Enhanced NMR for Sensing Target Biomolecules in the Cellular Environment

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Studying biomolecules such as proteins in their natural environment, *i.e*, the cell, using NMR spectroscopy is a recent challenge that can open the doors of new drug targets. Indeed, structure, dynamics as well as interactions in cells can be very different from the one observed in vitro, in particular, posttranslational modifications can't be assessed in classical studies led *in vitro*. However, in cell NMR is so far limited by, (i) the physiological protein concentrations that are very low, and result in very weak signal intensities, and (ii) the cell viscosity, resulting in line broadening. We are developing methods that can help resolving these two issues. On one hand, Dynamic Nuclear Polarization (DNP) that is developed in our lab, will allow a better signal to noise ratio in NMR experiments. On the other hand, the use of Long lived states (LLS) and Long Lived coherences (LLC), may help overcoming signal broadening. We have recently use LLS to characterize the N-terminal domain of c-Src kinase (Usrc), that is unfolded in vitro, and shown that LLS of the aliphatic protons of glycines have lifetimes approximately four times longer than their spin-lattice relaxation times.