Short Term Scientific Missions (STSM)

Action number (CM1405)

Title of the planned STSM

Unraveling the recognition mechanism of odorants with their binding proteins

Start and end dates:
15.12.2018-15.03.2018

The Applicant is **Miss Rahma Dahmani**. She got her Eng. **degree at the beginning of 2016** and started her PhD right afterwards in the group of Prof. Salima Boughdiri at the Theoretical Chemistry and Spectroscopy Laboratory (UR11ES19) in Tunis. **Her scientific interests** are quantum chemical calculations of different metal ligand complexes in connection with their biological activity and she wants to expand her expertise on classical mechanics techniques to tackle large scale molecular dynamics problems. **Her involvement in MOLIM will help on the promotion of WOMEN in science and motivate young people to envisage a scientific career in Europe.**

Name of the host institution:

MSME Laboratory
Theoretical Chemistry Group
University Paris-Est Marne-La-Vallée
5, Boulevard Descartes
77454, Marne-la-Vallée Cedex 2

Financial data (amounts requested for travel and subsistence).

1) Travel expenses: Flight ticket from Tunis to Paris (and back): **400 Euros**

2) Subsistence expenses (including lodging, local transportation, meals):
For a stay of 30 days (3 month): **800 Euros**

TOTAL: 2800 Euros

Work plan:

There are three important steps for the perception of smell: **(1)** Detection, **(2)** transduction, and **(3)** signal integration. Step 1 is unarguably the most important for chemists who work in the field of flavors and fragrances, since it represents the primary link between the odorant and the full perception process [1,2]. Although odorant detection is primarily due to the chemoreception of odorants by G-protein coupled, additional peri-receptor are likely to participate in olfactory signal start and termination [3]. These events are dominated by odorant-binding proteins, small highly soluble belonging to the lipocalin super family of transport proteins. They are thought to participate in the olfactory process by carrying odorant molecules to the olfactory receptors [4]. Inside their binding pocket, aromatic odorants such as phenyl acetate, phenetole, and strawberry aldehyde are able to bind

these specific amino acids over non-covalent interactions. However, the strength of the interaction will strongly depend on the orientation of the phenyl moiety and thus of the flexibility of the ligands (with respect to its soft-degree of freedom), as well as the amino acids inside the binding pocket.

The main objective of the proposed project is to unravel **(1) how the different types of aromatic phenyl compound vary in their conformational flexibility** to see how this affects their binding affinities and **(2) how they interact with odorant binding proteins at a molecular scale**. To achieve this, Miss Dahmani will apply to a multi-scale, bottom-up approach using **state-of-the-art *ab initio* calculations, molecular dynamics, and computational biology** methods. **The theoretical models will be validated with available experiments in the literature to guarantee their reliability.** The targeted phenyl ligands for the project feature different frame and electronic surrounding for the phenyl group, which is likely to influence the soft degree of freedom of the aromatic moiety, which may be the case for related phenyl compounds in the condensed phase (see Fig. 2).

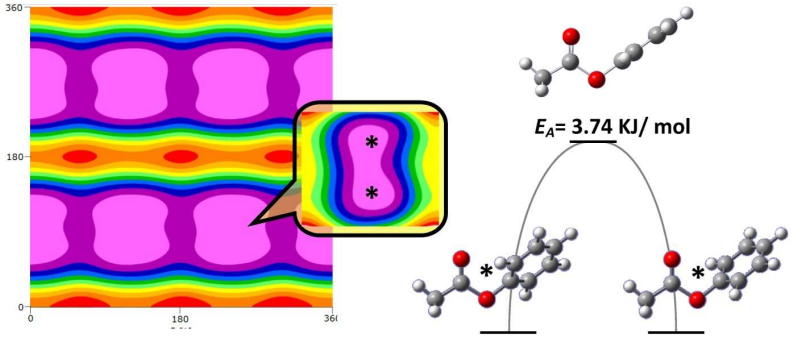

Fig. 3. *Potential Energy surface of phenyl acetate showing characteristic double minima. The barrier between the two enantiomers is only 3.74 KJ/mol and provide a soft-degree of freedom around the phenyl group in the molecule*

The work plan is thus to carry out an innovative research project between two groups that are actively participating in the theme of the COST ACTION MOLIM. At the MSME Laboratory (theoretical chemistry) in France, Miss Dahmani will be able to learn state-of-the-art molecular dynamics techniques to investigate protein-ligand interactions at a molecular scale. **This experience will allow acquire new skills, complete her knowledge in multi-scale simulation techniques to study large-scale biological problems, and provide her with a real chance to pursue a career in science**.

REFERENCES

References

[1] L. Buck, R. Axel, *Cell* **1991**, *65*, 175.
[2] U. J. Meierhenrich *et al.*, *Angew. Chem. Int. Ed*. **2004**, *43*, 6410.
[3] K. Lazard *et al.*, *Nature* **1991** , *349*, 790.
[4] S. Firestein. *Nature* **2001**,*413*, 211.