Applications of Weak Field Cross Polarization in Solution Biomolecular NMR

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First introduced by Chiarparin *et.al*,[1] the application of weak-field cross-polarization (WFCP, $\omega_I = \omega_S \leq J_{IS}$) to biomolecules in solution enables the exquisite manipulation of coupled spin pairs to achieve a number of desired spectroscopic outcomes ranging from the original application of selective coherence transfer to more recently, selective inversion of target spin populations,[2] and the selective removal of target spin pairs.[3] Such versatility results from the ability to manipulate specific cross-polarization parameters, such as RF field strength, contact time and frequency offsets, and through the combination with traditional pulse/delay elements, to design specific sequences that guide spin-trajectories towards desired states, while minimizing off-target effects. Furthermore, as a double resonance approach, WFCP can take advantage of the signal dispersal afforded in multidimensional experiments to achieve selectivity where traditional band-selective pulsing approaches may fail; and yet, as a spectroscopic tool, WFCP remains underappreciated. Here, we will detail novel applications of WFCP to biomolecular systems, including the recently described *S*elect*i*ve *E*xcipient *R*eduction/*R*emov*a*l (SIERRA) filter for elimination of signals arising from aliphatic excipients in natural abundance ^{1}H-^{13}C methyl spectra of biopharmaceutical products[3] (Figure 1). We will further discuss advances in the theoretical framework that have allowed for the continued development of these methods.

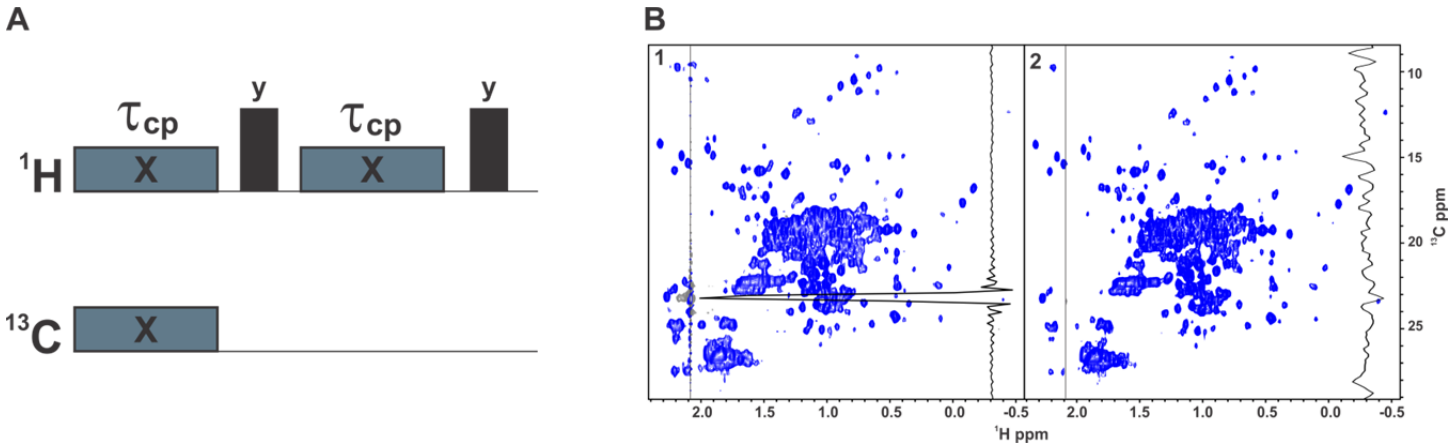

Figure 1 Applications of weak field cross-polarization. A) Schematic representation of the *S*elect*i*ve *E*xcipient *R*eduction/*R*emov*a*l (SIERRA) filter. B) Demonstration of the SIERRA filter on a signal arising from 10 mM sodium acetate buffer in a natural abundance ^{1}H-^{13}C gradient-selected HSQC spectrum of 40 mg/mL NISTmAb. Spectra shown are without (1) and with (2) the application of the SIERRA filter. 1D traces through the acetate signal along ^{13}C are shown to illustrate the completeness of signal removal.

References

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