Modeling & Design of Molecular Materials 2016

a meeting organized by

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Conference Program

June 26, 2016 (Sunday)

14:00-19:00	Registration
18:00-22:00	Grill

June 27, 2016 (Monday)

9:00-9:05	Opening ceremony
Session I:	**Modeling Interactions in Molecular Materials** (chair: T. Clark)
9:05	**L1**: R. Wade (EMBL, Heidelberg, Germany) - Simulation of protein adsorption on inorganic surfaces
9:50	**L2**: A. Sobolewski (Institute of Physics of Polish Academy of Sciences, Warsaw, Poland) - Photophysics of hydrogen bonded molecular systems: From theory to applications
10:35	Coffee break
Session II:	**Modeling Enzyme Reactions** (chair: E. Broclawik)
11:05	**L3**: A. Mulholland (University of Bristol, UK) - Multiscale modelling to predict and analyse enzyme activity
11:45	**L4**: T. Brinck (KTH Royal Institute of Technology, Stockholm, Sweden) - Computational tools in enzyme Design
12:25	**L5**: M. van der Kamp (University of Bristol,UK) - The use of QM/MM for enzyme activity screening: applications in antibiotic resistance and evaluation of biocatalysis
13:00	Lunch
Session III:	**Modeling Chemical Reactions** (chair: A. Mulholland)
15:00	**L6**: A. Toro-Labbe (Pontifica Universidad Catolica de Chile, Santiago de Chile, Chile) - Some Remarks on Activation and Relaxation Processes in Chemical Reactions
15:35	**L7**: E. Broclawik (Institute of Catalysis and Surface Science of Polish Academy of Sciences, Cracow, Poland) - Large versus small-scale modeling for TM centers in catalysis: is bigger always better ?
16:10	**L8**: S. Grabowski (Euskal Herriko Unibertsitatea UPV EHU, San Sebastian, Spain) - Tetrel bond as a preliminary stage of SN2 reaction
16:45	**L9**: J. Burda (Charles University, Prague, Czech Republic) - Reduction process of Pt(IV) in presence of dGMP; Computational DFT study
17:20	Coffee break
17:20-19:00	Poster Session I
19:00-21:00	Dinner

June 28, 2016 (Tuesday)

Session IV:	**Advances in Computational Methods** (chair: P. Szalay)

9:00	**L10**: K. Pernal (Technical University of Lodz, Poland) - Predicting electronic structure with correlated strongly orthogonal geminals
9:40	**L11**: N. Gresh (University Paris VI, France) - Addressing the issues of non-isotropy and non-additivity in the development of a quantum-chemistry-grounded polarizable molecular mechanics/dynamics potential. Applications to cation-ligand and ligand-receptor complexes
10:10	**L12**: B. Lesyng (Warsaw University, Warsaw, Poland) - Causality analysis of structural changes using vector signals based on quaternion formalism
10:40	Coffee break
Session V:	**Modeling Nucleic Acids** (chair: R. Wade)
11:10	**L13**: J. Rak (University of Gdansk, Poland) - Hydrated electrons and Trojan horse radiotherapy. Computational and experimental studies
11:40	**L14**: P. Szalay (Eötvos University, Budapest, Hungary) - Characterization of the excited states of DNA building blocks: a coupled cluster computational study
12:10	**L15**: L. Gorb (Institute of Molecular Biology and Genetics NAS, Kiev, Ukraine) - From isolated DNA bases to Dickerson dodecamer: results of recent quantum-chemical calculations
12:40	**L16**: R. Góra (Wrocław University of Science and Technology, Poland) - Photochemistry and photophysics of prebiotic precursors of nucleotides
13:00	Lunch
Session VI:	**Modeling Molecular Materials** (chair: Z. Latajka)
15:00	**L17**: B. Kuchta (Wrocław University of Science and Technology, Poland) - Heterogenous melting of methane confined in nano-pores
15:30	**L18**: P. Cysewski (Nicolaus Copernicus University, Bydgoszcz, Poland) - On the transferability of cocrystallization propensities
16:00	**L19**: I. Cukrowski (University of Pretoria, South Africa) - FAMSEC/IQA-deduced origin of the relative stability of cis- and trans-2-butene isomers
16:30	**L20**: A. Sikorski (University of Warsaw, Poland) - Monte-Carlo studies of two-dimensional polymer-solvent systems
17:00	Coffee break
17:30-19:00	Poster Session II

June 29, 2019 (Wednesday)

Session VII:	**Modeling Molecular Materials** (chair: A. Sobolewski)
9:00	**L21**: T. Clark (Erlangen-Nurnberg University, Erlangen, Germany) - Modeling real devices
9:30	**L22**: L. Firlej (Universite de Montpellier, France) - Modeling of low temperature adsorption of hydrogen in carbon nanopores

10:00	**L23**: M. Mitoraj (Jagiellonian University, Cracow, Poland) - Dihydrogen bonds in selected hydrogen storage materials - an insight from computational perspective
10:30	Coffee break
Session VIII:	**Modeling Molecular Materials** (chair: B. Kuchta)
11:00	**L24**: J. Urban (Komensky University, Bratislava, Slovakia) - Plasma surface interactions of mixed Be-W materials - theoretical study
11:35	**L25**: Z. Latajka (Wrocław University, Poland) - Theoretical modelling of selected model nanosystems
12:10	**L26**: M. Hennemann (Erlangen-Nurnberg University, Erlangen, Germany) - EMPIRE: New dimensions for materials modeling
12:35	**L27**: D. Kędziera (Nicolaus Copernicus University in Torun,Poland) - Chasing our limits, ytterbium dimer ground state calculations
13:00-15:00	Lunch
15:00-19:00	Excursion
19:00-22:00	Conference dinner

June 30, 2016 (Thursday)

Session IX:	**Modeling & Design of Drugs by Alumni of Wroclaw Universities** (chair: J. Leszczynski)
9:00	**L28**: J. Grembecka (University of Michigan,Ann Arbour, MI,USA) - Targeted inhibition of the menin-MLL interaction for cancer therapies
9:30	**L29**: M. Zakrzewska (Wroclaw University, Poland) - Design of fibroblast growth factor 1 for medical applications
10:00	**L30**: T. Cierpicki (University of Michigan,Ann Arbour, MI,USA) - Targeting RING ubiquitin ligase with small molecule inhibitors "
10:30	Coffee break
Session X:	**Modeling Molecular Materials** (chair: J. Burda)
11:00	**L31**: J. Leszczynski (Jackson State University, MS,USA) - Evaluating optimum pathways for potential prebiotic reactions
11:30	**L32**: A. Michalak (Jagiellonian University, Cracow, Poland) - Theoretical study on the electronic structure and properties of the PBI and tetrazole-derived polymers for fuel-cell applications"
12:00	**L33**: A. Kaczmarek-Kędziera (Nicolaus Copernicus University in Torun, Poland) - New materials designed for absorption of non-steroidal anti-inflammatory drugs
12:25	**L34**: A. Stachowicz-Kuśnierz (Jagiellonian University, Cracow,Poland) - The influence of air pollutants on structure and fuction of lung surfactant
12:50	Closing ceremony
13:00-15:00	Lunch

List of poster presentations

P1A Ivana Antol, Zoran Glasovac, Davor Margetić

P2A Wiktor Beker, W. Andrzej Sokalski

P3A Tomasz Buchała, Szczepan Roszak

P4A Krzysztof L. Buzar, Jerzy Trawczynski, Bartłomiej M. Szyja

P5A Radim Cajzl, Filip Šebesta, Jaroslav V. Burda

P6A Anna Chudoba, Zygmunt Flisak, Szczepan Roszak

P7A Diego Cortés-Arriagada, Alejandro Toro-Labbé

P8A Przemysław Czeleń

P9A Alexey A. Dmitriev, Nina P. Gritsan

P10A Justyna Dominikowska, T. Marek Krygowski, Wojciech P. Ozimiński, Marcin Palusiak

P11A Justyna Dominikowska, F. Matthias Bickelhaupt, Marcin Palusiak, Célia Fonseca Guerra

P12A Ege Dundar, Nicolas Chanut, Pascal Boulet, Philip L. Llewellyn, Bogdan Kuchta

P13A Olga Dvořáčková, Zdeněk Chval

P14A Karol Dyduch, Monika Srebro, Artur Michalak

P15A A. Kwocz, Jarosław J. Panek, Aneta Jezierska, Ł. Hetmańczyk, A. Pawlukojć, A. Kochel, Paweł Lipkowski, Aleksander Filarowski

P16A Anna A. Glagoleva, Valentina V. Vasilevskaya

P17A Liudmyla K. Sviatenko, Leonid Gorb, Danuta Leszczynska, Jerzy Leszczynski

P18A Dawid Grabarek, Elżbieta Walczak, Tadeusz Andruniów

P19A Izabela Grzelak, Ireneusz Kownacki, Marcin Hoffmann

P20A Francisca Cid, Alejandro Toro-Labbé, Soledad Gutiérrez-Oliva

P21A Susanta Haldar, Petra Kuhrova, Pavel Banas, Vojtech Spiwok, Jirí Sponer, Pavel Hobza, Michal Otyepka

P22A Karol Hęclik, Agnieszka Szyszkowska, Mirosław Tyrka, Iwona Zarzyka

P23A Karol Hęclik, Agnieszka Szyszkowska, Mirosław Tyrka, Iwona Zarzyka

P24A Jerzy Hładyszowski, Beata Żbikowska, Zbigniew Sroka

P25A James Hooper, Eva Zurek, Axel Enders

P26A Piotr Jankowski, P. Johansson, W. Wieczorek

P27A Wojciech Jankowski, Joanna Kurek, Marcin Hoffmann

P28A Jerzy J. Jański, Szczepan Roszak, Aleksander Koll, Janina Kuduk-Jaworska

P29A Dorota Jarmużek, Donata Pluskota-Karwatka, Marcin Hoffmann, Tomasz Pędziński, Kinga Salus

P30A Mateusz Jasik, Tadeusz Andruniów

P31A Wiktoria Jedwabny, Edyta Dyguda-Kazimierowicz, W. Andrzej Sokalski

P32A Kacper Błaziak, Jarosław J. Panek, Aneta Jezierska

P33A Andrzej Pihut, Aneta Jezierska

P34A Ludwik Komorowski, Piotr Ordon, Mateusz Jędrzejewski

P35A Mateusz Jędrzejewski, Piotr Ordon, Ludwik Komorowski

P36A Agnieszka Karczyńska, Artur Giełdoń, Paweł Krupa, Adam Liwo, Cezary Czaplewski

P37B Filip Formalik, Adam Olejniczak, Michael Fischer

P38B Hubert Kasprowski, Edyta Dyguda-Kazimierowicz

P39B Oskar M. Klaja, Bartłomiej M. Szyja, Jerzy Trawczynski

P40B Marta Kliber-Jasik, Małgorzata A. Broda, Joanna Nackiewicz

P41B Lidia Zapała, Małgorzata Kosińska, Tadeusz Pietryga, Jan Kalembkiewicz, Urszula Maciołek, Anna Kuźniar

P42B Lidia Zapała, Małgorzata Kosińska, Tadeusz Pietryga, Jan Kalembkiewicz, Urszula Maciołek, Anna Kuźniar

P43B Justyna Kozłowska, Agnieszka Roztoczyńska, Wojciech Bartkowiak

P44B Martyna Kuta, Marcin Hoffmann, Shozeb Haider

P45B Adam K. Sieradzan, Agnieszka G. Lipska, Adam Liwo

P46B Rabindranath Lo, Petr Švec, Zdeňka Růžičková, Aleš Růžička, Pavel Hobza

P47B Anna Kuźniar, Urszula Maciołek, Tadeusz Pietryga, Jan Kalembkiewicz, Małgorzata Kosińska, Lidia Zapała

P48B Anna Kuźniar, Urszula Maciołek, Tadeusz Pietryga, Janusz Pusz, Jan Kalembkiewicz, Małgorzata Kosińska

P49B Milan Melicherčík, Katarína Skúpa, Zuzana Šestáková, Ján Urban, Miroslav Piršel

P50B Roma Musik

P51B Adam Olejniczak, Bartłomiej Cichy, Wiesław Stręk

P52B Adam Olejniczak, Bartłomiej Cichy, Łukasz Radosiński, Wiesław Stręk

P53B Daniela E. Ortega, Diego Cortés-Arriagada, Oleksandra S. Trofymchuk, Diana Yepes, Soledad Gutiérrez-Oliva, René S. Rojas, Alejandro Toro-Labbé

P54B Anna Panek, Alina Świzdor, Natalia Milecka-Tronina, Jarosław J. Panek

P55B Aneta Jezierska, Jarosław J. Panek

P56B Bartosz Pawelczak, Krzysztof Marciniec, Anna Sulkowska

P57B Bartosz Pawelczak, Mariola Chudzik, Anna Sulkowska, Malgorzata Maciazek-Jurczyk

P58B Tomasz Pieńko, Aleksandra Wierzba, Monika Wojciechowska, Dorota Gryko, Joanna Trylska

P59B Tadeusz Pluta

P60B Justyna Rogacka, Lucyna Firlej, Bogdan Kuchta

P61B Filip Sagan, Mariusz P. Mitoraj

P62B Kinga Salus, Marcin Hoffmann, Donata Pluskota-Karwatka, Bożena Wyrzykiewicz

P63B Kinga Salus, Marcin Hoffmann, Donata Pluskota-Karwatka, Tomasz Siodła, Bożena Wyrzykiewicz

P64B Eric Schulze, Matthias Stein

P65B Filip Šebesta, Jaroslav V. Burda

P66B Katarína Skúpa

P67B Žofie Sovová, Filip Šebesta, Jaroslav V. Burda

P68B Adam Stępniewski, Ewa Broclawik, Mariusz Radoń, Kinga Góra-Marek

P69B Beata Szefler, Przemysław Czeleń

P70B Łukasz Wolański, Tadeusz Andruniów

P71B Yang Yi, Yong Li, Jun Li, Karol Jackowski, Szczepan Roszak

P72B Jarosław Zaklika, Paweł Kędzierski, Robert W. Góra

Lecture abstracts

in chronological order

Simulation of protein adsorption to inorganic surfaces

Rebecca C. Wade

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Zentrum für Molekulare Biologie (ZMBH), DKFZ-ZMBH Alliance and Interdisciplinary Center for Scientific Computing (IWR), Heidelberg University, Germany

Understanding protein–inorganic surface interactions is central to the rational design of new tools in biomaterial sciences, nanobiotechnology and nanomedicine. Although numerous experimental studies of protein adsorption onto solid substrates have been reported, many aspects of the mechanisms by which biomolecules recognize and interact with inorganic surfaces remain unclear. There are many challenges to the accurate modeling and simulation of protein-surface interactions, for review see [1]. Here, we discuss how simulations of protein-surface interactions can aid the interpretation of experimental data and provide insights into the determinants of protein-surface binding.

Using electrostatic calculations and our rigid-body Brownian dynamics docking methodology, we find that even a small fluorescent label attached to a protein to monitor adsorption processes can significantly change the interactions of the protein with a charged surface [2]. We show how the results of experiments with fluorescently labeled proteins can be interpreted by modeling the structures and computing the interaction properties of both labeled and unlabeled species.

We then combine Brownian dynamics and molecular dynamics simulations to investigate how proteins bind to a gold surface [3,4]. The results reveal a three-step adsorption process involving recognition, adsorption and induced fit, and provide structural models of the protein-surface complexes.

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Photophysics of hydrogen bonded molecular systems: From theory to applications

Andrzej L. Sobolewski

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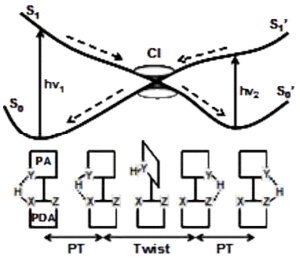
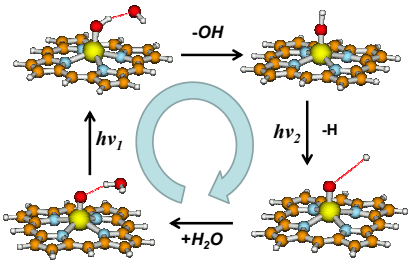
Proton is the lightest nuclei and its monatomic form (H_1) is the most abundant chemical substance in the Universe. The relative lightness and small size of this "quantum" particle explains the unusually high diffusion rate of the 'excess' proton through the hydrogen bond network of water molecules. We have shown recently that radiationless deactivation channel associated with conical intersection between the electronically excited state and the ground state for proton-transfer reaction along hydrogen bonds may provide a very effective mechanism for explanation of functionality of commercial organic photostabilizers, and the photostability of biological molecules such as DNA and proteins [1].

A question of control of proton motion with the aid of light fields is not only of fundamental interest, but may also results in some practical applications. Thus the mechanistic aspects of the excited-state intra-molecular proton-transfer (ESIPT) process may be utilized in construction of optically driven photostable molecular switches (a) [2], while the electron-driven proton-transfer (EDPT) phenomenon along the inter-molecular hydrogen bond(s) may provide a template for designing of macromolecular systems, which are able to oxidize water using solar radiation (b) [3,4].

(a)



(b)



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Multiscale modelling to predict and analyse enzyme activity

Adrian Mulholland

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Biomolecular simulations have advanced to the stage where they can provide reliable predictions of enzyme mechanisms and ligand binding, and can make direct connection with experiments [1], for both protein enzymes and ribozymes [2]. Classical molecular dynamics (MD) simulations can analyse conformational behaviour and can allow predictions of activity in some cases [3]. While large-scale quantum chemical calculations are now possible on enzymes [4], combined quantum mechanics/molecular mechanics (QM/MM) methods remain a good, practical approach to model reactions in enzymes. QM/MM methods can also now be applied to free energy calculations of protein-ligand binding affinities, providing a route to test MM forcefields and explore the contribution of ligand polarization to binding [5]. QM/MM, atomistic and coarse-grained methods can be combined in practical multiscale protocols to tackle a wide range of length- and timescales, e.g to model drug metabolism in cytochrome P450 enzymes [6-8]. QM/MM modelling can also analyse problems relevant to biocatalysis, e.g. the chemoselectivity of alkene oxidation by bacterial CYPs [9].

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Computational Tools for Enzyme Design

Tore Brinck

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In this talk I will present some of the computational tools that we have developed for the redesign of enzymes to change their reaction specificity. The foundation of our approach is to mine the protein data bank (PDB) for structures with suitable size and shape of their active sites, and then optimize their binding and reactive properties for a new reaction by active-site mutations.[1–3] We use a combination of computational methods, ranging from automated docking to large-scale molecular dynamics simulations and quantum chemical calculations throughout the design process. The most recent contribution to the toolbox is a novel method for predicting contributions of individual residues to the catalytic efficiency of an enzymatic reaction by calculations using the fragment molecular orbital theory (FMO). [4,5] This is a computationally efficient method that allows the individual catalytic effects of all residues to be estimated by two calculations, one on the reactive state and one on the transition state. The method has been found to properly account also for the effects of residues that are not directly interacting with the substrate.

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The use of QM/MM for enzyme activity screening: applications in antibiotic resistance and evaluation of biocatalysts

Marc W. van der Kamp

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Hybrid quantum mechanical / molecular mechanical (QM/MM) modelling of enzyme reactions is now a mature field. [1] It has been used extensively to reveal the intricate detail of reaction mechanisms of many enzymes. Application of QM/MM as a tool for in silico screening of enzyme activity is still limited, however. Recently, we showed that it is now possible to use QM/MM umbrella sampling simulations in a largely automated way to predict whether a β-lactamase can break down carbapenems ('antibiotics of last resort'). [2] We have now extended this research to show that predictions of similar accuracy can be obtained with a rapid protocol, so that screening can be performed on a clinically relevant timescale.

Similar rapid protocols, combined with newly developed automated procedures for simulation setup (see: https://github.com/marcvanderkamp/enlighten), have been used to investigate enzyme activity and selectivity in two enzymes that can be used as biocatalysts. The first example is neuraminic acid lyase, an aldolase that has undergone directed evolution to develop complementary stereoselective catalysts. [3] Recently, we revealed the mechanism of the rate limiting step of the wild-type enzyme in great detail. [4] The E192N variant with broader substrate specificity was used for the directed evolution experiments that led to *R*- and *S*-selective biocatalysts. [3] Further, a co-crystal structure of the E192N variant with a substrate analogue revealed two possible binding modes of a substrate analogue. Here, we show how the automated setup and rapid QM/MM activity screening correctly predicts the stereoselectivity of the variants, and how binding mode and selectivity are related differently than originally hypothesised.

The last example relates to a newly identified and characterised Diels-Alderase (DAse), with high potential for exploitation as a biocatalyst. [5] X-ray crystallography revealed the likely active closed structure of the DAse. Docking of the substrate and product of the natural reaction indicates a few possible binding modes. Rapid QM/MM reaction modelling aided by the automated setup procedures identifies the most likely Michaelis complex and the detailed reaction mechanism of this novel DAse.

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Some Remarks on Activation and Relaxation Processes in Chemical Reactions

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Activation and relaxation processes have been studied in many different contexts, mainly with the aim of getting insights on the physical nature of the forces that triggers these processes. The Marcus equation [1] is one of the most successful analytic forms that provides nice ways to rationalize the activation energy and to characterize the transition state through the Hammond postulate [2] and the Brönsted coefficient [3]. The Marcus' equation involves the reaction energy and the so-called Marcus' intrinsic activation energy that describes the structural distorsion of reactants at the transition state. On the other hand, activation and relaxation processes can be analyzed from the perspective of the reaction force [4,5], in this context rational partitions of direct and reverse activation energies emerges naturally. The activation and relaxation energies are characterized in terms of reaction works defined at the different regions along the reaction coordinate, thus producing interesting insights on energy barriers and rate and equilibrium constants. In this presentation, different approaches to activation and relaxation processes are discussed in the light of results obtaned for different kind of chemical reactions.

Acknowledgements. Financial support from ICM, Milenio Grant Nº 120082, Nucleus Millennium CPC and FONDECYT through projects Nº 1130072 and 1141098 is acknowledged.

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Large versus small-scale modeling for TM centers in catalysis: is bigger always better?

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The two quandaries while modeling catalytically relevant systems concern: i) QC suitable to solve the problem, and ii) the type and size of selected models. Points i) and ii) are critically interdependent and reasonable balance must be obeyed between the model size and the level of QC. We discuss this issue based on selected examples taken from our studies on the performance of ammonia-modified Co(II) sites in zeolites with respect to the activation of NO.

Zeolites are periodic structures built of Si- or Al-O_4 tetrahedrons (T). Exchanged TM cations (active sites for deNOx and fine chemistry) are usually diluted, linked to one or two T blocks. Working models may range from local clusters to periodic models of a real framework while QC from correlated wave function methods (WF) to DFT/BO-MD. Here we will illustarte which properties, and what credible insights may be provided by modeling (Table 1).

Model	Method	Properties
Cluster (S)	CASPT2, CC	spin state energetics, wave function analysis
Cluster (S,M)	DFT	geometries, frequencies, electron density analysis
Periodic	DFT	Co siting (static), geometries, frequencies (harmonic)
	B-O MD	Co siting (dynamic), relative populations, frequencies

Table 1: Models (S-small, M-medium) and QC methods versus accessible properties

Co(II) sites with bound NO pose serious challenge for QC as they are non-innocent, showing many close-lying spin states, distinctly varying in properties. Their electronic structure and charge transfer properties requires exact correlated WF methods, applicable only for very small models.

On the other hand, the speciation of Co(II) siting for centers modified by ammonia and NO sorption calls either for extremely large clusters or periodic modeling (including MD runs) to asses stable structures and their relative populations.

Fig. 1 shows experimental IR spectrum taken for Co/MOR after designed pre-treatment by NH_3 and NO. Our modeling[1] aided its understanding: experiment pointed to two peaks due to 3 (a) or 5 (b) NH_3 co-ligands. QC revealed new, unforeseen features due to the spin change: 3 donor co-ligands after spin-flip imposed larger red-shift of NO than 5 co-ligands; MD still enriched band assignment.

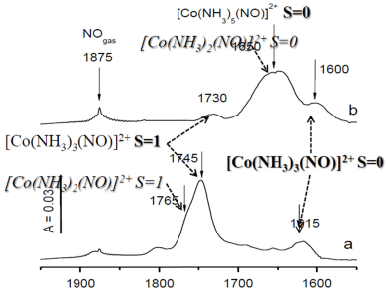

Figure 1: Re-interpretation of IR spectra for NO-CoMOR: EXP, **CASPT2/DFT**, *BO-MD*

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Tetrel bond as a preliminary stage of S_N2 reaction

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Some of noncovalent interactions are classified as σ-hole bonds, i.e. interactions between a covalently-bonded atom of Groups IV-VII acting as a Lewis acid and a Lewis base centre [1]. The Lewis acid centre is characterized by the positive electrostatic potential being the consequence of the loss of the electronic charge on the extension of one of the covalent bonds to the atom.

Such interactions where the Group IV atoms play a role of the Lewis acid [2], named as tetrel bonds [3,4], seem to be interesting since they often may be treated as initiating the S_N2 reaction [4]. The analysis of tetrel bonds show that they are characterized by similar properties as hydrogen bonds [4,5]. Very strong tetrel bonds are also observed which possess characteristics of covalent bonds, and where the tetrel centre may be treated as pentavalent, or at least pentacoordinated one. Fig. 1 presents two such systems linked by very strong tetrel bonds; similar systems were early classified by Martin as ¨frozen¨ transition states characterized by pentavalent centre [6]; they are the subject of this analysis.

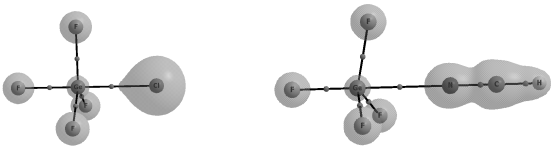

Figure 1: The molecular graphs of GeF_4-Cl^- and GeF_4-NCH; the $\nabla^2\rho(r)=0$ isosurfaces are presented.

Broad spectrum of tetrel bond interactions is analyzed with the use of QTAIM (Quantum Theory of Atoms in Molecules) approach [7] and other methods; related experimental systems are presented.

Acknowledgements. Financial support ; Eusko Jaurlaritza (Basque Government) - the Project No. IT588-13, and the Spanish Office of Scientific Research - Projects Nos. CTQ2012-38496-C05-01 and CTQ2015-67660-P.

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Reduction process of Pt(IV) complexes in presence of dGMP Computational DFT Study

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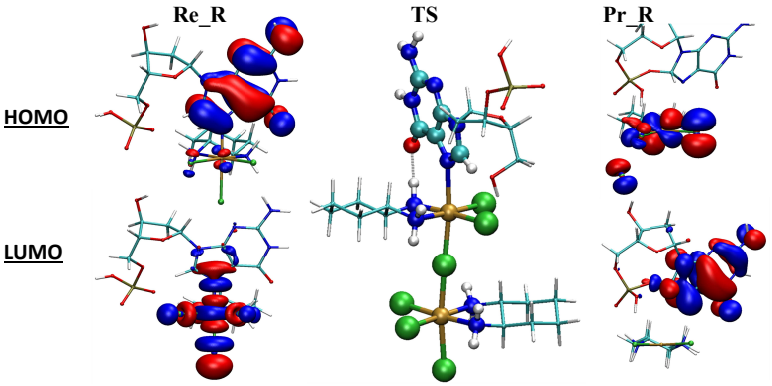
This contribution focuses on a reduction mechanism of $Pt^{IV}(DACH)Cl_4$ in the presence of dGMP. The first step represents a substitution reaction of a chloro-ligand by dGMP followed by a nucleophilic attack of phosphate or sugar oxygen to the C8 position of guanine. Subsequently, the reduction reaction occurs forming the $Pt^{II}(DACH)Cl_2$ complex. The whole process is completed by a hydrolysis. Two different pathways for the substitution reaction were examined: direct associative and Basolo-Pearson autocatalytic mechanism. Activation barriers were used for estimation of the rate constants (according to Eyring's TST) and compared with experimental values. Structures were optimized at the B3LYP-D3/6-31G(d) level with COSMO solvation model and single-point energetics was evaluated at the B3LYP-GD3BJ/6-311++G(2df,2pd) level with IEF-PCM/scaled-UAKS solvent approach. The rate determining step is the nucleophilic attack with a slightly faster performance in 3'-dGMP branch than in 5'-dGMP with the activation barrier of 21.1 and 20.4 kcal·mol^{-1} (experimental values are 23.8 and 23.2 kcal·mol^{-1}, respectively). The reduction reaction is connected with the electron flow from guanine. The whole redox process (substitution, reduction and hydrolysis reactions) is exoergic by 34 and 28 kcal·mol^{-1} for 5'-dGMP and 3'-dGMP, respectively.



Predicting electronic structure with correlated strongly orthogonal geminals

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Most computational chemistry methods cannot provide a uniformly accurate description of dynamic and static electron correlation. Geminal theories have been proposed as alternatives to one-electron Hartree-Fock method and, by relying on two-electron functions (geminals), they are potentially capable of accounting for static correlation effects. Imposing a strong orthogonality condition on geminals, and employing an antisymmetrized product of such geminals as an ansatz for a wavefunction, leads to a relatively simple optimization problem for the energy. This simplification, however, results in loosing a significant portion of electron correlation due to a lack of correlation among geminals.

Recently, we have proposed to correct the strongly orthogonal perfect-pairing geminal model by amending it with the correlation energy correction [1] derived from the extended random phase approximation (ERPA) [2]. On the examples of systems of diverse electronic structures we have shown that the resulting method greatly improves upon the noncorrelated strongly orthogonal geminal model. It recovers most of the electron correlation and it yields energy barrier heights of excellent accuracy. Thanks to a balanced treatment of static and dynamic correlation, the method stays reliable when one moves from systems dominated by dynamic electron correlation to those for which the static correlation comes into play [3,4].

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Addressing the issues of non-isotropy and non-additivity in the development of a quantum-chemistry-grounded polarizable molecular mechanics/dynamics potential. Applications to cation-ligand and ligand-receptor complexes

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We present results obtained in the recent years in the course of validations and applications of the polarizable molecule mechanics potential, SIBFA (Sum of Interactions Between Fragments Ab initio computed). We focus on the issues of separability, non-isotropy and non-additivity. Illustrative examples bear on the stacking interactions of cytosine and guanine, halogen bonding, and polyligated complexes of alkali metal cations. Applications are shortly presented on the impact of highly polarized water molecules in the vicinity of the dimetallic binding site of Superoxide Dismutase (SOD), and in the comparative interaction energies of inhibitors of a Zn-metalloenzyme. Newly emerging perspectives of applications of the massively parallel software, Tinker-HP, are mentioned.

Causality analysis of structural changes using vector signals based on quaternion formalism

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Molecular dynamics simulations (MD, QCMD, etc.) predict atomic/molecular motions, they do not contain, however, any explicit information about causal dependences of different structural changes between mobile parts of a molecular system. Post-processing of MD data should answer the question of whether the occurrence of an event in one part of the molecular system influences the probability of a subsequent event in another part of this system, delayed in time. If such influence exists we are talking about causal relations between these events, and the formal model is called the causality analysis (CA). An overview of a number of CA models for scalar-type signals drawn from MD simulations, developed in particular by us, is given in [1]. Recently we have developed a CA model for the time-dependent vector signals (positions, momenta, torques, etc…). For this purpose we use the quaternions algebra where MD signals are treated as time-dependent quaternions. The developed model is based on the autoregressive formalism:

$$\mathbb{x}(t) = \sum_{p=1}^{P} \mathbb{R}(p)\mathbb{x}(t - p\Delta t) + \mathbb{e}(t),$$

$$\mathbb{R}(p) = \begin{bmatrix} \mathrm{R}_1^1(p) & \cdots & \mathrm{R}_n^1(p) \\ \vdots & \ddots & \vdots \\ \mathrm{R}_1^n(p) & \cdots & \mathrm{R}_n^n(p) \end{bmatrix}$$

$$\mathbb{x}(t) = \begin{bmatrix} \vec{x}^1(t) \\ \vdots \\ \vec{x}^n(t) \end{bmatrix}, \quad \mathbb{e}(t) = \begin{bmatrix} \vec{e}^1(t) \\ \vdots \\ \vec{e}^n(t) \end{bmatrix},$$

Signal, **x**(t), is the sum of the causal part, dependent on the earlier signal values **x**(t−pΔt), and the stochastic part, **e**(t). R_j^i are rotation operators, capable also to change lengths of vectors. R_j^i should be parameterized - their quaternion representation reduces the number of fitting parameters and significantly accelerates computations. Analysis of **R**(p) allows detection of causal relations. The developed analytical formalism and its numerical implementation were validated using a simple molecular model – a benzene molecule in close proximity to a soft wall. More advanced molecular applications are being carried out.

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Hydrated electrons and Trojan horse radiotherapy Computational and experimental studies

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Ionizing radiation (IR) commonly used in radiotherapy of cancer is deleterious to the healthy tissues surrounding the tumor. The hypoxia of most solid cancer cells makes this situation even worse due to the so called oxygen effect, i.e. the fact that hypoxic cells are about three fold more resistant to IR than the normal oxic cells [1].

In order to improve the efficacy of radiotherapy radiosensitizers – substances that make cancer cells more susceptible to the IR-induced damage – should be employed. Modified nucleosides, which are incorporated into the genomic DNA during its biosynthesis and are sensitive to the product of water radiolysis, are good candidates for Trojan horse type radiosensitizers. Indeed, very recently we have demonstrated that substitution of any nucleobase with its brominated analogue leads to serious DNA damage induced by solvated electrons while under identical experimental conditions almost no damage has been observed to the native biopolymer [2].

In the current presentation we will show how DFT modeling along with negative ion photoelectron spectroscopy and radiation chemical studies coupled to MS spectroscopy enabled some uracil derivatives to be selected as new, potential radiosensitizers [3,4].

Moreover, various DNA degradation paths will be explored using 2-layer ONIOM (the ωB97XD functional with the 6-31++G(d,p) basis set is used for the high layer, while the Amber96 force field is employed for the real system) and a well-tempered QM/MM metadynamics (with three nucleotides in the QM part described at the M06-L/DZVP level) against 21 base pair double stranded DNA containing the adenine radical.

In summary, we will demonstrate that an efficient radiosensitizing nucleoside should have good electron acceptor properties. Furthermore, in order to assure effective dissociative electron attachment of the anion, the chemical bond holding together the substituent and nucleobase residue should be relatively weak. Finally, out of a number of possible processes triggered by the presence of nucleobase radical in DNA, its cyclization (exclusively for purine radicals) and β-elimination leading to single strand break seem to be most probable.

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Characterization of the Excited States of DNA Building Blocks: a Coupled Cluster Computational Study

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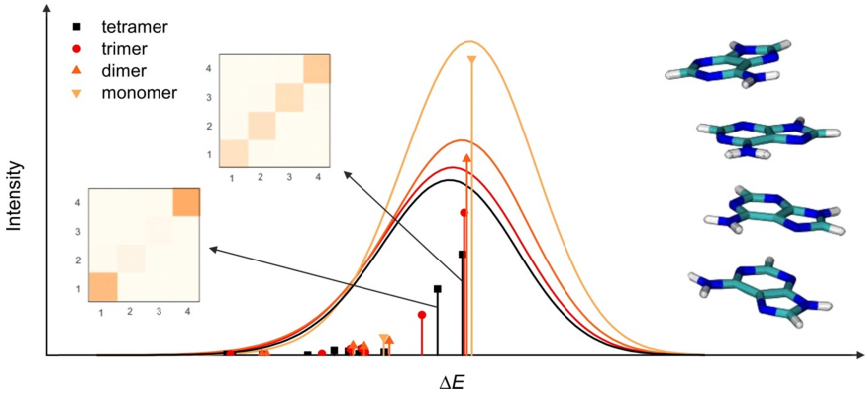
DNA building blocks consisting of up to four nucleobases are investigated with the EOM-CCSD and CC2-LR methods in two B-DNA-like arrangements of a poly-adenine:poly-thymine (poly-A:poly-T) system. Excitation energies and oscillator strengths are presented and the character of the excited states are discussed. Excited states of single-stranded poly-A systems are highly delocalized, especially the spectroscopically bright states, where delocalization over up to four fragments can be observed. In case of poly-T systems, the states are somewhat less delocalized, extending to maximally about three fragments. A single A:T Watson-Crick pair has highly localized states, while delocalization over base pairs can be observed for some excited states of the (A)2:(T)2 system, but intrastrand delocalization is more pronounced in this case, as well. As for the characteristics of the simulated UV absorption spectra, a significant decrease of intensity can be observed in case of single strands with increasing chain length; this is due to stacking interactions and is in accordance with previous results. On the other hand, the breaking of H-bonds between the two strands does not alter the spectral intensity considerably, it only causes a redshift of the absorption band, thus it is unable to explain the experimentally observed DNA hyperchromism on its own, and stacking interactions need to be considered for the description of this effect as well.



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From isolated DNA bases to Dickerson dodecamer: results of recent quantum-chemical calculations

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The results of the first comprehensive DFT study on the $d(A)_3\_d(T)_3$ and $d(G)_3\_d(C)_3$ nucleic acid duplexes are reported. The ability of mini-helixes to preserve the conformation of A- and B-DNA in the gas phase and under the influence of such factors as: solvent, uncompensated charge, and counter-ions was evaluated using M06-2X functional with 6-31G(d,p) basis set. The accuracy of the models was ascertained based on their ability to reproduce key structural features of natural A- and B-DNA. Analysis of the helicity suggests that the helical conformations adopt geometrical parameters which are close to those of the A- and B-DNA form.

The comparative analysis of parameters of isolated Watson–Crick base pairs versus A- and B-DNA conformations indicates the same tendency of base-pair polarization and hydration. Specifically, effects of polarization of nucleobases in continuum type dielectric medium mimicking water are stronger than those caused by the presence of backbone. Polar environment as well as the presence of counterions stabilizes duplexes, facilitating helix formation. Substantial conformational changes of nucleotides upon duplex formation decrease the binding energy. In spite of structural and energetic changes, the placement of a mini-helix into the gas phase does not lead to significant disruption of the structure. On the contrary, the duplex preserves its helicity and the strands remain bound.

The more detail investigation reveals the role of micro-hydration in structural adjustments of AT-containing fragment in B-DNA. It was studied at density functional theory B97-D/def2-SV(P) level. The $(dA{:}dT)_5$ complexes with 10 structural water molecules in minor groove and 15 water molecules in major groove were studied. The obtained network of hydrogen bonds in minor and major grooves revealed dependence between the grooves width and the types of water patterns. Depending on the minor groove width, the following patterns were observed: an inter-strand "water spine" similar to that of Dickerson water spine and inter-strand two-water bridges. Our calculations indicate that the features of A-tracts primarily are coupled with the specific locations of structural waters in the major and minor grooves. Network of structural waters in the major groove is more diverse than in the minor groove, which agrees with crystallographic data. As the major groove is wider, its water spine is enriched by structural water molecules which formed two- and three-water bridges and hydrogen bonded mainly with three hydrophilic centres. We suggest that formation of the specific water pattern in the major and minor grooves is the factor responsible for stabilization of conformations of A-tracts with narrowed minor groove, leading in turn to the strong intrinsic bending of A-tract in DNA in absence of any structural waters in grooves.

The described above results are compared with direct calculations of structural features of Dickerson DNA-dodecamer obtained at B97-D/def2-SV(P) level.

Photochemistry and photophysics of prebiotic precursors of nucleotides

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During the Archean eon (3.8-2.5 billion years ago), the Sun was much less luminous than today. However, the total amount of UV-light reaching the surface of early Earth was much larger due to lack of the ozone layer, and higher Solar activity in the UV range. This prolonged exposure to UV-light was probably a major selective factor at the early stages of abiogenesis that resulted in the remarkable photostability of naturally occurring nucleic acids, and peptides. UV-irradiation could also initiate prebiotically plausible reactions that would otherwise require significant amounts of heat or a specific catalyst. Thus for many decades UV-light has been considered as an important element of experiments targeted at syntheses of biomolecules, or their precursors, from simple feedstock molecules [1,2].

These synthetic reaction pathways often contain intermediates that had to accumulate in the environment over longer periods of time, and should evince resistance to different environmental conditions of early Earth including intense UV radiation.

During our theoretical studies on the photostability of two such intermediates: 2-aminooxazole (AMOX) and 4-aminoimidazole-5-carbonitrile (AICN)—appearing, respectively, in the Sutherland's synthesis of pyrimidine nucleotides and oligomerization of HCN leading to adenine suggested by Ferris—we observed an interesting mechanism of their non-radiative deactivation that could be described as electron-driven proton transfer (EDPT) [3,4]. More recently we observed this mechanism also in hydrated imidazole and adenine [5]. Although the ring-puckering processes, driven by $\pi\pi^*$ electronic states, remain usually the main deactivation channels, our non-adiabatic molecular dynamics simulations indicate a significant importance of the EDPT mechanism. The latter seems to occur quite commonly in the case of hydrated chromophores with low-lying $\pi\sigma^*$ electronic states. In such case, photoexcitation of the chromophore clustered with several water molecules leads to the ejection of an electron in the direction of the solvent molecules. The electron may be then followed by a proton from an amino, hydroxyl or imino group of the chromophore.

Subsequent proton transfers along H_2O wires result in the recombination of the migrating proton with the hydrated electron and eventually may enable photodeactivation via a conical intersection with the electronic ground-state (cf. Fig. 1).

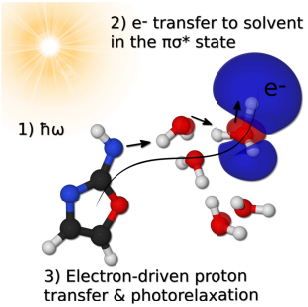

Fig. 1: Electron-driven proton transfer along H2O wires induces the formation of $\pi\sigma^*/S_0$ state crossing in 2-aminooxazole.

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Heterogeneous melting of methane confined in nano-pores

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It is well known that the nano-systems exhibit properties different from their bulk analogs. Typically, the phase diagrams are redefined because the position of coexistence lines depends on the size and shape of the nano-objects. This is related to the fact that nano-systems are characterized by high surface-to-volume ratio. The surface atoms are weakly bonded and their contribution to the latent heat is smaller. Consequently, the surface usually transforms at lower temperature and the whole transition may happen smoothly over a finite range of temperatures. This observation suggests that there is no temperature of melting (or any other structural change) in the conventional sense because the structural (phase) changes are gradual and phases are no longer distinguishable.

Here we discuss mechanism of methane melting [1-3] in confined nanoporous systems. The general analysis of methane in slit pores was already discussed by Miyahara and Gubbins [1]. In this paper, we emphasize the influence of structural heterogeneity on the mechanism of structural transformations. As an example, we discuss the differences in mechanism of melting of methane confined in two different structures: first, in 3 and 4 nm slit pores, then, in 2.8 nm square channels of SURMOF porous structure. Mechanism of melting transformation in both cases will be compared and the correlation between the nano-scale and heterogeneity will be emphasized and discussed.

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On the transferability of cocrystallization propensities

Piotr Cysewski

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Cocrystals taking advantage of newest opportunities of materials science are practically utilized in many branches of industry. This originates from the possibility of tuning properties of such multicomponent solids. Unfortunately it is not obvious to predict if a given pair of coformers can form molecular complexes in the solid state leading to homogeneous dispersion. This is why variety of screening procedures were formulated and validated. Nowadays [1], a new virtual cocrystal screening procedure was proposed, which takes advantage of the similarities between cocrystallization landscapes of different compounds. Assuming that affinities of coformers can be quantified by thermodynamics of mixing of liquid components under super cooled conditions, the quantitative rules were defined. First criterion requires high similarities expressed in terms of correlations between excess heat distributions obtained for a common set of conformers. Second criterion requires sufficiently high affinity of coformers, what means that estimated H_{mix} value should be within accepted range suggesting high probability of cocrystallization. Thus, it is not necessary to perform experimental cocrystallization of every pair of coformers since miscibility in the solid state of one compound can be transferred to another one. This was validated for aromatic or hetero-aromatic amides [1]. It was found that in this case selection of isonicotinamide can offer a very convenient comparative system since it is a common binary cocrystals constituent.

This approach seems to be general and can be applied for predicting of many other cocrystals formed by other groups of chemicals. For example in Fig 1. the efficacy of screening of dicarboxylic acids cocrystallization is documented. Many more examples will be presented during lecture.

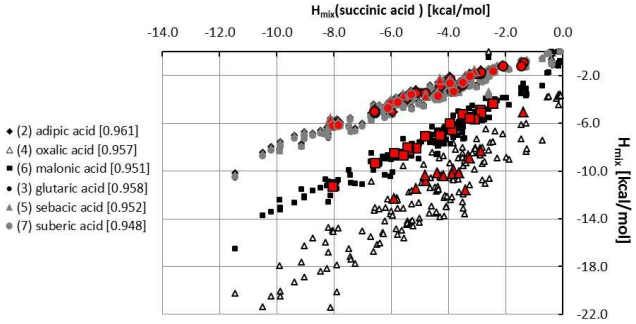

Figure 1: The correlation of H_{mix} distributions of selected dicarboxylic acids as a function of succinic acid (1) affinities for a common set of coformers. Red points characterize real cocrystals found in the CSD. Brackets in the legend contain the values of Spearman ranks (σ) quantifying correlations between distributions.

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FAMSEC/IQA-deduced origin of the relative stability of *cis*- and *trans*-2-butene isomers.

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Weinhold et al[1] have concluded from the NBO analysis that the H--H contact is involved in steric repulsion in *cis*-2-butene; this has been used to explain higher energy of this isomer relative to *trans*-2-butene. Matta et al[2] proposed different explanation from the QTAIM perspective; stability gained by the H•••H bonding interaction is cancelled mainly by the considerable destabilization of the ethylenic carbons.

This presentation will explain the relative stability of *cis*- and *trans*-2-butene using Fragment Attributed Molecular System Energy Change (FAMSEC)[3] and IQA schemes. Figure 1 shows that relative to *trans*-2-butene (i) the H--H and CH--HC molecular fragments $\mathcal{G}$ are stabilized in *cis*-2-butene, $E^{\mathcal{G}}_{\text{attr-loc}} < 0$, (ii) *cis*-2-butene is destabilized the most by H6C5=C7H8, $E^{\mathcal{G}}_{\text{attr-mol}} > 0$, and (ii) energy increase of H4 and H12 added the least to the higher energy of *cis*-2-butene. FAMSEC-based analysis showed that (i) in contrast to NBO analysis,[1] the H--H contact is not strained, showing several similar trends found for classical intramolecular H-bonding[3] and (ii) in line with QTAIM data,[2] middle part added most to the energy of *cis*-2-butene when it changed from *trans*-2-butene. The origin of computed energy contributions will be discussed in details.

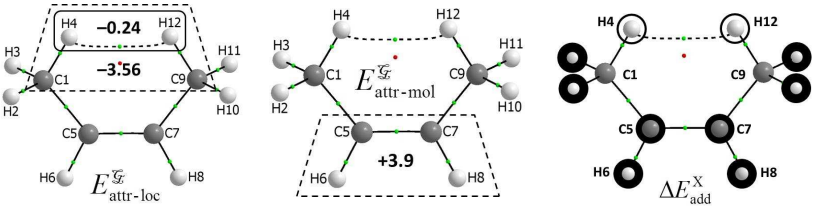

Figure 1: $E^{\mathcal{G}}_{\text{attr-loc}}$ and $E^{\mathcal{G}}_{\text{attr-mol}}$ describe a change in fragment's energy and energy contribution to *cis*-2-butene, respectively. $\Delta E^{X}_{\text{add}}$ is the change in additive energy of an atom – black rings represent a proportional increase in the energy. Values in kcal/mol from *trans*- to *cis*-2-butene.

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Monte-Carlo studies of two-dimensional polymer-solvent systems

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The structure of strictly two-dimensional athermal polymer films was studied by Monte Carlo lattice simulations using the cooperative motion algorithm (CMA) explicitly taking into account the solvent molecules [1]. The simulations were performed for a wide range of polymer chain length (from 16 to 1024 statistical segments) and concentration φ (from 0.0156 to 1). The results obtained for short chains were in good agreement with those of previous simulations [2]. For the longest chains some unexpected behavior in the dilute and semidilute regimes was found. A pronounced change in the concentration dependence of chain's size and shape was observed below a certain critical concentration (0.6 for the longest chains under consideration). Below this concentration longer chains became more extended. Behavior of single chain structure factors confirmed these changes in the fractal dimension of the chain as a function of the concentration. The observed phenomena are related to the excluded volume of solvent molecules leading to a modification of chain statistics in the vicinity of other chains, which effect is important in strictly two-dimensional systems [3].

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Modeling Real Devices

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It is now possible to treat up to 100,000 atoms with semiempirical molecular orbital (MO) theory.[1,2] This allows us to simulate charge transport through crystals,[3] in self-assembled monolayers (SAMs)[4] or across domain boundaries by using local ionization energy[5] and electron affinity[6,7] as the external potential in specific simulations of the quantum movement of the holes or electrons, respectively.[8] The charge-transport paths obtained with these techniques agree with each other and with calculations based on Landauer theory using the semiempirical wavefunction.[9]

Examples of simulations of crystals and SAMs will be given after a short outline of the theory and practice of MO calculations on very large systems.

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Modeling of low temperature adsorption of hydrogen in carbon nanopores

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Hydrogen is very likely the ultimate future of the energetic economy of the world: it is ubiquitous in the environment, it can be sustainably produced, and it holds the highest energy per unit mass of any fuel (except nuclear). If combusted, it produces only water. Therefore hydrogen, when used as energy vector, enters the natural water cycle of the Earth, with no impact on the planet's climate. Today the major issue of the widespread hydrogen use is its low mass and low volume storage, as the energy density of hydrogen gas is low. Physisorption in nanoporous materials seems to be the most promising way of storage, as it does not release much energy during adsorption and in principle do not require the energy input when hydrogen is released.

In this paper we will present the Grand Canonical Monte Carlo simulations of hydrogen adsorption in slit-shape carbon nanopores. Our calculations confirm the very controversial experimental results [1-3] showing that under confinement the density of hydrogen film adsorbed on the carbon wall exceeds that of the bulk liquid at low temperature and approaches that of solid hydrogen at extreme pressures. The densification of hydrogen is restricted to the layer in direct contact with the adsorbent, and does not depend significantly on the pore size (at least for the pores of the width from 0.6 to 3.0 nm) nor on the temperature (for 50 K< T < 180 K).

The simulations are confronted with the experimental isotherms of hydrogen adsorption in KOH - activated nanoporous carbons [3] obtained from biomass waste [4]. The numerical and experimental results are coherent and prove that the interaction between hydrogen molecules and carbon surface is strong enough to produce adsorbed layer with solid hydrogen density.

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Dihydrogen bonds in selected hydrogen storage materials – an insight from computational perspective

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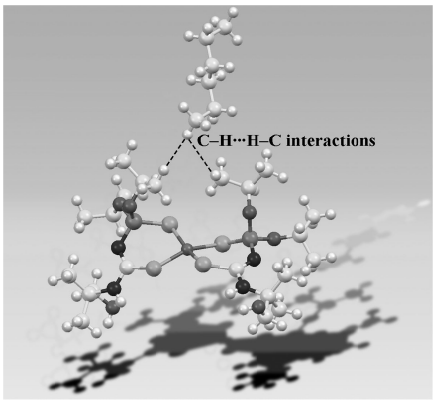
Polar dihydrogen bonds $X–H^{\delta+}\cdots{}^{-\delta}H–Y$ (X ≠ Y), known also as *proton-hydride* interactions, are considered nowadays as important class of non-covalent interactions. The N–H···H–B connections are of special interests due to their importance in hydrogen storage materials (as example one can provide the ammonia borane). In this contribution the nature of N–H···H–B bonding in ammonia borane will be at first place briefly discussed in terms of stability and reactivity. [1]



We have further analyzed the N–H···H–B interactions in the inorganic BN-analog of butane. Subsequently, the stability of mixed, organic-inorganic BN/CC derivatives will be characterized – such systems are obtained by simple substitution of the „BN" units in inorganic saturated systems by the isoelectronic „CC" fragments.[2a] At next stage we have extended the scope of our study by considering the homopolar *hydride–hydride* connections $B–H^{\delta-}\cdots{}^{-\delta}H–B$ in hydrogen storage materials which are traditionally considered in literature as destabilizing interactions.[3] In addition, we comparatively discuss the results on the nature of homopolar dihydrogen interactions C–H···H–C (and other non-covalent interactions) in the newly synthesized sterically crowded nickel complexes (see the Figure above) and have demonstrated the stabilizing role of "steric repulsion" (i.e. the sterically hindered complex with the bulky OiPr substituents being close to each other causes not only the deviation from planarity, but also superior stability over the other isomers where lack of "steric crowding" is noted).[2b]

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Plasma Surface interactions of mixed Be-W materials — theoretical study

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Beryllium and tungsten are considered as the main plasma-facing materials for the fusion reactor ITER and are being tested in the JET tokamak, tungsten for a divertor and beryllium as the first-wall material. [1] Computer simulations and theoretical calculations help to understand the underlying processes taking place during reactor's run since controlled experiments are often unavailable and represent essential input data needed for the modelling of erosion, transport and deposition in codes like WallDYN or ERO to get insight into such processes as BeD_x formation and sputtering. Presently, mixed Be/W surface erosion and morphology changes due to deuterium irradiation are studied by using molecular dynamics simulations as well as basic properties of these surfaces and sputtered molecules obtained by MD simulations and DFT tools are reported here.

Analytical bond-order potential(ABOP) [2, 3] was used to describe interactions in Be-W-D system during simulations of D bombardment of crystalline Be_2W and amorphous $Be_{12}W$ surfaces with impact energy range 10 to 30 eV. The sputtering yields, D implantation, D reflection and D depth profiles were analysed. The effect of the surface deuteration was observed in amorphous $Be_{12}W$. According to the bombardment simulations it affected the Be sputtering yields as well as D re-erosion and D reflection rates. However, this effect was almost negligible in Be_2W surface, which had a very structured form, its structure remaining unchanged over time during the simulations.

Surface binding energies as well as cohesive energies of these surfaces were calculated at DFT level of theory and compared with zero Kelvin MD ABOP optimization. The results showed that energies for Be vacancy are in good agreement, but SBE for W vacancies given by ABOP potential are distinctly higher than the corresponding DFT values.

In order to explain the inconsistency of MD simulations and experimental results concerning Be sputtering, the dissociation energies and thermodynamics of small beryllium deuterides were calculated and analysed using Gaussian G4 method. Subsequently, some possible reaction paths based on transition state theory were suggested and evaluated. Finally, the total electron-impact ionization cross sections and their corresponding reaction rates are presented here.

Acknowledgements. The MD simulations were performed on the LEO2 and LEO3 supercomputers at Innsbruck University.

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Theoretical modelling of selected model nanosystems

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Nowadays the advanced quantum chemical methods are very widely applied in study and design of new materials. First-principle methods enable one to study the electronic and geometrical structure of molecular systems as accurately as possible with modern computational effort. Moreover, using *ab initio* molecular dynamics methods, which calculate the forces exerted on atoms at each time step of simulation, one can calculate the evolution of atomic and electronic motions without assuming empirical parameters.

Very important and the most famous nanometer scale materials are fullerene. Although the number of papers devoted to fullerenes is large and growing rapidly, only a small proportion concerns fullerene oxides. Unlike the C_{60} molecule, C_{70} has five non-equivalent carbon atom types, which leads to eight non-equivalent C-C bonds. There are therefore at least eight *a priori* possible isomers of $C_{70}O$. A series of *ab initio* calculations have been carried out to determine the stability of different isomers of mono-oxides and mono-ozonides of C_{70}. On the basis of density functional theory method calculations and Born-Oppenheimer molecular dynamics will be presented a mechanism for the thermally induced dissociation of $C_{70}O_3$. It is interesting to note that the first to steps of studied process is identical with the general mechanism for ozonolysis of alkenes proposed by Criegee. Moreover, the results of molecular dynamics simulations of $C_{70}O_3$ doped with light molecules will be also discussed.

Carbon nanotubes (CNTs) play an important role in materials chemistry and are the subject of many experimental as well as theoretical studies. Open-ended single-walled carbon nanotubes (SWCNTs) are considered in many studies as a model system in nanoconfined chemistry. In the lecture will be presented analysis the noncovalent interaction between the cyclic formic acid dimer (FAD) and pyrene, which was used as a simple model for a CNT wall. Moreover, will be presented results for FAD in an armchair (6,6) SWCNT as an example for a smaller nanotube and in an armchair (8,8) SWCNT as an example for a larger one.

EMPIRE: New Dimensions for Materials Modeling

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The increasing role of quantum chemical calculations in drug and materials design has led to a demand for methods that can describe the electronic structures of large and complex systems. Semiempirical methods based on the neglect of diatomic differential overlap (NDDO) approximation (e.g., the MNDO, MNDO/d, AM1, AM1*, and PMx methods) are important representatives of such approaches. Many of these methods have been implemented in the massively parallel program EMPIRE, which makes the full quantum-mechanical treatment of systems containing 100,000 atoms or more possible [1].

Periodic boundary conditions (PBC) enable quantum chemical programs to treat condensed-phase systems, such as proteins in a periodic water box or solids. This allows molecular materials to be studied in their native environment, instead of comparing experimental bulk properties with gas-phase monomer calculations. For semiempirical methods, the most practical way of implementing PBC is the cyclic-cluster approach in which the system is approximated by a supercell and by imposing Born-von Karman boundary conditions. Using a large unit cell allows the calculation to be performed entirely in real space. This is easily affordable because of the generally low computational cost of NDDO calculations. The main advantage of this technique is that program features like the calculation of local properties or excited states are directly transferable from non-periodic calculations. EMPIRE, which was especially designed for calculations on systems with very many atoms, is also suitable for use on systems with very large unit cells (e.g., disordered and amorphous systems) [2].

EMPIRE can, for example, be used in combination with a classical molecular dynamics (MD) code to perform electronic structure calculations on snapshots from an MD run on a periodic system. A recent addition to EMPIRE makes it possible to perform MD calculations using semiempirical methods entirely. This enables the study of bond formation and breaking processes.

Configuration interaction (CI) calculations can be used to study the properties of biradicals and excited states. In CI calculations, the MOs for the ground state are calculated and then used unchanged to construct a series of further electronic configurations (microstates) that are mixed to form new electronic states. CI calculations give not only the ground state, but also the excited states that result from mixing the microstates used. They can therefore be used for the calculation of UV/vis spectra and second order hyperpolarizabilities etc. EMPIRE can perform CI calculations on systems containing 5,000 atoms or more.

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Chasing our limits, ytterbium dimer ground state calculations

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The great development of the experimental methods of modern molecular physics particularly in the field of ultra-cold gas physics, results in possibilities of obtaining of the previously unprecedented precision in the experimental measurements of the properties describing small molecular systems such as length scattering in the interatomic collisions, bond energies, polarizabilities, time of life in the resonant states and many others. As a consequence, the theoretical investigations get the unique chance of testing new theories and methodologies, that more and more accurately would describe the systems of the interest of chemistry and physics of cold molecules. Among many possible molecules, the ytterbium dimer was chosen. What makes Yb_2 molecule so interesting, is its usefulness for investigations of limitations of the non-Newtonian gravity. But for this purpose, quite accurate ytterbium dimer ground-state curve should be determined. During the lecture, systematic sequence of different computational approaches taking into account: electronic correlation, relativistic, finite nucleus size and DBOC corrections will be presented and analyzed. Additionally, the new scheme of relativistic two-component method will be presented.

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Targeted inhibition of the menin-MLL interaction for cancer therapies

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Menin is a protein that directly interacts with the Mixed Lineage Leukemia 1 (MLL1) and MLL2 histone methyltransferases. Menin also binds to MLL fusion proteins and this interaction is involved in acute leukemias with *MLL* translocations. Accumulating evidences suggest that the menin-MLL1/MLL2 interaction also plays an important role in solid tumors, including prostate cancer. Therefore, targeting the protein-protein interaction between menin and MLL1/MLL2 wild type or MLL fusion proteins with small molecules might result in novel therapeutics for acute leukemias and solid cancers.

We developed and optimized small molecules that specifically bind to menin with low nanomolar affinities and inhibit the menin-MLL interaction *in vitro* and in human cells. Substantial medicinal chemistry efforts combined with structure-based design led to the development of the menin-MLL inhibitors with optimized drug-like properties, including high selectivity and favorable pharmacokinetic profile. In MLL leukemia cells these compounds induce downregulation of *HOXA9* and *MEIS1* genes, associated with phenotypic changes, including inhibition of cell proliferation and induced differentiation. *In vivo* administration of these compounds results in a profound effect on MLL leukemia tumor burden and substantial extension in survival of MLL leukemia mice through on-target mechanism of action. Furthermore, the menin-MLL inhibitors we developed showed pronounced *in vitro* and *in vivo* efficacy in the metastatic castration resistant prostate cancer models through blocking the menin-MLL interaction. Overall, we demonstrate that pharmacologic inhibition of the menin-MLL interaction represents an effective treatment for MLL leukemias and a subset of solid tumors, providing a new potential therapeutic approach for hematologic and solid cancers. Efforts are undergoing to advance these compounds to clinical trials in cancer patients.

Design of fibroblast growth factor 1 for medical applications

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Fibroblast growth factor (FGF1) is a powerful mitogen exhibiting strong action on numerous different cell types. It is the only member of the FGF family that binds with high affinity to all isoforms of four FGF receptors (FGFR). Thus, FGF1 induced signaling leads to a wide range of cellular responses during development as well as in adult life, such as growth regulation, differentiation, survival, stress response, migration, and proliferation. Due to its angiogenic, osteogenic, neuroprotective and wound repair properties, this protein is a promising candidate for a therapeutic agent. However, low thermal stability, high sensitivity to proteases and thiol chemistry question medical applications of wild-type FGF1. Here, the engineering of FGF1 protein, involving the generation of variants tailored for regenerative medicine and for targeted therapy of FGFR-dependent cancer, will be presented.

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Targeting RING ubiquitin ligase with small molecule inhibitors

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RING E3 ubiquitin ligases belong to the class of novel valuable anti-cancer targets. Bmi1-Ring1B is a heterodimeric RING ligase which represents a central component of the Polycomb Repressive Complex 1 (PRC1) and ubiquitinates histone H2A on lysine K119. This epigenetic modification of H2A is required to maintain transcriptionally repressive state of many genes. Small molecule inhibitors of the Ring1B-Bmi1 E3 ligase activity have not been reported to date, but are highly desired as potential therapeutic agents targeting cancer stem cells. Employing fragment screening approach we identified small molecule inhibitors of Ring1B-Bmi1. Using medicinal chemistry, we developed potent compounds that bind to Ring1B-Bmi1 and inhibit E3 ubiquitin ligase activity with low micromolar affinities. In cells, Ring1B-Bmi1 inhibitors revealed robust downregulation of H2A K119 ubiquitination. Treatment of model cell lines enriched in leukemia initiating cells show that Ring1B-Bmi1 inhibitor block self-renewal and induce cellular differentiation. Our approach validates that RING ligases represent novel class of 'druggable' epigenetic targets.

Evaluating optimum pathways for potential prebiotic reactions

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Prebiotic chemistry refers to reactions occurring in natural environment before the advent of life on Earth. Life involves processes that establish a delicate balance of metabolism and genetic. There is a possibility of different chemical reactions that use various chemical elements widespread in the Universe. The studies using experimental techniques are aimed to provide details of processes that might be essential for prebiotic chemistry. There are still more questions than answers and computational chemistry provides efficient tools to augment experiments. The talk reviews our recent results, related to chemical reactions of small molecules, obtained using reliable computational chemistry methods. The studied phenomena could contribute towards understanding of possible prebiotic processes.

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Theoretical study on the electronic structure and properties of the PBI and tetrazole-derived polymers for fuel-cell applications

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While tetrazole has much lower basicity than imidazole and may not be fully protonated in the presence of phosphoric acid, the basicity of tetrazole groups can be increased by substituents. The main goal of the theoretical study presented here was to compare, based on the DFT calculation results, the effect of the polymer structure modifications on the geometry and the electronic structure of the PBI and tetrazole-derived polymers that can be potentially used as membranes in high temperature polymer electrolyte membrane fuel cells. Results indicate that the protonation energies can be strongly affected due to the changes in the molecular electrostatic potential distribution (Fig. 1). [1]

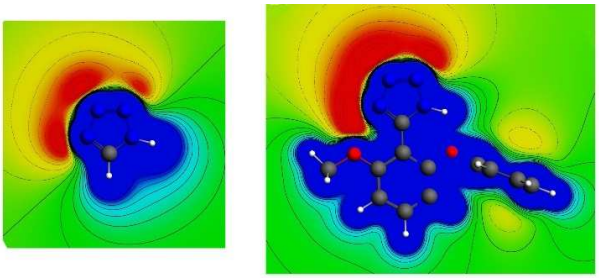

Figure 1: Effect of the ether groups on the molecular electrostatic potential of tetrazole; the contour maps are plotted in the plane containing heterocyclic ring; blue color corresponds to highest positive MEP and red to the lowest MEP values.

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New materials designed for absorption of non-steroidal anti-inflammatory drugs

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The adsorption of the non-steroidal antiinflammatory drugs (NSAIDs) from water environment is possible on the materials of properly designed properties. The main aim of the project is the preparation of such materials on the basis of biopolymers, namely chitosan, and their thorough analysis with respect to the interaction with NSAIDs. The procuration of the efficient and selective NSAIDs sorbents is crucial for various branches of science and technology, starting from the pollution detection and removal from the environment and finishing in nanomedicine and designing of the drug delivery systems. NSAIDs are available over-the-counter and are applied widely in chronic diseases and popular ailments such as headache, dismenorrhoea, muscle pains. Among their adverse effects the gastrointestinal problems, cardiovascular risk and erectile disfunction can be mentioned. NSAIDs themselves and their metabolites are discharged to the environment and can undergo the further photodegradation or other transformations that can possibly increase their hazardous action on living organisms. Despite their small amounts in environment (ppb) one does not know the precise influence of NSAIDs on the organisms assuming the long exposition times. Thus the current European Union regulations add diclofenac to the list of the most hazardous chemicals. Therefore, it is of particular importance to develop the methodology of NSAIDs detection and removal from the wastewaters and soils. Hence, the thorough knowledge of the mutual interaction of NSAIDs and their sorbents is compelling.

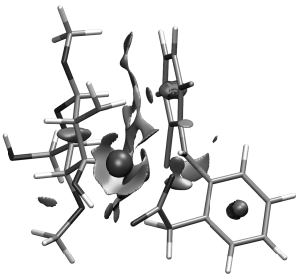

Figure 1: Diclofenac sodium-chitosan unit interaction.

The experimental part of the project covers the synthesis of various materials based on chitosan. It is supported by extensive computational study including the intramolecular interaction in chitosan chains, conformational study of chosen NSAIDs, their dimerization, and the influence of the chitosan modification on the mutual NSAID-biopolymer interaction.

Acknowledgements. Support from National Science Centre, Poland grant No. 2014/13/B/ST8/04342 is gratefully acknowledged. Calculations were performed in Wroclaw Centre for Networking and Supercomputing, Poznan Supercomputing and Networking Center and Academic Computer Centre Cyfronet AGH.

The influence of air pollutants on structure and function of lung surfactant

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Lung surfactants (LS) is a surface active monolayer which lines the air-water interface on the surface of alveoli. It is made of a mixture of lipids (mostly phospholipids) and proteins. Its' main function is the reduction of surface tension (γ) at the interface. On inspiration, this reduces the work needed to expand interfacial area, while on exhalation, it prevents alveolar collapse. LS also forms the first barrier preventing penetration of inhaled microorganisms and various pollutants into the organism.

In the present study we examine the interaction of LS with benzo[a]pyrene (BaP), a dangerous air pollutant from the family of polyaromatic hydrocarbons. BaP is produced during incomplete combustion of organic material, such as coal, wood, or automobile fuels, but also tobacco or foods. It is composed of five fused benzene rings. In human body BaP is metabolized to highly reactive benzopyrene diol epoxide, which can bind covalently to DNA and is thus strongly carcinogenic. BaP is hydrophobic, so during inhalation, on its' first contact with LS, it is accumulated in the monolayer. Such impurities can disturb proper functioning of lung surfactant, leading to respiratory disorders.

During tidal breathing, alveolar surface oscillates in the range of ±25-30%, which causes regular expansion and compression of LS monolayer. In this process γ changes from 30mN/m at full inhalation to 0mN/m at full exhalation. In this study we model the influence of BaP on this process by measuring experimental surface pressure-surface area isotherms and performing a series of molecular dynamics simulations for surface areas from 100 to 60Å^2 per lipid molecule. A 1:1 mixture of DPPC (dipalmitoylphosphatidylcholine) and POPC (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine) was used as a model of LS and 0,1 mole fraction of BaP was introduced to this system.

Our results show that initially BaP molecules are accumulated in the monolayer. For large areas (100-80Å^2/lipid) they reside parallel to the surface in the region corresponding to the boundary between lipids' heads and tails. For smaller areas (70-60Å^2/lipid) they are forced to adopt an orientation perpendicular to the surface and move to the head region. We show that addition of BaP has a condensing effect on the monolayer, which is reflected in lowering the values of γ and shifting the isotherm to smaller areas. A detailed molecular description of this process is obtained by analyzing structural properties of LS, such as radial distribution functions, density profiles, tilt angle and order parameters. We also observe that, for low surface areas, a significant number of BaP molecules cross the LS barrier and is released to the subphase.

Acknowledgements. Support from the Polish National Science Centre (grant no. UMO-2014/13/B/ST4/04995) is greatly acknowledged. Calculations were performed at the Academic Computer Centre CYFRONET.

Poster abstracts

in alphabetical order of the leading author's last name

Poster session A – June 27 (Monday)

Poster session B – June 28 (Tuesday)

DFT calculations vs. experiment for UV/vis spectroscopy: aryl guanidines and aryl guanidinium salts

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The hydrogen bond is a ubiquitous phenomenon in nature which is of great importance in functioning of living organisms and design of technologically interesting materials. Recently, an overview of a new discoveries in this research field has been published encompassing usage of hydrogen bonds from an anion binding to a construction of large polymeric structures[1]. To achieve an efficient binding of the anions, a various proton donating functional groups were used of which an guanidine functionality is especially interesting due to its acid/base properties[2]. Namely, specific Y-shaped structure of its protonated form allows efficient delocalization of the electrons which results in the high stability of its protonated form and therefore its unusually high basicity. It can be easily protonated and in this form, anion binding is assisted by coulombic charge-charge attractive forces, and therefore, we can expect that guanidines bind anions significantly stronger than akin urea, thioureas or amides.

Following our interest in the guanidine chemistry in the ground[3] and excited states[4], the UV/vis spectra of different guanidines (phenyl, napthyl, antracenyl, quinolinyl, antraquinonyl and cumarinyl) in acetonitrile have been simulated by TD-DFT calculations using the hybrid long range corrected CAM-B3LYP functional. Solvent effects were added by using polarizabile continuum model (PCM). Special emphasize was put to the effect of protonation on the excitation energies and absorption intensities. Also, the effect of complexation and specific interactions through hydrogen bonds with different anions (F^-, NO_3^-, $CF_3SO_3^-$, CH_3COO^- and $HCOO^-$) were examined. It was shown that the protonation of guanidine subunit shifts the low energy absorption bands toward higher energies (hypsochromic shift). The shift is reduced upon complexation with anions. In the phenylguanidine, λ_{max} of salts are clearly in a correlation to the anion basicity and strength of H-bonding. Observed changes are decreased upon increase of chromophoric size. To check the correctness of theoretical predictions, UV/vis spectra of available guanidine derivatives and their salts were measured and compared with the calculated data.

Acknowledgements. Support from the Croatian Science Foundation grant No. 9310 is acknowledged. The calculations were performed on the Isabella cluster (isabella.srce.hr) at the University of Zagreb Computing Center (SRCE).

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Combined molecular dynamics and differential transition state stabilisation approach to Kemp eliminase KE07 mutants

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Wroclaw University of Science and Technology

The general goal of this study is to examine a possibility of improvement of current enzyme design methodology. Our proposal is based on Differential Transition State Stabilisation (DTSS) concept [1,2], which, contrary to current enzyme design techniques, takes into account interactions between catalytic environment and both transition state and reactants. Focusing on electrostatic contribution to DTSS energy as its major component, a point charge and cumulative atomic multipole [3] representation of molecular charge distribution are used in this work. We test this approach on artificial Kemp eliminase KE07 and its seven mutants [4]. To take into account the dynamic aspect of protein environment, 30 ns molecular dynamics simulation of all of these enzymes has been performed, using produced trajectories to average the DTSS energy over an ensemble. Our findings suggest that qualitatively DTSS energy better agrees with experimental catalytic activities than standard transition state stabilisation. These findings provide a clue to find a better *de novo* catalyst design.

Acknowledgements. The work was financially supported by the Polish Ministry of Science and Higher Education from the funds for the studies in the years 2013-2016 as a part of the 'Diamond Grant' programme, research project no DI2012 016642. The partial support of the Wroclaw University of Technology financed by a statutory activity subsidy for Faculty of Chemistry by Polish Ministry of Science and Higher Education is acknowledged.

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Theoretical tools for designing conducting polymers pyrrole nad thiophene

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Theoretical simulations and analysis of materials allow to predict physical and chemical properties of materials reducing time and cost. Theoretical calculations and estimations allow to observe evolution of properties for both short-chain structures and long oligomers, but not for long-chain polymers. Therefore, these qualities have to be extrapolated. Observed modifications help to determine estimated parameters needed to design conducting polymers and influencing their properties. Presented study carried out for pyrrole and thiophene complexes can be easily compared with experimental results.

Ruthenium and iron metalloporphytrins as CO_2 hydrogenation catalysts

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The conversion of CO_2 to energy carrier molecules is possible only via application of specific catalysts that are able to activate inert molecule of carbon dioxide. In the presented study we investigate the mechanism of homogeneous hydrogenation of CO_2 with the heterocyclic catalysts – porphyrins [$Me^0C_{20}N_4H_{12}$]. The iron and ruthenium atoms have been selected as the centre of the macrocycle according to the literature suggestions [1].

Initial studies of the photochemical path suggest that the excited states of the investigated catalyst structure are not stable enough to bypass the thermodynamical barrier of the reaction suggested by the literature [1]. We have established the process of activation and coordination of the carbon dioxide with the catalyst molecule, which determines the later stages of the proposed reaction cycle. A few potential pathways were taken into consideration as was suggested by the models proposed in the literature [2].

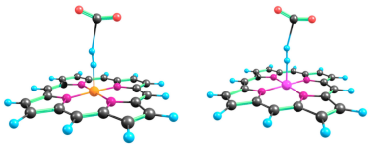

Figure 1: Similarity of the ruthenium (left) and iron (right) metalloporphyrin transition states of the CO_2 coordination via hydrogen molecule.

For the optimisation of the stationary states of the proposed reaction DFT mechanism application using ORCA code with PBE0 functional and Def2-TZVP basis set. A set of pathways was proposed and analysed as was suggested by the analysis of the literature. From the performed simulations we have derived that the coordination of the CO_2 can take place through the hydrogen molecule, an single hydrogen atom coordinated by the metallic centre or directly to the metallic centre of the porphyrin catalyst. As it was established, the chosen activation mode determines the optimal reaction pathway and the selectivity of the cycle that leads to the formic acid.

Acknowledgements. Calculations were carried out thanks to computational resources of Wrocław Centre of Networking and Supercomputing (WCSS), Academic Computer Centre in Gdansk (TASK).

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Cisplatin interaction with the tetrameric model of DNA, combined QM/MM MD Umbrella Sampling study

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Cisplatin is one of the most widely studied anticancer agents. To extend the knowledge of cisplatin binding mechanism, we present a combined QM/MM MD Umbrella sampling study of the reaction mechanism of hydrated cisplatin to two subsequent guanines located in the AGGT sequence.

We have found several structures of cisplatin interacting with both guanines in the AGGT sequence by hydrogen bonds between cisplatin hydrogens and oxygen and nitrogen atoms in guanine heterocycles. These adducts can be considered to be reactants for cross-linked structure formation. One of these structures is shown in Fig. 1. We have found the most energetically stable structures where cisplatin is bound to one of the guanines by a coordination covalent platinum–nitrogen bond.

The calculations were performed using the QMS program, [1] which couples QM and MM calculations performed in Gaussian and Amber software, respectively. QM part is calculated at the B3LYP/LanL2DZ level. [2] For MM parts, we have used the Amber force field. [3]

Currently we are looking for transition structures placed between the reactant and product structures. In future, we would like to calculate an dynamical QM/MM MD trajectory to obtain energetical profile of cisplatin binding to the AGGT sequence.

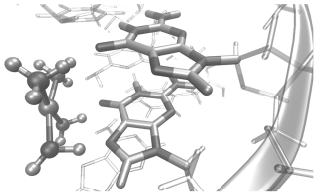

Figure 1: Reactant structure, cisplatin interacting with DNA by hydrogen bonds.

Acknowledgements. Computational resources were supplied by the Ministry of Education, Youth and Sports of the Czech Republic under the Projects CESNET (Project No. LM2015042) and CERIT-Scientific Cloud (Project No. LM2015085) provided within the program Projects of Large Research, Development and Innovations Infrastructures. This work is supported by the Czech Science Foundation (grant no. 16-06240S).

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Electrochemical oxidation of β-substituted thiophenes: a theoretical study

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Conducting polymers are valuable materials in the field of organic electronics. Due to the unusual electronic and optical properties [1], they find applications in the construction of dye-sensitized solar cells, organic light-emitting diodes and biosensors [2]. While the "synthetic metals" exhibit conductivities comparable to pure metals, they simultaneously retain certain favorable properties of polymers, such as processability, corrosion resistance and low density. The Nobel Prize in Chemistry, awarded in 2000 to Heeger, MacDiarmid, and Shirikawa, amplified interest in these materials.

An important group of conducting polymers that can be obtained *via* electropolymerization comprises the systems based on certain five-membered heterocyclic aromatic rings, such as thiophene and pyrrole. Anodic oxidation of the monomer molecule constitutes the first step in the electropolymerization process (see Fig. 1) [3]. Recently, we have investigated the propensity of various β-substituted pyrroles toward the oxidation [4]. In the current work, we focus on the selected thiophene derivatives incorporating both electron-donating and electron-withdrawing functional groups. Ionization energies and the electron spin density distributions in the reactants and products are examined by means of density functional theory. It is found that the amine group at the $\\beta$-position makes the oxidation process more favorable (IE=+7.40 eV) comparing with the unsubstituted thiophene (IE=+8.70 eV), while the nitro group has the opposite effect (IE=+9.52 eV).

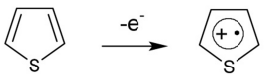

Figure 1: Oxidation of thiophene leads to the radical cation.

Acknowledgements. Calculations were performed at the Wroclaw Centre for Networking and Supercomputing.

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Removal of methylated arsenic pollutants with silicon doped graphene

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Pollution of drinking waters with arsenic (III and V) is a critical environmental problem because the exposure to methylated arsenic containing waters has been associated with alterations in the birth weight and gestational age, skin lesions, lung and bladder cancer, renal dysfunctions, among other effects on the human health [1,2]. Therefore, the development of new materials for the control and removal of methylarsenicals from the environment becomes an important effort. In recent years, graphene has emerged as a useful material for the development of new adsorbents for extraction of several organic and inorganic pollutants[3]. For the arsenic removal, intrinsic graphene has been determined with low efficiency from water sources; however, modified graphene composites have been reported as efficient adsorbent materials for the removal and/or detection of arsenic compounds [3]. In this framework, some recent works have reported the successful obtaining of silicon-doped graphene sheets (SiG), which showed an enhanced performance for the adsorption and sensing, and the Raman scattering of organic dyes [4]. Taking into account the rise of SiG and its potential applications, and the development of new adsorbent materials, we study by means of density functional theory calculations the removal of methylated arsenic pollutants using SiG sheets. The adsorption of trivalent and pentavalent forms of methylated arsenicals onto SiG was fully characterized from its geometrical parameters, energetic and binding properties. Solvent effects and molecular dynamics studies were also performed to account for the removal efficiency at water and ambient conditions.

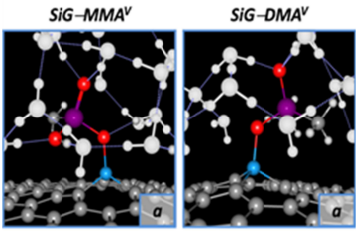

Figure 1. Trivalent and pentavalent methylarsenicals adsorbed onto SiG in an explicit water environment.

Acknowledgements. This work was supported by the projects FONDECYT/Postdoctorado no. 3140314, FONDECYT no. 1130072 and ICM grant no.120082.

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Docking and molecular dynamics study of CDK-2 and GSK3β enzymes inhibition

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Kinases are an important group of enzymes involved in regulation of cellular processes. The structural analysis of many of compared enzymes exhibit high similarity in terms of structure active sites of considered proteins, which often are related with control of completely different processes. For that group of proteins can be included Glycogen synthase kinase-3 (GSK-3β) [1] and Cyclin-dependent kinase 2 (CDK-2) [2], high similarity of this two enzymes is a source of large problems in developing of molecules with selective inhibition potential. The previous investigations show, that compounds classified as indirubin derivatives and analogs could exhibit such properties.

In this investigation, the group of indirubin derivative and analogs was analyzed as potential inhibitors of CDK-2 and GSK-3β proteins. Docking procedure was used to evaluate structures and binding affinity of complexes created by both proteins with ligand molecules. In the case of the ligand molecule characterized by highest differences in binding affinity towards both active sites, molecular dynamic procedure was applied. Molecular dynamics simulation of such complexes allows on simultaneous assessment of binding affinity and dynamic and structural properties of analyzed compound in the conformational space of active site. Calculations of the free energy were realized by Molecular Mechanic/Poisson-Boltzmann Surface Area (MM-PBSA) method [3].

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Theoretical study of the electronic structure and properties of lanthanide complexes with redox-active ligand, $[LnCp^*_2(SiMe_3N=)_2S]$ (Ln = Sm, Eu, Yb)

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Lanthanides are extensively used in the modern chemistry and material science, especially for creating the conductive, superconductive and magnetic materials, including the single molecule magnets. Many lanthanide complexes are characterized by high magnetic anisotropy, slow magnetization relaxation and intense luminescence [1]. This report presents the results of theoretical study of the electronic and magnetic properties of the lanthanide complexes, $[LnCp^*_2(SiMe_3N=)_2S]$ (**1**-**3**, Ln = Sm, Yb, Eu), synthesized recently by our colleges at the NIIC and NIOC SB RAS.

As in the case of lanthanides the relativistic effects are extremely important, the scalar relativistic DKH2 Hamiltonian and CASSCF or CASSCF/CASPT2 techniques with non-perturbative account of the spin-orbit interaction (SOC) have been employed. Active spaces for CASSCF calculations included 8 orbitals (seven 4f orbitals of Ln and SOMO of ligand) and n electrons (n = 6 for **1**, n = 7 for **2** and n = 14 for **3**). The g- and D-tensors for the pseudo-spin $\tilde{S}$ states of complexes **1** – **3**, their cations (**1**$^+$ - **3**$^+$) and atomic cations Ln^{3+} were calculated using the SINGLE-ANISO procedure. The temperature dependences of magnetic susceptibility of the polycrystalline samples of **1** - **3** were also calculated from the first principles. All calculations were performed using the MOLCAS suit of programs.

According to the calculations, all compounds under study (**1** – **3**) are the complexes of Ln^{3+} cation with radical anion, $[(Me_2SiN=)_2S]^{-\bullet}$. Magnetic properties of complexes **1**-**3** were analyzed using results of calculations and considering the exchange interactions (isotropic and asymmetric) between paramagnetic centers (cation Ln^{3+} and $[(Me_3SiN=)_2S]^{-\bullet}$). It was shown that complexes **1** and **2** are characterized by weak ferromagnetic exchange interaction ($J \leq 10$ cm^{-1}) between Ln^{3+} and radical anion. In turn, the exchange interaction in complex **3** is significantly larger and antiferromagnetic in nature. A substantial contribution of the temperature-independent paramagnetism (TIP) to the magnetic susceptibility of complexes **1** and **2** and their cations has been established. The accuracy of the calculations was analyzed using literature energy spectra of Ln^{3+} cations and NIR spectra of complexes **1** - **3**.

Acknowledgements. Support from Russian Science Foundation (project №16-13-10155) is acknowledged.

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Cooperativity in halogen-bonded haloamine tetramers

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Halomethane and haloamine tetramers (Fig. 1) were chosen as systems modelling the structural motif found in the crystal structure of anti α-bromoacetophenone oxime.[1]

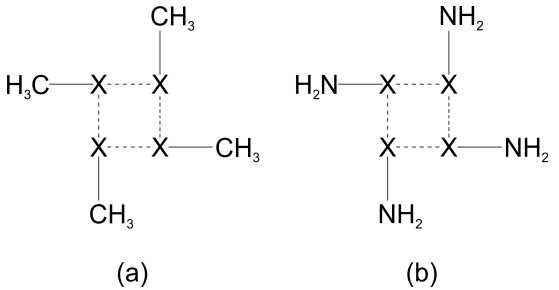

Figure 1: Schematic representation of model systems: halomethanes (a) and haloamines (b).

Kohn-Sham molecular orbital (MO) and energy decomposition analysis (EDA) in the framework of Ziegler-Rauk energy decomposition scheme [2,3] reveal a synergy that can be attributed to a charge-transfer interactions in the halogen-bonded tetramers.[4] Interestingly, halogen–halogen interaction in haloamines is the first known example of halogen bond for which the back-donation takes place. Additionally, for model systems, the direct relationship between the diminishment of accepting/donating orbitals energy gap, in a stepwise creation of a system from its subunits, and the cooperativity is found.[4]

Acknowledgements. The financial support from the Netherlands Organization of Scientific Research (NWO-CW, NWO-EW) is acknowledged. Calculations were performed in part at the Wroclaw Centre for Networking and Supercomputing.

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Polycalicenes: aromaticity induced by electric field

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A theoretical study of calicene and planar poly-1,7-[N]calicenes consisting of from 2-8 calicene units (see Fig. 1) was performed.

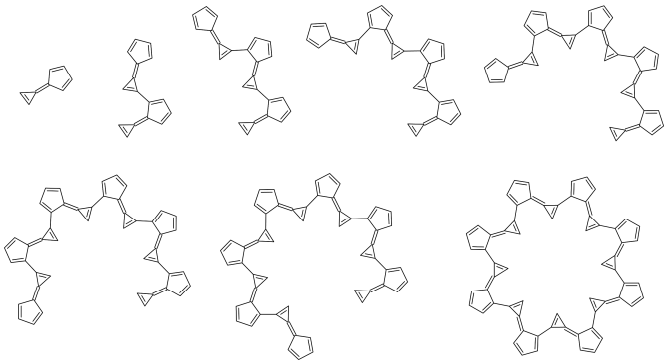

Figure 1: Calicene and planar poly-1,7-[N]calicenes (N ∈ [2,8]).

Local and global π-electron delocalization in these systems was investigated with use of aromaticity measures of different types. Systematic change of aromatic character is present along chains of connected calicene units. This phenomenon was compared with the properties of the isolated calicene molecule in external electric field, allowing to explain local aromaticity in polycalicenes in the context of calicene unit affected by its surroundings in polycalicene chains. Interrelations between local and global aromaticity in polycalicenes were established. Additionally, multidimensionality of the aromaticity phenomenon was studied with use of principal component analysis (PCA).

Acknowledgements. Calculations were performed in part at the Wroclaw Centre for Networking and Supercomputing.

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Modeling of adsorption of CO_2 in deformed pores of the MIL-53(Al)

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Carbon dioxide is a greenhouse gas implicated in global warming [1] but also used in existing hydrogen production processes [2]. Therefore, with a future world economy based on hydrogen as an energy vector, coupled with the recent commitments to the Kyoto Agreement whereby efforts must be made to reduce CO_2 emissions, there is a need for materials to efficiently capture and store CO_2 [3]. The MIL series of hybrid porous frameworks are candidates for the purpose of CO_2 adsorption. In particular, the breathing MIL-53 structures are of special interest because their adsorption properties could be modulated by applying external pressure to modify the geometry of pores [3, 4].

Molecular simulations were performed to predict CO_2 adsorption in flexible metal-organic frameworks. For this purpose, a generic force field was fitted to our experimental data to describe the non-bonded (electrostatic and Van der Waals) interactions between the CO_2 molecules and the large pore (lp) and narrow pore (np) forms of the MIL-53(Al) framework. With this force field validated, predictions of CO_2 uptake and enthalpy of adsorption at various applied external pressures were calculated. This was done by creating rigid intermediate structure forms between the lp and np shapes, and simulating adsorption of CO_2 in each of them.

In parallel, we have devised an experimental device in which it is possible to modulate the porosity of the MIL-53 material with the aid of external mechanical pressure. Equally, calorimetry experiments have been carried out on the unconstrained material to directly measure the adsorption enthalpies. This set of experiments allows a comparison of the isotherms on the material constrained to various mechanical pressures, and the enthalpies on the non-constrained material, with the results obtained by molecular simulation. This joint experimental-computational approach allows for us to further understand this flexible class of materials and is a way forward to understanding the possibility to optimize pore size for specific gas separations.

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The effect of pyridine X substituents on the kinetics of the hydration reactions of trans-$[Pt(NH_3)_2(pyr\text{-}X)Cl]^+$ complexes

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Platinum anticancer complexes are administered in its inactive (chlorinated) form and the activation by hydrolysis happens inside the cells. Affecting the speed of hydrolysis, as the rate determining step of subsequent reactions, is one of the ways to fine-tune the therapeutic effect.

We have studied the kinetics of the aquation reaction on the trans-$[Pt(NH_3)_2(pyr\text{-}X)Cl]^+$ complexes with the pyrimidine substituent X being OH, Cl, F, Br, NO_2, NH_2, SH, CH_3, CCH and several other groups. Reaction energy profiles, atomic charges, electron densities at bond critical points and ligand binding energies were calculated. All the structures along the reaction pathway were fully optimized using B3LYP/MWB-60(f)/6-31+G* method. Single point energies and molecular properties were evaluated using B3LYP/MWB-60(2fg)/6-311++G (2df,2pd) method both *in vacuo* and in implicit water environment (PCM method). To prove the findings, chosen complexes were studied adding empirical dispersion model GD3BJ as well as using the hybrid functional M06-2X.

The substituent ligand influences electron density on the pyridine ring and thus the electron donating ability of the heterocyclic nitrogen. Through the trans-effect the charge and binding energy of the Cl ligand are affected leading to the difference in the rate of the hydrolysis reaction of several orders of magnitude. On the opposite sides of the scale lie NO_2 and NH_2 ligands, as the least and most promoting substituents, respectively, leading to more than 1000 times diference in the rate of the hydration reaction *in vacuo*. The implicit water environment in general dampens all interactions, lowering the difference in the reaction rate between the studied complexes about one order of magnitude.

Acknowledgements. This work is supported by the Czech Science Foundation (grant No. 208/12/0622, No. 401/16/06240S). The access to computing and storage facilities of the National Grid Infrastructure MetaCentrum (grant No. LM2010005) is appreciated.

Exploring conformational space of bifunctional salen-cobalt(III) catalysts for CO2/epoxide copolymerization

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Copolymerization of CO_2 with epoxides represents so-called green polymerization processes which are of great importance as a possible large-scale utilization of CO_2 in chemical synthesis [1]. One of the most promising generation of catalysts, are bifunctional systems that combine in one structure organometallic complexes (electrophilic part) with quaternary amonium salts (nucleophilic part). Both parts play significant role during formation and growth of polymer chain [2]. The most successful examples involve Co(III) complexes with salen-based ligands incorporating ammonium salts connected to the salen core by aliphatic linkage ("chains"). These systems exhibit high catalytic activity, as well as high selectivity towards the transformation of CO_2 into biodegradeble policarbonates, [3]

Bifunctional Co(III)-salen catalysts are challenging for theoretical, mechanistic studies due to their size (hundreds of atoms) as well as high conformational flexibility. Extensive conformational search seems to be crucial for finding chemically significant minima of possible intermediates in studied catalytic cycles.

Hereby, we propose computational protocol employed in the search for viable energetic minima. It combines fast, and yet satisfyingly accurate, semiempirical PM7 method with DFT calculations. The first step involves PM7 evaluation of hundreds of thousands geometries resulting from extensive conformational search, combining various approaches. Further, selected structures are used in molecular dynamics simulations on the semiempirical level. Finally, two-step assessment of the structures on the DFT level is carried out: (i) geometry optimization in smaller basis set (frozen core, TZP/DZP); (ii) energy calculations in larger (all electron, TZP) basis set.

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Theoretical and experimental investigations of compounds with cycle-arranged hydrogen bridges

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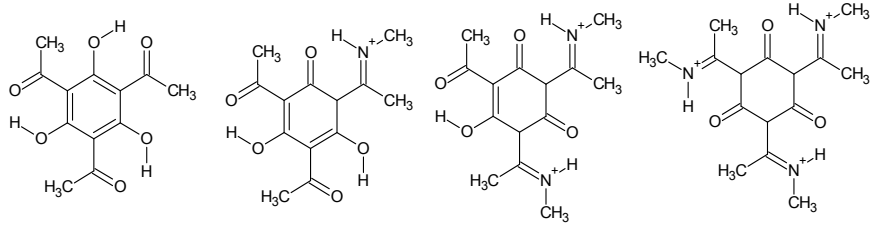
This report presents the studies of cycle-arranged hydrogen bridges in tris-hydroxy Schiff bases (Scheme). The studies have been completed by experimental (IR, Raman, IINS and X-ray) and computational (CPMD, CASTEP and DFT) methods. Significant dynamics of proton in hydrogen bridges of the studied compounds has been shown. The influence of substitutes on the hydrogen bonding strength has been examined. The interpretation of the studied IR, Raman and IINS spectra has been performed on the basis of the isotopic effect as well as PED analysis.



1 **2** **3** **4**

Scheme. Chemical structures of studied compounds: 1,1′,1″-(2,4,6-trihydroxybenzene-1,3,5-triyl)triethanone (**1**), (1*E*)-1-(3,5-diacetyl-2,4-dihydroxy-6-oxocyclohexa-2,4-dien-1-yl)-N-methylethaniminium (**2**), (1*E*,1′*E*)-1,1′-(5-acetyl-4-hydroxy-2,6-dioxocyclohex-4-ene-1,3-diyl)bis(N-methylethaniminium) (**3**) and (*E*,*E*,*E*)-(2,4,6-trioxocyclohexane-1,3,5-triyl)tris(N-methylmethaniminium) (**4**).

Adsorption of amphiphilic comb-like macromolecules on interfaces

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Comb-like amphiphilic macromolecules consist of a backbone and side groups, which interact specifically with each other and with different solvents or with different parts of heterogeneous surfaces. Being placed on the boundary between two phases (Fig. 1), such macromolecules can take a variety of conformations. In this case, structure of the macromolecular chain and presence of an interface as spatial constrains are the key factors influencing conformation behavior of a macromolecule. Thus, comb-like amphiphilic macromolecules are prospective for application in controlled polymer systems of different kind.

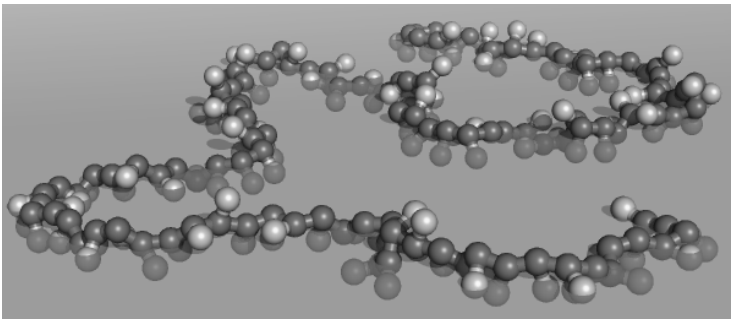

Figure 1: Snapshot of an amphiphilic comb-like macromolecule on a liquid-liquid interface.

In our work, we studied self-organization and conformational behavior of a single amphiphilic comb-like macromolecule on liquid-solid and liquid-liquid interfaces. The solid phase was represented by a patterned surface with areas, interacting with backbone and side groups of the macromolecule in different way. Liquid phases were selective solvents for backbone and side groups. Varying parameters of interaction between backbone, side groups and the surrounding media, we obtained a number of conformations and investigated transitions between them.

Computer simulations were carried out by means of molecular dynamics technique using LAMMPS program package.

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New semiempirical approach to predict kinetics of multistep chemical reactions: application in chemistry and biology

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We propose an efficient computational approach to analyze multi-step chemical reactions. The applied protocol includes a generation of multistep Gibbs free energy reaction profile for the transformations of the reagents to end-products. It is followed by evaluation of rate constants, creation of the corresponding kinetic equations and subsequent solution of the resulting equations. The mono- and bimolecular rate constants k_{uni} and k_{bi} are calculated using equations (1) and (2) and used to predict the rate of reactants decay and the rate of accumulation of products and intermediates. For this purpose, the system of differential equations having the following general form (3) is solved by using a Mathcad 15 program.

$$k_{uni} = \frac{k \cdot T}{h} \cdot e^{-\frac{\Delta G_i^{\neq}}{RT}} \quad (s^{-1}) \tag{1}$$

$$k_{bi} = \frac{k \cdot T}{h} \cdot e^{-\frac{\Delta G_i^{\neq}}{RT}} \cdot \left(\frac{1}{c}\right) \quad (L \cdot mol^{-1} \cdot s^{-1}) \tag{2}$$

$$\sum_i \frac{dn_i}{dt} = \sum_{\substack{j \\ (j \neq i)}} k_{ji} n_j - n_i \sum_{\substack{l \\ (l \neq i)}} k_{il}$$
$$\sum_i \frac{dn_i}{dt} = \sum_{\substack{j \\ (j,m \neq i)}} k_{ji} n_j n_m - n_i \sum_{\substack{l \\ (l,o \neq i)}} k_{il} n_o \tag{3}$$

This procedure is semi-empirical since to obtain the best accuracy it needs a limited amount of experimental data to accomplish a fitting. The procedure allows the experimentally-determined results to be significantly augmented by addition of computationally predicted data. Using this approach the kinetics of the reactions can be monitored such that one has an opportunity to trace decay or an accumulation for virtually any reactive species. It allows to analyze the kinetics of any step of the multistep chemical reaction and to predict intermediates even if one is not able to detect them experimentally.

This procedure was successfully applied to the prediction of kinetics of alkaline hydrolysis of such energetic materials as trinitrotoluene, dinitrotoluene, dinitroanisole, and hexahydro-1,3,5-trinitro-1,3,5-triazine, as well as to study interaction between 2′-deoxycytidine, 2′-deoxyguanosine, 2′-deoxyadenosine and *cis*-2-butene-1,4-dial, a reactive metabolite of furan.

Assessing the accuracy of various *ab initio* methods for geometries and excitation energies of retinal chromophore minimal model by comparison with CASPT3 results

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Retinal is a chromophore of proteins involved in light perception and active transport of ions. [1] It is covalently linked with the protein through protonated iminium moiety, thus it is commonly called retinal protonated Schiff base (RPSB, or simply PSB). Due to remarkable rate and efficiency of retinal photoisomerization process, theoretical chemistry and molecular modelling approaches are the most important and reliable tools to investigate virtually all retinal properties.

In the present work, we investigate the minimal model of retinal (PSB3). Although it is significantly truncated compared to the full model (Figure 1), it is extensively used to gain insight into qualitative properties and photoisomerization mechanism . [2-3] Its small size and possessing the most important qualitative retinal features make it a perfect model for our high-level of theory calculations.

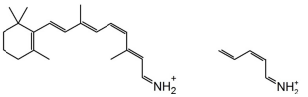

Figure 1: Comparison of full and minimal retinal models.

The first aim of the present work was to characterize performance of various *ab initio* methods, e.g. CC2, MP2, CASSCF, CASPT2 in describing the ground-state geometry of the PSB3 model in reference to the CASPT3 and CCSD(T) methods. Secondly, it was to assess performance of CASPT2//CASSCF protocol (extensively used for retinal properties investigation) in application to excitation energies against the CASPT3 results. To the best of out knowledge, it was the first attempt to investigate molecular properties of retinal model with CASPT3 method. Moreover, PSB3 system is probably the largest system for which geometry was optimized at this level of theory.

According to our results, only the CASPT3 method provides geometry in nearly perfect agreement with the CCSD(T) one. The resulting CASPT2 error in excitation energy is up to 0.16 eV and only 0.06 eV for the transitions to the S_1 and S_2 states, respectively.

Acknowledgements. This work was financed by Wroclaw Research Centre EIT+ under the project BIOMED "Biotechnologies and advanced medical technologies"' (POIG 01.01.02-02-003/08) financed from European Development Fund Operational Programme Innovative Economy 1.1.2. Calculations were performed at the Wroclaw Centre for Networking and Supercomputing and Academic Computer Centre Cyfronet AGH in Krakow.

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Computational studies of Iridium(III) complexes: towards organic light emitting diode (OLED)

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The research in the organic light-emitting diodes (OLEDs) has become one of the most interesting topics in the field of chemistry, physics and material science. Iridium (III) complexes possessing good thermal stabilities, microsecond excited-state lifetimes, and high luminescence efficiencies have been used as the emitting layers in organic diodes [1]. Rationally tuning the emission energy of Ir (III) complexes to range from blue to red light over the entire visible range is a key step for the realizing of full-color displays and large-area solid-state lighting in OLED fields.

We have undertaken computational studies have been carried out with the aim of better understanding the photophysical properties of such metal complexes. The electronic structures and phosphorescent properties of a series of iridium(III) complexes have been investigated by using density functional theory (DFT) and time-dependent density functional theory (TDDFT) methods, as described by Srinivasan et al. and Trani et al. [2,3]. The frontier orbital energies HOMO and LUMO and energy gaps between HOMO and LUMO have been calculated. Previous studies indicated that the energy gap between molecular orbitals is a critical parameter in determining molecular electrical transport properties because it is a measure of electron conductivity [4].

In summary, a new homologous series of Iridium(III) complexes has been synthesized and theoretical calculation were carried out to analyze their emission energies and predict the kinetic stability. The obtained results show that some complexes can be considered as potential candidate of blue-emitting material and indicated the substituents impact the optical properties with both electronic and geometric effects.

Acknowledgements: This research was supported in part by PL-Grid Infrastructure.

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Catalytic hydrogenation reaction of HCN

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Based on the experimentally determined network of hydrogenation processes of hydrogen cyanide (HCN) into methylamine (CH_3NH_2) that is, showing the possibility to hydrogenate a C≡N bond until full saturation in interstellar conditions[1], we study the mechanisms of hydrogenation of precursors needed in the amino acids formation reactions that takes place in the interstellar medium. The relevance of this combined approach both experimental and theoretical is that involves reactions occurring in gas-phase and at the surface of either icy particles, these latter acting as effective catalysts involving proton/electron transfer, nucleophilic/electrophilic attacks.

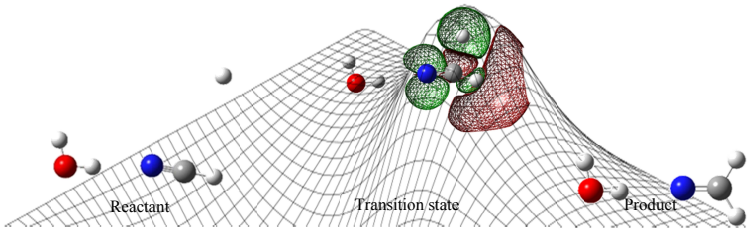

Figure 1: Reactants, transition state and product of hydrogenation of HCN using water as a catalyst

The study is based upon the reaction force analysis[2] and takes advantage of the partition of the reaction coordinate into reaction regions where different mechanisms might be taking place. A complete characterization of transition states and the determination of the physical nature of potential energy barriers in terms of the predominance of structural or electronic effects and the specific interactions driving the reaction mechanisms will be produced.

Acknowledgements. This work was supported by FONDECYT through project N° 1141098 and financial support from ICM through project N° 120082.

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Insights into stability and folding of GNRA and UNCG tetraloops revealed by microsecond molecular dynamics and well-tempered metadynamics

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The folding/un-folding pathway of two most biologically important RNA tetraloops (5'-GNRA-3' and 5'-UNCG-3') had been investigated at the molecular level using state-of-the-art all atom standard Molecular Dynamics (MD) and biased Well Tempered Metadynamics (WTMetaD) simulation. The Collective Variable (CV) based WTMetaD simulation provides useful information on the folding/un-folding mechanism for both the hairpins.

The unfolding and refolding mechanisms of the GNRA TL observed by well-tempered metadynamics agree with the (reverse) folding mechanism suggested by recent replica exchange molecular dynamics simulations[1]. The orientation of the glycosidic bond of the G_{L4} nucleobase is critical for the UUCG TL folding pathway, and our data strongly support the hypothesis that G_{L4}-*anti* forms a kinetic trap along the folding pathway.

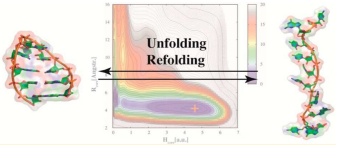

Figure 1. Free energy surface of folding/un-folding pathway for UUCG tetraloop.

Along with giving useful insight, our study also demonstrates that using only a few CVs apparently does not capture the full folding landscape of the RNA TLs. Despite using several sophisticated selections of the CVs, formation of the loop appears to remain a hidden variable, preventing a full convergence of the metadynamics. Finally, our data suggest that the unfolded state might be overstabilized by the force fields used.

Acknowledgements. This work was supported by grant P208/12/1878 (J.S., M.O., P.K.) from the Czech Science Foundation. This work was also part of the Research Project RVO:61388963 of the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, and was supported by Czech Science Foundation (P208/12/G016). (S.H., P.H.).

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Investigation on esters with imidazo[1,5-c]quinazoline ring by quantum computational calculations

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Compounds containing imidazoquinoline and imidazoquinazoline moieties have been reported to possess interesting properties. Until now, more than one hundred of imidazo[1,5-c]quinoline-2-one derivatives have been described in the literature, of which at least half show biological activity in various aspects, e.g. anticancer, antiviral, antibacterial or anticonvulsant [1]. Furthermore, their decomposition temperature is often over 400 °C, resulting in a wide field of research in the context of obtaining heat-resistant polymers.

1-phenyl-2H,6H-imidazo[1,5-c]quinazoline-3,5-dione reacts with ethyl bromoacetate under mild conditions to give 2-(etoxycarbonylmethyl)-1-phenyl-6H-imidazo[1,5-c]quinazoline-3,5-dione and next 2,6-bis(etoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione. The products were isolated at high yield and identified on the basis of IR, ^{1}H and ^{13}C NMR, UV spectroscopy and X-ray crystallography.

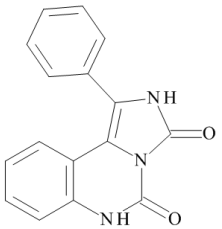

Figure 1: 1-phenyl-2H,6H-imidazo[1,5-c]quinazoline-3,5-dione half-structural formula

Diester can be presented by 16 possible pair of enantiomers. Only one pair of them is the most stable and crystallized, which shown crystallographic research. Based on of quantum-mechanical modelling with the use of DFT method, it was explained which conformers of mono and diester and why were formed. Theoretically there is 16 possible isomers of monoester, but after optimization are obtained two pairs of isomers only. Based on these results, the further modelling clearly indicates that four pairs of the diester conformers can be formed, which are able to mutual transformations. Therefore, finally only one pair of diester enantiomers crystallizes. Furthermore, a packing of diester molecules in the unit cell was explained.

Acknowledgements. The computational grant G49-12 from the Interdisciplinary Centre for Mathematical and Computational Modelling (ICM) at the Warsaw University is gratefully acknowledged.

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DFT calculations of bishydroxyakylated derivatives of 1-phenyl-2H,6H-imidazo[1,5-c]quinazoline-3,5-dione

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Based on DFT calculations of 2,6-bis(etoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoli-ne-3,5-dione, packing of diester molecules in the unit cell depending on the type of solvent was explained. X-ray crystallography investigations shown that the use of chloroform to 2,6-bis(etoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione crystallization causes formation only single four enantiomers (two identical pairs) in the unit cell. In turn, the crystallization of diester from benzene results in formation four pairs of two enantiomers in the unit cell. They are the same enantiomers as in the case of crystallization from chloroform.

As X-ray diffraction analysis shows (Figure 1), the imidazoquinazoline rings of diester enantiomers are parallel to each other and are set exactly above each other, however, they are rotated by 180° in the plane.

Quantum-mechanical calculations revealed the overlap between HOMO and LUMO molecular orbitals of the two enantiomers.

Electron transfer is possible due to the difference in the charge distribution in imidazoquinazoline rings of the enantiomers. For the HOMO orbitals, the electrons belonging to equivalent bonds (quinazoline ring edge of condensation), however, to two different molecules but from equivalent bonds (quinazoline ring edge of condensation) are overlapping, or better to say: fusing.

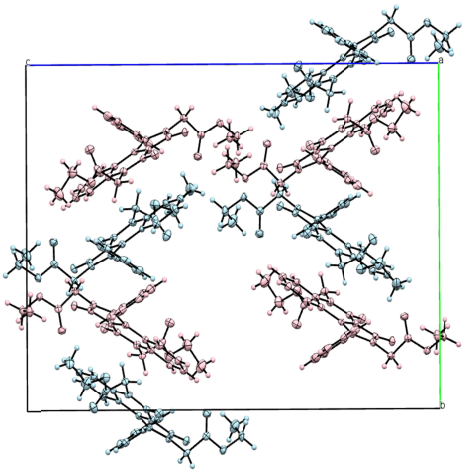

Figure 1: Unit cell of crystallographic network of 1-phenyl-2,6-bis(ethoxycarbonylmehtyl)imidazo[1,5-c]quinazoline-3,5-

The formation of charge-transfer complexes explains the relative position of the 2,6-bis(etoxycarbonylmethyl)-1-phenylimidazo[1,5-c]quinazoline-3,5-dione enantiomers in the crystal lattice.

Acknowledgements. The computational grant G49-12 from the Interdisciplinary Centre for Mathematical and Computational Modelling (ICM) at the Warsaw University is gratefully acknowledged.

Comparison of antiradical activity of luteolin and apigenin

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In our previous paper [1] we concentrated on antiradical activity of some chosen flavonoids. We established that generally flavonols were much more active than flavones. However, there was an exception, which was lutein. Lutein (5,7,3',4' – tetra hydroxyl flavone) exhibits activity comparable to that of flavonols, whereas lack of one hydroxyl group in its structure destroys this activity by several orders of magnitude. If the missing hydroxyl group is at position 3' we get apigenin which is much weaker antioxidant. If the structure of luteolin is changed by methoxylation at one of the positions 3' or 4' we get chrysoeriol or diosmetin, respectively. The both derivatives of luteolin structure are also much weaker antioxidants.

In the present study we compare hydrogen abstraction scheme from hydroxylated positions of flavones' ring B for luteolin, apigenin, chrysoeriol, diosmetin and 5,7,3'-trihydroxy flavone. The theoretical model is based on [1,2] taking into account reorganization energy. Computations are carried out using Gaussian09 software [3]. We use UB3LYP/6-31G(d,p) model chemistry and take into account a continuous polarizable dielectric (PCM SCRF) solvation model of the studied structures in methanol-water reaction medium. The experimentally carried out kinetic study of antiradical activity of: luteolin, apigenin, chrysoeriol, diosmetin and 5,7,3'-trihydroxy flavone was performed using FRAP test in 1:1 (vol/vol) methanol-water mixture at 37^{o}C.

Acknowledgements. Support from Wrocław Medical University ST grant No. 857 is acknowledged. Calculations were performed at the Wroclaw Centre for Networking and Supercomputing.

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Can Density Functional Theory predict ferroelectricity in self-assembled monolayers?

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Polar organic molecules which crystallize in their bulk form such that they exhibit ferroelectric behavior have recently attracted great interest; one example is croconic acid (CA)[1]. Such molecules may also be of interest when deposited on a surface to, for example, create a two-dimensional network with ferroelectric behavior. The ability to predict from computations alone whether or not such molecules will form interesting networks is a particularly challenging and enticing problem.

In this work, we use Density Functional Theory (DFT) to explore experimentally-characterized hydrogen-bonded networks which assemble from CA, from a topical quinonoid zwitterion (ZI), and from benzimidazole (BI) when they are deposited on the coinage metal surfaces, Cu(111), Ag(111), and Au(111)[2,3]. The networks are influenced by the substrate onto which they are deposited and, as could be expected from the literature, the Au(111) networks are readily predictable from gas-phase models, but the Ag(111) networks are not generally predictable from density-functional-theory (DFT) energies alone. We describe what is needed in order to be able to predict the proper networks without any input from experiment.

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DFT modelling of SEI-forming additives for Li-ion batteries

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Lithium-ion batteries (LIBs) have been replacing the conventional batteries (lead-acid, Ni-Cd) in a wide range of application since 1990s. However, despite almost quarter of a century of commercialization, they are still an area of intense studies – mainly focused on development of new electrode materials and compatible with them electrolytes. As stable interphases, created between these two key components, make possible to battery operation, the solid electrolyte interphase (SEI), a self-forming passivation layer on the anode electrode, significantly affects the battery performance [1].

In a typical electrolyte system – solution of $LiPF_6$ in a mixture of organic carbonates – the reduction of carbonates occurs at approximately 1 V vs. Li, and results in formation of passivation layer, which consists of Li_2CO_3 and some oligomer-like compounds [2]. Its task is to protect electrolyte against contact with negative electrode and not to hinder the transport of lithium cations between the electrolyte and the electrode. However, properties of such spontaneous formed layer are not good enough. Therefore, application of special additives, responsible of SEI-forming process, is highly recommended. Formation of the SEI in controlled way can improve many important parameters such as cycle life, coulombic efficiency, irreversible capacity, power density and safety. Most of them are very important from the point of view of the user.

Designing of new additives must be focused primarily on two issues: ability of reduction (high reduction potential is necessary) and products of reduction path (formation of oligomeric and polymeric structure is preferred). Both of them can be easily assessed with computations.

Presented results will show the line of thought that leads from the quantum modeling to the tests of new additives in real systems. Analysis of different sulfate compounds showed some important connection between structural parameters of compounds and their ability to reduction and formation of SEI. Based on that analysis, new SEI-forming additives were proposed.

Acknowledgements. This work was supported by National Science Center of Poland, grant no. 2015/17/N/ST4/03867. Calculations have been carried out at the Wroclaw Centre for Networking and Supercomputing (http://www.wcss.pl), grant No. 346.

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Quantum chemical calculations of complexes of colchicine with zinc(II)

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Colchicine is a tropolone alkaloid of Colchicinum autumnale. It shows antifibroatic, antimitotic and anti-inflammatory activity [1]. It can be used in the treatment of gout and Mediterranean fever [2]. Complexes with zinc may be interesting because zinc cations may modulate activity of alkaloids [3]. Moreover, zinc have substantial biological importance for plants and animals. It is second, after iron, most prominent metal in human body and is essential for growth, development and plays important role in various biological systems [4].

The colchicine complexes with Zn (II) cations have been investigated using DFT methods and obtained data was compared with experimental measurements. Counterpoise corrected and uncorrected interaction energies were calculated. We also calculated ^{1}H, ^{13}C NMR and IR spectra to compare theoretically and experimentally obtained data. All complexes were investigated in terms of quantum theory of atoms in molecules QTAIM. It has been shown that colchicine forms stable complexes of the 2:1 stoichiometry with Zn (II) cation and 1:1:1 and 2:1:1 stoichiometry with metal cation and nitrate ion.

Calculated and measured spectra showed differences before and after complexation. Calculated electron densities and bond critical points indicated bonds between ligands and central cation in the investigated complexes that satisfy the quantum theory of atoms in molecules.

Our calculations helped indicate atoms of colchicine which coordinates zinc (II). For each stoichiometry complexes Zn^{2+}…O6 interaction was the strongest. Most energetically favoured structure in 1:1:1 stoichiometry was obtained when colchicine coordinated via O1, O2, and O4 oxygen atoms. For stoichiometry 2:1 and 2:1:1 complexes most energetically favoured structure was obtained when both molecules of colchicine coordinated via O5 and O6 oxygen atoms.

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The leading contribution of cyklobutane ring in a carboplatin biotransformation

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The computational simulation was carried out on the reaction model mimicking the carboplatin transformation in biological milieu: sequential interaction of drug with electron and water molecule. The crucial steps of reaction course are illustrated by structures, (fig. 1 – 3) and corresponding energy effects.

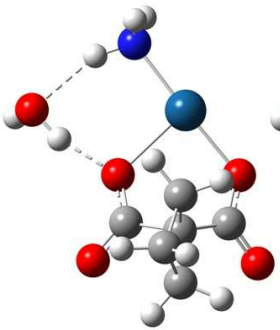

fig. 1

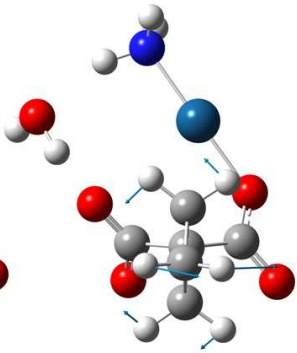

fig. 2

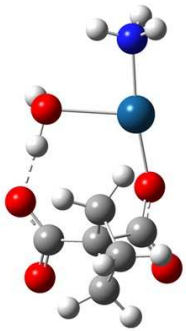

fig. 3

The coresponding scheme of reaction course:
{$[Pt(NH_3)_2(OOC\text{-}C_4H_4\text{-}COO)] + e^-$}+$H_2O \rightarrow (H_2O)[Pt(NH_3)(OOC\text{-}C_4H_4\text{-}COO)]^-$ (fig.1)
-7.5 kcal/mol → NH_3 + $(H2O)[Pt(NH_3)(OOC\text{-}C_4H_4\text{-}COO)]^-$ (fig.2) + 6.3 kcal/mol →
NH_3 + $[Pt(H_2O)(NH_3)(OOC\text{-}C_4H_4\text{-}COO)]^-$ (fig.3) - 0.5 kcal/mol

The most important changes are observed in geometry of anionic ligand, which are particularly visible in transition state (fig.2, imaginary frequency 80i cm^{-1}). Thus, it is justified to consider the function of cyclobutane ring as a leading in studied processes.

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Theoretical studies of fluvastatin photodegradation mechanism

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Knowledge of the photochemical properties of therapeutic agents is important with respect to their influence on the environment and to safe and effective treatment. Light, by causing drugs degradation, can essentially change their chemical and pharmacological properties leading to the formation of harmful decomposition products.

Statins are group of pharmaceuticals used in prevention and treatment of various cardiovascular diseases. Acting as competitive inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase they significantly reduce serum total cholesterol, LDL cholesterol, and triglyceride levels, while modestly raise HDL cholesterol [1-3].

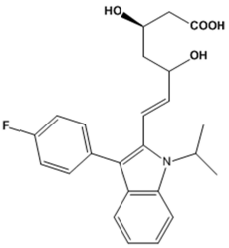

Figure 1: Structure of fluvastatin

Fluvastatin is a totally synthetic statin that is the first-line agent for lipid lowering in patients with atherosclerosis and cardiovascular disease. Fluvastatin is highly photochemically reactive. Exposed to light the compound forms a range of photoproducts. Although there have been a few investigations on fluvastatin photostability, previously described results are unclear and inconsistent [4, 5]. This fact prompted us to undertake more detailed kinetic studies on fluvastatin photodegradation. Both, experimental and computational methods, similar to our previous studies were applied to get insight into the possible mechanisms responsible for the fluvastatin photoproducts formation [6, 7].

All calculations were performed within DFT framework at the M06/6-31G(d) level of theory.

Acknowledgements. This research was supported in part by PL-Grid Infrastructure.

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Theoretical absorption spectra of rhodopsin and bathorhodopsin substituted with acyclic retinal analogues

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Rhodopsin, the visual pigment localized in the rod photoreceptor cells, is the earliest and most thoroughly investigated member of G protein-coupled receptor family. It gains its spectral properties from the chromofore 11-cis-retinal, linked covalently by a protonated Shiff base to Lys296 residue of opsin. Absorption of a photon induces the 11-cis to all-trans-photoizomerization of retinal which initiates the chain of conformational changes leading to activation of transducin, allowing transmission and intensification of the signal. An useful tools for investigating the rhodopsin function are retinal analogues which enable to identify the role of retinal structure in the protein functioning.

In the present work, the theoretical absorption spectra were constructed for systems comprising of rhodopsin models substituted with 11-cis-diethyl-ac-retinal and 11-cis-ethyl-methyl-ac-retinal as well as bathorhodopsin models substituted with all-trans- analogues of those compounds. Both of these acyclic retinal derivatives are proved to be able to form pigments and perform their function during all the activation phases until the equilibrium state of metarhodopsin I and metarhodopsin II [1]. Classical MD simulations were performed for described systems and obtained trajectories were then used as a source of structures for the QM/MM calculations. Using the QM/MM calculations the excitation energies as well as oscillator strengths were obtained for up to forty structures per system. Those values were then used to construct the desired spectrum. Such dualistic approach allows to account for both the biological environment of a protein and the dynamic nature of studied systems while also being able to correctly describe the electron absorption. The constructed spectra allow to predict the absorption maxima with good accordance with the experiment. The described protocol was also used to assess the effect of the relaxation of protein environment surrounding the chromofore. It was furthermore utilized to prove the significance of the hydrogen bond system formed by the residues Glu181, Tyr191, Tyr268 and the water molecule for the accuracy of the acquired absorption spectra.

Acknowledgements. This research was performed as a part of the research task: "Molecular modeling techniques that assist a reasonable design of inhibitors, biocatalysts, sensors, or molecular switches" in the "Biotechnologies and Advanced Medical Technologies" project (BioMed). Project no.: POIG 01.01.02-02-003/08-00. Calculations were performed at the Wrocław Center for Networking and Supercomputing.

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Modeling of inhibitory activity with long-range components of interaction energy

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In contrast to empirical approaches that are commonly used for design of novel ligands or inhibitors, quantum mechanical methods allow to understand the physical origin of intermolecular interactions, aiding the rational drug design methodology. [1] Hybrid Variational-Perturbational Theory (HVPT) was applied to determine leading interaction energy components in several receptor-ligand complexes. In addition to regular enzyme-inhibitor complexes of fatty acid amide hydrolase, FAAH and pteridine reductase 1, PTR1, complexes with small molecule inhibitors of menin-MLL and EphA2-ephrinA1 protein-protein interactions have also been included in this study. Overall, these receptor-ligand complexes encompass a variety of intermolecular interactions as both polar or charged and nonpolar aggregates are considered. Such a choice of receptor-ligand complexes enables derivation of nonempirical inhibitory activity models that are general enough to be applicable for a wide range of complexes.

Systematic analysis of prevailing interaction energy terms has led to conclusion that restriction to long-range components of interaction energy, namely electrostatic and dispersion interactions, is usually sufficient to reproduce the inhibitory ranking. Since ab initio calculations are time consuming for relatively large biomolecular complexes, nonempirical E_{Das} function [2] approximating the dispersion interactions, have been tested in combination with atomic multipole electrostatic energy $E_{EL,MTP}^{(10)}$. As demonstrated by correlation with experimentally established ligand affinity, $E_{EL,MTP}^{(10)} + E_{Das}$ nonempirical model appears to be an accurate and computationally affordable method for ligand scoring. Unlike empirical scoring methods, nonempirical approach proposed herein does not rely on arbitrary parametrization. Favourable performance of $E_{EL,MTP}^{(10)} + E_{Das}$ model over a range of receptor-ligand complexes further validates its general applicability in structure-based drug design. Possible limitations of $E_{EL,MTP}^{(10)} + E_{Das}$ model have also been discussed in our contribution.

Acknowledgements. We thank Prof. Rebecca C. Wade from Heidelberg Institute for Theoretical Studies (examination of *Tb*PTR1), Prof. Jolanta Grembecka and Prof. Tomasz Cierpicki from Department of Pathology of University of Michigan (studies on menin-MLL inhibition), and Prof. Alessio Lodola from Pharmacy Department of Università di Parma (work on FAAH and EphA2-ephrinA1 systems). This work was supported in part by Wrocław University of Science and Technology and Wrocław Research Centre EIT+ under the project BIOMED "Biotechnologies and advanced medical technologies" (POIG 01.01.02-02-003/08) financed from the European Regional Development Fund Operational Programme Innovative Economy 1.1.2. Calculations were performed at the Wroclaw Centre for Networking and Supercomputing.

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N-oxide derivatives with intramolecular hydrogen bonding – a ground and excited state study

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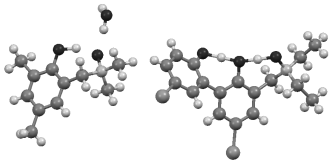
N-oxide derivatives 2-(N,N-dimethylamino-N-oxymethyl)-4,6-dimethylophenyl (SEHBEM) [1] and 5,5'-dibromo-3-diethylaminomethyl-2,2'-biphenol N-oxide (WUKMOE) [2] were investigated on the basis of Density Functional Theory. The structures of the studied compounds with their crystal codes are presented in Figure 1. This work is a continuation of our previous study of 2-(N-diethylamino-N-oxymethyl)-4,6-dichlorophenol [3]. Here, we present some results related to static DFT computations describing metric and electronic structure parameters. The simulations were performed *in vacuo* and with solvent reaction field.



Crystal structure codes: SEHBEM and WUKMOE respectively

Figure 1: The structures of investigated N-oxides.

The chemical composition of the two studied compounds comparing with the previously studied N-oxides forces different behavior of the H-bridge protons. The SEHBEM compound prefers to preserve the molecular structure whereas the WUKMOE derivative exhibits proton transfer phenomena.

Acknowledgements. The Authors would like to express their thanks to the Academic Computer Center (TASK) in Gdańsk and the HPC Centre at the ICM, University of Warsaw (grant no. G52-7, G50-2) for generous grants of the computing time and use of file storage facilities. Additionally, A.J. and J.J.P. would like to thank the National Science Centre (Poland) for supporting this study under the grant no. UMO-2015/17/B/ST4/03568.

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Metric and electronic structure study of selected fused-rings compounds: anthracene and quinoline derivatives

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Quantum-chemical simulations were performed for compounds presented in Figure 1 [1-5]. The compounds derive from two chemical groups possessing fused rings, diverse substituents and intramolecular hydrogen bonding (O-H…O and O-H…N types). Their chemical composition makes them interesting objects for various studies. Here, we report on DFT and MP2 computations performed *in vacuo* and with solvent reaction field. Metric parameters were computed and compared with experimental data available [1-5]. A detailed analysis on the intramolecular hydrogen bond was done scanning the bridge proton path. The electronic structure evolution and substituents effect upon the intramolecular reorganization were investigated.

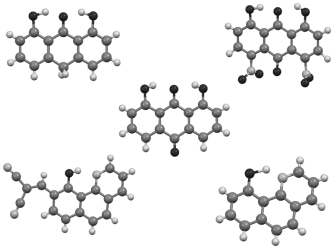

Figure 1: The structures of the studied anthracene and quinoline derivatives.

Acknowledgements. A.J. would like to express her thanks to the HPC Centre at the ICM, University of Warsaw for generous grants of the computing time and use of file storage facilities. Additionally, A.J. would like to thank the National Science Centre (Poland) for supporting this study under the grant no. UMO-2015/17/B/ST4/03568.

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The reaction spectrum for the analysis of structural evolution on the reaction path

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Properties of the hessian matrix calculated for the structures on the reaction path within the IRC scheme have been analyzed. The variable trace of the matrix contains all information concerning the structural changes in the evolving system, including the role of each atom within. Its derivative over the reaction progress allows for observation the crucial points on the IRC. Decomposition of the trace into atomic contributions led to an attractively simple, yet very informative picture, presenting the role of atoms in the structural modifications occurring on the subsequent reaction steps. The test reactions chosen as examples for the method are: CO + HF → HCOF and HONS → ONSH.

Atomic resolution for the energy derivatives on the reaction path

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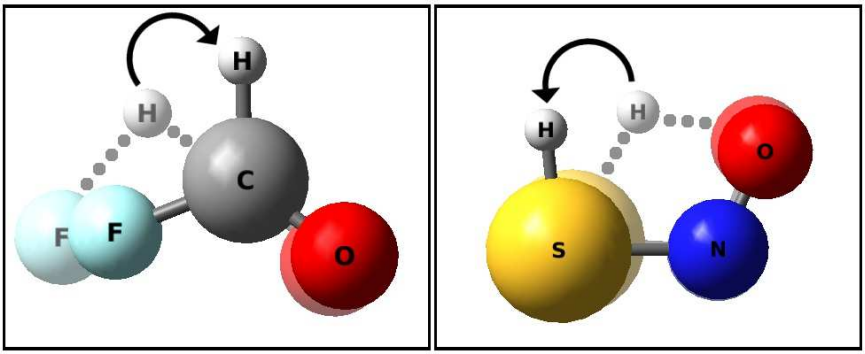
Definite algorithms for calculation of the atomic contributions to the reaction force F_ξ and the reaction force constant k_ξ (the first and the second derivatives of the energy over the reaction path step) are presented. The electronic part in the atomic and group contributions has been separated, and this opened the way to identification of the reactive molecule fragments on the consecutive stages of the reaction path. Properties have been studied for the two canonical test reactions: CO + HF → HCOF and HONS → ONSH [1].



Acknowledgements. The work was financed by a statutory activity subsidy from the Polish Ministry of Science and Higher Education for the Faculty of Chemistry of Wrocław University of Technology, ref. no. S50013/K0301. The use of resources of Wrocław Center for Networking and Supercomputing (WCSS) is gratefully acknowledged. We are indebted to a referee for the much enlightening remarks.

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The all-atom refinement of protein structures generated with the coarse-grained UNRES force field

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Knowledge of the protein structure is crucial for understanding of their function and role in biochemical processes. Nowadays, protein structure can be determined by experimental methods; however, despite their advances, it is very expensive and sometimes impossible (i.e. because of crystallization problems or conformational flexibility of the protein). Therefore, a variety of computational methods have been designed to predict protein structures when the experimental data are sparse, inaccurate, or non-existent. Coarse-grained models are very useful in predicting structure of large proteins and protein complexes which can subsequently be converted to all-atom representation. However, results from coarse-grained simulations, usually provide models with only middle or low resolution because of simplifications inherent in coarse-grained models. In order to enhance the quality of the predicted structures and to eliminate overlaps in all-atom structures, many different refinement approaches using all-atom force fields are used. Our refinement protocol, which based on the previously tested methods, includes simulations with positional restraints: energy minimization, heating and molecular dynamics simulations with the CHARMM or AMBER all-atom force fields, utilizing scoring function, and structure averaging. For small-size proteins, the current versions of our refinement protocol improves the RMSD, TMscore and GDT-TS values. Moreover, for all proteins, it eliminates atom-atom overlaps, that arise during the conversion of coarse-grained models to all-atom structures, and thus improves the local structure and MolProbity scores.

Acknowledgements. Supported by grant UMO-2013/10/M/ST4/00640 from the National Science Center of Poland. Computer resources were provided by the Informatics Center of the Metropolitan Academic Network (IC MAN) in Gdańsk and the Beowulf cluster at the Faculty of Chemistry, University of Gdańsk.

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Adsorption of small aromatic molecules in highly siliceous zeolites

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Zeolites attract lot of scientific attention especially with their possible applications to adsorption and separation processes. We study the process of adsorption of small aromatic molecules which could lead to a potential method of separation of such species, e.g. biomass-derived aromatics [1]. We used different types of molecular simulations to investigate phenomena of adsorption of benzene and phenol in all-silica and Al-containing zeolite structures.

First, molecular dynamics (MD) simulations were performed to calculate free energies of solvation of the species as the prerequisite for adsorption calculations. It was used to validate different force fields for applicability to our system. Most satisfactory results were obtained for Polymer Consistent Force Field (PCFF) as compared to reference data form FreeSolv database [2].

Zeolite structures (MFI, EUO, BEA) were optimized using four different force field to find most suitable one. We selected core-shell approach - Catlow force field [3] since it gives the lowest absolute error of cell parameters, bond lengths and T-O-T angles with comparison to the experimental data. Also Al atom was added in all possible sites in structure to determine most favorable configuration.

Finally, Grand Canonical Monte Carlo (GCMC) simulation of adsorption from gaseous phase were performed. Since phenol is generally adsorbed form water solution we used free solvation energies to calculate proper gas fugacities to perform adsorption simulations. We used PCFF and FHF [4] force field to describe interactions between framework atoms (Si, O, Al, H) and adsorbed molecules. For benzene adsorption in high-silica MFI and EUO structures we obtained very good agreement with experimental data for FHF for different temperatures. Both PCFF and FHF force field gave correct results for adsorption of phenol in MFI. For aluminated (Al/Si ratio – 95, 47, 23, 11) structures for PCFF we observed qualitative agreement with reference – decreasing of the amount of adsorbed molecules with increasing of Al/Si ratio.

We also examined different (3, 4 and 5-sites) models of water molecule in terms of adsorption in zeolites. Best results of saturation pressure of water in adsorbent were obtained for SPC/E and SPC (3-sites) model. We also noticed correct tendency of increasing amount of adsorbed water molecules while increasing of Al/Si ration. It was caused by the fact that applying aluminum atoms into the framework we change structure from hydrophobic (all-silica) to hydrophilic.

Acknowledgements: Numerical computations supported by WCSS (grant no. 172).

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Alkaline hydrolysis of organophosphorus pesticides: influence of the substitutions at the phosphorus atom

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Organophosphorus pesticides (OPPs) are extensively used for agricultural and domestic purposes. Their relatively small persistence, in comparison to other pesticides, together with acute toxicity to their specific target, make them very promising compounds that could serve as plant protective substances. Apart from the benefits in terms of crop protection and the potential increase in crop yields, OPPs attract much interest due to the adverse effects that organophosphorus pesticides can pose non-specifically to living beings other than the target organisms, with humans, especially children, being of special concern. Considering that few OPPs disposal methods are known, understanding the fundamental principles by which the hydrolysis is driven would be of great importance for development of novel approaches for safe organophosphate disposal.

Herein, the systematic ab initio study of gas-phase reaction mechanisms of alkaline hydrolysis of *p*-nitrophenyl dimethyl phosphate and its sulphur substituted derivatives: *p*-nitrophenyl dimethyl phosphothioate and *p*-nitrophenyl dimethyl phosphodithioate, is presented. As shown for other phosphotriesters, [1] hydrolysis reaction of these organophosphorus compounds might follow either a multistep addition-elimination mechanism, characterized by the presence of a pentavalent intermediate, or a one-step direct-displacement pathway, which proceeds through a single transition state. In addition to sulphur substitutions, we investigate the influence on the reaction mechanism of both incoming and leaving group conformations. Knowledge of the structural and energetic properties of particular hydrolysis pathways resulting from substrate conformation and composition might aid the rational design of catalysts capable of enhancing OPPs degradation.

Acknowledgements. Calculations were performed at the Wroclaw Centre for Networking and Supercomputing.

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Small Cu clusters as reaction centers for the CO_2 dissociation

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Utilization of CO_2 is a significant concern of our times. The reaction of reduction leads to production of fuel but the first electron transfers are kinetically unfavorable what makes the process very slow. Therefore electro- or photocatalysis is studied by researchers at present. Electrocatalysis on copper surface produces methane with limited effectiveness. Usage of photoinducable semiconductors coated with metal clusters is another way to provide electrons for the reduction and overcome high energy barriers [1].

In the presented work the dissociative adsorption of CO_2 on copper clusters in the gas phase was studied using Born-Oppenheimer Molecular Dynamics by means of the DFT theory with PBE density functional. The results for 4, 6, 7, 8, 13-atom clusters show that the adsorption is stronger on the smaller clusters especially those with planar geometry where adsorbed CO_2 molecule sets in plane. While adsorption weakens with the increasing cluster size for Cu_4, Cu_6, Cu_7, Cu_8, the Cu_{13} cluster behaves differently. Cu_{13} is able of forming specific adsorption site where the CO_2 is coordinated to as much as 4 atoms of Cu (Fig. 1a).

In order to find the most probable paths of dissociation one of the C-O bonds was successively elongated during the simulation. In the transition state the preferred geometry is or has a motif of tetra- or pentahedral bipiramid for Cu_6, Cu_7, Cu_8. The dissociation occurred in three different modes: on the edge (Cu_6, Cu_7, Cu_8), on the triangular face (Cu_6, Cu_7, Cu_8) and on the rectangular face of a cluster (only Cu_{13}). The last has a lowest transition state energy and enables the CO_2 molecule to coordinate to 4 atoms of Cu as in the case of adsorption but with the different geometry (Fig. 1b). In most cases the complex with dissociated CO_2 is of a similar thermodynamical stability as undissociated or greater for Cu_4 and Cu_{13}.

The results suggest that clusters of appropriate size, small enough to be flexible and loosely bonded and big enough to enable formation of specific active sites of molecular interactions, may be of special interest for the design of new better catalysts. Usage of clusters from this range of sizes may increase effectiveness of the reaction due to stronger adsorption and lower transition state energy.

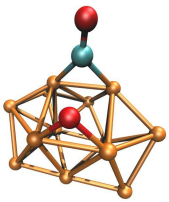

Figure 1: a) Adsorption on Cu_{13}, b) dissociation on the specific active site - rectangular face of Cu_{13} cluster

Acknowledgements. Calculations were performed at the Wroclaw Centre for Networking and Supercomputing and Centre for the Computational Scince – ICM Warsaw.

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Interactions of amino acids with selected phthalocyanines. DFT study

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We studied the geometric and electronic properties of aluminium-, gallium- and zinc octacarboxyphthalocyanines (Al(OH)PcOC, Ga(OH)PcOC and ZnPcOC) with eight carboxylic groups attached to the benzene rings (fig. 1), what make them water-soluble compounds. This is very important for practical applications e.g. as photo-sensitizers in photodynamic therapy (PDT) [1]. The complexes of phthalocyanines containing diamagnetic metals such as Zn^{2+}, Al^{3+}, Ga^{3+} are especially interesting in this respect because these complexes have a long triplet lifetimes and high triplet quantum yield what ensures high cytotoxicity against neoplasmic cells [2].

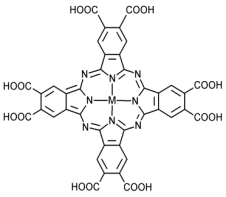

Figure 1: Structure of MPcOC, M – Al(OH), Ga(OH), Zn.

The presence of amino acids in the solution increases the photostability of the phthalocyanines. To explain this phenomenon we performed DFT calculations of 1: 1 phthalocyanine - amino acid complexes. The effects of axial and equational coordination on molecular structure and electronic absorption spectrum were investigated. The calculation results reveal that axial coordination significantly changes the planarity of the phthalocyanine ring and, thus, alters the electronic structure. On the other hand, hydrogen bonding of phthalocyanine side COOH groups with amino acids, in equatorial complexes, does not change the structure within the centre of the phthalocyanine and causes only a slight increase in UV-Vis bands intensity, what is in perfect agreement with experimental data.

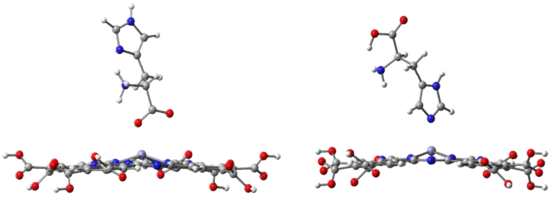

Figure 2: Structures of two types of ZnPcOC – histidine axial complexes.

Acknowledgements. Calculations were carried out in the Academic Computer Centre CYFRONET, AGH, Kraków.

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Determination of aqueous dissociation microconstants of anthranilic acid and its derivatives using DFT method

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The dissociation macroconstants are one of the fundamental properties of organic molecules which enable determination of degree of dissociation at a given pH, whereas microscopic constants provide information about specific sites of ionization. Both are key parameters especially for biological compounds containing ionizable groups, because they influence on many physicochemical properties, like lipophilicity, solubility, and permeability of molecule [1].

Anthranilic acid (AA) and its N-substituted derivatives (N-methylanthranilic acid – MeAA, N-phenylanthranilic acid – PhAA) may exist in four different microforms, namely as a cation (H_2R^+), zwitterion ($HR^{\pm}$), neutral species (HR^0) and anion (R^-) (Figure 1) and equilibria between these forms are expressed by the microconstants k_{11}-k_{22} [2].

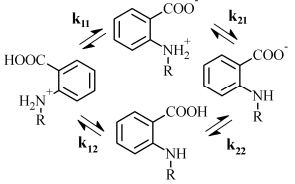

Figure 1: Equilibria of AA (R = H), MeAA (R = CH_3) and PhAAB (R = C_6H_5) in aqueous solution

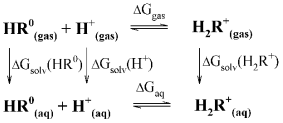

Figure 2: Thermodynamic cycle for calculation of the theoretical pk_{12} [3]

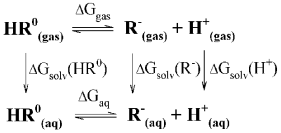

Figure 3: Thermodynamic cycle for calculation of the theoretical pk_{22} [3]

In this work, the k_{12} and k_{22} microdissociation contants of AA, MeAA and PhAA in aqueous solution were studied using the density functional theory (DFT) calculations with conductor-like polarizable continuum model (CPCM). Thermodynamic cycles for calculations of the theoretical pk_{a1} and pk_{a2} microdissociation constants are shown in the Figures 2 and 3. The of values of appropiate constants of investigated compounds were calculated by the equation (1):

$$pk_a^{DFT} = \Delta G_{aq}/2.303RT \qquad (1)$$

The pk_a values have been determined with the use of various functionals and basis set, taking into account the polarization as well as diffusion functions. The obtained results were compared to the experimental results [2].

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DFT and TD-DFT investigation of IR and UV spectra of N-phenylantranilic acid

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N-Phenylanthranilic acid (2-anilinobenzoic acid) belongs to fenamates: N-substituted anthranilic acid derivatives. The most known mefenamic acid, tolfenamic acid, meclofenamic acid are used clinically as nonsteroidal anti-inflammatory drugs (NSAIDs) for the treatment of fever, pain, and inflammation. N-Phenylanthranilic acid was established as the minimum structural requirement for achievement the biological properties of fenamates. It is widely used in medicine, pharmacy and analytical chemistry as starting material for synthesis of pharmaceutically important molecules such as antimalarials, anti-inflammatory and antineoplatics, comparative medical research and for metal ion determination [1].

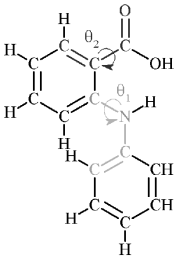

Figure 1: The molecular structure of N-phenylantranilic acid with defined the dihedral angles

N-Phenylantranilic acid and its derivatives have attracked attention, because of their complexing properties. The fundamental methods used to verify the complexing ability of ligand and changes after complexation are spectral methods such as absorption and infrared spectroscopy [2]. Therefore, the correct interpretation of the electronic and infrared spectra of parent ligand is necessary and in order to confirm the correct spectra interpretation the computational methods can be applied.

In the calculations the following procedure has been applied:

1. Conformational studies of the ground-state geometry of N-phenylanthranilic acid.
2. Calculation of the vibrational spectra.
3. Determination of the vertical electronic excitation energies using the TD-DFT framework.

Furthermore, in order to obtain the best compatibility with the experimental results, the calculations have been conducted with use DFT method and various functionals and basis set, taking into account the polarization and diffusion functions.

The results of calculations have been used in detailed interpretation of the experimental of FT-IR and UV-VIS spectra of the investigated amino acid.

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Assessment of DFT methods for computing linear and nonlinear electric properties of endohedral complexes

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The possibility of filling an internal empty space of carbon nanotubes (CNTs) cages with atomic, ionic or molecular guests has been recognized soon after their discovery by Iijima. Since the encapsulation of the molecule inside the carbon nanotube cage may influence both host and guest as well as can lead to various applications (eg. nanometer-sized capillaries, new containers of molecules and ions, nanoscale reactors or potential shuttles for drug-delivery) the endohedral complexes of CNTs are interesting objects in diverse areas of science and engineering. [1] In view of the prospects of applications, the prediction of physical and chemical properties of endohedral nanotube complexes on the basis of theoretical analysis seems to be quite important.

Among various properties of interest, apart from structure and energetics, are the linear and nonlinear electric properties of the CNTs endohedral complexes. [2] The challenge of theoretical work in this field is the demand of using highly correlated methods combined with flexible, sufficiently diffuse set of basis functions. However, taking into account the size of CNT cages, it is clear that performing high-level *ab initio* calculations for such extended systems might be cumbersome. As an alternative, electron correlation effect can also be assessed by adopting Kohn-Sham formulation of the density functional theory (DFT) that provides arrays of computationally efficient method in the description of electronic structure of molecules. Nevertheless, most of the conventional exchange-correlation functionals demonstrate limited applicability in the field of molecular nonlinear optics. Moreover, their performance depend on the nature and the size of the system. [3]

In this work a systematic evaluation of the performance of a wide range of exchange-correlation functionals was carried out, based on the calculations of dipole moment (μ), polarizability (α) and first hyperpolarizability (β) of endohdral complexes formed through the encapsulation of the LiF or HCl molecules inside carbon nanotubes of different diameter. An assessment was performed on the efficiency and consistency of *(i)* generalized gradient approximation *(ii)* meta-GGA, *(iii)* global hybrids and *(iv)* range-separated hybrids implemented in DFT against the values obtained using MP2 method. The magnitudes of electric dipole moments and (hyper)polarizabilities of investigated complexes were computed within the finite field method (FF). The obtained results demonstrate that the largest variations between data calculated using different exchange-correlation functionals occur in the case of dipole moment and first hyperpolarizability. This effect is particularly visible for molecular complexes formed with the carbon nanotube of the smallest diameter.

Acknowledgements. This work was supported by NCN Grant No.: DEC-2013/09/N/ST4/00325. The calculations were performed in the Wroclaw Centre for Networking and Supercomputing and PL-Grid Infrastructure.

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Interaction of G-quadruplex derived from NHE III1 region of *c-MYC* oncogene (Pu22) with small ligands

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The nuclease hypersensitivity element III_1 upstream of the P1 promoter of c-*MYC* controls 85–90% of the transcriptional activation of this gene (1). The *c-MYC* oncogene is overexpressed in a broad spectrum of human malignancies. Transcription of *c-MYC* is primarily regulated by a 27 base guanine-rich sequence present within the nuclease hypersensitivity element III1 (NHE III1). This duplex element can equilibrate between transcriptionally active forms (duplex and single-stranded DNA) and a silenced form. NHE III1 contain six consecutive guanine stretches and is able in conditions of K^+ solutions to form two different unimolecular G-quadruplex confromation (2,3). The first one is the chair form with three propeller loops and the second one is basket form with two lateral loops and central diagonal loop. Compounds that stabilize the intramolecular DNA G-quadruplex formed in the *c-MYC* promoter have been shown to inhibit the *c-MYC* gene, making G-quadruplex an attractive target for cancer and other diseases therapeutic intervention.

Chromophore is considered as a part of molecules which is strictly connected with their affinities to interact with G-tetrad and stabilization of the G-quadruplex structure. Aromatic chromophores possess conjugated double bond system with delocalized electrons which make them flat and increase their stability. Attractive nonbonded interactions between aromatic rings with conjugated double bonds (ligand-guanine) were found out as one of the most important interactions in those kind of complexes which increase the stability of them.

The screening of literature gives 106 aromatic chromophore without any side chains which potentially could interact with terminal G-tetrads. All ligands were docked into *c-MYC* structure of G-quadruplex (PDB id: 2L7V). Analysis of created ranking provide us insight on which aromatic chromophores are best candidates to modify in order to find best ligands which could potentially stabilize the structure of *c-MYC* G-quadrupex.

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New analytical potentials in physics-based coarse-grained force field

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Coarse-grained force fields, in which simplified representations of molecules are implemented, are widely used in biomolecular simulations because they offer a tremendous reduction of the cost of computations compared with the all-atom models. However, designing the functional forms of the coarse-grained energy terms poses a serious problem and these terms are very often imported from all-atom force fields or assigned on a heuristic basis. In such approaches at coarse-graining the multibody terms (which are necessary to generate regular structures [1]) are not considered and inadequate variables are often chosen to express the effective energy terms.

Based on statistical physics, the coarse-grained energy functions originate from the potentials of mean force (PMF) where the degrees of freedom that are not considered explicitly are integrated out [1]. Expansion of the PMF into Kubo cluster-cumulant functions [2], termed factor expansion (FE) [1] enables us to split the PMF into specific terms.

In this work, we used the factor approach to revise the local potentials in the coarse-grained UNRES force field for proteins. Unlike the former approach, in which the units to derive the local potentials were composed of whole terminally-blocked residues, we used three units: (i) terminally-blocked glycine residue to represent protein backbone; (ii) H-C^{α}(R)-$CONHCH_3$ and (iii) CH_3CO-NH-C^{α}-H(R), where R denotes a side chain. As opposed to the previous formulation, this dissection uses exactly the UNRES sites and, consequently, provides a clear separation of the backbone-only local potentials from those involving side chains. Consequently, the number of different potential types is significantly reduced. The respective energy surfaces were calculated by using the semi-empirical PM7 quantum mechanics method. The calculations were performed on a grid in the θ (C^{α}… C^{α}… C^{α}), or O (C^{α}… C^{α}… C^{β}), $\chi^{(n)}$ (rotational of side-chain dihedral angles) and either the $\lambda^{(1)}$ or $\lambda^{(2)}$ that describe the rotation of peptide group in the C^{α}… C^{α}… C^{α} frame. Based on the calculated potential-energy surfaces, the potentials of mean force in the C^{α}… C^{α}… C^{α}, R...C^{α}… C^{α}, and C^{α}… C^{α}...R virtual-bond angles and those in the C^{α}… C^{α}… C^{α}...C^{α}, R...C^{α}… C^{α}... C^{α}, C^{α}… C^{α}... C^{α}...R, and R...C^{α}… C^{α}...R were calculated. The PMF profiles will discussed in terms of formation of protein secondary structure.

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On the nature of the stabilisation of the E···π pnicogen bond in the $SbCl_3$···toluene complex

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The off-symmetrical structure of the toluene···$SbCl_3$ complex is a consequence of the off-centre location of the σ-holes at the Sb atom. The structure of the complex (along with the related complexes investigated)[1] is thus determined by the electrostatic attraction between the positive σ-hole of the Sb atom and the negative π-electrons of the aromatic ring, while their high stabilisation energies are because of both, polarization/electrostatic and the dispersion energy. The distinctive features of pnicogen bonding are thus an effect of the concert action of attractive dispersion and electrostatic interactions as well as of low exchange-repulsion interaction originating in polar flattening[2] of pnicogen atom in the pnicogen bond.

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HF and DFT methods in determination of dissociation constants of luteolin in aqueous solution

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Luteolin (Figure 1) is one of the naturally occurring flavonoids which is well known as a natural pigment as well as a biologically active compound. Because of the presence of ionizable hydroxyl groups, the knowledge of acid dissociation constants is a necessary parameter in ADMET research, because it allows to explain the chemical aspects of Absorption, Distribution, Metabolism, Excretion and Toxicity within the biological sense. Thus, dissociation constants often play the main role in understanding the pharmacodynamic properties of drug substances [1].

Currently, for the determination of pK_a values of flavonoids the potentiometric, spectrophotometric and capillary electrophoresis methods are used. An alternative is the use of molecular modelling.

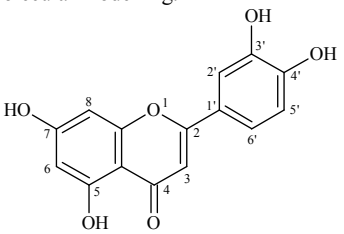

Figure 1: Molecular structure of luteolin

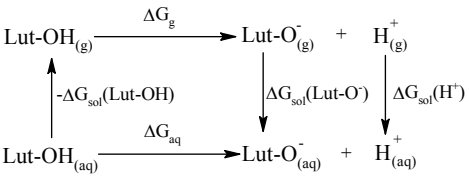

Figure 2: Thermodynamic cycle for the calculation of theoretical pK_a of luteolin (Lut-OH) [2]

In this work, the thermodynamic cycle presented in the Figure 2 was used for the calculations of theoretical dissociation constants of luteolin.

All computations have been carried out with the Gaussian09 package. HF and DFT methods have been applied for conformation analysis, geometry optimization and thermodynamic calculations. Different functionals and basis sets have been tested, taking into account the polarization and diffusion functions. Calculations in water solution have been carried out by means of the Solvation Model based on Density (SMD). The obtained theoretical dissociation constants were compared to the experimental data for luteolin available in literature [3,4].

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Spectroscopic (UV-VIS and IR) characterization of chrysin supported by DFT calculations

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Nowadays, computational calculations play an important role in many areas of flavonoids studies. They are used in theoretical investigations of physical and chemical properties of flavonoids to unveil the relationship between the structure and properties, and to predict the possible complexation sites or interpretation of changes after metal ions coordination [1].

In present work, theoretical and experimental results of the studies on the spectral properties of chrysin were shown. Chrysin is one of the less known flavonoids. It naturally occurs in passion flowers *Passiflora caerulea*, *Passiflora incarnata* and *Oroxylum indicum*. It is also found in chamomile, mushroom *Pleurotus ostreatus* and in honeycomb. Among the biological properties, anti-allergic, antioxidant, anti-inflammatory and anticancer activities are postulated for chrysin [2].

Additionally, due to the presence of functional groups at C4 and C5 positions, chrysin exhibit complexing properties. Therefore, well characterized spectral properties are necessary in comparative analysis with resulting complex.

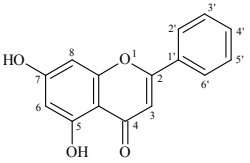

Figure 1: The molecular structure of chrysin

The molecular geometry and vibrational wavenumbers of chrysin have been calculated at ground state by using a DFT method and various functionals (B3LYP, B3PW91, B97D, pbe1pbe, X3LYP, M062X). Electronic absorption spectra of the title compound have been predicted with the use of the Time Dependent Density Functional Theory (TD-DFT) method and several different functional including B3LYP, CAM-B3LYP, BP86, B3P86, B3PW91, B97D, M062X. All calculations were performed with Gaussian09 software.

Simultaneously with computational calculations, the FT-IR (in KBr pellets) and UV-Vis spectra of the investigated compound dissolved in different solvents (ethanol, methanol, water and DMSO) were recorded.

The obtained theoretical infrared and ultraviolet-visible spectra were tested in range of the best fitting to the experimental data and used in the analysis of spectral properties of chrysin.

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The influence of site mutations on activity of XPB protein

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The ERCC3/XPB ATP-dependent DNA helicase is one of the ten subunits of the general transcription factor TFIIH. As the TFIIH is involved in transcription, nucleotide excision repair (NER) and cell cycle control the mutations in its subunits may have pleiotropic effects. There are known only several mutations not fatal for the cells, yet causing serious illnesses. Based on previous experimental work, we simulated wild type enzymes from archaebacteria and eukaryotes and 2 of its mutants.

All but one ERCC3 mutants were extremely sensitive to UV-irradiation. However, none of them was able to repair CPD or 6-4PP or to recover RNA synthesis after UV-irradiation. We have compared the most sensitive (UV24 cell line; S382P mutation) and most resistant (UV68 cell line; V471F mutation) mutants and found that the sensitive cells have more apoptotic cells, form more DSBs, have higher frequency of chromosomal aberrations and stronger G1/S block. Molecular dynamics analysis of the S382P ERCC3 protein has revealed significant fluctuation in protein loop next to DNA binding domain.

The effect of functional groups on the UV-Vis spectrum of dyes used in dye- sensitized solar cells

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The selection of appropriate dye is one of the most important steps in design of dye-sensitized solar cells. The following paper describes the influence of functional groups on the UV-Vis spectrum of dyes commonly used for the production of solar cells. The computational methods (DFT [1] and TD-DFT [2]) were applied for modelling in reported study. Five different dyes including: complexes of copper, zinc, osmium, and platinum were considered. To each dye, three functional groups were attached: carboxyl, phosphate and sulfate. The structures of molecules were optimized and applied for the simulation of excited states UV-Vis spectra. The final stage of the study was the comparison of obtained spectra with the spectrum of solar radiation.

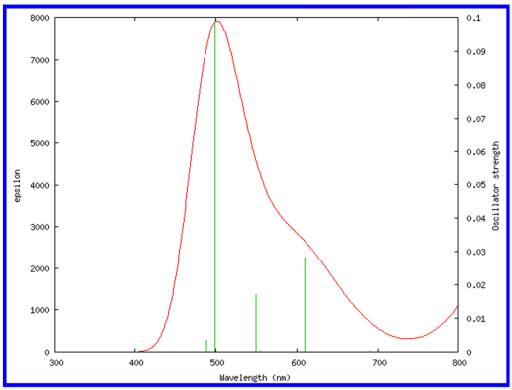

Fig 1. UV-Vis spectra for a platinum complex to the attached carboxyl group.

The calculations were done applying the Gaussian 09 [3] program. The absorption spectra were obtained using the program GaussSum [4] program. Calculations were performed at the Wroclaw Centre for Networking and Supercomputing.

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Mechanisms of surface charge state minimization in $AgInS_2$ quantum dots and its effect on defect states – DFT study

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Over the last years ternary I-III-VI group quantum dots (QDs) have found significant scientific attention due to their applicability in various priority areas of high social impact including i.e. the sun energy conversion for green energy sources and bio-medical imaging serving as one/two photon excited red-shifted luminescence agents for sensitive detection of various abnormalities.

Although, number of interesting applications of the QDs have already been reported, accurate description of complex kinetics of excited states relaxation in such systems is still far from understanding. Zero dimensionality, large tolerance to the off-stoichiometry and defect related properties of the compounds gives important physical premise to put more attention to the QD's surface regions where the physical properties like charge mobility or conductivity type may change by orders of magnitude comparing to regular crystal environment.

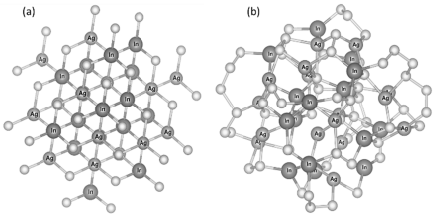

Fig. 1: Surface charge state minimization in pristine $AgInS_2$ cluster. Figure (a) represents ideal structure cut from model chalcopyrite crystal. In the figure (b) is shown corresponding cluster after structural optimization.

In this work we report on a possible pathways of surface charge minimization in the chalcopyrite quantum confined $AgInS_2$ (AIS) nanocrystals (Fig. 1).

We show the results of our investigation of the issues of formation of surface states, minimization of surface charge state and their influence on the mechanism of relaxation of excited states in AIS QDs. Presented results are based on calculations within the density functional theory for selected AIS clusters containing several-dozens atoms. Different hybrid functionals were used.

Our results show an essential influence of the surface and surface defects on the mechanisms of relaxation of fundamental excitations. Accurate knowledge about processes of relaxation of fundamental excitations in QDs will contribute to their more effective control and to the limitation of unfavorable nonradiative processes.

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Light-induced confinement of electrons due to sp^2-sp^3 hybridization in graphene bilayers – (TD-)DFT calculations

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Graphene can be potentially applied in a large variety of optoelectronic devices (very thin and elastic displays, transistors, photodetectors, lasers etc.). However, due to the zero-energy gap, no light emission form pristine graphene has already been reported.

Recent experiments [1] proved that it is the possible to generate the broadband white-light emission from graphene ceramics by excitation with continuous-wave (CW) laser operating in visible (VIS) or near infrared (NIR) region. However, such an emission is hard to be interpreted in terms of a black body radiation, as the temperature of the sample stays under 900 K for the highest excitation power (1.5 W), and the emission intensity remains constant up to 10 K. Some authors [2,3] suggested a formation of strong σ-bonds between graphene layers when graphite is irradiated with pulsed VIS laser (as an effect of a charge transfer between two graphene layers). Similar effects may also occur in multilayer disordered graphene during intense CW laser excitation.

We propose a theoretical model of light emission from locally interacting graphene bilayers. We assume that optically induced perturbations of graphene's ground state results in : (i) local change of hybridization $sp^2 \rightarrow sp^3$ and (ii) formation of transient interactions between carbon atoms from two opposite graphene layers (Fig. 1a). The resulting light-induced nanodomains are characterized by spatial confinement of the electrons on the p_z orbitals of the sp^2–sp^3 domain's interior and quantization of allowed electron's energy levels.

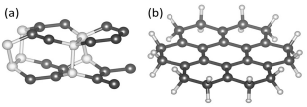

Figure 1: (a) Interlayer hybridization of graphene bilayer, (b) HHC24 graphene cluster. Two hydrogen atoms are bonded to each of 12 carbons on the cluster edge (sp^3 hybridization). The 12 carbons in the center remain in sp^2 hybridization with electrons on p_z orbitals.

The calculations have been performed using density functional theory (DFT) and time-dependent DFT, on model graphene nanodomains of different shapes and sizes, cut out from ideal graphene sheet. The sp^3-hybridized edge was achieved by attaching two hydrogen atoms to every carbon at the cluster's edge (Fig. 1b). We show that the quantized energy levels are separated by several eV, which allows the emission in UV/VIS/NIR range.

Acknowledgements. The computational support from Wrocław Centre for Networking and Supercomputing (grant no.172) is acknowledged.

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A theoretical study of the catalytic mechanism of ethylene polymerization with *N*-Arylcyano-β-diketiminateMethallyl nickel (II) complexes activated with BF_3 and $B(C_6F_5)_3$

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Density functional theory calculations were performed to study the ethylene insertions (**I_1**, **I_2** and **I_3**) onto a family of methallyl Ni(II) isomer catalysts toward ethylene polimerization, where a cyano group is located in *ortho* (complexes ***a, c***) or *para* (complexes ***b, d***) position of the respective aromatic ring; moreover, BF_3 (***a***,***b***) or $B(C_6F_5)_3$ (***c***,***d***) were used as co-catalytic additives in the complexes. For the **I_1** step, it was observed that the formation of a π-complex between complexes ***a***-***d*** and ethylene is a barrierless process, which occurs by the opening of three-coordinated methallyl ligand η_3-$(CH_2)_2CH_3$, giving the mono-coordinated η_1-$(CH_2)_2CH_3$species. In the chain growth (**I_2**), two pathways taken place: the first one allows the chain propagation; while, the second one leads to the β-hydrogen elimination for complexes ***a***, ***b*** and ***d.*** The latter agree with the experimental performance of complex ***c*** to give larger polymers compared to complexes ***a***, ***b*** and ***d***. The chain termination (**I_3**) step gives the β-agostic hydrogen intermediates, which act as new active species (***a1*** and ***c1***) and are formed with an average energy barrier of 14 kcal/mol for both isomers ***c*** and ***d***. This active species (***c1***) was explored in detail with two subsequent ethylene insertions **I_1** and **I_2** (where **I_1** originated a *β*-hydride transfer to C_β of the coordinating ethylene and **I_2**favored the *β*-hydrogen elimination). Finally, all the processes were studied through the Reaction Force analysis to characterize the structural and electronic events taking place in the chain initialization (**I_1**), propagation (**I_2**) and termination (**I_3**) steps.

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Steroids as enzyme substrates: docking studies on versatility of ligand-binding pockets of hydroxylases and monooxygenases

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Steroid hormones and their derivatives form a large group of useful pharmaceutical preparations employed in prevention and treatment of diverse diseases in gynecology, endocrinology, rheumatology, oncology, etc. Such compounds as hydrocortisone, dehydroepiandrosterone (DHEA), prednisolone are among the best known steroid drugs and food additives. The production of steroid drugs and hormones is based on combination of enzymatic reactions and chemical synthesis. Biooxidation reactions are among the most frequently employed steps [1]. Due to low concentration of natural steroid hormones, various biotransformation routes are pursued to convert naturally occurring steroids (e.g. phytosterols) into other bioactive compounds.

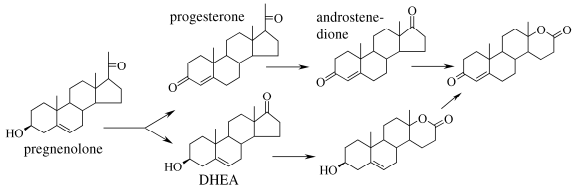

Figure 1. Biotransformations of pregnenolone in *Penicillium camemberti* AM83 [2]

Diversity of metabolic routes of steroids (see e.g. Figure 1) is, unfortunately, not accompanied by corresponding knowledge of enzymatic mechanisms of action on steroid substrates. In particular, structural information on the relevant enzymes is scarce. No structure of a fungal Baeyer-Villiger monooxygenase (BVMO) is to be found in the PDB database, and there are only a few reports on bacterial BVMOs [3] or steroid dehydrogenases [4]. Docking simulations are performed on the chosen enzymes acting on steroids [3,4]. The database of ligands consists of several representative steroid structures with hydroxyl or ketone functions at C-3 and other substitutions: DHEA, testosterone, pregnenolone, androstenedione, progesterone, etc. Dependence of the binding affinity (scoring function) on the molecular structure will be discussed.

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Biotin as a perfect ligand: docking and molecular dynamics studies on biotin-burkavidin and biotin-streptavidin systems

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Streptavidin together with avidin are the best-known members of a biotin-binding family of proteins. This exceptionally strong non-covalent binding (Kd ≈ $10^{-14} \div 10^{-16}$) makes these proteins useful in a variety of chemical and biochemical procedures, including purification, labelling (drug targeting), self-assembly of nanostructures. Artificial (metallo)enzymes can be based on the biotin technology [1-3]. The biotin-binding protein family was recently extended by a protein isolated from a human pathogen *Burkholderia pseudomallei*. The protein, burkavidin, was tested as a modified biotin host, exhibiting catalytic activity [4]. On the basis of homology modeling techniques we prepared a 3D model of burkavidin using MODELLER package.

```
STREPTAVIDIN: A---------GITGTWYNQLGSTFIV--TAGA-DGALTGTYESAV--GNAE-SRYVLTGRYDSAPAT-DG--
BURKAVIDIN:   DTSTAPNCQNPI-GSWLNELGSTMTIASISG--TGAITGTYVSPS--GTTG-QTFSLSGWFYAAPPANNGLD

STREPTAVIDIN: SGTALGWTVAWKNNYRN--AHSATTWSGQYVGGA-EARINTQWLLTSGTTEANAWKSTLVGHDTFTK--VKPS-
BURKAVIDIN:   QVTLVTFSVNWNN--TAARYNSITTWSGLCQITNNVPTITALYYYSNAFAQYS-WKHVNVGQDIFHP--IAP--
```

Figure 1. Alignment of burkavidin to the streptavidin template

In this study we report the impact of structural modifications of biotin (e.g. removal of hydrogen-bonding-capable functions, change of protonation state etc.) on the docking of biotin to streptavidin (as a control) and burkavidin. The impact is evaluated by the calculated "binding affinity" and by the percentage of successful finding the correct site by the docked molecule. Further, the dynamical nature of the biotin-protein contacts [3] was investigated by molecular dynamics calculations. AMBER force field was employed to represent the involved species.

Acknowledgements. We gratefully acknowledge computer time as well as the use of facilities granted by the Wrocław Centre for Networking and Supercomputing (WCSS), Poznań Centre for Supercomputing and Networking (PCSS) and Gdańsk supercomputing centre (CI TASK). This work has been supported by the National Centre of Science (NCN – Poland), grant no. UMO-2013/09/B/ST4/00279.

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Binding affinities for quinolinesulfonamides with bovine serum albumin. Computational studies

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Quinolinesulfonamides (QS) are biologically active compounds with potential antiviral, antitumor and neuroprotective action. These compounds can be distributed in human body probably in complexes with albumins. In preclinical studies bovine serum albumin (BSA) is widely used as a model plasma protein.

In this work we studied the interactions between BSA and two sulfamoyl quinoline derivatives: quinoline-2-sulfonamide (2QS) and quinoline-8-sulfonamide (8QS).

Computational experiment was performed using molecular docking techniques. The X-ray structure of BSA (4OR0.pdb) was downloaded from the Protein Data Bank [1]. Crystal structures of 2QS and 8QS were collected from Cambridge Structural Database [2, 3].

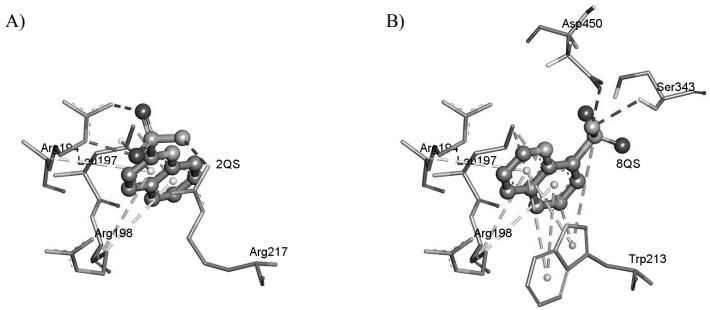

Figure 1: The comparison of binding conformation between 2QS (A) and 8QS (B) in their primary binding site in BSA. Binding interactions are shown in dashed lines

Acknowledgements. This work was supported by grant KNW-2-008/N/5/N from Medical University of Silesia, Katowice, Poland. Calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl), grant No. 382.

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The influence of the position of chlorines around the biphenyl rings in polychlorinated biphenyls on their interactions with human serum albumin

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Polychlorinated biphenyls (PCBs) are environmental toxicants which accumulate in human tissues. PCBs are classified as ortho-substituted or non-ortho-substituted congeners depending on theirs position of chlorine atoms around the biphenyl rings. PCB congeners belonging to these classes are different biologically activities and toxic effects. One of the dangers resulting from the presence of PCBs in human body is their ability to interact with carrier proteins. Human serum albumin (HSA) is a mainly plasma protein responsible for the distribution of drugs in human blood. Based on crystallographic studies it is known that HSA contains two hydrophobic drug-binding sites: Sudlow's site 1 and Sudlow's site 2 [1].

The aim of the present study was to investigate the influence of the position of chlorines around the biphenyl rings in PCBs on their binding properties in relative to HSA. Interactions between PCBs and HSA (1AO61.pdb) have been studied by means of molecular docking [2]. Conformation of ligands were energy-minimized using the Austin Model 1 (AM1) method.

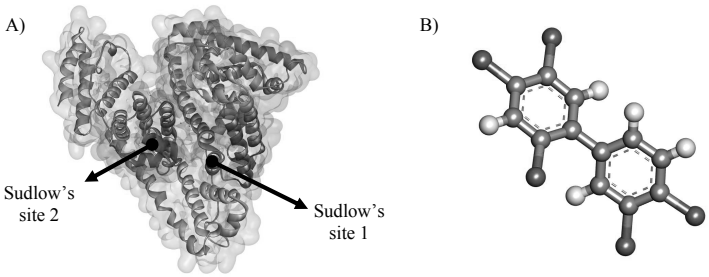

Figure 1: The three dimensional structures of HSA (A) and 2,3',4,4',5-pentachlorobiphenyl (B).

Acknowledgements. This work was supported by grant KNW-2-008/N/5/N from Medical University of Silesia, Katowice, Poland. Calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl), grant No. 382.

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Conformational dynamics of vitamin B_{12}-peptide nucleic acid conjugates revealed with molecular dynamics approach

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Vitamin B_{12} has been recognized as an efficient transporter of proteins, anticancer drugs and radioisotopes to eukaryotic cells [1]. We explore the idea to employ vitamin B_{12} for delivery of peptide nucleic acids (PNA) to bacterial cells. Peptide nucleic acid is a neutral DNA analogue that efficiently hybridizes with DNA and RNA and can be used in anti-sense or anti-gene applications. We have synthesized vitamin B_{12}-PNA conjugates and examined their structural properties with computational and experimental methods.

Molecular dynamics (MD) simulations have been conducted for free vitamin B_{12} and its conjugates with a 14-mer PNA of a sequence aimed to target an mRNA transcript encoding the red fluorescence protein (rfp). The following systems: vitamin B_{12}, B_{12}-PNA(C), B_{12}-PNA(anti-rfp), PNA(anti-rfp) were studied with employment of the AMBER force field [2]. The simulations were performed with NAMD [3] with the production trajectories up to 1 μsec. The method of conjugation of vitamin B_{12} and PNA was based on combined strategies described in [4] and [5, 6]. The series of 2D-NMR experiments (^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{1}H-^{1}H NOESY and ROESY) have been performed for the B_{12}-PNA(C).

In MD simulations we observed large conformational flexibility of vitamin B_{12}-PNA conjugates in aqueous environment. Intramolecular contacts between vitamin B_{12} and PNA within the conjugate have been identified using computational tools and will be verified with NMR analysis. Compactness of the PNA strand in water suggests its enhanced hydrophobic properties. In combination with hydrophilicity of vitamin B_{12}, it gives vitamin B_{12}-PNA conjugates an amphiphilic character that may play an essential role in their biological activity.

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Electric properties of light rare gas atoms. Accurate Coupled Cluster calculations

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Series of non-relativistic, Coupled Cluster (CC) calculations employing the hierarchy of the CC2, CCSD and CC3 approximations were performed in order to determine the following electric properties: dipole polarizability α, quadrupole polarizability *C*, dipole-dipole-quadrupole hyperpolarizability *B*, and second hyperpolarizability γ of the light rare gas atoms: He, Ne, and Ar. The closed-shell structure and the small size of the studied systems allowed us to study the effect of the basis set saturation on the properties of interest in a systematic manner. The quadrupole augmented cc-PV6Z (q-aug-cc-PV6Z) bases give practically the basis set limit values, at least for the dipole properties. Frequency-dependent dipole polarizability α(ω) is estimated using the following expansion:

$$\alpha(\omega) = \sum_{n=0}^{\infty} \omega^n D(n)$$

Where several values of the dispersion coefficient up to *D(10)* are also computed at the CC level.

The results indicate that the CC2 approximation tends to overestimate electric properties slightly, *e.g.* for the Ar second hyperpolarizability γ the difference between CC3 and CC2 for the q-aug-cc-pV6Z basis equals 70 a.u. or 6% of the CC3 value. The differences between CC3 and CCSD are much smaller. All calculations are carried out using the DALTON program [1].

Acknowledgements. The author acknowledges the computational grant from the Wrocław Centre for Networking and Supercomputing, in Wrocław.

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Modeling of low temperature adsorption of hydrogen in carbon nanopores

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During the last two decades a lot of effort has been devoted to develop a material that could store an applicable amount of hydrogen by physisorption. All these attempts have failed. Therefore, computer simulations have been used to guide the experiment and to determine in advance the potential storage capacity of a particular structure.

Usually, to simplify the interaction model and to spare the computation time, the simulations of hydrogen adsorption in nanoporous materials use the superatom representation of H_2 molecule with semi-empirical values of interaction model. This approach totally neglects the non-spherical shape of the molecule. However, this information may be crucial for the precise evaluation of the amount stored and the structure of the adsorbed layers, as packing of the spherical and elongated molecules is not the same. Therefore in the present work we compare the structure and storage of H_2 in slit-shaped, infinite carbon pores of nanometric width (from 0.6 nm to 2.5 nm), modeled using united atom (UA) and all atom (AA) representation of H_2 molecule.

We used Grand Canonical Monte Carlo technique to simulate H_2 adsorption isotherms at T = 77 K, either within Material Studio software (for AA model) or home-made code (for UA model). We shows that in both models the calculated amount of stored hydrogen is similar. This results confirm the validity of previous UA model-based estimations of storage capacity reported in the literature. Moreover, our simulation shows that UA model slightly overestimates the stored amount in narrowest pores (0.6 – 0.8 nm) and underestimates it in pores of width of 1.0 -1.2 nm. For pores larger than 1.5nm both models give the same results, at least at the adsorption pressure range studied here (1 – 700 bar). In particular, these observations do not depend on pressure.

Both models shows that the H_2 layer directly in contact with the pore wall is dense, with density largely exceeding the bulk density of liquid hydrogen at 33 K. This results confirm the recent experimental observations of hydrogen densification under confinement in carbon-based nanospaces [1, 2].

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An impact of non-covalent interactions on structure and stability of selected molecular materials

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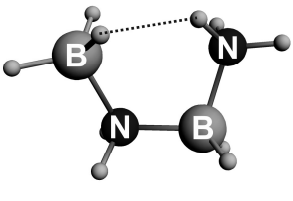
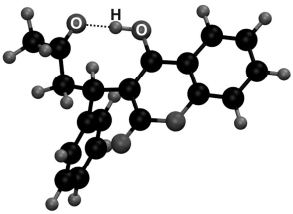
Non-covalent interactions are crucial for a range of physical and structural properties, such as high boiling point of water or secondary structure of proteins.

In this work we have demonstrated the importance of non-covalent interactions in various materials: hydrogen storage systems (the isosteres of BN/CC butanes)[1], the trioctylphosphine oxide (TOPO) capped CdS nanoparticles[2] and the coumarine derivatives[3] (see the Figure below).

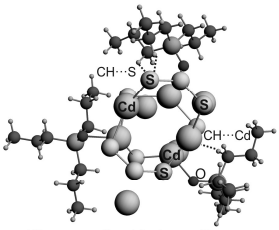
Briefly and more specifically, we have detected and described in detail (based on the charge and energy decomposition scheme ETS-NOCV) various types of dihydrogen interactions which appeared to be crucial for the stability and dehydrogenation of BN/CC butanes.[1] As far as the TOPO-capped CdS nanoparticles are concerned we have found that the high stability of such system originates from the strong Cd–O bonds as well as from the C–H···Cd and C–H···S interactions.[2] Finally, we have found that the intramolecular O···HO interactions are of great importance for the acidity of the coumarine derivatives – we have presented the satisfactory correlation between the calculated and experimental pK_a values.[3]



Dihydrogen bond in $BH_3NH_2BH_2NH_3$



Hydrogen bond in warfarin



Non-covalent interactions in TOPO-capped CdS

Acknowledgements. Results presented in this work were partially obtained using PL-Grid Infrastructure and resources provided by ACC Cyfronet AGH.

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DFT-GIAO calculations in structural studies of substituted etheno adducts of adenine nucleosides

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Etheno adducts are formed in reactions of DNA bases with chloroacetaldehyde, with lipid peroxidation products, and also with metabolites of vinyl chloride and furan. Presence of such modifications in genetic material may lead to errors in replication with consequences of mutations and even carcinogenesis. For an understanding of the biological significance of etheno adducts it is important to determine their structures. Structural identification is also essential for using these adducts as inflammatory or cancer biomarkers.

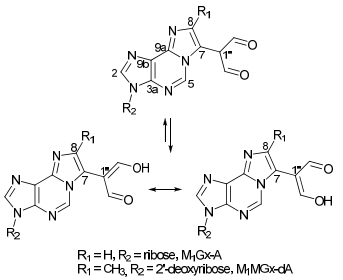

Figure 1: Structures of studied etheno adducts

NMR spectroscopy and theoretical methods have been used in structural studies on two adducts formed in reactions of malonaldehyde and glyoxal with adenosine (M_1Gx-A), and malonaldehyde and methylglyoxal with 2'-deoxyadenosine (M_1MGx-dA) (Figure 1) [1-3].

DFT-GIAO calculations were performed at M06/6-311++G(2df,2pd), B3LYP/6-311++G(2df,2pd) and M06/6-31++G(d,p) levels both in the gas phase and taking into account the effect of solvents (water, methanol and DMSO) using PCM approximation. It has been shown that when M06 or B3LYP functionals with the 6-311++G(2df,2pd) basis set are used, ^{1}H NMR chemical shifts very close to experimental values are obtained and surprisingly results of GIAO calculations at the M06/6-31++G(d,p) level have better correlation with measured ^{13}C NMR chemical shift values. PCM improves the correlation of results in all cases.

Acknowledgements. This research was supported in part by PL-Grid Infrastructure.

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Conformational studies on rotamers of *N*-acetylcysteine cross-links with adenine and adenosine aldehydic adducts

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M_1Gx-A-NAC, M_1MGx-A-NAC and M_1MGx-Ade-NAC (Figure 1) can represent model DNA-protein cross-links of *N*-acetylcysteine with aldehydic adducts of adenosine [1-3].

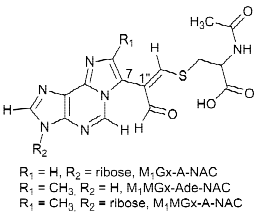

Figure 1: Structures of studied compounds

^{1}H and ^{13}C NMR spectra of M_1MGx-Ade-NAC and M_1MGx-A-NAC recorded at room temperature exhibited doubling of signals. A very intriguing was fact that no duplication of signals was seen in the spectra of M_1Gx-A-NAC. The three cross-linked products differ only with the substituent at C8; proton attached to C8 in M_1Gx-A-NAC is replaced in M_1MGx-Ade-NAC and M_1MGx-A-NAC by a methyl group. Presence of this group was supposed to cause hindered rotation over the C7-C1" bond resulted in existing of rotamers.

To confirm this hypothesis, variable-temperature ^{1}H NMR studies together with computational investigations were performed.

For these cross-links coalescence temperature was determined based on ^{1}H NMR studies. The Gibbs free energies for interconversion between rotamers of these compounds were calculated.

The aim of the quantum chemical investigations was to examine hindered rotation around the C7-C1" bond in M_1MGx-A-NAC and M_1MGx-Ade-NAC. The studies were performed with the use of DFT methods up to M06/6-31G(d), M06/6-31++G(d,p), B3LYP/6-31++G(d,p) and ωB97X-D/6-31G(d).

Additionally the Atoms in Molecules (AIM) theory was used to investigate the intramolecular hydrogen bond formation which may stabilize rotamers and inhibit their fast interconversion at room temperature.

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Binding kinetics of glycoproteins to their receptors by multi-scale molecular simulations

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The post-translational glycosylation of proteins can influence the protein-receptor binding kinetics due to both steric hindrance and alteration of electrostatic interactions. Both current developments in chemical force fields for carbohydrates and advances in sampling techniques for Molecular Dynamics (MD) simulations allow us to study glycan-protein interactions on a molecular level. This research aims at establishing a workflow for studying molecular interactions between glycosylated proteins and their receptors, as well as for predicting kinetic parameters.

We chose the human erythropoietin (EPO) as a testing and benchmark system because it has been extensively experimentally studied. The modeled EPO species are unglysoylated EPO, mono-N-glycoslyated EPO, and threefold N-glycosylated EPO, whereby the bi- or tetra-antennary glycans may carry terminal sialic acid (Neu5Ac) moieties. In our approach, we utilize a multi-scale simulation workflow: 1. Full-atomistic MD for sampling glycoprotein conformations; 2. Brownian Dynamics (BD) simulations for rigid-body association of the EPO species with their receptor (EPOR).

The full-atomistic simulations show that the glycosidic bond torsion conformational space of the glycan is well represented by only 5 to 10 clusters. This is because terminal sialic acid residues frequently deploy hydrogen bonds with the guanidine group of surface exposed arginines in the protein, resulting in a strong decrease in the flexibility of the glycan. Additionally, we find that the accessibility of the EPO-EPOR binding site is almost unaffected even by the large tetra-antennary glycosylation. From a multitude of unbiased BD simulations, protein-receptor interactions are investigated by monitoring inter-protein contacts. The BD docking simulations, which incorporate electrostatic interactions and hydrophobic desolvation, predict the EPO-EPOR complex crystal structure well (root mean square deviation < 6Å). This is a very promising approach for the computation of the rates of protein association (k_{on}). However, there is still manual interference required that obstructs high-throughput computation of various conformations in an automatized workflow.

In the long term, we expect this approach to be able to sufficiently predict k_{on} of any bimolecular system where glycosylation plays a key role.

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Study of Interaction of Hydrated Hg^{II} Ion with Thymine Using DFT and QM/MM MD Approach

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Double-stranded DNA with thymine mismatches represents an effective target for Hg^{II} cations, which bind between mismatched thymine (T) bases and form T-Hg^{II}-T metal-mediated base pairs. In addition, T-Hg^{II}-T base pairs can be localized next to each other. [1] This ability can be used for construction of electric sensors or charge-transporting materials.

In our contribution, we study a reaction coordinate corresponding to binding of the Hg^{II} cation to the N3 position of 1-methylthymine using QM/MM MD approach. Two different protonation states of the first solvation shell of the Hg^{II} cation are considered – solvation shell with one or two hydroxo ligands. In our simulations the QM part consists of 1-methylthymine and $[Hg(H_2O)_5\}(OH)]^+$ or $[Hg(H_2O)_4(OH)_2]$ cluster and the MM region is represented by surrounding solvent. The calculations are carried out at the B3LYP-GD3BJ/LANL2DZ/(Amber force fields) level using QMS 1.7 interface [2] for propagation. The free energy perturbation (FEP) method is subsequently used with larger basis set 6-31+G(d)/SDD in order to increase accuracy of the QM/MM energy profiles and the obtained results are compared with the previous ONIOM [3] and our DFT-D calculations.

Another interesting reaction with respect to possible mutations during DNA replication represents a transition between keto and enol form of thymine i.e. proton transfer from nitrogen N3 to oxygen O2. Particularly, we focus on the catalyzed proton transfer by hydrated metal cations. An effect of the hydrated Hg^{II} cation on the keto-enol transition is compared with an impact of biologically significant Zn^{II} and Mg^{II} cations. The structures are optimized at the B3LYP/6-31G(d)/SDD level and the first solvation shell (six water molecules) of metal cations is treated explicitly in these calculations. In orderto analyze the course of the studied keto-enol transition the reaction electronic flux [4] is determined along intrinsic reaction coordinates. Also Bader's AIM and ETS-NOCV analyses are carried out at the B3LYP/TZ2P (4f core for Hg) level using ZORA hamiltonian in order to observe changes in the electron density distribution.

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Red-shifting the wavelength of the Spinach aptamer, suggestions from QM:MM calculations

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Spinach aptamer was developed as an RNA analog of the Green Fluorescent Protein. The aptamer interacts with 3,5-difluoro-4-hydroxybenzylidene imidazolinone (DFHBI) molecule and modifies its electronic spectrum so that the chromophore emits bright light with wavelength of 501 nm. Song et al. have investigated modifications of the chromophore in their experimental study [1] and found that substitution of methyl group at position 2 by trifluoromethyl leads to emission wavelength of 523 nm in complex with the Spinach aptamer.

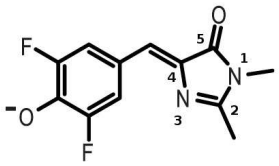

Figure 1: DFHBI molecule

The crystal structure of the Spinach aptamer in complex with its original ligand has been published in 2014 [2] and it enabled us to study the system computationally. In this contribution, we will report several new modifications of the chromophore that further red-shift absorption electronic spectrum of the complex. Our results are based on combined quantum mechanical / molecular mechanical calculations in ONIOM with the choice of DFT as the quantum mechanics method. These were used for geometry optimization. The quantum mechanical (QM) region contained the chromophore and nearby nucleotides. Excitation energies were calculated by TDDFT method on the QM region, optimized in ONIOM, embedded in PCM continuum with solvent of medium dielectric constant.

Acknowledgements. Support from the Slovak Scientific Grant Agency through VEGA 1/0878/15 grant is acknowledged.

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Comparison of amino acid's pKa computed by various DFT functionals and implicit solvent models

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Acid deprotonation constant, pKa, is difficult to obtain by theoretical methods because it is sensitive to accurate determination of free energy of deprotonation (an error of 1.36 kcal/mol in the change of free energy of deprotonation is an error of 1 pKa unit) [1]. This disadvantage turns into advantage in benchmark studies where tiny differences in energy are searched.

This benchmark study compares pKa values of several amino acids obtained by DFT calculations with 8 widely used functionals (B3LYP, M11, M11-L, M06-2X, PBE1PBE, PBEh1PBE, TPSSh and ωB97XD) combined with 3 basis sets (6-31+G*, 6-31++G(p,d) and 6-311++G(2df, 2pd)). Calculations are performed either in vacuum or in implicit solvent (IEF-PCM, D-PCM, C-PCM and COSMO/RS models are tested) with various definitions of cavities (UFF or UAKS topologies of cavities with atomic radii scaled by the electrostatic scaling factor of 1.1 or 1.2 are combined).

Our results show the importance of implicit solvent's model choice and cavity settings for proper reproduction of pKa. They favor D-PCM implicit solvent model combined with cavity scaling scheme proposed by Zimmermann and Burda [2] computed at the M11-L/6-311++G(2df, 2pd) level of theory.

Acknowledgements. Computational resources were provided by the CESNET LM2015042 and the CERIT Scientific Cloud LM2015085, provided under the program "Projects of Projects of Large Research, Development, and Innovations Infrastructures"

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Theoretical insight into NO activation/deactivation by ammonia modified cobalt centers in zeolites

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It is known that the interaction of non-innocent NO ligand and transition metals results in the complexes with intricate electronic structure, posing a challenge to computational chemistry. Therefore, the explanation of the NO activation by zeolitic cobalt centers modified by ammonia molecules is not a straightforward task. In order to deal with that we applied the CASSCF method, using the Pipek-Mezey procedure to localize active orbital. In the next step we obtained the relative shares of resonance structures: $Co^{I}NO^{+}$, $Co^{II}NO^{0}$, $Co^{III}NO^{-}$. In addition, SR-NOCV analysis based on DFT:BP86 approach was performed to investigate the electron density transfer between Co center and NO.

In our model NO was bonded to cobalt center, represented as single tetrahedron (labeled T1) where Co^{2+} was linked via two framework oxygen atoms. The model was extended by two water molecules to mimic the fourfold coordination. Ammonia-modified centers (no water molecules) were built in agreement with experimental suggestion and consisted of two or three NH_3 ligands. Furthermore, the complex with five NH_3 ligands, non-covalently interacting with the framework, was taken under consideration. Large T12 model for parent zeolite (no ammonia molecules) was optimized to validate the electronic and structural properties of small T1-based cluster.

Our research showed the strongest NO activation for the Co^{2+} site modified by three NH_3 ligands (singlet ground state). In this case the contribution of $Co^{III}NO^{-}$ resonance structure to wave function was high and equal to 25%. Interestingly, for full ammonia-saturated complex the share of $Co^{III}NO^{-}$ resonance structure was smaller by 8% while the contribution of $Co^{I}NO^{+}$ resonance structure was a little higher. Interpretation of SR-NOCV analysis depicted the stronger electron density transfer to NO antibonding orbital for singlet states of three ammonia T1-based cluster than complex with five ammonia molecules.

The protocol based on CASSCF calculations appeared to fully rationalize the NO activation, in dependence on as well the number of NH_3 ligands as the spin state of the Co^{2+} site. We assessed the limitation of SR-NOCV analysis being the less robust tool in this case [1], in contrast to our former research based on the selection of closed-shell ammonia fragment [2]. In the present study, SR-NOCV analysis can be used solely to compare electron transfers for the complexes, described by similar contribution of analogous leading configuration and the same type of examined bond.

Acknowledgements. We acknowledge the financial support provided by Grant No. 2013/11/N/ST4/00984 from the National Science Centre, Poland.

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Modeling of enzyme-ligand interactions, molecular dynamics approach

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Interaction protein–ligand is essential for all processes in living organisms; it involves the biological recognition, at the molecular level, that may be exploited by an appropriate functionalization of protein (homology of composing aminoacids) and/or chosen ligands at the active site, thus inducing a high specificity of the response (e.g., energetic signal, transformed substrate, etc.) of such interaction. A variety of molecular devices may be realized in this respect, with the aim of disease treatment.

Molecular dynamics simulation of drug complexes allows the simultaneous assessment of binding affinity and dynamic properties of analyzed compounds in the conformational space of protein active sites.

As a starting point in our molecular dynamics simulations, the complexes ligands - protein obtained during docking procedure were used. All simulations were done in explicit solvent environment. Calculations of the free energy were performed by using the Molecular Mechanic/Poisson-Boltzmann Surface Area (MM-PBSA) method. Structural and energetic parameters, including angles, distances, hydrogen bond creation, rmsd values and entropic contribution to binding affinity were collected and the results interpreted in the light of protein-ligand interaction.

Bond length alternation (BLA) as important parameter affecting the results of spectral properties calculations: CASPT2 & nevPT2 study of retinal chromophores

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The second-order perturbation theory with a complete active space self-consistent field reference function (CASPT2), which effectively includes electron correlation, can be a state-of-the-art method for many small-molecular systems. Unfortunately, in each formally rigorous method some degree of arbitrariness is always present. Indeed, the proper use of CASPT2 technique requires a careful discussion of number of parameters that have to be used. Choices of basis set, active space size, *LEVEL-shift* value and *IPEA-shift* value (important, but often omitted) are obviously significant. An additional difficulty is problem of choosing the suitable equilibrium geometry. It is neither easy nor obvious task.

The retinal molecule, which significant part is π-conjugated, is classical example of biochromophore. In such molecules the geometric and electronic structures are closely related. Of course, an accurate description of the ground-state structures is crucial prerequisite for the determination of valid spectral properties. However, comparing all of the geometrical parameters is a tedious and often even unnecessary work. More convenient is to use one parameter to describe chosen geometrical properties of molecule. The most useful in similar cases is the value of bond length alternation (BLA) - a geometrical parameter calculated as the difference between the average lengths of single bonds and double bonds in π-delocalized systems.

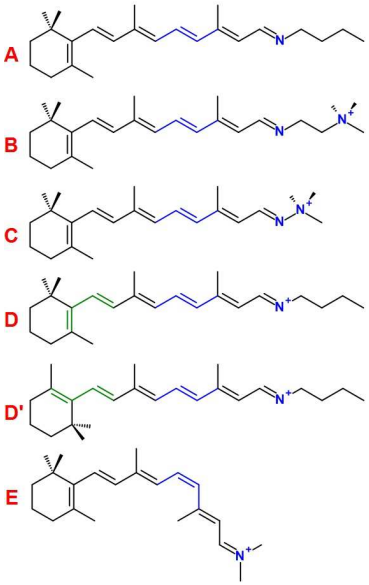

Figure 1: Set of retinal analogues (A-E) considered in our study

In our work we want to show the impact of the BLA parameter value on results calculated at CASPT2 level of theory. For comparison we present some results from nevPT2 and CC2 calculations.

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Theoretical studies of properties of active compounds of Rhubarb

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Rhubarb is one of the most widespread drugs used in China for thousands of years to produce various pharmacological and biological effects. The traditional Rhubarb has effects of diarrhea, anti-bacterial treatment of chronic renal failure, gallbladder jaundice, liver protection, stop bleeding and blood circulation, antipyretic, prevention and treatment of lung injury enterogenic and anti-senescence. Nowadays, scientists get new point that Rhubarb has the effect of anti-cancer. We are focused on its diarrhea and anti-cancer effects because they are most useful functions in our clinical treatments now and in the future. To study properties of active compounds in Rhubarb is our target. There are six compounds which are the most important in Rhubarb including Rheinanthrone, Emodin, Aloe-emodin, Rhein, Chrysophanol and Physcion. The most important component contributing to its multiple medicinal properties are anthrone and anthraquinones. Rheinanthrone which comes from Sennosides irritates the lining of the bowel and causes a laxative effect. And drugs containing an anthraquinone moiety such as Daunorubicin and Mitoxantrone being intercalator constitute some of the most powerful cytostatics. They suppress tumor growth mainly by interaction into DNA and inhibition of topoisomerase□, and are suspected to generate free radicals leading to DNA strand scission. We focused on its theoretical studies of Rhubarb using different methods at molecular level, besides, compared properties such as molecular structures, bond length, atomic charges, hybrid orbital, HOMO-LUMO gap, NMR spectrum as Emodin to qualify and quantify Rhubarb and studied its diarrhea and anticancer mechanism of active compounds. It is a new method to analysis Traditional Chinese Medicine using NMR in gas phase which is good for small organic molecules. NMR spectra of gaseous compounds and quantum chemical calculations are combined to determine new accurate values of shielding constants and chemical shift for compounds of Emodin, and show us what is the best theoretical method for Emodin. The absolute shielding constants in the studied molecules are obtained from DFT and HF which basis set are cc-pvdz and 6-31g(d).

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Studies on the photochemistry of psoralens intercalating DNA

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Psoralens are tricyclic furocoumarins used as therapeutic agents since ancient times. Nowadays they are routinely used in photochemotherapy with high-intensity UV-A irradiation. The underlying molecular mechanism is based on their strong tendency to intercalate with DNA [1-2]. Subsequent irradiation of the complex with UV-A (~360 nm) results in the 2+2 cyclo-addition of either of its two photoreactive sites with 5,6-carbon bonds of pyrimidines. Absorption of a second photon results in crosslinking of the DNA double-stranded helix. However, the reported quantum yields of this process are rather low (<9%) [2].

Recently Fröbel et al. observed significant reduction in the lifetime of the S_1 state of 4′-aminomethyl-4,5,8-trimethylpsoralen (AMT) using femtosecond transient absorption spectroscopy [2]. This singlet quenching appears to be due to ultrafast purine to AMT electron transfer and charge recombination implied by a low quantum yield of adduct formation. However, the mechanistic details of this processes were not investigated.

In here we report the results of our preliminary studies on the photochemistry of 4-hydroxymethyl-4,5,8-trimethylpsoralen (HMT) intercalated with model double stranded DNA. We used molecular mechanics and dynamics to find representative conformers of model intercalated DNA. Then, for the selected structures we constructed model systems for ab initio calculations. We performed calculations of the vertical excitation spectra, located the relevant minima on excited state surfaces and minimum energy crossing points, and calculated potential energy surface cuts using TD-DFT, ADC(2) and CASPT2/CASSCF methods. Our preliminary results confirm the experimental suggestions of the ultrafast DNA to psoralen charge transfer.

Acknowledgements. Most of the calculations were performed at the Wrocław Center for Networking and Supercomputing (WCSS) and Interdisciplinary Centre for Mathematical and Computational Modelling in Warsaw (ICM).

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