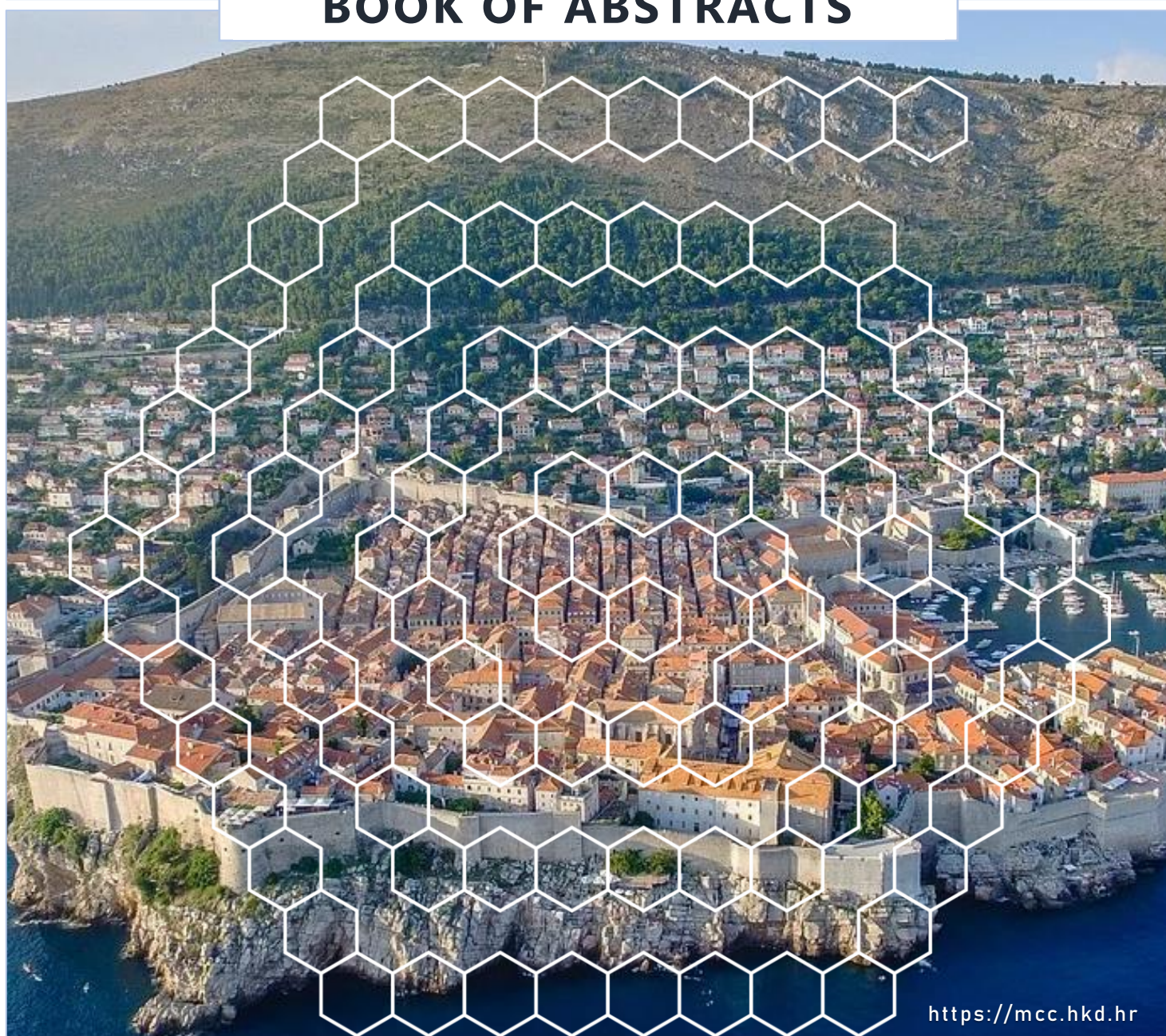


Math/Chem/Comp 2022 – 33rd MC² Conference

Inter University Centre Dubrovnik, 6 – 10 June 2022

BOOK OF ABSTRACTS

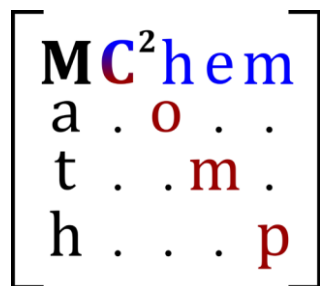


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Department of Chemistry, Faculty of Science, University of Zagreb, Croatia

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Math/Chem/Comp 2022 – 33rd MC² Conference
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IMPRESSUM

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**The 33rd International Course and Conference on the Interfaces among
Mathematics, Chemistry and Computer Sciences:
Mathematics, Chemistry, Computing (Math/Chem/Comp, MC²-33)**

Since 1986, the Math/Chem/Comp meetings have been bringing together researchers working on diverse subjects spanning mathematics, computer science, and chemistry. In continuation of this tradition, presentations concerning all aspects of current research on computer modeling, combinatorics, graph theory, and topology applied to any area of chemistry, physics, material and life sciences will be welcomed. The conference program will include invited plenary and special lectures workshops and posters. In particular, the MC²-33 meeting will revolve around the following topics:

1. Mathematical methods and computational algorithms in modeling of atoms, molecules, and chemical processes
2. Mathematical chemistry and chemical graph theory
3. Molecular modeling in practice (including molecular dynamics and aggregation)
4. Chemical experiments, industrial processes, and mathematical interpretation

The conference program will include invited lectures, contributed oral presentations, and posters. Moreover, we will offer a **Workshop: Aromaticity: Basis, Types, Rules, and Quantification**, which will be held by **Miquel Solà**, Institut de Química Computacional i Catàlisi i Departament de Química Universitat de Girona.

Proceedings

The papers presented at the MC²-33 meeting can be submitted to [Croatia Chemica Acta](#) to be published as proceedings.

All contributions will be refereed. The participants are encouraged to submit their manuscripts before the meeting or at the latest upon arrival in Dubrovnik. Those unable to attend are invited to send their manuscripts to the director of the conference.

Hrvoj Vančik and Jerzy Cioslowski

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12:00 – 13:00	Xabier Telleria-Allika: <i>Building Machine Learning Assisted Phase Diagrams: Three Chemically Relevant Examples</i>	
13:00 – 15:00	LUNCH BREAK	
CHAIR: Urban Bren		
15:00 – 16:00	Miquel Solà: <i>Photoinduced Charge Separation in Dyads Involving Complexes of C₆₀ and Nano hoops with Different Levels of π-extension and Aromaticity</i>	
16:00 – 17:00	Igor Rončević: <i>How Can We Tune the Properties of Organic Polymers?</i>	





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9:00 – 10:00	Jerzy Ciośłowski: <i>A New Formalism for Revealing Unknown Properties of Natural Orbitals</i>	
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10:00 – 11:00	Mihai V. Putz: <i>On the Valence Nature of The Chemical Bond: The Pauling Bondonic Qbits</i>	
11:00 – 11:15	COFFEE BREAK	
11:15 – 12:15	Sílvia Escayola: <i>The Intriguing Aromaticity of (Sub)phthalocyanines</i>	
12:15 – 13:15	Urban Bren: <i>Computational Chemistry as a Tool against the SARS-CoV-2 Virus</i>	
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POSTER SESSION

P01	Jadranko Batista, <u>Antonija Kraljević</u> , Bono Lučić Novel Structural Attributes Based on the Average Distances of Hydrophobic Amino Acids Improve Models for Predicting Protein Folding Rates
P02	<u>Iulia Păulescu</u> , Diana Dăescu, Diana-Maria Dreavă, Ioan Bîtcă, Mihai Medeleanu Theoretical and Experimental Studies on the Antioxidant Properties of New Flavylium Dyes
P03	<u>Ivan Pavlak</u> , Igor Rončević, Josef Michl Electronic Structure and Optical Properties of Metalloporphenes
P04	<u>Barbara Pem</u> , Danijela Bakarić Molecular Dynamics Study of Phosphatidylcholine Bilayers with the Addition of Phosphatidylglycerol
P05	<u>Gabrijel Zubčić</u> , Tomislav Portada, Davor Šakić Effects of an Rearrangement Reaction on the Product Distribution of the Hofmann-Löffler-Freytag Reaction

LECTURES

COMPLEXITY, SYSTEMS AND GRAPHS

Hrvoj Vančik

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Although the new sciences, the science about complexity, and the science about systems, have appeared in the same historical period during the first half of the last century, their interrelations has not been satisfactory studied and analyzed. By superficial view, both the sciences are based on the same principles of the holistic behavior of aggregates consisting of components. Theory of complexity is in the largest part of the literature known as the theory of chaos. Since this aspect of the theory of complexity is mostly discussed within the frame of the dynamical behavior of systems, its resemblance to the general system theory invented by K. L. von Bertalanffy is obvious.

The systems consist of the actual entities, actualities (the term borrowed from A. N. Whitehead), which have their position in the three-component "complexity space" (synchronic, diachronic, and combinatorial). Variously interconnected actualities form the system. As such, the system can be represented through graph theory as the topological object. The development of the graph descriptive determinant led to the polynomial which has the solutions known as the spectrum of the graph. It is argued how such a graph theoretical interpretation of systems could provide a new view on the teleological problem of the structure-function relationship.

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GRAPH THEORY OF GRAPHENE FLAKES: CLAR COVERS, AROMATICITY PATTERNS AND SPIN POPULATIONS

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This presentation has a character of a review of recent results in the field of constructing Clar covers of graphene flakes and using them for determination of various molecular properties of these molecules. Starting with a definition of a Clar cover (i.e., an extended Kekulé structure), we show how to construct the totality of Clar covers for an analyzed graphene flake and how to obtain their total number without their explicit construction. The resulting theory has a beautiful mathematical structure with connections to various fields of mathematics: graph theory, continued fraction theory, order theory, and combinatorics with particular focus on the enumeration of linear extensions of a certain family of partially ordered sets. Chemical applications of the presented theory will focus on the distribution of aromaticity patterns in graphene flakes and on the determination of spin populations in singly, doubly, and triply radical graphene flakes. The literature covering this field is very rich; the list below is supposed to give only a concise representation of the work performed in our laboratory.

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BUILDING MACHINE LEARNING ASSISTED PHASE DIAGRAMS: THREE CHEMICALLY RELEVANT EXAMPLES

Xabier Telleria-Allika, Jose M. Mercero, Xabier Lopez, and Jon M. Matxain

Kimika Teorikoa, Polimero eta Material Aurreratuak: Fisika, Kimika eta Teknologia Saila, Kimika Fakultatea, Euskal Herriko Unibertsitatea UPV/EHU, and Donostia International Physics Center (DIPC). P.K. 1072, 20080 Donostia, Euskadi, Spain

In this work we present a systematic procedure to build phase diagrams for chemically relevant properties by the use of a semi-supervised machine learning technique called uncertainty sampling. Concretely, in this work we focus on ground state spin multiplicity and chemical bonding properties. As a first step, we have obtained single-eutectic-point-containing solid-liquid systems which have been suitable for contrasting the validity of this approach. Once this was settled, on the one hand, we have built magnetic phase diagrams for several Hooke atoms containing few electrons (4 and 6) trapped in spheroidal harmonic potentials. Changing the parameters of the confinement potential such as curvature and anisotropy and interelectronic interaction strength, we have been able to obtain and rationalise magnetic phase transitions flipping the ground state spin multiplicity from singlet (non magnetic) to triplet (magnetic) states. On the other hand, Bader's analysis is performed upon helium dimers confined by spherical harmonic potentials. Covalency is studied using descriptors as sign for $\Delta\rho(r_C)$ and $H(r_C)$ and the dependency on the degrees of freedom of the system is studied i.e. potential curvature ω^2 and inter atomic distance R . As a result, we have observed that there may exist a covalent bond between He atoms for short enough distances and strong enough confinement. This machine learning procedure could, in principle, be applied to the study of other chemically relevant properties involving phase diagrams, saving a lot of computational resources.

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PHOTOINDUCED CHARGE SEPARATION IN DYADS INVOLVING COMPLEXES OF C₆₀ AND NANOHOOPS WITH DIFFERENT LEVELS OF π -EXTENSION AND AROMATICITY

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Conversion of the sunlight into chemical energy is considered to be one of the most important and fundamental chemical reactions in nature. A broad variety of artificial photosynthetic systems based on dyads, triads and up to pentads involving electron donor and acceptor moieties have been designed and synthesized to investigate artificial photoinduced energy and electron transfer processes. One type of dyads with potential applications in solar cells is the one combining C₆₀ complexed with nanohoops.^[1] In this work, we discuss a series of computational studies that involves the photoinduced charge separation in complexes of C₆₀ and Li⁺@C₆₀ with different nanohoops, such as the [10]cycloparaphenylene ([10]CPP) ring,^[2] π -extended CPPs bearing the hexa-*peri*-hexabenzocoronene (HBC) or the tribenzo[*fj,ij,rst*]pentaphene (TBP),^[3] and [n]cyclo-dibenzopentalenes ([n]CDBPs) as antiaromatic curved nanorings.^[4] The analysis of complexes of C₆₀ with nanohoops having different degrees of π -conjugation and aromaticity allow us to discuss the effect in the charge transfer separation and recombination on the level of π -extension and aromaticity present in the nanohoops.

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HOW CAN WE TUNE THE PROPERTIES OF ORGANIC POLYMERS?

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Organic semiconductor polymers are very attractive due to their potential use as molecular wires in molecular electronics.^[1] One of their main advantages is the possibility of tuning their properties, enabling the design of materials tailored to a specific purpose.^[2]

Using a combination theory and experiments, we will show that backbone torsion and solid-state packing play a major role in determining the electronic, optical, and transport properties of aromatic 1D polymers connected with an azodioxide bond (Figure 1).^[3] For these compounds, both hybrid DFT and GW-BSE calculations predict a linear relationship between the backbone torsional angle and the band gap. This angle can be increased by introducing substituents, or decreased by adsorbing the polymer on a surface. For example, we find a dramatic decrease of the dinitrosobenzene polymer band gap after adsorption to gold (2.39 eV \rightarrow 0.68 eV), which is well-reproduced by calculations and can mostly be attributed to planarization. Understanding the effects of torsion allows us to identify and quantify torsion-independent effects of solid-state packing using GW-BSE calculations, which are essential for accurate description of exciton binding.

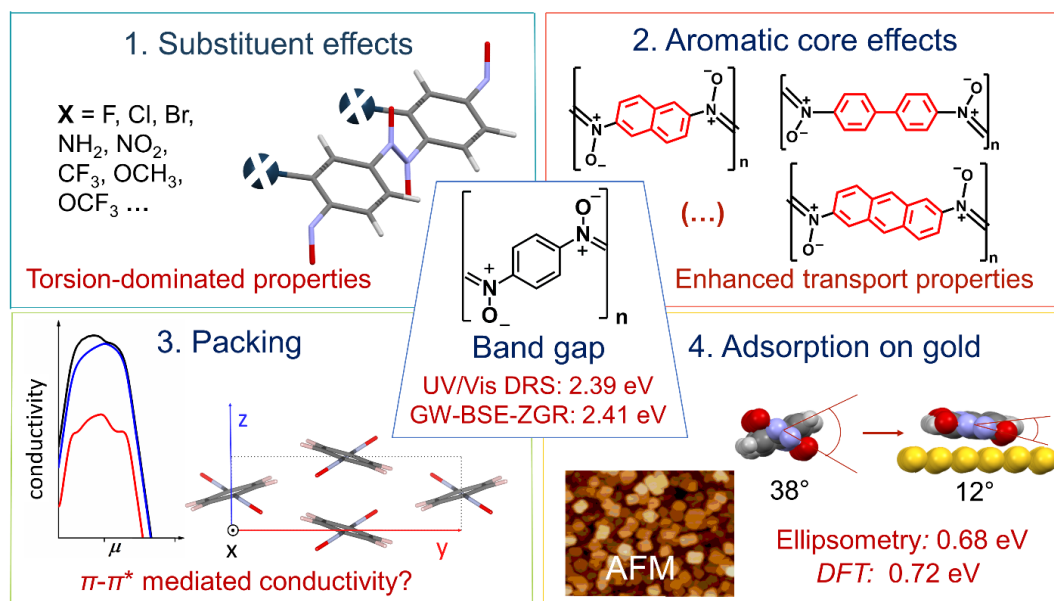


Figure 1. The effects of substituents, aromatic core, packing, and adsorption on the properties of polymers based on dinitrosobenzene.

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A NEW FORMALISM FOR REVEALING UNKNOWN PROPERTIES OF NATURAL ORBITALS

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Previously unknown properties of the natural orbitals (NOs) pertaining to singlet states (with natural parity, if present) of electronic systems with even numbers of electrons are revealed upon the demonstration that, at the limit of $n \rightarrow \infty$, the NO $\psi_n(\mathbf{r})$ with the n largest occupation number v_n approaches the solution $\phi_n(\mathbf{r})$ of the zero-energy Schrödinger equation

$T \{[\rho_2(\mathbf{r},\mathbf{r})]^{-1/8} \phi_n(\mathbf{r})\} - (\pi^2/\mu_n)^{1/4} [\rho_2(\mathbf{r},\mathbf{r})]^{1/4} \{[\rho_2(\mathbf{r},\mathbf{r})]^{-1/8} \phi_n(\mathbf{r})\} = 0$ (where T is the kinetic energy operator), whereas v_n approaches μ_n . The resulting formalism, in which the "on-top" two-electron density $\rho_2(\mathbf{r},\mathbf{r})$ solely controls the asymptotic behavior of both $\psi_n(\mathbf{r})$ and v_n at the limit of the latter becoming infinitesimally small, produces surprisingly accurate values of both quantities even for small n . It opens entirely new vistas in the elucidation of their properties, including single-line derivations of the power laws governing the asymptotic decays of v_n and $\langle \psi_n(\mathbf{r})|T|\psi_n(\mathbf{r}) \rangle$ with n , some of which have been obtained previously with tedious algebra and arcane mathematical arguments. These laws imply a very unfavorable asymptotics of the truncation error in the total energy computed with finite numbers of natural orbitals that severely affects the accuracy of certain quantum-chemical approaches such as the density matrix functional theory. The new formalism is also shown to provide a complete and accurate elucidation of both the observed order (according to decreasing magnitudes of the respective occupation numbers) and the shapes of the natural orbitals pertaining to the $^1\Sigma_g^+$ ground state of the H_2 molecule. In light of these examples of its versatility, the above Schrödinger equation is expected to have its predictive and interpretive powers harnessed in many facets of the electronic structure theory.

WIGNER LOCALIZATION IN ONE, TWO AND THREE DIMENSIONS: AN *AB INITIO* APPROACH

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Almost a century ago Eugene Wigner predicted that a system consisting of interacting electrons would, at sufficiently low density, form a crystalline structure with the electrons localized at lattice sites.^[1] In general, at low density, when localization is due to the electronic repulsion we speak of Wigner localization. We investigate Wigner localization at very low densities by means of accurate quantum chemistry methods, such as exact diagonalisation, full configuration interaction and CASSCF. In particular, we study systems containing few electrons, known as Wigner molecules. To accurately model Wigner molecules we have developed an approach that consists of three main principles: (i) the creation of a supercell that has the topology of a Clifford torus, which is a flat, finite, and borderless manifold; (ii) the renormalization of the distance between two points on the Clifford torus by defining it as the Euclidean distance in the embedding space of the Clifford torus; (iii) we use a grid of equidistant spherical gaussians as a basis for the Hamiltonian.^[2] We have validated our approach by comparing our results to a semi-classical model that becomes exact in the low-density limit. With our approach we are able to observe the Wigner localization without ambiguity.^[3]

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SOLITONIC NATURAL ORBITALS IN COULOMBIC SYSTEMS

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High-accuracy electronic structure calculations on the members of the helium isoelectronic series and the H₂ molecule with a stretched bond reveal that the ground-state wavefunctions of these Coulombic systems give rise to natural orbitals (NO) with unusual properties. These solitonic NOs (SoNOs) possess fewer nodes than expected from their small occupation numbers, exhibit substantial spatial localization, and respond (with approximate retention of their shapes) in a paradoxical manner (e.g. by moving away from nuclei upon increase in the nuclear charge or decrease in the internuclear distance) to changes in the underlying Hamiltonian. An efficient tool for the identification of the SoNOs is provided by an index constructed from two expectation values pertaining to a given NO and the corresponding occupation number. In the case of the helium-like species, the rapid decay of the occupation numbers of the SoNOs with increasing nuclear charge Z is governed by an asymptotic expression that involves the radial positions and spreads of the orbitals. Three s-type SoNOs (with the occupation numbers amounting to only ca. $7.9 \cdot 10^{-67}$, $6.8 \cdot 10^{-92}$, and $9.0 \cdot 10^{-113}$ in the case of the helium atom) are predicted to turn into unoccupied NOs (UNOs) at Z equal to ca. 2.673, 2.587, and 2.536, respectively. The persistence of the analogous p-type orbital beyond $Z=2$ is consistent with the computed properties of the σ_u -type SoNO of the H₂ molecule with a stretched bond. In particular, the profiles of this SoNO along two perpendicular lines bear great resemblance to the radial profiles of its p-type counterpart.

NATURAL-ORBITAL BASED MULTIREFERENCE DIAGNOSTIC FOR WAVEFUNCTION METHODS

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The treatment of electron correlation is always a challenge in theoretical chemistry computations and simulations. The popular Single Reference (SR) correlated wavefunction methods (MP2, CCSD, etc.) and Kohn-Sham DFT are good at capturing dynamic correlation, but poorly describe nondynamic correlation. When running a calculation, a diagnostic tool can help users decide whether to choose SR methods or Multi-Reference (MR) methods (CASSCF, DMRG, etc.), the latter being usually more complicated and expensive.

Although a series of MR diagnostics are available in the literature, a recent work by Kulik and coworkers^[1] have reported the disagreement between different diagnostic criteria. In recent years, our group proposed the dynamic and nondynamic indices I_D and I_{ND} in terms of natural spin-orbital occupancies.^[2,3] However, our I_{ND} is not size-intensive as it scales with system size.^[4] Hence, in this work, we firstly propose several approaches to ensure our indices to be size-intensive, we then analyze the performance of various diagnostics in an extensive dataset using CCSD and MP2 wavefunctions. We determine the critical value agreement between each pair of diagnostics, and classify them according to their ability to identify non-dynamic correlation. We find that our new MR natural orbital-based index, $I_{ND}^{\max} = \max \{ n_i^\sigma (1 - n_i^\sigma) \}$, provides the same information about the MR character compared with D_2 diagnostic,^[5] and the I_{ND}^{\max} is more general and available in many quantum chemistry methods.

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POSSIBILITY OF DISCRIMINATION BETWEEN APPROVED AND WITHDRAWN DRUGS USING MULTIVARIATE CLASSIFICATION STRUCTURE-PROPERTY MODELS BASED ON MOLECULAR DESCRIPTORS

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There is enormous public interest in the EU, but also the interest of the pharmaceutical industry in the possibility of finding significant factors that would make it possible to distinguish between approved drugs and drugs that have been withdrawn after several years of use. The EU responded to this interest by funding a large AI4EU project, which launched calls for proposals to develop various artificial intelligence (AI)-based computing solutions.^[1] Among them was the task to develop a predictive AI solution based on the deep neural network method to distinguish drugs from withdrawn drugs based on their structure.^[2] In this presentation, the process of defining the problem and creating a dataset will be elaborated, as well as related issues such as the different status of the same drug in different countries or regions, or the problem of cleaning datasets, as many drugs are not pure compounds but complexes. We have calculated comprehensive sets of molecular structure descriptors for the final sets of approved and withdrawn drugs. The analysis of the importance/usefulness of each structure-based molecular descriptor (including those related to ADMETox properties of drugs) in discriminating between approved and withdrawn drugs will be presented. As expected, the classification accuracy of the multivariate models based on descriptors is not high. Nevertheless, it is comparable to (or sometimes better than) more complex models and significantly higher than the accuracy achieved by random guessing (random model).

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- [2] The AI-on-demand platform, <https://www.ai4europe.eu/> and <https://www.ai4media.eu/project-overview/> (assessed on April 15, 2022)

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DERIVATION OF FORMULAE FOR CALCULATION OF MINIMAL AND MAXIMAL VALUES OF MODEL EVALUATION METRICS AND THEIR USE IN EVALUATION OF VARIABLE MONOTONICITY

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In the development of structure-property relationship models and multivariate models in general, there is a tendency to include as few structural variables (molecular descriptors) as possible in the final optimised models. Due to the ubiquitous digitisation of data and molecular fingerprints, molecular descriptors are increasingly binary variables with values of 1 or 0. Even the experimental properties of chemical compounds are expressed in binary values - e.g. toxic (1) or non-toxic (0). We have performed the calculation and simulation of the correspondence between the two binary variables in paired and unpaired sorting cases. These two experiments provide us with the maximum (in the paired sorting case) and minimum possible correspondence (unpaired sorting) of these variables. Theoretically, we have derived formulae for calculating the maximum and minimum agreement between two variables where x-values (first variable) and y-values (second variable) belong to class 1. The difference between the minimum and maximum values reflects the information content or monotonicity between the two variables. If we consider the case $x = y$, we obtain expressions that measure the monotonicity of a variable with x values in class 1 and $(N - x)$ values in class 0. If the number of elements in class 1 and class 0 is expressed by the values of the error matrix corresponding to a binary classification (TP - true positive, TN - true negative, FN - false negative, FP - false positive; $x = TP + FN$, $N - x = TN + FP$), we obtain general expressions for calculating the maximum and minimum values of any variable measuring the agreement, correlation or error between two classification variables. In addition to being used to evaluate the monotonicity of variables, the results obtained are also used to evaluate the quality of binary classification models.

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ON GINI INDEX OF TREES

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Gini index is used in the economy to measure the income inequality of social groups.^[1] The graph theoretical applications of Gini index for rooted trees was introduced in 2017.^[2] For this purpose, two distance based topological index (Gini index and level index) were introduced. In this note, we compute the Gini index and level index of some trees.

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COMPUTATIONAL STUDY OF THE HUMAN DPP III CATALYZED PEPTIDE HYDROLYSIS – DIFFERENCE BETWEEN “GOOD” AND “SLOW” SUBSTRATES

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Dipeptidyl peptides III (DPP III) is a two-domain zinc containing enzyme that cleaves dipeptide from the unsubstituted N-terminus of its substrates. Substrates are peptides of different sequences and sizes, with tetrapeptides to octapeptides being the best one^[1] There have been several attempts to explain DPP III broad substrate promiscuity and to rationalize why some of the peptides are effectively cleaved by DPP III (“good” substrates) while the others are not (“slow” substrates) showing high inhibition potency. Combining quantum molecular mechanics calculations, molecular dynamic simulations and the free energy calculations (MM/P(G)BSA) we have offered possible explanations.

The enzymatic cycle of human DPP III i.e. the substrate binding to the active site of the enzyme, the peptide bond hydrolysis and release of the products were described for enzyme in complex with tynorphin, “slow” substrate, and Leu-enkephalin. The study showed that the reason for much slower processing of tynorphin than Leu-enkephalin is not the difference in the reaction mechanism, but the significantly higher stabilization of the products of tynorphin hydrolysis, which impede the regeneration of the enzyme. That is, the energies required for nucleophilic attack of the catalytic water molecule and inversion at the nitrogen atom of the cleavable peptide bond, which corresponds to the rate-determining step of peptide hydrolysis by DPP III, are similar for both ligands.

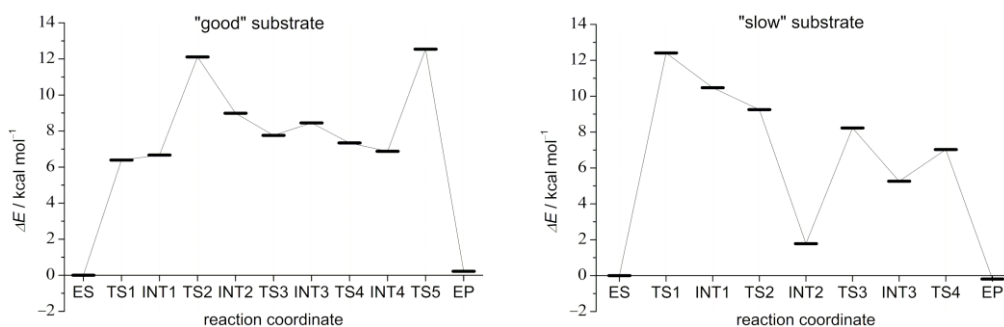


Figure 1. Energy profile for the hydrolysis of Leu-enkephalin (left) and tynorphin (right) in the active site of human DPP III. Calculations were performed at B97D/[6-31G(d)+LanL2DZ-ECP] +ZPVE_{B97D/[6-31G(d)+LanL2DZ-ECP]} level of theory.

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ON THE VALENCE NATURE OF THE CHEMICAL BOND: THE PAULING BONDONIC QBITS

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The still valence bond theory (VBT) enigma and cumbersome concepts of modern quantum chemistry in general and of bonding in special, the directional hybridization (as originating from the <paradoxal> linear combinations of directionless free-atom s,p,d,... orbitals) and the resonance hybrids (of two or more Lewis lone pairs and bonds' localized structures)^[1] are revisited from the quantum information perspective. That is, the quantum information (qbits) of the first and second degree are employed under Walsh-Hadamard (1Qbit for one-center/lone pair) and Bell (2Qbits for two centers/bonds) transformations to provides, respectively, the refreshing unified perspective on the nature of the chemical bonding, hybridization and resonance, while resembling the bosonic nature through the recent advanced bondonic theory^[2] and of its Bloch spherical realization of quantum information of the paradigmatic Heitler-London bonding potential.^[3] The present work advocates on reconsidering Pauling's VBT as a quantum information framework for further exotic valence based phenomena; such are those of collapsing all-pi hybridized wave functions of carbon-on-graphene to produce high electrical and inference signals.^[4] The earlier "(non)realistic/utilitarian" criticism to Pauling proto-quantum vision of chemical bonding, especially on "self-creation" of hybrid orbitals on the pre-bonding atoms-in-molecule, or on the arbitrariness/reference in localization of resonance states (*vis a vis* of natural bonding orbitals as molecular structural quantum solution from natural atomic and hybrid orbitals) may be conceptually integrated in the entangled nature of the bosonized electrons in the bondonic quasi-particles, being the latter responsible for chemical bonding stability in special and chemical reactivity in general.

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THE INTRIGUING AROMATICITY OF (SUB)PHTHALOCYANINES

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The theoretical description of the aromaticity of (sub)porphyrins and (sub)phthalocyanines is challenging because of their size, topological flexibility and the existence of multiple π -electron circuits that can contribute to their aromatic character ^[1]. Most of the aromaticity studies found in the literature are limited to the use of nucleus independent chemical shift (NICS) ^[2,3]. However, taking into account the complexity of these molecules and the limitations of NICS it is necessary to go beyond NICS measurements and make use of more specialized methods. In this work, we will study the aromatic character of S_0 and T_1 states of eight systems employing a wide range of global ^[4,5] and local aromaticity descriptors. We also analyze similarities and differences between phthalocyanines and porphyrins. The study was performed at the CAM-B3LYP/cc-pVTZ level of theory, including a wide range of aromaticity indicators based on geometric (harmonic oscillator model of aromaticity, HOMA), magnetic (GIMIC) and electronic (fluctuation index (FLU), electron density of delocalized bonds (EDDB) ^[4], AV_{\min} and AV_{1245} ^[5]) criteria. Our detailed analysis, provides new in-sights on the aromatic character of these molecules, which will be employed in the rational design of (sub)porphyrins and (sub)phthalocyanines derivatives with specific electronic structures.

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COMPUTATIONAL CHEMISTRY AS A TOOL AGAINST THE SARS-COV-2 VIRUS

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SARS-CoV-2, or severe acute respiratory syndrome coronavirus 2, represents a new pathogen from the family of *Coronaviridae* that caused a global pandemic of the COVID-19 disease. In the absence of effective vaccination strategies, research of novel therapeutic targets such as SARS-CoV-2 main protease (3CL^{pro}) or RNA-dependent RNA polymerase (RdRp) becomes essential. Therefore, we prepared a database of commercial small-molecule compounds and performed an *in silico* high-throughput virtual screening on the active site of both viral enzymes using ensemble docking. We identified novel classes of potential inhibitors and calculated favorable binding free energies of representative hits by molecular dynamics simulations coupled with Linear Interaction Energy calculations. This innovative procedure maximized the respective phase-space sampling and yielded non-covalent inhibitors representing small optimizable molecules that are synthetically readily accessible, commercially available as well as suitable for further biological evaluation and mode of action studies.^[1–3] Moreover, drug repurposing studies were performed applying our novel inverse molecular docking fingerprinting^[4] and the viral entry through the spike protein to neuropilin 1 binding pathway was inhibited.^[5]

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POSTERS

NOVEL STRUCTURAL ATTRIBUTES BASED ON THE AVERAGE DISTANCES OF HYDROPHOBIC AMINO ACIDS IMPROVE MODELS FOR PREDICTING PROTEIN FOLDING RATES

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Protein folding is a very important problem in life sciences that has been studied experimentally, but also through modelling (theoretical and simulation analyses).^[1] It is assumed that all the information that determines the protein folding process and the protein folding rate is contained in the primary structure of the proteins (i.e. in the sequence of the amino acids). Modelling the protein folding constants k_f (s⁻¹), which are equal to $1 /$ (time required for protein folding), is a size-dependent problem, which means that $\ln(k_f)$ depends on the length of the protein sequence. Here we have defined and calculated new descriptors (features) that take into account mutual arrangements of hydrophobic amino acids in the primary structure. We calculated the average distance between single hydrophobic amino acids and between multiple hydrophobic amino acids, as well as their average distance from the centre and from the N- and C- termini of the protein sequence. These attributes were found to have better agreement (correlation) with protein folding rates in three protein sets than protein length, relative contact order distance or other parameters calculated from the protein's primary sequence or its three-dimensional structure.

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THEORETICAL AND EXPERIMENTAL STUDIES ON THE ANTIOXIDANT PROPERTIES OF NEW FLAVYLIUM DYES

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Anthocyanins are the most researched class of natural flavylum dyes. They are water soluble compounds responsible for a multitude of colors found in plants, ranging from yellow-orange to violet-blue. Anthocyanins have been associated with numerous health benefits due to their multiple biological properties (anti-inflammatory, antimicrobial, antiproliferative and antioxidant properties). Their potential applications include their use as colorants for food and cosmetics, as pH freshness indicators in intelligent food packaging, and as photosensitizers for dye-sensitized solar cell (DSSC).^[1]

In this work the antioxidant properties of two series of bio-inspired anthocyanidins (from malvidin and poenidin) were investigated by both theoretical and experimental methods. DFT methods were used to compute some thermodynamic descriptors such as phenolic O-H bond dissociation energy (BDE), ionization potential (IP), proton dissociation enthalpy (PDE), proton affinity and electron transfer enthalpy (ETE) related to radical scavenging activity of phenolic antioxidants based on three main mechanisms: hydrogen atom transfer (HAT), single electron transfer-proton transfer (SETPT) and sequential proton loss-electron transfer (SPLET).^[2]

The antioxidant activity of the synthetic flavylum dyes was experimentally assessed by the DPPH radical scavenging assay which involves two possible antioxidative mechanisms: hydrogen atom transfer (HAT) or single electron mechanism (SET). While HAT measures the ability of a potential antioxidant to deactivate radicals by hydrogen donation, SET measures the ability to transfer one electron to reduce the radicals.^[3]

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ELECTRONIC STRUCTURE AND OPTICAL PROPERTIES OF METALLOPORPHENES

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Periodic two-dimensional polymers have been extensively researched in recent years due to their possible applications as optoelectronic materials,¹ molecular magnets,² energy storage media,³ etc. Recently, we have succeeded in the synthesis of a graphene analogue made of fully fused porphyrin rings, called porphene.⁴ Metalloporphenes containing an innocent metal ion exist in the form of two rectangular symmetry-equivalent D_{2h} valence tautomers with pronounced bond length alternation (BLA) and an indirect band gap, differing by the orientation of the rectangles along the x or y axes. They are connected via a saddle point of square D_{4h} symmetry and less BLA, at which the sheet is gapless (Figure 1). Some methods of calculation yield a shallow third minimum at the square geometry instead of a transition state. Metalloporphenes containing a metal ion with an incomplete shell of $3d$ electrons may have minima at rectangular and/or square geometries.

Here, we present predicted electronic structure and optical properties of metalloporphenes carrying a divalent first-row transition metal inside the porphyrin ring, obtained using the hybrid PBE38 functional. Both the D_{2h} and D_{4h} geometries are investigated, and all possible spin states are considered, resulting in a rich map of these tunable 2D materials.

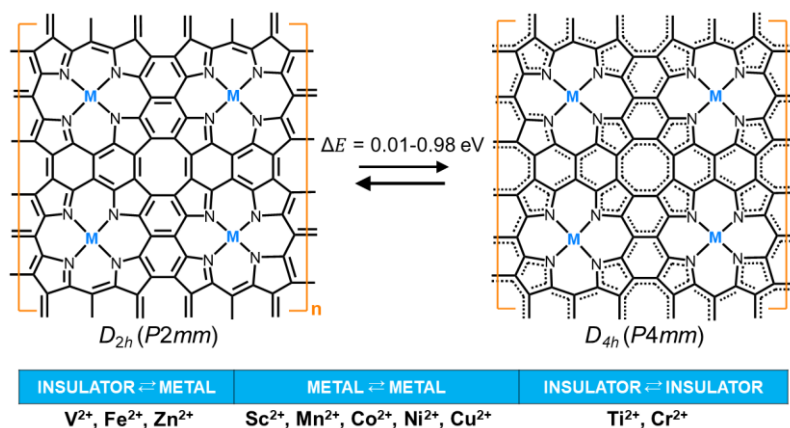


Figure 1. Interconversion between the rectangular D_{2h} and square D_{4h} geometries, and their predicted properties.

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MOLECULAR DYNAMICS STUDY OF PHOSPHATIDYLCHOLINE BILAYERS WITH THE ADDITION OF PHOSPHATIDYLGLYCEROL

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Unilamellar lipid vesicles are commonly used as models to study lipid-lipid and lipid-environment interactions of biological membranes.^[1] However, the preparation of unilamellar vesicles consisting of zwitterionic lipids such as 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC) often requires the addition of a charged lipid, *e.g.* 1,2-dipalmitoyl-*sn*-glycero-3-phosphoglycerol (DPPG), to maintain stability.^[2] The addition of anionic DPPG into the neutral DPPC membrane may influence both membrane properties and membrane hydration. The effect of 5 % DPPG on DPPC membrane properties and the arrangement of water was studied computationally by employing classical molecular dynamics. Lipid bilayers consisting of DPPC with and without 5 % DPPG were simulated in GROMACS, using the CHARMM36m force field, for a total of 100 ns. The bilayers of 128 molecules were simulated in the presence of 6400 water molecules and 100 mM NaCl, at 30 and 50 °C (below and above phase transition temperature). Membrane properties such as area per lipid, membrane thickness, deuterium order parameters and lateral diffusion of lipids were calculated, and membrane hydration was studied by analyzing hydrogen bonding networks, solvent orientation and radial distribution functions. Obtained results will be used to compare with experimental findings in order to gain insight into the behavior of mixed lipid bilayers and their suitability as model membranes.

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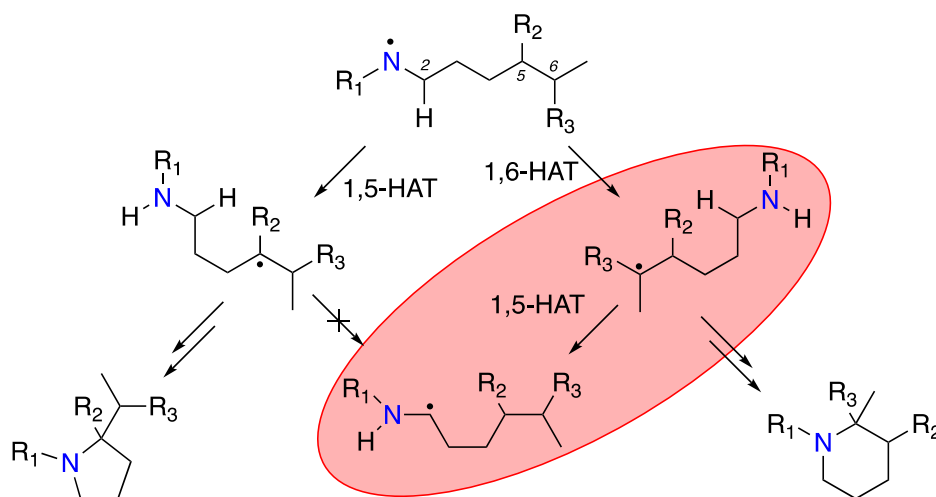
EFFECTS OF AN REARRANGEMENT REACTION ON THE PRODUCT DISTRIBUTION OF THE HOFMANN-LÖFFLER-FREYTAG REACTION

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Hofmann-Löffler-Freytag (HLF) is a well-established reaction used for late-stage functionalization for producing pyrrolidine rings, and more rarely piperidine rings, via C-H activation. However, according to Šakić and Zipse,^[1] the driving force for the formation of piperidine and pyrrolidine rings is roughly the same. Having this in mind, there are several published works where selective piperidine formation has been realized.^[2–4] It was hypothesized by Muñiz et al.^[2] that an intermolecular process leads to the formation of the piperidine ring. Nonetheless, intramolecular hydrogen atom transfer (HAT) processes are much faster in comparison with intermolecular HAT processes. Short et al.^[4] proposed an explanation for predominant piperidine formation when sulfoxide is in α -position.^[3,4] Namely, the elongated N-S and S-O bond and the compressed O-S-N angle geometrically favor seven-membered transition state, as in 1,6-HAT for the C-H abstraction. Herein we propose alternative explanation. After formation of a C₆ radical via 1,6-HAT, it subsequently rearranges via 1,5-HAT to a more stable C₂ radical. This depletes the pool of intermediates needed for piperidine synthesis. If C₆ radical is more stable than C₂, due to phenyl ring stabilization of C₆ radical,^[2] then the piperidine ring is formed. In this light, substitution of C₂ position is outlined as vital for a feasible synthesis of products containing piperidine. Therefore, relative stabilities of the C₂, C₅ and C₆ radicals have a crucial effect on the regioselectivity of the HLF reaction.



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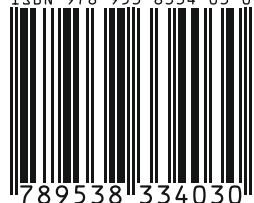
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