Density Matrix Formalism

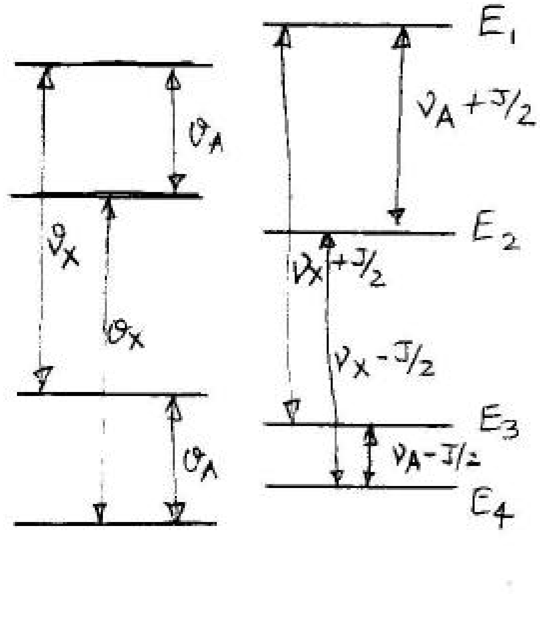
- only simplest NMR pulses can be properly described by vector representation

AX $I = \frac{1}{2}$ – with four energy levels E_1 to E_4

– assume $-\gamma$ (lowest energy E_4 level oriented against the field)
  - $\vec{\mu}$ with the field
  - spin & momentum against the field

+1	(↑↑)	$\vert ++\rangle$
0	(↓↑)	$\vert -+\rangle$
0	(↑↓)	$\vert +-\rangle$
−1	(↓↓)	$\vert --\rangle$

A, X – "kets"



Density Matrix of Two-spin System

$\lvert AX\rangle$	$\lvert ++\rangle$	$\lvert -+\rangle$	$\lvert +-\rangle$	$\lvert --\rangle$
$\lvert ++\rangle$	P_1	$1Q_A$	$1Q_X$	$2Q_{AX}$
$\lvert -+\rangle$		P_2	ZQ_{AX}	$1Q_X$
$\lvert +-\rangle$			P_3	$1Q_A$
$\lvert --\rangle$				P_4

- off diagonal elements connect pairs of different states ≡ coherences

$\lvert ++\rangle \rightarrow \lvert -+\rangle$ A nucleus flipped
single quant. coher.
$1Q_A$
symmetric matrix

$\lvert ++\rangle \rightarrow \lvert --\rangle$ $2Q_{AX}$

ZQ_{AX} flip/flop.
$E_2 \rightarrow E_3$
(non-zero energy).

- diagonal = populations.

Complete information on ensemble of spins..
obtain populations ,, macro Magnetizations ...

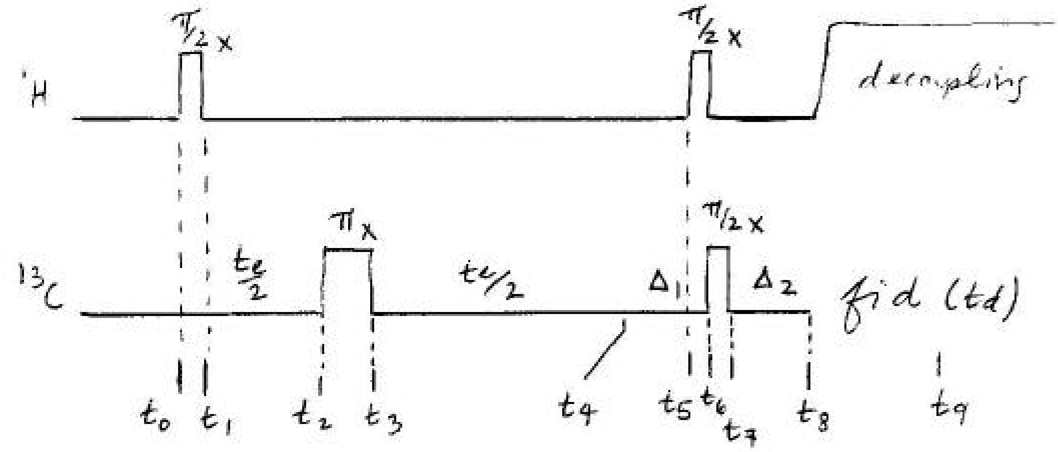
2D HETCOR (H/C COSY)

reveal pairwise correlation of diff. nuclear species ex) C-H or C-F based on scaler coupling

Calculation Procedure :

1) thermal ⇄ populations (zero offdiag and ϵ)
2) effect of rf pulses (rotations)
3) evolution betwn pulses
4) " during acq.
5) observ. magnetiz. determination.

A : ^{13}C X : ^{1}H



Equilibrium Populations

determ'd by Boltzmann dist.

$$\frac{P_i}{P_j} = \frac{e^{-E_i/kT}}{e^{-E_j/kT}} = e^{(E_j - E_i)/kT}$$

least populated level

$$\frac{P_2}{P_1} = e^{(E_1 - E_2)/kT} = e^{[h(\nu_A + J/2)/kT]}$$

10^8 Hz -vs- 10^2 ~ lim

neglect J/2 here (only)

$h\nu_{A}/kT$ are much smaller than 1.

A, X

$T = 4.7$ T

^{13}C $\nu = 50 \times 10^6$ Hz

$$p = \frac{h\nu_A}{kT} = \frac{6.6 \times 10^{-34} \, J s \cdot 50 \cdot 10^6 s^{-1}}{1.4 \times 10^{-23} (J/K) \cdot 300K} = .785 \times 10^{-5}$$

∴ 1st ord series expansion.

$$P_2 / P_1 = \exp(h\nu_A / kT) \simeq 1 + (h\nu_A / kT) = 1 + p$$

$$P_3 / P_1 = \quad \nu_X \quad \simeq 1 + (h\nu_X / kT) = 1 + q$$

$$P_4 / P_1 \cong 1 + [h(\nu_A + \nu_X)/kT] = 1 + p + q$$

for ^{13}C / ^1H 1 : 4 or $q = 4p$

Normalize sum of populations

$$P_1 = P_1$$
$$P_2 = (1+\rho)P_1$$
$$P_3 = (1+4\rho)P_1$$
$$P_4 = (1+5\rho)P_1$$
$$1 = P_1(4+10\rho) = P_1 S$$

so

$$P_1 = 1/S$$
$$P_2 = (1+\rho)/S$$
$$P_3 = (1+4\rho)/S$$
$$P_4 = (1+5\rho)/S$$

$S = 4 + 10\rho$ ← 10ρ is small

let $S \sim 4$

So matrix at $\rightleftharpoons$ is:

$$D(0) = \begin{bmatrix} P_1 & 0 & 0 & 0 \\ 0 & P_2 & 0 & 0 \\ 0 & 0 & P_3 & 0 \\ 0 & 0 & 0 & P_4 \end{bmatrix} = \frac{1}{4}\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1+\rho & 0 & 0 \\ 0 & 0 & 1+4\rho & 0 \\ 0 & 0 & 0 & 1+5\rho \end{bmatrix}$$

$$= \frac{1}{4}\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} + \frac{\rho}{4}\begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 4 & 0 \\ 0 & 0 & 0 & 5 \end{bmatrix}$$

↗ unit matrix
not affected by evolution or rotation.
(much larger in magnitude)

↗ Smaller
contains the population difference

$\rightleftharpoons$ matrix for other systems: built same way.

$t_0 \to t_1$ $\frac{\pi}{2}$ pulse (x axis)

(then pre — over R^{-1}; 1st post — under $D(0)\ R$)

$$D(1) = R^{-1}\ D(0)\ R$$

Rotation operator : $R_{90_x H} = \frac{1}{\sqrt{2}} \begin{bmatrix} 1 & 0 & i & 0 \\ 0 & 1 & 0 & i \\ i & 0 & 1 & 0 \\ 0 & i & 0 & 1 \end{bmatrix}$ $i = \sqrt{-1}$

$$R^{-1}_{90_x H} = \frac{1}{\sqrt{2}} \begin{bmatrix} 1 & 0 & -i & 0 \\ 0 & 1 & 0 & -i \\ -i & 0 & 1 & 0 \\ 0 & -i & 0 & 1 \end{bmatrix}$$

obtain by transposition & conjugation

follow Rules of matrix multiplication : $AB \neq BA$
not commutative

$A(BC) = (AB)C = ABC$
associative

$A(B+C) = AB + AC$
distributive

Result after multiplication :

(1QA, 1QX marked above columns 2 and 3; 1QX, 1QA marked beside rows 2 and 3)

$$D(1) = \frac{1}{2} \begin{bmatrix} 4 & 0 & -4i & 0 \\ 0 & 6 & 0 & -4i \\ 4i & 0 & 4 & 0 \\ 0 & 4i & 0 & 6 \end{bmatrix} = \begin{bmatrix} 2 & 0 & -2i & 0 \\ 0 & 3 & 0 & -2i \\ 2i & 0 & 2 & 0 \\ 0 & 2i & 0 & 3 \end{bmatrix}$$

verify Hermitian [E below diag. is complex conj of E above diag.]

Conclude : 90° (^1H) pulse created $1Q_H$, ~~don~~ didn't touch ^{13}C, redistrib. populations

$$D(1) = \begin{bmatrix} 2 & 0 & -2i & 0 \\ 0 & 3 & 0 & -2i \\ 2i & 0 & 2 & 0 \\ 0 & 2i & 0 & 3 \end{bmatrix}$$

Annotations on $D(1)$: element (1,2): 1Q ^{13}C; element (1,3): 1Q ^{1}H (circled); element (1,4): 2Q AX; element (2,4): 1Q ^{1}H (circled); element (3,4): 1Q ^{13}C; element (2,3): ZQ ^{13}C ^{1}H

$$D(0) = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 4 & 0 \\ 0 & 0 & 0 & 5 \end{bmatrix}$$

^{13}C unaltered

^{1}H single Q coherence.

AX $\quad |{+}{+}\rangle, \ |{-}{+}\rangle, \ |{+}{-}\rangle, \ |{-}{-}\rangle.$

(first sign: A → ^{13}C; second sign: X → ^{1}H)

$$\begin{bmatrix} P_1 & 1Q_A & 1Q_X & 2Q_{AX} \\ & P_2 & ZQ_{AX} & 1Q_X \\ & & P_3 & 1Q_A \\ & & & P_4 \end{bmatrix}$$

$t_1 \to t_2$ Evolution:

$$d_{mn}(t) = d_{mn}(0) \exp(-i\,\omega_{mn} t)$$

↗ matrix element, row m, column n

$d_{mn}(0)$ Starting pt just after the pulse

$$\omega_{mn} = (E_m - E_n)/\hbar$$

• angular freq of transition $m \to n$

• diagonal elements are invariant during evolution since $\exp[i(E_m - E_m)/\hbar] = 1$

• off diagonal: periodic evolution

• $\in$ of $d_{mn}(0)$ are $D(1)$ obtain $D(2)$ at t_2

elements d_{13} & d_{24}

(ignore relaxation during pulse sequence) Results generally the same.

ω_{proton} freq (transmitt) after $t_e/2$

$$d_{13} = -2i \exp(-i\,\Omega_{13} t_e/2) = B$$

$$d_{24} = -2i \exp(-i\,\Omega_{24} t_e/2) = C$$

where

$$\Omega_{13} = \omega_{13} - \omega_{proton}$$

$$\Omega_{24} = \omega_{24} - \omega_{proton}$$

so

$$D(2) = \begin{bmatrix} 2 & 0 & B & 0 \\ 0 & 3 & 0 & C \\ B^* & 0 & 2 & 0 \\ 0 & C^* & 0 & 3 \end{bmatrix}$$

B^*, C^* are complex conj. of B, C.

$t_2 \rightarrow t_3$ 2^{nd} PULSE

Rotation Operators:

$$R\pi^x_c = \begin{bmatrix} 0 & i & 0 & 0 \\ i & 0 & 0 & 0 \\ 0 & 0 & 0 & i \\ 0 & 0 & i & 0 \end{bmatrix} \quad R^{-1}_{(\ )} = \begin{bmatrix} 0 & -i & 0 & 0 \\ -i & 0 & 0 & 0 \\ 0 & 0 & 0 & -i \\ 0 & 0 & -i & 0 \end{bmatrix}$$

post

$$D_2 R_{180}{}^x{}_c = \begin{bmatrix} 0 & 2i & 0 & iB \\ 3i & 0 & iC & 0 \\ 0 & i & iB^* & 2i \\ iC^* & 0 & 3i & 0 \end{bmatrix}$$

pre $\bar{c}\, R^{-1}$

$$D_3 = \begin{bmatrix} 3 & 0 & C & 0 \\ 0 & 2 & 0 & B \\ C^* & 0 & 3 & 0 \\ 0 & B^* & 0 & 2 \end{bmatrix}$$

Results D_3 to D_2 π^x_c caused population inversion
(d_{11} x'chang. $\bar{c}$ d_{22})
interch. coherences B & C [d_{13} & d_{24}]

B, after evolved $\bar{c}$ ω_{13} during 1^{st} half.
now evolves with at ω_{24}

& C switches from ω_{24} to ω_{13}

$t_3 \to t_4$ Evolution

$$d_{13} = C \exp(-i\,\Omega_{13}\, t_e/2)$$

$$d_{24} = B \exp(-i\,\Omega_{24}\, t_e/2)$$

in lab frame $\quad \omega_{13} = 2\pi(\nu_X - J/2) = \omega_H + \pi J$

$\quad \omega_{24} = 2\pi(\nu_X - J/2) = \omega_H - \pi J$

in Rotating frame ω becomes Ω

Simplify: $\quad d_{13} = -2i \exp[-i(\Omega_H - \pi J)t_e/2]$

$\cdot \exp[-i(\Omega_H + \pi J)t_e/2]$

$= -2i \exp(-i\,\Omega_H t_e)$

$d_{24} = -2i \exp(-i\,\Omega_H t_e) = d_{13}$

Results: • D_4 doesn't contain J (decoupled)

Ω_H (avers. shift) is expressed, J is Not.
center of doublet

• J was present in D_2 & D_3

• $t_e/2 - \pi_C - t_e/2$ Refocusing Routine

protons fast (Ω_{13}) during 1st $t_e/2$ are slow (Ω_{24}) during 2nd $t_e/2$ ...

(they changed labels)

Δ_1

without $(d_{13} = d_{24})$ a useful signal is canceled.

Δ ~~rather~~ want max signal d_{13} & d_{24} must be = but opposite in sign.

Evolution during Δ_1

$$d_{13}(5) = d_{13}(4)\exp(-i\Omega_{13}\Delta_1)$$

$$= -2i\exp(-i\Omega_H t)\exp[-i(\Omega_H + \pi J)\Delta_1]$$

$$= -2i\exp(-i\Omega_H(t_e + \Delta_1))\exp(-i\pi J\Delta_1)$$

$$d_{24}(5) = -2i\exp(-i\Omega_H(t_e + \Delta_1))\exp(+i\pi J\Delta_1)$$

~~so~~ choose $\Delta_1 = \frac{1}{2J}$ (which implies) or $\pi J\Delta_1 = \pi/2$ to achieve goal. max signal

$$\exp(\pm i\pi/2) = \cos(\pi/2) \pm i\sin(\pi/2) = \pm i$$

$$\exp(-i\pi J\Delta_1) = -i$$

$$\exp(+i\pi J\Delta_1) = +i$$

so $d_{13}(5) = -2\exp[-i\Omega_H(t_e + \Delta_1)]$

$d_{24}(5) = +2\exp[-i\Omega_H(t_e + \Delta_1)]$

let $c = \cos(\Omega_H(t_e + \Delta_1))$

$s = \sin(\Omega_H(t_e + \Delta_1))$

use Euler's formula $e^{\pm ix} = \cos x \pm i\sin x$

which leads to $d_{13}(5) = -2(c - is)$

$d_{24}(5) = +2(c - is)$

$\therefore$

$$D_5 = \begin{bmatrix} 3 & 0 & -2(c-is) & 0 \\ 0 & 2 & 0 & 2(c-is) \\ -2(c+is) & 0 & 3 & 0 \\ 0 & 2(c+is) & 0 & 2 \end{bmatrix}$$

$t_5 \rightarrow t_7$

- two separate pulses applied sequentially $90_{x_H} \rightarrow 90_{x_C}$
can lump operator to ONE matrix

$$R_{90_x C,H} = R_{90_{x_C}} R_{90_{x_H}}$$

$$= \frac{1}{\sqrt{2}} \begin{bmatrix} 1 & i & 0 & 0 \\ i & 1 & 0 & 0 \\ 0 & 0 & 1 & i \\ 0 & 0 & i & 1 \end{bmatrix} \frac{1}{\sqrt{2}} \begin{bmatrix} 1 & 0 & i & 0 \\ 0 & 1 & 0 & i \\ i & 0 & 1 & 0 \\ 0 & i & 0 & 1 \end{bmatrix}$$

$$= \frac{1}{2} \begin{bmatrix} 1 & i & i & -1 \\ i & 1 & -1 & i \\ i & -1 & 1 & i \\ -1 & i & i & 1 \end{bmatrix}$$

$$\text{\&} \quad R^{-1}_{90_x C,H} = \frac{1}{2} \begin{bmatrix} 1 & -i & -i & -1 \\ -i & 1 & -1 & -i \\ -i & -1 & 1 & -i \\ -1 & -i & -i & 1 \end{bmatrix}$$

$D_5 \cdot R_{90xC,H} = \frac{1}{2}$ paste here

then $R^{-1}_{90xC,H} \cdot$

$$D_7 = \frac{1}{2} \begin{bmatrix} 5 & i-4is & 0 & -4ic \\ -i+4is & 5 & 4ic & 0 \\ 0 & -4ic & 5 & i+4is \\ 4ic & 0 & -i-4is & 5 \end{bmatrix}$$

1Qx (element d_{13}); 1Qx (element d_{24})

$D_5 \rightarrow D_7$ NOTE:

1) ^{13}C coherences created in d_{12}, d_{34} due to 90_{xC} pulse.

2) ^1H information:

$[s = \sin \Omega_H (t_c + \Delta_1)]$

transferred from d_{13}, d_{24} into ^{13}C coherences d_{12}, d_{34}.

$d_{12} = \frac{i - 4is}{2}$ $d_{34} = \frac{i + 4is}{2}$

∴ mixed $^{13}C/^1H$ information is carried into fid

Δ_2

observable signal $\propto$ $d_{12} + d_{34}$

without Δ_2 terms $\bar{c}$ "S" cancel

allow Δ_2 (short coupled evolution)

No more rf pulses – hence need on d_{12}, d_{34} to get observable $1Q_A$

at t_8 d_{12}, d_{34} become

$$d_{12}(8) = i(1/2 - 2s) \exp(-i \Omega_{12} \Delta_2)$$
$$d_{34} \text{ " } = i(1/2 + 2s) \exp(-i \Omega_{34} \Delta_2)$$

where $\Omega_{12} = \omega_{12} - \omega_{trc}$ & $\Omega_{34} = \omega_{34} - \omega_{trc}$

in ^{13}C Rotating frame $\omega_{tr,c}$ the ^{13}C transm. freq.

$$\nu_{12} = \nu_A + J/2 = \nu_C + J/2$$
$$\nu_{34} = \quad - \quad = \nu_C - J/2 \qquad \text{since } \omega = 2\pi\nu$$

$$\left.\begin{aligned} \Omega_{12} &= \Omega_c + \pi J \\ \Omega_{34} &= \Omega_c - \pi J \end{aligned}\right\}$$

so $d_{12}(8) = i(1/2 - 2s) \exp(-i \Omega_c \Delta_2) \exp(-i \pi J \Delta_2)$

$d_{34}(8) =$ " + " " " + "

Δ_2 (con't)

if $\Delta_2 = 0$ terms "s" (proton info.) are lost when $d_{12} + d_{34}$

as for Δ_1 best result $\Delta_2 = 1/2J$

$\Rightarrow \exp(\pm i \pi J \Delta_2) = \pm i$ (previously)

knowing $i = \sqrt{-1}$, $i^2 = (\ )^2 = -1$

$$d_{12}(8) = +(1/2 - 2s)\exp(-i\Omega_c \Delta_2)$$
$$d_{34}(8) = -(1/2 + 2s)\exp(-i\Omega_c \Delta_2)$$

Detection (evolution $\bar{c}$ proton decoupling) evolve at Ω_c

$$d_{12}(9) = +(1/2 - 2s)\exp(-i\Omega_c \Delta_2)\exp(-i\Omega_c td)$$
$$d_{34}(9) = - \quad " \quad " \quad "$$

observables: $M_{transverse\ ^{13}C} = M_{xC} + i M_{yC}$ — combines x, y components

$\rightarrow$ ^{13}C mag.

$$= -(4M_{0C}/p)(d_{12}^* + d_{34}^*)$$ reintroduce p/4 factor

$$= -M_{0C}(d_{12}^* + d_{34}^*)$$

$$\therefore M_{trans.\ ^{13}C} = 4M_{0C}\, s\, \exp(i\Omega_c \Delta_2)\exp(i\Omega_c td)$$

expanding in "s"

$$= 4M_{0C}\sin[\Omega_H(te + \Delta_1)]\exp(i\Omega_c \Delta_2)\exp(i\Omega_c td)$$

hence the final Result of C/H COSY analysis.
contains all information.

Findings 1) ^{13}C magnet. rotates by $\Omega_C t_d$
while modulated by proton. $\Omega_H t_e$

2) FT wrt each time domain (td, te) yields
a 2D spectrum

3) signal enhanced by factor of "4" γ_H/γ_C

4) polarization transfer cannot be
accounted for in other manners (vectors)

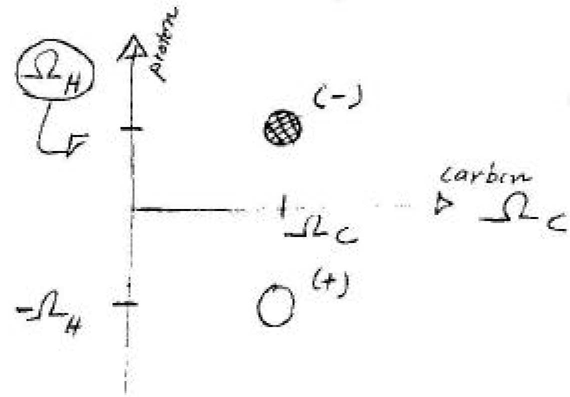
FT (td) of $\exp(i\Omega_C t_d)$ others const.
get Ω_C (single peak)

FT(te) of ~~H~~ $\sin[-\Omega_H(t_e+\Delta_1)]$ others const.

since $\sin\alpha = \dfrac{e^{i\alpha} - e^{-i\alpha}}{2i}$

both $+\Omega_H$ & $-\Omega_H$ are obtained

Result:



all positive c̄ magnitude calculation.

(fully decoupled)