AquaConSoil

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Investigating the microbial biodegradation of polyfluoroalkyl substances (PFAS) by molecular docking and molecular dynamic simulations

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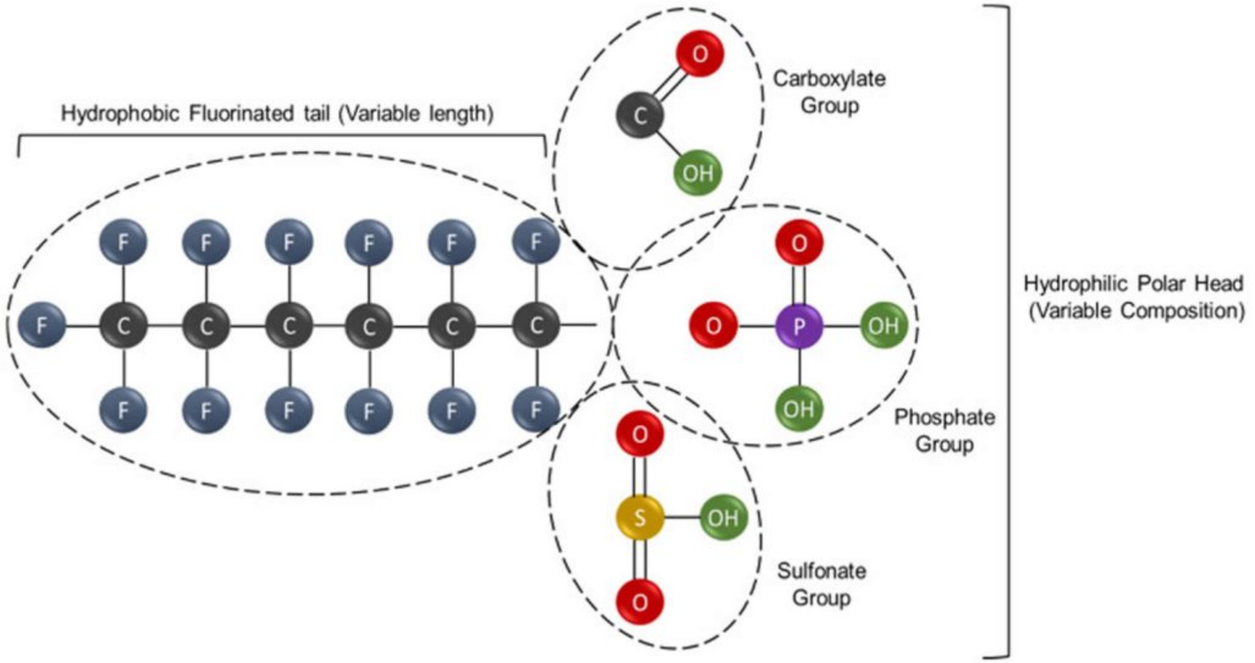
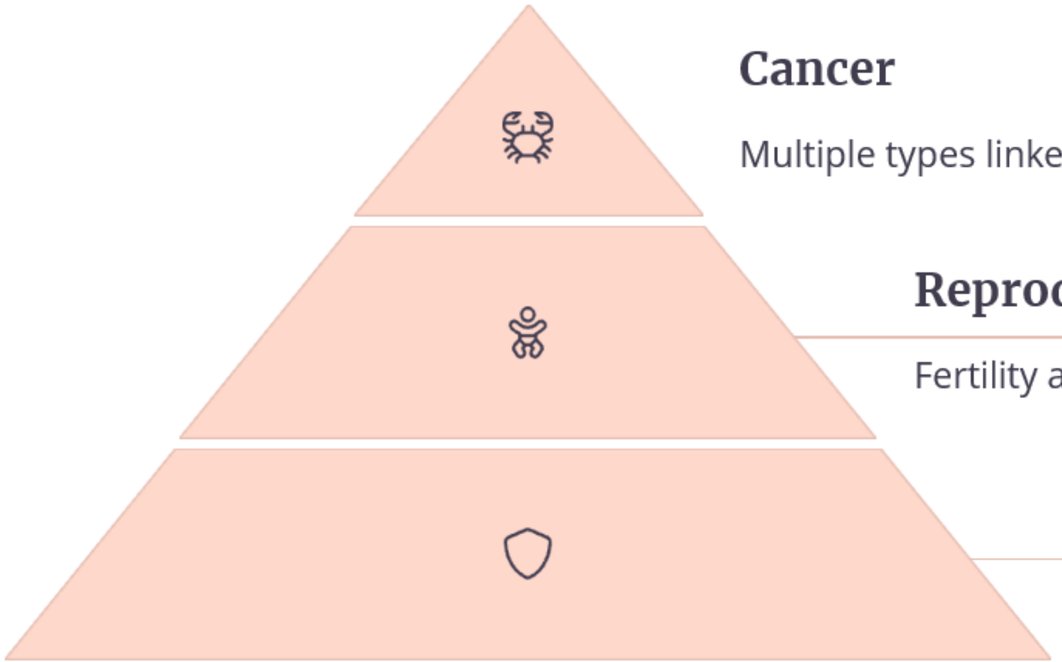
What is PFAS?

- Over 170 PFAS substances
-“Forever chemicals” due to strong C-F bond
- Found in everyday products from cookware to cosmetics
- Bioaccumulate in the environment and living organisms
- Significant technical challenges for PFAS removal



Health & Environmental Risks of PFAS



Cancer

Multiple types linked to exposure

Reproductive Issues

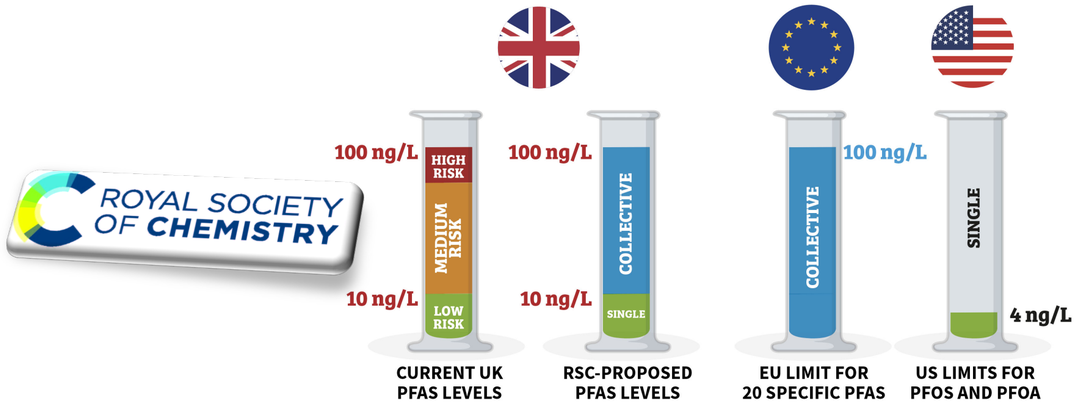
Fertility and developmental problems

Immune Suppression

Reduced antibody response to vaccines

Regulations for controlling PFAS

-In England and Wales 35 and 37 percent of water courses contain medium or high-risk levels of PFOS and PFOA respectively.
-UK water companies are not required by law to reduce them until they are deemed ‘high risk’.
-Concentrations of each individual PFAS is allowed at up to ten times the level considered ‘low risk’
-Currently no overarching limit on the total concentration when they are combined.



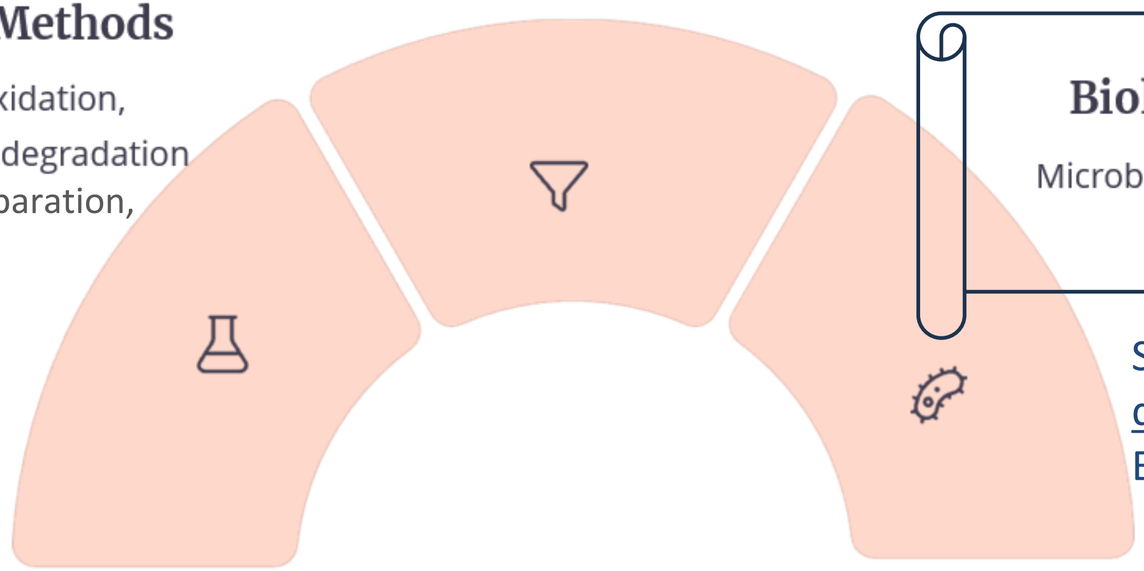
Overview of PFAS Removal Methods

Physical Methods

Activated carbon, ion exchange, membranes

Chemical Methods

Advanced oxidation, electrochemical degradation
Bubble and foam separation, Coagulation



Biological Methods

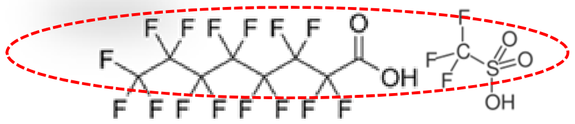
Microbial degradation, enzyme-based treatments

Smorada CM, Sima MW, Jaffé PR. Bacterial degradation of perfluoroalkyl acids. Curr Opin Biotechnol. 2024 Aug;88:103170.

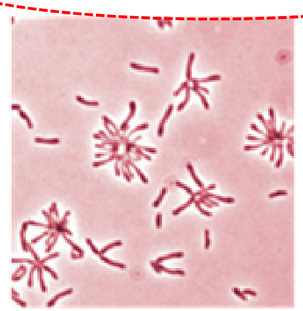
Project overview

PFAS

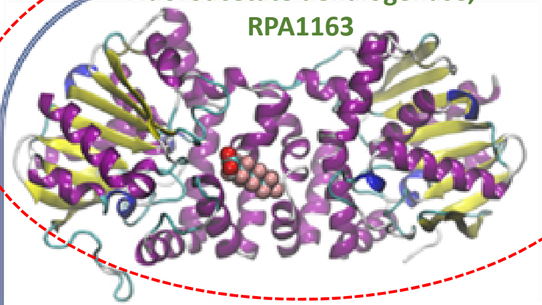
Bioremediation

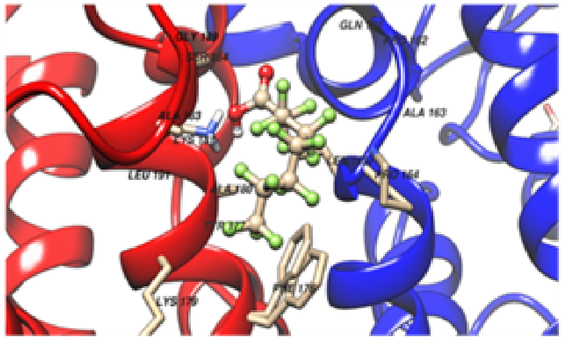


Rhodopseudomonas palustris

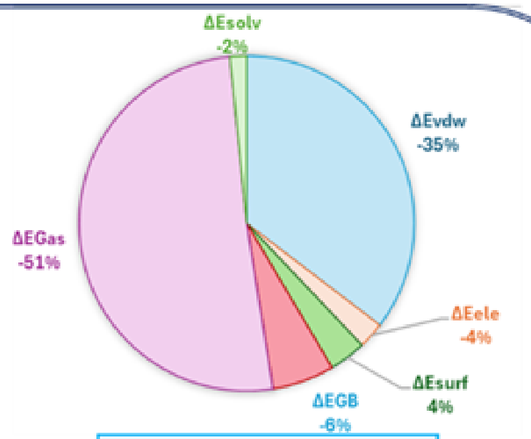


Fluoroacetate dehalogenase, RPA1163

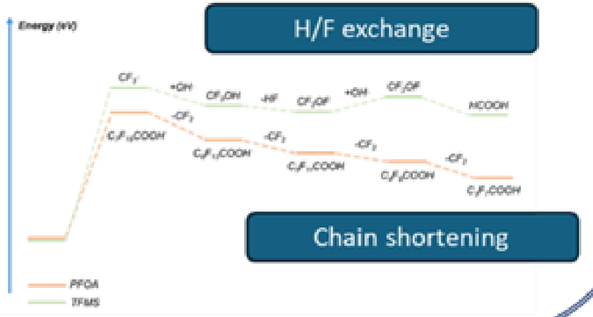




Molecular docking
Molecular dynamic simulation



Binding Energy



H/F exchange

Chain shortening

Methodology

In silico investigation of biodegradation of long chain and short chain PFAS with different functional group

-Enzyme Selection:

Nominated a model enzyme based on relevance to PFAS degradation pathways.

-Structure Acquisition:

Built the 3D structure of the enzyme (from PDB).

-Molecular Docking:

Docked PFAS molecules to the enzyme active site to predict binding poses and affinities (using AutoDock Vina).

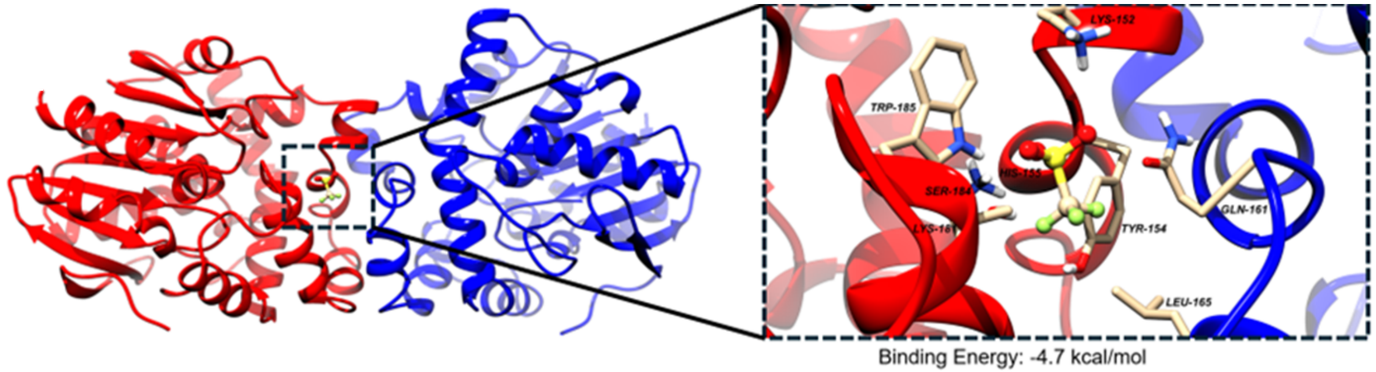
Molecular Dynamics Simulation:

Performed MD simulations to assess stability and dynamics of the PFAS-enzyme complex in solvated conditions (using GROMACS with AMBER 99SB force field)

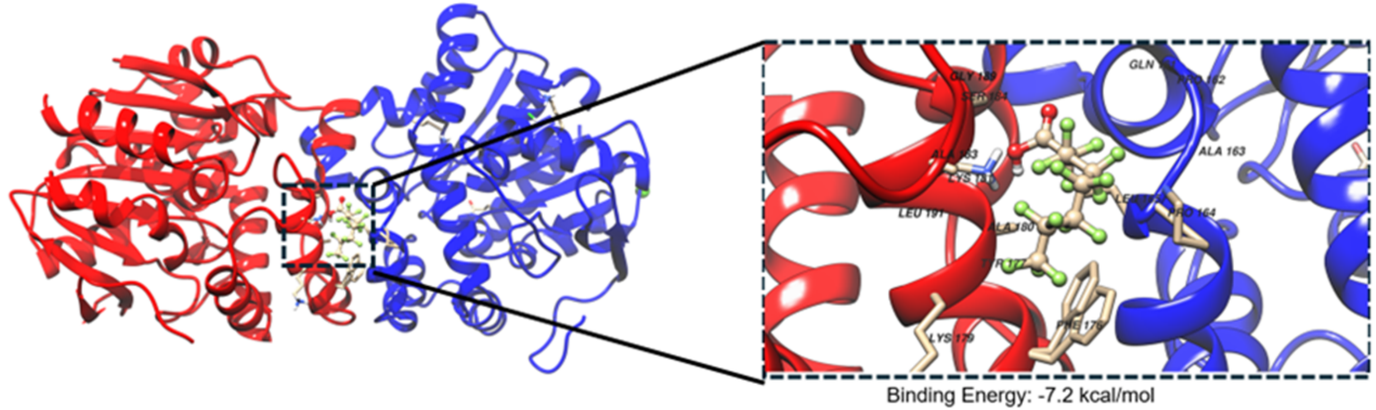
-QM/MM Calculations:

Applied quantum mechanics/molecular mechanics (QM/MM) hybrid methods to model electronic-level interactions at the active site.

Molecular Docking



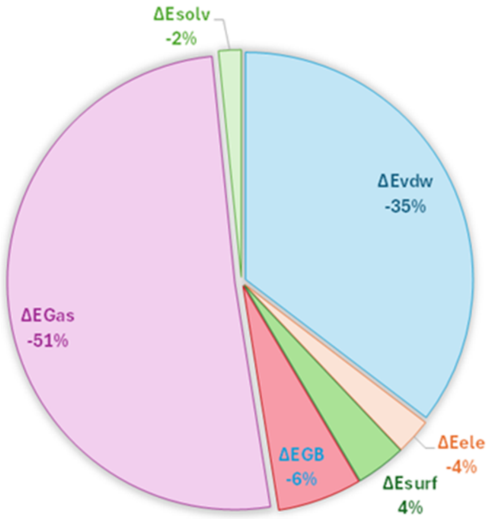
Binding Energy: -4.7 kcal/mol



Binding Energy: -7.2 kcal/mol

- AutoDock Tool, AutoDock Vina v1.2.x, CHIMARA software
- Scores of different ligand-protein poses are based on binding affinity and conformation of molecules at active sites of enzyme
- TFMS near TYR and HIS amino acid residue in enzyme
- PFOA in regions with Leu and Tyr
- Higher number of hydrogen-bond receptor in PFOA, higher binding affinity

Molecular Dynamic Simulation

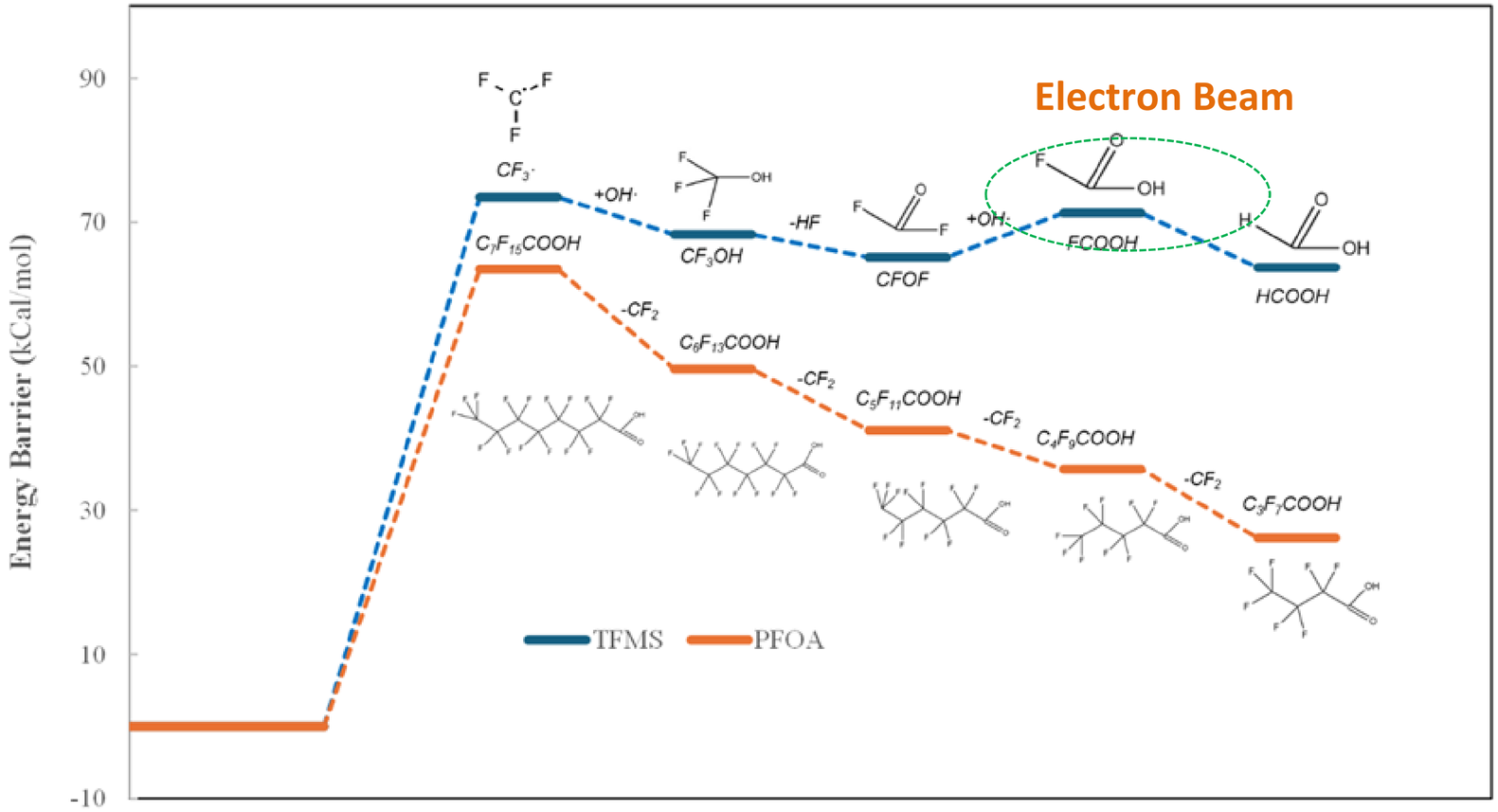


- Calculating binding energy using Gromacs
- Dominance of van der Waals due to the hydrophobic interactions
- Gas-phase energy an indication of intrinsic molecular mechanic and complementary shape of enzyme and ligand than solvent-mediated effect.

Enzyme should focus on hydrophobic residue to strengthen van der Waals interactions and geometry of binding pocket for better shape complementary.

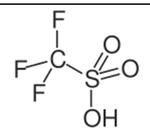
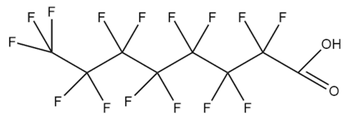
Degradation Pathway and Energy Barrier

Construct a reaction energy profile using QM/MM and DFT calculations



Conclusion

- ✓ Enzyme and PFAS interactions are investigated using simulation techniques
- ✓ Degradation of long chain and short chain PFAS were compared
- ✓ Fluoroacetate dehalogenase, RPA1163 could degrade only the PFAS containing acetate functional group

PFAS Compound	Molecular structure	Functional group	Binding energy	Activation energy	Pathway
TFMS		Triflate	-27.02	63.49	H/F exchang
PFOA		Acetate	-77.85	73.525	Chain shortening

Future Research Direction

- ✓ Integration of simulation and experimental evaluation to understanding biodegradation potential of different PFAS
- ✓ Using insight from MD simulation for enzyme engineering
- ✓ Looking through engineering biology solution for enhancing bacterial potential for PFAS biodegradation and biosensing for PFAS detection, through multidisciplinary collaboration

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