Two Dimensional NMR

The experiments and spectra so far described are one dimensional in the sense that the FID obtained is a function of a single time variable. It is possible to introduce a second time variable by including an incrementable delay in the pulse sequence. This incrementable delay is typically called $t_1$; the time period during which the FID is acquired is then known as $t_2$. We collect a series of FIDs corresponding to different values of $t_1$. This set of FIDs is a function of both time variables: $S(t_1,t_2)$. Fourier Transformation of these FIDS wrt $t_2$ and transposition of the data matrix yields a set of interferograms $G(t_1,\omega_2)$. Finally, FT wrt $t_1$ yields a 2D NMR spectrum $F(\omega_1,\omega_2)$. 2D spectra are typically displayed as contour plots.

The above description can be generalized to any number of dimensions by introducing additional incrementable delays in the pulse sequence. Practically, dimensionality greater than 4 is not useful. 3D and 4D experiments have become common since about 1990.

Homonuclear 2D-J-Resolved Spectroscopy

Good introduction to nD NMR, but no longer commonly used.
Uncoupled Spins

Consider the effect of this pulse sequence on two spins A and X. Initially, assume that they are not J-coupled so we can see the effect of the pulse sequence on chemical shifts.

Define magnetization vector for each transition
\( \propto \) population difference of states involved.

Figure 11-2
The effect of the \( \left( \frac{\pi}{2} \right) \) pulse is to bring both isochromats along the \( y' \) axis of the rotating frame.

Immediately after the \( \left( \frac{\pi}{2} \right) \) pulse, \( A \) and \( X \) are in phase.

However, with time, the magnetization in the \( xy \) plane will evolve. Consider time \( \frac{t_1}{2} \). Because of different precession frequencies of \( A \) vs \( X \), there will be a phase difference between them.

\[
\Delta \phi_1 = 2\pi (\Delta \nu_0) \left( \frac{t_1}{2} \right)
\]
If at this time a $\pi$-pulse is applied along $y'$ (by changing the transmitter phase), then

\[
\Delta \phi_1 (t = t_1) = -\Delta \phi_1 + \Delta \phi_2 = -\Delta \phi_1 + 2\pi \left(\Delta \nu_0 \right) \left(\frac{t_1}{2}\right) = 0
\]

So at the end of the evolution period, i.e., $t = t_1$, the two magnetization vectors are refocused: the signal at time $t_1$ is exactly the same as after the first $\pi/2$ pulse (except for homogeneous effects. . . $T_2$ relaxation during the time period $t_1$). Any dispersion due to magnetic field inhomogeneity is refocused as well.

Result: chemical shifts are refocused by the pulse sequence for any $t_1$ . . . i.e. chemical shifts are independent of $t_1$ and will not show up in the spectrum in $\omega_1$.

**Coupled Spins**

Now we want to look at how the $J$-coupling term of the Hamiltonian behaves under the pulse sequence. Assume $A$ and $X$ are now coupled, with coupling constant $J$:

\[
J \mathbf{I}_A \cdot \mathbf{I}_X \quad (A,X \text{ because } \delta >> J)
\]
Consider the effect of the pulse sequence on $A$ spins. Label the magnetization vectors $A_\alpha$ and $A_\beta$ corresponding to whether the coupling partner (X spin) is $\alpha$ or $\beta$. Then

After $\left(\frac{\pi}{2}\right)_{x'}$ pulse

After evolution for time $\frac{t_1}{2}$

$$\Delta \phi_1 = 2\pi J \frac{t_1}{2}$$

After $(\pi)_{y'}$ pulse

$(\pi)_{y'}$ pulse rotates the magnetization components $A_\alpha, A_\beta$ to mirror image position wrt the $y'$ axis. In this case, the $(\pi)_{y'}$ pulse has an additional effect: the state of the coupled X is inverted, so the precession frequencies of the two A magnetization vectors are swapped.
Result: At $t=t_1$, the components of A magnetization are separated by $2\pi J t_1$. Thus, $J$-coupling is not refocused by spin echo. Instead, it causes the components of the A magnetization to oscillate as a function of $t_1$ at frequencies $-\pi J$ and $+\pi J$.

The time-domain NMR signal will be of the following form:

$$s(t_1, t_2) = \frac{M_0^4}{2} \left[ e^{-t_1/T_2} e^{i\pi J t_1} e^{-t_2/T_2} e^{-i(\omega_0^A - \pi J) t_2} + e^{-t_1/T_2} e^{-i\pi J t_1} e^{-t_2/T_2} e^{-i(\omega_0^A + \pi J) t_2} \right]$$

In $t_2$, we detect both chemical shift and $J$-coupling ($\omega_0^A \pm \pi J$ terms above), while only the $J$-coupling shows up in $t_1$ terms.

$$F(\omega_1, \omega_2) = \int s(t_1, t_2) e^{-i\omega_1 t_1} e^{-i\omega_2 t_2} dt_1 dt_2$$
Predict resonances at

or

\[ \begin{align*}
\omega_1 & \quad \omega_2 \\
+ \pi J & \quad w_0^A + \pi J \\
- \pi J & \quad w_0^A - \pi J \\
\end{align*} \]

\[ \frac{J}{2} \quad \nu_0^A + \frac{J}{2} \]

\[ \frac{-J}{2} \quad \nu_0^A - \frac{J}{2} \]

\[ + \]

\[ - \]

massage data to simplify appearance

normal

tilted

spin-spin collapsed along \( f_2 \) axis, but oriented along \( f_1 \) axis

Figure 11-3
Correlation Experiments

The 2D-J-resolved experiment is an exception, in that it correlates one property of a particular spin with another property of the same spin. Most nD experiments are correlation experiments, correlating chemical shifts of pairs of spins which are related by e.g. J-coupling, dipole-dipole interaction, or chemical exchange. They may be homonuclear (all H’s) or heteronuclear (¹³C—¹H or ¹⁵N—¹H).

**Homonuclear:**

<table>
<thead>
<tr>
<th>Correlation via J-coupling</th>
<th>Correlation via Cross-relaxation</th>
</tr>
</thead>
<tbody>
<tr>
<td>COSY</td>
<td>NOESY</td>
</tr>
<tr>
<td>TOCSY</td>
<td></td>
</tr>
</tbody>
</table>

**COSY**

COSY gives crosspeaks between spins separated by two or three bounds only (vicinal, geminal protons).

**TOCSY**

TOCSY allows mixing of all spins or a spin system. For example, you will see a TOCSY crosspeak between A and X in an AMX spin system where $J_{AM}, J_{MX} \neq 0$, $J_{AX} = 0$.

An example:

CH₃—CH₂—CH₂OH

TOCSY, but no COSY

COSY and TOCSY
Dipole-Dipole Interactions

Two magnetic dipoles will interact through space (contrast with the J-coupling interaction, which occurs only through the intervening electron density of bonds). Detection of this interaction is evidence for spatial proximity of the spins (measurable for distances $\leq 5$ Å)

$\mathbf{\mu}_A \cdot \mathbf{R} \mathbf{\rightarrow} \mathbf{\mu}_X$

Let’s call $A$ spin $J$ and $X$ spin $S$. . . conventional nomenclature for what follows.

$$E_{dd} = \frac{\mathbf{\mu}_A \cdot \mathbf{\mu}_X}{R^3} - 3\left(\frac{\mathbf{\mu}_A \cdot \mathbf{R} (\mathbf{R} \cdot \mathbf{\mu}_X)}{R^5}\right)$$

$$= \gamma_A^2 \gamma_X^2 \left[ \frac{I_A \cdot I_X}{R^3} - \frac{3 (I_A \cdot \mathbf{R} (\mathbf{R} \cdot I_X))}{R^5} \right] \quad \text{(for } \gamma_A = \gamma_X)$$

$$= \gamma_I \gamma_S^2 \left[ \frac{I \cdot S}{R^3} - \frac{3 (I \cdot \mathbf{R} (\mathbf{R} \cdot S))}{R^5} \right] \quad \text{(generally)}$$

This interaction provides the main means by which spins $\frac{1}{2}$ exchange magnetization ($T_2$ processes — called cross-relaxation) or dissipate magnetization to the lattice in longitudinal relaxation.

The motion of $I$ relative to $S$ sets up local field fluctuations at $S$ (or, equivalently, modulates $E$ levels of $S$). There exists a component of this modulation at $S$ transition frequency, so the fluctuations can induce transitions.
**Solomon Equations**

The Solomon equations are a phenomenological description of the relaxation behavior of the \(Z\)-components of \(I\), \(S\) magnetization in a two-spin dipolar-coupled system.

\[
\frac{d}{dt} \langle I_Z \rangle = \frac{1}{T_{II}^I} \left( \langle I_Z \rangle - I_0 \right) - \frac{1}{T_{IS}^I} \left( \langle S_Z \rangle - S_0 \right)
\]

\[
\frac{d}{dt} \langle S_Z \rangle = \frac{1}{T_{IS}^I} \left( \langle I_Z \rangle - I_0 \right) - \frac{1}{T_{SS}^I} \left( \langle S_Z \rangle - S_0 \right)
\]

where \( T_{II}^I = W_0 + 2W_{II} + W_2 \)

\( T_{IS}^I = W_0 + 2W_{IS} + W_2 \)

\( T_{SS}^I = W_2 - W_0 \)

Here \( W \)'s are transition probabilities, related to molecular geometry and motion by time-dependent perturbation theory.

\[
W_0 = \frac{1}{10} \frac{\hbar^2 \gamma_I^2 \gamma_S^2}{R^6} \frac{\tau_c}{1 - \left( \omega_I - \omega_S \right)^2 \tau_c^2}
\]

\[
W_{II} = \frac{3}{20} \frac{\hbar^2 \gamma_I^2 \gamma_S^2}{R^6} \frac{\tau_c}{1 + \omega_I^2 \tau_c^2}
\]

\[
W_{IS} = \frac{3}{20} \frac{\hbar^2 \gamma_I^2 \gamma_S^2}{R^6} \frac{\tau_c}{1 + \omega_S^2 \tau_c^2}
\]

\[
W_Z = \frac{3}{5} \frac{\hbar^2 \gamma_I^2 \gamma_S^2}{R^6} \frac{\tau_c}{1 + \left( \omega_I + \omega_S \right)^2 \tau_c^2}
\]

where \( \tau_c \) = rotation correlation time for \( \dot{R} \)

\[
(\omega_I \tau_c \approx 1 \quad \text{for} \quad \tau_c \approx 10^{-9} \quad \text{S for} \quad ^1\text{H at 500 mHz})
\]

**Main Result**  If in a two spin system, there exists nonequilibrium \(Z\)-magnetization, there will be magnetization exchange between \(A\) and \(X\).