Ch122a

Fall term 1997

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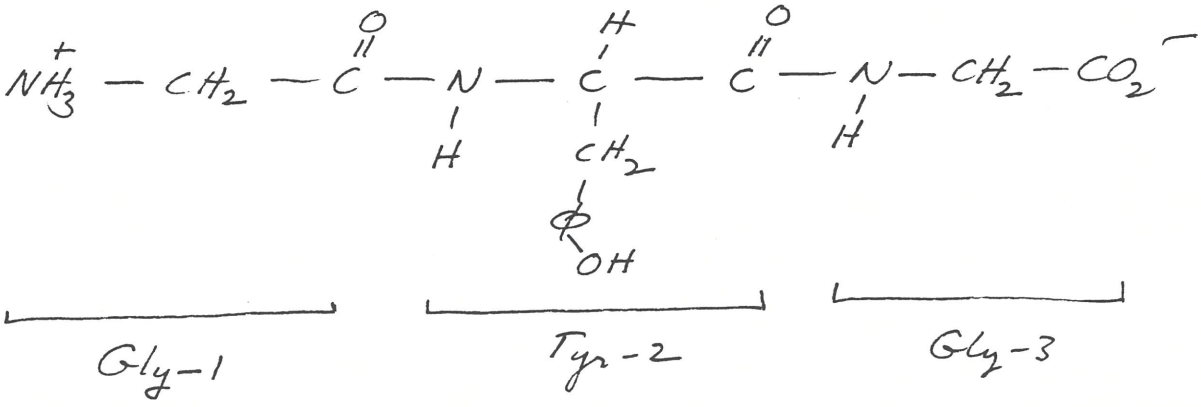
Lecture 18

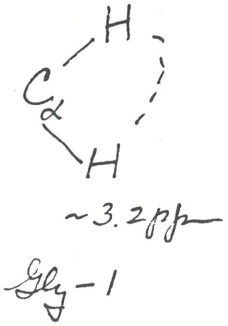
November 12, 1997

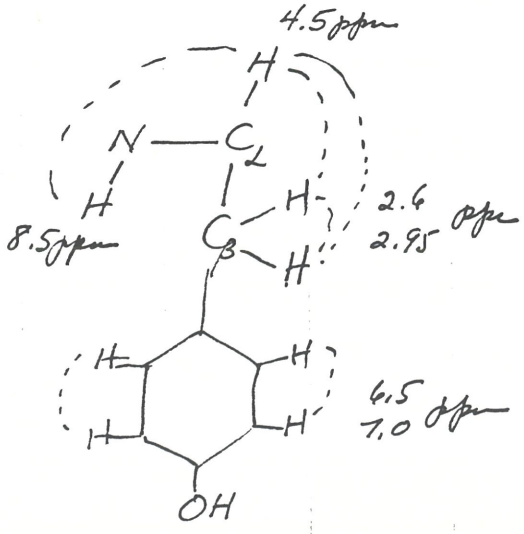
# DQF-COSY and TQF-COSY (continue)

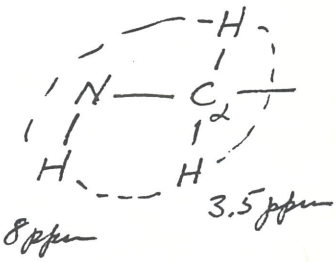
Example tripeptide Gly-Tyr-Gly



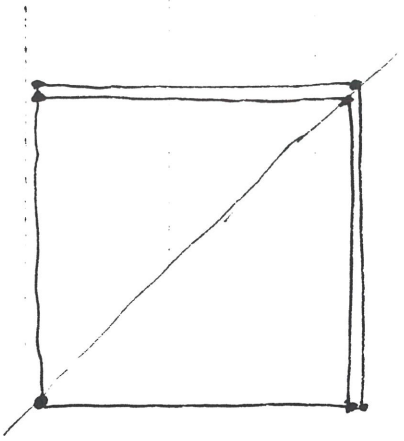

Spin systems



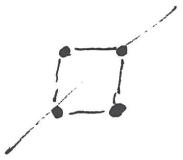
Gly-3



NH
8 ppm

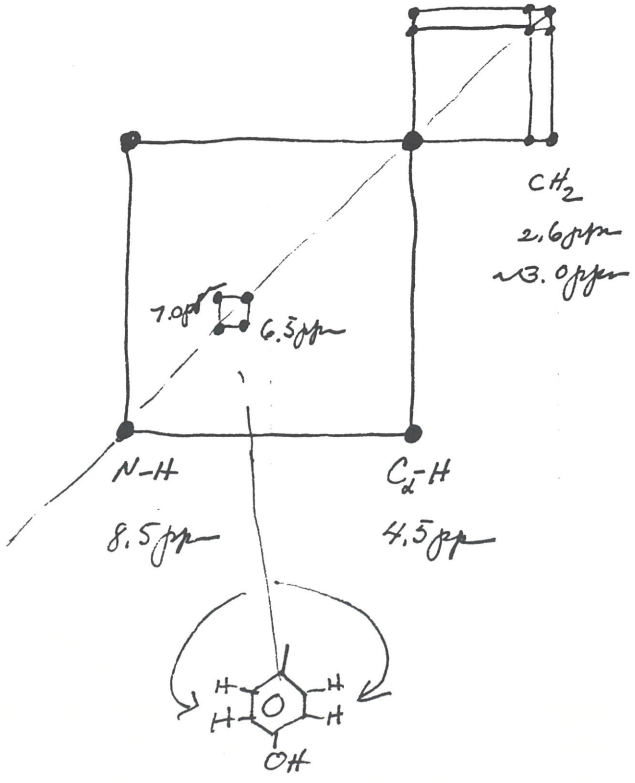
$CH_2$
~3.5 ppm

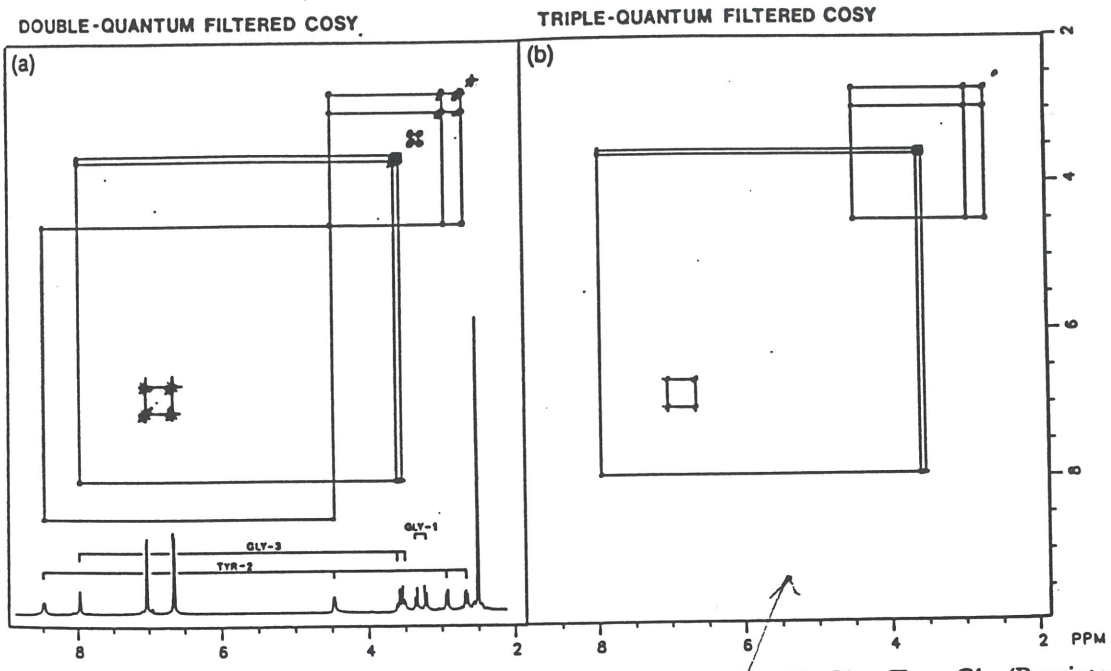
Gly-1



~3.2 ppm

Tyr-2





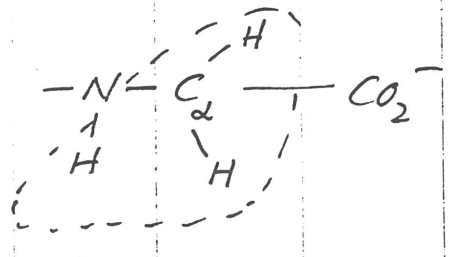

Double- and triple-quantum filtered COSY spectra of the tripeptide Gly—Tyr—Gly. (Reprinted from ref. 7, Ch. 1 with permission.)

Triple-Quantum Filtered COSY

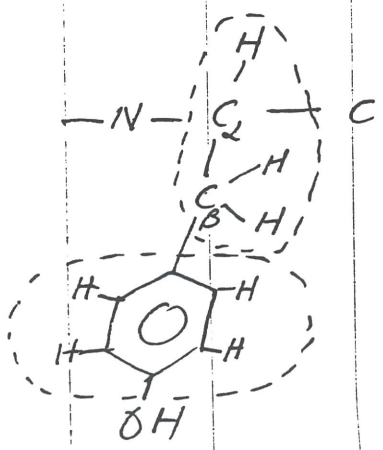
(1) All 1-quantum and 2-quantum coherences are eliminated

(2) Only spin multiplets involving $\geq$ 3 or more protons contribute to the TQF-COSY

e.g.



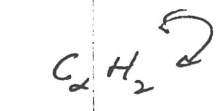
Gly-3



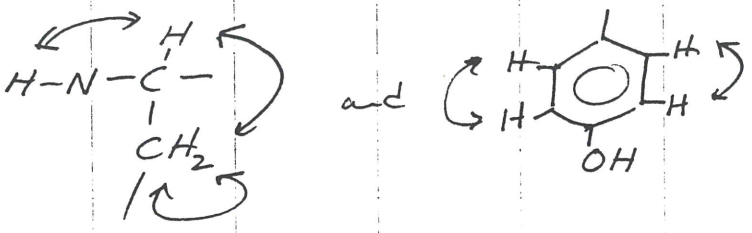
Tyr-2

## DQF-COSY

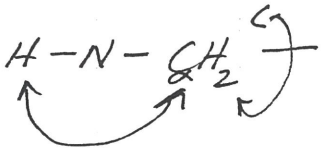
Gly-1



Tyr-2

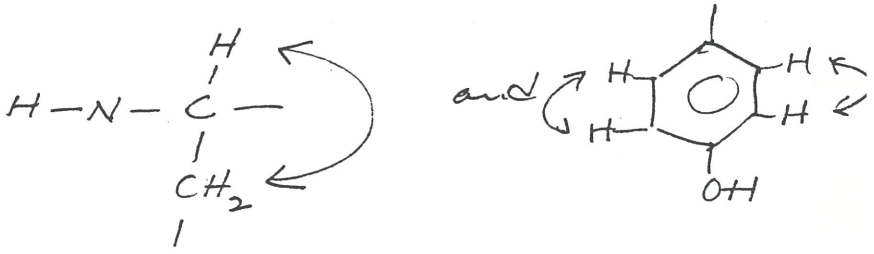


Gly-3

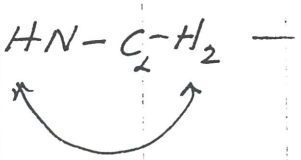


## TQF-COSY

Tyr-2



Gly-3



## Summary on COSY

(1) Siglets, i.e., resonances arising from spins that are not scalar coupled to any other spin show up along diagonal of 2-D spectrum

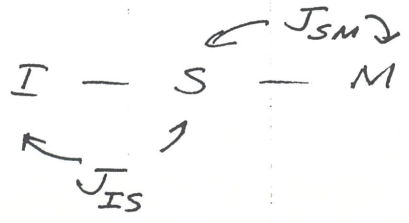
(2) All spin multiplets contribute to diagonal as well as cross-peaks, a pair of cross peak for every pair of spins coupled at $-\Omega_I$ and $-\Omega_S$, if I and S are the spins coupled. Intensities are determined by 1-quantum coherences.

(3) Only spin multiplets contribute to DQF-COSY. Intensities are determined by 2-quantum, 3-quantum, ---- p-quantum coherences, where p is the number of $I=\frac{1}{2}$ spins in spin multiplet.

(4) Only spin multiplets containing 3 or more coupled spins contribute to TQF-COSY. All 1-quantum and 2-quantum coherences are eliminated. Intensities of cross peaks determined by 3-quantum coherences.

## RELAY-COSY Experiment

A method to identify an "S" spin that is simultaneously coupled to an "I" spin as well as an "M" spin




But $J_{IM} = 0$, i.e., I & M spins are not scalar couple

Pulse sequence

π-pulse here in the middle of the 2τ delay is to refocus chemical shift

$$\left(\frac{\pi}{2}\right)_x - t_1 - \left(\frac{\pi}{2}\right)_\phi - \tau - \left(\frac{\pi}{2}\right)_{\phi+\frac{\pi}{2}} - \tau - \left(\frac{\pi}{2}\right)_\phi - t_2$$

← additional delay (2τ) → and RF pulses to transfer coherence between I and S spins to M spin so that coherence is established between I and M spins. — relayed coherence transfer

Following second $\frac{\pi}{2}$ pulse, the transverse S magnetization $2 I_z S_y \sin\omega_I t_1 \sin\pi J_{IS} t_1$ can undergo relayed coherence transfer from I to M via S. Because the π-pulse is the 2τ interval, the evolution of S due to chemical shift becomes refocused at the end of this delay and so can be ignored. Only have to worry about the evolution of S due to scalar coupling of S spin with I-spin, and scalar coupling of S spin with M spin. Therefore, this term in $\sigma_3$ evolves as follows:

$$2 I_z S_y \sin\omega_I t_1 \sin\pi J_{IS} t_1 \xrightarrow{\pi J_{IS} 2\tau I_z S_z} \xrightarrow{\pi J_{SM} 2\tau S_z M_z}$$

$$[2I_z S_y \cos\pi J_{IS} 2\tau \cdot \cos\pi J_{SM} 2\tau - 4 I_z S_x M_z \cos\pi J_{IS} 2\tau \cdot \sin\pi J_{SM}$$

$$- S_x \sin\pi J_{IS} 2\tau \cdot \sin\pi J_{SM} 2\tau - 2 S_y M_z \sin\pi J_{IS} 2\tau \cdot \sin\pi J_{SM} 2\tau]$$

$$\sin\omega_I t_1 \quad \sin\pi J_{IS} t_1$$

In order for coherence to be transferred from I to M, the transverse S magnetization needs to evolve in phase with respect to $J_{IS}$ and in antiphase with respect to $J_{SM}$.

The last term above is converted to observable M magnetizati after the last 90° pulse

$$- 2 S_y M_z \sin\pi J_{IS} 2\tau \cdot \sin\pi J_{SM} 2\tau \cdot \sin\omega_I t_1 \cdot \sin\pi J_{IS} t$$

$$\xrightarrow{\frac{\pi}{2}(I_x + S_x + M_x)} 2 S_z M_y \sin\pi J_{IS} 2\tau \cdot \sin\pi J_{SM} 2\tau \sin\omega_I t_1 \sin\pi J$$

$\uparrow$ $t_2$ $\qquad$ $\uparrow$

This term defines a cross-peak at $\omega_1 = \omega_I$ and $\omega_2 = \omega_M$ with antiphase doublet structure in both dimension

$\longrightarrow$ $2\tau$ chosen so that $\sin\pi J_{IS} 2\tau$ and $\sin\pi J_{SM} 2\tau \neq 0$

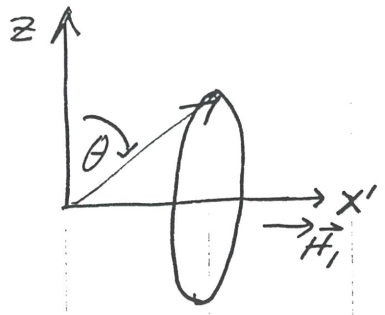
Ideal $\quad 2\pi J_{IS}\tau = \frac{\pi}{2}$ and/or $2\pi J_{SM}\tau = \frac{\pi}{2}$

or $2\tau \sim \frac{1}{2J_{IS}}$ and/or $\frac{1}{2J_{SM}}$ !

Pulse sequence (HOHAHA)

Spin lock sequence replaced by MLEV-17 or DIPSI-X composite pulses

Cross-peaks observed for all spins scalar coupled. Characteristic 2-D patterns for various spin multiplets.




If $\theta = 0$ initially, then

in time $t = t_{\frac{\pi}{2}} = \frac{\pi}{2\omega_1}$, $\vec{\mu}$ will be in xy plane

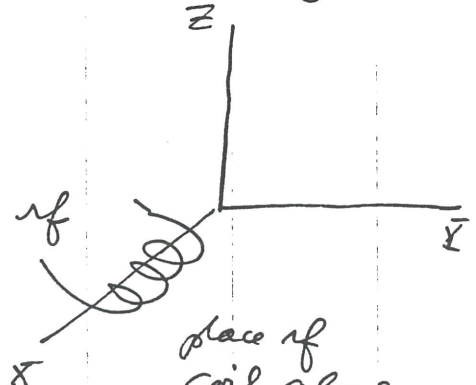
$(\omega_1 t_{\frac{\pi}{2}} = \frac{\pi}{2})$

and in time $t = t_\pi = \frac{\pi}{\omega_1}$, $\vec{\mu}$ will be opposed to $\vec{H}$ (inverted!)

$(\omega_1 t_\pi = \pi)$

This is the phenomenon of magnetic resonance.

— How to generate rotating fields?




Then,

$2 H_1^x \cos \omega_f t$

$= H_1^x (e^{i\omega_f t} + e^{-i\omega_f t})$

anticlockwise component

clockwise component

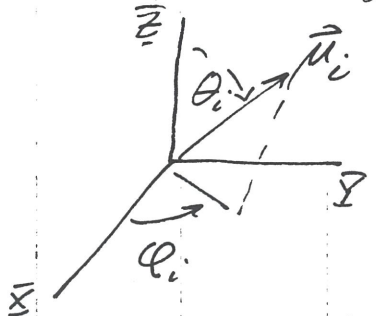
(sum of two rotating components)

- Many spins — Concept of Magnetization

In general, there are many spins in the sample. To describe the system, we can exploit the concept of magnetization ($\vec{M}$). If the spins interact only weakly among themselves, then we can write

$$\vec{M} = \sum_k \vec{\mu}_k \quad \text{or} \quad \begin{cases} M_X = \sum_k \mu_k^X \\ M_Y = \sum_k \mu_k^Y \\ M_Z = \sum_k \mu_k^Z \end{cases}$$

Even for a sample where all the spins are the same (same $\gamma$'s and chemically identical), the various spins or $\mu$'s have different orientations with respect to the applied magnetic field;




i.e., $\theta_i$, $\varphi_i$ vary

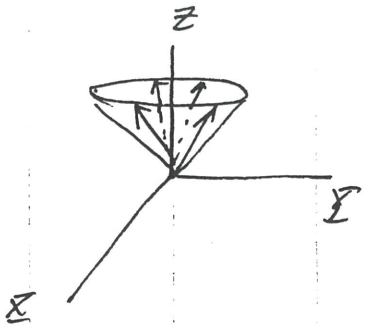
The energy of the spin is independent of the azimuthal angle $\varphi$

but it depends on the polar angle $\theta_i$.

Specifically, Energy $= -\vec{\mu}_i \cdot \vec{H} = -\mu_i H_0 \cos\theta_i$.

This means that all $\vec{\mu}_i$'s with the same $\theta_i$ share the same energy. However, at thermal equilibrium, all $\varphi_i$'s are equally probable (the so-called random phase approximation)

So at thermal equilibrium,




all $\theta_i$'s equally probable

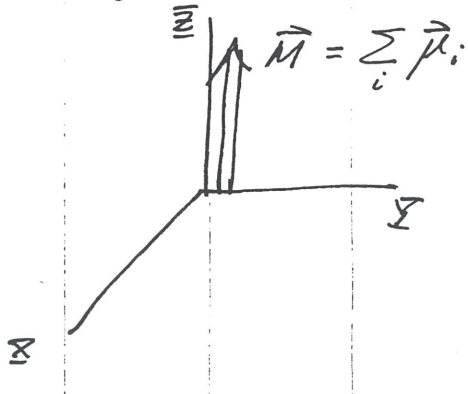
$$M_x(\theta) = \sum_i \mu_i^x = 0$$
$$M_y(\theta) = \sum_i \mu_i^y = 0$$
$$M_z(\theta) = \sum_i \mu_i^z = N(\theta)\,\gamma\hbar|\mu|\cos\theta$$

and

$$M_x = \sum_\theta M_x(\theta) = 0$$
$$M_y = \sum_\theta M_y(\theta) = 0$$
$$M_z = \sum_\theta N_\theta\,\gamma\hbar|\mu|\cos\theta$$

and $N_\theta$ is determined by the Boltzmann formula.

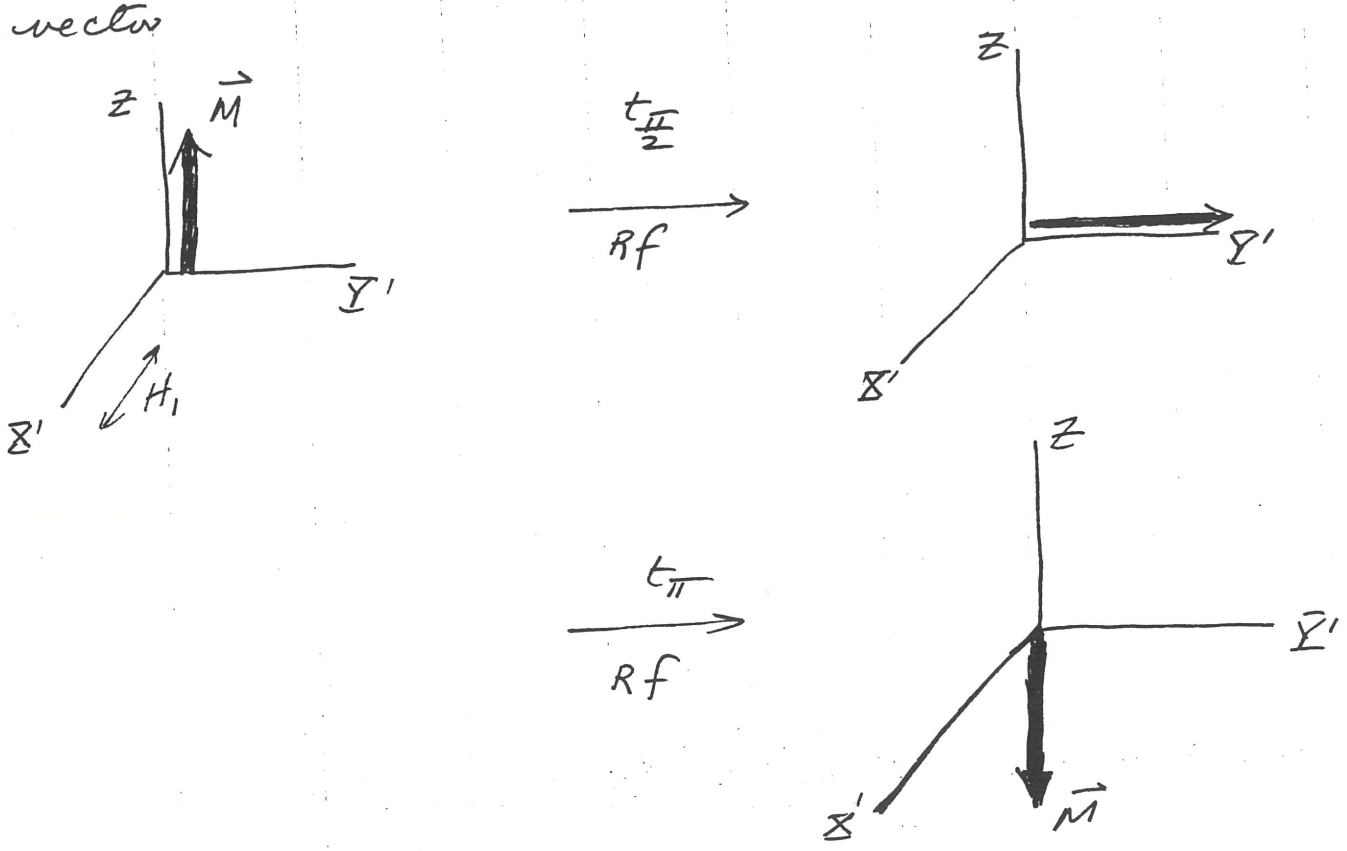
Therefore, at the beginning of an NMR experiment, when the system is supposedly at thermal equilibrium, we have




and we follow only this <u>macroscopic</u> magnetization in an NMR experiment!

Note that all spins with the same $\gamma$'s, all spins with the same $\gamma$'s even in different chemical environments, all spins with different $\gamma$'s, etc., contribute to $\vec{M}$. In practice it may not be possible to excite them all at the same time or not, that is,

- For the many-spin problem, magnetic resonance can be described in terms of "motion" of the bulk magnetization vector




- In practice, must include relaxation terms, as $M_X$, $M_Y$, $M_Z$ depart from equilibrium values as in above, to describe the temporal behavior of $\vec{M}$. The result is the Bloch equations

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{H} - \vec{i}\frac{M_X}{T_2} - \vec{j}\frac{M_Y}{T_2} - \frac{(M_Z - M_0)}{T_1}$$

or $$\frac{dM_x}{dt} = \gamma(M_y H_0 + M_z H_1 \sin \omega_{rf} t) - \frac{M_X}{T_2}$$

$$\left(H_1^{\mathcal{E}} = H_1 \cos\omega_{rf} t \;,\quad H_1^{\mathcal{I}} = H_1 \sin\omega_{rf} t\right)$$

$$\frac{dM_y}{dt} = \gamma(M_z H_1 \cos\omega_{rf} t - M_{\mathcal{E}} H_0) - \frac{M_y}{T_2}$$

$$\frac{dM_z}{dt} = -\gamma(M_x H_1 \sin\omega_{rf} t + M_y H_1 \cos\omega_{rf} t) - \frac{(M_z - M_0)}{T_1}$$

where $M_0$ = equilibrium magnetization

$T_1$ = longitudinal relaxation time
or spin lattice relaxation time

$T_2$ = transverse relaxation time
or spin-spin relaxation time

The magnitudes of $M_{\mathcal{E}}$, $M_{\mathcal{I}}$, $M_{\mathcal{Z}}$ vary as $\vec{M}$ evolves with time

## Relaxation Processes and Measurement of NMR Signals

## Free-induction Decay

after $\frac{\pi}{2}$ pulse, $M_{xy} \neq 0$, non-equilibrium, so $M_{xy}$ must decay with time. Rate of decay depends on how the individual spins that make up the magnetization can get out of phase, and this decay thus depends on

a) different frequencies of precession of various spins that are excited by rf

$$\Delta\omega_0 : \omega_1^0, \omega_2^0 \ldots\ldots$$

b) magnetic field inhomogeneity over the sample

c) variations in the precession frequencies due to fluctuations in the local magnetic field at the nucleus

$$\overline{\Delta(\omega-\omega_0)^2}^{1/2}$$

In any case, FID $\equiv$ NMR spectrum in time domain

In the pulse experiment, rf is on for a time necessary to turn $\vec{M}$ by $\pi/2$. Since $T_2$ can be pretty short, require

$$t_{\pi/2} \ll T_2 \quad , \text{ a condition}$$

which often times require $H_1^{rf}$ to be large

$$\left(\text{Note} \quad t_{\pi/2} = \frac{\pi}{2\gamma H_1^{rf}}\right)$$

However, in pulse experiments, one is trying to excite all the spins at the same time (usually spins of same $\gamma$)

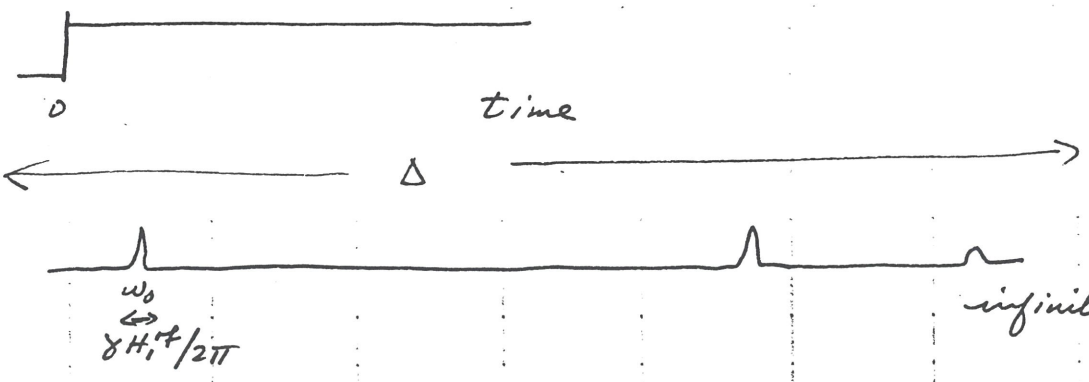
$$\therefore \gamma H_1^{rf} \gg 2\pi\Delta \qquad \Delta \text{ spectral width}$$

$t_p \ll \frac{\pi}{2(2\pi\Delta)} = \frac{1}{4\Delta}$ if condition is to be satisfied.


$\therefore t_p \ll T_2$ or $\frac{1}{4\Delta}$ which ever is shorter.

- Continuous wave Experiment

obtained by sweeping the frequency of rf or magnetic field through resonance slowly.
In this expt., as opposed to pulse expt. that gives FID, rf is on continuously, however $H_1$ is small so that only one resonance is excited at a time.




Far from resonance $\vec{H}_{eff} = \left(\vec{H}_0 + \frac{\omega_{rf}}{\gamma}\right) \sim \vec{H}_0$

at or near resonance $\vec{H}_{eff} = \left(\vec{H}_0 + \frac{\omega_{rf}}{\gamma}\right) + \vec{H}_1 \sim \vec{H}_1$