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Computational Characterization of the Protein Binding of Persistent Organic Pollutants

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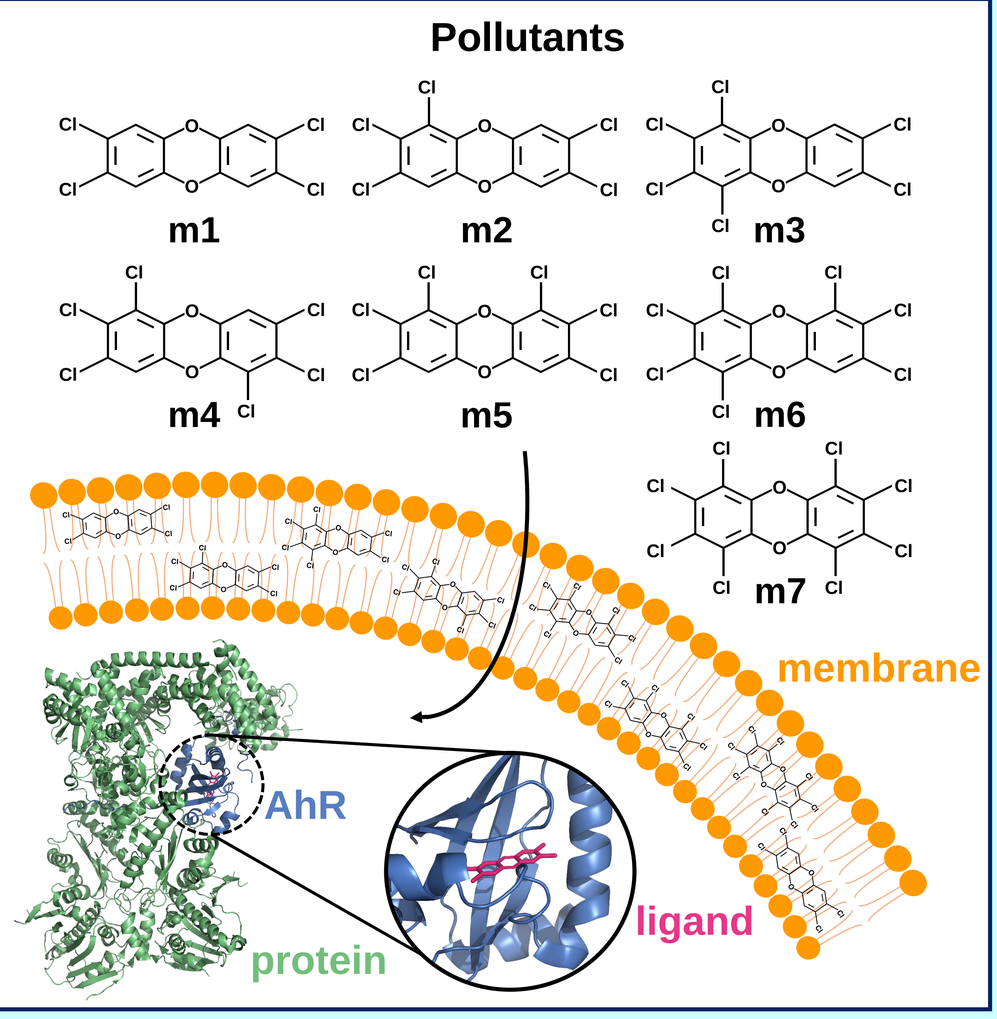
INTRODUCTION

- Polychlorinated dibenzo-p-dioxins (PCDDs) and other halogenated aromatic hydrocarbons (HAHs) known as "dioxin-like" compounds are widespread persistent environmental pollutants.
- PCDDs are unwanted by-products from combustion and industrial processes.
- The toxic equivalency factor (TEF) approach reflects the potential of these compounds to induce AhR activation in comparison with the most toxic congener.

TEF: 1 ← m1 m2 m3 m4 m5 m6 m7 → 0

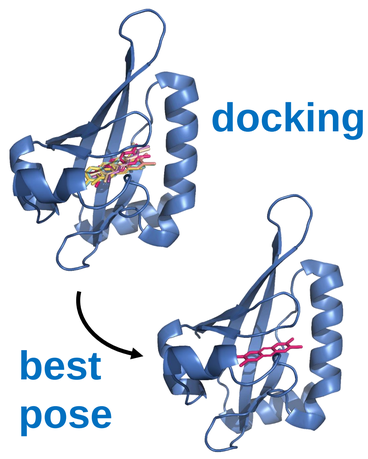
MOTIVATION

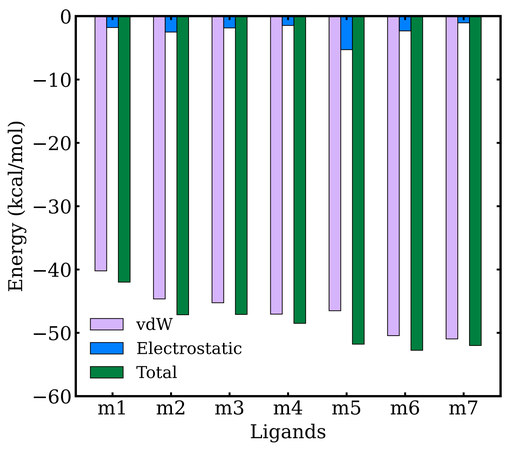
- The study of the binding mechanism between these contaminants and the AhR is important to find a structure/toxicity relation.



METHODS AND RESULTS

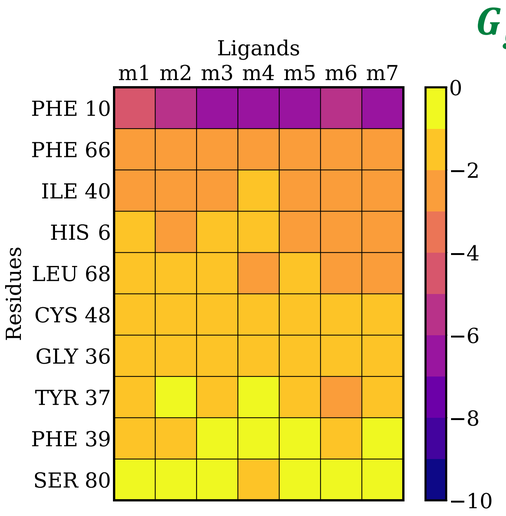
1. Molecular Docking + Molecular Dynamics + MMGBSA

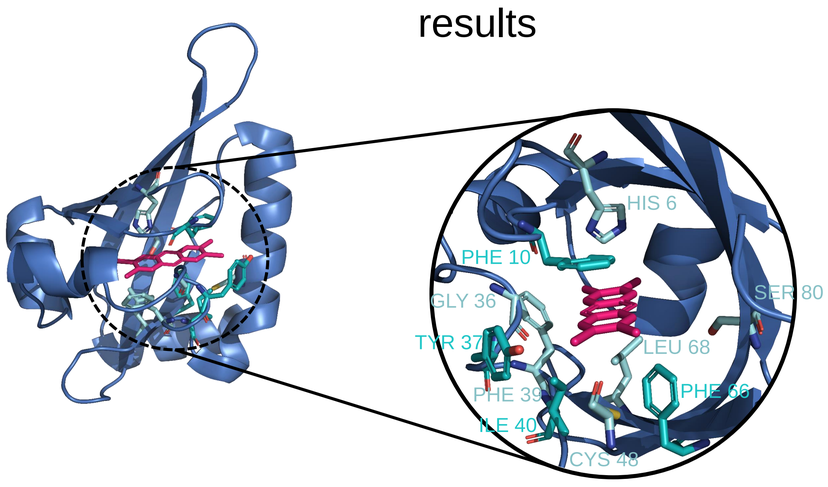




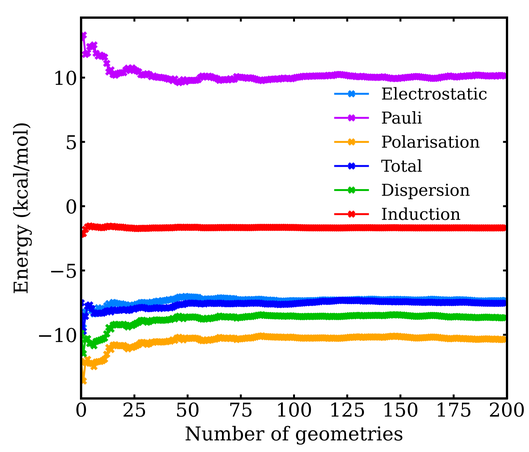
$$G_{gas} = E_{elec} + E_{vdW}$$

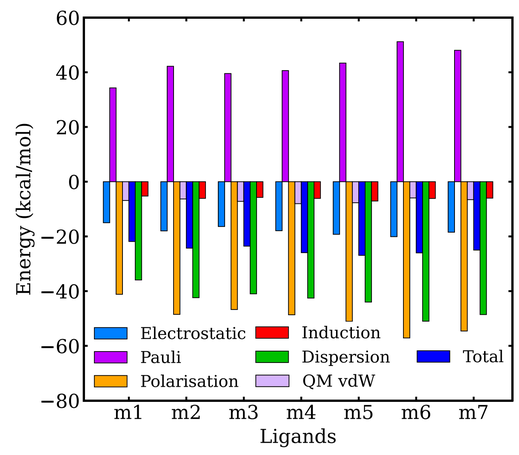
- vdW is the dominant component
- vdW increases with the number of Cl atoms
- The residues with highest interaction energies coincide with the experimental results





2. Energy Decomposition Analysis



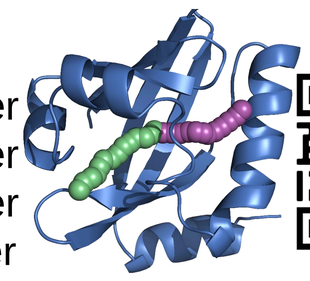


- 50 geometries is enough to converge energy
- Polarisation term increases with the number of Cl atoms

$$E_{int} = E_{Pauli} + E_{elec} + \underbrace{E_{disp} + E_{ind}}_{\text{Polarisation}}$$

3. Umbrella Sampling

- There are two tunnels
- It is expected that larger number of Cl atoms, lower energy dissociation barrier and larger association barrier



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