HOW DO PFAS POLLUTANTS INTERACT WITH PROTEIN IN LIVING BODIES ? INSIGHT FROM MOLECULAR DYNAMICS SIMULATIONS

LABORATORY : Institut Lumière Matière

LEVEL : M1 / M2
TEAM(S) : THEOCHEM

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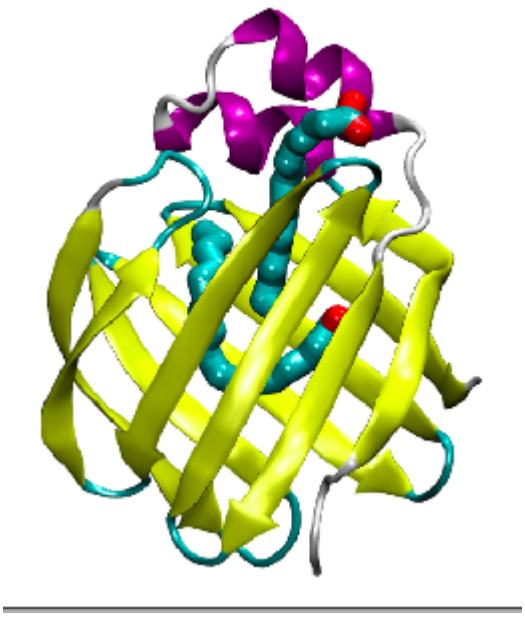
KEYWORD(S) : Protein / molecular dynamics simulations / PFAS

SCIENTIFIC CONTEXT :

Per- and polyfluoroalkylated substances (PFAS) are a family of artificial chemical compounds with a wide range of properties: non-stick, waterproofing, heat resistance, etc. There are several thousands of them on the market in various day-to-day products. Because of the high stability of the carbon-fluorine bond, they are the most persistent man-made pollutant known to date, and exposure to PFAS can lead to serious adverse health effects. Some specific interaction between PFAS and proteins have been described, and molecular modeling can help to decipher how some PFAS can be transported by proteins in the body (Delva-Wiley, J. 2021). The aim of this project, financed by the CNRS, is to model the molecular interactions between PFAS and the FABP family of proteins (Fatty Acid Binding Protein), to describe the pathways of PFAS in the body and their actions on human metabolism.



X-ray structure of rat liver FABP, complexed with two oleic acetates, which can be replaced by PFAS.

MISSIONS :

After some bibliography work, the student is going to use different numerical modeling techniques to map the interaction and dynamics of the PFAS/FABP complex. The conformations of the protein FABP are described by molecular dynamics (MD) simulations. Common conformations are used to perform molecular docking, with an algorithm that finds probable conformations of the PFAS/FABP complex. The student will then perform molecular dynamics simulations of these PFAS/FABP complex and investigate their stability, find relevant molecular interactions. We shall focus on differences between different PFAS and try to understand which PFAS are interacting more strongly with the FABP. Finally, we wish to investigate the dynamics of dissociation, by using the τ-RAMD (for Random Accelerated Molecular Dynamics) method (Kokh,2028 and 2020). This accelerated MD method, implemented in the GROMACS software, will enable us to compare complexes according to their dissociation times.

The student will also interact with the two other teams that are implied in the project (from the Laboratoire des Biomolecules, in Paris, and from the lab Matrice Extracellulaire et Dynamique Cellulaire in Reims).

OUTLOOKS :

The project may be continued as a phD thesis provided that a doctoral school grant is obtained.

BIBLIOGRAPHY :

Delva-Wiley, J. et al. (2021). Computational Analysis of the Binding Mechanism of GenX and HSA. ACS Omega. 6, 43,
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Kokh, D. (2020). tauRAMD. github repository https://github.com/HITS-MCM/tauRAMD