

Inter-nuclear dipolar interaction is anisotropic, and becomes a source of noise in systems that undergo rotational motion, for example in liquids. This noise causes spin relaxation; the relaxation rates for the two spins L and S participating in a dipolar interaction are:

$$r_L = \frac{\gamma_L^2 \gamma_S^2 \hbar^2}{10} \left(\frac{\mu_0}{4\pi} \right)^2 \frac{\tau_c}{r_{LS}^6} \left(\frac{3}{1 + \omega_L^2 \tau_c^2} + \frac{6}{1 + (\omega_L + \omega_S)^2 \tau_c^2} + \frac{1}{1 + (\omega_L - \omega_S)^2 \tau_c^2} \right) \quad (1)$$

$$r_S = \frac{\gamma_L^2 \gamma_S^2 \hbar^2}{10} \left(\frac{\mu_0}{4\pi} \right)^2 \frac{\tau_c}{r_{LS}^6} \left(\frac{3}{1 + \omega_S^2 \tau_c^2} + \frac{6}{1 + (\omega_L + \omega_S)^2 \tau_c^2} + \frac{1}{1 + (\omega_L - \omega_S)^2 \tau_c^2} \right)$$

This, however, is not the only dipolar relaxation process in the system – the two spins also start to exchange magnetisation, the so-called *cross-relaxation* process:

$$\frac{d}{dt} \begin{bmatrix} \langle \hat{L}_Z \rangle \\ \langle \hat{S}_Z \rangle \end{bmatrix} = - \begin{bmatrix} r_L & x_{LS} \\ x_{LS} & r_S \end{bmatrix} \begin{bmatrix} \langle \hat{L}_Z \rangle - \langle \hat{L}_Z^{eq} \rangle \\ \langle \hat{S}_Z \rangle - \langle \hat{S}_Z^{eq} \rangle \end{bmatrix} \quad (2)$$

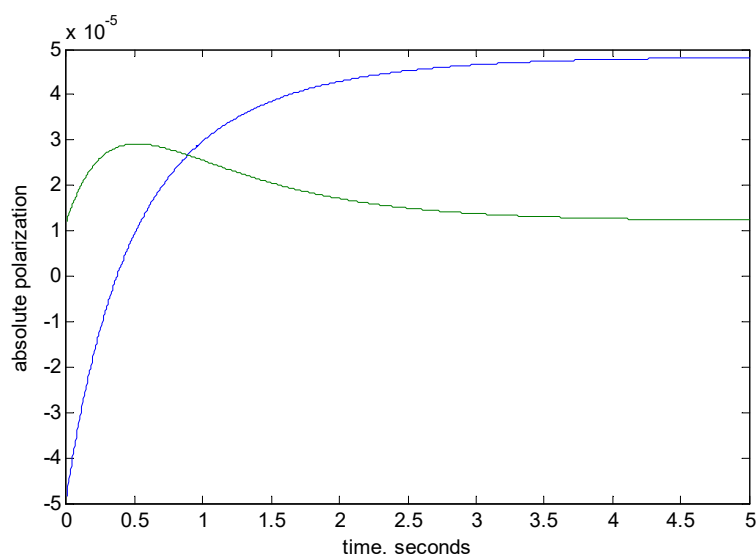
These are called Solomon equations, and the *cross-relaxation rate* is:

$$x_{LS} = \frac{\gamma_L^2 \gamma_S^2 \hbar^2}{10} \left(\frac{\mu_0}{4\pi} \right)^2 \frac{\tau_c}{r_{LS}^6} \left(\frac{6}{1 + (\omega_L + \omega_S)^2 \tau_c^2} - \frac{1}{1 + (\omega_L - \omega_S)^2 \tau_c^2} \right) \quad (3)$$

This cross-relaxation process is called the *nuclear Overhauser effect* (NOE). Unlike the self-relaxation rate (which is always positive), this expression can change sign, meaning that (for example) the proton-proton NOE is negative for small molecules in non-viscous liquids, but becomes positive for large molecules in viscous liquids and / or strong magnetic fields. Because of its distance dependence, NOE is the cornerstone of NMR structure determination.

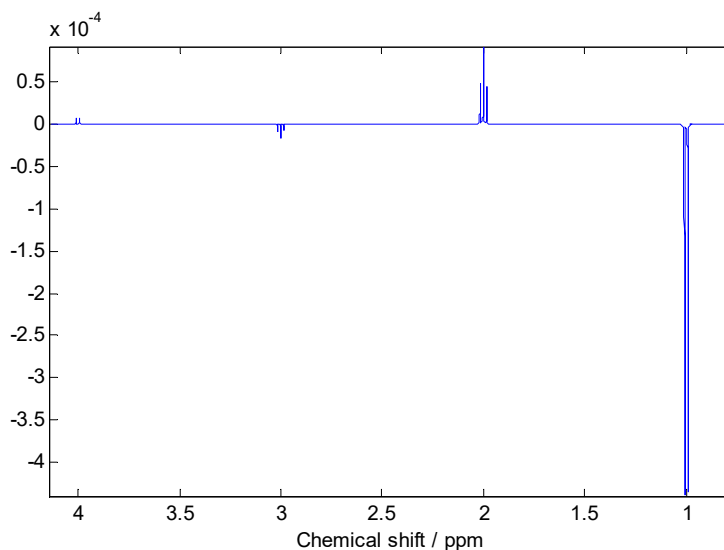
Distance determination using nuclear Overhauser effect

Assuming a room temperature ^1H - ^{13}C spin system in a 600 MHz magnet with inter-nuclear distance of 1.03 Angstrom and a rotational correlation time of 100 ps with proton magnetization inverted at time zero, we get the following curves for the time dependence of the longitudinal magnetization:



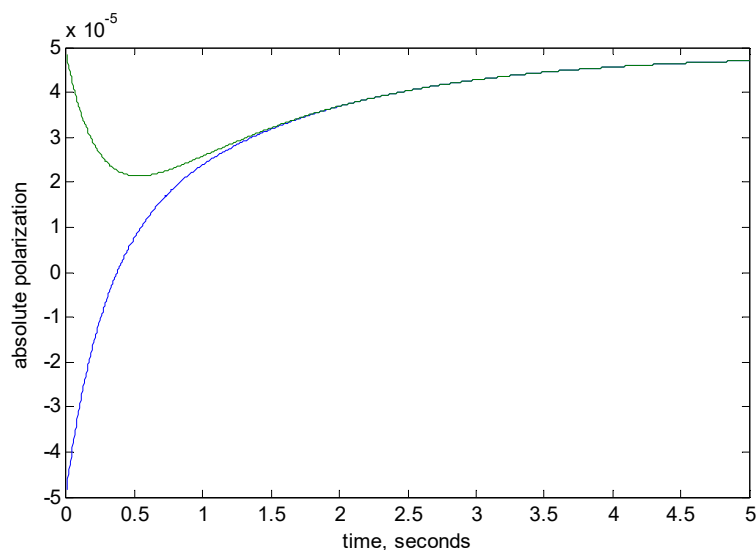
Several things in this figure are worth noting. Firstly, the room temperature equilibrium polarization of ^{13}C is approximately a factor of four smaller than that of protons, a consequence of the smaller magnetogyric ratio. Secondly, an enhancement of ^{13}C polarization, by nearly a factor of three may be obtained via the Overhauser effect if the nearby proton is inverted. Thirdly, the three relaxation parameters ρ_{II} , ρ_{SS} and σ_{IS} may be extracted by fitting Equation (2). Inter-atomic distance and rotational correlation time may then be determined by solving Equations (1) and (3).

A manual NOE measurement experiment involves inverting the source spin, waiting for a variable “mixing” time and running a pulse-acquire experiment. A typical picture (a chain of four protons with 2 Angstrom spacing at 600 MHz and a correlation time of 200 ps) is given below



The peaks are integrated, the integrals plotted against time and fitted to Equation (2), in most cases directly with respect to the distance and the correlation time.

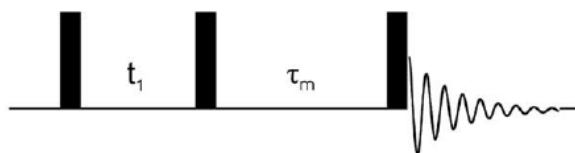
As expected from the appearance of Equation (3), homonuclear Overhauser effect becomes negative for long correlation times. Longitudinal magnetization dynamics in a room-temperature ^1H - ^1H spin system in a 600 MHz magnet with the a distance of 2.00 Angstrom and a correlation time of 1 ns is shown below



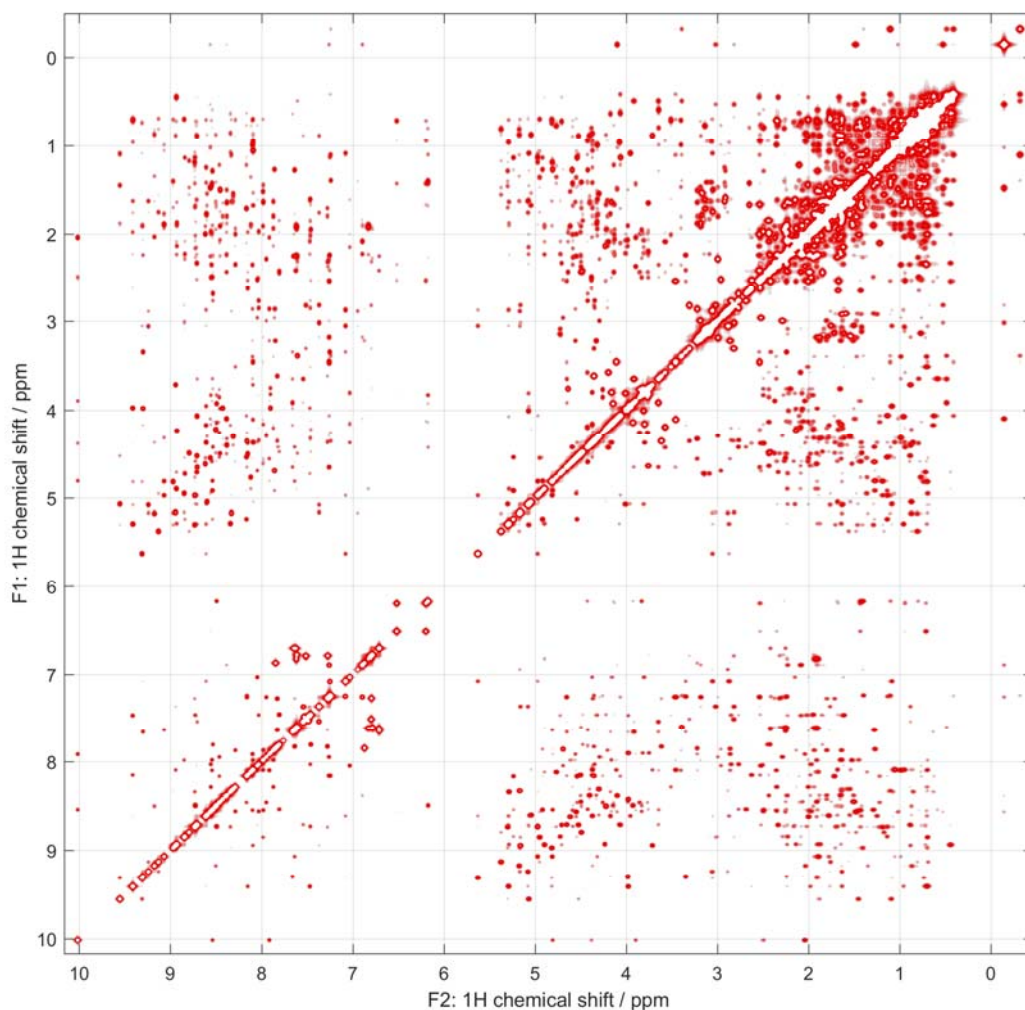
In multi-nuclear systems the two-spin approximation described above is often invalid and the distances resulting from such fitting runs can only be viewed as approximate.

NOESY pulse sequence

The 2D pulse sequence that takes advantage of the nuclear Overhauser effect is NOESY. The difference with COSY is that NOESY peaks are indicative of spatial proximity rather than J -coupling.



The sequence starts off in the same way as COSY, and has the same indirect evolution period. However, the transverse magnetisation is destroyed after the second pulse (using gradients), and the longitudinal magnetisation is allowed to cross-relax during the second evolution period, called *mixing time*. The magnetisation is then made transverse by the last pulse and detected. From the practical perspective, the existence of a NOESY cross-peak simply indicates spatial proximity.



Cross-peak intensity is a function of spin-spin distance, and NOESY spectra can therefore contain vast amounts of information on molecular geometry. An example (ubiquitin) is shown above.