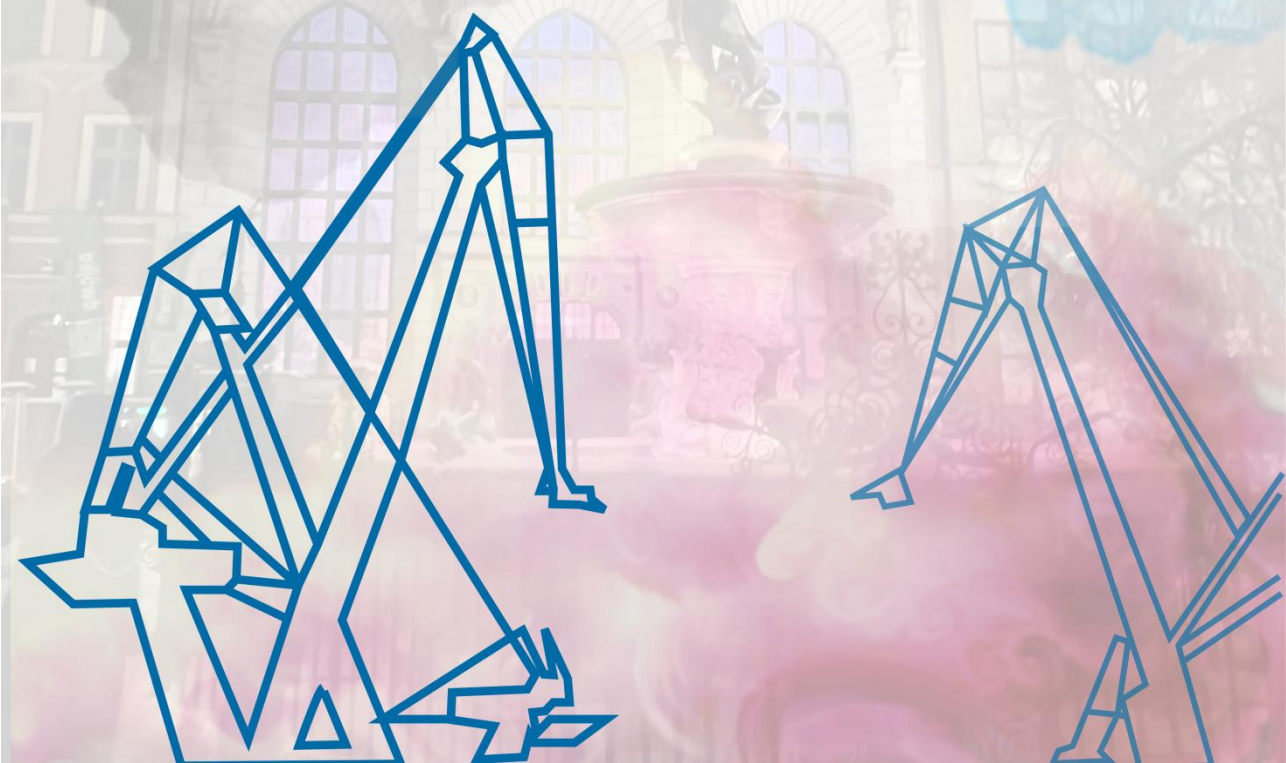
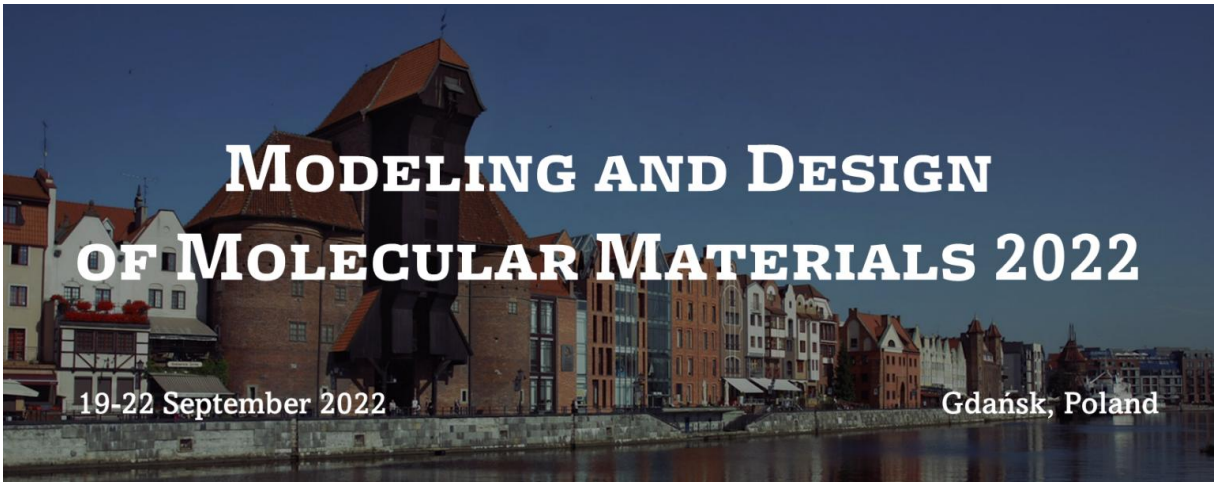
MDMM
2022

Modeling and Design
of Molecular Materials 2022

19 - 22
September 2022
Gdańsk, Poland

BOOK OF ABSTRACTS





BOOK OF ABSTRACTS

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Modeling and Design of Molecular Materials 2022

University of Gdańsk
Gdańsk, Poland
19 - 22 September 2022

Conference Chair
Prof. Janusz Rak, PhD, DSc

Organised by
Univeristy of Gdańsk

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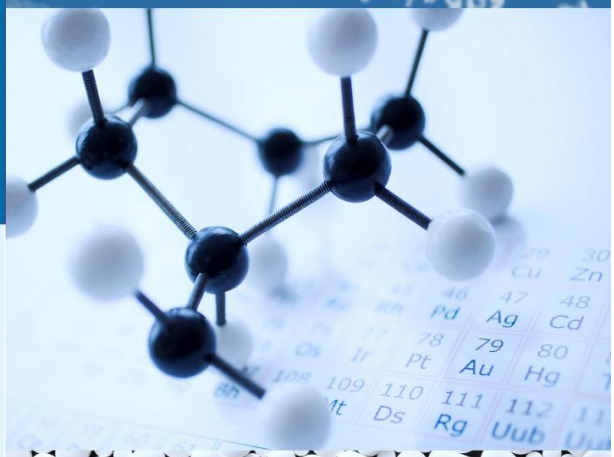

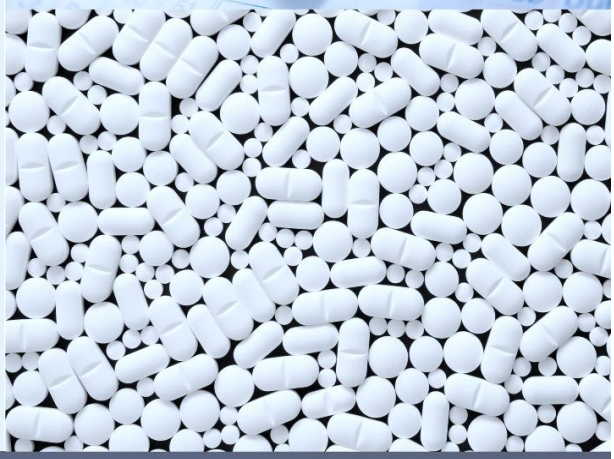

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Molecular materials
As the key word

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9th edition:

MODELING AND DESIGN OF MOLECULAR MATERIALS 2022

19 - 22 September

Gdańsk, Poland

University of Gdańsk | Jagiellonian University in Kraków | Wrocław University of Science and Technology | Jackson State University

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Day 1 - 19 September 2022 (Monday)

8:00-9:00 Registration

9:00-9:10 **Opening ceremony** - Vice-Rector for Research of the University of Gdańsk, Prof. Wiesław Laskowski and Chairman of the MDMM 2022 conference, Prof. Janusz Rak

Session I: Materials for medical treatment - part I (chair: L. Gorb)

9:10-9:40 **Jolanta Grembecka** *Structure-based Development of Menin Inhibitors for Leukemia Treatment: from Benchside to the Clinic*

9:40-10:10 **Michael Mitchell** *Biomaterials for Cancer Immunotherapy and Genome Editing*

10:10-10:40 **Tomasz Cierpicki** *Role of the Dynamics in Assessing Protein Druggability*

10:40-11:00 Coffee break

Session II: Materials for medical treatment - part II (chair: M. Mitchell)

11:00-11:30 **Seungpyo Hong** *Dendritic Nanoparticle Platform for Enhanced Cancer Immunotherapy*

11:30-12:00 **Leonid Gorb** *Static and Dynamic DFT Calculations of DNA mini-helixes*

Oral presentations

12:00-12:15 **Joao Ameixa** *Mechanisms of Radiosensitization in Fluorinated DNA: DNA Origami Studies* (Young Researcher Award)

12:15-12:30 **Anna Stachowicz-Kuśnierz** *Congo Red as a Supramolecular Carrier System for Doxorubicin: an Approach to Understand the Mechanism of Action*

12:30-12:45 **Farhad Izadi** *Decomposition of the Sanazole Radiosensitizer by Low-Energy Electrons*

12:45-13:00 **Joanna Panecka-Hofman** *Non-Equilibrium Simulations of Pteridine Reductase 1 Reveal its Flexibility Hot-Spots*

13:00-13:15 **Magdalena Muszyńska** *Characterizing Molecular Machines Using SwitchSENSE® Technology* (Sponsor presentation, Dynamic Biosensors)

13:15-14:30 Lunch

Session III: Molecular anions - part I (chair: S. Denifl)

14:30-15:00 **Kit H. Bowen** *Electron Induced Proton Transfer*

15:00-15:30 **Xue-Bin Wang** *Cryogenic Photoelectron Spectroscopy of Microsolvated Anions and Hydrogen Bonded Clusters*

15:30-17:00 **Poster session and coffee - odd posters' numbers**

17:00-18:30 Welcome meeting

Day 2 - 20 September 2022 (Tuesday)

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8:30-9:00 **Sylwia Rodziewicz-Motowidło** *How to Become a Cyborg to Live Longer? New Biomaterials in the Regeneration Process*

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9:00-9:30 **Nohad Gresh** *Simulations of Ligand-Zn-Eetalloenzyme Complexes. Prospects for Large-Scale Polarizable MD Simulations of Ligand-Macromolecule Complexes*

9:30-10:00 **Pedro Fernandes** *The Interplay Between Enzyme Flexibility, Reaction Mechanism and Reaction Rate*

10:00-10:30 **W. Andrzej Sokalski** *Use of Catalytic Fields for Better Understanding of Enzyme Catalytic Activity and Inverse Theozyme Design*

10:30-11:00 **Carme Rovira** *Computer Simulation of Mechanisms in Glycoprocessing Enzymes Using QM/MM Approach*

11:00-11:30 Coffee break

Session VI: Modelling catalytic reactions (chair: T. Clark)

11:30-12:00 **Wojciech Macyk** *Selected Aspects of Modeling of Photocatalytic Reactions*

12:00-12:30 **Detlef Bahnemann** *Mechanism(s) of Photocatalytic Processes: Revisited!*

12:30-13:00 **Rafał Szabla** *Predicting Photochemical Reactivity Based on Computational Characterization of Reaction Mechanisms*

13:00-13:30 **Marcin Hoffmann** *Hydrosilylation versus Hydrogermylation of Alkenes – DFT Studies on Reactions' Mechanisms*

Oral presentations

13:00-13:45 **Zdenek Futera** *Mechanism of Electron Transport through Metal-Protein-Metal Junctions*

13:45-15:00 Lunch

Session VII: Molecular anions - part II (chair: K. H. Bowen)

15:00-15:30 **Janina Kopyra** *Decomposition of Biologically Relevant Molecules Triggered by Low Energy Electrons*

15:30-16:00 **Stephan Denifl** *Low-energy Electron Attachment to Potential Radiosensitizers*

16:00-16:30 **Ilko Bald** *Low-energy Electron Induced Processes in Biological and Plasmonic Materials - Implications for Cancer Treatment and Catalysis*

16:30-18:00 **Poster session and coffee - even posters' numbers**

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9:30-10.00 **Timothy Clark** *Quantum Chemistry for Very Large Systems*

10:00-10:30 **Tomasz Wesolowski** *Recent Progress In Frozen-Density Embedding Theory based Multi-level Simulations for Condensed Phase*

10:30-11:00 Coffee break

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11:30-12:00 **Artur Michalak** *Theoretical Study on Polymeric Materials for Fuel-Cell Applications*

12:00-12:30 **George Froudakis** *Traditional Theoretical Methodologies vs Novel Machine Learning Techniques for Addressing the Gas Storage Problem in Nanoporous Materials*

12:30-13:00 **Donald Siegel** *Discovery and Demonstration of Metal-Organic Frameworks for the Storage of Hydrogen and Natural Gas*

13:00-14:00 Lunch

14:00-18:30 **Excursion**

20:00-00:00 **Conference dinner**

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Oral presentations

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9:45-10:00 **Karol Baran** *Driving Forces of Carbon Dioxide Absorption in Novel Ionic Liquids from Molecular Simulations Perspective*

10:00-10:15 **Anna Kaczmarek-Kędziera** *Influence of Hydrogen and Halogen Bonds on Photophysical Properties of Squaraine Dyes*

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10:45-11:15 Coffee break

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Oral presentations

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13:00-13:15 **Piotr Wróbel** *IR Spectra of Liquids Modelling with MD Simulations*

13:15-14:30 Lunch

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15:00-15:30 **Jacek Korchowiec** *The Lung Surfactant Activity Probed with Molecular Dynamics Simulations*

Oral presentations

15:30-15:45 **Saruti Sirimatayanant** *Two-Photon Absorption Spectrum of Rhodopsin Calculated using TD-DFT/ MM with Polarizable Embedding Scheme*

15:45-16:00 **Nicolas Callebaut** *Quantum Mechanical Study of Size and Sequence Effects on the Ionization Potential of Stacked DNA Bases*

16:00-16:15 **Hari Desai** *DFT Studies on Adsorption of Hg Vapors on Sulfur Impregnated Activated Carbon*

16:15-16:30 **Valery Lutsyk** *Extending the Martini 3 Coarse-Grained Force Field to Carbohydrates*

16:30-16:45 **Piotr Ordon** *Theory and Applications of the Reaction Fragility Spectrum*

17:00-17:15 **Awards and Closing ceremony**

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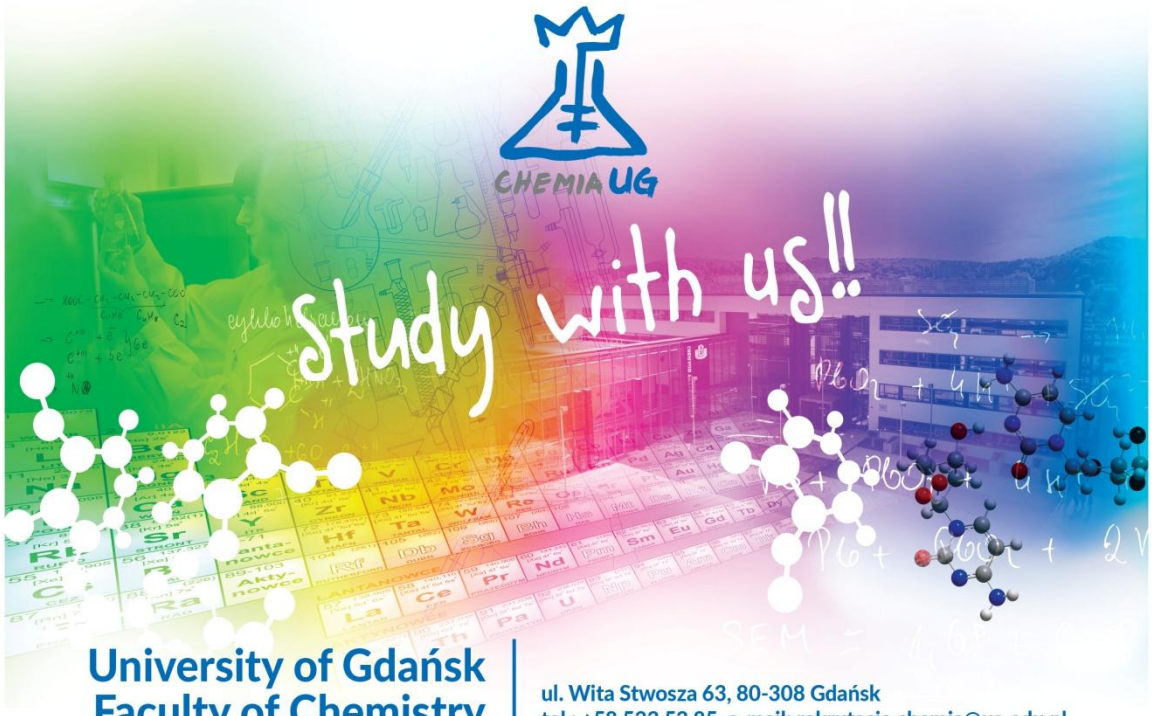

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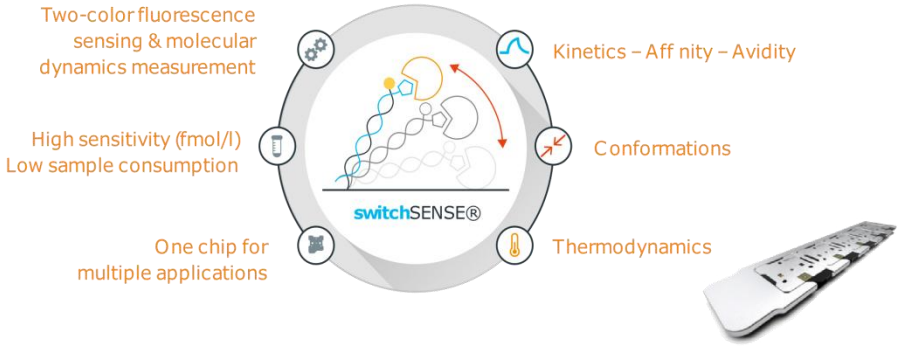

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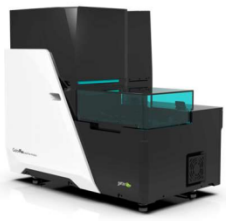

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SPEKTROMETRIA

Dear Colleagues,

It is a great pleasure to welcome you to the **Modeling & Design of Molecular Materials 2022** (**MDMM 2022**) conference. This is an interdisciplinary meeting that will be devoted to the various aspects of conceiving materials with pre-defined properties. The key term is "molecular material" which in the context of the conference means **drugs** and **drug carriers** (focused on cancer), **catalysts with emphasis on photocatalysts** (e.g. solar energy conversion) or **theozymes** (theoretically designed biocatalysts), **materials for hydrogen storage** (green fuel), **conductive polymers** (e.g. electronics, biosensors), etc. Nowadays, computer modeling seems to be a crucial step for the rational design of materials with demanded properties. Thus, during this prospective event we gather specialists who develop computational methods useful in the computer-aided design of materials as well as those who employ molecular modeling at the very early stage of their projects and for whom computational approach leads eventually to practical solutions.

The present conference is a continuation of a 8 biannual MDMM meeting series which has been ignited in 2004 by Prof. Sokalski. Over years, the conference has developed into the well-established tradition of alternating Polish–Czech–American workshops involving Profs. Sokalski, Burda and Leszczynski from Technical University of Wrocław (Poland), Charles University in Prague (Czech Republic), and Jackson State University (USA), respectively, as the main organizers of meetings taking place in Lower Silesia in Poland (MDMM), Czech Republic (Modeling Interactions in Biomolecules (MIB)) and Jackson, Mississippi, USA (Current Trends in Computational Chemistry (CCTCC)).

In 2022 the 9th edition of Modeling & Design of Molecular Materials will be held in Gdańsk (Poland) at the Baltic Campus, a modern academic center comprising most departments of the University of Gdańsk. The current meeting gather not only computational chemists, but also physicochemists, material chemists, photochemists, etc., i.e. all those who not only develop but also use computational chemistry in their everyday research, from all over the world. The conference should illustrate well both the challenges in the field of molecular modeling and the significant progress that has been achieved in the last few years towards solving practical problems in materials science, biotechnology and medicine.

Prof. Janusz Rak
Chair of **MDMM 2022**

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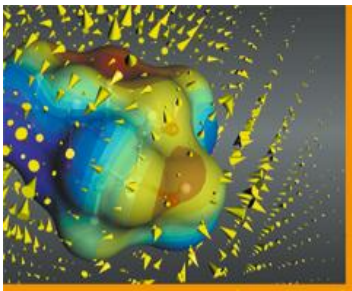

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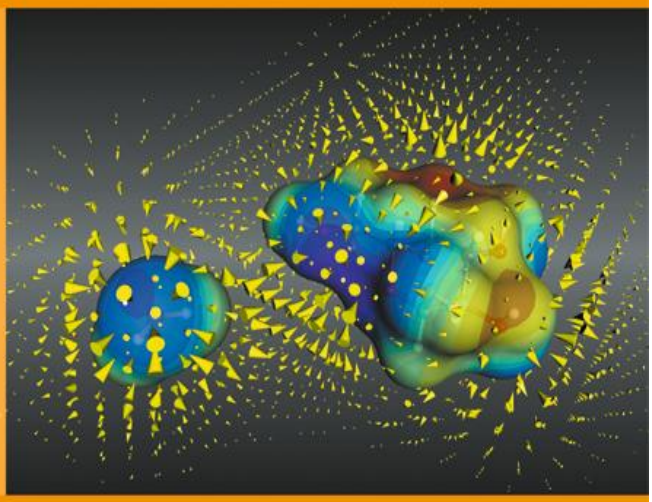

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Submission to first decision (Median): *26 days*
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GENERAL INFORMATIONS

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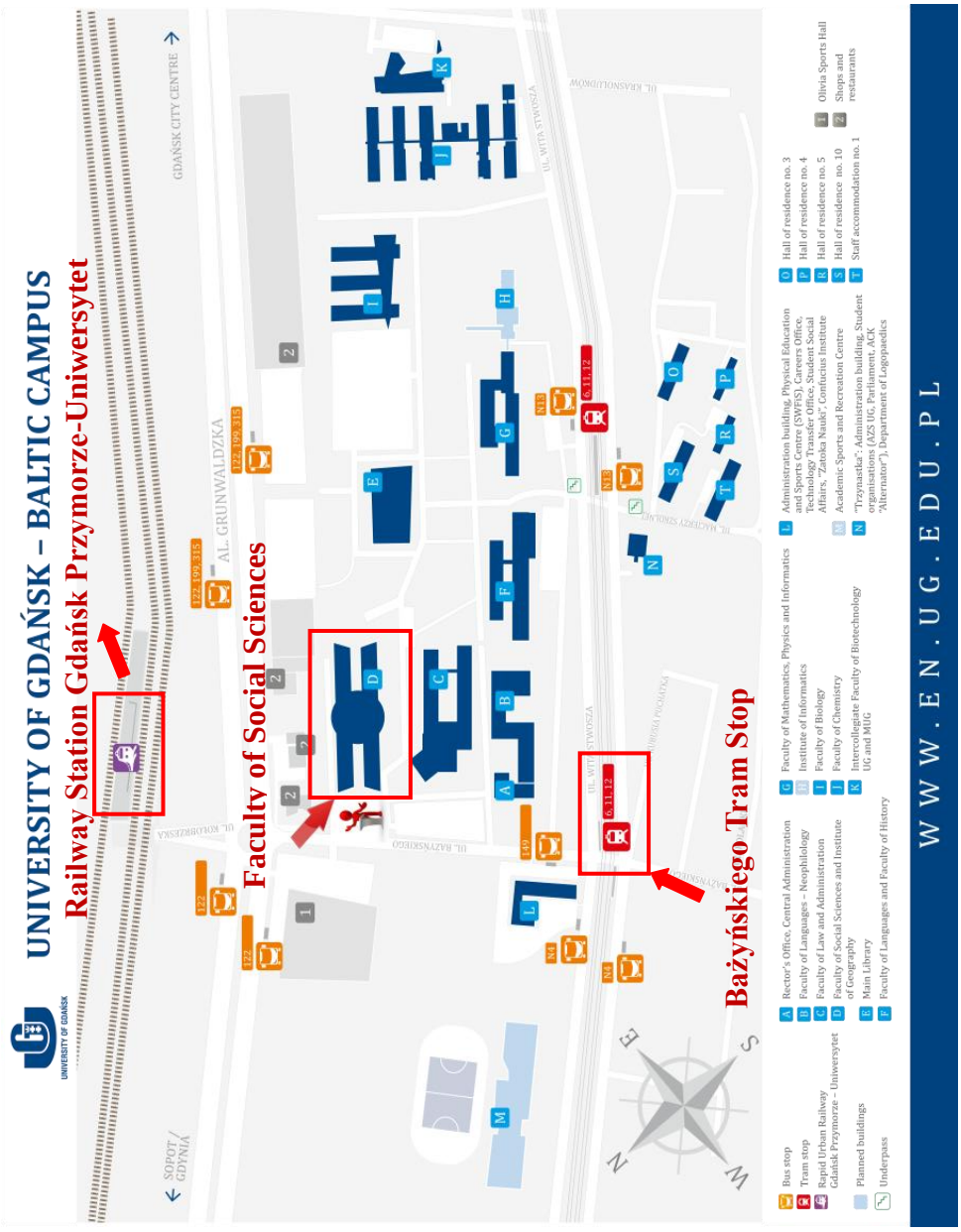


Baltic campus

The University of Gdańsk is a dynamically developing institution of higher learning, and one that combines respect for tradition with a commitment to the new. It offers education in nearly all fields of academic knowledge, in sought-after professions on the job market and in state-of-the-art facilities in its Gdańsk, Sopot and Gdynia campuses. It is currently one of the most modern academic centres in the north Poland.

The University of Gdańsk's investment in development is concentrated in the expansion of the University on three campus sites: in Oliwa (The University of Gdańsk Baltic Campus), in Sopot, and in Gdynia. The University's infrastructure has been developed in recent years principally through financial support obtained through European Union programs. New faculty buildings, and work units, and laboratories, provided with state-of-the-art equipment, open up new possibilities for scientific and scholarly research, and for cooperation with the economy and with business.

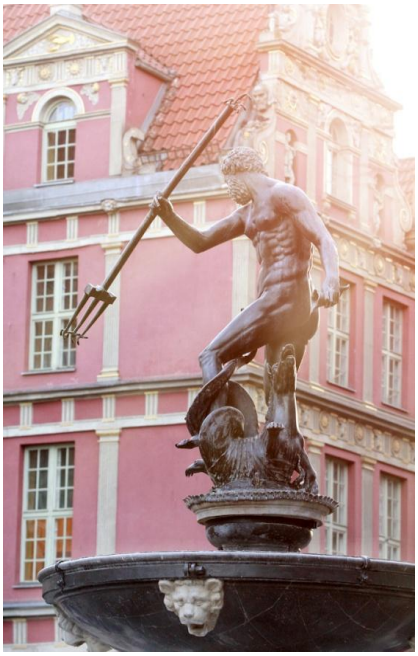
20th March 2020 will mark the 50th anniversary of the founding of the University of Gdańsk, at present the largest university in the Pomeranian region, which has had an indisputable influence on the development of modern Poland, science and higher education. We have eleven faculties with almost twenty six thousand students, doctoral students and post-graduates.

Gdańsk city

Gdańsk is one of the most beautiful cities in Poland. It is located at the Baltic Sea and together with Gdynia and Sopot, it forms an agglomeration called the Tri-City, with nearly 1.1 million inhabitants. Due to its location, Gdańsk has been developing intensively since the beginning of its existence (it was one of the first cities in Poland, the settlement has already existed here in the 8th century). It belonged to a group of Hanseatic League cities which participated in maritime trade. Gdańsk played an important role in history. In 1939, it was one of the hot spots of World War II, and later, in 1980, it became the birthplace of the Solidarity workers movement, which contributed to the end of communist domination in Eastern Europe.

Most main attractions are located in **The Main Town**. Although the destruction of World War II is still a place with one of the most valuable historic ensembles in Poland. The most valuable monuments are located along the **Royal Road** (Droga Królewska) guiding from the **Highland Gate** (Brama Wyżynna) to the **Green Gate** (Brama Zielona) located close to the **Motława's Rriver**. By the Motława's Rriver we can admire the **Granary Island** (Wyspa Spichrzów) with picturesque, eighteenth-century granaries, the **Polish Baltic Philharmonic** and the **Gdańsk Crane** - a historic medieval port crane. Between the gates there is the **Coal Market** (Targ Węglowy), where you can see the **Prison Tower** (the **Amber Museum** is also located here). Short way off is the **Golden Gate** (Złota Brama) beginning of the **Long Street** (Ulica Długa) and the **Long Market** (Długi Targ).

Following this route there are beautiful tenement houses. The **City Hall** is definitely worth a visit (the Historical Museum of the City of Gdańsk is located here), with an 83-meter tower. One of the most characteristic places on the **Long Market** (Długi Targ) is the **Neptune's Fountain** and the **Artus Court**, a place where merchants, politicians and other wealthy residents of the city met to discuss in past times. Behind the town hall building is **Basilica of the Assumption of the Blessed Virgin Mary**, it is the largest brick church in the Europe. The building, with its grandeur and interiors, creates an amazing impression, and the Tower viewpoint offers a beautiful view of the Gdańsk Old Town.



Recommended museums in Gdańsk are the **European Solidarity Centre** and the **Museum of the Second World War**.

Another interesting and worth visiting place in Gdańsk, near to Baltic Campus is Oliwa's district. For centuries it was a monastery village. There are the **Oliwa Cathedral**, which dates back to the 12th century and the monastery garden, which over time grew and was transformed into the **Oliwa Park** (there is a botanical garden and the **Abbots' Palace**). A walk through the park's alleys, among the well-kept trees, bushes and ponds where ducks and swans live, is a great idea to spend a day off.

How to get to Gdańsk

Plane

Gdańsk has only one airport. You can get from Gdansk Lech Walesa Airport to the city centre:

1. by **PKM trains** (Pomeranian Metropolitan Railway)
    - Route: Gdańsk Port Lotniczy > Gdańsk Wrzeszcz*
2. by **public transport buses**
    - Line 110 (Route: Port lotniczy > Wrzeszcz PKP)
    - Line 210 (Route: Port lotniczy > Dworzec Główny)
    - Night line N3 (Route: Port lotniczy > Wrzeszcz PKP > Dworzec Główny)
3. by **taxi**
    - Neptun Taxi: (+48) 800 170 700

*If you travel directly to the Conference venue from the airport, you can get off at the Strzyża Station (Gdańsk Port Lotniczy > Strzyża > Gdańsk Wrzeszcz), and you can go by tram (line 5, 6, 12; you have to get off at the Bażyńskiego tram stop).

Train

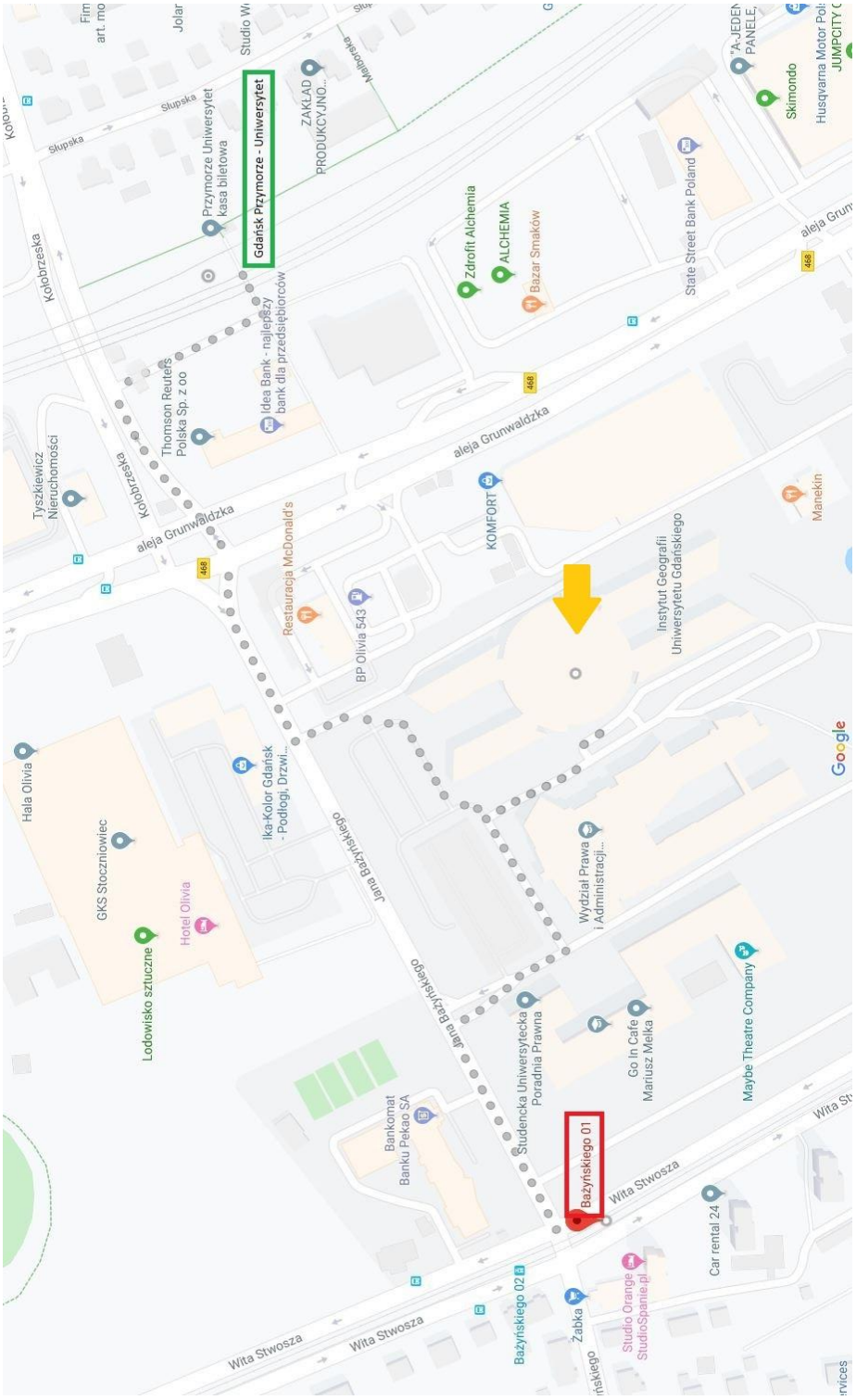
If you travel from e.g. Warsaw or Cracow city, you can get to Gdańsk by PKP Intercity trains (https://www.intercity.pl/en/). The trains arrive directly at the Gdańsk Główny or Gdańsk Wrzeszcz Station.

Communication within the Gdańsk

The MDMM 2022 Conference is located in Baltic Campus of University of Gdańsk. The venue can be reached:

1. By **SKM (Szybka Kolej Miejska) trains**
    - Route: Gdańsk Główny > Gdańsk Przymorze - Uniwersytet
    - Route: Gdańsk Wrzeszcz > Gdańsk Przymorze - Uniwersytet
2. by **tram**
    - from Gdańsk Główny: line 6, 12
    - from Gdańsk Wrzeszcz: line 5, 6, 12

In both cases you have to get off at the Bażyńskiego tram stop.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Przymorze Uniwersytet kasa biletowa
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Słupska
Kołobrzeska
Thomson Reuters Polska Sp. z oo
Idea Bank - najlepszy bank dla przedsiębiorców
Tyszkiewicz Nieruchomości
aleja Grunwaldzka
Restauracja McDonald's
BP Olivia 543
KOMFORT
Zdrofit Alchemia
ALCHEMIA
Bazar Smaków
State Street Bank Poland
Skimondo
Husqvarna Motor Pol
Manekin
Instytut Geografii Uniwersytetu Gdańskiego
Hala Olivia
GKS Stoczniowiec
Lodowisko sztuczne
Hotel Olivia
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Jana Bażyńskiego
Wydział Prawa i Administracji...
Studencka Uniwersytecka Poradnia Prawna
Go In Cafe Mariusz Melka
Maybe Theatre Company
Bankomat Banku Pekao SA
Bażyńskiego 01
Bażyńskiego 02
Wita Stwosza
Car rental 24
Żabka
Studio Orange StudioSpanie.pl
Google

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Emergency Information

All emergencies: 112 (no area code needed)
Ambulance and health emergencies: 999 or 112
Fire brigade: 998 or 112
Police: 997

SOCIAL EVENTS

EXCURSION

OLD TOWN
AND BOAT CRUISE

Today's Gdansk is a rapidly growing European city. Its unusual location and more than a thousand years of history make it unique. At the same time, it is a city that still holds many secrets and has that "something" that makes it impossible to be mistaken for any other.

Participants of the MDMM2022 conference will have a chance to explore the history of beautiful Gdansk by taking part in a scheduled tour on 21st September. It includes a guided walk through the Old Town and then a cruise on the pirate ship from Gdansk to Westreplatte - an extremely important place in Polish history, associated clearly with the moment when World War II broke out.

Tour schedule:*

14:00 departure from the UG campus

14:30 walking tour of Gdansk with a guide

16:00 pirate ship cruise to Westerplatte and back

18:00 return by bus to the UG campus

*times of individual tour points are subject to change.

CONFERENCE DINNER

WHITE MARLIN

restaurant & lounge

White Marlin is one of the most beautiful and atmospheric restaurants in Northern Poland!

The restaurant is located in one of the wings of the Southern Baths in Sopot. The former bathing resort building perfectly represents the resort architecture of the seaside city, which was formerly known as the North Riviera. The interior of the restaurant has been designed with the idea of vacation rest Wood, white, beige and natural light are just some of the elements of a Boho style décor.

The Conference Dinner will be given in White Marlin on the 21st of September, starting at 8 p.m. A three-course meal and a four-hour open bar (house wine, regional beer, mineral water, juices, tea and coffee) will be served to satisfy the participants of MDMM2022.

We recommend taking a taxi or using the SKM train to the Sopot stop, followed by about a 15-minute walk to get to White Marlin.

Adress:

White Marlin
Aleja Wojska Polskiego 1
81-769 Sopot
Reception number phone:
0048 784 629 283

ABSTRACTS OF INVITED LECTURES

Structure-Based Development of Menin Inhibitors for Leukemia Treatment: from Benchside to the Clinic

Jolanta Grembecka

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Menin is a protein that directly interacts with the Mixed Lineage Leukemia 1 (MLL1) histone methyltransferase, and this protein-protein interaction (PPI) is required for recruitment of MLL1 to the target genes and plays a critical role in acute leukemia with mutations in *nucleophosmin* (*NPM1*) gene. Menin also binds to MLL fusion proteins and this interaction is involved in acute leukemia with *MLL1* translocations, which lead to poos prognosis in acute myeloid leukemia (AML) patients (<35% 5-year survival). Therefore, small molecule inhibition of the menin-MLL1 interaction might represent novel promising strategy for the treatment of different subtypes of AML.
We developed small molecules that specifically bind to menin and inhibit the menin-MLL1 protein-protein interaction both *in vitro* and in cells. Crystallography studies demonstrate that these compounds bind to the MLL1 binding site on menin and closely mimic the key MLL1 interactions with menin. Using structure-based design, we extensively optimized these compounds, which resulted in sub-nanomolar menin-MLL1 inhibitors with favorable drug-like properties. These compounds demonstrate strong effect and specific mechanism of action in leukemia cells and block progression of acute leukemia in mouse models of *MLL1*-rearranged and *NPM1*-mutated leukemia, including complete, long-lasting remission in mice. One of our menin inhibitors was introduced to clinical trials in AML patients and demonstrated encouraging initial clinical efficacy. Our work provides a strong example of successful targeting of PPIs with small molecules for new therapeutic applications. We also demonstrate how systematic structure-based optimization of PPI inhibitors can lead to *in vivo* active compounds and potentially new therapeutics.

Lipid Nanoparticles for Overcoming Biological Barriers to Nucleic Acid Delivery

Michael J. Mitchell

Department of Bioengineering, University of Pennsylvania, Philadelphia, PA

Significant advances have been made in the development of nucleic acid therapeutics to both generate therapeutic proteins (via mRNA, pDNA) and silence proteins that trigger disease progression (via siRNA, miRNA, antisense oligonucleotides (ASOs)). Most recently, the development of gene editing technologies (CRISPR-Cas, TALENs, zinc finger nucleases (ZFNs)) have opened new opportunities to precisely edit the genome, target disease causing mutations, and potentially enable one-time cures of genetic diseases. However, these therapeutics must overcome numerous obstacles to be successful, including rapid *in vivo* degradation, poor uptake into target cells, required nuclear entry, and potential *in vivo* toxicity in healthy cells and tissues. In this talk, I will discuss our efforts towards the development of new lipid nanoparticles (LNPs) that enable the delivery of nucleic acid therapeutics to target cells and tissues *in vivo*. Furthermore, I will describe new therapeutic strategies utilizing these LNPs for (i) mRNA CAR T cell engineering for cancer immunotherapy, and (ii) in utero mRNA delivery for treating disease before birth.

Keywords*: lipid nanoparticles, mRNA*

Role of the Dynamics in Assessing Protein Druggability

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Prediction of protein druggability could facilitate development of novel drug candidates. Druggability of a given protein depends on the physicochemical and topological properties of small-molecule binding sites and many tractable drug targets such as protein kinases, GPCRs and channels present well-defined binding pockets. On the other hand, protein-protein interaction (PPI) binding sites are typically more flat and larger, and are consequently more challenging for development of small molecule inhibitors. Protein druggability can be predicted based on computational approaches and experimental methods, such as fragment screening. Here, we evaluated the druggability of BTB domains, which are common PPI motifs present in transcription factors and epigenetic proteins and are attractive targets for inhibitor development. We carried out fragment screening against the BTB domains of KAISO, LRF, and MIZ1, and we identified multiple small-molecule ligands that bind to MIZ1, but we found no hits for KAISO and LRF. To rationalize this unexpected finding, and to elucidate the biophysical and structural bases of ligandability of these BTB family members, we investigated BTB domain dynamics using solution NMR spectroscopy. Our findings argue that protein dynamics may be a broadly applicable tool in drug discovery to assess the druggability of novel and challenging targets.

Dendritic Nanoparticle Platform for Enhanced Cancer Immunotherapy

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Dendritic polymers have drawn considerable attention to be used as a nanocarrier platform for various therapeutic agents over the past few decades. Major advantages of the macromolecules include: i) the ability to mediate strong multivalent binding; ii) efficient, controlled tumor penetration due to their sub-10 nm size and deformability; and iii) facile multifunctionalization through various conjugation chemistries. In this presentation, our recent efforts on using poly(amidoamine) (PAMAM) dendrimers for immunotherapy will be summarized. Immune checkpoint inhibitors (ICIs), either in a form of antibody or engineered peptide, targeting programmed death-ligand 1 (PD-L1) on tumor cells were conjugated to a generation 7 (G7) PAMAM dendrimer, followed by characterization, binding kinetics measurements, in vitro cell assays, and in vivo biodistribution/efficacy studies. The three independent binding measurements using surface plasmon resonance (SPR), bio-layer interferometry (BLI), and atomic force microscopy (AFM) all revealed that the dendrimer-ICI conjugates exhibited a significantly greater binding kinetics than corresponding free ICIs, by up to five orders of magnitude. Such enhancement was likely achieved through the multivalent binding effect mediated by dendrimers, along with the folding structure stabilization of various peptides. The enhanced binding kinetics was translated into significantly improved immunotherapy efficiency and *in vivo* efficacy when tested using a syngeneic mouse model. Our results demonstrate that the dendrimer-based platform has great potential to enhance therapeutic efficacies of various immunotherapeutic drugs.

Acknowledgements: Milton J. Henrichs Chair Professorship; NSF DMR-2211932.

Keywords*: dendrimer, nanoparticle, cancer immunotherapy, immune checkpoint inhibitor*

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Static and Dynamic DFT Calculations of DNA Mini-Helixes

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We report a comprehensive quantum-chemical study on $d(A)_5{\cdot}d(T)_5$, $d(G)_5{\cdot}d(C)_5$ DNA mini-helixes and Dickerson dodecamer d[CGCGAATTCGCG] possessing A and B forms. The research was performed to model an evolution of the spatial structure of $d(A)_5{\cdot}d(T)_5$ and $d(G)_5$ $d(C)_5$ DNA mini-helixes from vacuum to water bulk. The influence of such external factors as the presence of counterions and the extent of hydration was included. The comparison of limited calculations has been carried out on the Dickerson dodecamer. In the case of static calculations, the study has been performed at the density functional theory level with ωB97XD exchange-correlation functional augmented by the 6-31G(d,p) basis set. In the case of dynamic calculations, the PBE functional augmented by the single-ζ valence SZV basis set and Goedecker-Teter-Hutter (GTH) pseudopotential was used.

The static calculations reveal that $(dA)_5{\cdot}(dT)_5$ anion when placed in a vacuum, forms a DNA duplex which possesses an intermediate form between a helix and a ladder. The presence of compensating Na^+ counterions or explicit micro-hydration of minor and major groves stabilizes a DNA mini-helix of a B-shape. Such factor as water bulk plays a minor role. Somewhat different behavior has been found in case of the $(dG)_5{\cdot}(dC)_5$ duplex. In this case we observe the formation of B-type mini-helixes even for $(dG)_5{\cdot}(dC)_5$ anion placed in vacuum. This is due to an additional stabilization originating from the appearance of an extra hydrogen bond, comparing to an AT base pair. The example of obtaining results is placed in Figure 1.

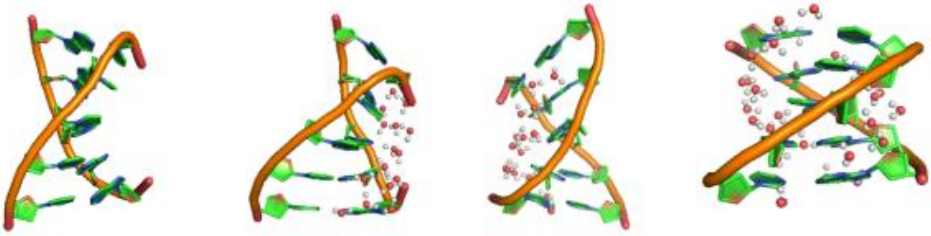

Fig. 1. Geometry of (dA)5·(dT)5 mini-helixes in vacuum (main view).

Electron Induced Proton Transfer

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This talk will report on the developing saga of electron induced proton transfer (EIPT), beginning with previous work on thymine-glycine heterogeneous dimer anions and ammonia-hydrogen halide anions. After presenting new work on the latter systems, which further supports and refines the model for EIPT, we will present results which show that small ammonia cluster anions are, in all likelihood, EIPT systems.

***Keywords**: ammonia cluster anions*

Cryogenic Photoelectron Spectroscopy of Microsolvated Anions and Hydrogen Bonded Clusters

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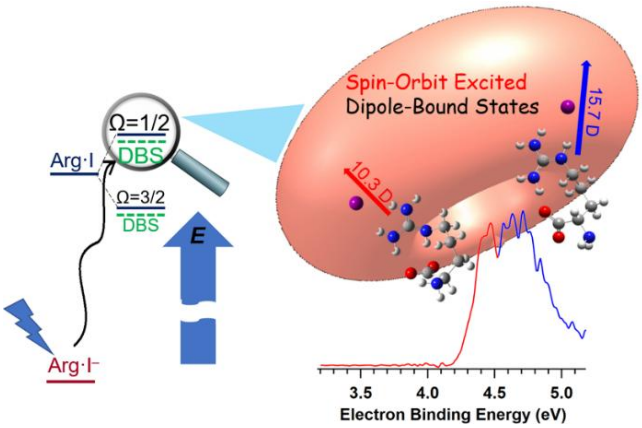
Employing size-selective cryogenic photoelectron spectroscopy (cryo-PES) coupled with electrospray ionization (ESI), we have been studying the physical and chemical properties of a wide variety of complex molecular clusters ranged from micro-solvated biological molecules to atmospherically relevant pre-nucleation clusters, and hydrogen bonded complexes. We revealed distinct solvation motifs of kosmotropic versus chaotropic anions regarding their ability in organizing local solvent structures, observed enormous difference of intermolecular interactions critical to biogenic aerosol formation, and probed proton location and proton transfer in a series of hydrogen bonded clusters. Our latest research focuses on probing photochemistry of hydrated anions and characterizing ion-molecular cluster conformations [1] via anion resonant states.



Electronic excitement of arginine-iodide molecular clusters can produce spin-orbit excited dipole-bound states. These states can be used as electronic Feshbach resonances that allow researchers to distinguish between complex arginine-iodide cluster isomers based on molecular dipole moments.

Acknowledgements: The work was supported by the U.S. Department of Energy (DOE), Office of Science, Office of Basic Energy Sciences, Division of Chemical Sciences, Geosciences, and Biosciences, and performed using EMSL, a national scientific user facility sponsored by DOE's Office of Biological and Environmental Research and located at Pacific Northwest National Laboratory, which is operated by Battelle Memorial Institute for the DOE.

***Keywords**: anion photoelectron spectroscopy, molecular clusters, anion resonant states*

References:
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How to Become a Cyborg to Live Longer? New Biomaterials in the Regeneration

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A cyborg is a human being supported by electronic or mechanical devices, possessing additional skills or enhancing natural skills or performance. According to this definition, a cyborg can also be defined as a human whose damaged tissues or organs are replaced by new ones. The field that deals with the restoration of damaged or lost tissues or organs is regenerative medicine, which requires the integration of knowledge from the physical and natural sciences with materials science and clinical medicine to learn to trigger the regeneration of failed human organs and tissues. People in the world are living longer and aspire to a higher quality of life at an advanced age. In addition, women's fertility is falling in developed countries, which means that global economies will have to keep humans functional as long as possible, using, among others, regenerative medicine. Regenerative technologies based on new materials, devices and cell therapies have also created new solutions for people who are victims of trauma, disease and birth defects. In a new era of regenerative human repair, materials have transformed from being primarily mechanical functions to advanced regulators of biological activity - "smart biomaterials". In modern biomaterials, molecular biological information is encrypted in such a way as to quickly start regeneration where it does not occur spontaneously. In addition, new biomaterials create the necessary bioactive architecture so that they integrate into the human body in the least invasive way. Additionally, the bioactive structure of the biomaterial can act as a carrier for drugs or cells. The vision of regenerative medicine is to regenerate the soft and hard tissues, organs, and nerves responsible for major human disability. The present lecture will be devoted to molecules which are designed to assemble into cell scaffolds for human repair and provides examples relevant to wound healing, skeletal muscles and brain damage, fractures of the skeleton and cartilage destruction.

Acknowledgements: Work supported by the National Centre for Research and Development of Poland, No. STRATEGMED1/235077/9/NCBR/2014 and No. TECHMATSTRATEG2/406384/7/NCBR/2019 and No. TECHMATSTRATEG2/410747/11/NCBR/2019. Work supported by the National Science Centre of Poland, No. 2019/35/B/NZ5/01555.

***Keywords**: biomaterials, scaffolds, regenerative medicine*

Simulations of Ligand-Zn-Metalloenzyme Complexes. Prospects for Large-Scale Polarizable MD Simulations of Ligand-Macromolecule Complexes

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Zn-metalloenzymes when overexpressed are involved in numerous pathologies and are a major target for the design of therapeutic drugs. Molecular dynamics (MD) simulations of ligand-Zn-metalloenzyme complexes are the next frontier for free energy simulations. Such complexes are challenging owing to the onset of very strong polarization/charge transfer and non-additivity. It is essential prior to such simulations to evaluate how well ΔE from polarizable multipolar potentials such as SIBFA [1] compares to ΔE(QC) in a diversity of multi-molecular complexes extracted from ligand-metallo-enzyme complexes which encompass the Zn-binding core. This was performed on the complexes of the extended recognition site of the VIM-2 (Verona-Integron Metallo-β-Lactamase) with five inhibitors having an anionic triazole-thione (TZT) as an anchor in the dizinc core and two side-chains substituting its C atom and an N atom *ortho* to it. They total up to 280 atoms. Whether with, or without, 14 structural waters, ΔE(SIBFA) reproduced BSSE-corrected ΔE(QC) with relative errors < 1.5%, as well as the QC ranking of the five ligands [2].

A next stage of refinement is the calibration of the SIBFA potential on the basis of SAPT-DFT calculations [3]. This was performed for four end-side chains of proteins: formamide, imidazole, formate and methanethiolate, and on the guanine base, all probed in detail by a dipolar probe, water, and a dicationic probe, Zn(II). This enabled each of the six SAPT-DFT energy contributions to be fit by refining the relevant parameters of their SIBFA counterparts by Least-Squares Fit with a BFGS minimizer. Validations were subsequently performed on multimolecular complexes of formamide (n=4-24), stacked guanine tetramers, and several oligoligated complexes of Zn(II).

The SIBFA potential and its analytical gradients have been ported in the Tinker-HP package [4]. This enabled the first molecular dynamics (MD) simulations on liquid water with this potential to be performed lending itself to comparisons with several experimental results [5].

Acknowledgements: ANR grant ANR-14-CE16-0028-01; Grand Equipement de Calcul Intensif (GENCI); Institut du Developpement et des Ressources Informatiques (IDRIS); Centre Informatique de l'Enseignement Superieur (CINES), project x-2009-07509; Centre Regional Informatique et d'Applications Numeriques de Normandie (CRIANN), project 1998053.

Keywords*: polarizable potentials; Quantum-Cheristry; ligand-macromolecule complexes; molecular dynamics*

References:

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The Interplay between Enzyme Flexibility, Reaction Mechanism and Reaction Rate

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This talk will address our most recent work on understanding enzyme reaction mechanisms using QM/MM methods[1]. First, the talk will overview the fields we work in, with selected examples to illustrate the concepts. Particular emphasis will be given to the fields of snake venom chemistry [2] and bioplastic degradation [3] Next, we will focus on structure-activity relationships, explaining the enzyme's precise structural and electrostatic requisites to catalyze a chemical reaction [4-6]. Finally, based on the refined understanding of the structure-activity relationship, we will discuss methods to predict rate-enhancing mutations to engineer more efficient enzymes [3,4].

From a more broad point of view, we will discuss the insights that computer simulations brought into the general understanding of how enzymes work and how the flexible enzyme machinery influences and dictates the reaction rate and controls the chemical pathway it catalyzes

Acknowledgements: This work was supported by UIBD/50006/2020 with funding from FCT/MCTES through national funds. PAF acknowledges the Fundação para a Ciência e Tecnologia through the Grants PTDC/QUI-QFI/28714/2017 and PTDC/QUI-OUT/1401/2020 for financial support.

***Keywords**: QM/MM, enzymes, reaction mechanisms, molecular modelling*

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Use of Catalytic Fields for Better Understanding of Enzyme Catalytic Activity and Inverse Theozyme Design

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The electrostatic nature of enzyme catalytic activity postulated by Warshel using empirical valence bond approach [1] confirmed by rigorous non-empirical perturbational analysis [2-3] and vibrational Stark spectroscopy experiments [4] has been used to derive alternative bottom-up methodology based on static [5] and dynamic [6] catalytic fields yielding electrostatic properties of an ideal catalytic environment. Static catalytic fields Δ_S describing at the same time transition state stabilization and substrate destabilization have been applied to Baker theozymes [7] to explain role of mutations introduced by directed evolution [5], to model nonadditivity of multiple mutations[5], analyze alternative enzyme reaction mechanisms [8] and predict substitution effects in substrate assisted catalysis [9]. Whenever necessary electrostatic model could be extended to include intermolecular correlation effects by application of SAPT based non-empirical dispersion functions [10].

Dynamic catalytic field Δ_D vectors derived directly from transition state and substrate wavefunctions indicate the most favorable changes in catalyst charge distribution coupled to the reaction coordinate and enhancing catalytic activity [6]. Δ_D vectors calculated at midpoints of hydrogen bonds forming network in ketosteroid isomerase indicate that optimal collective zero point proton displacements for each of two stages of isomerisation reaction proceed in opposite directions [6]. As the proton oscillations in strong hydrogen bonds are very rapid, this could explain why KSI belongs to fastest enzymes known. Evaluation of Δ_D is much less costly and requires the knowledge of stationary point structures and the positions of O or N atoms forming the hydrogen bond network only. So the dynamic catalytic fields could be useful to determine possible role of proton wires in the catalytic activity of large molecular systems, where the conventional computational techniques could not be applied.

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***Keywords**: catalyst design, theozyme, proton wire, catalytic field*

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Computer Simulation of Reaction Mechanisms in Glycoprocessing Enzymes Using QM/MM Approaches

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Glycosidases or glycoside hydrolases (GHs) constitute the main machinery for the degradation of glycosidic bonds in Nature. These enzymes are growing in importance as drug targets to treat diseases such as diabetes, infection and lysosomal-storage diseases, and they are also relevant in the production of energy from bio-mass. We will here present recent examples of the application of free energy quantum mechanics/molecular mechanics (QM/MM) simulations to unravel catalytic mechanisms in GHs [1-5], from classical Koshland mechanisms for retaining and inverting GHs [1-3], to recently discovered mechanisms involving an epoxide intermediate [4] or a metal-coordinated cysteine nucleophile [5].

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***Keywords**: enzymes, carbohydrates, chemical reactions, quantum mechanics/molecular mechanics, metadynamics*

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Selected Aspects of the Modeling of Photocatalytic Reactions

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Due to the dynamic development of research on both catalysis and photocatalysis, modeling of these processes attracts growing attention. Modeling of adsorption processes, reaction pathways, *etc*. is usually based on classical quantum chemical calculations, however, modeling of other important processes, like heat transfer, requires another approach. In this work, the results of modeling of self-sensitized degradation of organic pollutants at TiO_2 will be presented [1]. It appears, that photocatalytic oxidation of colorless organic pollutants can be promoted by visible light due to the formation of surface charge transfer complexes capable of visible light absorption. Both experimental and theoretical studies confirm the role of intermediates in the complete mineralization of pollutants.

The purpose of another part of our work was to describe the thermodynamic properties of TiO_2, in particular its properties related to heat transfer and dissipation. Calculations with the use of molecular dynamics methods gave us a picture of the time-dependent temperature distribution within the material upon photons absorption. The results shine a light on the conditions required to observe photothermal effects, which may play a key role in photocatalysis and photothermal catalysis.

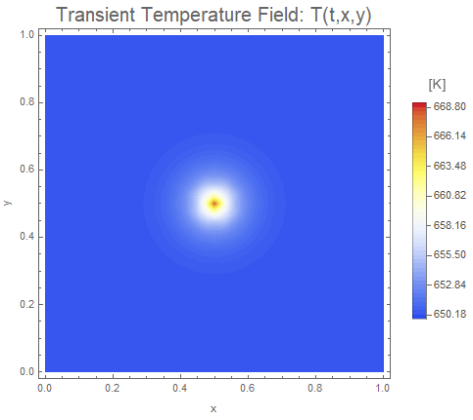

Fig.1. Surface temperature distribution within anatase TiO_2 for heat source equivalent to 3.2 eV at 650 K 2 ns after e^-/h^+ recombination.

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***Keywords**: photocatalysis; titanium dioxide; photosensitization; heat transfer*

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Mechanism(s) of Photocatalytic Processes: Revisited!

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Charge carrier transfer processes are very important and play a vital role in photocatalytic reactions. The fundamental study of the dynamics of these charge transfer processes is thus crucial from the viewpoint of developing efficient photocatalytic systems for largescale industrialization. The current presentation mainly reviews recent efforts on understanding the charge transfer kinetics in photocatalytic processes. Some fundamental aspects involved in charge transfer processes, such as, charge carrier generation, charge carrier trapping, charge carrier recombination, and electron and hole transfer are discussed based on the results published in the past decades. Moreover, recent studies focusing on the enhancement of the photocatalytic efficiency by improving the charge carrier transfer and separation will also be discussed here. Noble metal loading, plasmonic structure, and graphene loading have been found to be efficient methods to improve charge carrier separation and to suppress charge carrier recombination. Although there have been significant advances in the research of charge transfer dynamics, there are still many processes not fully understood, especially on the molecular-level. There are, for example, hardly any studies associated with electron and hole transfer kinetics in photocatalytic reactions on single crystal TiO2 surfaces. Most researchers have studied the charge transfer kinetics on a very short timescale, while the charge transfer on a more extended timescale is still unclear. This review highlights the importance of charge transfer processes in photocatalytic reactions the understanding of which can provide possibilities to significantly improve photocatalytic efficiencies.

Keywords*: photocatalysis, mechanistic studies, time-resolved investigations*

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Predicting Photochemical Reactivity Based on Computational Characterization of Reaction Mechanisms

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Organic photochemistry has been demonstrated as an effective way of overcoming high energy barriers and attaining high selectivity in the synthesis of various organic compounds. However, prediction of the outcomes of photochemical reactions of organic chromophores has posed notorious challenges for synthetic chemists, particularly since small changes and substitutions to organic chromophores can greatly affect the order of electronically excited states, each offering different reactivity. In addition, different organic solvents can strongly interact with the photoexcited solute molecule and lead to photoredox chemistry, which is difficult to predict without quantum chemical modeling. In this talk, I will demonstrate how thorough characterization of molecular mechanisms of specific photochemical transformations can be used to improve the reaction yields and transfer similar reactivity to related but modified organic chromophores. To achieve this, we apply highly accurate methods of quantum chemistry including multiconfigurational approaches such as CASPT2/CASSCF as well as the single reference algebraic diagrammatic construction to the second order [ADC(2)] coupled with our in-house codes for the optimization of state crossings and calculation of electron transfer rates. I will focus on the most recent achievements from our group including a photocyclization reaction of substituted dihydropyridazines to diazetidines and a DNA modification enabling highly efficient photoinduced electron transfer along the nucleic acid strand and self-repair of photodamages [1].

Acknowledgements: The work has been supported by a grant from the National Science Centre, Poland (2020/37/B/ST4/04092 to R.S.).

***Keywords**: organic photochemistry, electron-transfer, reaction mechanisms, DNA, theoretical chemistry*

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Hydrosilylation versus Hydrogermylation of Alkenes – DFT Studies on Reactions' Mechanisms

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We present the results of our DFT studies on catalytic hydrosilylation and hydrogermylation of alkenes catalysed by sodium trialkylborohydrides. On the basis of the investigation of the potential energy hypersurface at the M06-2X/6-31++G(d,p)//M06-2X/6-31+G(d) level of theory, we propose a detailed mechanism and energy profile for the reactions and describe geometric and electronic structures of stationary points corresponding to each step. The results of quantum-chemical computations not only provide a consistent explanation of the high (α) regioselectivity of $NaHBEt_3$-catalysed hydrosilylation, but are also in good agreement with the experimental yields depending on the substrates used, hence they not only further support the mechanism presented, but also make a computational toolkit for predicting reactivities. On the other hand supposedly similar hydrogermylation is also highly regioselective yet it leads – in contrast to the analogous hydrosilylation process – to *β*-germylated products. The nature of this process is very different to the hydrosililation as the mechanism proceeds via a trisubstituted germanide anion whose attack on the terminal vinyl carbon is the source of selectivity.

***Keywords**: catalysis, hydrosilylation, hydrogermylation*

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Decomposition of Biologically Relevant Molecules Triggered by Low Energy Electrons

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Reactions initiated by electron attachment to molecules, including those which result in molecular dissociation, drive plenty of the important processes in many fundamental areas of technology, chemical engineering, atmosphere, radiation physics and chemistry.

It is by now well known that low energy electrons (LEEs), the secondary species of the interaction of ionizing radiation with matter, efficiently produce structural and chemical modifications of many complex biostructures. These secondary electrons with a kinetic energy distribution up to 20 eV [1] are created in numbers of $5x10^4$ per 1 MeV of primary energy deposited [2] that makes them the most abundant radiolytic species.

Recent two decades have witnessed a remarkable growth in the scientific interest in studying the low energy electron attachment to biologically relevant molecules. Among them, a wealth of experimental and theoretical data have been devoted to nucleic acids and their building-blocks [3,4] in order to unravel the molecular mechanism how LEEs damage macromolecules.

In the present contribution I shall present experimental gas phase studies on dissociative electron attachment to halo-substituted derivatives of DNA/RNA sub-units. Such chemical compounds are frequently used as biological modifiers able to alter the response to radiation. Nowadays radiation-induced responses are being increasingly used for modification of radiotherapy based on advancements in radiobiology. Therefore, it is needed to determine the behaviour of these compounds under reductive conditions. In particular, during the talk emphasis will be placed on the description of the formation of the transient negative ions and the comparison of the fragmentation patterns of halogenated biologically relevant compounds.

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***Keywords**: halo-substituted biomolecules, dissociative electron attachment, negative ions*

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Low-Energy Electron Attachment to Potential Radiosensitizers

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Various types of molecules have been considered as potential radiosensitizers for hypoxic tumors which are characterized by a lack of oxygen [1]. Among them are nitroimidazolic compounds, which are suggested to mimic the oxygen effect as well as compounds like modified nucleobases and tirapazamine, which form free radicals upon activation. The desired benefit of radiosensitizers may also partially be ascribed to the action of low-energy secondary electrons (LEEs). This species is generated in abundant amounts during the irradiation of biological tissue. The kinetic energy distribution of secondary electrons formed finds its maximum below 10 eV. LEEs may activate radiosensitizers upon reduction. In this case, they are captured by the molecules which leads to the formation of transient negative ions. Those states may lead to long-lived anions or they may decay by molecular dissociation in competition to spontaneous electron emission.

In this talk, I will review our recent electron attachment studies with various classes of radiosensitizers in the gas phase. The setup used for these studies was an electron monochromator combined with a quadrupole mass spectrometer. The electron monochromator offers the generation of an electron beam with an energy resolution of ~100 meV, which is significantly higher compared to standard electron sources. The results will be compared with the situation, when the radiosensitizer is micro-hydrated or in solution.

Acknowledgements: This work was supported by the FWF, Vienna (P30332, I5390).

Keywords*: electron attachment, reduction, mass spectrometry, nitroimidazoles, modified nucleobases*

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Low-Energy Electron Induced Processes in Biological and Plasmonic Materials - Implications for Cancer Treatment and Catalysis

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Low-energy electrons play an important role in different fields such as radiation damage to biological systems and catalysis. When high-energy radiation traverses biological media, a shower of low-energy (i.e. < 20 eV) electrons is generated that can damage DNA effectively.[1] We have used the DNA origami technology to quantify single- and double strand breaks in oligonucleotides of well-defined sequence and could confirm that also oligonucleotides show the same resonant features of strand break cross sections peaking around 10 eV as plasmid DNA.[2] As the DNA origami technique allows for analysis of well-defined oligonucleotide sequences, it is particularly suitable to study the effect of radiosensitizers that are incorporated into the DNA with the aim to make tumor tissue more prone to radiation damage.[1]

In a different context, low-energy electrons are formed when visible light interacts with noble metal nanoparticles resulting in the excitation of surface-plasmon resonances, which leads to the formation of so-called hot electrons having energies below about 3 eV.[3] They can be transferred to adsorbed molecules and induce dissociation or other more complex chemical transformations. We have studied the mechanisms of some model reactions using surface-enhanced Raman scattering (SERS) and X-ray photoelectron spectroscopy (XPS)[4] and the latest results will be presented as well as similarities to DNA radiation damage and finally open questions will be discussed.

Acknowledgements: ERC consolidator Grant 772752.

***Keywords**: low-energy electrons, DNA origami, DNA damage, radiosensitizers, plasmon chemistry*

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Approaching Exact Quantum Chemistry by Stochastic Wave Function Sampling and Deterministic Coupled-Cluster Computations

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It is well established that the exponential wave function ansatz of coupled-cluster (CC) theory and its extensions to excited, open-shell, and multireference states are among the most efficient ways of incorporating many-electron correlation effects in molecular applications. In this talk, we will discuss novel ways of obtaining accurate energetics equivalent to high-level CC calculations, such as CCSDT, CCSDTQ, and EOMCCSDT, at small fractions of the computational costs, even when multireference correlation effects become significant, which result from the merger of moment expansions defining the CC(*P*;*Q*) formalism [1] with Quantum Monte Carlo (QMC) propagations in the many-electron Hilbert space [2,3]. We will also demonstrate that one can use the merger of the CC and stochastic configuration interaction (CI) ideas to extract the exact, full CI (FCI), or near-exact energetics out of the early stages of FCIQMC propagations [4–6] with the help of the relatively inexpensive polynomial steps similar to those of CCSD, eliminating exponential complexity of conventional FCI Hamiltonian diagonalizations altogether. The advantages of the new methodologies will be illustrated by chemical bond dissociations and reaction pathways [2,4], singlet–triplet gaps and excited electronic states [3,7], many-electron systems beyond the reach of FCI [5], and strongly correlated systems that emerge in modeling metal–insulator transitions [6].

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***Keywords**: molecular electronic structure, coupled-cluster theory, CC(P;Q) formalism, configuration interaction Quantum Monte Carlo, semi-stochastic computations*

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Quantum Chemistry for Very Large Systems

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The ability to perform quantum chemical calculations on very large systems (100,000 atoms and larger [1] or periodic systems with up to 50,000 atoms in the repeat unit [2]) opens new opportunities for the electronic characterization of materials or biological systems. In this talk, I will describe recent developments in the EMPIRE semiempirical molecular orbital program and present applications in which a variety of quantum mechanical techniques have been used in the areas of photovoltaic systems and covalent organic frameworks. In all cases, quantum calculations allow a better understanding of the electronic characteristics of the system.

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Recent Progress in Frozen-Density Embedding Theory Based Multi-Level Simulations for Condensed Phase

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In the first part, we present our recent work on Frozen-Density Embedding Theory (FDET): a) extension from its original version for variationally obtained embedded wavefunction [1] to nonvariational methods [2], b) non-decomposable approximations for the nonadditive kinetic potential [3], c) interpretation of the electronic polarization of the environment in FDET based simulations [4]. In the second part, recent examples of application of the FDET-based simulation for one- and two-photon absorption [5,6] and nuclear quadrupole splittings [7] will be overviewed.

***Keywords**: quantum-embedding, FDET, multi-scale simulations, two-photon absorption, electric field gradient, electronic polarization, continuum models*

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Classical and Ab Initio Molecular Dynamics Modeling of Interactions in Electrolytes for Me-Ion Batteries

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There is no doubt that efficient energy storage is one of key challenges of sustainable development. Large effort is therefore invested in research on metal-ion batteries. The Li-ion cells proved to be very successful devices; nevertheless, alternative chemistries of "beyond lithium" batteries (Na or Mg based) also attract increasing attention. Experimental works on Me-ion batteries and electrolytes have been supplemented and supported by theoretical modeling.

Molecular dynamics (force field or first principles-based) simulations are routinely used to study properties of liquids. Here we will present the results of MD investigations of Li, Na or Mg-conducting electrolytes based on molecular or ionic liquids.

We will focus on ion-ion or ion-solvent interactions: speciation of ion aggregates and structure of the system, effects of correlations for transport properties of the electrolyte, and the manifestations of interactions in vibrational spectra (IR and Raman).

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***Keywords**: molecular dynamics, electrolytes, ionic liquids, interactions, vibrational spectroscopy*

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Theoretical Study on Polymeric Materials for Fuel-Cell Applications

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The prospects for the wide use of fuel cells, in particular in transport and electronics, increase the interest in research topics related to polymer membranes for applications in fuel cells. However, the possibility of practical applications of technologies based on polymer fuel cells with proton-exchange membranes (PEM-FC) seems to be limited due to the necessity to use it - with mass application - large amounts of platinum. Possible solutions to this problem include use of the high-temperature PEM-FC (HT-PEM-FC), or the alkaline anion-exchange-membrane fuel cell (AEM-FC), both allowing for use of much cheaper, more accessible metals. However, in both cases the stability of membranes is insufficient, due to the fast decomposition processes.

In the present account the results of our recent theoretical DFT studies will be presented, focused on modeling and design of polymeric materials for possible use as membranes in fuel-cells. These studies have been performed in close collaboration with experimental groups and were focused on polybenzimidazole-based (PBI) systems [1-4] for AEM-FC and the novel tetrazole-substituted polymers for HT-PEM-FC [5-6].

***Keywords**: DFT modeling, membranes for fuel cells*

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Traditional Theoretical Methodologies vs Novel Machine Learning Techniques for Addressing the Gas Storage Problem in Nanoporous Materials

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Machine learning techniques (ML) are powerful tools already used in science and industry since their computational cost is by several orders of magnitude lower than that of the "conventional" approaches. However, their ability to provide accurate predictions strongly depends on the correct identification of those parameters (descriptors) that will allow the algorithm to effectively learn from past data. Other critical factors that affect the quality of the predictions are the size and the quality of the dataset used for the training of the algorithm as well as the correct estimation of the training size.

Aiming at both, the transferability of our model and the reduction of the training data set, we introduce 2 different classes of descriptors, based on fundamental chemical and physical properties: Atom Types and Atom Probes [1,2]. Our descriptors are based on the chemical character of the atoms which consist the skeleton of the materials and not their general structural characteristics employing in this way "chemical intuition" in our model.

On parallel, an automatic procedure of identifying the appropriate size of the training set for a given accuracy was developed [3]. A novel training algorithm based on "Self-Consistency" (SC) replaced the standard procedure of linearly increasing of the training set. Our SC-ML methodology leads to significantly more accurate predictions, while the number of MOFs needed for the training of the ML algorithm can be reduced by an order of magnitude.

Despite the progress in the field and the improved models that have been recently developed, ML algorithms fail to classify new materials with improved properties compared to the known ones. To the best of our knowledge the previous point has never been addressed since extrapolation is an inherent drawback of ML. In lack of such information, we propose a new methodology for the construction of artificial data with the desired properties that will be used for ML training [4]. This will enable ML algorithms to achieve improved predictions, in particular for high-performing materials.

Keywords*: machine learning, multi-scale, AI, gas storage*

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Discovery and Demonstration of Metal-Organic Frameworks for the Storage of Hydrogen and Natural Gas

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An overview is presented of recent computational and experimental efforts to discover and demonstrate metal-organic frameworks (MOFs) for the storage of hydrogen and natural gas. High-throughput screening of MOFs is used to pinpoint promising known and hypothetical MOFs. The screening employs a variety of computational techniques, including empirical correlations, atomic simulations, and machine learning. Correlations between elementary MOF properties and gas storage performance are identified. These predictions are used to guide experimental synthesis and characterization efforts. These experiments subsequently demonstrate the ability of several of the identified MOFs to out-perform class-leading materials and validate the usefulness of computation in guiding materials discovery.

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***Keywords**: hydrogen storage, MOFs, natural gas storage, materials discovery, machine learning*

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Electronic Excited States of Conjugated Molecules and their Lifetimes

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Vertical absorption spectra of selected molecules (pyrimidine nucleobases and 5-azacytosin, 2-amino-1,3,5-triazine, 2,4-diamino-1,3,5-triazine, 2,4,6-triamino-1,3,5-triazine, and s-triazine) were performed using TD-DFT, post-HF, and semiempirical OM2/MNDO methods. In the second part of the project also electronic excited states in the series of the conjugated polyenes from C2 to C22 were explored. From comparing a relatively large set of functionals from the different rungs of Jacob's DFT ladder, the important role of the exact exchange interaction is demonstrated. TD-DFT results with the ωB2GP-PLYP functional (and a few others) are comparable with the post-HF methods. An important finding is also a good accuracy of the semiempirical OM2 approximation, which is used for estimations of lifetimes of the excited states for the same set of molecules. The lifetimes' determination is based on a stochastical treatment of a swarm of MD trajectories. The time-dependent Schrödinger equation is solved for the electronic degrees of freedom while the dynamics of nuclei is treated classically in each trajectory step applying Tully's fewest switch algorithm. The probability of individual states in time is determined and compared with both experimental and computational studies. Our results are in fair accord with available experiments. The nucleobases relatively quickly deactivate – all the relaxation times are below 0.5 ps (in very good accord with measured values). Much longer lifetimes (a few hundred ps) were obtained for other molecules: 5-azacytosin, 2,4-diamino-1,3,5-triazine, and 2,4,6-triamino-1,3,5-triazine. Also, in agreement with experimental data, 2-amino-1,3,5-triazine returns to the ground state on a nanosecond scale. As to polyenes, the longest lifetime of the first excited state (S1) was found for decapentaene (about 5 ps). Further elongation of the conjugated chain caused a mild decrease of this value to ca 1.5 ps for docosaundecaene.

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***Keywords**: lifetime determination, semiempirical methods, multireference appoach, MD simulations*

Chemioinformatics for Materials Safe-by-Design

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Materials science is rapidly growing, but the related enthusiasm needs to be balanced against the potential toxicity effects that several types of engineered materials can induce. Many countries, including the European Union, have introduced specific regulations on the necessary risk assessment procedures before introducing new products to the market. Ideally, the risk should be identified and eliminated at the earlier possible design stage to reduce unnecessary costs and time. This leads to the modern idea of developing new materials being safe-by-design.

The use of computational techniques enables predicting properties of new materials based on their 'digital twins' (virtual molecular models) at the early screening stage. This also applies to various toxicological endpoints that need to be evaluated in the context of risk assessment.

Nowadays, chemoinformatics, which stands for data-based computational methods utilizing structural information and machine learning methods (e.g., Quantitative Structure-Activity Relationships, Read Across), provides an array of tools for materials designers.

The lecture aims to give a flavor on the progress of chemoinformatics and challenges that need to be faced shortly, based on several case studies. How to model ionic liquids? How to appropriately represent the molecular structure of multicomponent materials? How to consider the dependence of the structure on the surrounding environment (e.g., pH, salinity in natural waters, the presence of proteins and other molecules in the organism)? Although we will probably not answer all these questions, I hope they will stimulate a new generation of chemoinformatitians to make further developments in the field.

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***Keywords**: chemoinformatics, safe-by-design, machine learning, molecular descriptors*

Importance of Structure-Activity Relationship (SAR) Studies of Sulfonamide Moiety in Current and Future Therapy

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Antibiotic resistance is a global problem, and one promising solution to overcome this issue is using metallodrugs, agents containing metal ions and ligands. These complexes are superior to free ligands in various characteristics including anticancer properties and mechanism of action. The pharmacological potential of metallodrugs can be modulated by an appropriate selection of ligands and metal ions. It seems that a good example of proper coordination is the combination of a trivalent metal ion of Ru, Rh, Os, and Ir with selected sulfonamide derivatives.

In our project, we focus on the synthesis and studies of Ru, Rh, Ir, and Os - sulfonamide complexes, their bioinorganic profiles determination, biological properties, and activity characterization as well as the methods used to determine the biomolecules' interaction modes with them. We relate these interaction results to the mechanism of antimicrobial(anticancer) activity and structure-activity relationships. The interactions between these complexes and DNA should show close similarities to those of covalent polycyclic aromatic carcinogens, especially to N7-alkylating intercalation compounds. Up-to-date results of our work will be shown in this presentation in this regard.

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***Keywords**: sulfonamides, metallodrugs, trivalent metal ion complexes, physicochemical and biological properties*

Isotopic Consequences of Non-Covalent Interactions

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Secondary isotope effects are associated with atoms which covalency does not change in the physical or chemical processes. In this presentation we will discuss recent computational developments in this area from our laboratory on such isotope effects in binding of ligands to proteins [1] chromatographic separation [2], hydrogen-bonding [3], formation of nanomaterials [4], as well as caging [5].

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Mechanisms of Ion Translocation Through Transmembrane Channels Revealed by Molecular Dynamics Simulations

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Translocation of ions through channels and pores is fundamental for numerous physiological processes, especially in excitable and energy-transducing membranes. Single channel recordings provide an insight into channels' functional characteristics, including conductance states, selectivity and gating, while structural studies can reveal their architecture in atomic detail. However, the link between these two descriptions tends to be unclear making it difficult to understand the mechanisms underlying transmembrane transport and the design of channel-forming agents. By capturing conformational energetics and thermally activated dynamics, molecular simulations offer a unified view of ion transport in which conductance properties can be rigorously derived from a microscopic interaction model. In this talk, I will summarize the results of two case studies, in which multiscale molecular dynamics simulations were applied to elucidate the mechanism of action of a pore-forming antibiotic and the proton-driven F_o motor of ATP synthase.

Amphotericin B is known to permeabilize fungal cell membranes in a sterol-dependent manner. Unfortunately, the structure of AmB channels has long eluded researchers, hampering the development of safer alternatives. By matching the predicted channel conductance with our and previous measurements, we predict that AmB forms octameric pores. We then use free energy calculations to explain the effect of sterols on the pore stability and discuss the observed ion transport mechanism and selectivity in structural terms.

Despite a rapid increase in the number of high-resolution structures of ATP synthase, the mechanism of tight coupling between proton transport and motion of the F_o motor remains elusive. Using free energy simulations, we show how the motor's directionality and efficiency naturally arises from the interplay between intraprotein interactions and energetics of protonation of the c-ring. Our calculations reveal that the strictly conserved arginine in the a-subunit is adapted to three different tasks: it dictates rotation directionality, controls the protonation behavior, and separates the two proton-access half-channels.

The Lung Surfactant Activity Probed with Molecular Dynamics Simulations

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The surface of pulmonary alveolar subphase is covered with a mixture of lipids and proteins. This lung surfactant (LS) plays a crucial role in lung functioning. During tidal breathing LS is subject to dynamic changes in surface area. It shows a complex phase behavior which can be altered by the interaction with third molecules such as drugs or pollutants. LS is in constant contact with ambient air and constitutes the first barrier for pathogen uptake into the body. For studying multicomponent biological systems, it is of interest to couple experimental approach with computational modelling yielding atomic-scale information. Simple two, three, or four-component model systems showed to be useful for getting more insight in the interaction between lipids, lipids and proteins or lipids and proteins with drugs and impurities. These systems were studied theoretically using molecular dynamics (MD) simulations and experimentally by means of the Langmuir technique [1]. A better understanding of the structure and behavior of lung surfactants obtained from this research is relevant for developing new synthetic surfactants for efficient therapies, and may contribute to public health protection.

It was demonstrated that the results obtained from molecular dynamics simulations coupled to physicochemical experiments reveal the details of physiologically important processes taking place in the lung surfactant system. It has to be stressed that theoretical findings depend on the quality of the approximations used. Therefore, a special care has to be taken when choosing MD protocol. For example, an important point in this regard is the choice of water model. Despite of that, the recent developments in MD techniques lead to improved agreement with experimental results and provide more reliable predictions.

Acknowledgements: The calculations reported in this presentation were performed using PL-Grid infrastructure at ACK CYFRONET.

Keywords*: lung surfactant, monolayer degradation, air pollutants, surface-pressure isotherms, water models*

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ABSTRACTS OF ORAL PRESENTATIONS

Mechanisms of Radiosensitization in Fluorinated DNA: DNA Origami Studies

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Fluorinated nucleosides, such as gemcitabine (2',2'-difluoro-2'-deoxycytidine, Gem), are widely administered in cancer chemoradiation therapy due to their radiosensitizing action[1]. Gem can enhance the effects of ionizing radiation via dissociative electron attachment (DEA) reactions with secondary low-energy electrons produced along the radiation track inducing DNA single- and double-strand breaks [2]. According to the experimental scheme illustrated in Figure 1, we exposed two different DNA origami nanotriangles designs carrying two sequence-specific DNA oligonucleotides towards a highly energetic electron beam (16 MeV) in dry and aqueous conditions, hence a *step-closer* to a more biologically relevant environment. In the fluorinated sequence, one cytidine nucleoside was replaced by 2'-fluoro-2'-deoxycytidine ($^{2'F}$C), a representative model system for Gem. Following the irradiation, atomic force microscopy (AFM) analysis allowed to determine the number of DNA single-strand breaks as a function of the delivered dose. Our results suggest that the fluorination at the sugar moiety, irrespective of the position in the oligonucleotide sequences, does not affect the response towards high-energy electrons, in the form of single-strand breaks. This indicates that not only DEA processes, but also further physico-chemical mechanisms underlie the radiosensitization of fluorinated DNA. This study has implications for the rational design of new radiosensitizer agents with promising physicochemical features for cancer chemoradiation therapy.

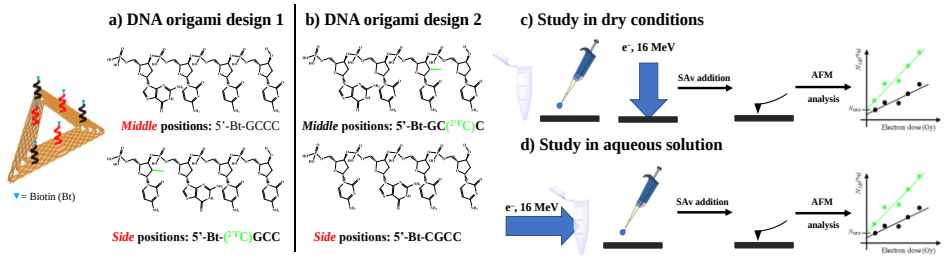

Fig. 1. Experimental scheme for quantitative determination of DNA single strand breaks as a function of the dose using AFM imaging. DNA origami nanotriangles with different target oligonucleotide sequences were designed according to a) design 1 and b) design 2. In dry conditions (c), DNA origami nanotriangles were deposited onto silica chips and subsequently irradiated at a given electron dose, while in aqueous conditions (d) the solution was directly irradiated. In both studies, the remaining target strands are marked with streptavidin (SAv) for subsequent AFM analysis.

***Keywords**: cancer therapies, DNA origami, atomic force microscopy, radiosensitizers*

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Congo Red as a Supramolecular Carrier System for Doxorubicin: an Approach to Understand the Mechanism of Action

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Doxorubicin (DOX) is a common anticancer drug belonging to the anthracycline family. It is used in treatment of various types of cancer, e.g. leukemia, lymphoma, breast, liver, lung, or ovary cancer. However, it also causes many side effects. The most serious of them are: cardiotoxicity leading to serious heart damage, and decrease in the number of myeloid cells. DOX is genotoxic to neoplastic cells. Its activity is related with the presence of a system of conjugated aromatic rings which intercalates DNA strands, interacts with base pairs and disrupts replication and metabolism of cancer cells. Unfortunately, the same mechanism applies to healthy cells. It is therefore desirable to design new carriers for DOX, which would enable targeted delivery of this drug to cancer cells and in this way reduce the side effects.

In the present study transfer of DOX through lipid membranes is examined. Raman imaging of MCF7 line cells showed little uptake of DOX from solution. When Congo Red (CR) was also present, DOX uptake was observed. To analyze this result, Langmuir through experiments on model DPPC monolayers were carried out. These measurements showed increased adsorption to the monolayer from subphases containing DOX/CR and CR. Molecular details of these processes were examined with MD simulations. In agreement with our previous study [1], it was shown that in DOX/CR system, large aggregates of DOX molecules were not formed. Instead smaller, mixed DOX/CR clusters were present. Transient association of DOX/CR and CR clusters with lipid heads was observed. In the free energy profiles for transfer of DOX and CR though a monolayer, a stabilizing interaction between CR and DPPC heads was identified. Analysis of the trajectories and radial pair distribution functions revealed occurrence of a DPPC-CR complex, stabilized via interactions between the SO_3 group of CR and choline groups of DPPC. When placed in the hydrophobic part of the monolayer, CR clusters exhibited tendency to leave towards the headgroups. On the other hand DOX/CR clusters remained in the hydrophobic part of the monolayer. All of the above results indicate that CR can be considered as a potential carrier of DOX through biological membranes.

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***Keywords**: doxorubicin, Congo red, drug-membrane interactions, MD simulations*

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Decomposition of the Sanazole Radiosensitizer by Low-Energy Electrons

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Water ionization associated with the interaction of high radiation with living cells generates highly reactive oxygen species (ROS) capable of reacting with DNA, as well as a substantial number of secondary low-energy electrons (LEEs) with an energy distribution peaking around 10 eV. LEEs may contribute to DNA damage in this energy range by primarily inducing single- and double-strand breaks through dissociative electron attachment (DEA) [1,2]. In other words, the capture of electrons by compounds results in the formation of transient negative ions, which can dissociate via DEA. When radiosensitizer derivatives are integrated into DNA, they form radical species that cause DNA damage. Molecules of this class are still being researched. In this work, a crossed electron-molecular beam setup combined with a quadrupole mass spectrometer was used to study electron attachment to sanazole (AK-2123). Sanazole is a hypoxic radiosensitizer and is specifically used in the treatment of stage III cervical cancer [3,4]. Therefore, the findings of dissociative electron attachment to sanazole in the gas phase provides basic information on its reduction properties and will be presented. The sample vapour was introduced in the interaction region of a hemispherical electron monochromator (HEM) via a 1 mm stainless-steel capillary and crossed an electron beam. The HEM was used to form an electron beam with an energy resolution of 120 meV at full width at half maximum (FWHM) and an incident electron current of 10–30 nA. We observed 16 fragment anions, which indicates that low-energy electrons with kinetic energies ranging from 0 to 12 eV strongly decompose the molecule. The results show that $(NO_2)^-$ and the parent anion are efficiently formed upon electron attachment to sanazole.

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Keywords*: low energy electrons (LEEs), dissociative electron attachment (DEA), electron capture, radiosensitizer, Sanazole*

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Non-Equilibrium Simulations of Pteridine Reductase 1 Reveal its Flexibility Hot-Spots

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Pteridine reductase 1 (PTR1), the key enzyme of the folate pathway of pathogenic trypanosomatids, is a promising drug target. The dynamics of the enzyme has not been studied in detail so far. The functional form of the enzyme is a homotetramer, with four equivalent binding sites, each - binding a cofactor and a ligand. Partial occupancies and single empty sites observed in some liganded crystal structures of PTR1 homotetramers suggest negative cooperativity of ligand binding. Additionally, analysis of crystal structures [1] and normal mode analysis [2] demonstrated flexibility of substrate loops flanking the binding sites. In order to further investigate the large-scale dynamics and the cooperativity between the active sites, we applied the non-equilibrium method - Rotamerically Induced Perturbations [3]. The found flexibility hot-spot residues [2] were also identified in the molecular dynamics studies as the important residues interacting with substrates and products of the catalyzed enzymatic reaction, and are conserved among PTR1 from different species.

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***Keywords**: molecular dynamics, non-equilibrium method, enzyme, inhibitor, allostery*

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Characterizing Molecular Machines Using SwitchSENSE® Technology

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switchSENSE® is an automated, fluorescence-based biosensor chip technology that employs electrically actuated DNA nanolevers for the real-time measurement of binding kinetics (k_a, k_d) and affinities (with KD values down to the fM range). Interactions between proteins, DNA/RNA, and small molecules can be detected with femto-molar sensitivity. At the same time, conformational changes and complex binding events can be measured using minimal amounts of sample.

In this work, we present an overview of different applications of the switchSENSE® technology for the detection of sequence-specific DNA/RNA binding as well as kinetic and activity rates of enzymes (such as DNA/RNA polymerases, reverse tanscriptases and helicases).

Different measurement modes can be combined in the heliX® biosensor to achieve the best sensitivity for every experiment. By using a sensitive FRET read-out, we can analyze complex binding modes, such as the kinetics of a RNA-binding protein to two different RNA recognition motifs. By using fluorescence proximity sensing, we measured the association of Bst DNA polymerase to a DNA template. Subsequently, the elongation of the DNA primer was measured in real-time and the Michaelis constant K_M was obtained.

In summary, this work provides insights on the versatility of the switchSENSE® technology for DNA/RNA-binding proteins and enzymes. The results obtained by researchers using this technology are contributing to better understand gene expression and cellular mechanisms involved in several diseases as well as supporting bringing better drugs to the market.

***Keywords**: switchSENSE technology, molecular interactions, biophysical parameters, helix® biosensor*

Mechanism of Electron Transport through Metal-Protein-Metal Junctions

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Motivated by the high efficiency of electron transfer over large distances, redox proteins have been recently incorporated in solid-state metal/protein/metal junctions in nanoelectronic devices. However, unexpected physical phenomena emerged when the electric currents or conductance were measured as a function of applied bias potentials. In contrast to an aqueous solution, where an electronic charge is transferred by a thermally activated hopping mechanism, temperature-independent currents were detected in protein junctions, suggesting coherent tunneling as the undergoing mechanism. Yet, the current magnitudes are relatively large, even in wide 3-5 nm junctions, which is unexpected for tunneling transport [1].

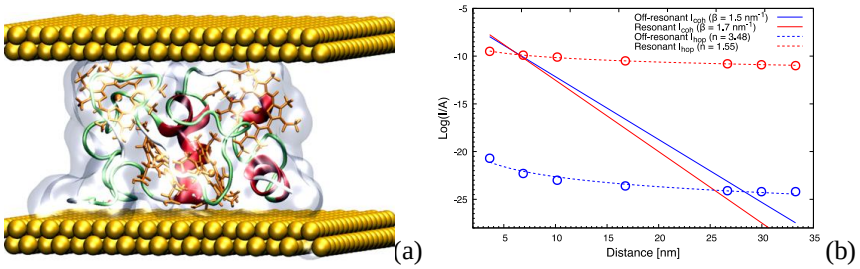

Fig. 1. (a) DFT model of Au/STC/Au junction, and (b) distance dependence of junction currents.

To investigate these processes, we use computer simulations based on combinations of classical molecular dynamics (MD), hybrid quantum-mechanical/molecular-mechanical (QM/MM) approaches, and density functional theory (DFT). We employ the Marcus theory of electron transfer for a description of the hopping mechanism while the Landauer formalism is applied to coherent tunneling. We demonstrate the performance of these techniques by studying the charge transport properties of small tetraheme cytochrome (STC) and blue-copper protein azurin in contact with the gold electrodes [2]. Electronic level alignment between the protein and the metal electrodes and the interfacial electronic coupling was identified as the key factors determining the electron transport mechanism [3].

Acknowledgements: We gratefully acknowledge funding by the Czech Science Foundation GAČR in the context of Project No. 20-02067Y.

***Keywords**: protein junction, electron transport, coherent tunneling, DFT, nanobioelectronics*

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Surfactant Molecules Used for Contaminant Removal in Aqueous Media

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Using Molecular Dynamics simulations, we investigate the role of surfactant molecules as agents for contaminant removal in bulk water phases and on solid surfaces. Surfactants are used to study retention of metallic particles, lead (Pb) and Mercury (Hg), in water to investigate the efficiency of amphiphilic molecules to capture polluting particles. Simulations were performed for different metallic particle concentrations and number of surfactant molecules. Data was analysed in terms of radial distribution functions, radial density profiles and isotherm curves, indicating that metallic particles are captured by the surfactant polar groups. The results show that the retention of the metallic particles increased with the SDS concentration. It is also observed that the metallic particles modify the structure of the micelles characterized by their radius and their moments of inertia.

Surfactant molecules are also tested as agents to adsorb contaminants on solid modified surfaces. CO2 adsorption on graphite and zeolite surfaces were conducted using an anionic, *Sodium dodecyl sulfate* (SDS), surfactant at different compositions. The results show that gas adsorption is affected by the amount of SDS on the solid surfaces. Adsorption was studied in term of density profiles and pair correlation functions.

Acknowledgements: DGAPA-Mexico grant IN102017, Conacyt-Mexico grant A1-S-29587, DGTIC-UNAM grant LANCAD-UNAM-DGTIC-238.

***Keywords**: surfactants, removal, contaminants*

Driving Forces of Carbon Dioxide Absorption in Novel Ionic Liquids from Molecular Simulations Perspective

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Carbon Capture and Storage (CCS) and especially techniques of absorption in green solvents like ionic liquids are widely studied as a promising tool for reducing harmful effects of anthropogenic carbon dioxide emissions [1]. Despite 20 years of research, some mechanistic details are still unclear. Fractional free volume (FFV) and anion type are believed to be the two most important factors which determine carbon dioxide solubility in ionic liquids (ILs) [2]. Due to the increasing scientific interest in multi-cationic ILs and ILs which can absorb gas via chemisorption (e.g., ones with amino acid anion) both factors are optimized in order to obtain better sorbents. Amino acid ionic liquids (AAILs) are believed to be both prominent carbon dioxide sorbents and environment friendly solvents. In this work, the importance of free volume and possible chemical sorption was critically tested via comparison of ILs with both high and low FFV and amine group available or blocked for reaction with CO_2 molecule. Studied systems contained choline or 4-centered imidazolium based cation and alanine or N-acyl alanine anion (which leads to 4 systems total). The possibility of chemical reaction was established using tight binding parametrization-based calculations, while sorption in the liquid phase was studied using molecular dynamics (liquid phase characteristics and FFV calculation) and XTB Monte Carlo (gas uptake) simulations. The study shows significant disproportion in FFV according to cation type and lower impact of anion structure on FFV. Alanine N-acylation was confirmed as factor making chemisorption of CO_2 in AAIL energetically unfavorable. Gas uptake simulated via Monte Carlo methods was compared to values from literature and predicted by in-house QSPR models involving FFV as a molecular descriptor. Conducted simulations reveal how FFV and anion type affect gas solubility and each other. Multi-cationic ILs with amino acid anions are identified as potentially good materials for CCS absorption-based techniques.

Acknowledgements: Financial support of these studies from Gdańsk University of Technology by the DEC-15/RADIUM/2021 grant under the RADIUM - 'Excellence Initiative - Research University' program is gratefully acknowledged.

***Keywords**: molecular dynamics, ionic liquids, carbon dioxide, absorption*

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Influence of Hydrogen and Halogen Bonds on Photophysical Properties of Squaraine Dyes

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A supramolecular strategy of tuning of photophysical properties of squaraine dyes by hydrogen and halogen bonding is investigated with quantum chemistry tools. A central squaraine unit bound by strong hydrogen bonds with 4-substituted N,N′-diphenylurea and, alternatively, N,N′-diphenylthiourea molecules, exhibits strongly modified electron accepting character in comparison to the isolated dye [1]. The replacement of oxygen by sulfur atoms in the central ring, known to affect its photophysical behavior, provides a way of modifying the strength and nature of the intermolecular contacts. The introduction of the sequence of the substituents of varying electron-donating or electron-withdrawing characters in the position 4 of N,N′-diphenyl(thio)urea subsystems allows to finely tailor the hydrogen bonding with the central squaraine unit by modification of the N–H bond characteristics. All of these structural factors lead to the controlled adjustment of the electron density distribution, and thus, the properties affected such as transition moments and absorption intensity. Ab initio calculations give strong support for the reasonability of such an approach to the fluorophore design due to the obtained strong hypsochromic shift of the maximum one-photon absorption wavelength observed particularly for thiosquaraine complexes and increase in the TPA wavelength together with the enhancement of the TPA cross section. For the first time, the linear dependence of the non-additivity in the interaction energy on the Hammett substituent constant is reported. In the case of the halogen bonds to iodoperfluorobenzene, the observed effects vary in the sequence of squaraines with the modified heterocyclic side substituents and central squaric acid unit by the O→S→Se→Te replacement and are strongly dependent on the binding site employed.

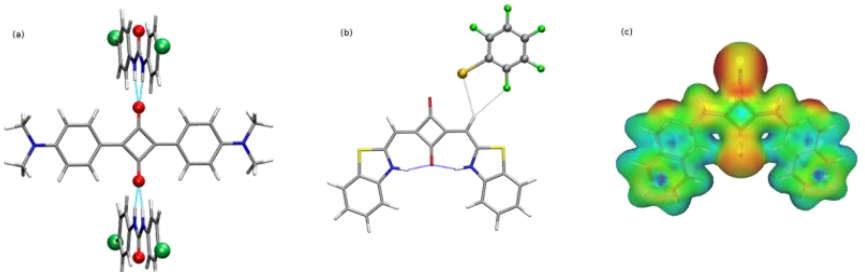

Fig. 1. Exemplary complexes (a) and (b) and electrostatic potential (c) for a squaraine dye

***Keywords**: hydrogen bond, photophysical properties, squaraine dyes, ab initio, interaction*

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Investigation of Reorganization Free Energy of Azurin Oxidation on Gold Electrodes by PMM and QM/MM Techniques

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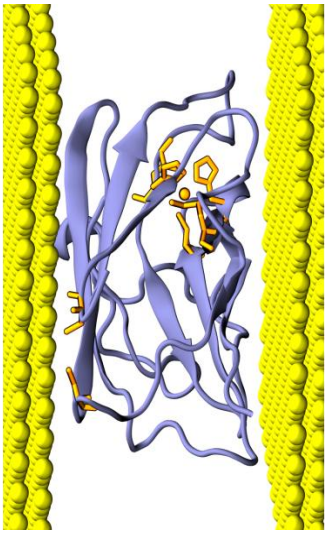
Reorganization free energy quantifies structural and electronic changes of a molecular system when an electron-transfer (ET) event proceeds. This descriptor plays a key role in the Marcus theory of ET where, together with the redox-potential difference, determines the heights of free-energy barriers and so the kinetics of the ET processes. Computationally, the reorganization free energy can be calculated by statistical approaches based on molecular dynamics (MD) techniques and QM/MM sampling. However, the complexity and cost of these calculations grow with the size of the studied system, in particular its redox-active part, and its flexibility. Therefore, fast yet accurate semi-empirical approaches of well-tested applicability are desired. One of such techniques is the Perturbed Matrix Method, PMM [1], which allows rapid evaluation of charge-transfer quantities on thousands of MD samples.

Motivated by the recent development of nano-bio-electronics where charge-transport properties of biomolecules like peptides and proteins are utilized, we investigated the reorganization free energy of blue-copper protein azurin upon its extraction to vacuum and adsorption to gold surfaces [2]. Using the accurate QM/MM description we have shown that the energy is, rather surprisingly, not reduced in dry protein because the loss of the hydration shell is compensated by increased flexibility of the protein matrix near the Cu redox site. Then, we carefully benchmarked the PMM on these data and investigated its robustness with respect to various parameters including the choice of the QM region, quality of the non-perturbed Hamiltonian, or the number of samples. In general, PMM performs quite well both in solution and on the bio/metallic interfaces, not only at a qualitative level but also quantitatively.



Acknowledgements: We gratefully acknowledge funding by the Czech Science Foundation GAČR in the context of Project No. 20-02067Y.

***Keywords**: azurin, reorganization energy, perturbed matrix method, QM/MM, metal interface*

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DFT Determination of Structure and Spectroscopic Properties of Selected Metabolites from *Chelidonium majus*

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Chelidonic acid (4-oxo-4H-pyran-2,6-dicarboxylic acid, see Fig. 1) is present in plants of *Papaveraceae* family, especially *Chelidonium majus* (Fig. 2). The plant has been known from their anticancer, antibacterial, hepatoprotective and antioxidant properties.

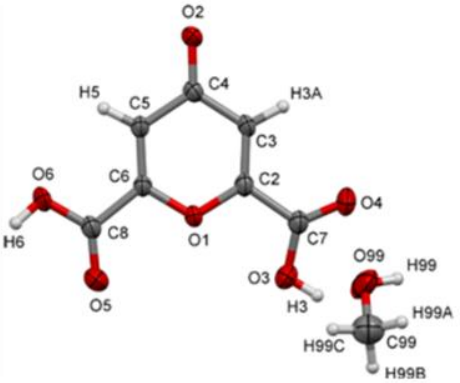

Fig. 1. Methanol solvate of chelidonic acid Fig. 2. Chelidonium majus

Among the bioactive metabolites are chelidonic acid, meconic acid and coptisine. In this study we will report on their structure, vibrational IR/R parameters and NMR spectra. In particular, we will assess the performance of DFT-B3LYP for predicting structural and spectroscopic data of selected γ-pyrone derivatives *vs* experiment and CCSD results with smaller basis set. A very good agreement between B3LYP/CBS estimated bond lengths and experimental data for the studied γ-pyrone derivatives was observed.

Acknowledgements: Partial support obtained from the Faculty of Chemistry, University of Opole.

***Keywords**: chelidonic acid, DFT, γ-pyrone, molecular structure, spectroscopy*

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Change in the Nature of the ZSM-5 Zeolite Depending on the Type of Metal Adsorbent - Analysis of DOS and Orbitals for the Iron Metal

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The emission of nitrogen oxides NOx has become the main problem among air pollutants emitted from various sources, such as automotive, energy and heavy industry. In addition, these oxides are a very serious problem both in terms of impact on human health and the environment cause for eg. acid rains and photochemical smog [1]. Currently, regulations require a significant reduction of these harmful oxides and the existing thresholds may be lowered again in the near future. The most effective way to dispose of nitrogen oxides to meet the required limits is the SCR deNOx reaction. Transition metal modified zeolites have recently gained the greatest interest among scientists [2-4].

Ab initio calculations within the density functional theory were used. The exchange and correlation functional is approximated with a Perdew-Burke-Ernzerhof (PBE) functional. Cluster models of ZSM-5 ($Al_2Si_{18}O_{53}H_{26}$) zeolites (Fig. 1) have been used with Fe particles adsorbed above aluminium.

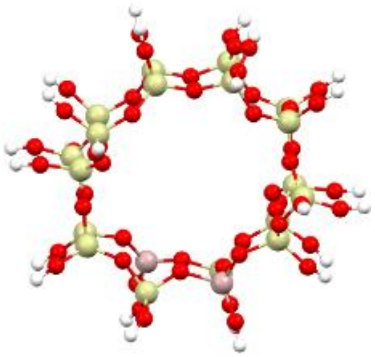

Fig. 1. Structure used to calculations ZSM-5 zeolite ($Al_2Si_{18}O_{53}H_{26}$).

The adsorption of three iron adsorbates inside the pores of the zeolite ZSM-5 - Fe, FeO and FeOH was carried out with different arrangement of aluminum atoms in the zeolite structure. The DOS diagram and the HOMO and LUMO molecular orbitals for these systems were analyzed. It has been shown that depending on the adsorbate and the position of aluminum atoms in the pore structure of the zeolite, the systems can be described as insulators or conductors, which significantly affects their activity. The main aim of the research was to understand the behavior of these types of systems in order to select most efficient for deNOx reaction.

Acknowledgements: Research was financial supported by CASALE S.A company.

***Keywords**: ZSM-5, DOS, molecular orbitals, DeNOx, DFT*

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Interactions of Cationic Surfactant-Fatty Alcohol Monolayers with Natural Human Hair Surface: Insights from Dissipative Particle Dynamics

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Fatty alcohols (C_nFAs) combined with cationic surfactants are common ingredients of lamellar-phase personal care liquids. We employ mesoscopic modelling to study how surfactant-C_nFA monolayers originating from the corresponding bilayers of the personal care liquids interact with the human hair surface above and below the fluid-gel transition temperature as well as in and out of equilibrium. For the monolayer model, we consider the single-tail cationic surfactant cetyltrimethylammonium chloride (CTAC) and an excess of C_nFAs with their alkyl tail equally long to or longer than the CTAC alkyl tail. The hair surface mimics keratin surface proteins covered by a film of lipid molecules covalently bonded to the proteins. Our modelling shows a formation of dense adsorbed layer due to the interactions of the CTAC and C_nFA alkyl tails with the hydrophobic hair surface. The adsorption and the behaviour of the adsorbed layer is different under fluid and gel conditions. The differences are related to the structure of the adsorbed layer as characterised by the density profiles across the adsorbed layer and the orientational order parameters of the molecules within the adsorbed layer. Under steady-state shearing (an approximation of real life non-equilibrium conditions), increasing the shear rate above a threshold leads to continuous or abrupt desorption of the CTAC and C_nFA molecules under fluid or gel conditions, respectively; the freed molecules can then form various self-assembled structures in the bulk solution. The underlying mechanism of CTAC and C_nFA desorption from the adsorbed layers is closely related to the corresponding adsorption mechanism.

Acknowledgements: This work was supported by the Ministry of Education, Youth and Sports of the Czech Republic through the e-INFRA CZ (ID:90140).

***Keywords**: dissipative particle dynamics, complex fluids, adsorption, polymer brush*

Molecular Dynamics Investigation of Correlations in MeTFSI/EMIM-TFSI (Me = Li, Na) Electrolytes

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Classical polarizable and nonpolarizable molecular dynamics simulations have been performed for MeTFSI (Me = Li, Na) solutions in the EMIM-TFSI ionic liquid.[1,2] Different temperature or pressure values and salt concentrations have been examined. The structure and dynamics of the solvation shell of Me^+ cations, diffusion coefficients of ions, conductivities of the electrolytes, and correlations between motions of ions have been investigated. Contributions to the total conductivity of the electrolyte arising from motions of different ions and cross-correlations between them have been analyzed.

The results indicated that regardless of the conditions or force field, significant correlations are present in all systems. The degree of correlations depends mainly on the salt fraction in the electrolyte and is much less affected by temperature and pressure changes. Regardless of the type of Me^+ cation, motions of Me^+ ions and ionic liquid anions are positively correlated, contributing toward conductivity decrease and leading to negative transference numbers of metal ions. The simulations have confirmed experimental findings of negative transference numbers of Li^+ and have suggested that the effect of Me-anion correlations in certain concentration range is a general feature of Me^+ solutions in ionic liquids.

Acknowledgements: The PL-Grid infrastructure was used in the computations. This work was supported by the Faculty of Chemistry of the Jagiellonian University.

***Keywords**: ionic liquids, electrical conductivity, electrolytes, ions, molecular dynamics*

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IR Spectra of Liquids Modelling with MD Simulations

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Vibrational spectroscopy is commonly used to investigate interactions between molecules through the changes of vibrational frequencies.

Computational methods are used to support the experiment, e.g. to identify individual bands observed experimentally or to predict possible shape of the spectrum. The most simple approach based on using quantum chemical calculations for isolated molecule in vacuum may provide some useful hints, but usually it is insufficient for condensed phase systems.

Our research concentrates on using molecular dynamics (MD) to model IR spectra of liquids, in particular systems that are used as electrolytes for batteries, such as ionic liquids or salt solutions in organic solvents. MD approach does not suffer from limitations of implicit solvent methods because solvent molecules are explicitly included in the modelled system. However, classical MD based on force fields usually cannot correctly reproduce the band shifts related to changes in salt concentration and ab initio MD needs to be applied.

The IR spectrum can be obtained from the total dipole moment of the system as the Fourier transform of dipole moment autocorrelation function. More detailed information about contribution of different parts of the system to the whole spectrum is available from Fourier transforms of geometrical parameters such as bond lengths or angles. In this way, the features of the spectrum can be related to local environment of vibrating molecules.

In the presentation examples of MD-based investigations of interaction-induced spectral shifts will be shown. Discussed systems include Na salt in an ionic liquid [1] and Mg or Na/Li salts in organic solvents [2,3]. The results show that the approach based on ab initio MD can satisfactorily reproduce the changes induced in IR spectra by solvent interactions with metal ions.

Acknowledgements: The PL-Grid infrastructure was used in computations.

***Keywords**: electrolytes, molecular dynamics, infrared spectroscopy*

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Two-Photon Absorption Spectrum of Rhodopsin Calculated Using TD-DFT/MM with Polarizable Embedding Scheme

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We assess the performance of polarizable embedding scheme within the single-point, post Molecular Dynamics (MD), Time-Dependent Density Functional/Molecular Mechanics (TD-DFT/MM) method for computing the One and Two-Photon Absorption (O/TPA) spectra of Rhodopsin. Following our previous performance assessment of density functionals on TPA spectra of reduced retinal models; BHandHLYP is employed as the functional of choice for calculating the 3 lowest lying excited states and their corresponding electronic properties within the polarizable embedding scheme (PE). Arbitrary frames post equilibrium of QM/MM MD were chosen to perform OPA and TPA calculations. Comparison against the prominent electrostatic embedding (EE) scheme of Olivucci et al 2019 with the more advanced perturbation method (XMCQDPT2)[1], and Palcewska et al. 2014 with TD-DFT[2], yield that our TD-DFT PE system is able to quantitatively reproduce Olivucci's work where Palczewska doesn't. PE allows for the mutual polarization of the quantum region, governed by TD-DFT, while the MM region, is governed by classical mechanics. This mutual polarization allows for a more realistic description of the interaction between the two regions, as opposed to EE that only allows interaction of MM region to the quantum region, but not vice versa. TD-DFT with PE, even at our small size of 77 atoms, is able to reproduce the XMCQDPT2 excitation energies at the S_0-S_1 excited state, although TPA intensities are underestimated by up to an order of magnitude. On the other hand, excitation from S_0 to S_2 or S_3 have only slightly underestimated energies. XMCQDPT2 method places the wavelength of S_2 and S_3 at approximately 678nm and 644nm respectively [1], conversely, results we present here ranges at 608nm and 557nm. TPA intensities are also reproducible for the excitation to the same states. Excitation to the S_2 and S_3 states are merely underestimated by 10s to a few 100s of GM, respectively, a stark difference to the results reported by Palczewska's team where TPA intensities are underestimated as low as 3 orders of magnitude[2].

Acknowledgements: Calculations were performed at the Wroclaw Centre for Networking and Supercomputing (WCSS). Massimo Olivucci and team is thanked for providing parameters and trajectories of classical MD for Rhodopsin. Jógvan Magnus Haugaard Olsen is also thanked for providing guidance on using PyFrame and Dalton.

***Keywords**: One-photon Absorption, Two-photon Absorption, polarizable embedding, Time-Dependent Density Functional Theory, BHandHLYP, rhodopsin, retinal, electrostatic embedding, Quantum Mechanical/Molecular Mechanics*

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Quantum Mechanical Study of Size and Sequence Effects on the Ionization Potential of Stacked DNA Bases

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The deoxyribonucleic acid (DNA) is exposed to many environmental influences, including both natural and artificial ionizing radiation. These can cause mutation of the cell's DNA, which can lead to cancer disease. The influence of ionizing radiation on DNA has been intensively investigated by different approaches from a macroscopic view to a microscopic picture of the DNA building blocks. It is known that guanine (G) has the lowest ionization potential among the four DNA bases [1-2] (lower than single adenine, cytosine, and thymine), and that the vertical ionization potentials (vIPs) tend to decrease with increasing system size [3]. However, no convergence of the vIP values has yet been achieved up to the maximum size considered [4] and no study has provided a systematic investigation of vIPs as a function of the DNA sequence.

In our work, we have developed a DFT-based (*Density Functional Theory*) computational approach with an optimized medium-sized basis set to investigate the vertical ionization potential of short single-stranded DNA sequences of different lengths and types in the gas phase. This approach allows to recover a large part of the electronic correlation energy at reasonable computational expense despite the large size of the DNA complexes. We have achieved a systematic study of the ionization potential of all combinations of two, three and four stacked nucleobases.

Our investigation of the ionization potential is also extended to sequences containing 5-methylated cytosine (5-mC). Quantum mechanics calculations carried out on single methylated cytosine as well as on two- and three-base stackings containing 5-mC indicate that methylation tends to decrease the vIP of the DNA base sequence.

Acknowledgements: N.C. thanks the FRIA (Belgium) for a PhD fellowship. This work is financially supported by the "Fonds de la Recherche Scientifique" - F.R.S-FNRS (Belgium).

***Keywords**: quantum chemistry, DFT, base stacking, DNA damage, ionization*

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DFT Studies on Adsorption of Hg Vapors on Sulfur Impregnated Activated Carbon

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Mercury vapors (Hg) are released from coal fired power plants, during extraction of natural gas and many other industries. The inhalation of mercury vapor may produce harmful effects on the nervous, digestive, and immune systems, lungs, and kidneys, and may be fatal. Adsorption being an economical, simple, and effective process may be used for removal of mercury vapors from atmosphere. Activated carbon (AC) being the most widely used adsorbent due to its properties like high surface area, high micro pore volume. Mercury is supposed to have a good affinity towards sulfur (S) and hence sulfur impregnated activated carbon is famous for removal of Hg vapors from air. The impregnated sulfur reacts with mercury to form mercury sulfide thereby removing it from vapor streams.

In the present study we have investigated the adsorption S on AC surface and followed by chemisorption of Hg vapors on S adsorbed AC. All the simulations were performed on Gaussian 16 software. Gas phase simulations were carried out in the present study. Optimization and frequency calculations have been carried out using the B3LYP functional which is a hybrid type and also one of the most used one. 6-31G is the basis set used for C, H and S atoms in the system as it maps the properties and has a balance between accuracy and computational cost. Since 6-31G is only available up to Zn in periodic table, for mercury atoms LanL2DZ was used. To model the AC surface for adsorption of S, graphene sheet with 16 C atoms was used. Three sites for the AC namely armchair edge, zigzag edge, and graphene surface was used in the present investigation. AC surface with two different functional groups namely, hydroxyl and carboxylic acid were also studied for adsorption of S. S was modeled using cluster atoms varying from 2 to 7. To assess the chemisorption of Hg on AC surface with S containing functional groups like thiol, sulfonic acid, sulfenic acid, sulfinic acid and two edge H atoms replaced by two S atoms in AC surface was investigated.

The results were analyzed using parameters such as adsorption energy, reaction energy, bond lengths, change in entropy of the system. The results suggested that S cluster with two edge H atoms in the graphene sheet was most reactive and hence was used for adsorption on AC. Zigzag edge was the most favorable for adsorption of S. Among the functional groups present on the AC hydroxyl was favored for adsorption of S. The trends for chemisorption of Hg vapors on S adsorbed surface was same as that of adsorption of S on AC. For the chemisorption of Hg on S present as functional groups on AC, the edge where two H atoms were replaced by two S atoms was most favored for chemisorption of Hg. A reaction pathway was proposed for chemisorption of Hg on S adsorbed armchair and zigzag edge, after the transition state simulations were carried out.

***Keywords**: Hg vapors, activated carbon, sulfur impregnation, chemisorption, sulfur functionalization*

Extending the Martini 3 Coarse-Grained Force Field to Carbohydrates

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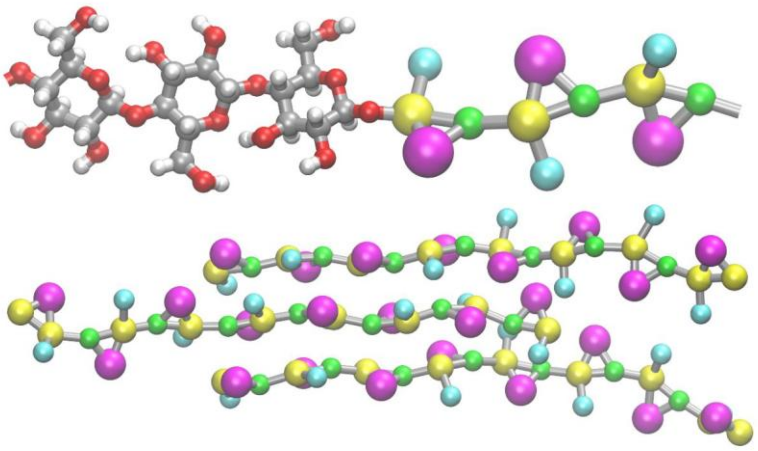
Carbohydrates play an essential role in a large number of chemical and biochemical processes. High structural diversity and conformational heterogeneity make it problematic to link their measurable properties to molecular features. Molecular dynamics simulations carried out at the level of classical force fields are routinely applied to study the complex processes occurring in carbohydrate-containing systems while the usefulness of such simulations relies on the accuracy of the underlying theoretical model. I would like to present a newly developed the coarse-grained force field dedicated to glucopyranose-based carbohydrates and compatible with recent version of the Martini force field (v. 3.0). The parameterization was based on optimizing bonded and non-bonded parameters with a reference to the all-atom simulation results and the experimental data. Application of the newly-developed coarse-grained carbohydrate model to oligosaccharides curdlan and cellulose displays spontaneous formation of aggregates of experimentally-identified features. In contact with other biomolecules, the model is capable to recover the protective effect of glucose monosaccharides on a lipid bilayer and correctly identify the binding pockets in carbohydrate-binding proteins. The features of the newly-proposed model make it an excellent candidate for further extensions, aimed at modeling more complex, functionalized and biologically-relevant carbohydrates.



Acknowledgements: This research was funded by the National Science Centre, Poland (contract financed in 2020–2024 under no. 2019/35/B/ST4/01149 OPUS 18).

***Keywords**: carbohydrates, glucose, molecular dynamics, force field, coarse-grained*

Theory and Applications of the Reaction Fragility Spectrum

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We have introduced the Reaction Fragility Spectrum as a new method for the comprehensive studies on the mechanism of the chemical reaction. It reveals the evolution of the electronic structure and provides quantification for both the sequence of bond breaking and forming and the evolution of the bond order modifications along the chemical reaction path. The new DFT Connectivity Matrix has been introduced: its elements are the divergences over the atomic displacements of the Hellmann–Feynman forces acting on atoms in a molecule. The DFT Connectivity Matrix elements have been proved to describe how the atoms in a molecule are actually connected with chemical bonds. Other very important theoretical result derived from our concept is the new approximation for the Fukui Function. Numerous applications to various chemical reactions are presented.

Keywords*: reaction mechanism, IRC, Hellmann-Feynman force, energy Hessian*

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ABSTRACTS OF POSTER PRESENTATIONS

P1. Computational Evaluation of Photoinduced Electron Transfer Rates in DNA

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The vulnerability of DNA and RNA to the harmful effects of UV-radiation is particularly intriguing in the context of origins of life. Many fundamental aspects of the photochemistry of nucleic acid oligomers are still obscure, including the contribution of locally-excited (LE) and the extent of the charge-transfer (CT) character in DNA/RNA strands, and the availability of different photorelaxation pathways in such assemblies. Thus, characterization of photoinduced processes in oligonucleotides based on highly accurate quantum-chemical methods is urgently needed.

In this contribution ground and excited states equilibrium geometries were optimized using MP2, ADC(2) and the the spin-component scaled variant of the latter, using a set of four basis sets: def2-SVP, cc-pVDZ, aug-cc-pVDZ and cc-pVDZ-F12. Vertical excitation energies were obtained at the same level of theory. Calculations were performed using the TURBOMOLE 7.3 package The optimization of minimum-energy crossing points (MECPs) between two electronic states was performed employing the CIOpt package. A more complete understanding of the photodynamics of **D7A** (7H-diaminopurine-adenine) and **A7A9** (7H-adenine-9H-adenine) base pairs is gained after the calculation of the absorption cross-section spectra and trajectories using the software Newton-X version 2.4. At stationary level, both base pairs are predicted to have significant UV induced electron transfer, having minima of the donor and acceptor states. The conical intersection S_1/S_0 is expected to be reached in a barrierless fashion, suggesting the photostability of evaluated base pairs. The population of the CT state is still challenging within nonadiabatic molecular dynamics approximation, what might be related to the zero point energy leakage.

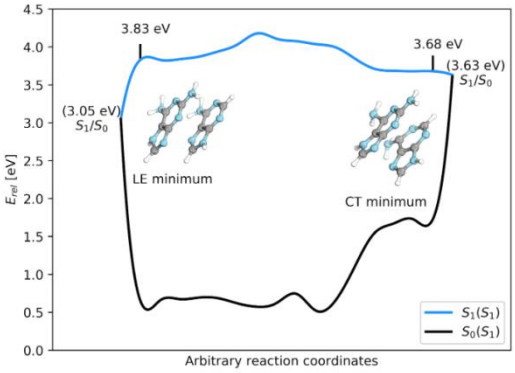

Fig. 1. Potential energy profile computed at MP2/ADC(2)/def2-SVP level of theory of D7A.

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

***Keywords**: electron transfer, ab initio, base pairs, conical intersections, non-adiabatic dynamics*

P2. The Acid-Base Profiles as a Consequence of the Schiff's Bases Structures Formed by Sulfa Drugs Analogues

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The structural modification of compounds with proven biological activity is mostly considered to obtain new active substances. Predicting the effect of compound structural changes on its activity allows the efficacy and possible use of a new medicinal product to be assessed. To achieve this goal has to determine the stability and acid-base properties of the substance received. It is crucial for indicating the possibility of the compound studied penetrating biological barriers and interacting with molecules present in the cells of a living organism. The structure modification investigations of compounds with therapeutic effects and multidirectional pharmacological use are currently recognized as top and evidenced by numerous reports about the skeletons design as well as synthetic procedures diversity [1,2]. The main aim of the presented study was to determine the physicochemical parameters *in silico* of four selected heterocyclic Schiff's bases belonging to the anilinesulfonamide derivatives (sulfathiazole and sulfacetamide drugs modified by pyrrole motives, **Fig. 1**). The M06/6-311++G(2d,2p) method was used to obtain the complete analysis of structural and ionic forms of objects studied in the gas phase. The acid-base properties in water described by pKa values were received by SMD/M06/6-311++G(2d,2p) method.

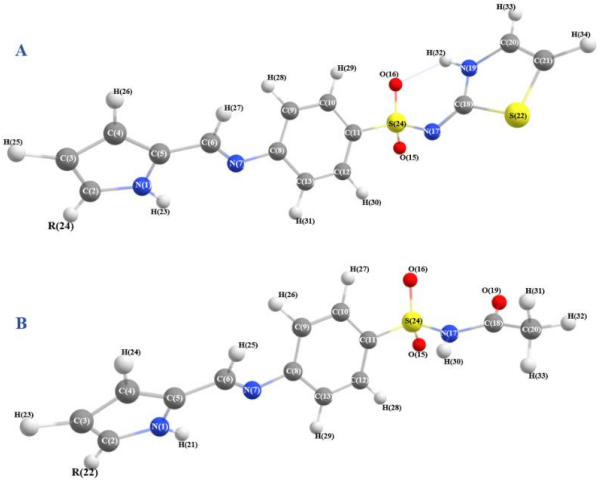

Fig. 1. The optimized Schiff's bases structures based on: ***A.*** *sulfathiazole;* ***B.*** *sulfacetamide, where R denotes H or Br atoms present in the modifier.*

Acknowledgements: This work was supported by the Polish National Science Centre under Grant [UMO-2019/33/B/ST4/00031].

Keywords*: sulfonamides, Schiff's bases, structural analysis, tautomers, pKa values*

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P3. The Affinity of Small Molecules to DNA - Optimization of the New, Innovative SwitchSense Technology

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The switchSense is a new, innovative technology that allows studying of biomolecules interactions in real-time. For the best possible measurement results, specially chips have been dedicated. The surface of the chip is covered with gold, on which is anchored double-stranded DNA labeled with a fluorophore. The ligand may be bound to the DNA helix. The analyte-ligand interaction results in fluorescence changes. So far applications of this technology have included macromolecular systems in which the analytes are, for example, proteins [1-4]. But not only macromolecules may be characterized by pharmaceutical potential. Moreover, DNA is a desirable target for many therapies. That is why it has become so important to study the interaction of small molecules with this biomolecule.

In this presentation, the results of method optimization (used in the switchSense technology) for the new application - study to small molecules-DNA interaction have been presented. In this case, the measuring system (see Fig. 1) is only a DNA helix labeled with a fluorophore (without ligand) and the analyte is a small molecule [4].

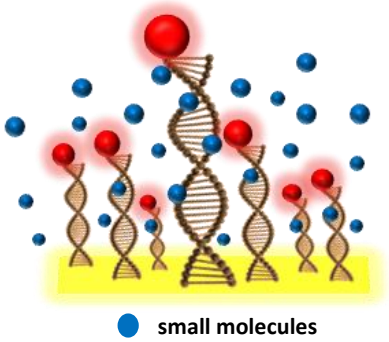

Fig. 1. The measurement system.

Acknowledgments. This work was supported by the Polish National Science Centre (NCN) under Grant No. UMO-2019/33/B/ST4/00031.

***Keywords**: switchSense, DNA interaction, small molecules.*

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P4. $P2X_7$ Receptor as a Target for Purinergic Approach to Synergistic Anticancer Action

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The purinergic signaling pathway is the oldest evolutionarily known transduction system. This pathway regulates many physiological and pathophysiological processes in the central nervous system. The problem of the interaction of purinergic compounds with drugs used for many diseases is rarely touched. For this reason, our focus was to clarify the relationship between the purinergic signaling pathway and the chemotherapeutic drug - temozolomide (TMZ) used in human glioma treatment.

In the theoretical part of the presented work, a homologous model of the human $P2X_7$ receptor was created. Molecular docking methods were then applied, during which ATP and TMZ were docked into the receptor structure. This approach allowed the identification of potential binding pockets for TMZ. The experimental part of the study involved retinoic acid-induced differentiation of A172 glioma cells and examined $P2X_7$ receptor expression in undifferentiated and differentiated gliomas. The study compared the effects of $P2X_7$ receptor agonists/antagonists and their interaction with TMZ in both cell types by evaluating cell proliferation, viability, and migratory properties.

The results indicate that the differentiated cells are more sensitive to the influence of ATP and TMZ alone and to the combined effects of TMZ and ATP (what was also predicted by theoretical studies). The synergistic effects caused by the action of ATP and TMZ include reduced viability and reduced migration ability of differentiated A172 glioma cells. Significantly, both compounds achieved promising results at low and non-toxic concentrations.

Based on the results, we can conclude that an appropriate concentration of ATP molecules in the microenvironment of glioma cells is necessary to achieve synergistic interaction with TMZ for enhanced anti-tumor activity. Achieving such a concentration of ATP may shorten the therapy and reduce the chemotherapeutic agent's side effects. The proposed approach of interacting the drug with a purinergic agent opens up new possibilities for developing novel combination cancer therapies.

Acknowledgements: WN acknowledges the partial financial support by the National Science Center grant 2016/23/B/ST4/01770.

***Keywords**: glioma, purinergic signaling, temozolomide, $P2X_7$ receptor, molecular docking*

P5. Ruthenium Complexes as Potential Radiosensitizers for Use in Radiotherapy

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Radiotherapy (RT) is one of the fundamental methods of cancer treatment [1]. It should be emphasized that cancer cells in tumors are characterized by hypoxia, which greatly reduces the effectiveness of ionizing radiation (IR). Radiosensitizers are chemical compounds that sensitize cancer cells to IR and one group of radiosensitizers constitute modified nucleosides (MNs). MNs due to their similarity to native nucleosides can be incorporated into cellular DNA during replication or repair and after irradiation with IR undergo degradation induced by hydrated electrons (dissociative electron attachment, DEA). The latter are one of the main products of water radiolysis in cells under hypoxic conditions [2].

To be incorporated into DNA, MN must undergo phosphorylation by cellular kinases and be processed by DNA polymerases. However, a chemical modification of nucleoside may lead to a derivative which is not a good substrate for the mentioned above enzymes. Thus, the present project aims at exploring a new concept of delivering radiosensitizing nucleosides/nucleobases to the genomic DNA that enables the enzymatic pathways related to DNA replication or repair to be bypassed. Hence, the main goal of the current studies is to synthesize and evaluate physicochemical properties of ruthenium complex with a radiosensitizing derivative of uridine that can intercalate to DNA and in this way efficiently deliver the radiosensitizer to the biopolymer [3,4].

In this report, we present the successful coordination of the 5-bromouracil anion (BrU) and 2,2'-bipyridine (bpy) to the Ru(II) cation (Fig. 1). The stability of the obtained complex in water, acetonitrile and methanol has been tested and the results showed its degradation in all solutions. In the next step we will continue the synthesis and stability tests of Ru(II) complex with DNA intercalating ligand – dipyrido[3,2-*a*:2',3'-*c*]phenazine (dppz).

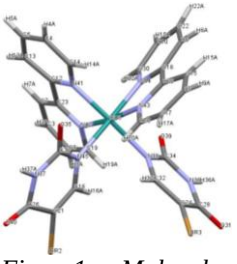

Fig. 1. Molecular structure of the Ru(II) complex with bpy and a BrU ligands.

Acknowledgements: This work was supported by grant from the Ministry of Science and Higher Education in Poland (DS/531-T080-D494-21 to J.R.) and Young Scientists Research grant (BMN 2021, University of Gdansk, Faculty of Chemistry).

***Keywords**: ruthenium complexes, radiotherapy, ionizing radiation, radiosensitizers, DNA*

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P6. Stationary Radiolysis of Adenine Derivative – a Potential Radiosensitizer

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More than 80% of cancer cases world-wide are solid tumours characterized by high levels of hypoxia (so called oxygen effect), which result in their radioresistance to ionizing radiation (IR). The oxygen effect can be mitigated by using compounds that sensitize cancer cells to IR - radiosensitizers (RS). A promising group of RS are modified nucleosides (Mnucs), where the derivatives of pyrimidine nucleobases have been mainly studied so far. Only few examples of radiosensitizing substituted purine nucleobases are described in the literature. Well known examples are 8-bromo-2'-deoxyadenosine and 8-bromo-2'-deoxyguanosine which were investigated both experimentally and computationally [1,2,3,4]

In the present project the results of stationary radiolysis performed for a new adenine derivative, 8-thiometyladenine ($ASCH_3$), are reported. In order to verify the susceptibility of $ASCH_3$ to decomposition induced by the attachment of solvated electron (DEA) radiolysis in an aqueous solution was carried out in the presence of a hydroxyl radical scavenger. Despite a favourable DEA profile, $ASCH_3$ does not undergo the IR induced decomposition in water. This seeming controversy between the experiment and theory prompted us to check if the protonation of the primary anion, $ASCH_3^{\bullet -}$, might be responsible for the observed lack of the radiolytic activity of $ASCH_3$ in water. Thus, the radiolysis of $ASCH_3$ in aprotic solvents, tetrahydrofuran (THF) and acetonitrile (ACN), was additionally carried out. Although no $ASCH_3$ decay was detected in THF, its decomposition products were observed in ACN. Our experimental findings were confirmed with the help of quantum chemical modelling of reaction profiles. The decomposition of $ASCH_3$ observed in an aprotic solvent of medium polarity seems to be a strong argument for our tentative hypothesis.

Acknowledgements: This research was conducted with the financial support of the National Science Centre (NCN) as part of the project number UMO-2020/02/Y/ST4/00110.

***Keywords**: radiosensitizers, stationary radiolysis, adenine derivative, modified nucleosides*

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P7. Polyamide Decomposition: Theoretical Investigation of the Process

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The theoretical description of the polymer degradation process requires taking into account many possible reaction paths. The detailed mechanism investigation, as well as optimal conditions description of the studied process, is essential for the effective processing of the polymer on an industrial scale. One of the best-known synthetic polymers, from the polyamide family, is nylon 6. This polymer is widely used due to a number of significant physicochemical properties [1]. Thermal degradation of nylon 6 leads to the formation of a stable cyclic product - ε-caprolactam (Figure 1b).

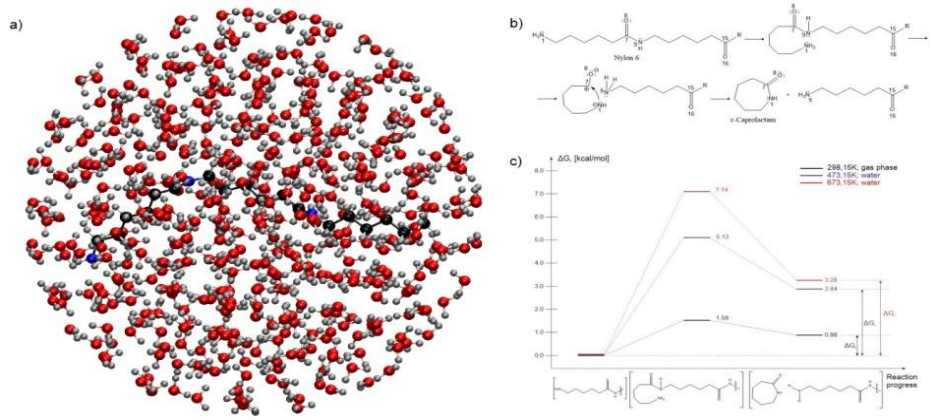

Fig. 1. a) Geometric structure of the nylon 6 thermal degradation substrate surrounded by water molecules;b) scheme of the nylon 6 thermal degradation mechanism; c) the influence of temperature and the solvent presence on the calculated thermodynamics data of studied process.

In this study, the influence of environmental conditions, in particular temperature and the presence of a solvent, on the degradation mechanism was investigated. Quantum chemical calculations were carried out in Gaussian 09 [2] and ADF 2019 [3] software. Additionally, different DFT functionals (B3LYP, BP86, B3LYP-D3, BP86-D3) and basis sets (TZP, TZ2P, QZ4P) were used. The presence of a solvent was studied using both *implicite* (SCRF and COSMO continuous solvent model respectively) and *explicite* models. Selected results were compared with the available experimental data as well [4].

Acknowledgments: This work was supported by grant IDUB/DigiWorld/2022/14 1027.0641.363.2019 from Jagiellonian University. This research was also supported in part by PLGrid Infrastructure.

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P8. Feasibility of Nonempirical Ligand Scoring in Binding Affinity Predictions

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Reliable assesment of the ligand inhibitory activity remains a challenge, as the performance of commonly used empirical scoring functions is still insufficient [1]. In particular, a single empirical scoring function is not capable of providing reasonable binding affinity estimates in all the protein-ligand complexes [2] and its usage precludes investigation of the physical nature of ligand binding. On the other hand, accurate quantum chemical calculations are resource-consuming and so impractical in routine *in silico* screening of a large ligand library.

To overcome these obstacles, we propose a first-principles based ligand scoring scheme (MED) accounting for long-range interaction energy terms as a useful and reliable tool for predictions of the relative binding energy in receptor-ligand complexes [3]. The MED model presented herein combines the computational efficiency with the lack of arbitrary parametrization and appears to peform favourably in a number of cases, including the challenging inhibitors of protein-protein interaction [4]. In this contribution we compare the performance of MED model for various protein-ligand systems with the empirical scoring, demonstrating the predictive capabilities of MED scheme and discussing the possible limits of its applicability.

Acknowledgments: NCN OPUS 02NO/0021/18 Catalytic fields as the tool for theoretical analysis and design of biocatalysts.

Keywords*: computed-aided drug design, nonempirical interaction energy, protein-ligand complexes*

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P9. Amphotericin B and Thiadiazole Derivatives - Theoretical Binding Site Study

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Fungal diseases are estimated to be responsible for over 1.5 million deaths every year. Antifungal antibiotics, such as Amphotericin B (AmB), are often used to treat them, but, unfortunately, the use of AmB is associated with a high toxicity [1]. Therefore, novel alternative treatments are sought after, in which AmB is combined with other potential drugs that reduce its toxicity towards human cells while maintaining its potency against fungal cells. In one such treatment, AmB is combined with thiadiazol derivatives to give systems with lesser toxicity and better antifungal properties [2].

The exact mechanism of interaction between AmB and thiadiazole derivatives is currently unknown. In order to understand this mechanism the nature of how thiadiazole derivatives bind to AmB molecules was studied computationally. To accomplish this, possible binding sites of thiadiazole derivatives to AmB were determined based on extensive docking studies between the two molecules with the DFTB method [3]. The computed binding energies show that multiple thiadiazoles will readily bind to AmB in an energetically favorable way, while it was also determined that entropy and solvation effects play a major role in the studied interaction.

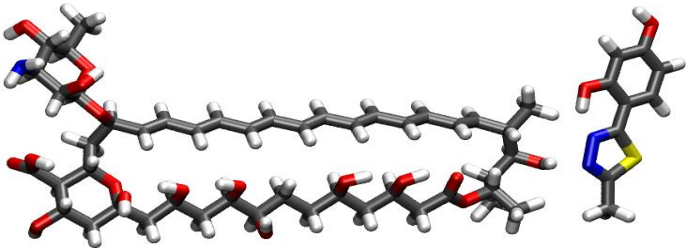

Fig. 1. Geometry of possible binding site between amphotericin B (left) and thiadiazol derivative (right).

Acknowledgments: Experimental studies were done by prof. Arkadiusz Matwijczuk and were the inspiration for this research. This work was supported by PL-Grid Infrastructure (ACC Cyfronet AGH).

***Keywords**: antifungal, density functional tight-binding, conformation study, docking*

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P10. Computational Perspectives about the Role of Anion-π Interactions in Molecular Crystals

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Many examples have been reported in the recent literature of families of supramolecular crystals whose structures are all geometrically similar, but their differing constituents lead to altered electronic properties across a chemical series. Among them are families of molecular crystals that are designed such that anion-π interactions, that is to say quite strong non-covalent interactions between simple/complex anions and strong π-acceptors such as 1,4,5,8,9,12-hexaazatriphenylenehexacarbonitrile ($HAT(CN)_6$), play an important role in stabilizing and determining both the atomic and electronic structures [1,2]. Some new functionality, described herein, is explored by computationally studying the influences of intermolecular interactions on the properties of molecular crystals that contain simple anions, $HAT(CN)_6$, and cationic transition metal complexes with phenanthroline ligands. Using a series of anions it was found that a family of crystals could be created which all adopt the same basic framework, within which the anions are inserted into available pores and cavities.

A computational analysis of the intermolecular interactions in each structure confirms that the main differences between them lie within the relative strengths of the $[M(phen)_3]^{2+}$- $HAT(CN)_6$ and anion-$HAT(CN)_6$ interactions. Density functional theory and density functional tight-binding theories are further used to discuss the influence of the anion-π interactions on the electronic structures of the metal complexes and to propose further directions for designing new spin-crossover materials.

Acknowledgements: This work was supported by the PL-Grid Infrastructure (ACC Cyfronet AGH).

***Keywords**: anion-π interactions, density functional tight-binding, molecular crystals*

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P11. The Reaction Fragility Spectrum in Solvent Obtained with C-PCM Model

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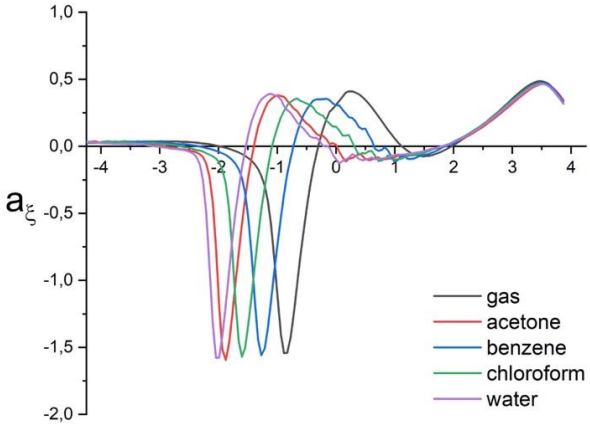
Recently we have introduced and developed the Reaction Fragility Spectrum (*J. Chem. Phys.* ***2017***, *147, 134109*, *J. Phys. Chem. A*, **2020**, *124* (6), 1076-1086) as a convenient and instructive method of visualization of electronic reorganization in a reacting molecular system. This method relies on tracing the evolution a divergence of the Hellmann-Feynman forces and to represent elasticity of the atomic structure over the reaction progress. Depiction of the course of the reaction is achieved by a diagram, analogous to a spectrum, that correlates with the formation and breaking of bonds. This work provides analysis and the numerical results of the effect of the solvent influence on the mechanism of the reaction revealed by the Reaction Fragility Spectrum. Our results show how the sites positions on the IRC path of bond breaking and forming depend on the solvent and its dielectric constant.



Acknowledgements: Calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl), grant No. 249.

Keywords*: chemical reaction mechanism, IRC, Hellmann-Feynman force, Reaction Fragility, C-PCM solvent model*

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P12. Charge Transfer Properties of Cytochrome b_{562} Investigated by QM/MM Sampling Techniques

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Life driving processes such as respiration, photosynthesis, and many enzymic catalytic reactions are based on electron transfer reactions facilitated by redox proteins. Cytochrome b_{562} found in *Escherichia coli* is one among these proteins. It consists of a heme ($Fe^{2+/3+}$) center covalently bonded to the protein matrix. The central iron cation is further coordinated to axial histidine and methionine ligands (Fig. 1). Recently, electrochemical scanning tunneling microscopy (EC-STM) was utilized to probe the conductive properties of single cytochrome b_{562} on solvated gold surfaces [1]. Motivated by the availability of such detailed experimental data, we study the charge-transport properties of the cytochrome b_{562}, first in bulk solution and later on the gold-electrode interfaces.

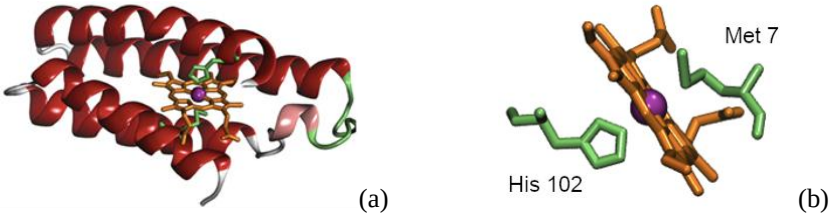

Fig. 1. (a) crystal structure of the cytochrome b_{562} protein (PDB id 2BC5), and (b) detail of its redox-active heme site (purple: Fe, orange: porphyrin ring, green: axial histidine and methionine).

We employ various computational techniques to study these electron transport properties. Classical molecular dynamics (MD) methods are used for studying structural and dynamical aspects of the protein configuration, while the hybrid quantum mechanical/molecular mechanical (QM/MM) approach based on DFT is applied to investigate the electronic properties. Here, we focus on the process of cytochrome b_{562} oxidation, which we describe within a frame of the Marcus theory of electron transfer. We calculate the reorganization free energy as the key parameter determining the free energy barrier for the charge transfer. The robustness of the obtained results is validated by the available experimental data with respect to different force-field parameters and solution compositions.

Acknowledgements: We gratefully acknowledge funding by the Czech Science Foundation GACR in the context Project No. 20-02067Y.

***Keywords**: cytochrome b_{562}, reorganization free energy, molecular dynamics, QM/MM, DFT*

References:
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P13. Characteristics of the Adsorption Process of Volatile Organic Compounds from the Gas Phase on Modified Activated Carbon

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Volatile organic compounds (VOCs) are substances characterised by high vapour pressure and a boiling point below 250°C at atmospheric pressure. VOCs include compounds belonging to different groups of organic compounds such as aliphatic hydrocarbons, aromatic hydrocarbons, alcohols, esters, and ketones. Volatile organic compound's pollution is mainly caused by industrial processes, but also by the use of combustion vehicles. Some of these compounds are also secreted by plants in the form of secondary metabolites. Currently, efforts are being made to reduce VOC emissions, which are provided for by legal acts in the form of regulations, European Union regulations, e.g. Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on industrial emissions (integrated pollution prevention and control). The control of VOC concentrations in waste gases is due to their adverse environmental effects. They contribute to the formation of tropospheric ozone and secondary organic aerosols. They adversely affect human health due to their mutagenic and carcinogenic properties. One effective method of air purification is adsorption on activated carbon. [1-3]

This study aims to evaluate the mutual influence of the components of the purified air stream from VOC vapours on the process of adsorption from the gas phase on DL-malic acid modified activated carbon WG-12 (Grand Activated Sp. z o.o.). The adsorption of mixtures of acetone, ethyl acetate, n-butyl acetate and acetone, ethyl acetate, toluene was investigated. Gas chromatography was used to determine the outlet concentrations of the individual adsorbates, and then bed breakthrough curves were prepared to show changes in concentration over time. The process was characterised in terms of mass transfer in the adsorption bed. It was found that in the case of the three-component systems studied, competitive adsorption occurs, resulting in a mutual displacement of the adsorbed components from the bed. Modifications with DL-malic acid increased the adsorption efficiency, especially towards the less volatile components.

Acknowledgements: This work was supported by Rector of The West Pomeranian University of Technology in Szczecin for PhD students of the Doctoral School, grant number ZUT/8/2022.

***Keywords**: multicomponent adsorption, volatile organic compounds, modified activated carbon*

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P14. Specificity in Detection of PTCs in mRNA by NMD and its Network, Insights from Cancer Perspective

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Nonsense mediated mRNA decay (NMD; Figure 1) is a quality-control checkpoint that detects and eliminates aberrant messenger RNAs (mRNAs) with premature termination codons (PTCs). The NMD pathway plays an important role in the degradation of mRNA containing PTCs, but the molecular mechanism and structural rearrangements (with exon junction complex; EJC and eukaryotic release factors; eRFs) during this process has not been fully delineated. The object of our project is to understand the mechanism with dynamic and structural properties of proteins from the NMD, EJC, and eRFs complexes that are involved in the recognition or binding to mRNA or the PTCs. Herein, we studied the binding network between the protein-RNA / protein or RNA-RNA components using molecular modeling / dynamics approaches, as well as by applying the cross-linking MS-based structural techniques (XL-MS).

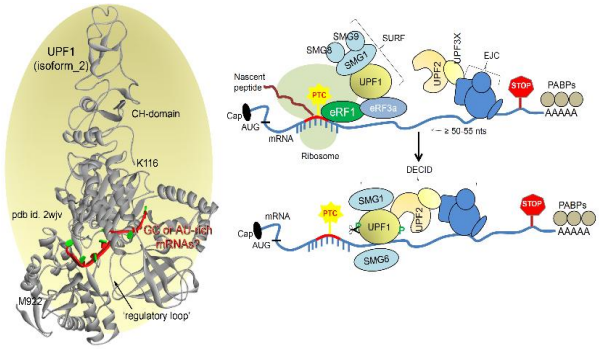

Fig. 1. The master regulator of the NMD (nonsense-mediated mRNA decay) pathway: UPF1 (UP-frameshift 1). Optimized UPF1 isoform_2 model structure and interactions with the poly(U) mRNA motif (https://doi.org/10.3390/ijms222312744).

PTCs cause a multitude of human diseases and there are no established therapeutic options for their therapeutic management. In addition, the overall cancer patient survival status relating to the components from NMD, EJC, and eRFs suggest that there is substantial decrease in the survival in the patients from the altered group. It has been estimated that up to 30% of all mutations resulting in human genetic disorders result in PTCs, and this PTCs represent a unique constellation of diseases. In addition, investigating the mutational effect on the stability and binding or protein-protein, protein-RNA, and RNA-RNA can provide new insights into the molecular mechanisms of this complex process and assist in development of novel therapeutic approaches. Our initial findings highlighted two distinct conformations between 1B and RecA2 domains of the UPF1 protein (master regulator of NMD): 'open (isoform_2; without insertion)' and 'closed (isoform_1; with insertion)'. These structural movements correspond to an important stacking pattern in mRNA motifs, i.e., absence of stack formation in mRNA, with UPF1 isoform_2 results in the 'open conformation'. In addition, lower fluctuating GC-rich mRNA motifs have better binding with UPF1, compared with AU-rich sequences.

***Keywords**: PTC, nonsense mediated mRNA decay, cross-linking mass spectrometry, molecular dynamics, structural properties*

P15. Sink or Soar? A Predictive TD-DFT Study on the Selected Properties of Novel Oxazole-Based Diarylethenes

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1,2-diarylethenes are organic compounds composed of two aromatic fragments linked together with an ethylenic bridge[**1**]. Since the two arene moieties may take either *cis* or *trans* configuration relative to the double bond, the molecules may normally appear in form of two stable geometric isomers (*Z*/*E*). These, however, may convert into each other upon absorption of light by the process of photoisomerization (***1*** in *Fig.1*). On the other hand, the *cis* (*Z*) isomer may alternatively undergo the reaction of photocyclization, resulting in the light-induced formation of an additional link between the arene rings (***2*** in *Fig.1*). As such transformation remains, in general, reversible, it has been successfully implemented for the construction of the so called 'molecular photoswitches'[**1,2**].

The design of these highly applicable compounds consists mainly in functionalization of the symmetric diarylethenic building blocks, composed of relatively simple aromatic rings, such as benzene or tiophene[**1**]. Quite recently, the idea of replacing one of the subfragments with oxazole ring (***R₁*** in *Fig.1*) has been considered[**3**]. Since the photophysical and photochemical properties of the resulting styryloxazole molecules turned out to be quite promising, we have decided to dwell a little more into this issue. Consequently, a pilotage computational study has been carried out with the TD-DFT methodology[**4**] in order to predict the possible results of the remaining benzene fragment substitution with naphthalene(***R₂*** in *Fig.1*). The selected (photo)physical and (photo)chemical properties of the molecules under investigation were simulated and thoroughly scrutinized. The designated results, unveiling the not-so-obvious characteristics of the studied systems, are being presented and critically discussed. Eventually, the aspects of their potential applicability are also assessed.

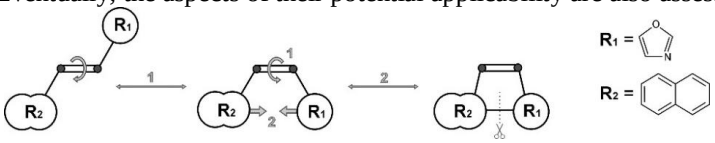

Fig. 1. Schematic depiction of the diarylethenic systems under consideration and two crucial light-triggered processes, i.e. photoisomerization and photocyclization, expected to occur within them.

Acknowledgements: All the calculations were performed thanks to the **Eagle** HPC cluster resources by **PCSS** (**PLGrid** Infrastruct.).

Keywords*: asymmetric diarylethenes, photosensitive materials, photochemical processes, isomerism, Time-Dependent DFT, UV-Vis spectra*

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P16. Analysis of Enzyme Reaction Mechanisms by Catalytic Fields

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Static catalytic field Δs derived from transition state and substrate wavefunctions represents the charge distribution of a molecular environment exerting optimal catalytic activity for any chemical reaction [1,2]. It can be used to evaluate the catalytic role of specific amino acid residues, and the gradient of Δs was even used to discover the paths of concerted proton dislocation along the reaction pathway [3]. Within a family of homologous enzymes, the charge distribution of strictly conserved charged amino acid residues correspond to the catalytic field Δs, and in principle it could be used to validate alternative enzyme reaction mechanisms. Such analysis is presented for the reaction catalyzed by a family of histydyl t-RNA synthetases, where three alternative reaction mechanisms have been proposed [4].

Acknowledgements: Research sponsored by NCN grant No 2017/27/B/ST4/01327.

Keywords*: catalytic field, differential transition state stabilization, enzymatic catalysis, reaction mechanism*

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P17. Theoretical Study of the Partial Oxidation of Methane into Methanol on Ru-Porphyrin

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The reaction mechanism of the Partial Oxidation of CH_4 into methanol is a major goal of heterogeneous catalysis [1,2]. Over the years, many modifications to this process have been developed, but the catalysts employed so far have not given very good results [3]. Hence, there are numerous experimental investigations confirming that ruthenium complexes often show very good catalytic activity in similar processes [4].

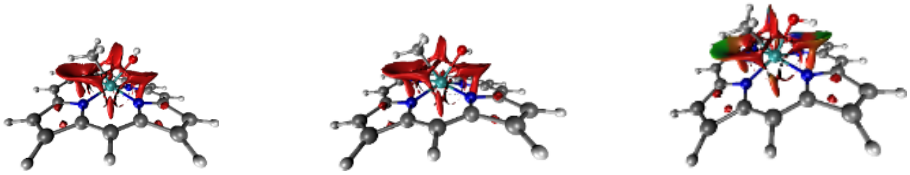

Fig. 1. NCI index surface representation (isovalue ± 0.5 [a.u.]) of the Ru-porphyrin complexes.

Density Functional Theory (DFT) has been applied to analyze the steps in the partial oxidation of methane to methanol using Ru-porphyrin complexes. The Quadratic Synchronous Transit (QST 2; QST 3) methods were followed to investigate localized transition states (TS) in the reaction. The non-covalent interaction index (NCI) was applied to characterize the non-covalent interactions in this process, thus providing description of these linkages (see Fig. 1).

The results indicate that the Spin Crossover (SCO) phenomenon occurring in the reaction significantly changed the physico-chemical properties of the complexes studied. Despite the rather high energy barriers, the process deserves attention due to the significant role of the SCO in the reaction kinetics. Strong repulsive interactions were noted between the CH_4 molecule and the metalloporphyrin in the partial oxidation reaction, as revealed by the NCI plots.

Acknowledgements: The Authors gratefully acknowledge generous grants of CPU time and support, provided by the Wrocław Centre for Networking and Supercomputing (WCSS), Poznań Supercomputing and Networking Center (PSNC) and Academic Computing Centre Cyfronet-Kraków (Prometheus supercomputer, part of the PL-Grid infrastructure).

***Keywords**: Partial Oxidation, SCO, DFT, NCI*

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P18. Influence of type Amino Acid on Thermochemical and Antimicrobial Properties of Active Pharmaceutical Ionic Liquids

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The ester prodrugs gain growing interest in the field of development and application of pharmaceutical ingredients since they may improve pharmacological activity and safety profile. This is due to the simplicity of synthesis and biotransformation into an active form, at the same time preventing the rapid metabolism of the drug substance, as well as the possibility of achieving increased solubility and improved absorption [1].

Active Pharmaceutical Ionic Liquids (AAILs) have been studied extensively as replacements for commonly used drug salts. The topical and transdermal drug delivery allows for reducing undesirable side effects, avoiding first-pass metabolism in the liver, and minimizing gastrointestinal side effects. The novel concept of obtaining AAILs and using them in drug delivery systems may ensure the effective delivery of poorly soluble drug molecules through the skin [2].

In this study, we present the thermochemical data obtained by DSC (differential scanning calorimetry) of a series of analogues drugs from the group of non-steroidal anti-inflammatory drugs and L-amino acid isopropyl esters. The effect of the amino acid structure on the thermal stability, and phase transition temperatures of the obtained salts will be presented, which may influence the bioavailability and effectiveness of the drug administration. Moreover, the antimicrobial activity of studied compounds will be described.

Acknowledgements: this work was supported by Rector of the West Pomeranian University of Technology in Szczecin for PhD students of the Doctoral School, grant number: ZUT/7/2022.

***Keywords**: Active Pharmaceutical Ionic Liquids, amino acids ester prodrugs, non-steroidal anti-inflammatory drugs*

References:

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P19. New Ligands Targeting TRF1/TRF2 Proteins Modulating their Telomeric Function.

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Choosing a proper molecular target is an important milestone in drug discovery research, and therefore searching for new valuable targets is a challenging process. Small chemical compounds are one of the primary choices in pharmaceutical industries and the chemistry-based approach in finding new medication cannot be ignored by the researchers. [1] Exploring new biological (enzymes, structural and/or functional proteins) targets is one of the mayor challenges in the discipline of medicinal chemistry, especially anticancer drug design. Therefore within the last few years the researchers focused on a telomere fail-safe protein called shelterin complex. Several diseases linked to shelterin, or their malfunction are known, in example glioblastoma [2], where TRF1 and TRF2 overexpression, is a significant factor for the development of the disease. Dyskeratosis congenita is related to TIN2 and TPP1 mutation and in some cases of chronic leukemia, is linked with POT1b mutation. [3] In response to this work, several research groups started to design potential modulators of shelterin components, applying Computer-Aided Drug Design (CADD). [4] There are several techniques which are involving CADD, such as High-Throughput Screening (HTS), for searching initial chemical hits, later the chosen hits are improved through Lead Optimization, which may include scaffold replacement, Fragment-Based Drug Design (FBDD) or generating a pharmacophore [1]. A pharmacophore is a set of molecular features which possess optimal steric conformation, electronic properties, to induce a desired biological response of a targeted molecule. [5] Herein, are presented the results which involve Computer-Aided Drug Design such as FBDD and generation of a pharmacophore set in order to obtain new derivatives of confirmed active compound modulating TRF1/2, which was developed earlier through high-throughput screening method in our research group.

***Keywords**: telomere, TRFH domain, computational methods in medicinal chemistry*

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P20. Comparison of the Catalytic Activity of W-SBA-15 and Ti-SBA-15 Materials in the 1,5,9-Cyclododecatriene Epoxidation Process

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The epoxidation of 1,5,9-cyclododecatriene (CDT) results in 1,2-epoxy-5,9-cyclododecadiene (ECDD) formation. ECDD, due to the high degree of functionalization of the molecule, finds many applications. It can be used as a component of epoxy resins and coatings. There are also reports of its possible use as an ingredient in perfumes. One of the more promising applications of ECDD appears to be the production of laurolactam and dodecanedioic acid [1].

The vast majority of studies on the CDT epoxidation process have been conducted using homogeneous catalysis (traditional as well as phase-transfer catalysis) with catalysts containing tungsten or molybdenum atoms [2]. There are several literature reports on the use of heterogeneous catalysts of the mesoporous silica type containing a titanium atom as the active center [1]. There are no reports on the use of any other heterogeneous catalysts in the studied process.

A comparative study of the activity of SBA-15-type mesoporous catalysts containing a tungsten atom (W-SBA-15) or a titanium atom (Ti-SBA-15) as the active center was carried out. The W-SBA-15 catalyst showed higher activity in the studied process.

Acknowledgements: This work was supported by Rector of the West Pomeranian Universityof Technology in Szczecin for PhD students of the Doctoral School, grant number: ZUT/9/2022.

***Keywords**: mesoporous silica, Ti-SBA-15, W-SBA-15, epoxidation, 1,5,9-cyclododecatriene*

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P21. A Theoretical Model of On-Surface Ullmann Coupling

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The chemistry of nanomaterials is still growing. Researchers look for precise and tailored methods of obtaining desired polymers. One of the more promising methods of covalent structure construction is on-surface Ullmann coupling. On-surface self-assembly on metal crystals is a favourable and developing research subject.

In our investigation, a Monte Carlo method coarse-grained simulation program was proposed to explore the creation of organometallic precursors of polyaromatic hydrocarbons in Ullmann coupling on metal crystal surface in the canonical ensemble. Studied systems comprised PAH derivatives molecules, represented as carbon segments and directional interactions, and divalent metal atoms in stoichiometric proportions. Copper crystal ((111) symmetry) was chosen as a surface and a reagent. Particle movement was restricted to lattice nodes to mirror the behaviour of PAHs on a crystal. Periodic boundary conditions were implemented to minimise edge effects.

The poster presents the exemplary results of simulations conducted for particles with different PAH backbones – naphthalene, anthracene, phenanthrene and tetracene. We've observed numerous different topologies of the obtained systems in dependence on the number and direction of interactions. The enantiomers of given PAH derivatives in a mixture and their influence on obtained results were investigated and compared to enantiopure systems.

The results of performed simulations may be used as preliminary research in the experimental trials of the method and as the method of eliminating PAH derivatives unsuitable for nanopolymers production.

Acknowledgements: This work was supported by the National Science Centre, Poland research grant 2018/31/B/ST4/01759.

***Keywords**: on-surface synthesis, Ullmann coupling, simulation, Monte Carlo method, PAHs*

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P22. Selected Structural and Vibrational Properties of Eggshell, African Snail and Red Coral. DFT *vs*. Experiment

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Eggshell is a common biowaste, which have a wide range of potential usage in the production of dietary supplements for humans, pharmaceuticals, cosmetics, foods, pro-healthy products for animals, fertilizers and feed. So, it is necessary to control the quality of the eggshell. Non-destructive IR/Raman spectroscopy is one of the appropriate techniques for this purpose. However, the interpretation of experimental spectra is not easy in many cases. Therefore, we determined selected structural and spectroscopic parameters of main components (calcium carbonate, collagen and polyene pigments) simple models: single molecules of $CaCO_3$, n-methylformamide, glycine and proline, Gly-Pro and Pro-Gly dimers, *in silico* and compared the results with the available experimental data. All calculations were provided in the gas phase using hybrid functionals B3LYP and BLYP to analyse the vibrations using harmonic and anharmonic model. In addition, the theoretical results were also compared with the experimental data for the African snail and red coral shell, as their chemical composition is similar to that of an eggshell.

Fig. 1. Eggshell (A), red coral (Corallium rubrum, B) and African snail (Helixia aspersa, C)

Acknowledgements: Partial support from ALVANAEKO Sp. z o. o. and the Faculty of Chemistry, University of Opole.

***Keywords**: DFT, eggshell, African snail, red coral, IR/Raman spectroscopy*

References:
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P23. Can Interactions between Carbon Nanotubes and Proteins Act as an MIE According to AOP 173?

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Carbon nanotubes (CNTs) are widely used in the application of nanotechnology and industries, due to their unique physicochemical characteristics. Consequently, their exposure to humans and the ecosystem is growing. Although the studies aimed at assessing the toxicity of carbon nanotubes have been extensively provided for more than one decade, the mechanism of the induced adverse effects is still challenging.

Recently, our group published a new article on the concept of adverse outcome pathway (AOP) for lung fibrosis induced by MWCNTs triggered by agranulocyte adhesion and diapedesis pathway [1]. According to our previous study, we concentrate following questions: (1) Can Carbon nanotubes and protein act as Molecular Initiative Events (MIEs) according to AOP 173? (2) How does the aspect ratio (length/diameter) of CNTs influence proteins? (3) How do distinct geometric shapes of CNTs and their functionalization influence the protein functions as well as binding interactions?

Based on the above questions, we generated the geometry optimization for three distinct models of CNTs employed with density functional theory (DFT) of B3LYP/6-31G* used. The three-dimensional structure of L-Selectin_mouse was developed by using Modeller10.3 software. To find the molecular interactions with CNTs, the docking studies were used to extract the best conformations of protein-CNTs, and further, molecular dynamic (MD) simulations were performed with protein-CNTs complex to analyze the dynamic behavior. In addition, the MD/MMPBSA method was utilized to select the lowest binding energy models of CNTs.

Acknowledgements: This work was funded via the National Science Centre (NCN TransNANO project, No 2020/37/B/ST5/01894).

***Keywords**: CNTs, AOP 173, MIE, DFT, Modeller, docking, MD*

References:

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P24. Interactions between $[PdCl_4]^{2-}$ Dianions in Crystals

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Palladium centers are currently being considered as potential building blocks for materials useful in optoelectronics and photovoltaic applications as perovskites and important synthons of biological systems. In the frame of our projects [1,2] two crystalline solids including tetrachloridopalladate(II) units differing in size of organic counterions were synthesized and evaluated using a variety of the quantum chemical methods. From the crystal structures data of obtained compounds, an interesting structural motif concerning Pd···Cl contact between anionic $[PdCl_4]^{2-}$ subsystems (Fig.1) was found. The double negative charge on each unit suggested presence of highly repulsive forces. In the absence of any surrounding environment these two dianions dissociated in preliminary computational tests, indeed. However, the inclusion of the surrounding counterions ($[NH_3\text{-}(CH_2)_n\text{-}NH_2]_4$, n= 4 or 6) along with the constellation of the H-bonds which they form to these dianions, permits the entire system to be held together as seen in the solid state. This finding is supported by the MEP, QTAIM, NCI and NBO analyses. Similar structural pattern was discovered within CSD survey for other members of Group 10 as well as it was successfully modelled for other $(MX_4)^{2-}$ (M= Ni, Pt) species using theoretical protocols [1].

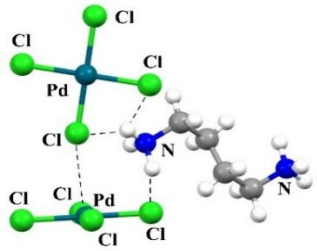

Fig. 1. View of the excerpt of the crystal structure of the studied system (CSD Refcode: NETMOO).

In our further theoretical examinations, we took a closer look at the nature of this interaction. It has been demonstrated that the stabilizing effect of the counterions is partly due to the dispersal of the negative charges on the Pd anionic units and consequently the reduction of the negative electrostatic potential of the π-hole at Pd atom. The result is that the anionic subunits come closer together and the apparently counterintuitive Pd···Cl interaction appears [2].

***Keywords**: molecular anions, noncovalent interactions, DFT study, CSD survey, Pd(II) complex*

References:

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P25. Neural Networks in the Design of Molecules with Affinity to Selected Protein Domains

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Drug design via machine learning can speed up new drug discoveries. While current databases of known compounds are magnitudes of orders smaller (approximately 10^8) [1], the number of small drug-like molecules is estimated to be between $10^{23} - 10^{60}$ [1]. The use of molecular docking algorithms [2] can help in new drug development by sieving out the worst drug-receptor complexes. New chemical spaces can be efficiently searched with the application of artificial intelligence [1]. From that, new structures can be proposed. The paper given below aims to create new chemical structures via a neural network that will possess affinity to selected protein domains (see **Figure 1.**). Transferring chemical structures into SELFIES [3] code allowed us to pass chemical information to a neural network. On the basis of vectorized SELFIES new chemical structures can be created. With the use of the created neural network, novel compounds that are chemically sensible can be generated. Newly created chemical structures are sieved by the Quantitative Estimation of Drug-Likeness descriptor [4] value and the SYnthetic Bayesian Accessibility classifier score [5]. The affinity to selected protein domains has been checked with the use of the AutoDock tool [2]. The results of the paper are the structures that possess affinity to selected protein domains.

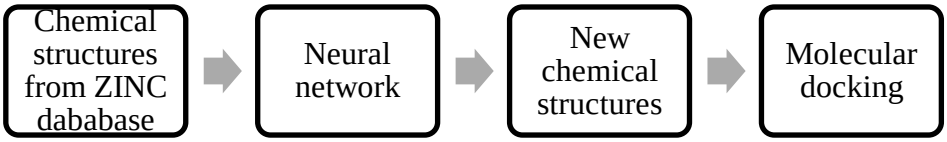

Fig.1. Simplified scheme of the realization of the experiment.

***Keywords**: machine learning; neural networks; molecular docking; ROR-γ; drugs design*

Acknowledgements: The author expresses gratitude to Dr. Rafał Bachorz, Head of the Molecular Modeling Laboratory at the Institute of Medical Biology, for allowing calculation inducement and for his invaluable assistance during code preparation. A special thanks to Dr. Esben Jannik Bjerrum, AstraZeneca's Principal Scientist, for the concept of the predictive model. The author also thanks Professor Marcin Hoffmann for all the comments and discussions that led to the publication of this paper. I would also like to thank my parents for all their support during my studies.

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P26. Synthesis, Structural Characterization and Theoretical Calculations of Interaction Energies for Pharmaceutical Crystals Derived from Acridine and Selected Hydroxybenzaldehydes

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One of the greatest challenges of today's scientists is to invent innovative ways to address various conditions in order to eliminate them or minimise their negative effects. For the pharmaceutical industry, it is particularly important that a potential medicinal product has the best possible physicochemical parameters, such as, for example: bioavailability, solubility, thermal stability or tabletability. Equally important is the economic issue – the product should be profitable, have relatively low production and storage costs and the manufacturing method should have the least possible impact on the environment. Drugs in the form of a multicomponent crystals allow for pharmacological modification of drug action [1-2] which make it possible to obtain the aforementioned industry-desired characteristics and properties.

An Active Pharmaceutical Ingredients: acridine and hydroxybenzaldehyde derivatives, were selected for the study. Acridine is able to intercalate into the DNA double strand, causing deactivation of the parasite's genetic material [3], while hydroxybenzaldehydes can enhances xenophagy [4] – a specific type of autophagy that inhibits the spread of pathogens.

The study presents a description of the synthesis of two multicomponent crystals derived from acridine and selected hydroxybenzaldehyde derivatives: 4-hydroxybenzaldehyde and 3-hydroxybenzaldehyde, results of structural studies by X-ray structural analysis, analysis of inter- and intramolecular interactions in the crystal lattice of the compounds, thermal stability studies and theoretical calculations of inter- and intramolecular interaction energies.

Acknowledgements: The research was financed from Faculty of Chemistry, University of Gdansk, Poland (grant No. 531-T080-D738-22 and grant No. 539-T080-B029-22).

***Keywords**: pharmaceutical crystals, X-Ray Diffraction, Active Pharmaceutical Ingredients, acridine, benzaldehydes*

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P27. Hydrogermylation of Styrenes Initiated by Trialkylborohydrides – a Quantum-Chemical Study of the Mechanism

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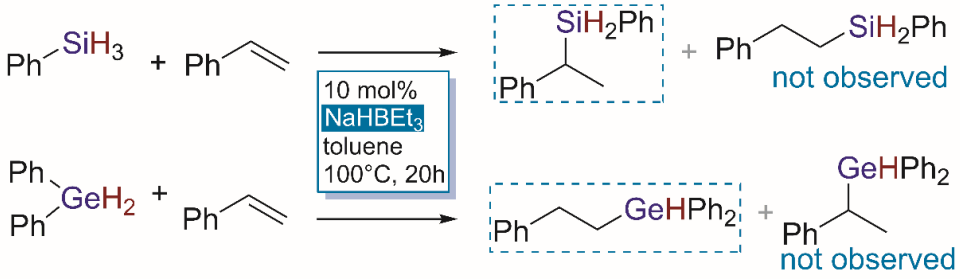
Hydrogermylation of aromatic alkenes was found to proceed in the presence of sodium trialkylborohydrates.[1] In contrast to analogous hydrosilylation reactions,[2] the reactions of phenylgermane and diphenylgermane with styrenes accompanied by 10 mol% of trialkylborohydrates proceeded in a highly selective mode to give β-addition products.

DFT calculations were employed to explain the mechanism of this process, which revealed that the mechanism assigned to hydrosilylation[3] did not apply to hydrogermylation. Further research led to a conclusion that the latter proceeded via a trisubstituted germide anion, whose attack on the terminal vinyl carbon is the source of selectivity. Hence, the reaction should be classified as a "living" process rather than a typically catalytic one.



Scheme 1. Opposite selectivity of hydrosilylation and hydrogermylation under the same conditions.

Acknowledgements: Computations were carried out using the PL-Grid infrastructure. grant № START 96.2020 financed by the Foundation for Polish Science and grant no. POWR.03.02.00-00-I020/17 co-financed by the European Union through the European Social Fund under the Operational Program Knowledge Education Development are gratefully acknowledged.

***Keywords**: quantum chemistry, DFT, hydrogermylation, triethylborohydride, styrene*

References:

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P28. Structural and Spectroscopic Studies of Two Novel Potentially Photoswitchable Nitro Complexes of Ni(II) and Pd(II) with a (N,N,O)-Donor Supporting Ligand.

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Two new potentially (photo)switchable compounds, i.e. analogous nitro complexes of Ni(II) and Pd(II) with a (N,N,O)-donor supporting ligand (referred to as **1a-Ni** and **1a-Pd**) were synthesized according to the literature procedure [1]. Schematic representation of both studied compounds is shown in Scheme 1 below.

Scheme 1. Schematic representation of the studied systems.

Crystallization of **1a-Ni** and **1a-Pd** was carried out with the use of various solvents. It turned out that the studied compounds crystallize differently depending on the solvent and crystallization method. In the case of the Pd(II) complex it was possible to obtain solvatomorphs containing DCM or $CHCl_3$ in the crystal structure and also a non-solvent crystal structure when crystallized from acetone or acetonitrile. All crystal structures were determined using single-crystal X-ray diffraction method and profoundly analyzed. Additionally, bulk samples of both complexes were studied using solid-state IR spectroscopy regarding photoswitchable properties. It appeared that the Ni(II) system based on structural examination exhibits higher photoswitchable potential which was indeed confirmed by the IR spectroscopic results. The changes in the IR spectra upon irradiation with the LED with the central wavelength of 530 nm indicate nearly 100% nitro-to-nitrito isomerization of **1a-Ni**. The light-induced linkage isomer is stable up to 240 K. In turn, **1a-Pd** does not exhibit photoswitchable properties in the solid state form.

Acknowledgements: The Wrocław Centre for Networking and Supercomputing (grant No. 285) is gratefully acknowledged for providing computational facilities. The in-house X-ray diffraction experiments were carried out at the Department of Physics University of Warsaw on Rigaku Oxford Diffraction SuperNova diffractometer which was co-financed by the European Union within the European Regional Development Fund (POIG.02.01.00-14.122/09).

***Keywords**: solvatomorph, photoswitchable, organic ligand, nitrite ligand, N,N,O-donor square complexes*

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P29. Effect of Process Conditions on Photocatalytic Water Disinfection in a Hybrid Photoreactor with a Rotating Magnetic Field Generator

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Ever-dwindling supplies of drinking water and insufficient sanitization of water from currently available sources are causing a constant search for new, effective and inexpensive methods of water treatment. A promising method is photocatalytic water disinfection and magnetic water purification. Combining the methods would result in an effective and environmentally friendly method of water purification. Photocatalytic disinfection involves the in-situ generation of highly reactive oxygen species that cause the oxidation of organic pollutants and pathogenic microorganisms, while magnetic purification processes allow for the enhanced separation of pollutants.

The effect of the process parameters on efficiency of water disinfection in a "hybrid" reactor (photoreactor with rotating magnetic field generator) was the aim of the research.

Two reference strains of bacteria Gram-negative *Escherichia coli* K12 (ATCC 29425) and Gram-positive *Staphyloccocus epidermidis* (ATCC 49461) and three copper-modified titanium photocatalysts (0.5Cu@HomoP25, 2.0Cu@HomoP25, 5.0Cu@HomoP25) were used. The influence of copper amount, light, rotating magnetic field (RMF) and synergistic effect of light and RMF on photocatalytic disinfection process were determined. The experiments were performed in a self-designed and constructed photoreactor with a rotating magnetic field generator. Light-emitting diodes (LEDs) emitting radiation in the visible range were used as the light source. The concentration of photocatalyst was 0.1 $g \cdot dm^{-3}$. RMF in the frequency 5, 25 and 50 Hz were applied. Each experiment lasted 3 hours and samples were taken in 0, 1 and 3 hours of process. A series of decimal dilutions were made, and the diluted solutions were plated on solid media appropriate for type of bacteria. The inculcated plates were incubated at a temperature of 37ºC for 24 h. Then visible colonies were counted. The results obtained were used to develop an artificial neural network models in Statistica 13.3, through which the effect of the various process conditions on the efficiency of water disinfection was determined. The control experiment under dark conditions was also performed.

The results clearly indicate that photocatalytic process supported by rotating magnetic field has a positive effect on water disinfection efficiency. The total disinfection of water was obtained in a shorter time. The frequency of the applied magnetic field did not effect on the efficiency of disinfection. The process duration was the main factor determining the removal of bacteria from water. The best antibacterial properties against Gram-positive *Staphylococcus epidermidis* bacteria had 5.0Cu@HomoP25. Moreover, 2.0Cu@HomoP25 had excellent properties against Gram-negative *Escherichia coli*. In both cases, the full water disinfection effect was achieved after 1 h of running the process in the presence of light and a rotating magnetic field.

Acknowledgements: The authors are grateful for the financial support within the Project No. 2021/41/N/ST8/00482 (Preludium 2021) from the National Science Center, Poland.

***Keywords**: photocatalysis, rotating magnetic field, titanium dioxide, disinfection, water purification*

P30. Interactions of Gold(I) Complexes with Models of Thioredoxin Reductase; DFT & QM/MM Studies

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One of the treatment options for oncological diseases is programmed cell death (PCD) induced by increased oxidative stress. One of the main PCD types is so-called apoptosis, which is regulated by thioredoxin systems. [1] The thioredoxin reductase enzyme, one of the key thioredoxin system components, can be blocked by gold(I) complexes and hence cause therapeutic oxidative stress. [2]

First, we investigated the interactions of a selected gold(I) complex with the active site of the enzyme using the density functional method. For this purpose, structures of reactants, transition states, and products in different redox states and (de)protonations of the active site were explored. From these calculations, Gibbs activation energies and standard reaction energies of the reaction profiles were determined.

Recently we performed QM/MM MD calculations with Umbrella sampling technique on the more extended systems where the quantum core comprised tetrapeptide sequence on the C-end of the enzyme together with the gold(I) complex. This active site was completed by the rest of the enzyme and explicit solvent water treated by classical MD force field.

All the computational models predict spontaneous gold coordination to both S- and Se- sites especially in neutral and basic environments.

***Keywords**: thioredoxin reductase, gold(I) complexes, DFT, QM/MM*

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P31. Thymidine Kinase 1 Case – on the Importance of the Starting Structure for QM/MM Mechanistic Studies

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The exact mechanism of action of human Thymidine Kinase 1 (*hTK1*), a phosphotransferase responsible for the first phosphorylation step of thymidine (T) is unknown. While there are no experimental reports on the binding of both its substrates at the active site of the enzyme, structural studies on the homolog *Thermotoga maritima* TK (*Tm*TK) (36% identity and 55% similarity to the *h*TK1) show that substrate binding influences the quaternary structure of the whole enzyme, "opening" its conformation. To study these change in *h*TK1,we performed a 1 μs Molecular Dynamics (MD) on *h*TK1 with a ligand that promoted an open conformation in *tm*TK studies, observing the transition of *h*TK1 to the open conformation with similar metrics to those described for *Tm*TK experimentally.

Yet, the QM/MM umbrella sampling studies performed on the MD-obtained active conformation of *h*TK1 produced an unfavorable activation barrier for the phosphorylation reaction amounting to 25.3 kcal/mol, over a total of 12 ps simulation per window. By hypothesizing that the choice of starting structure could be responsible for the unfavorable result, we resorted to analogous QM/MM calculations on the homolog *tm*TK, as an X-ray structure of an open conformation binding both native reactants is available for this enzyme.

The umbrella sampling QM/MM simulations on *tm*TK showed free energy barriers were equal to 11.5 kcal/mol and 11.7 kcal/mol, over a total of 8 ps simulation per window, depending on the MD equilibration protocol that was performed prior to the QM/MM simulations. These barriers are much lower from those obtained for *h*TK1 and raise a question whether (1) the QM/MM starting structure choice or (2) whole MD simulation protocol of "opening" the enzyme is to be refined for *h*TK1, or (3) is it impossible to obtain a reasonable structure of *h*TK1 for QM/MM studies with such procedure.

Acknowledgements: This work was supported by Polish National Science Center (NCN) under the Grant No. UMO-2018/29/N/ST4/00507 (S.R.). This research was supported in part by PLGrid Infrastructure (plgsamanta).

***Keywords**: Thymidne Kinase 1, QM/MM, hTK1, starting conformation, umbrella sampling*

P32. Inclusion Complexes of Cannabidiol and Tetrahydrocannabinol with β-Cyclodextrin: a DFT Study with Dispersion Correction

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Cannabidiol (CBD) and Δ^9-tetrahydrocannabinol (THC) (Fig.1) are essential phytocannabinoids, which acidic precursors are found in *Cannabis sativa L.*[1]. The non-psychotropic CBD exhibits anti-inflammatory, antibacterial and antiviral properties and reduces psychoactive effects of THC [1]. Despite few approved medical applications such as the treatment of epilepsy, the use of CBD in the therapy of other diseases is still under investigation [2]. The further development of its potential is hindered by a very low solubility in water. This, however, could be overcome by preparing inclusion complexes with cyclodextrins (CDs). According to other studies, CBD forms inclusion complexes with βCD at a 1:1 stoichiometric ratio.

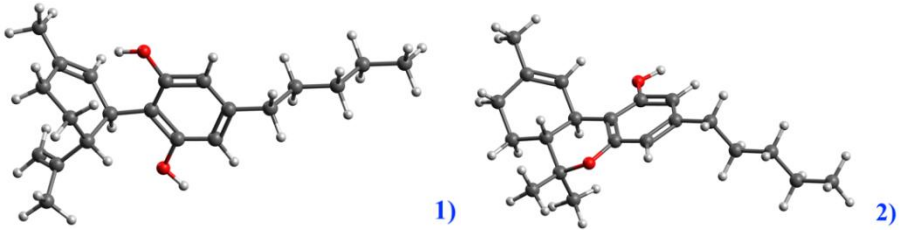

Fig. 1. Selected low-energy conformers of 1) CBD 2) THC

In this work, interaction of CBD and THC with βCD is examined at the B3LYP/6-31G(d,p) level of theory. Several stable conformers of CBD and THC were considered to determine the lowest energy complex with βCD. Moreover, two initial orientations of CBD and THC with respect to βCD were tested, namely the head (ring first) or the tail (n-pentane chain first) were placed vertically in the host cavity. Computation of geometry structures of host-guest complexes were performed in the vacuum or in water using the polarizable continuum model (PCM). Additionally, calculations were extended with implementing the Grimme's dispersion correction (GD3) term [3] into each type of approach. The results suggest, that in order to obtain reliable geometry structures and interaction energies of CBD(THC)- βCD complexes, it is necessary to include GD3 term into calculations.

Acknowledgements: Wroclaw Centre for Networking and Supercomputing.

Key words: *cannabinoids, β-cyclodextrin, Grimme's correction, inclusion complex*

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P33. Energetics of Homopolar Dihydrogen Non Covalent Interactions Exhibited in Polyborane Complexes

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Dihydrogen interactions are a group of non-covalent interactions attracting increasing attention of researchers with their applications in hydrogen storage materials and crystal engineering. More widely-known are polar (δ+)X-H···H-Y(δ-) bonds, which are especially crucial for hydrogen storage materials due to the facilitation of H_2 elimination, but homopolar H-H contacts: (δ+)X-H···H-Y(δ+) and (δ-)X-H···H-Y(δ-) also exist. Their stabilizing energetics has been proved in a range of bulky systems, and attributed mostly do London dispersion forces. Their stabilization in smaller species, or within single molecule is still, however, a matter of debate.

In the following work, a pair of promising hydrogen storage materials: alkenyldecaborane 6,9-(H_2C=C{CH_2-(C_6H_{11})}]$_2B_{10}H_{12}$ and a smaller $B_9H_{13}NH_2(CH_2Ph)$ [1], are studied by means of several bonding analysis methods, both real-space-based (QTAIM, IQA, NCI) and molecular orbital-based (ETS-NOCV, LED), in order to shed some light on the nature of their numerous C-H···H-C and B-H···H-B homopolar dihydrogen contacts. Dimers of said molecules were found to be stabilized by dispersion and charge delocalization in H···H regions between molecules. While the C-H···H-C contacts proved to be stabilizing in the two-atomic QTAIM perspective despite unfavorable electrostatics, the negatively charged hydrogen atoms in B-H···H-B contacts made the latter interaction repulsive. This (B-H···H-B) contact, however, is also stabilized by the electrostatics of B-H···B, resulting in a net attraction between BH moieties. Overall, a picture of cooperative stabilization stemming from joint interactions between BH and CH groups emerges.

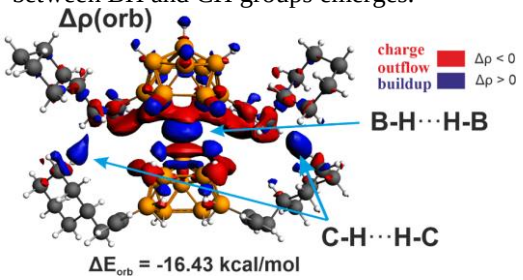

Fig. 1. Structure of the dimer of 6,9-(H2C=C{CH_2-(C_6H_{11})}]$_2B_{10}H_{12}$ with electronic differential densities illustrating homopolar dihydrogen C-H···H-C and B-H···H-B interactions.

Acknowledgements: This research was supported in part by PLGrid Infrastructure. M. P. M. acknowledges the financial support of the Polish National Science Center within the Sonata Bis Project 2017/26/E/ST4/00104.

Keywords: *homopolar dihydrogen interactions, charge and energy decomposition, bonding theory, hydrogen storage materials*

References:

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P34. Cisplatin-Crosslinked DNA Origami Nanostructures as Drug Delivery Systems

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Cisplatin is widely utilized as a chemotherapeutic agent; however, the accompanying side effects limit its use requiring targeting strategies to deliver it selectively to tumor cells [1]. The use of DNA-based nanocarriers like DNA origami nanostructures (DONs) is a promising approach to package drugs like cisplatin. DONs are ideal for targeting due to their functionalizability and they offer design flexibility to engineer various controlled release mechanisms [2]. The stability of these nanostructures is however challenged by environmental factors requiring some degree of crosslinking.

In this work, we demonstrate the use of cisplatin as a crosslinker and cytotoxic agent in DONs for potential drug delivery applications [3]. We studied the effect of the initial cisplatin concentration and loading time on the amount of bound cisplatin and the corresponding structural effects on the DON carrier using inductively coupled plasma mass spectrometry (ICP-MS), agarose gel electrophoresis (AGE), and atomic force microscopy (AFM). Localization of cisplatin on the DONs is mapped using scanning transmission electron microscopy with energy dispersive X-ray spectroscopy (STEM-EDX). We observe that DONs can be loaded with up to 1000 cisplatin molecules per nanostructure before significant distortions to the structure occur. The cytotoxicity of cisplatin-loaded DONs is then tested on the FaDu cell line using MTT assays. Only nanomolar quantities of cisplatin-loaded DONs are required to reduce cell viability to 50% after 48 and 72 hours. These results can provide insights into optimizing DNA-based drug delivery systems with DNA-binding/intercalating payload, especially for tandem chemo-radiotherapy.

Acknowledgements: Praemium Academiae, and projects “Center for Tumor Ecology - Research of the Cancer Microenvironment Supporting Cancer Growth and Spread” (Reg. No. CZ.02.1.01/0.0/0.0/16_019/0000785) and CARAT (Reg. No. CZ.02.1.01/0.0/0.0/16_026/ 0008382) supported by the Operational Programme Research, Development and Education.

***Keywords**: cisplatin, DNA origami, drug delivery, electron microscopy, AFM*

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P35. Contaminant Desorption on Solid Surfaces with Surfactants Molecules by Molecular Dynamics

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Studies of hydrocarbons desorption from solid surfaces (dolomite/graphite) are investigated. Removal studies of alkanes from graphite/dolomite plates were conducted with simulations of three different surfactants, *Cocamidopropyl betaine* (CAPB), N-dodecyl-*N.N-dimethyl-3-ammonio-1-propane*-sulfonate (SB3-12), *Sodium dodecyl sulfate* (SDS), and their mixtures at different compositions. Simulations were carried out with different concentrations on the surface and in all cases the alkane molecules were adsorbed on the plates in a layer structure, two or four layers, suggested by the density profiles. It is also observed that the surfactants tails interact with hydrocarbon alkane chains promoting desorption of the last molecules. In some cases, the anionic-betaine mixtures with compositions work better to desorb the contaminant molecules.

The results show that the graphite surfaces with surfactants are more efficient for alkenes desorption.

Acknowledgement*:* DGAPA-Mexico grant IN102017, Conacyt-Mexico grant A1-S-29587 DGTIC-UNAM grant LANCAD-UNAM-DGTIC-238.

Keywords*: surfaces, surfactants, desorption, hydrocarbons*

P36. Role of Acidic Amino Acid Residues in Sequence-Specific DNA-Protein (SSDP) Interactions

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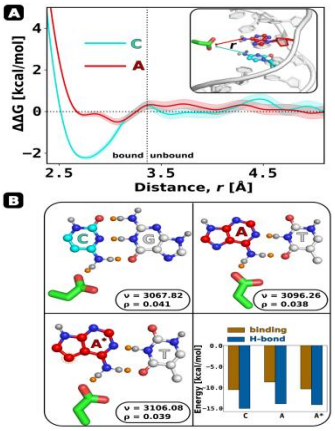

How a specific DNA-binding protein finds its target substrate-DNA sequence and discriminates all the off-target sequences is an intriguing question, and essential for the understanding of several biological phenomena. Aside from the kinetic aspects, a DNA-binding protein must follow a certain pattern like compact binding to the target site, and loose binding to off-target sites. Therefore, noncovalent interactions such as hydrogen bonding, electrostatic interactions, and hydrophobic interactions (*viz*, VdW) play an important role in sequence-specific DNA-protein interactions. It is well established that the majority of the sequence-specific DNA-protein interactions occur in the major groove of DNA as the functional group of DNA bases are easily accessible for direct interactions/readout (mainly *via* H-bonds) with the amino acid motif of a partner protein. One way to decipher this direct readout is through base-amino acid preference. Hence, we gathered interfacial interaction information of all the DNA/protein complexes from the PDB database. In a previous study from our group on the telomeric repeat-binding factor 1 protein, the role of a specific *Asp* residue in the recognition of the human telomeric sequence containing three consecutive cytosines has been explored by per-residue decomposition of the binding free energy [1]. Interestingly, in this current study, we found that both acidic residues, *Asp* and *Glu*, are quite frequently present at the negatively charged DNA-protein interface, they interact unfavorably with the DNA backbone and thereby may be expected to destabilize the complex. Further analyses suggest that acidic residues can take part in the direct readout *via* interacting with the amino group of cytosine. At the same time, this observation raises the question, of why acidic residue prefers only cytosine and not adenine, even though adenine also has an amino group available for forming H-bond in the major groove? *Asp/Glu* lower the affinity for non-cytosine sites and thus act as negative selectors preventing off-target binding. At cytosine-containing sites, the favorable contribution does not merely rely on the formation of a single H-bond but requires the presence of positive potential generated by multiple cytosines, consistently with the observed excess of cytosine in the target sites. Finally, we show that the preference of Asp/Glu for cytosine over adenine is a result of the repulsion from the adenine imidazole ring and the tendency of purine-purine dinucleotides to adopt the BII conformation. Our results show that acidic residue is mainly involved in the discrimination of off-target sites; sensing the absence of cytosine, Asp/Glu decreases the binding affinity for off-target sites. Finally, using the multiscale modeling (viz, QM, QM/MM) we explain the preference of acidic residues toward cytosine over adenine.

References:

[1] Wieczór, M. et al. *Nuc. Acids Res.*, **2017**,45, 7643-7654.

P37. pH-Dependent Models of the Cellular Uptake Mechanism of NPs for Effective Drug-Delivery for Cancer Treatment: Insights from a Computational Study

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Newly synthesised nanoparticles with an amphiphilic character of hydrophilic γ-polyglutamic acid (γ-PGA) with the hydrophobic drug methotrexate (MTX) [1] (so-called MTX-SS-PGA) have been widely used for precise drug release in a redox-sensitive manner at the site near the nucleus. The released nanoparticles cause less damage to normal cells and, at the same time, act against cancer cells by releasing the drug efficiently. This new transformed MTX-SS-PGA formulation has a higher therapeutic effect against cancer than free MTX. The efficiency of cellular uptake of newly designed MTX-SS-PGA systems may be controlled by pH and NPs structure, charge, and geometry. However, there is still a lack of systematic knowledge about pH-dependent behaviour and the cell uptake of newly designed NPs.

Thus, we proposed molecular dynamics simulation to determine the effects of cell uptake mechanisms of drug-loaded nanoparticles with three different models of the modeled lipid membrane bilayer (POPC) with three different pH states such as (a) 7.0 (neutral), (b) 6.4 (Tumeric range), and (c) 2.0 (stomach range), respectively, shown in the figure below. Our MD study suggests that the Tumeric pH range of the model's uptake is faster than other models. Specifically, we observed that the stomach pH range started to be delivered to the drug due to destabilization [2] of the system with more acidic environmental conditions. In this context, here, we hypothesize that the charge, geometry, and energetics of the NP structure strongly influence the mechanism of cellular uptake. While at lower pH, it increases protonation states. The observed mechanism of cellular uptake is stronger in certain states. Thus, the proposed study provides systematic knowledge about the relationship between pH and the mechanism of cellular uptake of newly designed MTX-SS-PGA systems. The knowledge about the relationship between pH and MTX-SS-PGA structure may be crucial to designing the theoretical model for an efficient drug delivery system.

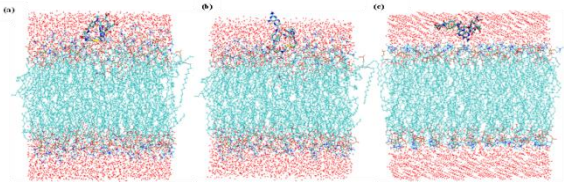

Fig. 1. Drug-loaded nanoparticle (MTX-SS-PGA) present in the lipid bilayer in threedifferent pH states (a) neutral (7.0), (b) tumeric (6.4) (c) stomach (2.0).

***Keywords**: cell uptake, drug-loaded nanoparticle, drug delivery, anticancer drug, MD*

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P38. Interactions Containing Nitro Groups in the Crystals Formed from Dinitrobenzoic Acids and Nitrogen Containing Heterocycles

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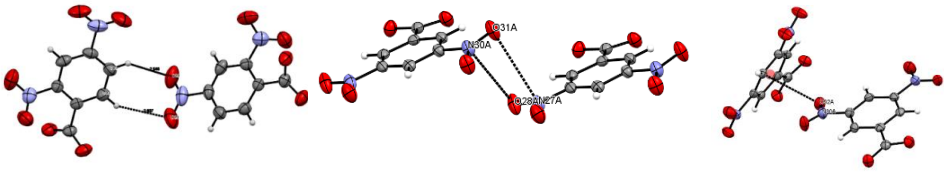
The nitrobenzoic acids are an interesting object of research from a crystal engineering viewpoint. It is due to that nitro groups may participate in various interactions, such as: $NO_2\cdots H–X$, $NO_2\cdots NO_2$, and $NO_2\cdots\pi$ resulting different supramolecular synthons (Fig. 1) [1-2]. The energies of these interactions are comparable to those of classical hydrogen bonds [3-4].



E= –3.2 kJ/mol E= –6.5 kJ/mol E= –12.4 kJ/mol

Fig. 1. Examples of interactions containing NO_2 groups in the crystals formed from dinitrobenzoic acids and nitrogen containing heterocycles.

In this presentation, we report on the crystal structures, analysis and theoretical calculations of intermolecular interactions containing nitro groups in the crystals formed from dinitrobenzoic acids and nitrogen containing heterocycles.

Acknowledgement*:* The research was financed from Faculty of Chemistry, University of Gdańsk, Poland (grant No. 531-T080-D738-22).

Keywords*: nitrobenzoic acids, interactions containing nitro groups, crystal engineering*

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P39. Theoretical Studies on a Novel Zn(II) Turn-On Fluorescent Chemosensor

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In recent years, fluorescent chemosensors have attracted a great deal of attention for detecting various (bio)chemical analytes because of their simplicity, high sensitivity, and real-time monitoring with fast response [1,2]. In particular, there is a high demand for development of novel fluorescent probes for selective sensing of biologically relevant transition-metal ions, such as, among others, Cd(II), Hg(II), and Zn(II), due to their potential environmental and biological applications. Up to now, several chemical pathways that control photophysical properties of such fluorescence-based sensors have been described. The most explored signaling mechanisms involve photo-induced electron transfer (PET), chelation-enhanced fluorescence (CHEF), intramolecular charge transfer (ICT), and metal-to-ligand charge transfer (MLCT) effects; aggregation-induced emission (AIE), C=N isomerization, and excited-state intramolecular proton transfer (ESIPT) have also recently been reported [2,3]. Since assigning a proper signaling mechanism is not a straightforward task, especially because the effects may coincide, quantum-chemical calculations appear to be indispensable to fully understand photophysics of a system of interest.

In this contribution, results of combined experimental and theoretical studies on a newly proposed Schiff-base chemosensor for selective detection of Zn(II) will be presented from the (TD-)DFT perspective [4]. Quantum-chemical calculations, along with a detailed analysis of the computed photophysical properties of the naphthylmethylene-hydrazine-based probe and the metal complex (Figure 1), indicate that turn-on emission signaling behavior is associated with intramolecular rotation and nitrogen lone-pair quenching effects.

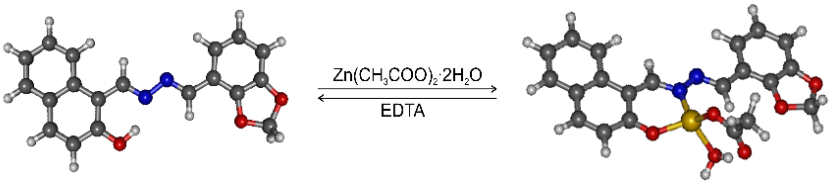

Fig. 1. Complexation / decomplexation process of Zn(II) with naphthylmethylene-hydrazine-based probe.

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

Keywords*: Schiff base, Zn(II) chemosensor, fluorescence, intramolecular rotation, (TD-)DFT*

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P40. Studies of Interactions Between Abiotic Sequence-Defined Oligomers and Bisphenol-A

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Recent advances in polymer synthesis bring us closer to the biopolymer archetype, where synthetically-made polymers are of uniform length and have a strictly defined monomeric sequence [1]. Such macromolecules, built out of abiotic monomers display folding abilities into novel secondary structures depending on stereochemical differences [2, 3]. Therefore, they may exhibit functions coded in three-dimensional structure, similar to natural proteins. Here, we have investigated molecular interactions of stereocontrolled oligocarbamates with Bisphenol A (BPA) using experimental and theoretical means. Pentamers of different stereochemistry were designed to maximize the number of possible attractive interactions (hydrogen bonds, Van der Waals interactions and π-π stacking) towards a target – BPA. Conformation spaces of systems composed of pentamer and BPA have been searched by Multiple Simulated Annealing - Molecular Dynamic (MSA-MD) and subsequently binding free energies were assessed by Molecular Mechanics - Generalized Born Surface Area (MM-GBSA) methodology. Experimental values of binding free energies were obtained by two approaches the Dose-Response and modified Stern-Volmer model based on fluorescence measurements [4–7]. Both approaches have indicated a similar trend in energy change with an arrangement of stereocenters. The study confirms a direct influence of stereochemistry on binding strength oligomer - BPA and it can be precisely followed by theoretical tools.

Acknowledgement*:* R.S., M.S. (NCN scholarship) are highly grateful to the Polish National Science Centre (2018/31/D/ST5/01365) for financial support. R.S. and S.K. thank the Łukasiewicz Centre for the financial support (grant PolyProbe: 4/Ł-PORT/CŁ/2021). R.S. and W.F. thank the National Centre for Research and Development for the founding (LIDER/27/0148/L-12/20/NCBR/2021). Calculations have been carried out using resources provided by Wroclaw Centre for Networking and Supercomputing (http://wcss.pl).

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P41. A First-Principles Study on the Competitiveness of Protonation and Dissociative Electron Attachment in an Aqueous Solution of Uracil Derivatives

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In the so-called "Trojan horse" therapy, a modified nucleoside, the "Trojan horse" incorporated into DNA undergoes a dissociative electron attachment (DEA) process in the presence of solvated electrons formed during water radiolysis. DEA leads to the formation of an active nucleoside radical which, in secondary reactions, may result in single- or double- DNA strand breaks. The consequence of this process can be a cancer cell death.

The radiobiological studies on 5-iodo-4-thio-2'-deoxyuridine (5ISdU) and 5-bromo-4-thio-2'-deoxyuridine (5BrSdU) indicate that 5ISdU exhibits radiosensitizing properties, while its sister derivative, 5BrSdU, does not display such behaviour. The quantum-chemical calculations at the DFT level have shown that the activation barrier for the halide anion release for the $5BrSdU^{\bullet-}$ radical anion is almost twice as high as that for $5ISdU^{\bullet-}$. This barrier height difference makes the dissociation time of the C-Br bond by almost 200 fold longer compared to that for the C-I bond breakage. Such a long lifetime of the $5BrSdU^{\bullet-}$ anion is probably sufficient for its protonation which blocks the DEA process [1].

The current studies aim at investigating the kinetics of competitive protonation and dissociation reactions for the two above mentioned systems using the quantum chemistry (QM), molecular dynamics (MD) and ab initio molecular dynamics (AIMD) methods. We determined the proton affinities of protonacceptor centers in the studied molecular systems at the DFT level and compared them to the available literature data. Although the C5 atom is the most proton affinic center in both studied anions, our MD simulations show that the O2 center forms the highest number of hydrogen bonds with the water molecules while the C5 site is not involved in the hydrogen bonding at all. The studied anions have been optimized at the AIMD level and in the further steps, the potential of mean force for the halide anion release and the anion protonation will be carried out using umbrella sampling. These calculations should explain at the molecular level the radiosensitizing properties of 5ISdU and the lack of such properties for very similar 5BrSdU.

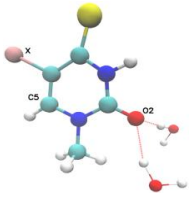

Fig. 1. Uracil derivative with visible hydrogen bonds through which proton transfer can occur.

Acknowledgements: This research was conducted with the financial support of the National Science Centre (NCN) as part of the project number UMO-2020/02/Y/ST4/00110.

***Keywords**: cancer, radiosensitizers, DEA, protonation, QM, molecular dynamics, AIMD*

References:

[1] Spisz, P. et al. *Molecules*, **2019**, 24, 2819-2836.

P42. Charge Dystribution in Simple Alkohol Homologue Serie from Self-Consistent Polarization Method

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Rapidly developing classical molecular dynamics (MD) methods are widely used in computational chemistry. MD methods are commonly used in simulations of large systems, especially in biological research. To perform MD simulations numerous approximations are required. The most significant is force field (FF), which defines forces influencing atoms in a system, types of atoms and their arrangement, and partial charges of atoms. Partial charge of an atom is not observable, thus to determine the value various computational methods may be implemented. In this work we present application of self-consistent polarization (SCP) method in deriving atomic charges of alcohol molecules in water solutions. SCP method is iterative method, based on determination of energy and charge of an atom in field of the remaining atoms in system [1,2].

Four alcohol molecules were studied: methanol, ethanol, 2-propanol and t-butanol. In our work we used DFT method with two XC functionals (M06-2X and B3LYP), four population analyses (CHELP, CHELPG, HLY, MK), different widths of solvation shell radius (4 Å, 6 Å, 8 Å, 10 Å) and cc-pVQZ basis set, which was used in SCP method calculations of a single alcohol molecule in water. Based on our results, we designated the M06-2X functional, MK population analysis and 8 Å shell radius, as the most efficient in terms of the quality of results and computational costs. As a comparator to the experimental data we provided radial distribution functions of different alcohol solutions using the partial charges derived.

In our research we demonstrate that implementation of the SCP method is simple, and it is also associated with moderate computational costs. We also demonstrate that its employment can improve MD results in terms of distribution of molecules, determining values of dipole moments and conformations of molecules in the system.

***Keywords**: molecular dynamics (MD); self-consistent polarization method (SCP)*

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P43. Quadripartite Bond Length Rule Applied to Two Prototypical Aromatic and Antiaromatic Molecules

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In 2000, a remarkably simple relationship was introduced[1], which connected the calculated geometries of isomolecular states of three different multiplicities. These encompass interatomic distances (**R**) in a ground singlet state($\mathbf{R}^{0}_{gs}$), the first excited triplet state($\mathbf{R}^{0}_{T1}$), as well as related radical anion ($\mathbf{R}^{-}_{gs}$) and radical cation ($\mathbf{R}^{+}_{gs}$). The rule allows prediction of geometry of one of the species if the three remaining ones are known. The equation is satisfied:

$$\mathbf{R}^{+}_{gs} + \mathbf{R}^{-}_{gs} - \mathbf{R}^{0}_{gs} - \mathbf{R}^{0}_{T1} \approx 0.$$

Here, we verify applicability of this bond length rule for two small planar organic molecules, *i.e.* benzene and cyclobutadiene, which stand as prototypical examples of, respectively, aromatic and antiaromatic systems.

Our computations were performed on different levels of theory. Firstly, two multireference wave function based approaches were utilized: complete active space self-consistent field method (CASSCF) and basing on its wavefunction second-order perturbation theory (CASPT2). Secondly, as effective and accurate for theoretical researches of small and medium-sized organic molecules coupled-cluster based methodology (CC2) – a reasonable compromise between computational cost and quality of results. Finally, mainly for comparison purposes, all investigated structures were additively optimized at (U)B3LYP, (U)M06-2X and (U)CAM-B3LYP density functional theory levels of theory. Dunning and coworkers correlation-consistent basis sets (aug-)cc-pVXZ (X = D, T, Q) and Pople's 6-31G(d,p) basis sets were utilized.

All obtained results leads us to conclusion, that the rule applies semi-quantitatively to these cyclic systems and in the case of benzene it works independently for quinoid as well as for anti-quinoid minima.

Acknowledgements: W.G. gratefully acknowledges annual support from the Ministry of Education and Science. Calculations have been carried out using resources provided by *Wroclaw Centre for Networking and Supercomputing* (http://wcss.pl), grant No. 484.

***Keywords**: aromaticity, antiaromaticity, benzene, cyclobutadiene, molecular orbital theory*

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AUTHOR INDEX

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