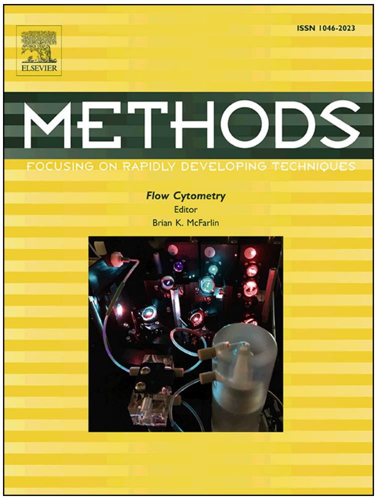

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Intermolecular Interactions Determined by NOE Build-up in Macromolecules from Hyperpolarized Small Molecules

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Abstract

The nuclear Overhauser effect (NOE) is a primary means to characterize intermolecular interactions using modern NMR spectroscopy. Multiple experiments measured using different mixing time can be used for quantifying NOE buildup and measuring cross-relaxation rates. However, this approach using conventional multi-dimensional NMR is time consuming. Hyperpolarization by dissolution dynamic nuclear polarization (D-DNP) can generate deviations from equilibrium spin polarization by orders of magnitude, thereby enhancing signals and allowing to characterize NOE build up in real-time. Since most small molecules can be hyperpolarized using D-DNP, this method is applicable to the study of intermolecular interactions between small molecules and macromolecules. This application is demonstrated using a model system for host-guest interactions including the third generation polyamidoamine dendrimer (G3 PAMAM) and the pharmaceutical phenylbutazone (PBZ). After mixing ^{1}H hyperpolarized PBZ with PAMAM, the NOE build up is directly observed at different sites of the dendrimer in series of one-dimensional NMR spectra. Cross relaxation rates specific to individual source and target spins are determined from the build up curves. Further, the polarization enhancement is shown to be sufficiently large to allow identification of cross-peaks not observed in a conventional 2D-NOESY spectrum. The improved signal-to-noise ratio provided by hyperpolarization allows for characterizing the intermolecular interaction in an almost instantaneous measurement, opening an application to macromolecular and biomacromolecular NMR.