Use of Fluorine NMR to Describe Molecular Interactions
Laboratory of Dr. Bruno Kieffer - Biomolecular NMR team

Context: The NMR platform is investing into a new cryoprobe that allows the observation of fluorine nucleus with very high sensitivity.

Project:

The applications of fluorine NMR in life science are based on two main features of this nucleus: the 19F is highly abundant and nearly as sensitive as the proton, it is not present in biomolecules allowing the specific observation of fluorine labelled compounds in very complex biological media. Furthermore, the chemical shift of the fluorine nucleus is very sensitive to the environment, offering a powerful mean to detect and monitor subtle changes in the structure and/or dynamics of macromolecules. These features have motivated the developments of efficient methods to observe the interactions between drugs and biological targets (such as large protein complexes) or to follow the activity of protease activity using fluorinated substrates. These applications are possible thanks to the existence of many drugs bearing fluorine atoms in the pharmacopoeia and the availability of many fluorinated variants of amino-acids or nucleosides. Here, we wish to take advantage of the fluorine probe to investigate the details of the molecular events involved in a signaling cascade related to the action of retinoic acid in cells. In particular, we will investigate the interaction between a SH3 domain and the polyproline rich region of the NTD of the Retinoic Acid nuclear Receptor (RAR) using peptides containing fluoro-prolines. Preliminary results indicate the possibility to measure on and off rates of these interaction enabling a complete understanding of the mechanism by which phosphorylation of residues within the proline rich domain leads to a modulation of the affinity for the SH3 domain.

Related publications of the team:

