KATEDRA FYZIKÁLNÍ CHEMIE
UNIVERZITY PALACKÉHO V OLOMOUCI

INSTITUTE OF MOLECULAR AND TRANSLATIONAL MEDICINE

8th Advanced in Silico Drug Design workshop 2025

Olomouc

27th – 31st January 2025

Book of Abstracts

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8ADD workshop (27.1.2024 – 31.1.2024) is focused on using in silico tools and approaches in drug design. We cover both structure-based drug design (molecular docking, molecular dynamics, structural bioinformatics tools) and ligand-based drug design (QSAR, pharmacophores, deep learning) with lectures and on-hand tutorials.

Welcome to Olomouc! Karel Berka and Pavlo Polishchuk

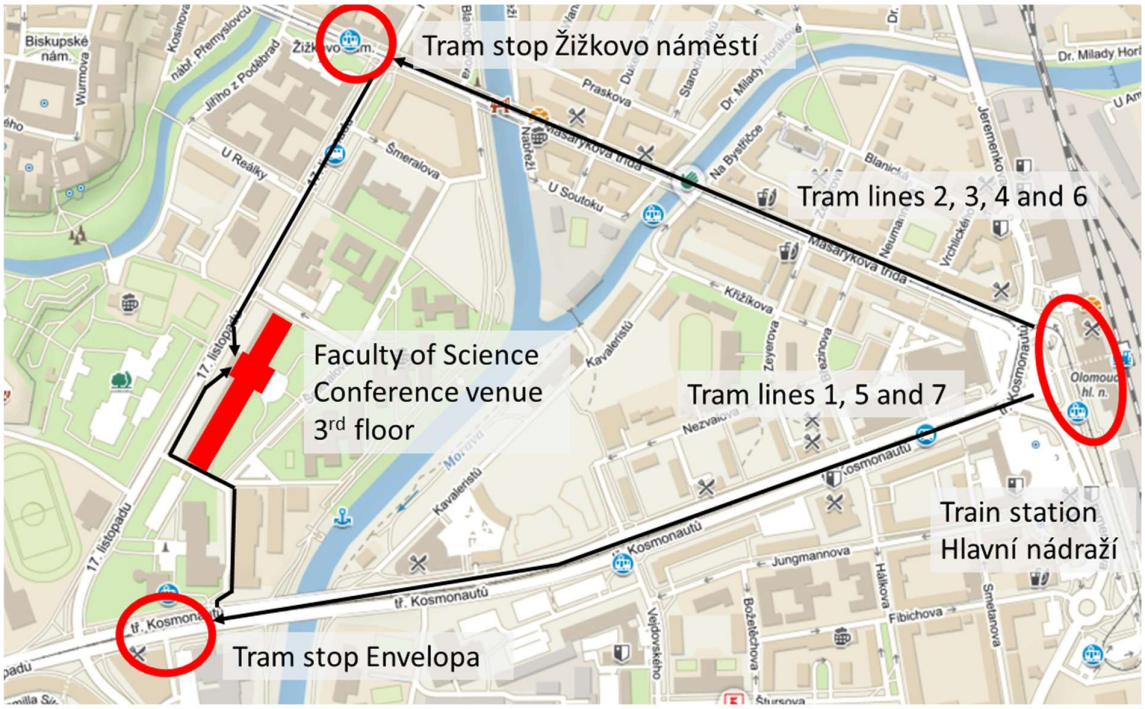
Invited Lecturers

- Thierry Langer (UniVie, Vienna)
- Alexandre Varnek (Uni Strasbourg)
- Hanoch Senderowicz (Bar-Ilan University)
- Johannes Kirchmair (UniVie, Vienna)
- Wim Dehaen (UCT Prague)
- Semen Yesylevskyy (IOCB Prague, IOP Kiev, KFC UPOL, Receptor.AI)
- Federica Moraca (UNINA, Napoli)
- Martin Šícho (UCT Prague)
- Wim Dehaen (UCT Prague)
- Martin Lepšík (IOCB Prague)
- Thomas Evangelidis (AIffinity)
- Marián Hajdúch (IMTM UPOL)
- Alexander Dömling (IMTM UPOL)
- Olexandr Isayev (Carnegie Mellon University, Pittsburg)
- Miroslav Lžičař (Deep MedChem)

Local Organizers

- Karel Berka (KFC UPOL)
- Pavel Polishchuk (IMTM UPOL)
- Guzel Minibaeva (IMTM UPOL)
- Aleksandra Ivanova (IMTM UPOL)
- Václav Bazgier (KFC UPOL)
- Kateřina Storchmannová (KFC UPOL)
- Dominik Martinát (KFC UPOL)
- Anna Špačková (KFC UPOL)
- Elizabeth Kolářová (KFC UPOL)
- Jan Solomon (KFC UPOL)

Venue



Faculty of Science, Palacky University Olomouc, Czech Republic
tř. 17. listopadu 12, Olomouc
GPS: 49.5924922,17.2632337
3rd floor PC room 3.002 + lecture room 3.003

Faculty building in Google Street View

List of On-Site Participants

1. Tereza Kubátová – University of Vienna, AT
2. Andrea Nedělníková – Palacký University Olomouc, CZ
3. Jozef Fülöp – University of Chemistry and Technology Prague, CZ
4. Jan Kachnowicz – University of Wrocław, PL
5. Lina Ould Mohamed – University of Science and Technology Houari Boumediene, DZ
6. Khoroshyy Petro – Institute of Organic Chemistry and Biochemistry, CZ
7. Filip Kapral – University of Chemistry and Technology Prague, CZ
8. Parnia Jabbari – Istituto di Blostrútture a Bioimaging, CNR, IT
9. Alladi Chaharanraj Goud – Palacký University Olomouc, CZ
10. Pavel Polishchuk – Palacký University Olomouc, CZ
11. Gizem Nur Duran – Gebze Technical University, TR
12. Vít Škrhák – Charles University Prague, CZ
13. Gorkha Raj Giri – Tribhuvan University, NP
14. Semanur Bulut - Gebze Technical University, TR
15. Dinesh Kumar Sriramulu – Palacký University Olomouc, CZ
16. Elina Shaniiazova – Constructor University Bremen, DE
17. Modupe Omoniyi – University of Vermont, US
18. Khem Raj Joshi – Pokhara University, NP.
19. Sami Ahmed Mohammed Ali Hamdoun – Monash University Malaysia, MY
20. Rajamanikkam Kamaraj – Charles University Prague, CZ
21. Mária Bajnoková – Charles University Prague, CZ
22. Carlo Apuzzo – University Federico II of Naples, IT
23. Stefano Cimmino – University Federico II of Naples, IT
24. M. Isabel Agea – MSD, CZ
25. Oliver Vaverka – Gymnázium Hejčín, Olomouc, CZ
26. Natalia Mikłuszka – University of Wrocław, PL
27. Lukáš Kerti – Comenius University Bratislava, SK
28. Anastasiia Krokhina – University of Strasbourg, FR
29. Tomáš Basl – University of Chemistry and Technology Prague, CZ
30. Ekaterina Sosnina – AT
31. Sergey Sosnin – University of Vienna, AT
32. Alessandra Guarracino – University Federico II of Naples, IT
33. Miloš Halda - Institute of Organic Chemistry and Biochemistry, CZ
34. Oriana Vitale - University Federico II of Naples, IT
35. Riccardo Fusco – Palacky University Olomouc, CZ
36. Aleksandra Ivanova – Palacky University Olomouc, CZ
37. Elizabeth Kolářová – Palacky University Olomouc, CZ
38. Jan Solomon – Palacky University Olomouc, CZ
39. Dominik Martinát – Palacky University Olomouc, CZ
40. Markéta Grulichová – Palacky University Olomouc, CZ
41. Barbora Hubálková – Palacky University Olomouc, CZ

Poster Abstracts

Elucidation of the Fe3+ Ion Transfer Mechanism in Neisseria Meningitidis

Gizem Nur DURAN, Mehmet ÖZBİL

Gebze Technical University, Biotechnology Institute, Kocaeli, TURKEY

Neisseria meningitidis, commonly known as meningococcus, is a Gram-negative bacterium responsible for severe diseases such as meningitis and meningococcemia, posing significant challenges for children and adults. The bacterium's survival depends on acquiring iron (Fe3+), which it obtains from human serum transferrin (hTf) via two surface proteins, transferrin-binding proteins A (TbpA) and B (TbpB). TbpB is extracellular, while TbpA is an integral membrane protein. Together, they form a ternary complex with hTf to extract and transport Fe3+ ions into the bacterial cell.

In 2012, Noinaj et al. resolved x-ray structures of TbpA, TbpB, and the TbpA-hTf binary complex, proposing that Fe3+ ions pass through a beta-sheet channel in TbpA. However, the absence of the ternary complex's three-dimensional structure left key mechanistic details unresolved.

This study models the TbpA-TbpB-hTf complex using classical and steered molecular dynamics (MD) simulations. Starting from known binary structures, the ternary complex was constructed for the first time. Additionally, a mutant TbpA structure (Lys359Ala) was generated to investigate the role of Lys359 in ion release. Simulations revealed that Lys359 weakens Fe3+ binding, initiating its release, while structural changes in TbpA and TbpB stabilize the complex and guide the ion through TbpA’s channel. The mutant structure exhibited reduced ion release efficiency, confirming Lys359’s critical role.

By elucidating the TbpA-TbpB-hTf complex's dynamics and Fe3+ ion pathway, this study advances our understanding of N. meningitidis iron acquisition and identifies potential therapeutic targets for disrupting this essential process.

Keywords: ion channels, Neisseria meningitidis, molecular dynamics simulations, transferrin-binding proteins

In Silico Analysis of Hemagglutinin N-Glycosylation in Swine Influenza A (H3N2)

Semanur Bulut, Mehmet Özbil

Gebze Technical University, Biotechnology

Monitoring influenza A viruses (IAV) is crucial for updating vaccines, tracking the emergence of drug-resistant viruses, and following zoonotic infections. Understanding the relationship between antigenic variations and changes in the sialic acid receptor-binding properties of the HA glycoprotein is particularly significant. Swine are hypothesized to act as "mixing vessels" for human, avian, and swine IAVs, potentially leading to the emergence of pandemic IAVs. The emergence of the 2009 H1N1 pandemic virus (H1N1pdm09) has strengthened this hypothesis.In this project, we aim to investigate the antigenic differences and binding efficiency of four structurally uncharacterized A/H3N2 strains isolated from swine between 2019 and 2024 using computational methods. N-glycosylation plays a critical role in masking antigenic epitopes and limiting the binding of host antibodies. Characterizing the antigenic properties of these viruses is crucial because H3 viruses acquire a new glycan site approximately every five to seven years, posing a potential outbreak risk.the HA proteins of these swine-isolated strains will be modeled, and N-glycosylation modifications will be introduced at positions predicted by the NetNGlyc 1.0 server near the protein’s head region, specifically in proximity to the A antigenic site and the receptor-binding site (RBS). At the predicted positions, glycan groups with a core structure containing GlcNAc and Mannose (GlcNAc2Man3) will be covalently linked to the amide nitrogen of the HA protein to form N-glycosidic bonds.The binding efficiency of the HA proteins from the four selected strains to porcine respiratory epithelial cells (α2,6-SiaGal) and the S139/1 Fab antibody will be analyzed and comparisons will be made between N-glycosylated and non-glycosylated trimeric HA protein structures in complexes with α2,6-SiaGal and S139/1 Fab in the presence of varying amino acids in antigenic regions.

Exploring electronic structure as well as polymorphism in selected Schiff Bases

Natalia Mikłuszka, Aneta Jezierska

University of Wrocław, PL

Many pharmacologically active substances exist in different polymorphic forms, which exhibit significantly different properties such as bioavailability. Some drugs undergo polymorphic transitions during storage, altering their activity. As a result, understanding polymorphism is crucial for analyzing active substances [1]. Schiff bases containing an aromatic ring with a hydroxyl group in the ortho position directly linked to an imine group, can form intramolecular resonance-assisted hydrogen bonds that increase the thermodynamic stability of the molecule [2]. In case of 2-(E)-[5-methylthiazol-2-ylimino)methyl]phenol, the presence of a single N-C bond allows for thiazole ring rotation, which causes a fomation of conformational polymorphs [3]. Comparison of crystallographic data and quantum simulations based on Density Functional Theory (DFT) shows that gas-phase and solvent models effectively replicate molecular structures. Simulated IR and NMR spectra at various computational levels of theory provide data of the structural parameters. Using the “scan” method within DFT geometry optimization, the energy associated with the bridged proton transfer in the intramolecular hydrogen bond was determined. The obtained energy barriers are low enough to allow spontaneous proton transfer. Additionally, CP-MD (Car-Parrinello Molecular Dynamics) [4] simulations provide time-evolution details of selected parameters.

We gratefully acknowledge Polish high-performance computing infrastructure PLGrid (HPC Center: ACK Cyfronet AGH) for providing computer facilities and support within computational grant no. PLG/2024/017802. Results were also obtained using resources provided by Wroclaw Centre for Networking and Supercomputing- grant no. 206.

[1] K. Raza, SOJ Pharm Pharm Sci, 2014, 1 (2), 10–20

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[4] R. Car, M. Parrinello, Phys Rev Let, 1985, 55, 2471-2474

In silico studies of enantiomeric substitution in MUC7 fragment complexes

Jan Kachnowicz, Klaudia Szarszoń, Joanna Wątły, Aneta Jezierska

University of Wrocław, Chemistry Department, F. Joliot-Curie 14, 50-383 Wrocław

The problem of drug resistance in pathogens is getting more serious each year. We are observing the emergence of an increasing number of multidrug-resistant (MDR) microorganisms. We estimate that from year 2050 around 10 million people will be dying every year from infections caused by MDR bacteria. [1] That is why we are searching for new solutions to fight with drug resistant microbes. One of the most promising ideas that could replace antibiotics are antimicrobial peptides (AMPs). [2] Certain fragments of proteolytic digestion of MUC7 glycoprotein present in human saliva are examples of AMPs. One of those fragments is a peptide with EGRERDHELRHRRHHHQSPK sequence. [3] Moreover, its biological activity is enhanced by coordination of metal ions e.g. Cu(II) and Zn(II). However, this peptide is susceptible to proteolytic degradation. To address this issue two L-amino acids (in the most prone site to enzymatic cutting) were exchanged for their enantiomers obtaining EGRERDHELRHRrhHHQSPK peptide (where small letter indicate D-amino acids), which exhibits new coordination properties. In order to investigate this phenomenon, conformational studies were performed using classical molecular dynamics. To determine the most stable sets of donor groups binding Cu(II) and Zn(II) ions in both peptides, Monte Carlo simulations based on trajectories generated from molecular dynamics runs were used. It allowed to characterize influence of Cu(II) and Zn(II) ions on the structure of both ligands using a novel method on the basis of a mean deviation of dihedral angles from ideal α-helix.

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[2] S.-U., Gorr, Front. Oral Biol., 2012, vol. 15, pp. 84–98.

[3] K. Szarszoń, S. Andrä, T. Janek and J. Wątły, Inorg. Chem., 2024, vol. 63, pp. 11616–11627.

Turning it off and on again: a possible new way of enhanced sampling in MD

Tomáš Basl, Vojtěch Spiwok

UCT Prague, CZ

Molecular dynamics (MD) simulations are a computational tool used to study the dynamics of molecular systems and processes such as protein-folding. Nonetheless, this method still faces high computational and temporal costs when employed on systems containing large numbers of atoms and thus can be effectively utilized only for simple models and small proteins. Many methods are constantly being developed to help accelerate MD simulations. This work focuses on stochastic resetting (SR), which is a method used to study non-deterministic systems. During stochastic resetting, a system undergoing a random process is returned to its default state at either random or defined time intervals. Recent studies show that SR can accelerate molecular dynamics simulations in certain situations. In this work, the ways by which chignolin escapes energy minima during its folding process are comparatively studied by molecular simulations with implemented stochastic resetting and by MD simulations alone. The goal is to evaluate the potential of stochastic resetting to enhance the process of studying protein's behaviour around its energy minima by MD. That could lead to faster and easier sampling which could consequently advance experimental work, such as drug design and synthetic protein development.

Dataset Composition and Machine Learning Performance in Virtual Screening

Anastasiia Krokhina[1, 2], Hanoch Senderowitz[1]

1. Bar-Ilan University, IL. 2. University of Strasbourg, FR

Common practices suggest that predictive Machine Learning (ML) models should be developed using well-balanced datasets. This study explores the influence of dataset class composition on the binary classification performances of ML models in virtual screening. Specifically, we evaluated the performance of k-nearest neighbors and extreme gradient boosting models trained on datasets with balanced and imbalanced class distributions on selected examples taken from two widely used virtual screening datasets: LIT-PCBA (1) and DUD-E (2). Furthermore, during model training, hyperparameter tuning was performed via cross-validation using two virtual screening-aware metrics: the area under the receiver operating characteristic curve (ROC AUC) and the Matthews correlation coefficient (MCC).

Our results indicate notable model performance differences depending on the dataset composition. Specifically, when hyperparameters were optimized using the MCC metric , models trained on imbalanced datasets consistently outperformed those trained on balanced datasets. The superior performance of models developed from imbalanced datasets and optimized for MCC suggests their utility in real-world scenarios, where imbalances are often unavoidable.

This work emphasizes the need to carefully consider dataset properties and evaluation metrics in developing predictive ML models, taking into consideration the intended usage of these models and, therefore, contributing valuable insights into designing robust machine-learning workflows in chemoinformatics.

1. Tran-Nguyen, V.-K., Jacquemard, C. & Rognan, D. LIT-PCBA: An Unbiased Data Set for Machine Learning and Virtual Screening. J. Chem. Inf. Model. 60, 4263–4273 (2020).

2. Mysinger, M. M., Carchia, M., Irwin, John. J. & Shoichet, B. K. Directory of Useful Decoys, Enhanced (DUD-E): Better Ligands and Decoys for Better Benchmarking. J. Med. Chem. 55, 6582–6594 (2012).

Computational Protocols for Accurate Interactions at Insulin–Receptor Interface

Miloš Halda[1,2], Yevgen P. Yurenko[1], Martin Lepšík[1]

1 Inst Org Chem Biochem, Czech Acad Sci, Prague, CZ; 2 Fac Science Charles Uni

The quantitative characterization of residue contributions to protein-protein binding across extensive flexible interfaces poses a significant challenge for biophysical computations. This study leverages recent advancements in semiempirical quantum-mechanical and implicit solvent approaches embodied in the PM6-D3H4S/COSMO2 method for the development of a hierarchical computational protocols encompassing molecular dynamics, fragmentation, and virtual glycine scan techniques for the investigation of flexible protein-protein interactions. As a model, the binding of insulin to its receptor is selected, a complex and dynamic process that has been extensively studied experimentally. The interaction energies calculated at this level in ten molecular dynamics snapshots did not correlate with molecular mechanics/generalized Born interaction energies because only the former method is able to describe non-additive effects. This became evident in the examination of the energetics in small-model dimers featuring all the present types of non-covalent interactions with respect to DFT-D3 calculations. The virtual glycine scan has identified 16 hotspot residues on insulin and 15 on the insulin receptor, and their contributions have been quantified using PM6-D3H4S/COSMO2. The accuracy and credibility of the approach are further supported by the fact that all the insulin hotspots have previously been confirmed by biochemical and structural evidence. The modular nature of the protocol has enabled the formulation of several variants, each tailored to specific accuracy and efficiency requirements. The developed computational strategy is firmly rooted in general biophysical chemistry and is thus offered as a general tool for the quantification of interactions across relevant flexible protein-protein interfaces.

Cheminformatics Analysis of RNA-Binding Ligands

Jozef Fülöp, Andrea Brancale, Daniel Svozil

University of Chemistry and Technology, Prague & CZ-OPENSCREEN

This project systematically investigates the chemical properties and structural features that distinguish RNA-binding ligands from protein-binding counterparts. Large and diverse chemical libraries were examined and curated through a comprehensive cheminformatics workflow, incorporating molecule standardization and chemical space visualization techniques. Advanced machine learning approaches, including ensemble methods (e.g., XGBoost) and graph neural networks, were employed to classify RNA-targeting compounds, uncovering high-impact features such as certain substructural patterns and the amount of hydrogen-bond donors. These findings provide deeper insights into small molecule–RNA interactions, which are critical for guiding the rational design of novel therapeutics targeting RNA-related diseases. Overall, this work highlights the potential of integrating cheminformatics and machine learning to elucidate RNA-ligand specificity, thereby contributing to advances in drug discovery and medical research.

ChemPatentizer: Transforming Chemical Patents into Actionable Scientific Data

Riccardo Fusco, Alexander Domling

Palacky U Olomouc, CZ

Chemical patents are a rich yet challenging source of structure and activity data, with significant obstacles arising from their format and lack of standardization. Often, these documents are presented as scanned images, making data extraction through classical OCR methods unreliable. Furthermore, unstructured activity data and non-standard layouts compound the difficulty, as identifiers are frequently poor in quality and patents can exceed hundreds of pages. Nevertheless, the potential for high-quality data within chemical patents, particularly through standardized assays and significant matched pair transformations, underscores the need for an effective extraction solution. In response, we present a semi-autonomous pipeline, ChemPatentizer, that combines human expertise with DECIMER, a tool for recognizing chemical structures, to segment and convert patent content into a usable format. Unlike fully automated approaches, our pipeline leverages chemist input to guide patent selection and initial data segmentation, addressing the nuanced and varied nature of patent data. Following manual segmentation, our pipeline automates the creation of structure-activity tables and facilitates downstream analyses, such as molecular matched pair studies and Deep QSAR modeling. ChemPatentizer's modular design allows human verification at each step, enhancing accuracy and reliability. Our approach, validated with patents on the GLP-1 receptor, demonstrates the value of combining automation with expert oversight in extracting meaningful data from chemical patents.

StreaMD: a tool to perform high-throughput molecular dynamics simulations

A. Ivanova[1], O. Mokshyna[2], P. Polishchuk[1]

1. Palacký University , CZ; 2. Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences, CZ

In our research, we introduce a sequential pipeline that automatically processes the preparation and simulation of molecular dynamics simulations. This pipeline handles different scenarios, including simulations of protein in water, and protein with ligand and/or cofactors. Users only need to provide a PDB file of the protein and, if necessary, SDF or MOL files for any ligands or cofactors. By utilizing the dask module, our tool simultaneously prepares and runs simulations on single or multiple servers, enabling efficient parallel processing. After the simulations are finished, the tool automatically performs basic analyses. The pipeline also features advanced options such as contact analysis via ProLIF and binding free energy calculations using gmxMMPBSA. Additionally, it allows for the extension or resumption of incomplete simulations.

To validate the described instrument we ran 10 ns simulations and computed the Generalized Born Surface Area (GBSA) energies for 166 molecules of human beta-secretase 1, 63 molecules of human α-thrombin and 51 molecules of bovine trypsin. The resulting Pearson correlation coefficients between GBSA energies and pKd values were found to be 0.49, 0.69, 0.64 for the BACE1, thrombin and trypsin datasets, respectively. The utilization of this high-throughput molecular dynamics tool not only simplifies the process of running or extending simulations for a given set of compounds but also facilitates a more detailed analysis in the routine of drug design. The tool is available as an open-source package at https://github.com/ci-lab-cz/md-scripts.

This work was supported by the Ministry of Education, Youth and Sports of the Czech Republic through INTER-EXCELLENCE II LUAUS23262, the e-INFRA CZ (ID:90254), ELIXIR-CZ (LM2018131, LM2023055), CZ-OPENSCREEN (LM2018130, LM2023052) grants and by European and Regional Fund project ENOCH (No. CZ.02.1.01/0.0/0.0/16_019/0000868).

Key Factors and Insights for Improving Multi-Task Learning in Drug Discovery

Ekaterina A. Sosnina

Independent Researcher, Vienna, Austria

Multi-task learning (MTL) is a machine learning approach that leverages shared knowledge across tasks to make predictions using a single model. It is widely used in drug discovery, but there are questions that remain open, such as selecting the right modelling approach (descriptor-based vs. interaction-based), improving training data, and designing effective test datasets.

MTL is an approach, that can avoid using predefined descriptors by relying on shared information across tasks only. In this study I compares descriptor-based models, which use molecular and target descriptors, with interaction-based models, which rely solely on compound-target interaction data. While interaction-based models perform well for compounds ot targets already used in model training, their main limitation is their inability to predict the activity of new compounds or targets not included in the training set, a critical challenge addressed by descriptor-based models.

To improve test data design, I focuses on investigation warm-start predictions (for compounds present in training data) and cold-start predictions (for new compounds). I show that MTL models, despite their ability to generalize, struggle with cold-start predictions for compounds dissimilar to training data. Therefore, model evaluation should use multiple test sets to balance diversity and similarity between test and training data.

Investigating training data enrichment as a way of model improvement, I demonstrate that adding diverse and informative data improves performance and generalization. However, the degree of enhancement depends on the proportion of new data relative to the original dataset.

The main outcome of this study are practical insights for optimizing MTL in drug discovery, including selecting appropriate modeling approaches, enriching training data, and designing test datasets.

Multiscale Computational Protocols for Accurate Residue Interactions at Flexible Insulin Receptor Interface

Miloš Halda[1,2], Yevgen P. Yurenko[1], Martin Lepšík[1]

1 Inst Org Chem Biochem, Czech Acad Sci, Prague, CZ; 2 Fac Science Charles Uni

This study[1] leverages recent advancements in semiempirical quantum-mechanical (SQM) and implicit solvent approaches embodied in the **PM6-D3H4S/COSMO2 method**[2] for the development of hierarchical computational protocols encompassing molecular dynamics (MD), fragmentation, and virtual glycine scan (VGS)[3] techniques for the investigation of flexible insulin receptor (IR) binding. Solely the PM6-D3H4S/COSMO2 method, but not molecular mechanics/generalized Born (MM/GB), is able to describe quantum effects, such as chalcogen bonds or non-additivity. The VGS approach has identified 16 hotspot residues on insulin which had previously been found experimentally, and quantified their contributions. The developed computational strategy is stems from biophysical chemistry and is thus offered as a general tool for the quantification of interactions across flexible protein protein interfaces.

Eliminating artifacts in current RNA force fields in the cUUCGg tetraloop backbone

Jan Salomon, Marie Zgarbová, Petr Jurečka

Department of Physical Chemistry, Palacký University Olomouc, Czech Republic

The structural dynamics of the UUCG tetraloop is a critical component in RNA folding. This research highlights one of the challenges in experimentally determining this structure, the GL4-GS+1 backbone step. Comparative analysis of available experimental structures and structures from simulations in the widely used ff99bsc0χOL3 force field identified artifacts in the description of UUCG in this force field. Quantum chemical calculations serve as benchmarks for assessing force field modifications aiming to improve the description of the structural equilibrium. Experimental force field combinations were introduced to destabilize the artifacts observed in the ff99bsc0χOL3 force field. The OL21-RNA modification was found to be the most promising in the description of the backbone equilibrium in the GL4-GS+1 step, despite some shortcomings. The results, supported by eNOE reweighted MD simulations and QM calculations, suggest that the native α/γ flip is the major conformation in the UUCG tetraloop, which stands in contrast to the current consensus.

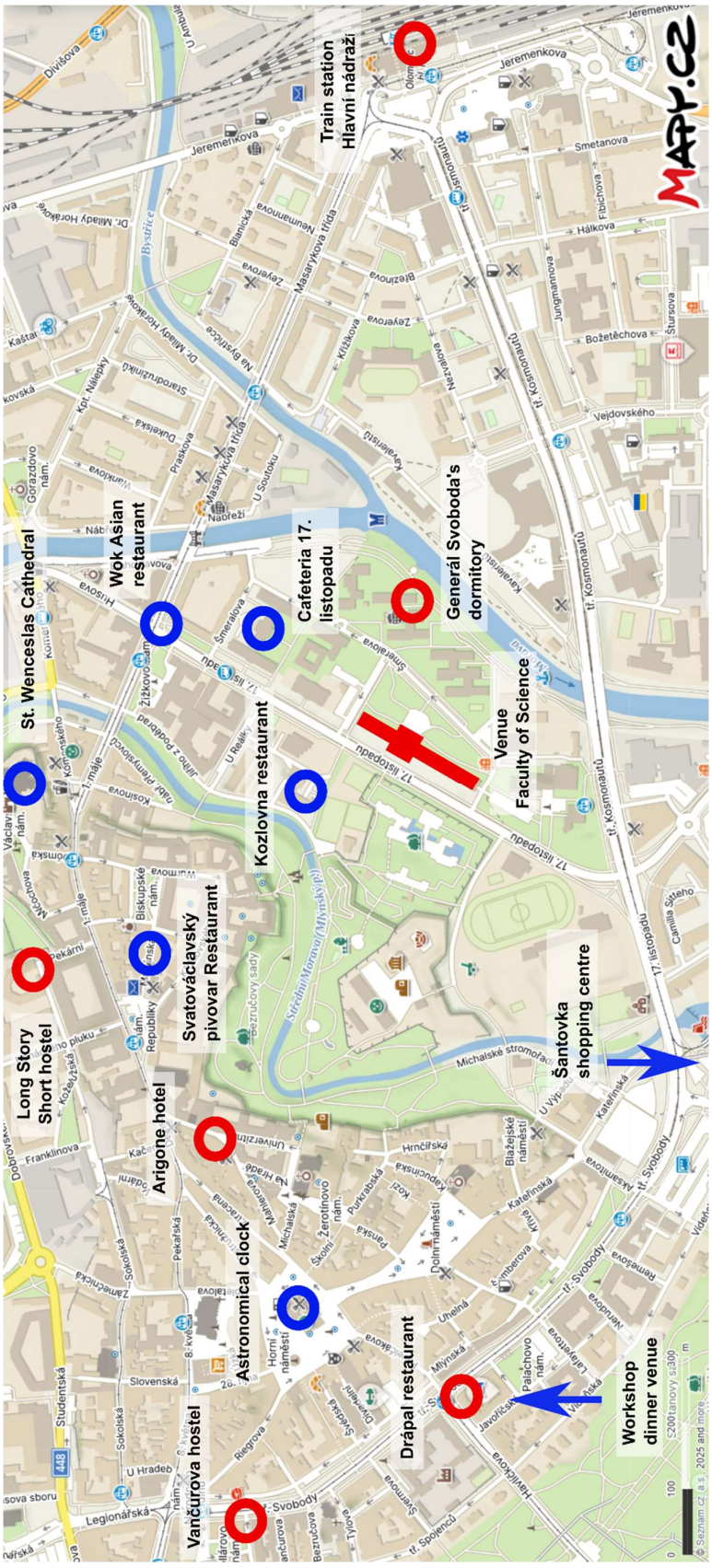
Study of non-canonical backbone conformation substates in DNA and protein-DNA complexes

Elizabeth Kolářová, Petr Jurečka

Department of Physical Chemistry, Palacký University Olomouc, Czech Republic

This thesis will look at molecular dynamic's simulations of DNA and protein-DNA complexes that provide useful information on stability, energetics or dynamics in order to gain a deeper understanding of the interactions between these molecules. Classical molecular dynamics is used for the simulations to allow detailed analyses. The work focuses on four different structures of single DNA and two protein-DNA complexes that contain non-canonical conformations, with the main focus on the non-canonical α/γ states of the sugar-phosphate backbone. This will include the BB02, BB03, BB12, BB13 conformations but also the unassigned NANT conformations for which an attempt will be made to define them using nine torsion angles. Molecular dynamics simulations were performed in force fields from the AMBER family, namely the bsc1, OL15 and the newly developed OL21 force field. The results of this work point to the possible stable occurrence of some non-canonical α/γ states in unusual DNA structures and in protein-DNA complexes in functional segments. The newly defined conformational states may contribute to the refinement of the description of non-canonical conformers in crystallographic databases.

Accommodation, Restaurants and Sights



Notes

Program

Monday, January 27, Introductions

10:00 – 12:00		Registration
12:00 – 12:15		Start
12:15 – 13:00	**Karel Berka**	Drug design intro
13:00 – 14:00	**Marián Hajdúch**	Drug Research and Development in Academia: Lessons Learned
14:00 – 15:00	**Johannes Kirchmair**	Introduction to cheminformatics
15:00 – 15:15		Coffee
15:15 – 16:15	**Alexandre Varnek**	Chemography concept in chemical exploration
16:15 – 19:00		Poster session

Tuesday, January 28, Structures

9:00 – 10:00	**Karel Berka**	Structure sources
10:00 – 11:00	**Martin Lepšík**	QM in Drug Design
11:00 – 11:15		Coffee
11:15 – 12:00	**Semen Yesylevskyy**	AI in Drug design
12:00 – 13:00		Lunch
13:00 – 14:00	**Thierry Langer**	Pharmacophores
14:00 – 18:00	**Thierry Langer**	Pharmacophores tutorial
15:00 – 15:15		Coffee
19:00 – 22:00		Conference dinner

Wednesday, January 29, Structure-based methods

9:00 – 10:00	**Federica Moraca**	Molecular docking
10:00 – 11:00	**Semen Yesylevskyy**	Molecular dynamics
11:00 – 11:15		Coffee
11:15 – 12:15	**Hanoch Senderowicz**	CFTR Modelling
12:15 – 13:00		Lunch
13:00 – 15:00	**Federica Moraca**	Molecular docking tutorial
15:00 – 15:15		Coffee
15:15 – 16:00	**Pavel Polishchuk** **Guzel Minibaeva**	Easydock
16:00 – 18:00	**Aleksandra Ivanova**	MD tutorial
19:00 – 22:00		Excursion to IMTM

Thursday, January 30, Ligand-based methods

9:00 – 10:00	**Wim Dehaen**	QSAR
10:00 – 10:45	**Pavel Polishchuk**	Multi-instance learning
10:45 – 11:00		Coffee
11:00 – 12:00	**Martin Šícho**	De novo design
12:00 – 13:00		Lunch
13:00 – 15:00	**Wim Dehaen**	QSAR tutorial
15:00 – 15:15		Coffee
15:15 – 16:30	**Martin Šícho**	Chemical space visualization tutorial
16:30 – 18:30	**Martin Šícho** **Pavel Polishchuk**	De novo tutorial

Friday, January 31, Applications

9:00 – 10:00	**Alexander Dömling**	No one left behind: Innovative drug discovery tools in the Domling group
10:00 – 11:00	**Karel Berka**	Alphafoldology
11:00 – 11:15		Coffee
11:15 – 12:00	**Pavel Polishchuk**	CACHE
12:00 – 13:00		Lunch
13:00 – 14:00	**Olexandr Isaev**	AIMNet2: Foundation neural network potential for molecules, reactions, and CADD applications
14:00 – 14:30	**Thomas Evangelidis**	Drug Design using NMR
14:30 – 15:00	**Miroslav Lžičař**	CHEESE: 3D Shape and Electrostatic Virtual Screening in a Vector Space
15:00 – 15:15		Coffee