NOESY – Applications to Proteins

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The field seen at nucleus A fluctuates as a molecule tumbles and $\theta$ changes.

The interaction operator, $V$, is distance dependent ($1/r^3$) and contains several types of operators: $Iz, I+, I-, I+, I++,$ etc. 

$(I+, I-, etc$ are linear combinations of $Ix, Iy)$

These operators can cause several types of transitions:
one quantum, $W_1$, two quantum, $W_2$, zero quantum, $W_0$

The magnitude of $\mu_B$ is important – an unpaired electron is $(2000)^2$ more efficient than a proton at the same distance
Some magnetization precessing at $\omega_a$ in $t_1$ can precess at $\omega_b$ in $t_2$. 
Periodic Inversion Sets Stage for Magnetization Transfer During Mixing Time

For short $T$, Large $\tau_c$, $\Delta I \propto 1/r^6$

$T = 0$

$T = \Delta T$
NOE (Nuclear Overhauser Effect)
depends on competition between $W_0$ and $W_2$ processes
NOEs are Positive for Small Molecules, Negative for Large

\[ \eta = \frac{-1 + \frac{6}{1+4\omega_0^2\tau_c^2}}{1 + \frac{3}{1+\omega_0^2\tau_c^2} + \frac{6}{1+4\omega_0^2\tau_c^2}} \]
In Practice Data May be Collected for Cross Peaks at a Series of Mixing Times

\[ I_{cp} = C\{\exp(-\rho T) \cdot (1 - \exp(-2\sigma T))\} \]

\[ \rho = 2W_1 + W_2 + W_0, \quad \sigma = (W_2 - W_0) \]

[Graph showing \( dI_{cp}/dT \propto 1/r^6 \)]
NOEs Give Structural Information

\[ \frac{\sigma_{14'}}{\sigma_{12}} = \frac{r_{12}^6}{r_{14'}^6} \]

\[ r_{12} = 2.5 \text{ Å}, \quad \frac{\sigma_{14'}}{\sigma_{12}} = 4.0, \quad \text{implies: } r_{14'} = 3.15 \text{ Å} \]
Potential NOE Interactions

In an Idealized $\alpha$-Helix
NOEs for Intermediate Sized Molecules: ROESY

- Short peptides and oligosaccharides often have tumbling times near $1/\omega_0$, and NOEs near zero.
- ROESY – Rotating Frame Overhauser Effect Spectroscopy – offers a solution – cross-relaxation in the low effective field of a “spin-lock”.
- Cross-peaks and auto-peaks are always of opposite sign. Still $1/r^6$ dependent. $\frac{1}{2}$ the intensity for a large molecule.

\[ 90x \quad \tau_m \quad \text{spin-lock} \quad t2 \]