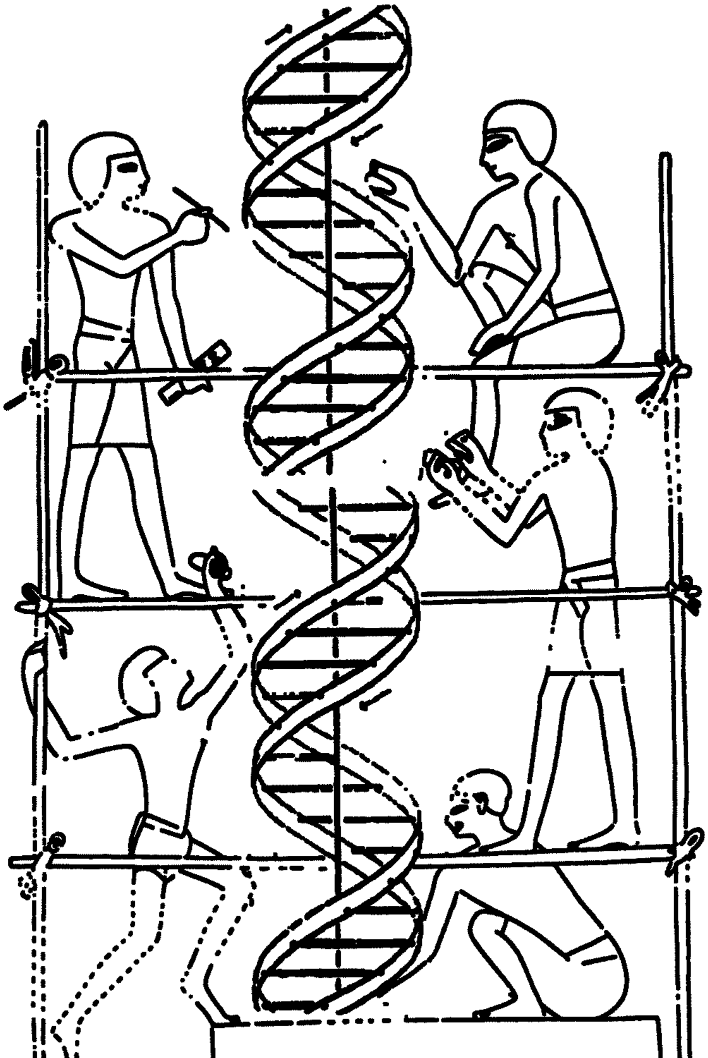
Modeling & Design of Molecular Materials 2006

Wrocław, 10-15 September 2006



Program & Book of Abstracts

Modeling & Design of Molecular Materials 2006

a conference and workshop organized by

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

NSF Computational Center for Molecular Structure and Interactions,
Jackson State University (JSU), MS, USA

Charles University in Prague, Czech Republic

Wrocław Center for Supercomputing and Networking (WCSS)

Conference website: www.mml.ch.pwr.wroc.pl/workshop an event supported by

Wrocław University of Technology

and

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Conference and workshop program

September 10, 2006 (Sunday)

16.00-20.00 Registration - Entrance to B-4 building
(corner of Smoluchowskiego & Łukasiewicza Streets)
16.00-20.00 Welcome reception

September 11, 2006 (Monday)

8.00-9.00 Registration - Entrance to B-4 building
9.00-9.10 Workshop opening - Room 409 B-4 building

SESSION I - Room 409 B-4 building (Chair - J. Leszczyński)
9.10-10.00 **L1**: W. Minor - *Structural Genomics Changes the Molecular Modeling Approach*
10.00-10.45 **L2**: T. Brinck - *Computational Design of New Enzyme Catalysts*

10.45-11.00 Coffee break

SESSION II - Room 409 B-4 building (Chair - G. Náray-Szabó)
11.00-11.40 **L3**: A. Koliński - *Modeling Protein Structure and Interactions in Reduced Conformational Space*
11.40-12.20 **L4**: L. Piela - *Theoretical Model of Conformational Autocatalysis*
12.20-13.00 **L5**: B. Lesyng - *Causality Analysis - A Strategy for the Analysis of Molecular Dynamics Data*

13.00-15.00 Lunch break

SESSION III - Room 409 B-4 building (Chair - T. Brinck)
15.00-15.45 **L6**: G. Náray-Szabó - *On the Mechanism of Action of Enzymatic Phosphate Hydrolysis*
15.45-16.30 **L7**: P. Paneth - *Application of Different QM/MM Schemes to Studies of Enzyme-Catalyzed Reactions*
16.30-17.00 *FQS POLAND software presentation*

17.00-17.15 Coffee break

SESSION IV - Rooms 448 & 446 B-4 building
Optional session for participants registered earlier
17.15-18.45 L. Firlej, B. Kuchta - *Monte Carlo and Statistics*

SESSION V - 4th floor B-4 building
19.30-21.00 Poster session A (P2-P6, P8-P11, P13-P14, P16-P28, P30-P38, P56)

September 12, 2006 (Tuesday)

SESSION VI - Room 409 B-4 building (Chair - L. Piela)
9.00-9.45 **L8**: H. Cheng - *Design and Development of Efficient Hydrogen Storage Materials to Enable the Hydrogen Economy*
9.45-10.30 **L9**: W. Grochala - *Towards the ”Hydrogen economy” Dream – Catalysis of the Homo- and Heterolytic Splitting of the H2 Molecule*
10.30-11.00 **L10**: B. Kuchta - *Adsorption and Phase Transitions in Nanopores*

11.00-11.15 Coffee break

SESSION VII - Room 409 B-4 building (Chair - P. Paneth)
11.15-11.50 **L11**: P. Politzer - *Halogen Bonding as a Basis for the Design of New Materials*
11.50-12.25 **L12**: C. Ramseyer - *Modelling of Ionic Channels at the Molecular Level: Achievements and Perspectives*
12.25-13.00 **L13**: A. Miniewicz - *Design of Photochromic Polymers and Liquid Crystals for Dynamic Holography*
13.00-15.00 Lunch break

SESSION VIII - Room 409 B-4 building (Chair - C. Ghio)
15.00-15.40 **L14**: J. Leszczyński - *Nerve Agents - How To Uncover Their Characteristics and Not Get Killed?*
15.40-16.20 **L15**: I. Majerz - *Isotope Effects in Strong Hydrogen Bonds*
16.20-17.00 **L16**: J. Burda - *Computational Approach to Anticancer Metallodrugs*

17.00-17.15 Coffee break

SESSION IX - Rooms 448 & 446 B-4 building
Optional session for participants registered earlier
17.15-19.00 L. Firlej, B. Kuchta - *Monte Carlo and Statistics*

September 13, 2006 (Wednesday)

9.30-10.00 Panorama Racławicka Gallery tour (Purkyniego Street)
optional upon request
10.00-13.00 Wrocław sightseeing (starting from Panorama Racławicka Gallery)
optional upon request, free

SESSION X - Rooms 448 & 446 B-4 building
Optional session for participants registered earlier
15.15-19.00 L. Firlej, B. Kuchta - *Monte Carlo and Statistics*

19.30-21.00 Conference reception - Museum of Architecture (Bernardyńska Street)

September 14, 2006 (Thursday)

	SESSION XI - Aula B-4 building (Chair - P. Kafarski)
9.00-9.40	**L17**: L. Hua - *What controls enantioselectivity of carbonyl reductase?*
9.40-10.20	**L18**: C. Ghio - *Computational Prediction of Regio- and Stereoselectivities in the Hydroformylation of Chiral Olefins*
10.20-10.45	**L19**: N. Mishra - *A Theoretical Study of the Comparative Binding Affinities of PAIIL towards Monosaccharides*
10.45-11.00	Coffee break
	SESSION XII - Aula B-4 building (Chair - L. Komorowski)
11.00-11.40	**L20**: T. Wesołowski - *First-principles Treatment of the Interface Between the Orbital and Orbital-free Levels of Description in Multi-scale Modelling*
11.40-12.25	**L21**: A. Tachibana - *A New Energy Density Visualization Scheme for External Field Effects on Molecular Systems*
12.25-13.00	**L22**: A. Daini - *The Effect of Interaction Range and Anisotropy on Surface Tension*
13.00-15.00	Lunch break
	SESSION XIII - Aula B-4 building (Chair - Z. Latajka)
15.00-15.40	**L23**: J. Sauer - *Treating Dispersion Effects in Extended Systems by Hybrid MP2:DFT calculations: Hydrocarbons on Catalyst Surfaces*
15.40-16.20	**L24**: J. Wojdeł - *Computational Modelling of Double Metal Cyanide Catalyst for Propoxylation Reaction*
16.20-17.00	**L25**: E. Brocławik - *CYP 3A4: Modelling Substrate Binding and Electronic State of Oxyferryl Active Site Helps to Understand Reactivity*
17.00-17.15	Coffee break
	SESSION XIV - Rooms 448 & 446 B-4 building Optional session for participants registered earlier
17.15-19.00	L. Firlej, B. Kuchta - *Monte Carlo and Statistics*
	SESSION XV - 4th floor B-4 building
19.30-21.00	Poster session B (P1, P3, P7, P12, P15, P17, P29, P31, P39-P55, P57-P58, P59)

September 15, 2006 (Friday)

	SESSION XVI - Aula B-4 building (Chair - J. Sauer)
9.00- 9.35	**L26**: M. Cieplak - *Stretching to Understand Proteins*
9.35-10.10	**L27**: S. Grabowski - *Characteristics of a Wide Spectrum of Dihydrogen Bonded Materials*
10.10-10.45	**L28**: H. Dodziuk - *Why Are Strained Hydrocarbons Worth Studying?*
10.45-11.00	Coffee break
	SESSION XVII - Aula B-4 building (Chair - J. Burda)
11.00-11.35	**L29**: P. Cysewski - *Accuracy of Gas Phase Acidities of Carboxylic Acids Predicted by Direct Scaling of Harmonic Vibrational Frequencies rom ab initio Calculations - A Perspective for Precise pKa Estimation*
11.35-12.00	**L30**: Z. Vokáčová - *NMR Parameters in RNA Molecules and Their Correlation with Molecular Structure*
12.00-12.20	**L31**: M. Pavelka - *Quantum Chemical Study of Cu(I)/Cu(II) Cations in a Peptide Environment*
12.30	Farewell - main campus building (A-1) photograph of workshop participants on the stairs

Conference posters

No.	Session	Main author	Title
P1	B	T. Borowski	*DFT Studies on the Reaction Mechanisms of Intra- and Extradiol Dioxygenases*
P2	A	G. Brancolini	*Mechanism for DNA Triple Helix Formation: a Computational Study*
P3	B	E. Broniatowska	*PLDB - Protein Ligands DataBase*
P4	A	H. Chojnacki	*Multiple Proton Transfer in Some Molecular Systems. Implications for Crystalline Phases*
P5	A	P. Czeleń	*Molecular Dynamic Simulation of the Effects of Oxidative Damage on the Structure of Telomeric DNA*
P6	A	M. Doskocz	*Studies of Hydrogen Bonds in C-H···O=P by NMR Chemical Shifts and 3hJ(13C-31P) Spin-Spin Coupling. Correlation of Experimental and ab inito Data*
P7	B	M. Doskocz	*The Theoretical Study of Five Heterocyclic Derivatives of Carbazole – Monomers Electroconducting Polymers*
P8	A	M. Feliks	*Reactivation mechanisms for sarin-inhibited acetylcholinesterase by oxime: a model DFT study*
P9	A	M. Fiet	*Theoretical Study of Concerted Proton Transfer in the Ground Electronic State of the Double Hydrogen Bonded Formic Acid Dimer*
P10	A	Z. Futera	*Activation of Ruthenium(II) Complexes and their Interactions with DNA bases*
P11	A	P. Gauden	*CO2 Sorption on N-, O-, and OH-substituted Carbonaceous Materials. A computational Chemistry Study*
P12	B	P. Gauden	*Argon Adsorption on Heterogeneous Carbon Surfaces: Accesible Pore volume and Width*
P13	A	A. Gorączko	*Modeling of Isotopomeric Molecular Clusters in Electron Ionisation Mass Spectra*
P14	A	H. Grebneva	*Causes of Rare Tautomer Forms Stabilization of DNA Bases Under Dimers Formation and DNA Synthesis*
P15	B	H. Grebneva	*Changes in Structure of DNA Bases as one of Reasons of the Untargeted UV-mutagenesis*
P16	A	D. Gront	*Optimizing the Parallel Tempering Monte Carlo method for biomolecular systems - insights from stat. thermodynamics*
P17	B	D. Gront	*BBQ - Backbone Building from Quadrilaterals: An Algorithm That Outperforms Existing Methods*
P18	A	R. Grzywa	*The Molecular Basis of Urokinase Inhibition: From the Analysis of Intermolecular Interactions to the Prediction of Binding Affinity*
P19	A	J. Handzlik	*DFT Study of Molybdena-silica System in Olefin Metathesis*
P20	A	K. Hernik	*cis-Diammine(orotato)platinum(II) - a Cisplatin Analogue. Density Functional Study*
P21	A	J. Hładyszowski	*DFT Study of Dihexanoyle Phosphatidylcholine Monolayer*
P22	A	T. Jaroń	*DFT Studies of Novel Hypothetical Hydrides of Late Lanthanide Metals: Route to high-TC Superconductivity?*
P23	A	A. Kaczmarek	*Experimental and Theoretical Investigations of Spectroscopic Properties of Azobenzene Derivatives in 1,1,2-trichloroetan*
P24	A	J. Kamiński	*Accuracy of Various Approximations to the Non-additive Kinetic Functional in Exactly Solvable Cases*

No.	**Session**	**Main author**	**Title**
P25	A	M. Kluba	*Molecular Basis of Vampirism - Designing Anti-porphyria Drugs*
P26	A	S. Kmiecik	*De Novo Simulations of Protein-folding Pathways in a Reduced Conformational Space*
P27	A	M. Kurciński	*Model of Three-dimensional Structure of the Vitamin D Receptor Bound with Peptide Ligand Mimicking Co-activator Sequence*
P28	A	M. Kwiatkowski	*A Clustering Based Approach to Adsorption Modeling*
P29	B	M. Kwiatkowski	*Computer Analysis of Nitrogen Adsorption Isotherms on Active Carbons by an Employment of the New LBET Class Models*
P30	A	D. Latek	*Theoretically Predicted Contacts and Sparse NMR Data in De novo Protein Structure Prediction*
P31	B	J. Lundell	*Quantum Chemical Studies of Xenon Insertion Compounds of Formic Acid*
P32	A	J. Lundell	*Computational Study of Formic Acid Dimers Involving the Higher-energy Conformer, cis-HCOOH*
P33	A	Ł. Maj	*Design of Ti/Si/H Clusters and Surfaces of Cubic TiSi for Heterolytic Addition of H2*
P34	A	L. Michera	*Theoretical Study of Cisplatin Interactions with Glycine in Gas-phase and Implicit Water Solution – COSMO*
P35	A	P. Miszta	*Homology Modelling of G-protein Coupled Odorant Receptor AgOR1 from Malaria Mosquito Anopheles Gambiae*
P36	A	J. Mrázek	*Computational DFT Study of the Non-heme Iron Center of Photosystem II*
P37	A	J. Murray	*The Two Components of the Activation Energy*
P38	A	W. Niewodniczański	*Electronic Structure of Pyridinium N-phenolate Betaine Dye*
P39	B	S. Orłowski	*Locally Enhanced Sampling Molecular Dynamics Study of the Dioxygen Transport in Human Cytoglobin*
P40	B	A. Panczakiewicz	*Implementation of the QM/QM Method Based on the LocalSCF Algorithm*
P41	B	P. Paneth	*Continuum Solvent Models of Body Fluids on the Example of Serum*
P42	B	Ł. Pepłowski	*Insights Into the Catalytic Activity of Industrial Enzyme Co-Nitrile Hydratase. Docking Studies of Nitriles and Amides*
P43	B	J. Pietkiewicz	*Glycolytic enzyme enolase as a plasminogen receptor: in vitro interaction and theoretical modeling.*
P44	B	Y. Pivak	*Defect Transport Modelling in Monoclinic La(2-x)Pr(x)Ti(2-y)Nb(y)SiO(9+d)*
P45	B	M. Radoń	*Peculiarities of the Electronic Structure of Cytochrome P450 Active Site (Compound I) - DFT and CASPT2 Modeling*
P46	B	P. Rejmak	*Cu(I) Sites in Faujasite and their Interactions with the CO Molecule - Theoretical Studies*
P47	B	M. Rostkowski	*Charge Localization in Monothiophosphate Monoanions*
P48	B	D. Rutkowska-Zbik	*Preliminary Theoretical Studies on TiO2 Anatase System*
P49	B	J. Sebek	*Modeling of Circular Dichroism Spectra of Flexible Peptides in Water Solutions with Using Molecular Dynamics and Quantum Mechanics*
P50	B	W. Szczepanik	*Linear Response Kohn-Sham Equations with Constrained Electron Density Applied to a Nonheme Fe(IV)=O Complex*
P51	B	B. Szyja	*Modeling the Adsorption of Aromatic Compounds on a TiO2/SiO2 Catalyst*

No.	**Session**	**Main author**	**Title**
P52	B	K. Świderek	*Modeling Properties of Iridium Complexes*
P53	B	M. Ullrich	*Modelling of Transition States in Stereoselective Addition of Diethylzinc to Benzaldehyde Catalyzed by N,S-camphor Based Catalysts*
P54	B	Z. Velkov	*Predicted Antioxidant Activity of Amide and , Thioamide of o-Coumaric Acid*
P55	B	P. Wielgus	*Theoretical Description of Ge/Si Microclusters*
P56	A	M. Wiśniewski	*On the Reactivity of Curved Carbon Nanostructures to Amidogen*
P57	B	M. Wiśniewski	*Towards the Reactivity of Carbon to Izoelectronic (Cl- and K+) Adsorbates*
P58	B	T. Zimmermann	*The Interactions of Platinum Complexes with Sulfur-Containing Amino Acids; Theoretical Calculations*
P59	B	A. Zwiefka	*Study of Binding of Pseudomonas aeruginosa Alginate by Toll-Like 4 and CD18 Receptors*

Lecture abstracts

in chronological order

Structural Genomics Changes the Molecular Modeling Approach

Władysław Minor

Department of Molecular Physiology and Biological Physics,
University of Virginia, Charlottesville VA, United States of America

The Protein Structure Initiative (PSI) is a federal, university, and industrial effort with the objective of achieving high-throughput determination of protein structures on a genome-wide scale. The long-range goal of the PSI is to employ modeling to make the three-dimensional atomic-level structures of most proteins easily obtainable from the knowledge of their corresponding DNA sequences.

Experimental procedures are being developed to expedite and automate all stages of the experimental protein structure determination process (e.g. target selection, cloning, expression, crystallization, data collection, processing, phasing, and deposition into the Protein Data Bank). The data management effort evolved from simple data collection and storage to a comprehensive effort that includes information integration and mining, target selection and prioritization, experiment design and tracking, automated data collection and processing, and automated dissemination and report generation. The main bottleneck can be associated with the lack of adequate computer software and integration of the whole process. The next step is to integrate modeling techniques to create a new system to perform research in structural biology.

Computational Design of New Enzyme Catalysts

Tore Brinck

Physical Chemistry, Royal Institute of Technology, Stockholm, Sweden

In recent years it has become evident that many enzymes can use alternate catalytic mechanisms, and that it is possible to change the reaction mechanism and reaction specificity by active-site modifications. We have demonstrated, together with experimental collaborators, that it is possible to convert the Candida antarctica lipase B (CALB) into an aldolase by the mutation of a single residue, the catalytic serine[1]. It is one of the first examples where a successful redesign of the reactive mechanism has been based on computer modeling. Recent studies have shown that the same mutant is also capable of catalyzing Michael Type additions[2] and epoxidations of α-β unsaturated carbonyl compounds.

In this talk we will discuss how computational chemistry can be combined with experimental studies in the process of redesigning enzymes for catalysis of unnatural reactions. In order to obtain an efficient catalyst it is necessary to optimize the entire catalytic process from the substrate binding, via the transition state to the expulsion of products. We therefore use a combination of quantum chemistry and molecular dynamics methods to analyze the effects of different mutations on the catalysis. The computational data is continously evaluated against the results of kinetic measurements, and the combined results of theory and experiments guide the designing process.

[1] Branneby, C.; Carlqvist, P.; MAgnussen, A.; Hult, K.; Brinck, T.; Berglund, P. *J. Am. Chem. Soc.* **2003**, *125*, 874.

[2] Carlqvist, P.; Svedendahl, M.; Hult, K.; Brinck, T.; Berglund, P. *ChemBioChem* **2005**, *6*, 331.

Modeling Protein Structure and Interactions in Reduced Conformational Space

Andrzej Koliński

Laboratory of Theory of Biopolymers, Faculty of Chemistry, Warsaw University, Poland

Systematic sequencing of numerous genomes provides an enormous library of protein sequences. Only for a small fraction of these proteins the three dimensional structures have been determined. The knowledge of protein structures is necessary for understanding and controlling their biological functions. It is also important to know the protein folding mechanisms and the dynamic and thermodynamic characteristics of the denatured state. Understanding protein dynamics and folding mechanisms may be even more challenging than the theoretical prediction of protein structure. Classical molecular dynamics methods are applicable only to not too large systems and/or to a relatively narrow time frame. The time scale of biomacromolecular processes is orders of magnitude wider, therefore simplified models could be very useful.

The reduced representation of the CABS model[1] employs four interaction centers per residue (alpha carbon, beta carbon, the center of mass of the side group and the center of peptide bond). The main chain backbone is confined to a lattice grid, thereby enabling extremely fast conformational updating and energy evaluation. The force field of CABS consists of several potentials of mean-force derived from the statistical analysis of structural regularities observed in already solved protein structures. The sampling of conformational space is done with Monte Carlo methods, including computationally efficient replica exchange MC algorithms. Versatile tools of bioinformatics have been developed to handle data processing and analysis of large scale simulations of protein systems using the CABS model[2]. CABS methodology has proven to be one of the best performing methods for protein structure prediction. It has been demonstrated during the sixth CASP (Critical Assessment of protein Structure Prediction) community-wide experiment[3] that the CABS-based modeling technique is applicable to an entire spectrum of structure prediction problems; from comparative modeling to de novo prediction of new folds.

In this contribution we describe some of the newest applications of the CABS modeling technique[4]. These applications include: prediction of protein structure, modeling of folding mechanisms, protein - protein interactions, and fully flexible docking of peptide-type ligands to protein receptors. The CABS reduced model could be easily integrated with all-atom approaches. Namely, the united atom models from CABS simulations are accurate enough for a reasonably fast rebuilding of atomic details. Consequently, the proposed methodology enables multiscale simulations of large biomolecular systems.

[1] Kolinski, A. *Acta Biochimica Polonica* **2004**, *51* (2), 349–371

[2] Gront, D.; Kolinski, A. *Bioinformatics* **2005**, *22* (5), 621–622

[3] Kolinski, A.; Bujnicki, M. *Proteins* **2005**, *61* (Suppl 7), 84–90

[4] Kmiecik, S.; Kurcinski, M.; Rutkowska, A.; Gront, D.; Kolinski, A. *Acta Biochimica Polonica* **2006**, *53* (1), 131-143

Theoretical Model of Conformational Autocatalysis

Lucjan Piela

Quantum Chemistry Laboratory, Department of Chemistry, University of Warsaw, Poland

A model of key-lock, template and hand-glove intermolecular interactions will be illustrated by an example of conformational autocatalysis based on the interaction of protein molecules (within the newest empirical force field, highly successful in CASP6 predictions). First, an oligopeptide (32 amino acids, aa) is designed in such a way as to ensure the existence of the global minimum basin of the alpha-helical character and a metastable basin of the beta type. Among 14 candidates satisfying this requirement, only one exhibits autocatalytic behaviour of the following kind. A single molecule of the protein, when subject to an extensive Monte Carlo conformational search (replica method), practically always attains the alpha-helical global minimum if the temperature exceeds a minimum temperature. Below this minimum temperature the beta form is stable, although of higher energy. If, however, two proteins interact, and one of them is frozen in the beta (metastable) form, and the second is allowed to fold, then it practically always folds to the beta i.e. metastable form. It was proved also that the third protein molecule continues to form a stack of molecules with such beta conformations (conformational autocatalysis). This model [1] seems to mimic the main features of the spreading the prion diseases.

Acknowledgements: Support from the Polish Ministry of Science within the PhD grant of E. Małolepsza is acknowledged.

[1] Malolepsza, E.; Boniecki, M., Kolinski A., Piela L. *Proc. Natl. Acad. Sci.* **2005**, *102* (22), 7835–7840.

Causality Analysis - A Strategy for the Analysis of Molecular Dynamics Data

Andrzej Górecki[1,3], Joanna Trylska[2], Bogdan Lesyng[1,3]

[1]Faculty of Physics, [2]ICM, [3]CoE BioExploratorium, Warsaw University, Poland

Our ability to carry out high-quality quantum-mechanical calculations and/or quantum, classical or quantum-classical molecular dynamics simulations for (bio)molecular or nano-systems does not automatically lead us to a satisfactory description and understanding of the mechanisms of their functioning. Typically, causal relations between such events as proton transfer processes and conformational changes of the molecular scaffold, or time-ordered correlations between conformational changes are required for the rational description of such mechanisms. Therefore, in post-processing of simulation data we are interested in extracting correlations among various events, as well as in extracting their mutual influence and temporal ordering.

The problem is more general and refers to complex systems in natural sciences, as well as in economy. In 2003, Granger received the Nobel prize for his contribution to the causality analysis in economy [1]. The method analyzes signals (time series) generated by complex systems affected by stochastic fluctuations, assuming linear relations between a present variable and its values in preceding time-steps. An extended, multi-channel Granger-type analysis is also applied in causality analyses of EEG signals (http://brain.fuw.edu.pl).

We applied the same strategy in the analysis of MD simulation results [2]. Input signals are trajectories or their combinations, and thermal interactions with the environment are responsible for the stochastic perturbations. We applied a *Multi-Variate Autoregressive Model* (MVAR) and the *Directed Transfer Function* (DTF) method for the analysis of MD data. DTF is equivalent to Granger analysis, but its computational implementation is simpler. The MVAR-DTF method filters out the thermal noise and detects causal relations among selected degrees of freedom treated as signals. Applications of the developed analysis tool were tested on the dynamics of two model systems: linear chains of atoms, and a malonaldehyde molecule (SCC-DFTB MD data for malonaldehyde [3] were used). The MVAR-DTF method detected independent and correlated motions in subunits of the chains, and in malonaldehyde, correlations between motions of the donor and acceptor oxygen atoms, and the proton transfer processes (hoppings).

Causality cannot be easily derived from other conventional analyses. We are currently carrying out similar studies for larger systems, such as proteins. To detect causality relations, we have also been testing another approach, which is based on a concept of *transfer entropy*.

Acknowledgements: Support - CoE BioExploratorium and Warsaw University BST funds.

[1] Granger, C.W.J. *Econometrica* **1969**, *37*, 424–438.
[2] Gorecki, A; Trylska, J.; Lesyng, B. *Europhysics Letters* **2006**, *75*, 503–509.
[3] Walewski, L.; Krachtus, D.; Fischer, S.; Smith, J.C.; Bala, P.; Lesyng, B. *Int. J. Quant. Chem.* **2006**, *106*, 636–640.

On the Mechanism of Action of Enzymatic Phosphate Hydrolysis

Gábor Náray-Szabó

Chemistry Department, Eötvös Loránd University, Budapest, Hungary

Phosphate hydrolysis is the key step in several important enzymatic reactions. Two alternative mechanisms have been proposed, the reaction proceeds either via a loose transition state (dissociative path) or through a high-energy intermediate (associative path). We performed ab initio quantum mechanical calculations on large models of the active sites of HIV integrase and dUTPase and compared the results. While in the case of the reaction catalyzed by HIV integrase no high-energy intermediate could be located, providing evidence for an SN2-type mechanism, for dUTPase we found a high-energy, pentacoordinate intermediate with a trigonal bipyramidal structure. This indicates that this reaction follows the associative path. We compared the reaction paths for two substrates of dUTPase. One is the natural substrate of the enzyme, deoxi-uridine-5'-triphosphate (dUTP), which reacts relatively easily, the other is its nitrogen analogue, deoxi-uridine-5'-phosphate-imino-diphosphate (dUTP-PNP), which reacts much slower. The difference between the reaction rates of these compounds is appropriately reproduced, and the relative stability of the high-energy intermediate of dUTP is larger than that of dUTP-PNP.

Application of Different QM/MM Schemes to Studies of Enzyme-Catalyzed Reactions

Piotr Paneth

Institute of Applied Radiation Chemistry, Technical University of Łódź, Poland

Several QM/MM schemes will be reviewed based on the experience of the previous and current research in my group, starting with an early approach to introduce the polarization of the MM layer in AM1/ESFF calculations of the ATCase-catalyzed reaction between carbamyl phosphate and aspartate[1]. Problems in dealing with decarboxylation reactions, where single C-C bond dissociation is used as a reaction coordinate, will be illustrated on the example of AM1/CHARMM studies of the mechanism of ornithine decarboxylase[2]. The same level of theory will be also used to illustrate problems with open-shell systems and hydrogen atom transfer[3]. These studies were carried out on the first step of the pre-steady state phase of the reaction catalyzed by methylmalonyl-CoA mutase. The ONIOM approach at the BP86/Amber level to the mechanism of the second step, the homolysis of the C-Co bond, will also be presented[4].

We will conclude with the presentation of our own program, QM^{2}Manager[5], which aims at combining various levels from different programs. In the current implementation it allows methods from Spartan to be combined with LocalSCF. We will compare our previous results obtained at the B1LYP/PM3 level (QM/QM) for haloalkane dehalogenase DhlA[6] to those for haloalkane dehalogenase LinB obtained with QM^{2}Manager at the B3LYP/AM1 (QM/QM) theory level. Present calculations allow the optimization of the whole enzyme at the (semiempirical) quantum level with the active site refined at the DFT level.

Acknowledgements: The presented studies were supported through a series of grants from the State Committee for Scientific Research (KBN) in Poland. Allocation of the computational time at the Poznan Supercomputer and Networking Center and at the Warsaw Interdisciplinary Center for Modeling is gratefully acknowledged.

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Design and Development of Efficient Hydrogen Storage Materials to Enable the Hydrogen Economy

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Computational chemistry is playing an increasingly important role in materials design and development. In this talk, I will outline our effort to develop and utilize computational chemistry methods to identify carbon-based materials capable of storing hydrogen via physical and chemical adsorption processes.[1-3] For H_2 physisorption, our main focus is on single-walled carbon nanotubes. We show that H_2 adsorption capacity and strength are strongly dependent on nanotube diameters and packing, but less on nanotube chirality. The calculated diffusion coefficients are much higher than what has been reported for H_2 in microporous materials such as zeolites, suggesting a superb transport property of these materials. For chemisorption, we have identified a series of polyaromatic compounds as hydrogen carriers. Some of these compounds can be liquefied and a novel storage concept was proposed, which suggests that using the organic liquids as hydrogen carriers would require little infrastructural change for the hydrogen economy. The predicted chemical and physical properties were validated by a series of experiments.

Acknowledgements: This work is supported in part by funding provided by the US Department of Energy's Office of Energy Efficiency and Renewable Energy within the Center of Excellence on Carbon-based Hydrogen Storage Materials (DE-FC36-05GO15074).

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Towards the "Hydrogen economy" Dream – Catalysis of Homo- and Heterolytic Splitting of the H_2 Molecule

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The realization of the 'Hydrogen Economy' dream will largely rely on the existing low-Z stores of hydrogen (H_2O, NH_3, $LiBH_4$, $LiAlH_4$, LiH, $LiNH_2$, etc.) [1]. Three crucial properties of these and composite materials, however, should be greatly improved: (i) the thermal decomposition temperature, T_{dec}, should be brought down to 60-90 °C; (ii) the kinetics of the thermal decomposition and H_2 reabsorption should be accelerated; (iii) the pressure of H_2 necessary for on-board recharging should be decreased to 10-20 atm [1]. Therefore, the existing technologies for hydrogen storage require efficient (single- or multicomponent) catalysts, their properties being crafted separately for every single hydrogen store.

Fast progress of quantum methods and computing power now allow for the careful design of novel hydrogen transfer catalysts. In this contribution we will present state-of-the-art solutions in catalysis of hydrogen evolution and uptake from H_2 stores (various compounds of Ti, Fe, Si), followed by selected results *in silico*. We will discuss recent advances in the theoretical design of transition metal and main group element (Ti, Ni, Si) catalysts for the reductive homolytic [2] and heterolytic [3,4] splitting of H_2:

$$H_2 + 2e^- \rightarrow 2H^- \quad (1)$$

$$H_2 \rightarrow H^+ + H^- \quad (2)$$

Figure 1: Fleet of BMW 750 hL (liquid H_2-powered vehicles).

Three 'perverseness laws' related to H_2 absorption and desorption will be described: (a) the low T_{dec} versus thermodynamic irreversibility; (b) the large weight % H versus high T_{dec} for heterolytic stores; (c) the request for thermodynamic stability versus heat elimination during on-board recharging for chemical stores (entropy burden). These annoying relationships constitute the major challenges of all modern H_2 storage technologies.

Acknowledgements: Support from ICM and Dept. Chem. is gratefully acknowledged. Calculations were performed at ICM supercomputers.

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Adsorption and Phase Transitions in Nanopores

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It is well known that thermodynamic properties of materials are modified in confined geometries. In particular, molecular liquids and solids in porous materials show properties which are not predictable by macroscopic methods. In such situation, the computer simulations allow one to model and analyze microscopic mechanisms responsible for the observed behavior. In this communication, we present results of Grand Canonical Monte Carlo simulations of layering (that is, the formation of mono- or multi-layer structure by physical adsorption) and melting transitions in nanometric cylindrical pores.

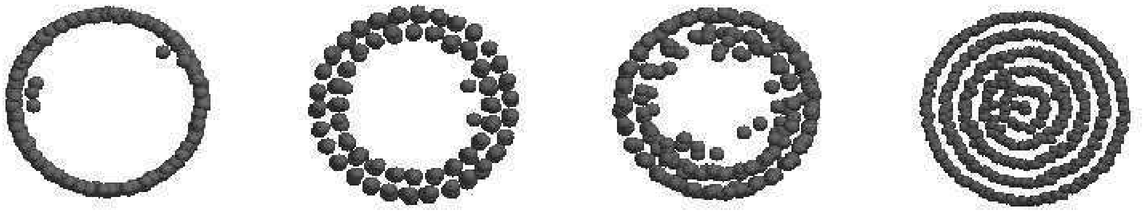

Figure 1: Examples of different phase situations of adsorption in cylindrical pores.

We discuss the influence of the pore size on the mechanism of transitions. We emphasize the fact that there is a strong correlation between layering and melting. We focus our discussion on the first two adsorbed layers, where the influence of the interaction with the pore wall is crucial for the mechanism of the transitions. Finally, we discuss the influence of heterogeneity of the pore wall structure on the phase properties. The picture which emerges from this analysis of the phase situation in nanometric pores shows an intricate situation of adsorbed system with heterogeneous phase structure and, as a consequence, phase transition mechanism totally different from their 3D analogs [1-3].

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Halogen Bonding as a Basis for the Design of New Materials

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Halogen bonding is a noncovalent interaction between a halogen atom on a "donor" molecule and a Lewis base "acceptor."ă It is analogous to hydrogen bonding, but its importance is not as widely recognized.ă Halogen bonding is due to a small region of positive electrostatic potential that forms on the ends of bromine, ăiodine, and sometimes chlorine atoms, particularly when bonded to electron-withdrawing systems.ă There is now a growing awareness that halogen bonding is of considerable significance in many areas, inluding molecular biology and materials science.

After a brief overview of the origins and properties of halogen bonds, this presentation will focus upon their increasing importance in the design and development of new materials, sometimes described as "crystal engineering."ă Computational results will be presented that relate specifically to haloacetylenes, cyanogen halides and haloacetylene nitriles as building blocks for polymers.

Modeling of Ionic Channels at the Molecular Level: Achievements and Perspectives

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Although the presence of the membrane helps cells to retain vital ingredients, ion permeation is crucial for a variety of biological functions such as nervous signal transmission and osmotic regulation. Ion channels are proteins inserted in the membrane lipid bilayer that form aqueous pores. They are extraordinary machines acting at the nano-meter scale that allow ions to cross the hydrophobic barrier of the core membrane, guarantying to the cell a controlled exchange of ionized particles. As all membrane proteins, ionic channels are difficult to crystallize and up to 1995, no high resolution structure of a potassium channel was available. It was impossible to relate their structures to their specific functions.

In 1995, the cloning of the first bacterial gene from streptomyce lividans encoding for a potassium selective channel (the KcsA gene) opened the avenue to large production of purified K^+ channel. The crystallization of the KcsA and the determination of its structure by X-ray diffraction have allowed an unprecedented investigation of diffusion channels using theoretical calculations based on microscopic description of the interactions inside the protein [1]. In this communication, it will be shown how Molecular Dynamics simulation [2], Brownian Dynamics and ab initio calculations [3] can explain the permeation, the selectivity between ions, the diffusion, and more recently the gating of KcsA channel [4]. The concerted motions between ions, water molecules and atoms constituting the backbone of the protein will be presented as a key factor for the comprehension of this ionic pore.

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Design of Photochromic Polymers and Liquid Crystals for Dynamic Holography

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Photorefractive and photochromic materials are extensively studied because of their dynamic holographic properties (low light intensity induced reversible refractive index change). These materials are used in optical signal processing: light switching, spatial and frequency modulation, dynamic optical memory systems, etc. [1]. For these applications the time scale of photo-induced phenomena and magnitude of photo-induced anisotropy is of the primary importance.

We have undertaken the systematic investigations of two groups of photoactive materials: (i) dye-functionalised polymers in which molecular orientation can be controlled by polarised light by means of the coupling of optical field with the anisotropic absorption of molecules and (ii) low-molecular mass liquid crystals in which spatially modulated optical field acting through phtoconductivity via space charge electric field introduces optical anisotropy. We limit our interest to azobenzene-containing polymers and nematic liquid crystals interacting with photoconducting polymeric surface.

It is of primary importance to develop material in which complex refractive index can be changed by low intensity light. The model compound is photochromic azobenzene-derivative covalently bonded to the polymer main chain. The interplay between *cis-trans* photoisomerisation process and polymer matrix interaction with photoactive molecules is a challenging problem in achieving the best performance - fast (1 ms - 1 s), large ($\Delta d \approx 0.05$) and reversible refractive index changes. We show, on some examples, how chemical design of both optically nonlinear chromophores and polymeric matrix contribute to optimum performance materials. Part of the holographic-type experiments is explained by Monte Carlo simulations of light-induced microscopic events taking place in azobenzene-containing polymers.

In another group of materials suitable for real-time holography the photoconducting polymers (PVK:TNF) are combined to act together with optically birefringent nematic liquid crystals. This unique material combination gives a new photorefractive hybrid system of excellent performance characteristics. The optimization requires the design of highly birefringent nematic liquid crystalline mixtures and photoconducting polymer substrate able to align liquid crystal molecules by anchoring them on the surface and create surface potential

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Nerve Agents - How To Uncover Their Characteristics and Not Get Killed?

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The efficient decomposition of chemical warfare agents is a matter of urgency due to their dangerous storage, environment contamination, and terrorism threats. Highly toxic common nerve agents are organophosphorus compounds and they act as acetylcholine esterase (ACHE) inhibitors. The mechanism of the toxic action of these compounds has been interpreted as the blockage of hydrolysis of the neurotransmitter molecule ACH, through competitive binding with the active part of the cholinesterase enzyme. Since ACH adopts a specific conformation while binding with the active cholinesterase site, it could be imagined that the nerve gases would adopt similar conformation during the competitive binding process. The quantum chemical studies on nerve gases reveal that they have less conformational flexibility with respect to ACH in both gas-phase and in aqueous medium. The active site of the nerve gases resemble the active site of ACH and the application of QM/MM technique has shown that they bind more strongly than ACH in the active cavity of ACHE, mostly through hydrogen bonding and non-bonded interaction.

The toxic effect of the nerve gases in the atmosphere could be deactivated through hydrolysis on metal oxide surfaces. The decomposition of nerve agents from soils and groundwater is of practical interest since it is of relevance to the agricultural, industrial, and military applications of these species. The development of cost effective, cleanup technologies for nerve agents is a high priority for environmental restoration research. Such development involves the coordination of experimental and theoretical investigations to integrate both technological and fundamental aspects of key processes. Although the major processes affecting the natural and engineered treatment of nerve agents appreciated qualitatively, many questions remain regarding reaction mechanisms. Quantum chemical analysis provides a wide array of powerful tools that have been underutilized in deciphering the complex reactions affecting warfare agents.

The talk reveals the results of the high performance computational studies of the JSU group on nerve agents. Their molecular structures, properties, interactions with soils, metals and their oxides have been studied using reliable, ab initio techniques. These investigations provide new insight into the studied phenomena and reveal efficient ways of decomposition of nerve agents.

Acknowledgements: This research was supported by the CMCM grant from the ERDC (Vicksburg, MS) and the Army High Performance Computational Research Center (University of Minnesota).

Isotope Effects in Strong Hydrogen Bonds

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The importance of the hydrogen bond is well known, as the hydrogen bond is very abundant in biological systems responsible for the molecular and macroscopic properties of materials, molecular recognition, and supramolecular structure. The most important problem in investigating the hydrogen bond is the degree of proton transfer, which determines all the properties of the hydrogen bond. Very strong hydrogen bonds are, in addition to the properties of the proton donor and acceptor, also sensitive to temperature and the surroundings of the hydrogen bridge. These hydrogen bonds are rather rare and only a few such complexes have been investigated by neutron diffraction, which allows for a precise localization of the proton in the hydrogen bridge [1-4]. Only for 4-methylpyridine-pentachlorophenol complex [3] the continuous proton migration from donor to acceptor in strong OHN hydrogen bond was systematically investigated using the neutron diffraction technique. The deuterated pentachlorophenol - 4-methylpyridine complex is not isomorphic with the protonated analogue and temperature change causes a phase transition connected with the passing of the deuteron through the center of the hydrogen bridge.

In potassium hydrogen dichloromaleate two very short OHO hydrogen bonds are present [4]. Several different types of refinements were applied, including an unconventional model with all atoms except hydrogen constrained in P-1, but with hydrogen allowed to refine without any constraints in P1. Standard deviations and significance tests clearly showed that the 'heavy-atom' structure is best described as centrosymmetric. However, even when the heavy-atom structure was constrained to be perfectly centrosymmetric, the protons still refined to off centred positions. This structure was described as 'pseudocentrosymmetric with non-centred protons'.

Furthermore, the behaviour of H_2 is very interesting: at 295 K and 170 K it is located on one side of the symmetry centre but at 90 K and 30 K it is located on the other side. A detailed determination of the unit-cell parameters by X-ray diffraction in the whole temperature range from 30 K to 295 K has revealed a phase transition connected with the location of H_2 in relation to the $O\cdots O$ centre. These effects disappear with replacing of hydrogen atoms by deuterium.

Isotopic substitution is very popular in spectroscopy and many other investigative techniques as the method which does not perturb the structure of molecule. This assumption is true with reference to most molecules. The only exceptions are some hydrogen-bonded complexes in which the proton in the hydrogen bridge is replaced by deuteron. When the hydrogen bond is extremely strong, the isotopic substitution causes drastic changes in the geometric parameters of the hydrogen bond as well as in the symmetry of the crystal.

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Computational Approach to Anticancer Metallodrugs

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Pt(II)-Pt(IV) complexes

Cisplatin (diammine-dichloro-platinum(II) complex) and its Pt(IV) analogues are known for their high activity in anticancer treatment. In the first part of my contribution I will concentrated on the physical background of the activation of these drugs in the hydration process of replacing chloro-ligards by water molecules. Thermodynamic and kinetic parameters were determined for this hydration reaction. Comparing with experimental data it can be seen very good agreement of both characteristics. The process of cisplatin activation can be understand purely on the thermodynamical footings as formation of less stable Pt-complexes under the LeChatelier-Braun-van Hoff's principle of chemical equilibrium.

Interaction of cisplatin with various model of single-stranded and double-helix DNA was also examined thoroughly. Here, not only Pt-bridges between purine bases were considered but guanine-cytosine cross-link, too. Influence of the sugar-phosphate backbone was explored in the dinucleotide DNA model, as well. Recently also interactions with amino acids was performed and some of the most important results will be discussed, too.

Dinuclear Rh(II) complexes

Preference for coordination of diaqua-tetrakis-μ-acetatodirhodium to purine DNA bases was examined in the next part of this project. Higher thermodynamic affinity of the Rh-complex to adenine was found in accord with HSAB principle.

Ru(II)-piano-stool complexes

Detachment of the chloro-ligand in [Ruthenium(II)(Arene)(en)Cl]$^+$ was studied in connection with cisplatin activation. Similarly, transition state for process of the water replacement was searched and both thermodynamical and kinetical data for activation and interactions with DNA bases were estimated.

What Controls Enantioselectivity of Carbonyl Reductase?

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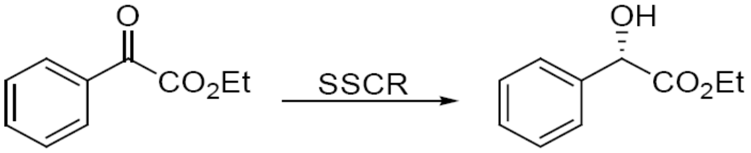
Enantiometrically pure alcohols are important and valuable intermediates in the synthesis of pharmaceuticals and other fine chemicals. Enzymatic reduction of prochiral ketones is the method of choice because of its environmentally benign reaction conditions, broad substrate scope, and high stereo- and regioselectivity. Many alcohol dehydrogenases reduce prochiral ketones to chiral alcohols following Prelog rule, only a handful of dehydrogenases give anti-Prelog alcohol products. We have studied the synthetic application of several alcohol dehyddrogenases, the carbonyl reductase from Sporobolomyces salmonicolor (SSCR) shows different enantiopreference for similar substrates as shown in equation (1) and (2). We have identified the residues in contact with the substrates and changed one or more of these residues caused the enantiopreference reversal of acetophenone reduction (equation (3) and (4)). The docking studies are engaged to understand what controls the enantioselectivity of this enzyme in the enantioselective reduction of ketones, α and β-ketoesters to their corresponding chiral alcohols.



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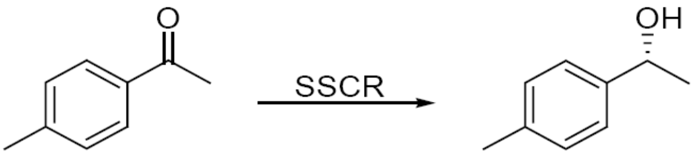

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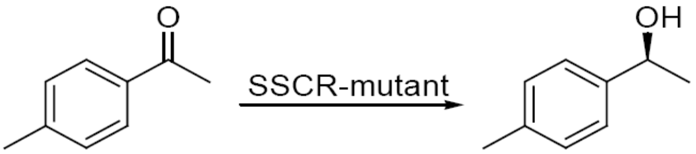

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Computational Prediction of Regio- and Stereoselectivities in the Hydroformylation of Chiral Olefins

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The hydroformylation of chiral substrates produces a mixture of the linear aldehyde (L) and two diastereomers of the branched aldehyde (b and b') whose population, using an unmodified rhodium catalyst (H-Rh$(CO)_3$) under mild reaction conditions, depends on their relative stability at the alkyl-rhodium transition state (TS) level [1]. To determine the overall populations, all possible rotamers of the various Rh-carbonyl adducts must be considered. Alkyl rhodium TS were earlier established as the key step determining the hydroformylation regioselectivity, if the reaction is not reversible at room temperature, by comparing computational and experimental results [2]. Examining the influence of method and basis set on the relative stabilities of the lowest energy alkyl rhodium TS for related chiral olefins, the agreement with available experimental results was only qualitative at the B3P86/3-21G/L2DZ (L2DZ standing for LANL2DZ) level, while a quantitative accord was obtained both at the B3P86/6-31G*/L2DZ or at the B3LYP/SBK(d) levels [3]. Furthermore, the structural features of alkyl rhodium TS (where a second chiral center at the inner olefin carbon appears upon complexation), with larger basis sets, do not present major variations in the distinct computational descriptions for each substrate. Significant differences in relative stabilities of L (actually `l` and `l`'), b and b' can be properly detected in the case of chiral vinylethers, whereas for chiral alkenes, consistently with their lack of selectivity, only small energy gaps were computed. Thus these computational methods should allow the prediction of regio- and stereoselectivity for chiral olefins not yet experimentally screened.

The effect on the hydroformylation reaction regio- and diastereoselectivities due to bulky aromatic substituents, such as benzene or pyrrole rings, as well as of alkyl groups of increasing steric hindrance (methyl, ethyl, n-propyl, i-propyl or t-butyl) at the chiral center is considered. The generation of a new stereocenter with the aid of a chiral catalyst or by substrate-based asymmetric induction is an interesting topic, especially if the involved processes match criteria of atom economy. Olefin hydroformylation, incorporated into a domino sequence, would be the ideal transformation if stereoselectivity could be controlled. A new example of complete 1-3 substrate-induced diastereoselectivity is presented, with a tetrahydroindolizine (coming from intramolecular cyclization of a chiral aldehyde intermediate on the 2-pyrrole position) obtained as the sole diastereomer with the same absolute configuration at C6 and C8 [4], confirmed via NMR (^{1}H, ^{13}C) and IR spectra.

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A Theoretical Study of the Comparative Binding Affinities of PAIIL towards Monosaccharides

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Pseudomonas aeruginosa is an opportunistic gram-negative pathogen responsible for a variety of diseases, which are often life threatening for the patients suffering from cystic fibrosis [1]. It synthesises two lectins: glactophilic PAIL and fucophilic PAIIL [1]. Its virulance is associated with its ability to form biofilms and to secrete toxic compounds. It was demostrated that *P. aeruginosa* induced otitis externa diffusa as well as several respiratory tract infections could be cured by simply the administration of PAIL and PAIIL specific sugars [2]. Previous studies manifests that the PAIIL exhibit a unique binding mode with L-fucose mediated via two calcium ions [3, 4].

To evaluate the high binding affinity of PAIIL towards the fucose and its derivatives, we performed a theoretical investigation of their interaction energies and geometrical flexibilities around binding site. The 10-ns long molecular dynamics simulations of PAIIL, PAIIL-fucose, PAIIL-mannose, PAIIL-fructose, and PAIIL-Me-arabinose were performed in the explicit solvent with physiological condition (NaCl concentration$\approx$0.154 mol/l). It has been observed that ions play crucial role in the active site of PAIIL. More detailed solvent analysis was done. By separating the calculated binding free energies into contributing terms we observed that the most significant contribution comes from the van der Waals and electrostatic energy terms.

Theoretical results of PAIIL systems and phenomenological high binding affinity towards fucose will be argued. The analysis of interaction energy and structural flexibility around the binding site can be exploited for designing ligands molecules, which would have highest affinity towards PAIIL.

Acknowledgements: We gratefully acknowledge support from the Ministry of education, youth and sport of the Czech Republic (grant No. MSM0021622413 and LCO6030). Calculations were performed at the Supercomputing center, Brno, Czech Republic.

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First-Principles Treatment of the Interface Between the Orbital and Orbital-Free Levels of Description in Multi-Scale Modeling

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In various methods used in computer simulations, orbitals are used to describe only a part of the investigated system (*subsystem A*) whereas the rest (*environment*) is described without orbitals. In such methods, the effect of the environment is represented by some additional component of the potential (*embedding potential*), which is usually system dependent and takes different forms in different embedding schemes. It has been shown that the exact embeding potential in such a case can be expressed using universal functionals of electron density[1]:

$$V_{eff}^{emb}\left[\rho_A, \rho_{Total}-\rho_A\right](\vec{r}) = -\sum_a^{N_B} \frac{Z_a^B}{\left|\vec{R}_a^B-\vec{r}\right|} + \int \frac{\rho_B(\vec{r}')}{|\vec{r}-\vec{r}'|} d\vec{r}' + \left.\frac{\delta E[\rho]}{\delta\rho}\right|_{\rho=\rho_{Total}} - \left.\frac{\delta E_{xc}[\rho]}{\delta\rho}\right|_{\rho=\rho_A} + \left.\frac{\delta T_a^{nad}[\rho_1,\rho_{Total}-\rho_1]}{\delta\rho_1}\right|_{\rho_1=\rho_A} \quad (1)$$

where $T_s^{nad}\left[\rho_1\rho_2\right] = T_s\left[\rho_1+\rho_2\right] - T[\rho_1] - T[\rho_2]$ denotes the bifunctional, i.e. the functional of two electron densities, representing the nonadditivity of the kinetic energy of the reference system of non-interacting electrons $T_s[/rho]$. Other terms in the above equation are defined as in the Kohn-Sham formulation of DFT. In the recent years, the embedding potential of the Eq. (1) form has been used in multi-level type of computer simulations of various embedded systems in condensed phase [2]. The potential of the Eq. (1) form differs from the Kohn-Sham orbitals. They are neither the Kohn-Sham orbitals for the isolated *subsystem A* nor form a subset of Kohn-Sham orbitals for the whole system. Morover, the embedding potential of Eq. (1) differs fundamentally for embedding potentials in most of empirical embedding methods because it is neither linear nor homogenous in ρ_A. n this talk, the physical meaning of such differences will be discussed using model system and such common ideas of computational chemistry as orthogonality, charge-fransfer, polarization [3-4].

Acknowledgements: Support from Swiss FNRS is acknowledged.

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A New Energy Density Visualization Scheme for External Field Effects on Molecular Systems

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n the intrinsic field theory of chemical reactions, we have shown that the external field effects on chemical reaction system gives rise to the dynamical potential fields as well as the electrostatic ones. The dynamic as well as the static external filed effects on chemical reaction systems has also been formulated in terms of the differential geometry and called the theory of string model. The string model has been successfully applied to study solvent effects on chemical reactions [1].

In Fig.1, The external effect for chemical reaction systems is shown, where a chemical reaction system A embedded in the environmental medium M is modeled as a parallel-plate capacitor filled with a dielectric. Active role of the dynamic electron transfer from region to region within the chemical reaction system A has also been studied in terms of the Regional DFT; and it should be extended to incorporate the explicit electro "dynamic" nature that obeys the Maxwell's equations [2].

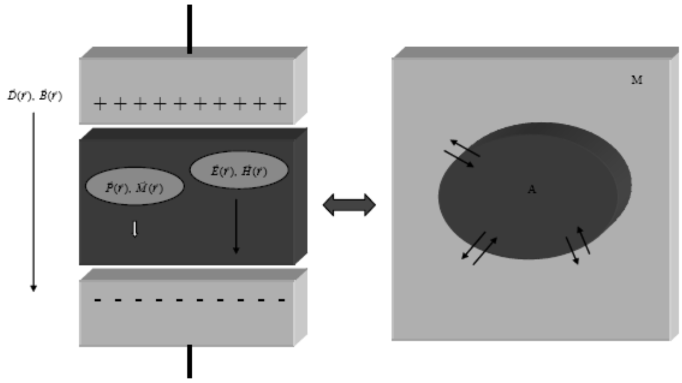

Figure 1: A model of the RIgged QED to incorporate the external motion (M) effects on molecular systems (A).

In order to treat this generic situation systematically, we have developed the Rigged Quantum Electrodynamics (QED) theory which incorporates the field theories of the electromagnetism and quantum mechanics and provides a new energy density visualization scheme [2].

Acknowledgements: This work has been supported in part by Center of Excellence for Research and Education on "Complex Functional Mechanical System" as a COE Program of the Ministry of Education, Culture, Science and Technology of Japan.

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The Effect of Interaction Range and Anisotropy on Surface Tension

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The interfacial tension between two coexisting phases results from differences in the mean intermolecular interactions and microscopic structure in each of the phases. This quantity is important in the nucleation and growth of phases in supersaturated systems (e.g, droplets in a superheated vapor phase).

In this work, multi-canonical Monte Carlo simulations combined with parallel tempering are used to study the structural and thermodynamic properties of an anisotropic-square-well fluid [1]. For this fluid, molecules are modeled as hard spheres that possess attractive patches which can lead to strongly directional interactions. This model has been commonly used to describe the thermodynamic properties of simple fluids and has been previously applied to globular proteins [2]. We have studied the influence of the range of the attractive interaction, as well as the degree and geometry of anisotropy, on the phase behavior and interfacial properties.

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Treating Dispersion Effects in Extended Systems by Hybrid MP2:DFT calculations: Hydrocarbons on Catalyst Surfaces

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Currently used density functionals do not properly account for dispersion interactions which limits the use of density functional theory (DFT) in applications that involve both bond rearrangements and van-der-Waals interactions. Prominent examples are catalytic transformations of organic substrates in the binding pockets of enzymes or on solid surfaces. We will consider the example of hydrocarbon transformations in the pores of zeolites.

Here we propose use of a hybrid QM:QM method [1] which is designed for a reaction between a small or medium sized substrate molecule and a very large chemical system. It combines MP2 calculations for the reaction site with DFT calculations for a large system under periodic boundary conditions. A hybrid MP2:DFT structure optimisation for a cluster embedded in the periodic model is the first of three steps in a multi-level approach. The second step is extrapolation of the MP2 energy to the complete basis set (CBS) limit. The third step is extrapolating the high-level (MP2) correction to the limiting case of the full periodic structure. This is done by calculating the "high-level" correction for a series of cluster models of increasing size, fitting an analytic expression to these energy corrections, and applying the fitted expression to the full periodic structure. We assume that, up to a constant, the high-level correction is described by a damped dispersion expression. Combining the results of all three steps yields an estimate of the MP2 reaction energy for the full periodic system at the CBS level.

For adsorption of isobutene in zeolite H-ferrierite [2], the energies obtained for the formation of the ?-complex, the isobutoxide, the *tert*-butoxid and the *tert*-butyl carbenium ion are -78, -73, -48, and -21 kJ/mol, respectively [3]. This corresponds to corrections of the pure DFT results [2] by -62, -70, -67,and -29 kJ/mol, respectively. Hence, the MP2-corrections are substantial and, perhaps more importantly, not the same for the different hydrocarbon species in zeolites.

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Computational Modeling of Double Metal Cyanide Catalyst for Propoxylation Reaction

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Double Metal Cyanide (DMC) catalysts are a class of molecular salts comprising of a metal cyanide crystalline framework with two different metal centres (M_1=Co,Fe, M_2=Zn)[1, 2]. In recent years DMC catalysts have become industrially important for polyol preparation processes. Their main advantages over more traditional potassium base (KOH) catalyst are twofold: much higher activity, and highly reduced unsaturation of the obtained polyols [3]. Both features result in the possibility of reaching much higher molecular weights than using KOH catalyst. DMC catalysts have been relatively thoroughly investigated with respect to their activity in different preparation routes and operating conditions [2, 3]. At the same time, we are not aware of any theoretical investigation into the exact mechanism of the DMC mediated catalysis to date.

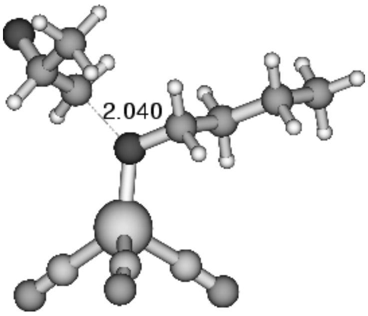

Figure 1: Transition state in the first step of PO polymerisation

In the presented study, we start with the crystal structure of the DMC precursor salt, which has been refined from powder diffraction data. The DMC bulk is then constructed by the substitution of hydroxyl group with chloride anion. The resulting structure is optimised using fully periodic Density Functional (DF) calculations in the planewave pseudopotential formalism with respect to both lattice parameters and atomic positions. Further, the slab model is used to calculate a reconstructed surface of DMC catalyst. From this periodic structure, relevant cluster models are extracted for further calculations of the catalytic cycle.

The full catalytic cycle is investigated in cluster DF calculations using the B3LYP functional and the Los-Alamos Effective Core Potential basis sets. In calculating transition states for the propylene oxide polymerisation, we test for the bimetallic interaction, similar to the one proposed by Moore et. al. [4], but conclude that the spatial constraints of DMC surface render it impossible. In the case of monometallic catalytic centres, our calculations suggest highly active intermediate products, leading to cascade of further polymerisation steps before product re-anchoring to the surface and its final release.

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CYP 3A4: Modeling Substrate Binding and the Electronic State of Oxyferryl Active Site Helps to Understand Reactivity

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Cytochrome P450 enzymes catalyze primary oxidations of endobiotics and xenobiotics and metabolize majority of drugs, transforming the substrate either to active form or to toxic compounds. Hydroxylation of the C-H bond is the main metabolism step thus the understanding of its mechanism and prediction of metabolites is a big challenge in drug design. Quantum chemical modeling has already provided extensive information on major steps in catalytic cycle of cytochrome CYP450 [3]. substrate binding, oxidation of the native form of the enzyme into the active oxyferyl form, and subsequent metabolism. Here we utilize the oxyferryl model of the active center (Cpd I) [3] and focus on its electronic structure (CASPT2) and the substrate transformation (DFT). The metabolism substrate is (S)-N-[1-(3-morpholin-4-ylphenyl)ethyl] - 3-phenylacrylamide (1), active in a cortical spreading depression model of migraine.

Preliminary CASSCF investigation of Cpd I show peculiarities of its antiferromagnetically coupled doublet electronic state with delicate balance between configurations with radical centered either on porphyrine or on cysteine. Only after including dynamical correlation within PT2 scheme the porphyrine-centered doublet becomes the candidate for the ground state, in accord with experimental predictions. Porphyrine radical is believed to play the major role in the activation of C-H bond and in catalytic oxidation of the substrate. Therefore dynamics of electronic structure reorganization may be of significant importance in drug transformation and directing the metabolism towards desired products.

The substrate (1) is believed to metabolize on CYP 3A4 mainly by hydroxylation of the phenyl ring on N-phenylmorpholine moiety. DFT calculations show that all steps in the metabolism proceed on the doublet potential energy surface, with antiferromagnetic coupling preserved in the encounter complex. Transition-state structure for the formation of strongly bound complex reveals the role of morpholine nitrogen bound in ortho position to the oxidized site [4]. Its configurational flexibility compensates for the aromaticity loss on formation of the σ-complex with oxyferryl site, which substantially lowers the energy barrier for the rate-determining step in the drug metabolism. Two geometrical conformations found for the TS, with the phenyl ring either parallel or perpendicular to the porphyrin plane, may lead to two distinct metabolites. Therefore protein environment may favor one of the conformations and become the metabolism router by positioning the substrate and selecting viable conformation of the TS.

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Comprehensive Study of the Effects of Methylation on Tautomeric Equilibria of Nucleic Acid Bases

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Minor tautomers of nucleic acid bases can result by intramolecular proton transfer. These rare tautomers could be stabilized through the addition of methyl groups to DNA bases. A comprehensive theoretical study of this possibility was performed. Molecular geometries of all tautomers were obtained at the DFT and MP2 levels with the 6-31G(d,p) basis set, and single point calculations were performed at the CCSD(T)/6-311G(d,p) level. Tautomers obtained by protonation at the preferred protonation site for methylated isolated bases was compared to their nonmethylated counterparts. The effects of methylation on the relative stabilities of nucleic acid base tautomers are also compared and discussed in this work. The results suggest that some sites on the bases may not be mutagenic and may even stabilize the canonical Watson-Crick form. The results also show that a number of methylation sites can stabilize the tautomers, suggesting possible mechanisms for mutagenic changes. These findings are presented in this work.

Stretching to Understand Proteins

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Mechanical stretching of single proteins has been studied experimentally for about 50 proteins yielding a variety of force patterns and peak forces. Here, we perform a theoretical survey of 7749 proteins of known native structure and map out the landscape of possible dynamical behaviors unders stretching at constant speed. The model used is constructed based on the native geometry. It is solved by methods of molecular dynamics and validated by comparing the theoretical predictions to experimental results.

We characterize the distribution of peak forces and on correlations with the system size and with the structure classification as characterized by the CATH scheme. We identify proteins with the biggest forces and show that they belong to few topology classes. We determine which protein segments act as mechanical clamps and show that, in most cases, they correspond to long stretches of parallel beta-strands, but other mechanisms are also possible. We then consider stretching by fluid flows. We show that unfolding induced by a uniform flow shows a richer behavior than that in the force clamp. The dynamics of unfolding is found to depend strongly on the selection of the amino acid, usually one of the termini, which is anchored. These features offer potentially wider diagnostic tools to investigate structure of proteins compared to experiments based on the atomic force microscopy.

Characteristics of a Wide Spectrum of Dihydrogen Bonded Materials

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The dihydrogen bond (DHB) is a special type of hydrogen bond where the proton acceptor is a hydrogen atom center with excess negative charge. Such interactions are usually designated as X-H$^{+\delta}\ldots{}^{-\delta}$H-Y [1]. Early studies on DHBs indicated that Y is a transition metal or borine, while X-H is typically a proton-donating bond such as O-H, N-H [1]. Later studies justified the existence of a wider spectrum of DHB interactions, even C-H. . .H-C [2].

We have analyzed different complexes where DHBs exist, from those bordering with the weak van der Waals interactions [3] to the very strong interactions which are mostly covalent in nature [4]. The geometrical, energetic and topological parameters derived from Bader theory [5] were analyzed and their continuous changes were found. For example, Figure 1 presents the relationship between the H. . .H distance (in) for the DHBs systems analyzed and the electron density at the corresponding bond critical point (ρ in au), CADHBs(+) designate positively charge assisted dihydrogen bonds which are strong and covalent in nature interactions, closed-shell interactions correspond to those of the medium strength and also to DHBs which border with van der Waals interactions, H■2 molecule is also indicated. It is well known that the greater electron density at BCP corresponds to the stronger interaction [2-5]. For the narrow ranges of distances this relationship is linear but for the wider spectrum of interactions this is exponential or of the similar functional type, but non-linear. Such a situation is observed in our complexes (Figure 1). The analyses of the nature of DHBs seem to be very important since it was pointed out that such interactions are very often the preliminary stage of the uptake of free gaseous hydrogen. Thus, these systems may be treated as those where hydrogen storage is possible.

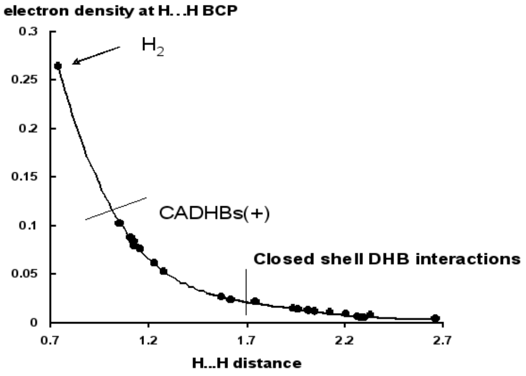

Figure 1: The H. . .H distance versus the electron density at BCP.

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Why Are Strained Hydrocarbons Worth Studying?

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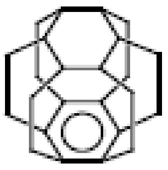
Progress in organic synthesis in the recent 50 years has allowed chemists to obtain hydrocarbons with spatial structures strongly departing from the standard ones in harmony with van’t the Hoff and LeBel hypotheses. This domain is exemplary for the mutual cooperation of synthetic and theoretical chemistry, and the question why such systems are worth studying often arises. In particular, it is of importance for the justification of grant proposals, which nowadays are required to show immediate applications. We were confronted with the question of applicability when reporting a computational grant on cyclophanes such as hexahydrosuperphane [1].

Serendipity, in which scientific discoveries find their ways to marketable applications, will be shown stressing that, contrary to engineering, the aim of science is to gain a better understanding of the world surrounding us and to satisfy our curiosity. In the shorter or longer run, this can bring practical applications, but in most cases one cannot foresee them. One of the best examples of a complicated way of development of a scientific domain are fullerenes. The prediction of C_{60} (**2**) by theoreticians has been forgotten and the Kroto, Smalley, and Curl analysis of their experimental finding has been extremely difficult without the knowledge of the works by Osawa, Yoshida, Bochvar, and Galpern [2]. Numerous exciting applications, mainly ǎof endohedral fullerene complexes, have been proposed [3], none of which has been realized until now. Nevertheless, molecules with cage structures of usually high symmetry, exhibiting the system of nonplanar conjugated bonds and untypical salt character, are fascinating objects for studying although we do not know when these studies will bring practical gains. As shown by the discussion of the existence of the central bond in [1.1.1]propellane (**3**), studies of hydrocarbons with unusual spatial structures allow us to better understand the nature of the chemical bond [4].



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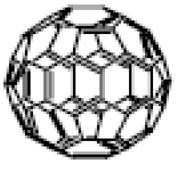

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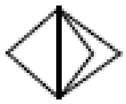

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Acknowledgements: I thank ICM, Warsaw University for a computational grant.

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Accuracy of Gas Phase Acidities of Carboxylic Acids Predicted by Direct Scaling of Harmonic Vibrational Frequencies rom *ab initio* Calculations - A Perspective for Precise pKa Estimation

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The gas phase Gibbs free energies for the dissociation reaction ($\Delta G^{298.15}$) of fourteen carboxylic acids were calculated on the SCF, G3, and CBS-Q levels. The accuracy of calculations was critically compared to experimental data. Since all results suffer from systematic errors, the procedure of vibrational frequencies scaling was proposed. Thus, two parameters were adjusted for best fitting theoretical to experimental values of $\Delta G^{298.15}$. The scalling frequencies was performed for both the deprotonated and neutral form of carboxylic acids. Results suggest the great effectiveness of such a procedure since for all applied basis sets within the SCF framework an accuracy was achieved below the experimental error. Besides, what is most promising, low level HF calculations lead to accuracy comparable to or even exceeding the precision offered by sophisticated model chemistries.

Acknowledgements: Results were in part obtained based on computational grants from PCSS (Poznań Supercomputing and Networking Centre, Poland). The allocation of computing time is greatly appreciated.

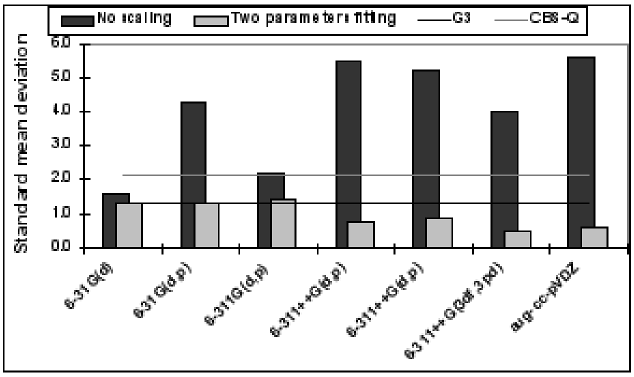

Figure 1: The accuracy of $\Delta G^{298.15}$ prediction by means of SCF calculations In variety of basis sets as well as by G3 and CBS-Q model chemistries.

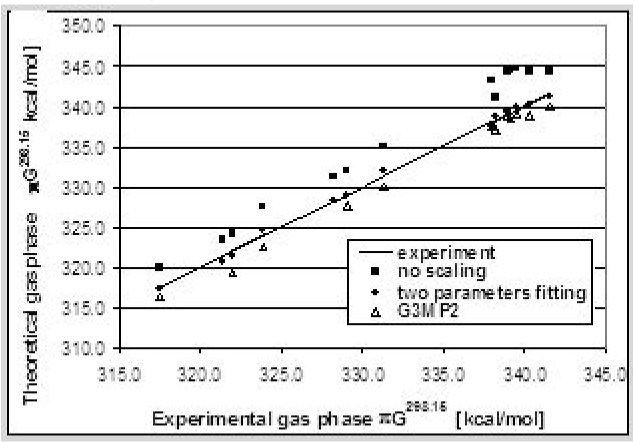

Figure 2: The correlation between theoretical and experimental values of $\Delta G^{298.15}$ calculated on HF/aug-cc-pVDZ and G3 levels.

NMR Parameters in RNA Molecules and their Correlation with Molecular Structure

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The functional diversity of nucleic acids (NAs) makes their study crucial for deeper understanding of biological processes. Structure parameters used for the description of NAs are torsion angles of the backbone (α, β, γ, δ, $epsilon$, ζ) shown in Figure 1, sugar conformation (C2'-endo or C3'-endo), and glycosidic torsion angle (χ) which designate orientation of nitrogenous base relative to sugar moiety.

The goal of this study was to determine the correlation between parameters of nuclear magnetic resonance (NMR) spectroscopy and the local architecture of distinct patterns of RNA dinucleotides.

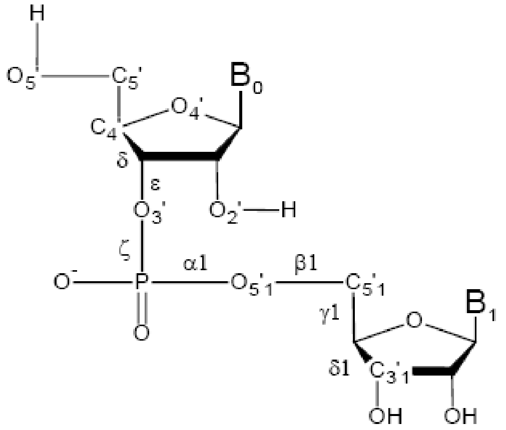

Figure 1: Scheme of dinucleotide monophosphate.

Distinct patterns of RNA dinucleotides were studied by quantum chemistry calculation methods with the aim to obtain NMR shifts and spin-spin coupling constants, including water solvent modeled by the PCM method. Calculated NMR parameters, in particular the J-couplings, were correlated with the structure of RNA dinucleotides. In addition we calculated the effect of substitution of nitrogenous bases on J-coupling in the backbone. The three bond J-coupling constants can be used for the determination of torsion angles. Our theoretical data were compared with available experiment from the literature as well as with empirical Karplus curves [1, 2].

The torsion angles can be naturally grouped into the three group according to correlation with similar NMR parameters: α can be grouped with ζ, β with ϵ, and γ with δ. Torsions β and ϵ can be determined by the three-bond coupling constants which are known and frequently measured. Torsion angles γ and δ can be correlated with the three-bond coupling constants, we also calculated the correlation between the torsion angles with the two- and the four-bond coupling constant. Torsions α and ζ can't be associated with any of the three-bond coupling constants but we calculated their correlation with the two bond coupling constants ^{2}J(C,P).

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Quantum Chemical Study of Cu(I)/Cu(II) Cations in a Peptide Environment

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The first part of this work[1] concerns small complexes of Cu(I)/Cu(II) cations with variable hydrogen sulphide-amine-aqua ligand field. Investigations of such complexes are neccesarry in order to obtain deeper insight into normal behavior of copper cations in the presence of S-, N-, and O-types of ligands. These ligands represent biologically most common environment for copper. At the DFT level of theory, energy analyses revealed several trends: (i) The am(m)ine complexes are the most stable, followed by those containing the aqua and hydrogen sulfide ligands, which are characterized by similar stabilization energies. (ii) The most preferred Cu(I) coordination number is 2 in am(m)ine or aqua ligand fields. A qualitatively different binding picture was obtained for complexes with H_2S ligands where the 4-coordination is favored. (iii) The 4- and 5-coordinated structures belong to the most stable complexes for Cu^{2+}, regardless of the ligand types.

The second stage of present work concerns active centers (figure 1) of reduced and oxidized blue copper proteins. The study is based on partially and fully optimized models. Both gas phase and in polarized continuum model (water and protein-like environment) approaches were used at the DFT level. Single-point analyses examine energetic relations, spectral features, and vertical and adiabatic ionization potentials.

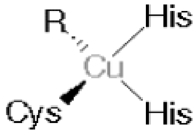

Figure 1:

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Poster abstracts

in alphabetical order of the presenting author’s last name

Poster session A (Session V) - September 11 (Monday)
Posters: P2, P4-P6, P8-P11, P13-P14, P16, P18-P28, P30, P32-P38

Poster session B (Session XV) - September 14 (Thursday)
Posters: P1, P3, P7, P12, P15, P17, P29, P31, P39-P55, P57-P58, P59

DFT Studies on the Reaction Mechanisms of Intra- and Extradiol Dioxygenases

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The catalytic reaction mechanisms of three different ring-cleaving dioxygenases have recently been studied with the hybrid density functional B3LYP. The enzymes studied are: Fe(II)-dependent human homogentisate dioxygenase (HGD) [1], Mn(II)-binding homoprotocatechuate 2,3-dioxygenase (MndD) [2], and the Fe(III)-dependent protocatechuate dioxygenase (PCD) [3]. All these metalloenzymes catalyze the oxidative ring fission where both atoms of dioxygen are incorporated into the acyclic products. In these theoretical investigations reliable models of the enzyme-substrate complexes (up to 90 atoms) have been used to characterize the structures and energetics of intermediates and transition states defining the enzymatic reaction path. The comparison of these results, which is presented in this poster, provides valuable insights into the similarities and differences between the mechanisms utilized by these enzymes, including the factors controlling the type of the cleavage reaction, i.e. intra or extradiol.

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Mechanism for DNA Triple Helix formation: a Computational Study

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We present a theoretical study of the mechanism of formation of triple helical structure by association of a double helix containing an oligopyrimidine · oligopurine (oligoY · oligoR) sequence with a single-stranded triple helix-forming oligonucleotide (TFO) [1]. The formation of this type of triplex critically depends on the protonation of the imino group of the TFO cytosines [2], forming Hoogsteen hydrogen bonds with guanine of a GC Watson-Crick base pair.

As a first step we investigate the thermodynamics of the triplex $\leftrightarrow$ duplex $+$ TFO transition by computing the entalphy of formation of three different system involving 15 mer pyrimidine oligonucleotide as third strands. The calculations are done using AMBER99 force field of the TINKER package [3] and GB/SA implicit solvent model for the water.

Insights into the mechanism of these reactions can be provided by investigation of the potential energy surface of the proposed zipping pathway (Figure 1). Initial guess of stationary points, both minima and transition states, can be obtained by rotation around dihedral backbone angles of the third strand of the triplex. Results of the calculations allow us to describe a reaction mechanism that agrees quite well with the proposed nucleation-zipping model.

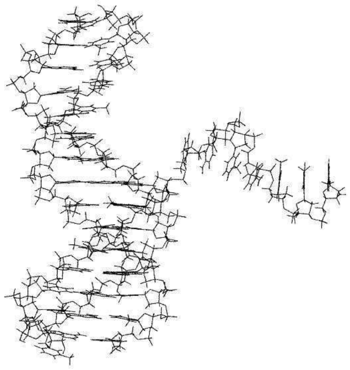

Figure 1: Zipping Mechanism.

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PLDB - Protein Ligands DataBase

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The biological activity of proteins relies on their interaction with non-protein-molecules which are stated as ligand. Term "ligand" regards to all small molecules which are the part of the protein in its natural state (in vivo). Ligands participate very frequently in enzimatic reactions being generally responsible for biological activity of the protein. The computer simulation of protein-ligand interaction requires the information about properties of ligand molecule (e.g. its electronic structure, partial charges, van der Waals paramters).

The Protein Data Base, PDB, [1] contains information (crystal structure) about proteins also in form of their complexes with ligands. The simulation of protein - ligand interaction requires the knowledge of parameters describing the ligand molecules. The extraction of the ligands present in the PDB and creation of the library of ligands bound to proteins (natural and engineered) is assumed to be presented in the assumed library. This library will contain:

1. a complete set of ligands,
2. optimal structure according to quantum chemistry calculations,
3. partial charges distribution - according to quantum chemistry calculations,
4. parameters for torsional potential (free rotations),
5. parameters for non-bonding interactions,
6. structural differences between optimal (step 1.) and complexed structural forms,
7. energy comparison between free molecule and its complexed form.

Such a ligand library will be useful not only for fast identification of natural ligands of proteins and access to the set of parameters characterized ligands' molecules but also for computer aided drug design created on the basis of the natural ligands. The library of this type can be also useful for simulation of pathological processes like complexation of toxins during the therapeutical procedures or in case of pathological metabolisms of some chemical compounds. The search for potential target protein molecules binding these non natural ligands can also be performed on the basis of the ligands library. Particularly, the investigation of all interactions of unproper metabolites of aspirin, as an example of application the ligand library is planned. The ligand library will be applied for drug design for individual therapy, which is planned to be introduced in medicine in a close future.

Our ligand library is based on MySQL system with access by WWW and is operated by PHP. All quantum chemical calculation will be done by using Gaussian03 package [2].

Acknowledgements: Chemical quantum calculations are performed at the Research Centre in Juelich (project no. 2249).

[1] www.rcsp.org
[2] www.gaussian.com

Multiple Proton Transfer in Some Molecular Systems. Implications for Crystalline Phases

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The proton transfer reactions are the simplest but very important in many chemical problems as well as in some biological processes. The multiple proton transfer seems to play an important role in quantum chemical interpretation at molecular level of some biological processes like mutations, aging and cancerogenic action. It has been illustrated that in most cases the proton is transferred, however, there are systems where at least in the excited electronic states hydrogen atom might be responsible for the tautomeric interconversion [1].

In the case of model molecular systems the ab initio methods have been applied for cases known to require the multireference description i.e. the non-dynamical correlation energies have been studied within the different basis sets for model hydrogen bonded systems. We have shown that the non-dynamical correlation energy does not influence to a great extent the results of calculation for hydrogen bonded systems.

In the solid state the single and double proton transfer processes were investigated for a number of model molecular systems These processes have been studied for crystalline hydrogen bonded systems at non-empirical level where one, two and three-dimensional crystals were considered. The results of computations enable for reasonable interpretation of low potential barrier for the proton transfer observed experimentally by NMR technique for molecular crystals of carboxylic acid dimers [2]. The possible mechanism of the proton movement [3] was considered as well.

Acknowledgements: This work has been partly sponsored by Wrocław University of Technology. The numerical calculations were performed in part at Wrocław Networking and Supercomputing Center.

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Molecular Dynamic Simulation of the Effects of Oxidative Damage on the Structure of Telomeric DNA

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Very important part of chromosomes are their ends caled telomers. Telomers are protein - DNA complexes. In their structure we can find two repeating binding factors (TRF1 and TRF2), which are specifically bound with telomeric DNA.

Telomers play a critical role in keeping genomic stability.

It has been proved that mild oxidative stress induces loss of telomeric DNA. Some studies have reported that a presence of single 8-oxo-guanine in telomeric DNA reduced the percentage of bond protein binding factors by 50%, compared with standard nondamaged DNA. The presence of multiple 8-oxo-guanine lesions in thandem thelomeric repeats, has more dramatic conseqences and make binding proces nearly impossible [1].

Name	Seqence
Stand.	CCGTACTTAGGGTTAGGGTTAACA
8oxo1	CCGTACTTAGXGTTAGGGTTAACA
8oxo2	CCGTACTTAGXXTTAGGGTTAACA
8oxo3	CCGTACTTAXXXTTAGGGTTAACA
8oxo1-1	CCGTACTTAGXGTTAGXGTTAACA

Table 1: Oligonucleotides used in MD simulations.

In my research I want to define how the presence of 8-oxo-guanine changes structure of telomeric DNA. I used molecular dynamic methods to obtain structures of standard and modificated telmeric DNA. In my simulations I used oligonucleothides which consist of 24 base pairs.

[1] Opresko, P. L.; Fan, J.; Danzy, S.; Wilson, D. M. III; Bohr, V. A. *Nucleic Acids Res.* **2005**, *33* (4), 1231–1239.

Studies of Hydrogen Bonds in C-H· · ·O=P by NMR Chemical Shifts and $^{3h}J(^{13}C\text{-}^{31}P)$ Spin-Spin Coupling. Correlation of Experimental and *ab inito* Data

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Wrocław University of Technology, Poland,
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Jackson State University, MS, United States of America,
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Hydrogen bonds are fundamentally important in stabilizing specific intermolecular interactions. They are important in the formation of secondary structures, conformational preferences, and aggregation processes. The hydrogen bonds C-H· · ·O are much weaker interactions, but there are some examples where they are manifested. Organophosphonic compounds reveal diverse and interesting biological and biochemical properties, and are used as inhibitors of various enzymes, antibacterial agents, plant growth, calcium metabolism regulators and hypertensive and immunosuppressive agents.

We present NMR experiments, which shows phosphoryl oxygen (P=O) interactions; intermolecular with C-H proton from chloroform, and with CH_2 protons from diethylphosphonate dimer, and intramolecular interaction with protons from CH_2 group in compound show in Figure 1. The ^{13}CNMR spectrum for the CH_2CH_3 group (Figure1) indicate the presence of $^{3h}J_{CP}$ spin-spin interactions across C-H· · ·O=P.

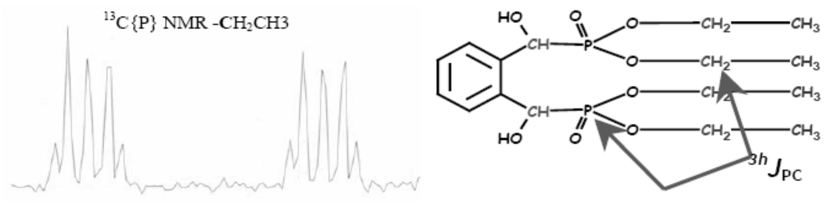

Figure 1: ^{31}C{P}NMR spectrum group CH_2.

An analysis of the CSD crystallographic database for C-H· · ·O=P interactions shows a correlation between *ab initio* calculated and experimental values - basicity of phosphoryl oxygen atoms, chemical shift, and spin-spin coupling.

Acknowledgements: Calculations were performed at the Wrocław Centre for Networking and Supercomputing, Poznań Supercomputing Networking Center, and Academic Computer Centre in Gdańsk.

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The Theoretical Study of Five Heterocyclic Derivatives of Carbazole – Monomers Electroconducting Polymers

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Polymers containing carbazole and fluorene moieties in the main chain or side chain have attracted much attention because of their unique properties which allow various photonic applications such as photoconductive, electroluminescent, and photorefractive materials. To control the electronic and optical properties of such polymers one may introduce electron-rich heterocycles at the terminal polymerization sites to prepare multi-ring electropolymerizble monomers. The introduced heterocycles possessing the ability to electrochemical polymerization are: thiophene, ethylenedioxynothiophene, furane, methylopyrrole, and pyrrole.

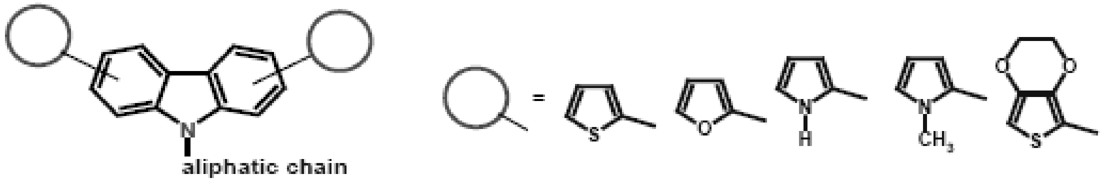

Figure 1: The structrure derivatives of carbazole.

The differences between HOMO-LUMO gaps, vertical ionization potentials, and distribution of total atomic spin densities of radical cations of the studied molecules could indicate the expected electropolymerization properties.

The electronic states of derivatives of these carbazoles and fluorenes were elucidated by molecular orbital calculations using the density functional theory (DFT) utilizing the Becke-type three parameters functionals (B3LYP) and the 6-311G(d,p) basis set. The reactivity for coupling reaction of thiophenes derivatives are inferred from calculated unpaired electron spin densities of the respective radical cations, and ionization potentials which correspond to energies for generating radical cations during oxidative processes.

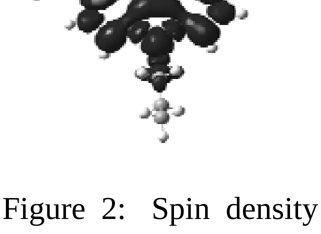

Figure 2: Spin density of N-butylo-3,6-bis (2-furane)carbazole.

Acknowledgements: Support from Wrocław University of Technology grant No. 332079 is acknowledged. Calculations were performed at the Wrocław Centre for Networking and Supercomputing.

Reactivation Mechanisms for Sarin-inhibited Acetylcholinesterase by Oxime: A Model DFT Study

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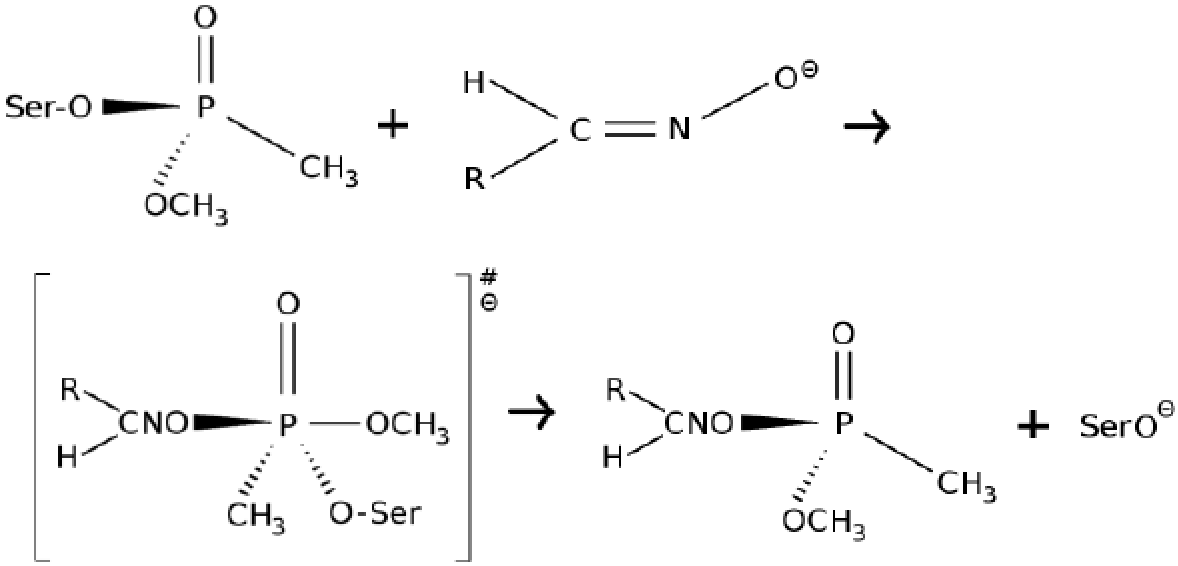
Acetylcholinesterase (AChE) is the enzyme responsible for signal transducing in neural synapses. Various organophosphate neurotoxic agents - sarin, tabun, soman and VX - have the ability to form phosphonate ester bond to the serine in the active site of AChE. The enzyme activity is blocked due to more stable nerve agent AChE adducts. These adducts are proposed to undergo dealkylation by a carbonium ion mechanism, resulting in C-O bond cleavage of the phosphonate ester bond and the loss of the enzyme activity of AChE (aging). In most cases this leads to death by respiratory failure. Experimental investigations reveal that the enzyme activity can be efficiently recovered by applying the oxime as the antidote. It is therefore crucial to shed light on the characterizations of mechanisms on the reactivation of the nerve agent inhibited AChE by oxime as follows:



In our study the above pathway for the reaction between the sarin-AChE adduct and oxime has been theoretically explored at B3LYP/6-311G(d,p) level.

Theoretical Study of the Concerted Proton Transfer in the Ground Electronic State of the Double Hydrogen Bonded Formic Acid Dimer

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The carboxyl functional group (-COOH) is a fundamental building block of organic acids, whose simplest representative is formic acid. The formic acid dimer is one of the most extensively studied systems both experimentally and theoretically since it forms a quite strong double hydrogen bond and the measurement of its gas phase IR and Raman spectra is fairly easy [1-3]. It is also one of the simplest model systems in which a multi-proton transfer can be observed.

The fundamental motivation of this study was relatively small amount of information concerning the electronic structure and proton transfer dynamics in the excited states of the formic acid dimer. Therefore, we have determined the structural parameters of the formic acid monomer and dimer, its IR and UV-VIS spectra as well as the ionization potentials. Moreover, we have investigated the mechanism of the concerted intermolecular proton transfer. The ground and low-lying excited state properties of the monomer and dimer of formic acid have been established using complete active space self-confident field (CASSCF) and second order multireference Möller-Plesset perturbation theories (CASPT2) in the ANO-S basis set.

Acknowledgements: We thank the Wroclaw Supercomputing and Networking Center (WCSS) for a generous allotment of computer time.

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Activation of Ruthenium(II) Complexes and their Interactions with DNA bases

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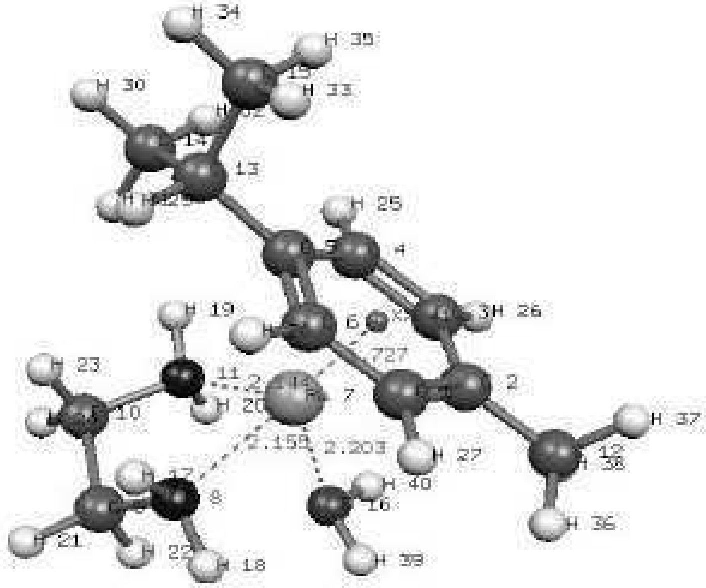
Recently, Ru(II)-piano-stool complexes were reported as promissing anticancer drugs in Sadler's group [1,2]. Replacement reactions between [Ruthenium(II)(Arene)(en)X]$^{2+}$ complexes (X=Cl$^-$, H_2O, OH$^-$, guanine, adenine, cytosine, and thymine) were studied. DFT/MP2 calculations were performed in both gas phase and COSMO regimes. Bonding energies of individual ligands were determined. Relatively strong metal-arene interactions were found in comparison with DNA base coordinations.

In the supermolecular approach, reaction profile for process of the chloride replacement by water was examined. Both thermodynamical and kinetical description of this process was obtained and compared with similar process of the cisplatin activation.



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CO_2 Sorption on N-, O-, and OH-substituted Carbonaceous Materials. A computational Chemistry Study

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Physicochemistry of Carbon Materials Research Group, Toruń, Poland

It is well-known that the detailed and complete description of the sorption processes on carbonaceous adsorbents is still a key problem, the solution of which is still far from complete. Many aspects should be taken into account in modeling sorption processes: different types of the intermolecular interactions, the orientation of adsorbate molecules with respect to the adsorbent, the deformation of the adsorbent and adsorbate, the influence of doping atoms (treated as a source of heterogeneity), and so on. Thus, theoretical studies of intermolecular interactions between an adsorbate and adsorbent on the basis of computational chemistry (ab initio, DFT, and QM/MM) have recently played a very important role [1].

A systematic molecular modeling study of CO_2 chemisorption on carbonaceous surfaces has been performed by Montoya et al. [2] and Radovic [3]. The first observed that the enthalpy of sorption remains almost constant as the model size increases, and it is distinctively different for formation of the same complex on different types of active sites. Radovic noticed that simply removing H atoms from the graphene edge ('creating' carbon active sites) without examining the resulting spin multiplicity issues is convenient, but may be unrealistic and misleading.

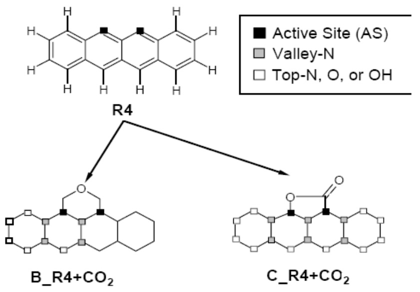

Figure 1: Different CO_2-carbon modelclusters: parent (R4) and N-, O-, and OH-containing ones.

In this study we investigated the reaction of carbon dioxide with different four ring (R4) models with two adjacent unsaturated atoms (treated as the active site) in the zig-zag position. Lactone and heterocyclic complexes were taken into account. We extended investigations for homogeneous systems [2, 3] to those containing N-, O-, or OH- (Fig. 1). Calculations were performed using Gaussian 98 (B3LYP with the 6-31G(d,p) basis set) [4]. The mechanisms of CO_2 chemisorption are discussed on the basis of well-known reactivity parameters and enthalpies of reactions (T=298 K, p=1 atm.).

Acknowledgements: The authors acknowledge the computer cluster at the Information and Communication Technology Center of the Nicolaus Copernicus University (Toruń, Poland).

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Argon Adsorption on Heterogeneous Carbon Surfaces: Accesible Pore volume and Width

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[2]Institute of Physical Chemistry, Polish Academy of Science, Warsaw, Poland

Most carbonaceous adsorbents are disordered materials. Several authors investigated the effects of geometric heterogeneity on adsorption and on the results of characterization methods by performing advanced numerical studies using simple models (i.e. slit - like pores) [1]. On the other hand, other studies suggested that deviations from this ideal pore geometry significantly change the behavior of confined fluids [2]. Consequently, the estimation of surface area, pore volume or density of adsorbate is very complicated (for defected narrow pores, especially). Moreover, the results of our recent studies [1] and those published by Wongkoblap and Do [3] show that the selection of the potentials for molecular simulations should be made with care.

In the current study, we investigate the influence of the defect of ideal graphitelike surface (i.e. a graphitized carbon black surface and the walls of carbon slit-shaped pores) on adsorption. Firstly, we assume infinite carbon slit pores in order to model carbon blacks. The infinite pore model is too ideal to reflect the carbon structure since the pore length is strictly finite and the real carbon contains functional groups, chemical impurities and defects on the basal graphene layers [2]. As a result, the interaction potential between a molecule and a solid surface is not only a function of the distance z between the molecule and the surface but also on the location *(x, y)* with respect to the surface. To describe correctly the physical adsorption, a real carbon pore of finite length and carbon surfaces as graphene layers comprising of carbon atoms arranged in a hexagonal pattern as well as the surface heterogeneity should be taken into account. The grand canonical Monte Carlo (GCMC) simulation [4] is used to study the adsorption, the calculation of effective pore width, pore volume, and density of adsorbate.

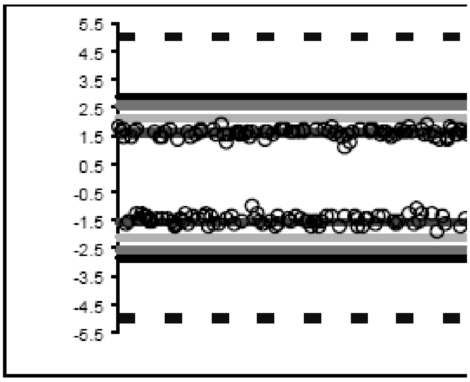

Figure 1: Snapshot of Ar atoms (circles) adsorbed in an ideal carbon pore (lines - effective pore widths calculated assuming the various definition).

Acknowledgements: The authors acknowledge the computer cluster at the Information and Communication Technology Center of Nicolaus Copernicus University (Toruń, Poland).

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Modeling of Isotopomeric Molecular Clusters in Electron Ionisation Mass Spectra

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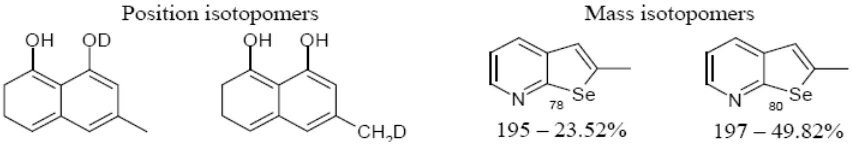
Each ionic species produced in a mass spectrometer is normally observed as a cluster of peaks. The intensity ratios for these peaks are a unique representation of the isotopic abundance ratios of the elements that are comprised in the ion. The term "isotopomers = isotopic isomers" denotes compounds with the same elemental composition and structure but different isotopic composition and refers to compounds of different isotope locations.



The isotopomer pattern can give valuable information about the elemental composition of an ion and its molecular precursor. An understanding of the isotopomer pattern facilitates a more effective interpretation of a mass spectrum.

The mass of the isotopomer defined as $(E_1)_{n1}(E_2)_{n2}(E_3)_{n3}\ldots(E_z)^+_{nz}$ can be calculated by

$$m_j = \sum_{i=1}^{z}(n_i \cdot m_{E_i})$$

in which n_i denotes the number of the isotope atoms and m_E the accurate mass of the isotope. The fractional abundance of the single isotopomer is dependent on the natural isotope abundances, $A_j = \prod_{i=1}^{z} A_i^{n_i}$, and the peak $A_j = \sum_{k=1}^{p}\left(\prod_{i=1}^{z} A_i^{n_i}\right)_{m_i=const}$ intensity is the sum of all isotopomers with the same masses.

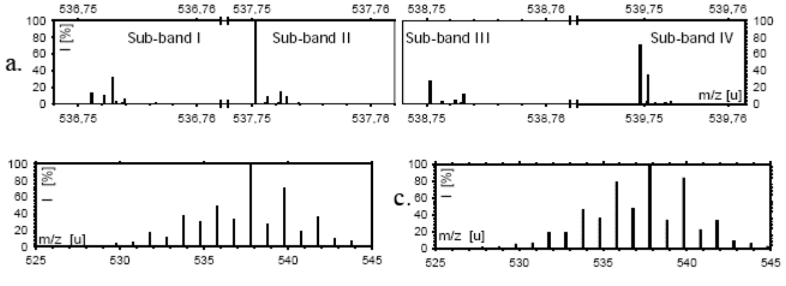


Figure 1: Modeling of the molecular ion cluster of the tris(benzo[*b*]selenopheno) [2,3:2',3':2",3"] benzene $C_{24}H_{12}Se_3$: a) a fragment of the accurate mass model, b) high-resolution model, c) low resolution model.

$$\text{high resolution model (b)}: I_{l-r} = \underset{i=\left(\frac{m}{z}-0.5\right)}{\overset{\left(\frac{m}{z}+0.49\right)}{\mathbf{MAX}}}(I_p), \quad \text{low resolution cluster (c)}: I_{l-r} = \sum_{i=\left(\frac{m}{z}-0.5\right)}^{\left(\frac{m}{z}+0.49\right)} I_p$$

Causes of Rare Tautomer Forms Stabilization of DNA Bases Under Dimers Formation and DNA Synthesis

Helen A. Grebneva

Donetsk Physical and Technical Institute, NAS of Ukraine, Donetsk, Ukraine

After ultraviolet (UV) irradiation, photoproducts are formed in a DNA molecule. In most cases these are cyclobutane pyrimidine dimers and (6-4) adducts. At present, the generally accepted hypothesis, in its various modifications, relates the nature of a mutagenesis exclusively to properties of a DNA-polymerase, which sometimes wrongly incorporates accidental nucleotide bases opposite the dimers instead of correct ones. There is a number of experimental facts which contradict the standard hypothesis. A mechanism of changes in the tautomeric state of bases has been worked out for the case of ultraviolet quantum absorption by DNA molecule. It is shown tautomeric state of bases may change under dimer formation. It is founded 7 new rare tautomeric forms of the guanine and cytosine and 5 in thymine and adenine. It is shown such rare tautomeric forms are main cause of targeted and untargeted mutagenesis [1].

All rare tautomeric forms of bases will be stable as upon dimer formation the DNA strand becomes curved resulting in the elongation or breakage of hydrogen bonds between the bases. In the case of elongation the shape of potential curve changes. The second minimum becomes deeper. That's why, the hydrogen atom will come to the partner in hydrogen bond, as a result of processes described in [1], and the new tautomeric state will be stable at a small elongation of the hydrogen bond.

An important stage for increasing the accuracy of DNA synthesis is that of identification of nucleotides and nucleotide pairs. The identifying ability of polymerases is improved, in particular, by removing water from enzyme's active center. The absence of water at the active centers of polymerases provides the conservation of tautomeric states of bases participating in DNA synthesis,. when the DNA molecule is single-stranded.

It is not excluded that when different enzymes are active the DNA molecule will for a time exist in the form of one strand. Let us estimate a possibility, for the bases in rare tautomeric forms, of transformation to canonical tautomeric states because of the contact with water molecules. The experiment shows that the lifetime of "free" guanine, i. e. the time till it links a water molecule, makes 0,1 to 10 s and even 1000 s, where the meant are guanine molecules that are in water medium. For guanine present in DNA strand the time is much higher. Different DNA polymerases synthesize nucleotides at a rate of 10 to 1000 per a second. Let during DNA synthesis the DNA strand be (in the single-stranded form). The time for which there will be no enzyme protection is defined by the rate of enzyme activity. For the DNA polymerase V it will be not higher than 0,1 second. As the time for the base to link water molecule and to change the tautomeric state is higher than 0,1 s, we see that the process is low-probable.

Acknowledgements: This work was facilitated by The State Fund for Fundamental Research of Ukraine (Grant No F7/208-2004).

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Changes in Structure of DNA Bases as one of the Reasons of the Untargeted UV-mutagenesis

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At present, the generally accepted explanation of mutagenesis nature rests exclusively upon the idea that it is conditioned by sporadic errors of DNA polymerases devoid of the exonuclease (proof-reading) activity, such as the NA polymerase IV or V E. coli. However, such an approach can't explain some phenomena of UV mutagenesis ad contradicts some experimental facts. Mutations occur frequently opposite the dimers (the targeted mutagenesis). Sometimes they originate in a small vicinity of dimers (the untargeted mutagenesis).

A model of ultraviolet mutagenesis has been developed. It rests on the fact that during the formation of photodamages the tautomeric state of their constituent DNA bases can change [1]. It is shown that opposite such photodamages the DNA polymerase incorporates canonical bases which can form hydrogen bonds with template bases. The SOS synthesis with the help of the DNA polymerase III, when exonucleases are suppressed by the "sliding clamp" mechanism, or with the help of the DNA polymerases IV or V E. coli having no exonuclease activity at all has been analyzed. It has been shown that in this cases the photodimers with bases in rare tautomeric forms can result in transitions, transversions and one-nucleotide gaps of targeted and untargeted types [2].

Several mechanisms of the untargeted mutagenesis have been developed. Rare tautomeric state of the G-C pair, when here occurs the double protonic transitions (G*-C*), is stable. It is shown that when the DNA with such damages is synthesized with the help of DNA polymerases IV or V E. coli, the G-C→A-T transitions and G-C→C-G homologous transversions will grow in number rapidly. These results completely agree with the experimental data on the operation of genes mutators. The same mutations will be formed during the SOS synthesis if G* or C* will be in a close (10-15 bases) vicinity of dimer [2].

The five new tautomeric states of thymine and adenine and the seven of cytosine and guanine will be stable in a small vicinity of dimer [3]. They may become a source of mutations during the SOS synthesis. We consider that the base pair with Watson-Crick type geometry are formed when the hydrogen bonds are formed between template and incorporated bases. All the types of transitions, transversions as well as one nucleotide gaps are potential in that case. In the case of closely located dimers in the both strands, the adenines A^*_i (i=1-5) or guanines G^*_i (i=1-7) that are in rare tautomeric states can be a source of untargeted mutations [2].

Acknowledgements: This work was facilitated by The State Fund for Fundamental Research of Ukraine (Grant No F7/208-2004).

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Optimizing the Parallel Tempering Monte Carlo Method - Insights from Statistical Mechanics

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The Parallel tempering (PT) Monte Carlo sampling scheme has been already applied to study different systems, including spin glasses and biomolecules. In this work we examine the efficiency of PT simulations and propose an iterative procedure for the optimal selection of the replicas' temperatures. The method returns a set of temperatures for a PT simulation for which the overlap of distribution of states (referred as an overlap ratio) measured for every pair of adjacent replicas remains constant. To illustrate this idea we test the procedure on a lattice Go-type protein model. The proposed approach is based on the most fundamental thermodynamic properties of modeled system. Thus, the method could be applied to virtually any system governed by the canonical ensemble. We also discuss the connection between the overlap ratio and the efficiency of sampling. In particular, for the model protein system studied in this work, we found that there exists an optimal spacing of replica's temperatures for which the folding time is the shortest with well-separated distributions of the near-native states and random coil states, respectively.

BBQ - Backbone Building from Quadrilaterals: An Algorithm That Outperforms Existing Methods

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In this contribution we present an algorithm for protein backbone reconstruction that comprises great computational efficiency with high accuracy. **BBQ** program has been extensively tested both on native structures as well as on near-native decoy models. Obtained results provide a comprehensive benchmark of existing tools and evaluate their applicability to a large scale modeling in a reduced representation.

BBQ combined with our larger project **BioShell** creates a toolkit for performing common tasks in protein structure modeling like structure clustering, distance geometry calculations, data conversion between various file formats, fast data processing and analysis.

The Molecular Basis of Urokinase Inhibition: From the Analysis of Intermolecular Interactions to the Prediction of Binding Affinity

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Urokinase–type plasminogen activator (uPA) is a trypsin–like protease that plays a crucial role in angiogenesis process. In addition to the physiological role in healthy organisms, angiogenesis is extremely important in cancer growth and metastasis and its control constitutes a promising approach in anticancer therapy. The (α–aminoalkyl)phosphonate diphenyl esters are well known as highly efficient serine protease inhibitors. In general, it has been suggested that specificity in this case depends essentially on the inhibitor–protein interactions in S1 pocket [1]. However, the actual mode of this class of urokinase inhibitors binding has not yet been confirmed experimentally. Since the X–ray structure of urokinase is available, it can be used to propose the molecular mechanism of diphenylphosphonate derivatives binding.

In this contribution, we performed flexible docking calculations of one novel and four already known [2] urokinase phosphonic inhibitors with available experimental activity. The docking results are consistent with the previously suggested mode of inhibitors binding [1]. To further determine the physical nature of interactions as well as the role of particular active site residues, the protein–ligand complexes were subjected to rigorous non–empirical analysis of intermolecular interactions. The binding energy was partitioned according to the variation–perturbation procedure [3] into the electrostatic, exchange, delocalization and correlation contributions. The overall methodology was successfully applied for other classes of enzymes (*e.g.*, phenylalanine ammonia–lyase [4]). Since the preliminary results suggested that several crucial active site contacts were too short, the optimal distances corresponding to the minimum *ab initio* interaction energy were also evaluated. Despite the deficiencies of force field–optimized enzyme–inhibitor structures, the satisfactory agreement with experimental inhibitory activity was obtained for the electrostatic interaction energy, suggesting its possible application in the binding affinity prediction.

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DFT Study of the Molybdena-silica System in Olefin Metathesis

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Theoretical studies of supported catalysts enable detailed description of the active sites properties. Such results can be complementary to the experimental findings. Olefin metathesis proceeds according to the carbene mechanism, involving metal-carbene and metallacyclobutane complexes. In the case of the heterogeneous molybdenum catalysts, surface Mo-alkylidene species are formed after the contact with alkene or cycloalkane [1-3]. Molybdena-silica systems exhibit high activity in olefin metathesis if a suitable preparation and activation procedure is applied [1-3]. In the present work, properties and metathesis activity of Mo sites on silica are investigated, using density functional theory. The geometries of the potential energy minima and the corresponding transition states have been optimized within a framework of the conventional cluster approach, as well as with the application of the hybrid ONIOM method.

For photoreduced molybdena-silica systems treated with cycloalkane, IR measurements confirmed the presence of Mo-alkylidene and molybdacyclobutane species on the catalyst surface [2,3]. In this study, the scaled theoretical wavenumbers of the C-H stretching vibrations for Mo-methylidene, Mo-ethylidene and molybdacyclobutane centres have been compared with the reported IR data. This is a continuation of the previous work [4] with employing new models of the active sites. On the basis of the theoretical results obtained, it is concluded that stable molybdacyclobutane complexes were experimentally found on the catalyst surface, while other molybdacyclobutane intermediates, playing a crucial role in the catalytic cycle of olefin metathesis, were not experimentally detected.

Ethene metathesis proceeding on differently located Mo-methylidene centres has been studied as well. The Mo sites are placed both on fully hydroxylated and partially dehydroxylated silica surface. It is concluded that the structure and surroundings of the Mo-alkylidene centres affect significantly their metathesis activity. The Mo centres which are predicted to be the most active in olefin metathesis are placed on the partially dehydroxylated SiO_2 surface.

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cis-Diammine(orotato)platinum(II) - a Cisplatin Analogue. Density Functional Study

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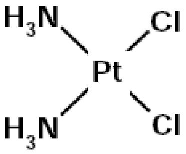
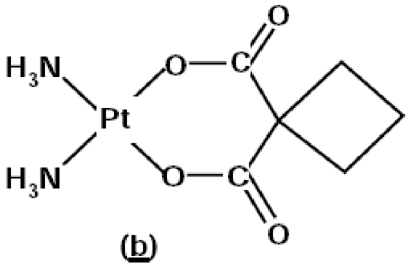
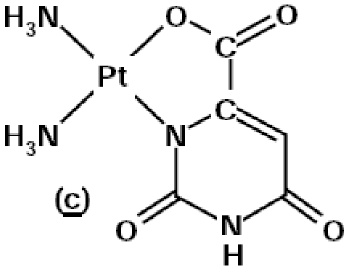
Orotic acid (vitamin B_{13}) is a key intermediate in biosynthesis of the pyrimidine nucleotides in living organisms, moreover, it may serve as the biological carrier for some metal ions. cis-Diammine(orotato)platinum(II) (c) can be considered as a new potential cisplatin analogue.



(a)
cisplatin



(b)
carboplatin



(c)

The molecular structure, vibrational frequencies, and the theoretical infrared and Raman intensities have been calculated by the density functional mPW1PW91 method. The detailed vibrational assignment has been made on the basis of the calculated potential energy distribution. The theoretically predicted IR and Raman spectra [1] show very good agreement with experiment. Natural Bond Orbital (NBO) analysis has provided new data on the electronic structure and hybridization of atoms [2]. It is suggested that strong hydrogen bonding between the carbonyl oxygen atom of the uracilate ring and the ammonia molecule in the complex may hinder the cleavage of the Pt-orotate bonds in biological systems. This may lead to lower cytotoxicity of the title complex, in comparison to cisplatin and carboplatin.

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DFT Study of Dihexanoyle Phosphatidylcholine Monolayer

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Flat twodimensional quasi-crystalline periodic structure of DHPC (dihexanoyle phosphatidylcholine) was optimized in Gaussian 03 Rev. C.02 in LSDA/3-21G* model chemistry. The unit cell consisted of four DHPC molecules. The computations were started from the geometry of the optimized tetramer of DHPC in the same model chemistry (LSDA/3-21G*). The average surface area per one DHPC molecule in a monolayer was about 50.8A. Such optimized periodic geometry of DHPC tetramer was taken as the starting geometry in B3LYP/3-21G* computations in Gaussian 03. The average surface area per one DHPC molecule in a monolayer was about 57.5A^2 on this model chemistry. In both cases the dipole moment of the periodic structures proved to be perpendicular to translation vectors. One can make a judgment, that neglectance of water in the model does not influence much the average surface per one molecule (experimental value ca. 60 A^2 measured for DPPC in lipid membrane) but the geometry of alkyl chains of DHPC molecules.

Acknowledgements: Support from ICM computational grant is acknowledged. Calculations were also performed at the Wroclaw Centre for Networking and Supercomputing.

DFT Studies of Novel Hypothetical Hydrides of Late Lanthanide Metals: Route to High-T_C Superconductivity?

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Despite the presence of light H atoms and contrary to predictions of the BCS theory of superconductivity, hydride materials (PdH_x, Th_4H_{15}) do not enjoy much success as high-temperature superconductors, the record critical temperature value (T_C) not exceeding 20 K. High-frequency H-related phonons could in principle be utilized to significantly increase T_C, but only if the electronic density of states at the Fermi level has a significant contribution from H (1s) states. This may occur for main group hydrides only at ultra-high pressures, as shown for SiH_4 [1,2].

Extending our preliminary theoretical study [3], we now show that two novel ternary hydrides of Yb, $Yb^{II}BeH_4$, and $Cs_3Yb^{III}H_6$, might be prepared under appropriate conditions. $Yb^{II}BeH_4$ should form from binaries even at ambient pressure, while $Cs_3Yb^{III}H_6$ should be achievable at increased pressures of H_2 (similar to the known $Yb^{II}(Yb^{III}H_4)_2$ [4]).

$Cs_3Yb^{III}H_6$ is particularly interesting as it features unprecedented strong mixing of the 4f states of Yb and 1s states of H. The f electrons no longer form an inner shell, but are engaged in genuine σ bonding to H. In this unusual compound of trivalent ytterbium, the late lanthanide element resembles actinides or even outer-transition metals; it manages to introduce holes to the hydride band. A f^{13} electron count in the vicinity of shell closure (resembling the d^9 count for parent oxocuprates) and the involvement of H (1s) states are likely to promote superconductivity in this fascinating material.

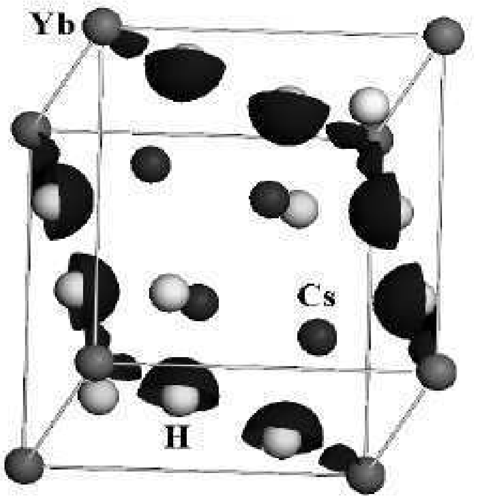

Figure 1: Spin density (black) in the primitive unit cell of hypothetical $Cs_3Yb^{III}H_6$ ternary hydride; note significant contributions from H atoms.

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Experimental and Theoretical Investigations of Spectroscopic Properties of Azobenzene Derivatives in 1,1,2-trichloroetan

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Due to the possible reversible photoisomerisation between *cis* and *trans* conformations [1], azobenzene derivatives are still interesting systems for numerous photonic applications. The photochromic behavior of azobenzene derivatives depends on many factors such as environment or substituents attached to the azobenzene core. The terminal groups can strongly influence the spectroscopic properties of azobenzenes. As a consequence the nonlinear optical properties may also be strongly affected [2]. Polymeric matrices with photoactive azobenzenes can be used for many applications such as surface relief gratings [3] or all optical memories [4].

In the present study, we report on the spectroscopic characterization of new photochromic co-polymers of PMMA containing azobenzene derivatives (Fig. 1). The spectra were measured in 1,1,2-trichloroetan. We support the experimental results with the calculations using density functional theory with PBE0 and B3LYP functionals. The preliminary results show very good agreement between theoretical and exprimental data.

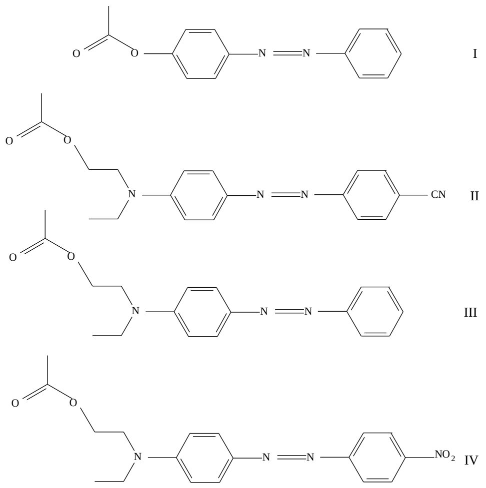

Figure 1: Schematic representation of the investigated model molecules.

Acknowledgements: This research was supported by the grant 3 T08E 08430 from the Polish Committee for Scientific Research. One of the authors (RZ) is scholarship holder of the Foundation for Polish Science '06

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Accuracy of Various Approximations to the Non-additive Kinetic Functional in Exactly Solvable Cases

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One of the key elements in subsystem formulation of density functional theory [1] as well as in the orbital-free embedding formalism [2], is so called non-additive kinetic energy bifunctional, $T_s^{nadd}[\rho_A, \rho_B]$ which is defined as:

$$T_s^{nadd}[\rho_A, \rho_B] = T_s[\rho_A + \rho_B] - T_s[\rho_A] - T_s[\rho_B] \tag{1}$$

The associated functional derivative with respect to ρ_A is one of the components of the effective potential in one-electron equations for embedded orbitals:

$$\left[-\frac{1}{2}\nabla^2 + v_{eff}^{KS}[\rho_A, \mathbf{r}] + v_{eff}^{emb}[\rho_A, \rho_B, \mathbf{r}] \right] \phi_{Ai} = \varepsilon_{Ai}\phi_{Ai} \tag{2}$$

where:

$$v_{eff}^{emb}[\rho_A, \rho_B, \mathbf{r}] = -\sum_{i=1}^{Nuc_B} \frac{Z_i}{|\mathbf{r} - \mathbf{R_i}|} + \int \frac{\rho_B(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}' + v_{xc}[\rho_A(\mathbf{r}) + \rho_B(\mathbf{r})] - v_{xc}[\rho_A(\mathbf{r})] + \frac{\delta T_s^{nadd}[\rho_A, \rho_B]}{\delta \rho_A} \tag{3}$$

In practical calculations, $T_s^{nadd}[\rho_A, \rho_B]$ and $\frac{\delta T_s^{nadd}[\rho_A,\rho_B]}{\delta\rho_A}$ are approximated using one of the well known kinetic energy functionals. For some cases, exact expressions for $T_s^{nadd}[\rho_A, \rho_B]$ can be derived [3] (four-electron systems: Li^+-He, Li^+-H_2, H_2-H_2, He-He). The main aim of the present study is to test the accuracy of common approximations to the kinetic energy and the associated derivatives (potentials) for such cases.

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Molecular Basis of Vampirism - Designing Anti-porphyria Drugs

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Porphyria has been suggested as an explanation for the origin of vampire legends, based upon a number of similarities between the condition and the folklore that was first speculated upon by biochemist David Dolphin in 1985. In his work he demonstrated, that Dracula was suffering from porphyria. Most vampiric features can be found among porphyria symptoms. For example, garlic, being the most common protection against vampires, has an influence on the porphyrin biosynthesis pathway. Some of porphyrias manifestate themselves as a pathological sensitivity of the skin exposed to light causing scarring and disfiguration. Gums can shrink, so the teeth look like fangs and in some extreme cases accumulation of porphyrins in bones and teeth can even cause red fluorescence of these tissues [1].

Porphyria is a group of different (inherited or acquired) disorders caused by abnormalities in the heme biosynthetic pathway. In general, they are classified as hepatic or erythropoietic porphyrias, based on the site of the enzyme defect and the resulting overproduction and accumulation of the porphyrins. In humans, porphyrins are the main precursors of heme, an essential component of hemoglobin, myoglobin, catalase, peroxidase and cytochromes. Deficiency in the porphyrin pathway enzymes leads to an insufficient production of heme. Since heme metabolism plays a central role in a cellular metabolism, disruption of the neuroendocrine and cardiovascular systems can occur in such attacks. An additional problem in these deficiencies is the accumulation of porphyrins, which are not toxic to tissues in darkness, but upon UV radiation they produce cytotoxic compounds. The chemical properties of porphyrin intermediates determine in which tissues they accumulate, whether they are photosensitive, and how the compound is excreted - either in urine or feaces.

The natural bond orbital analysis (NBO) of fully optimized hemine and other porphyrin derivates have been performed by using the density functional methods (B3LYP) with the extended 6-311+G(d,p) basis set. Natural bond orbital analysis based on Löwdin's concept of "natural" orbitals, is used to describe the unique set of orthonormal 1-electron functions $\theta_i(\vec{r})$ and to express the density $\rho(\vec{r})$ of Ψ. This approach, adapted by Frank Weinhold and co-workes [2] in NBO's package provides information about charges, bond types and hybrid directions.

The results of such an analysis allow for the properties of the investigated molecules to be compared. In particular, the changes in iron properties and the corresponding influence on the heme system can be evaluated. All these information are very useful in drug design.

Acknowledgements: Calculations were performed at Poznań and Wrocław Centres for Networking and Supercomputing.

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De Novo Simulations of Protein-folding Pathways in a Reduced Conformational Space

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Determining the folded structure is a priority for a full biochemical protein characterization. But a detailed understanding of the folding process requires characterization of all alternate protein conformations populated along the folding pathway including the unfolded state and partially folded intermediates. Large theoretical and experimental research efforts are devoted to understand how a protein folds into its native structure.

To address this question we have used reduced protein lattice model and Monte Carlo dynamics to perform equilibrium folding simulations in various folding stages, beginning from the denatured state. The use of a reduced representation of polypeptide chains enable significant reduction of the conformational space and allow the search for the native state on a reasonable time scale.

Compared to the experimental results we have obtained similar sequence of folding events and have located crucial interactions for the folding process. Our simulations, strongly suggest that the topology of the native state plays an important role in the folding process.

Model of the Three-dimensional Structure of the Vitamin D Receptor Bound with Peptide Ligand Mimicking Co-activator Sequence

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We developed a fully flexible docking method that uses a reduced lattice representation of protein molecules, adapted for modeling peptide - protein complexes. The CABS model (Carbon Alpha, Carbon Beta, Side Group) employed here was initially designed for single-chain protein folding and performed well in many applications. Instead of full-atomic protein representation the CABS model incorporates three pseudo-atoms per residue - C?, C? and the center of the side group. Force field used by CABS was derived from statistical analysis of non-redundant database of protein structures. In test applications the native state of the complex was reconstructed from separated molecules of the receptor and the peptide ligand. It was performed for a set of protein complexes, for which three-dimensional structures are known, including the rat vitamin D receptor bound to short peptide mimicking coactivator sequence. Accuracy of obtained models, calculated as cRMSD (coordinate Root-Mean-Square Deviation) between the experimental and model structures, varied from 0.7Åup to 4Å, which is competitive with experimental methods, such as crystallography or NMR.

Construction of a fast and accurate flexible docking procedure is nowadays one of the most important tasks of bioinformatics and is crucial for rational drug design. Forthcoming modeling study should lead to better understanding of mechanisms of macromolecular assembly and will explain coactivators' effects on receptors activity, especially on vitamin D receptor and other nuclear receptors.

A Clustering Based Approach to Adsorption Modeling

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In the authors' scientific team the new clustering based approach to modeling adsorption processes based on entropy formula was proposed. The mentioned approach is based on theăclassical BET approach to the multilayer adsorption description. However the clustering based approach takes into account theăpresence of branched clusters and the heterogeneity of surface. Ităis worth emphasizing that the proposed approach considers heterogeneity both from theăgeometrical and energetic points of view. What is more, this approach discusses geometrical and energetic limitations of creating clusters and theăadhesive forces in layers higher than the first one are taken into account.

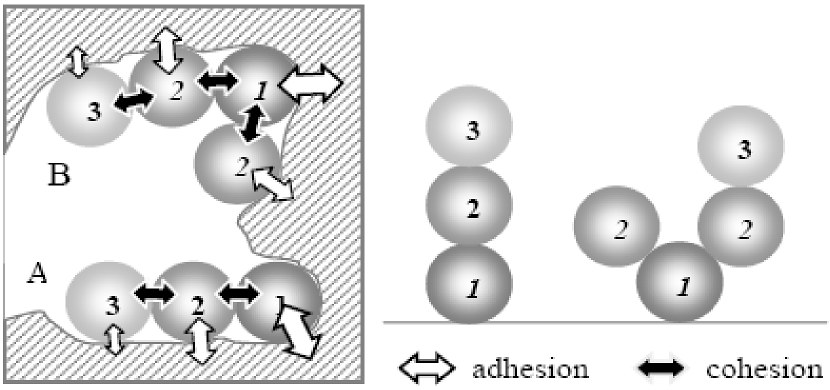

Figure 1: Illustration of adsorbate molecules clusterization mechanisms in presented approach to adsorption modeling: a) A - an individual cluster limited to 3 layers by the pore geometry, B - an individual cluster with the second adsorption layer branched, limited to 3 layers by the pore geometry, b)ămodels of molecules clusterisation (*BET*-like stacks).

Acknowledgements: The research is led within the University grants 11.11.210.122.

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Computer Analysis of Nitrogen Adsorption Isotherms on Active Carbons by an Employment of the New LBET Class Models

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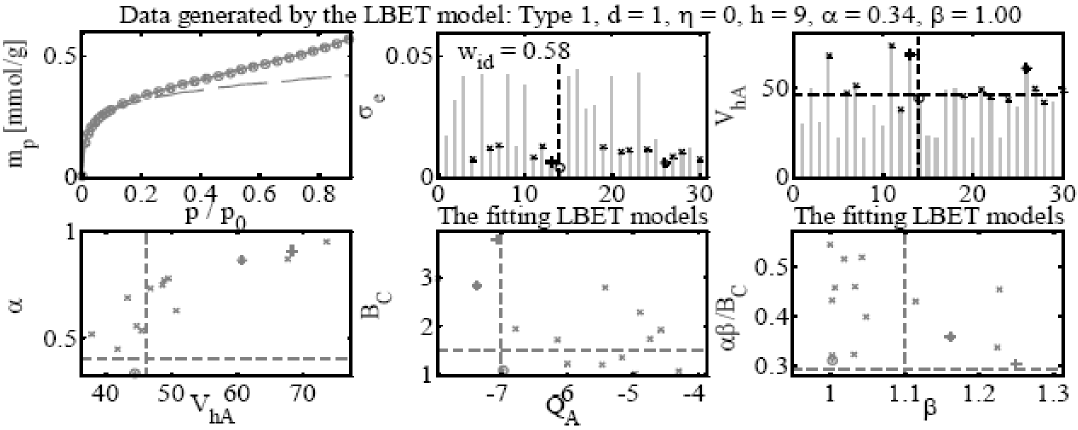
The reported research concerns properties of the new *LBET* class models designed to describe the heterogeneous adsorption on microporous carbonaceous materials [1,2]. The purpose of the numerical analysis and calculations was to verify the *LBET* class adsorption models and to test their applicability to the analysis of nitrogen adsorption isotherm. Theăresearch was divided into two stages. In the first stage the adsorption isotherms were generated by the *LBET* formulas with adequate energetic and structural parameters. Then, the parameters were identified, using the full set of variants of the *LBET* formulas with fixed values of the system parameters and a selected energy distribution variant. The proposed multivariant identification of adsorption systems, based on fitting of the *LBET*-type models, was found to be useful for the analysis of empirical isotherms N_2 - WA2 and N_2 - WA4 taken from literature [3]. The obtained results show that the *LBET* class models give good insight into the adsorption mechanisms and structure of pores. Moreover, fitting of *LBET* models provides information on properties of adsorbate clusters deposed in the material. It makes possible to deduce the pore structure properties.


Data generated by the LBET model: Type 1, d = 1, η = 0, h = 9, α = 0.34, β = 1.00

The fitting LBET models

The fitting LBET models

Figure 1: The multivariant identification results for an isotherm generated by the *LBET* model.

Acknowledgements: The research is led within the University grants 11.11.210.122.

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Theoretically Predicted Contacts and Sparse NMR Data in De novo Protein Structure Prediction

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A straightforward de novo approach is successful in structure prediction of small, globular proteins, however, the prediction of larger and more complex folds is still a challenging task. De novo protein structure prediction with the simplified CABS model could be significantly improved by combinations of theoretical approach with sparse experimental data. In this work we implemented two kinds of data, which could be obtained with relatively small effort: theoretically predicted contacts and sparse NMR data such as chemical shifts [1, 2]. Such combined approach accelerates determination of protein structure without limiting the model resolution. We successfully tested our approach on several proteins of different size and topology, which do not have any homologous in the PDB database.

Acknowledgements: This work was partially supported by the Polish Committee for Scientific Research (KBN) Grant No. PBZKBN-088/P04/2003. Computational part of this work was done using the computer cluster at the Computing Center of Faculty of Chemistry, Warsaw University.

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Quantum Chemical Studies of Xenon Insertion Compounds of Formic Acid

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Computational Study of Formic Acid Dimers Involving the Higher-energy Conformer, cis-HCOOH

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Formic acid (HCOOH) is the simplest organic acid exhibiting rotational isomerism, and it exists in two planar structures: the *trans* and *cis* conformers with H-C-O-H dihedral angles 180^o and 0^o, respectively. The *trans*-form is the most stable and the predominant one in the gas phase, while the higher-energy *cis*-form has been hard to characterise spectroscopically due to its fast tunneling relaxation into the more stable form.[1] Formic acid is also found to readily engage into intermolecular interactions that allows studies on properties and reactions involving the C-H. . .O and O-H. . .O non-covalently bonded systems - picturing small models for many processes including the science of life. In the gas phase, the *trans*-formic acid forms a symmetric cyclic dimer, which is the most stable structure among several hydrogen-bonded complex structures described by computational studies [2]. However, various asymmetric cyclic structures have been assigned in He droplets and solid argon experiments [3,4]. Computational studies have also described a few *trans-cis* dimers, which appear relevant to high-pressure solid phase of formic acid [5].

In our computational study, we have applied quantum chemical calculations to study the structural, energetical and vibrational properties of *trans-trans, trans-cis* and *cis-cis* formic acid dimers. Especially, we are interested to provide adequate predictions of the IR-spectra of dimer species that could be realised in solid noble gas matrices based on the previous knowledge of the *trans-trans* dimers in solid argon, laser activation of the higher-energy *cis*-form of formic acid monomer [6] and the very recent observation of the first *trans-cis* dimer in solid argon [7]. To suggest possible experimental photoactivation possibilities, we have extended our computational simulations to the anharmonic vibrational calculations that allows us to predict also the combination and overtone modes besides the fundamental modes, as well as their band intensities.

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Design of Ti/Si/H Clusters and Surfaces of Cubic TiSi for Heterolytic Addition of H_2

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Proton/hydride low-Z compounds ($LiBH_4/H_2O$, $LiH/LiNH_2$, etc.) constitute an important family of hydrogen stores [1,2]. H_2 fuel is liberated from these composite materials via a generalized reaction: $H^+ + H^- \rightarrow H_2$. The standard enthalpy of such reactions is most often large and negative. In consequence, many of them cannot be reversed at modest H_2 pressures.

The emerging proton/hydride technologies often utilize Ti-based catalysts (more suitable for homo- rather than for the heterolytic split of H_2), while many traditional hydrogenation catalysts (Pd, Ni) fail to cooperate with these storage systems. Appreciable thermodynamic stability of the hydrogenated forms of Group 10 catalysts is likely to be blamed for this shortcoming.

In this contribution we describe our attempts to design, from the first principles, a novel family of hydrogen transfer catalysts, which exhibit (i) a negative but modest enthalpy of H_2 addition (*i.e.* -0.4 to -0.5 eV per H_2), and (ii) a very small electronic barrier of this process (< 0.1 eV) [3,4]. Such catalysts break the Hammond's rule, but they ideally fulfill the requirements posed by the lightweight proton/hydride stores with favourable thermodynamics (Li_2NH, $Li_2Mg(NH)_2$).

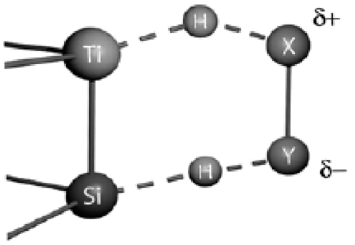

Figure 1: Representation of H−2 transfer from a Ti/Si compound (or from a surface defect of c-TiSi) to the discharged store of H_2.

We report - based on the DFT calculations for various isomers of a hypothetical $Ti_4Si_4H_8$ molecule - that a coordinatively unsaturated >Ti=Si< group exhibits an unprecedented flexibility for the addition of H_2. A perplexing variety is seen of energetically-equivalent isomers with three-center Ti. . .H. . .Si and terminal Ti-H and Si-H bonds. Small barrier for H_2 attachment is mainly due to an interstitial nature of the product hydride. Richness of the possible arrangements of H atoms might result in a new versatile H_2 transfer catalyst, if $Ti_4Si_4H_8$ could be prepared.

Results for molecular species are compared to those for H_2 attachment to selected surfaces and surface defects of as yet unknown cubic TiSi polymorph.

Acknowledgements: Support from ICM and Dept. Chem. is gratefully acknowledged. Calculations were performed at ICM supercomputers.

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Theoretical Study of Cisplatin Interactions with Glycine in the Gas-phase and Implicit Water Solution - COSMO

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Interactions of hydrated cisplatin complexes with glycine were explored. The square-planar cis-$[Pt(NH_3)_2(H_2O)X]^+$ complexes (where X=Cl, OH and H_2O) were chosen as models for mono- and dihydrated reactants. Theoretical calculations using DFT techniques with B3LYP functional were performed. Both gas-phase and polarizable continuum model (in COSMO version) were employed for the reaction energies and bonding energies determinations in approach of isolated molecules as well as supermolecular complexes. The formations of monodentate complexes by replacing aqua-ligand with N and O atoms of the amino acid represent exothermic processes. The stronger BDE was found in structures with Pt-N coordination. This bonding energy is about 60 kcal/mol. This correlates well with other calculations on cysteine and methionine complexes. The formation of chelate structures is an exothermic reaction for dihydrated form of reactants.

Homology Modeling of G-Protein Coupled Odorant Receptor AgOR1 from Malaria Mosquito *Anopheles Gambiae*

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Over 3 billion people live under the threat of malaria transmitted by female *Anopheles gambiae* mosquitos. Malaria kills over one million of humans each year - mostly children. Insect repellents help to reduce exposure to dangerous bites. Perhaps the most popular repellent is DEET (N, N-diethy-3-methylbenzamide) but over the long history of its usage some toxic reactions have occurred. We have computationally studied alternatives to DEET: 1-methylisopropyl 2-(2-hydroxyethyl) piperidine-1-carboxylate (Picardin) and 2-methylpiperidinyl-3-cyclohexene-1-carboxamide (AI3-37220, 220) [1]. Using hierarchical overlaying the activity of diastereomers was correlated with molecular structures. Quantum-chemically optimized structures may be docked to target insect proteins, however there are no structures of odorant receptors.

In order to get some qualitative picture of possible repellent-receptor site interactions we constructed a crude model of G-protein coupled receptor of a hypothetical odorant receptor (OR) from *Anopheles gambiae* AgOR1. Recently Zweibel *et al.*, using bioinformatics tools for scanning of mosquito genome, have indicated a familly of 79 putative OR proteins [2]. Special attention is devoted to AgOR1 since female specific expression of this gene was reported [3, 4].

Homology modeling of AgOR is very difficult since only one transmembrane GPCR protein (rhodopsin) is published in the Protein Data Bank. We used several servers [5-6] to indicate transmembrane regions [7], then helices indicated by SOSUI [6] with the rhodopsin template were used to construct a 3D model of AgOR1. Software tools embedded in the DS suite [8] were employed. Preliminary results of DEET and 220 docking to this model are presented.

Acknowledgements: This research was supported by UMK grant #380F. P.M. thanks the Marshal's Office of kujawsko-pomorskie voivodeship for a PhD scholarship "Krok w przyszłość".

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Computational DFT Study of the Non-heme Iron Center of Photosystem II

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Photosystem II is large membrane-bound molecular complex utilized by higher plants, algae and cyanobacteria for trapping the light energy by the means of rapid electron transfer (ET). The non-heme iron center constitutes a bridge between two quinone molecules: Qa and the terminal electron acceptor, Qb. However, its role in the ET process remains unclear [1]. Experimental studies suggest that, unlike in bacterial reaction centers, in PS II the ET from Qa to Qb could be modulated by binding of various ligands to the iron cation [2].

We present a density functional theory investigation for molecular models of the iron center. Calculations on the small model system predict the high spin state to be the ground state. Spin states energies are only slightly affected when the bicarbonate ligand is removed. The Fe-Qa model shows that the reduction of Qa is accompanied by proton transfer from the H-bonded histidine residue, in accord with previous studies on Zn-replaced center [3].

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The Two Components of the Activation Energy

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The reaction force is the derivative of the potential energy of a process along the intrinsic reaction coordinate. It has a universal form that provides insight into the mechanisms of chemical reactions. **A particularly important feature of the reaction force is that it shows that an activation barrier is composed of two components: *the first reflects primarily initial structural changes that will facilitate the subsequent process, while the second corresponds to the electronic changes that occur before the transition state.*** Recognition of these two contributions to the activation energy can provide significant insight into reaction mechanisms, for example in elucidating the nature of solvent effects.

Electronic Structure of Pyridinium N-phenolate Betaine Dye

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2,6-diphenyl-(2,4,6-triphenyl-1-pyridinium)-N-phenoxide betaine, also known as Reichardt's betaine, exhibits the largest measured shift of the S_0-S_1 absorption band maximum (-9730 cm^{-1}), when going from diphenyl ether to water [1]. Hydrogen bonds created between betaine oxygen atom and solvent molecules significantly influence betaine dyes electronic structure [3]. This molecule, containing seven aromatic rings, is still untractable by accurate quantum chemical methods. It is well established that electronic transfer upon excitation takes place in the central part of molecule [2]. Hence, the simplest derivative (4-(1-pyridinium-1-yl)phenolate) is a good starting point for the description and understanding of the origin of solvatochromic behavior in Reichardt's betaine.

In the present report, the results of the quantum chemical studies of interaction between 4-(1-pyridinium-1-yl)phenolate betaine and water molecules are presented. Supermolecular approach as well as polarizable continuum model (PCM) method has been used. The optimal geometry has been obtained at the MP2/6-31++G(d,p) level of theory. This structures has been used to calculate spectroscopic parameters with configuration interaction with singlets (CIS, CIS(D)) method and time-dependent density functional theory (PBE0, B3LYP functionals). Atom in molecules (AIM) [4] analysis has been carried out on the optimized geometries. The critical points were analyzed in terms of electron densities and their Laplacians, additionally the energetic characteristics of critical points were taken into account.

Acknowledgements: Calculations were performed at the Wroclaw (WCSS) and Mississippi (MCSR) Centre for Networking and Supercomputing.

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Locally Enhanced Sampling Molecular Dynamics Study of Dioxygen Transport in Human Cytoglobin

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Recently to the vertebrate heme globin family a new member - cytoglobin (Cyg) - has been added [1]. This protein is usually six-coordinated. In the absence of gaseous ligand (e.q. O2) the sixth coordination position is occupied by distal HisE7 residue. Cyg displays a classical globin fold, so-called three-on-three alpha-helical sandwich and is expressed in many different tissues. The physiological role of Cyg is still not clear. In this presentation the results of molecular dynamics simulations of diooxygen diffusion inside Cyg are discussed. In addition to classical trajectory approximate Locally Enhanced Sampling method (LES) [2,3] has been employed as implemented in NAMD [4] code. CHARMM27 all-atom force field was used. Classical reaction paths were carefully analyzed using methods similar to described in recent study on mini-hemoglobin [5]. It has been found that there are multiple paths possible and two main cavities are present. One may expect that dioxygen diffusion is slower than that in mini-hemoglobin and human myoglobin.

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Implementation of the QM/QM Method Based on the LocalSCF Algorithm

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Molecular modeling and simulation of large systems remains a very difficult process because of their complexity and diversity. Despite increasing computational capability available nowadays, investigations at the atomic level are still a challenge to computational chemists.

Currently, QM/MM methods proved to be the most successful theoretical approach to studying biomolecular systems. Mixed quantum mechanics/molecular mechanics schemes combine the accuracy of the quantum mechanical description with the efficiency and low computational cost of molecular mechanics.

However, molecular mechanics (MM) force fields are unable to describe the changes in the electronic structure of a system undergoing a chemical reaction. Such changes in the electronic structure in processes that involve breaking or forming a bond or a charge transfer require quantum mechanics (QM) for the proper treatment. However, due to high computational cost, the application of QM is still limited to relatively small systems. Therefore, significant effort is being made to develop new schemes that will make it possible to study the entire protein on the quantum theory level.

We present a unique implementation of the QM/QM algorithm, based on Jaguar [1], which is a very fast quantum mechanics code, and LocalSCF methods [2]. LocalSCF is a novel linear scaling quantum mechanics method implemented at present in the semiempirical framework. The computer program [3], named after the mathematical method, has been designed for fast electronic structure calculations of large, complex protein systems consisting of up to 100000 atoms.

In our work we prepared fully automatic algorithm implemented as a routine that connect Jaguar and LocalSCF in a QM/QM scheme. This in-house routine was written in Perl and can be extended to work with another quantum mechanics codes, like Turbomole, Gaussian or GAMESS.

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Continuum Solvent Models of Body Fluids on the Example of Serum

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We present continuum solvent models of body fluids, on the example of blood serum, that are based on the SM5 solvent model framework [1]. Two models have been prepared; the first one includes optimization of geometries in the reaction field of the implicit solvent within the semiempirical AM1 formalism [2]. In the second model, energies of reactants in solution are obtained from the gas phase geometries obtained using MPW1K density functional theory [3]. This new strategy for preparing models of body fluids is validated on the experimental difference in the enthalpies of activation of a methyl transfer reaction carried out in blood serum and in water.

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Insights Into the Catalytic Activity of the Industrial Enzyme Co-Nitrile Hydratase. Docking Studies of Nitriles and Amides

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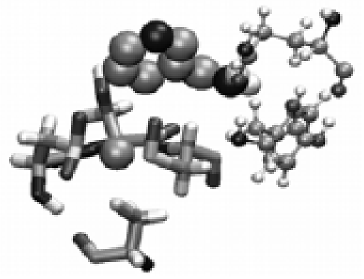
Nitrile hydratase (NHase) is an important industrial enzyme with a nonstandard active center containing Fe^{3+} or Co^{3+} ion, that catalyzes the hydration of nitriles to corresponding nitriles [1]. In year 2000 production of acryloamide, using this biotechnology tool, achieved 200.000 tons. Amides are used as a flocculants, a components of synthetic fibers, vitamins (PP), or a soil conditioners. The biggest NHase plants are in Japan (Mitsubishi Rayon Co., Ltd), France (SNF Floerger) and China (Lonza Guangzhou Fine Chemicals).

In spite of many researches [2-4] catalytical mechanism of conversion nitriles to amides is not known yet. Docking investigations may help to answer how enzymes work.



Here we present docking studies of substrates (acrylonitrile, benzonitrile and nicotinonitrile) and products (acryloamide, benzoamide, nicotinamide) into cobaltous NHase enzyme (pdb code 1IRE [1]) from Pseodonocardia thermophila JCM 3095. Docking was performed using AutoDock 3.0.5 package [5]. We applied 256 starts of genetic algorithm for every substrate and every product into crystal structure with and without water molecules. We focused only in hits in the closest neighborhood of active site and channel leading to active site. In all cases we obtained 3072 binding sites.

We discovered that statistically aromatic substrates and products more often dock in the neighborhood of the active center than aliphatic ones. This is in accordance with the nature, because that enzyme prefers aromatic substrates. Our studies shows that αGln89 and αTyr114 can be critical in pushing off a product from the active center of Co-NHase (see Figure 1).

Acknowledgements: This research was supported by MEiN grant no. 2P04A07229 and grant "Krok w przyszłość - Stypendia dla doktorantów".

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Glycolytic Enzyme Enolase as a Plasminogen Receptor: *in vitro* Interaction and Theoretical Modeling

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Plasminogen is a plasma protein-precursor of plasmin, which as a serine protease degrades blood cloths in the fibrinolytic system. Plasmin plays important role in a variety of other activation cascades and has been implicated in embryogenesis, tissue remodeling, angiogenesis, wound healing and also pathogen and tumor cell invasion and metastasis ("pericellular proteolysis") [1]. Both prokaryotic pathogenic microorganism and eukaryotic cancer cells recruit plasmin's proteolytic activity to their surface to facilitate cell invasion and migration through tissue layers . Plasminogen interacts with target cells via specific receptors. A strong plasminogen-binding protein on the surface of mammalian and pathogenic bacterial and fungi cells appears enolase [2]. Enolase, although traditionally considered for glycolytic enzyme localized in cell cytoplasm, proved to be a multifunctional protein, incliding cell-surface factor for binding some ligands [3]. In our studies we detected significant expression of enolase as a surface protein on normal and transformed rat muscle cells and human sarcoma cells using immunofluorescence method. Moreover, we observed enolase catalytic activity of intact cells of mammals and bacterial cell cultures. Therefore this protein exposed on plasmatic membrane maintains native enzyme structure as the one existing in cytoplasmic compartment. Immunobloting experiments allowed to prove interaction of plasminogen with purified human muscle-specific enolase and with enzyme isolated from cells of Gram-negative bacteria *Klebsiella pneumoniae*. The topography of 248-252 aminoacid motif of human enolase as the site of plasminogen binding was demonstrated in 3D model, based on crystal structure of human enolase [4], and localization of surface interaction plasminogen with enolase from *Streptococcus pneumoniae* [5]. Moreover we tried to establish a model of interactions between structural kringles of plasminogen and native molecule of human enolase. The interactions were predicted by docking each structural kringle to the enolase structure. The non-bonded protein-protein interactions were evaluated by a scoring function. We also attempted to model the plasminogen structure by homology.

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Defect Transport Modeling in Monoclinic $La_{2-x}Pr_xTi_{2-y}Nb_ySiO_{9+\delta}$

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Oxygen ion-conducting solid electrolytes are key materials for numerous high-temperature electrochemical devices, such as solid oxide fuel cells (SOFCs). Although the use of the SOFCs for electric power generation is characterized by a high energy-conversion efficiency, environmental safety and fuel flexibility, their practical application is, however, still limited due to high costs of the component materials and processing. Developments of novel low-cost materials with optimized transport and thermomechanical properties are of vital importance in this field. Recently, a considerable attention has been focused on the silicates with the apatite-type structure, $A_{10-x}Si_6O_{27-\delta}$. Possessing a relatively high level of oxygen-ionic conductivity, moderate thermal expansion and relatively good stability these may be of a substantial interest when considering the low cost of raw materials and well-developed technologies for SiO_2-based film processing in the electronic industry.

This work continues our search for alternative groups of silicate-based materials with oxygen ionic transport, and summarizes computer simulation results and experimental data on monoclinic $La_{2-x}Pr_xTi_{2-y}Nb_ySiO_{9+\delta}$ (xǎ= 0-1.0; yǎ= 0-0.2). The atomic modeling studies were performed using the GULP software, on the basis of the Born model for ionic solids and Mott-Littleton approach for defect calculations. The crystal lattice, formation of oxygen vacancies and interstitial anions, and ion migration processes were simulated. The results are compared to the experimental data obtained by the X-ray diffraction analysis, impedance spectroscopy, and modified faradaic efficiency and electromotive force methods for the determination of ion transference numbers.

The simulated and experimental structural parameters of $La_{2-x}Pr_xTi_{2-y}Nb_ySiO_{9+\delta}$ were found very similar, within the limits of experimental uncertainty. Using the formation energy of isolated point defects, the oxygen-ion migration pathways and activation energies were estimated. Contrary to the apatite-type silicates where a primary contribution to ionic conductivity is due to oxygen interstitial diffusion, the ion migration processes in the $La_{2-x}Pr_xTi_{2-y}Nb_ySiO_{9+\delta}$ were found to occur via the vacancy mechanism. This conclusion was confirmed by the experimental data on Nb-substituted silicates exhibiting a relatively low ionic transport, and by the oxygen partial pressure dependencies of ionic and electronic conductivities. The estimated activation energies for oxygen ion transport in the monoclinic silicates are in a reasonable agreement with the experimental values, varying in the range of 1.2-1.4 eV.

Peculiarities of the Electronic Structure of Cytochrome P450 Active Site (Compound I) – DFT and CASPT2 Modeling

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Electronic structure of cytochrome P450 active site compound I (modeled as [Fe(O)(SH)P] with C_S symmetry) was studied by means of unresticted DFT (B3LYP, BLYP) and CASSCF / CASPT2. The study has been prompted by expected open-shell chracter of the prospective ground state candidate with antiferromagnetic electron coupling, hardly covered by widely used DFT methodology. Indeed, in agreement with literature[1] the lowest lying states of each symmetry and spin arise in DFT results from ferro- or antiferromagnetic coupling between FeO triplet (2 unpaired electrons) and doublet (1 unpaired electron) located either on porphirine a_{2u} (so called A_{2u} states) or on sulphur π lone pair (Π_S states). B3LYP gives ${}^2A_{2u}$ or ${}^4A_{2u}$ (almost degenerate) as ground state. However, important differences between hybrid and non-hybrid functional are apparent in many aspects: relative energies (esp. lack of expected almost-degeneracy between doublets and quartets of the same radical character), geometries, bond orders and occupations of natural orbitals. This could suggest that BLYP applied to doublets prefers 1 over 3 unpaired electrons.

Since DFT results seemed unstable with respect to calculational parameters while multi-configurational character of low lying states was apparent, we employed CASSCF/CASPT2 methodology to resolve the doubts. No successful study at this level has been reported in literature. In spite of technical difficulties due to the problem size, we managed to select reasonable set of active orbitals. CASSCF active spaces explored by us consisted of maximum 3 Fe d orbitals ($3d_\sigma$, $3d_\pi$) with their partners on oxygen ($2p_\sigma$, $2p_\pi$), 4 porphyrine frontiers (a_{1u}, a_{2u}, e_g) and 2 orbitals on sulphur (π_S, σ_S). CASPT2 resulted in either ${}^2A_{2u}$ or ${}^4A_{2u}$ (almost degenerate) ground state, in agreement with our B3LYP results, literature[2] and experiment[3]. Computed spin densities and spin natural orbitals were consistent with those from DFT and illustrated nicely radical character of Cpd I. Interesting effects of strong dynamic correlation at CASPT2 level has been noticed: rotation of the ground state in comparison to CASSCF (where it was Π_S) and strong mixing between CASSCF roots in Multi-State CASPT2[4]. Strong influence of dynamic correlation could also support good performance of DFT in assigning intricate electronic states.

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Cu(I) Sites in Faujasite and their Interactions with the CO Molecule - Theoretical Studies

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Copper exchanged zeolites are intensively studied due to their unusually high activity of Cu(I)-ZSM-5 in NOx decomposition reactions,[1] as well as their catalytical applications in many organic reactions.

We focus on Cu(I) sites in faujasite (FAU), high alumina zeolite. We have investigated Cu(I) sites alone as well as interacting with CO molecule, widely used as a probe molecule in infrared spectroscopy. We apply the combined quantum mechanic/interatomic potential functions method (QM-Pot),[2] which is particularly useful in studies of the extended systems. Within the QM-Pot approach investigated system is divided into the cluster, treated at high level computational methods of the quantum mechanic (QM) Ű Density Functional Theory in our case, and the periodic environment, described by less exact methods of the molecular mechanic (MM). Calculations are performed using the QMPOT program, coupling the Turbomole package in QM part with the GULP program in MM part. The QM-Pot enables to obtain more reliable results than free cluster modeling with less computational effort than full QM periodic calculations.

Our calculations predict Cu(I) positions in sites IŠ and II (with threefold coordination) much more stable than the ones in site III (twofold coordination). CO binding is the stronger the weaker is Cu(I) binding. CO frequencies are obtained using semiempirical scaling based on the CO bond lengths.[3] CO frequencies in FAU are site specific and depend on the number of Al atoms in the nearest neighborhood of the adsorbed molecule. All results are in well agreement with experimental data.

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Charge Localization in Monothiophosphate Monoanions

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Chemical and physical properties of chemical species lead to forces that can combine two or more atoms together or decompose molecules. The most important among these forces is electrostatics resulting from interaction between charges. Keeping that fact in mind, we can deduce that this phenomenon can play a crucial role in character of chemical reactions. In case of molecules we can think about local charges, so called partial atomic charges. Despite the fact that partial atomic charges have no physical meaning and they cannot be evaluated experimentally, they can be treated as a very convenient way for justification and prediction of chemical processes. Partial atomic charges can be calculated with many different computational methods but sometimes they can yield different results.

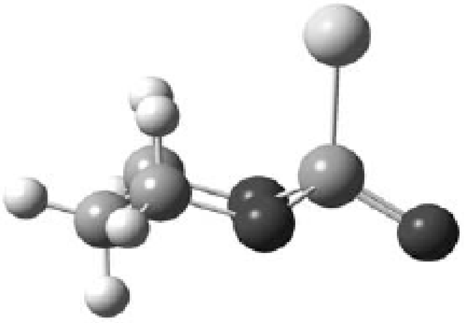

Figure 1: Monothiophosphate monoanion.

Thiophosphates (Figure 1.) are important compounds because of their usefulness in ion exchange, catalysis, non-linear optics, and in stereochemical investigation of biochemical processes. We present calculations on charge distribution in monothiophosphate monoanions using 10 different partial atomic charges schemes. We use B3LYP DFT method with different basis sets in the gas phase and continuum solvation model (CPCM). We test these schemes for different oxygen-bounded substituents and two thiophosphate conformations. Finally, we have added metal ion in opposite to the negative charged group to check its effect on geometry and charge distribution.

We concluded, that choosing different substituents and charge partition scheme, independently of basis set functions and theory level, does not change much the results. On the other hand, we have observed considerable differences in case of using different types of counter-ion.

Preliminary Theoretical Studies on TiO_2 Anatase System

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Nowadays, titanium dioxide constitutes one of the most studied transition metal oxide systems. This is due to its numerous applications, which, among others, include its application as white pigment (e.g. in paints and cosmetics), coatings (e.g. for corrosion protection) and gas sensor. In catalysis, it is widely used as a support for various types of catalysts (e.g. metals, oxides). Additionally, its photochemical properties are at the origin of its application as a photocatalyst for degradation of organic pollutants.

The main goal of our work is the characterization of one of TiO_2 forms - the anatase system by the Density Functional Theory (DFT) method. The stress is put on the investigation of the (001) surface. The choice of this surface follows from the fact that this is one of the mainly exposed ones in the commercial anatase powders (Degussa P25, Merck).

The electronic and geometric properties of the investigated structures are studied by ab initio DFT approach within cluster and periodic models using TURBOMOLE and VASP program packages. Electron exchange and correlation are calculated within gradient corrected density approximations. The results are discussed in terms of geometric and electronic parameters such as bond lengths, valence angles, atomic charges and densities of states.

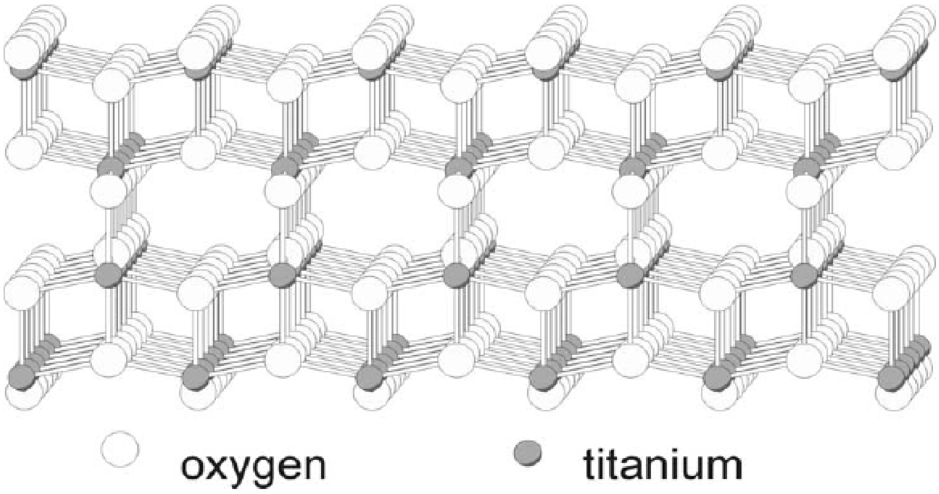

Figure 1: Structure of the (001) surface of anatase TiO_2.

Acknowledgements: Support from Polish Catalysis Network "Nanomaterials as catalysts for new, environment friendly processes" is acknowledged.

Modeling of Circular Dichroism Spectra of Flexible Peptides in Water Solutions Using Molecular Dynamics and Quantum Mechanics

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The electronic circular dichroism (ECD) spectroscopy is often used for structural anddynamical studies of peptides and proteins. The aim of our work is to explain mainspectroscopic features of peptides on the basis of ab initio computations. The role of geometry fluctuations and the polar solvent (water) in formation of the spectral shapes of usual peptide secondary structures is investigated on model simple molecules. The solvent is modeled explicitly as well as by polarizable continuum dielectric models (PCM).

Spectra of Ala-Ala dipeptide in all three ionic forms were simulated using combined quantum mechanics and molecular mechanics (QM/MM). Calculated spectral frequencies and intensities reasonably well correspond to the experiment. The geometry dispersion and participation of water orbitals have to be included for faithful modeling. A further extension with a semiempirical transition dipole coupling (TDC) model enabled us to estimate ECD shapes of common peptide and protein conformations [1].

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Linear Response Kohn-Sham Equations with Constrained Electron Density Applied to a Nonheme Fe(IV)=O Complex

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The theoretical description of solvent effects on absorption spectra is a big challenge. Time Dependent Density Functional Theory calculations are very time consuming and computational cost grows very rapidly with the size of the system therefore solvent molecules cannot be treated explicitly. In the subsystem formulation of density functional theory the total system is divided into two subsystems. One of them is usually treated with high accuracy and another, which describes environment modifies properties of the first one. All the terms representing interactions between subsystems are functionals of electron density [1][2] (formalism was developed for weakly interacting molecular systems (weakly overlapping electron densities)). Time dependent response theory applied to Kohn-Sham equations with constrained electron density [3] allows for a proper and reliable description of the environment and considerably reduces the time of TDDFT calculations. The formalism have been applied to the calculations of excited states of a nonheme Fe(IV)=O complex which is very interesting due to similarity to some enzymes.

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Modeling the Adsorption of Aromatic Compounds on a TiO_2/SiO_2 Catalyst

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Sol-gel process combined with supercritical drying allow to obtain aerogel, solid material of very low density which results from very high pore volume and high surface areas. Titania-silica catalyst in this form should be active in photocatalytic degradation of organic pollutants in water/air. However, studies of titania-silica aerogels involves, beside photocatalysis as a one of Advanced Oxidation Processes, epoxidation or pohotacytalytic production of hydrogen.

The adsorptive properties of the catalyst surface is of great importance in determining the overall catalytic activity. In the present study we have used the Grand Canonical Monte Carlo (GCMC) method to analyze these properties. Adsorption isotherms as well as the distribution of mass of the reagents indicate that toluene, phenol and salicylic acid undergo multilayer adsorption.

Mass cloud visualisation indicates strong interactions between adsorbate molecules. Molecule s tend to concentrate in groups, which is visible especially in case of toluene. Adsorption isotherms confirmed this effect by very strong influence of pressure on the number of adsorbed molecules.

This seems to be of lesser importance in case of salicylic acid. Adsorption is still multilayer, however host-guest interactions prevail over the interactions between sorbate molecules.

The result show, that there is a considerable difference in behavior of the TiO_2 and SiO_2 surface. The molecules of the salicylic acid adsorb only to the titania surface, it is possible that the hydrogen bonds are formed between the guest molecule and the host hydroxyl groups. It seems interesting that the water molecules do not adsorb to the surface. In most cases the energy of interaction between water and the catalyst is equal to 0.

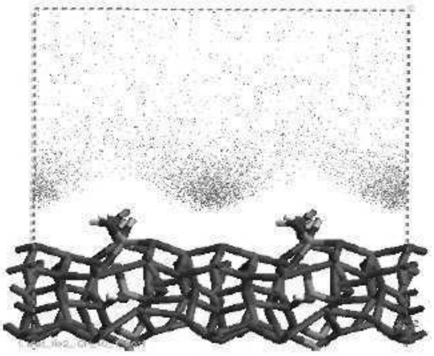

Figure 1: Distribution of mass of salicylic acid in the proximity of catalyst surface.

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

Modeling Properties of Iridium Complexes

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Cyclometalated complexes of Ir(III) are under intensive development as luminescent dopands in organic light-emitting diodes (OLEDs). The reason these d^6 complexes are attractive in photochemical applications is that they have long-lived excited states and good photoluminescence efficiencies. OLEDs prepared with this heavy metal complexes are the most efficient OLEDs reported to date.

Class of highly phosphorescent Ir complexes have two cyclometalated ligands and a single bidentate, monoanionic ancillary ligand, making the complexes neutral. The emission color from the complex dependents on the choice of cyclometalating ligand, from green to red.

This work presents calculations and validation of excited state properties obtained from time-dependent density functional theory (TD-DFT) and from the configuration interaction singles (CIS) for iridium complexes. The majority of the studies have been focused on optimization of the geometry for bis(2-phenylene pyridine) acrylate iridium $(ppy)_2Ir(acac)$ (Figure 1) and bis(2-(p-tolyl)pyridine) acrylate iridium $(tpy)_2Ir(acac)$, and electronic excitation energies for bis(2-phenylene pyridine) acrylate iridium $(ppy)_2Ir(acac)$. To describe geometries of complexes the density functional theory (B3LYP B3P86) was used. The accuracy of density functional theory has been assessed by comparison to experimental data.

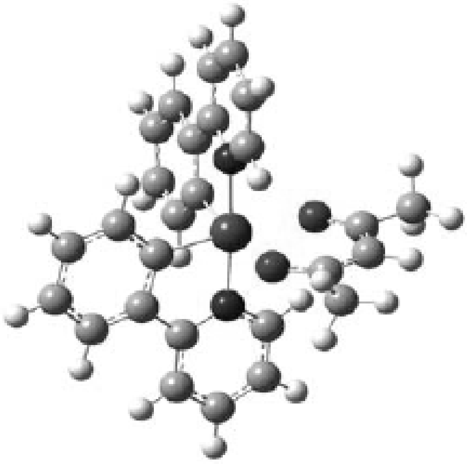

Figure 1: Structure of $(ppy)_2Ir(acac)$.

We report application of TD-DFT and CIS to calculate photophysical data of iridium complex like absorbance and emission for $(ppy)_2Ir(acac)$ in the gas-phase and in solution-phase. Obtained findings were compared with experimental data for $(ppy)_2Ir(acac)$ in degassed 2-MeTHF, at room temperature.

All of the reported computation methods can be useful for exploration of new types of ligands.

Modeling of Transition States in Stereoselective Addition of Diethylzinc to Benzaldehyde Catalyzed by N,S-camphor Based Catalysts

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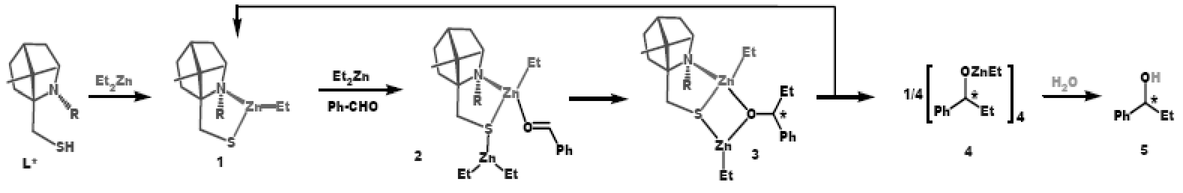
Effective stereoselective synthesis is important in modern material science. Camphor based catalysts allow for stereoselective addition of diethylzinc to benzaldehyde, leading to chiral secondary alcohols [1]. The mechanism of this stereoselection has been computationally studied [2] but the understanding of this reaction is still rather limited [3]. In order to find the most plausible bulky substituents in a group of newly designed N,S-camphor catalysts (see Fig.) we performed extensive PM3 quantum-chemical study involving hypothetical transition states of organometallic complexes of the catalysts with diethylzinc and benzaldehyde. The PM3 method applied here, has been proved in earlier studies to be adequate [4, 5].



It has been found that out of eight possible arrangements of ternary TS [2→3] diethylzinc-catalyst-aldehyde complexes only three forms are sterically allowed and one is favorable. Molecular structures obtained allow us to rationalize the mechanism of stereoselectivity and to predict what enantiomer should be produced with the highest enantiomeric excess.

In a good chiral ligand L* the substituent R (see Fig.) can't be neither too small ($R \neq H$) nor too large ($R \neq$ Pri, But, Bus, 1-Me-alkil). The best substituent should have the CH_2 group neighbouring nitrogen atom.

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Predicted Antioxidant Activity of Amide and Thioamide of *o*-Coumaric Acid

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Thioamides are close structural analogs of the abundant in nature amides. Therefore, the former are often used for modeling of amide-containing biotransformations. However, charge distribution in the thioamide group differs substantially from that in the amide function which often leads to incomprehensible experimental results.

Antioxidant activity can be predicted using various descriptors such as energy of HOMO, dissociation energy of the radicals producing bonds, stability and/or spin density distribution in the radicals obtained, etc. Thioamides feature better bond delocalization than amides and we expect the former to produce more stable radicals and thus more effective antioxidants. Presently, no experimental tests have been reported in support of this assumption.

So far, quantum-chemical estimations have addressed mainly small thioamide molecules: thioformamide, thioacetamide, thiocarbamide, and their alkyl derivatives. The present investigation concentrates on larger systems with π-conjugation. Appropriate study cases for the purpose are the amide and thioamide of o-hydroxycinnamic acid and the neutral radicals they form. The latter are attractive as antioxidants. To substantiate the above stated hypothesis UHF and DFT calculations with 6-31G(d), 6-31+G(d) basis sets for the amide and thioamide of o-hydroxycinnamic acid and their hydroxyl radicals are carried out.

The results support the supposition for enhanced stability of the thioamide radicals. Their vibrational spectra are in excellent agreement with the theoretically predicted ones.

Theoretical Description of Ge/Si Microclusters

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Theoretical study on the $\mathrm{Ge}_m\mathrm{Si}_n$ heteroclusters has been performed using the single determinant perturbative methods. Several possible geometries of these clusters have been studied to locate the energetically most favorable isomers. It is observed that the properties of both types of atoms inside the clusters become equivalent. The formation of Si-Si bond is preferred among the three types of bonds available. It is shown that the small interatomic charge transfer is essential to gain the stability of the clusters, nevertheless the Ge/Si bonds do not reveal a significant ionic character. The unusual L–shaped structure of the GeSi_2 molecule is explained by the comparison to other triatomic species. With the absence of significant interatomic charge donation the ionization process leads to the bonds elongation. The vertical and adiabatic ionization potentials only slightly depend on the size of the cluster. The electron density at the bond critical points together with its laplacian indicate that the Ge/Si bonds reveal intermediate properties and cannot be classified as a one of the two limiting types of interatomic interactions. The *ab initio* calculated dissociation energies agree well with the experimental data. The experimental atomization enthalpies are improved by replacing Gibbs energy functions with fully theoretical thermal functions.

On the Reactivity of Curved Carbon Nanostructures to Amidogen

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Single-walled carbon nanotubes (SWNTs) described as rolled graphene sheets have induced great research interest because of their unusual physical and chemical properties [1]. Understanding the chemistry of SWNTs is a viable route to developing controlled synthesis methods, enhance their solubility, and make them more amenable for the assembling of nanostructure precursors. The chemical reactivity of the exterior surface of SWNTs to many kinds of molecules and atoms has been revealed both experimentally and theoretically [2]. The adsorption changes the electronic structure of the SWNT, and in turn imoses modifications in the electronic properties of the tube. Also, interest in the chemical reactivity on the sidewall of SWNTs has greatly increased to improve the solubility and processibility of functionalization in SWNTs.

A detailed and complete description of the sorption processes on carbonaceous adsorbents is still a key problem and the solution to which is still far from complete. Many aspects (e.g. the intermolecular interaction, the orientation of adsorbate molecules with relation to the adsorbent, the deformation of adsorbent and adsorbate, the influence of the doping atoms on the adsorption process) should be taken into account in adsorption processes. Thus, the theoretical studies of intermolecular interaction between adsorbate and carbonaceous adsorbents on the basis of computational chemistry (ab initio, DFT, and QM/MM) have recently been attracting great attention [3].

In this work, we study the chemical reactivity of exterior surface of curved carbon nanostructure (in the form of *(n,0)* SWNTs) to amidogen radical using DFT calculations. The calculations were performed using the Gaussian 98 program (B3LYP with the 6-31G(d,p) basis set) [4]. The mechanisms of $\cdot NH_2$ adsorption was discussed, among other things, on the basis of the calculation of reactivity parameters and the enthalpy of reactions (T=298 K, p=1 atm.).

Acknowledgements: The authors acknowledge the use of the computer cluster at the Information and Communication Technology Center of the Nicolaus Copernicus University (Toruń, Poland).

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Towards the Reactivity of Carbon to Izoelectronic (Cl^- and K^+) Adsorbates

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Physicochemistry of Carbon Materials Research Group, Toruń, Poland.

Ab initio, Density Functional Theory (DFT), and Quantum Mechanics/Molecular Mechanics (QM/MM) are promising to the investigation of the sorption mechanisms on the carbonacous materials. Therefore, the theoretical studies taking into account the intermolecular interactions between adsorbate molecules and the adsorbent structure, on the basis of computational chemistry, have recently been attracting great attention [1].

A very important problem during the study of adsorption mechanism on the carbonaceous adsorbents using quantum calculations is the choice of the shape and size of the graphene layer and the location of unsaturated carbon active sites, defects, doped atoms, etc. On the other hand, there are not the models of the structure of the porous carbon that can successfully explain all its measured experimentally physical and chemical features [2]. On the other hand, some models of carbonaceous materials assume that structures of randomly connected graphene clusters consisting of several aromatic carbon atoms (3-7 rings) [2]. Several models have been proposed to predict and simulate different primary structures possible to be found in a carbonaceous material (basal plane, armchair, zigzag, and tip models) [1, 3]. Since an electron does not delocalize through single bonds efficiently, it is reasonable to assume that the reactivity of each graphene cluster is not affected by the remaining structure. Therefore, carbon active sites are considered as unsaturated carbon atoms in carbonaceous models [1].

In the current studies we focus on the utility of HSAB in the description of the reaction of chloride anion (Cl^-) and potassium cation (K^+) with different types of 2-radical graphene sheets possessing various numbers of benzene rings. We limited considerations to two neighboring unsaturated carbon atoms in the zig-zag position. The calculations were performed using Gaussian 98 (B3LYP with the 6-31G(d,p) basis set) [4]. Additionally, to study the chemisorption of Cl^- and K^+ ions on the mentioned above graphene sheets the well- known reactivity parameters and the enthalpy of reactions (T=298 K, p=1 atm.) are taken into account. A systematic theoretical study shows that for the chloride anion charge transfer is significant. The opposite result is obtained for the second ion. Therefore, we observe that the enthalpy of sorption remains almost constant as the model size increases for K^+ in contrast to Cl^-.

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The Interaction of Platinum Complexes with Sulfur-Containing Amino Acids; Theoretical Calculations

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The cisplatin interactions with sulfur containing amino-acids in vacuum and with implicit solvent were simulated. We considered two cisplatin hydrated forms, cis-$[Pt(NH_3)_2(Cl)H_2O]^+$ and cis-$[Pt(NH_3)_2(OH)H_2O]^+$ and two sulfur-containing amino acids cysteine and methione as a reactants. In the first step, reaction mechanism involves formation of monodentate intermediates, where aqua ligand is replaced with amino acid. For coordination, all three active sites of amino acid were considered: sulphur, nitrogen and oxygen. In the next stage, the another platinum ligand is replaced by one of the remaining donor atoms of the amino acid creating the chelate structure. Reaction energies were determined in the so-called supermolecular approach as well as in the model of isolated molecules. In order to describe solvent effects SCRF/CPCM method was used.

Structures were optimized using DFT method in split valence double-zeta basis set with polarization and diffusion functions on heavy atoms. Core electrons of platinum, sulfur and chlorine atoms were described by quasirelativistic pseudopotentials. Single point calculations together with the NPA population and MO analyses were performed using 6-311++G(2df,2pd) basis set.

Solvent effects exhibit strong influence on structures and calculated thermodynamic data. The difference between vacuum and PCM reaction Gibbs free energies were found up to 20 kcal/mol. Methionine and cysteine sulfur is preferred monodentate donor atom in both chloro and hydroxo complexes. However, in case of methionine, formation of the complex with Pt-N coordination shows very similar thermodymic characteristics. In comparison with vacuum results, first reaction steps are less exotermic in contrast to the chelation step, which is facilitated by presence of water environment. The only exception is methionine κ^2S,O chelate in hydroxo complexes. Generally, the formation of chelate structures is exotermic in case of hydroxo complexes and endotermic in case of chloro complexes. In accord with experimental observations the formation of κ^2S,N chelate structures is thermodynamically preferable.

Study of the Binding of *Pseudomonas aeruginosa* Alginate by Toll-Like 4 and CD18 Receptors

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Bacteria possess adhesion substances that play essential roles in targeting host cells and in propagating infection. *Pseudomonas aeruginosa* cause hospital-acquired and often persistent infections. The pulmonary infections with *P. aeruginosa* remain a serious clinical problem for cystic fibrosis, immunocompromised and mechanically ventilated patients. In these patients mucoid *P. aeruginosa* produce exopolysaccharide also referred to as alginate and persistently colonize lung. This alginate is a random polymer of D-mannuronic acid (M) and L-guluronic acid (G) residues linked SS1-4.

Here we report on the results of molecular dynamics simulations carried out on complexes between the alginate structure and the pathogen recognition cell surface receptors :Toll -like 4 (TLR) and CD11/CD18, required for many cellular adhesive interactions and during the immune response to microbial infections. Molecular simulations (using Accelrys Insight II software) were carried out for complexes containing an alginate (mannuronic-mannuronic-guluronic-mannuronic acids-MMGM) and leucine-rich repeat (LRR) sequences of TLR4 as well as for complexes containing beta -2 integrine - a part of CD11/CD18 receptor. The four binding site of alginate found in the present study were located within domain LRR.

Our computational studies demonstrate that the beta -2 integrine may be involved in *P. aeruginosa* adherence to host cells. The alginate polymer with beta-2 integrine created three complexes and many of hydrogen bonds were formed. On the basis of energy of interactions, in spite of lowest Ludi Score, only one structure was mostly stable. It was characterized by hydrogen bonds.

This studies shed light on the molecular mechanisms bacterial adhesion. Understanding the invasive capacity of mucoid *P.aeruginosa* should open up new avenues to inhibition of infections. The host cells treatment with receptor blocking antibody or pharmacological inhibitors may limit bacterial adherence.

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