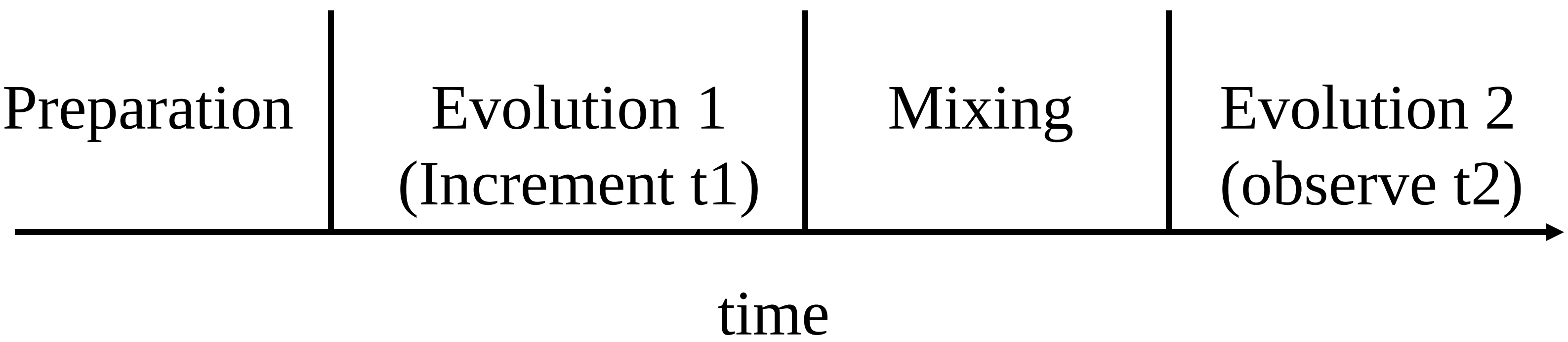
COSY by PRODUCT OPERATORS

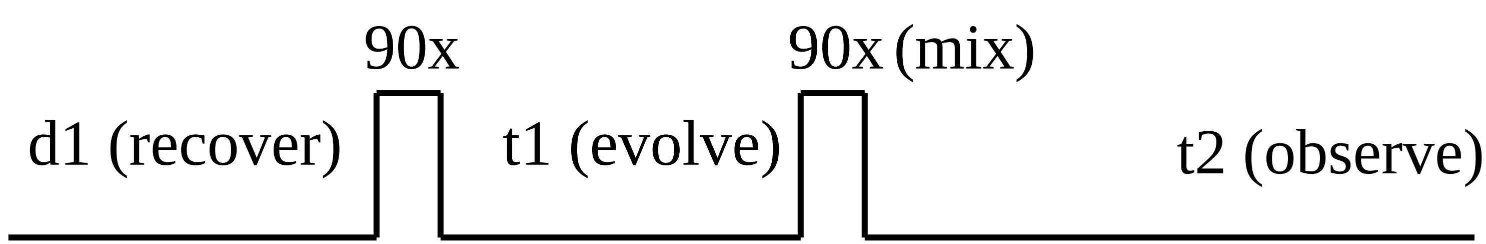
BCMB/CHEM 8190

Two Dimensional NMR Spectra

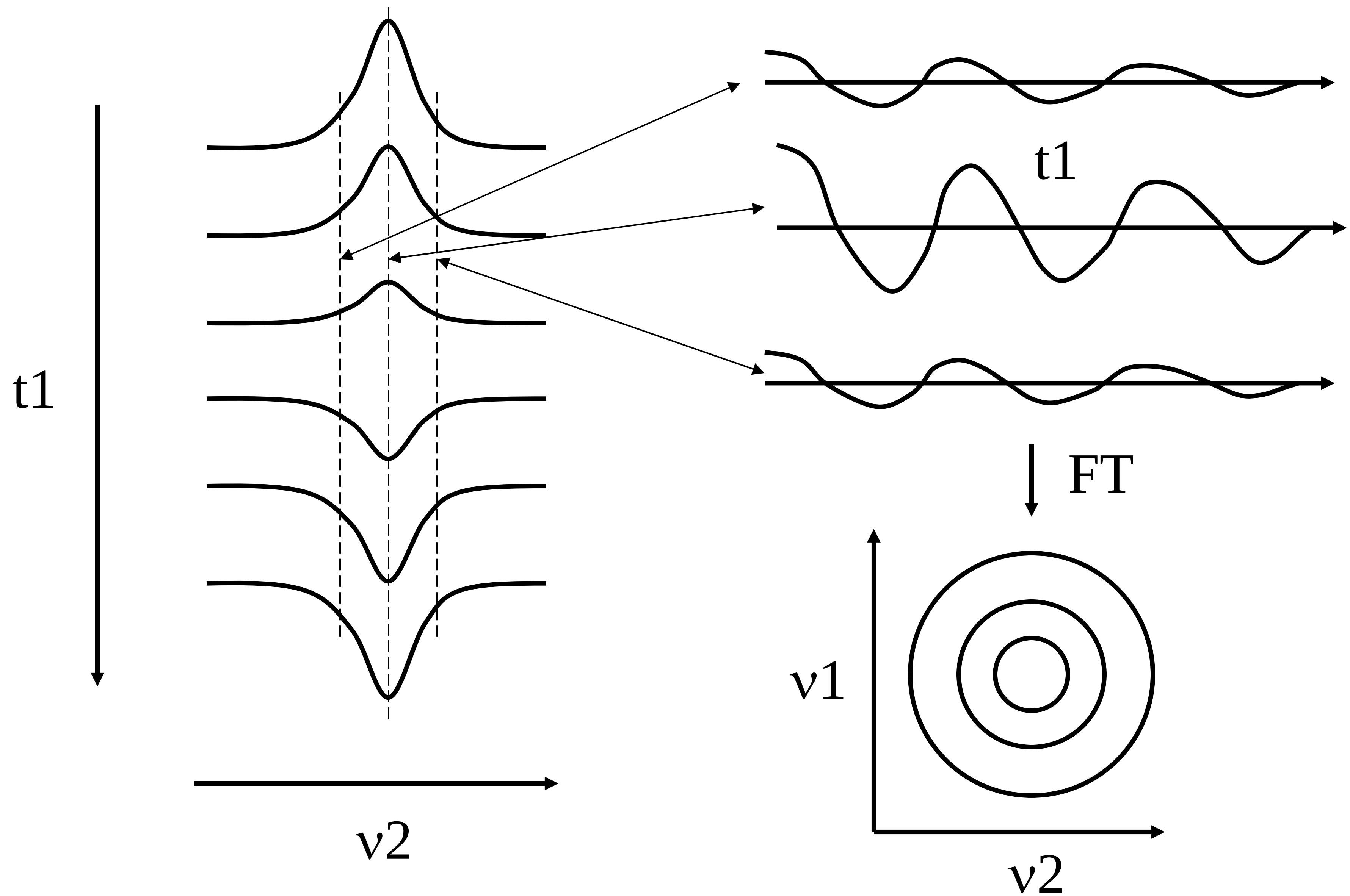
A General Scheme: other mixing and evolution periods can be added to increase dimensions



Example: COSY – mixing is scalar coupling



2D –NMR - FIDs are Transformed in t2, then in t1



COSY for an AX Spin System
Using Product Operators

Hamiltonian: $\mathbf{H} = -\gamma B_0(1-\sigma_A)\mathbf{I}_{\mathbf{ZA}} - \gamma B_0(1-\sigma_X)\mathbf{I}_{\mathbf{ZX}} + 2\pi J\, \mathbf{I}_{\mathbf{ZA}} \cdot \mathbf{I}_{\mathbf{ZX}}$

chemical shift scalar coupling

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

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

- `step1:=spinsystem([A,X]);`

$$step1 := Iz_A + Iz_X$$

- `step2:=xpulse(step1,{A,X},Pi/2);`

$$step2 := -Iy_A - Iy_X$$

Evolution Step Combines All parts of Hamiltonian in Kanters' POF Approach

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

$$
\begin{aligned}
step3 := & -\mathrm{Cos}(2\,\pi\,W_A\,t1)\,Iy_A\,\mathrm{Cos}(\pi\,J_{A,X}\,t1) \\
& + 2\,\mathrm{Cos}(2\,\pi\,W_A\,t1)\,Ix_A\,Iz_X\,\mathrm{Sin}(\pi\,J_{A,X}\,t1) \\
& + \mathrm{Sin}(2\,\pi\,W_A\,t1)\,Ix_A\,\mathrm{Cos}(\pi\,J_{A,X}\,t1) \\
& + 2\,\mathrm{Sin}(2\,\pi\,W_A\,t1)\,Iy_A\,Iz_X\,\mathrm{Sin}(\pi\,J_{A,X}\,t1) \\
& - \mathrm{Cos}(2\,\pi\,W_X\,t1)\,Iy_X\,\mathrm{Cos}(\pi\,J_{A,X}\,t1) \\
& + 2\,\mathrm{Cos}(2\,\pi\,W_X\,t1)\,Ix_X\,Iz_A\,\mathrm{Sin}(\pi\,J_{A,X}\,t1) \\
& + \mathrm{Sin}(2\,\pi\,W_X\,t1)\,Ix_X\,\mathrm{Cos}(\pi\,J_{A,X}\,t1) \\
& + 2\,\mathrm{Sin}(2\,\pi\,W_X\,t1)\,Iy_X\,Iz_A\,\mathrm{Sin}(\pi\,J_{A,X}\,t1)
\end{aligned}
$$

Can Also use Transformation Table

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

$$\mathbf{I_{YA}} \xrightarrow{(\pi J t_1)\mathbf{2I_{ZA}I_{ZX}}} \cos(\pi J t_1)\mathbf{I_{YA}} - \sin(\pi J t_1)\mathbf{2I_{XA}I_{ZX}}$$

$$\cos(\pi J t_1)\mathbf{I_{YA}} \xrightarrow{(\omega_A t_1)(\mathbf{I_{ZA}}+\mathbf{I_{ZX}})} \cos(\pi J t_1)\cos(\omega_A t_1)\mathbf{I_{YA}} - \cos(\pi J t_1)\sin(\omega_{\mathbf{A}} \mathbf{t_1})\mathbf{I_{XA}}$$

$$-\sin(\pi J t_1)\mathbf{2I_{XA}I_{ZX}} \xrightarrow{(\omega_A t_1)(\mathbf{I_{ZA}}+\mathbf{I_{ZX}})} -\sin(\pi J t_1)\cos(\omega_A t_1)\mathbf{2I_{XA}I_{ZX}} - \sin(\pi J t_1)\sin(\omega_A t_1)\mathbf{2I_{YA}I_{ZX}}$$

Repeat for $\mathbf{I_{YX}}$ **-** get four more terms

Now the effect of another X pulse:

$$\mathbf{I}_{XA} + \mathbf{I}_{XX}$$

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

$$
\begin{aligned}
step4 := & -Cos(2\,\pi\,W_A\,t1)\,Iz_A\,Cos(\pi\,J_{A,X}\,t1) \\
& - 2\,Cos(2\,\pi\,W_A\,t1)\,Ix_A\,Iy_X\,Sin(\pi\,J_{A,X}\,t1) \\
& + Sin(2\,\pi\,W_A\,t1)\,Ix_A\,Cos(\pi\,J_{A,X}\,t1) \\
& - 2\,Sin(2\,\pi\,W_A\,t1)\,Iz_A\,Iy_X\,Sin(\pi\,J_{A,X}\,t1) \\
& - Cos(2\,\pi\,W_X\,t1)\,Iz_X\,Cos(\pi\,J_{A,X}\,t1) \\
& - 2\,Cos(2\,\pi\,W_X\,t1)\,Ix_X\,Iy_A\,Sin(\pi\,J_{A,X}\,t1) \\
& + Sin(2\,\pi\,W_X\,t1)\,Ix_X\,Cos(\pi\,J_{A,X}\,t1) \\
& - 2\,Sin(2\,\pi\,W_X\,t1)\,Iz_X\,Iy_A\,Sin(\pi\,J_{A,X}\,t1)
\end{aligned}
$$

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 ($\mathbf{I_{XA}}+\mathbf{I_{XX}}+\mathbf{I_{YA}}+\mathbf{I_{YX}}$). I is Y component

```
> step5:=observe(step4, {A,X}, t2,0);
```

$$
\begin{aligned}
step5 := &\frac{1}{2} Sin(2\pi W_A t1)\, Cos(\pi J_{A,X} t1)\, Cos(2\pi W_A t2)\, Cos(\pi J_{A,X} t2) \\
&+ \frac{1}{2} I\, Sin(2\pi W_A t1)\, Sin(\pi J_{A,X} t1)\, Sin(2\pi W_X t2)\, Sin(\pi J_{A,X} t2) \\
&+ \frac{1}{2} I\, Sin(2\pi W_X t1)\, Sin(\pi J_{A,X} t1)\, Sin(2\pi W_A t2)\, Sin(\pi J_{A,X} t2) \\
&+ \frac{1}{2} Sin(2\pi W_X t1)\, Sin(\pi J_{A,X} t1)\, Cos(2\pi W_A t2)\, Sin(\pi J_{A,X} t2) \\
&+ \frac{1}{2} Sin(2\pi W_X t1)\, Cos(\pi J_{A,X} t1)\, Cos(2\pi W_X t2)\, Cos(\pi J_{A,X} t2) \\
&+ \frac{1}{2} I\, Sin(2\pi W_X t1)\, Cos(\pi J_{A,X} t1)\, Sin(2\pi W_X t2)\, Cos(\pi J_{A,X} t2) \\
&+ \frac{1}{2} I\, Sin(2\pi W_A t1)\, Cos(\pi J_{A,X} t1)\, Sin(2\pi W_A t2)\, Cos(\pi J_{A,X} t2) \\
&+ \frac{1}{2} Sin(2\pi W_A t1)\, Sin(\pi J_{A,X} t1)\, Cos(2\pi W_X t2)\, Sin(\pi J_{A,X} t2)
\end{aligned}
$$

Note: t1 must reach ~1/(2J) or sin terms make crosspeaks small

Useful Trigonometric Identities:

- $\sin(A)\cos(B) = \frac{1}{2}[\sin(A+B) + \sin(A-B)]$
- $\cos(A)\sin(B) = \frac{1}{2}[\sin(A+B) - \sin(A-B)]$
- $\sin(A)\sin(B) = \frac{1}{2}[\cos(A-B) - \cos(A+B)]$
- $\cos(A)\cos(B) = \frac{1}{2}[\cos(A+B) + \cos(A-B)]$

Previous expressions evolve at $\omega \pm \pi J$

Transforming these in t1 and t1 Gives a series of Absorptive and Dispersive peaks at v +/- J/2

```
> spec1:=
evalc(Re(FT(FT(step5,0,t2,v2),0,t1,v1)));
```

$$+\frac{1}{16}\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v1\right)$$
$$+\frac{1}{16}\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v1\right)$$

$$\mathit{spec1} := \frac{1}{16}\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v1\right)$$

$$-\frac{1}{16}\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v1\right)$$

$$+\frac{1}{16}\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v1\right)$$

$$+\frac{1}{16}\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v1\right)$$

$$-\frac{1}{16}\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v1\right)$$

$$+\frac{1}{16}\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v1\right) - \frac{1}{16}\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v1\right)$$

$$+\frac{1}{16}\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v1\right) - \frac{1}{16}\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v1\right)$$

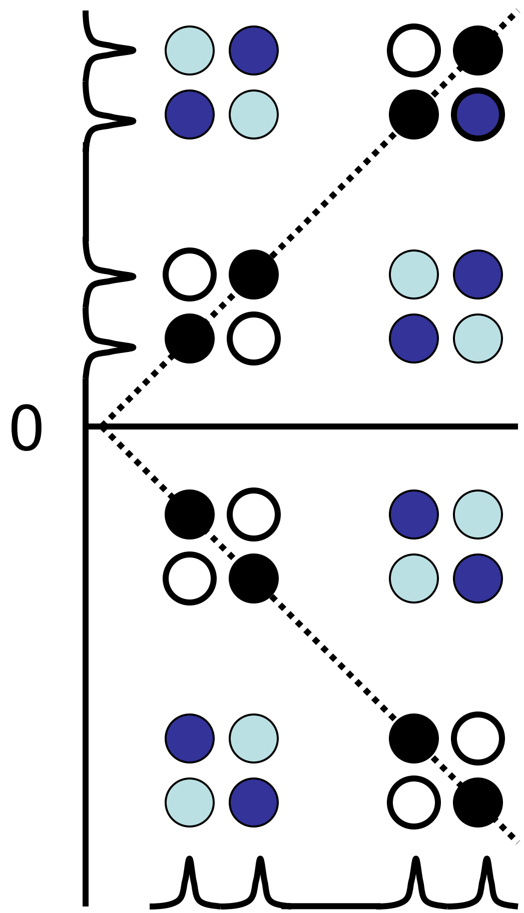
$$-\frac{1}{16}\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Di}\left(W_X-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v1\right)$$

$$-\frac{1}{16}\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X-\frac{1}{2}J_{A,X}, v1\right) - \frac{1}{16}\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A-\frac{1}{2}J_{A,X}, v1\right)$$

$$+\frac{1}{16}\mathit{Di}\left(W_A-\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_X+\frac{1}{2}J_{A,X}, v1\right) + \frac{1}{16}\mathit{Di}\left(W_A+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v1\right) - \frac{1}{16}\mathit{Di}\left(W_X+\frac{1}{2}J_{A,X}, v2\right)\mathit{Ab}\left(W_A+\frac{1}{2}J_{A,X}, v1\right)$$

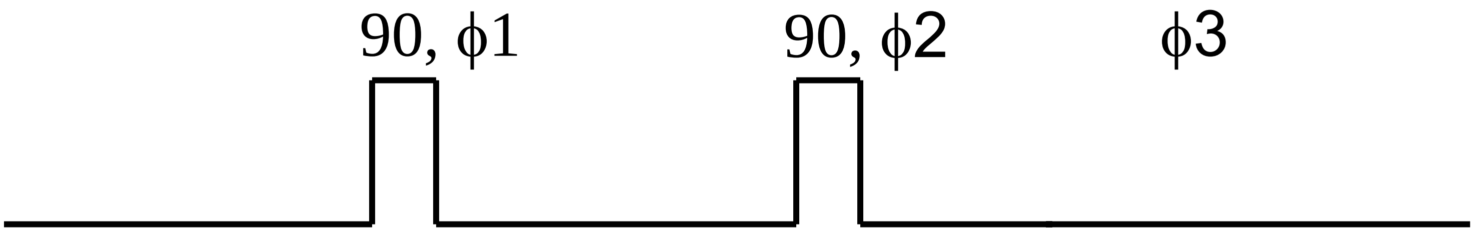
Sequence has no quadrature in V1

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



- Cos(w) = 1/2 (exp(iw) + exp(-iw)) two opposite rotating components
- Sin(w) = -i/2 (exp(iw) – exp(-iw)) sum of two terms (i*sin) gives +w
- Solution: collect a second set 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

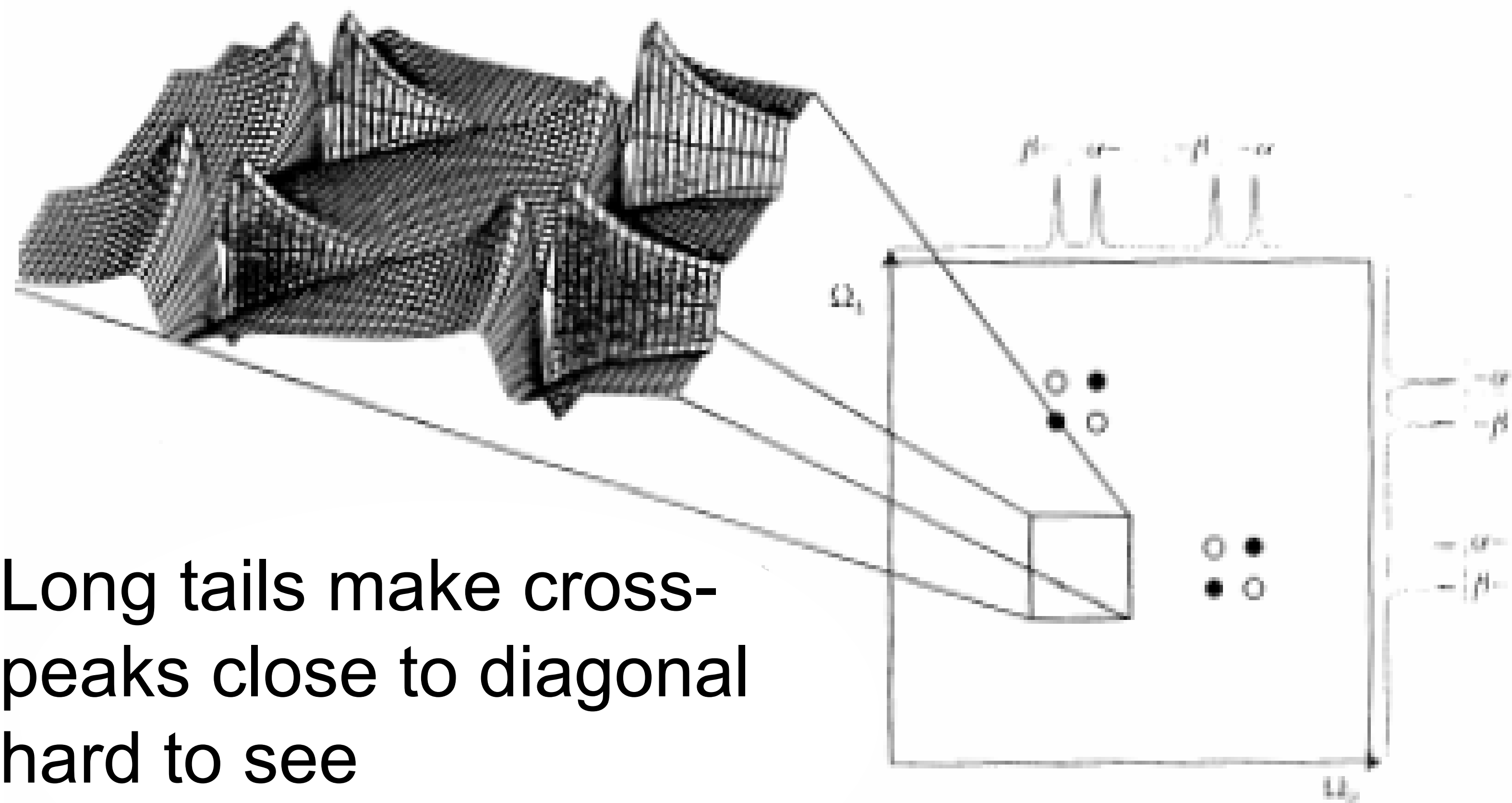
Elementary Phase cycle for COSY



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

φ2	φ2	φ2	memory
x	x	+	real
-x	x	-	real
x	y	+	imag
-x	y	-	imag

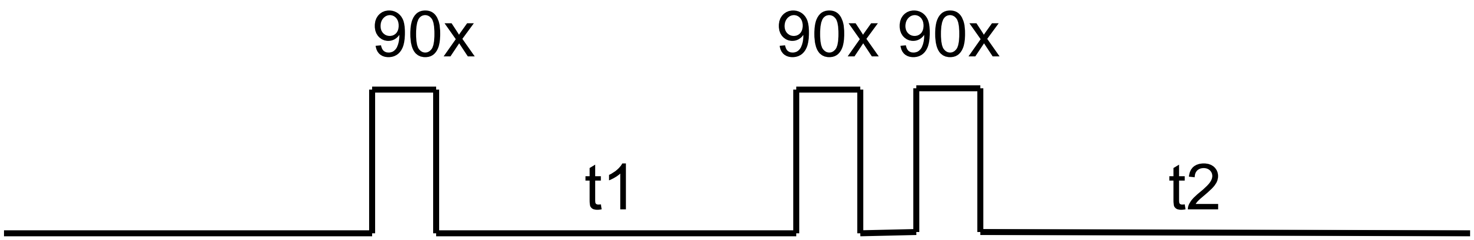
Another problem: Dispersive and Twisted Auto-Peaks (or Cross-Peaks)



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

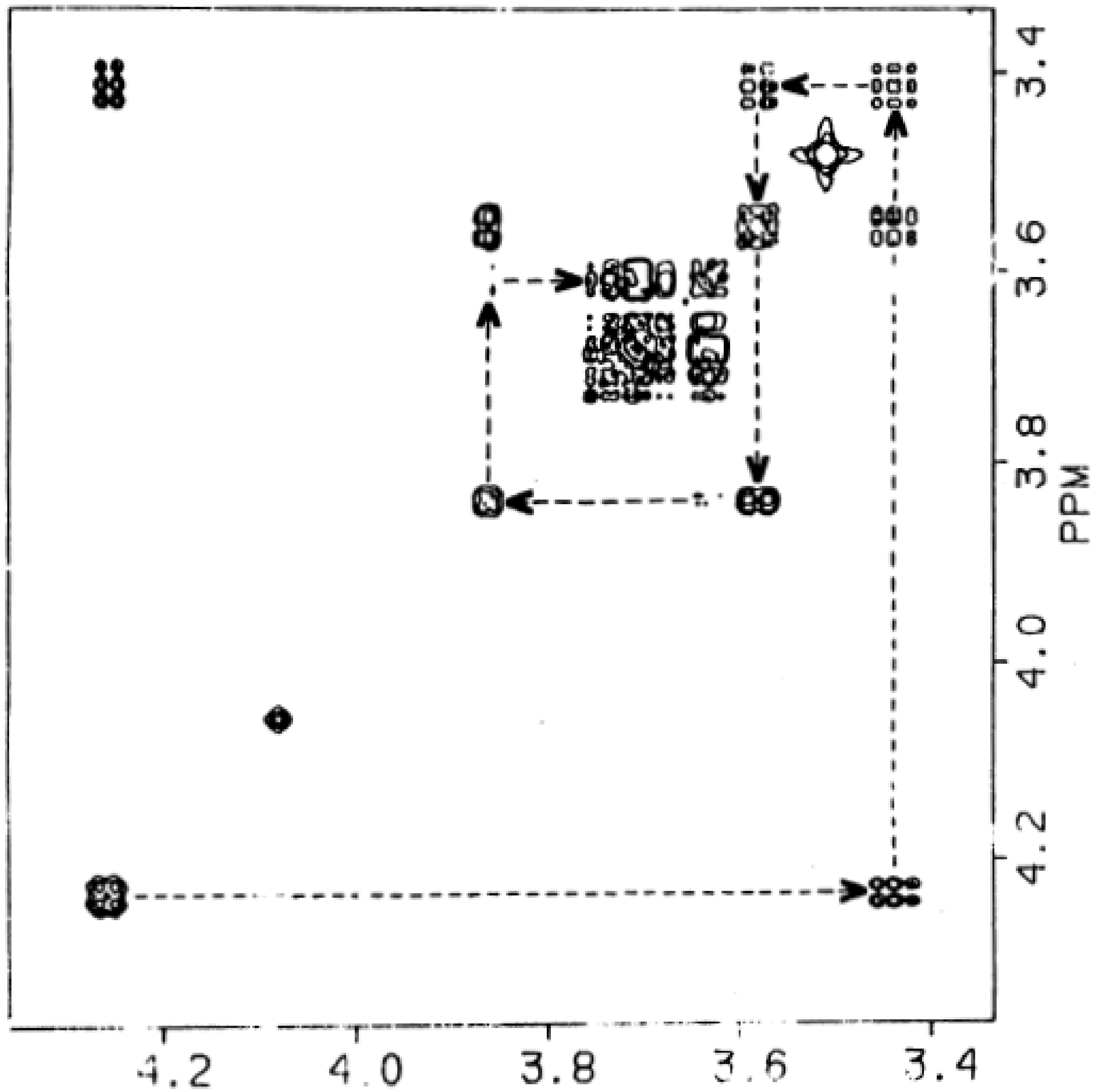
- One solution: magnitude spectrum – but lines are still broad

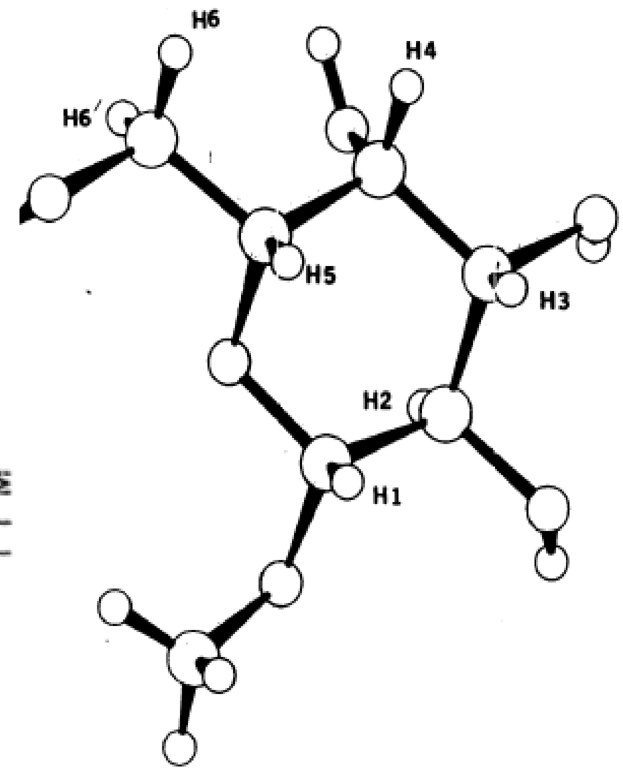
Double-Quantum Filtered COSY



- Consider MQ term from page 7 and add x pulse
- $-2I_{1X}I_{2Y} -(I_{1X}+I_{2X})\rightarrow -2I_{1X}I_{2Z}$ … auto-peak
- $-2I_{1Y}I_{2X} -(I_{1X}+I_{2X})\rightarrow -2I_{1Z}I_{2X}$ … 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