



PFAS Bioaccumulation in Great Lakes Chinook Salmon: A Molecular Level Study

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Introduction

- Per fluorinated alkyl substances are toxic synthetic chemicals
- Build up of PFAS in the Great Lakes has led to **bans on drinking water and fish**
- It is unknown how PFAS is affecting the fish of the Great Lakes on the molecular level
- Recent studies claim that docking simulation can be used to estimate how PFAS bioaccumulates
- Our research shows that only docking is insufficient
- A deeper molecular level study is needed to understand what **makes PFAS toxic**

Computation

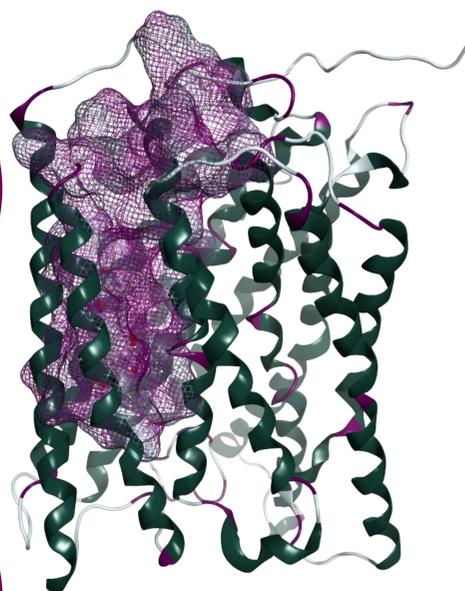
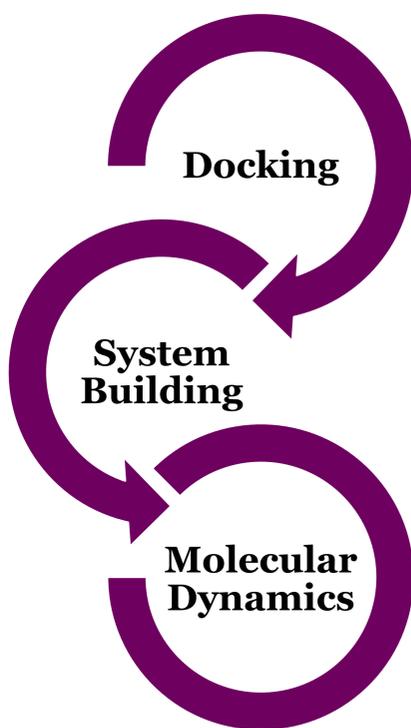


Figure 1. Cytochrome c Oxidase subunit 1 from Chinook Salmon with potential docking site shown in a grid form.

- **Docking:** Placement and evaluation of multiple ligand binding poses within a specified site
- **System Building:** Combining the ligand and protein, then recreating physiological conditions within an appropriate water box
- **Molecular Dynamics:** Simulating the dynamics of the system and evaluation of the ligand protein interactions

Results

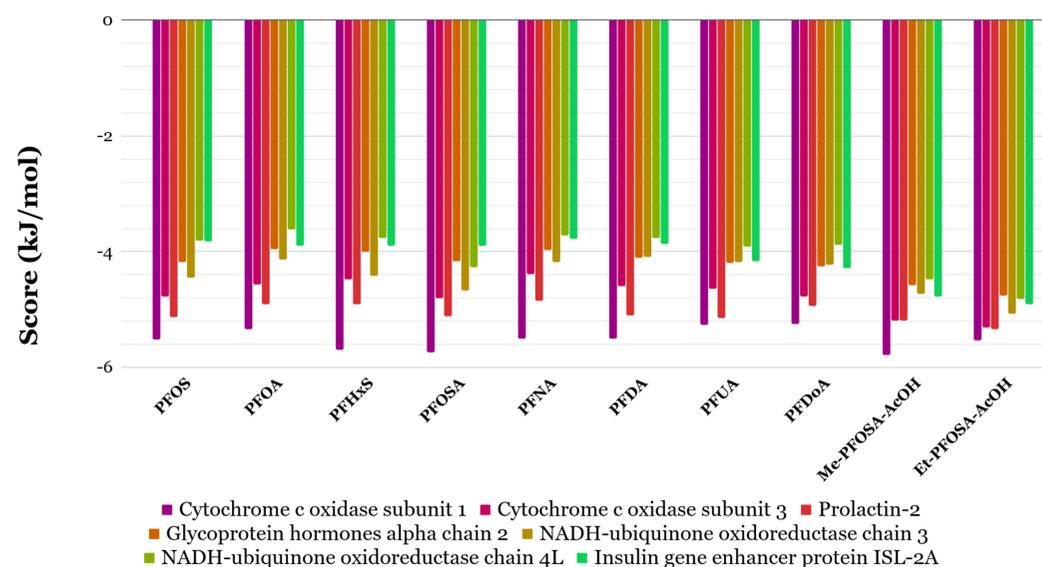


Figure 2. Docking scores from selected PFAS molecules in various proteins from Chinook Salmon. The highest score only is shown

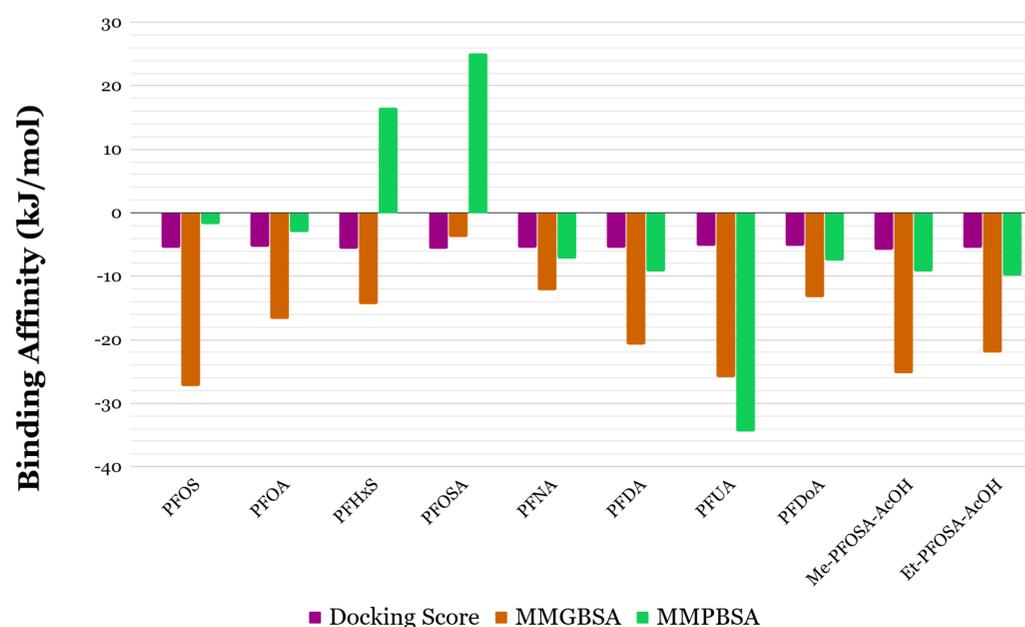


Figure 3. Binding affinity calculation results using MD simulation data of PFAS ligand in cytochrome c oxidase subunit 1 protein.

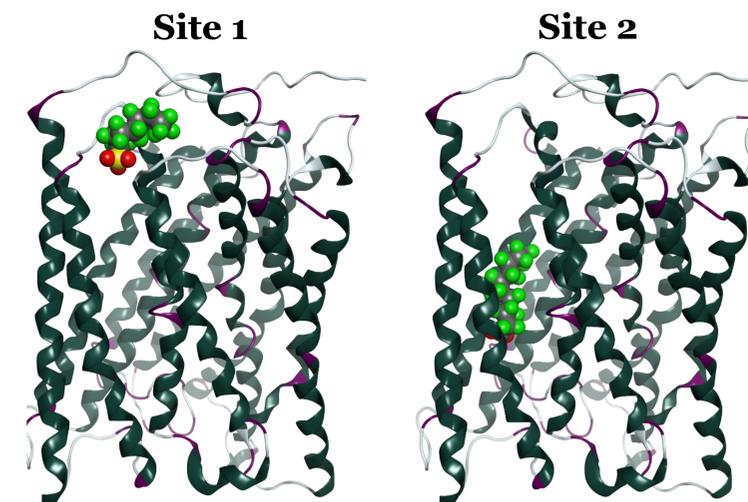


Figure 4. Two tested docking sites for PFAS in the cytochrome c oxidase I. PFOSA is docked to the Site 1 shown on left and PFUA docked to the Site 2 shown on right.

- PFAS docked in chinook salmon protein keeping the best pose
- 500 poses were tested per PFAS protein combination
- Docking yielded similar scores for each combination
- Multiple sites were tested for each docking calculation
- MD simulations provided information for further binding affinity calculation
- In cytochrome most PFAS docked in site 1 but MMPSA and MMGBSA calculation showed it was not very stable in some cases
- This was due to solvent interactions with the ligand

Summary

- Protocol developed to quickly dock PFAS in various proteins
- Molecular dynamical simulations provided deeper insight into ligand binding
- Docking may not provide accurate estimates

Acknowledgment

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References

1. Carla A. Ng and Konrad Hungerbuehler *Environmental Science & Technology* **2015** 49 (20), 12306-12314 DOI: 10.1021/acs.est.5b03000
2. *Molecular Operating Environment (MOE)*, 2016.08; Chemical Computing Group Inc., 1010 Sherbooke St. West, Suite #910, Montreal, QC, Canada, H3A 2R7, **2016**.

Future Work

Steered molecular dynamics and umbrella sampling to better understand the binding mechanism of PFAS.