Understanding protein-ligand interactions:

from Medicinal Chemistry to Biotechnology

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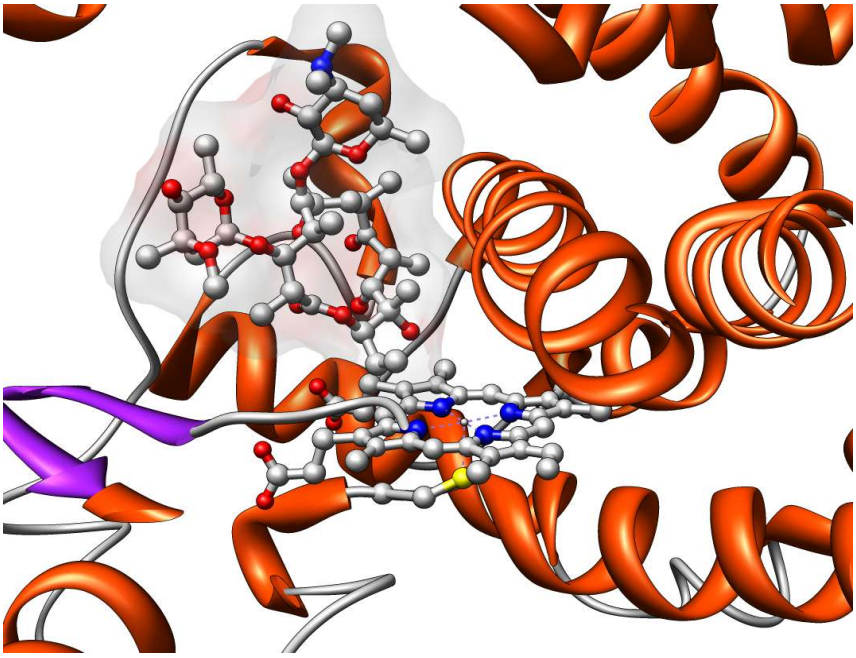
The interactions between proteins and chemical ligands, endogenous (NADPH, co-enzymes,..) or exogenous (drugs, contaminants,...), are involved in many biological processes and the general state of health of any living organism is highly sensitive to these mechanisms. Understanding the rules that define how proteins recognize and associate with these compounds is a key question of different fields like pharmacology or medicinal chemistry.

Studies aimed to decode protein-ligand interactions are frequently multidisciplinary and combine experimental and theoretical approaches. However, during the last decades, computational techniques have become one of the cornerstones of the field; a phenomenon resulting from the general improvement of the models used for the molecular description as well as the increase of computer power. These methods can be apply to investigate a wide range of questions e.g. Can we find a ligand that binds to a target protein? Can we apply chemical modifications of the ligand to increase/decrease its binding affinity or catalytic activity? Why are some protein mutations leading to specific resistance? Can we modify the protein to allow it to perform new reactions?

In this talk, using my personal experiences in this field, I'll present different studies where the understanding of protein-ligand interactions is a critical issue. After a short overview of the different techniques and there limitations, I'll segment my talk in two distinct parts, one dedicated to applications in the biomedical field (drug design and metabolism of drugs), the other to the recent design of a new “hemozyme”.



Crystallographic structure of the antibiotic Erythromycin bound to the human Cytochrome P450 3A4