

NHR-project hbc00062:
**Adsorption of pharmaceuticals and personal care products in zeolites
studied with density functional theory calculations**

NHR Project ID:	hbc00062
NHR-Centers	NHR@ZIB, NHR-Nord@Göttingen
Run time:	I/2022 – III/2025 (initial phase + three continuation phases)
Project Leader:	PD Dr. Michael Fischer
Project Scientists:	PD Dr. Michael Fischer, Lobna Saeed, Jakob Brauer
Affiliation:	Crystallography & Geomaterials Research Group, Faculty of Geosciences, University of Bremen, 28359 Bremen; Bremen Center of Computational Materials Science and MAPEX Center for Materials and Processes, University of Bremen, 28359 Bremen

Overview

Electronic structure calculations in the framework of density functional theory (DFT) are used to investigate the interaction of selected pharmaceuticals and personal care products with zeolites. Throughout the project, focus is placed on different organic species that are important in the context of wastewater treatment (pollutant removal) or drug delivery, with separate studies investigating the adsorption of carbamazepine (an anticonvulsant medication), triclosan (a disinfectant), and 5-fluorouracil (an anticancer drug). The calculations are used to obtain a detailed understanding of the host-guest interactions and, in more recent studies, of the competitive adsorption of water, which is important in real-world scenarios. Collaborative projects done with experimental partners focus on the adsorption of organic UV filters and drug molecules in cationic zeolites.

Scientific background

Zeolites are inorganic crystalline materials whose structures are constituted by frameworks of corner-sharing TO_4 tetrahedra (where $\text{T} = \text{Si}, \text{Al}, \dots$). More than 250 zeolite framework types have been reported, with distinct topologies being assigned three-letter codes like FAU, MFI, or MOR.[1] The presence of accessible cavities or channels is a distinctive feature of zeolite structures. This intrinsic porosity is pivotal for their large-scale industrial applications in catalysis, ion exchange, and separation. Apart from these established uses, zeolites could also be employed in applications involving the adsorption of functional organic molecules. On the one hand, zeolites could find use in the adsorption-based removal of emerging organic contaminants from wastewaters. In this context, the active ingredients of pharmaceuticals and personal care products (PPCPs) have been identified as pollutants of particular concern.[2] On the other hand, zeolites could also be suitable host materials for the encapsulation of drugs or other active compounds, such as organic UVfs that are used in sunscreen lotions.[3]

With regard to the potential use in PPCP removal, highly siliceous zeolites appear as the most promising zeolitic adsorbents, as their hydrophobicity limits the co-adsorption of water.[4,5,6] Two DFT investigations carried out in the initial phases of this HLRN project focused on the adsorption of carbamazepine (CBZ) and triclosan (TCS). For both species, several structurally distinct all-silica frameworks were considered, allowing insights into the relationships between zeolite topology and affinity towards organic contaminants. The study of TCS adsorption also evaluated the impact of framework protons on the affinity towards TCS, as well as including

the co-adsorption of water. More recently, emphasis was placed on the adsorption of 5-fluorouracil (5-FU), an anticancer drug for which highly siliceous FAU-type zeolites have been proposed as carrier materials in prior experimental work.[7] In order to investigate the relationship between adsorption behavior and different features in the local structure, interactions with framework protons, which have Brønsted acidic properties, and with Lewis acidic octahedral aluminium atoms were studied.

Whereas these purely computational investigations concentrated on hydrophobic high-silica zeolites, the adsorption of functional organic molecules in low-silica aluminosilicate zeolites was studied together with experimental collaboration partners. One project, pursued in collaboration with researchers from Modena and Turin (Italy), looked at the adsorption of organic UVfs in Na-containing zeolite FAU, with emphasis on the analysis of vibrational (infrared) spectra. Another, ongoing collaboration with researchers from Poznan (Poland) addresses the adsorption of several drug molecules such as the antibiotic ciprofloxacin (CIPRO) in zeolites exchanged with different types of extra-framework cations.

Funding of this research is provided through a Heisenberg grant to PD Dr. Michael Fischer (Deutsche Forschungsgemeinschaft project no. 455871835, Fi1800/6-1). The associated PhD candidates are funded by the DFG (Jakob Brauer, DFG project no. 492604837) and by the Central Research Development Funds of the University of Bremen (Lobna Saeed).

Project results I: Hydrophobic zeolites for the removal of PPCP contaminants

A detailed DFT investigation considering eleven different all-silica frameworks revealed a large influence of the zeolite topology on the affinity towards CBZ.[P1] **Figure 1** illustrates that CBZ fits nearly perfectly into the zig-zag channels of zeolite IFR, maximizing attractive van der Waals interactions. In contrast, the adsorption in the straight channels of zeolite MOR requires a significant deformation (“flattening”) of the guest molecule, resulting in a reduced adsorption energy. Further calculations considering the adsorption of CBZ dimers showed that attractive guest-guest interactions between co-adsorbed guest molecules are usually much weaker than host-guest interactions. They may, however, become significant in zeolites with relatively spacious pores, such as FAU, where the CBZ dimers can assume an energetically optimal arrangement.

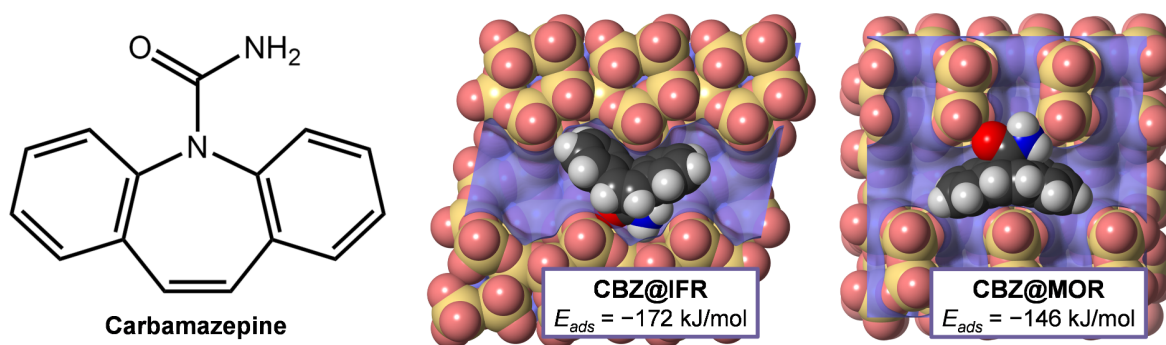


Figure 1: Left: Molecular structure of carbamazepine. Middle and right: Space-fill representation of low-energy adsorption complexes of CBZ in zeolites IFR and MOR. Insets indicate the adsorption energy, with more negative values signifying stronger interaction.

The subsequent study of TCS adsorption showed that the higher flexibility of the TCS molecule results in a less pronounced dependence of the adsorption energy on the pore shape in comparison to the more rigid CBZ.[P2] This finding underlines the key role of guest molecule rigidity/flexibility in determining the overall host-guest interaction. Calculations for TCS adsorbed in highly siliceous aluminosilicate zeolites delivered a stronger interaction compared to the all-silica counterparts, which was attributed to stabilizing hydrogen bonds involving zeolite framework protons. However, DFT-based molecular dynamics (MD) simulations

revealed that these hydrogen bonds are not stable in the presence of co-adsorbed water molecules. In fact, they are quickly broken when water molecules are present, and the TCS molecule is displaced from its initial position. It is thus clearly important to consider competitive water adsorption when investigating PPCP adsorption in systems that contain hydrophilic sites.

Project results II: Adsorption of 5-FU at different types of acid sites

Due to the continued interest in zeolites as materials for the controlled release of 5-FU, the adsorption of this anticancer drug was studied in depth using DFT calculations. A first investigation considered the adsorption in FAU-type aluminosilicates containing different numbers of framework protons within a single twelve-membered ring of TO_4 tetrahedra.[P3] With its two negatively polarized carbonyl groups, the 5-FU molecule can simultaneously interact with two framework protons (**Figure 2**), resulting in a considerable additional stabilization compared to the interaction with a single proton. However, as for TCS, DFT-based MD simulations indicated that the hydrogen bonds to framework protons are quickly broken upon interaction with co-adsorbed water molecules. It was inferred that loading of 5-FU from non-aqueous solvents and subsequent exposure to humidity in the human body could be a viable pathway to release the drug in a controlled way.

In an experimental study of 5-FU adsorption in FAU, only partial release of the drug was observed, which was tentatively explained with an irreversible binding of 5-FU to octahedrally coordinated aluminium atoms.[7] In order to investigate the adsorption at such sites, a model of FAU containing a framework-associated octahedral Al atom was constructed, and different 5-FU adsorption complexes were investigated using DFT calculations and DFT-based MD simulations.[P4] It was found that the 5-FU molecules remain bonded to the octahedral Al atom in the presence of water, in contrast to the observations made previously for the interaction with framework protons. This finding corroborates the previous assumption that the presence of octahedral Al atoms in the zeolite pores has a detrimental impact on the 5-FU release properties. A DFT-calculated infrared spectrum of FAU containing Al-coordinated 5-FU showed good agreement with experimental data, providing further evidence that the adsorption at octahedral Al sites was indeed an important process in previously investigated samples.[7]

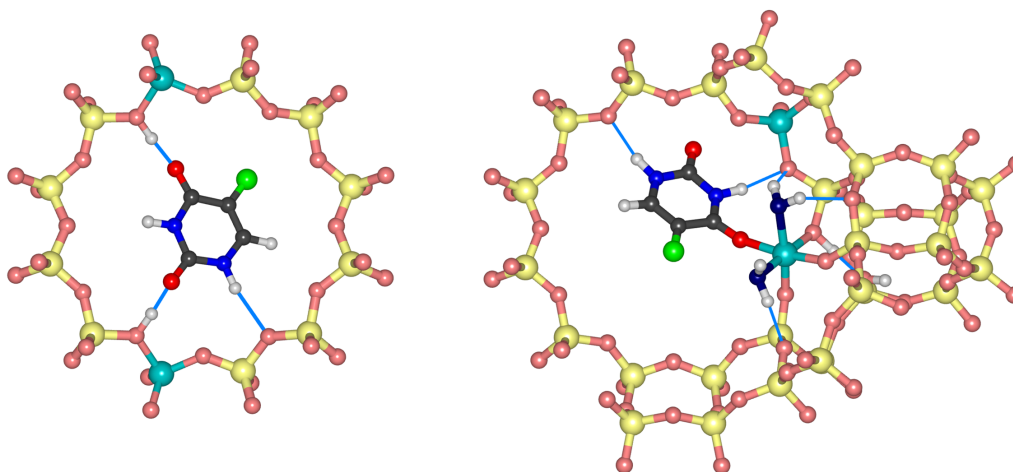


Figure 2: **Left:** “Multi-site” interaction of 5-FU with two framework protons. **Right:** Representative adsorption complex of 5-FU interacting with an octahedral aluminium site. For simplicity, both panels show only the surrounding part of the zeolite framework.

Project results III: Combining experiments and calculations to study adsorption in cationic zeolites

A comparative experimental study of a series of zeolites with different topologies, Si/Al ratios, and charge-balancing cations showed that a FAU-type zeolite X with a Si/Al ratio close to 1 that contains Na⁺ cations, dubbed NaX in the following, is a suitable material for the encapsulation of the organic UVfs octinoxate (OMC) and avobenzone.[3] The adsorption into the pores of NaX improves the stability of the organic species by preventing unwanted decomposition reactions, at the same time retaining the UV filtering ability. Due to the disorder of the UVf molecules in the pores, diffraction methods cannot provide any detailed insights into the local structure of the host-guest system. Therefore, infrared spectroscopy experiments on OMC-loaded NaX samples were combined with DFT calculations to obtain a microscopic picture of the dominant interactions.[P5] In addition to electrostatic interactions between Na⁺ cations and oxygen atoms of OMC, interactions between the cations and the OMC aromatic ring were found to play a significant role in stabilizing the adsorbed molecule. The DFT calculations also helped to understand why OMC is dominantly adsorbed in the *trans* form, which has a higher UV absorption capacity than the *cis* isomer.

Cationic zeolite X samples were also used in a series of experiments investigating the storage and release of CIPRO, a widely used fluoroquinolone antibiotic. While the parent form NaX was found to exhibit no appreciable CIPRO adsorption, forms exchanged with divalent cations (Mg²⁺, Ca²⁺, Sr²⁺, Zn²⁺) adsorbed different amounts of the drug.[P6] Among the four zeolites, MgX and ZnX took up considerably larger amounts of CIPRO than CaX and SrX, and this behavior was mirrored in the DFT adsorption energies, which were considerably more negative for MgX and ZnX. Whereas MgX released most of the drug within a few hours in simulated body fluid, only partial release occurred for ZnX. An explanation for this distinctive behavior was provided by the DFT calculations, which predicted an additional binding of CIPRO to framework aluminium atoms for ZnX, but not for any of the other zeolites.

Outlook

The investigations summarized above focused on the equilibrium adsorption of guest molecules, mostly neglecting the aspect of diffusion (although some preliminary predictions of diffusion coefficients using empirical parameters were made in [P2] and [P5]). In the final phase of the project, machine learning methods will be used to develop a set of DFT-based neural network potentials that may allow accurate predictions of guest molecule diffusion, concentrating in the first place on CBZ diffusion in hydrophobic zeolites. Further calculations on cationic zeolites address the adsorption of bisphosphonate drugs, which are intensively studied by the experimental collaboration partners in Poznan. Finally, the project is also extended towards the adsorption at external surfaces of zeolites, rather than in the pores, looking at PPCP adsorption on clinoptilolite, a natural zeolite mineral that could find use as a low-cost adsorbent in wastewater treatment.

Publications

- P1** M. Fischer, *Adsorption of Carbamazepine in All-Silica Zeolites Studied with Density Functional Theory Calculations*, ChemPhysChem 24, e202300022 (2023)
- P2** M. Fischer, *Density functional theory study of hydrophobic zeolites for the removal of triclosan from aqueous solution*, Environ. Sci. Adv. 2, 1082–1098 (2023)
- P3** M. Fischer, *Adsorption of 5-fluorouracil, an anticancer drug, in faujasite-type zeolites: understanding storage and release with density functional theory calculations*, CrystEngComm 26, 3795–3807 (2024)
- P4** M. Fischer, *Adsorption of 5-fluorouracil, an anticancer drug, in faujasite-type zeolites: understanding storage and release with density functional theory calculations*, ChemRxiv preprint (2025), link: <https://doi.org/10.26434/chemrxiv-2025-bkwp1>

- P5** M. Fischer, R. Fantini, R. Arletti, J. Brauer, L. Mino, *Unraveling the Molecular Structure of Zeolite–Octyl Methoxycinnamate Hybrid UV Filters: A Combined Spectroscopic and Computational Approach*, *J. Phys. Chem. C* **127**, 24242–24252 (2023)
- P6** A. Domke, M. Fischer, M. Jakubowski, A. Pacholak, M. Ratajczak, A. Voelkel, M. Sandomierski, *Experimental and computational study on the Ca²⁺, Mg²⁺, Zn²⁺ and Sr²⁺ exchanged zeolites as a drug delivery system for fluoroquinolone antibiotic – Ciprofloxacin*, *J. Drug Delivery Sci. Technol.* **99**, 105997 (2024)

Presentations

Selection of oral conference presentations by the project leader or collaborators

- O1** R. Fantini, G. Vezzalini, G. Confalonieri, F. Di Renzo, L. Mino, R. Cavalli, M. Argenziano, M. Fischer, R. Arletti, *Microporous Minerals Catching Sun: UV filters encapsulation in Zeolites*, Geosciences for a sustainable future - SGI-SIMP2022, Turin (Italy), 19th to 21st September 2022
- O2** M. Fischer, J. Brauer, *Atomistic modelling approaches to study the adsorption of emerging organic contaminants in hydrophobic zeolites*, European Zeolite Conference (FEZA2023), Portorož (Slovenia), 2nd to 6th July 2023
- O3** R. Fantini, G. Vezzalini, G. Confalonieri, F. Di Renzo, L. Mino, R. Cavalli, M. Argenziano, M. Fischer, M. Sisti, R. Arletti, *Characterization and technological performances of zeolite-encapsulated organic UV filters*, EUROCLAY 2023, International Conference of European Clay Groups Association, Bari (Italy), 24th to 27th July 2023
- O4** M. Fischer, J. Brauer, *Computational studies of zeolites as adsorbents for the removal of pharmaceuticals and personal care products*, MinWien2023, Joint Meeting of the German, Austrian, and Slovakian Mineralogical Societies, Vienna (Austria), 17th to 21st September 2023
- O5** M. Fischer, L. Mino, R. Fantini, J. Brauer, R. Arletti, *Combining IR spectroscopy and density functional theory calculations to investigate the interaction of functional organic molecules with zeolites*, Annual Meeting of the German Crystallographic Society (DGK), Bayreuth (Germany), 18th to 21st of March 2024
- O6** R. Arletti, R. Fantini, M. Fischer, J. Brauer, R. Cavalli, M. Argenziano, L. Mino, *Zeolite for an effective solar protection: understanding the stability, unravelling the structure*, European Mineralogical Conference emc2024, Dublin (Ireland), 18th to 23rd of August 2024
- O7** M. Fischer, *Interaction of the anticancer drug 5-fluorouracil with Brønsted and Lewis acid sites: Insights from density functional theory*, 6th Euro-Asia Zeolite Conference, Alicante (Spain), 19th to 23rd of January 2025

References

- [1] C. Baerlocher, D. Brouwer, B. Marler, L.B. McCusker, *Database of Zeolite Structures*; <http://www.iza-structure.org/databases>
- [2] M. Patel, R. Kumar, K. Kishor, T. Misra, C. U. Pittman Jr, D. Mohan, *Chem. Rev.* **119**, 3510–3673 (2019)
- [3] R. Fantini, G. Vezzalini, A. Zambon, E. Ferrari, F. Di Renzo, M. Fabiani, R. Arletti, *Microporous Mesoporous Mater.* **328**, 111478 (2021)
- [4] A. Martucci et al., *Microporous Mesoporous Mater.* **148**, 174–183 (2012)
- [5] D. J. de Ridder, J. Q. J. C. Verberk, S. G. J. Heijman, G. L. Amy, J. C. van Dijk, *Separ. Purif. Technol.* **89**, 71–77 (2012)
- [6] N. Jiang, R. Shang, S. G. J. Heijman, L. C. Rietveld, *Water Res.* **144**, 145–161 (2018)
- [7] A. Datt, E. A. Burns, N. A. Dhuna, S. C. Larsen, *Microporous Mesoporous Mater.* **167**, 182–187 (2013)