Colloquia in Cellular Signaling

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Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**".
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NMR and intermolecular interactions: applications in drug design and studies of protein (de)stabilization

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Abstract:

It is in the study of intermolecular interactions that NMR spectroscopy reveals its full potential and great versatility as a technique of structural investigation. In fact, when applied to dynamic processes, NMR allows to characterize, with atomic resolution, phenomena of molecular interaction on a wide variety of time scales both in chemical and biological systems.
In this lecture I will introduce the NMR toolbox for the study intermolecular interactions. To illustrate the applicability and limitations of the technique two different research contexts will be used: protein-ligand interactions in a drug design context and the study of ion liquid effects on protein stabilization.

In the context of drug research NMR is nowadays used both as a screening technique for the identification of candidates as well as for the establishment of structure-activity relationships. For this purpose, complementary protein and ligand-based observe NMR techniques have been developed. The application of the Saturation Transfer Difference (STD-NMR)[1] technique will be introduced to exemplify the development of a rapid, ligand-based, methodology to study the interaction between drugs and drug candidates with the two isoforms of cyclooxygenase (COX),[2] followed by other examples in a drug design context.
In recent years ionic liquids (ILs) have attracted much attention in a wide range of chemical and biochemical applications. ILs physical and chemical properties can be enhanced and modified by both their cationic and anionic moieties and this is the reason for their broad range of applications. A promising field of application of ILs is as protein structure modulators. Inspired in the high concentrations of organic charged metabolites found in cell milieu and in our previous studies with imidazolium-based ILs,[3] we have started to address the importance of ion-pairs and its consequences on protein stability in conditions under artificial crowding conditions mimicking the cell milieu. We look to understand the molecular mechanisms of ion specific effects on proteins towards protein stabilization and/or destabilization using different protein systems and ILs.

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[3] A. M. Figueiredo *et al. Phys. Chem. Chem. Phys.* **2013,** *15*, 19632–43; M. Silva *et al. Phys. Chem. Chem. Phys.* **2014,***16*, 23394–403**.**