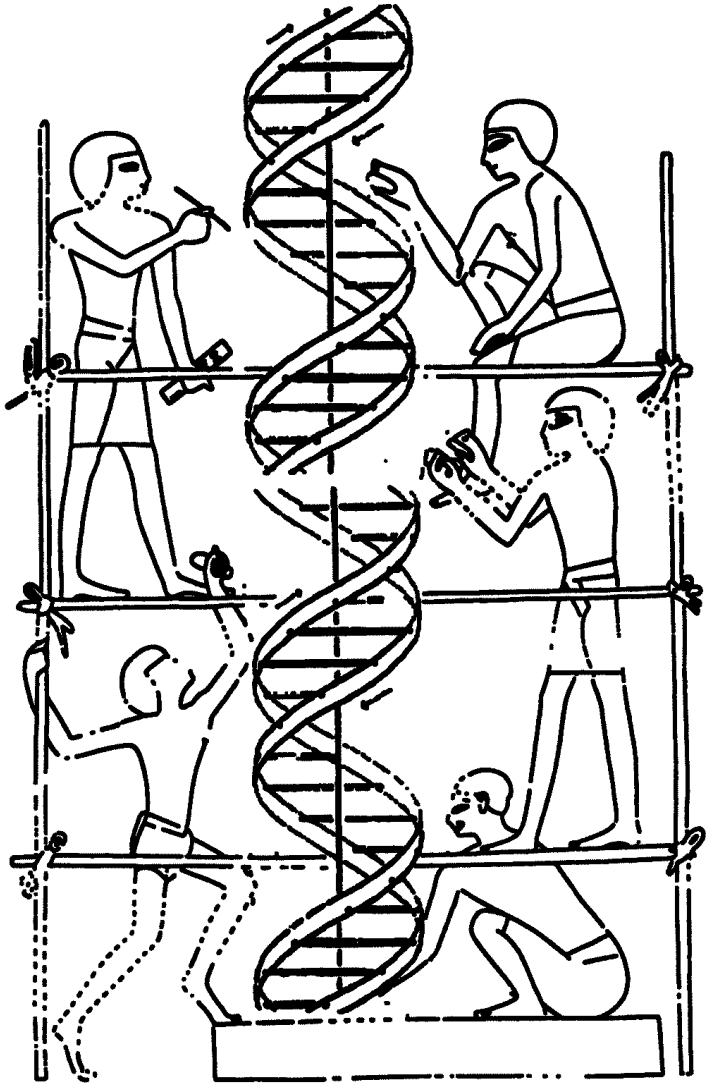
Modeling & Design of Molecular Materials 2014

Kudowa Zdrój, Poland – June 29 - July 3, 2014



Conference program & abstracts

Modeling & Design of Molecular Materials 2014

a meeting organized by

Molecular Modeling & Quantum Chemistry Laboratory
Wrocław University of Technology (WUT), Wrocław, Poland

NSF Interdisciplinary Center for Nanotoxicity
Jackson State University, Jackson, MS, USA

Charles University in Prague, Czech Republic

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Conference program

June 29, 2014 (Sunday)

14:00-18:00	Registration
18:00	Opening ceremony
Session I	chair: J. Leszczyński
18:05	**Keynote (L1): D. B. Janssen (University of Groningen, Netherlands)** *Discovery and engineering of biocatalysts supported by computational design*
18:40	**L2: K. Maruszewski (EU Joint Research Center, Ispra, Italy)** *Science based policy making: who does what?*
19:15-22:00	Grill

June 30, 2014 (Monday)

Session II	**Modeling Reactions & Catalyst Design** (chair: P. Paneth)
9:00	**L3: M. B. Hall (Texas A&M University, United States of America)** *Metal bis(dithiolenes) as electro catalysts*
9:30	**L4: J. Sauer (Humboltd University, Germany)** *Ab initio free energy calculations with chemical accuracy for molecule - surface interactions*
10:00	**L5: E. Brocławik (J. Haber Institute of Catalysis, Kraków, Poland)** *Donor modifiers of Co(II) acitive site properties: explicit spin and charge transfer channels for NO - NH3 co-adsorption in zeolites*
10:30	Coffee break
Session III	**Modeling Reactions & Catalyst Design** (chair: J. Sauer)
11:00	**L6: T. Brinck (Royal Institute of Technology, Stockholm, Sweden)** *Redesigning enzymes for non-native reactions: the case of Diels-Alderases*
11:25	**L7: V. Moliner (Universitat Jaume I, Castellón de la Plana, Spain)** *Theoretical studies of dynamic and quantum tunnelling effects in enzymes*
11:50	**L8: P. Paneth (Łódź Technical University, Poland)** *To B3LYP or not to B3LYP?*
12:20	**L9: T. Borowski (J. Haber Institute of Catalysis, Kraków, Poland)** *Reaction mechanisms of selected mononuclear non-heme oxygenases – insights from computational studies*
12:40	**L10: B. Szyja (Westfaelische Wilhelms-Universität Münster, Germany)** *Design of hierarchical zeolite catalysts*
13:00	Lunch

Session IV	**Modeling Molecular Materials for Molecular Electronics** (chair: O. Shishkin)
15:00	**L11: O. Prezhdo (University of Rochester, United States of America)** *Quantum dynamics of solar energy materials*
15:25	**L12: T. Clark (Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany)** *Novel multiscale simulations of molecular electronics*
15:50	**L13: M. Natarajan Arul (Royal Institute of Technology, Stockholm, Sweden)** *Multiscale modeling approaches for diagnostic probes design*
16:10	**L14: F. Blockhuys (University of Antwerp, Belgium)** *Hybrid organic-inorganic conjugated oligomers: the best of both worlds*
16:30	**L15: P. Szarek (Osaka University, Japan)** *The physicochemical aspects of conduction in molecular junction*
16:50	**L16: B. Szefczyk (Wrocław University of Technology, Poland)** *Discovering the structure of NaYF4 hexagonal phase*
17:10	Coffee break
17:40-19:10	Poster Session I

July 1, 2014 (Tuesday)

Session V	**Modeling Interactions in Molecular Materials** (chair: T. Clark)
9:00	**L17: M. Head-Gordon (University of California, Berkeley, United States of America)** *Advances in density functional theory calculations for intermolecular interactions*
9:30	**L18: M. Szczęśniak (Oakland University, Rochester, MI, United States of America)** *Gold-gold and gold-ligand interactions: separating true from pretend*
10:00	**L19: J. Gu (Shanghai Institute of Materia Medica, China)** *Electron-DNA interactions: a DFT investigation*
10:30	Coffee break
Session VI	**Modeling Reactions & Catalyst Design** (chair: J. Murray)
11:00	**L20: A. Mulholland (University of Bristol, United Kingdom)** *Computational biochemistry: enzyme dynamics, conformations and catalysis*
11:30	**L21: H. Cheng (National University of Singapore, Singapore)** *First principles modeling guided discovery of efficient hydrogenation catalysts*
12:00	**L22: J. Burda (Charles University, Prague, Czech Republic)** *Reactions of Ru(II) complexes; quantum mechanical and combined QM/MM MD study*
12:30	**L23: J. Leszczyński (Jackson State University, United States of America)** *Los Angeles Clippers team has been estimated at $1B – How much could a computational chemistry group be worth?*
13:00	Lunch

Session VII	**Advances in Computational Methods** (chair: G. Chalasiński)
15:00	**L24: P. Politzer (University of New Orleans, United States of America)** *σ-hole interactions: a physical interpretation*
15:30	**L25: J. Murray (University of New Orleans, United States of America)** *Expansion of the π-hole concept*
15:55	**L26: A. Tachibana (Kyoto University, Japan)** *Spin vorticity and stress tensor of electron*
16:20	**L27: I. Cukrowski (University of Pretoria, South Africa)** *Exploring intramolecular interactions using the fragment attributed molecular energy change method*
16:40	**L28: I. Grabowski (Nicolaus Copernicus University in Toruń, Poland)** *Simple non-empirical procedure for spin-component-scaled MP2 methods applied to the calculation of dissociation energy curve of noncovalently interacting systems*
17:00	Coffee break
17:30-19:00	Poster Session II

July 2, 2014 (Wednesday)

9:00-13:00	Excursion
13:00-15:00	Lunch
Session VIII	**Modeling Materials** (chair: O. Prezhdo)
15:00	**L29: M. L. McKee (Auburn University, AL, United States of America)** *Computational modeling of lattice free energies. From solids to solvated ions*
15:25	**L30: O. V. Shishkin (Institute for Single Crystals, Kharkov, Ukraine)** *How are molecular crystals organized?*
15:50	**L31: Z. Latajka (Wrocław University, Poland)** *Xenon compounds - theoretical studies of molecular complexes*
16:15	**L32: S. Zarić (Texas A&M University at Qatar)** *Non-covalent interactions of aromatic molecules*
16:35	**L33: P. Cysewski (Nicolaus Copernicus University in Toruń, Poland)** *Factors contributing to stabilization of glycine crystal polymorphs*
17:00	Coffee break

Session IX	**Modeling Biomolecules** (chair: A. Wierzbicki)
17:30	**L34: J. Šponer (Academy of Sciences of Czech Republic, Brno, Czech Republic)** *Large-scale quantum chemical computations of nucleic acids*
17:55	**L35: N. Gresh (University Paris 05, France)** *Further progress in the developments of an anisotropic, polarizable molecular mechanics/dynamics potential. Applications to ligand-protein complexes and extensions to nucleic acids*
18:20	**L36: A. Lodola (Universita degli Study di Parna, Italy)** *Insights into the mechanism of EGFR covalent inhibition by QM/MM and enhanced sampling approaches*
18:45	**L37: B. Lesyng (University of Warsaw, Poland)** *A QM-MD simulation approach to the analysis of FRET processes in (bio)molecular systems*
19:10	**L38: G. Pályi (University of Modena and Reggio Emilia, Italy)** *Stochastic models of the absolute asymmetric synthesis by the Soai-autocatalysis*
20:00-22:00	Conference dinner

July 3, 2014 (Thursday)

Session X	**Modeling Biomolecules** (chair: A. Mulholland)
9:00	**L39: P. Carloni (German Research School for Simulation Sciences GmbH, Jülich, Germany)** *Multiscale modeling of membrane and membrane proteins*
9:30	**L40: A. Wierzbicki (University of South Alabama, United States of America)** *Collagen-hydroxyapatite interactions and the molecular-scale architecture of bone*
10:00	**L41: M. Kotulska (Wrocław University of Technology, Poland)** *Computational modeling of amyloid peptides*
10:30	Coffee break
Session XI	**Advances in Computational Methods** (chair: J. Burda)
11:00	**L42: A. Michalak (Jagiellonian University, Kraków, Poland)** *Theoretical description of chemical bonding based on natural orbitals for chemical valence (NOCV)*
11:30	**L43: S. Grabowski (University of Basque Country, San Sebastian, Spain)** *σ-hole bond versus hydrogen bond in simple complexes and large clusters*
12:00	**L44: A. Sikorski (University of Warsaw, Poland)** *Adsorption of non-linear polymers. A Monte Carlo study*
12:20	**L45: M. Jabłoński (Nicolaus Copernicus University in Toruń, Poland)** *Charge-inverted hydrogen bond as a new type of interaction*
12:40	Closing ceremony

MDMM 2014 conference posters

No.	Presenting authors	Title
P1/A	Wiktor Beker W. Andrzej Sokalski	*Catalytic activity of Kemp eliminase theozyme (KE07) mutants interpreted by electrostatic multipole term of differential transition state stabilization*
P2/A	Sławomir A. Bojarowski Prashant Kumar Paulina M. Dominiak	*A comparative study of transferable theoretical aspherical pseudoatom data bank and classical force field in predicting the electrostatic interaction in molecular dimers*
P3/A	Mateusz Brela Monika Srebro Artur Michalak	*Theoretical study on structure-activity relationships in ethylene polymerization catalyzed by half-metallocene titanium(IV) complexes*
P4/A	Tomasz Buchała Szczepan Roszak	*The evolution of charge transfer properties for pyrrole and 3,6-bis(2-pyrrolo)carbazol oligomers – precursors of conducting polymers*
P5/A	Zdeněk Chval Ingrid Romancová Ondřej Kroutil Miroslav Šíp	*Structure and dynamics Cy3 and Cy5 cyanine dyes terminally attached to DNA: a combined theoretical study*
P6/A	Katarzyna Czarnecka Tadeusz Andruniów	*Effect of His202 protonation on zFP538 chromophore geometry - molecular dynamics study*
P7/A	Przemysław Czeleń Beata Szefler	*Molecular dynamics study of ChEMBL474807 inhibition properties against GSK3 and CDK2 enzymes*
P8/A	Silvia Díaz Mateusz Brela Soledad Gutiérrez-Oliva Alejandro Toro-Labbé Artur Michalak	*Comparison of the reaction electronic flux and ETS-NOCV picture of the HCN→CNH isomerization reaction assisted by water*
P9/A	Justyna Dominikowska Marcin Palusiak	*On cations of polycyclic aromatic hydrocarbons*
P10/A	Agnieszka Drzewiecka-Matuszek Maria Oszajca Alicja Franke Dorota Rutkowska-Żbik Małgorzata Brindell Małgorzata Witko Grażyna Stochel Rudi van Eldik	*Reactivity of model complexes for Cpd I and Cpd II - theoretical studies*
P11/A	Olga Dvořáčková Zdeněk Chval	*Influence of the substitution effects in the pyridine ring on the reactivity of the trans-$[Pt(NH_3)_2(pyr{-}X)Cl]^+$ complex*
P12/A	Karol Dyduch Monika Srebro Artur Michalak	*Theoretical studies on the cobalt(III)-based catalysts for CO_2/epoxide copolymerization*

P13/A	Edyta Dyguda-Kazimierowicz Wiktor Beker W. Andrzej Sokalski	*Modeling the catalytic activity of enzyme mutants with differential transition state stabilization approach*
P14/A	Maciej Dziubiński Bogdan Lesyng	*Analysis of molecular interactions and internal tensions along a collective variable*
P15/A	Şerafettin Ekinci Mustafa Taşyürek Humar Kahramanlı Kadir Sabancı	*Modelling of the tensile properties of high density polyethylene/carbon nanotube composites via ANN*
P16/A	Ruslan Garifullin Turan S. Erkal Sezen Tekin Bülend Ortaç Ayşe Gül Gürek Vefa Ahsen H. Gul Yaglioglu Ayhan Elmali Mustafa O. Guler	*Encapsulation of a zinc phthalocyanine derivative in self-assembled peptide nanofibers*
P17/A	Michael Gastegger Philipp Marquetand Christoph Flamm Leticia González	*An evolutionary approach to computational de-novo enzyme design for olefin metathesis*
P18/A	Davy Geldof Frank Blockhuys	*Chemical surface modification of titanium oxide using organophosphonic acids*
P19/A	Ewa Gołaś Cezary Czaplewski Harold A. Scheraga Leslie Glasser Adam Liwo	*Structural insight through mechanical stretching: steered molecular dynamics simulations of a small heat shock protein*
P20/A	Łukasz Golon Lidia Chomicz Janusz Rak	*Theoretical investigation of brominated uracil radiosensitization mechanism*
P21/A	Izabela Grzelak Marcin Hoffmann	*Computational studies of potential inhibitors of sulfatase steroid*
P22/A	Teodora E. Harsa Alexandra M. Harsa Beata Szefler	*QSAR of dopamine derivates by similarity cluster prediction*
P23/A	Rocío Durán Bárbara Herrera Alejandro Toro-Labbé	*Reaction force and reaction flux analysis of proton transfers on DNA bases*
P24/A	Drahomír Hnyk Jan Macháček Derek A. Wann Paul D. Lane Jindřich Fanfrlík Adam Pecina Martin Lepšík Adam Přáda Josef Holub	*The structural consequences of functionalising and/or removing the cluster atoms of icosahedral closo-$B_{12}H_{12}^{2-}$. Possible applications*

P25/A	James Hooper	*Modelling the influences of the substrate and coverage on surface assemblies of 3-hydroxyphenalenone*
P26/A	Kate E. Horner Joseph M. Tresise Peter B. Karadakov	*Exploring the molecular properties of nucleobases with magnetic shielding calculations*
P27/A	Wojciech Jankowski Marcin Hoffmann Beata Jasiewicz Anna Gąsowska Karolina Malczewska-Jaskóła	*Quantum chemical calculations on complexes of anabasine with zinc(II) and copper(II) ions*
P28/A	Robert J. Floor Hein J. Wijma Dick B. Janssen	*Computational redesign of epoxide hydrolase for enantioselective synthesis*
P29/A	Mateusz Jasik Borys Szefczyk	*Parameterization of the menthol force field for ionic liquids simulations*
P30/A	Aneta Jezierska-Mazzarello Jarosław J. Panek	*Properties of hydrogen bridges of polycyclic aromatic systems with O-H···O bonds - a Car-Parrinello study*
P31/A	Gemma K. Kinsella Natalie-Anne Ward Jonathan Williams Simon C. Hirst John B.C. Findlay	*Melanocortin-4 receptor (MC4R) mutations – predisposition to obesity*
P32/A	Piotr Niemiec Renata Tokarz-Sobieraj	*Redox properties of modified Keggin heteropolyacids*
P33/A	Paweł Rejmak Jorge S. Dolado Malcolm J. Stott Andrés Ayuela	*Computational ^{29}Si NMR in hydrated cement pastes*
P34/B	Eliza A. Roszak Maciej Chorowski	*Adsorption characteristics of carbon materials in low temperature range*
P35/A	Rafał Roszak Szczepan Roszak	*"Frustrated Lewis pair" with light metals – tunable materials for hydrogen storage*
P36/A	Jakub Šebera Lukáš Trantírek Yoshiyuki Tanaka Vladimír Sychrovský	*Theoretical study of repairing function of hOGG1 enzyme*
P37/A	Hüseyin Ünver C. Tuğrul Zeyrek Hamit Alyar Mustafa Yildiz Nefise Dilek	*Molecular structure and quantum chemical computational studies of a new Schiff base*
P38/A	Jarosław Zaklika Paweł Kędzierski	*Improvement in analysis of nature of interactions in cathepsin L – inhibitor complex due to optimization of Lennard-Jones parameters*

P39/B	Jan Konieczny Renata Grzywa Edyta Dyguda-Kazimierowicz W. Andrzej Sokalski	*Nonempirical atom-atom potential functions representing intermolecular interaction energy components*
P40/B	Ondřej Kroutil Milan Předota Zdeněk Chval	*Structural and dynamic properties of the water hydration shell of the square planar platinum(II) complexes: ab initio MD study*
P41/B	Martyna Kuta Marcin Hoffmann Agata Głuszyńska	*Quantum mechanical and molecular modeling of carbazole ligands, potential telomerase inhibitors of antitumor activity*
P42/B	Dorota Latek	*Impact of cellular localization of proteins on docking accuracy*
P43/B	Elena Lilkova Peicho Petkov Damyan Grancharov Petko S. Petkov Nevena Ilieva Leandar Litov	*Estimating protein-protein binding free energies by the unit interval approach*
P44/B	Agnieszka Lipska Adam K. Sieradzan Paweł Krupa Magdalena Mozolewska Sabato D'Auria Adam Liwo	*Application of UNRES force field to coarse-grained molecular dynamics simulations of arginine-binding protein from Thermotoga maritima*
P45/B	Donatella Callegari Daniele Pala Silvia Rivara Marco Mor Alessio Lodola	*Comparative analysis of virtual screening approaches in the search for EphA2 receptor antagonists*
P46/B	Piotr Lodowski Maria Jaworska Tadeusz Andruniów Pawel M. Kozłowski	*Photochemical properties of base-off methylcobalamin. DFT and TD-DFT study*
P47/B	Rabindra Nath Manna Agnieszka Dybala-Defratyka	*A QM/MM study of dehalogenation of hexachlorocyclohexane (HCH) isomers catalyzed by LinA and LinB dehalogenases*
P48/B	Murat Mirik Mustafa Taşyürek Şerafettin Ekinci	*Notch impact resistances of carbon nanotubes reinforced high density polyethylene nanocomposite materials*
P49/B	Piotr Niemiec Renata Tokarz-Sobieraj	*Electronic structure of Cu containing Dawson heteropolyacids. DFT cluster calculation*
P50/B	Justyna Dominikowska Marcin Palusiak	*On cooperativity of halogen bonding*
P51/B	Jarosław J. Panek Aneta Jezierska-Mazzarello	*Free energy profiles for proton motion in hydrogen bridges of quinoline derivatives - CPMD-based investigations*
P52/B	Tadeusz Pluta	*Electric properties of carbazole and fluorene*

P53/B	Maciej Przybyłek Piotr Cysewski Tomasz Miernik Mirosław Kobierski Dorota Żiółkowska	*On the origin of benzoic acid crystals morphology trimming by surfaces in thin films crystallization*
P54/B	Mariusz Radoń Ewa Brocławik	*Metal–nitrosyl bonding in transition metal complexes: role of resonance structures and spin states*
P55/B	Paweł Rejmak Marcin Klepka Aleksandra Drzewiecka-Antonik Anna Wolska Kinga Ostrowska Elżbieta Hejchman	*Computational and spectroscopic characterization of Cu(II) complexes with derivatives of hydroxycoumarins*
P56/A	Rafał Roszak Szczepan Roszak	*Hydrogen uptake by beryllium doped graphene – ab initio molecular dynamics study*
P57/B	Rafał Roszak Szczepan Roszak	*Carbon-based materials for selective electrochemical oxygen reduction*
P58/B	Agnieszka Rugor Anna Wójcik Stefan Mordalski Andrzej Bojarski Maciej Szaleniec	*Structural modelling of a novel molybdoenzyme: steroid C25 dehydrogenase from Sterolibacterium denitrificans*
P59/B	Kadir Sabancı Şerafettin Ekinci Mustafa Taşyürek	*Determination of nitinol fibers performances by means of embedded systems*
P60/B	Jakub Šebera Jaroslav V. Burda Michal Straka Akira Ono Chojiro Kojima Yoshiyuki Tanaka Vladimír Sychrovský	*Formation of a T-Hg(II)-T metal-mediated DNA base pair: theoretical calculation of the reaction pathway*
P61/B	Filip Šebesta Jaroslav V. Burda	*Autocatalytic mechanism of binding $Pt^{IV}(DACH)Cl_4$ to dGMP and followed-up formation of $Pt^{II}(DACH)Cl_2$*
P62/B	Szymon Śmiga Adam Buksztel Ireneusz Grabowski	*Assessment of quality of OEP2-SOS functionals applied to quantum chemical calculations*
P63/B	Daniel Smykowski Bartek Szyja Ionut Tranca Emiel J. M. Hensen Jerzy Szczygieł	*Computational study of carbon dioxide electroreduction on Cu/Ni surfaces*

P64/B	Marcin Sobieraj K. A. Krzyśko A. Jarmuła M. W. Kalinowski Bogdan Lesyng M. Prokopowicz Joanna Cieśla Adrian Gojdź B. Kierdaszuk	*Analysis of enzyme-ligand FRET in the complexes of E. coli purine nucleoside phosporylase and its mutants with formycin A*
P65/B	Monika Srebro Jochen Autschbach	*Delocalization error and 'functional tuning' in Kohn-Sham calculations of molecular properties*
P66/B	Adam Stępniewski Ewa Brocławik Kinga Góra-Marek Mariusz Radoń	*Electron transfer processes crucial for coadsorption of NO and small ligands on cobalt sites in zeolites*
P67/B	Beata Szefler	*QSPR/QSAR studies by similarity clustering prediction*
P68/B	Piotr Talaga Mateusz Brela Artur Michalak	*ETS-NOCV description of changes in the electronic structure along the reaction path of the double proton transfer in the formamide dimer and related systems*
P69/B	Can Alaşalvar Mustafa Serkan Soylu Zeliha Hayvali Hüseyin Ünver	*Spectroscopic studies, structure and DFT calculations of 4-4E-[(2-fluorophenyl)imino]methyl-2-methoxyphenol*
P70/B	Anna Wójcik Ewa Brocławik Per E. M. Siegbahn Tomasz Borowski	*How subtle differences in enzyme structures affect the reaction outcome? Theoretical studies on HMS and HPPD*
P71/B	Łukasz Wolański Tadeusz Andruniów	*Fluorescent proteins' chromophores in vacuo: a benchmark study of spectral properties*
P72/B	Sirous Yourdkhani Tatiana Korona	*On the influence of local approximations to electron correlation on the quality of QTAIM parameters*
P73/B	Wiktor Beker Jarosław Zaklika Aleksandra Ziobro Józef Lipiński Ludwik Komorowski Piotr Ordon	*Atomic polarization justified Fukui index as affinity indicator in aromatic heterocycles and nucleobases*
P74/B	Snežana D. Zarić Goran V. Janjić Dusan N. Sredojević Dragan B. Ninković Jelena M. Andrić Dusan Ž. Veljković	*Influence of hydrogen bonds on non-covalent interactions of aromatic molecules*
P75/B	Mateusz Brela Artur Michalak	*Theoretical analysis of ion-polymer interactions in PBI-based membranes with ETS-NOCV method*

P76/B	Przemysław Czeleń Żaneta Czyżnikowska	*Physical nature of intermolecular interactions within Sir2 homolog active site: molecular dynamics and SAPT-DFT study*
P77/B	Wiktoria Giedroyć-Piasecka Edyta Dyguda-Kazimierowicz Marco Mor Alessio Lodola W. Andrzej Sokalski	*Simple nonempirical scoring model of fatty acid amide hydrolase inhibition*

Lecture abstracts

in chronological order

Discovery and engineering of biocatalysts supported by computational design

Dick B. Janssen, Robert J. Floor, Hein J. Wijma

[1]Biotransformation and Biocatalysis, Groningen Biomolecular Sciences
[2]Biotechnology Institute, University of Groningen, the Netherlands

The feasibility of novel processes in the emerging biobased economy is to a large extent dependent on the discovery and engineering of enzymes for industrial-scale biocatalytic conversions. Naturally occurring enzymes usually require tailoring of properties such as thermostability, solvent tolerance, substrate range, and chemo-, regio- or stereoselectivity. Established protein engineering methods are directed evolution based on (semi-)random mutagenesis and high-throughput screening, and rational design, based on insight in structure-function relationships.

The integration of computational methods in directed evolution strategies improves the efficiency of searching of protein sequence space for enzyme variants with improved properties [1-3]. For enhancing thermostability, we explored a strategy (FRESCO, Framework for Rapid Enzyme Stabilization by Computation [3]) in which point mutants and disulfide bond mutants are first generated by computational design and high-throughput calculation of differences in free energy of folding ($\Delta\Delta G^{Fold}$). Next, molecular dynamics simulations and scoring for local flexibility (RMSF) are used to rank promising variants. After using these high-throughput computational tools, the highest ranking variants are expressed and tested in the laboratory. Experimentally confirmed beneficial mutations are combined, again after testing multiple combinations by molecular dynamics simulations. This gave a spectacular stability increase of different enzymes in only two or three rounds of laboratory testing.

Similar computational strategies are explored to design mutant libraries with enzymes possessing altered stereoselectivity. Using tools of computational protein design, in silico enzyme variants are generated that are expected to bind the transition state of an enzyme-catalyzed reactions. Predicted variants are subjected to molecular dynamics simulations with scoring for near-attack conformers, after which small sets of the most promising variants are tested in the laboratory.

The results show that the use of high-throughput computational methods can rapidly increase enzyme properties that are relevant for applied biocatalysis. The methods used for screening mutants can potentially also be used to facilitate discovery of useful enzymes in genomic sequences.

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[1] Wijma, H. J., Janssen, D. B. *FEBS J.* **2013**, 280, 2948–2960.
[2] Wijma, H. J., Floor, R. J., Janssen, D. B. *Curr. Opin. Struct. Biol.* **2013**, 23, 588–594.
[3] Wijma, H. J., Floor, R. J., Jekel, P. A., Baker, D., Marrink, S. J., Janssen, D. B. *Protein Eng. Des. Sel.* **2014**, 27, 49-58.

Science based policy making: who does what (and why)?

Krzysztof Maruszewski

European Commission Joint Research Centre, Institute for Health and Consumer Protection, Ispra, Italy

Increasing awareness of health, safety and security issues and growing risk aversion among citizens creates an increasing societal demand to understand uncertainty, estimate probability, and eventually manage and reduce risks. While this growing demand brings more and more aspects of policymaking within the orbit of science, we need to ask ourselves what sort of information we expect from science, and what are the science's limits and role in the face of uncertainty.

Mechanism of electrocatalytic purification of olefins by metal bis(dithiolenes)

Michael B. Hall

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Nickel bis(dithiolene) complexes have been reported as electro-catalysts for the purification of alkenes. Initial reports suggested that neutral complex reacts with an alkene (and not its common impurities) to produce the *cis*-interligand adduct, which upon reduction releases the alkene. More recent experimental work shows that intraligand addition to a single dithiolene dominates in the absence of the anion. Furthermore, this intraligand adduct readily decomposes; thus, the anion appears to catalyse formation of the *cis*-interligand adduct and to prevent formation of the intraligand adduct. Recent density functional theory (DFT) calculations show that the relative energies for the species involved in this reaction are very dependent on the functional and comparisons with CCSD calculations suggest that the BMK and ωB97X-D functionals perform best for this system. With these functionals a new mechanism has been uncovered that explains the catalytic activity of the anion. The mechanism involves formation of a dinuclear, neutral-anion complex that assists the binding of the alkene to Ni and its migration to the *cis*-interligand adduct, the key to the catalysis by the anion. Other metals including cobalt and copper have also been studied computationally.

Chemical accuracy for molecule-surface interactions: *ab initio* energies and entropies

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A hybrid method that combines MP2 on cluster models with DFT+dispersion on periodic models (plus ΔCCSD(T) corrections) is presented that yields binding energies of molecules on (simple) metal oxide surfaces *ab initio* and with chemical accuracy. Examples are the binding of CO and CH_4 on Mg(001), of H_2, CH_4, CO and CO_2 on the internal surfaces of metal organic frameworks (MOF), as well as the adsorption of hydrocarbons in zeolites. Entropies of adsorption can also be calculated with chemical accuracy from vibrational partition functions calculated by DFT+dispersion, when anharmonicities are included. This is shown for adsorption of CH_4 on MgO(001) and in a zeolite with Bronsted sites (H-chabazite).

Donor modifiers of Co(II) active sites: explicit spin and charge transfer channels for NO - NH_3 co-adsorption in zeolites

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Electronic factors essential for the catalytic activity of Co^{2+}-exchanged zeolites towards NO are examined by DFT modeling for cluster models and the analysis of natural orbitals for chemical valence (NOCV) [1]. The interpretation of charge transfers between the ammonia-modified cobalt center and the non-innocent NO ligand is given, supported by the analysis of the electronic contributions to the Co(II)-NO bond [2]. NH_3 co-ligation is shown to highly modify donor properties of a cobalt site and its activation ability, evidenced by calculated and measured red-shift of NO stretching frequency and ascribed to enhanced backdonation [3]. Calculations indicate that versatility of amine nitrosyl complexes showing variable activation of NO, differing as well in the number of NH_3 ligands as in the geometry and electronic structure of Co-N-O unit may co-exist in zeolite frameworks. Their relative stabilities might depend on fine structural features of the zeolite and on experimental conditions. Fine features of the electronic status of the cobalt center may tune population of antibonding orbitals on NO as this may be accomplished selectively through several independent electron density transfer channels of distinct provenience, active either cumulatively or selectively for different spins. It appears that some channels do not efficiently transmit the electron density to the NO ligand.

Combined analysis of experimental and calculation results indicates at the forms containing three or five NH_3 co-ligands as decisive. The novel finding concerning the interpretation of discussed IR spectra is the assignment of the most down-shifted bands at 1600-1615 $cmcm^{-1}$ to the singlet state of $[Co(NH_3)_3(NO)]^{2+}$ adduct, which supplements the interpretation due to obtrusive feature belonging to the spectrum of pentaammine adducts. Theory points also to the exchangeable Co^{2+} (with manifold of close-lying electron and spin states) as a very good candidate for the center designated to act as the electron transmitter, providing tunable electron transfer channels. In consequence, the influence of electron donor species co-ligated to Co(II) center on the weakening of NO bond may offer the opportunity for targeted N-O activation.

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Redesigning Enzymes for non-native reactions: the case of Diels-Alderases

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I will present some of our recent work on the computational design of Diels-Alderases. Our approach is to mine the protein data bank (PDB) for structures with suitable size and shape of their active sites, and then rationally (re)design them by introducing new catalytic residues and optimizing the shape. 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 this toolbox is a novel method [1] for predicting contributions of individual residues to the catalytic efficiency of an enzymatic reaction by calculations using the fragment molecular orbital theory (FMO) [2]. Results will be presented both for the design of enzymes that catalyze Diels-Alder by hydrogen bonding [3–5], and for an enzyme that uses a novel acid-base mechanism for catalysis [6]. The predicted catalytic performance of these enzymes will be compared to the designs by Siegel et al. [7].

Fig. 1: Snapshot from a molecular dynamic simulation of a designed Diels-Alderase showing the substrates (green and blue) prepositioned for transition state formation. Bond forming (CCX) and hydrogen bonding (HbX) interactions are indicated.

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Theoretical studies of dynamic and quantum tunnelling effects in enzymes

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Transition state stabilization in a preorganized active site seems to be the major source of catalysis although some degree of protein flexibility is needed to reach the maximum catalytic efficiency [1]. Development of a new enzyme must then consider the inclusion of TS stabilizing interactions either in a pre-existing enzymatic structure (enzymatic re-design) or in a completely new designed enzyme (*de novo* design). However, the moderate success obtained until now using this strategy has reignited the debate about the origin of the catalytic power of natural enzymes [2, 3]. While it is generally accepted that enzymes are flexible entities with active motions before, after and during the chemical transformation, the controversial subject is the proposal about the active role played by some protein motions driving the conversion of substrates into products. This proposal comprises both slow conformational changes, related with protein loop motions, and fast vibrational motions, termed as promoting vibrations. These proposals are often presented under the denomination of "dynamical effects".

According to the Born-Oppenheimer approximation, changing the mass of atoms belonging to a molecular system does not change the forces acting on the system but alters the frequencies, which in turn can affect the rate constant. Based on this idea, experiments of wild type and isotopically substituted enzymes have been used to quantify the role of these motions in recent years [4]. We will show how analysis of free energy surfaces, obtained as a function of independent substrate and environment reaction coordinates [5] can be applied to the comparative study of light (wild-type) and heavy enzymes to shed light into the controversial debate on whether protein dynamics are linked to the chemical reaction step of enzymatic processes [6, 7]. The relative small effect on reducing the effective free energy barrier would be in agreement with our successful results on designing new biocatalysts using the substrate-protein equilibrium approximation [8–10].

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To B3LYP or not to B3LYP?

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Recent years witness strong development of the DFT resulting in plethora of new functionals that improve particular aspects of the deficiencies of the theory. This rapid development raises a few practical questions. The obvious one is how good these new functionals are. This question is partly answered by a number of articles that report results of benchmark calculations. The question that we would like to address is how well are the "old" functionals. In particular, B3LYP may be considered one of the most exploited functionals in the history of chemical DFT calculations; its popularity was based on its robustness in calculations of organic systems. Is there still a place for B3LYP calculations? We will address this questions based on the comparison of theoretical predictions of isotope effects with the experimental results both obtained in our laboratory.

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Reaction mechanisms of selected mononuclear nonheme oxygenases - insights from computational studies

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In this contribution we present and discuss computational results from studies focusing on reaction mechanisms of mononuclear nonheme metalloenzymes and biomimetic synthetic complexes. The reactions studied involve: dioxygen activation by α-ketoglutarate dependent oxygenases [1], coupled aromatic ring hydroxylation and rearrangement elicited by Fe(IV)=O species [2, 3], and oxidative C-C bond cleavage catalyzed by a Cu(II) synthetic complex [4]. Each of these systems presents a different challenge, and hence, an array of computational methods has been used to tackle them, i.e. CCSD(T), DFT: B3LYP, TPSSh, ONIOM(DFT:AMBER) and MD(AMBER).

Despite the fact that the mechanisms of oxygen activation by α-ketoglutarate dependent oxygenases, which leads from ketoacid-Fe(II) complex through binding of O_2 to formation of the Fe(IV)=O species and release of CO_2, has been studied with computational methods for more than a decade now [1], it is still unsettled, mostly due to the fact that various functionals give very different description of the lowest energy surface at the beginning of this process. More specifically, for the Fe-α-ketoglutarate-O_2 adduct the ground state features high-spin iron II or III when B3LYP is employed, whereas hybrid functionals with 10% of HF exchange, i.e. TPSSh and BP86+10%HF, favor intermediate-spin Fe(IV). In an attempt to resolve this issue we have undertaken a CCSD(T) study to benchmark DFT methods, as experimental data are scarce for this particular process.

HPPD is a widespread in nature α-ketoacid dependent oxygenase catalyzing and intriguing reaction of aromatic ring hydroxylation coupled with 1,2-rearrangement [2, 3]. Experimental measurements of kinetic isotope effect (KIE) with ring deuterated substrate revealed that Fe(IV)=O species decays in a process characterized by inverse KIE, which was originally interpreted in favor of direct oxygen atom insertion into the ring. Results of our ONIOM study, however, suggest a different explanation of the origin of the inverse KIE and provide strong argument against the original interpretation.

Oxidative cleavage of C-C bonds is one of processes with potential application in biomass conversion. A synthetic Cu(II) complex catalyzing oxidation of an enolate substrate has recently been characterized, where chloride anion plays a catalytic role [4]. Results of DFT investigations allowed us to propose a probable mechanism and explain of the role of Cl^-.

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Design of the hierarchical zeolite catalysts

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Synthetic zeolites are one of the most important materials in catalysis due to highly ordered regular porous structure, which can be controlled by using different Structure Directing Agents (SDA) during the synthesis. This porous structure consists of micropores with the diameter typically less than 2 nm, and therefore it imposes a limitation on the diffusive properties of the bulky molecules. Considerable effort has been put in the synthesis of mesoporous zeolites, in order to combine the high acidity of crystalline zeolites with easy diffusion of bulky molecules through mesopores. The synthesis of zeolite nanosheets first reported by Ryoo et al [1] describes the thickness of the nanosheet is uniform and amounts to 2 nm, whereas small nanoslabs of varying thickness have been obtained with conventional hydrothermal method with tetraalkylamonnium SDAs.

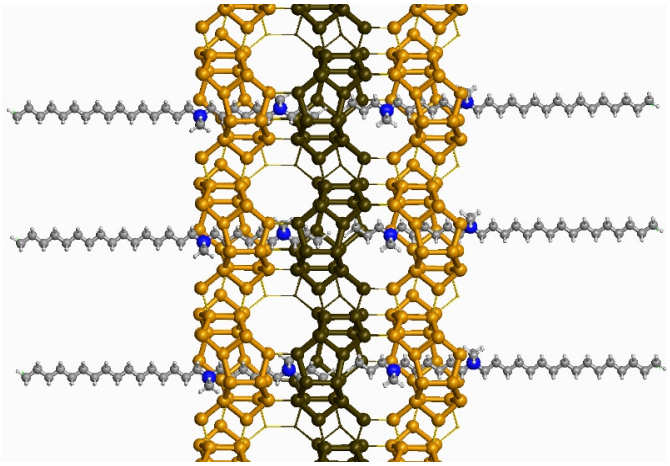

Fig. 1: Most stable configuration of SDA in MFI nanosheet.

Our study aims to explain the nature of the structure-directing effect of such templates by means of the Molecular Dynamics simulations. We have studied the interaction of a number of SDAs with a MFI framework nanosheet and nanoparticles taking part in the process.

By comparison of energies, we conclude that the straight configuration of the SDA is only more stable by 7 kcal/mol as compared to other configurations in which the SDA occupies the zigzag channels. Interestingly, the terminal C_6 chain is too long to fit in the central pore, and it needs to bend and take the position in the zig-zag pore, which is less energetically preferred. The other possibility is to use the shorter terminal chain (C_3) in the SDA. The experimets confirmed that the crystallinity of the material obtained with the shorter chain is is higher.

The interaction with the template with the longer side chains is significantly stronger though, and suggests that propyl side chains could be better SDAs to form the MFI nanosheet. This however does not find the confirmation with experiment – the structure of the material obtained is much more disordered, and crystal intergrowth are observed. We conclude that the explanation of this fact lays in the earlier stage of zeolite formation.

This also explains the negative effect of the propyl side chains on the crystallinity of the obtained material. The model consisting of two SDAs located on both sides of the Si_{33} nanoparticle is significantly more stable if the side chains used are longer.

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Quantum dots – artificial atoms, large molecules or small pieces of bulk? Insights from time-domain *ab initio* studies

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Quantum dots (QD) are quasi-zero dimensional structures with a unique combination of solid-state and atom-like properties. Unlike bulk or atomic materials, QD properties can be modified continuously by changing QD shape and size. Often, the bulk and atomic viewpoints contradict each other. The atomic view suggests strong electron-hole and charge-phonon interactions, and slow energy relaxation due to mismatch between electronic energy gaps and phonon frequencies. The bulk view advocates that the kinetic energy of quantum confinement is greater than electron-hole interactions, that charge-phonon coupling is weak, and that the relaxation through quasi-continuous bands is rapid. QDs exhibit new physical phenomena. The phonon bottleneck to electron energy relaxation and generation of multiple excitons can improve efficiencies of photovoltaic devices. Our state-of-the-art non-adiabatic molecular dynamics techniques, implemented within time-dependent density-functional-theory, allow us to model QDs at the atomistic level and in time-domain, providing a unifying description of quantum dynamics on the nanoscale.

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Novel multiscale simulations of molecular electronics

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Organic components are playing an increasing role in modern low-energy electronic devices and in the next generation of solar cells. Modeling these components presents very diverse challenges; the nature of the interface to inorganic components [1,2], the conformational freedom of flexible organic moieties [3], the physical effects of the organic components themselves [4] and, above all, techniques for simulating the charge transport itself [5,6].

These challenges require the use of wide variety of existing theoretical techniques from classical molecular dynamics, periodic density-functional theory, semiempirical molecular-orbital theory and Landauer transport theory.

However, new developments are also necessary; very large scale semiempirical MO calculations [7], local properties as external potentials in transport calculations [5] and new methods for simulating charge transport. Our work in this area will be described.

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Computational biomarkers design

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Biomarkers play a key role in the current health-care system as diagnostic agents [1]. Most of the currently used agents involve high energy radiation or the use of heavy metals and radioactive nuclei [1, 2] and it is of paramount importance to design alternative agents with reduced or no health-risk. Our research efforts are devoted to this subject and we propose organic molecules or proteins based biomarkers for (one and two photon) fluorescence imaging of bio-structures or physiological conditions responsible for or associated with the diseases. Using computational modeling approaches we study various biomarkers and understand their working mechanism. We also aim to establish structure-property relationship and based on which the one and two photon absorption properties can be improved for the real world imaging applications. In this presentation I will discuss about the integrated approach based modeling of optical properties of biomarkers in the explicit bio-environment or in presence of different physiological conditions (like pH and ionic strength) [3–7]. The results on the optical properties of molecules in presence of bio-structures like protein, fibril and membrane will be presented [5–7]. The discussion will also deal with the modeling of metal probes and pH probes [3, 4].

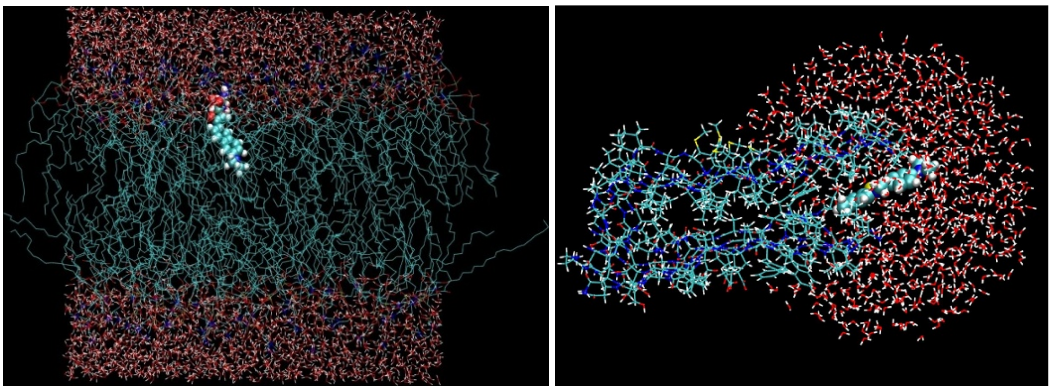

Fig. 1: Fibril probe and membrane probe.

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Hybrid organic/inorganic conjugated oligomers: the best of both worlds?

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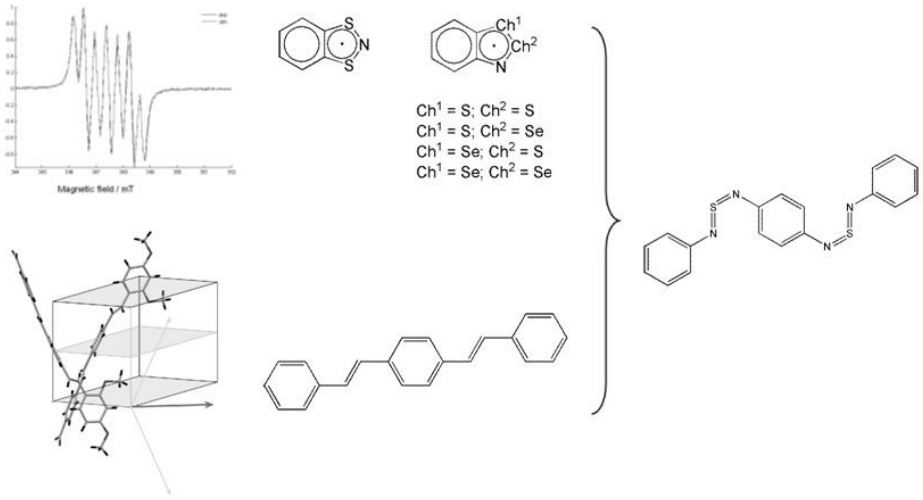
Within the class of low-molecular-weight organic semiconductors distyrylbenzene (DSB) and its derivatives have been successfully applied as materials for opto-electronic applications such as organic light-emitting diodes (OLEDs) and ion-selective sensors [1,2]. More recently, their non-linear-optical (NLO) properties have become the focus of attention through the analysis of the supramolecular structures of asymmetrically substituted, dipolar derivatives of DSB [3].

Likewise, 1,2,3-benzodithiazolyls and their isomeric 1,3,2-dithiazolyl derivatives, commonly referred to as Herz radicals, have become of considerable interest to contemporary material science as promising building blocks in the design and synthesis of molecular magnets and/or conductors. Assignment of their EPR spectra [4] has relied heavily on the results of quantum chemical calculations at the level of DFT, which, at the same time, has clearly illustrated the problems associated with finding an appropriate combination of functional and basis set.

The success of these two classes of materials prompted us to combine their basic units into a new hybrid structure, *i.e.*, a compound containing three aromatic rings linked by nitrogen-sulfur-nitrogen (–N=S=N–) linkages. A computational study was performed in order to gain insight into these new compounds' properties, focussing mainly on conformational and configurational preferences and conjugation, both for the neutral compounds and the radical ions. In parallel, attempts were made to prepare these materials and structurally characterise them. Our preliminary results are reported.



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The physicochemical aspects of conduction in molecular junction

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The model of conduction through a molecule has been developed, which presumes the transmission of current across a chain of atoms in the molecular junction is due to electrostatic induction-like mechanism. The first principle calculations of electric current passing through a single molecule were based on uncertainty principle and founded on theories describing charge transfer phenomena in chemical reactions. The model has been applied to study the single molecule detection of DNA bases. The trends of I-V characteristics were found to be in reasonable agreement with non-equilibrium Green's function evaluations of previous works. The analysis of results leads to relationship between molecular dipole moment and electric current, suggesting that the current in molecular junction might be modulated by affecting the linear and nonlinear optical properties of the trapped molecules.

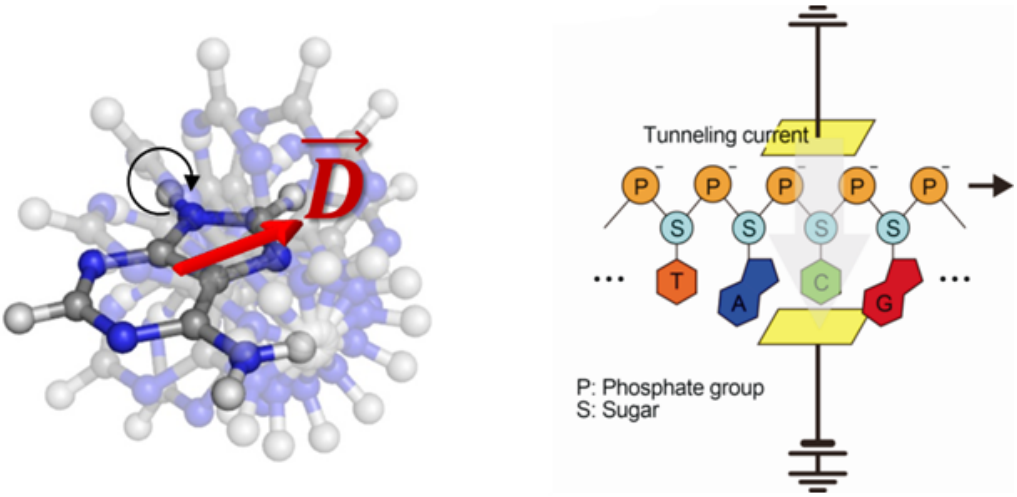

Fig. 1: The dipole moment and the rotamer of DNA base with respect to the N-glycosidic sugar-base σ-bond, and conceptual diagram of single-molecule tunneling current measurement for single strand DNA sequencing using nanogap electrodes.

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Discovering the structure of $NaYF_4$ hexagonal phase

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Hexagonal phase of $NaYF_4$ nanocrystals is one of the most promising hosts for materials with up-converting properties. When doped with lanthanides such as erbium, ytterbium or thulium, it absorbs IR radiation and in turn, emits visible light in a broad and tunable range. [1] These nanocrystals are passivated e.g. by coating with silica or monolayer of polymer, such as PEG. [2] However neither the structure of the bulk material, nor of the surface are well understood.

In the talk, results of Car-Parrinello molecular dynamics (MD) simulations of the $NaYF_4$ crystal models will be presented. [3] These models are build using space groups proposed in literature. The calculations show that models based on $P\bar{6}$ and $P\bar{6}2m$ space groups lead to identical structure, while model based on the $P6_3/m$ group behaves differently. Results of MD simulations of selected surfaces will be shown as well. These DFT calculations are the first step towards understanding of interactions between $NaYF_4$ surface and monolayers of passivating agents.

Acknowledgements: The work has been financed from the state grant no. 0543/IP3/2011/71 awarded by the Ministry of Science and Higher Education (Poland) within the project *Iuventus Plus*.

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Advances in density functional theory calculations for intermolecular interactions

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Progress in electronic structure calculations depend upon advances in the underlying methods, and also the tools available for analyzing the results of calculations using the resulting methods. In this talk, I shall discuss progress made in my group on both fronts.

With regard to core methodology, I will report on the development of an improved density functional. The design principles for this functional are novel and will be discussed. The final functional is the one that emerges as most transferable from tests of over 10,000 competing functional forms. Quite remarkably, the resulting functional involves substantially fewer empirical parameters (only 10) than many existing alternatves. Due to the design choices together with the training procedure, it outperforms every existing density functional tested for intermolecular interactions. It performs competitively with the best existing functionals for applications to thermochemistry and chemical kinetics. Progress towards assessing the best functionals from tests of much larger numbers of competing functional forms will also be reported if progress permits.

With regard to analyzing electronic structure calculations, I shall discuss an approach to intermolecular energy decomposition analysis (EDA) that my group has been developing to permit interpretation of density functional theory calculations. This EDA allows one to separate so-called "frozen" interactions, induced electrostatic polarization, and dative donor-acceptor interactions. As the EDA is performed variationally, one can also assess the role of these distinct contributions on experimental observables. A variety of examples will be presented to show the usefulness of the approach at present. I shall finish with a discussion of limitations and future challenges.

Gold-gold and gold-ligand interactions: separating true effects from artifacts

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Donor-acceptor interactions are notoriously difficult and unpredictable for conventional density functional theory (DFT) methodologies. This is because local and semilocal DFT approximations are rife with self-interaction error, as well as fail to describe the derivative discontinuity at integer numbers of electrons. This work will present a reliable computational treatment of gold-ligand interactions of the donor-acceptor type within DFT. These interactions require a proper account of the ionization potential of the electron donor and electron affinity of the electron acceptor. This is accomplished in the Generalized Kohn Sham framework that allows one to relate these properties to the frontier orbitals in DFT via the tuning of range-separated functionals. A donor and an acceptor typically require different tuning schemes. This poses a problem when the binding energies are calculated using the supermolecular method. A two-parameter tuning for the monomer properties ensures that a common functional, optimal for both the donor and the acceptor, is found. A reliable DFT approach for these interactions also takes into account the dispersion contribution. The approach is validated using the water dimer and the $(HAuPH_3)_2$ aurophilic complex. Binding energies are computed for Au4 interacting with the following ligands: SCN^-, benzenethiol, benzenethiolate anion, pyridine and trimethylphosphine. The results agree with coupled-cluster reference values for the right reasons. By contrast, standard GGA and hybrid functionals misrepresent donor-acceptor abilities of gold+ligand couples. If the results of these approaches happen to agree with the reference data, it is for the wrong reasons.

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Electron-DNA interactions: A DFT investigation

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In exploring the electronic structures of DNA system the density functional theory is one of the effective and practical approaches. Among various functionals, M06-2X is the most reliable and applicable in the study of electron-DNA interactions. This functional predicts correct electron affinity of DNA bases, describes appropriate base-base stacking interactions and H-bonding interactions, and allows performing the calculations for the system large as a few hundred atoms. In the present report, M06-2X is applied in the study of the electron attachment to the short DNA fragments such as dGpdC duplex, dCpdC duplex, and dCpdGpdC duplex. The results demonstrate that the excess electron can locate on different cytosine in these systems. The electron attachment induced inter-strand proton transfer is found to further stabilize the anionic radicals in aqueous solutions. Non-adiabatic electron steps from cytosine to cytosine might be an energy viable pathway for electron migrating through DNA.

Computational biochemistry: enzyme dynamics, conformations and catalysis

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Enzymes are outstanding natural catalysts and are crucial in most biological processes. Better understanding of the mechanisms underlying their catalytic properties promises technological spin-offs such as better drug design (many drugs are enzyme inhibitors, which bind to enzymes and prevent them from functioning), analysis of the effects of genetic variation and mutation (for example in predicting drug metabolism and mechanisms of drug resistance) and the design of new catalysts (for example biomimetic catalysts or engineered enzymes). Computational modelling and molecular simulation has a vital role to play in analysing enzymes, providing a level of detail beyond that achievable in experiments alone, for example in identifying reaction mechanisms, analysing unstable species in enzyme-catalysed reactions and catalytic contributions. The field of enzyme modelling has grown enormously in recent years, and has matured to the point that computational enzymology is increasingly recognised as essential for understanding these fascinating biological catalysts. Combined quantum mechanics/molecular mechanics (QM/MM) methods allow reactions within enzymes to be modelled. Molecular dynamics simulations (e.g. using GPUs) can now reach long timescales, allowing investigation of drug binding, enzyme conformational changes and dynamics. Combined with theoretical modelling, simulations allow analysis of the role of dynamics and quantum tunnelling in enzyme catalysis. Recent applications include identification of a novel role for methionine in catalysis; the effects of isotopic substitution on reaction in heavy and light dihydrofolate reductase; mechanisms of bacterial antibiotic resistance; drug resistance in influenza neuraminidase (e.g. H7N9 and H1N1 strains); covalent inhibition of the drug target fatty acid amide hydrolase; and conformational changes in the reaction cycle of terpene synthases, which are potentially useful biocatalysts for the synthesis of valuable compounds such as anticancer drugs and antibiotics.

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First principles modeling guided discovery of efficient hydrogenation catalysts

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The majority of petrochemical and a significant portion of fine chemical, agrichemical and pharmaceutical processes involve heterogeneous catalytic hydrogenation. Currently, most of the reaction is realized on supported metal catalysts in two consecutive steps. H_2 molecules first undergo a dissociative chemisorption process on metal catalyst surfaces to form hydrides. Subsequently, the negatively charged H atoms on catalyst surfaces attack the unsaturated bonds to form hydrogenation products. Hydrogen bronze materials, such as H_xMoO_3 and H_xWO_3, have been known to play an important role in catalytic hydrogenation. However, the detailed mechanisms have not been well understood. Using density functional theory, we performed systematic calculations to model the dissociative chemisorption process of H_2 molecules and hydrogenation of unsaturated molecules on the $MoO_3(010)$ and the $WO_3(001)$ surfaces. In contrast to the case in metal hydrides, H atoms in these bronze materials were found to behave like protons. We show that these hydrogen atoms are chemically active and capable of selectively hydrogenating unsaturated bonds with favorable thermodynamics and kinetics. Dehydrogenation of several selected cycloalkanes can also be catalyzed by these metal oxides to form bronze materials. Guided by the theoretical predictions, we carried out a series of experiments to understand the catalytic reactivity of the metal oxide materials toward hydrogenation and dehydrogenation. Our studies have led to the discovery of several efficient and cost effective catalysts.

Reactions of Ru(II) complexes; quantum mechanical and combined QM/MM MD study

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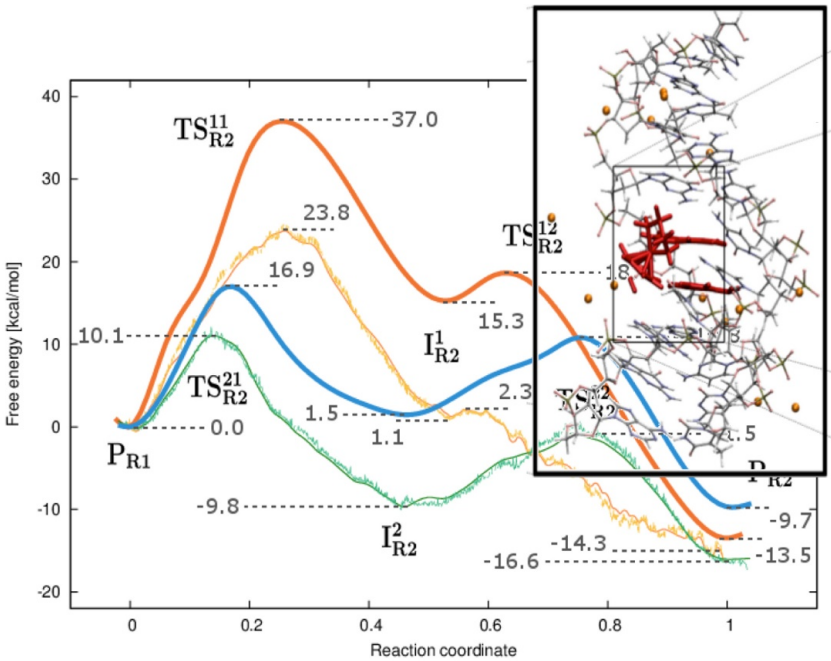
Biologically relevant interactions of piano-stool ruthenium(II) complexes with ds-DNA are studied in this paper by hybrid QM/MM computational technique. The whole reaction mechanism is divided into three phases: i) hydration of the $[Ru^{II}(\eta^6\text{-benzene})(en)Cl]^+$ complex, followed by ii) monoadduct formation between the resulting aqua-Ru(II) complex and N7 position of one of the guanines in the ds-DNA oligomer model and the final phase – iii) formation of the intra-strand Ru(II) bridge (cross-link) between two adjacent guanines. Free energy profiles of all the reactions are explored by QM/MM MD umbrella sampling approach where the Ru(II) complex and two guanines represent a quantum kernel, which is described by DFT methods. The combined QM/MM scheme is realized by our own software (QMS v. 1.4), which was developed to couple several quantum chemical programs (in this study Gaussian 09) and Amber 11 program. Calculated free energy barriers of the both ruthenium hydration and Ru(II)-N7(G) DNA binding process are in good agreement with experimentally measured rate constants. Then this method was used to study a possibility of cross-link formation. One feasible pathway leading to Ru(II) guanine-guanine cross-link with synchronous releasing of benzene ligand is predicted. The cross-linking is exergonic process with energy barrier lower than for monoadduct reaction of Ru(II) complex with ds-DNA



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σ-Hole interactions: a physical interpretation

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The anisotropic electronic densities of covalently-bonded Group IV-VII atoms frequently give rise to regions of positive electrostatic potential on the extensions of single covalent bonds to these atoms. Through such positive "σ-holes," the atoms can interact attractively and highly directionally with negative sites such as the lone pairs of Lewis bases, anions, π electrons, etc. [1,2]. In the case of Group VII, this is called "halogen bonding." Hydrogen bonding can be viewed as a less directional subset of σ-hole interactions. Since positive σ-holes often exist in conjunction with regions of negative potential, such atoms can also interact favorably with positive sites. In accordance with the Hellmann-Feynman theorem, all of these interactions are purely Coulombic in nature (which encompasses polarization and dispersion). The strength of σ-hole bonding increases with the magnitudes of the potentials of the positive σ-hole and the negative site.

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Expansion of the π-hole concept

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Regions of lower electronic density above and below atoms in planar portions of molecules have been labeled "π-holes" [1]. These are in contrast to σ-holes, which are regions of lower electronic density along the extensions of many single bonds [2]. Both can lead to regions of positive electrostatic potential that drive interactions with negative sites. In this talk, we expand the concept of π-holes to include more extensive regions of lower electronic density above and below planar portions of molecules and discuss the interactions of such regions with negative sites.

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Spin vorticity and stress tensor of electron

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We have developed the concept of energy density using the stress tensor of QED (Quantum Electrodynamics) [1-5]. The symmetric component of the electronic stress tensor has been proved to predict the emergence of the covalent bond in terms of the spindle structure [4]. The theory of the spindle structure has been developed to visualize the regional chemical potential of chemical reactivity and the bond order of chemical bond [6-12]. Quite recently, we have found a new picture of electron spin torque driven by the antisymmetric component of the stress tensor of electron through the spin vorticity [13-15], where the chirality of the electronic structure has played an essential important role [5,8,12]. The theory of the electron spin torque has been developed to visualize the chirality characteristics of atoms and chiral molecules [16-18].

Acknowledgements: This work was partially supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (25410012).

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Exploring intramolecular interactions using the fragment attributed molecular system energy change method

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Numerous methods were developed to gain information about the nature and strength of intramolecular interactions but they still remain elusive, particularly when compared with an insight one can gain from an analysis of intermolecular interactions. An IQA-based fragment attributed molecular system energy change (FAMSEC) method, developed recently by us, will be presented. Its applicability and usefulness will be demonstrated by exploring intramolecular interactions, regardless whether a QTAIM-defined bond path is or is not present, in molecules where (i) a classical H-bond is formed and (ii) steric clash take place.

The FAMSEC method is of a general nature as it explores global variations in the total and self-atomic energies as well as all possible diatomic interaction energies (all terms as defined in the IQA method [1]) when a molecule (or a molecular system, such as a dimer) changes from an initial (used as a reference state, *ref*) to its final configuration, *conf*. The diatomic fragment, {A:B}, attributed molecular energy change, ${}^{\rm ref}_{\rm conf}\delta E^{\rm \{A:B\}}_{\rm attr\text{-}m}$, is defined by Eq. 1

$$ {}^{\rm ref}_{\rm conf}\delta E^{\rm \{A:B\}}_{\rm attr\text{-}m} = {}^{\rm ref}_{\rm conf}\sum \delta E^{\rm \{A:B\}}_{\rm self} + {}^{\rm ref}_{\rm conf}\delta E^{\rm A,B}_{\rm int} + {}^{\rm ref}_{\rm conf}\sum \delta E^{\rm \{A:B\},X}_{\rm int}, \qquad (1) $$

where ${}^{\rm ref}_{\rm conf}\sum \delta E^{\rm \{A:B\}}_{\rm self}$, ${}^{\rm ref}_{\rm conf}\delta E^{\rm A,B}_{\rm int}$ and ${}^{\rm ref}_{\rm conf}\sum \delta E^{\rm \{A:B\},X}_{\rm int}$ is the change in the self-atomic energy of {A:B}, interaction energy between atoms A and B, and interaction energy between the fragment {A:B} and all the remaining atoms X in a molecule, respectively, when going from the *ref* to *conf* state of a molecule. The first two terms in Eq. 1 describe a localized, to within a molecular fragment {A:B}, energy change within a molecule. Eq. 1 can be re-written in more convenient for calculation form, Eq. 2 (it makes the study of intramolecular interactions in large molecules possible as expensive IQA calculations are performed only for atoms A and B)

$$ {}^{\rm ref}_{\rm conf}\delta E^{\rm \{A:B\}}_{\rm attr\text{-}m} = {}^{\rm ref}_{\rm conf}\sum \delta E^{\rm \{A:B\}}_{\rm total} - {}^{\rm ref}_{\rm conf}\sum \delta E^{\rm \{A:B\}}_{\rm int} - {}^{\rm ref}_{\rm conf}\delta E^{\rm A,B}_{\rm int}, \qquad (2) $$

where ${}^{\rm ref}_{\rm conf}\sum \delta E^{\rm \{A:B\}}_{\rm total}$ accounts for the change in the total atomic energies of atoms in {A:B}. Besides classical de- and stabilizing diatomic interactions (they are not only fully recovered but also explored by the FAMSEC method) a steric H--H clash in the planar biphenyl will be discussed in details and its FAMSEC-based interpretation proposed.

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Simple non–empirical procedure for spin–component–scaled MP2 methods applied to the calculation of dissociation energy curve of noncovalently–interacting systems

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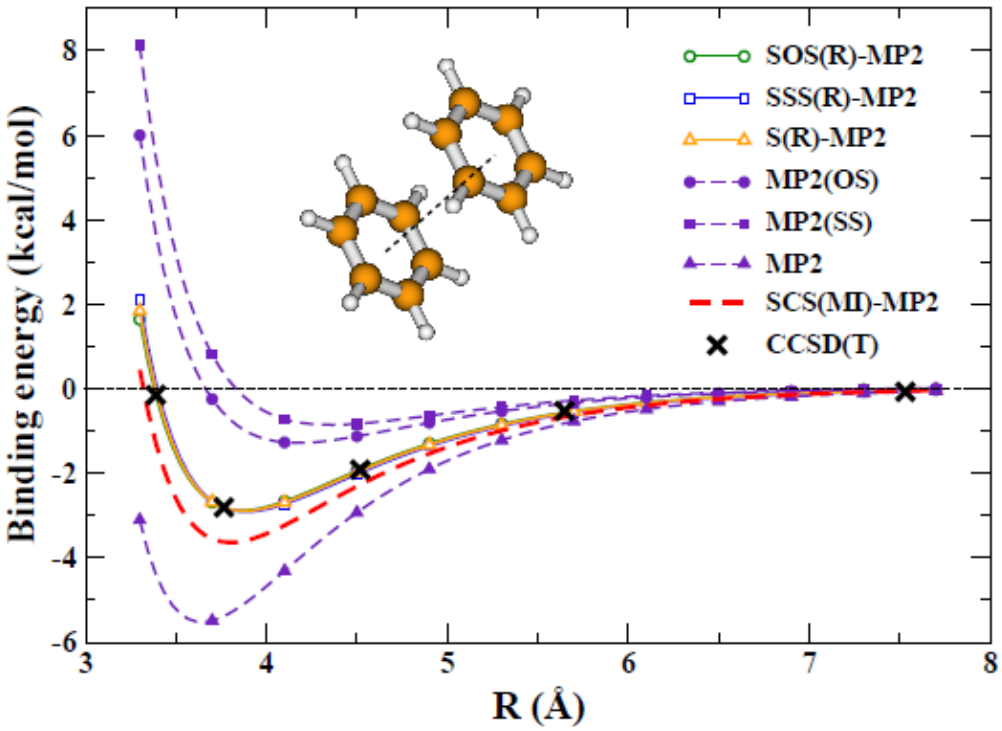
We present simple and non–empirical method to determine optimal scaling coefficients, within the (spin–component)–scaled MP2 approach, for calculating intermolecular potential energies of noncovalently–interacting systems. The method is based on an observed proportionality between (spin–component) MP2 and CCSD(T) energies for a wide range of intermolecular distances and allows to compute with high accuracy a large portion of the dissociation curve at the cost of a single CCSD(T) calculation.

The accuracy of the present procedure is assessed for a series of noncovalently–interacting test systems: the obtained results reproduce CCSD(T) quality in all cases and definitely outperform conventionalMP2, CCSD and SCS–MP2 results. The difficult case of the Beryllium dimer is also considered.



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Computational modeling of lattice free energies. From solids to solvated ions

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Periodic plane-wave methods have been used to compute lattice energies and cohesion energies for several examples of solids dominated by electrostatic and dispersion forces,

for example, $Na_5B(SO_4)_4/K_5B(SO_4)_4$ as well as $[(CH_3)C][HCB_{11}Cl_{11}]$ and $[LiC_{60}][PF_6]$. In addition, the pair of solids Na_2O_2 and $Na_2O_2.8H_2O$ has been studied where the peroxide dianion (O_2^{2-}) can exist in the lattice without abstracting a proton from adjacent water molecules. Likewise, in solid $K_2C_2.2NH_3$, the dicarbide (C_2^{2-}) can exist next to ammonia molecules without abstracting a proton. In both examples, the greater lattice energies allow the dianion to exist next to the extractable protons. Free energies are computed for the steps solid→gas-phase and gas-phase→aqueous ions to determine K_{sp} values.

Acknowledgements: Calculations were performed at the Alabama Supercomputer Center.

How are molecular crystal organized?

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It is quite clear that structure of molecular crystals is determined by energy of interactions between molecules. Interatomic distances in the crystal are just consequences of energetic of interactions including not only specific interactions such as hydrogen bonds or stacking interactions but also general dispersion and electrostatic interactions. Therefore the most efficient and unambiguous consideration of crystal structure should be based on analysis of topology of intermolecular interactions in the crystal in terms of their energy and directionality [1,2].

Application of this approach allows recognizing only four type of organization of molecular crystals [2] which may be described by directed rhomb (Fig.1). Any crystal is built by building units (molecules or molecular complexes). The most strongly bonded building units may form columns/chains, layers or three-dimensional assemblies which may be considered as basic structural motif (BSM) of the crystal. According to this analysis all intermolecular interactions in the crystal may be considered as primary synthons (responsible for the formation of BSM) or auxiliary synthons which provide packing of BSMs. It should be noted that general electrostatic and dispersion interactions also may provide the formation of supramolecular synthons.

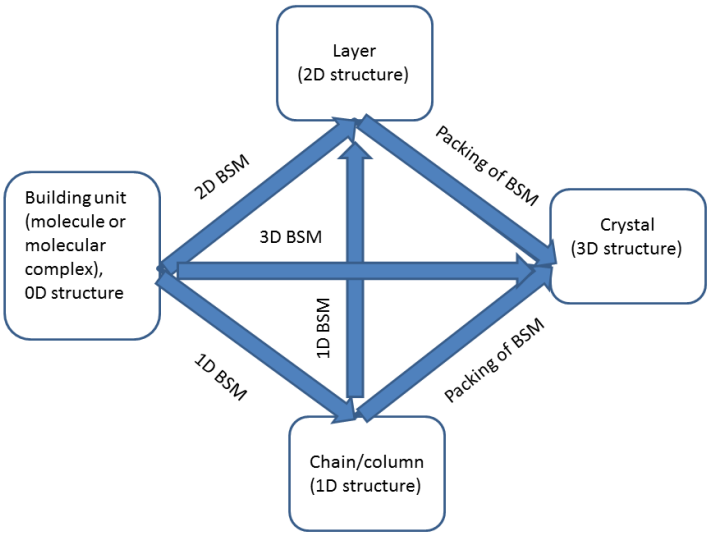

Fig. 1: Directional rhomb of supramolecular architecture of molecular crystals. Vertices corresponds to different fragments of crystal and vectors represent way of organization of these fragments from left to right.

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Xenon compounds – theoretical studies of molecular complexes

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Noble gases (Ng) are usually considered as chemically inert due to their stable electronic structure of valence electrons unfavorable to formation of chemical bonds. The inertness of noble gases has been used e.g. in the development of low-temperature matrix isolation technique since the early 1950s.

The first chemical compound containing noble gas atom, $Xe^{+}[PtF_6]^{-}$, was experimentally prepared 50 year ago. The last four decades have introduced a rich and interesting world of noble gas chemistry.

Recently, a new class of noble gas containing molecules, HNgY (where Y – an electronegative group), have been prepared and characterized in the low-temperature matrices IR spectroscopy [1]. Usually molecules are experimentally prepared in low-temperatures matrices by photodissociation of a hydrogen containing precursor and thermal mobilization of the photodetached hydrogen atoms.

In order to understand the nature of chemical bonds in molecular systems containing Ng atoms we have applied the topological analysis of the electron localization function (ELF). Via ELF analysis we can obtain information on the degree of ionic and covalent bonding in studied systems. The results of *ab initio* calculations, the SAPT analysis, the topological analysis of the ELF and the discussion of the nature of molecular interactions as well as chemical bonds with Xe atom will be presented for following molecular complexes:

- $HXeOH\ldots H_2O$ and $XeH_2\ldots H_2O$ (example of dihydrogen bonds),
- $HXeBr\ldots CO_2$ and $HBr\ldots CO_2$ (for comparison),
- $HXeI\ldots HX$ (where X = Br, I),
- $HXeY\ldots H_2O$ (where Y = Cl, Br, and I).

The geometry optimization of HXeY complexes at high level of theory (MP2 and CCSD(T)) yields several minima on the potential energy surface. Moreover, the HXeY complexes are more stable than the analogical HY complexes. The SAPT analysis of $HBr\ldots CO_2$ and $HXeBr\ldots CO_2$ complexes clearly indicate on importance of dispersion and electrostatic terms in the total interaction energy.

Interaction of HXeY subunit with other molecules has a strong effect on vibrational properties of HXeY molecules. All studies HXeY complexes exhibit large blue shifts of the H-Xe stretching mode up ca. +160 cm^{-1}.

Acknowledgements: The authors would like to gratefully acknowledge the National Centre for Research and Development of Poland (grant ERA-CHEMISTRY-2009/01/2010) for the support of this research. Calculations were performed at the Wrocław Centre for Networking and Supercomputing.

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Non-covalent interactions between metal complexes and aromatic rings

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Metal complexes and organic aromatic molecules are very common constituents of materials and their interactions have been recognized as important force responsible for properties of materials. Moreover, metal complex/aromatic interactions are essential in a number of other biological and chemical systems.

The interactions between water molecules (non-coordinating and coordinating) and aromatic rings (OH/π and parallel interactions) were studied by analyzing data in the Cambridge Structural Database (CSD) and by quantum chemical calculations. Crystallographic analysis shows that water/aromatic contacts prefer parallel interaction to much better known OH/π interaction, indicating importance of parallel interaction. The data from the CSD and quantum chemical calculations reveal influence of water coordination to a metal ion; interactions of coordinating water are stronger even if the aqua complex is neutral. [1, 2] Positively charged complexes form very strong interactions; the strongest calculated MLOH/π interaction energy is -14.85 kcal/mol, while the strongest calculated parallel interaction energy is -14.89 kcal/mol.

Study of the crystal structures from the Cambridge Structural Database showed that organic aromatic rings prefer stacking with chelate rings to other organic aromatic rings. Calculations have shown that the nature of metal ions strongly influences the strength of these interactions. Very accurate calculations at CCSD(T)/CBS level showed that the energies of stacking interactions of copper and nickel six-membered chelate rings with benzene are -6.39 kcal/mol and -4.77 kcal/mol, respectively. [3, 4] These results can be very important for numerous systems that contain metal-chelate rings and organic aromatic molecules, most notably organic-inorganic materials.

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Factors contributing to stabilization of glycine crystals polymorphs

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Glycine exhibits intriguing diversity in solid forms. There are deposited 99 records in Cambridge Crystallographic Database classified in five polymorphic forms. The versatility of observed contacts of glycine in crystals is presented in Fig.1. Unfortunately data obtained by different authors, with variety of equipment and measurement conditions, with divers refinement protocols and corresponding errors (R-factors) suffer from serious incongruences. Some CIF's are even deficient from geometric parameters. That is why optimization of molecular geometries were performed for all structures based on capabilities of Accelrys Material Studio 6.1. The experimental values of cell parameters were preserved and only relaxation of molecular geometry was allowed. This led to congruent set of data used for further intermolecular interaction energies (IIE) computations based on *first principle* and *ab initio* approaches. Several decomposition schemes were adopted for elucidation of energetic origins of observed heterogeneities in glycine crystals and interesting trends were noticed leading to deeper understanding of this unusual phenomenon of glycine. For example the β forms are characterized by lowest compressibility, while the contrary δ form has highest susceptibilities to pressure stress. Also some methodological issues are addressed.

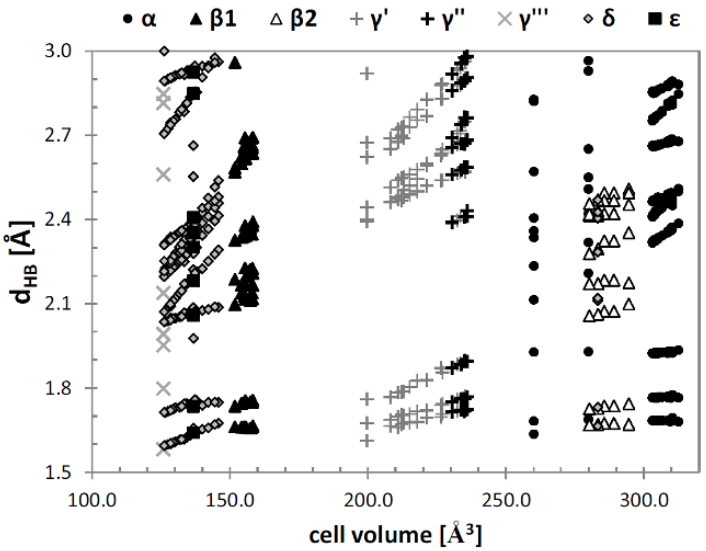

Fig. 1: Distributions of hydrogen bond lengths found in molecule shells of all known glycine crystals.

Large-scale quantum chemical computations of nucleic acids

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Due to the recent developments of DFT-D3 methodology, it is now feasible to perform sufficiently accurate QM computations on complete nucleic acids building blocks such as quadruplex DNA stems or RNA building blocks. Such computations may decisively enhance our capability to study nucleic acids using advanced computational tools. However, as any computational methods, these computations have also limitations. I will discuss the advance of large-scale QM computations of nucleic acids, show their synergy with classical MD simulation studies, and analyze their advantages and limitations, namely limited conformational sampling and utilization of continuum solvent.

Acknowledgements: Support from the Czech Science Foundation project P305/12/G034 is acknowledged.

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Further progress in the developments of an anisotropic, polarizable molecular mechanics/dynamics potential. Applications to ligand-protein complexes and extensions to nucleic acids

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To be able to reliably match quantum-chemistry (QC) results of intermolecular interaction energies, a polarizable molecular mechanics/dynamics force-field should have three essential features: separability, anisotropy, and non-additivity. Examples for each are provided in several test cases comparing the results from the SIBFA potential to those from QC, such as halogen bonding, the stacking of two nucleic acid bases, and multiply H-bonded water oligomers. Results from ongoing simulations on complexes of inhibitors with target proteins are then presented. The impact of structured, highly polarized water molecules on molecular recognition is also addressed.

Insights into the mechanism of EGFR covalent inhibition by QM/MM and enhanced sampling approaches

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Irreversible EGFR inhibitors can circumvent resistance to first-generation reversible, ATP-competitive inhibitors in the treatment of non-small-cell lung cancer, including gefitinib. They contain an electrophile warhead, generally an acrylamide group, that binds covalently a non-catalytic cysteine (Cys797) of EGFR ensuring [1]. While acrylamide-based inhibitors of EGFR are currently employed in therapy, the chemical details of their reaction with EGFR are still unclear. With this in mind, we used a hybrid quantum mechanics/molecular mechanics potential (QM/MM) in combination with steered-MD and umbrella sampling approaches to elucidate, at atomic level, the mechanism of alkylation of Cys797 by the prototypical acrylamide-based inhibitor PD168393.

Calculations show that Cys797 reacts with the acrylamide group of PD168393 through a "direct addition" mechanism [2], with Asp800 acting as a general base/general acid in distinct moments of the reaction (Figure 1). As a base, aspartate 800 activates the thiol group by deprotonating it, favoring the nucleophile attack at the β-carbon of the acrylamide. As an acid, aspartic acid 800 transfers a proton to the α-carbon of the reacting acrylamide, leading to the final product of the reaction. The QM/MM simulations also show that acrylamide participates to the reaction in its *s-cis* configuration and that only a limited structural adaptation of the EGFR kinase domain is required to allow the formation of a covalent bond between the sulfur atom of Cys797 and the β-carbon of the inhibitor. The calculated free-energy barrier for the overall process (13 kcal/mol) is in agreement with experimental constants of inactivation [3], which correspond to energy barriers of 10-12 kcal/mol.

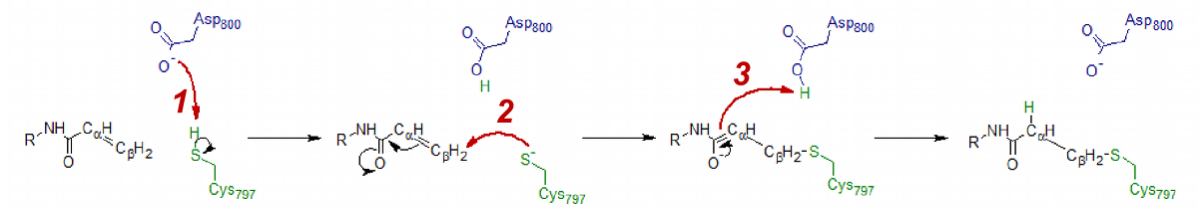

Fig. 1: Proposed mechanism of alkylation of EGFR Cys797 by PD168393.

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A QM-MD simulation approach to the analysis of FRET processes in (bio)molecular systems

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Nonradiative Förster resonance energy transfer (FRET) occurs from a donor molecule to an acceptor molecule, $D^* + A \rightarrow D + A^*$, and results from a dipole-dipole interaction between their electronic states. Transfer occurs when the oscillations of an optically induced electronic coherence on D^* are resonant with the energy gap of A. FRET is a phenomenon used in molecular biophysical studies, including protein conformational changes, protein-protein interactions or protein–DNA interactions, as well as in fluorescence microscopy applications. Predicting FRET pathways in proteins using computer simulation techniques is very important for reliable interpretation of experimental data. A novel and relatively simple methodology has been developed and applied to purine nucleoside phosphorylase (PNP) complexed with a fluorescent ligand – formycin A (FA). FRET occurs between an excited Tyr residue (D^*) and FA (A).

MD simulations for the protein molecule containing D^*, and complexed with A, are carried out. Interactions of D^* with its molecular environment are accounted by including changes of the ESP charges in S_1, compared to S_0, and computed at the SCF-CI level. FRET probability W_F depends on the inverse six-power of the D^*–A distance, R_{da}. The orientational factor $0 < \kappa^2 < 4$ between D^* and A is computed and included in the analysis. Finally, W_F is time-averaged over the MD trajectories resulting in its mean value.

$$W_F(t) = \frac{3\kappa^2(t)}{2\tau_d}\left(\frac{R_F}{R_{da}(t)}\right)^6, \quad \kappa = \boldsymbol{\mu}_d\boldsymbol{\mu}_a - 3\left(\frac{\mathbf{R}_{da}}{R_{da}}\boldsymbol{\mu}_d\right)\left(\frac{\mathbf{R}_{da}}{R_{da}}\boldsymbol{\mu}_a\right), \quad W_F^{\mathrm{mean}} = \frac{1}{T}\int_0^T W_F(t)dt$$

where $\boldsymbol{\mu}_d$ and $\boldsymbol{\mu}_a$ are electric transition moments of the donor and acceptor molecules, respectively. In course of MD they change their orientations. $\mathbf{R}_{da}$ is vector from D^* to A - a few definitions have been considered and final results compared. Other parameters in these formulae are taken from experiments. Possible deactivation paths, including FRET ones, are considered. One should note that because FRET processes are sensitive to charges of residues, prior to simulations the protein molecule should be virtually titrated - for methodology see e.g. [1]. Comparison of experimental and theoretical data for PNP as well as its two mutants, PNP F159A and PNP F159Y - in complex with FA, are reported in [2].

Acknowledgements: These studies were supported by the MNiSW grant (NN202105536). Computations were carried out using Biocentrum-Ochota (POIG.02.03.00-00-0030/09) and ICM UW infrastructures.

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Stochastic models of the absolute asymmetric synthesis by the Soai-autocatalysis

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Absolute asymmetric synthesis (AAS) is the preparation of pure (or excess of one) enantiomer of a chiral compound from achiral precursor(s) by a chemical reaction, without enantiopure chiral additive and/or without applied asymmetric physical field. Only one well-characterized example of AAS is known today: the Soai-autocatalysis [1]. This reaction (addition of dialkylzinc reagent to N-heterocyclic aldehydes) gives medium-to-high excesses of one enantiomer of the product (chiral secondary alcohol), but it can not be said in advance, *which* enantiomer will be in excess. It would be of great practical value to control the direction of this reaction towards one or the other enantiomer of the product. This requires better understanding of the mechanism.

We made an attempt at clarification of the mechanism by *stochastic analysis* of several parallel AAS experiments. Our results show that the *initial steps* of the reaction might be controlled by simple *normal distribution* ("coin tossing") formalism. Advanced stages of the reaction, however, appear to be of more complicated nature. *Symmetric beta distribution* formalism could not be brought into correspondence with the experimental observations. A *bimodal beta distribution* algorithm provided suitable agreement with the experimental data. The parameters of this bimodal beta function were determined by a Polya-urn experiment (simulated by computer). Interestingly, parameters of the resulting bimodal beta function give a *golden section ratio*. These results show, that in this highly interesting autocatalysis at least two, most probably three catalytic cycles are cooperating.

The most important details of this modelling procedure will be reported in the lecture.

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Multiscale modeling of membrane and membrane proteins

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The interactions between membranes and membrane proteins with chemicals are crucial processes for all forms of life. Here we will present a variety of molecular simulation approaches, from quantum to coarse grain, to gain insights on ion transport and ligand binding to some of these very important biomolecules. We will also discuss possible ways to use the results from these simulations for modeling signaling cascades.

Collagen-hydroxyapatite interactions and the molecular-scale architecture of bone

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The remarkable mechanical properties of bone are determined by the organization and strength of binding at the mineral-collagen interface. While the process through which collagen becomes mineralized has been extensively studied, little is known about the mechanisms or energetics that underlie the organization of this mineral-matrix composite. One obvious question regarding bone architecture arises from the fact that bone apatite platelets do not exhibit the hexagonal crystallographic symmetry of hydroxyapatite. We investigated collagen-mineral interactions by combining dynamic force spectroscopy measurements of binding energies with molecular dynamics simulations of binding and atomic force microscopy observations of collagen adsorption on single crystals of calcium phosphate for four mineral phases of potential importance in bone formation. We determined the magnitude and mode of collagen-hydroxyapatite binding, and comparison between the orientations seen on the different mineral surfaces and transmission electron microscopy analyses of bone and dentine showed that only calcium-deficient apatite provides an interface with collagen that is consistent with the organization seen in mineralized tissues. The calcium-deficient apatite is likely to possess monoclinic symmetry and forms through recrystallization of either amorphous calcium phosphate or octacalcium phosphate, and it can express the observed characteristic platelet habit of bone apatite.

Computational modeling of amyloid peptides

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Amyloids are proteins capable of forming fibrils whose intramolecular contact sites form a characteristic zipper pattern. A number of diseases related to amyloid proteins is constantly increasing and include Alzheimer's disease (proteins Aβ and tau), Parkinson's disease (α-synuclein), type 2 diabetes (amylin), Creutzfeldt-Jakob's disease (prion), Huntington's disease (huntington), amyotrophic lateral sclerosis (SOD1), and many others. Recognition of factors responsible for protein misfolding and subsequent cascade of events can contribute to better understanding of the diseases mechanisms and potential drug design. Recent studies indicate that short segments of aminoacids, which are believed to be 4-10 residues long and called *hot-spots*, can underly amyloidogenic properties of a protein. Those fragments can be harmless when they are burried inside a protein. Other studies indicate that the neurodegenerative processes is related only to transient amyloid oligomers and may correspond to their incorporation into cell membranes, creating weakly cation-selective ion channels that allow uncontrolled influx of calcium or other ions into nerve cells. In the talk we will present our results of computational methods that recognize amyloidogenic hot-spots and their propensity to forming double strands, based on classical machine learning methods, probabilistic formal grammars, and our original method based on site specific co-occurrence pattern [1–3]. Preliminary results on modeling hypothetical structures of the amyloid pores will also be discussed.

Acknowledgements: Support from NCN grant No. N N519 643540 is acknowledged. Calculations were in part performed at the Wroclaw Centre for Networking and Supercomputing.

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Theoretical description of chemical bonding based on natural orbitals for chemical valence (NOCV)

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Recently developed ETS-NOCV scheme [1] for chemical bond analysis is based on Natural Orbitals for Chemical Valence (NOCV) [2,3] combined with the Extended Transition State (ETS) bond-energy decomposition [4]. NOCV provide a simple mothod for decomposing the deformation density, $\Delta\varrho$, into the different components (such as σ, π, δ, etc.). Within the ETS-NOCV analysis it is possible to obtain in addition the corresponding energy contributions to the total bond energy.

In the present account the applications of the ETS-NOCV scheme in a description of various types of chemicals bond will be presented. This appraoch is particularly useful for transition metal complexes, as it allows to separate the donation/back-bonding charge-transfer channels. However, it is as well suitable for a description of typical covalent bonds, and the relatively weak interactions, such as agostic connections between C-H and the metal, hydrogen and halogen bonds. In particular, the recent applications of the ETS-NOCV scheme in analysis of changes in chemical bonding along pathways of chemical reactions will be presented.

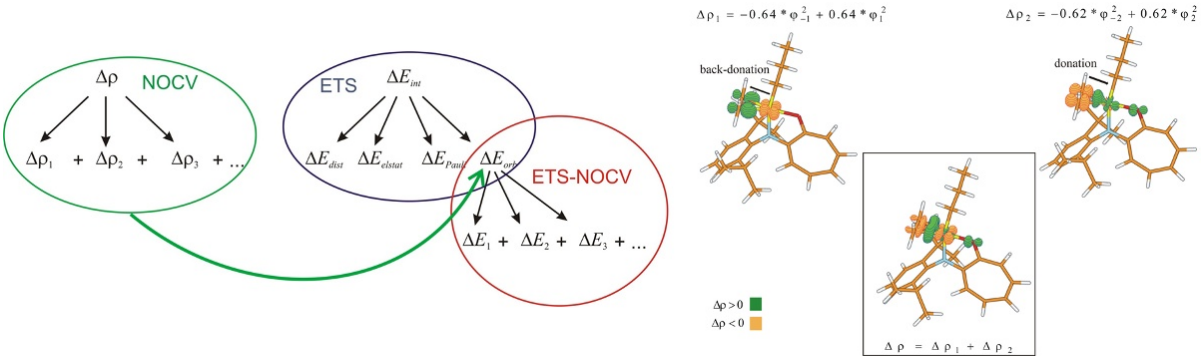

Fig. 1: The main idea of the ETS-NOCV scheme (left part) and the donation/back/bonding components of $\Delta\varrho$ describing bonding of ethylene to Ni-anilinotropone complex (right part).

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σ-hole bond versus hydrogen bond in simple complexes and large clusters

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The hydrogen bond and halogen bond often play the key role in reactions and physicochemical processes, such as for example, the proton transfer or the S_N2 reaction. However there are other Lewis acid – Lewis base interactions which are important in numerous chemical processes. It seems that the σ-hole concept often explains the formation of such interactions and the accompanying mechanisms [1,2].

The σ-hole bond is defined as a noncovalent interaction between a covalently bonded atom of groups IV–VII and a Lewis base center [2,3]. It is often competitive to the hydrogen bond interaction. For example, for the ZFH_3^+ ions acting as the Lewis acids the Z-H...B hydrogen bonds or the F-Z...B σ-hole bonds may be formed (Z is the element of the Vth group while B designates the Lewis base center) [4]. For the NH_4^+ cation the N-H...B hydrogen bond is formed and not the N...B σ-hole bond. However in a case of more Lewis base ligands firstly the N-H...B H-bonds are formed and if all N-H bonds of ammonia ion are saturated thus the nitrogen Lewis acid sites are involved in the N...B interactions [5].

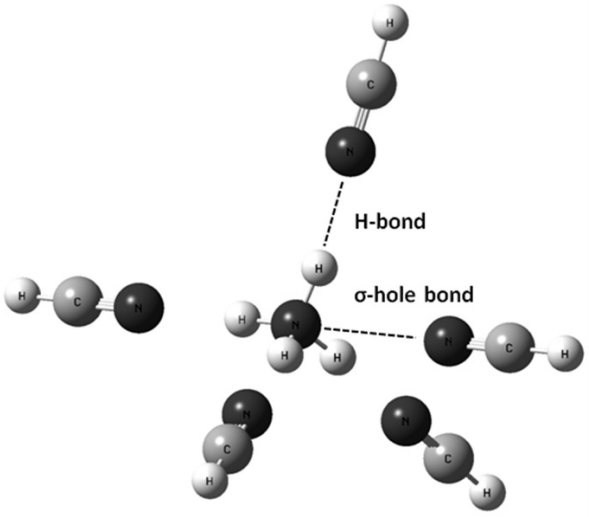

Fig. 1: The NH_4^+...$(NCH)_5$ cluster

Figure 1 presents the NH_4^+...$(NCH)_5$ cluster where four N-H...N hydrogen bonds were detected and next, the N...N σ-hole bond. The IIIrd group elements, X, were analyzed as potential Lewis acid centers and it seems that there are rare cases where the X...B interactions may be classified as the σ-hole bonds [6].

Acknowledgements: Financial support comes from Eusko Jaurlaritza (GIC 07/85 IT-330-07) and the Spanish Office for Scientific Research (CTQ2012-38496-C05-04). Technical and human support provided by Informatikako Zerbitzu Orokora - Servicio General de Informatica de la Universidad del Pais Vasco (SGI/IZO-SGIker UPV/EHU).

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Adsorption of non-linear polymers. A Monte Carlo study

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In this work we investigated the structure and the dynamic properties in two-dimensional systems containing long flexible polymer chains [1]. Computer simulations of idealized models of macromolecules at interfaces were performed by means of the Monte Carlo method. The coarse-grained models chains were approximated as sequences of beads and were embedded to a pseudo-crystalline lattices. We studied the following chain's internal architectures: linear, star-branched and cyclic with different sequences of two kinds of beads: hydrophobic (H) and hydrophilic (P): homopolymers, random copolymers, alternating copolymers and block copolymers [2]. The polymer beads interacted with a long-distance contact potential and were placed near an impenetrable and attractive surface. The properties of the model system were determined using the Random Sequential Adsorption, the Replica Exchange Monte Carlo and the Dynamic Lattice Liquid algorithms. The influence of the temperature, the strength of the adsorption, the sequence of beads and the macromolecular architecture on the properties of chains were studied. The changes of the polymer film structure in the presence of certain patterns on the adsorbing surface was also presented and discussed [3].

Acknowledgements: The authors gratefully acknowledge the computational grant 77/2012 from the Supercomputing and Networking Center (PCSS) in Poznan, Poland. The computations were also carried out using the computer cluster at the Computing Center of the Department of Chemistry at University of Warsaw, Poland.

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Charge-inverted hydrogen bond as a new type of interaction

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By performing *ab initio* calculations for a wide range of dimers with various types of interactions involving a hydridic hydrogen atom (hydride hydrogen bond, dihydrogen bond, agostic bond, etc.) we show that the recently proposed charge-inverted hydrogen bond (CIHB) [1–4] should indeed be investigated as a new type of interaction. This conclusion is obtained on the basis of formal definitions of relevant interactions as well as on the quantum theory of atoms in molecules and the hybrid variational-perturbation scheme of the decomposition of the interaction energy. Particular attention is paid to comparison of CIHB with agostic-type interactions. Additionally, it is shown that CIHB is somewhat similar to strong dihydrogen bonds. The origin of this finding is also presented.

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Poster abstracts

in alphabetical order of the leading author's last name

Poster session A - June 30 (Monday)
Posters: P1-P38

Poster session B - July 1 (Tuesday)
Posters: P39-P77

Catalytic activity of Kemp eliminase theozyme (KE07) mutants interpreted by electrostatic multipole term of differential transition state stabilization

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Recent successful theoretical design of several enzymes, possessing new functions unknown in nature, constitutes the major breakthrough in biocatalysis research [1-3]. However, the activities of theozymes are rather low and subsequent directed evolution experiments resulted in considerably enhanced performance, so it is obvious that the design methodology has room for improvements. In this contribution we wonder how to explain the role of several mutations introduced additionally to the theoretically designed KE07[2].

The increasing catalytic power of in vitro engineered descendants of KE07 was analysed within the Differential Transition State Stabilisation (DTSS) concept [4] and Cumulative Atomic Multipole Moment (CAMM) approximation of electrostatic multipole term [5]. The results provide hope that this phenomenon can be explained by rather simple electrostatic model, opening the perspective to develop more robust theozyme design methods.

Acknowledgements: This work was funded by Wroclaw Research Center within the project 'Biotechnology and advanced medical technology' – BioMed (POIG.01.01.02-02-003/08) supported by the European Regional Development Fund (Innovative Economy Operational Programme, subtask 1.1.2 Calculations were performed at the Wroclaw Centre for Networking and Supercomputing.

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A comparative study of transferable theoretical aspherical pseudoatom data bank and classical force field in predicting the electrostatic interaction in molecular dimers

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Electrostatic interactions are extremely essential in biological system and it is also well known that ab-initio calculations are very expensive and time consuming in case of macromolecules. In this study we have evaluated electrostatic interaction energy (EES) of S66 [1] and S66_8 [1] data sets, total 66 different molecular complexes.

These complexes are representative of a range of chemical and biological systems for which hydrogen bonding, electrostatic, and van der Waals interactions play important roles. S66_8 set cointains same molecular dimers as S66 set, but they are embedded at 8 points around the equilibrium geometries. Electrostatic energy calculated on the basis of UBDB [2] databank of aspherical models were compared with corresponding reference results. Further, results were also compared with energies computed with use of widely used force fields.

	0.90	0.95	1.00	1.05	1.10	1.25	1.50	2.00
UBDB+EPMM	1.81	1.43	1.20	1.06	0.99	0.85	0.56	0.43
AM1-BCC	7.88	5.79	4.34	3.31	2.56	1.27	0.47	0.34
RESP	7.33	5.26	3.86	2.88	2.18	1.00	0.33	0.24
RESP-SCRF	5.23	3.33	2.11	1.37	0.96	0.77	0.78	0.66
CGenFF	8.19	7.10	4.62	3.59	2.83	1.49	0.63	0.47

Table 1: RMSD in kcal/mol.

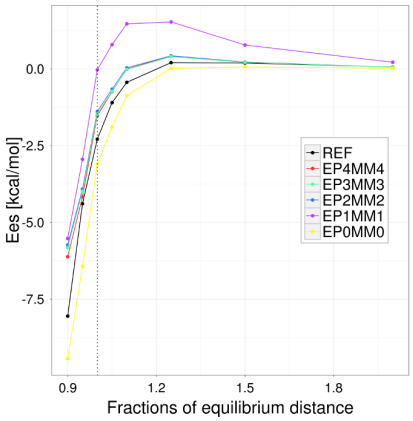

Fig. 1: Benzene-benzene $\pi - \pi$ interaction. Digits in methods names represent the level of truncation - $L_{\max}$.

Verification of the results on S66_8 data set gave an important knowdlege which parts of UBDB+EPMM method are essential for good estimation of electrostatic interaction energies. The EPMM [3] method consist of two different aproach: EP - Exact Potential - which evaluates the exact Coulomb integral and MM - Multipole Method - Buckingham-type multipole approximation. In UBDB+EPMM method below the critical distance (here $R_{crit} = 4.5$) EES is evalueted by the Exact Potential method. Appart from interactions between multipoles, EP contains the penetration energy. For electrostatic dominated systems (i.e. H-bonded) dipole expansion is sufficient for EES calculation. For such systems UBDB+EPMM with $L_{\max} = 1$ fits the results obtained with $L_{\max} = 4$ whereas for dispersion dominated systems truncation should be at least at quadrupole level ($L_{\max} = 2$). This study shows that estimation of electrostatic interaction energy using UBDB databank is more accurate and fast when compared to other known methods and opens new possibility of applying on macromolecules.

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Theoretical study on structure-activity relationships in ethylene polymerization catalyzed by half-metallocene titanium(IV) complexes

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Half-metallocene complexes represent an important class of organometallic compounds that are applicable as catalysts in the homogeneous polymerization of olefins. The modification of the ligand in the complexes is the main route used for tuning their properties of these complexes. Many structural modifications, including steric tuning, changing the ligand backbone structure, and altering the chelating heteroatoms, have been pursued on the ancillary ligand (see Fig. 1a). Ligand electronic effects have been observed in many catalytic systems. [1-3] Recently, it was shown by experimental study that derivatives of half-metallocene titanium(IV) complexes exhibit a relatively high polymerization activity.

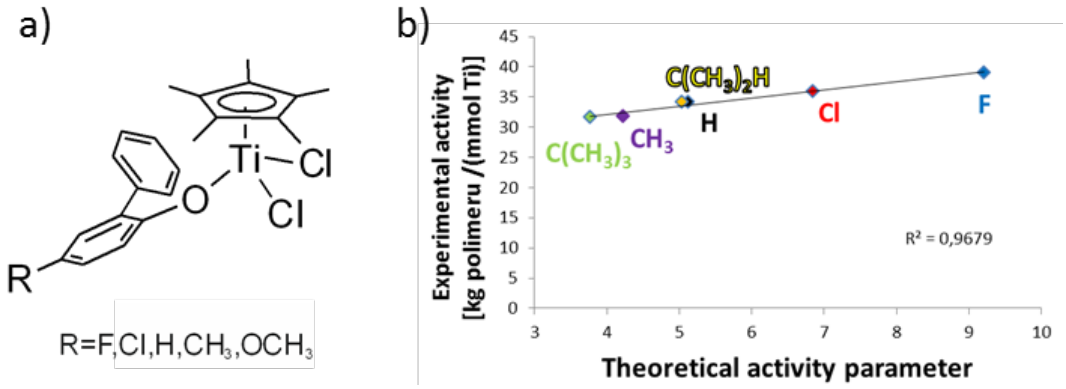

Fig. 1: Titanium catalyst considered in the present study (left part) along with corelation between theoretical activity parameter and experimental activity (right part).

In Fig. 1b. the correlation between experimental activities and the theoretical activity parameters have been depicted. Introduction of the substituent R into the phenoxy ligand leads to a decrease in the Ti-O bonding energy, mostly due a decrease in the orbital interaction contributions. It is shown that the strength of the covalent bond correlates with the theoretical activity parameter of the catalyst. This suggest that changes in the experimental activity , reflected by the strength of the Ti-O bond, are directly rationalized via orbital interaction contributions.

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The evolution of charge transfer properties for pyrrole and 3,6-bis(2-pyrrolo)carbazol oligomers – precursors of conducting polymers

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Conducting polymers are important for organic electronics. They are used, among other things in dye-sensitized solar cells (DSSCs), organic light-emitting diodes OLED and biosensors. An important feature of these materials is semiconducting.

Physical and chemical properties of these materials can be modified by chemical changes in the structure providing or withdrawing electrons from the polymer chain. Chemical modifications allow to controlling band gap energy difference between HOMO, and LUMO orbitals.

The following properties were studied: spin electron density, ionization energy, distribution of molecular orbitals HOMO / LUMO, the energy band structure, the formation of the conduction band in the material and structural features such as the dihedral angle between the mers.

Structure and dynamics Cy3 and Cy5 cyanine dyes terminally attached to DNA: a combined theoretical study

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Cyanine Cy3 and Cy5 are fluorescent dyes are often used for molecular labeling (e.g. in DNA microarrays) or together as the donor - acceptor pair in the fluorescence resonance energy-transfer (FRET) experiments to investigate structure and dynamics of biomolecules.

In this contribution the structure and dynamics of cyanine Cy3 and Cy5 dyes terminally attached to the 5'-end of the CCACTAGTGG oligonucleotide were studied by molecular dynamics (MD), essential dynamics, metadynamics, and density-functional (DFT) calculations. Nine and seven main binding patterns between the last GC base pair and the cyanine dye were found for the Cy3-DNA and Cy5-DNA complexes, respectively. Both dyes interact with the highest probability with the last CG base pair by the stacking interactions between the distal indole ring and guanine base and the corresponding structures are in excellent agreement with previous experimental evidence.1 The Cy3 dye shows very high flexibility and all possible combinations in the stacking interactions between the distal and proximal indole rings of Cy3 and the guanine and cytosine rings were observed. Cy5-DNA complex was similarly flexible but structures with stacking interactions of proximal indole ring were not populated due to increased length of the polymethine linker. Only in 0.3% and 1.0% of the structures the Cy3 and Cy5 dyes, respectively, were completely unstacked and tilted off the last base pair. With 9.7% and 10.1% probabilities the two dyes did not interact with the GC base pair through stacking interactions of the indole rings but only through dispersion interactions of the delocalized π-electrons of the polymethine linkers.

Acknowledgements: This work is supported by the Czech Science Foundation (grant no. P208-12-0622).

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Effect of His202 protonation on zFP538 chromophore geometry - molecular dynamics study

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Fluorescent proteins (FPs) had great contribution in development of modern molecular biology. Over past 20 years, this genetically encoded fluorescent probes have been used to localize biomolecules expression, monitor secondary messengers, study promotors activity and investigate protein-protein interactions, contibuting to our understanding of living organisms.

zFP538, GFP-like protein from the button polyp *Zoanthus sp.*, is one of two known examples of natural yellow FPs. Remington et al. proposed the red shift in absorption and emission spectra (λ_{ex} = 528 nm; λ_{em} = 538 nm) compared to GFP (Green Fluorescent Protein, first discovered and the best known FP from bioluminescent jellyfish *Aequorea victoria*) might be attributed to additional heterocyclic ring in zFP538 chromophore (formed from Lys66-Tyr67-Gly68), which physically extends π-bond conjugation by C=N double bond [1]. However, the role of amino acids residues present in vicinity of the chromophore is not determined.

Molecular dynamics simulations of zFP538 (PDB: 2OGR [2]) were carried out to investigate influence of His202 protonation on the chromophore geometry and hydrogen bond network in proximity of the chromophore.

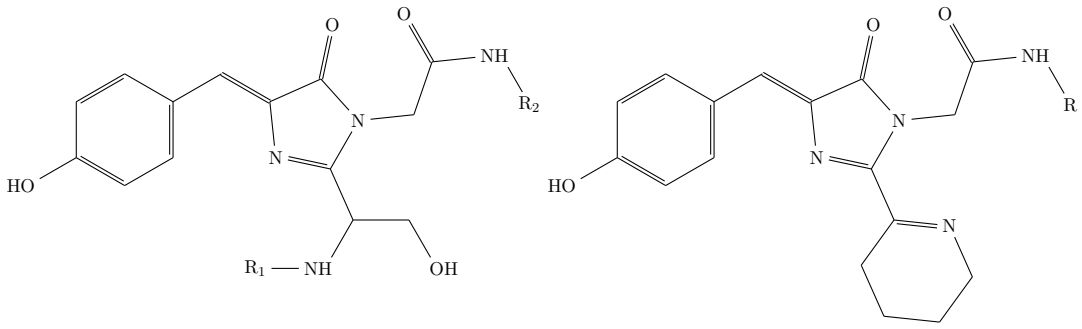

Fig. 1: Neutral form of GFP (left) and zFP538 (right) chromophores

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

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Molecular dynamics study of ChEMBL474807 inhibition properties against GSK3 and CDK2 enzymes

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The indirubin derivatives represent a significant group of ATP-competitive inhibitors. During investigations, inhibition properties of ChEMBL474807 (1-(4-amino-1,2,5-oxadiazol-3-yl)-5-(piperidin-1-ylmethyl)-N'-(pyridin-4-ylmethylene)-1H-1,2,3-triazole-4carbohydrazide towards two enzymes, namely glycogen synthase kinase-3β (GSK-3β) and cyclic dependent kinase-2 (CDK-2), were analyzed. The close resemblance of amino acid sequence of the considered enzymes (25% identity and 41% similarity) [1] proves that a large group of indirubin derivatives are inhibitors of both analyzed active sites [2]. Such a situation requires search for drugs characterized by high selectivity.

Molecular dynamics simulation of drug complexes allows on simultaneous assessment of binding affinity and dynamic properties of analyzed compound in the conformational space of active site. Complexes of ChEMBL474807 with GSK-3β and CDK-2 obtained during the docking procedure were used as starting points in molecular dynamic simulations realized in explicit solvent environment. Calculations of the free energy were realized by Molecular Mechanic/Poisson-Boltzmann Surface Area (MM-PBSA) method [3].

	GSK-3β 1-conf	GSK-3β 2-conf	CDK-2
ΔH	-26.01	-17.53	-28.29
TΔS	-18.00	-23.73	-10.61
ΔG	-8.00	6.20	-17.68

Table 1: The free energy values of binding (kcal/mol) for the ChEMBL474807 GSK-3β and CDK-2 complexes observed during MD simulations.

The structural and energetic characteristics of the considered complexes unambiguously indicate differences in dynamic properties of analyzed ligands in complexes with both active sites, manifested in the frequency of hydrogen bond creation, rmsd values and entropic contribution to binding affinity. The observed differences clearly indicate a higher affinity of the considered ligand towards CDK-2 than GSK-3β active site.

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Comparison of the reaction electronic flux and ETS-NOCV picture of the HCN→CNH isomerization reaction assisted by water

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The HCN→CNH isomerization reaction, and the corresponding reaction assisted by water, have been extensively studied by many theoretical methods. Changes in the electronic structure during the reaction were described using various theoretical concepts, e.g., bond orders, charge distribution as well as frontier orbitals analysis.

The main goal of this study was to analyze and compare the changes in the electronic structure along the IRC for the HCN→CNH isomerization reaction assisted by water. Emerging from two, relatively new theoretical approaches: the reaction electronic flux (REF) [1], and ETS-NOCV method [2]. The REF provides information about the electronic activity that can be decomposed into the polarization and charge transfer components. The ETS-NOCV allows to analyze the changes in the bond-energy components along the reaction path, and in particular, to rationalize the changes in the orbital-interaction contribution in terms of the deformation-density components. The results show the complementarity of both methods.

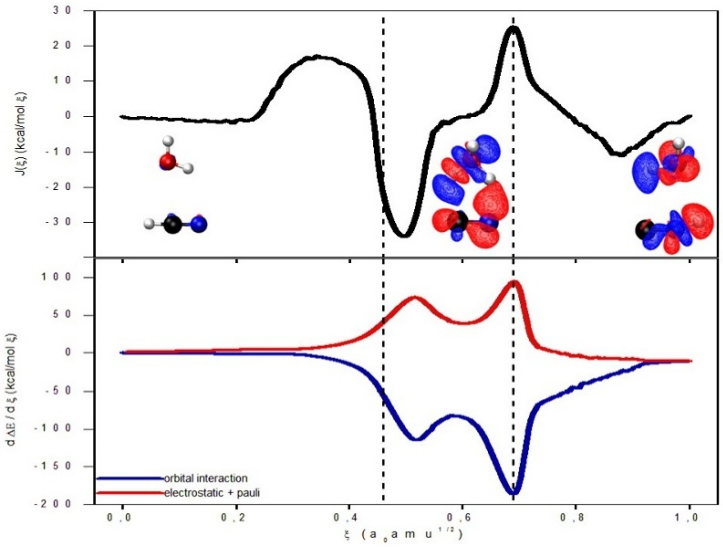

Fig. 1: REF and ETS-NOCV representations for HCN→CNH isomerization assisted with water are depicted in top and bottom panel repsectively.

Acknowledgements: Work supported by FONDECYT Grants No 1100881. S.D. wishes to thank CONICYT for Doctoral fellowships.

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On cations of polycyclic aromatic hydrocarbons

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The concept of Clar's π-electron aromatic sextet is tested against a set of polycyclic aromatic hydrocarbons (PAHs) in their neutral and doubly charged forms. Increasing attention is being paid to cationic PAHs due to the fact that this class of chemical species is assumed to be present in interstellar space.[1-3] Systems containing different types of rings (in the context of Clar's concept) are chosen, including benzene, naphthalene, anthracene, phenanthrene and triphenylene. In the case of dicationic structures both singlet and triplet states are considered. It is found that for singlet state dicationic structures the concept of aromatic sextet can be applied and the local aromaticity can be discussed in the context of Clar theory, whereas in the case of triplet state dicationic structures the model rather fails.[4] The interdependence between the values of different aromaticity indices applied to neutral and charged systems in singlet and triplet states is also discussed.

Acknowledgements: Financial support from National Science Center of Poland (Grant No. 2012/05/N/-ST4/00203) and University of Łódź Foundation (University of Łódź Foundation Award) is acknowledged. Calculations were partly performed at the Wroclaw Centre for Networking and Supercomputing (WCSS).

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Reactivity of model complexes for Cpd I and Cpd II - theoretical studies

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In the catalytic cycles of heme enzymes such as catalase, peroxidase and cytochrome P450, the high-valent iron(IV)-oxo species are postulated as key intermediates in the oxygenation reactions of inert organic substrates. While most of the concern has been devoted to very high reactive iron(IV)-oxo cation radical porphyrin species, termed compound I (Cpd I), its one-electron reduced form, i.e. iron(IV)-oxo porphyrin (Cpd II) for a long time was not considered as reactive species in C-H hydroxylation or other oxidation reactions. Recent findings revealed that Cpd II, although less reactive than Cpd I, can be regarded as complementary oxidant in the bio-mimetic catalysis. In this context, our work focuses on a comparative mechanistic study on the reactivity of Compound (Cpd) I and II analogues without and with different axial ligands (hydroxo or N-methylimidazole).

The theoretical studies were performed within Density Functional Theory (DFT), as implemented in Turbomole v. 6.3 with the hybrid B3LYP functional. All electron basis sets of def-TZVP quality were employed for all atoms. A complete geometry optimization was performed for every system and localization of energetic minima was confirmed by vibrational analysis. The resulting structures were characterized by structural parameters (bond lengths, valence and torsion angles), Mulliken charges and spin densities. For transition states one imaginary frequency, corresponding to H abstraction, was found. In every studied reaction, -H (with respect to the substrate phenyl ring) is abstracted by Cpd II species, and an intermediate OH group, attached to Fe porphyrin, is formed. The calculated transition state barriers for Cpd II do not depend on the type of axial ligand, which agrees with the experimental results.

The study indicates that oxidation of the selected substrates by the oxidizing Cpd II species is an enthalpy-controlled process. In contrast, different results were found for reactions with the application of the Cpd I mimic. Depending on the nature of the substrate, the reaction at room temperature can be entropy-controlled or enthalpy-controlled. Thiss indicates that the commonly assumed correlation between the rate constant with C-H bond strength (BDE) may not be valid sometimes since a large contribution of $\Delta S^{\neq}$ to $\Delta G^{\neq}$ leads to a significant temperature dependence of the activation barrier. The meaningful contribution of the activation entropy to the oxygenation process indicates that the reaction mechanism in biomimetic studies can be tuned by systematically varying temperature.

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Influence of the substitution effects in the pyridine ring on the reactivity of the trans-$[Pt(NH_3)_2(pyr{-}X)Cl]^+$ complex

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Platinum anticancer complexes are administered in its inactive form and the hydrolysis step is needed for their activation. The activated drug reacts rapidly with DNA or proteins and the hydrolysis step is the rate determining step of the whole process. Thus, the modification of the speed of hydrolysis is one of the ways of a new drug development.

In the present work we have studied the kinetics of the aquation reaction on the trans-$[Pt(NH_3)_2(pyr{-}X)Cl]^+$ complex (X = OH^-, Cl^-, NO_2^-, NH_2, SH^-, CH_3). All possible positions *ortho-*, *meta-* and *para-* of the substituent X in the pyridine ring were considered and reaction energy profiles, atomic charges, electron densities at bond critical points, ligand binding energies were calculated. All the structures along the reaction pathways were fully optimized using B3LYP/MWB-60(f)/6-31+G* method. Single point energies and molecular properties were evaluated by B3LYP/MWB-60(2fg)/6-311++G(2df,2pd) method.

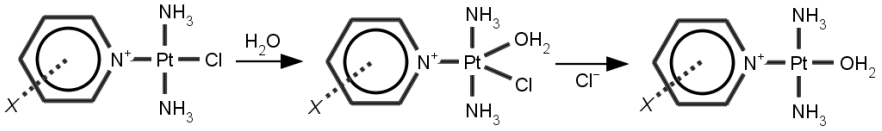

Fig. 1: Reaction mechanism of the aquation reactions.

The substituent ligand influences electron density on the pyridine ring and thus the electron donating ability of the heterocyclic nitrogen. Thus, through the trans-effect the charge and binding energy of the Cl ligand are affected. The substituent ligands on the pyridine ring can be ordered according to their ability to promote the aquation reaction as follows: $NH_2 > OH^- > SH^- \sim CH_3 > NO_2^- > H > NO_2^- \sim Cl$. The largest selectivity offers the substitution in the *ortho-* position leading to almost 400 times difference in the rate of the reaction between the fastest *o*-NH_2 and the slowest *o*-Cl^- ligand in the gas phase. In the water environment described by the PCM method this difference is lower by about one order of magnitude.

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Theoretical studies on the cobalt(III)-based catalysts for CO_2/epoxide copolymerization

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Over the last few years highly active and selective catalytic systems toward transformation of CO_2 into biodegradeble policarbonates has been reported [1]. One of the most promising catalyst generation is based on cobalt(III)-salen-type scafolds, which can be divided in two groups: binary and bifunctional catalytic system [2]. Frist consist of electrophilic part – electroneutral metaloorganic complexes of cobalt (III) and nuclephilic part – quaternary amonium salts as a co-catalyst. Both parts play significant role during formation and growth of polymer chains [2]. For bifunctional system electrophilic and nucleophilic part are incorporated in single chemical being, where quaternary amonium salt is connected to the salen core by aliphatic linkage, forming so-called "chains".

Presented theoretical (DFT) studies are focused on the relation between structure and activity of interesting model systems – electrophilic part of binary catalysts and the real, bifunctional molecules. The static DFT calculations as well as Born-Oppenheimer molecular dynamic approach were used. Among factors addressed in these studies are variation on conformation of octahedral cobalt(III) complexes [3] and influence of length and number of quaternary-amonium-salt chains (N^+-chains) [4].

Static DFT calutalions for model systems indicate that, in the absence of N^+-chains, salen-type ligand adopts square planar, trans coordination. For bifunctional systems the lowest energy structures are observed for cis-β conformation, where 3 donor atoms of salen are planar while the fourth atom is in the axial position. Moreover these preferences are strongly affected by the length and the number of N^+-chains. Molecular dynamic simulations for bifunctional catalysts indicate that these preferences are attained over time, no sponatious transitions between conformations are observed. Additionally, adopted conformation of octahedral cobalt (III) complex affects movement of chains and their orietnation toward metal center, and thus, may have implications on polymerisation mechanism.

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

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Modeling the catalytic activity of enzyme mutants with differential transition state stabilization approach

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Recent advances in computational design of biocatalysts have led to the development of enzymes exhibiting novel catalytic properties [1, 2]. However, catalytic activity characterizing designed enzymes is not as remarkable as that of natural ones. Significant improvement in catalytic properties of enzymes designed theoretically can be obtained with experimental approaches (e.g., directed evolution) indicating, that computational methodology has not yet grasp all the determinants of a successful biocatalyst.

A possible improvement in the design methodology might involve application of the Differential Transition State Stabilization (DTSS) approach [3]. DTSS method combined with decomposition of the interaction energy reveals the factors that influence the catalysis in terms of both the physical nature of enzyme-ligand interactions and the catalytic contribution of enzyme residues. The designed organophosphate degrading enzyme and its experimentally improved variants [2] were studied herein as a test case to evaluate the performance of DTSS method. Based on the QM/MM structures of enzyme in complex with substrate and transition state, the catalytic contribution of amino acid residues undergoing the mutations was evaluated within the scope of DTSS methodology. Unlike transition state stabilization values, that are currently employed in computational biocatalyst design, DTSS approach yields qualitatively correct estimate of the catalytic activity of enzyme mutants, that would possibly allow for limiting the amount of experimental work necessary for refinement of catalytic properties of designed enzymes. Dominant electrostatic multipole DTSS contribution offers more robust biocatalyst design methodology.

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Analysis of molecular interactions and internal tensions along a collective variable

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Functional motions of (bio)molecules are related to structural transitions between their meta-stable states. The source of these transitions are thermal fluctuations and/or free energy consumption (e.g. ATP hydrolisys), but also mutual interactions between atoms of the molecule. In any case, an effective "driving force" is required to make a transition. The question is: how to identify groups of atoms, which contribute to such a force?

We aimed to develop a procedure for the identification of molecular subsystems, whose internal interactions push the whole system forward or backward along a given collective variable (reaction coordinate). Our analysis is based on data acquired from classical molecular dynamics (MD) simulations, however it can also be extended to use QM/MD simulation data.

The basic idea is to express the change along a given collective variable in terms of pairwise cooperation between atoms. Such cooperation can support/block the whole molecule's tendency to go forward/backward during transition. Having defined a measure of pairwise cooperation between atoms, we were able to cluster them into groups using the *affinity propagation* clustering algorithm [1]. Also, we used a bootstrapping scheme (see e.g. [2]) to assess the quality of the clustering, as well as to distinguish between noise resulting from thermal fluctuations, and actual cooperation within the molecule.

We applied our approach to an 11-atom toy model with three meta-stable states and a natural collective variable. For this simple case we could confront the results of our analysis with intuition and knowledge about the molecule's properties. Our method revealed which atoms cooperate at consecutive values of the collective variable. We could also examine how different types of interactions influence the mechanical properties of our model.

Preliminary results obtained for the simple model show that our analysis is capable of detecting cooperating groups of atoms in molecules. Although our approach should still be validated for larger, more complex (bio)molecules, it seems to be a promising method for detecting mechanisms that drive cooperative conformational transitions.

Acknowledgements: Studies supported by the University of Warsaw BST 163500/BF funds, as well as by the Biocentrum-Ochota project (POIG.02.03.00-00-003/09).

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Modelling of the tensile properties of high density polyethylene/carbon nanotube composites via ANN

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For the attempts in order to enhance mechanical properties of composite materials, carbon-nanotubes (CNTs) have been used with polymers from the date of their introduction to make composites having better properties. Polyethylene (PE) multiwalled carbon nanotubes (MWCNTs) with weight fractions 1, 3, 5 wt% were prepared by melt blending using a twin screw extruder. Multi-wall carbon nanotube (MWNT) /HDPE composite were fabricated using the injection technique as tensile test bar. Tensile tests were performed by universal tensile testing device according to ASTM D 638 test standards. The four different Artificial Neural Network (ANN) models have been designed to predict the maximum load, elongation at break and maximum stress. To evaluate the success of systems various statistical measures such as MAE, RMSE and R2 have been used. The results show that the ANN model trained using Levenberg–Marquardt (LM) algorithm has produced more accurate results.

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Encapsulation of a zinc phthalocyanine derivative in self-assembled peptide nanofibers

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We demonstrate encapsulation of octakis(hexylthio) zinc phthalocyanine molecules by non-covalent supramolecular organization within self-assembled peptide nanofibers. Peptide nanofibers containing octakis(hexylthio) zinc phthalocyanine molecules were obtained via a straightforward one-step self-assembly process under aqueous conditions. Nanofiber formation results in the encapsulation and organization of the phthalocyanine molecules, promoting ultrafast intermolecular energy transfer.

The morphological, mechanical, spectroscopic and non-linear optical properties of phthalocyanine containing peptide nanofibers were characterized by TEM, SEM, oscillatory rheology, UV-Vis, fluorescence, ultrafast pump–probe and circular dichroism spectroscopy techniques. The ultrafast pump–probe experiments of octakis(hexylthio) zinc phthalocyanine molecules indicated pH controlled non-linear optical characteristics of the encapsulated molecules within self-assembled peptide nanofibers. This method can provid e a versatile approach for bottom-up fabrication of supramolecular organic electronic devices.

An evolutionary approach to computational *de-novo* enzyme design for olefin metathesis

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One of the most tantalizing challenges in computational chemistry and bioinformatics is the design of artificial enzymes, tailored specifically to catalyze any desired chemical transformation.

Here we describe the computational *de-novo* design of a metalloenzyme capable of catalyzing the ring closing metathesis of diallylether, a reaction with no natural counterpart. The "inside-out" enzyme design protocol was employed for this task, where a theoretically engineered novel active site is introduced into the scaffold of an existing protein [1]. The active site was modeled after motifs present in the popular second generation Grubbs ruthenium-based metathesis catalyst [2]. In order to efficiently search for active site configurations with high catalytic activity, a newly developed genetic algorithm was used, combining high throughput quantum-chemical computations on DFT-level with a stochastic optimization procedure. The ROSETTA suite of programs [3] was then used to screen a database of protein crystal structures for scaffolds where these model active sites could be realized and to optimize catalytic interactions via a subsequent step of sequence design. This procedure resulted in four promising candidate metalloenzyme designs for experimental expression.

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Chemical surface modification of titanium oxide using organophosphonic acids

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Chemical surface modification is an important aspect of a large number of applications such as sensors, diodes, separation technology, functionals coatings, adsorbents etc. Different types of surface modification methods to graft organic functional groups onto the surface of metal oxides are currently known, the most important being organosilylation and reactions with organophosphonic (OP) acids. Grafting with (OP) acids is being applied to organically modify metal oxide supports, based on the esterification reaction between OP acids and the hydroxyl groups on the surface of the support. A large number of aspects of the materials resulting from this modification method remain subjects to heated debate [1–3]. Key issues are the precise mechanism of their preparation and the precise assignments of important peaks in both NMR and IR spectra, which are fundamental to a full understanding of these functionalized surfaces.

Titanium oxide exists in nature as rutile, anatase and brookite, but nanocrystalline titanium oxide prefers the anatase form due to the lower surface free energy of its stable (101) facet. Therefore, previous studies focused on the modification of the (101) facet with OP acids. Although (001) is a minority facet in anatase, its reactivity is higher compared with the (101) facet and several studies succeeded to characterize a larger portion of the anatase (001) facet [4]. We present the surface modification of the anatase (001) surface with methyl phosphonic acid (MPA) and compare the obtained results with those using the (101) facet and results obtained with the rutile polymorph.

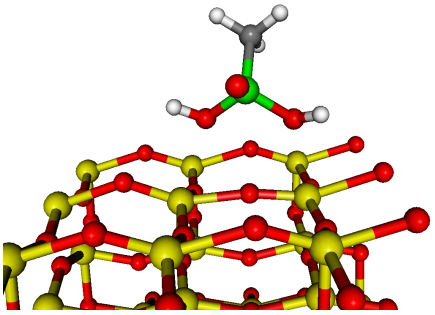

Fig. 1: MPA adsorption at the (001) anatase surface.

Acknowledgements: This work was carried out using the Turing HPC infrastructure at the CalcUA core facility of the University of Antwerp, a division of the Flemish Supercomputer Center VSC, funded by the Hercules Foundation, the Flemish Government (department EWI) and the University of Antwerp.

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Structural insight through mechanical stretching: steered molecular dynamics simulations of a small heat shock protein

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Alpha A-crystallin is a dominant constituent of the mammalian lens, and contributes to its refractive and mechanical properties. Acting as a chaperone, this small heat protein (sHSP) helps to prevent aggregation within the glassy solution of proteins that comprise the lens. The present study explores the mechanical properties of bovine Alpha A-crystallin by Steered Molecular Dynamics simulation. In particular, an external pulling force is applied to the protein in a series of unfolding experiments. The effect of L- to D-amino acid substitution on the protein's mechanical strength and stability is further explored by the stretching of variants carrying a specific D-residue substitution. A Principal Component Analysis (PCA)-based approach is applied to extract trends that associate high tensile strength with elements of secondary protein structure. Four systems are investigated: the native protein, two serine D-amino acid analogues, and one D-threonine variant. An examination of force profiles, unfolding pathways, and PCA trends reveals that the response and mechanical strength of the protein is significantly modulated by the introduction of a D-amino acid, and that the extent of this effect is highly dependent on residue position. Finally, since such L to D racemization occurs in parallel to lens ageing, biological implications are addressed.

Acknowledgements: This project is supported by the MPD Program of the Foundation for Polish Science „Bio-Molecular Chemistry: An Interdisciplinary Approach to Protein Structure-Function Relationships", and is co-financed by the European Union from its Regional Development Fund [MPD/2010/5].

Theoretical investigation of brominated uracil radiosensitization mechanism

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One of the greatest problems in radiotherapy comes from the radiation sensitivity of neoplasms which is often lesser than that of normal tissue. This may be caused by the tumor outgrowing its blood supply: cancer cells are hypoxic while the presence of oxygen can make a cell 2.5-3 times more susceptible to ionizing radiation. This phenomenon has made scientists seek alternative ways to increase sensitivity to radiation, such as the compounds known as radiosensitizers.

The radiosensitizing properties of a brominated pyrimidine – 5-bromouracil - have been known for more than half a century. It is known that it can be incorporated into DNA as a thymine analogue and such labeled DNA is more sensitive to radiation damage like single and double strand breaks. However the exact mechanism of damage formation is still unknown. It is thought to rely on hydrated electrons as the presence of free radical scavengers has little influence on the amount of damage. Recently we proposed a mechanism for electron induced single strand break formation in DNA labeled with a brominated purine – 8-bromoadenine [1].

In the current work we investigate whether the radiosensitizing properties of 5-bromoracil can be explained with a similar mechanism. We also examine its isomer – 6-bromouracil – as a potential radiosensitizer. We use the B3LYP/6-31++G(d,p) level of theory to describe the response of model nucleotides, 5-bromo-2'-deoxyuridine 3',5'-diphosphate (5-BrdUDP) and 6-bromo-2'-deoxyuridine 3',5'-diphosphate (6-BrdUDP), to electron attachment.

We found out that both compounds are characterized by adiabatic electron affinities significantly larger than that of their thymine analogue. In 6-BrdUDP electron attachment causes immediate barrier free bromide anion release, while for 5-BrdUDP there is a small barrier. The product of the former process, 6-radical (6-*dUDP), abstracts a hydrogen atom from the 3'- or 5'-position of the ribose residue. For 5-radical (5-*dUDP) such reaction is hindered sterically. Moreover, 1,2-hydrogen shift, transforming the 5-radical into 6-radical, is kinetically forbidden. The 3'-radical (3'-*dUDP) and 5'-radical (5'-*dUDP) formed in the hydrogen abstraction step can undergo the O-P bond break at the respective sites to produce either a ketone or an aldehyde and a phosphoryl radical. Due to positive free energy the 5' O-P bond break reaction is unlikely to happen in contrast to the 3' O-P bond break.

We conclude that the mechanism of radiosensitization by 5-bromouracil cannot be explained by a simple intranucleotide reaction. It might be based on the abstraction of hydrogen from an adjacent sugar residue or a water molecule. The mechanism we propose for 6-bromouracil could be confirmed by identifying a 3-ketone product in radiolytic experiments with labeled DNA.

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Computational studies of potential inhibitors of sulfatase steroid

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The aim of the study was to assess the conformational flexibility of potential steroid sulfatase inhibitors and to investigate the interaction modes between particular ligand and the receptor structure.

Preliminary selection of 16 potential inhibitors took place based on the previous research, similarity searching and structure clustering. In the first step, 200 conformers for every ligand were generated with the help of MarvinSketch program. On the basis of the energy values obtained at molecular mechanics level as implemented in MarvinSketch, 20 conformers were choosen for further studies. These selected structures were further optimized by semiempirical PM3 method. Subsequently, 10 conformers were chosen to the next step of research. The selection of conformers was guided by the lower energy and larger RMSD values. In the next step we optimized the structures up to B3LYP/6-31G* level. The conformational flexibility of the ligands was assessed on the basis of the RMSD value and the value of torsion angles. Next, the docking of inhibitors to the steroid sulfatase by means of AutoDock program was carried out.

The computational approaches used in this context showed, that the number of the rotational bonds influences the conformational flexibility of the analysed compounds. The study indicated that all ligands bind in the active site of the steroid sulfatase The main role in stabilizing the ligand protein interaction was the creation of hydrogen bonds between the inhibitor and the enzyme. The key role played amino acids residues of the human steroid sulfatase: Lys368, Gly100, His290 i Asn447. Additionally the presence of the sulfamate group favours interaction between the inhibitor and steroid sulfatase.

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QSAR of dopamine derivates by similarity cluster prediction

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A novel QSAR approach, based on correlation weighting and alignment over a hypermolecule, that mimics the investigated correlational space, was performed on a set of 40 dopamines, downloaded from the PubChem database. The best models describing log P and LD50 of this set of dopamine derivatives were validated in the external test set and in a new version of prediction by using clusters of similarity.

Reaction force and reaction flux analysis of proton transfers on DNA bases

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The reaction force and the reaction electronic flux [1,2] are very useful tools to fully analyze a particular reaction in order to understand the structural and electronic rearrangements that take place along the reaction coordinate.

In this work we have applied this indexes along with structural and NBO population analysis [3], in order to characterize the intramolecular proton transfer on the DNA basis, Adenine, Citosine, Guanine and Thymine, at the intrinsic reaction coordinate (IRC), implemented at Gaussian 09 [4], at B3LYP/6-311g(d,p) basis set [5]. Our results indicate that although all the electronic rearrangements occur at the transition state, there is a different behavior of the electron transfer due to the differences of donor and acceptor atoms.

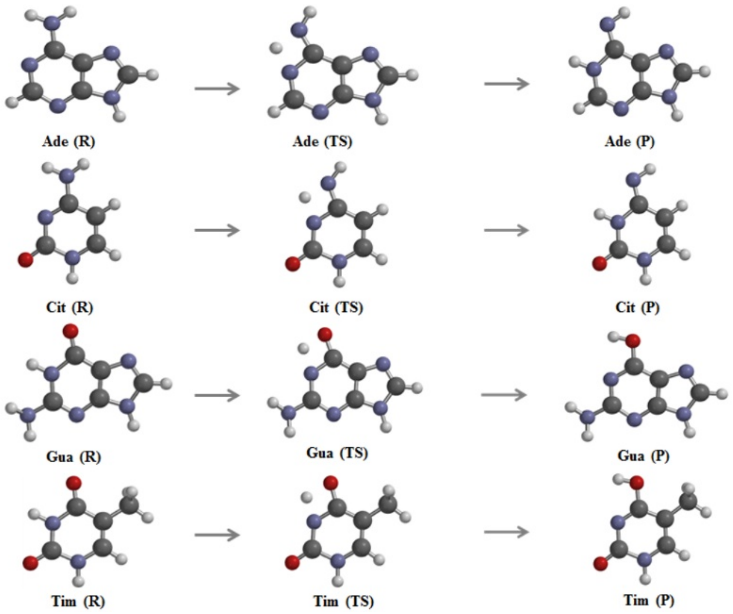

Fig. 1: Proton Transfers on DNA basis of this work.

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The structural consequences of functionalising and/or removing the cluster atoms of icosahedral *closo*-$B_{12}H_{12}^{2-}$. Possible applications

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Boron is one of only a few elements that are capable of forming extended binary hydrides. Due to the electron deficiency of boron, the corresponding boron hydrides do not resemble hydrocarbons in terms of molecular shapes. The geometries of boron clusters are based on various polyhedra, with the icosahedron being the most prominent. Indeed, *closo*-$B_{12}H_{12}^{2-}$ represents one of the most important building blocks in boron cluster chemistry and, moreover, is the most symmetrical and stable geometric arrangement of boron and hydrogen atoms (I_h point-group symmetry). Departure from this symmetry may be achieved by replacing boron with heteroatoms, such as e.g.carbon and/or chalkogens, in various positions within the cage, by replacing hydrogen atoms with a variety of substituents (halogens, SH, and alkyls are often seen), and, finally, by removing one, two, or more vertices, resulting in further classes of boron clusters, such as *nido* or *arachno*. Boron based icosahedra also tend to be joined in various modes of sharing common vertices to get *macropolyhedral* clusters as a consequence.

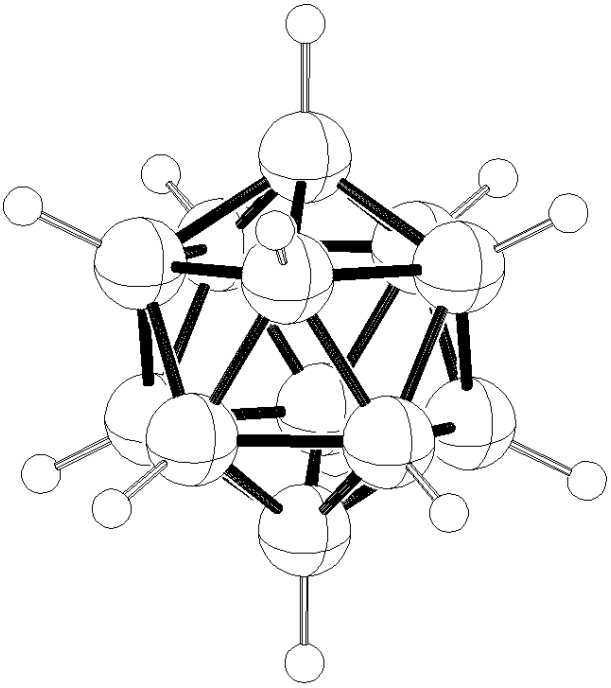

Fig. 1: closo-$B_{12}H_{12}^{2-}$

Experimentally known examples derived by substituting carbon or sulfur atoms into *closo*-$B_{12}H_{12}^{2-}$, by replacing hydrogen atoms with other atoms or moieties, by the removal of the aforementioned carbon atoms, and by sharing two icosahedra in different modes were studied using gas electron diffraction in conjunction with *ab initio* and DFT computational protocols of various quantities, the latter being sometimes the only possible structural tool applicable. Selection of such types clusters, their structural studies and outline of possible applications in materials science and medicine is the subject of this presentation.

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Modelling the influences of the substrate and coverage on surface assemblies of 3-hydroxyphenalenone

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The field of "organic electronics" continues to receive a great deal of attention; efforts in the field may provide a means, for example, of designing compact and flexible materials which can be used in information storage and processing or, when depositing organic molecules on a surface, creating chiral binding sites over the otherwise achiral surface. The polar molecules of 3-hydroxyphenalenone (3-HPLN) and croconic Acid (CA) are two examples of molecules which crystallize in a bulk form with ferroelectric behavior [1]. When deposited on metal surfaces, both 3-HPLN and CA tend to form extended chiral Kagome lattices which change on different substrates [2,3]. Calculations suggest that, unlike the bulk crystalline forms, the dipole moments of the surface-adsorbed molecules tend to align in such a way that they cancel each other out.

In this work, the results of an extensive computational study on the networks which 3-HPLN and CA form when adsorbed to metallic slabs is discussed. The dependence of the 3-HPLN/CA network architecture on the substrate is compared with, in particular, the strength of the inter-molecular binding (ie. hydrogen-bonding), the preferential binding sites for the organic molecule on the substrate (ie. epitaxy), and the electrostatic interactions caused by charge-transfer to and from the adsorbate upon adsorption, which are all factors that are typically used to rationalize network formation in molecular networks. It is found that these arguments can differ slightly when different Density Functional Theory (DFT) models are used and, alone, are not sufficient to explain the observed structures. The analogy of the way which 3-HPLN/CA molecules pack with simple models of packing in two-dimensional arrays of hard rounded triangles [4], however, suggests that the contribution of entropy to the networks' free energies is of equal importance.

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Exploring the molecular properties of nucleobases with magnetic shielding calculations

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DNA and RNA, key instructions for the creation of life contain only 5 natural nucleobases. However, despite extensive research into these important biological targets, there is still much debate surrounding their properties.

For example, uracil, a base found in RNA, has been studied by various methods. One computational study concluded that uracil is non-aromatic [1] whilst other work found uracil to be of an aromaticity intermediate between that of a non-aromatic compound and benzene [2]. With so much debate, a novel approach is required, one which can investigate aromaticity as well as other key properties.

Arguably, some of the most promising aromaticity descriptors in use are magnetic properties which employ the relationship between the magnetic field on a nucleus, $\mathbf{B}_J$, with an applied magnetic field, $\mathbf{B}_0$ expressed by

$$\mathbf{B}_J = (1 - \boldsymbol{\sigma}_J)\mathbf{B}_0 \qquad (1)$$

where $\boldsymbol{\sigma}_J$ is the second-rank shielding tensor of *J*. This shielding tensor can also be evaluated at an off-nucleus position, where there is a non-negligible electronic density, and denoted as $\boldsymbol{\sigma}(\mathbf{r})$. One of the most popular examples of this type of calculation is the NICS technique [3], which involves a single calculation of this type, usually at a ring centre or 1 Å above it. Our method involves magnetic shielding calculations at points placed at 0.05 Å intervals across grids positioned through the molecular plane and 1 Å above.

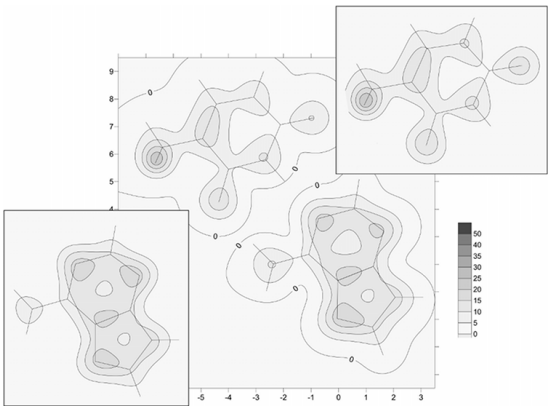

Fig. 1: Contour plots of the isotropic chemical shielding (ppm) across the plane 1 Å above the adenine-thymine base pair (centre) with the analogous plots of lone adenine (left) and thymine (right) overlaid for reference.

We have previously shown that this technique is highly successful in characterising aromaticity across a selection of heterocycles, but it also provides detailed information on the nature of bonding. Using these kinds of calculations it is possible to investigate the molecular properties of the nucleobases as well as the changes in these properties upon base-pairing. In particular, the effect of hydrogen-bonding on aromaticity and covalent bonding within the component bases can be seen, along with the effect of the amino group pyramidalisation. Many subtle features are seen by this sensitive method and could be used to explain the behaviour of base pairs. For example, to guide the synthesis of synthetic base analogues to produce more natural-behaving bases or to understand disease by studying DNA methylation.

Acknowledgements: We thank the University of York for a teaching scholarship awarded to KEH.

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Quantum chemical calculations on complexes of anabasine with zinc(II) and copper(II) ions

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Anabasine cooper(II) and zinc(II) complexes have been studied using quantum chemical calculations to help elucidate the unexpected experimental results. The main aim of this study was to check which nitrogen atom of anabasine (from piperidine ring or from pyridine ring) is involved in the formation of a coordination bond. We also calculated predicted chemical shifts of ^{13}C NMR spectra to match to which from many examined complexes belongs shifts from experimentally measured spectra. We also wanted to check if we are able to confirm which atom of nitrogen anabasine uses for coordination on the basis of analysis of molecular orbitals.

All calculations were performed within DFT framework at M06/SDD[1,2] level, and to assess basis set effects on the results we also performed calculations in composite basis set. For the hydrogen, oxygen, nitrogen, and carbon atoms we used 6-31+G(d)[3] basis set, while for the zinc and cooper atom we used SDD basis set in which zinc atom with electrons core was described by pseudopotential. For chemical shifts calculation we used GIAO[4] (Gauge-Independent Atomic Orbital) method.

On the basis of our calculations we found that anabasine prefers to coordinate to zinc(II) or cooper(II) by nitrogen atom of piperidine ring. We also calculated population of conformers using a standard Boltzmann formalism which showed that mixtures of conformers will mainly consist of complex with anabasine connected via piperidine ring nitrogen atom but it is also possible to obtain complexes with one anabasine connected via piperidine ring nitrogen atom and one connected via pyridine ring nitrogen atom. Complexes with anabasine connected only via piperidine ring nitrogen atom were not likely to observe.

Our calculations led to the identification of a compound which corresponds to the experimentally obtained spectrum for both zinc(II) and cooper(II) complexes. We also were able to assign each chemical shift from experimental spectra for atom of anabasine and to indicate which carbon atom of anabasine change its chemical shift after changing nitrogen atom which anabasine molecule use to coordinate with central zinc(II) or cooper(II) ion.

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Computational redesign of epoxide hydrolase for enantioselective synthesis

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The ability to redesign naturally occurring enzymes to a desired regio- and enantioselectivity would have great benefits for the synthesis of specialty chemicals and pharmaceuticals [1-2]. Current methods mostly rely on directed evolution or rational protein engineering. We recently explored a strategy (CASCO, Catalytic Sites by Computation) in which most experimental screening is replaced by computational methods. The strategy was applied to the redesign of a thermostable variant of limonene epoxide hydrolase for conversion of cyclopentene oxide to optically active diols, which requires different substrate binding modes in the active site (Fig. 1). First, active site redesign towards binding of transition state models is performed with Rosetta software [3], which produces a range of promising designs that should bind substrate in a reactive position for the desired selectivity. Next, the reactivity of the bound substrates is estimated by calculating the frequency of occurrence of near-attack conformations during molecular dynamics simulations [4].

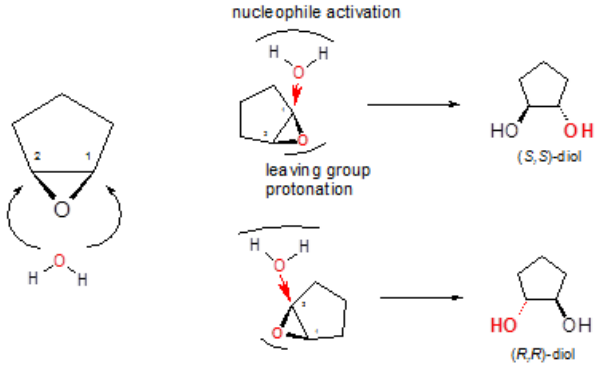

Fig. 1: Product enantioselectivity in epoxide hydrolase. The positioning of the substrate relative to the nucleophilic water determines regioselectivity and whether (*R,R*) or (*S,S*) product is formed.

Twenty-nine epoxide hydrolase variants were computationally designed and tested experimentally. Of the variants that were designed to be (*S,S*)-selective, 63% was correctly predicted, and of the variants designed to be (*R,R*)-selective 85% was correct. Both for (*S,S*)-diol and (*R,R*)-diol enantioselectivities exceeding E=80 were observed. The final enzyme variants obtained were as enantioselective as those obtained by a directed evolution experiment [5], but with strongly reduced experimental screening.

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Parameterization of the menthol force field for ionic liquids simulations

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Ionic liquids (ILs) are, by commonly used criterion, defined as molten salts, composed solely of ions, with the melting point below 373 K. This quickly developing class of chemical substances possesses a range of attractive characteristics: low vapour pressure, stability at wide range of temperatures, good solving properties for many organic, inorganic and organometallic molecules. An interesting new class of these compounds are menthol-substituted, imidazolium-based ILs. Menthol's various biological properties make it useful for medical and cosmetological applications, while its three centres of asymmetry provide that it is used in a range of organic reactions. Menthol-substituted ILs have been found to indicate promising antimicrobial and antielectrostatic properties [1], as well as being useful in organic catalysis [2] and biochemical studies [3].

Computational methods, including molecular dynamics (MD), have been widely used to elucidate basic physical chemistry of ILs properties [4]. The crucial element of performing reliable MD simulations of ILs is a properly chosen force field [4]. In the present work the construction and validation of force field parameters designed to reproduce the macroscopic properties of menthol and menthol-substituted, imidazolium-based ILs is presented. Several sets of OPLS-AA compatible parameters were created and carefully optimized. The refinement of parameters included fitting of partial atomic charges and their polarization, optimization of Lennard - Jones parameters and recalculation of the dihedral angle parameters to reproduce the energy profiles calculated using the quantum mechanical method. To validate the force field, a variety of physicochemical properties were calculated for menthol and menthol-substituted ILs. Both thermodynamic and kinetic properties were taken into account, including density, surface tension, heat of vaporization and shear viscosity. The final acquired force field was able to accurately reproduce the properties of investigated compounds while being fully compatible with OPLS-AA force field.

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Properties of hydrogen bridges of polycyclic aromatic systems with O-H···O bonds - a Car-Parrinello study

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The current study is a part in a series of investigations of polycyclic aromatic compounds containing intramolecular hydrogen bonds. Close proximity of the coupled aromatic system and hydrogen bridges gives rise to resonance-assisted hydrogen bonding phenomena. Substituted naphthols are ideally suited for this kind of investigations. Figure 1 describes structure of the parent compound, 1-hydroxy-8-methoxy-3-methylnaphthalene, with known crystal structure [1]. Its derivative, 1-bromo-5-hydroxy-4-isopropoxy-7-methylnaphthalene [2], will be also described.

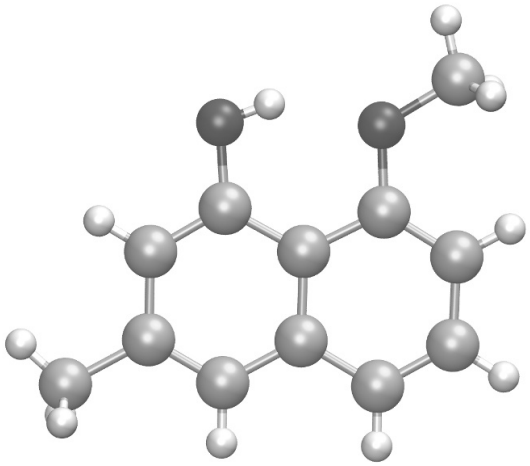

Fig. 1: Molecular structure of 1-hydroxy-8-methoxy-3-methylnaphthalene.

Car-Parrinello molecular dynamics (CPMD) [3] is chosen as a theoretical background for this study. The computational setup (exchange-correlation functional: PBE, kinetic energy cut-off: 100 Ry, pseudopotential scheme: norm-conserving Troullier-Martins PPs) was chosen on the basis of initial trials. Further, gas phase and solid state simulations were carried out. The effect of Grimme's dispersion corrections was also studied. The report presents time evolution of structural parameters, spectroscopic signatures based on the CPMD simulations, and comparison with available experimental data.

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Melanocortin-4 receptor (MC4R) mutations – predisposition to obesity

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Mutated versions of membrane proteins often fail to express at the plasma membrane, but instead are trapped in the secretory pathway, resulting in disease. The retention of these mutant proteins is thought to result from local misfolding, which prevents export from the ER (endoplasmic reticulum), targeting the receptor for degradation via the ER-associated quality control system. The rhodopsin-like G-protein-coupled MC4R (melanocortin 4 receptor) is an example of such a membrane protein. MC4R is important in energy homeostasis and food intake and the resulting failure to activate produces an insatiable appetite, leading to in gross obesity.

Our aim is to show proof of concept that selective compounds can rescue the function of MC4R mutants by increasing their cell-surface expression, and further to this, examine whether the rescue profile differs between mutants. Whole-cell ELISA and 96-well fluorescence-based assays with N-terminally HA (haemagglutinin)-tagged and C-terminally mCherry-tagged mutant MC4Rs were used to screen a number of novel MC4R-selective compounds. A total of four related compounds increased the cell-surface expression of wild-type and three intracellularly retained mutant MC4Rs, thus acting as pharmacological chaperones. Additionally, we are pursuing computational drug design techniques to identify and validate novel MC4R pharmacological chaperones utilizing a developed MC4R homology model and a molecular docking protocol.

There appears to be a unique rescue efficacy profile for each compound that does not correlate with potency, suggesting distinct receptor conformations induced by the different mutations. A degree of functionality of V50M and S58C was also rescued following relocation to the cell surface.

Redox properties of modified Keggin heteropolyacids

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Polyoxometalates (POMs) are a large class of metal-oxygen cluster anions, the properties of which can be modified by changing their size, shape charge and chemical composition [1]. In this work calculations for two groups of modified heteropolyacids, namely tungsten and molybdenum Keggin anions were performed. Calculations were performed for systems with general formula $H_nPW_{11}TMO_{39}$ and $H_nPMo_{11}TMO_{39}$, where TM = Cr^{3+}, Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+}.

Studies of different HPAs were carried out within the DFT approach with cluster model using Turbomole code. Optimized geometries, densities of states, population analysis, as well as the character and energy of boundary orbitals were determined. Additionally for both $H_nPW_{11}TMO_{39}$ and $H_nPMo_{11}TMO_{39}$ systems the Natural Orbital Chemical Valence method was used to investigate the role of introduced addenda atom on the activation process of small molecules (O_2, OOH*) in terms of quality and quantity. The effect of the solvation by CH_3CN and H_2O was taken into account within COSMO approximation.

For all studied $H_nPW_{11}TMO_{39}$ and $H_nPMo_{11}TMO_{39}$ systems calculated density of states spectra show that the valence band close to the Fermi level is dominated by 2p orbitals of the oxygen bridging centers. On contrary the conduction band comes mainly from the d orbitals of addenda metal cations, in particular, from the introduced new one. In addition, the chemical character of the introduced addenda atoms determines the energy levels of frontier orbitals and the size of band gap. Moreover, the size of band gap is a reflection of the reduction abilities of the systems. According to the NOCV analysis the activation process of small molecules is dependent on the nature of transition metal introduced into the Keggin framework.

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Computational ^{29}Si NMR in hydrated cement pastes

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Hydrated Portland cement consists mainly of of calcium–silicate–hydrate (C–S–H) gel, an amorphous solid responsible for majority of the cement mechanical properties. Although C–S–H gel is the most widely manufactured material in the world, its exact nanostructure is not fully explained yet. The present atomistic models of C-S-H gel are based on two layered inosilicate minerals, either jennite or tobermorite [1]. These models were proposed on the basis of several experimental techniques, among which ^{29}Si MAS NMR is one of the most important in cement science. However, NMR results are not able to unambiguously elucidate the structure of this complex material.

We here present the first, up to the best of our knowledge, theoretical simulation of ^{29}Si MAS NMR spectra for the structural models of C–S–H gel [2]. Magnetic shielding tensor was calculated at the density functional theory level employing Gauge Including Projector Augmented Waves method [3]. The chemical shifts was obtained using selected silicates as the references. In order to simulate NMR spectra of amorphous C–S–H gel we sampled fifteen different periodic models, derived from the experimental structures of jennite and tobermorite. We found the best agreement between calculated and experimental MAS NMR spectra of C–S–H gel for tobermorite based models with high Ca loading. We also investigated ^{29}Si chemical shift anisotropies and showed that this quantity can discriminate various Si sites in C–S–H gel in much clearer way than isotropic chemical shift only [4].

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Adsorption characteristics of carbon materials in low temperature range

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Interest of scientists in low temperature adsorption used to be limited to very few groups in the past years. Most of efforts were focused on characterization of materials in ambient and high temperature. Things have changed since development of equipment like cryo-sorption pumps started. Nowadays interest in low temperature adsorption has increasing tendency. One of potential areas where such results can be utilized is gas storage. Thanks to low temperature of adsorption process gas can be adsorbed in storage tank under lower pressure than in ambient temperature. This results in avoiding compressors during filling process of adsorption tanks. Recently low temperatures can be easily obtained by utilization of latent heat of LNG vaporization. Analysis of coupling of LNG vaporization and natural gas adsorption process can be found in [1]

Proposed coupling of processes requires reliable data concerning adsorption characteristics of potential sorbents. Due to this need experimental research of adsorption of methane gas onto variety of materials are conducted. Presentation shows equipment which is used to determine adsorption characteristics in low temperature range (120 – 250 K) and results of experimental characterization of activated carbon.

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"Frustrated Lewis pair" with light metals – tunable materials for hydrogen storage

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Frustrated Lewis pair is a term commonly used to describe compounds bearing Lewis acid and Lewis base fragments which are sterically protected and cannot form adduct. Compounds with frustrated Lewis pair (FLP) are known to be able to split hydrogen molecule which makes them catalyst for hydrogenation reaction [2]. However FLP concept can be useful also for design material for adsorption hydrogen storage.

Interactions between light metal complexes bearing empty p-orbital (Lewis acids) with σ-orbital of hydrogen molecule were previously reported [3]. The hydrogen adsorption properties of such materials can be further enhanced by interactions with lone pair of electronegative atom (Lewis base). The Adsorption energy can be easily tuned by changing Lewis base part of metal complexes, e.g. in MgN_4 complex (where N_4 is tetradentate ligand with nitrogen atoms), presence of Lewis base fragment can increase adsorption energy of hydrogen from 1.5 kcal/mol to 6.0 kcal/mol. The examples of FLP material with light metal center (Be and Mg) are presented in this work together with ETS-NOCV [4] analysis of the hydrogen interaction with both Lewis acid and Lewis base part.

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Theoretical study of repairing function of hOGG1 enzyme

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The low-energy pathway for excision of 8-oxoguanine (OxoG) catalysed with the human 8-oxoguanine glycosylase 1 (hOGG1) base excision repair enzyme was proposed by means of theoretical calculations [1]. Initiation of the reaction proceeds via attacked glycosidic nitrogen of OxoG residue with Nε-ammonium group of lysine 249 that is key catalytic residue of hOGG1 protein. The oxidation of normal guanine at carbon C8 is well known damage of normal nucleobase that occurs rather frequently. The oxidative damage results in nonplanar geometry at the glycosidic nitrogen and loss of the five-membered ring aromaticity [2]. The modified electronic character of glycosidic nitrogen enhances stability of the interactions with lysine 249. The calculated activation energy of glycosidic bond cleavage proceeding via attack of lysine 249 to glycosidic nitrogen of OxoG was significantly lower than activation energies of alternative S_N2 cleavage mechanisms.

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Molecular structure and quantum chemical computational studies of a new Schiff base

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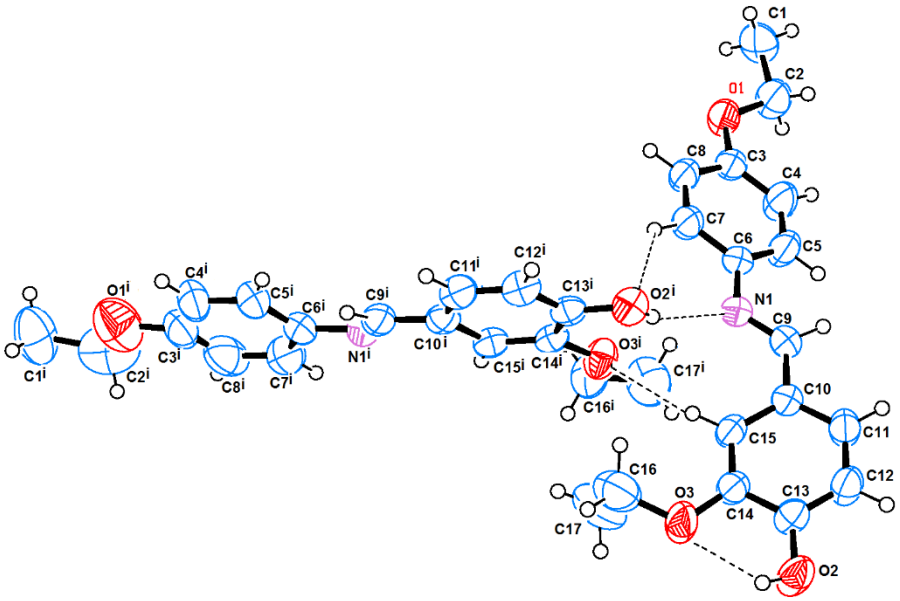
Synthesis, crystallographic characterization, spectroscopic (FT-IR) and density functional modelling studies of the Schiff base seen in Fig. 1 have been reported. The molecular structure obtained from X-ray single-crystal analysis of the investigated compound in the ground state has been compared using Hartree-Fock (HF) and density functional theory (DFT) with the 6-311++G(d,p) basis set. In addition to the optimized geometrical structures, atomic charges, molecular electrostatic potential (MEP), natural bond orbital (NBO), nonlinear optical (NLO) effects and thermodynamic properties of the compound have been investigated by using DFT. The experimental (FT-IR) and calculated vibrational frequencies (using DFT) of the title compound have been compared. The solvent effect was also investigated for obtained molecular energies and the atomic charge distributions of the compound. There exists a good correlation between experimental and theoretical data. The predicted NLO properties of the compound which calculated by the B3LYP method with 6-31G(d), 6-31+G(d,p), 6-31++G(d,p), 6-311+G(d) and 6-311++G(d,p) basis sets are greater than ones urea.



Improvement in analysis of nature of interactions in cathepsin L – inhibitor complex due to optimization of Lennard-Jones parameters

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Analysis of interactions within the active site of enzymes is the basis for rational design of novel inhibitors or redesign of the enzyme specificity. The hybrid variational-perturbational method of interaction energy decomposition of Sokalski and Roszak [1] have been used successfully for this task previously [2]. Such analysis requires optimized coordinates of the protein-ligand complex, a task not easily achievable without forcefield parameterization of the ligand.

In an attempt to analyze interactions of cathepsin L with its inhibitors we have found that standard CHARMM Generalized Force Field (CGenFF) approach [3] to generate parameters for organic compounds does not reproduce intermolecular distances with sufficient accuracy, and also that the atomic charges fitted with CGenFF method do not offer an advantage in comparison to charges derived using Merz-Singh-Kollman (MSK) method. An alternative method of optimization of Lennard-Jones parameters with fixed MSK charges is proposed to improve the reproduction of geometry of protein-ligand complexes. Electrostatic component of interaction energies for complexes optimized with this new parametrization procedure better reproduce the *ab initio* results.

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

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Nonempirical atom-atom potential functions representing intermolecular interaction energy components

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Universal atom-atom potential functions representing short range electrostatic penetration, exchange and delocalization terms have been derived for benchmark S66x8 set of dimers [1]. Complete model involving additional long range electrostatic multipole term estimated from Cumulative Atomic Multipole Moments [2] and dispersion term derived by Pernal et al. [3] has been tested for set of urokinase inhibitors interacting with corresponding active site residues [4].

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Structural and dynamic properties of the water hydration shell of the square planar platinum(II) complexes: *ab initio* MD study

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Neutral cisplatin as a prodrug needs one or more hydrolysis steps prior to binding to nucleic acids, their supposed pharmacological target. Thus, a detailed understanding of cisplatin interactions with water solvent molecules is of primary importance and it has been studied extensively by both experimental and theoretical methods. In this contribution we are dealing with the structure and dynamics of the hydration shells of neutral cisplatin $[Pt(NH_3)_2Cl_2]^0$ and its charged and hydrolyzed forms $[Pt(NH_3)_2Cl(H_2O)]^{1+}$, $[Pt(NH_3)_2OH(H_2O)]^{1+}$ and $[Pt(NH_3)_2(H_2O)_2]^{2+}$.

Ab-initio molecular dynamics simulations with explicit water molecules and using PBE functional with dispersion corrections were used to study influence of the molecular charge on the dynamic behavior of water in the first solvation shell of the complexes and in so called meso-shell [1]. By the meso-shell we mean an axial region within ~0.3 nm of the central platinum atom. For neutral cisplatin it was observed [2] that water molecule(s) interact with the platinum atom 'inversely' by the hydrogen atom (so-called inverse hydration). Here we show that inverse hydration takes place even for the charged Pt(II)-complexes. Radial distribution functions, exchange probabilities, water binding energies and structures of the meso-shell of the studied complexes are compared and possible impact on the interactions of Pt(II)-complexes with biomolecules is discussed.

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Quantum mechanical and molecular modeling of carbazole ligands, potential telomerase inhibitors of antitumor activity

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Cancer is the major cause of death worldwide and creates the most diverse group of diseases. Recently the strongest hope gives the process of telomerase inhibition. Telomerase is an enzyme, which is active in more than 85% cancer cell, where causes the repetition of the telomere sequences to replace those that are lost during DNA replication. It is suggested that inhibition of formation telomerase - telomeric DNA complex results in inhibition of telomerase activity [1–3]. Compounds that stabilize the intramolecular DNA G-quadruplex formed in the human telomeric sequence have been shown to inhibit the activity of telomerease and disrupt telomere capping and maintenance, making intramolecular human telomeric DNA G-quadruplex an attractive target for cancer therapeutic intervention [3, 4].

All suggested carbazole ligands containing heterocyclic benzothiazolium group (possessing positive charge) and additional substituents (functional groups, C=C bond) were examined with the use of quantum mechanics methods. 200 conformers for every ligand were generated with the help of MarvinSketch program. These selected structures were further optimized and selectioned by the lower energy and larger RMSD values. Subsequently the structures were optimized at HF/STO-3G, HF/6-31G*, B3LYP/6-31G* and APFD/6-31G* levels. The conformational flexibility of the ligands was assessed on the basis of the RMSD value and the value of torsion angles. The docking of selected inhibitors to the different structures of G-quadruplex DNA structure by means of AutoDock program was carried out.

Research have shown that the compounds which are characterized by two benzothiazole substituents bounded to the central carbazole possess larger conformational flexibility than the ligands with the same substituent on the nitrogen atom of carabazole molecule. Obtained results have shown that carbazole derivatives are capable to bind to G-quadruplex structures in two different ways.

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Impact of cellular localization of proteins on docking accuracy

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Here, three case studies of small molecule docking with varied cellular localization of a receptor and the surrounding environment of its active site are presented. The first study is concentrated on chiral recognition of pyrolidyn-2-one derivatives by AGP (orosomucoid), a glycoprotein which is commonly used in HPAC. It was showed that information obtained from docking to such globular proteins with the water-accessible binding site as AGP, accurately reproduce the chromatographic data such as retention factors and selectivity factors. The second case is docking of ergotamine, a small molecule agonist, to 5HT1B and 5HT2B serotonin receptors. As was shown by our recent GPCRDOCK 2013 results (the group named Warsaw), the water-accessible binding site of those membrane G protein-coupled receptors can be easily reproduced by homology modeling [1] giving accurate ligand binding modes. The last case is focused on two proteins with the lipids-accessible binding site. The first one, V-ATPase is a membrane rotor protein with the potential binding site of archazolide localized inside the lipid bilayer [2]. The second protein, RPE65, is a peripheral membrane protein with the binding site surrounded by lipids molecules of bilayer. Both, V-ATPase and RPE65 represent the most difficult case of docking, in which most of the docking scoring functions fail to select the most accurate ligand pose.

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Estimating protein-protein binding free energies by the unit interval approach

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Protein-protein interactions play fundamental role in many biochemical processes. Therefore, techniques for simulating large protein-protein complexes, calculating binding energies, identifying crucial for the binding inter-protein interactions and assessing the effects of different mutations attract great interest. However, these simulations are quite challenging as they usually include enormous amount of atoms, which makes them extremely computationally demanding and time consuming.

The complexity of protein-protein interaction simulations requires the use of advanced sampling techniques. These include potential of mean force or free energy pathway methods. Another option is to reduce the number of degrees of freedom by using implicit solvent description. Nevertheless, current methods are more or less applicable to investigating protein-ligand complexes, where one of the interacting molecules is fairly small. They are not really well suited for studying large protein-protein complexes due to slow convergence, limited sampling issues and prohibitively time-consuming and resource-demanding simulations.

Here, we describe an alternative to the common biasing and alchemical methods computational protocol for calculating free energies of large macromolecular systems from standard molecular dynamics (MD) simulations. Our approach is based on an implementation of Jayaram and Beverige's unit interval renormalization methodology [1] and relies on collecting statistical data from MD simulations. This technique belongs to the "end point" methods, where rather than simulating the binding/dissociation process along some reaction coordinates or using a coupling parameter, the binding free energy is calculated using a thermodynamic cycle, whereas only the initial (free proteins) and the final (complex) states are simulated.

The protocol was tested on the particular cytokine – receptor system of human interferon gamma (hIFNγ) and its cellular receptor hIFNγRα. This system was chosen, because hIFNγ exhibits different binding affinity towards the receptors, depending on the cytokine chain length [2] and thus is suitable for calibration of the protocol.

Acknowledgements: Financial support is acknowledged from Grants DMU03/23/12.12.2011 of the Bulgarian National Science Fund and Grant BG051 PO001-3.3.06-0057 of the Operational Programme "Human Resources Development" co-financed by the European Social Fund of the European Union.

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Application of UNRES force field to coarse-grained molecular dynamics simulations of arginine-binding protein from *Thermotoga maritima*

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The arginine-binding protein from *Thermotoga maritima* (TmArgBP) possesses a typical two-domain structure of the periplasmic binding protein family. These domains are linked by a rotating hinge that can make the protein change its conformation from an open to a closed form and vice versa, depending on the absence or presence of the ligand (Figure 1). The protein is characterized by a high specificity and affinity for binding a single molecule of L-arginine [1]. The objective of this study was to inv

The objective of this study was to investigate the dynamics of the TmArgBP in the presence of arginine and without the presence of arginine. The state of protein (closed or open) can be determined by monitoring the distance between residues D18 and K145 both located near active site but on different domain each. We used molecular dynamics simulations with the coarse-grained UNRES force field to determine the distance distribution between the C^{α} atoms of these two residues, depending on the presence of arginine.

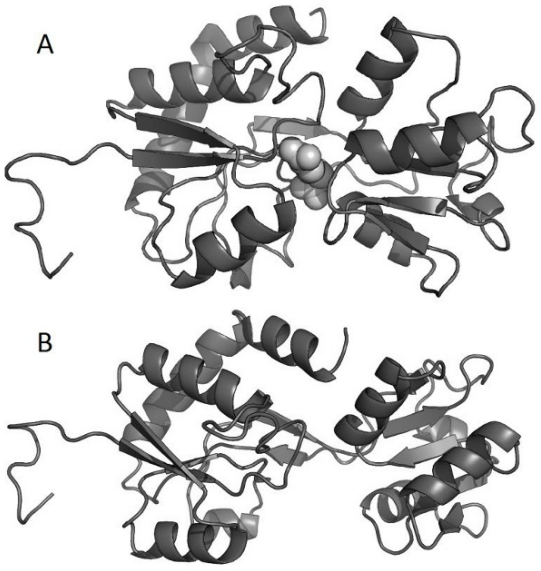

Fig. 1: Arginine-bound closed (A) andarginine-unbound open (B) state of TmArgBP.

All simulations were carried out with the UNRES package [2] (www.unres.pl). In the UNRES model, a polypeptide chains is represented as a sequence of C^{α} atoms with united side chains attached to them and peptide groups positioned halfway between the consecutive C^{α}'s; this reduction of the number of the degrees of freedom results in an over 1000-fold speed-up of calculations, compared to the all-atom treatment [3]. The results of simulations agree with the experimental data which suggest that binding arginine makes it more likely for the protein to adapt a closed conformation.

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Comparative analysis of virtual screening approaches in the search for EphA2 receptor antagonists

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EphA2 is a member of the Eph subfamily of tyrosine kinase receptors and it is activated by membrane-anchored ligands called ephrins. EphA2 receptor and its ephrin-A1 ligand form an important cell communication system, which has been found overexpressed in many cancer types and involved in tumor growth and angiogenesis.1 Recent medicinal chemistry efforts have identified the bile acid derivative UniPR129,2 and the ephrin-A1 derived peptide YSA3 as low micromolar binders of the EphA2 receptor. However, these compounds suffer for poor physicochemical properties or limited metabolic stability hampering their use in vivo. In this scenario, the identification of compounds able to disrupt the EphA2-ephrinA1 complex either lacking the bile acid scaffold or a peptidic structure may lead to new pharmacological tools suitable for in vivo studies.

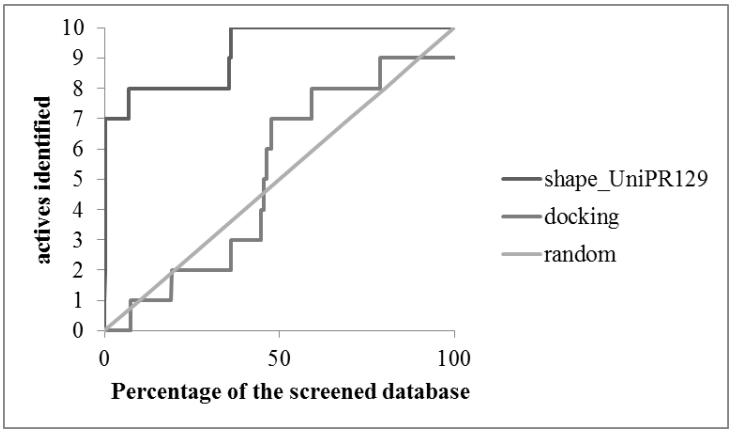

Fig. 1: Enrichment curves for VS approaches

To identify the most promising virtual screening protocol aimed at finding novel EphA2 antagonists, we investigated the ability of both ligand-based and structure-based approaches to retrieve known EphA2 antagonists within a library of drug-like decoys. While ligand-based methods, i.e. shape-similarity and pharmacophore search, were conducted using UniPR129 and Ephrin-A1 ligands reference structures, structure-based screenings were performed with Glide, employing the X-ray structure of the EphA2 receptor-ephrin-A1 complex.

A comparison of enrichment factors showed that ligand-based approaches outperformed the structure-based ones. That said, different pitfalls can be identified for each approach. In particular, shape-similarity was strongly affected by the choice of the reference molecule, thus giving artificial enrichments when the query compound was structurally-related to the active ones. Taken together, the results suggested that the shape-screening method conducted using the G-H loop as the query structure appeared as the most promising protocol for searching for EphA2 antagonists lacking the bile acid nucleus.

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Photochemical properties of base-off methylcobalamin. DFT and TD-DFT study

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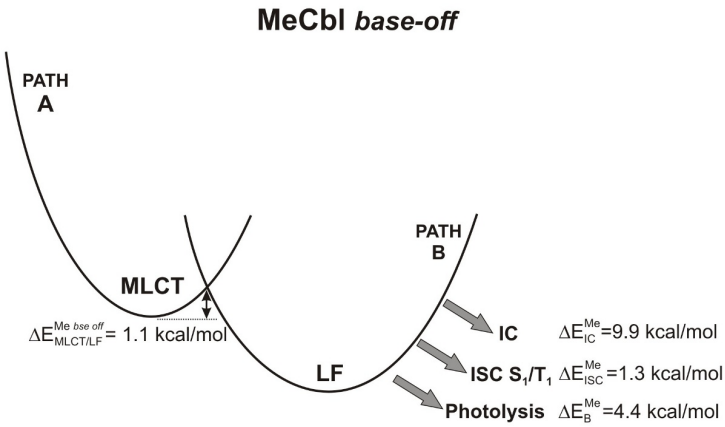
Derivatives of vitamin B_{12} are important bioinorganic cofactors, which possess rich and complex photolytic properties mediated by their electronically excited states. These properties primarily depend upon the nature of their axial ligands and also depend on the environment, such as solvent or enzyme. In acidic conditions when the lower axial dimethylbenzimidazole (DBI) base is replaced by water, a new channel for fast nonradiative decay is opened and formation of a radical pair following bond hemolysis [1].



The analysis of the electronic structure of base-off MeCbl was performed by means of time-dependent density functional theory (TDDFT). Calculations were carried out using the gradient corrected Becke–Perdew (BP86) functional together with the TZVPP basis set and COSMO solvent model with water as solvent. In the calculations a simplified model was used, in which all the corrin side chains were replaced by hydrogen atoms and the 5,6-dimethylbenzimidazole trans axial base was replaced by water. The calculations were carried out with the use of TURBOMOLE program.

For the S_1 excited state the PES surface was determined relative to R_{Co-C} and R_{Co-O} axial bond lengths. Based on the results of theoretical studies the two possible path of photoreaction were identified. First (A), that directly from minimum S_1 state leads to photodissociation of methyl ligand and second (B), on which the first step of photoreaction is disconnection of water molecule from cobalt. Path A is practically inactive because the energy barrier associated with direct dissociation of methyl ligand is higher in energy then barrier of MLCT/LF intersection of two excited states during stretching of Co-O bond. Methyl dissociation and S_1/S_0 internal conversion follow on the path B from LF excited state of MeCbl after total or partial detachment of the lower ligand (H_2O molecule). On path B the S_1/T intersystem crossing may be effective and methyl photolysis from the triplet state is possible.

Acknowledgements: This work was supported by National Science Centre, Poland, under grant No. UMO-2013/09/B/ST4/03014. The TURBOMOLE calculations were carried out in the Wrocław Centre for Networking and Supercomputing, WCSS, Wrocław, Poland, under calculational Grant No. 18.

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A QM/MM study of dehalogenation of hexachlorocyclohexane (HCH) isomers catalyzed by LinA and LinB dehalogenases

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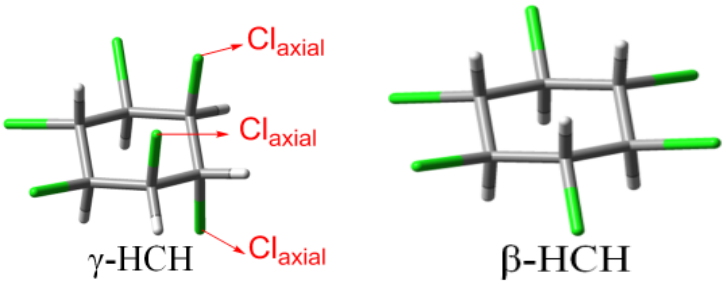
Hexachlorocyclohexane (HCH) isomers are highly persistent chlorinated pollutants used in agriculture as pesticides over the past four decades. The use of HCH has been banned in most of the countries. LinA dehalogenase dehydrochlorinates α-, γ-, δ-HCH isomers via an E2 elimination mechanism in which active site His73-Asp25 amino acids act as catalytic dyad but has very low activity for β-HCH isomer, because β-HCH lacks adjacent trans-diaxial H/Cl pair. LinB catalyses the hydrolytic dechlorination of β-HCH (not α- and γ-HCH) via SN2 mechanism in which an active site Asp108 acts as a nucleophile. The elimination mechanism proposed for the dehydrochlorination reactions of γ- and β-HCH catalyzed by LinA enzyme so far although provides useful starting point information raises several questions related to the protonation state of the imidazole ring of His73 which may influence the sequence of chemical steps in the active site. Therefore, the role of His73-Asp25 catalytic dyad on possible mechanisms of the HCH substrates dehydrochlorination in the active site of LinA has been explored using quantum mechanical/molecular mechanical (QM/MM) umbrella sampling simulations as well as micro-macro iteration optimization schemes. The free energies of activation have been calculated using one and two dimensional potentials of mean force obtained at the PM3/MM (MM=amberff99SB, TIP3P) level of theory. The energetic pictures of each of the considered scenarios have been subsequently corrected using density functional theory methods and used for the discussion on the most probable mechanistic scenario.



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Notch impact resistances of carbon nanotubes reinforced high density polyethylene nanocomposite materials

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In this study, Multiwall Carbon Nanotubes (MWNT) reinforced High Density Polyethylene (HDPE) materials were used. Mechanical properties of the samples reinforced with Carbon Nanotubes at weight ratios of 1%, 3% and 5% were investigated. Reinforced samples were compared to samples produced with pure High density Polyethylene. Two different methods were used for sample production. The first method is cutting samples from plates that were produced by hot hydraulic compression. Other one is plastic injection method in a hot mold. The samples were then subjected to experiments and impact resistance values were measured in accordance with ASTM D6110 standards. Also Thermogravimetric Analyses (TGA) was performed for and Multi-Wall Carbon Nanotubes within the High Density Polyethylene. At the end of the study, it was observed that impact resistance decreased with increasing carbon nanotube reinforcement amount. Impact resistance of samples produced by means of plastic injection was improved by 35% comparing with samples produced from pure YYPE. Impact resistance of samples produced by means of hot compression, in the other hand, was decreased by 51%. These results were explained with the fact that structures of composite materials were transformed to a tougher and fragile phase. In the TGA investigations, it was seen that mass loss breakdown temperature and melting point temperature increased by MWNT ratio in the composite samples.

Acknowledgements: The authors acknowledge the support of this study by the Scientific Research Projects Coordination Office of Cumhuriyet University

Electronic structure of Cu containing Dawson heteropolyacids. DFT cluster calculation

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Polyoxometalates (POMs) are well-known metal-oxygen cluster species with diverse compositional range and enormous structural variety [1]. POMs have been found their potential applications in many fields such as catalysis, medicine, nanotechnology, material science and so on [2]. The structure of HPA allows for many different modification of primary, secondary and tertiary structures providing an opportunity to tailor their catalytic properties.

In this work calculation for copper modified heteropolyacids with Dawson structure will be compare with systems, where different transition metal cations was introduce as a one addenda atom. The systems with general formula $PW_{17}TMO_{61}^{8-}$, where TM = Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} were performed.

Electronic structure of modified HPA were carried out within the DFT approach with cluster model, using Turbomole code. Optimized geometries, densities of states, population analysis, as well as the character and energy of boundary orbitals were determined. The effect of solvation by water was taken into account within COSMO approximation. The results of calculations for modified HPAs show that changes in chemical composition lead to the changes in physicochemical properties of the studied system. The analysis of character of frontier orbitals and spectrum of density of states suggests that in modified system the reduction process will occur with participation of TM ion. What is more the impact of the position of Cu in Dawson structure will be discussed.

Acknowledgements: This work is supported by the project financed by National Science Center DEC 2011/03/B/ST4/01216.

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On cooperativity of halogen bonding

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The many-body theory was applied in order to estimate the character of interaction in quadruple complex consisting of four bromomethane molecules. The scheme of such system is shown in the Figure 1.

The tetrameric complex used as a model system was found in the crystal structure in which the halogen bonds were stabilizing the solid state structure [1]. Decomposition of interaction energy [2] on two-, three- and four-body terms allowed to conclude that the individual halogen bonds in tetramer rather do not cooperate forming the complex. The non-additive contribution to interaction energy is negative, but of very small value in respect to total interaction energy (less than 0.01%), indicating very weak cooperativity of halogen bridges. Moreover, a few Basis Set Superposition Error (BSSE) [3] schemes (namely: SSFC [4], PAFC [4], VMFC [5] and TB [6]) were applied in order to study the influence of BSSE on the interaction energy and its terms. Both structural and energetic consequences of complexation were investigated. The importance of the chemistry model used in calculations was also studied.

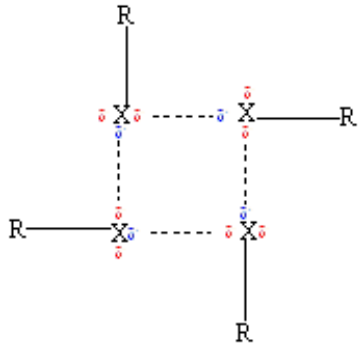

Fig. 1: The scheme of the structural motif that occurs in the system under investigation.

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Free energy profiles for proton motion in hydrogen bridges of quinoline derivatives - CPMD-based investigations

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Quinoline derivatives, interesting from the point of view of medicine and organic LED material chemistry, can be devised to exhibit medium-strong and strong intramolecular hydrogen bonding. A chosen set of twelve such compounds [1] contains diverse types of H-bonds of varying strength. Their structural properties were studied. Our earlier studies encompassed calculations of the energy of the H-bond and its dependence on the particular substitution pattern. Further, the pathway of the bridged proton movement from the donor to the acceptor was examined. This part of study, devoted to static investigations, was complemented by analysis of the electron density parameters derived from the Atoms in Molecules (AIM) theory.

The current report is based on Car-Parrinello molecular dynamics (CPMD) [2]. The CPMD served as a theoretical background to calculate free energy profiles for the proton motion using enhanced sampling methodology of metadynamics.[3,4] The chosen two compounds for this part, 8-hydroxyquinoline N-oxide and 2-carboxyquinoline N-oxide (quinaldic acid N-oxide), contain short O-H···O bonds suggesting strong proton delocalization. We employed PBE exchange-correlation functional, Troullier-Martins pseudopotential scheme and plane wave basis set with 95 Ry kinetic energy cutoff. The time step of 3 a.u. was used in propagation of the CPMD equations. The choice of several collective variables was carried out, and metadynamics parameters (hill shape, hill accumulation frequency) were tuned to sample the free energy profile. Problems encountered during the simulations (e.g. various manifestations of energy transfer into unwanted channels) are described. Finally, two-dimensional free energy maps are presented and related to the experimental and previously calculated properties of the two investigated molecules.

Acknowledgements: We gratefully acknowledge generous grant of computer time and facilities provided by the Wrocław Centre for Networking and Supercomputing (WCSS) and Interdisciplinary Centre for Mathematical and Computational Modeling (ICM, University of Warsaw). This work has been supported by the Polish National Science Centre (NCN), grant no. UMO-2011/03/B/ ST4/00699.

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Electric properties of carbazole and fluorene

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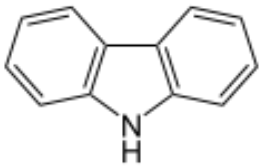
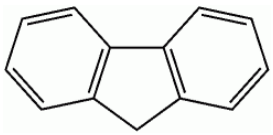
Carbazole and fluorene are isoelectronic, aromatic molecules with tricyclic structure (Fig.1a, 1b). Geometry, dipole moment, all components of the static and dynamic polarizability tensor (α), components of the static hyperpolarizability (β) tensor were determined for these molecules by means of the DFT calculations. In order to validate the electric property results accurate Coupled Cluster (linear and quadratic response CCSD) calculations were also performed. The Pol basis set specifically developed for electric properties calculations [1], and its more compact Z3Pol version [2] were used in all calculations.

It has been found that the values of the static polarizability components for both studied molecules are very close, while the off-diagonal β component differs widely reflecting the difference in polarity of the studied molecules. Coupled Cluster results agree very well with the DFT values for the polarizability tensor components. However, there is a sharp disagreement for the hyperpolarizability components calculated at the DFT and CCSD levels of theory. Good performance of the compact Z3Pol basis for the polarizability calculations is demonstrated.

Dynamic polarizability of carbazole evaluated at frequencies close to the resonance obtained at the DFT level was calculated as the first step toward simulating the Raman spectrum.



(a) Carbazole



(b) Fluorene

Fig. 1: Chemical structures of the two molecules studied

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On the origin of benzoic acid crystals morphology trimming by surfaces in thin films crystallization

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It is well known that crystal morphology can be affected by many factors like, solvent polarity, tailor-made additives and nucleation conditions. One of the promising methods of controlling crystal morphology is polymer induced heteronucleation. In this work, we examined morphology of crystals obtained through evaporative crystallization of benzoic acid from methanolic solutions on three different polar surfaces: glass, polyvinyl alcohol, gelatin and on non-polar paraffin layer. The influence of different surfaces on benzoic acid crystal faces growth was investigated using powder X-ray diffraction (PXRD) measurements. As we found, in all cases the most intense PXRD peak was located at 2θ value of 8.1°, which corresponds to Miller plane (002).

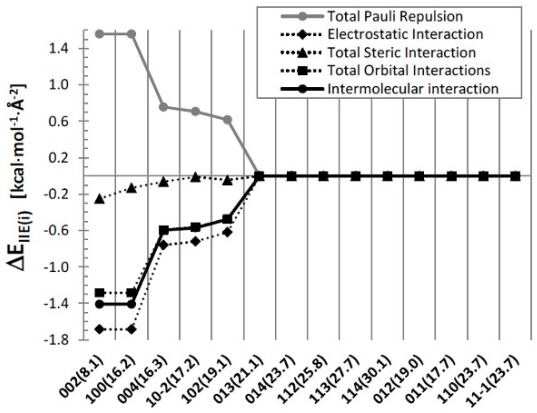

Fig. 1: Energy contributions to intra-layer stabilization of benzoic acid crystal faces.

In order to elucidate origin of observed intriguing properties of (002) face the intra- and inter- layer intermolecular interaction energies were computed. The distributions of surface densities of energy contributions were documented on Fig.1. As we found, faces exhibiting the highest stability and at the same time the strongest adhesion appeared on X-ray powder spectra with highest intensities. The observed "pseudo-mono-morphology" only partly originate from orientation effect. Presented on Fig.1. detailed decomposition into energy contributions confirmed uniqueness of (002) and (100) planes.

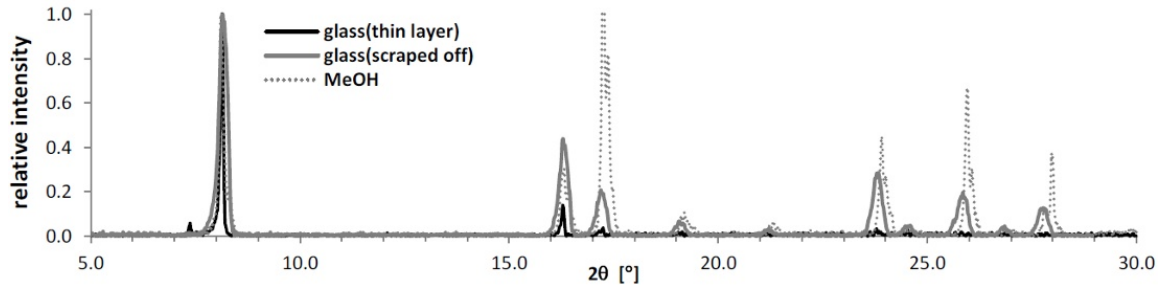

Fig. 2: The powder X-ray spectra of benzoic acid thin layers formed on glass.

Metal–nitrosyl bonding in transition metal complexes: role of resonance structures and spin states

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We elucidate the quantum mechanical descriptors of the metal–nitrosyl bonding in transition metal complexes [1, 2] using DFT and *ab initio* calculations. To this end, a few model complexes with various transition metals (M = Fe, Co, Mn, Ni, and Cu) are studied; these complexes belong to different Felthan-Enemark classes and show distinct M−N−O geometries. Using the approach proposed in ref. [3] (with some new improvements), the multiconfigurational CASSCF wave function is analyzed in terms of resonance structures with a definite charge assigned to the nitrosyl and the metal fragment. The analysis allows to quantify the role of main resonance structures (M^n-NO^0, $M^{n+1}-NO^-$, and $M^{n-1}-NO^+$) participating in the M−NO bond and to quantify a donation form the NO σ lone pair (occurring in the complexes with a linear M−N−O motif). It is shown that the degrees of charge transfer and covalency vary a lot in the studied series of complexes.

We also present a striking example of how an existence of multiple spin-states can affect the mechanism and the energetics of nitric oxide bonding to Mn(II) porphyrin, as compared with an analogous Co(II) porphyrin. To make the Mn−NO bond, the spin state of manganese has to change twice. This makes the Mn−NO bond energy very sensitive to a description of the spin-state energetics of the parent Mn(II) porphyrin. We show that the latter energetics is very deficiently described by many common DFT methods, leading to large discrepancies of the calculated bond energies with the experimental data. Once the mentioned problem is corrected, it is possible to get the correct bond energy for both Mn−NO and Co−NO simultaneously. This interpretation is also confirmed by the bond energies estimated from high-level CCSD(T) calculations for the small mimics of the studied complexes, using the method proposed in ref. [4].

Acknowledgements: We acknowledge support from Ministry of Science and Higher Education, grant No. IP2011 044471 and from National Science Centre, grant No. UMO-2011/01/B/ST4/02620. Some calculations were performed at the Wroclaw Centre for Networking and Supercomputing (WCSS) and Academic Computer Centre CYFRONET, Kraków, and in part thanks to the PL-GRID infrastructure.

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Computational and spectroscopic characterization of Cu(II) complexes with derivatives of hydroxycoumarins

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Coumarin derivatives are an important pharmacophore present in numerous compounds which can be isolated from natural sources. They show wide range of biological activity, such as antibacterial, anitiviral and anticancer [1]. Cu complexes are reported to show the enhancement of pharmacological activity in comparison to parent ligand, combined with lower toxicity [2]. This makes study on Cu(II) complexes with coumarins particularly interesting. Structural studies on Cu(II) complexes with perspective pharmaceutical applications are essential for the understanding of structure activity relationship [3].

The Cu(II) complexes with acetyl derivatives of 7-hydroxy-4-methylcoumarin have been obtained by electrochemical synthesis. These compounds were consequently characterized by means of X-ray absorption (at MAX-lab synchrotron laboratory), ultraviolet-visible and infrared spectroscopies. The density functional theory (DFT) level calculations were performed with gradient PBE and hybrid PBE0 functionals for proposed structural models. DFT results were used for clarifying of observed spectra. Our study shows that combination of spectroscopic and computational techniques enables structural characterization of studied compounds in lack of crystallographic data.

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Hydrogen uptake by beryllium doped graphene – ab initio molecular dynamics study

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Carbon-based materials doped with light elements are promising material for the adsorption hydrogen storage. Beryllium is the least studied dopant, however it effect on hydrogen adsorption is greater compare to boron or nitrogen. Be_2-moiety incorporated into carbon material can increase hydrogen adsorption energy by the factor of 5 [1] and does not disturb local structure of carbon material [2]. The effect of Be_2 on hydrogen adsorption is local hence concentration of Be_2 fragment in adsorbent structure should be relatively high.

The aim of this work is to find maximum possible concentration the of Be_2 moiety within 2D carbon framework. Structure of such material as well as hydrogen adsorption properties were studied using Born-Oppenheimer molecular dynamics.

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Carbon-based materials for selective electrochemical oxygen reduction

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Electrochemical oxygen reduction reaction (ORR) is a cathode process of most fuel cells. ORR can proceed through two paths: i) less efficient indirect two-electron (eq. 1) or ii) desirable direct four-electron mechanism (eq. 2).[1]

$$\mathrm{O_2} + 4\,\mathrm{e} + 2\,\mathrm{H_2O} \longrightarrow 4\,\mathrm{OH^-} \qquad E = 0.401V \tag{1}$$

$$\mathrm{O_2} + 2\,\mathrm{e} + \mathrm{H_2O} \longrightarrow \mathrm{OOH^-} + \mathrm{OH^-} \qquad E = -0.065V \tag{2}$$

The ORR limits overall efficiency of fuel cell and hence requires effective catalyst which ensures high kinetic and selectivity toward four-electron pathway.

Carbon-based materials doped with boron and/or nitrogen are active catalysts for ORR. [2] Moreover doped carbon materials are cheaper and possess higher stability in comparison to commercial Pt-based catalysts. The mechanism of ORR on modified carbon material is known [3], selectivity is controlled by dissociation of OH^- or OOH^- anion from gt-OOH structure (gt = carbon material). However the dopant effect on selectivity have not been systematically studied. The influence of B and N doping on ORR selectivity in presented in this work.

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Structural modelling of a novel molybdoenzyme: steroid C25 dehydrogenase from *Sterolibacterium denitrificans*

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Steroid C-25 dehydrogenase (S25DH) is an oxygen sensitive, αβγ heterotrimeric molybdenum enzyme isolated from cholesterol-degrading, denitrifying bacterium *Sterolibacterium denitrificans* (Chol-1ST) belonging to so-called EBDH-like class of DMSO reductase family [1]. The enzyme catalyzes regioselective hydroxylation at the C-25 tertiary carbon atom of the aliphatic side chain in cholest-4-en-3-one and its derivatives [1].

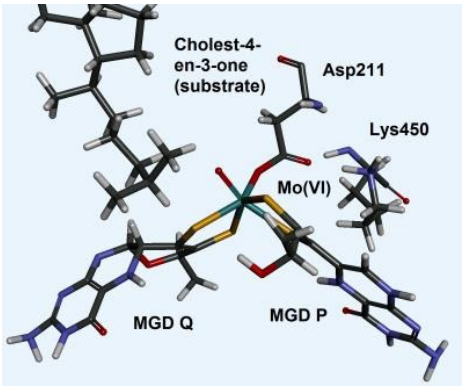

Fig. 1: Active site of S25DH with docked substrate

As the crystal structure of the enzyme is still unknown we developed a homology model of S25DH catalytic α subunit using ethylbenzene dehydrogenase (EBDH) as a template [2] (sequence identity 40%, similarity 96%). The catalytically active structure of the molybdenum cofactor (MoCo) was obtained from QM:MM modeling of the EBDH α subunit. In the catalytically active, oxidized form of the cofactor Mo atom is coordinated by six ligands: four sulphur atoms from two pyranopterin-guanine dinucleotides (MGD-Q, MGD-P), OG1 from Asp^{211} residue and catalytically active oxo ligand (Fig. 1).

100 homology models were developed in MODELLER 9v7 and the best models that could accommodate test substrates were used in molecular dynamics (MD) simulations. MD simulations were conducted in Amber12 software in order to obtain reliable model of S25DH in complex with native substrate. Missing parameters for the MoCo and the Fe-S cluster were derived from the quantum mechanical (QM) calculations. The model comprised of 14450 atoms and 30 000 water molecules in a periodic box extending 10 Å from the protein surface. The MD production was conducted for 30 ns in 303 K under constant pressure.

The obtained results showed that the structure of MoCo is comparable to those obtained in QM:MM studies, confirming quality of the parameterization. Analysis of MD trajectories enabled insight into dynamics of substrate aliphatic chain in the enzyme active site and revealed important interactions between cofactor, amino acid residues, substrate and water molecules present in the active site. The cooled model was used for docking experiments with other substrates as well as QM:MM calculations aimed at the modeling of the reaction mechanism.

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Determination of nitinol fibers performances by means of embedded systems

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Utilization of shape memory alloys is rapidly spreading to many technological areas. From this point, alloys with shape memory are used in various fields such as temperature sensors in electronics, test valves in medicine, radiator fans in automotive and multi leg mobile robots. Application of nitinol fibers, which are actually shape memory alloys, as muscle fibers in industrial robots are increasing day by day.

In this study, several tests were carried on aiming for the operational performance of nitinol fibers that are easy to control, economic, silent, harmless to environment and that have increasing utilization in recent motion technology. By using embedded systems, contraction (spasm) ratios and electrical current passing through the fibers were measured after 0.04 and 0.06 inch nitinol fibers were subjected to various voltages. Additionally, yielding limit value of nitinol fibers at split (breaking) point were detected. In the realized test system, ATmega 2560 microprocessor was took part as an embedded system in the Open Source Arduino Mega electronic card.

Acknowledgements: Calculations and experiments were conducted in Laboratories of Electric Electronic Engineering Department, Batman University.

Formation of a T-Hg(II)-T metal-mediated DNA base pair: theoretical calculation of the reaction pathway

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We proposed and calculated the reaction mechanism describing the substitution of two imino protons in thymine-thymine (T:T) mismatched DNA base pair with mercury dication that resulted in formation of (T)N3-Hg^{II}-N3(T) metal-mediated base pair [1]. The mechanism assumes two basic steps. The formation of first Hg^{II}-N3(T) bond is triggered by deprotonation of N3 imino nitrogen in thymine with hydroxo ligand of Hg^{II}. The formation of second Hg^{II}-N3(T) bond proceeds via water-assisted tautomerization of remaining, metal non-bonded, T base. The thermodynamic parameters ΔG_R = -9.5 kcal mol^{-1}, ΔH_R = -4.7 kcal mol^{-1}, and ΔS_R = 16.0 cal mol^{-1} K^{-1} calculated with ONIOM (B3LYP:BP86) method agreed well with the isothermal titration calorimetric (ITC) experiment. The peculiar positive reaction entropy measured previously was explained as effects of both the metal dehydration and the change of chemical bonding. The chemical modification of T:T mismatch to T-Hg^{II}-T metal-mediated base pair modelled for the middle base pair within tri-nucleotide B-DNA duplex confirmed complete dehydration of Hg^{II} during the reaction that was recently determined experimentally [2].

Acknowledgements: This work was supported by the Grant Agency of the Czech Republic 13-27676S. Y.T. and V.S. acknowledge the Young Investigator's Grant of the Human Frontier Science Program (HFSP). V.S and Y.T were supported by Daiichi-Sankyo Foundation of Life Science and the Invitation Fellowship for Research in Japan (Short-Term) from JSPS. The access to the MetaCentrum computing facilities is appreciated.

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Autocatalytic mechanism of binding $Pt^{IV}(DACH)Cl_4$ to dGMP and followed-up formation of $Pt^{II}(DACH)Cl_2$

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Pt(II) complexes are widely used in anticancer treatment and they are active against many types of tumor cells. Nevertheless, new organometallic complexes are investigated in order to find drugs which have milder side effects and can be used in the cases of platinum(II)-resistant tumors. Pt(IV) complexes represent one of such classes of substances. Due to their high kinetic stability, a reduction to the Pt(II) analogues must initially occurs in an activation mechanism. [1] This study focuses on the reduction process of the platinum complex $Pt^{IV}(DACH)Cl_4$ (DACH=diaminocyclohexane) in the presence of 5'-dGMP (2'-deoxyguanosine-5'-monophosphate) or 3'-dGMP.

The reaction is initiated with substitution of a chloride ligand by dGMP which leads to formation of the coordinate-covalent bond Pt-N7. We consider an association and autocatalytic Basolo-Pearson mechanism for this step. In the next part a nucleophilic attack by oxygen of a phosphate group (for 5'-dGMP – blue pathway) or from a hydroxyl group (for 3'-dGMP – red pathway) to the C8 site occurs (see Fig. 1). Subsequently the Pt(IV) complex is reduced to $Pt^{II}(DACH)Cl_2$ while dGMP is oxidized to 8-oxo-dGMP. [2]

The explored structures were optimized at the B3LYP/6-31G(d) computational level using GD3BJ dispersion corrections and CPCM/Klamt solvation model. Single-point energy parameters were determined at the B3LYP-GD3BJ/6-311++G(2df,2pd) level using IEFPCM/sUAKS solvation model developed in our laboratory recently. [3] Obtained rate constants are compared with experimental values. Analyses of changes in the electron density distribution along the reaction coordinate were performed to get deeper insight into the reaction mechanism.

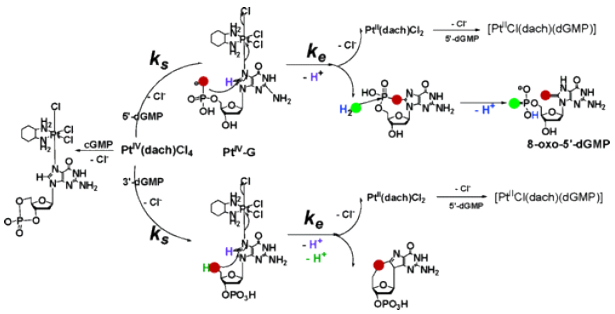

Fig. 1: Scheme of the explored reaction

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Assessment of quality of OEP2-SOS functionals applied to quantum chemical calculations

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The performance of correlated optimized effective potential (OEP) functionals based on the spin–resolved second–order correlation energy [1] is analyzed. Special attention is dedicated in particular to the recently proposed scaled–opposite–spin OEP functionals (OEP2-SOSa, OEP2-SOSb, OEP2-SOSh) [2–4] which are the most advantageous from the computational point of view (scaling – N4). We find that a composite approach, named OEP2–SOSh, based on a post–SCF rescaling of the correlation energy can yield high accuracy for many properties (total energies, correlation energies, ionization potentials, HOMO–LUMO gap energy differences), being comparable with the most accurate OEP procedures previously reported in the literature but at substantially reduced computational effort. The methods were also applied to the calculation of dissociation energy curve of noncovalently iterating systems. Detailed analysis of those results will be presented on a poster.

Acknowledgements: This work was supported by the National Science Center under Grants No. DEC–2012/05/N/ST4/02079 and DEC–2013/08/T/ST4/00032.

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Computational study of carbon dioxide electroreduction on Cu/Ni surfaces

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At the moment, there is no effective technology for utilization of CO_2, however catalytic reduction of carbon dioxide into useful products (especially the ones that can be used as fuels or fuel components) is an innovative and promising research area. This solution can be treated as CO_2 recycling and could be used for production of fuels with simultaneous decreasing of CO_2 emission and saving of fossil resources [1].

One of the articles [2], where a mechanism of carbon dioxide electroreduction to methane was proposed, has been published by the group of J. K. Nørskov. In this work, CO_2 reduction was simulated using DFT and a potential reaction mechanism was proposed.

Another mechanism of reduction of CO_2 on Cu (110) has been proposed by S. Sakong [3]. In the reasearch published group of M. Koper [4, 5] the possibility of C-C bond formation in the process of carbon dioxide electroreduction, what is essential in production of hydrocarbons. It was also revealed [6], that the reactivity may be tuned by introduction of monolayer of different metal.

Nickel is another metal, on which CO_2 decomposition reaction exhibits favourable thermodynamics [7]. Additionally, both Cu and Ni have fcc structure and similar lattice constants. At the same time the electronic structure of Cu and Ni is different [8]. A system consisting of Ni layer covered by Cu monolayer may be an interesting material for electroreduction of CO_2, where the reaction mechanisms may be different than on pure Cu.

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Analysis of enzyme-ligand FRET in the complexes of E. coli purine nucleoside phosporylase and its mutants with formycin A

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Purine nucleoside phosphorylase (PNP) is the enzyme which uses orthophosphate to cleave the N-glycosidic bond of β-(deoxy)ribonucleosides. Formycin A (FA) is its aromatic, competitive inhibitor with strong fluorescence capabilities. Absorption and emission spectra of PNP result from the presence of tyrosine residues and are characterized with the maxima around 277 and 305 nm, respectively. Since FA exhibit absorption and emission spectra red-shifted relative to PNP, with the maxima at 295 nm and 340 nm, respectively, one observes the existence of fluorescence resonance energy transfer (FRET) processes between protein tyrosine residues and the ligand.

This study aims to interpret experimental data that, among others, suggests the absence of FRET for the PNPF159A mutant in complex with FA, based on novel theoretical methodology. Tyr 160 in its S1 excited state was identified as the most probable energy donor, and FA as the acceptor. QM computations for tyrosine and FA were carried out using the TURBOMOLE package at the SCF-CI level. Changes in the interaction potentials were accounted by modifying atomic charges of the Tyr residue in its excited state. Local molecular motions of the residues and the ligand were simulated using the MD method, with the NAMD package and the CHARMM force field. Energy transfer probabilities (ETP) were computed based on the nonradiative dipole–dipole coupling model. This model results in the inverse six-power dependence of the donor-acceptor distance on ETP. The orientational factor $\kappa 2$ of the donor and the acceptor was also computed and included in the analysis. Total FRET probabilities were obtained by computing the FRET time-averages over the MD trajectories. Theoretical analysis was capable to qualitatively interpret experimental data. A more detailed analysis of the developed methodology will be presented during the conference talk (BL).

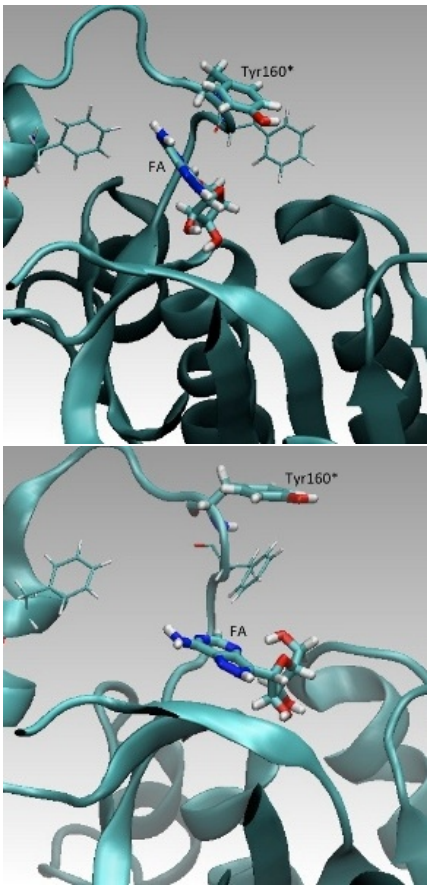

Fig. 1: Most effective (left) and least effective (right) conformations in FRET.

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Delocalization error and 'functional tuning' in Kohn-Sham calculations of molecular properties

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Theoretical methods based on Kohn-Sham density functional theory (DFT) and its time-dependent (TD) extension remain the 'workhorse' of numerical quantum chemistry, especially for first-principles calculations of ground- and excited-state properties for larger systems, including electronic spectra, electronic dynamic and static linear and higher order 'response' properties, or conformational and/or dynamic averaging of spectra and response properties. Despite widespread popularity and great success of (TD)DFT in determination of various properties for a wide variety of systems, several problems have been noted in practical calculations that can be traced back to the static correlation problem, and to the delocalization error. [1]

In the present work we explore the sometimes dramatic impact of the delocalization error and possible benefits from the use of long-range (LC) corrections and 'tuning' of functionals in (TD)DFT calculations of molecular ground-state and response properties. Tuning refers to a non-empirical molecule-specific determination of adjustable parameters in functionals to satisfy known exact conditions, for instance that the energy of the highest occupied molecular orbital (HOMO) should be equal to the negative vertical ionization potential (IP), or that the energy as a function of fractional electron numbers follows straight-line segments. [2] As has been shown in recent years, the use of LC functionals, functional tuning, and explicit quantification of the delocalization error, have provided valuable insight regarding the performance of (TD)DFT for molecular properties. This is illustrated further by scrutinizing selected molecular properties which probe different aspects of electronic structure. [3,4] The findings may provide clues for future improvements of DFT methods since different molecular properties exhibit varying sensitivity to approximations in the electronic structure model.

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Electron transfer processes crucial for coadsorption of NO and small ligands on cobalt sites in zeolites

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Our theoretical investigation refers to the change of catalytic property of cobalt cation introduced to the framework of zeolite in the exchange position. We undertake the analysis regarding the interaction of modified Co^{2+} site with NO [1]. The main task is to determine the influence of coadsorbed NH_3 or CO on the strength of NO bond what is reflected by IR frequency shifts with respect to free molecule. To that end, the simplest conceivable model consists of single aluminium tetrahedron $[Al(OH)_4]^-$, labeled as T1, and cobalt Co^{2+} coordinated to two oxygens atoms is applied. The previous study [2] has showed that the approximation of zeolitic evironment with T1 is sufficient to obtain the reliable result. In the case of NH_3 coadsorption, the most ammonia-saturated Co^{2+} site is modelled by bare cation due to its weak bonding to the lattice in porous material. The process of bond formation is described in terms originating from the Dewar-Chatt-Duncanson model including donation and backdonation of electrons between the ligand and the transition metal. To examine the independent charge flows between well-defined fragments of a complex the SR-NOCV (spin resolved natural orbitals for chemical valence) method [3] is employed. Moreover, we observed that for studied systems the dative bond is perturbated by the partial spin separation leading to weak covalent one. The balance between these two contributions decides about the propensity towards NO activation or deactivation. The calculations are carried out by means of DFT:BP86 approach [4].

The interesting feature of the adduct with coadsorbed NH_3 or CO is close lying triplet and singlet state with the different ability to shift the IR frequency of NO. The energy gap between them strongly depends on the used functional. Thus, we did the recalculations at PBE, PBE0, B3LYP, TPSSh and CASPT2 level. Furthermore, the advanced CASSCF/CASPT2 method facilitates the interpretation of electron density channels from SR-NOCV analysis. It is worth noting that expressing the wave function with natural orbitals allows to detect the left-right correlation reflecting the weak covalent bond.

The electron transfer channels obtained in our work for various adducts can be interpreted withing SR-NOCV analysis but for deeper insight into the electronic configurations of the structures the CASSCF calculations are indispensable.

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QSPR/QSAR studies by similarity clustering prediction

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Molecular properties, either physico-chemical or biological ones, can be modeled by using topological and quantum descriptors, in the frame of a Hypermolecule that mimics the biological receptors to be accessed by the ligand small molecules. In the present study we will focus on a novel algorithm, called "similarity cluster prediction". The general procedure for developing and validating the models using the above concept is given. The algorithm is exemplified on a set of 60 indolizines and the modeled property is log P.

Acknowledgements: The work was supported by computational grant no. 133, PCSS (Poznań, Poland).

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ETS-NOCV description of changes in the electronic structure along the reaction path of the double proton transfer in the formamide dimer and related systems

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ETS-NOCV method [1,2] is a combination of NOCV (Natural Orbitals for Chemical Valence) analysis with the Ziegler-Rauk method of the interaction-energy partitioning (ETS, Extended Transition State). Usefulness of the ETS-NOCV scheme in a description of chemical bonding has been demonstrated for many examples, involving transition metal complexes, molecules with covalent bonds, as well as for the weak interactions, e.g., agostic, hydrogen and halogen bonds.

In the present work, the ETS-NOCV method has been used to analyze the changes in bonding along the IRC pathways from the DFT calculations for the double proton transfer reaction in formamide dimer (see Fig. 1) and the sulfur-based related systems. The main goal was to compare the ETS-NOCV results with the recent analysis based on the Reaction Electronic Flux (REF) scheme by Toro-Labbé [3, 4].

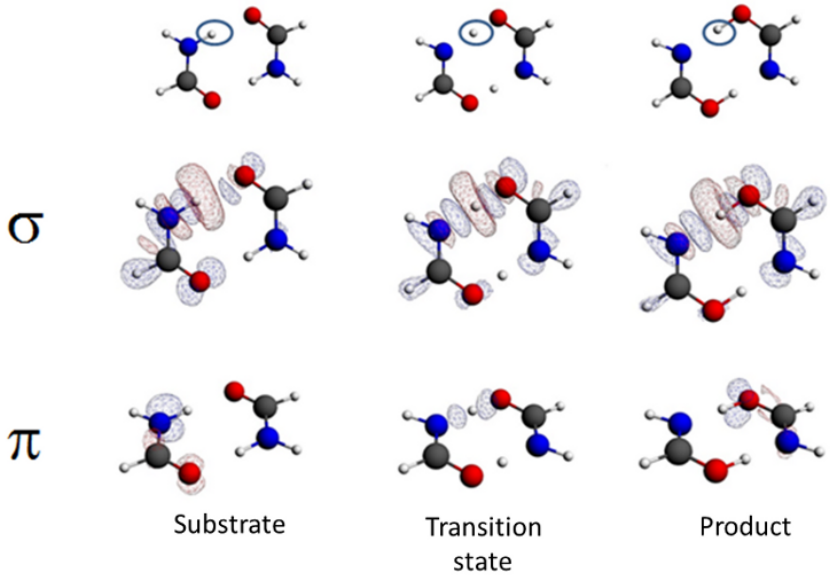

Fig. 1: Changes in bonding of the transferred H atom in formamide dimer: the dominating NOCV-contributions to deformation density $\Delta\varrho$; the two considered fragments (marked in the top part of the figure) are: the H atom and the remaining part of the molecule.

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Spectroscopic studies, structure and DFT calculations of 4-4E-[(2-fluorophenyl)imino]methyl-2-methoxyphenol

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The Schiff base compound 4E-[(2-fluorophenyl)imino]methyl-2-methoxyphenol has been synthesized and characterized by using FT-IR, ^{1}H and ^{13}C NMR spectroscopic and X-ray crystallographic techniques. The crystal structure has been solved by direct methods and refined by full-matrix least squares. The title compound crystallize in the Tetragonal space group $P4_32_12$ with $a = 12.7581(2)$, $b = 12.7581(2)$, $c = 14.6508(4)$ Å, $V = 2384.70(8)$ Å^3, D_x = 1.366 g.cm^{-3} respectively (R1=0.0307 and wR2=0.0744 for 2696 reflections [I>2σ(I)]. The molecular geometry, vibration frequencies, NMR chemical shift values of the title compound have been calculated by using the density functional theory (B3LYP) with the 6−31G (d,p) basis set. The calculated results show that the optimized geometry parameters, the theoretical vibration frequencies and chemical shift values show good agreement with experimental values. In addition, HOMO – LUMO energy gap, molecular electrostatic potential map, and thermodynamic properties were calculated by using same method and discussed.

How subtle differences in enzyme structures affect the reaction outcome? Theoretical studies on HMS and HPPD

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Hydroxymandelate synthase (HMS) and 4-hydroxyphenylpyruvate dioxygenase (HPPD) are related Fe(II)-dependent dioxygenases characterized by high degree of sequence and structure similarity. Both enzymes belong to α-keto acid dependent dioxygenases. HMS is required for biosynthesis of p-hydroxyphenylglycine, a skeletal component of macrocyclic peptide antibiotics such as vancomycin, whereas HPPD catalyzes the second step of tyrosine catabolism, which in plants is coupled with biosynthesis of liophylic cofactors necessary for photosynthesis. HMS and HPPD catalyze oxidative decarboxylation and subsequent hydroxylation of the same substrate (4-hydroxyphenylpyruvate), leading to different products, i.e. (S)-4-hydroxymandelate (HMA) and homogentisate (HG), respectively. The initial steps of their catalytic reactions, yielding the reactive Fe(IV)=O species, are believed to have a common scenario [1,2]. Once the enzyme-Fe(IV)=O-hydroxyphenylacetate complex is formed, the reaction paths diverge: HMS catalyzes hydrogen atom abstraction followed by OH^{-}rebound process yielding HMA, whereas the HPPD reaction runs through aromatic ring hydroxylation and side-chain rearrangement giving its final product, i.e. HG [2]. The present computational studies are aiming at factors responsible for regioselectivity of the reactions involving Fe(IV)=O in these enzymes, as well as insight into the reaction mechanisms [3]. Molecular dynamics (MD) simulations, performed for catalytic domains of HMS and HPPD hosting the oxoferryl intermediate provided starting structures used in construction of quantum chemical (QM) and QM/MM models of the active site regions in HMS and HPPD. QM DFT mechanistic studies conducted with models of increasing size helped to identify the role of Serine 201, which by adopting different conformations in HPPD and HMS active sites orient the substrate differently in the two enzymes and, hence, influence the course of the reaction. The mechanism of HPPD is still under debate, thus hybrid QM/MM studies were performed to analyze different scenarios and also to reproduce experimental kinetic isotopic effects (KIE). Results of QM/MM studies reproduce the observed reverse KIE and allowed us to propose a refined mechanism of the HPPD catalytic reaction.

Acknowledgements: Project operated within the Foundation for Polish Science MPD Programme co-financed by the EU European Regional Development Fund. This research project was supported by grant No DEC-2011/01/N/ST4/02330 (A.W.) and is supported by grant No UMO-2011/01/B/ST4/02620 (E.B.) from the National Science Centre, Poland.

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Fluorescent proteins' chromophores in vacuo: a benchmark study of spectral properties

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Fluorescent proteins are very important group of useful proteins, that are often utilized for labelling biological specimens including even whole body imaging. They are used in fluorescent microscopy, to construct biodetectors, nanosensors and even new kind of Light-Emitting Diodes (LEDs). Owing to these many applications, fluorescent proteins and its chromophores are intensively investigated by many research teams.

So far, spectroscopic studies have provided insightful information about fluorescent proteins as well as their chromophores both in solution and *in vacuo*. Unfortunately, absorption spectra of chromophores *in vacuo* are rarely measured experimentally.

Therefore, in our view it is valuable to investigate spectral properties of fluorescent proteins' chromophores in gaseous state in terms of various computational method such as TDDFT, CC2, CASPT2 and nevPT2.

Acknowledgements: The research was supported by Wroclaw Research Centre EIT+ under the project "Biotechnologies and advanced medical technologies" – BioMed (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 and at the Academic Computer Centre CYFRONET AGH Cracow, Poland (MNiSW/Zeus_lokalnie/ /PWrocł./068/2012; MNiSW/*/PWrocł./060/2012)

On the influence of local approximations to electron correlation on the quality of QTAIM parameters

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The local treatment of electron correlation is gaining an increasing popularity in the last years. Most studies in this field is focused on an accurate description of the total correlation energy, while only limited investigations are available for other properties of the ground state, especially on the level of coupled cluster theory (see e.g. [1]). It is however known already that these properties are usually more demanding than the energy itself as far as the selection of proper local parameters is concerned. It is therefore of interest to study how the localization of the electron correlation influences one-electron densities, which can be used to calculate first-order one-electron properties, such as e.g. dipole moments. Since the detailed analysis of the densities can be performed through means of Quantum Theory of Atoms in Molecules (QTAIM) [2], we have decided to apply this method to investigate possible changes in various parameters at critical points, such as charge densities, Laplacian of charge densities, etc., induced by the local description of the correlated part of the density. To this end we analyze the expectation-value coupled-cluster singles and doubles (XCCSD) density matrix, as defined in Ref. [3], as well as its variants in two popular localization schemes, for a set of model molecules. We also apply the same localization conditions to the local MP2 density, and compare the results with parameters obtained from the canonical MP2. Our results show that often the localization of electron correlation does not lead to significant differences of QTAIM parameters for covalent bonds in comparison to the parent nonlocal method, and therefore cheaper locally-correlated approaches can be utilized to produce one-electron densities for the QTAIM analysis.

Acknowledgements: S.Y. acknowledges the scholarship from the Ministry of Science, Research and Technology of Iran. T.K. acknowledges the partial support from the National Science Centre of Poland through grant 2011/01/B/ST4/06141.

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Atomic polarization justified Fukui index as affinity indicator in aromatic heterocycles and nucleobases

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Polarization justified Fukui functions [1,2] have been successfully tested as an adequate reactivity indicator for a set of five member ring heterocycles [3]. In this work, the Fukui functions condensed to atomic FF indices have been demonstrated, exploring the concept of AIM basins by Bader. On the ground of formal analysis of the polarization effect, the atomic or group reactivity indicators and softness have been defined. These indices are potentially applicable to test a sensing effect on a molecule, induced by an approaching point agent nucleophilic (-) or electrophilic (+) at a distance in the order of v. d. Waals radii. Calculated atomic and group indices have been proved to be consistent with the well established trends of reactivity for a control group of the five member ring heterocycles (imidazole, oxazole, thiazole). They have been applied to the analysis of nucleobases in order to reproduce the geometrical ordering of the complementary bases (adenine, guanine, cytosine, thymine, uracyl).

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

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Influence of hydrogen bonds on non-covalent interactions of aromatic molecules

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Interactions of organic aromatic molecules are very well investigated, since these interactions are essential in a number of other biological and chemical systems. These interactions are of great importance in various materials.

The influence of hydrogen bonding on the geometries of parallel interactions between pyridines was studied by analyzing data from Cambridge Structural Database (CSD) and by *ab initio* calculations. The pyridines with hydrogen bonds show the pronounced preference for offsets of 1.25–1.75 Å, close to the position of the calculated minimum; however, the pyridines without hydrogen bonds do not show a preference for certain values. [1] This is because stacking interactions of pyridines without hydrogen bonds are less strong (-4.08 kcal/mol) than interactions with hydrogen bonds (-6.86 kcal/mol), and they are more susceptible to the influence of supramolecular structures in crystals.

These results indicate the large influence of hydrogen bonding on paralellel interactions of pyridines. However, the data in crystal structures from the CSD and *ab initio* calculations show less influence of simultaneous classical hydrogen bonds on CH/O interactions of pyridine with water molecule. The results show that simultaneous hydrogen bond strengthens CH/O interactions by about 20%, whether they are linear or bifurcated. The energies of most stable (meta/para bifurcated) CH/O interactions calculated at CCSD(T)(limit) level for pyridine without and with hydrogen bond are -2.30 and -2.69 kcal/mol, respectively. [2]

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Theoretical analysis of ion-polymer interactions in PBI-based membranes with ETS-NOCV method

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Polybenzimidazolium-based (PBI) materials are potentially useful in today's industry in, for example, electrodialisys, electrodeionisation of water and membranes in alkaline anionic exchange membrane fuel cells (AAEMFC). Currently, a large number of experimental studies are focused on possible usage of PBI-derivatives. [1]

The main goal of the present study is to use theoretical calculations to the effect various ligands on the geometric and electronic structure of the cationic polymers and theirs interaction with anions. The models based on PBI (see Fig. 1) were investigated with static DFT calculations, as well as Born-Oppenheimer Molecular Dynamics (BO-MD). [2] Changes in the charge distribution were characterized based on atomic charges and the molecular electrostatic potential distribution (see Fig. 2.). Furthermore, the interaction of the model polymer-chains with various anions (OH^-, F^-, Cl^-, Br^-, I^-, HCO_3^-, BF_4^-) was characterized based on the ETS-NOCV bond-analysis. [3,4] The results help to rationalize the stability of systems observed in experiment and indicate differences in the character of bonding of OH^- as well as F^- and other ions.

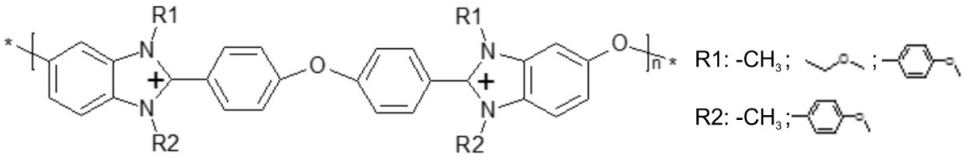

Fig. 1: Considered structures based on PBI.

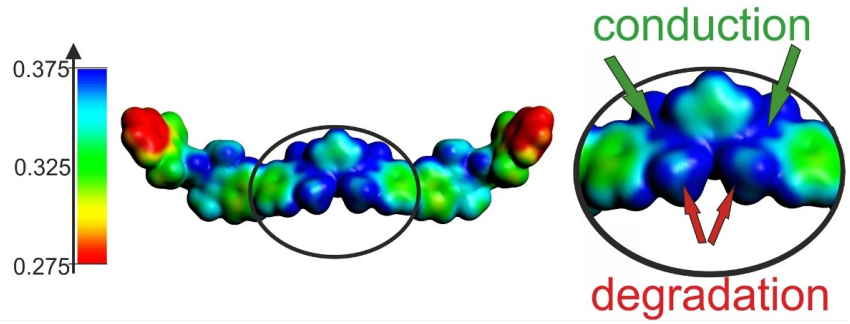

Fig. 2: Molecular electrostatic potential (MEP) for the models of methylated PBI.

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Physical nature of intermolecular interactions within Sir2 homolog active site: molecular dynamics and SAPT-DFT study

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In the present study we analyze the interactions of NAD+-dependend deacetylase (Sir2 homolog yeast Hst2) with carba-nicotinamide-adenine-dinucleotide (ADP-HPD). Due to their biochemical properties Sir2 proteins are involved in various biological processes such as DNA metabolism, regulation and repair [1,2].

For the Sir2 homolog, yeast Hst2 docking procedure was applied in order to gain an insight into the structural and energetical basis of enzyme inhibition. An orientation of ADP-HPD in the enzyme active site achieved during this stage, exhibits a high similarity relative to experimental structure, 1SZC deposed in Protein Data Bank [3]. The structure of protein – ADP-HPD complex obtained during docking procedure was used as a starting point for molecular dynamics simulation. Structural analysis, including stability of hydrogen bonds and mobility of the ligand was done for geometries collected during 50 ns of equilibrated trajectory.

The protein-ADP-HPD complex resulting from molecular dynamics simulation was used in DFT-SAPT calculations. The total intermolecular energy was divided into physically relevant terms determining the nature of interactions in complex in question. The analysis was performed for ADP-HPD and 18 amino acids forming deacetylase binding pocket. The results indicate that although the first-order electrostatic interaction energy is substantial, the presence of multiple hydrogen bonds in investigated complexes leads to significant value of induction component. Moreover, the dispersion energy is found to be quite important stabilizing factor.

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Simple nonempirical scoring model of fatty acid amide hydrolase inhibition

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Fatty acid amide hydrolase (FAAH) is an enzyme hydrolysing fatty acid ethanolamide neuromodulators, low levels of which are connected with series of pathologies in humans [1]. Therefore, the design of potent and selective FAAH inhibitors is of therapeutic importance.

Qualitative prediction of enzyme-inhibitor binding affinity, together with the insights in the physical nature of FAAH inhibition, is presented. The ab initio calculations of FAAH-inhibitors binding energy performed herein enabled to determine the protein residues that are key for the specificity of inhibitor binding. Due to the predominantly nonpolar characteristics of the interacting monomers, electron correlation effects appear to be crucial for the proper description of the binding affinity. Since the computational cost of obtaining the dispersion contribution is prohibitive when it comes to its appliaction in virtual high-throughput screening, a simple atom-atom potential fitted to ab initio values [2] was tested. Finally, the performance of ab initio methods applied herein was examined and compared with the results obtained with commonly used empirical scoring functions.

Overall, the approximate model of FAAH inhibitor activity proposed herein does not require any empirical parameters, therefore it could serve as a unique opportunity for inhibitor design or virtual screening based on first principles.

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