

REMINISCENCES ON ANTE GRAOVAC - *SPIRITUS MOVENS OF MCC*

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In November 2012 our dear friend and outstanding scientist Ante Graovac passed away. This was the great shock for Croatian and international scientific community, since Ante (or Tonko as his family and close friends called him) was always full of energy and ideas and he was a *spiritus movens* of many activities in science and education in Croatia and abroad.

Ante Graovac had published 150 scientific articles and was author and editor of 30 books and special issues of journals in the field of mathematical chemistry. I met Ante for the first time in 1974, at the second year of my Chemistry studies at Faculty of Science in Zagreb. He was lecturing in course "Mathematical methods in Chemistry". We students immediately got in love with his lecturing, because we recognized his unconventional approach and his availability in communication and discussions, and his simple but not trivial way of explaining difficult scientific issues. Ante knew how to elaborate different research problems and topics in understandable way, what we students appreciated very much.

Later, when I got a job at Ruđer Bošković Institute in 1979, Tonko and me have became colleagues and soon very good friends, not only because of common scientific interests, but also because of close tastes in music, literature, paintings and travelling.

During my stay in USA, from 1991 to 1994, Tonko had visited me and my family in Bethesda, MD and later in Rochester, MN, for several times. During his stays we had great social life and fruitful scientific exchange of ideas, also working on scientific articles. Later when I came back to Croatia, Tonko and me were travelling together several times abroad on scientific conferences and scientific collaborations - Germany, Hungary, Romania and Canada - always having interesting happenings.

The greatest legacy of Tonko, in my opinion, is the organization of annual Math/Chem/Comp (MCC) International Courses and Conferences in IUC in Dubrovnik, of which he was one of the founders and actively involved in MCC from its beginning in 1986 to 2011 (I joined Tonko in MCC from 1993).

Tonko's legacy is preserved in many scientific articles and books but especially in Math/Chem/Comp courses and conferences, which are world renowned and which thanks to his friends and collaborators will continue to be organized.

Dear Tonko, we thank you for all what you learnt us and for giving yourself to us!

A CHARGE-GRANULARITY CORRECTION TO THE ELECTROSTATIC SELF-ENERGY OF A CHARGE DISTRIBUTION IN TWO DIMENSIONS

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The electrostatic self-energy $E(N)$ of a set of N unit charges confined to a plane is investigated. Contingent upon satisfaction of certain conditions, $E(N)$ is shown to possess an asymptotic expansion at the limit of $N \rightarrow \infty$. The first two leading terms of this expansion are evaluated in closed forms. As expected, the first term is identical with the self-energy of a continuous charge distribution with density $\rho(\mathbf{r})$ that corresponds to the bulk limit of its discrete counterpart. The second term, which accounts for the Madelung energy, is given by a complicated functional of $\rho(\mathbf{r})$. For radially symmetric $\rho(\mathbf{r})$, this functional reduces to the previously derived variational local-density expression.

ONE-ELECTRON REDUCED DENSITY MATRICES OF STRONGLY CORRELATED HARMONIUM ATOMS

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Explicit asymptotic expressions are derived for the reduced one-electron density matrices (the 1-matrices) of strongly correlated two- and three-electron harmonium atoms in the ground and first excited states. These expressions, which are valid at the limit of small confinement strength ω , yield electron densities and kinetic energies in agreement with the published values. In addition, they reveal the $\omega^{5/6}$ asymptotic scaling of the exchange components of the electron-electron repulsion energies that differs from the $\omega^{2/3}$ scaling of their Coulomb and correlation counterparts. The natural orbitals of the totally symmetric ground state of the two-electron harmonium atom are found to possess collective occupancies that follow a mixed power/Gaussian dependence on the angular momentum in variance with the simple power-law prediction of Hill's asymptotics. Providing rigorous constraints on energies as functionals of 1-matrices, these results are expected to facilitate development of approximate implementations of the density matrix functional theory and ensure their proper description of strongly correlated systems.

MIXED ATIYAH DETERMINANTS FOR GRAPHS IN THE EUCLIDEAN OR HYPERBOLIC SPACE

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Abstract :

In 2001 Sir Michael Atiyah , inspired by physics (Berry Robbins problem related to spin statistics theorem of quantum mechanics) associated a remarkable determinant to any n distinct points in Euclidean 3-space (or hyperbolic 3-space) ,via an elementary construction. Although the problem of nonvanishing of the Atiyah determinants is very intricate (Atiyah and Atiyah -Sutcliffe conjectures) ,we shall show how one can associate a mixed Atiyah determinant to any graph with the given points as vertices . For the sum of all mixed determinants we can prove an identity ($n!$ conjecture) which implies that for any configuration of n distinct points in hyperbolic 3-space at least one of the mixed determinants is nonzero.

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EDGE REALIZABILITY OF CHEMICAL GRAPHS

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We study necessary and sufficient conditions for existence of a simple graph G , and for a simple and connected graph G' with given numbers m_{ij} of edges with end-degrees i, j for $i \leq j \in \{1, 2, \dots, \Delta\}$ where Δ denotes the maximum degree of G or G' .

Applications in Mathematical Chemistry are to optimization of bound additive topological indices. Algorithms for drawing these graphs are also provided.

COMPUTATIONAL APPROACHES FOR THE PREDICTION OF pKa OF POLYPHENOLIC COMPOUNDS AT DIFFERENT THEORY LEVELS

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Knowing the pKa of a compound gives insight into many properties relevant to industries, in particular the pharmaceutical industry during drug development processes [1]. Acid-base dissociation constants (pKa values) are important in understanding the chemical, environmental and toxicological properties of molecules. Though various methods have been developed to predict pKa by experimental and theoretical models, prediction of pKa is still complicated [2]. Hence, a new approach for predicting pKa using the OH group philicity concept has been attempted. Presence of known OH functional groups in a molecule is utilized as the most important indicator to predict pKa. The power of this descriptor in describing pKa for the series of polyphenolic compounds is probed. Results reveal that the group electrophilicity is suitable for effectively predicting the pKa values. Mechanism of antioxidant action of polyphenols in different cell conditions, reliable estimate of dissociation constants of their OH groups is of utmost importance. Polyphenols having more than one OH group have, aside from the first pKa, also pKa values of higher orders. Modelling at different levels of molecular structure representation were performed in order to produce reliable structure-property (pKa) models starting from available experimental pKa values of polyphenols and related compounds. DFT (Density Functional Theory) and semi-empirical methods were used for calculation of molecular structure and estimation of pKa values of flavonoid baicalein and selected related polyphenolics. Accuracy of theoretical estimation of pKa values of baicalein (whose antioxidant properties were intensively investigated in my previous studies), and related polyphenols will be verified by experimental and literature data.

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FREE RADICAL SCAVENGING POTENCY OF QUERCETIN AND ITS CATECHOLIC COLONIC METABOLITES: A DFT STUDY

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Flavonoids are thought to contribute to the beneficial health effects through diet rich in fruits and vegetables [1]. However, flavonoids generally have a low bioavailability (in nM range) suggesting that their bioactivity may be associated with their colonic metabolites which are present in systemic circulation at much higher concentrations (in μ M range) [2]. Majority of ingested structurally diverse flavonoids (95%) undergo extensive colonic metabolism [3] producing the common set of simpler hydroxybenzoic acids and phenols [4].

Free radical scavenging potency of quercetin and its six catecholic colonic metabolites were studied *in silico* employing DFT approach as implemented in Gaussian 09 package [5]. Geometry optimizations and frequency calculations were carried out using the M05-2X/6-311++G(d,p) level of theory, in conjunction with the SMD solvation model [6]. Two mechanisms of free radical scavenging reaction were considered: double hydrogen atom transfer (HAT) and double sequential proton loss electron transfer (SPLET). Obtained thermodynamic results indicate that all catecholic metabolites possess higher free radical scavenging potency than the parent quercetin molecule. They all have been found more potent scavengers than quercetin itself, able of deactivating various free radicals (HO^\bullet , HOO^\bullet , $\text{CH}_3\text{O}^\bullet$, and $\text{CH}_2=\text{CH}-\text{O}-\text{O}^\bullet$). Additionally, second HAT and SPLET processes have been estimated to be less energy demanding than the first ones indicating $2\text{H}^+/2\text{e}^-$ processes as inherent to catecholic moiety.

Our results suggest that recently proposed complete abandonment of free radical scavenging as one of possible mechanisms contributing to the health benefits of polyphenols [7] appears to be premature.

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COOPERATIVE BINDING OF AFLATOXIN B₁ BY CYTOCHROME P450 3A4: A Computational Study

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Aflatoxin B₁ (AFB₁) - the most potent natural carcinogen known to men - is metabolized by cytochrome P450 3A4 (CYP3A4), either to the genotoxic AFB₁ exo-8,9-epoxide or to the detoxified 3 α -hydroxy AFB₁. The activation of the procarcinogen proceeds in a highly cooperative fashion, which differs from common allosteric regulation in the sense that it can be attributed to simultaneous occupancy of a single large and malleable active site by multiple ligand molecules. Unfortunately, unlike in the case of ketoconazole, there is currently no experimental structure available for the doubly ligated CYP3A4-AFB₁ complex. Therefore, we employed a sequential molecular docking protocol to create various possible doubly ligated complexes and subsequently performed molecular dynamics simulations and free-energy calculations to check for their consistency with the available experimental data on regio- and stereo-selectivity of both AFB₁ oxidations as well as with available kinetic data. Only the system in which the first AFB₁ molecule was bound in a face-on C8–C9 epoxidation mode and the second AFB₁ molecule was bound in a side-on 3 α -hydroxylation mode - a result of an unconstrained molecular docking protocol - has successfully fulfilled all the imposed criteria and is therefore proposed as the most likely structure of the doubly ligated complex of CYP3A4 with AFB₁. The empirical Linear Interaction Energy method revealed that shape complementarity through nonpolar dispersion interactions between the two bound AFB₁ molecules is the main source of the experimentally observed positive homotropic cooperativity. The reported study represents a nice example of how state-of-the-art molecular modeling techniques can be used to study complicated macromolecular complexes, whose structures have not yet been experimentally determined, and to validate these against the available experimental data. The proposed structure will facilitate future studies on the rational design of successful AFB₁ modulators or on human subpopulations characterized by specific CYP3A4 polymorphisms that are especially sensitive to AFB₁.

MOLECULAR ELECTRIDES AND SUPERELECTRIDES

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Ionic compounds are chemical compounds consisting of positive and negative ions held together by electrostatic forces. Electrides are unique ionic compounds where the anionic part is constituted only by isolated electrons. These new type of compounds were postulated and synthesized first by Dye [1]. They have interesting physicochemical properties that make them suitable for certain technological applications that range from electron emitters to reversible H₂ storage devices. Thus far, only solid-state electrides have been reported. Electrides were shown to exhibit large non-linear optical properties (NLOP) [2], non-nuclear attractors (NNA) of the electron density, and electron localization function (ELF) basins. However, several molecules show some of these properties without the presence of an isolated electron. Therefore, none of these properties alone are sufficient to characterize electrides. In this work, we provide an unambiguous computational means to distinguish molecular electrides from similar species [3]. We analyze seven species that were previously considered molecular electrides on the basis of large NLOPs and frontier orbitals with large density values in the vicinity of the position where one would expect the isolated electron of the electride. We will show that some of them are actually not electrides [3]. Finally, we present some examples of what we called molecular superelectrides, which are defined as electrides having more NNA than atoms. These species are relevant as they can be considered molecular models for the study of the metallic bond [4].

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2D-QUANTITATIVE STRUCTURE ACTIVITY STUDY AND THE COMPUTATIONAL PREDICTION OF ANTIBACTERIAL ACTIVITY FOR SERIES OF QUINOLONE DERIVATIVES

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Abstract: *Quantitative structure–activity relationship (QSAR) models are useful in understanding how chemical structure relates to the biological activity of natural and synthetic chemicals and for design of newer and better therapeutics. In the present study, 15 quinolones derivatives were evaluated as antibacterial inhibitors, expressed by the cytotoxicity of these compounds (MIC). Based on these data, different molecular descriptors were used to solve this problem. A linear QSAR model was developed using Multiple Linear Regression technique, while Genetic Algorithm was adopted for selecting the most appropriate descriptors. The predictive activity of the model was evaluated by means of external validation set and the Y-randomization technique, and its structural chemical domain has been verified by the leverage approach.*

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HOW TO PLAY A PIANO LIKE A VIOLIN? INTEGER PARAMETERS AS CONTINUOUS VARIABLES IN MOLECULES, ANTI-QUANTIZATION, RE-QUANTIZATION, AND THE UNIVERSAL MOLECULE MODEL

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A well-tuned piano can produce only “quantized” frequency sounds, but a violin has no such restriction: by shifting your finger along the string, the frequency can be modified continuously. However, while tuning a piano, one can also produce continuously any intermediate frequency, thereby “anti-quantizing” the piano, but when the tuning is done, “re-quantization” occurs, and again, only specific frequencies can be heard.

In molecular modelling the “quantized” integer parameters of molecules, for example, nuclear charges, can also be “anti-quantized” if taken as continuous variables. The extra freedom obtained leads to new, valid relations between real, “re-quantized” molecules, having again only integer nuclear charges. Such “anti-quantization, re-quantization” approach applies to other integer parameters as well.

These non-integer values correspond to non-physical, impossible “molecules”, but a continuous change through such models still can give valid relations between real molecules, for their energies and other properties. This is reminiscent to the use of complex functions, where, for example, contour integration through non-physical values on the complex plane is used to obtain real, and valid physical quantities. If all parameters are taken as continuous variables, one obtains the “Universal Molecule Model” that connects all real molecules, even seemingly unrelated molecules, to one another through impossible, non-physical models within a single mathematical framework [1,2]. This anti-quantized and re-quantized “Universal Molecule Model” provides new, valid relations on energy and other properties of real molecules, and all actual molecules may then be regarded as special cases of the “Universal Molecule”.

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SIMULATION AND CONTROL OF LIGHT-INDUCED DYNAMICS IN COMPLEX MOLECULAR SYSTEMS

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Interaction of molecules with light induces a multitude of dynamical phenomena such as internal conversion, isomerization, or photochemical reactions. The simulation of such processes requires an atomistic description of the coupled electron-nuclear dynamics including the driving light field. For this purpose, we have developed the field-induced surface-hopping method (FISH) [1], which combines classical nuclear dynamics „on the fly” with quantum mechanical electronic population dynamics. This allows for an efficient treatment of complex systems including all degrees of freedom. The electric fields initiating and/or steering the photodynamics are incorporated straightforwardly without approximations, thus enabling the use of arbitrarily complex pulse shapes. On this basis we have devised a methodological framework for simulating time-resolved spectroscopic signals which can be directly compared with the experiment [2]. Specifically, we will present the simulation of time-resolved photoelectron imaging spectra, providing unique insights into the relaxation dynamics of photoexcited molecules [3]. Furthermore, the broad scope of the FISH method for exploring control strategies in complex systems and unravelling the underlying mechanisms will be illustrated on examples in the condensed phase. It will be shown how FISH simulations employing experimentally shaped fields reveal the mechanism responsible for optimal dynamic discrimination between two spectroscopically almost identical biomolecules [4]. Moreover, the theoretical design of laser pulses capable to extend the excited state lifetime of the DNA base adenine will be presented [5]. Finally, it will be demonstrated how a combination of quantum chemistry with classical electrodynamics allows for the optimal control of spatio-temporal field localization in a molecular-sized nanostructure [6].

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RELIABILITY OF THE STABILITY CONSTANTS PREDICTION BY TOPOLOGICAL INDEX ${}^3\chi^v$

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Linear, as well as quadratic correlation functions of stability constants of coordination compounds, $\log K$ or $\log \beta$, on topological indices, and especially on connectivity index ${}^3\chi^v$ were applied on many systems [1]. The majority of our calculations were done on copper(II) and nickel(II) complexes of amino acids and their *N*-substituted derivatives [2], along with small peptides [3], but we also studied complexes of monocarboxylic acids with other metals, including cadmium and lanthanides [4,5]. The systematic analysis of the regression results revealed that models gave relative error, expressed as $S.E./(\log K \text{ range})$ usually smaller than 0.1, and in the range 0.017 – 0.21. This is a strong indication for the validity of our method, showing that the models are more dependent on the set of stability constants used for their calibration, than on the form of regression function. Are the stability constants negatively or positively correlated on ${}^3\chi^v$, it seems to depend on the mode of ligand binding.

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SAMPLING STRATEGIES FOR QM/MM CALCULATIONS IN CONDENSED PHASE

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An overview of our most recent projects in the theoretical treatment of enzymatic catalysis is presented, focusing on Mo-dependent enzymes^[1-3] and the difficulties encountered in simulating reactions in the condensed phase. In pathways where strong Coulomb interactions in the active site have to be balanced by neighboring residues or solvent molecules, the use of an effective dielectric constant and a continuum description of the environment are insufficient. Quantum mechanics/molecular mechanics (QM/MM) molecular dynamics are too costly, since the number of degrees of freedom to sample outside the active site is too large and the two systems (QM and MM) are strongly coupled.

In order to address this problem, we have recently explored the Perturbative QM/MM Monte Carlo scheme of Truong and Stefanovich,^[4] whereby a separation of the two sampling spaces is possible. We show that with some simple extensions to the method, the number of QM calculations can be kept to a minimum, while thoroughly sampling the configurational space. Model applications of the method to free energy profiles are presented, discussing the robustness of different models for strong/weak overlapping states.

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SPECTROSCOPIC INVESTIGATION OF SILVER(I) COMPLEXES WITH HALOGEN SUBSTITUTED PYRIDINES

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Microbial resistance to antibiotics has become a worldwide concern. Recently, silver(I) compounds have attracted attention as potential antimicrobial agents.^{1,2} Combining of silver salts with organic ligands may result in obtaining complexes with broader spectra of activity.

We have synthesized a series of 1:2 complexes of silver(I) nitrate with 2- and 3-halopyridine, $[\text{Ag}(\text{NO}_3)(\text{Xpy})_2]$, X = Cl, Br, I, in order to investigate the potential biological activity and put some more insight in structure-function relationship as to their solid state structure as well as through characterization the species that exist in solution. We have chosen NO_3^- anion because it is well known that in metal complexes it could act as a counterion or a ligand and could assist in metallophilic interactions.

All compounds were analysed by NMR in solutions and in the solid state and FT-IR and MS. The X-ray crystal structure was also determined (Fig. 1.). Solid state NMR parameters were used as a reference for solution study results. Starting from the experimental geometries, we performed quantum-mechanical calculations of complexes at different DFT levels of theory and compared data with spectroscopic results.

Preliminary antimicrobial activities of the complexes against two Gram-negative strains: *M. catarrhalis* ATCC 23246 and *E. coli* AcrAB- were evaluated.

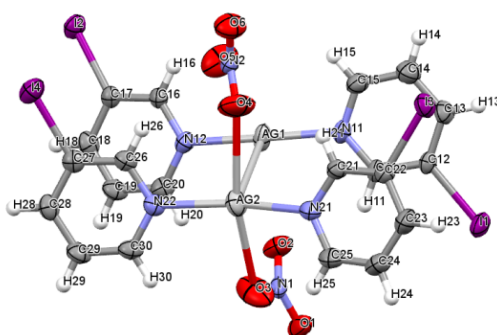


Fig. 1. The crystal structure of $[\text{Ag}(\text{NO}_3)(3\text{-I-py})_2]$.

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ITERATED ALTANS AND THEIR PROPERTIES

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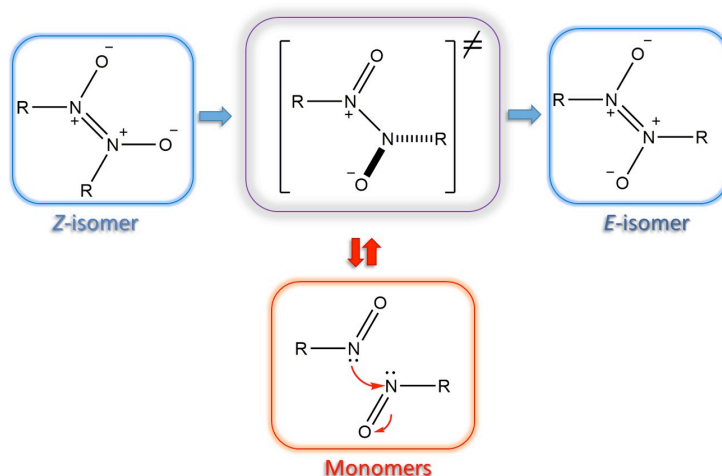
Recently a class of molecular graphs, called *altans*, became a focus of attention of several theoretical chemists and mathematicians. In this talk we will present iterated altans and show, among other things, their connections with nanotubes and nanocaps. The question of classification of bipartite altans will be also addressed. Using the results of Gutman we are able to enumerate Kekulé structures of several nanocaps of arbitrary length.

CHEMICAL BONDS AND TOPOCHEMICAL EFFECTS

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The thermally induced *E-Z* isomerization of the benzeneazodioxide derivatives is studied in the solid polychrystalline state. The reactions are studied from the kinetic and mechanistic aspects. In contrast to the solution, where isomerizations of azodioxides proceed through the formation of corresponding nitroso monomers, in solid state the reaction follows the mechanism that includes formation of the “torsional” transition state, as it is the case in other known *cis-trans* isomerizations. It is proposed that both the reactions in solid state, the nitroso monomer-dimer equilibrium, and isomerization about the azodioxide N=N bond involve similar transition states. The drift for the transformation of *Z*- to *E*-isomer is the phase transformation, since the *E*-isomer crystal phase of the product is significantly more stable than the *Z*-crystal phase. Similar concurrent reactions were found in the solid-state polymerizations of 1,4-dinitrosobenzenes. The reactivity of dimereization and isomerization strongly depends on the topochemical conditions. We demonstrate that the strong topochemical effect can stabilize the structures in the potential energy minima that are shorter than van der Waals bonds and longer than the normal covalent bond.



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A (VERY) SHORT INTRODUCTION TO COMPUTATIONAL CHEMISTRY

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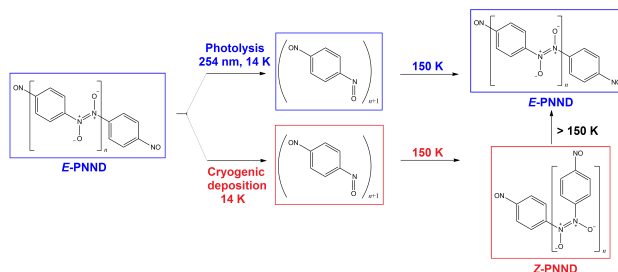
The purpose of this short course is the introduction to the basic principles and methods of computational chemistry, its applications and possible developments. The lecture will consist of following topics. After short introduction, overview of different approaches to energy calculations of microscopic systems will be given, with the main attention to *ab initio* and DFT methods. Then follows the wave function analysis, with comparison of different population analysis approaches. After introducing the concept of potential energy surface, attention will be given its stationary points and calculation of reaction paths, followed by the methods of thermodynamic and kinetic parameters calculations. Approaches to the calculation of excited states and spectroscopic properties will briefly mentioned, as well as different ways to tackle the solvation effects problem. At the end, the overview of multilayered approach to complex biomacromolecules calculations will be presented.

KINETICS OF FORMATION OF POLYBENZENE AZODIOXIDE

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Polymerization 1,4-dinitrosobenzene was examined to gain a deeper understanding of solid-state reactions. The experimental part included the study of depolymerization and low temperature polymerization of 1,4-dinitrosobenzene in the solid state by IR spectroscopy.[1] The dissociation of azodioxide bonds was induced either by 254 nm UV irradiation at cryogenic temperatures or by sublimation. Monomers start to form azodioxy bonds at around 150 K. While *E*-polymers were obtained from monomers prepared by UV photodissociation, *Z*-forms were detected in samples prepared by sublimation and subsequent deposition on a CsI surface. Because *Z*-forms isomerize to more stable *E*-polymers above 150 K, these isomers are probably kinetically stabilized by interactions with alkali halide surface. Since polymerization is accompanied by phase transition, a non-linear Avrami-Erofeev kinetic analysis was utilized to determine kinetic parameters.[2] The results suggest a one-dimensional phase growth, as was expected for a linear polymer. The structure of oligomers was also studied computationally. DFT methods were used for shorter polymers, while longer ones were calculated by Fragment Molecular Orbitals method. Both methods suggest helical *E*-conformations to be the most stable, with a full helix turn after 38 Å. Lower stability of *Z*-isomers is explained by electrostatic repulsions between oxygen atoms which are spaced much more closely than in *E*-isomers. Since FMO method shows good correlation with the DFT results and is much faster, we find it suitable for theoretical study of similar polymers and further investigation.[3]



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QUANTUM MOLECULAR DYNAMICAL STUDIES OF THE Li(+)-FERROCENE COMPLEX

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Alkali metal cations, as well as tetraalkylammonium cations, are in general attracted to the π face of aromatic structures by strong noncovalent bonding forces [1]. However, in various cases electrophilic substitution reactions of ferrocene, which bears two aromatic cyclopentadienyl rings, are known to proceed via precomplexation of the iron atom by the electrophile [2], which is counterintuitive. In this vein, earlier theoretical studies [3], demonstrated that the Li(+)-Ferrocene complex with a direct Li(+)-to-iron interaction is a metastable complex, protected from the most stable π -complex by a sizable barrier of ~ 16 kcal/mole. Furthermore, experimental evidence of the existence of such kind of complex was then provided by the synthesis and the elucidation of the molecular structure Li(+)-[1.1]diborataferrocenophane by X-ray crystallography [4].

In this communication, the dynamics of the Li(+)-Ferrocene complex will be discussed based on Quantum Molecular Dynamical Studies of the complex bearing the direct Li(+)-to-iron interaction. It will be shown that this compound can be best seen as a planetary like system with the Li(+) "orbiting" in the plane perpendicular to the five-fold symmetry axis of the ferrocene which contains the iron atom. In accordance to the calculations performed, the complex is predicted to have a long enough lifetime as to allow for experimental detection and spectroscopic characterization.

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MODELLING OF SCREEN-PRINTED SENSOR RESPONSE PARAMETERS BY USE OF MICROSOFT EXCEL SOLVER

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Solver is a spreadsheet optimization modeling system that is incorporated into Microsoft Excel for Windows, which can be used for solving various linear, nonlinear or integer problems [1,2]. When applied to analysis of a scientific data set, it can yield the same results as commercial analysis software packages [3]. The investigations presented describe modelling of response parameters of a potentiometric surfactant screen-printed sensor by using potentiometric data set of some anionic surfactants. The theoretical models for the potentiometric titration curves were elaborated too. The experimental data were compared with appropriate theoretical curves in which the sensor response parameters and analyte properties (sensor slope, constant potential term, solubility product constant, analyte concentration) were estimated and optimized with *Solver* (Excel) using least-squares criterion to fit theoretical curves to an experimental data set. The initial parameter settings were defined, and no constraints on the variables were applied. The macro SolvStat provided the regression statistics of the *Solver* by calculation of the standard deviations of the parameters, correlation coefficients and standard errors of the y estimate $SE(y)$. The theoretical models fit satisfactorily to the experimental values for the investigated surfactants.

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MATHEMATICAL RESEARCH OF MOLECULAR DESCRIPTORS

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Mathematical chemistry is interdisciplinary research area. The development of molecular descriptors relies on graph theory and statistics. Here, several results will be presented that demonstrate:

- 1) Usage of extremal graph theory
- 2) Realizability problems in graph theory
- 3) Computer assisted search for molecular descriptors

Adriatic indices will be presented here and the above three topics will be exemplified on them. Further, possible use of complex networks in studying of molecular descriptors will be mentioned.

Also, molecular descriptor that are used in biophysics (which are not based on graph theoretical representation of molecules) will be presented and some of possibilities of their application will be discussed.

COMPUTATIONAL ALGORITHMS IN CONFORMATIONAL ANALYSIS OF CYCLIC AND NON-CYCLIC MOLECULES

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Conformational analysis is a search through conformational space leading to a set of conformers for a given molecule. The main problem in conformational analysis is finding reasonable initial guess for structures that will be subsequently optimized. This initial guess can be obtained by sampling coordinate space or phase space. Usually, coordinate space search is conducted stochastically by generation of randomly distorted geometries and their optimizations. If the number of degrees of freedom is sufficiently small, complete coordinate search can be performed using the potential energy surfaces spanned by torsional degrees of freedom. Phase space search is conducted by molecular dynamics simulations and random selection of geometries for optimization from the trajectories. In addition, complete molecular dynamics trajectories can be analyzed using tensor decomposition tools and valuable information can be obtained. Conformational analysis of cyclic and non-cyclic molecules will be presented by showing examples of stochastic and grid search as well as examples of numerical processing of molecular dynamics trajectory data.

SELF ORGANIZING CARBON STRUCTURES IN TIGHT BINDING MOLECULAR DYNAMICS CALCULATIONS

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Graphene is a two-dimensional building material for the zero-dimensional fullerenes and the one-dimensional nanotubes. Using mathematical constructions and identifying some atoms, these materials can be rolled up from appropriate patterns cut out from the hexagonal lattice of carbon atoms. The question arises if there is a realistic formation process behind this idealized construction. Although the first time the C₆₀ and C₇₀ fullerenes were produced by laser irradiated graphite, the fullerene formation theories are based on various fragments of carbon chains, and networks of pentagonal and hexagonal rings [1-2]. The first successful results concerning fullerene formations in a priori molecular dynamics simulations based on a true quantum chemical potential was published twenty-one years after discovering the buckminsterfullerene. The greater application of fullerenes and nanotube faces the lack of selective growth and assembly processes. Here we present quantum chemical molecular dynamics calculations which selectively produce the buckminsterfullerene C₆₀, the C₇₀ [3], the armchair and the zigzag nanotubes depending on the initial structure of patterns cut out from the graphene [4-7].

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STUDIES ON DEUTERIUM ISOTOPE EFFECTS IN ^{13}C NMR SPECTROSCOPY*

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Deuterium is often studied isotope due to easy of its incorporation into the molecules and because of large fractional mass changing upon deuteration. Deuterium substitution gives rise to some unexpected effects in molecules: optical activity, *e.g.* in CXYHD, small dipole moment (10^{-2} - 10^{-4} D) *e.g.* in monodeuterated benzene and acetylene, which enables the measuring of pure rotational spectra of these compounds, long-range effects in NMR.

The most unusual feature of deuterium labeling is the existence of long range deuterium isotope effects (LRDIE) on ^{13}C NMR chemical shifts. The high magnetic field NMR spectrometers has recently enabled detection of very fine LRDIE even through 12 bonds, as small as 0.1 Hz, in π -electron systems. The calculations of LRDIE are still challenging because of their rather low magnitude (1 ppb - 300 ppb) and lack of reliable theoretical underpinning for isotope interactions through many bonds.

Generally, isotope effects on chemical shifts are interpreted in terms of vibrational and rotational averaging of nuclear shielding. Changes in nuclear shielding with bond extension and/or bond angle deformation accompany deuteration. In the theoretical approach to LRDIE at least two contributions have to be taken into account: (1) the secondary change in shielding at remote C-atom due to shorter C-D than C-H mean bond length at the site of deuteration and (2) the primary change in remote C-atom shielding, due to change in mean bond length at this remote site. We have postulated that LRDIE predominantly arise from (1), *i.e.* primary change of bond length at the site of deuteration, since vibrational differences at remote C-atoms in isotopomers are very small. The C-D bond was modeled by reduction of the corresponding C-H bond in the range 0.003-0.018 Å. Nuclear shieldings (GIAO) and atomic charges (Löwdin, Mulliken) were calculated by different *ab initio* basis sets. For C-atoms more than four bonds away from the deuteration site the differences of shielding and charges between protonated and deuterated molecules correlate fairly good with experimental LRDIE. By this approach experimental LRDIE can be successfully calculated, even those over 10 and 12 C-C bonds.

*Dedicated to prof. dr. sc. Ante Graovac

¹D. Vikić-Topić, M. Hodošček, A. Graovac, E. D. Becker, G. Lodder, and H. Zuilhof: On the Calculations of Deuterium Long Range Isotope Effects on C-13 Chemical Shifts, in Nuclear Magnetic Shieldings and Molecular Structure. J. A. Tossell, ed., Kluwer Academic Publishers, Dordrecht, NATO ASI Series C **386**, 574 (1993)