs with weak ferromagnetic coupling within the edge and antiferromagnetic coupling between the edges. Our molecular and periodic broken-symmetry calculations suggest that a recently synthesised GNR is a suitable candidate for testing these predictions in practice.

References:

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[2] M. Slota, A. Keerthi, W. K. Myers, E. Tretyakov, M. Baumgarten, A. Ardavan, H. Sadeghi, C. J. Lambert, A. Narita, K. Müllen, L. Bogani, *Nature* **557** (2018) 691–695.

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σ-Aromaticity in Dicationic Halogenated Cycloalkanes

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Traditionally, aromaticity is associated with π-electron delocalization, while σ-electron delocalization represents a less common form of stability in cyclic systems. This study investigates oxidation-induced σ-aromaticity in inherently non-aromatic halogenated cycloalkanes [1]. By employing different aromaticity descriptors, such as magnetically induced current densities (MICD), the electron density of delocalized bonds (EDDB), and aromatic stabilization energy (ASE), it is demonstrated that oxidation transforms halogenated cycloalkanes into σ-aromatic systems. The resulting σ-electron delocalization in these dications closely mirrors the prototypical double-aromatic $C_6I_6^{2+}$ system. Notably, certain deviations from Hückel's rule suggest that the observed aromaticity is better explained by orbital selection rules. These findings provide a unified view of how oxidative processes trigger aromatic character across different molecular architectures.

References:

[1] S. Radenković, S. Đorđević, *Phys. Chem. Chem. Phys.* **27** (2025) 25422-25432.

Role of Acid Additives in the C–H Bond Activation by Palladium(II) Acetate

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Palladium-mediated carbon–hydrogen (C–H) bond activation is a well-established transformation that plays a central role in metal-catalyzed functionalization of organic compounds, both in solution and in the solid state [1]. Studies suggest that acids promote the activation by palladium(II) acetate ($Pd(OAc)_2$) *via* activating the $Pd(OAc)_2$ trimer and facilitating anion exchange at the palladium center [2]. Since our group reported the first solid-state C–H bond activation in 2014 [3], our research was expanded to the solid-state functionalization of organic molecules and the effects of different palladium sources, as well as the roles of basic and acidic additives, on the reaction course in the solid state [4].

Here, we present a computational rationalization of the influence of acidic additives on azobenzene C–H bond activation by $Pd(OAc)_2$. By combining experimental and computational approaches, we correlate the pK_a values of the employed acids (Figure 1) with the reaction outcome, highlighting the critical role of acid strength in promoting $Pd(OAc)_2$ trimer dissociation and accelerating C–H bond cleavage.

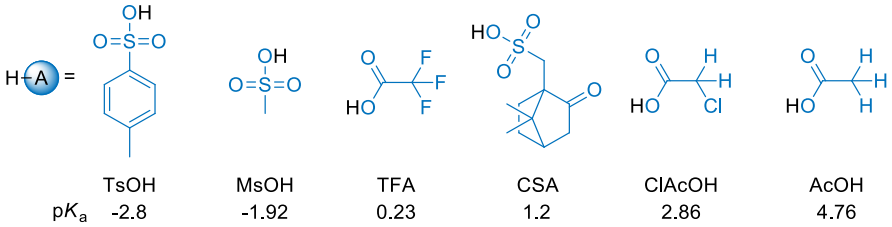

Figure 1. Acids used as additives in azobenzene C–H bond activation by $Pd(OAc)_2$

This work was financed by Croatian Science Foundation grants no. IP-2019-04-9951, DOK-2020-01-7515 and IP-2025-02-3843. Computations were performed at Supek cluster, SRCE, Zagreb.

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Machine-Learning Based Non-Adiabatic Molecular Dynamics for Nano-Porous Graphene

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Nano-porous graphene (NPG) offers great potential for a variety of applications from electronics to photocatalysis. Its band gap can be tuned over a wide range of values, just by changing structural parameters [1]. Often, only ground-state properties have been studied for NPG. However, in order to optimize NPG for photo-physical and photo-chemical applications, their excited-state properties need to be studied. One method to study dynamic excited-state properties is non-adiabatic molecular dynamics (NAMD). Unfortunately, conventional NAMD employing *ab-inito* methods to describe ground- and excited-state potential energy surfaces is computationally expensive, particularly for periodic systems. Employing machine-learning methods can significantly reduce the computational cost of NAMD without compromising accuracy [2].

In this work, we trained machine-learning interatomic potentials for the ground state and the five lowest excited states for a specific NPG. We used these potentials to run NAMD simulations for the NPG, describing the transitions between states using Landau-Zener surface hopping [3]. Our findings show that the number of excited states included in the NAMD simulations affects the relaxation to the ground state. Furthermore, our NAMD simulations reveal the limitations of the chosen approach to NAMD simulations. Together with the advantages of the approach employed in this work, the limitations, possible solutions, and potential further developments will be discussed in this contribution.

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Are Energies of Hydrogen Bonds of Metal Complexes Predictable? Computational Study in the Gas Phase

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Noncovalent interactions in the second coordination sphere of metal complexes are of great importance for their physical and chemical properties; the ability to predict and tune their energies is essential for many applications, among them catalytic activity [1].

We have performed DFT calculations in the gas phase on hydrogen bonds of 180 aqua and ammine metal complexes to study the various factors that could influence their strengths – charge of the complex, metal oxidation state (OS), metal coordination number (CN), nature of the metal and the other ligands in the complex. In addition, we have studied the nature of these hydrogen bonds by performing the calculations based on Symmetry Adapted Perturbation Theory (SAPT).

The calculations have shown that the strength of hydrogen bonds is dependent only on two factors – the charge of the complex and the ratio of metal oxidation state and metal coordination number (OS/CN); the influence of all other factors is practically negligible [2]. All the complexes with the same charge and OS/CN ratio have very similar energies (Figure 1), as well as the same nature, as evidenced by similarities in their SAPT energy components [2]. Hydrogen bonds become stronger with the increase of positive charge of the complex, as well as the increase of the OS/CN ratio, with both correlations being highly linear [2]. We show that the strength of hydrogen bonds of metal complexes can be predicted solely by knowing their simple descriptors, providing valuable guidelines for the fine tuning of their properties in various applications.

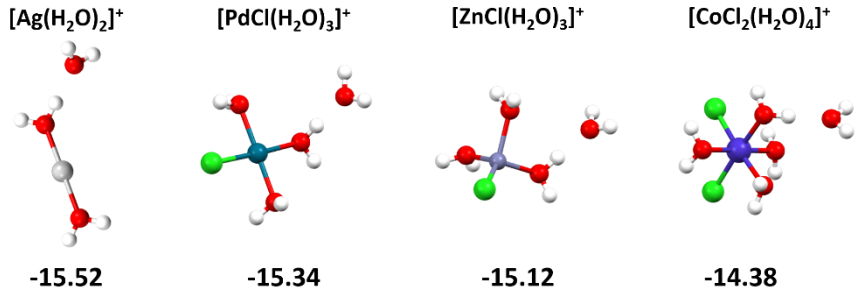

Figure 1. M06L-D3/def2-TZVPP energies (in kcal/mol) of selected hydrogen bonds of 1+ charged complexes with different composition, but the same OS/CN ratio (0.50)

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Changing Basis Sets: A Computational Chemist's Journey into Start-up World

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Scientific research trains us to value rigor, reproducibility, and depth. Startups demand speed, adaptability, and strategic storytelling. In this presentation, I will share the intellectual and psychological transition from academic quantum chemistry to co-founding and leading TINFE HTS, a fluorescence spectroscopy company. I will discuss how core competencies developed in computational chemistry—modeling, abstraction, systems thinking—became unexpectedly useful in entrepreneurship, while also highlighting the challenges: compressed timelines, investor-facing narratives, pitch competitions, and the reframing of "failure" as iteration. The talk offers an analytical reflection on how scientific identity evolves when theory meets market reality, and how stepping outside academia can become an accelerated learning process in itself. Additionally, I will explore how participation in startup accelerators, bootcamps, and pitch competitions reshapes scientific communication—requiring translation of technical depth into clear value propositions without sacrificing intellectual integrity. The journey reveals that while the domain may change—from wavefunctions to fluorescence spectra—the underlying cognitive toolkit of a scientist remains the foundation on which success can be built. The key transformation lies not in abandoning scientific thinking, but in changing the basis in which problems are expressed.

Predictive Atomistic Modeling of Antitumor Drug Encapsulation within Supramolecular Hosts

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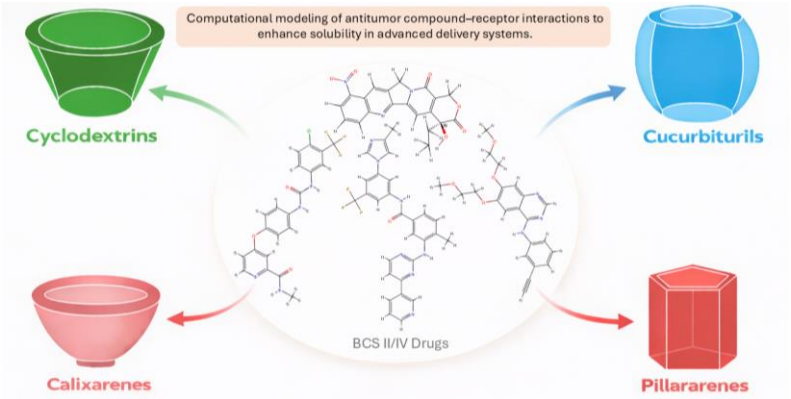
Supramolecular inclusion complexes based on macrocyclic receptors such as cyclodextrins and cucurbiturils offer promising strategies for improving the physicochemical and pharmacokinetic properties of antitumor drugs through non-covalent encapsulation. However, the molecular determinants of binding affinity, selectivity, and stability remain insufficiently understood [1].

In this study, a computational framework combining quantum chemical calculations, restrained electrostatic potential charges, molecular docking, molecular dynamics simulations, and binding free energy analysis was applied to investigate host–guest complexes of representative macrocycles and antitumor drugs [2].

The results provide atomistic insight into binding modes and key interactions, enabling quantitative affinity comparison and supporting predictive design of macrocycle-based drug delivery systems [3].



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Posters

Differences in Aggregation Profiles Between Coarse-Grained and All-Atom Simulations: a Case Study of the IMGIIA Hexapeptide

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Supramolecular peptide nanostructures derive their function out of the combination of self-assembly morphology and sequence chemistry of their peptide building blocks. Depending on sequence design, their applications range from peptide glass, biosensors, drug delivery hydrogels, and cell culture scaffolds [1]. Modeling self-assembling peptides is commonly approached through molecular dynamics (MD): all-atom (AA) simulations resolve precise binding mechanisms, while coarse-grained (CG) methods enable screening of larger systems and longer timescales [2]. While CG has this advantage, AA is more accurate because they capture hydrogen bonding directly. In CG, backbone properties are predefined based on assumed hydrogen bonding and are less reliable for sidechain interactions.

Here we aim to test multiple backbone setups and concentrations to determine which CG simulations are the closest to AA results based on simulation setups from a previous paper [3].

For this purpose, we simulated the IMGIIA hexapeptide [4] in CG simulations using 200 peptides in an 8000 nm^3 box and in AA simulations using 30 peptides in a 125 nm^3 box. Inter-chain contact events were used to quantify aggregation kinetics, aggregate size and distribution, residue contact frequency, interaction types, and pairwise peptide alignments present during the simulations. A contact event was defined using distance cutoffs of 5.1 Å (AA) and 7.05 Å (CG) and this was measured and processed using a Python code built on MDAnalysis.

The results showed that CG simulations with nonpolar backbones are the closest in cluster size and peptide pair populations to AA.

This work offers an alternative aggregation propensity measurement through aggregate population analysis and shows how AA and CG can simulate complete aggregation through different mechanisms by observing pairwise peptide binding.

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High-Throughput Quantum-Chemical Docking for Novel Compounds as Potential Alzheimer's Therapeutics

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Alzheimer's disease, a devastating neurodegenerative disorder, progressively impairs cognitive function and memory [1]. The cholinergic hypothesis links disease progression to acetylcholine (ACh) deficiency, a compound vital for the transmission of nerve signals. ACh is degraded by the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), which are the targets of current Alzheimer's disease symptom treatments focused on cholinesterase inhibition [2]. This study investigates novel, selective and joint AChE and BChE inhibitors *via* semi-flexible quantum-chemical molecular docking.

Building upon previous research [3] and employing a rational drug design approach, a diverse set of 27 novel peptidomimetic compounds was methodically synthesized. These were specifically designed to enhance interactions with cholinesterases. A parallelized high-throughput *Monte Carlo* algorithm generated diverse configurational landscapes that accounted for all degrees of freedom and eliminated overlapping structures (Fig. 1). Binding energies within the AChE and BChE active sites were estimated using the PM7 Hamiltonian, followed by geometry optimization and calculation of standard Gibbs energies of binding for the top 1000 local minima. Structures were clustered and ranked by binding energies. Automated interaction analysis, assisted with visual inspection, identified promising candidates. The goal is to identify compounds with high affinity and selectivity for inhibiting both AChE and BChE. Targeting both enzymes may offer a more comprehensive approach to treating Alzheimer's disease and lead to improved therapeutics.

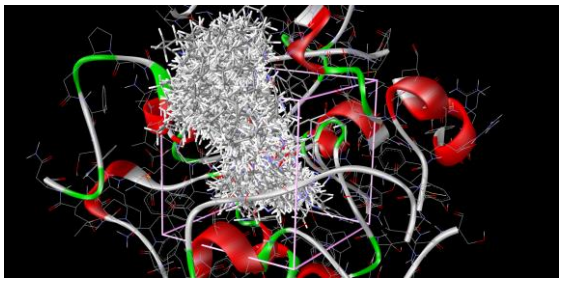

Figure 1. Configurational landscape in AChE for one of the investigated compounds

This work was supported by the *Croatian Science Foundation* under the project number HRZZ-IP-2022-10-9525.

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DFT-Guided Insights into Zeolite-Based Catalysts for DeNOx-SCR Reaction

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Nitrogen oxides (NOx) are among the largest air pollutants and their abatement is a focus of intense ongoing research. One of the best ways of NOx abatement is through selective catalytic reduction of nitrogen oxides (DeNOx-SCR) [1]. In this work, we investigated the design and improvement of zeolite-based catalysts for DeNOx-SCR reaction by combining experimental methods and density functional theory (DFT). Several catalysts were synthesized, and their activity and selectivity were screened under various operating conditions. After screening, the best performing catalysts were thoroughly characterized and modeled using DFT-based methods.

Identification of key reaction intermediates provided mechanistic insights for DFT modeling and enabled us to propose multiple, simultaneous reaction pathways. The findings deepen the understanding of zeolite-based DeNOx-SCR catalysts and provide guidelines for optimization and deliberate design.

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Sampling the Wigner Distribution Obtained from Correlated Vibrational Wave Functions

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Without a sufficiently accurate representation of the initial phase space distribution, subsequent surface hopping simulations won't yield meaningful results [1, 2]. Sampling from the harmonic Wigner distribution is a popular choice since it is a computationally cheap way to account for zero-point energy that works reasonably well for rigid systems. However, it often fails to properly describe large amplitude motion. In the case of methylhydroperoxide, this leads to a qualitatively wrong distribution of products in subsequent surface hopping simulations [1, 2]. We recently proposed a sampling procedure using the Wigner distribution obtained from a vibrational self-consistent field (VSCF) wave function, and found that it was able to mitigate this error. Since the anharmonicity is treated in a mean-field manner, it remains very efficient compared to other sampling procedures [2]. However, neglecting the explicit vibrational correlation could also lead to qualitatively wrong results.

In this work, we investigate the Wigner distributions obtained from the correlated vibrational wave functions of two systems. The first is a model sombrero potential for which the VSCF calculation using linear coordinates does not converge. However, even a relatively low number of products of linear basis functions can properly describe the curved motion. The second system is methylhydroperoxide, whose VSCF Wigner distribution was found to be reasonable, but not quantitatively correct [2]. The problem that arises when one includes correlation is that both the time to sample the 2N dimensional phase space and to evaluate the Wigner distribution at a single point increases rapidly with the size of the system. To remedy this problem, we treat the system within the vibrational active space self-consistent field framework, where the molecule is partitioned into active modes, for which the correlation is treated explicitly, and bath modes, which are treated in a mean field manner [3]. The modes which should be grouped together in the active subspace(s) can be identified from the initial VSCF calculation. The results obtained indicate that the method could be applied to large systems with strongly correlated modes while remaining computationally inexpensive.

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Deciphering the Strength of Cation-π Interactions of Benzene Sandwich Compounds with the Help of AIM, XEDA and NOCV

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Cation-π interactions are significantly stronger with benzene sandwich compounds than with (uncoordinated) benzene [1]. In this work we analyzed and compared the nature of cation-π interactions of benzene and benzene sandwich compounds $(Cr(benzene)_2$, $Mo(benzene)_2$ and $W(benzene)_2)$ with six cations (Be^{2+}, Mg^{2+}, Ca^{2+}, Li^+, Na^+, K^+) using three different methods: AIM, XEDA and NOCV. All cation-π complexes were optimized at the B3LYP-D3/def2TZVP level of theory, which was also used for interaction energy calculations.

Topological analysis using Atoms in Molecules (AIM) helped to explain that cation-π interactions involving the Be^{2+} cation have a covalent character ($\nabla^2\rho(r) > 0$, $H(r) < 0$ and the ratio $-G(r)/V(r) < 1$) for all systems, while the interactions with other cations are classical non-covalent interactions ($\nabla^2\rho(r) > 0$, $H(r) > 0$ and the ratio $-G(r)/V(r) > 1$). The Xiamen Energy Decomposition Analysis (XEDA) revealed that the electrostatic component is very important for the interaction, but the polarization component is the key component that is responsible for the remarkable strength of these interactions. The Natural Orbitals for Chemical Valence (NOCV) analysis determined that, in addition to π orbitals of aromatic ring, d orbitals of the metal in the sandwich compounds are also involved in the interaction with orbitals of the cation, providing additional stabilization for cation-π interactions of sandwich compounds.

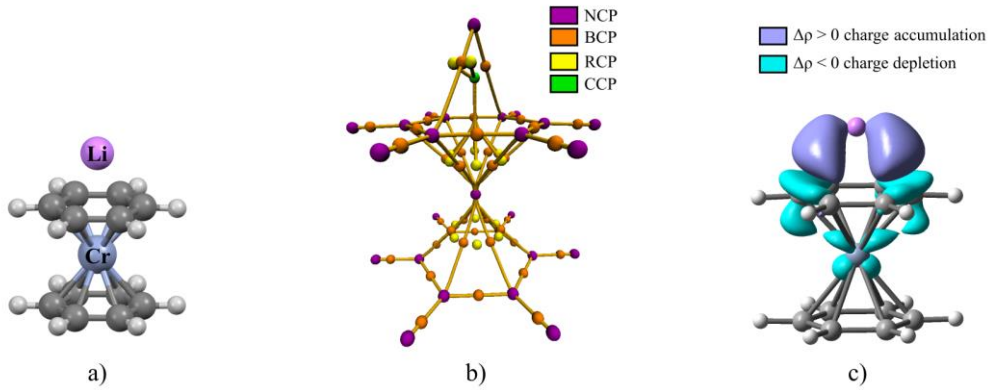

Figure 1. Cation-π interaction between Li^+ and $Cr(benzene)_2$: a) side-view, b) AIM critical points (Nuclear, Bond, Ring and Cage Critical Points) and c) NOCV pair depicting the strongest orbital interaction.

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Computational Modeling of Phosphorus-Based Metal-Free Hydride Donors

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Phosphorus-based hydrides have recently attracted attention as promising metal-free hydride donors. One important factor that controls their reactivity is the polarity of the P–H bond. By introducing electron-donating groups, the P–H bond becomes more polarized, with increased negative charge on the hydrogen atom [1]. This makes the release of a hydride ion (H^-) easier. A further enhancement in hydride-donating ability can be achieved by stabilizing the positively charged species that forms after hydride release. In the systems studied here, such stabilization is associated with the formation of an intramolecular P→P dative interaction, which lowers the energy of the resulting dication. By combining these two design strategies, electronic tuning and structural stabilization, we designed a series of new compounds with some of the best known hydricities [2]. Hydricities of all compounds were calculated in acetonitrile using density functional theory at the (PCM)ωB97X-D/6-311++G(d,p)//(PCM)ωB97X-D/6-31G(d,p) level. Notably, all designed systems exhibit hydricities sufficiently low to enable the reduction of CO_2, as shown in Figure 1, placing them among the strongest known metal-free hydride donors.

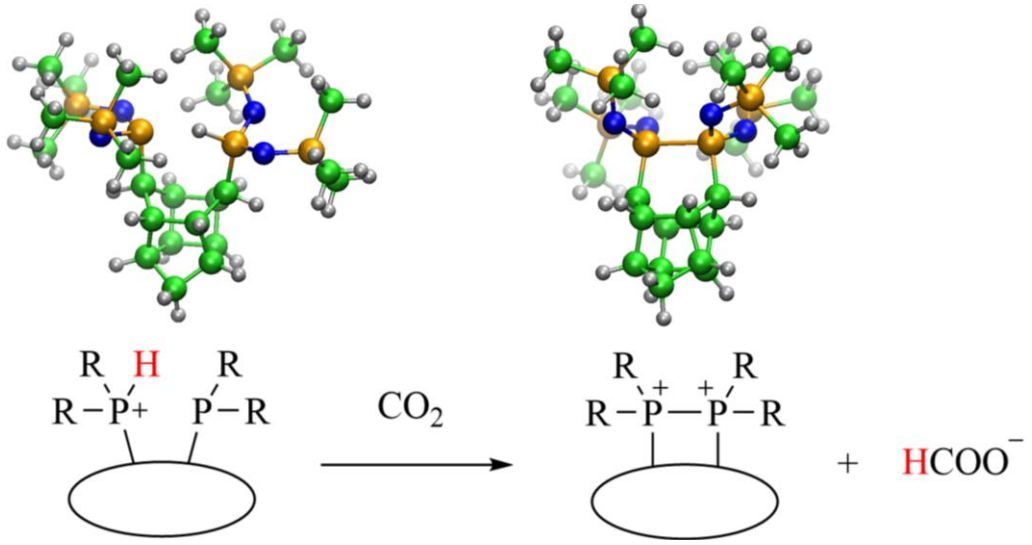

Figure 1. 3D picture of hydride donor with its dication form and scheme of hydride transfer on CO_2

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Combined DFT and Experimental Study of Anti-Corrosion Coatings for Dental Implants

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With increasing life expectancy and improved quality of life, the demand for dental implants continues to grow. Although the current success rate of dental implant therapy exceeds 95%, certain patient groups, including diabetics, smokers, elderly patients, and oral cancer patients, may experience adverse reactions such as allergic responses, increased susceptibility to inflammation, or incomplete osseointegration, that is, the formation of a stable and functional bond between the implant and the surrounding bone tissue.

Recent research has therefore focused on surface modification of titanium implants with organic, inorganic, or biomolecular coatings to improve corrosion resistance and bioactivity, which are essential for successful osseointegration. In this study, titanium dental implants were functionalised with (*i*) alendronate, a drug commonly used in the treatment of bone diseases, and (*ii*) collagen, a structural biopolymer responsible for the mechanical stability of bone and connective tissue. The main objective of the functionalisation was to form protective coatings that increase the corrosion resistance of titanium in simulated artificial saliva, as a prerequisite for long-term biocompatibility.

The corrosion behaviour of the functionalised implants was investigated *in situ* using electrochemical impedance spectroscopy (EIS) in artificial saliva during a 7-day immersion period. Quantum-chemical calculations at the density functional theory (DFT) level enabled determination of the formation mechanisms of both coatings and revealed a key difference in their binding modes, which was reflected in the corrosion behaviour of the coated implants. The calculated Gibbs free energies for the implant–alendronate (ΔG^*_{INT} = -13.64 kcal mol^{-1}) and implant–collagen (ΔG^*_{INT} = -6.45 kcal mol^{-1}) interactions indicate a more spontaneous formation of the alendronate coating on the titanium surface. The DFT results also showed that the collagen coating is further stabilised by hydrogen bonding, which proved crucial for the stability of the implant in artificial saliva.

EIS measurements confirmed that the collagen coating provides about 99% protection of titanium, whereas the alendronate coating provides about 92% protection under the same conditions. The combined experimental and DFT approach was essential for interpreting the observed corrosion behaviour, which could not be fully explained based on experimental results alone.

Tuning Excited-State Pathways for Ultrafast Aza-Quinone Methide Formation

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Aza-quinone methides (aza-QMs) are important intermediates in the synthesis of aza-heterocycles, yet mild and efficient methods for their photochemical generation remain limited. Here, we combine computational and spectroscopic studies to elucidate the excited-state mechanisms governing aza-QM formation from substituted o-hydroxymethylaniline derivatives and to guide the rational design of improved precursors.

Photochemical elimination of H_2O from 2-aminobenzyl alcohol (**1**) serves as a promising starting point [1]. We show that the reaction proceeds *via* a relatively slow, multistep mechanism involving heterolytic C–O bond cleavage in the S_1 state, formation of a contact ion pair, internal conversion to S_0, and subsequent deprotonation to yield the aza-QM. In contrast, the newly designed N-Boc-O-Ac-aminobenzyl alcohol (**5**) exhibits a different behavior, where aza-QM formation occurs in an ultrafast, intermediate-free process via the S_1/S_0 conical intersection.

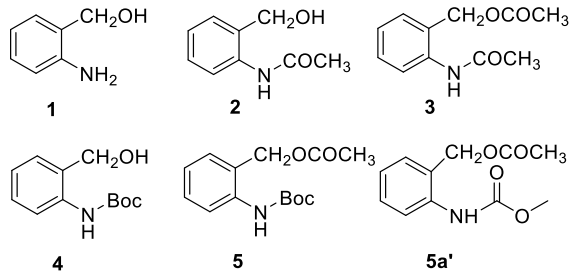

Figure 1. Investigated aniline derivatives **1**-**5** and **5a'** undergoing photoelimination to aza-QMs

Computational results indicate that C–O bond cleavage in both systems is mediated by higher-lying dissociative nσ* states, which become stabilized upon elongation of the benzylic C–O bond. In **5**, substitution effects further stabilize a low-lying nπ* state and facilitate access to the dissociative pathway, leading to efficient OAc elimination and rapid aza-QM formation.

These mechanistic insights provide a framework for the rational design of aza-QM precursors and highlight how excited-state engineering (systems **1**-**5**) can be used to control photochemical reactivity in organic synthesis and in biological applications.

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Combined Experimental and Molecular Dynamics Insight into Assembly of Fmoc-Amino Acid Building Blocks

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Low molecular weight gelators based on Fmoc-amino acids are versatile building blocks for functional supramolecular materials due to their simplicity, tunability and biocompatibility [1]. In this work, we investigate the self-assembly of Fmoc-Histidine (Fmoc-His), Fmoc-Cysteine (Fmoc-Cys) and their co-assembled system (Fmoc-Cys:Fmoc-His, 1:1) by combining molecular dynamics (MD) simulations with experimental characterization. MD simulations reveal distinct self-assembly pathways, where Fmoc-His forms fibril-like assemblies, Fmoc-Cys forms compact aggregates, while the co-assembled system gives rise to branched fibrous structures. Intermolecular interaction analysis shows that Fmoc-His primarily governs the morphology, whereas Fmoc-Cys contributes to increased compactness and may enhance intermolecular order within the co-assembled system. Co-assembly stabilizes interactions between Fmoc-His and negatively charged C-termini, as evidenced by coordination number analysis, modulating the local environment of Fmoc-His and potentially influencing its catalytic activity. Experimentally, scanning electron microscopy (SEM) also reveals distinct morphologies: Fmoc-His forms crystalline structures, Fmoc-Cys forms fibrous network and the co-assembled system develops fiber-bundle-like morphology and forms a hydrogel. These structural differences are accompanied by differences in catalytic activity, measured using p-nitrophenyl acetate (pNPA) hydrolysis, with the highest activity observed for Fmoc-His, followed by the co-assembled system and Fmoc-Cys. Overall, this study demonstrates that small changes in molecular building blocks strongly influence self-assembly pathways, resulting in distinct morphologies and functions. Co-assembly of Fmoc-Cys and Fmoc-His provides a simple strategy to obtain hydrogel and tune functional behaviour in minimalistic amino acid-based systems, while MD simulations offer molecular-level insight into the governing interactions.

Acknowledgements: Croatian Science Foundation (Grant No. DOK-NPOO-2023-10-8638; IP-2025-02-3357); COST Action SNOOPY (Grant No. CA23111); MOBILIsE project funded by the European Union's Horizon 2020 research and innovation programme (Grant No. 951723).

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Metal-Driven Allosteric Regulation of the MtsR Metalloregulator: Mechanistic Insights into Activation and DNA Binding

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Streptococcus pyogenes is a human pathogen responsible for infections ranging from mild to life-threatening, rendering its virulence mechanisms important targets for therapeutic intervention. Manganese homeostasis in this organism is regulated by MtsR, a DtxR-family metalloregulatory transcription factor whose activation mechanism remains incompletely understood. Members of the DtxR family share a conserved modular architecture and undergo metal-induced allosteric transitions that reorganize their DNA-binding domains in response to fluctuations in intracellular metal availability [1–3]. Here, we combine molecular dynamics (MD) simulations with EPR spectroscopy, circular dichroism (CD), and differential scanning calorimetry (DSC) to characterize Mn^{2+}-dependent conformational changes in MtsR. Comparative analysis of *apo*, partially metallated, and fully metallated states indicates that Mn^{2+} binding progressively restricts conformational heterogeneity rather than inducing a discrete structural transition. The fully metallated form adopts a compact arrangement of DNA-binding domains, in which the α3 recognition helices are positioned at a separation compatible with simultaneous engagement of adjacent major grooves in B-form DNA. In contrast, the *apo* ensemble samples expanded and misaligned conformations that are structurally incompatible with productive DNA binding. At the molecular level, Mn^{2+} coordination stabilizes an Arg157-centered interaction network that allosterically couples the regulatory core to the DNA-binding domains. These interactions are persistent in the metallated state, but weak or absent in the *apo* form. Experimental biophysical measurements support this model.

Acknowledgments: This work was supported by the Croatian Science Foundation under the project IP-2020-02-3446 – “Manganese metallosensors”

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Band Gap and CO_2 Capture Engineering in Porphyrin-Based Porous Organic Polymers

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The development of new sustainable materials for gas adsorption and photocatalytic transformations offers a promising strategy to address environmental challenges and energy scarcity. Porous organic polymers (POPs) are attractive candidates for photocatalytic applications because of their high porosity, physicochemical stability, and tunable structure. Previous research has shown that porphyrin-based POPs with azo linkages show great potential for CO_2 capture [1]. Furthermore, replacing azo linkages with ethynyl linkages can yield semiconducting polymers with low optical band gaps [2]. The electronic properties of POPs and the band gap can be further tuned through careful selection of linear spacers [3]. In this study, we computationally investigate how substituents (−H, $-CH_3$, −OH) on phenyl spacers influence the band gap and CO_2 adsorption properties of porphyrin-based POPs featuring azo and ethynyl linkages. Structurally, these POPs form 2D frameworks, whose crystal structures were optimized using periodic DFT calculations with the CRYSTAL23 program. The optimized structures were then subjected to grand canonical Monte Carlo (GCMC) simulations using RASPA program, and the resulting CO_2 adsorption isotherms were compared. Band gaps were determined from structures reoptimized using the hybrid PBE0 and B3LYP functionals, which can be particularly reliable for reproducing experimentally reported optical band gaps when no charge transfer excitation is involved [4]. The calculated CO_2 uptake and electronic properties were compared with experimental data obtained from UV-Vis diffuse reflectance measurements. These results demonstrate that periodic DFT can be used to investigate and optimize the adsorption and electronic properties of functionalized POPs.

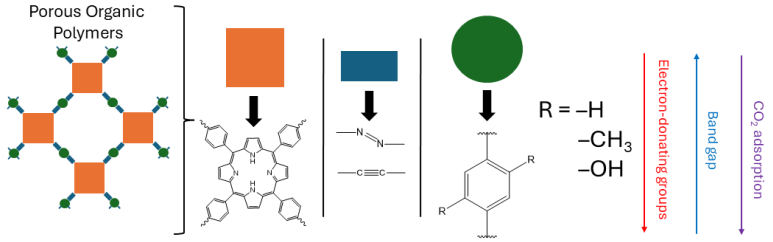

Figure 1. Porous organic polymers with tunable adsorption and electronic properties

Acknowledgement: This research was supported by the European Union – NextGenerationEU through the National Recovery and Resilience Plan 2021-2026 Institutional grants of University of Zagreb Faculty of Science (NextGenChem).

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Tuning Hydricity of the Benzimidazole Hydride Donors – A Computational Approach

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Hydride donors are essential in modern research, with demand increasing alongside rising atmospheric CO_2 levels [1]. Non-metallic hydride donors are particularly compelling because they are more cost-effective, tunable, and easier to recycle than metal-based alternatives. Benzimidazoles (**BIM**) have emerged as a promising group of donors; their hydricity is remarkably close to that of formic acid, meaning properly substituted BIMs can reduce CO_2 to formic acid—a process already experimentally confirmed [2].

To enlarge the pool of BIM derivatives capable of transforming CO_2 to formic acid, we modelled a pool of *α*- and *β-substituted* 2-methylbenzimidazoles, as well as 4-X-phenyl substituted benzimidazoles (Figure 1) by the CPCM(ACN)/wB97xD/aug-cc-pVTZ//CPCM(ACN)/wB97xD/6-31+G(d,p) calculations. In addition to typical substituents such as $–NMe_2$, –OMe, and halides, superbasic (SB) groups—encompassing guanidine, cyclopropenimine, and phosphazene—were included. The changes in hydricity are interpreted using Hammett and Taft-type analyses of substituent effects. A strong deviation from linearity of amino derivatives was found. The correlation between hydricities and the change in aromaticity upon hydride transfer confirms that aromaticity is a very important property of the electronic structure governing the process.

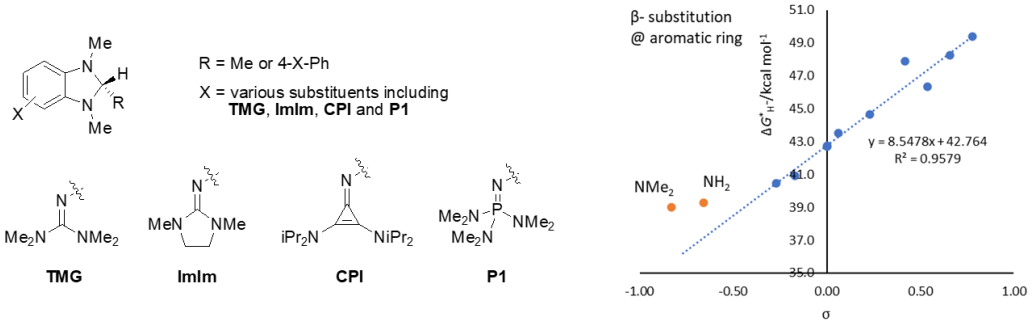

Figure 1. Structures of the investigated **BIM** derivatives and the example of the Hammett-type correlation for β-substituted benzimidazole derivatives.

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Reactive Force-Field Parameter Optimization for Fe/P/C/O/H Systems

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Mesoscale modeling of processes in $LiFePO_4$ batteries should ideally involve molecular dynamics methods available to describe bond rearrangement and preferably also electron transfer reactions. Reactive force field approach as implemented in *ReaxFF* code has potential for satisfying both the above requirements [1]. In a recent work, we developed Li/O *ReaxFF* force field and implemented the optimization protocol relying on the *Optuna Python* package [2]. In this work we proceed to use this protocol to develop reactive force field (ie. optimize parameters) for systems containing Fe/P/C/O/H atoms. The extensive training set of more than 400 structures is used, of which about 10% is selected for validation and excluded from parameter training. A number of these is evaluated using *Gaussian 16* commercial code at the density-functional (DFT) level of theory thus yielding charges and energies for additional training. We validate the force field by the quality of reproduction of the (crystal) structures on a set of 30 crystal structures and 21 molecules including DFT calculated energies and charge distributions for comparison. Finally, a validation is also performed comparing equation-of-state like energy-volume diagrams of six simple iron-phosphorus crystals. Based on these results, the performance of the developed force field, its quality, behavior and stability are evaluated. This is to the best of the authors' knowledge the first Fe/P *ReaxFF* force field available.

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100 years of the Croatian Chemical Society and 55 years of the Section for Theoretical and Computational Chemistry

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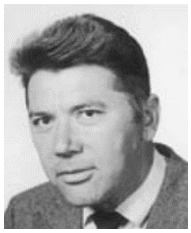
The society was founded on 23 January 1926 in Zagreb as the Zagreb Section of the *Yugoslavian Chemical Society*, marking the beginning of organised chemical activity in Croatia. The first president was Vladimir Njegovan. From then on, the Society's main goal is to develop and promote scientific, professional, and teaching activities in all areas of pure and applied chemistry in Croatia.

Vladimir Njegovan

Building at Maruličev trg 19, Zagreb, where the founding meeting was held

Some important years in the history of Croatian Chemical Society:

- in 1927, the journal '*Arhiv za Hemiju i Farmaciju*' was started
- in 1939, the society adopted the name **Croatian Chemical Society (CCS)**, further defining its national identity.
- in 1940, the Nobel lecture of Leopold Ružička was organised in Zagreb
- in 1955, the society's journal changed its name to *Croatica Chemica Acta*
- in 1958, the first branch was established in Rijeka
- in 1969, the first HSKIKI conference was held
- in 1971, the Section for theoretical chemistry was initiated
- in 1976, branch in Split was established
- in 1979, branch in Osijek was established
- in 1988, the award *Božo Težak* medal was established and awarded to Linus Pauling
- in 1989, Vladimir Prelog was awarded the medal
- in 1993, society became a member of IUPAC and FECS
- in 1995, the award *Vladimir Prelog* for young chemists in the field of organic chemistry was established
- in 1997, branch in Varaždin was established
- in 2003, the award *Leopold Ružička* for young chemists in the field of chemistry was established
- in 2012 branch in Pula was established



Milan Randić

In 1971 Section for theoretical chemistry has been initiated by Milan Randić, who was at the time a leader of the newly established Theoretical Chemistry Group at the Ruđer Bošković Institute. The Section activities were mostly manifested by organising lectures of the leading scientists in the field, especially of those recognized at the global level. It is worth to mention the visits by E. Heilbronner, H. J. Monkhorst, F. E. Harris, C. Trindle and F. Harary, and later by H. Lischka, Z. Janko, H. Schwarz, H. F. Schaefer III, H. Maskill and L. Radom. Their visits were possible owing to professional connections of the Croatian theoretical chemists (Z. B. Maksić, N. Trinajstić, T. P. Živković, Z. Meić, A. Graovac, S. Bosanac and A. Sabljić) who started their careers at the same time or soon after. After Randić moved to USA, the Section was led by Nenad Trinajstić, and later by Ante Graovac and Zvonimir Maksić. Through its prominent members, the Section also participated in organising scientific conferences, for example *International Symposium on Aromaticity* (Dubrovnik, 1979.) and *International Symposium on Theoretical Organic Chemistry* (Dubrovnik, 1985.). Since 2011, the Section has been led by Borislav Kovačević. In recent years, through active involvement of the Section members, it has increasingly contributed to the organisation of specialized events in computational chemistry. In 2017 and 2019, two mini-symposia dedicated to radical enzymes were held at the Ruđer Bošković Institute. In 2022, Croatia joined the central European countries organising the *Central European Symposium on Theoretical Chemistry* (CESTC), with two appointed representatives (Nada Došlić and Tomica Hrenar). In 2024, the CESTC meeting was hosted in Sveti Martin na Muri. Another meeting series, held under the name *Computational Chemistry Day* (CCD), was established in 2018 and has since been organised on annual basis, with only occasional interruptions.

Nenad Trinajstić

Ante Graovac

Zvonimir Maksić

Participants of the CCD meetings in 2018 and 2019

Quantum Chemical Prediction of Spectra for Key Prebiotic Molecules

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The search for the origins of life necessitates understanding the formation and evolution of complex organic molecules in astrochemical environments [1]. Regions like star-forming cores and protoplanetary disks exhibit rich molecular inventories, and identifying the spectral signatures of key prebiotic molecules is crucial for interpreting astronomical observations [2]. This work presents a detailed quantum chemical investigation of the spectroscopic properties of several astronomically relevant molecules: glycolonitrile (HOCH2CN), aminoacetonitrile (NH2CH2CN), glycolaldehyde (HOCH2CHO), formamide (NH2CHO), methyl formate (HCOOCH3), glycolamide (NH2COCH2OH) and 2-(methylideneamino)acetonitrile (CH2=NCH2CN). These molecules are considered building blocks for more complex biomolecules and have been detected or proposed in interstellar space [3,4].

We employed density functional theory and various functionals to determine conformational spaces, optimize the molecular geometries and estimate vibrational frequencies. Rotational constants were calculated to aid the interpretation of rotational spectra expected from sensitive radio telescopes such as ALMA. Particular attention was paid to identifying key vibrational modes likely to be observed in infrared spectra from space-based observatories such as JWST. Calculated vibrational frequencies were compared with experimental data (where available) and scaled to improve agreement. We investigate the influence of hydrogen bonding, which is particularly relevant in interstellar ice mantles, on the vibrational modes of these molecules using dimer calculations. These findings could aid future observations aimed at unraveling the chemical pathways that lead to the emergence of life's building blocks in the cosmos.

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Low-Lying ππ* Excited States in Five-Membered Ring Heterocycles: a Continuing Challenge

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Five-membered ring heterocycles are simple model systems that have been extensively studied in both experimental and theoretical works, as they are essential building blocks of biomolecules and systems relevant for optoelectronic applications [1]. Despite their small size, quantum chemical methods often fail to accurately describe their excited states, leading to inconsistent predictions of excited-state ordering [2]. Therefore, understanding how the choice of theoretical approach influences excited-state characters is essential for further progress in the field.

In this work, we investigate the hidden character of low-lying ππ* excited states in five-membered ring heterocycles. Heterocycles are compared to the simplest polyenes (cis-butadiene) and acenes (benzene) using various computational methods combined with wavefunction analysis. We focus on analyzing the configuration weights of the first bright and dark excited states, commonly referred to as L_a and L_b, respectively. The performance of different excited-state methods is evaluated by comparing their predictions with the coupled-cluster singles, doubles, and triples (CC3) reference method [3]. Correlation effects are further examined through the series of algebraic diagrammatic construction (ADC) methods, as well as linear-response time-dependent density functional theory (TDDFT).

ADC(1) fails to correctly predict the L_b state since it cannot capture any double-excitation character. In contrast, ADC(2) provides a good balance for both states, with relatively small errors in case of heterocycles. ADC(3) yields only a slight improvement over ADC(2), despite its high computational cost. For the TDDFT, we found that different functional families exhibit varying accuracy for the L_a and L_b states, often leading to incorrect state ordering.

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DFT Study of Cyclophosphamide/Ifosfamide Chlorination: Effects of Speciation, Conformation and Explicit Solvation

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Quantum-chemical methods are essential for mechanistic elucidation of chlorination reactions of environmentally relevant pharmaceuticals. Our previous studies have shown that a correct mechanistic description of chlorination of formally inert nitrogen-containing functionalities requires three elements: (i) a suitably benchmarked theoretical protocol, (ii) identification of the chemically relevant reactive species, including the appropriate ionization state and/or tautomeric form, and (iii) an explicit and chemically meaningful description of the aqueous medium. In the case of amides (e.g. acetaminophen), accurate reproduction of experimental chlorination kinetics required consideration of the less stable but much more reactive iminol tautomer, together with water-assisted transition structures and benchmarking against higher-level methods [1].

The same principle was confirmed recently for sulfonamides, where the chlorination mechanism could only be described correctly after explicit consideration of speciation and tautomerism (e.g. sulfamethoxazole). In neutral aqueous solution, the anionic form was identified as the relevant reactant, whereas under acidic conditions the neutral form and its tautomeric imide structures may also contribute. In addition, explicit water molecules were found to be essential for obtaining realistic transition structures and barriers [2].

In the present work we extend this mechanistic framework to phosphorodiamidates, specifically cyclophosphamide (CPA) and ifosfamide (IFO). In contrast to amides and sulfonamides, chlorination of phosphorodiamidates is additionally conformation-dependent, meaning that not only ionization and isomeric states but also the conformational properties of the reactant must be taken into account. Accordingly, a realistic mechanistic treatment of CPA and IFO chlorination requires benchmarking of the computational method, differentiation between the neutral and anionic chlorination pathways, and evaluation of the relevant isomeric/conformational space of the parent reactants.

Acknowledgment:

Our thanks go to the Croatian Science Foundation (Grant IP-2022-10-2634) and the project FarmInova (KK.01.1.1.02.0021), funded by the European Regional Development Fund. Computational resources were provided by the Advanced Computing Service on Cluster Supek, EU funded through KK.01.1.1.08.0001, at the University of Zagreb University Computing Centre (SRCE).

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Structural and Electronic Properties of 1- and 2-Naphthylamines in Aqueous Solutions

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Previous studies of *ortho*-, *meta*-, and *para*-aminobiphenyl [1] isomers have demonstrated distinct photochemical pathways involving proton transfer or water-assisted proton transfer from the NH_2 group to an aromatic ring carbon atom. While all isomers undergo water-assisted excited-state proton transfer (ESPT), the *meta*- isomer uniquely exhibits an additional photoredox pathway mediated by proton-coupled electron transfer (PCET), leading to water splitting. Motivated by the relevance of photocatalytic water activation, we investigate analogous processes in simpler organic chromophores.

Here, we examine 1- and 2-naphthylamine using a combined computational and experimental approach, focusing on isomer- and conformer-dependent photochemistry, including microsolvated water clusters. Our results reveal distinct excited-state deactivation pathways for the two isomers. In aqueous environments, 1-naphthylamine undergoes both water-assisted ESPT and a PCET-mediated photoredox process, whereas 2-naphthylamine exhibits exclusively ESPT reactivity. These differences are attributed to the intrinsic electronic characteristics of the La and Lb excited states in the two isomers. More broadly, our findings raise the question of whether such divergent photochemical behavior can be rationalized in terms of excited-state antiaromaticity relief.

Acknowledgement. This research has been supported by the Croatian Science Foundation grants (HRZZ-IP-2019-04-8008, HRZZ-IP-2022-10-4658, and HRZZ-IP-2024-05-8565) and the ADRIS foundation.

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E/Z Isomerization of Brilliant Yellow: A Theoretical Study of Its Photoactive Forms

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Brilliant Yellow (BY) is an azo dye exhibiting photoinduced E/Z isomerization, which governs its optical properties and potential applications in photonic and bioanalytical systems. In this work, a comprehensive theoretical investigation of multiple conformational and configurational isomers of BY was performed in order to elucidate their structural and spectroscopic characteristics. Geometry optimizations were performed by applying density functional theory (DFT), followed by time-dependent DFT (TD-DFT) to simulate the electronic absorption spectra in solution. Several exchange–correlation functionals in combination with basis sets were employed to evaluate their potential applicability in predicting the excitation energies and spectral features. The nature of the electronic transitions was analyzed based on molecular orbital contributions, showing that the main absorption bands originate predominantly from π→π* transitions localized on the azo chromophore. The calculated UV/Vis spectra reveal distinct differences among the isomers, with significant shifts in absorption maxima and oscillator strengths depending on the E/Z configuration. The theoretically obtained results are further compared to experimental data to provide evidence of the most suitable combination of a method/ basis set. Falling in line with other studies provided in scientific literature, the presented results demonstrate that photoinduced interconversion between photoactive forms can indeed lead to measurable spectral changes, thus providing insight into the structure–property relationship in azo dyes and supporting their application in photoresponsive systems [1-2].

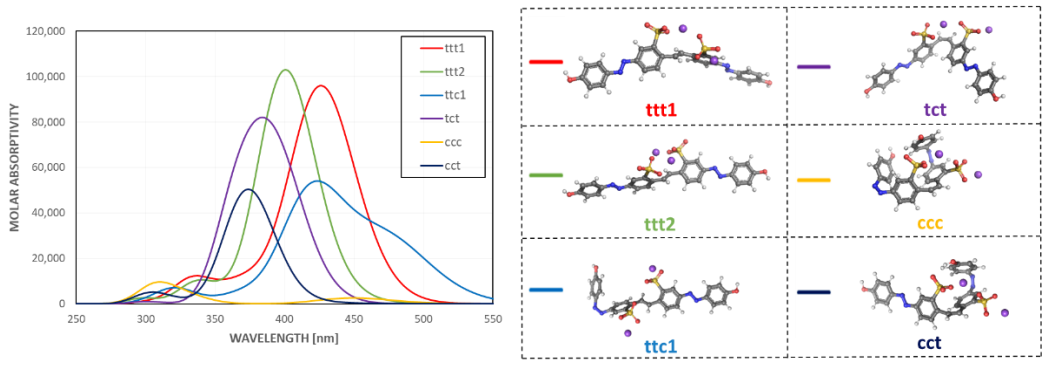

Figure 1. Optimized geometries and simulated UV–Vis absorption spectra of the six possible conformational isomers of the BY-2Na dye

Funding:

This research was financed by the Bulgarian National Science Fund, grant number KP-06-M98/01 of 01.12.2025 (project “Azo Dyes in Polymer Matrices as Media for Optical recording”).

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Molecular Dynamics Study of Microplastic-Pollutant Adsorption

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Microplastics (MPs), polymer particles smaller than 5 mm, are increasingly recognized as contaminants of emerging concern due to their persistence, accumulation and potential environmental risks. In aquatic systems, MPs can adsorb a wide range of organic and inorganic contaminants, while processes such as ageing, and surface modification significantly alter their behaviour and associated risk. Experimental studies of MP-pollutant interactions are often time-consuming and subject to considerable methodological variability, resulting in inconsistent findings across studies. To overcome this, our study combines molecular dynamics (MD) simulations with experimental analysis to investigate the adsorption of selected pesticides onto polyethylene terephthalate (PET) MPs. Two atomistic PET models were constructed: (i) a single, continuous 150-mer chain representing a pristine PET MPs, and (ii) an aggregate of thirty 5-mer chains representing a fragmented, aged-like structure with a higher density of terminal functional groups. The simulation results show that the fragmented PET model exhibits stronger interactions with all tested pesticides compared to the continuous chain model. This arises from an increase in both Coulombic and Lennard-Jones (LJ) interactions. The increase in Coulombic interactions is attributed to the presence of additional oxygen-containing functional groups. At the same time, the stronger LJ potential is attributed to increased structural flexibility and more pollutant-surface contacts. Experimental results further confirm a significant increase in adsorption capacity following the ageing of PET MPs. Surface characterization indicates that aged MPs exhibit rougher and more heterogeneous morphologies compared to pristine MPs, leading to a greater number of available adsorption sites. In agreement with these observations, MD simulations reveal that surface oxidation at the atomistic level enhances adsorption by increasing the density of reactive functional groups. Overall, this combined approach provides detailed molecular-level insight into MP-pollutant interactions, highlighting the critical role of surface chemistry. These findings also underscore the need for more advanced simulation frameworks incorporating surface heterogeneity, longer timescales, and environmental complexity to improve predictions of MPs behaviour in real-world systems.

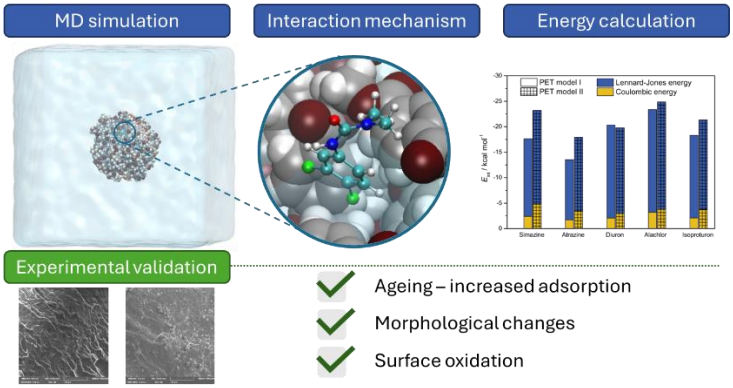

Figure 1. Molecular dynamics study of microplastic-pollutant adsorption

Small Mutation, Big Impact: How a Single Change Influences Electrostatic Interactions and Performance of MAO-A Enzyme Linked to Brunner Syndrome

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Enzymes are finely tuned molecular machines, and even one single-point mutation can dramatically affect their function. This is especially critical when such mutations involve charged residues, which play a fundamental role in stabilizing transition states during catalysis. In this study, we focus on clinically observed mutations in monoamine oxidase A (MAO-A)—a mitochondrial enzyme essential for the breakdown of neurotransmitters such as serotonin. Disruption of its function has been linked to Brunner syndrome, a rare neurodevelopmental disorder characterized by impulsivity, aggression, and intellectual disability [1,2].

Using a multiscale simulation approach, we investigated how specific MAO-A mutations affect the catalytic mechanism of serotonin degradation [3]. Our methods combined classical molecular dynamics (MD) with the empirical valence bond (EVB) technique to quantify changes in activation free energy and electrostatic contributions. The studied variants, including C266F, V244I, and E446K, were found to increase the activation barrier by several kcal/mol, resulting in reaction rate reductions of up to ~18,000-fold. These effects are functionally equivalent to a complete loss of enzymatic activity. Electrostatic analysis revealed that the mutations compromise transition state stabilization by disrupting the preorganized charge distribution in the active site. Additionally, subtle structural shifts propagate throughout the protein, affecting folding and active-site accessibility. Together, these findings illustrate how a seemingly minor genetic change can lead to severe functional consequences and provide a clear molecular link between genotype and phenotype in MAO-A–related disorders.

This work underscores the broader significance of atomic-level interactions in enzyme catalysis and illustrates how computational modeling can reveal the molecular origins of disease. Our approach provides a powerful framework for assessing the functional consequences of genetic mutations and supports the application of structure-based simulations in the context of precision medicine.

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Investigating Photodynamics of Nucleobase–Water Systems

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This study examines the photodynamics of weakly bound hydrogen-bonded molecular systems, with a primary focus on developing a pragmatic computational protocol that incorporates flexibility and quantum distributions of initial conditions for nonadiabatic dynamics. As a case study, the photodynamics of 2,6-diaminopurine nucleobase-water clusters has been investigated 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 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.

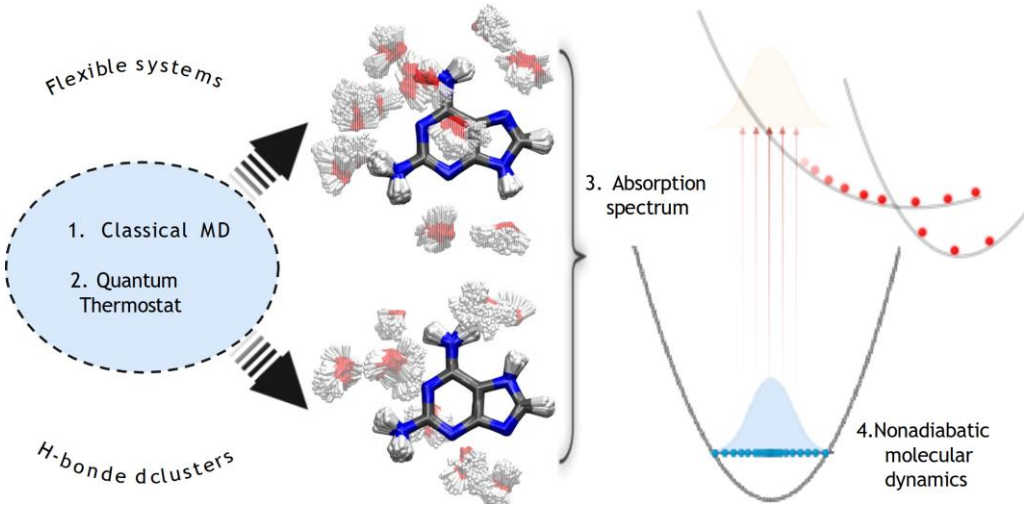

Figure 1. Schematic representation of workflow for simulating ultrafast relaxation of 2,6-diaminopurine nucleobase-water clusters

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Substituent Effects on the Intramolecular Cyclization of Dibenzoguanidine Precursors: A Computational Study

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The intramolecular cyclisation that leads to dibenzoguanidine frameworks is a key step in the synthesis of rigid receptors for anion recognition. Previous experimental work showed that conversion of intermediate **1** to compound **2** (Figure 1) occurs only after reduction to a more reactive triamine, highlighting the importance of both electronic factors and molecular preorganization [1].

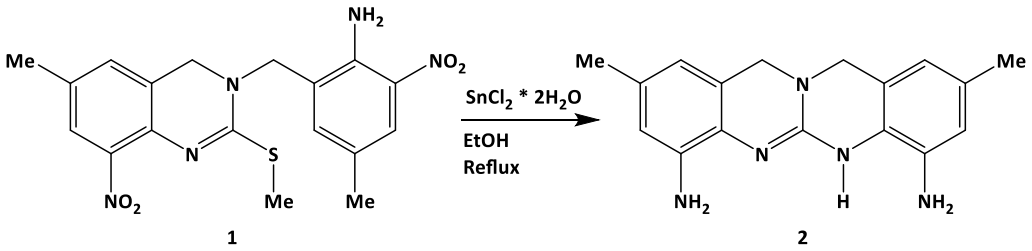

Figure 1. The intramolecular cyclization

In our work, we attempted to carry out this cyclization using an unsubstituted system (R = H at the 2,9-positions). However, synthesis of compound **2** under these conditions was unsuccessful, indicating that the absence of substituents significantly affects the reaction outcome. This observation prompted a detailed computational investigation.

Density functional theory (DFT) calculations (M062X/6-31G* level of theory) were employed to locate and analyze transition states for a series of substituted systems (R = H, CH_3, Ph,...). Particular attention was given to how electronic effects and steric constraints influence activation barriers and transition-state geometries.

This study aims to provide insight into substituent-controlled intramolecular reactivity, with emphasis on the interplay between nucleophilicity and conformational preorganization, and to support the rational design of preorganized guanidine-based systems.

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Electroporation of a Native-like *E. Coli* Membrane Model

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Electroporation refers to the application of short, high-voltage electrical pulses designed to temporarily increase cell membrane permeability. Exposure of the cell to an external electric field leads to a reversible destabilization of the lipid bilayer, enabling the controlled uptake of molecules such as drugs or DNA [1]. The fundamental mechanism of electropore formation can be considered identical in both lipid bilayers and simple alkane systems (e.g. octane) in terms of the sequence of events. The process is initiated by the formation of "water wires," followed by the subsequent expansion of the pores [2]. However, the diversity of lipid types, their chemical structures and charges result in distinct physical properties of membranes depending on their composition [3]. Research has shown that during the translocation of a DNA molecule through a pore, interactions occur between the DNA and the polar lipid headgroups, leading to the formation of DNA/membrane complexes [4]. Therefore, for MD simulations to faithfully reproduce *in vitro* experiments and capture all relevant interactions, it is essential to simulate structurally complex systems and move away from simplified models. In this study, a native-like *Escherichia coli* membrane model consisting of 14 lipid components (the *Avanti* model [3]) was implemented using the CHARMM36 force field. A transverse electric field was applied along the z-axis. Several DNA molecules were positioned near the membrane. Preliminary results reveal membrane curvature under the influence of the external electric field, the emergence of water wires, and the formation of a pore.

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Convergent Transcriptomic and Pharmacophore Evidence for CDK4/6, HDAC and MEK Inhibitor Repurposing in Urothelial Carcinoma

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Urothelial carcinoma (UC) has limited therapeutic options, making drug repurposing an attractive strategy [1]. We applied a four-axis framework to 15 CDK4/6, HDAC and MEK inhibitors: LINCS L1000 transcriptomic reversal scoring against a UC patient-derived GEO cohort signature, SMARTS-based pharmacophore modelling with literature validation, seven-descriptor physicochemical profiling (RDKit) [2] and rule-based ADMET assessment. Only compounds satisfying strict reversal criteria (both cell lines, NES > 2, ≥3 oncology and ≥5 total gene sets) were retained. PCA of Morgan fingerprints segregated the target classes into distinct chemical-space clusters (Fig. 1A–B); romidepsin was structurally isolated due to its macrocyclic scaffold, exhibiting incomplete pharmacophore coverage (3/4 features) and the worst ADMET profile of the panel, while the highest intra-class similarity (palbociclib–SHR6390, T = 0.75) reflects a productive CDK4/6 analogue series. Pharmacophore validation confirmed class-specific binding motifs in the remaining 14 compounds: hinge-region H-bond donor/acceptor and hydrophobic adenine-pocket fill for CDK4/6, zinc-binding groups (hydroxamic acid or benzamide) for HDAC, and halogen-mediated Ser212 contacts for MEK allosteric inhibitors. Palbociclib led by oncology pathway coverage (150 pathways, rank 2/112) with a clean ADMET profile (low hERG/CYP3A4, zero Lipinski violations), albeit at moderate potency (IC_{50} = 11 nM). Trametinib combined the highest reversal score (5.28) with sub-nanomolar potency (IC_{50} = 0.92 nM, rank 9/112) but showed high hERG risk and MW = 615 Da. Entinostat achieved the broadest reversal (118 pathways, rank 5/112) while vorinostat offered a complementary profile (MW = 264 Da, clean ADMET, reversal score 5.06) with narrower reversal (32 pathways). Multi-criteria integration identified palbociclib as the overall priority candidate, with trametinib, entinostat and vorinostat as class-specific leads warranting further in vitro evaluation.

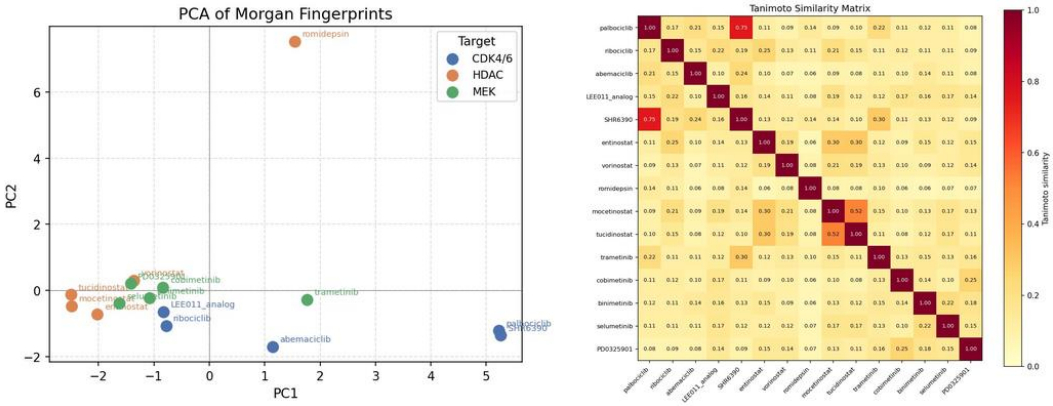

Fig. 1. (A) PCA of Morgan fingerprints showing chemical-space separation of CDK4/6 (●), HDAC (■) and MEK (▲) inhibitors; romidepsin is structurally isolated. (B) Tanimoto similarity heatmap.

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Computational Analysis of Isoindole-Based Reagents for Guanidinylation

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2*H*-Isoindoles are highly reactive heterocyclic intermediates of theoretical and practical interest and are widely used as building blocks in organic and pharmaceutical synthesis [1]. Although isoindoles possess an aromatic π-system, the position of the nitrogen atom prevents the formation of a Clar aromatic sextet in any six-membered ring, resulting in enhanced reactivity relative to indole isomers. Their cycloaddition reactivity is driven by restoration of aromaticity in the fused aryl system, and it is comparable to that of isoacenofurans, which are isoelectronic with the iso[aceno]indoles discussed here [2].

The cycloaddition reactivity of N-amidino benzannulated isoindoles was studied experimentally and computationally using DFT at the M06-2X/6-311+G(d,p) level. Linear homologation significantly increases reactivity, which is attributed to the intrinsic instability of the isoindole framework and energetic stabilization upon re-aromatization in cycloadducts.

Two homologated derivatives, 2*H*-benzo[*f*]isoindole and 2*H*-naphtho[2,3-*f*]isoindole, were synthesized *via* multistep routes. Their cycloaddition reactivity toward dienophiles was evaluated, and pronounced instability in solution was confirmed.

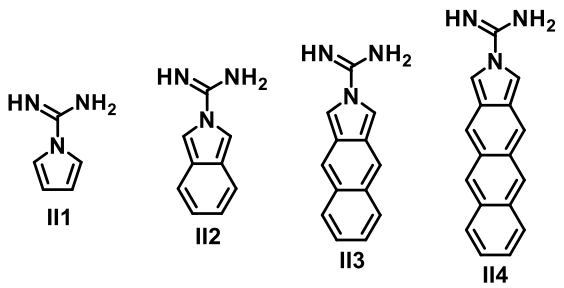

Figure 1. Isoindole linear homologs **II1**–**II4** used in computational analysis

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Yellow K2 – Potential Next Generation NSAID

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One of the main imperatives of medicine and pharmacy is the treatment of pain, inflammation, and fever [1]. Non-steroidal anti-inflammatory drugs (NSAIDs) are leading medicines for treatment, yet current NSAIDs suffer from various limitations (such as efficacy, adverse effects, and/or potential abuse) [2,3]. The relatively recent development of precise *in silico* bioinformatic and chemoinformatic tools can substantially optimize and fast-track the process of drug development. Along with exponentially increasing knowledge of molecular mechanisms underlying pathological states, it enables proper ground for engineering and development of better NSAIDs with more precise targeting without undesired side effects.

A newly developed compound "Yellow K2", with potential use as an NSAID with a functional group of increased cyclooxygenase-2 (COX-2) affinity, has been engineered and developed using contemporary chemoinformatic and bioinformatic methodologies of *in silico* molecular engineering. The lead compound development and optimization included *in silico* design, pharmacokinetic and pharmacodynamic studies, molecular docking simulations, and structural studies with the use of Virtual reality (VR), followed by a computer-assisted exploration of reverse synthesis – possible pathways of organic synthesis from economically viable constituent reagents.

The project was wrapped up by conducting ground *in vitro* cytotoxicity studies on human embryonic kidney 293 cell lines using MTT assay to test the *in silico* obtained projections.

Building upon promising results of this small, economically viable molecule, the research is scheduled to proceed into the second phase of preclinical trials – *in vitro* immunofluorescence pharmacokinetic and pharmacodynamic studies on a wider array of mammalian cell cultures – traditional liquid cultures and novel 3D cell cultures (organs-on-a-chip and organoids).

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Tunneling Splittings of the Enolic Acetylacetone

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Proton transfer reactions play a central role in many chemical and biological processes, ranging from enzymatic catalysis and hydrogen-bond rearrangements to proton transport in condensed phases. The study of such tunneling processes provides valuable insight into the quantum nature of molecular dynamics in hydrogen-bonded systems. Acetylacetone represents a well-known example of an intramolecular proton transfer system. In its enol form, the molecule contains a strong intramolecular hydrogen bond that forms a six-membered quasi-ring structure. Within this configuration, the proton can be located on either of the two oxygen atoms, leading to two equivalent minima on the potential energy surface (Figure 1). In the case of acetylacetone, the tunneling process is not governed solely by the motion of the proton along the hydrogen bond. Instead, it involves a multidimensional large-amplitude motion of the molecular framework. It has been shown that the proton transfer is strongly coupled to several additional motions, including deformation of the six-membered quasi-ring and torsional motions of the methyl groups attached to the carbon skeleton. These coupled motions significantly influence the tunneling dynamics of the system [1]. Tunneling splittings 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.

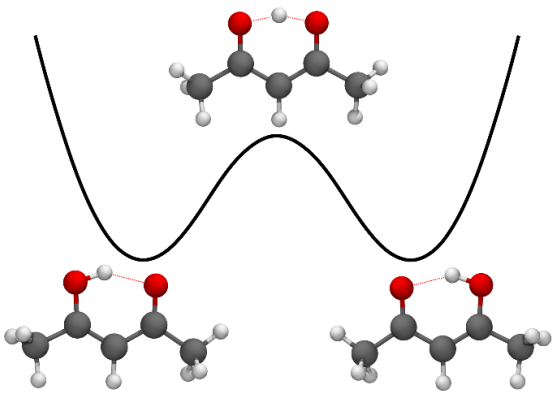

Figure 1. The proton transfer in the enolic form of acetylacetone

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Single-Cell Metabolite Annotation by Tandem Mass Spectrometry and *Ab Initio* Molecular Dynamics

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Accurate single-cell mass spectrometry (MS) imaging and metabolite identification remain challenging due to the small size of cells, the limited quantity of desorbed material, and the high density of m/z values in metabolite databases. A highly sensitive analytical approach that enables metabolite annotation by matching m/z values from single-cell MS/MS (tandem mass spectrometry) spectra with fragment m/z values calculated using *ab initio* molecular dynamics was developed.

This method was applied to annotate a signal at m/z 337.11 Da, which is elevated in chronic lymphocytic leukemia [1]. Five candidate compounds were selected through database searching. Prior to single-cell MS/MS imaging, the procedure was conducted on S-nitrosoglutathione (GSNO), one of the candidates. Five fragment ions were consistently observed in both experimental and *in silico* spectra of the GSNO solution.

After optimizing the sensitivity of single-cell MS imaging, MS/MS spectra were acquired from individual lymphocytes. These spectra revealed 0–3 fragment matches with *in silico* spectra of three glutathione-related compounds. In contrast, no correspondence was found between experimental and calculated spectra for the remaining candidate compounds.

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SARS-CoV-2 Spike Protein Interaction with Monoamine Oxidase B: Implications for Neurodegeneration

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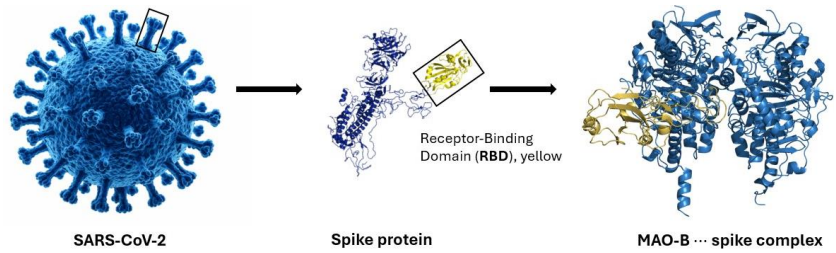
COVID-19, caused by **SARS-CoV-2**, is primarily a respiratory disease but is also associated with neurological complications. One proposed mechanism involves interactions between viral components and monoamine oxidase (**MAO**) enzymes [1]. Here, we investigate the binding of the SARS-CoV-2 spike protein to monoamine oxidase B (**MAO-B**), hypothesizing disruption of monoaminergic homeostasis and potential links to neurodegeneration [2].

An integrated computational approach combining molecular docking, molecular dynamics (**MD**) simulations, and **MM-GBSA** calculations was used to characterize MAO-B· · · spike interactions. Multiple high-affinity binding sites were identified, with stable binding observed in MD simulations and significant effects on binding energetics of substrates and inhibitors, suggesting interference with MAO-B function.

Overall, the findings indicate a potential molecular basis for SARS-CoV-2-induced disruption of monoaminergic signaling, warranting further investigation [3,4].



Research Rationale

Spike protein can bind to **MAO-B**, impacting its activity and altering neurotransmitter levels. This disruption suggests increased risk for neurodegenerative diseases.

Acknowledgement: Croatian Science Foundation, grant number IP-2024-05-3953.

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From Structure to Function: UCP1 Cavity Interactions Revealed by Molecular Dynamics Simulations

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Mitochondria, the cell's powerhouses, primarily produce adenosine triphosphate (ATP), but under cold exposure, brown adipose tissue (BAT) uniquely utilizes non-shivering thermogenesis to dissipate energy as heat instead. Central to this process is uncoupling protein 1 (UCP1), which, in the presence of long-chain fatty acids (FAs) or other uncouplers like dinitrophenol and CCCP, facilitates a regulated transport of protons across the inner mitochondrial membrane, thereby generating heat. While nucleotides inhibit this process, FAs function as weak, protein-independent uncouplers, mainly limited by the transport of the FA anion across the membrane. According to the fatty acid cycling hypothesis [1], UCP1 catalyzes this crucial step. Nonetheless, the specific molecular mechanisms underlying both the UCP1-facilitated transport of FA anions and its inhibition remain poorly understood.

In our study, we propose two distinct pathways for FA anion translocation (sliding) at the UCP1 protein-lipid interface, converging at critical arginine residues, R84 and R183, located in the nucleotide-binding region. Our findings indicate that the protonation of the FA anion facilitates its release from the protein-lipid interface [2]. Interestingly, the addition of ATP prior to the introduction of FAs entirely inhibits protein-mediated proton transport, through binding to both R84 and R183. In contrast, when ATP is introduced in the presence of FAs, the inhibition is only partial, suggesting that the competition between ATP and FAs alters the degree of proton transport regulation. Molecular dynamics (MD) simulations are conducted on cryo-EM structures of UCP1 in both nucleotide-free (PDB: 8HBV) and ATP-bound (PDB: 8HBW) states, with results correlating well with conductance measurements of membranes reconstituted with UCP1 [3].

Taken together, our findings enhance the understanding of UCP1's role in regulating the proton gradient. Unraveling the precise molecular mechanisms of proton transport is crucial for comprehending the processes of non-shivering thermogenesis and energy balance in mammals, both of which are fundamental to cellular function.

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Molecular Dynamics Study of Ion-Mediated DNA-Membrane Interactions

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Interaction of DNA and membranes are crucial for understanding basic cellular processes. Depending on the membrane content and properties of the DNA molecule, representative native-like systems for studying mentioned interactions can be constructed *in silico*. Novel *in silico* model of *Avanti* lipid membrane provides a platform for conducting realistic computational research. It consists of 14 different lipids and presents one of the most complex and most realistic *in silico* models of membranes [1]. *Avanti* membrane represents *Escherichia coli* polar lipids extract used *in vitro* and it was proved to maintain stable membrane properties across a physiologically relevant temperature range.

For this study, using *Avanti* membrane, a system of two lipid bilayers enclosing two DNA molecules of different sizes and structures was constructed. Linear double stranded DNA promotor region of 78 bp and a homohexameric assembly of 50 bp per subunit were generated in *silico*. The membrane patches were expanded four times their original size to reduce artefacts of boundary effects and the DNAs were oriented for the optimal fit between the opposing membrane surfaces. The system was solvated with TP3P water model molecules and neutralized with Na^+ and Cl^- ions reaching a concentration of 0.1 M. In this study, we examine the effect of temperature, pressure and ionic strength on the sandwich-like system. Temperature is raised to 320 K and subsequently to 500 K while pressure is raised to 10, 50 and 100 bar. In a neutralised system, ionic strength is increased by adding various cations, namely Ca^{2+}, Mg^{2+} and K^+. The properties of bilayer and DNA, DNA-bilayer distance and potential insertion of DNA molecules into the bilayer were studied.

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In Silico Prediction of Pharmaceutical Cocrystal Formation Using Explainable Machine Learning

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Pharmaceutical cocrystals are multicomponent crystalline systems composed of an active pharmaceutical ingredient (API) and a coformer, assembled by noncovalent forces. The design of such cocrystals has become an important strategy for improving the physicochemical properties of APIs, such as solubility, chemical stability, and bioavailability [1]. In general, screening of new cocrystals involves experimental identification with a large number of coformers, thus being time-consuming, laborious and expensive. The application of computational (*in silico*) methods for the prediction of cocrystal formation, such as machine learning (ML), can significantly reduce the time and cost required for cocrystal screening [2]. Classification ML models can be used to predict whether a given API–coformer combination will form a cocrystal, providing useful preliminary information for the selection of potential coformers. In this study, a classification ML model was developed using experimental data reported in the literature. Molecular descriptors were generated from the SMILES representations of APIs and coformers using the RDKit toolkit. These descriptors quantitatively describe molecular properties and are used as input features for the ML model. Although ML models can be useful for *in silico* cocrystal screening, they are often considered black-box models with limited interpretability. The lack of interpretability can reduce trust in model predictions and limit the extraction of meaningful scientific insights [3]. To address this limitation, explainable artificial intelligence (XAI) methods are used to provide insight into model predictions and help identify the key factors influencing cocrystal formation.

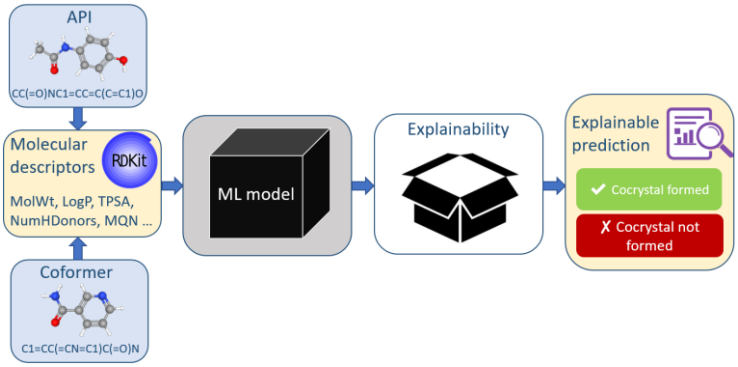

Figure 1. Workflow of explainable machine learning classification for cocrystal prediction

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Impressum

Name of the conference: Computational Chemistry Day 2026

Organizers: Ruđer Bošković Institute, University of Zagreb Faculty of Pharmacy and Biochemistry, University of Zagreb Faculty of Science, Croatian Chemical Society and University of Zagreb University Computing Centre SRCE

Place: University of Zagreb University Computing Centre SRCE, Zagreb, J. Marohnića 5; Ruđer Bošković Institute, Zagreb, Bijenička 54, Croatia

Date: May 8-9, 2026

Organizing Committee: Darko Babić (RBI, Zagreb), Danijela Barić (RBI, Zagreb), Branimir Bertoša (UniZG-FS, Zagreb), Marko Cvitaš (UniZg-FS, Zagreb), Ines Despotović (RBI, Zagreb), Luca Grisanti (CNR-IOM, Trieste), Emir Imamagić (SRCE, Zagreb), Ivan Kodrin (UniZg-FS, Zagreb), Boris Kovačević (RBI, Zagreb), Janez Mavri (NIC, Ljubljana), Tomislav Piteša (RBI, Zagreb), Marin Sapunar (RBI, Zagreb), Višnja Stepanić (Head of the Organizing Committee, RBI, Zagreb), Davor Šakić (UniZg-FPB, Zagreb), Tana Tandarić (RBI, Zagreb), Mario Vazdar (UCT, Prague), Robert Vianello (RBI, Zagreb) and Valerije Vrček (UniZg-FPB, Zagreb)

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Abstracts were prepared by the authors.

Editor: Darko Babić

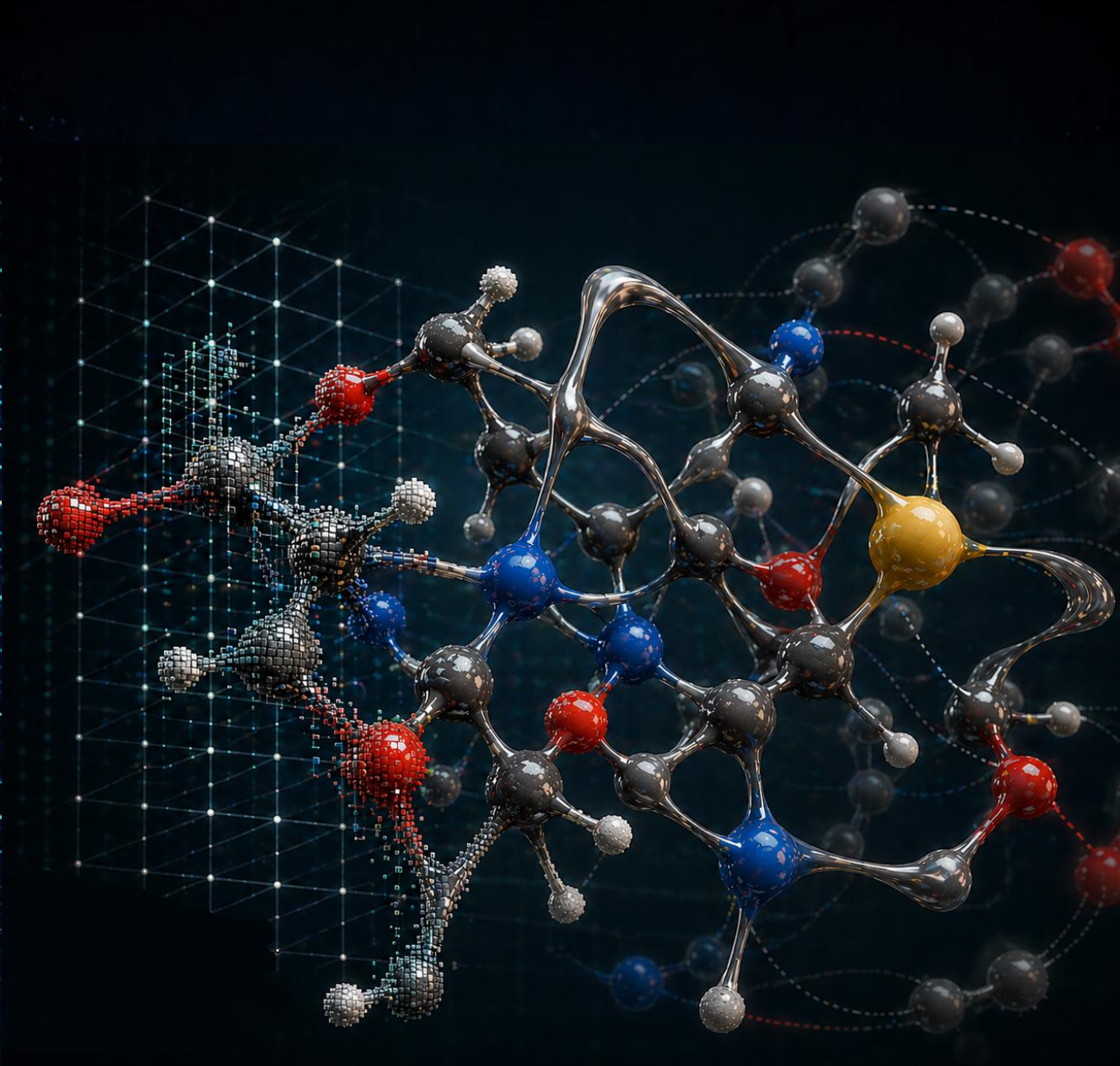
Publisher: Ruđer Bošković Institute

Cover image generated with AI assistance from ChatGPT

ISBN: 978-953-7941-61-1

Organization of the Computational Chemistry Day 2026 was financially supported by:

- The Croatian Science Foundation, through the projects: IP-2024-05-3953, IP-2024-05-7730, IP-2025-02-7105, and UIP-2025-02-1368
- University of Zagreb Faculty of Pharmacy and Biochemistry
- The Ruđer Bošković Institute, Zagreb
- University of Zagreb University Computing Centre SRCE
- O2 d.o.o.
- Informos d.o.o.



ISBN 978-953-7941-61-1