COSY by PRODUCT OPERATORS

BCMB/CHEM 8190
Two Dimensional NMR Spectra

A General Scheme: other mixing and evolution periods can be added to increase dimensions

Preparation | Evolution 1 (Increment t₁) | Mixing | Evolution 2 (observe t₂)

Example: COSY – mixing is scalar coupling

d₁ (recover) 90x t₁ (evolve) 90x (mix) t₂ (observe)
2D -NMR - FIDs are Transformed in t2, then in t1
COSY for an AX Spin System
Using Product Operators

Hamiltonian: \[ H = -\gamma B_0 (1-\sigma_A) I_{ZA} -\gamma B_0 (1-\sigma_X) I_{ZX} + 2\pi J I_{ZA} \cdot I_{ZX} \]

chemical shift \quad scalar coupling

Basis set: \((\alpha\alpha, \alpha\beta, \beta\alpha, \beta\beta)\)

Using product operator transformation tables, or Kanters’ POF procedures for MAPLE:

\[
\begin{align*}
\text{step1} &:= \text{spinsystem}([A,X]); \\
\text{step2} &:= \text{xpulse}(\text{step1},\{A,X\},\pi/2);
\end{align*}
\]
Evolution Step Combines All parts of Hamiltonian in Kanters’ POF Approach

> step3 := evolve(step2, {A, X}, t1);

\[
\begin{align*}
\text{step3} & := -\cos(2\pi W_A t1) Iy_A \cos(\pi J_A X t1) \\
& \quad + 2 \cos(2\pi W_A t1) Ix_A Ix X \sin(\pi J_A X t1) \\
& \quad + \sin(2\pi W_A t1) Ix_A \cos(\pi J_A X t1) \\
& \quad + 2 \sin(2\pi W_A t1) Iy_A Ix X \sin(\pi J_A X t1) \\
& \quad - \cos(2\pi W_X t1) Iy_X \cos(\pi J_A X t1) \\
& \quad + 2 \cos(2\pi W_X t1) Ix_X Ix A \sin(\pi J_A X t1) \\
& \quad + \sin(2\pi W_X t1) Ix_X \cos(\pi J_A X t1) \\
& \quad + 2 \sin(2\pi W_X t1) Iy_X Ix A \sin(\pi J_A X t1)
\end{align*}
\]
Can Also use Transformation Table

Because elements of $H$ commute
operators can be applied successively

\[(\pi J_t)2I_{ZA}I_{ZX}\]
\[I_{YA} \rightarrow \cos(\pi J_t)I_{YA} - \sin(\pi J_t)2I_{XA}I_{ZX}\]

\[(\omega_A t_1)(I_{ZA} + I_{ZX})\]
\[\cos(\pi J_t)I_{YA} \rightarrow \cos(\pi J_t)\cos(\omega_A t_1)I_{YA} - \cos(\pi J_t)\sin(\omega_A t_1)I_{XA}\]

\[(\omega_A t_1)(I_{ZA} + I_{ZX})\]
\[-\sin(\pi J_t)2I_{XA}I_{ZX} \rightarrow -\sin(\pi J_t)\cos(\omega_A t_1)2I_{XA}I_{ZX} - \sin(\pi J_t)\sin(\omega_A t_1)2I_{YA}I_{ZX}\]

Repeat for $I_{YX}$ - get four more terms
Now the effect of another X pulse:

\[ I_{XA} + I_{XX} \]

```plaintext
> step4 := xpulse(step3, {A,X}, Pi/2);

step4 := -Cos(2 \pi W_A t1) I_x A \cos(\pi J_{A,X} t1) \\
- 2 \cos(2 \pi W_A t1) I_x A I_y X \sin(\pi J_{A,X} t1) \\
+ \sin(2 \pi W_A t1) I_x A \cos(\pi J_{A,X} t1) \\
- 2 \sin(2 \pi W_A t1) I_x A I_y X \sin(\pi J_{A,X} t1) \\
- \cos(2 \pi W_X t1) I_x X \cos(\pi J_{A,X} t1) \\
- 2 \cos(2 \pi W_X t1) I_x X I_y A \sin(\pi J_{A,X} t1) \\
+ \sin(2 \pi W_X t1) I_x X \cos(\pi J_{A,X} t1) \\
- 2 \sin(2 \pi W_X t1) I_x X I_y A \sin(\pi J_{A,X} t1)
```

some of the above are not observable (MQ,Z) – only retain observables
some X observables were modulated by properties of A in t1 – crosspeaks
some X observables were modulated by properties of X in t1 - autopeaks
Observe: take the trace of result with Mx and My operators \((I_{XA} + I_{XX} + I_{YA} + I_{YX})\). \(I\) is Y component.

\[
\text{step5} := \frac{1}{2} \sin(2 \pi W_{A} t1) \cos(\pi J_{A,X} t1) \cos(2 \pi W_{A} t2) \cos(\pi J_{A,X} t2) \\
+ \frac{1}{2} I \sin(2 \pi W_{A} t1) \sin(\pi J_{A,X} t1) \sin(2 \pi W_{X} t2) \sin(\pi J_{A,X} t2) \\
+ \frac{1}{2} I \sin(2 \pi W_{X} t1) \sin(\pi J_{A,X} t1) \sin(2 \pi W_{A} t2) \sin(\pi J_{A,X} t2) \\
+ \frac{1}{2} \sin(2 \pi W_{X} t1) \sin(\pi J_{A,X} t1) \cos(2 \pi W_{A} t2) \sin(\pi J_{A,X} t2) \\
+ \frac{1}{2} \sin(2 \pi W_{X} t1) \cos(\pi J_{A,X} t1) \cos(2 \pi W_{X} t2) \cos(\pi J_{A,X} t2) \\
+ \frac{1}{2} \sin(2 \pi W_{X} t1) \cos(\pi J_{A,X} t1) \sin(2 \pi W_{X} t2) \cos(\pi J_{A,X} t2) \\
+ \frac{1}{2} \sin(2 \pi W_{A} t1) \cos(\pi J_{A,X} t1) \sin(2 \pi W_{A} t2) \cos(\pi J_{A,X} t2) \\
+ \frac{1}{2} \sin(2 \pi W_{A} t1) \sin(\pi J_{A,X} t1) \cos(2 \pi W_{X} t2) \sin(\pi J_{A,X} t2)
\]

Note: \(t1\) must reach \(~1/(2J)\) or sin terms make crosspeaks small.
Useful Trigonometric Identities:

\[
\begin{align*}
\sin(A)\cos(B) &= \frac{1}{2} [\sin(A+B) + \sin(A-B)] \\
\cos(A)\sin(B) &= \frac{1}{2} [\sin(A+B) - \sin(A-B)] \\
\sin(A)\sin(B) &= \frac{1}{2} [\cos(A-B) - \cos(A+B)] \\
\cos(A)\cos(B) &= \frac{1}{2} [\cos(A+B) + \cos(A-B)]
\end{align*}
\]

Previous expressions evolve at $\omega \pm \pi J$.
Transforming these in $t_1$ and $t_1$ gives a series of Absorptive and Dispersive peaks at $\nu +/− J/2$

\[
> \text{spec1} := \text{evalc(Re(FT(FT(step5,0,t2,v2),0,t1,v1))});}
\]
Sequence has no quadrature in V1

- Can set transmitter rf is to one side of spectrum, but this reduces sensitivity

\[ \cos(w) = \frac{1}{2} (\exp(iw) + \exp(-iw)) \]
\[ \text{two opposite rotating components} \]

\[ \sin(w) = -\frac{i}{2} (\exp(iw) - \exp(-iw)) \]
\[ \text{sum of two terms (i*sin) gives +w} \]

- Solution: collect a second set of data with sin modulation in t1: accomplished by setting by setting second pulse to 90y, and adding acquisitions to imaginary part of memory
Elementary Phase cycle for COSY

- Implement quadrature in t1
- Correct for T1 recover in t1 – would give axial peak
- Phase cycle:

<table>
<thead>
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<th>φ2</th>
<th>φ2</th>
<th>φ2</th>
<th>memory</th>
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<tr>
<td>x</td>
<td>x</td>
<td>+</td>
<td>real</td>
</tr>
<tr>
<td>-x</td>
<td>x</td>
<td>-</td>
<td>real</td>
</tr>
<tr>
<td>x</td>
<td>y</td>
<td>+</td>
<td>imag</td>
</tr>
<tr>
<td>-x</td>
<td>y</td>
<td>-</td>
<td>imag</td>
</tr>
</tbody>
</table>
Another problem: Dispersive and Twisted Auto-Peaks (or Cross-Peaks)

- Long tails make cross-peaks close to diagonal hard to see

- One solution: magnitude spectrum – but lines are still broad
Double-Quantum Filtered COSY

- Consider MQ term from page 7 and add x pulse
- $-2I_{1x}I_{2y} -(I_{1x}+I_{2x}) \rightarrow -2I_{1x}I_{2z} \ldots$ auto-peak
- $-2I_{1y}I_{2x} -(I_{1x}+I_{2x}) \rightarrow -2I_{1z}I_{2x} \ldots$ cross-peak
- Note: both are absorptive (still antiphase)
- Phase cycling needed to remove other pathways
- Resonances from single lines (solvent) removed
Example of 2Q-Filtered COSY

β-Me-Galactose