37th MMWS Erlangen

MMWS2025.MGMS-DS.DE

MOLECULAR MODELLING WORKSHOP ERLANGEN

31/03-02/04/2025

CHEMIKUM, NIKOLAUS-FIEBIGER-STRAßE 10, 91058 ERLANGEN

PLENARY SPEAKERS:

CHRISTOPH BANNWARTH (AACHEN)

JAN MEISNER (DÜSSELDORF)

REINHARD MAURER (WARWICK)

RENANA PORANNE (TECHNION CITY)

molecular graphics modelling society

NHR FAU

C3 Computer Chemie Centrum

CAMP@EAM

FAU Friedrich-Alexander-Universität Erlangen-Nürnberg

MOLECULAR MODELLING WORKSHOP 2025

Welcome to the 37th Molecular Modelling Workshop (MMWS)

It is with utmost pleasure to write these introductory remarks to this year's molecular modelling workshop in Erlangen, already the 37th in a long and successful series of meetings, organised by the *Molecular Graphics and Modelling Society – Deutschsprachige Sektion e.V.* (MGMS-DS). As a characteristic, the workshop covers a broad range of topics in the field of molecular modelling, such as structural modelling, molecular (dynamics) simulations with various flavours, multi-scale approaches, chemoinformatics and machine learning-based techniques, to name a few, and their applications in various fields.

As such, it is only natural that the workshop is also supported as an activity of the CECAM (*Centre Europeen de Calcul Atomique et Moleculaire*) node "Mathematics and Computation in Molecular Simulation". The node is hosted by the Atomistic Simulation Centre, a consortium that consists of three national supercomputer centres: NHR@ZIB in Berlin, PC2 in Paderborn, and NHR@FAU in Erlangen. The centres of the NHR alliance provide Tier 2 computing infra-structure, training, and expert support to researchers throughout Germany and as such provide high-performance computing facilities which are substantial for high-level molecular modelling and simulations. NHR@FAU is not only helpful for computational scientists in and outside Erlangen, the organisers of the MMWS2025 are also grateful for direct support of the workshop. The first day of the workshop is therefore acknowledged as NHR@FAU-day.

We are looking forward to, in total, three inspiring days with presentations and discussions, with coffee and snacks, with old and new friends, with new impressions and future nice memories.

Scientific program

Prof. Dr. Carolin Müller

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DEAR FRIENDS AND COLLEGUES,

the 37th Molecular Modelling Workshop 2025 (from March 31st to April 2nd) in Erlangen aims for providing young scientists with a platform to present their research, exchange ideas with peers, and connect with others in the field. Presentations by scientists early in their career and of work in progress are therefore highly encouraged.

Additionally, the workshop offers a valuable networking opportunity, both within academia and with industry representatives. The workshop feeds from the warm and friendly atmosphere generated by its participants.

The thematic focus of MMWS 2025 is "Bridging Molecular Modelling between Ground- and Excited States". However, the organizing committee invites submissions for poster or oral presentations in English, covering all topics of molecular modelling, work on methods and applications alike, in and across all disciplines.

We are excited to announce this year' plenary speakers (in order of their presentations) and are looking forward to welcoming you to an inspiring Molecular Modelling Workshop in Erlangen!

PROF. DR. RENANA GERSHONI-PORANNE
Technion, Israel

PROF. DR. REINHARD MAURER
University Warwick, UK

PROF. DR. CHRISTOPH BANNWARTH
RWTH Aachen, Germany

PROF. DR. JAN MEISNER
HHU Düsseldorf, Germany

AWARDS

Traditionally, there will be two *Poster Awards* of 100 Euro each and three *Lecture Awards* for the best talks sponsored by the MGMS-DS:

1st Winner
Travel bursary to the *Young Modellers Forum* in the United Kingdom (travel expenses are reimbursed up to 500 Euro)

2nd Winner
up to 200 Euro travel expenses reimbursement

3rd Winner
up to 100 Euro travel expenses reimbursement

Only undergraduate and graduate research students qualify for the poster and lecture awards.

MGMS-DS E.V. ANNUAL MEETING

The general meeting of the MGMS, German Section (MGMS-DS e.V.) will be held during the workshop (in German language). We cordially invite all conference delegates to take the opportunity and join the society to participate in the annual meeting!

FEES

The conference fee amounts to 100 Euro (students: 50 Euro); online-only participation reduces the fee by 50%. This fee includes the annual membership fee for the MGMS-DS e.V.

WI-FI ACCESS

During the workshop, Wi-Fi access is possible via **eduroam** (SSID). Please have your Wi-Fi configured in advance or ask your local administrator for detailed information about your eduroam access. Links to general information about eduroam can be found on the workshop website mmws2024.mgms-ds.de

PRE- AND POST-CONFERENCE WORKSHOP

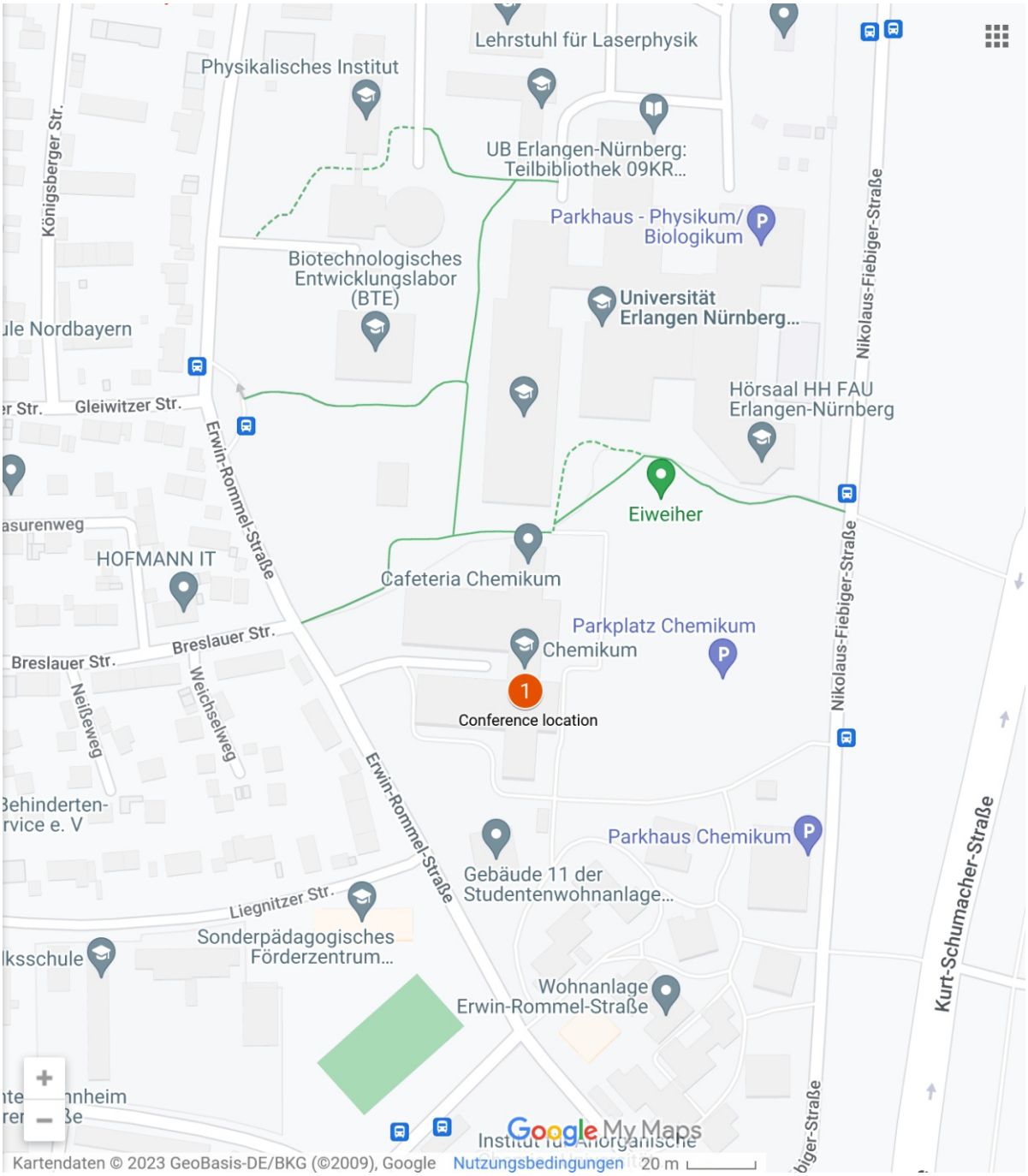
We are delighted to renew the pre-COVID tradition of workshops held before and after the conference. Please inspect the lectures program for more details.

LOCATION

Conference location: All talks, coffee breaks, the poster sessions and the buffet dinner on Monday, March 31st will take place at the Chemikum I, Nikolaus-Fiebiger-Straße 10, 91058 Erlangen, located on the southern campus of the university. The registration desk is next to lecture hall C1.

The *Social Event "Visit at a typical Erlanger Gasthaus"* will take place at "Steinbach Bräu" (https://steinbach-braeu.de), Vierzigmannstraße 4, 91054 Erlangen, on Tuesday evening. Food and drinks will be available at your own expense.

Public transport is available (www.vgn.de) by bus line 287 or 293 from the city center / railway station to the southern campus ("Technische Fakultät").



Lectures Program

PROGRAM

Monday, March 31st 2025 ***NHR@FAU-day***

10:00-12:00	**Pre-Conference Workshop** Schroedinger Suite
11:00-14:00	**Registration**
14:00-14:10	**Welcome remarks / Agenda review**
14:10-15:00	**PLENARY LECTURE I: Renana Gershoni-Poranne** Mission ImPASsible: Decoding Polycyclic Aromatic Systems with Deep Learning
15:00-15:25	**L01: Anna Kahler (Erlangen, Germany)** Performance optimization of GROMACS on modern Hardware
15:25-15:50	**L02: Louis Thirion (Erlangen, Germany)** A Neural-Network-Based Selective Configuration Interaction Approach to Molecular Electronic Structure
15:50-16:30	**Coffee Break**
16:30-16:55	**L03: Krzysztof Bojarski (Gdańsk, Poland)** Bridging Molecular Modeling and Machine Learning: New Perspectives on Protein-Glycosaminoglycan Recognition
16:55-17:20	**L04: Damian Suchomski (Gdańsk, Poland)** Molecular modeling of glycosaminoglycan-binding regions on the surface of procatepsin K key to its allosteric regulation
17:20-17:45	**L05: Nicolas Tielker (Dortmund, Germany)** Insights from the first *euroSAMPL* blind prediction challenge
18:00-21:00	**Poster Session & Buffett – Dinner**

Tuesday, April 1st 2025

09:00-09:50	**PLENARY LECTURE II: Reinhard Maurer** Machine-learning-enabled modelling of ultrafast dynamics at surfaces
09:50-10:15	**L06: Christian Ritterhoff (Erlangen, Germany)** The influence of strain-induced ferroelectricity on the fracture of oxide perovskites
10:15-11:00	**Conference Photo & Coffee Break**
11:00-11:25	**L07: Tom Frömbgen (Bonn, Germany)** Chiral induction in ionic liquids
11:25-11:50	**L08: Maximilian Tiefenbacher (Vienna, Austria)** Excited-state nonadiabatic dynamics in explicit solvent using machine learned interatomic potentials
11:50-12:15	**L09: Debabrata Halder (Erlangen, Germany)** Atomic-Scale Insights into the Interaction of Cobaltabis(dicarbollide) with DNA: A Molecular Modelling Perspective
12:15-14:00	**Lunch**
14:00-14:50	**PLENARY LECTURE III: Christoph Bannwarth** Potential energy surfaces exploration tools for simulation of molecular photophysics and photochemistry
14:50-15:15	**L10: Jesús L. Tamudo (Regensburg, Germany)** First principles prediction of wavelength-dependent isomerization quantum yields of a second-generation molecular nanomotor
15:15-15:40	**L11: Martina Hartinger (Eralngen, Germany)** Unraveling Excited-State Mechanisms: Computational Insights into Photoswitching
15:40-16:30	**Coffee Break**
16:30-16:55	**L12: Maria Fyta (Aachen, Germany)** Unraveling the molecular interactions of single nucleobases and amino acids within material openings
16:55-17:20	**L13: Dipti Potdar (Helsinki, Finland)** Molecular dynamics simulations of poly(2-oxazolines) for drug delivery applications
17:20-17:45	**L14: Moritz Macht (Erlangen, Germany)** pH-dependent simulations of API precipitation and dissociation
18:00-19:00	**Annual Meeting of the MGMS-DS e.V.**
19:30	**MMWS Social Event @ Steinbach-Bräu**

Wednesday, April 2nd 2025

09:00-09:50	**PLENARY LECTURE IV: Jan Meisner** Computational Reaction Discovery and Construction of Reaction Networks
09:50-10:15	**L15: Nico Kißing (Bremen, Germany)** Simulating Pressure on Molecules in Implicit Solvation Environments with the X-HCFF and GOSTSHYP methods
10:15-10:40	**L16: Rupam Gayen (Erlangen, Germany)** Molecular Dynamics Modelling of Mechanical Activation and Catalysis in Ball-Milling Mechanochemistry
10:40-11:15	**Coffee Break**
11:10-11:35	**L17: Jacqueline Calderón (Erlangen, Germany)** Metadynamics-based protocols applied to G-protein coupled receptors
11:35-12:00	**L18: Frank Beierlein (Erlangen, Germany)** Probing DNA/RNA Conformation: A Multi-Technique Approach
12:00-12:25	**L19: Gunther Stahl (OpenEye / Cadence)** Automated Identification of Cryptic Pockets for Drug Discovery
12:25-12:55	**Poster & Lecture Awards, Closing**
14:00-16:00	**Post-Conference Workshop:** ProteinsPlus – Supporting Structure-Based Design on the Web

Poster Session

POSTER SESSION

Monday, March 31st 2025 18:00-21:00

P01 **Frank R. Beierlein (Erlangen, Germany)**
Probing DNA Conformation: A Multi-Technique Approachs

P02 **Vipul K. Ambasta (Erlangen, Germany)**
Machine Learning in Predicting Electronic Absorption Properties of Molecules and Materials

P03 **Piet Ankermann (Erlangen, Germany)**
Molecular Case Studies of GALC Mutations Causing Krabbe Disease

P04 **Barışcan Arıcan (Erlangen, Germany)**
A Multiscale MD-QM/MM Approach for Modeling Fracture Behavior in Epoxy Resins

P05 **Abdessamad Belasri (Wuppertal, Germany)**
Computational Investigation of Gas Pollutants Adsorption on Copper Squarate

P06 **Arsha Cherian (Erlangen, Germany)**
Influence of Ligand Modifications on Catalyst Positioning in Supported Ionic Liquid Phase (SILP) Systems

P07 **Olena Denysenko (Erlangen, Germany)**
A comparative molecular dynamics study of bovine antibodies

P08 **Rustam Durdyyev (Erlangen, Germany)**
Impact of reduction, oxidation and ligand modification on the physicochemical properties of magic gold nanoclusters

P09 **Christiane Ehrt (Hamburg, Germany)**
Mining Macromolecular Binding Interfaces

P10 **Emily Groß (Regensburg, Germany)**
Computational Studies on Ion Pairing and Hydrogen Bonding

P11 **Elias Harrer (Erlangen, Germany)**
Assessing the dynamics of hemithioindigo-based photoswitches using multi-state molecular mechanics

P12 **Christophe Jardin (Nuremberg, Germany)**
The effect of somatic mutations in the voltage-gated proton channel hHV1 from molecular simulations

P13 **Nico Kißing (Bremen, Germany)**
Simulating Pressure on Molecules in Implicit Solvation Environments with the X-HCFF and GOSTSHYP methods

Please kindly remove your posters on tuesday evening!

POSTER SESSION

Monday, March 31st 2025 18:00-21:00

P14 **Max Kroesbergen (Erlangen, Germany)**
Computing Molecular Excited States and Spectra with Neural-Network-Supported Configuration Interaction

P15 **Alexander Mielke (Regensburg, Germany)**
Exploring the influence of electron donor and acceptor substituents on photochemical properties of a light-driven molecular nanomotor

P16 **Jules C. E. Ndongue (Erlangen, Germany)**
Towards automated exploration of enzymatic reactions

P17 **Sampanna Pahi (Erlangen, Germany)**
What is the impact of covalent-network formation on the curing kinetics of thermosets?

P18 **Philippa Petersen (Erlangen, Germany)**
What is the role of puckering in the thermal ratcheting steps of HTI based molecular motors?

P19 **Simon Schäfer (Erlangen, Germany)**
ManifoldX: A Parallel Wrapper for FoldX with Integrated Structure Preprocessing

P20 **Marlene Sell (Erlangen, Germany)**
Optimizing Parameters in Metadynamics Simulations for Free Energy Calculations

P21 **Fabian Sendzig (Dortmund, Germany)**
Solvent-controlled separation of integratively self-sorted supramolecular coordination cages

P22 **Cyrille N. Tahabo (Mainz, Germany)**
Designing Transmembrane Signaling Systems in Artificial Cells using DNA Structures

P23 **Dustin Vivod (Jülich, Germany)**
Exploring the ionomer-platinum interface in the cathode catalyst layer of polymer electrolyte membrane fuel cells via molecular dynamics simulations

P24 **Leon Völker (Erlangen, Germany)**
Mode of Metal Ligation Governs Inhibition of Carboxypeptidase A

P25 **Senta Volkenandt (Erlangen, Germany)**
Exploring bimodal equilibrium in MBD2 protein recognition of methylated CpG dinucleotides

Please kindly remove your posters on tuesday evening!

POSTER SESSION

Monday, March 31st 2025 18:00-21:00

P26 **Silvana S. Zurmühl (Erlangen, Germany)**
Detection of pH induced structural changes in helical peptides

P27 **Anselm H. C. Horn (Erlangen, Germany)**
NHR@FAU: Booster For Your Atomistic Simulations

All abstracts are available on the conference web site:
www.mmws2025.mgms-ds.de

Please kindly remove your posters on tuesday evening!

Abstracts

Mission ImPASsible: Decoding Polycyclic Aromatic Systems with Deep Learning

Renana Gershoni-Poranne
Schulich Faculty of Chemistry, Technion – Israel Institute of Technology, Israel

Polycyclic aromatic systems (PASs) present a seemingly insurmountable challenge: vast chemical spaces, complex electronic structures, and elusive aromatic properties. Our mission, should we choose to accept it, is to harness the power of deep learning to decode these molecular mysteries. In this talk, we embark on a journey through this complex chemical space, combining traditional computational methods with cutting-edge artificial intelligence tools. We demonstrate how neural networks can be trained to predict electronic properties with unprecedented speed and accuracy. More importantly, we show how they can be used interpretably to extract chemical insight.

To enable the application of such techniques to the design of novel functional PASs, we established the COMPAS Project – a COMputational database of Polycyclic Aromatic Systems – which already contains ~1 million molecules in three datasets [1–4]. We also developed two new types of molecular representation to enable efficient and effective machine- and deep-learning models to train on the new data: a) a text-based representation [5] and b) a graph-based representation [6]. By analyzing thousands of PAS structures with our dedicated representations, our AI agents not only achieve higher predictive ability with fewer data but have also uncovered hidden patterns and structure-property relationships that traditional methods might have missed.

Finally, we implemented the first guided diffused-based model for inverse design of PASs: GaUDI [7]. Our model generates new PASs with defined target properties. In addition to its flexible target function and high validity scores, GaUDI also accomplishes design of molecules with properties beyond the distribution of the training data.

From small benzenoid systems to extended graphene-like structures, we show how deep learning can navigate this complex chemical landscape, offering new insights into molecular design and property prediction. This talk will not self-destruct in five seconds, but it will revolutionize how we think about combining artificial intelligence with molecular science.

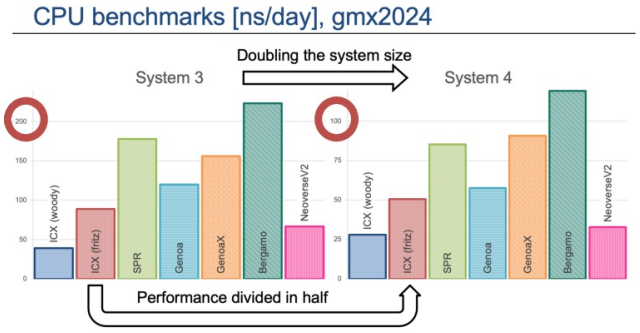
[1] A. Wahab, L. Pfuderer, E. Paenurk, R. Gershoni-Poranne, *J. Chem. Inf. Model.* **2022**, *62*, 3704.
[2] E. Mayo Yanes, S. Chakraborty, R. Gershoni-Poranne, *Sci. Data* **2024**, *11*, 97.
[3] S. Chakraborty, E. M. Yanes, R. Gershoni-Poranne, *Beilstein J. Org. Chem.* **2024**, *20*, 1817–1830.
[4] A. Wahab, R. Gershoni-Poranne, *Phys. Chem. Chem. Phys.* **2024**, 26, 15344–15357.
[5] S. Fite, A. Wahab, E. Paenurk, Z. Gross, R. Gershoni-Poranne, *J. Phys. Org. Chem.* **2022**, e4458.
[6] T. Weiss, A. Wahab, A. M. Bronstein, R. Gershoni-Poranne, *J. Org. Chem.* **2023**, *88*, 9645–9656.
[7] T. Weiss, E. M. Yanes, S. Chakraborty, L. Cosmo, A. M. Bronstein, R. Gershoni-Poranne, *Nat. Comput. Sci.* **2023**, *3*, 873–882.

Performance optimization of GROMACS on modern Hardware

Anna Kahler, Thomas Zeiser, Gerhard Wellein

Erlangen National High Performance Computing Center
Friedrich-Alexander-Universität Erlangen-Nürnberg

The MD simulation code GROMACS runs out of the box on CPUs and has been able to offload time-consuming calculations of electrostatics that use the Particle Mesh Ewald approach to GPU since version 2018. In the past years, GROMACS developers have added GPU offloading for bonded interactions and for the calculation of updates and constraints. With these code changes, the following questions may arise: Which hardware yields the best performance results? What are the optimized runtime parameters? How does the performance change across different hardware and software versions?



To find answers, a variety of benchmarks is run on different hardware architectures including CPUs and GPUs. The results not only give insights into scaling behavior regarding system size or show performance increases with the most recent program version or on the newest GPU but also reveal a need to assess runtime parameters for each project individually and based on the used hardware.

A Neural-Network-Based Selective Configuration Interaction Approach to Molecular Electronic Structure

Louis Thirion[1,2], Pavlo Bilous[3], Yorick L. A. Schmerwitz[2,4], Max Kroesbergen[1], Gianluca Levi[2], Elvar Ö. Jónsson[2], Hannes Jónsson[2], Philipp Hansmann[1,2]

[1] Friedrich-Alexander University of Erlangen-Nürnberg — [2] University of Iceland, Reykjavik — [3] Max Planck Institute for the Science of Light, Erlangen — [4] Max Planck Institute for Coal Research, Mühlheim

A novel method is presented for efficient *ab initio* calculations of molecules' ground and excited electronic states. Combining Hartree-Fock with a neural-network-based configuration interaction (NNCI) algorithm enables selective configuration interaction calculations that mitigate the exponential growth of the Hilbert space. Using our recently developed Python library SOLAX [1], a neural network classifier iteratively selects basis elements relevant for the targeted states, optimizing the many-body basis. Applied to the N_2 molecule, NNCI reproduces full configuration interaction (FCI) results obtained on nearly 10^{10} Slater determinants by using only 4×10^5 [2]. We find that rather than being hindered by combinatorial growth, NNCI benefits from increasing the number of single-particle degrees of freedom, providing a scalable alternative to standard truncation schemes. Future directions are committed to extending this approach to a multi-tier embedding scheme, thereby trying to enhance the accuracy of electronic structure calculations for surface reactions in the context of heterogeneous catalysis.

[1] Louis Thirion, Philipp Hansmann, and Pavlo Bilous, "SOLAX: A Python solver for fermionic quantum systems with neural network support," *SciPost Phys. Codebases* (2025)

[2] Yorick L. A. Schmerwitz, Louis Thirion, Gianluca Levi, Elvar Ö. Jónsson, Pavlo Bilous, Hannes Jónsson, and Philipp Hansmann, "A Neural-Network-Based Selective Configuration Interaction Approach to Molecular Electronic Structure," *Journal of Chemical Theory and Computation* (2025)

Bridging Molecular Modeling and Machine Learning: New Perspectives on Protein-Glycosaminoglycan Recognition

Krzysztof K. Bojarski

Department of Physical Chemistry, Gdańsk University of Technology, 80-233 Gdańsk, Poland

In recent years, glycosaminoglycans (GAGs) have gained increasing attention due to their structural diversity and critical biological functions. These negatively charged, sulfated, and linear carbohydrates are composed of repeating disaccharide units, typically consisting of an amino sugar and either glucuronic or iduronic acid (except for keratan sulfate). GAGs are primarily found in the extracellular matrix and lysosomes, where, with the exception of hyaluronic acid, they are covalently attached to proteoglycans. Through predominantly electrostatic interactions, they modulate the biological activity of various protein targets, including cathepsins, growth factors, chemokines, antithrombin, and bone morphogenetic proteins. GAGs play essential roles in cell signaling, adhesion, angiogenesis, anticoagulation, and apoptosis. Their dysregulation has been implicated in numerous pathological conditions, including cancer, autoimmune disorders, Alzheimer's and Parkinson's diseases, arthritis, and mucopolysaccharidoses. A deeper understanding of protein-GAG interactions is thus crucial for developing novel therapeutic strategies targeting these diseases.

In molecular studies of protein-GAG interactions, *in silico* methods often complement experimental approaches. However, designing a computational pipeline for molecular modeling of these interactions presents several challenges due to the unique properties of GAGs. These molecules are highly flexible, with their conformational variability arising from glycosidic linkages and ring puckering, making it difficult to define a preferred conformation. Additionally, GAGs can bind to multiple regions of a protein with similar free energy values, further complicating the identification of the most favorable binding mode. Despite their relatively simple carbohydrate backbone, GAGs exhibit significant structural complexity due to their sulfation patterns, which play a crucial role in protein recognition, structural properties, and biological activity. Moreover, protein-GAG complexes can display comparable stability even when GAGs bind within the same region but adopt different conformations. These factors collectively make it challenging to determine the native binding pose and conformation. Machine learning (ML) algorithms, which are increasingly employed in molecular modeling, also face limitations in this context due to the scarcity of high-quality experimental structural and thermodynamic data. As a result, developing accurate scoring functions remains a considerable challenge. Nevertheless, despite these obstacles, *in silico* methods have been successfully applied numerous times to characterize the complex nature of protein-GAG interactions.

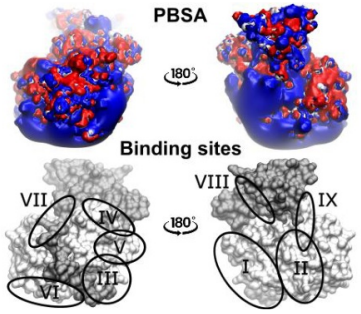
This study provides an overview of recent advancements in molecular modeling of protein-GAG systems. First, the ff14SB/GLYCAM06 (AMBER) and CHARMM36m (CHARMM) force fields are compared in terms of their ability to describe the conformational and energetic properties of protein-GAG interactions. While both force fields yield comparable energy profiles for GAG unbinding, they differ in their description of conformational properties, such as protein root mean square fluctuation (RMSF) and glycosidic linkage flexibility. Second, the impact of five explicit solvent models on the structural properties of heparin is assessed. Results suggest that in CHARMM, the choice of solvent model may have a lesser impact on heparin structure compared to AMBER. Finally, the Repulsive Scaling Replica Exchange Molecular Dynamics (RS-REMD) method is implemented in CHARMM as an advanced molecular docking approach and tested on seven protein-carbohydrate systems. The predictive power of MM-GBSA-based scoring is evaluated, and a deep learning-based scoring function is introduced, significantly improving the selection of the most accurate binding structures.

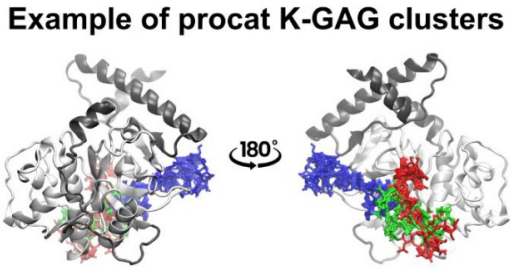
Molecular modeling of glycosaminoglycan-binding regions on the surface of procatepsin K key to its allosteric regulation.

Damian Suchomski

Department of Physical Chemistry, Gdańsk University of Technology, 80-233 Gdańsk, Poland

Procathepsin K is the precursor of cathepsin K, a key proteolytic enzyme involved in bone resorption and extracellular matrix remodeling. The allosteric regulation of cathepsin activity by glycosaminoglycans (GAGs) has recently gained scientific interest, yet its exact mechanisms remain unclear. Overexpression or overactivity of cathepsin K is linked to serious health conditions, including osteoporosis, pycnodysostosis, and various tumors, primarily due to its role in bone degradation. The maturation of inactive cathepsin forms is crucial for their activation at the right time and place. GAG binding can induce conformational changes that influence propeptide flexibility, either accelerating maturation or stabilizing structures where the proregion blocks the active site. However, little is known about the allosteric regulation of procathepsin K by GAGs.





This study aimed to screen a set of ligands, identify the most promising candidates, and determine their binding sites on procathepsin K. Molecular modeling techniques, including PBSA (Poisson-Boltzmann Surface Area) electrostatic potential analysis, molecular docking, molecular dynamics (MD) simulations and MM-GBSA (Molecular Mechanics-Generalized Born Surface Area) binding free energy calculations, were employed using AMBER21 package [1]. The set of potential glycosaminoglycan-binding sites was narrowed down to a few of the most promising ones with potential significance for the allosteric regulation of procathepsin K activity. Notably, these sites overlapped with those previously identified for the mature enzyme through both experimental [2, 3] and computational studies [4-7]. The charge and length of the GAG chains were found to influence binding. Chains with lower charge formed complexes with the lowest binding free energy values (the highest stability). In addition, shorter chains were preferred over longer ones at binding sites where the positive electrostatic area was narrower or unfavorably located for longer chains. The obtained results provide a solid foundation for further studies on the allosteric regulation of procathepsin K enzymatic activity by glycosaminoglycans and will serve as a basis for the next stages, where more advanced methods allowing for better sampling of conformational properties will be utilized.

[1] D. A. Case et al. Amber 2021. University of California, San Francisco, 2021.
[2] BA. H. Aguda et al., *PNAS* 111.49 (2014), pp. 17474–17479.
[3] Z. Li et al., *Journal of molecular biology* 383.1 (2008), pp. 78–91.
[4] K. Bojarski et al., *Journal of Molecular Graphics and Modelling* 113 (2022), p. 108153.
[5] M. Novinec, B. Lenari, and B. Turk, *BioMed research international*, 2014.1 (2014) p. 309718.
[6] M. Novinec, *PLoS One* 12.8 (2017), e0182387.
[7] G. V. Rocha, L. S. Bastos, and M. G. Costa, *Proteins* 88.12 (2020), pp. 1675–1687.

Insights from the first *euroSAMPL* blind prediction challenge

Nicolas Tielker[1], Michel Lim[2], Patrick Kibies[1], Juliana Gretz[3], Björn Hein-Janke[4], Ricardo A. Mata[4], Paul Czodrowski[2], Stefan M. Kast[1]

[1]Fak. Chemie und Chemische Biologie, Technische Universität Dortmund, [2]Dept. Chemie, Johannes-Gutenberg-Universität Mainz, [3]Fak. Chemie und Biochemie, Ruhr-Universität Bochum, [4]Inst. Phys. Chemie, Georg-August-Universität Göttingen

The FAIR (Findable, Accessible, Interoperable, and Reusable) principles for sustainable research data management (RDM) are vital for maximizing reproducibility of computational chemistry data and results, and to easily verify and use newly developed methods. This includes methods such as the automated or manual annotation of generated research data with relevant author- and domain-specific metadata, shared indexing between experimental and computational data, persistent storage, and the transparent and automated analysis of raw computational data.

To advance and encourage the adoption of RDM methods, we organized a pK_a blind prediction challenge as a community task for testing models in the spirit of the SAMPL (Statistical Assessment of the Modeling of Proteins and Ligands) series of challenges. [1,2,3] The first *euroSAMPL* challenge [4] was based on experimental aqueous pK_a measurements of 35 small, drug-like molecules done in-house, and allowed participants to submit computational predictions over a timeframe of three months before the experimental values were published. Compounds were selected according to novelty, existence of only one protonation equilibrium in the experimental pH range between 2 and 12, no significant populations of additional tautomeric microstates, and chemical diversity.

Processing and initial analysis of participants' data was automated, with final scores weighting not only the accuracy of the predicted values but also the submissions' RDM quality to generate the final ranking. The latter was judged by questionnaire-based peer evaluation by all other participants. Results of the challenge reveal good agreement between predicted and experimental values for some of the methods, including QM-based and ML-based methods, but the quality of the RDM still has significant room for improvement. Here, one of the submissions received the clear first place with respect to its "FAIRness", with three other submissions on a shared, but distant, second place, indicating a need for more standardization and awareness of proper research data management. Individual prediction results are compared to a "consensus prediction" from either all, or a subset of the submissions, and discussed with a perspective on best practices in the application of pK_a predictions in industry and academia.

All data and statistical analyses are collected in a GitLab repository, [5] to be published as part of the "SAMPL Special Collection" in Phys. Chem. Chem. Phys. Collectively, insights gathered in terms of challenge design and technical implementation stimulate ideas for future rounds.

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Machine-learning-enabled modelling of ultrafast dynamics at surfaces

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Electronic excitations at surfaces can be created either by electromagnetic radiation or the ultrafast motion of molecules, for example in photocatalysis or hyperthermal molecular scattering. Such excitations, while short-lived, will trigger coupled and concerted nonadiabatic motion of electrons and nuclei at short time scales that can measurably affect chemical dynamics by introducing energy dissipation, dynamical steering effects, and by contributing to state-dependent reaction probabilities. [1]

I will present our recent efforts to establish methods able to capture nonadiabatic and excited-state effects during ultrafast dynamics at surfaces. We employ a range of methods such as molecular dynamics with electronic friction and surface hopping dynamics. [2] By combining first principles electronic structure calculations [3] with high-dimensional machine-learning representations, [4,5] we are able to simulate measurable observables with statistical averaging over thousands of reaction events. Doing so enables us to directly compare our results to experiments and to assess the limitations of different methods. Recent relevant results include the vibrational state-to-state scattering of H_2 on copper surfaces [5], NO on Au(111), [6] and the light-driven hydrogen evolution reaction.

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The influence of strain-induced ferroelectricity on the fracture of oxide perovskites

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The cleaving of bulk crystals using mechanical force is a common procedure to obtain well-defined surfaces under UHV conditions. While this method avoids chemical changes in the surface composition due to etching and annealing procedures, the strain necessary for cleavage can induce ferroelectric phase transitions during the fracture process whose influence is still visible on the as-cleaved surface, as shown, for example, by Sokolović et al. [1] for mechanically cleaved SrTiO3. Here, we present density-functional theory calculations to discuss the influence of increasing strain on the magnitude of possible ferroelectric distortions and the development of a spontaneous polarization for three prototype perovskite oxides: cubic SrTiO3, ferroelectric BaTiO3, and polar KTaO3. First, we estimate the critical strain for mechanical cleavage in fracture Mode 1 and Mode 2. Subsequently, we calculate the polarization of the material at the point of fracture and discuss the implication on surface charges and the formation of surface defects.

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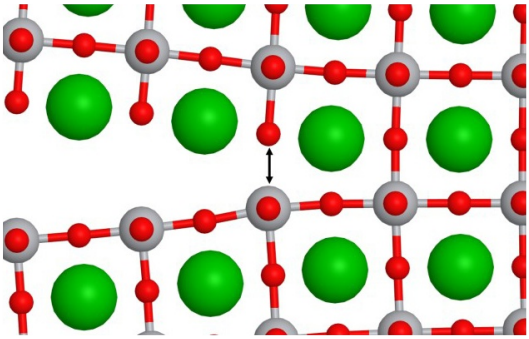

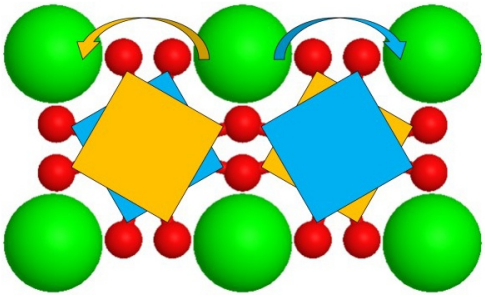

Chiral induction in ionic liquids

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Chiral ionic liquids (CILs) exhibit potential utility both as solvents in asymmetric synthesis and as selectors in the enantiomeric recognition of small molecules. The effective use of CILs in these applications requires a comprehensive understanding of the structure and dynamics. Due to their sensitivity to molecular conformations and conformational changes, chiroptical spectroscopy methods such as vibrational circular dichroism (VCD) offer unique opportunities to study the structure of CILs and in particular the occurrence of chirality induction effects.

In this talk, we present the combined results of our recent studies on CILs. The first part involves ab initio molecular dynamics (AIMD) simulations of the CIL 1-ethyl-3-methylimidazolium L-alaninate ([C2C1Im][L-ala]) [1,2], elucidating the induction of chirality from the anionic to the cationic moiety, thereby inducing a perturbation within the conformational landscape of the cation. Based on these findings, we investigate two prototypical molecular arrangements involving (R)- or (S)-butan-2-ol solutes within $[C_2C_1Im][L\text{-ala}]$ to uncover chiral recognition mechanisms. VCD spectra and structural analyses reveal discriminative interactions between the CIL and the enantiomers of butan-2-ol.

While the focus of the first study is on the chiral induction in ionic liquid cations, the second investigation [3-5] examines effects on the anionic components. Using AIMD simulations of (R)-propylene oxide dissolved in the achiral IL 1-ethyl-3-methylimidazolium bis-(trifluoromethylsulfonyl)imide ($[C_2C_1Im][NTf_2]$), we observe an induction of chirality from propylene oxide to the anion, monitored by theoretical and experimental VCD spectroscopy. These results are remarkable because (i) the cation only plays a minor role in the chiral induction and (ii) this is the first time that a chiral induction to an ionic liquid anion is observed.

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Excited-state nonadiabatic dynamics in explicit solvent using machine learned interatomic potentials

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Simulating complex systems containing thousands to millions of atoms remains a major challenge in computational chemistry, particularly for excited-state dynamics, where classical force fields fail to capture quantum effects. The Quantum Mechanics/Molecular Mechanics (QM/MM) approach has been widely used to study such systems, but it suffers from the inherent computational cost and poor scaling of quantum mechanical methods.

Recent advancements in machine-learned interatomic potentials offer a promising alternative by replacing the quantum mechanical treatment in QM/MM simulations, significantly accelerating calculations. One such model, FieldSchNet[1], incorporates the electric field generated by MM atoms to capture electrostatic interactions between the different regions, mimicking the electrostatic embedding in a QM/MM description. In this work, we apply FieldSchNet to excited-state surface hopping dynamics. Using nonadiabatic QM/MM simulations of furan in water, we generate training data for the five lowest singlet states and assess the performance of different training and testing strategies in reproducing the original dynamics.

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Atomic-Scale Insights into the Interaction of Cobaltabis(dicarbollide) with DNA: A Molecular Modelling Perspective

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Boron neutron capture therapy (BNCT) is an emerging cancer treatment strategy that relies on boron-containing agents to selectively target tumor cells. Cobaltabis(dicarbollide) ([COSAN]$^-$), a metallacarborane complex with a high boron content, is a promising candidate for BNCT. However, its interaction with nucleic acids, a key determinant of its therapeutic potential, remains controversial.

In this work, we employ a multiscale molecular modelling approach, integrating microsecond long molecular dynamics (MD) simulations, hybrid quantum mechanics/molecular mechanics (QM/MM) calculations, and binding free energy estimations, to resolve the binding mechanism of [COSAN]$^-$ with DNA at an atomic level.

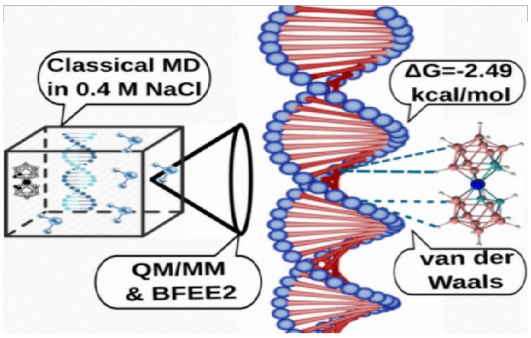

Figure 1: Atomic-scale insights into [COSAN]$^-$ interactions with DNA from MD and QM/MM simulations, revealing weak binding energetics.

Our findings reveal that [COSAN]$^-$ interacts weakly with DNA, preferentially binding to the major groove via dihydrogen B–H· · ·H–N bonding [1]. Moreover, our results demonstrate a strong dependence on ionic strength, with binding events observed primarily at high NaCl concentrations. These insights contribute to a fundamental understanding of metallacarborane interactions with biomolecules and provide a molecular basis for designing improved boron delivery systems for BNCT

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Potential energy surfaces exploration tools for simulation of molecular photophysics and photochemistry

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In this presentation, we will discuss quantum chemistry methods that enable the simulation of flexible molecules with focus on determining their spectroscopic properties and photochemical reaction mechanisms.

First, state-of-the-art methods in quantum chemistry for conformational sampling will be outlined [1–3] and how these are integrated into a workflow for the simulation of observable properties of molecules in the thermodynamic equilibrium. It will be demonstrated that accounting for the different conformers and their Boltzmann weights appropriately is essential for the simulation of electronic circular dichroism (ECD) spectra, a technique that is used for the determination of the absolute configuration of chiral molecules. [4]

Next, we will turn to the elucidation of photochemical reaction mechanisms and show how potential energy exploration tools can be used for this purpose. In particular, an efficient exploration technique for identifying important state crossing points between the ground and the lowest excited state is presented. [5] At comparably low computational cost, previously unknown photocatalytic processes can be investigated this way, leading to a better understanding of their mechanism. Real-life examples from collaborative research projects will be highlighted. [6, 7]

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First principles prediction of wavelength-dependent isomerization quantum yields of a second-generation molecular nanomotor

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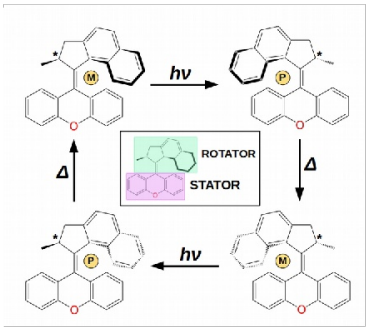
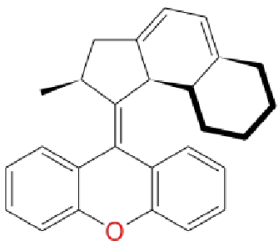
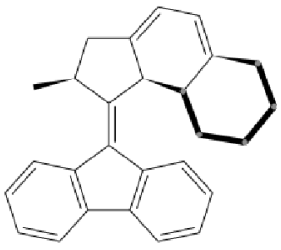
Figures: If you like, you can include figures in your abstract. We recommend to use figures in the size shown below. Please do not use figures larger than 5 cm (1.97 inch) in height. We recommend NOT to use figure captions.

Second-generation molecular nanomotors (MNMs) are gaining interest in biomedical applications due to their potential for light-induced ultrafast photoisomerization [1,2]. The rotational motion of this kind of MNMs is based on a two-step process. First, light absorption induces an E-Z photoisomerization around the central carbon-carbon double bond, converting the molecule into an unstable conformer. This step is followed by a thermal helix inversion, where the molecule undergoes a conformational change that restores the stable conformer but with a different spatial orientation. Repeating these two steps in sequence enables a full 360º unidirectional rotation. A fundamental challenge in their design is achieving unidirectional rotation during isomerization and thermal helix inversion. In this contribution, we aim at determining a way to ensure that unidirectionality [3]. For that, we investigate and compare the excited-state dynamics of all the possible conformers of two different second-generation Feringa-type MNM using non-adiabatic trajectory surface hopping molecular dynamics based on time-dependent density functional theory (TDDFT).

We simulate the photoisomerization of both M- and P-conformers and calculate quantum yields for clockwise and anti-clockwise rotations. Our results reveal that the helicity of the starting conformer determines the isomerization direction. Excitation in the wavelength range where the most stable conformer exhibits maximum absorption and quantum yield, maximizes unidirectional rotation. Additionally, we report excited-state lifetimes and detailed structural dynamics, providing new insights into the photochemical behavior of MNMs. These findings contribute to the rational design of more efficient molecular nanomotors for biomedical applications.







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Unraveling Excited-State Mechanisms: Computational Insights into Photoswitching

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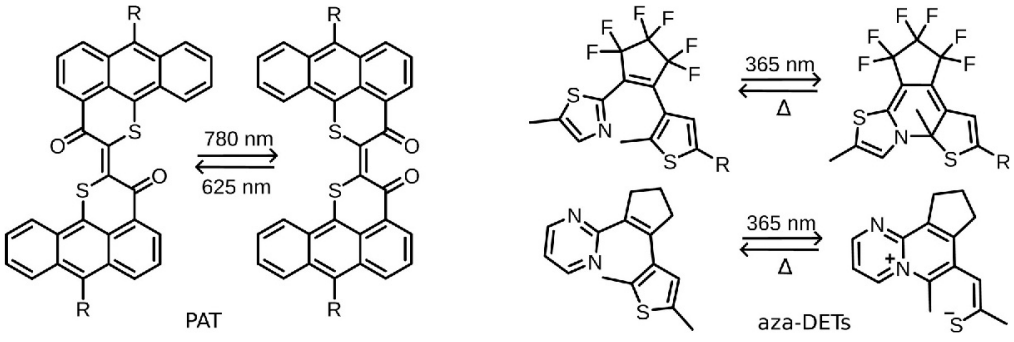
Light-driven molecular motion is at the heart of photochemistry, enabling the conversion of photon energy into electronic and structural changes. In particular, photoswitches and photomotors have emerged as key players in applications spanning nanotechnology, catalysis, and drug delivery. However, understanding their photoreaction mechanisms remains a formidable challenge due to the ultrafast nature of light-induced processes, which complicates a targeted reaction optimization. While spectroscopic experiments provide crucial insights, they often lack the structural details needed to comprehend excited-state dynamics. Consequently, computational methods have become essential tools in unraveling excited-state reactivity. In this context, we present different approaches to elucidate the fundamental principles governing photochemical reactivity.

In a first case study, we explore π-extended thioindigoid photoswitches, particularly peri-anthracene-thioindigo (PAT),[1] which represents a breakthrough in shifting absorption into the red and near-infrared region, along with its small brother peri-naphthalenethioindigo (PNT). Combining (TD-)DFT and ADC(2) calculations with steady-state and femtosecond time-resolved spectroscopy, we reveal an *E/Z*-isomerization mechanism driven by efficient population of the triplet manifold.

Secondly, we investigate aza-diarylethenes (aza-DETs),[2,3] a novel class of photoswitches exhibiting distinct photochemical pathways. Using state-of-the-art quantum chemical methods such as QD-NEVPT2 and MRSF-TDDFT, we dissect the mechanistic differences between aza-DETs forming closed-ring and zwitterionic photoproducts.

These insights enhance our understanding of photochemical transformations and pave the way for the rational design of next-generation photoswitches.



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Unraveling the molecular interactions of single nucleobases and amino acids within material openings

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The specific interactions of single biomolecules, such as DNA, RNA, and peptides with a material can be tailored in order to give rise to novel biosensors. These are made of a material part in which a nanometer-sized pore is drilled and can electrophoretically thread charged (bio)molecules through in the presence of an electrolyte solution [1]. This molecular transport through the material pore can be detected by ionic and/or electronic current signals. Both types of currents, though different in nature, inherently include the analyte information, that is the length, type, and sequence. At the same time, these currents map the explicit interactions of the threaded (bio)molecule to the surface of the material. The exact chemical details of both the (bio)molecule and the material, as well as their relative orientation strongly influence the interactions of the two and define the transport properties of the molecule through the material opening [2]. In order to unravel these exact interactions and their effect on the measurable current signals, two separate types of materials are probed: (a) two-dimensional graphene and molybdenum-disulfide [3] and (b) a biomimetic graphite-based structure [4]. The molecular transport and its interplay with the electrolyte solution through these materials are unraveled using atomistic simulations. At the same time, the electronic tunneling current, which is enhanced by the molecular transport through the material opening is calculated using quantum transport simulations. Both the ionic and electronic currents that are calculated, as well as those measured in relevant experimental setups need to be analyzed by applying Machine Learning schemes [5] in order to provide the exact chemical information on the (bio)molecule threading the material pores. These schemes are being integrated in the novel nanopore sequencers as part of the next generation sequencing schemes.

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Molecular dynamics simulations of poly(2-oxazolines) for drug delivery applications.

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Poly(2-oxazolines) or POx are emerging as promising alternatives to polyethylene glycol (PEG) in drug delivery due to their biocompatibility, tunable properties, and high functionalization potential [1, 2]. To investigate how stereochemistry and solvent polarity influence their structural behavior, we conducted molecular dynamics (MD) simulations on chiral poly(2-oxazoline) polymers with varying side-chain compositions in different solvents. This study aims to provide molecular-level insights into how these molecular features influence the structural dynamics and stability of these polymers in drug formulation and drug delivery.

Simulations of enantiopure and racemic conformers of poly(2-propyl-4-methyl-2-oxazoline) (pPrMeOx), poly(2-ethyl-4-ethyl-2-oxazoline) (pEtEtOx), and poly(2-butyl-4-ethyl-2-oxazoline) (pBuEtOx) were conducted in methanol, ethanol, and butanol using GROMACS software with the OPLS-AA force field. The results show that solvent polarity and side-chain structure strongly affect polymer dynamics and stability.

Our findings offer valuable insights into the design of poly(2-oxazoline)-based drug delivery systems. Solubility and structural behavior are strongly influenced by chain length, side-chain composition, and enantiomeric ratio, indicating that optimizing these parameters can enhance drug formulation process. The agreement between our simulations and experimental data further supports these observations [3], highlighting the role of poly(2-oxazolines) for enhanced drug delivery applications.

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pH-Dependent Molecular Dynamics Simulations of Active Pharmaceutical Ingredient Precipitation and Dissociation

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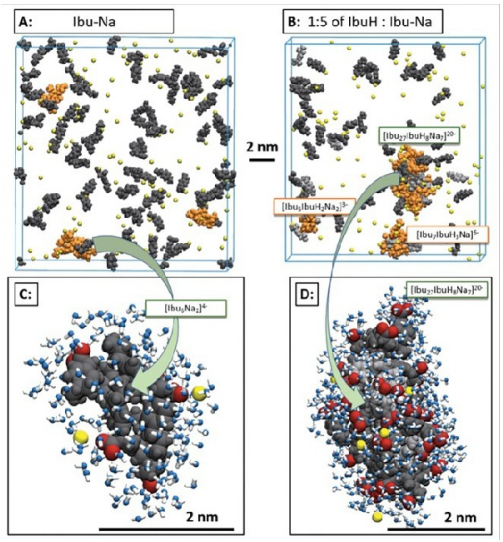

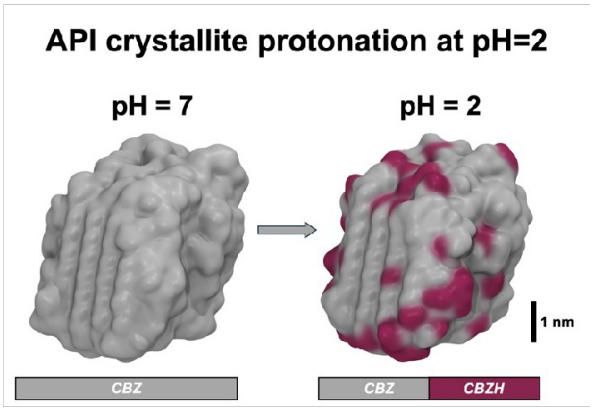

Modern pharmacology must integrate sometimes controversial aspects of drug discovery and formulation into collaborative research and development efforts, such as contrasting precipitation environments with the area of application and the favorable solubility of precipitates. The success of a new active pharmaceutical ingredient (API) candidate critically depends on its bioavailability, especially considering that a significant proportion of newly developed APIs fall under the biopharmaceutical classification system (BCS) class II substances, which are primarily limited by solubility. In many cases, this restricts drug uptake in the bloodstream after the dissolution of the API crystals in the gastrointestinal system. The need for molecular-scale insights becomes particularly evident for contrasting systems precipitated in an aprotic solvent while featuring constituents that can be protonated once the tablet reaches the intestinal system. Quantification and control of acid-induced precipitation and dissociation are critical to provide well-defined kinetics of drug release to the patient [1].

Conversely, our comprehension of crystal dissolution remains relatively limited and generally depends on the premise of a simple reversal of the growth process, namely ion-by-ion or molecule-by-molecule dissolution. However, in real-world situations, the dissolution of an API constitutes a complex, multi-faceted process, which may encompass the wetting of a solute phase, successive solvent penetration into the solute, initial fragmentation of crystals into crystallites, followed by the de-aggregation or dissolution of APIs into the solvent. This presentation focuses on the final stage of the dissolution process, which entails the disintegration of a small API crystal into the solvent to elucidate the underlying mechanisms or driving forces that facilitate acid-induced API crystallite dissolution [2,3].

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Computational Reaction Discovery and Construction of Reaction Networks

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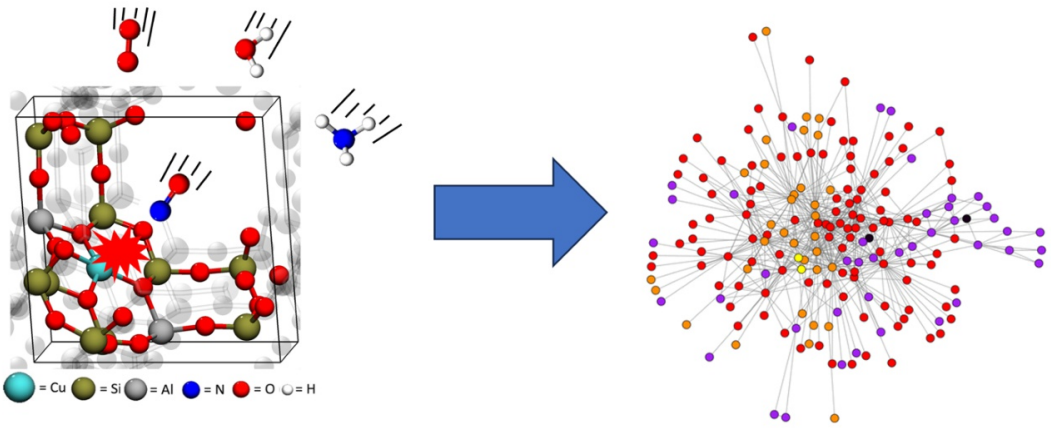

Recent developments of efficient computational methods make it possible to discover chemical reactions starting from basic principles and elucidate novel reaction mechanisms that might otherwise have been overlooked. Entire reaction networks can be discovered autonomously, which enables a complete investigation of chemical systems with all their elementary steps, intermediates, and side reactions. In this talk, modern approaches for the computational discovery of chemical reactions are presented. The capabilities of *ab initio* molecular dynamics accelerated by different external forces, coined nanoreactor molecular dynamics (NMD), [1] are demonstrated and improvements of reaction network construction and visualization are shown. [2,3] Recent studies span the fields of combustion chemistry, atmospheric chemistry, and catalysis. [3,4]

The extension of NMD to periodic systems also allows the investigation of surface reactions and porous media. Here, an application of periodic NMD simulations to construct a complex reaction network for zeolite catalysis in the context of Selective Catalytic Reduction (SCR) is given, which elucidates the reaction mechanism of the unwanted SCR side reaction of N_2O formation.

[1] L.-P. Wang *et al.*, *Nat. Chem.*, **2014**, 6, 1044-1048
[2] J. A. Meissner, J. Meisner, *J. Chem. Theory Comput.*, **2025**, 1, 218-229
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[4] R. Xu *et al.*, *Chem. Sci.*, **2023**, 14 (27), 7447-7464
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Simulating Pressure on Molecules in Implicit Solvation Environments with the X-HCFF and GOSTSHYP methods

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The investigation of molecular properties under pressure in the gigapascal regime is significant for gaining a deeper understanding of materials under extreme circumstances. Theoretical methods are required to supplement experimental data because the latter can only provide indirect information about pressure-induced changes at the molecular level. Both combined allow complete insight into the effects of pressure on molecular systems. [1]

In this context, it is essential to consider the chemical surrounding of the desired molecular system. However, the simulation of pressure applied to liquid-phase compounds is far from straightforward. As a first approach to implicitly include solvent effects in pressure simulations, the pressure models eXtended Hydrostatic Compression Force Field (X-HCFF) [2] and Gaussians On Surface Tesserae Simulate HYdrostatic Pressure (GOSTSHYP) [3] were used together with the Conductor-like Polarizable Continuum Model (C-PCM). [4, 5] All of these methods require discretized molecular surfaces for their functionality. In previous implementations of X-HCFF and GOSTSHYP, the combination of these pressure models with C-PCM led to instabilities in the quantum chemical software Q-CHEM [6] due to simultaneous usage of the discretization routine. Therefore, an independent way of discretizing and handling molecular surfaces for X-HCFF and GOSTSHYP is introduced, enabling a stable way to include implicit solvent effects in high-pressure simulations.

To investigate the effects of implicit solvation on molecules, those that can occur in a zwitterionic and a neutral state are of special interest. For glycine and sulfamic acid, it could be shown that high pressure applied with the GOSTSHYP model tends to stabilize the solvated zwitterionic state of the compounds in an aqueous environment. Additionally, intramolecular proton transfers at high pressure could be identified for some compounds.

The improved way of handling molecular surfaces in the pressure models also allows the straightforward implementation of new surface grid methods. Vibrational frequency calculations under pressure could benefit from being performed with a static surface grid. This could allow a better reproduction of pressure-induced red shifts of selective modes in experimental vibrational spectra. A corresponding implementation is currently in progress.

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Molecular Dynamics Modelling of Mechanical Activation and Catalysis in Ball-Milling Mechanochemistry

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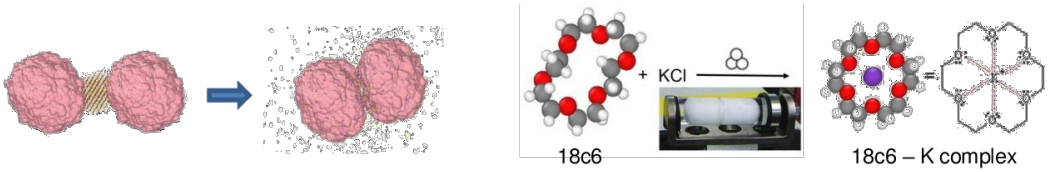
Mechanochemistry involves transformations driven or assisted by mechanical force [1]. Ball milling (BM) is the most widely used method in modern mechanochemistry, but its inherent nature makes it challenging to study individual impacts experimentally [2]. To overcome this limitation, molecular dynamics (MD) simulations offer a powerful tool to gain molecular-level insight into mechanical activation events.



We perform MD simulations using GROMACS package to describe mechanical activation by fragmentation of crystal particles down to individual atoms, ions and ion pairs and their subsequent recrystallization. To achieve this, we incorporate neutral, rigidly constrained amorphous balls to exert mechanical force on the crystal. Furthermore, we use the host-guest complexation reaction of 18-crown-6 ether (18c6) with KCl, as our model system and monitor subsequent product formation and rate of agglomeration under neat and liquid-assisted conditions. We demonstrate that a small amount of the liquid additive facilitated product formation, while too much of it destabilized the product by stabilizing the reactants. Our findings signify the importance of not only impacts for reactant activation, but also the immediate surroundings of the activated species for stability. This approach provides a fresh and detailed view of mechanochemistry that could allow for its theoretical optimization and guide the targeted use of catalysts in mechanochemical reaction.

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Metadynamics-based protocols applied to G-protein Coupled Receptors

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G protein-coupled receptors (GPCRs), which represent the largest family of membrane proteins in the human genome, play important roles in signal transduction by detecting extracellular stimuli and activating intracellular downstream signaling pathways. Signaling by GPCRs usually occurs via ternary complexes formed under cooperative binding between the receptor, a ligand, and an intracellular binding partner (a G-protein or β-arrestin). The three processes associated with GPCR signaling are ligand binding/dissociation, which we have traditionally called ligand binding/unbinding, receptor activation/inactivation and G-protein coupling/uncoupling. These processes are usually very slow in comparison to typical molecular dynamics (MD) simulation times (several μs to a millisecond), so that either enhanced sampling or steered MD techniques are needed to investigate them. Metadynamics has proven to be very successful for reconstructing the free energy hypersurface and for accelerating rare events in complex biomolecular systems. However, metadynamics is limited in the number of collective variables (CVs) it can handle as the computational cost scales exponentially with the number of CVs, hence finding and improving CVs is the object of intense investigation. Our own work in this field includes developing metadynamics protocols to investigate different steps in the GPCR signaling process. For receptor activation, we defined a generally applicable activity index[1] (A^{100}) for class A GPCRs. This index is a linear combination of five inter-helix distances between α-carbons that allows us to characterize the activation state. This activity index represents an effective CV for simulating activation/deactivation free-energy profiles for class A GPCRs with metadynamics.[2] A further important development is that our binding/unbinding protocol for small-molecule ligands[3] has been adapted and extended to consider peptide ligands for class A GPCRs.[4] This extension requires that the conformational sampling, the mechanical integrity, and the extension into the extracellular medium of the protocol be improved. These new metadynamics-based protocols generate results compatible with previous simulation and experimental studies at a relatively low computational cost.

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[2] J.C. Calderón, P. Ibrahim, D. Gobbo, F. L Gervasio, T. Clark,. *J. Chem. Inf. Model.* **2023**, 63, 3105−3117.
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Probing DNA/RNA Conformation: A Multi-Technique Approach

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The determination of distances between specific points in nucleic acids is essential to understanding their behaviour at the molecular level. The ability to measure distances of 2–10 nm is particularly important: deformations arising from protein binding commonly fall within this range, but the reliable measurement of such distances for a conformational ensemble remains a significant challenge. In addition to FRET-based techniques, EPR-(DEER) experiments are valuable tools to determine distances in biological macromolecules. We here show that MD simulations are a robust tool to interpret electron paramagnetic resonance (EPR) measurements of DNA oligonucleotides spin-labelled with triazole-appended nitroxides at the 2' position. For two nitroxide spin-labels attached to B-form DNA duplexes, we present results from EPR spectroscopy, MD simulations, X-ray crystallography, and NMR spectroscopy. These four methods are mutually supportive and pinpoint the locations of the spin labels on the duplexes. In doing so, this work establishes 2'-alkynyl nitroxide spin-labelling as a minimally perturbing method for probing DNA conformation. We further show how the spin labels established for DNA can be used to investigate DNA/RNA hybrid duplexes, and compare the experimental data with our MD results.

[1] J. S. Hardwick, M. M. Haugland, A. H. El-Sagheer, D. Ptchelkine, F. R. Beierlein, A. N. Lane, T. Brown, J. E. Lovett, E. A. Anderson, *Nucleic Acids Res.* **2020**, *48*, 2830-2840. (DOI: 10.1093/nar/gkaa086)
[2] M. M. Haugland, A. H. El-Sagheer, R. J. Porter, J. Pena, T. Brown, E. A. Anderson, J. E. Lovett, *J. Am. Chem. Soc.* **2016**, *138*, 9069-9072. (DOI: 10.1021/jacs.6b05421)
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Automated Identification of Cryptic Pockets for Drug Discovery

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The pharmaceutical industry is always on the lookout for new therapeutic targets. Many proteins found in signaling pathways have historically been considered "undruggable" as no points of attack for classical drug development work can be identified. The proteins do not show obvious "active sites" that can be targeted with e.g. classic virtual screening techniques due to their smooth protein surface or large inherent protein motion.

In recent years, many advances have been made in MD (Molecular Dynamics) simulations algorithms as well as compute power that drives them, to allow the study of the dynamic behavior of such undruggable proteins. Long timescale protein motions can, in many cases, reveal pockets that typically do not exist in an apo form where a ligand is not present, but can open during simulations. These so-called "cryptic pockets" have been studied and exploited so that now the first drugs binding to cryptic pockets are on the market.

The Weighted Ensemble toolkit WESTPA [1] allows for automated simulation of these slow and rare pocket opening events in reasonable time scales to identify potential cryptic pockets. Integration of WESTPA into OpenEye's cloud-native computing platform ORION provides the scalability for parallel computing that is needed to run, detect and classify such cryptic pockets through embarrassingly parallel simulations. We will use the GTPase KRAS protein as example how one can identify cryptic pockets in proteins that were thought to be undruggable.[2]

[1] J. Russo et al., *J. Chem. Theory Comput.* **2022**, 18, 638-649
[2] N. Vithani et al., *J. Chem. Inf. Mod.,* **2024**, 64(21), 8258–8273.

Probing DNA Conformation: A Multi-Technique Approach

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[2] *Computer-Chemistry-Center and Interdisciplinary Center for Molecular Materials, Department of Chemistry and Pharmacy, Friedrich-Alexander-Universität Erlangen-Nürnberg, Nägelsbachstr. 25, 91052 Erlangen, Germany*

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[4] *Chemistry Branch, Department of Science and Mathematics, Faculty of Petroleum and Mining Engineering, Suez University, Suez 43721, Egypt*

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The determination of distances between specific points in nucleic acids is essential to understanding their behaviour at the molecular level. The ability to measure distances of 2–10 nm is particularly important: deformations arising from protein binding commonly fall within this range, but the reliable measurement of such distances for a conformational ensemble remains a significant challenge. We show that MD simulations are a robust tool to interpret electron paramagnetic resonance (EPR) measurements of oligonucleotides spin-labelled with triazole-appended nitroxides at the 2' position. For two nitroxide spin-labels attached to B-form DNA duplexes, we present results from EPR spectroscopy, MD simulations, X-ray crystallography, and NMR spectroscopy. These four methods are mutually supportive and pinpoint the locations of the spin labels on the duplexes. In doing so, this work establishes 2'-alkynyl nitroxide spin-labelling as a minimally perturbing method for probing DNA conformation.

[1] J. S. Hardwick, M. M. Haugland, A. H. El-Sagheer, D. Ptchelkine, F. R. Beierlein, A. N. Lane, T. Brown, J. E. Lovett, E. A. Anderson, *Nucleic Acids Res.* **2020**, *48*, 2830-2840. (DOI: 10.1093/nar/gkaa086)
[2] M. M. Haugland, A. H. El-Sagheer, R. J. Porter, J. Pena, T. Brown, E. A. Anderson, J. E. Lovett, *J. Am. Chem. Soc.* **2016**, *138,* 9069-9072. (DOI: 10.1021/jacs.6b05421)

Machine Learning in Predicting Electronic Absorption Properties of Molecules and Materials

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Predicting the excited state properties, such as the HOMO-LUMO or band gaps as well as absorption spectra for materials and molecules using machine learning (ML) models have gained attention from the researchers across the world [1–5]. ML models can help in predicting the local minimum in potential energy landscape, excited properties of materials and molecules in more faster and acccurate way [6,7]. ML applications in this field are broad, with one major branch dedicated to predicting quantum chemistry-level properties from molecular and material structures. A key research direction focuses on the prediction of primary, secondary, and tertiary properties. Primary properties, such as the Hamiltonian and charge density, form the basis for deriving secondary properties, including physical observables like energies, band gaps, and dipole moments. Tertiary properties, particularly in spectroscopy, include computed spectra such as absorption spectra, obtained from transition dipole moments and vertical transition energies.

While numerous studies have investigated ML-based prediction of tertiary properties, a comprehensive assessment of model effectiveness and optimal input representations remains an open challenge. This poster presents a literature overview of existing ML approaches for predicting tertiary properties, exploring different model architectures, feature representations for molecules and materials, and recent advancements in the field. Finally, we highlight current trends, key challenges, and future opportunities in leveraging ML for direct property prediction in computational chemistry.

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Molecular Case Studies of GALC Mutations Causing Krabbe Disease

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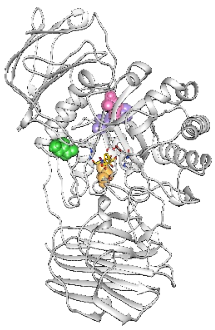
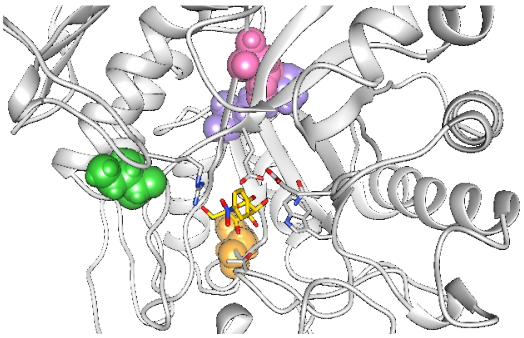
Globoid cell leukodystrophy, also known as Krabbe disease, [1] is a rare lysosomal disorder affecting the white matter of the central and peripheral nervous system. It is characterized by neurodegeneration and the most common form being infantile Krabbe cases, thus is usually diagnosed within the first year of life and with high morbidity and mortality. This autosomal recessive disease is caused by mutations in the GALC gene, which encodes the lysosomal enzyme galactocerebrosidase. [2] This study focuses on examining the structural effects of galactocerebrosidase variants found as mutations in the GALC gene of patients with Krabbe disease.





To investigate the effects of these mutations on protein structure, a structural model of human galactocerebrosidase was build. This model served as the basis for a series of all-atom molecular dynamics (MD) simulations to analyze the structural stability of the wild type and the mutated enzyme variants. Since galactocerebrosidase is subcellularly localized in the lysosome (pH 4.5-5.5), MD simulations were performed with protonation states corresponding to pH 4.5.

Differences in protein flexibility and intramolecular interactions between the wild type and the mutated enzymes were observed. Similarly, we detected effects of the mutations on the size of the substrate binding pocket, although the mutation site itself is not part of the active site/binding site of the enzyme.

Overall, our MD simulations shed light on how these mutations affect the structure of human galactocerebrosidase in the lysosome and they offer possible explanations as to why these mutations have an effect on enzyme function.

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A Multiscale MD-QM/MM Approach for Modeling Fracture Behavior in Epoxy Resins

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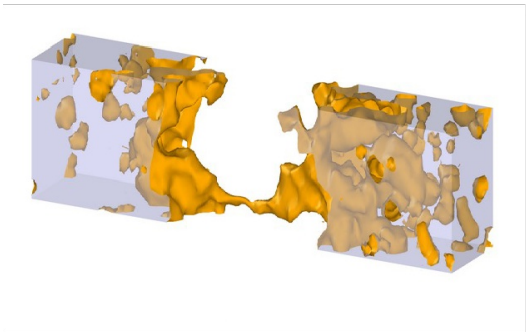
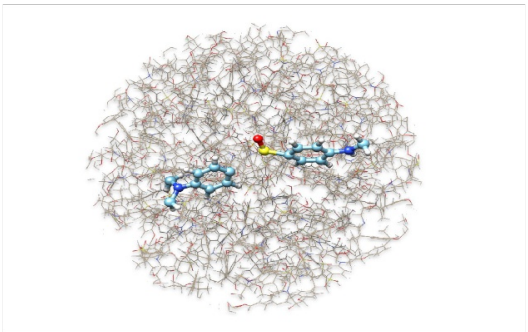
Epoxy resins are essential in advanced engineering applications due to their superior mechanical properties. However, predicting their fracture behavior at the molecular level remains challenging. This study introduces a multiscale framework that integrates molecular dynamics (MD) simulations with quantum mechanics/molecular mechanics (QM/MM) calculations, specifically employing the ONIOM method[1], to examine bond rupture and crack propagation in epoxy networks subjected to tensile straining. This approach leverages MD to capture the overall mechanical response of the material, while transitioning to QM/MM to accurately describe the inherently quantum mechanical nature of bond breaking. The framework utilizes spin density as a quantum mechanical criterion for bond breakage, where many previous approaches have relied solely on geometric distance criteria.





The MD simulations monitor strain accumulation and identify bonds that have elongated beyond critical thresholds, indicating impending fracture. Upon reaching these thresholds, the simulation transitions to QM/MM calculations. In this phase, bond breakage is dynamically assessed using the spin density, while explicitly considering long-range interactions and charge distributions within the surrounding chemical environment. This approach necessitates updating the molecular topology and recalculating partial atomic charges to accurately represent the evolving chemical structure during fracture events. Our method employs the block chemistry approach[2] to maintain charge-neutrality and ensure a chemically accurate representation of fractured sites. This on-the-fly methodology enables efficient and precise modeling of fracture events and their impact on larger-scale material behavior, providing a foundation for future studies of epoxy resin failure mechanisms.

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[2] M. Livraghi, S. Pahi, P. Nowakowski, D. M. Smith, C. R. Wick, A.-S. Smith, J. Phys. Chem. B, 2023, 127, 7648–7662.

Computational Investigation of Gas Pollutants Adsorption on Copper Squarate

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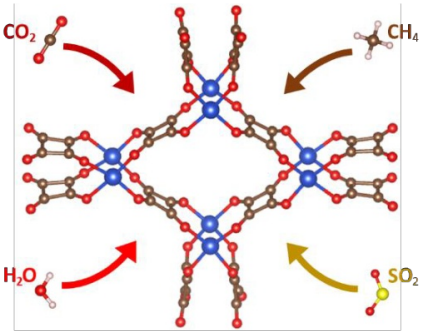

Copper squarate is a metal-organic framework (MOF) that is recognized for its potential in adsorbing gas pollutants due to its porous structure [1-3]. This study explores the adsorption of CO_2, CH_4, SO_2, and H_2O by copper squarate using density functional theory (DFT) calculations performed with the TURBOMOLE program. Following approaches [4] for other MOFs, we explore cluster representations of copper squarate. The structures of different cluster models with and without adsorbed pollutants were optimized, followed by frequency calculations to confirm their stability. Adsorption energies were then computed to assess the interaction strength, alongside an analysis of the adsorption nature. Our findings offer valuable insights into the adsorption behavior of copper squarate and pave the way for more advanced simulations, such as IR spectra and the temperature dependence of adsorption and desorption. These advancements are crucial for enhancing pollutant capture and demonstrating its potential for gas separation in environmental applications.

[1] C. Adjal, N. Guechtouli, V. Timón, F. Colmenero, D. Hammoutène, *Molecules*, **2024**, *29*, 3140.
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Influence of Ligand Modifications on Catalyst Positioning in Supported Ionic Liquid Phase (SILP) Systems

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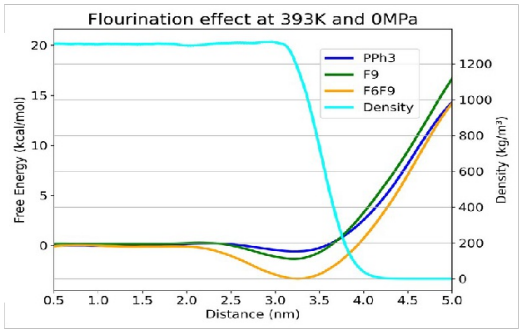
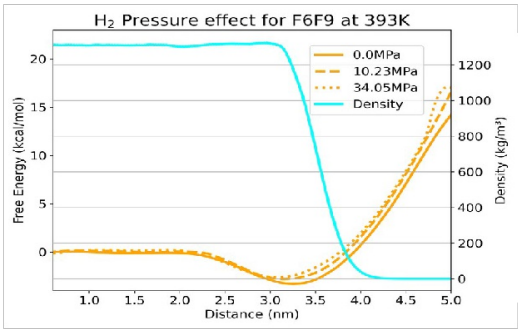
Supported Ionic Liquid Phase (SILP) catalysis utilizes a thin film of ionic liquid (IL) containing a homogeneous catalyst and is widely applied in hydrogen-involved catalytic systems. Understanding the interfacial behavior of the catalyst under reaction conditions is crucial for optimizing performance. Our study investigates how ligand modifications and interface dynamics influence catalyst positioning at IL/gas interfaces in the presence of a reactant gas. We selected Wilkinson's catalyst, a well-known hydrogenation catalyst, and H_2, the key reactant in hydrogenation reactions, for this study.

We performed Molecular Dynamics (MD) simulations on mixtures of [BMIM][NTf_2] and Wilkinson's catalyst (represented as PPh_3) or its two derivatives flourinated to different degrees (represented as F9 and F6F9) under pressurized H_2 across varying temperatures and pressures. The influence of H_2 on interfacial properties, and the impact of fluorinated ligands in enhancing catalyst surface affinity were examined. To further explore the local solvation environment of the catalyst, we conducted a 3D density analysis of atomic distributions within a defined spatial region around Rhodium (Rh), revealing preferential accumulation of ions of the IL and gas molecules.





Our findings indicate mild surface enrichment of H_2, which decreases with increasing pressure and temperature, mirroring trends in IL surface tension.[1,2] The increase in the degree of fluorination of the ligands enhances the surface affinity of the catalyst, as evidenced by computed potential of mean force (PMF) profiles depicted above, and the corresponding free energy gain upon surface accumulation. Specifically, the fluorinated catalyst (F6F9) exhibited a four-fold increase in surface affinity compared to its unmodified counterpart, Wilkinson's catalyst (PPh_3). To understand the molecular origin of this design, we analyze in detail the non-homogeneous environment of the catalysts in the bulk liquid and at the interface. The obtained insights highlight how interfacial modifications and ligand engineering can enhance the surface enrichment of the catalyst, potentially improving the performance of SILP catalytic systems.

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DOI: 10.1016/j.molliq.2023.122388

A comparative molecular dynamics study of bovine antibodies

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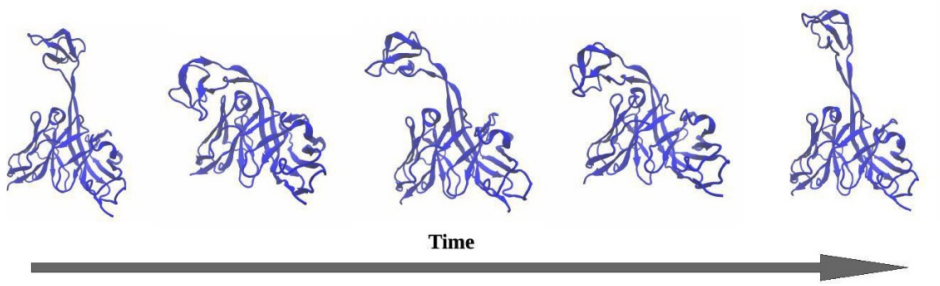

Antibodies are indispensable elements of the adaptive immune system in vertebrates, characterized by their extensive diversity, which enables them to recognize a wide array of antigens. Conventional antibodies are composed of heavy and light chains, each with constant and variable domains. The variable domains, particularly the complementarity-determining regions (CDRs), play a crucial role in antigen recognition. Among these, cow antibodies (CABs) with ultralong CDRH3 regions have shown exceptional ability in binding cryptic viral epitopes, positioning them as promising candidates for antiviral applications [1, 2].

Crystal structures of CABs showed that the ultralong CDRH3s form an elongated stalk and a globular knob at the distal ends of the stalk thus conveying the picture of a rather rigid core-stalk-knob arrangement. However, this finding is questioned by the presence of extensive crystal packing. To gain insight into the dynamics of CABs, we have therefore performed a large-scale comparative molecular dynamics study that included 19 unique CAB structures.

Our data shows that all CABs exhibit high flexibility of their knob domains as exemplified above for CAB BLV1H12 (PDB:4K3D [3]). However, we noted significant differences in the degree of flexibility, the observed knob orientations, and the frequency of the motions. In this context, interactions between the knob of the CDRH3 and the light chain of the CAB seem to play an important role for the stabilizations of distinct knob orientations.

These insights into ultralong CDRH3 antibodies could significantly enhance immunization strategies and antibody engineering, further elucidating their role in the bovine immune response and paving the way for novel antiviral therapies. This work not only underscores the unique capabilities of bovine antibodies but also provides a foundation for future research into their applications across different medical challenges.

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Impact of reduction, oxidation and ligand modification on the physicochemical properties of magic gold nanoclusters.

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In this work, we elucidate the impact of reduction and oxidation (red/ox) on the physicochemical properties of different thiolated gold nanoclusters (NC) of type $[Au_{25}(C_nH_m)_{18}]^x$ (with x=-1,0,+1) in two molecular solvents. Gold NCs have gained growing interest as building blocks for nano-clustered materials and devices due to their size specific geometry, symmetry and extraordinary high stability[1,2]. In e.g. the smallest cluster $Au_{25}(CH_3)_{18}$ an icosahedral core consisting of Au_{13} is protected by six V-shaped motifs [-S-Au-S-Au-S]. In our study, we decorate each thiolate atoms with alkyl chains of increasing length from C_4H_9, C_5H_{11} to C_6H_{13} and investigate the gas-phase and liquid properties of electro neutral, single reduced and oxidized species. It is expected that the ligand length affects the separation of the gold NCs due to different interaction strength between the ligands and the surface of HPLC column, however the influence of red/ox states of the gold NC is less studied.

Experimentally, the stability of gold NC upon ionization and reduction was proven and $[Au_{25}(CH_3)_{18}]^x$ can be obtained in the red/ox states x= -1,0 to +1. To understand the charge distribution along the NC and ligands, we conducted DFT calculations and parametrized a force field to enable the investigation of bulk and transport properties via Molecular Dynamics simulations.

We observed that the actual red/ox state has minor impact on the structural behavior of the different magic gold NCs and only the Au core is participating in the red/ox reactions. However, we observed significant charges of the liquid properties upon ligand modifications.

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Mining Macromolecular Binding Interfaces

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Protein-protein interactions (PPIs) are crucial for physiological processes and their modulation is of interest for studying signaling pathways and pharmacological research.[1] However, methods for mining interfaces between protein chains are sparse and often heavily sequence-dependent.

By mining macromolecular databases, we can extract valuable knowledge from available structures of biologically relevant protein-protein interfaces. The number of known physical interfaces was estimated to be more than 100,000 in 2014, already.[2] Protein-protein docking to predict the structure of protein-protein complexes is computationally expensive and heavily relies on prior knowledge of the potential interaction partners. Thus, the development of reliable PPI comparison tools is key to supporting protein-protein complex prediction by detecting potential interaction partners.

In this poster, we present PiMine [3] – a method for comparing predicted or known interfaces to biologically relevant interfaces [4] in individual databases of protein complexes and its performance in comparison to commonly applied methods. It relies on the comprehensive GeoMine [5] database and mining system. We will introduce retrospective and prospective application scenarios for predicting protein-protein complexes with PiMine. Furthermore, we will give a perspective on the method's potential to predict host-pathogen interactions based on AlphaFold2 models of global health proteomes.[5]

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Computational Studies on Ion Pairing and Hydrogen Bonding

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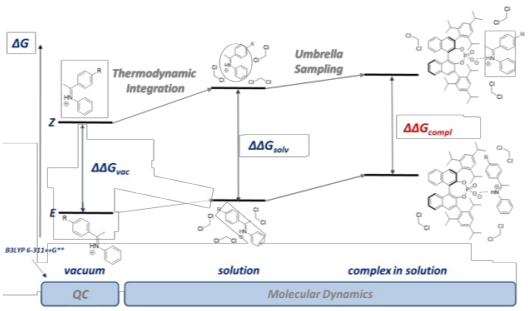
University of Regensburg



Quantum chemical calculations of the enantioselectivity in the transfer hydrogenation of imines in dichloromethane catalyzed by BINOL phosphoric acids showed poor performance.

Here we present a thermodynamic cycle that predicts the enantioselectivity using a combination of quantum chemistry and QUBEKit (Quantum mechanical Bespoke Kit) force field molecular dynamics simulations. [1] This combined QC/MD approach results in better agreement with experimental data for two selected imines. Details of the force field development are presented.

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Assessing the dynamics of hemithioindigo-based photoswitches using multi-state molecular mechanics

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In the realm of nanotechnology and molecular engineering, photoswitches play a key role as structural elements converting light into mechanical work. In particular, switchable chromophores embedded in complex molecular environments – such as molecular machines and self-assembled monolayers on surfaces – offer unique opportunities for the precise control of material properties and molecular motion. [1] A relatively new but emerging class of photoswitches is based on hemithioindigo (HTI) chromophores, which feature high thermal bistability, bright absorption bands in the visible region of the electromagnetic spectrum, and chemical durability. Upon photon absorption, HTIs readily undergo double bond isomerization, resulting in the formation of either *Z*- or *E*-isomers. By using HTI photoswitches as core structures, future photoresponsive (nano-)devices are accessible via HTI functionalization to tailor the light-induced motion, aggregation, and self-assembly on substrate surfaces. [2]

Excited state dynamics simulations are powerful tools to investigate the photoinduced processes in individual photoswitchable molecules [4-6]. However, in most light-responsive devices, the motion of the photoswitch is strongly coupled to a complex environment – e.g. explicit solvent shells or ensembles of photoswitches – requiring an atomistic treatment of 1000s of molecules paired with ns-scale dynamics. While this presents a significant challenge for fully *ab initio* treatment, an approximate approach, as suggested by Duchstein et al. for azobenzene chromophores, involves multiple molecular mechanics models, each describing a separate electronic state under consideration. [3] Here, we present an adaption of this methodology to the widely employed HTI chromophors. For this, we revisit the static theoretical description of the excited states of HTI [7-8] using high-level multireference calculations and investigate the role of the triplet state in *E-Z* (photo-) isomerization. The multi-state molecular mechanics are demonstrated for the exemplary case of photoswitching on the first triplet (T_1) surface applying dynamics in different explicit solvation environments and gaining atomic-scale insight into energetic and kinetic effects.

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The effect of somatic mutations in the voltage-gated proton channel hHV1 from molecular simulations

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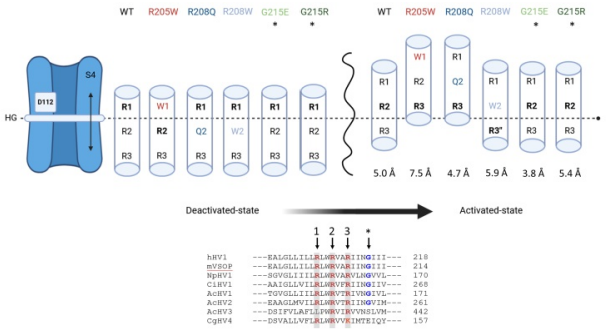

Somatic mutations are common in cancer, with only a few driving progression of the disease, while most are silent passengers. Some mutations may hinder or even reverse cancer progression. The voltage-gated proton channel (H_V1) plays a key role in cellular pH homeostasis and shows increased expression in several malignancies. Inhibiting H_V1 in cancer cells reduces invasion, migration, proton extrusion, and pH recovery, impacting tumor progression. Focusing on HVCN1, the gene coding for human H_V1 (hH_V1), we identified 197 mutations essentially clustered in two hotspots: the central region of the N-terminus and the region coding for the S4 transmembrane domain, which contains the channel's voltage sensor. We selected five mutations within the S4 segment (R205W, R208W, R208Q, G215E, and G215R) for electrophysiological analysis and MD simulations. Our findings reveal that while all mutants remain proton-selective, they all exhibit reduced effective charge displacement and proton conduction. The mutations differentially affect hH_V1 kinetics, with the most pronounced effects observed in the two Arg-to-Trp substitutions. Mutation of the first voltage-sensing arginine (R1) to tryptophan (R205W) causes proton leakage in the closed state, accelerates channel activation, and diminishes the voltage dependence of gating. Except for R205W, the mutations promote the deactivated channel configuration. Altogether, our findings are consistent with impairment of hH_V1's function by mutations in the S4 transmembrane segment, potentially affecting pH homeostasis of tumor cells. This work has been published recently [1].

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Simulating Pressure on Molecules in Implicit Solvation Environments with the X-HCFF and GOSTSHYP methods

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The investigation of molecular properties under pressure in the gigapascal regime is significant for gaining a deeper understanding of materials under extreme circumstances. Theoretical methods are required to supplement experimental data because the latter can only provide indirect information about pressure-induced changes at the molecular level. Both combined allow complete insight into the effects of pressure on molecular systems. [1]

In this context, it is essential to consider the chemical surrounding of the desired molecular system. However, the simulation of pressure applied to liquid-phase compounds is far from straightforward. As a first approach to implicitly include solvent effects in pressure simulations, the pressure models eXtended Hydrostatic Compression Force Field (X-HCFF) [2] and Gaussians On Surface Tesserae Simulate HYdrostatic Pressure (GOSTSHYP) [3] were used together with the Conductor-like Polarizable Continuum Model (C-PCM). [4, 5] All of these methods require discretized molecular surfaces for their functionality. In previous implementations of X-HCFF and GOSTSHYP, the combination of these pressure models with C-PCM led to instabilities in the quantum chemical software Q-CHEM [6] due to simultaneous usage of the discretization routine. Therefore, an independent way of discretizing and handling molecular surfaces for X-HCFF and GOSTSHYP is introduced, enabling a stable way to include implicit solvent effects in high-pressure simulations.

To investigate the effects of implicit solvation on molecules, those that can occur in a zwitterionic and a neutral state are of special interest. For glycine and sulfamic acid, it could be shown that high pressure applied with the GOSTSHYP model tends to stabilize the solvated zwitterionic state of the compounds in an aqueous environment. Additionally, intramolecular proton transfers at high pressure could be identified for some compounds.

The improved way of handling molecular surfaces in the pressure models also allows the straightforward implementation of new surface grid methods. Vibrational frequency calculations under pressure could benefit from being performed with a static surface grid. This could allow a better reproduction of pressure-induced red shifts of selective modes in experimental vibrational spectra. A corresponding implementation is currently in progress.

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Computing Molecular Excited States and Spectra with Neural-Network-Supported Configuration Interaction

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Our newly developed Python library for selective configuration interaction (CI) calculations of fermionic quantum systems, SOLAX [1], is applied to compute the ground and excited electronic states of molecules. We employ a novel state-specific CI approach, where the Hartree-Fock reference is obtained by variationally optimizing the orbitals for a specific excited state in a plane-wave representation [3]. Both full CI and selective CI calculations are performed, the latter using a recently proposed Neural-Network Supported CI approach (NNCI) [2]. The performance of the method is assessed by analysing the expansion of the many-body states in the Slater determinant basis and the distribution of relevant configurations. Preliminary calculations on Rydberg excited states of the H_2, N_2, and NH_3 molecules indicate that variationally optimizing the orbitals for the excited state not only improves mean-field solutions [3] but also improves the efficiency of the CI calculations, as accurate results are achieved with fewer relevant determinants compared to calculations using ground state optimized orbitals. Additionally, we present a newly implemented SOLAX algorithm to compute spectral functions within the NNCI scheme without the need for an explicit calculation of excited eigenstates and show how our methodology bridges the interdisciplinary gap between quantum chemistry and theoretical solid state physics.

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Exploring the influence of electron donor and acceptor substituents on photochemical properties of a light-driven molecular nanomotor

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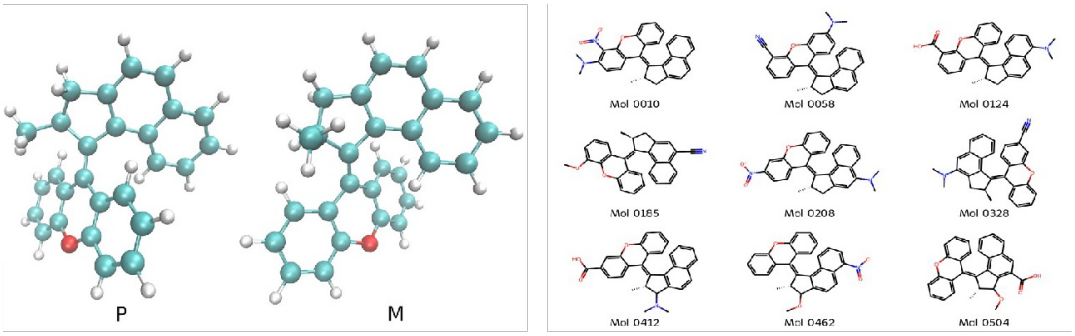
Universität Regensburg



We report an analysis of the impact of the molecular structure on the photochemical excited state properties of a comprehensive dataset of 2016 compounds based on the structure of a second-generation light-driven molecular nanomotor. [1,2] The two main helical conformers of the base structure were modified with all combinations of one electron donor and one acceptor group from a pool of three each on eight possible positions. We performed ground state geometry optimizations and excited-state calculations using time-dependent density functional theory to obtain the excitation energies, oscillator strengths and two photon absorption strengths of the first two excited states. [3] To identify the reactive state, transition densities were calculated and compared with the unsubstituted nanomotors. Further, a benchmark study of three machine learning models and three molecular descriptors was performed to accelerate the identification of promising candidates for future applications in living tissue without the need for expensive quantum mechanical calculations.

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Towards automated exploration of enzymatic reactions

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Mapping out a reaction mechanism involves optimizing the reactants and products, finding the transition state and following the reaction path connecting them. Enzymes, however, consist of several thousand atoms, and about one order of magnitude more electrons, a system size that is not easily tractable. Modelling enzymatic pathways is challenging because of the complexity of the system. The numerous degrees of freedom in an enzymatic system, out of which many can be relevant for the reaction and its energetic profile, at least indirectly, render the notion of "the reaction mechanism" naïve. Instead many reaction pathways are conceivable, which might be different conceptually such as a dissociative vs. an associative pathway. One approach to overcome previous difficulties is to use transition network approach to sample conformational transitions in proteins, to explore enzymatic reaction pathways [1].

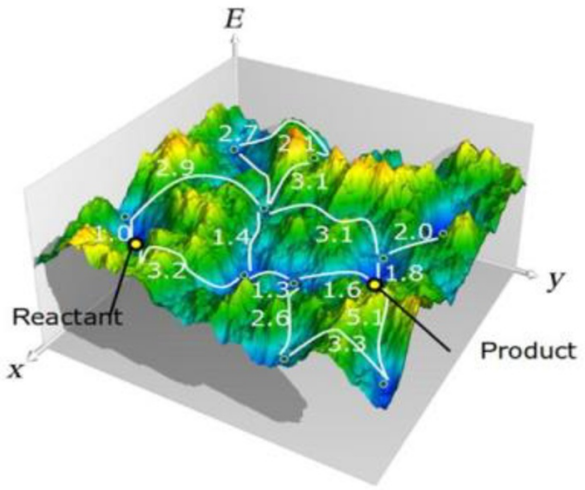

Figure: Schematic energy landscape with "valleys" (blue) and "mountains" (yellow/orange). Yellow points mark end states and green dots are intermediate states. White connections with transition barriers indicate a variety of possible pathways. Figure is taken from [1]

Carboxypeptidase A (CPA) an exopeptidase secreted by the pancreas which catalyzes the elimination of the C-terminal amino acid via hydrolysis, with a preference toward residues with hydrophobic side chains [2]. CPA occupies a special place in enzymology as the third enzyme whose three dimensional structure was determined with hight resolution by X-ray diffraction. Despite the abundance of structural information, however, there are still controversies concerning its catalytic mechanism.

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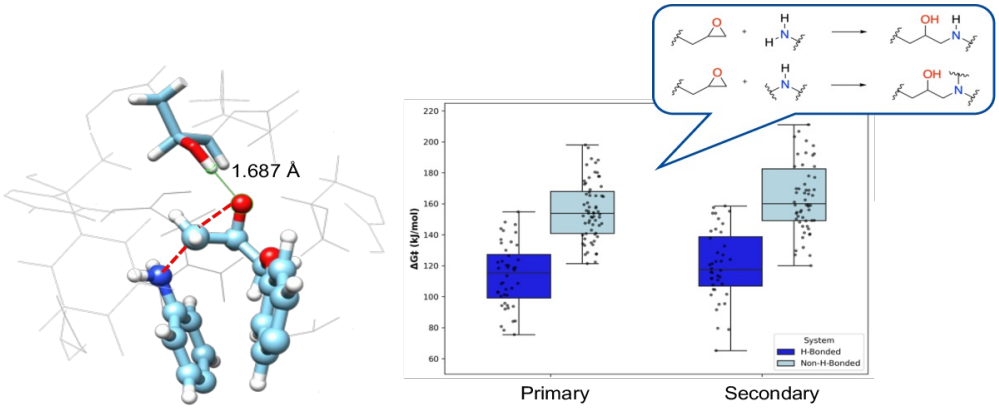
What is the impact of covalent-network formation on the curing kinetics of thermosets?

•SAMPANNA PAHI[1], CHRISTIAN WICK[1,2], and ANA SUNČANA SMITH[1,2,3] — [1]PULS Group, Institute for Theoretical Physics, FAU Erlangen-Nürnberg, Germany — [2]Group of Computational Life Sciences, Division of Physical Chemistry, Ruđer Bošković Institute, Zagreb, Croatia — [3]Competence Unit for Scientific Computing (CSC), FAU, 91058 Erlangen, Germany



In this work, we used a combination of reactive molecular dynamics and QM/MM modelling to fully understand the impact of the local network structure on the kinetics of the curing reaction of thermosets on the atomistic scale. Thermosets are covalently cross-linked glassy network materials, which are widely applied in e.g. airplane construction, as flooring materials or in the renewable energy sector. The attractive mechanochemical properties of thermosetting polymers are strongly coupled to the chemical formation of a covalent network, which happens in the so-called curing reaction of the material. During curing, typically a liquid mixture is converted into a glassy polymeric material in a highly exothermic process. However, the curing kinetics of the individual chemical reaction is strongly dependent on the local environment of the reactive sites, which we expect to strongly depend on the degree of cross-linking. Using a DGEBA/DDS based epoxy example system, we investigated the differences in the curing kinetics starting from isolated gas-phase systems to micro-solvated systems using different continuum approaches. We find that the curing reaction is strongly depended on the reaction geometry and can be facilitated by hydrogen bonding interactions on both the amine and the epoxy sites. However, while such simplified models do qualitatively reflect experimentally observed reaction energetics, they cannot elucidate the effect of the evolving network structure on the reaction mechanism during curing. Therefore, we increase the model complexity by sequentially coupling reactive molecular dynamics simulations [1] to QM/MM transition state (TS) analyses, which allows us to investigate mechanisms and energetic barriers during in silico curing of epoxy thermosets. Our findings underline the importance of hydrogen bonding, which generally lowers the activation energy, though its effect strongly depends on bond type and reactive site. When hydrogen bonds are present on both reactive sites (N and O), the activation energy is significantly reduced, approaching experimental values (70 kJ/mol vs. 50 kJ/mol). Hydroxyl (OH) bonding at the epoxy oxygen (O) and sulfonyl (SO) bonding with amine (N-H) led to the lowest activation barriers, highlighting their critical role in reaction kinetics. Finally, our methodology will allow us to investigate the curing kinetics as a function of the curing degree and observe the influence of the emerging network structure on the curing reaction.

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What is the role of puckering in the thermal ratcheting steps of HTI based molecular motors?

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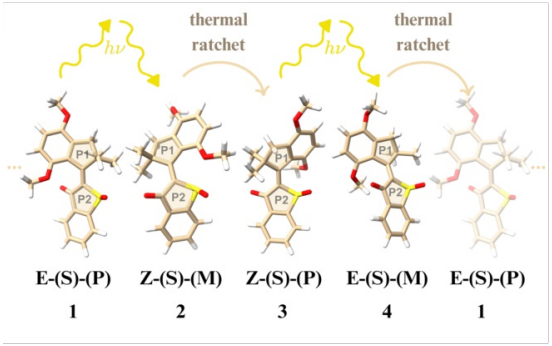
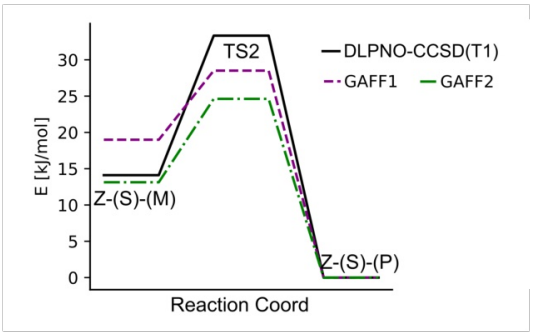
In this contribution, we will employ a combination of classical molecular dynamics simulations and static high-level ab initio calculations to elucidate the role of puckering in the ratcheting mechanism of Hemithioindigoid (HTI)-based molecular motors. HTI based molecular motors are small molecular machines, which utilize visible light to power directional thermal rotations of a small molecular rotor substructure relative to a so-called stator part. The thermal rotations are typically known as thermal ratcheting steps and involve a local unidirectional helix inversion, while the HTI chromophore allows E to Z photoisomerization with nondamaging visible light.[1]





In preliminary calculations, we observed that the motor states 1 to 4 all exhibit distinguished puckering conformations, which are likely induced due to steric effects of the methoxy and methyl substituents. In this work, we further investigate the role of puckering in the full thermal ratcheting mechanism with a combination of static ab initio calculations and molecular mechanics based MD simulations. Using geometric criteria obtained from NEB calculations and steered Molecular Dynamics Simulations, we identify the collective variables that are key to understanding the reaction mechanism of the thermal ratcheting steps. Finally, we perform 1 and 2 dimensional umbrella sampling in dichloromethane to unravel the energetic and geometric factors that underly the thermal ratcheting mechanism.

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ManifoldX: A Parallel Wrapper for FoldX with Integrated Structure Preprocessing

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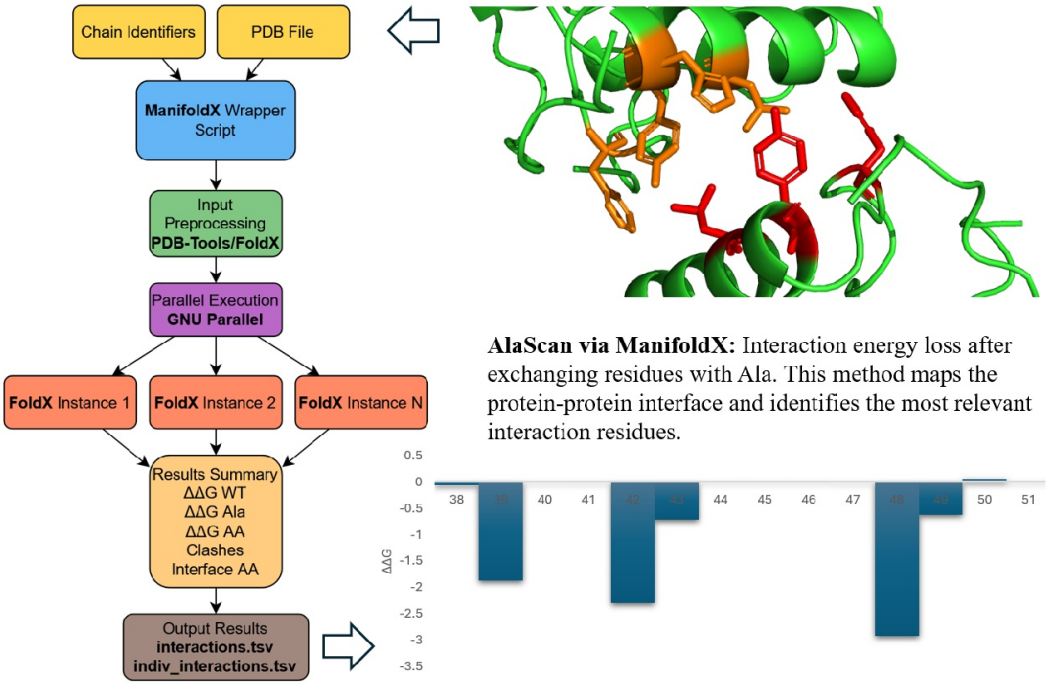
We introduce **ManifoldX**[1], a pipeline that wraps the FoldX[2] software to enhance its performance and usability. ManifoldX supports FoldX workflows such as *in silico* alanine (Ala) scanning[3] and comprehensive 20 amino acid (20AA) substitution scans, facilitating free energy (ΔΔG) interaction mapping and stability analysis for static protein-protein complexes. By providing FoldX with a scalable wrapper suitable for high-performance computing (HPC) and incorporating quality control (QC) features, ManifoldX substantially improves processing speed and simplifies workflows.

ManifoldX enables parallel computing through multithreading, significantly accelerating large-scale protein stability and interaction analyses. Additionally, it features integrated input file preprocessing, automating the preparation and formatting of input data to ensure compatibility with FoldX to minimise manual intervention. Results are summarized as automated reports to minimise raw output data postprocessing. FoldX is freely available as academic[4] license, and we provide ManifoldX on GitHub[1] under a MIT open-source license.



AlaScan via ManifoldX: Interaction energy loss after exchanging residues with Ala. This method maps the protein-protein interface and identifies the most relevant interaction residues.

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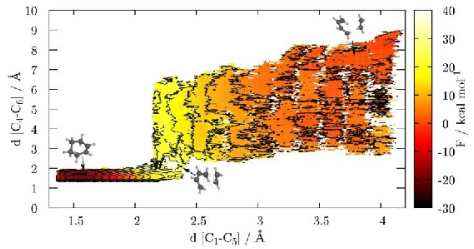
Optimizing Parameters in Metadynamics Simulations for Free Energy Calculations

Marlene Sell, Azad Kirsan, Bernd Meyer

Interdisciplinary Center for Molecular Materials
and Computer Chemistry Center, FAU Erlangen-Nürnberg



The calculation of free energy surfaces (FES) is essential for understanding chemical reactions. Especially the free energy differences between educts, products and possible transition states, as well as the structure of the latter, allow insight into the nature of the reactions. Well-sliced metadynamics (WS-MTD) [1] is a novel method to calculate FES. It combines umbrella sampling and metadynamics in order to speed up the simulations. However, it employs several fine-tuning parameters whose exact influence on the efficiency and accuracy of the results is not yet well understood.

In this study, the FES of the reaction of 1,3-butadiene and ethylene to cyclohexene, the simplest Diels-Alder reaction, was calculated by WS-MTD. This reaction is well studied, both experimentally and theoretically, and could thus be used to compare the influence of the studied parameters. Using FES calculated with different values of the relevant parameters, the free energy differences between the educts, transition state and products were determined in the form of the activation barrier and reaction energy. These were compared to literature values from experimental and other theoretical studies.

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Solvent-controlled separation of integratively self-sorted supramolecular coordination cages

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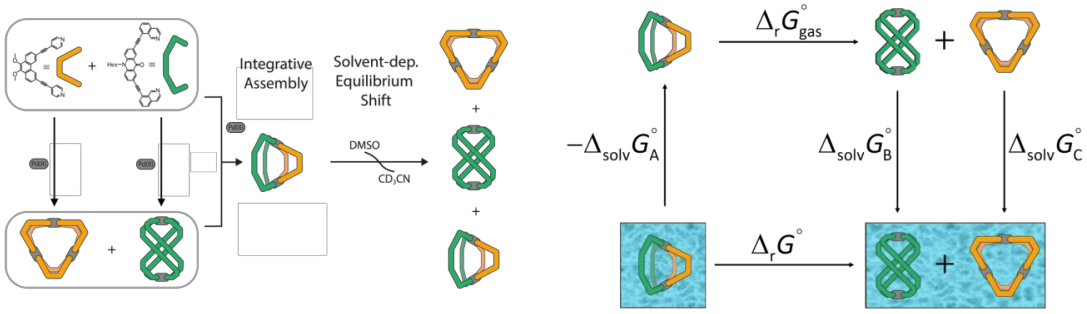
In the field of metallosupramolecular coordination cages several strategies, e.g., the method of shape complementary assembly, have been established to achieve the formation of heteroleptic cage species. [1-3] Hereby the aim is to assemble only a single complex structure of a well-defined size and shape and avoid statistical product mixtures. This goal can be realized by focusing on the cage formation reaction thermodynamics. Besides the release of strain and reduction of assembly nuclearity, the influence of solvent on the cage equilibria plays a major role which must be considered. [4-6]

We here present a joint experimental and theoretical investigation of a system of integrative self-sorting palladium cages whose equilibrium is determined by the chosen solvent. [7] While only the heteroleptic cage species forms in dimethyl sulfoxide, a mixture of the latter with two homoleptic species is observed in acetonitrile. To understand the driving force of these reactions, cage assembly thermodynamics was characterized experimentally and by calculations using liquid-state integral-equation theory. Both, a high-level quantum-mechanical (QM) approach using the embedded cluster reference interaction site model (EC-RISM), and a force field (FF) model based on the three-dimensional RISM were used to model the reaction. [8]



The joint ansatz yields deep insight into the reaction thermodynamics on a molecular level. Both the QM and FF-based methods reproduce the experimental reaction Gibbs energy well. With the RISM-based approaches, guided by an experimental van't Hoff analysis, the reaction thermodynamics could be further decomposed into energetic and entropic contributions. The results indicate that the solvation entropy is the driving force due to changes in solvent-accessible volumes of the reaction partners. A more detailed solvent-structure analysis was enabled by RISM-calculated three-dimensional and radial solvent distribution functions within and around the cages.

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Designing Transmembrane Signaling Systems in Artificial Cells using DNA Structures

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Building an artificial cell is an essential step to creating artificial life-like systems and a critical step in this endeavour is to design molecular systems which enable the communication of an artificial cell with its environment. Such artificial life-like systems hold great promise for biomedical engineering. In biomedical applications, such nanoscopic artificial life-like system will be able to, e.g., shape artificial tissues, as part of entirely novel therapeutic strategies. By mimicking biological mechanisms to enable the transmission of information from the exterior of artificial cells across membranes to their interior [1], we will contribute to creating new artificial life-like systems and gain insights to essential biological information processing mechanisms [2] and advance simulation method development [3]. In this work, we will design novel DNA-based transmembrane signaling systems using multi-scale simulations [1], [4]. DNA structures can be synthesized to function as receptors in artificial life-like systems. These DNA structures transmit signals across the membrane which mark the external boundary of artificial cellular systems. Using an atomistic molecular dynamics simulation approach, we study DNA attached to molecule of Cholesterol Tetraethylene glycol (CholTEG) in lipid membranes. In the simulations we investigate how CholTEG interacts with the membranes and how DNA-CholTEG changes local membrane structure.

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Exploring the ionomer-platinum interface in the cathode-catalyst layer of polymer electrolyte membrane fuel cells via molecular dynamics simulations

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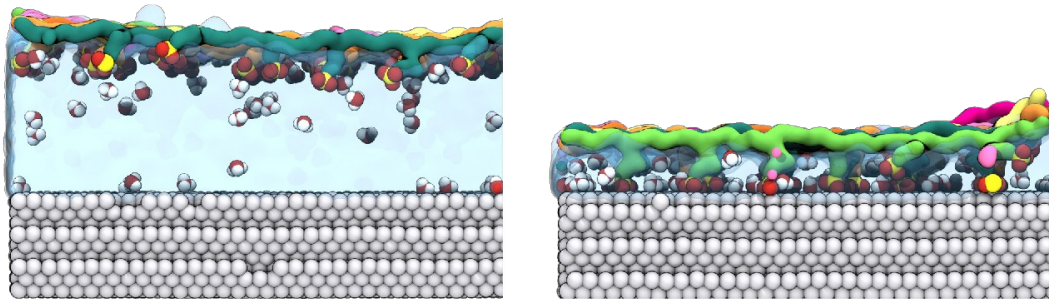
Polymer electrolyte membrane fuel cells (PEMFCs) play a vital role in establishing a sustainable hydrogen economy, making research into their performance and durability an important endeavor. For the performance of PEMFCs, the cathode-catalyst layer (CCL) plays an important role. This layer consists of a mixture of a proton-conducting ionomer phase and platinum catalyst supported on carbon substrate. At the platinum surface, the oxygen reduction reaction (ORR) takes place reducing the supplied oxygen gas to form water. The ionomer plays an important role in facilitating the transport of protons to the catalyst surface, as required for the electrochemical reaction. While most product water molecules evaporate and escape from the interface, some residual water remains and forms a water film at the ionomer-platinum interface, which impacts the transport of the ORR reactants (both oxygen and protons) and, thus, the CCL performance [1].

Currently one of the most used ionomers is Nafion, which features a perfluorinated alkane backbone. In line with current efforts to reduce usage of such molecules extensive research is performed in order to identify novel ionomers with similar or even better characteristics for usage in PEMFCs.



Using molecular dynamics simulations, we investigate the interface between Nafion and platinum to elucidate structure-function relationships and identify materials descriptors determining their performance as components in CCLs. In this study we focus our efforts on the influence of the water film that is present between the catalyst and the ionomer layer. The thickness of the water film is dependent on multiple factors such as the operating conditions, the local electrochemical environment, and hydrophilicity of the adjacent layers [1,2,3]. From our simulations of water films of varying thickness, we analyze the distributions of reactant species and orientation of water dipoles at the catalyst surface, and assess influence of the water film on the local ionomer structure and the transport of protons within the boundary layer.

These analyses provide insight into the structural and dynamical properties of CCLs at an atomistic scale. The developed workflow will guide future simulations exploring non-fluorinated ionomers as Nafion alternatives with better environmental friendliness to be used in CCLs for PEMFCs.

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Mode of Metal Ligation Governs Inhibition of Carboxypeptidase A

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Carboxypeptidase is a Zn-dependent protease that specifically recognises and hydrolyses peptides with a hydrophobic side chain at the C-terminal residue. According to hydrolysis mechanisms proposed in the literature, catalysis requires a water molecule to be close to the Zn ion so as to be activated as a nucleophile. Among small molecules that resemble the slowly hydrolysed Gly-Tyr peptide, which have been previously designed as inhibitors and characterised structurally, a variant with the terminal amino acid in a D-configuration has been the most effective. Our molecular dynamics simulations of carboxypeptidase complexed with different variants of those inhibitor ligands as well as variants of the Gly-Tyr peptide show that the strength of the inhibitory effect is not related to the binding strength of the ligand. Our data rather support an earlier notion that the inhibition is, at least partially, due to blocking a coordination site at the Zn ion by the ligand coordinating the metal ion in a bidentate fashion.

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Exploring bimodal equilibrium in MBD2 protein recognition of methylated CpG dinucleotides

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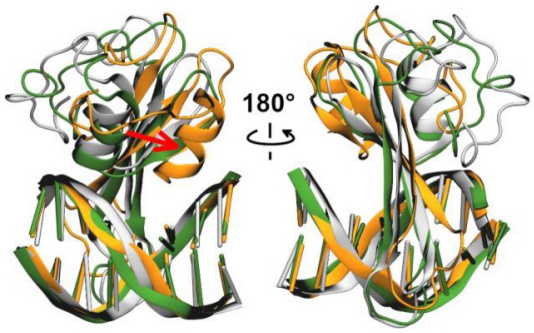
Transcription factors are proteins that regulate gene expression by binding to sequence-specific DNA target sites. The search mechanism for finding this target site can be explained by the model of facilitated diffusion, where the protein switches from three-dimensional diffusion in bulk solution to a one-dimensional sliding motion along the DNA surface [1]. While the sliding process has been studied computationally at atomistic and coarse-grained resolution, little is known about the search-to-recognition process at the atomistic level [2].

MBD2 is a transcription factor and member of the methyl-CpG binding domain (MBD) protein family that selectively recognises mCpG dinucleotides, i.e. a methylated cytosine followed by a guanine. DNA methylation is a mechanism for epigenetic regulation, meaning it affects gene expression.



We performed extensive classical MD simulations to investigate the recognition complex formation of MBD2 and mCpG DNA. When being placed one base-pair away from the specific site, MBD2 formed a stable complex at the target site on the order of microseconds. Surprisingly, RMSD clustering analysis revealed two stable conformations at the recognition site of which only one (green) resembles the original crystal structure (grey). Characterisation of these two states showed different DNA conformation as well as different hydrogen bond interactions between MBD2 and the DNA. Due to the absence of the hydrogen bond between S47 and the DNA backbone of a methylated cytosine in the secondary state, we performed additional simulations of the S47A mutant. These indeed resulted in structures that closer resemble the secondary state than the recognition state from the crystal structure. NMR experiments of our collaborators ultimately confirmed mCpG selectivity for the S47A mutant but showed also reduced binding affinity in agreement with our MD simulations. With these findings, our study illustrates that MBD2 explores a bimodal equilibrium in the process of mCpG recognition.

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Detection of pH induced structural changes in helical peptides

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[2]*Erlangen National High Performance Computing Center (NHR@FAU), Friedrich-Alexander-Universität Erlangen-Nürnberg*
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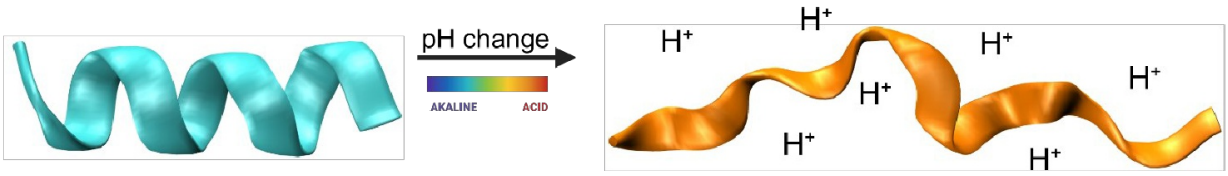

Helices are the most common structural element in proteins, which are often stabilised by interactions between oppositely charged side chains. Consequently, changes in the pH of the solvent, which cause a change in the protonation of these side chains, can lead to destabilisation of the helix, thereby affecting the structure and function of the protein. This is exploited by nature to trigger a variety of physiological processes[1], but can also lead to undesirable processes such as protein aggregation[2]. In addition, pH-dependent helix-coil transitions have the prospect of technical applications including biomaterials and engineered pH switches[3]. For the computational study of the above-mentioned processes, a correct prediction of pH-dependent effects on the structure of α-helices is of utmost importance.

To investigate whether the pH-dependent unfolding of α-helices can be adequately described by MD simulations, we have compiled a set of benchmark peptides known experimentally to undergo a pH-dependent helix-coil transition. We compared the performance of two popular AMBER force fields (ff14SB and ff19SB) with respect to their ability to reproduce the experimentally observed difference in helical content (HC). Each simulation was carried out over a time span of 1 µs and was simulated in triplicate in order to increase the reproducibility and structural convergence. Our simulations show that both ff14SB and ff19SB are able to detect pH-dependent structural changes for the benchmark peptides. However, on a quantitative level, there are distinct differences between the two force fields with respect to the change in helical content or the relative strength of polar intramolecular interactions. Finally, we investigated the performance of ff14SB and ff19SB for two peptides (O13 and O16) that have been optimised for helix stability, but the pH dependence of their stability is unknown.[4] Both force fields model a decrease in HC at acidic pH for O13. We were able to confirm these observations with circular dichroism (CD) spectroscopy measurements of in-house synthesised peptides. All simulations of O16 show a consistently high HC under different pH conditions, suggesting that O16 is stable at basic and acidic pH. Our experimental measurements corroborate these findings. Thus, our results indicate that both force fields, ff14SB and ff19SB, can be used to identify pH-dependent switches in peptides.

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NHR@FAU: Booster For Your Atomistic Simulations

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The Erlangen National High-Performance Computing Center (NHR@FAU) at FAU Erlangen-Nürnberg [1] was established in 2021 as a national center for HPC at German universities. Together with eight other institutions, it forms the NHR-Alliance [2]. NHR@FAU operates large-scale HPC systems and provides HPC services, related user support, and HPC training to members of German universities.

A strong focus of NHR@FAU lies on atomistic simulations and it also provides tailored hardware solutions in this area. As a key component of the NHR program, it offers exceptional competence and conducts extensive research in the field of atomistic simulations of molecular structures, with broad applications in chemistry, life sciences, materials science, and physics. With bundled atomistic structure simulation expertise, NHR@FAU helps users to select and use atomistic simulation methods in an HPC environment and actively accompanies and coordinates the development of high-performance simulation codes. An interdisciplinary approach promises not only synergy effects, e.g., through the exchange and joint development of simulation and evaluation tools, but in particular a cross-fertilization of materials and life sciences, which often use the same or similar simulation techniques.

The HPC research activities at NHR@FAU focus on performance engineering and modelling, performance tools, and research software engineering. NHR@FAU investigates and further develops hardware-efficient building blocks, programming concepts, and numerical algorithms for scalable, efficient, and robust iterative sparse matrix applications and stencil-based solvers on large-scale HPC systems.

A further core project is the education and lifelong training of scientists and engineers. The close cooperation among theory, simulation, and experiment, which has a long tradition in Erlangen, ensures that the training is not aimed specifically at modelers, but also made available to experimental colleagues. This is of particular importance in the light of increasing digitalization in science. NHR@FAU makes an essential contribution to the key technologies of scientific computing and scientific software development through the sustained concentration of methodological competence in both the application and development of computer codes and their hardware-related optimization.

NHR@FAU main compute clusters:

← Fritz (CPU)

Alex (GPU) →

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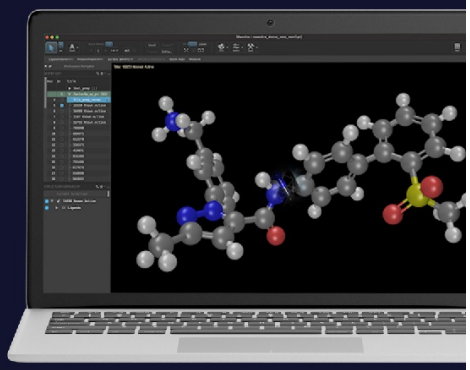
Schrödinger

A digital chemistry platform for modern drug discovery teams



Comprehensive molecular modeling solutions across the full drug discovery pipeline:

- Protein structure prediction and binding site analysis
- Comprehensive hit discovery and virtual screening workflows
- Precise property predictions for rapid lead optimization
- Solutions for small molecule and biologics drug discovery

Learn hands-on molecular modeling with Schrödinger Online Courses:
www.schrodinger.com/learn/training/schrodinger-online-learning

Request a free software evaluation:
www.schrodinger.com/request-sales-information

Boehringer Ingelheim

www.boehringer-ingelheim.com

Life forward

Our Company

Founded in 1885

Human Pharma and Animal Health Business Units

Global, research-driven company

≈ 53,500 employees

+130 markets served

Human Pharma

20,774 million EUR net sales in 2023

10.3% growth rate currency adjusted

up to **25** new molecular entity launches

Global manufacturing footprint across **12** sites

Key areas

- Oncology
- Respiratory diseases
- Mental health
- Retinal health
- Cardiovascular, renal and metabolic health (CRM)

Boehringer Ingelheim worldwide, 2023

2023 Sales

25,611 million EUR

Americas	Europe	Asia / Australia / Africa
12,206 million EUR	**8,279** million EUR	**5,129** million EUR

Our Impact

>61 million patients reached in 2023

Every minute, our pet para products treat **700** pets

520 poultry vaccinations every second

INGELVAC CIRCOFLEX® has protected **4 billion** pigs from Porcine circovirus associated disease since 2009

Animal Health

4,724 million EUR net sales in 2023

67% Companion Animals

#2 in the Animal Health industry

33% Livestock

60% Pets	7% Equine	12% Swine	8% Poultry	11% Cattle	2% VPH*

*Veterinary Public Health

Innovation & Science

5.8 billion EUR invested in Research & Development (R&D) in 2023

>150 joint projects in collaboration with more than 120 academic institutions

5 fast track
1 FDA breakthrough therapy
1 EMA PRIME designations in 2023

11,031 employees in Human Pharma R&D and Animal Health

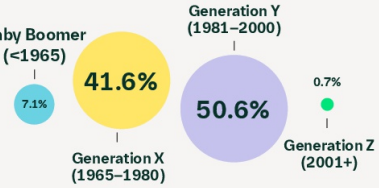
22.5% of sales

Our People

All workforce:

49.7 % Female
50.1 % Male

138 nationalities

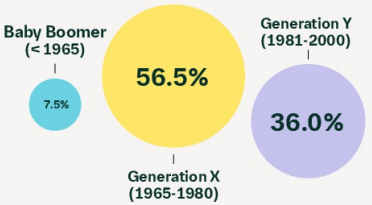


Supervisors:

Overall headcount: 8,691

40.4 % Female
59.5 % Male

81 nationalities



Making More Health

Making More Health (MMH) is a global, long-term initiative which leverages innovative social entrepreneurial solutions to improve the health of people, animals and their communities.

MMH social entrepreneurs are from 46 countries

+15 million lives impacted

+22,000 employees engaged

161 MMH social entrepreneurs supported


Roche

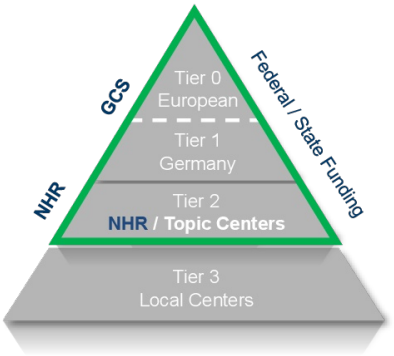
Friedrich-Alexander-Universität
Erlangen-Nürnberg

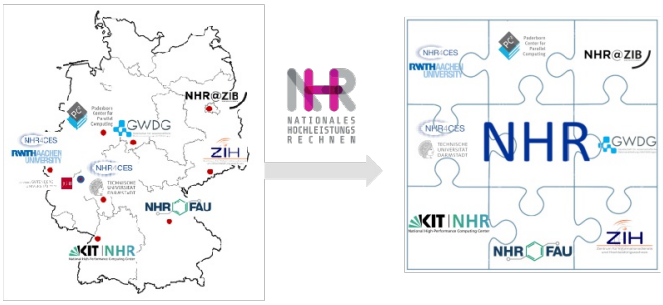
Erlangen National High Performance Computing Center
(NHR@FAU)

Martensstraße 1, 91058 Erlangen, Germany

NHR FAU

NHR (Nationales Hochleistungsrechnen) as Part of High Performance Computing in Germany





	# Nodes	Node configuration	Storage	Typical job sizes	Peak (FP64)
CPU Fritz	992 Intel ICL (71,424 cores)	2 * 36 c (8360Y) 256 GB 1 x HDR100	Shared PFS • 3.5 PB • 80 GB/s	1 – 64 nodes	5.2 PF/s
	64 Intel SPR (6656 cores)	2 * 52 c (8470) 1 TB / 2 TB	Shared PFS	---	---
GPU Alex	38 NVIDIA A100 (304 A100)	8 * A100 2 * 64 c (AMD) 1 TB 2 x HDR200	Node local 14 TB NVMe	1 – 8 GPUs	5.0 PF/s
	44 NVIDIA A40 (352 A40)	8 * A40 2 * 64 c (AMD) 0.5 TB	Node local 7 TB NVMe	1 – 8 GPUs	---

Access to NHR@FAU Resources

- Open to researchers at all German Universities – free of charge
- Peer-reviewed application process
- Simplified procedure for projects reviewed by DFG and others
- Application via JARDS central portal: **https://jards.nhr-verein.de**
- General user/project support available through NHR-centers

Application Focus

Atomistic simulations by Quantum mechanical (QM) and classical molecular dynamics (MD) methods for computational chemistry, life sciences, and materials science.
Installed **Molecular Dynamics simulation codes** (working out of the box):
Amber, Gromacs, LAMMPS, NAMD

https://doc.nhr.fau.de

For questions please send an e-mail to **hpc-support@fau.de**

INFOSHEET

OpenEye | cadence MOLECULAR SCIENCES

Accelerating Drug Discovery Through Computational Molecular Design

ROBUST SCIENCE | EXTREME SPEED | UNPRECEDENTED SCALE

Robust Science - Use physics-based design and machine learning to advance:

- Hit identification, hit-to-lead, and lead optimization
- Molecular dynamics simulations, binding free energies, and induced fit posing
- Shape and electrostatic similarities
- Membrane permeability pathway modeling
- Cryptic pocket detection
- Quantum chemistry calculations
- Antibody discovery
- Pharmaceutical formulations

Extreme Speed - Delivered the way you need, with:

- Orion's web-based cloud native modeling platform
- Desktop applications for local hardware
- Cheminformatics and modeling toolkits
- Expert consulting services and custom methods development

Unprecedented Scale - Perform extreme-scale search and screening on:

- Billions of molecules using ligand (2D/3D) and structure-based (3D) methods
- Millions of sequences from Next Generation Sequencing data
- Hundreds of thousands known and putative protein-ligand binding sites for off-target effects
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Virtual screening against billions of molecules in the Enamine REAL Database

2D ligand similarity in	3D ligand similarity in	3D ligand-protein docking in
SECONDS	**MINUTES**	**HOURS**

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SCIENCE FOR SCIENTISTS

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EMPIRE

EMPIRE is a modern, highly parallel semiempirical molecular-orbital program that can treat extremely large systems. It has been tested up to 100,000 atoms for non-periodic calculations and for repeat units in periodic calculations up to 50,000 atoms.

EH5CUBE

EH5cube reads EMPIRE .h5 files and creates Gaussian cube files containing the electron density, molecular orbitals, electrostatic potential or local properties (local ionization energy, local electron affinity or local polarization), that can be used for visualization or modeling.

PARASURF

ParaSurf uses output from a semi-empirical molecular orbital program like EMPIRE to construct molecular surfaces and calculate local properties and descriptors. The surface-based modeling techniques implemented in ParaSurf provide in silico screening, modeling and simulation techniques designed to give accurate, generally applicable predictions of biological activity, reactivity, ecological impact and ADME and physical properties.

CIMATCH

CImatch uses a genetic algorithm to overlay molecules based on the isodensity surfaces (calculated by ParaSurf), either alone or combined with a local property. It provides molecular superimposition that is independent of the 2D scaffolds of the molecules and depends only on their shape and binding properties. It is therefore ideal for QSAR applications.

WEB-BASED TOOLS

CADDLE

CADDLE is an entirely web-based molecular modeling system that offers high-quality interactive 3D-visualization combined with advanced workflows and protocols for simple modeling tasks.

SAR-CADDLE

SAR-caddle is a web-based tool for building and applying robust QSAR/QSPR models with applicability domain analysis and 3D visualization. It features Shepard interpolation, PLS and bagged stepping linear regression.

CADDLE and SAR-caddle can be used on any device equipped with a suitable web browser.

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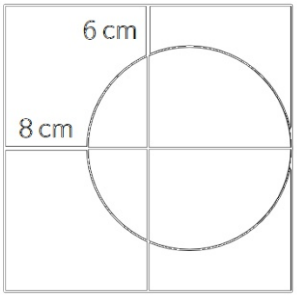
sanofi	**www.sanofi.de**
Schrödinger	**www.schrodinger.com**

MATH CHALLENGE

(www.mathe-kaenguru.de)

A large square is divided into four smaller squares. A circle within the large square touches the midpoint of the square's right edge (cf figure on the right, not to scale). How long is the edge?



IMPRINT

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