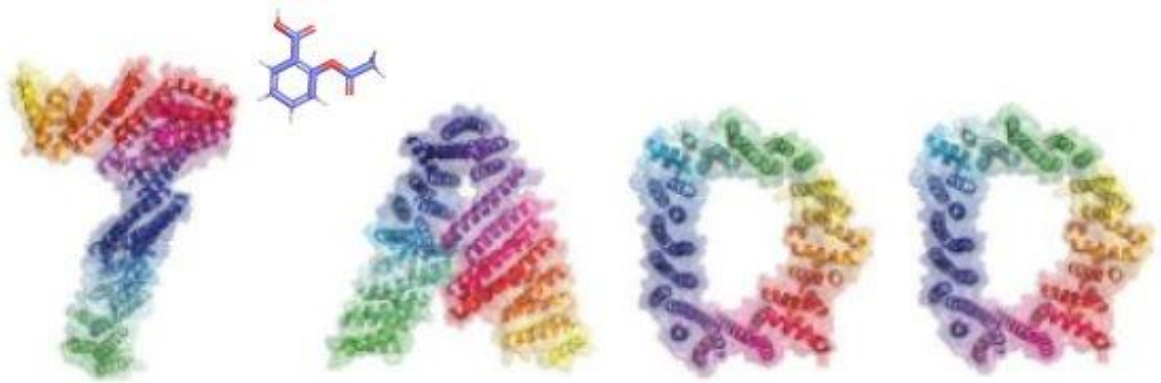
KATEDRA FYZIKÁLNÍ CHEMIE
UNIVERZITY PALACKÉHO V OLOMOUCI

INSTITUTE OF MOLECULAR AND TRANSLATIONAL MEDICINE

7th Advanced in Silico Drug Design workshop 2024

Olomouc

29th January – 1st February 2024



Book of Abstracts

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7ADD workshop (29.1.2024 – 1.2.2024) 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

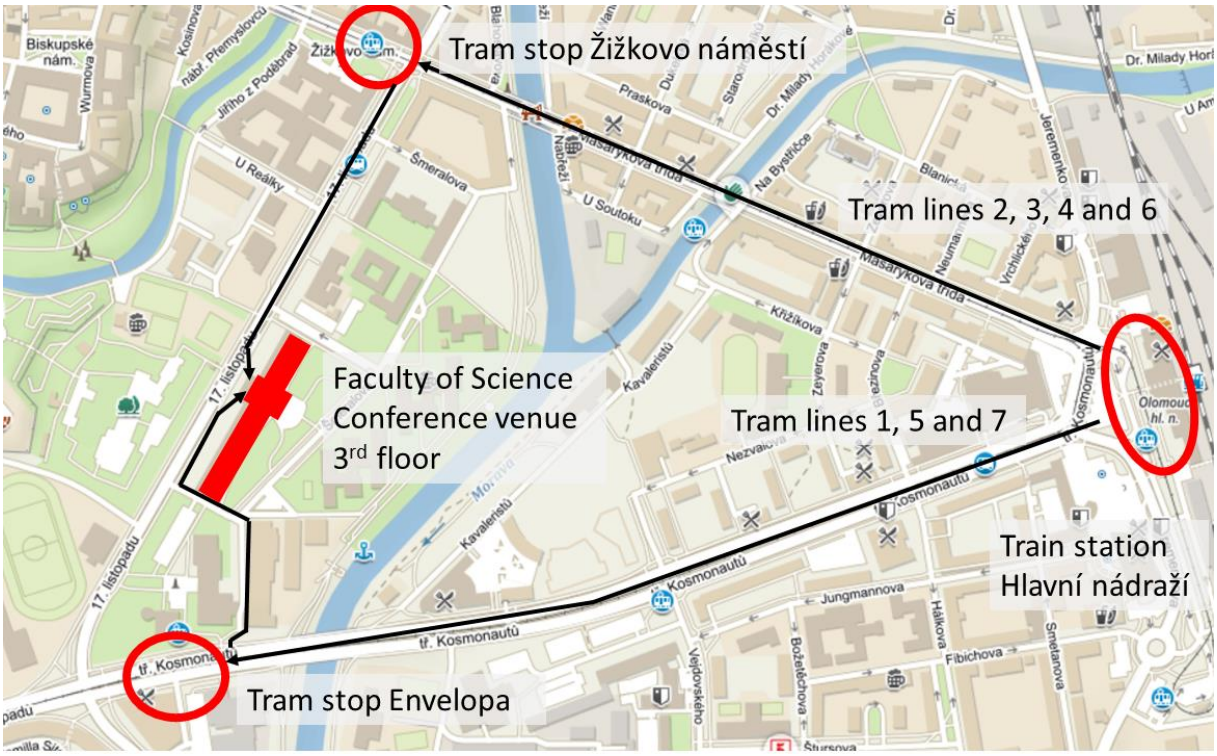
Invited Lecturers

- prof. Thierry Langer (UniVie, Vienna)
- assoc. prof. Johannes Kirchmair (UniVie, Vienna)
- dr. Alžběta Tuerková (CelerisTx, Graz)
- dr. Wim Dehaen (UCT Prague)
- dr.habil. Semen Yesylevskyy (IOCB Prague, IOP Kiev, KFC UPOL, Receptor.AI)
- dr. Martin Lepšík (IOCB Prague)
- dr. Federica Moraca (UNINA, Napoli)
- dr. Paulyna Magana (EMBL-EBI)
- dr. Genevieve Evans (EMBL-EBI)
- dr. Marian Novotný (Charles University, Prague)

Local Organizers

- doc. Karel Berka (KFC UPOL)
- dr. Pavel Polishchuk (IMTM UPOL)
- Guzel Minibaeva (IMTM UPOL)
- Aleksandra Ivanova (IMTM UPOL)
- dr. Václav Bazgier (KFC UPOL)
- Kateřina Storchmannová (KFC UPOL)
- Dominik Martinát (KFC UPOL)
- Anna Špačková (KFC UPOL)
- Nina Kadášová (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. Adam Tywoniak – University of Chemistry and Technology, Prague, CZ
2. Aleksandra Ivanova – Palacky University Olomouc, CZ
3. Andriy Lubskyy – Palacky University Olomouc, CZ
4. Anna Špačková – Palacky University Olomouc, CZ
5. Ariadna Llop Peiro – University of Rovira i Virgili, IT
6. Asma Haffouz – University of Sfax, TN
7. Atilio Reyes Romero – Palacky University Olomouc, CZ
8. Daniel Lee Číp - Palacky University Olomouc, CZ
9. Darina Barkhatova – Institute of Science and Technology Austria, AT
10. Dominik Martinát – Palacky University Olomouc, CZ
11. Embolo Enyuegue Elisee Libert – Institute of Medical Research and Medicinal Plant Studies, CM
12. Ermin Schadich – Palacky University Olomouc, CZ
13. Eugen Hruška – Charles Universitz, CZ
14. Federica Moraca – University of Naples Federico II, IT
15. Guzel Minibaeva – Palacky University Olomouc, CZ
16. Jan Mičan – Masaryk University, CZ
17. Jindřich Lněnička – Palacky University Olomouc, CZ
18. Jiří Žák – IOCB Prague, CZ
19. Jozef Fülöp - University of Chemistry and Technology, Prague, CZ
20. Kaoud Salama – Palacky University Olomouc, CZ
21. Karoll Ferrer - Palacky University Olomouc, CZ
22. Kusuma sai Davuluri – Palacky University Olomouc, CZ
23. Manikandan Mithun – Institute of Physics of the Czech Academy of Sciences, CZ
24. Maryna Krautsova – Palacky University Olomouc, CZ
25. Michał Sobieraj – Adam Mickiewicz University in Poznań, PL
26. Mithun Manikandan - Institute of Physics AS CR, CZ
27. Nina Kadášová – Palacky University Olomouc, CZ
28. Tereza Kubátová – University of Vienna, AT
29. Yevgen Yurenko – IOCB Prague, CZ

Poster Abstracts

Structural Studies of Self-assembling Polymers on Crystal Surface

Mithun Manikandan, Paolo Nicolini, Prokop Hapala

Institute of Physics, Czech Academy of Sciences

In biological systems, molecular motors and machines play crucial roles in various essential processes. Hydrogen bonding, a fundamental molecular interaction, serves as a key element in molecular switches and motors controlled by factors such as light, electrons, pH, and chemical reactions [1]. However, understanding the structural characteristics of molecules and designing them presents an ongoing challenge. In this study, we aim to computationally design photosensitive polymers capable of self-assembling on crystal surfaces, with the potential for integration into surface science and molecular electronics. To achieve this, we explore a vast array of monomers and polymers and employ ab-initio calculations to investigate the atomic details of the optimal structures on different crystal surfaces.

Identification of antileishmanial piperazines

Ermin Schadich[1], Susanne Nylén[2], Soňa Gurská[1,3], Jana Kotulová[1], Pavel Polishchuk[1], Marián Hajdúch[1,3], Petr Džubák[1,3]

1, Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry and University Hospital, Palacky University Olomouc, Czech Republic

2, Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Solna, Sweden

3, Catrin - Czech Advanced Technology and Research Institute, Palacky University Olomouc, Czech RepublicUsing the RDKit software, a series of eleven compounds including eight 1-aryl-4-(phthalimidoalkyl) piperazines and three 1-aryl-4-(naphthalimidoalkyl) piperazines were retrieved from a proprietary library based on their high pharmacophore similarity to haloperidol, an antipsychotic drug with antiparasitic properties, and evaluated in vitro as the potential antileishmanial scaffolds. These compounds were tested for antileishmanial activity against promastigotes of Leishmania major and Leishmania mexicana in dose-response assays. Two of 1-aryl-4-(naphthalimidoalkyl) piperazines, compounds 10 and 11, were active against promastigotes of both Leishmania species without being toxic to human fibroblasts. When structure-activity relations were analyzed, it was found that their activity correlated with the length of their alkyl chains. In assays with the infected mouse J774 macrophages, it was found that compound 11 was also active against intracellular amastigotes of both Leishmania species. Subsequent analyses revealed that compound 11 induced collapse of the mitochondrial electrochemical potential and increased the intracellular Ca2+ concentration in promastigotes of both species. Thus, it may serve as a promising scaffold for the development of novel antileishmanial drugs.

PDB-CAT: Classification and Analysis Tool for PDBx/mmCIF

Ariadna Llop-Peiró, Gerard Pujadas, Santiago García-Vallvé

University of Rovira i Virgili

Biological databases, such as the PDB (Protein Data Bank), face challenges due to the accumulation of new entries. Consequently, the PDB is undergoing a format change, transitioning to PDBx/mmCIF files. Moreover, the escalating volume of data presents difficulties for some applications, especially virtual screening set up, which requires classification based on ligand-protein complex interactions. Currently, no tool or database option facilitates this classification based on the type of bond between the protein and the ligand. To address this necessity, PDB-CAT classifies PDBx/mmCIF files into ligand-free and covalent and non-covalent complexes, determining the ligand code and whether it is a peptide ligand. Additionally, for datasets involving the same protein, the program enables the identification of sequence mutations by comparing to a reference structure. The program is implemented as a Jupyter Notebook, and it requires pdbecif and biopython libraries and Python 3.10 for optimal performance.

PDB-CAT was tested with SARS-CoV-2 Main Proteases. In this example, the workspace included 50 files downloaded from the PDB. Executing the code with the mutational analysis option, using 5R7Y as the reference structure, outputs a CSV information file within a few minutes. In the local environment, a classification was conducted to distinguish between mutated and non-mutated structures. Non-mutated structures were further categorized as ligand-free structures (in the absence of a ligand), covalent complexes, or non-covalent complexes. This process resulted in 40 non-mutated structures, classified into 10 free enzymes, 15 covalent complexes, and 15 non-covalent complexes. This work was supported by the project PID2022-138327OB-I00 financed by MCIN/AEI/10.13039/501100011033/FEDER, UE.

Quantification of Non-covalent Interactions at Protein-Protein Interface

Y. P. Yurenko, A. Muždalo, M. Černeková, A. Pecina, J. Řezáč, J. Fanfrlík, L. Žáková, J. Jiráček, P. Hobza, M. Lepšík

Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Prague, Czech Republic

The quantitative characterization of insulin/insulin receptor binding has posed a significant challenge due to the considerable size of the interface, its inherent flexibility, and the absence of suitable computational tools for the reliable assessment of non-covalent interactions. In this study, we present a comprehensive computational protocol employing molecular dynamics (MD), fragmentation, and quantum chemical (QM) as well as molecular mechanical (MM) calculations. These calculations are performed on a cryo-electron microscopy (cryo-EM) structure of the insulin/insulin receptor (IR) complex, aiming to pinpoint interaction "hotspots" within the primary site of the IR.

Through this hierarchical computational approach, we successfully identified interaction hotspots in insulin Site 1, including Ile A2, Glu A4, Tyr A19, Cys B7, Val B12, Glu B13, Tyr B16, Phe B24, and Phe B25. Notably, these findings exhibit excellent agreement with experimental data. The established protocol not only enhances our understanding of insulin binding but also provides a versatile tool for investigating the binding of insulin analogs. Additionally, it can be employed in the design of new insulin analogs with predefined properties, offering promising applications in the field.

Why Did the Compound Cross the Bilayer: Making Sense of Permeability Values

Adam Tywoniak[1]; Kateřina Storchmannová[2]; Martin Balouch[1]; Jakub Juračka[2]; František Štěpánek[1]; Karel Berka[2]

(1) Department of Chemical Engineering, UCT Prague, CZ

(2) Department of Physical Chemistry, Palacky U, Olomouc, CZ

Passive permeability is a crucial molecular property in drug discovery, as it co-determines pharmacokinetics whenever drug molecules cross phospholipid bilayers, e.g., in the gastrointestinal tract or across the blood-brain barrier. Its quantitative measure is the permeability coefficient P (cm/s), acting as the coefficient of proportionality of molar flux to a difference in concentration gradient: $J = P \cdot \Delta c$. It is often reported as logPerm = − log[10] P.

Many methods for determination of permeability have been developed, including cell line assays with colon carcinoma or kidney cells. Cell-free model systems include parallel artificial membrane permeability assays mimicking e.g., gastrointestinal epithelia or the skin, as well as the Black lipid membrane (BLM) and sub-micrometre liposomes. Unlike cell-based methods, these reduced models exclude active or paracellular transport and metabolism. In silico approaches are now established as well, based on molecular dynamics, or e.g., the solubility-diffusion model.

This contribution aims to interpret reported permeability values in proper physical context, as well as to showcase existing discrepancies in existing datasets.

Relevant thresholds are identified and discussed, incl. method-specific lower limits linked to experimental timescales and instrumental quantitation limits, underestimations caused by the presence of a stagnant water layer adjacent to any membrane, as well as upper limits pertaining to unrestrained self-diffusion in solution.

Permeability data sourced from literature (including ChEMBL) was aggregated and curated in MolMeDB (https://molmedb.upol.cz), a FAIR database of compound-membrane interaction data. For this contribution, the set was narrowed down to permeabilities measured or predicted for uncharged small molecules at a neutral pH across cellular, intestinal, or artificial membranes. Distributions for values from individual methods and their correlations are identified and discussed.

Docking Cytochrome P450

Eugen Hruška

Charles University, CZ

The metabolism of drugs in the human body is performed mostly by Cytochrome P450. For virtual screening of drug candidates, a rapid and accurate estimation of metabolisation by the most common isozymes of Cytochrome P450 is beneficial to avoid compounds with adverse metabolism. The site of metabolism for each drug candidate can be estimated by the proximity to the enzymatically active heme centre. The proximity can be obtained by docking the compound into the active site of Cytochrome P450. A comparison of docking results with different software into Cytochrome P450 isozyme active site was performed.

Structure analysis of Organic cation transporters in the SLC22

Nina Kadášová, Karel Berka

Dpt Physical Chemistry, Palacky University, Olomouc, Czech Republic

Solute carrier transporters (SLC) comprise a diverse group of membrane-bound proteins, with over 500 representatives classified into 65 families based on sequence homology and transport function. SLCs are crucial for transporting a wide range of solutes across biological membranes. Dysfunctions in these transporters contribute to the development of various diseases. Therefore, investigating these proteins is essential for understanding metabolic principles in the human body and disease mechanisms. This study focuses on the SLC22 family, specifically, organic cation transporters (OCTs) subclades. To investigate the ligand binding properties of OCT1 and OCT2, AI-predicted models generated by AlphaFold and SWISS-MODEL were utilized, along with the available cryo-EM structures of OCTs. Molecular docking using AutoDock Vina was performed identify suitable ligands transported by these proteins. The results aim to determine the efficacy of the prediction methods and the preferred structural models for understanding the ligand binding of OCTs.

ChannelsDB 2.0: A Comprehensive Database of Protein Tunnels and Pores in AlphaFold Era

Anna Špačková[1], Ondřej Vávra[2,3], Tomáš Raček[4,5], Václav Bazgier[1], David Sehnal[4,5], Jiří Damborský[2,3], Radka Svobodová[4,5], David Bednář[2,3], Karel Berka[1]

(1) Department of Physical Chemistry, Faculty of Science, Palacký University, Czech Republic

(2) Loschmidt Laboratories, Department of Experimental Biology and RECETOX, Faculty of Science, Masaryk University, Czech Republic

(3) International Clinical Research Center, St. Anne's University Hospital Brno, Czech Republic

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ChannelsDB 2.0 has been upgraded to offer a comprehensive insight into protein channels' structural characteristics, geometry, and physicochemical attributes, encompassing both tunnels and pores. These channels are computed on deposited biomacromolecular structures originating from the PDBe and AlphaFoldDB databases. In the new version of the ChannelsDB database, we have incorporated data generated through the widely used CAVER tool, augmenting the insights previously acquired only through the original MOLE tool. Additionally, we have extended the database's coverage by introducing tunnels originating from cofactors localised within the AlphaFill database or from cognate ligands within PDB structures. This expansion has increased the available channel annotations by almost five times. ChannelsDB 2.0 houses information concerning geometric properties such as length and radius and physicochemical attributes based on the amino acids lining the channels. These stored data are intricately linked with the existing UniProt mutation annotation data, facilitating in-depth investigations into the functional roles of biomacromolecular tunnels and pores.

In summary, ChannelsDB 2.0 represents an invaluable resource for conducting in-depth analyses of the significance of biomacromolecular channels. The database is freely accessible to the public at the address https://channelsdb2.biodata.ceitec.cz.

MolMeDB - Molecules on Membranes Database

Jakub Juračka[1], **Kateřina Storchmannová[1]**, Dominik Martinát[1], Václav Bazgier[1], Jakub Galgonek[2], Karel Berka[1]

(1) Dpt Physical Chemistry, Palacky University, Olomouc, Czech Republic
(2)
(3) Institute of Organic Chemistry and Bioichemistry, Czech Academy of Sciences, Prague, Czech Republic

Biological membranes are natural barriers of cells. The membranes play a key role in cell life and also in the pharmacokinetics of drug-like small molecules. There are several ways how a small molecule can get through the membranes. Passive diffusion, active or passive transport via membrane transporters are the most relevant ways how the small molecules can get through the membranes. There is an available huge amount of data about interactions among the small molecules and the membranes also about interaction among the small molecules and the transporters. MolMeDB (https://molmedb.upol.cz/detail/intro) is a comprehensive and interactive database. Data is available from 52 various methods for 40 biological or artificial membranes and for 184 transporters in MolMeDB. The data within the MolMeDB is collected from scientific papers, our in-house calculations (COSMOmic and PerMM) and obtained by data mining from several databases. Data in the MolMeDB are fully searchable and browsable by means of name, SMILES, membrane, method, transporter or dataset and we offer collected data openly for further reuse. Newly are data available in RDF format and can be queried using SPARQL endpoint (https://idsm.elixir-czech.cz/sparql/endpoint/molmedb). Federated queries using endpoints of other databases are also possible. Lately this database has been used for analysis of different functional groups influence on molecule-membrane interactions.

Proteome secondary structures generated by AlphaFold

Ivana Hutařová Vařeková[1]; **Dominik Martinát**[1]; Radka Svobodová[2,3]; Karel Berka[1]

1. Department of Physical Chemistry, Faculty of Science, Palacký University Olomouc

2. CEITEC – Central European Institute of Technology, Masaryk University Brno

3. National Centre for Biomolecular Research, Faculty of Science, Masaryk University Brno

The AlphaFold[1] algorithm and its associated database[2] provide convenient access to the structural data for entire proteomes across various species, facilitating comprehensive statistical analysis. In our study, we examined the distribution of secondary structures, specifically alpha helices and beta strands, within the proteomes of model organisms and those of relevance to human health. While there seems to be a general distribution of secondary structures within proteins in all analyzed life forms, our findings reveal several noteworthy functional exceptions: 1) abundance of short proteins with small amounts of secondary structures in plant proteomes, 2) spike of structures with 9-12 alpha helix count in some mammals (e.g., mice or rat) from the abundance of olfactory receptors from GPCR family and 3) enhanced presence of long proteins with abundant secondary structures (50+) in the human proteome. These insights contribute to a deeper understanding of the structural diversity within proteomes, shedding light on specific patterns and variations across different species and functional categories of proteins.

1. Jumper J., Evans R., Pritzel A. et al. Highly accurate protein structure prediction with AlphaFold. Nature 596, 583–589 (2021). https://doi.org/10.1038/s41586-021-03819-2

2. Varadi M., Anyango S., Deshpande M. et al. AlphaFold Protein Structure Database: massively expanding the structural coverage of protein-sequence space with high-accuracy models, Nucleic Acids Research, Volume 50, Issue D1, D439–D444 (2022), https://doi.org/10.1093/nar/gkab1061

Structure-based generation of synthetically feasible molecules

Guzel Minibaeva, Pavel Polishchuk

Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry, Palacký University, Czech Republic

Identifying molecules that selectively interact with a biological target is a key step in drug discovery. Nowadays, computer-aided molecular design plays an important role in the development of new drugs. In particular, de novo approaches are increasingly used to search for new biologically active molecules. In this case, new compounds with desired pharmacological properties are assembled in the target cavity guided by the general principles of intermolecular interaction. One of the problems of de novo design tools is difficulty to control synthetic feasibility of generated compounds.

In this work, a tool for the design of drug-like compounds inside protein binding sites was developed. This tool includes the use of the CReM method [1] to generate ligand structures and molecular docking by EasyDock [2] which automates docking with multiple docking tools to assess their binding to a target protein. The CReM method is intended for generating new compounds based on interchangeable fragment databases. The main idea of the CReM method is to consider the nearest chemical environment of a fragment when performing a replacement: if the nearest environment (chemical contexts) of two fragments is the same, the fragments are interchangeable.

The developed tool has two modes: i) iterative growing of a fragment co-crystallized with a protein preserving the position of the parent part of the molecule and ii) de novo compound generation. In the latter case we use a preliminary created set of staring fragments from ChEMBL compounds. Those fragments have from 8 to 15 heavy atoms, from 1 to 5 distinct hydrogen-bond donor/acceptors centers, logP < 2, TPSA > 25A^2, at most one halogen atom, at most two rotatable bonds and no structural alerts. These starting set of fragments is docked and iteratively grown. We implemented several strategies to select molecules on each iteration: greedy, Pareto or clustering-based selection. The developed tool was used to grow small ligands co-crystallized with 3C-like protease of SARS-CoV-2 (5RGX, 5RH2) and to de novo generation of ligands form CDK2, dopamine D2 and other targets frequently used in benchmarking studies. During testing of the tool, it was studied how the choice of the following parameters such as fragment databases and context radius affected the structural diversity and synthetic accessibility of the generated compounds. Based on obtained results, we concluded, the synthetic complexity of the generated structures decreases with increasing radius, as well as with using a base of fragments obtained from synthetically more accessible compounds.

This work was funded by the INTER-EXCELLENCE II LUAUS23262 project (MEYS), the European Regional Development Fund - Project ENOCH (No. CZ.02.1.01/0.0/0.0/16_019/0000868).

References

1. Polishchuk, P.,CReM :Chemically reasonable mutations framework for structure generation, Journal of Cheminformatics, 2020, 12, 1, 1-18.

2. Minibaeva, G.; Ivanova, A.; Polishchuk, P. EasyDock: customizable and scalable docking tool. Journal of Cheminformatics, 2023, 15, 1, 102.

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

Aleksandra Ivanova[1], Oleksandra Mokshyna[2], Pavel Polischchuk[1]

1 Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry,

Palacký University Olomouc, Czech Republic

2 Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences, Czech Republic

Molecular dynamics plays an important role in drug discovery. It helps not only more accurately evaluate binding energy of promising ligands but also to investigate binding modes or protein conformational flexibility. Despite crucial significance, the molecular dynamics method still requires effort and knowledge to use it in every day routine. There are some instruments implemented but so far none of them provide a convenient pipeline focused on running, analysis and if need continue simulations of different systems.

In this study, we have developed a sequential pipeline which automatically processes the preparation and simulation of molecular dynamics. The pipeline handles various systems, including protein-only simulation in water, protein-ligand, protein-cofactors, protein – ligand – cofactors systems. To utilize the tool, the user simply needs to provide a PDB file of a protein and, if needed, SDF or MOL files of ligands or cofactors. The underlying dask distribution module enables simultaneous preparation and execution of simulations across one or multiple servers, facilitating efficient parallel processing. After the simulations are finished, the tool automatically performs basic analyses such as calculation of root-mean-square deviation (RMSD) and root-mean-square fluctuation (RMSF). Furthermore, the tool offers additional functionalities, including contact analysis using prolif and binding free energy calculation pipeline based on gmxMMPBSA. Additionally, the tool provides the possibility to continue not finished simulation or to expand ones for more time.

The tool has been already applied in a few practical tasks [1, 2]. To validate the described instrument we run 10 ns simulations and computed the Generalized Born Surface Area (GBSA) energies for 166 molecules of human beta-secretase 1 and 51 molecules of bovine trypsin. The resulting Pearson correlation coefficients between GBSA energies and pK_i values were found to be 0.5 and 0.46 for the trypsin and thrombin datasets, respectively.

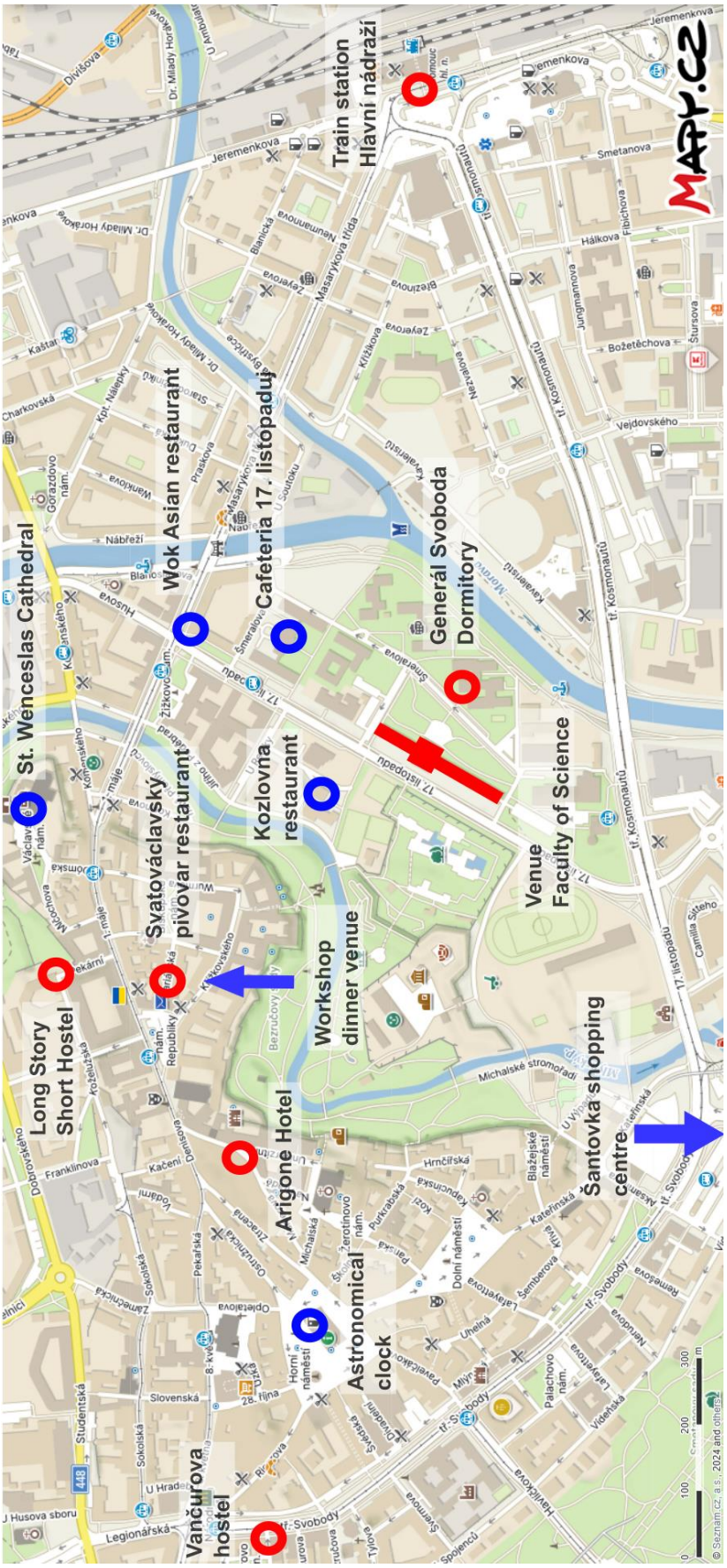
The utilization of this high-throughput molecular dynamics tool not only simplifies the process of running or extending simulations for a given set of compounds but also facilitates a more detailed analysis in the routine of drug design. The tool is available as an open-source package at https://github.com/ci-lab-cz/md-scripts.

1. Jurášek, M., et al. (2023). Triazole-based estradiol dimers prepared via CuAAC from 17α-ethinyl estradiol with five-atom linkers causing G2/M arrest and tubulin inhibition. Bioorganic Chemistry, 131, 106334.

2. Řehulka, J., et al. (2022). Anticancer 5-arylidene-2-(4-hydroxyphenyl)aminothiazol-4(5 H)-ones as tubulin inhibitors. Archiv Der Pharmazie, 355(12), 2200419.

The work was supported by the Ministry of Education, Youth and Sports of the Czech Republic through INTER_EXCELLENCE II grant LUAUS23262, the e-INFRA CZ (ID:90254) and projects ELIXIR-CZ (LM2023055) and CZ-OPENSCREEN (LM2023052).

Accommodation, Restaurants and Sights



Notes

Program

Monday, January 29

11:00am		Registration
12:15pm		Start
12:30pm	**Karel Berka**	Drug design intro (lecture)
1:15pm	**Genevieve Evans/ Paulyna Magana**	PDBe/PDBe-KB (lecture/tutorial)
3:15pm		Coffee
3:30pm	**Marian Novotný**	Binding site identification (lecture)
4:15pm	**Alžběta Tuerková**	Insights from a Biotech Startup: How Computational Chemists Shape theDesign of Proximity-Inducing Compounds (lecture)
5:00pm		Poster session

Tuesday, January 30

9:15am	**Pavel Polishchuk**	Virtual screening (lecture)
10:00am	**Martin Lepšík**	QM in drug design
11:00am		Coffee
11:15am	**Semen Yesylevskyy**	AI in drug design
12:00pm		Lunchtime
1:00pm	**Johannes Kirchmair**	Frequent hitters (lecture)
2:00pm	**Wim Dehaen**	QSAR (lecture)
3:00pm		Coffee
3:15pm	**Wim Dehaen**	QSAR (tutorial)
7:00pm		Conference dinner

Wednesday, January 31

9:15am	**Karel Berka**	Alphafoldology (lecture)
10:00am	**Federica Moraca**	Molecular Drug design (lecture)
10:45am		Coffee
11:00am	**Federica Moraca**	Molecular docking (lecture)
12:00pm		Lunchtime
1:00pm	**Federica Moraca**	Molecular docking (tutorial)
3:00pm		Coffee
3:15pm	**Aleksandra Ivanova**	MD (tutorial)
6:30pm	**Pavel Polishchuk**	Excursion to IMTM

Thursday, February 1

9:15am	**Pavel Polishchuk**	De novo (lecture)
10:15am		Coffee
10:30am	**Pavel Polishchuk/ Guzel Minibaeva**	De novo (tutorial)
12:00pm		Lunchtime
1:00pm	**Pavel Polishchuk**	CACHE (lecture)
2:00pm	**Thierry Langer**	Pharmacophores (lecture)
3:00pm		Coffee
5:15pm	**Thierry Langer**	Pharmacophores (tutorial)
6:30pm		Farewell party