COST-COSY School
CPCS-2025

Computational Physics of Confined Systems:
From Life to Material Sciences

Bogolyubov Institute for Theoretical Physics
of the National Academy of Sciences of Ukraine

June 24-26, 2025

Computational Physics of Confined Systems: From Life to Material Sciences

The school is organized in Kyiv on the basis of the Bogolyubov Institute for Theoretical Physics of the National Academy of Sciences of Ukraine (BITP) under the umbrella of COST Action CA21101 / Confined molecular systems: from a new generation of materials to the stars (COSY).

The school aims to introduce students and early-career scientists to computational research in confined systems, bridging the disciplines of life and material sciences. With its focus on cutting-edge topics, the school intends to inspire young researchers to explore this interdisciplinary field through lectures, hands-on tutorials, and skill-building sessions in scientific communication. The scope of the school will cover the structure of biomolecules, the physical properties of novel materials, and methods to model their physical properties at different levels of organization. The tutorials will demonstrate the students how to use in practice advanced computational methods. The participants from Kyiv are expected to be present in person. The participants from other cities in Ukraine and from Europe will join the event online via Zoom.

Scientific committee

Sergiy Perepelytsya

Bogolyubov Institute for Theoretical Physics of the NAS of Ukraine

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COST ACTION CA21101 – CONFINED MOLECULAR SYSTEMS: FROM A NEW GENERATION OF MATERIALS TO THE STARS (COSY)

The COST Action COSY aims to provide a computationally and experimentally sound foundation for the fundamental understanding and control of confined molecular systems. The resulting outcome will be translated into useful knowledge forming the basis for applications. These range from creating a new generation of materials including biomaterials, with immediate transfer to industry, to disclosing the chemistry occurring in space. To this end, COSY will combine new cutting-edge experimental techniques for the synthesis of novel nanomaterials and high-resolution characterization thereof, with state-of-the-art first principles modelling. The most advanced methods for molecular motion as well as modern artificial intelligence, machine learning technologies, and big data science will be applied.

COSY COST Action coordinators: María Pilar de Lara-Castells (Chair), Cristina Puzzarini (Vice Chair).

Program

Tuesday, 24.06.2025

10-00 10-10	**OPENING** **Sergiy Perepelytsya** (Bogolyubov Institute for Theoretical Physics of the NAS of Ukraine) **Maria Pilar de Lara-Castells** (COSY COST Action Chair) **Cristina Puzzarini** (COSY COST Action Vice Chair)	
10-10 11-10	**Aatto Laaksonen** https://youtu.be/grdNmuYNcsM?si=LBfRILNcS_wr-QBS *Stockholm University, Sweden* "Modeling polymers constrained by Nature"	10
11-10 12-10	**Francesca Mocci** https://youtu.be/a1fULQ7MZA0?si=799U3dfx2IgpdCib *University of Cagliari, Italy* "Multiscale Molecular Modeling of DNA: Toward Simulating Its Naturally Confined Environment"	11
12-10 12-30	**COFFEE BREAK**	
12-30 13-30	**Sergiy Perepelytsya** https://youtu.be/JqekZHz6TFM?si=RQ94InB8Eb67CxGv *Bogolyubov Institute for Theoretical Physics of the NAS of Ukraine* "Counterions confined in DNA nanomaterials: Insights form modeling and simulation"	12
13-30 14-30	**LUNCH**	
14-30 15-30	**Sonja Grubisic** https://youtu.be/aYntKIEu9Os?si=ZJVO6F4k7e-qpQMZ *University of Belgrade, Serbia*	14

	"Biomolecular Force Fields: Recent Advances in Nonstandard Amino Acid and Nucleic Acid Development"	
15-30 16-30	**Valeriya Trusova** https://youtu.be/SDjdLm01Vg4?si=8au6r602JAHtEUIc *V.N. Karazin National University, Kharkiv, Ukraine* "From molecular simulations to functional design: computational insights into theranostic protein-based nanostructures"	15
16-30 18-00	**Evening Scientific Mixer**	

Wednesday, 25.06.2025

10-00 11-00	**Anna Shestopalova** https://youtu.be/_9wYnpC36A0?si=Bd_66voujcW6kpVP *O.Ya. Usikov Institute of Radiophysics and Electronics of the NAS of Ukraine, Kharkiv, Ukraine* "Drug Design and Repurposing: An Overview with Selected Examples"	16
11-00 12-00	**Tetiana Bubon** https://youtu.be/-IcPZ2fhVms?si=4VUmEbi3gfrP2XgU *Bogolyubov Institute for Theoretical Physics of the NAS of Ukraine, University of Trieste, Italy* "Modeling of the Structure and Dynamics of the DNA Hydration Shell"	18
12-00 12-30	**COFFEE BREAK**	
12-30 13-30	**Ali Hassanali** https://youtu.be/vlmQopVriT0?si=nRYAalAjDJDF0Ino	19

	The Abdus Salam International Center for Theoretical Physics, Trieste, Italy "Chemical continuum: overcoming discrete notions in the chemical physics of water"	
13-30 14-30	**LUNCH**	
14-30 15-30	**Dmytro Piatnytskyi** https://youtu.be/HbWx1D-gm7Q?si=fzW6qdsh2aa12Uuj *Bogolyubov Institute for Theoretical Physics of the NAS of Ukraine* "Quantum chemical calculations basics"	20
15-30 16-30	**Piotr Żuchowski** https://youtu.be/B9Jm14Gpem8?si=5Q9a_bhirmHkPJsi *Nicolaus Copernicus University, Poland* "Molecular interactions with quantum chemistry methods"	21
16-30 18-00	**Excursion for the participants attending in person**	

Thursday, 26.06.2025

10-00 11-00	**Andrij Baumketner** https://youtu.be/ix6flt0QP8Y?si=l7skMFS_e56HY733 *Institute of Condensed Matter Physics of the NAS of Ukraine, Lviv, Ukraine* "What can we learn about quantum dots from computer simulations?"	22
11-00 12-00	**Carlo Maria Carbonaro** https://youtu.be/FTMiIbkubfQ?si=pJvBC6Anw21m6uTo *Physics Department in University of Cagliari, Italy*	23

"Experimental and computational characterization of carbon dots"

12-00 12-30	**COFFEE BREAK**	
12-30 13-30	**Valentyna Kuznetsova** https://youtu.be/kY9OQXtnJL8?si=Al-9ca8D_xukjmVk *Department of Physics at the University of South Bohemia in Ceske Budejovice, Czech Republic* "How to give a good presentation"	24
13-30 14-30	**LUNCH**	

14-30	**PARTICIPANT PRESENTATIONS**	

Dragan Popović 25
University of Belgrade – Institute of Chemistry, Technology and Metallurgy, National Institute of the Republic of Serbia
"Energetics of steps in proton pumping mechanism of cytochrome c oxidase"

Yevhen Osokin 26
Bogolyubov Institute for Theoretical Physics of the NAS of Ukraine
"Features of dπ-pπ-BONDING OF Cu(I) π-complexes with some unsaturated acids"

Aamir Saeed 27
Department of Geological and chemical sciences, University of Cagliari
"Insights into small molecule stabilization of viral G-quadruplexes via molecular dynamics and docking simulations"

Olha Vlasiuk 31

National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute"
TBA

Anita Lazić 32
The Innovation Centre of the Faculty of Technology and Metallurgy, University of Belgrade
"Structural effects on the antioxidant potential and drug-likeness of selected xanthene derivatives"

Giulia Olla 33
Department of Chemical and Geological Sciences, University of Cagliari
"Molecular dynamics simulations of 143d and 1kf1 G-quadruplexes"

Enrico Puddu 34
Department of Chemical and Geological Sciences, University of Cagliari
"Temperature-dependent stability of a viral G-quadruplex: a computational approach"

Zaira Carboni 35
Department of Physics, University of Cagliari
"Optical behavior and structural insights into nitrogen-doped carbon dots"

17-00 **Closing**

MODELING POLYMERS CONSTRAINED BY NATURE

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Nature is the most brilliant "trial-and-error" material designer, crafting biopolymers constrained for specific functional reasons. This talk gives an overview of how computer simulations can explain these natural constraints through multi-scale modeling approaches, spanning from atomic to mesoscopic scales. Through hierarchical coarse-graining and inverse problem-solving methodologies, this presentation introduces two key case studies: the transformation of plant cellulose and lignin into thermoplastic materials and the organization of DNA into chromatin. Computational strategies, including MD simulations, illustrate how chemical modifications and the introduction of plasticizers can overcome the natural rigidity in plant biopolymers, thus making it possible use them in bioplastics in a sustainable wyay. Additionally, the complex problem of DNA packaging into nucleosomes is discussed by employing successive hierarchical coarse-graining methods, giving insights into genome organization and gene regulation. These examples highlight how computational physics and chemistry not only increases our understanding of nature's intricate materials but also guides us toward sustainable, bio-inspired solutions in Material Sciences.

MODELING OF DNA: TOWARD THE SIMULATION IN THE NATURAL CONFINING ENVIRONMENT

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Understanding DNA behavior in its native, highly confined environments, such as chromatin, requires bridging multiple spatial and temporal scales. This talk explores how coarse-grained (CG) simulation approaches, both top-down and bottom-up, allow us to overcome the limitations of atomistic molecular dynamics in modeling large, complex biomolecular systems. After introducing the challenges of simulating DNA structure and dynamics across biological length and time scales, we compare several CG strategies, including the 3SPN and Ouldridge models, Martini [1], and systematically derived models using Inverse Monte Carlo (IMC) [2] and related bottom-up methods. Focus is given to the capability to incorporate ion-specific interactions [3], model sequence-dependent flexibility, and reproduce experimental observables such as persistence length and DNA condensation. We present applications to DNA duplexes, nucleosome core particles, and non-canonical structures like G-quadruplexes, highlighting the versatility and limitations of current CG models. The importance of matching model resolution to the property of interest is emphasized, alongside a discussion of hybrid schemes and emerging developments in multiscale modeling.

[1] H.M. Khan, D.P. Tieleman, Coarse Grained Models: The Martini Force Field, in Molecular Dynamics Simulations and Reaction Rates, eds. A. Laaksonen, F. Mocci, in Comprehensive Computational Chemistry, Vol. 3, eds. R.J. Boyd, M. Yáñez (Elsevier, 2024), pp. 660–673.
[2] A.P. Lyubartsev, A. Naômé, D.P. Vercauteren, A. Laaksonen, J. Chem. Phys. 143, 243120 (2015).
[3] F. Mocci, A. Laaksonen, *Soft Matter* **8**, 9268 (20120

COUNTERIONS CONFINED IN DNA NANOMATERIALS: INSIGHTS FORM MODELING AND SIMULATION

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From the very first works by Watson, Crick, Wilkins, and Franklin, it was known that the structure of the DNA molecule significantly depends on environmental conditions. This is due to the fact that the nitrogenous bases of DNA are hydrophobic (they tend to avoid contact with water), whereas the phosphate groups, located on the outside of the double helix, are hydrophilic. The phosphates of DNA carry a negative charge (-e) and in an aqueous environment are neutralized by positively charged metal ions (e.g., K^+, Mg^{2+}) or molecular ions such as polyamines (spermidine^{3+} and spermine^{4+}).

Considering the key role of counterions in stabilizing the DNA structure, understanding their spatial arrangement around the double helix in confined environments is essential. In this context, one of the first models that provided some physical insight into the distribution of counterions around DNA was the Manning model [1], revealing that counterions condense onto DNA, forming a layer of ionic atmosphere around the macromolecule. The system of DNA with counterions can be also considered as a lattice of ionic crystal [2,3]. This approach made it possible to investigate the vibrations of DNA counterions. The lecture will provide a brief overview of these approaches.

On the other hand, apart from analytical models, numerical simulation methods have proven to be extremely fruitful for studying the DNA system in an aqueous environment with confined ions. Over the past decades, these methods have become a separate field that complements experiments on one hand and bridges to analytical physical models on the other. The lecture will outline several results in this field, including the simulations of DNA with

polyamine molecules [4-6] and alkali metal counterions with different hydration characteristics [7,8].

Despite the key biological role of DNA, its unique properties make it an attractive material for use in various nanotechnologies. DNA nanotechnology originated in the 1980s and has seen rapid development over the past two decades. The lecture will outline various types of DNA nanotechnologies, including the application of DNA in lithium-ion batteries [9,10], as well as the fundamental problems addressed through the use of molecular dynamics methods.

[1] G. S. Manning, Q. Rev. Biophys. 11, 179 (1978).
[2] S. M. Perepelytsya and S. N. Volkov, Ukr. J. Phys. 49, 1072 (2004).
[3] S. M. Perepelytsya and S. N. Volkov, Eur. Phys. J. E 24, 261 (2007).
[4] S. Perepelytsya, J. Uličný, A. Laaksonen, and F. Mocci, Nucleic Acids Res. 47, 6084 (2019).
[5] S. Perepelytsya, T. Vasiliu, A. Laaksonen, L. Engelbrecht, G. Brancato, and F. Mocci, J. Mol. Liq. 389, 122828 (2023).
[6] S. Perepelytsya, T. Vasiliu, A. Laaksonen, L. De Villiers Engelbrecht, F. Mocci, Low Temp. Phys.50, 219–230 (2024).
[7] S. M. Perepelytsya, J. Mol. Model. 24, 171 (2018).
[8] S. M. Perepelytsya, Ukr. J. Phys. 65, 510 (2020).
[9] S. B. Mitta, R. Harpalsinh, J. Kim, H. S. Park, and S. H. Um, Adv. Mater. Interfaces 9, (2022).
[10] S. B. Mitta, J. Kim, H. H. Rana, S. Kokkiligadda, Y. T. Lim, S. H. Bhang, H. S. Park, and S. H. Um, PNAS Nexus 3, pgae213 (2024).

BIOMOLECULAR FORCE FIELDS: RECENT ADVANCES IN NONSTANDARD AMINO ACID AND NUCLEIC ACID DEVELOPMENT

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The accurate modeling of biomolecular systems, particularly proteins and nucleic acids, is fundamental to our understanding of biological function and the development of therapeutic strategies. Central to this effort is the ongoing refinement of molecular mechanics force fields, which simulate the physical interactions between atoms to predict the structure, dynamics, and energetics of macromolecules. Given that amino acids and nucleic acid bases are the primary building blocks of proteins and DNA/RNA, their accurate representation with force fields is therefore critical for reliable molecular simulations. This lecture will provide an in-depth overview of the development of force fields tailored to these key biomolecular components. Emphasis will be placed on the methodologies used for parameterization, validation against experimental and quantum mechanical data, and the trade-offs between accuracy and computational cost. Participants will be introduced to both widely used and emerging force fields for biomolecules, along with current challenges such as modeling peptides that contain α-tetra-substituted non-natural amino acids [1,2].

[1] S. Grubišić, I. Đorđević, D. Popović, Optimization of non-polarizable and polarizable force fields and their application to model compounds, Comprehensive Computational Chemistry, Elsevier, Volume 3, 2024, 964-986 (2024) book chapter.
[2] S. Grubisić, G. Brancato, A. Pedone, V. Barone, V., 2012. Extension of the AMBER force field to cyclic α,α dialkylated peptides. Phys. Chem. Chem. Phys., 14, 15308–15320 (2012) https://pubs.rsc.org/en/content/articlelanding/2012/cp/c2cp42713c

FROM MOLECULAR SIMULATIONS TO FUNCTIONAL DESIGN: COMPUTATIONAL INSIGHTS INTO THERANOSTIC PROTEIN-BASED NANOSTRUCTURES

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Protein-based nanostructures represent promising drug delivery and theranostic platforms due to their inherent biocompatibility and reduced immunogenicity. These systems enable simultaneous therapeutic delivery and diagnostic imaging for personalized medicine applications [1]. Computational approaches have transformed protein nanocarrier design through molecular dynamics simulations and enhanced sampling techniques [2]. All-atom simulations reveal that electrostatic interactions dominate polar drug binding, while π-π stacking governs aromatic molecule interactions. Advanced methods like umbrella sampling and metadynamics enable accurate binding free energy calculations and exploration of drug-protein interaction mechanisms. Coarse-grained modeling facilitates studies of protein self-assembly and nanoparticle formation, demonstrating assembly through primary particle formation followed by coagulation. Specialized computational approaches provide insights into hybrid protein-inorganic systems and cellular uptake mechanisms through receptor-mediated endocytosis. These computational insights directly inform rational design of next-generation protein-based theranostic nanostructures, establishing molecular modeling as essential for modern nanocarrier development with enhanced clinical translation potential [3].

[1] S. Hong, D. Choi, H. Kim et al., Pharmaceutics **12**, 604 (2020).
[2] T. Ashwini, R. Narayan, P. Shenoy, U. Nayak, J. Mol. Liq. **368**, 120596 (2022).
[3] I. Munir, F. Nazir, G. Yesiloz, ACS Appl Mater Interfaces **16**, 70187 (2024).

DRUD DESIGN AND REPURPOSING: AN OVERVIEW WIT SELECTED EXMPLES

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Drug design and repurposing are interdisciplinary approaches to modern therapeutics. The primary goal of drug design is to identify or create novel compounds that can safely and effectively treat specific diseases by targeting their underlying biological mechanisms. This field exemplifies interdisciplinary integration, combining advances in medicine, chemistry, pharmacology, biochemistry, biotechnology, molecular biology, molecular biophysics, bioinformatics, computer modeling, artificial intelligence, and even quantum computers. Drug design relies on the accurate prediction of interactions between small molecules and biomacromolecular targets such as proteins and nucleic acids. It is grounded in a fundamental understanding of biological, chemical, and physical principles of bionanostructures organization. While rooted in the natural sciences, drug design is an applied discipline with critical importance in molecular pharmacology and medicine. The current progress in drug design has been made possible not only by advances in the aforementioned scientific fields but also by the availability of high-speed internet and the development of diverse, specialized databases. Despite this progress, the drug design process remains time-consuming and costly, often requiring years of research and billions of dollars to bring a single drug to market. Drug repurposing, also known as drug repositioning or drug reprofiling, refers to the process of identifying new therapeutic uses for existing drugs. These may include drugs that are already approved, discontinued, or still under investigation. While the concept is not entirely new, it has gained significant attention in the past decade. Currently, approximately one-third of all newly approved drugs result from repurposing efforts. The importance of drug repurposing lies in its advantages over traditional drug development. It is often faster, less expensive, and safer, as much is already known about the pharmacokinetics, pharmacodynamics, and safety profiles of the compounds involved. Due to time constraints, only a

limited portion of the vast field of drug design can be covered in the lecture. However, the audience will be introduced to this fascinating and dynamic area of modern scientific research, at least at a popular-science level. The presentation begins with an introductory overview of drug design, including fundamental definitions and core concepts. Key methods will be briefly discussed, with a particular focus on rational drug design. A short historical overview of drug development will also be provided. Selected case studies will illustrate the principles of rational drug design, including the development of inhibitors targeting essential proteins in the Human Immunodeficiency Virus (HIV) life cycle. These proteins include protease (an enzyme that cleaves viral polyproteins), reverse transcriptase (which converts viral RNA into DNA), and host cell receptors such as CD4, along with the coreceptors CCR5 and CXCR4, which facilitate viral entry into T-lymphocytes. Examples of drug repurposing will also be presented, highlighting recent efforts to reposition existing antiviral drugs for the treatment of COVID-19 caused by SARS-CoV-2. The lecture will describe results related to blocking the interaction between SARS-CoV-2 and the angiotensin-converting enzyme 2 (ACE2) receptor. This includes a computational study aimed at identifying potential inhibitors of the SARS-CoV-2 spike glycoprotein by targeting its receptor-binding domain and its interface with ACE2 [1]. The lecture concludes with final remarks and a set of supplementary materials, including links to online resources and tools for further exploration of drug design. These materials are intended to support and encourage continued self-directed learning in this rapidly evolving field.

[1] K.V. Miroshnychenko, A.V. Shestopalova. J. Biomol. Struct. Dyn, **40**, 8672 (2022).

MODELING OF THE STRUCTURE AND DYNAMICS OF THE DNA HYDRATION SHELL

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Under physiological conditions, DNA adopts a double-helical structure, with hydrophobic nucleic base pairs positioned inside and negatively charged phosphate groups exposed to the surrounding solution [1]. The negative charges of the phosphate backbone are neutralized by metal ions (such as Na^+, K^+, and Mg^{2+}), as well as by molecular ions (polyamines). Early studies of DNA structure demonstrated that the ion-hydration environment stabilizes the macromolecule [2]. Additionally, it was shown that the dynamics of the DNA double helix and its ion-hydration shell are interrelated [3], playing a role in biological processes within living cells [4]. Therefore, understanding the structural and dynamical features of the ion-hydration shell is key to revealing the physical mechanisms underlying DNA function. In this lecture, we will explore current insights into ion-hydration shell properties, with a special emphasis on the advantages of molecular dynamics simulations for studying such complex systems at the atomic level.

[1] W. Saenger, Principles of Nucleic Acid Structure (Springer, New York, 1984).
[2] R.E. Franklin, R.G. Gosling, Acta Cryst. **6**(8–9), 673 (1953)
[3] E. Dubou´e-Dijon, A.C. Fogarty, J.T. Hynes, D. Laage, J. Am. Chem. Soc. **138**(24), 7610 (2016).
[4] B. Jayaram, T. Jain, Annu. Rev. Biophys. Biomol. Struct. **33**, 343 (2004)

CHEMICAL CONTINUUM: OVERCOMING DISCRETE NOTIONS IN THE CHEMICAL PHYSICS OF WATER

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QUANTUM CHEMICAL CALCULATIONS BASICS

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This talk explores fundamental issues in quantum chemical calculations, focusing on the approximations and computational methods that underpin modern theoretical chemistry. Key aspects of basis sets are discussed, with illustrative examples demonstrating their significance. Additional topics include solvent models, vibrational frequency analyses, and the treatment of basis set superposition error (BSSE), offering a broader perspective on advanced features in quantum chemical modeling. The presentation also covers relevant software applications used in practice. To illustrate the concepts discussed, example calculations for the hydrogen peroxide (H_2O_2) molecule are provided.

MOLECULAR INTERACTIONS WITH QUANTUM CHEMISTRY METHODS

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WHAT CAN WE LEARN ABOUT QUANTUM DOTS FROM COMPUTER SIMULATIONS?

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Colloidal quantum dots (QD) are recognized as an important new class of nanomaterials designed specifically for optical applications. Nucleation and growth of QDs represent a unique example of the self-assembly process whose mechanistic details, including factors controlling geometry and relevant growth characteristics, are of primary interest to fundamental research both in physics and in chemistry. Surfactant ligands are essential for the entire life cycle of colloidal nanocrystals (NCs), starting from nucleation/growth phase and ending with the thermal stability. How ligands attach to NCs is difficult to study by experimental means because of the intrinsic limitations of the latter, such as insufficient resolution. In our talk, we will focus on what can be learned about ligand-NCs interactions using atomistic simulations. We will begin by sketching out the challenges facing such simulations as they pertain to lead-halide quantum dots – a latest addition to the QD family with unique properties. Next, we will introduce methods of enhanced conformational sampling and provide concrete examples of how to use them by the computation of potential of mean force by umbrella sampling[1] and conformations of ligands bound to the surface of NC by replica-exchange method[2]. Finally, we will formulate the outlook for future developments in the field.

[1] A. Stelmakh, M. Aebli, A. Baumketner, and M. V. Kovalenko, Chemistry of Materials 33, 5962 (2021).
[2] V. Morad et al., Nature 626, 542 (2024).

EXPERIMENTAL AND COMPUTATIONAL CHARACTERIZATION OF CARBON DOTS

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Carbon dots (CDs), particularly nitrogen-doped CDs (N-CDs), are carbon-based nanoparticles (<10 nm) with outstanding photoluminescence properties, including high quantum yield and tunable emission across the visible spectrum. Their remarkable optical characteristics, combined with chemical stability, photobleaching resistance, and biocompatibility, make them highly attractive for applications in bioimaging, sensing, and environmental monitoring. However, the lack of precise control over their synthesis and an incomplete understanding of their structure-property relationship remain key challenges. In particular, the mechanisms governing nucleation, growth, and carbonization—as well as the link between their atomic structure and optical properties—are still not fully elucidated.

In this lecture, beside some basic concepts of photophysics and computational modelling useful to understand the background of CDs, I will present our recent efforts to unravel the formation and optical properties of archetypal N-CDs synthesized from citric acid with urea. By combining advanced experimental techniques (NMR, XPS, and mass spectrometry) with reactive molecular dynamics simulations, we have investigated the atomistic pathways of cyclization, condensation, and carbonization. Our simulations reveal key intermediates and plausible growth mechanisms, while spectroscopic analyses confirm the correlation between molecular fluorophores formed during synthesis and the observed optical properties. We also built a model to understand how the formed molecules interact with the CD, showing that the presence of N in the carbon network favours the π-π interactions of the molecules with the external layers of the CD. We believe that our findings represent a significant step toward the rational, bottom-up design of tailored fluorescent carbon nanomaterials.

SCIENTIFIC COMMUNICATION

Valentyna Kuznetsova

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In science, groundbreaking research can be lost if it's not communicated effectively. This talk explores how young scientists can master the art of scientific presentation and self-presentation - whether speaking to peers, the public, or potential collaborators. Using real-life examples from my research on laser-controlled photoreactions in proteins, we'll explore how to tailor your message for different audiences, use storytelling and analogies to explain complex ideas, and present yourself with clarity and confidence. From conference talks to poster sessions, from faculty meetings to outreach events—this session offers practical strategies to ensure your science is heard, understood, and remembered.

ENERGETICS OF STEPS IN PROTON PUMPING MECHANISM OF CYTOCHROME *C* OXIDASE

Dragan M. Popović,[1] Ivana Đorđević,[1] Dragana Mitić[2]

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Cytochrome *c* oxidase (CcO) links the reduction of O_2 to H_2O with proton pumping across the mitochondrial membrane, generating an electrochemical proton gradient that conserves energy in aerobic cells [1]. The coupling of protonation and redox reactions is essential in this process. Recent time-resolved optical and electrometric experiments have anticipated a sequence of reaction steps for the proton translocation mechanism in CcO. DFT/ electrostatic calculations are employed to obtain energetics of the proton and electron transfer reaction steps during the O→E transition. The energy profile of the reaction mechanism is studied by examining how the redox state of the metal centers, dielectric solvation effects, and membrane potential gradient influence the energy levels and potential leakage of the protein pump through the Glu242 gating site. Particular emphasis is made on side reactions that may short-circuit the pump, resulting in a loss of proton pumping, and how this may be avoided in natural biological systems [2-5].

[1] D.M. Popović, I.S. Đorđević, *J. Serb. Chem. Soc.* **85**, 1429 (2020).
[2] D.M. Popović, *Adv. in Biology* **2**, 1 (2022). New York: Nova Science.
[3] D.M. Popović, *Amino Acids* **45**, 1073 (2013).
[4] Popović, Quenneville, Stuchebrukhov, *J. Phys. Chem. B* **109**, 3616 (2005).
[5] J. Quenneville, D.M. Popović, A.A. Stuchebrukhov, *BBA-Bioenerg.* **1757**, 1035 (2006).

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FEATURES OF dπ-pπ-BONDING OF Cu(I) π-COMPLEXES WITH SOME UNSATURATED ACIDS

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π-complexes of transition metals occupy a special place in the chemistry of coordination compounds due to a certain specificity of the interaction of the central atom with the ligand. Here, not only covalent σ-bonds are formed due to the placement of the donor electron pair on the vacant orbitals of the acceptor, but also additional π-bonds are formed due to the fact that the π-orbital of the unsaturated (C=C)-fragment of the ligand can interact with some valence electrons of the central atom. Therefore, quantum-chemical modeling of the structural features of σ- and π-complexes of Cu^{2+}, Cu^{+} ions [1] and Cu^{0} atoms [2] with some unsaturated carboxylic acids was carried out. The modeling of the probable mechanisms of the course of chemical and electrochemical processes in solutions containing maleic, fumaric and acrylic acids, which are capable of forming strong π-complexes with Cu^{+} ions, was carried out. The features of the dπ-pπ-bonding between the C=C fragment of an unsaturated carboxylic acid and the Cu^{+} ion were studied using the QTAIM theory.

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INSIGHTS INTO SMALL MOLECULE STABILIZATION OF VIRAL G-QUADRUPLEXES VIA MOLECULAR DYNAMICS AND DOCKING SIMULATIONS

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G-quadruplexes (G4s) are noncanonical four-stranded nucleic acid secondary structures formed by guanine-rich sequences that stack into planar G-tetrads stabilized by Hoogsteen hydrogen bonding and monovalent cations [1]. Many regulatory genomic regions, including telomeres, promoters, and untranslated regions, contain sequences capable of forming G4s, often referred to as putative G-quadruplex sequences (PQs). G4s play essential roles in viral genome stability, transcription, and replication [2]. While their functions have been extensively studied in human genomes, their presence and regulatory significance in viral genomes, particularly in the RNA genome of Zika virus and the DNA genome of Monkeypox virus, remain largely unexplored. Understanding the structural stability and dynamics of viral G4s could reveal novel regulatory mechanisms and potential antiviral targets. Due to the absence of experimentally resolved three-dimensional structures of viral G4s, we investigated PQ motifs from Monkeypox (MPG4: GGTCTAGGATGAGGATCAGG) and Zika (ZRG4: GGUGGGGGACUGG) viruses using a comparative modeling approach. Structural templates were selected from the RCSB PDB based on sequence alignment and structural similarity to the human telomeric G-quadruplex (PDB: 1KF1) [3] and a GGA triplet motif (PDB: 1OZ8) [4]. Homology screening identified 1KF1 and 1OZ8 as the closest structural matches, which were modified using PyMOL mutagenesis and energy minimization to construct two-quartet G4 models for DNA (MPG4) and RNA (ZRG4). Molecular dynamic simulations were performed to evaluate the structural dynamics and ion stability of the modeled G4s. Amber OL15 [5] and OL3 [6] force fields were used in 1 μs simulations under both Langevin and Berendsen thermostats. Under Langevin dynamics at 300 K [7], both G4s

remained structurally stable, maintaining intact G-quartet (GQ) cores, with RMSD values of approximately 4 Å for MPG4 and 1.5 Å for ZRG4 (Figure 1A and 1B). Both systems exhibited stable RMSD oscillations averaging around 1.5 Å, indicating rigidity in the GQ framework (Figure 1A and 1B). The coordinated K^+ ion, essential for neutralizing the negative charge density and maintaining the Hoogsteen hydrogen bonding (HHB) network, remained stably positioned throughout the simulations. In MPG4, the K^+ ion exhibited slightly larger oscillations of about 0.7 Å, reflecting the intrinsic flexibility of the loop regions. In ZRG4, the K^+ ion remained consistently coordinated with only minor displacements of approximately 0.2 Å, suggesting strong interactions with O6 atoms. ZRG4 maintained RMSD values between 2.5 and 3 Å, further supporting stable ion coordination and HHB integrity. In contrast, simulations using the Berendsen thermostat [8] led to substantial RMSD increases and partial destabilization of both G4 models. The Berendsen thermostat's limitations in temperature and pressure coupling led to increased fluctuations and destabilization, whereas Langevin dynamics, with its additional friction and random noise, ensured better structural preservation. These findings support the structural stability of G4s in the genomes of Monkeypox and Zika viruses, reinforcing their potential regulatory roles in viral gene expression. Additionally, the observed differences between Langevin and Berendsen thermostat simulations highlight the importance of choosing appropriate simulation parameters when modeling G4 structures over extended timescales. This work lays a computational foundation for future studies exploring viral G4s as potential antiviral targets. Targeting G4s stability with small molecules could provide novel antiviral strategies, with their effect on G4 formation and stability validated through circular dichroism (CD) spectroscopy.

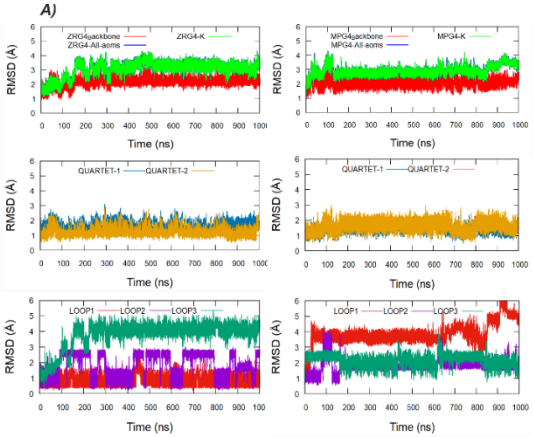

Figure 1: (A) Molecular dynamics simulations of ZRG4 and MPG4 G-quadruplex structures were performed under a Berendsen thermostat at 300 K for 1000 ns. RMSD plots illustrate structural fluctuations over time, highlighting deviations in the backbone, all atoms, K^+-coordinated core, individual G-quartets, and loop regions.

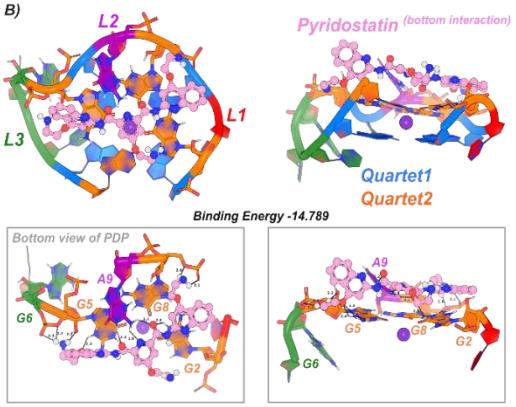

Figure 2 (B) Molecular docking of Pyridostatin with ZRG4 reveals the ligand bound at the base of the second G-quartet in a fully stacked conformation. The complex is stabilized through multiple hydrogen bonds with guanine bases, reinforcing the structural integrity of the G-quadruplex.

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Li-DNA SYSTEMS FOR NEW BATTERY TECHNOLOGIES

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STRUCTURAL EFFECTS ON THE ANTIOXIDANT POTENTIAL AND DRUG-LIKENESS OF SELECTED XANTHENE DERIVATIVES

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Fused aromatic or heteroaromatic moieties arranged in linear, angular or clustered geometries have emerged as valuable structural motifs in the design of new pharmaceuticals [1]. Oxygen-containing tricyclic compounds are commonly found in natural products with diverse pharmacological activities [2]. In this study, we synthesized a small library of eight xanthene derivatives. Their antioxidant activity was evaluated *in vitro* using the 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) method, while the pharmacokinetically relevant properties were predicted using established computational tools. The antioxidant potential was primarily attributed to the presence of phenolic functionalities, identified as key pharmacophores. The obtained results offer valuable insights for the rational design of promising xanthene-based antioxidant agents.

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MOLECULAR DYNAMICS SIMULATIONS OF 143D AND 1KF1 G-QUADRUPLEXES

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DNA in the cell nucleus is typically arranged in the well-known double helix structure, but it can also form secondary structures like G-quadruplexes (G4s), which are involved in gene regulation and DNA replication. This study focuses on telomeric G4s, located at chromosome ends, known to inhibit telomerase activity. Their stability can be enhanced by ligands that bind and preserve their structure. Previously, molecular dynamics (MD) simulations showed that the porphyrin-based ligand p11b stabilizes a parallel G4 structure (PDB: 1KF1) [1]. Here, the analysis is extended to a hybrid G4 topology (PDB: 143D) with the same sequence, to assess whether p11b also stabilizes this form. MD simulations were performed using the OL15 force field for DNA, GAFF for the ligand, and SPCE water model at 300 K (NPT) and higher temperatures (500–550 K, NVT) to evaluate thermal stability. RMSD analysis was used to monitor unfolding and determine the ligand's stabilizing effect. Preliminary results suggest that the ligand stabilizes the parallel topology but not the hybrid topology.

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TEMPERATURE- DEPENDENT STABILITY OF A VIRAL G-QUADRUPLEX: A COMPUTATIONAL APPROACH

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G-quadruplexes (G4s) are DNA structures involved in various cellular processes and hold significant promises for biomedical applications. They are stabilized by Hoogsteen hydrogen bonds between guanine tetrads, coordinated metal ions in the central cavity, and π-π stacking of aromatic moieties. G4 formation in gene promoters has been shown to regulate gene expression [1], highlighting their potential as targets for drug development. The G4 studied here belongs to the Papillomavirus family, specifically HPV-52, an oncogenic type associated with cervical cancer [1]. Its stability was evaluated using Molecular Dynamics simulations in a 150 mM NaCl aqueous solution, using sodium ions as counterions. Simulations were performed at 300 K for 1000 ns (NPT conditions) and at 500 K, 550 K, and 600 K for 200 ns (NVT conditions): elevated temperatures accelerate denaturation kinetics without altering the pathway [2], enabling shorter simulations with meaningful insights. Structural stability was assessed via the Root Mean Square Deviation of guanine tetrads and loops. The G4 remained stable at 300 K and 500 K and denatures at higher T. As a future goal, we plan to carry out new Molecular Dynamics simulations with and without a ligand, with the aim to identify a molecule capable of stabilizing the structure and inhibiting viral replication.

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OPTICAL BEHAVIOR AND STRUCTURAL INSIGHTS INTO NITROGEN-DOPED CARBON DOTS

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Carbon Dots (CDs) are a novel class of luminescent carbon-based nanomaterials that have attracted increasing attention due to their unique photoluminescent properties, low toxicity, chemical stability, and biocompatibility. Typically quasi-zero-dimensional, these nanoparticles exhibit a hybrid sp^2/sp^3 carbon core and a surface enriched with oxygen- or nitrogen-containing functional groups, offering great potential for applications ranging from bioimaging to optoelectronics.

In this study, we present a combined experimental and theoretical investigation of nitrogen-doped CDs synthesized from citric acid and urea in a 1:1 molar ratio.

The optical properties were characterized via UV-Vis absorption, steady-state photoluminescence, and time-resolved photoluminescence measurements.

To complement the experimental findings, molecular dynamics simulations were performed using GROMACS 2023.4 on the LUMI supercomputer. Two representative CD models were constructed: a pure CD functionalized with hydroxyl groups, and a nitrogen-doped CD featuring surface amine groups and graphitic nitrogen, simulating the 1:1 synthesis ratio. Structural characterization was carried out by analyzing the density distribution and the radius of gyration. The layer density distribution was measured to determine the distance between layers, and the radius of gyration was used to study the evolution of the system's compactness.

We further explored the interaction between these CD models and key fluorophores such as citrazinic acid, citrazinic acid amine and citrazinic acid amine amide. This multiscale approach offers insights into the structural and photophysical behavior of CDs, shedding light on the role of nitrogen doping and functional surface groups in tuning their emission properties.