5. DENSITY MATRIX DESCRIPTION OF COSY (HOMONUCLEAR CORRELATION SPECTROSCOPY)

COSY (**CO**rrelation **S**pectroscop**Y**) is widely used, particularly for disentangling complicated proton spectra by proton-proton chemical shift correlation and elucidation of the coupling pattern. Of course, other spin 1/2 systems such as ^{19}F can be successfully studied with this 2D sequence. The basic sequence is shown in Figure I.11.

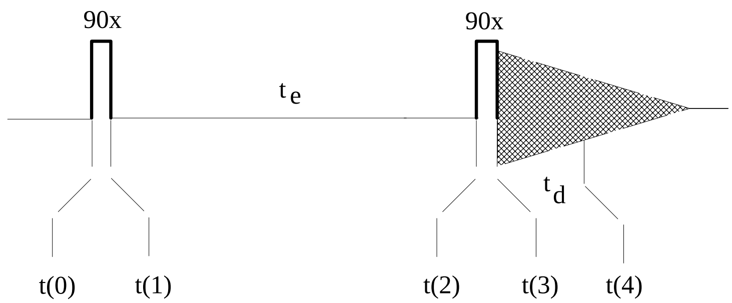

Figure I.11. The Basic COSY sequence (without phase cycling): $90x - t_e - 90x -$ AT

5.1 Equilibrium Populations

Since we deal with a homonuclear AX system, the populations at thermal equilibrium follow a pattern identical to that of INADEQUATE (see I.60 and I.61). The initial density matrix is:

$$D(0) = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 2 \end{bmatrix} \qquad \text{(I.90)}$$

5.2 The First Pulse

Here, also, we can use the results from INADEQUATE (I.63) since the first pulse is a nonselective 90*xAX*:

$$D(1)=\frac{1}{2}\begin{bmatrix}2 & -i & -i & 0\\ i & 2 & 0 & -i\\ i & 0 & 2 & -i\\ 0 & i & i & 2\end{bmatrix} \tag{I.91}$$

5.3 Evolution from *t* (1) to *t* (2)

Only nondiagonal terms are affected by evolution. The single-quantum coherences will evolve, each with its own angular frequency, leading to:

$$D(2)=\begin{bmatrix}1 & A & B & 0\\ A^* & 1 & 0 & C\\ B^* & 0 & 1 & D\\ 0 & C^* & D^* & 1\end{bmatrix} \tag{I.92}$$

where

$$\begin{aligned}A&=(-i/2)\exp(-i\Omega_{12}t_e)\\ B&=(-i/2)\exp(-i\Omega_{13}t_e)\\ C&=(-i/2)\exp(-i\Omega_{24}t_e)\\ D&=(-i/2)\exp(-i\Omega_{34}t_e)\end{aligned} \tag{I.93}$$

5.4 The Second Pulse

To calculate $D(3)=R^{-1}D(2)R$, we use the rotation operators for the 90*xAX* pulse given in (I.34)

$$R=\frac{1}{2}\begin{bmatrix}1 & i & i & -1\\ i & 1 & -1 & i\\ i & -1 & 1 & i\\ -1 & i & i & 1\end{bmatrix} \quad ; \quad R^{-1}=\frac{1}{2}\begin{bmatrix}1 & -i & -i & -1\\ -i & 1 & -1 & -i\\ -i & -1 & 1 & -i\\ -1 & -i & -i & 1\end{bmatrix}$$

The postmultiplication $D(2)R$ yields

$$\frac{1}{2}\begin{bmatrix} 1+iA+iB & i+A-B & i-A+B & -1+iA+iB \\ i+A^*-C & 1+iA^*+iC & -1+iA^*+iC & i-A^*+C \\ i+B^*-D & -1+iB^*+iD & 1+iB^*+iD & i-B^*+D \\ -1+iC^*+iD^* & i+C^*-D^* & i-C^*+D^* & 1+iC^*+iD^* \end{bmatrix}$$

We then premultiply this result by R^{-1} and obtain

$$D(3) = R^{-1}D(2)R$$

$$= \frac{1}{4}\begin{bmatrix} \begin{matrix} 4+iA-iA^* \\ +iB-iB^* \\ +iC-iC^* \\ +iD-iD^* \end{matrix} & \begin{matrix} +A+A^* \\ -B+B^* \\ +C-C^* \\ +D+D^* \end{matrix} & \begin{matrix} -A+A^* \\ +B+B^* \\ +C+C^* \\ +D-D^* \end{matrix} & \begin{matrix} +iA+iA^* \\ +iB+iB^* \\ -iC-iC^* \\ -iD-iD^* \end{matrix} \\ \\ \begin{matrix} +A+A^* \\ +B-B^* \\ -C+C^* \\ +D+D^* \end{matrix} & \begin{matrix} 4-iA+iA^* \\ +iB-iB^* \\ +iC-iC^* \\ -iD+iD^* \end{matrix} & \begin{matrix} +iA+iA^* \\ -iB-iB^* \\ +iC+iC^* \\ -iD-iD^* \end{matrix} & \begin{matrix} +A-A^* \\ +B+B^* \\ +C+C^* \\ -D+D^* \end{matrix} \\ \\ \begin{matrix} +A-A^* \\ +B+B^* \\ +C+C^* \\ -D+D^* \end{matrix} & \begin{matrix} -iA-iA^* \\ +iB+iB^* \\ -iC-iC^* \\ +iD+iD^* \end{matrix} & \begin{matrix} 4+iA-iA^* \\ -iB+iB^* \\ -iC+iC^* \\ +iD-iD^* \end{matrix} & \begin{matrix} +A+A^* \\ +B-B^* \\ -C+C^* \\ +D+D^* \end{matrix} \\ \\ \begin{matrix} -iA-iA^* \\ -iB-iB^* \\ +iC+iC^* \\ +iD+iD^* \end{matrix} & \begin{matrix} -A+A^* \\ +B+B^* \\ +C+C^* \\ +D-D^* \end{matrix} & \begin{matrix} +A+A^* \\ -B+B^* \\ +C-C^* \\ +D+D^* \end{matrix} & \begin{matrix} 4-iA+iA^* \\ -iB+iB^* \\ -iC+iC^* \\ -iD+iD^* \end{matrix} \end{bmatrix} \quad \text{(I.94)}$$

One can check that the population sum $d_{11}+d_{22}+d_{33}+d_{44}$ (trace of the matrix) is invariant, i.e., it has the same value for *D*(0) through *D*(3). Also, *D*(3) is Hermitian (the density matrix always is). In doing this verification we keep in mind that the sums $A+A^*$, $B+B^*$, etc., are all *real* quantities, while the differences $A-A^*$, $B-B^*$, etc., are *imaginary*. This can be used to simplify the expression of *D*(3) by employing the following notations:

$$A=(-i/2)\exp\left(-i\Omega_{12}t_e\right)=(-i/2)\left(\cos\Omega_{12}t_e-i\sin\Omega_{12}t_e\right)=$$
$$=(-i/2)(c_{12}-is_{12})=-(1/2)(s_{12}+ic_{12})$$
$$A^*=-(1/2)(s_{12}-ic_{12})$$

With similar notations for *B*, *C*, and *D* we obtain:

$$\begin{aligned}
A&=-\left(1/2\right)\left(s_{12}+ic_{12}\right)\ ;\ A+A^*=-s_{12}\ ;\ A-A^*=-ic_{12}\\
B&=-\left(1/2\right)\left(s_{13}+ic_{13}\right)\ ;\ B+B^*=-s_{13}\ ;\ B-B^*=-ic_{13}\\
C&=-\left(1/2\right)\left(s_{24}+ic_{24}\right)\ ;\ C+C^*=-s_{24}\ ;\ C-C^*=-ic_{24}\\
D&=-\left(1/2\right)\left(s_{34}+ic_{34}\right)\ ;\ D+D^*=-s_{34}\ ;\ D-D^*=-ic_{34}
\end{aligned} \tag{I.95}$$

With the new sine/cosine notations, *D*(3) becomes:

$$\frac{1}{4}\begin{bmatrix}
\begin{matrix}4+c_{12}+c_{13}\\+c_{24}+c_{34}\end{matrix} & \begin{matrix}-s_{12}+ic_{13}\\-ic_{24}-s_{34}\end{matrix} & \begin{matrix}ic_{12}-s_{13}\\-s_{24}-ic_{34}\end{matrix} & \begin{matrix}-is_{12}-is_{13}\\+is_{24}+is_{34}\end{matrix}\\[2ex]
\begin{matrix}-s_{12}-ic_{13}\\+ic_{24}-s_{34}\end{matrix} & \begin{matrix}4-c_{12}+c_{13}\\+c_{24}-c_{34}\end{matrix} & \begin{matrix}-is_{12}+is_{13}\\-is_{24}+is_{34}\end{matrix} & \begin{matrix}-ic_{12}-s_{13}\\-s_{24}+ic_{34}\end{matrix}\\[2ex]
\begin{matrix}-ic_{12}-s_{13}\\-s_{24}+ic_{34}\end{matrix} & \begin{matrix}is_{12}-is_{13}\\+is_{24}-is_{34}\end{matrix} & \begin{matrix}4+c_{12}-c_{13}\\-c_{24}+c_{34}\end{matrix} & \begin{matrix}-s_{12}-ic_{13}\\+ic_{24}-s_{34}\end{matrix}\\[2ex]
\begin{matrix}is_{12}+is_{13}\\-is_{24}-is_{34}\end{matrix} & \begin{matrix}ic_{12}-s_{13}\\-s_{24}-ic_{34}\end{matrix} & \begin{matrix}-s_{12}+ic_{13}\\-ic_{24}-s_{34}\end{matrix} & \begin{matrix}4-c_{12}-c_{13}\\-c_{24}-c_{34}\end{matrix}
\end{bmatrix} \tag{I.96}$$

5.5 Detection

Since no other pulse follows after $t(3)$ we will consider only the evolution of the observable (single quantum) elements d_{12}, d_{34}, d_{13}, and d_{24} in the time domain t_d. Before evolution they are (from I.96):

$$\begin{aligned} d_{12}(3) &= (i/4)(+is_{12} + is_{34} + c_{13} - c_{24}) \\ d_{34}(3) &= (i/4)(+is_{12} + is_{34} - c_{13} + c_{24}) \\ d_{13}(3) &= (i/4)(+c_{12} - c_{34} + is_{13} + is_{24}) \\ d_{24}(3) &= (i/4)(-c_{12} + c_{34} + is_{13} + is_{24}) \end{aligned} \qquad \text{(I.97)}$$

Their complex conjugates, which are needed for the calculation of magnetization components, are:

$$\begin{aligned} d^*_{12}(3) &= (i/4)(+is_{12} + is_{34} - c_{13} + c_{24}) \\ d^*_{34}(3) &= (i/4)(+is_{12} + is_{34} + c_{13} - c_{24}) \\ d^*_{13}(3) &= (i/4)(-c_{12} + c_{34} + is_{13} + is_{24}) \\ d^*_{24}(3) &= (i/4)(+c_{12} - c_{34} + is_{13} + is_{24}) \end{aligned} \qquad \text{(I.98)}$$

Each of the four matrix elements above contains all four frequencies evolving in domain t_e, namely: $\Omega_{12}t_e$, $\Omega_{34}t_e$, $\Omega_{13}t_e$, and $\Omega_{24}t_e$. During detection, each of them will evolve with its own frequency in the domain t_d:

$$\begin{aligned} d^*_{12}(4) &= (i/4)(+is_{12} + is_{34} - c_{13} + c_{24})\exp(i\Omega_{12}t_d) \\ d^*_{34}(4) &= (i/4)(+is_{12} + is_{34} + c_{13} - c_{24})\exp(i\Omega_{34}t_d) \\ d^*_{13}(4) &= (i/4)(-c_{12} + c_{34} + is_{13} + is_{24})\exp(i\Omega_{13}t_d) \\ d^*_{24}(4) &= (i/4)(+c_{12} - c_{34} + is_{13} + is_{24})\exp(i\Omega_{24}t_d) \end{aligned} \qquad \text{(I.99)}$$

Expression (I.99) shows that each t_d frequency is modulated by all four t_e frequencies. Thus, we expect sixteen peaks in the 2D plot. Actually, there will be 32 peaks, because only the t_d domain is phase modulated, while the t_e domain is amplitude modulated (i.e., it contains sine/cosine expressions).

Each sine or cosine implies both the positive and the negative frequency according to

$$c_{jk} = \cos\Omega_{jk}t_e = \frac{1}{2}\left[\exp\left(i\Omega_{jk}t_e\right) + \exp\left(-i\Omega_{jk}t_e\right)\right]$$

$$is_{jk} = i\sin\Omega_{jk}t_e = \frac{1}{2}\left[\exp\left(i\Omega_{jk}t_e\right) - \exp\left(-i\Omega_{jk}t_e\right)\right]$$

This leads to the 32 peak contour plot in Figure I.12.

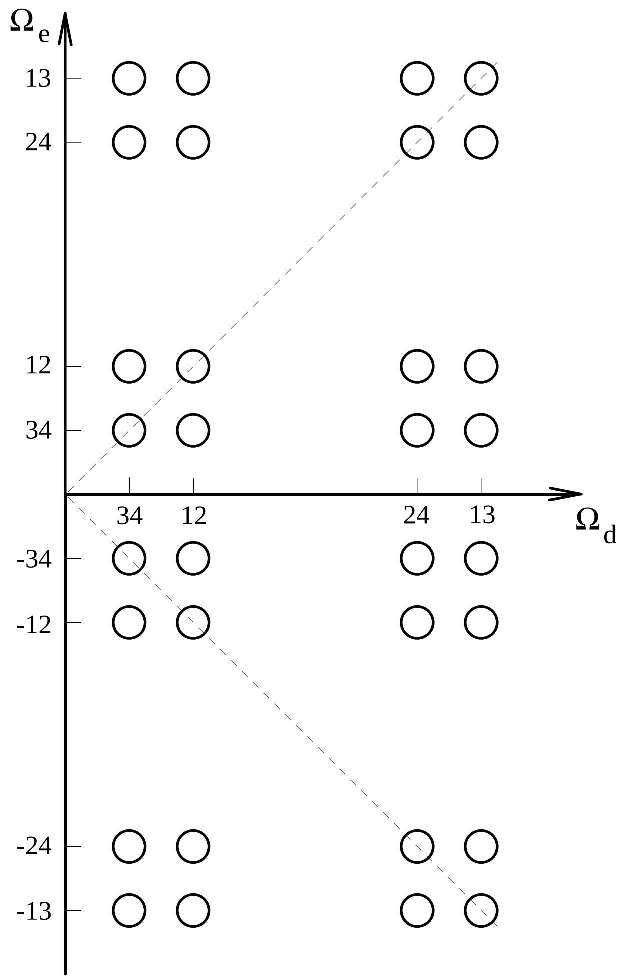

Figure I.12. Contour plot of COSY without phase cycling. The transmitter frequency is on one side of the spectrum.

We can plot the positive frequencies only, but the amplitude modulation in domain t_e still is a major drawback since it requires placing the transmitter frequency outside the spectrum (i.e., we lose the advantage of quadrature detection in both domains). The spectral widths have to be doubled and the data matrix increases by a factor of four.

If the transmitter is placed within the spectrum (e.g., between Ω_{12} and Ω_{24}), a messy pattern is obtained as shown in Figure I.13. The next section shows how this can be circumvented by means of an appropriate phase cycling.

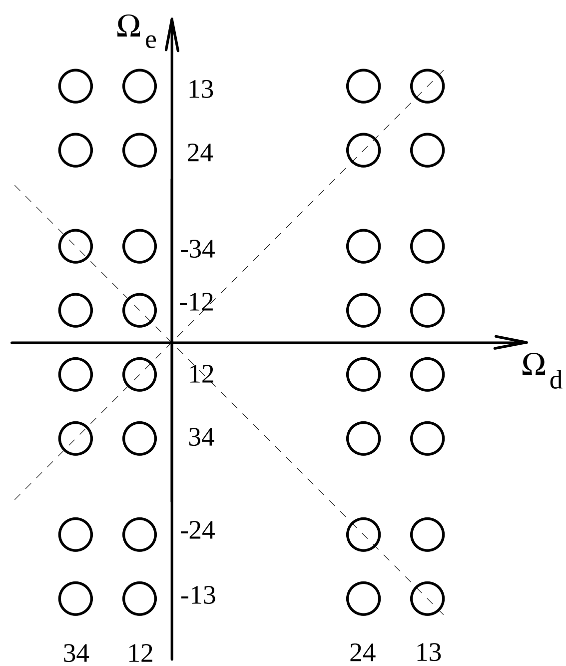

Figure I.13. Contour plot of COSY without phase cycling. If the transmitter is placed within the spectrum, it causes overlap of positive and negative frequencies.

6. COSY WITH PHASE CYCLING

6.1 Comparison with the Previous Sequence

The sequence for COSY with phase cycling shown in Figure I.14 differs from that discussed above (Figure I.11) only by the cycling of the second pulse.

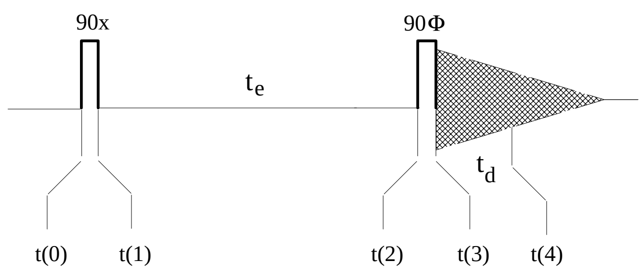

Figure I.14. COSY sequence with phase cycling of second pulse: $90x - t_e - 90\Phi - \mathrm{AT}$

Moreover, only two steps are theoretically necessary to eliminate negative frequencies in domain t_e. The second pulse is successively phased in x and y. Rather than doing the density matrix calculations for an arbitrary phase Φ, we will take advantage of the fact that we have already treated the x phase in the previous section. Only the effect of $90yAX$ must then be calculated (see Figure I.15).

Since the two sequences in Figures I.11 and I.15 have a common segment [$t(0)$ to $t(2)$], we can take $D(2)$ from the previous section [see (I.92). and (I.93)].

$$D(2) = \begin{bmatrix} 1 & A & B & 0 \\ A* & 1 & 0 & C \\ B* & 0 & 1 & D \\ 0 & C* & D* & 1 \end{bmatrix} \qquad \text{(I.100)}$$

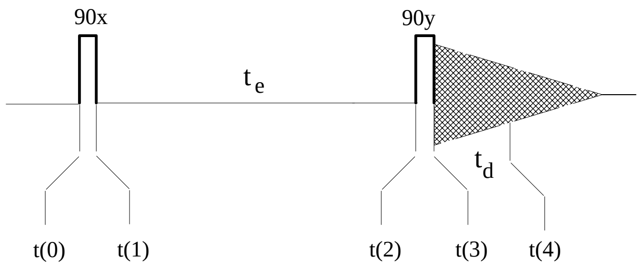

Figure I.15. The second step of the phase cycled COSY sequence: $90x - t_e - 90y - \mathrm{AT}$

6.2 The Second Pulse

The rotation operator for the 90*yAX* pulse can be obtained by multiplying R_{90yA} by R_{90yX}. These operators are (see Appendix C):

$$R_{90yA} = \frac{1}{\sqrt{2}}\begin{bmatrix} 1 & 1 & 0 & 0 \\ -1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & -1 & 1 \end{bmatrix} \quad ; \quad R_{90yX} = \frac{1}{\sqrt{2}}\begin{bmatrix} 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 1 \\ -1 & 0 & 1 & 0 \\ 0 & -1 & 0 & 1 \end{bmatrix}$$

The result of the multiplication, $R = R_{90yAX}$, is shown below together with its reciprocal, R^{-1}.

$$R = \frac{1}{2}\begin{bmatrix} 1 & 1 & 1 & 1 \\ -1 & 1 & -1 & 1 \\ -1 & -1 & 1 & 1 \\ 1 & -1 & -1 & 1 \end{bmatrix} \quad ; \quad R^{-1} = \frac{1}{2}\begin{bmatrix} 1 & -1 & -1 & 1 \\ 1 & 1 & -1 & -1 \\ 1 & -1 & 1 & -1 \\ 1 & 1 & 1 & 1 \end{bmatrix} \qquad \text{(I.101)}$$

The postmultiplication $D(2)R$ yields

$$\frac{1}{2}\begin{bmatrix} 1-A-B & 1+A-B & 1-A+B & 1+A+B \\ -1+A^*+C & 1+A^*-C & -1+A^*-C & 1+A^*+C \\ -1+B^*+D & -1+B^*-D & 1+B^*-D & i+B^*+D \\ 1-C^*-D^* & -1+C^*-D^* & -1-C^*+D^* & 1+C^*+D^* \end{bmatrix}$$

Premultiplying this result by R^{-1} gives

$$D(3) = R^{-1}D(2)R =$$

$$\frac{1}{4}\begin{bmatrix}
\begin{matrix} 4-A-A^* \\ -B-B^* \\ -C-C^* \\ -D-D^* \end{matrix} &
\begin{matrix} +A-A^* \\ -B-B^* \\ +C+C^* \\ +D-D^* \end{matrix} &
\begin{matrix} -A-A^* \\ +B-B^* \\ +C-C^* \\ +D+D^* \end{matrix} &
\begin{matrix} +A-A^* \\ +B-B^* \\ -C+C^* \\ -D+D^* \end{matrix} \\ \\
\begin{matrix} -A+A^* \\ -B-B^* \\ +C+C^* \\ -D+D^* \end{matrix} &
\begin{matrix} 4+A+A^* \\ -B-B^* \\ -C-C^* \\ +D+D^* \end{matrix} &
\begin{matrix} -A+A^* \\ +B-B^* \\ -C+C^* \\ +D-D^* \end{matrix} &
\begin{matrix} A+A^* \\ +B-B^* \\ +C-C^* \\ -D-D^* \end{matrix} \\ \\
\begin{matrix} -A-A^* \\ -B+B^* \\ -C+C^* \\ +D+D^* \end{matrix} &
\begin{matrix} +A-A^* \\ -B+B^* \\ +C-C^* \\ -D+D^* \end{matrix} &
\begin{matrix} 4-A-A^* \\ +B+B^* \\ +C+C^* \\ -D-D^* \end{matrix} &
\begin{matrix} +A-A^* \\ +B+B^* \\ -C-C^* \\ +D-D^* \end{matrix} \\ \\
\begin{matrix} -A+A^* \\ -B+B^* \\ +C-C^* \\ +D-D^* \end{matrix} &
\begin{matrix} +A+A^* \\ -B+B^* \\ -C+C^* \\ -D-D^* \end{matrix} &
\begin{matrix} -A+A^* \\ +B+B^* \\ -C-C^* \\ -D+D^* \end{matrix} &
\begin{matrix} 4+A+A^* \\ +B+B^* \\ +C+C^* \\ +D+D^* \end{matrix}
\end{bmatrix} \qquad \text{(I.102)}$$

With the same notations as in (I.95) :

$$\begin{aligned}
&A=-(1/2)(s_{12}+ic_{12}) \;;\; A+A^*=-s_{12} \;;\; A-A^*=-ic_{12}\\
&B=-(1/2)(s_{13}+ic_{13}) \;;\; B+B^*=-s_{13} \;;\; B-B^*=-ic_{13}\\
&C=-(1/2)(s_{24}+ic_{24}) \;;\; C+C^*=-s_{24} \;;\; C-C^*=-ic_{24}\\
&D=-(1/2)(s_{34}+ic_{34}) \;;\; D+D^*=-s_{34} \;;\; D-D^*=-ic_{34}
\end{aligned} \qquad \text{(I.103)}$$

$D(3)$ becomes

$$\frac{1}{4}\begin{bmatrix}
\begin{matrix}4+s_{12}+s_{13}\\ +s_{24}+s_{34}\end{matrix} & \begin{matrix}-ic_{12}+s_{13}\\ -s_{24}-ic_{34}\end{matrix} & \begin{matrix}+s_{12}-ic_{13}\\ -ic_{24}-s_{34}\end{matrix} & \begin{matrix}-ic_{12}-ic_{13}\\ +ic_{24}+ic_{34}\end{matrix}\\
\begin{matrix}+ic_{12}+s_{13}\\ -s_{24}+ic_{34}\end{matrix} & \begin{matrix}4-s_{12}+s_{13}\\ +s_{24}-s_{34}\end{matrix} & \begin{matrix}+ic_{12}-ic_{13}\\ +ic_{24}-ic_{34}\end{matrix} & \begin{matrix}-s_{12}-ic_{13}\\ -ic_{24}+s_{34}\end{matrix}\\
\begin{matrix}+s_{12}+ic_{13}\\ +ic_{24}-s_{34}\end{matrix} & \begin{matrix}-ic_{12}+ic_{13}\\ -ic_{24}+ic_{34}\end{matrix} & \begin{matrix}4+s_{12}-s_{13}\\ -s_{24}+s_{34}\end{matrix} & \begin{matrix}-ic_{12}-s_{13}\\ +s_{24}-ic_{34}\end{matrix}\\
\begin{matrix}+ic_{12}+ic_{13}\\ -ic_{24}-ic_{34}\end{matrix} & \begin{matrix}-s_{12}+ic_{13}\\ +ic_{24}+s_{34}\end{matrix} & \begin{matrix}+ic_{12}-s_{13}\\ +s_{24}+ic_{34}\end{matrix} & \begin{matrix}4-s_{12}-s_{13}\\ -s_{24}-s_{34}\end{matrix}
\end{bmatrix} \qquad \text{(I.104)}$$

We have to consider only the observable matrix elements :

$$\begin{aligned}
d_{12}(3)&=(i/4)(-c_{12}-c_{34}-is_{13}+is_{24})\\
d_{34}(3)&=(i/4)(-c_{12}-c_{34}+is_{13}-is_{24})\\
d_{13}(3)&=(i/4)(-is_{12}+is_{34}-c_{13}-c_{24})\\
d_{24}(3)&=(i/4)(+is_{12}-is_{34}-c_{13}-c_{24})
\end{aligned} \qquad \text{(I.105)}$$

Comparing the results for phase y (I.105) with those for phase x (I.97) shows that c and $-\ is$ are interchanged in all terms. This will lead to the desired phase modulation. Addition of (I.97) and (I.105) gives

$$
\begin{aligned}
d_{12}(3) &= (i/4)\left[(is_{12}-c_{12})+(is_{34}-c_{34})+(c_{13}-is_{13})+(-c_{24}+is_{24})\right]\\
d_{34}(3) &= (i/4)\left[(is_{12}-c_{12})+(is_{34}-c_{34})+(-c_{13}+is_{13})+(c_{24}-is_{24})\right]\\
d_{13}(3) &= (i/4)\left[(c_{12}-is_{12})+(-c_{34}+is_{34})+(is_{13}-c_{13})+(is_{24}-c_{24})\right]\\
d_{24}(3) &= (i/4)\left[(-c_{12}+is_{12})+(c_{34}-is_{34})+(is_{13}-c_{13})+(is_{24}-c_{24})\right]
\end{aligned}
\tag{I.106}
$$

The complex conjugates of the matrix elements above (needed for the expression of the magnetization components) are

$$
\begin{aligned}
d^*_{12}(3) &= (i/4)\left[(is_{12}+c_{12})+(is_{34}+c_{34})+(-c_{13}-is_{13})+(c_{24}+is_{24})\right]\\
d^*_{34}(3) &= (i/4)\left[(is_{12}+c_{12})+(is_{34}+c_{34})+(c_{13}+is_{13})+(-c_{24}-is_{24})\right]\\
d^*_{13}(3) &= (i/4)\left[(-c_{12}-is_{12})+(c_{34}+is_{34})+(is_{13}+c_{13})+(is_{24}+c_{24})\right]\\
d^*_{24}(3) &= (i/4)\left[(c_{12}+is_{12})+(-c_{34}-is_{34})+(is_{13}+c_{13})+(is_{24}+c_{24})\right]
\end{aligned}
\tag{I.107}
$$

We observe that every parenthesis represents an exponential, therefore we can use the notation

$$e_{jk} = c_{jk} + is_{jk} = \exp\left(i\Omega_{jk}t_e\right) \tag{I.108}$$

With this notation (I.107) becomes

$$
\begin{aligned}
d^*_{12}(3) &= (i/4)(+e_{12}+e_{34}-e_{13}+e_{24})\\
d^*_{34}(3) &= (i/4)(+e_{12}+e_{34}+e_{13}-e_{24})\\
d^*_{13}(3) &= (i/4)(-e_{12}+e_{34}+e_{13}+e_{24})\\
d^*_{24}(3) &= (i/4)(+e_{12}-e_{34}+e_{13}+e_{24})
\end{aligned}
\tag{I.109}
$$

The reader is reminded that the above expressions represent the summation from two acquisitions, one with phase *x* and the other with phase *y* for the second pulse. Instead of sines or cosines, they contain only exponentials. In other words we have achieved phase modulation in the domain t_e.

6.3 Detection

The evolution during t_d is identical for the two acquisitions, therefore we can apply it after the summation (in I.109).

$$
\begin{aligned}
d_{12}^*(4) &= (i/4)(+e_{12}+e_{34}-e_{13}+e_{24})\exp(i\Omega_{12}t_d) \\
d_{34}^*(4) &= (i/4)(+e_{12}+e_{34}+e_{13}-e_{24})\exp(i\Omega_{34}t_d) \\
d_{13}^*(4) &= (i/4)(-e_{12}+e_{34}+e_{13}+e_{24})\exp(i\Omega_{13}t_d) \\
d_{24}^*(4) &= (i/4)(+e_{12}-e_{34}+e_{13}+e_{24})\exp(i\Omega_{24}t_d)
\end{aligned}
\qquad \text{(I.110)}
$$

The expressions (I.110) correspond to a contour plot with 16 peaks, as represented in Figure I.16. This pattern is no longer dependent on the position of the transmitter since we have achieved the equivalent of quadrature detection in both domains. There are four diagonal terms, each having the same frequency in both domains t_e and t_d. If the two frequencies differ only by J (e.g., we have Ω_{12} in domain t_e and Ω_{34} in domain t_d) we have a "near-diagonal" peak. There are four such peaks. The remaining eight are referred to as *off-diagonal* or *cross-peaks* and their presence indicates that spins A and X are coupled. Two noncoupled spins will exhibit only diagonal peaks. We can verify that this is so by discussing what happens if J becomes vanishingly small. In this case $\Omega_{12} = \Omega_{34} = \Omega_A$ (center of the doublet); likewise $\Omega_{13} = \Omega_{24} = \Omega_X$. Therefore each group of 4 peaks in Figure I.16 collapses into a single peak in the center of the corresponding square. The diagonal and near-diagonal peaks of nucleus A are all positive and they collapse into one diagonal peak, four times larger. The same is true for nucleus X. The off-diagonal peaks come in groups of four, two positive and two negative. When they collapse (J=0) they cancel each other and there will be no off-diagonal peak. The net result is a spectrum with just two peaks, both on the diagonal, with frequencies Ω_A and Ω_X. The above discussion shows that COSY is not suited for spectra with ill-resolved multiplets because there will be destructive overlap in the off-diagonal groups.

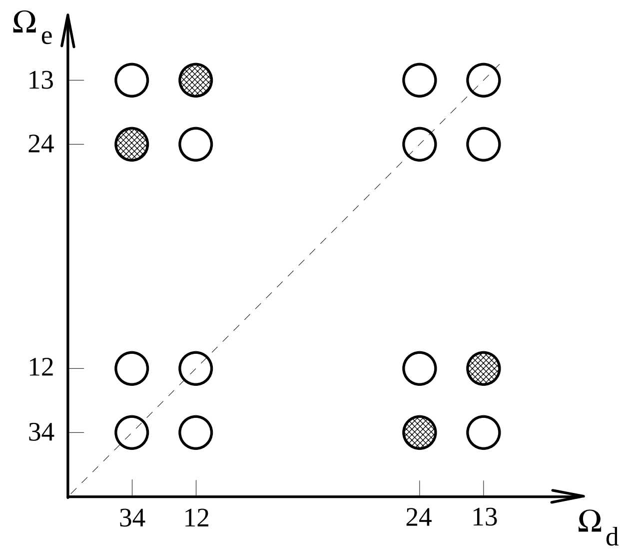

Figure I.16. Contour plot of COSY with phase cycling. Open circles are positive peaks; shaded circles are negative peaks.

There is one more observation. It is common practice to plot the 2D spectra in the "magnitude calculation" (MC) or "absolute value" mode, to avoid phasing problems. The magnitude calculation (the absolute value of a complex quantity) is performed by the computer after Fourier transform in both domains. Two peaks, one positive and one negative, will both become positive in MC, provided they are well resolved. If they are ill-resolved, they will cancel each other partially and will yield a much smaller signal. The MC is applied to this signal and it cannot represent the original amplitude of the two peaks. Therefore the use of magnitude calculation does not provide a solution for poorly resolved multiplets.

One word about the utility of phase cycling. While it is well known that this procedure helps canceling out radiofrequency interferences and pulse imperfections, we have just seen that it can be useful for other purposes. In INADEQUATE it helps eliminate the NMR signal from the ^{13}C-^{12}C pairs while preserving that from ^{13}C-^{13}C pairs. In COSY it helps achieve phase modulation in domain t_e. In both cases a two step cycling is theoretically sufficient. However, to efficiently compensate for hardware imperfections, cycling in more than two steps is generally employed.

7. CONCLUSION OF PART I

The density matrix approach described above constitutes a very clear and useful means for understanding the multipulse sequences of modern NMR. The limitation of this approach is the rapidly increasing volume of calculation with increasing number of nuclei. The size of the matrix goes from 16 elements for a two spin 1/2 system to 64 and 256 elements for three and four spin systems, respectively.

We must therefore resort to an avenue which affords a "shorthand" for the description of rotations and evolutions. The new avenue we present in the second part of this monograph is the *product operator* formalism.

Answer to the problem on page 44: The contour plot in Figure I.10 is the carbon-carbon connectivity spectrum of 2-bromobutane.