

SHORT TERM SCIENTIFIC MISSION (STSM) – SCIENTIFIC REPORT

Action number: COST Action CM1405

STSM title: Unraveling the recognition mechanism of odorants with their binding proteins

STSM start and end date: 15/12/2018 to 15/03/2019

Grantee name: Rahma Dahmani

PURPOSE OF THE STSM

Odorant binding proteins (OBP) are a subclass of lipocalins. They play an important role in the recognition and transport of hydrophobic odorants towards specific olfactory receptors present in large amounts in the respiratory and olfactory nasal mucosa in mammals.

The main objective of the proposed project is to unravel how different types of ligands (such as aromatic phenyl compounds) vary in their conformational flexibility to see how this affects their binding affinities and how they interact with odorant binding proteins at a molecular scale.

DESCRIPTION OF WORK CARRIED OUT DURING THE STSMS

- Conformational Sampling of the ligand

Conformational analyses of several aromatic ligands and octen-3-ol were carried at molecular mechanics and quantum chemical level to sample the most stable geometries. Optimizations were carried out at MP2/6-311++G(d,p) and B3LYP/6-311++G(d,p) level of theory. Atomic charges of ligand were calculated using Natural Population Analysis (NPA).

- MD simulation of the protein

We compared the structure of protein during simulation at 50 ns and 250 ns with crystal structure from PDB database (PDB-IDs: 1E00, 1UHB).

- Docking and MD simulation of ligand – protein complexes

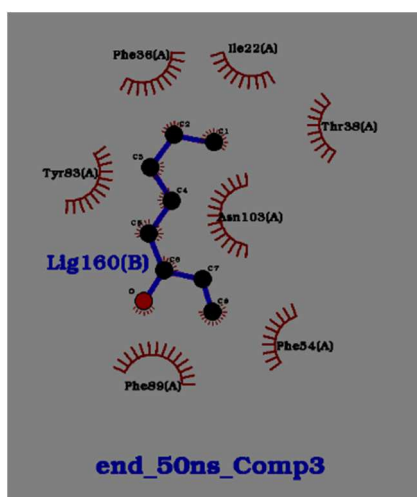
Using Autodock as starting point for the binding of , MD simulation were carried out using AMBER 2010 Force Field to insure interactions established between ligand (OCT) and protein (pOBP) .

The work plan allowed me to learn state-of-the-art molecular dynamics techniques to investigate protein-ligand interactions at a molecular scale. **This experience allowed me to acquire new skills, complete my knowledge in multi-scale simulation techniques to study large-scale biological problems. I believe that this will give me a real chance to pursue a career in science after obtaining my PhD.**

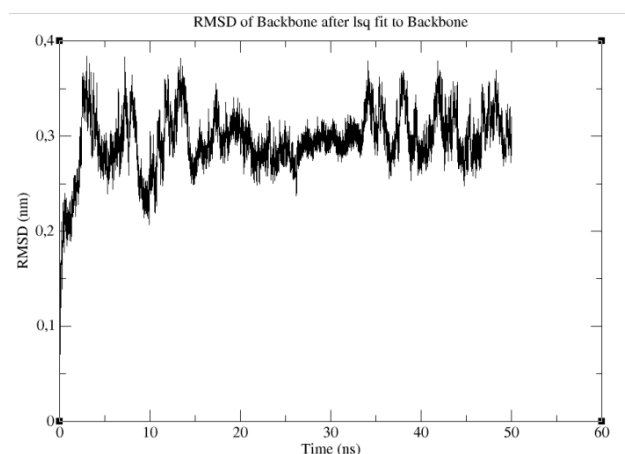
DESCRIPTION OF THE MAIN RESULTS OBTAINED

- Conformational analysis of 3 different ligands (2 aromatic and octen-3-ol) at different level of theory
- Validated structure and Dynamics of porcine OBP in explicit water
- Binding geometries of the ligand-protein complexes

Altogether, I have successfully analyzed the conformational dynamics of the protein and its ligands and studied the binding configurations of the protein-ligand complex.



Protein – Ligand Interactions (snapshot of OBP-octen-3-ol complex after 50 ns)



RMSD of pOBP in explicit water (Equilibration MD).

FUTURE COLLABORATIONS (if applicable)

The results obtained during my stay with the MOLIM STSM are crucial to know which conformations are be most relevant for the activation of ligand-protein-complexes in biological media and provide a stepping stone for future studies. In addition, I was able to highly benefit from my visit to plan future projects within the scope of my PhD thesis in the field of molecular dynamics simulations for biological applications. The STSM helped us to start a collaboration on these systems with Dr. S. Abeln at the Vrije Universiteit Amsterdam.

I agree with Miss R. Dahmani's STSM report.

H. Mouhib

Champs, 15/03/2019

