

Spin echoes, inhomogeneous fields, relaxation and chemical exchange.

Dušan Uhrín
School of Chemistry
University of Edinburgh



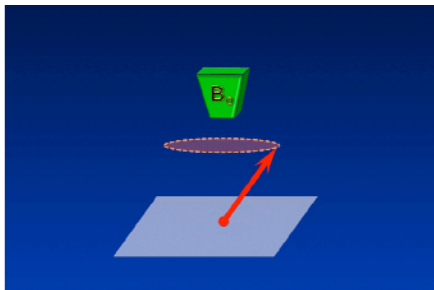
3rd SNUG meeting

August 2017

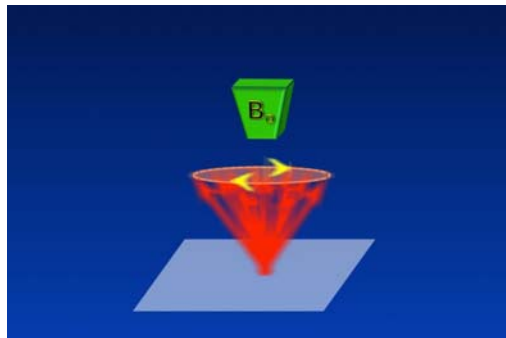
Rotating frame – a very useful concept in NMR

Spin precession in a magnetic field

slow

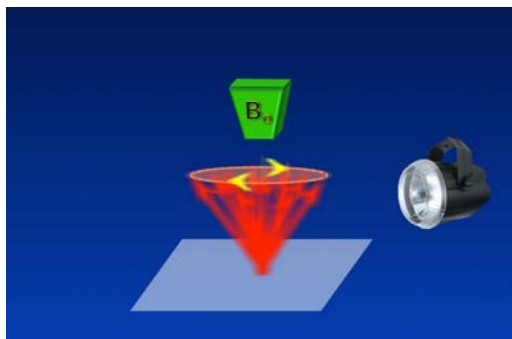


fast

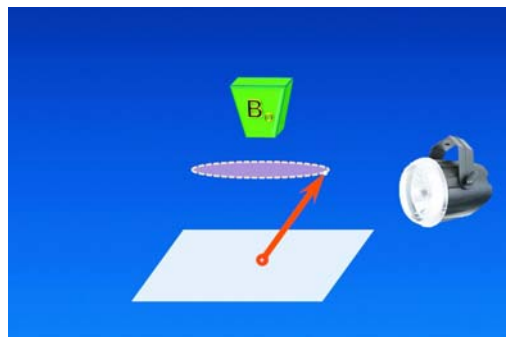


Stroboscope

off



on - at the resonance frequency – spin appears to be stationary



Merry-go-round

stay put

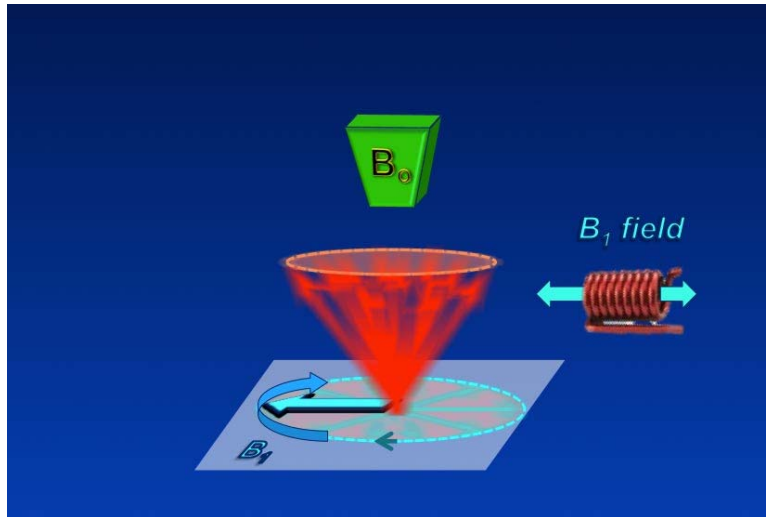


run around at the spinning frequency



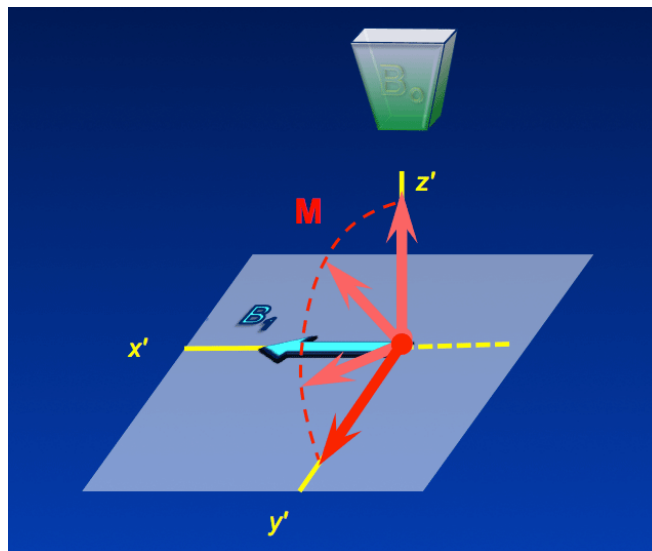
<http://mriquestions.com/rotating-frame.html>

Radiofrequency pulse in a rotation frame



Radiofrequency pulse oscillating (intensity B_1) at the resonance frequency is stationary in the rotating frame....

....spin does not feel the external field anymore, only the B_1 field, starts rotating around it.



Keeping the r.f. on, can place the spin into $y'z'$ plane at an arbitrary place

.... but usually chose a 90° rotation (as here) or a 180° rotation ($-z'$)

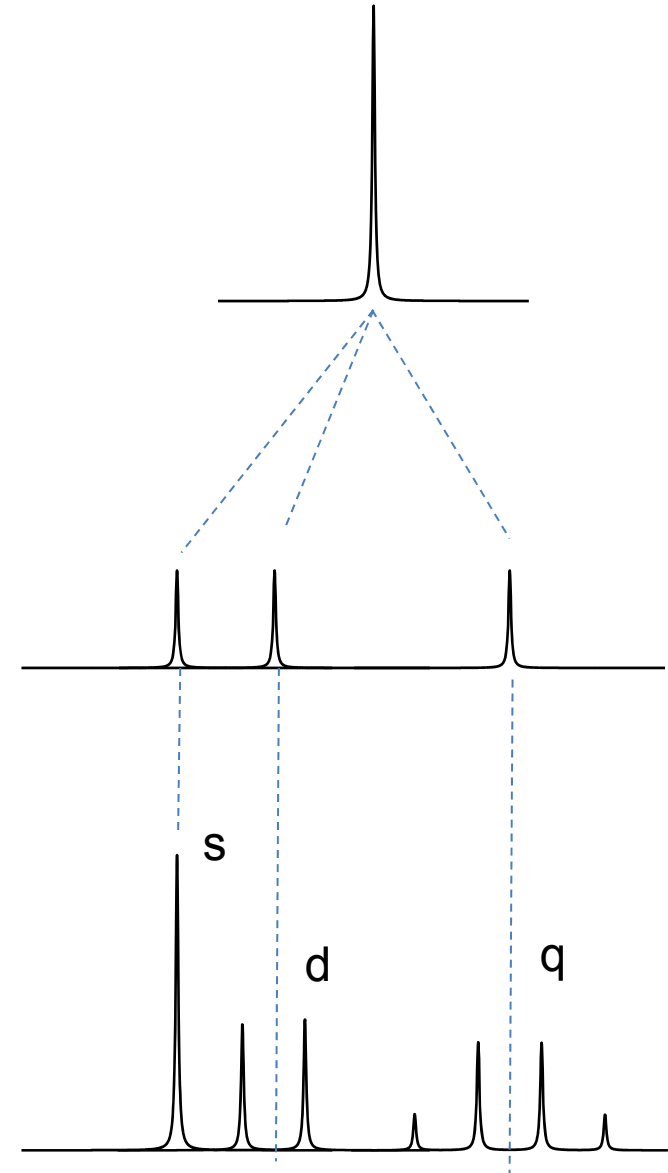
NMR resonance condition

$$\nu = \gamma B_0 / 2\pi$$
 - basic resonance condition

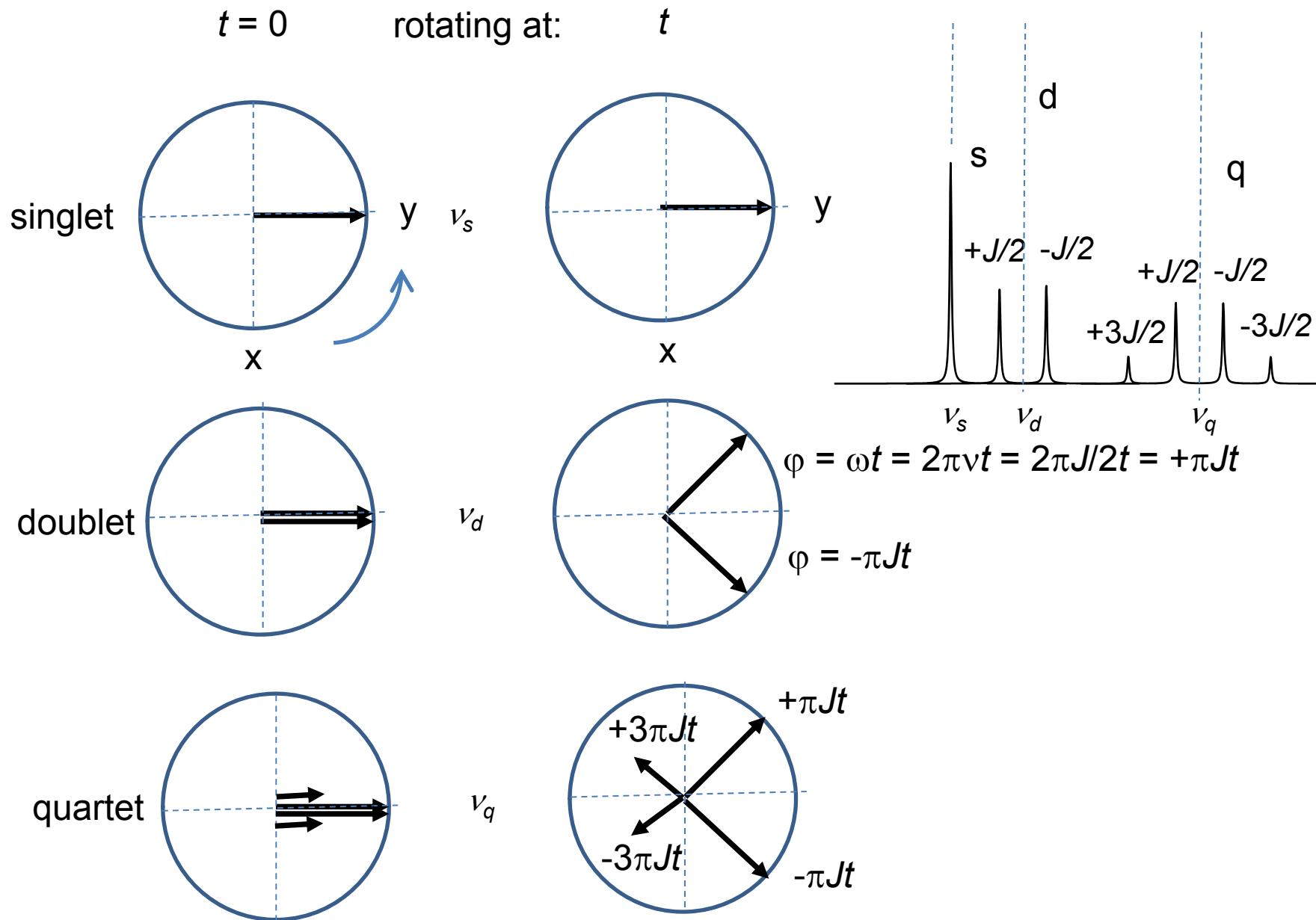
$$\nu_{Ai} = \gamma_A B_o(1-\sigma) / 2\pi - \sigma \text{ is the shielding constant}$$

$$v_{Ai} = \gamma_A B_o(1-\sigma) / 2\pi - \sum_{(X \neq A)} J_{AX} m_X$$

m_X is the magnetic quantum number

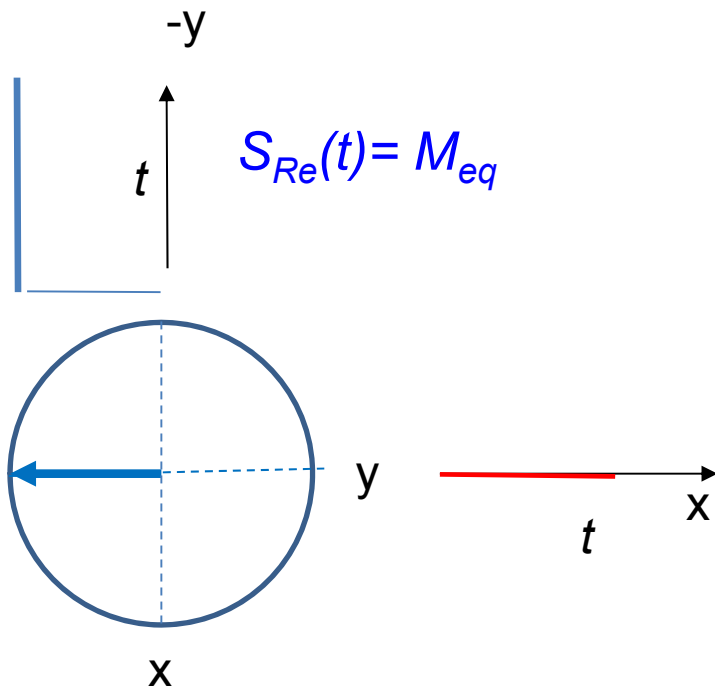


Multiplets in a rotating frame (after a 90° pulse)



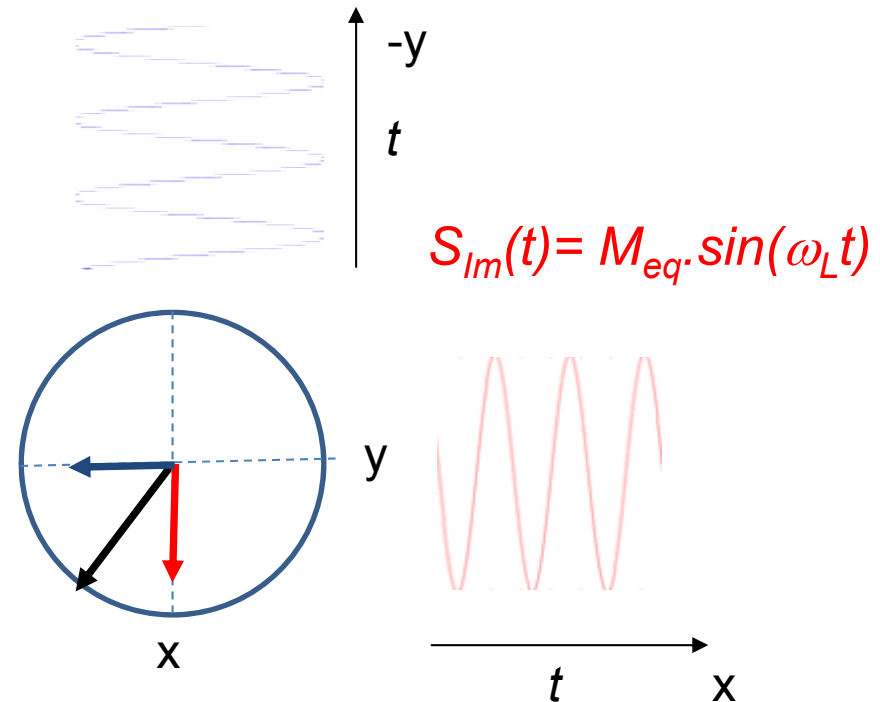
Signal detection along the x and y axis

On-resonance singlet



Off-resonance singlet

$$S_{Re}(t) = M_{eq} \cdot \cos(\omega_L t)$$

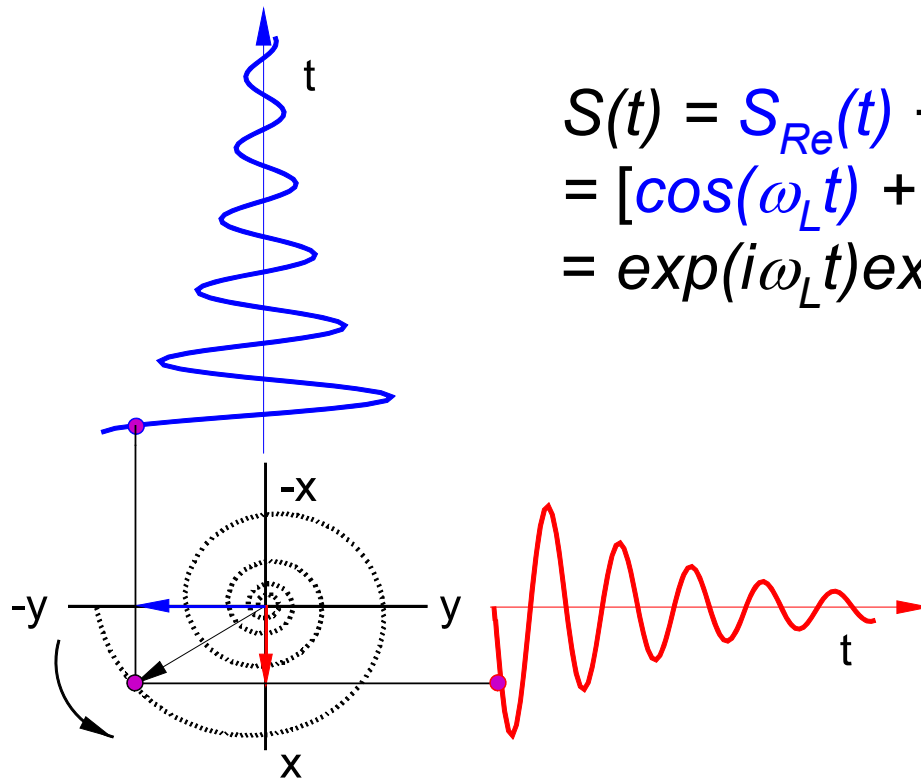


Oscillating current induced by rotating magnetic moments =
= Free Induction Decay or FID

No relaxation considered here!

FID of an off-resonance relaxing singlet

$$S_{Re}(t) = M_{eq} \cdot \cos(\omega_L t) \exp(-t/T_2)$$



$$\begin{aligned} S(t) &= S_{Re}(t) + iS_{Im}(t) \\ &= [\cos(\omega_L t) + i\sin(\omega_L t)] \exp(-t/T_2) \\ &= \exp(i\omega_L t) \exp(-t/T_2) = \exp[-(1/T_2 - i\omega_L)t] \end{aligned}$$

$$S_{Im}(t) = M_{eq} \cdot \sin(\omega_L t) \exp(-t/T_2)$$

FT of FID yields a Lorentzian line

$$S(t) = \exp[-(1/T_2 - i\omega_L)t] \leftarrow \text{FID}$$

$$S(\omega) = \int_0^{\infty} S(t) \exp(-i\omega t) dt \quad \swarrow \text{Guess function}$$

$$S(\omega) = \int_0^{\infty} \exp\{-[1/T_2 + i(\omega - \omega_L)t]\} dt$$

$$S(\omega) = \frac{1}{(1/T_2) + i(\omega - \omega_L)} =$$

$$S(\omega) = \frac{1}{(1/T_2) + i(\omega - \omega_L)} \frac{(1/T_2) - i(\omega - \omega_L)}{(1/T_2) - i(\omega - \omega_L)}$$

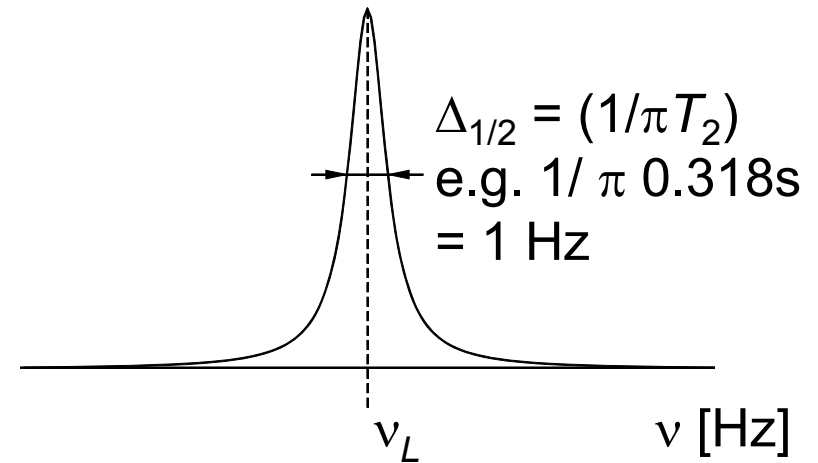
$$S(\omega) = \frac{(1/T_2)}{(1/T_2)^2 + (\omega - \omega_L)^2} + i \frac{(\omega_L - \omega)}{(1/T_2)^2 + (\omega - \omega_L)^2}$$

$$= A(\omega) + iD(\omega) \text{ or}$$

Absorption + Dispersion Lorentzian line

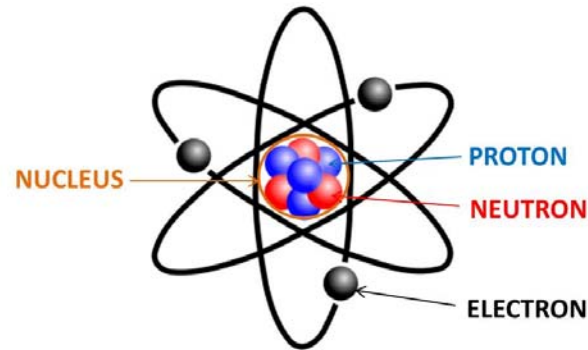
Absorption Lorentzian line.

$$S(\nu) = \frac{(1/T_2)}{(1/T_2)^2 + 4\pi^2(\nu - \nu_L)^2}$$

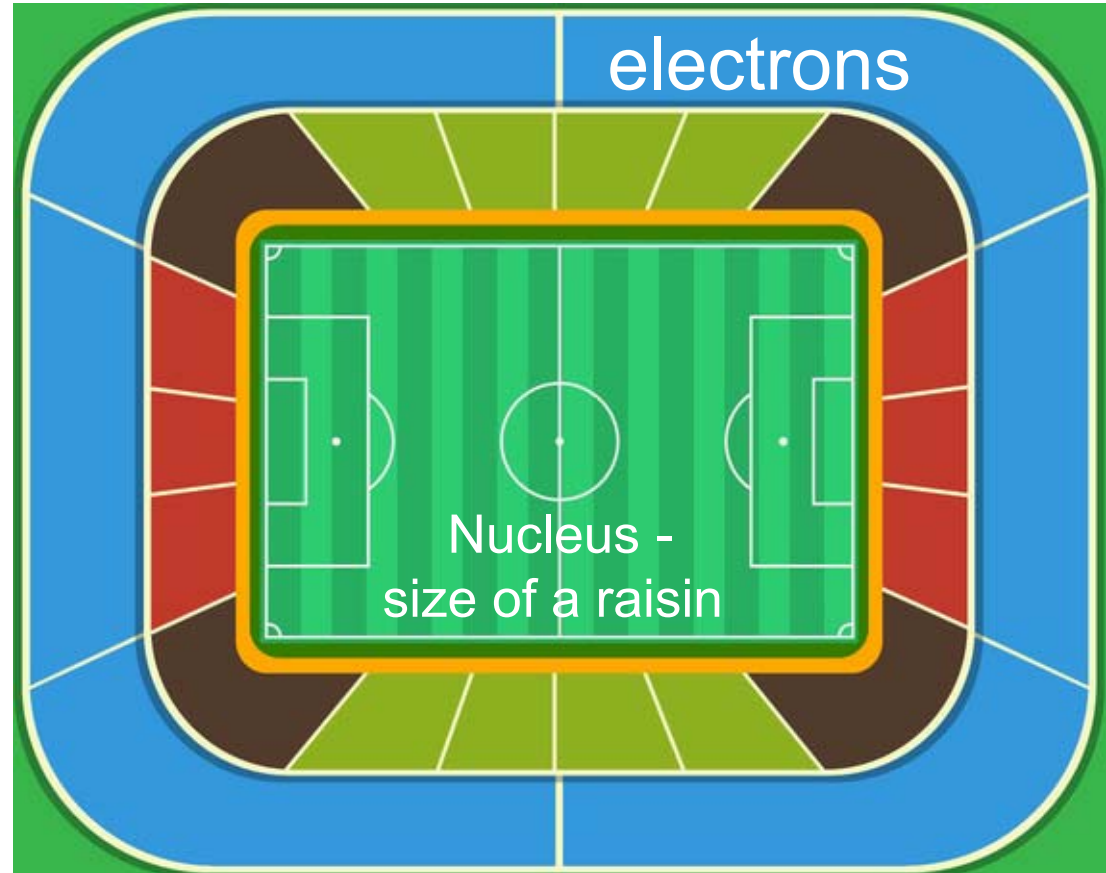


T_2 - spin-spin relaxation time [s]
 $R_2 = 1/T_2$ - spin-spin relaxation rate [Hz]

Why are nuclear excited states so long-lived?

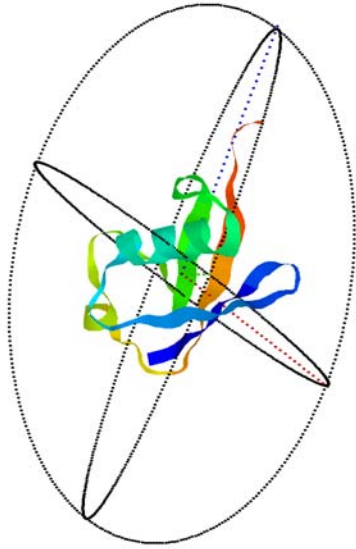


1. Large, empty spaces surround nuclei
2. Nuclear magnetic moments are only sensitive to other magnetic moments



What are the driving forces behind relaxation?

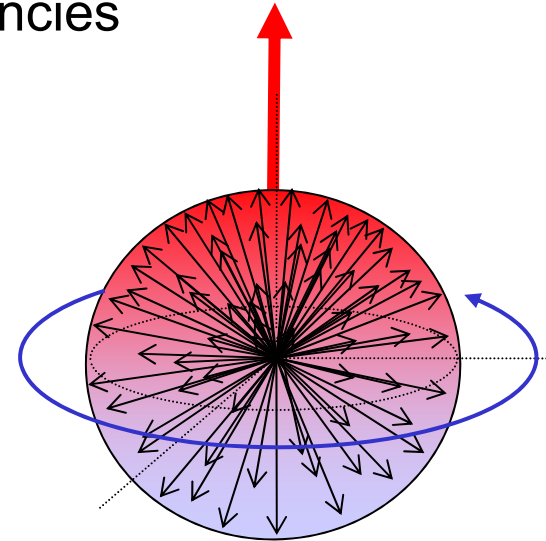
Molecules rotate violently



The time it takes for a molecule to rotate 1 radian (ca 60°) is referred to as a rotational correlation time, τ_c .

$$\tau_c = 10^{-12} - 10^{-9} \text{ s}$$

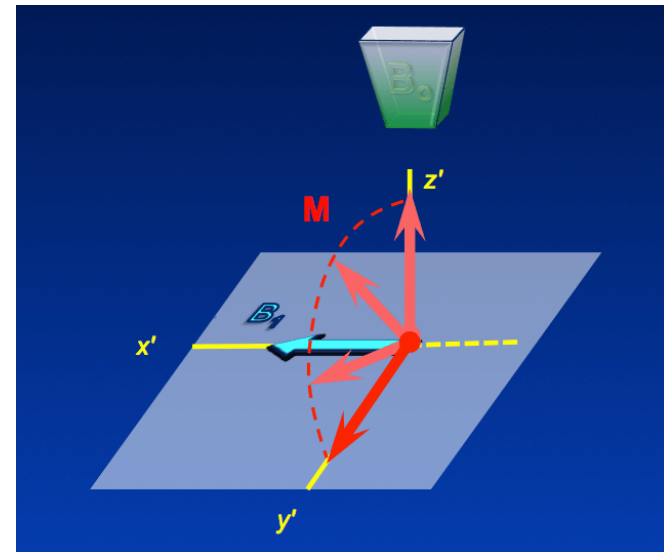
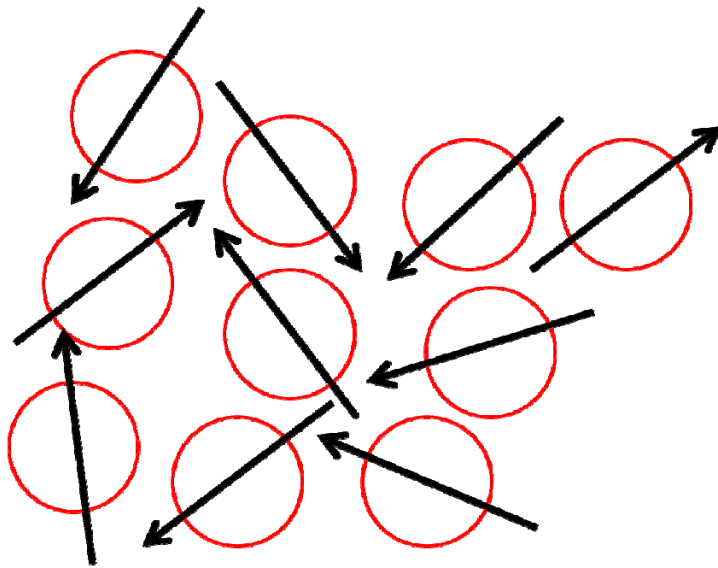
Spin rotate at their Larmor frequencies



Temporarily, these motion create a magnetic moment of one nucleus that is stationary in the rotating frame of another spin.

While ship rotates violently, spin stay stationary as keel
of a ship, unless ...

... the magnetic fields cause them to rotate for a moment.

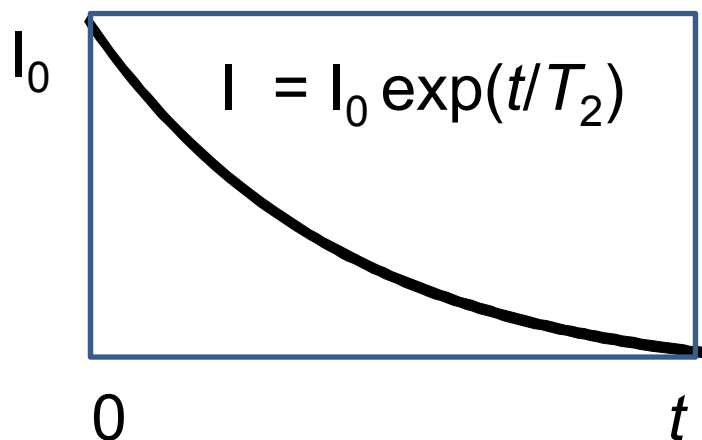
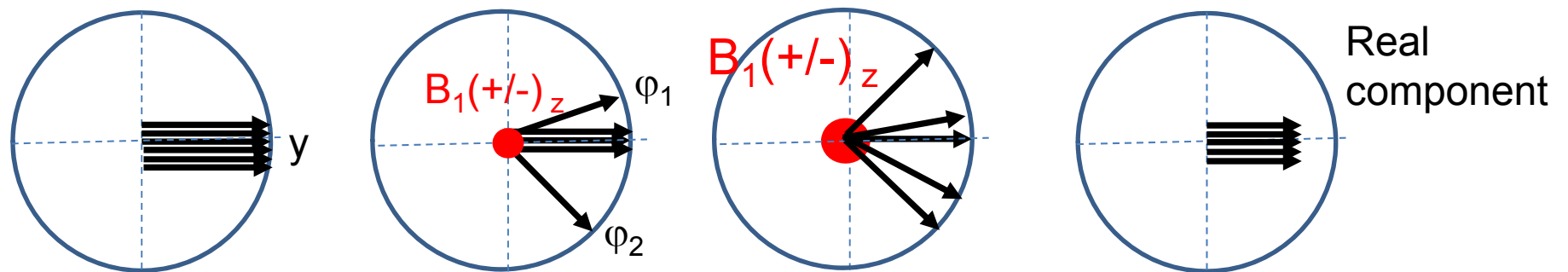


Local pulse of a random flip angle and random direction in a
single molecule – **this is the mechanism of relaxation**

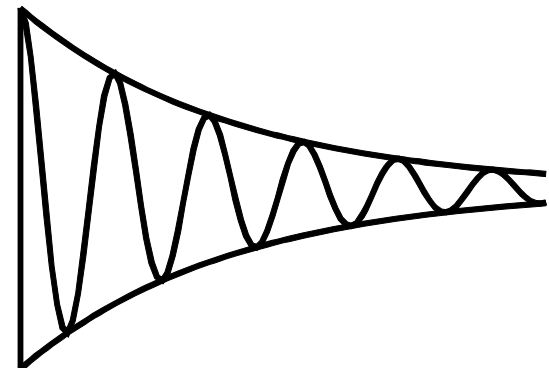
T_2 relaxation seen in the rotating frame

On resonance singlet (five molecules)

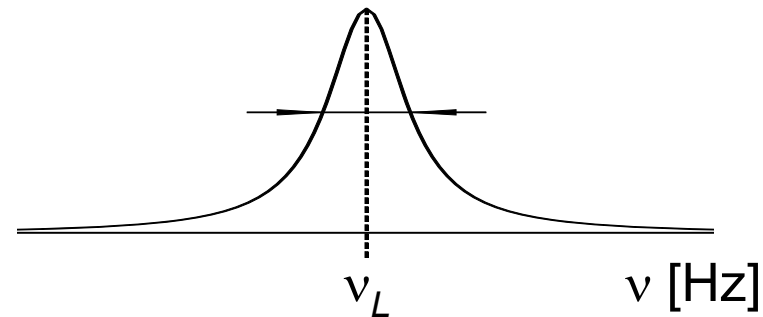
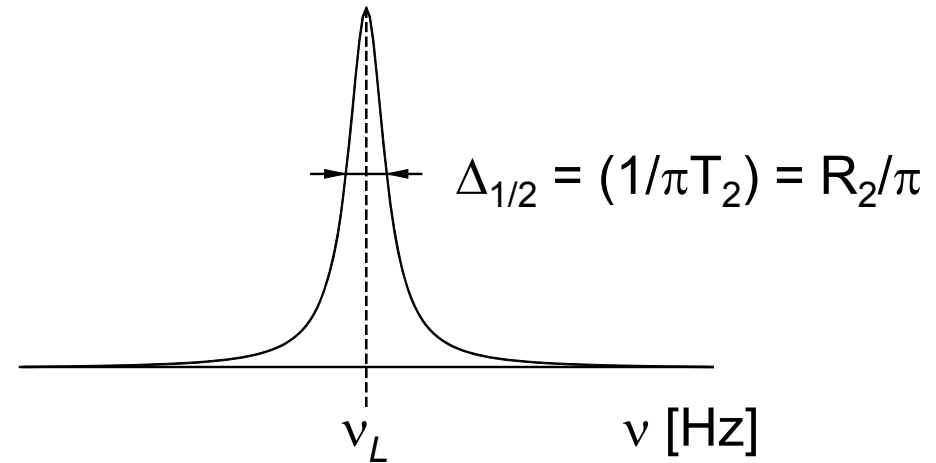
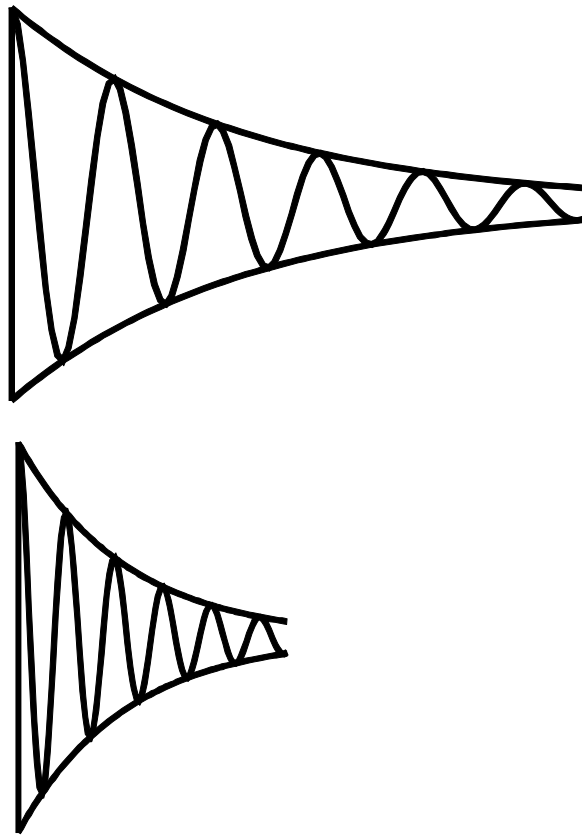
A magnetic moment of a nearby dipole becomes stationary along the z (or $-z$) axis of the rotating frame. This acts as a local z -pulse and moves a spin in two molecules by φ_1 and φ_2



Off-resonance singlet



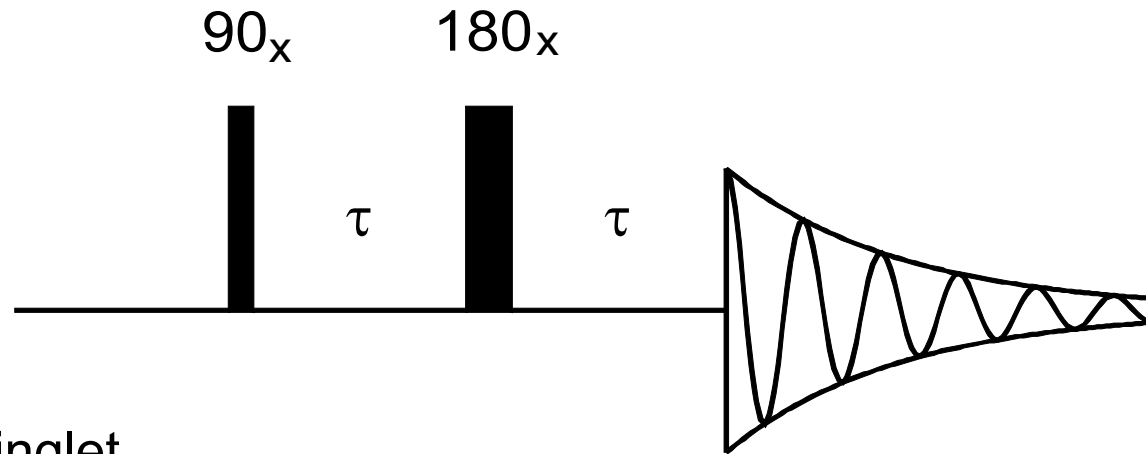
Shorter T_2 , or faster relaxation rate, R_2 , = broader lines



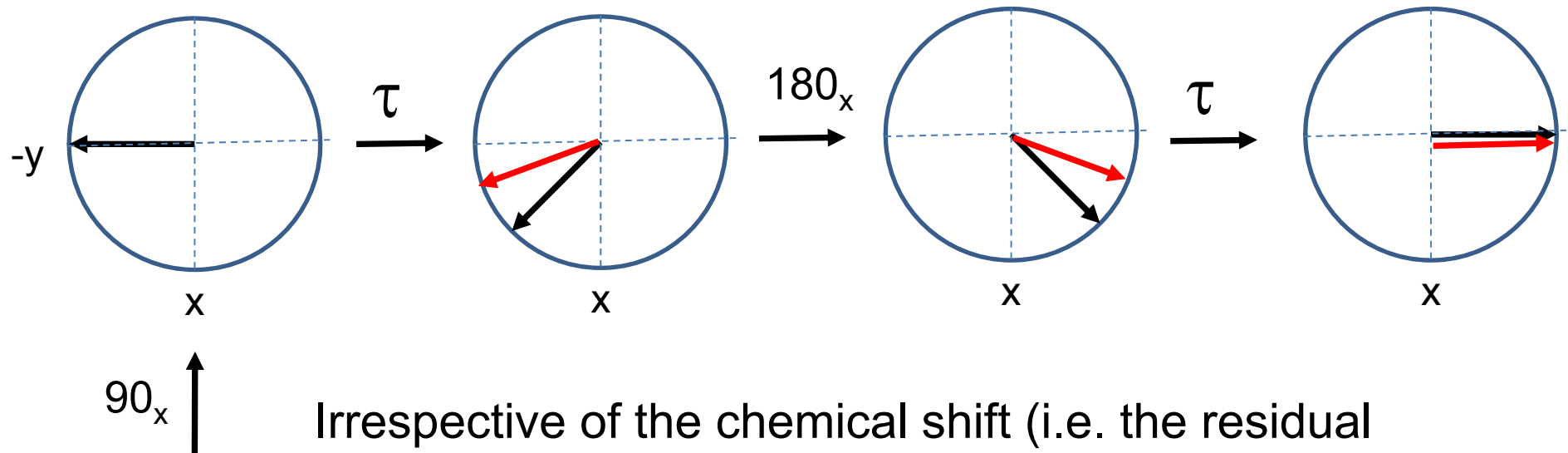
Sources of spin-spin relaxation:

- Natural relaxation – size of the molecules
- Magnetic field inhomogeneity
- Chemical exchange

Spin-echo – the most important building block of FT NMR

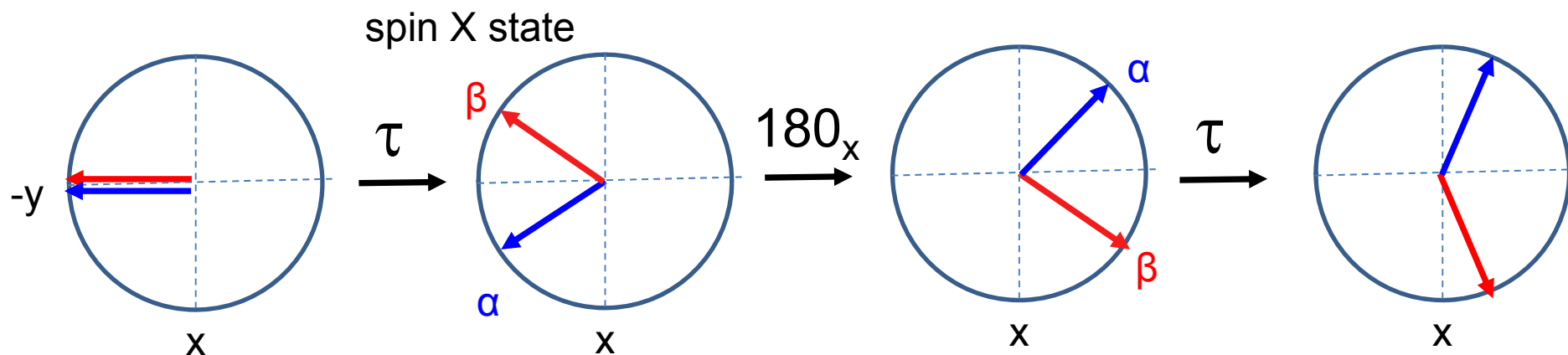
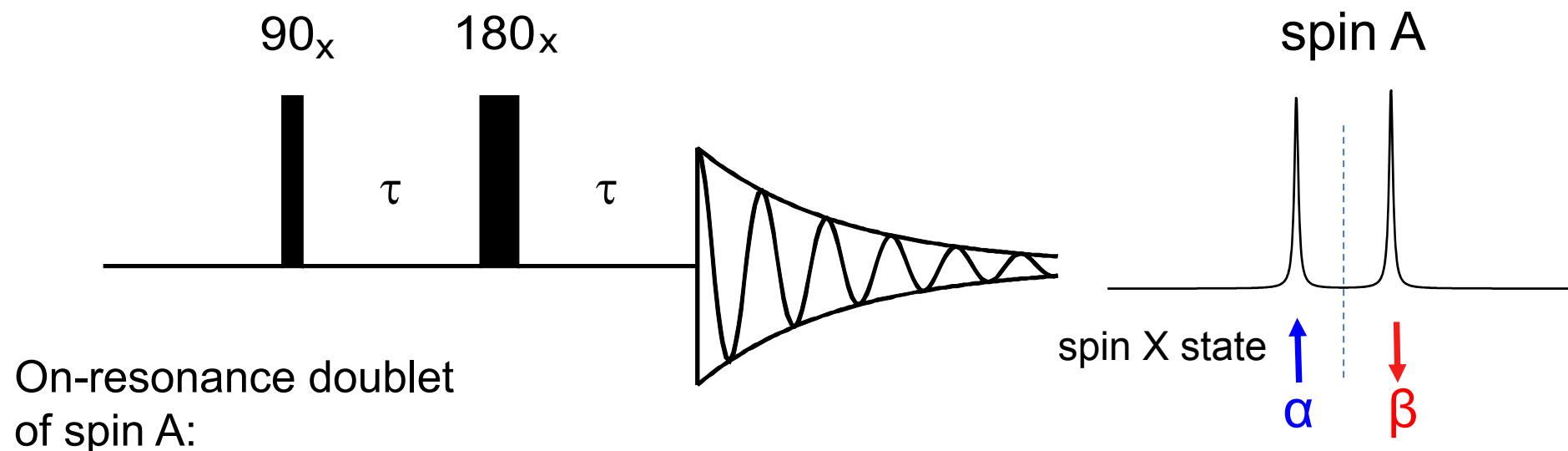


Off-resonance singlet



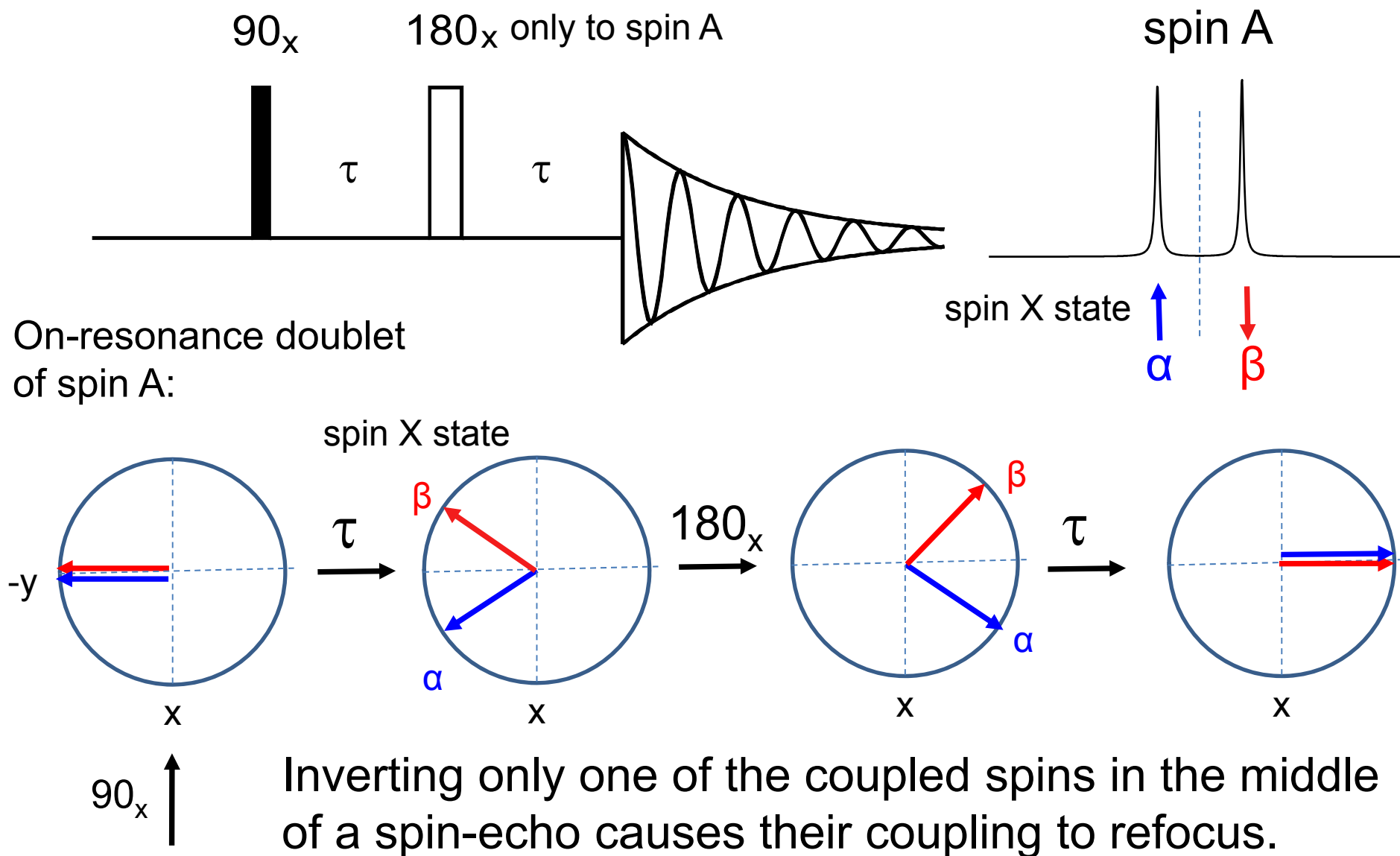
Irrespective of the chemical shift (i.e. the residual frequency in the rotating frame) all singlets align again by the end of the spin echo

Spin-echo of coupled AX spins – a doublet case

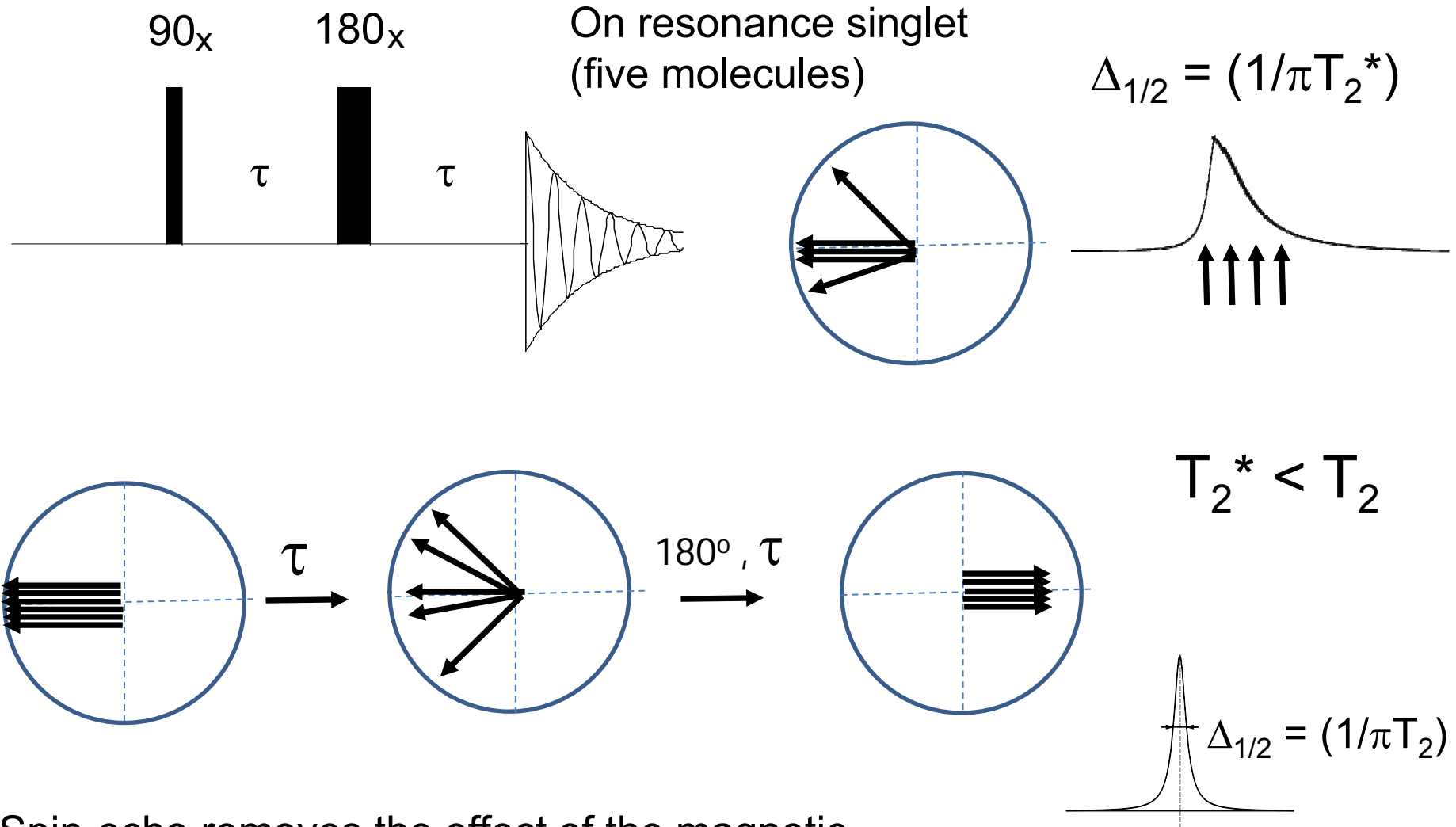


Inverting both coupled spins in the middle of a spin-echo cause the coupling to evolve. It only refocuses chemical shift, not the coupling.

Selective spin-echo of coupled AX spins



Spin-echo and magnetic field inhomogeneity

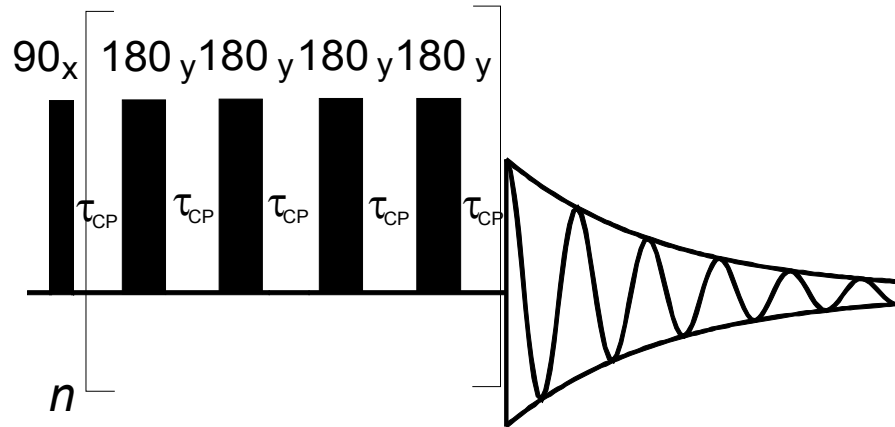


Spin-echo removes the effect of the magnetic field inhomogeneity. It does not stop relaxation. Signal still gradually disappears.

Signals sampled during the spin-echo are narrower

How do we measure T_2 relaxation times?

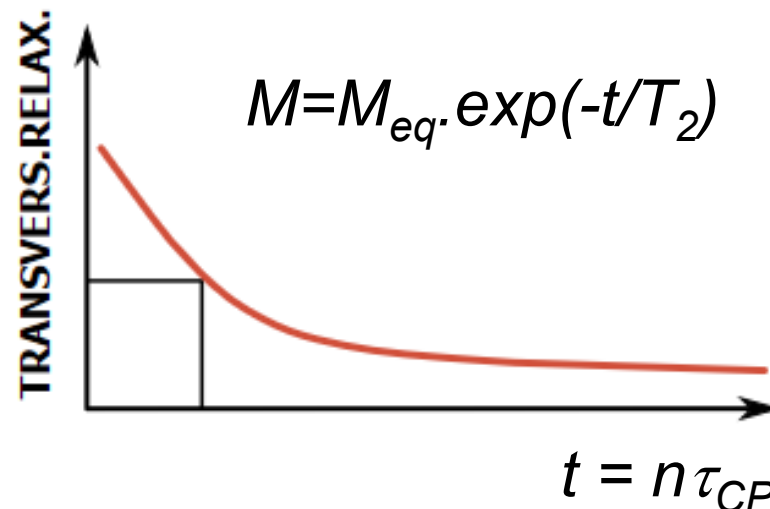
CPMG: Carr-Purcell, Meiboom-Gill



The time evolution due to J -modulation becomes negligible when

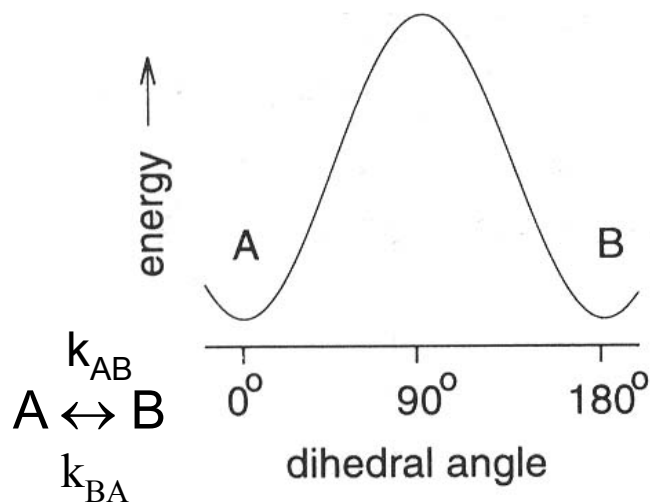
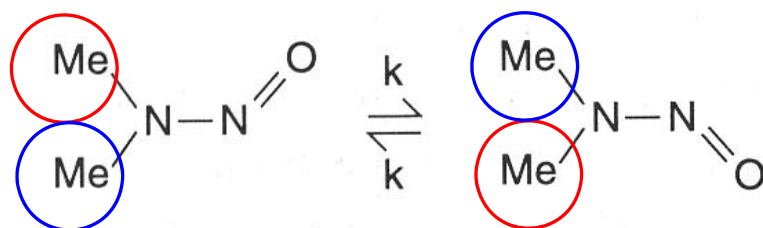
$$\tau_{cp} \cdot \sqrt{\delta^2 + J^2} \ll 1$$

where τ_{cp} is an interpulse delay (in s), J is the coupling constant (in Hz), and δ is the chemical shift difference (in Hz) between the coupled spins.



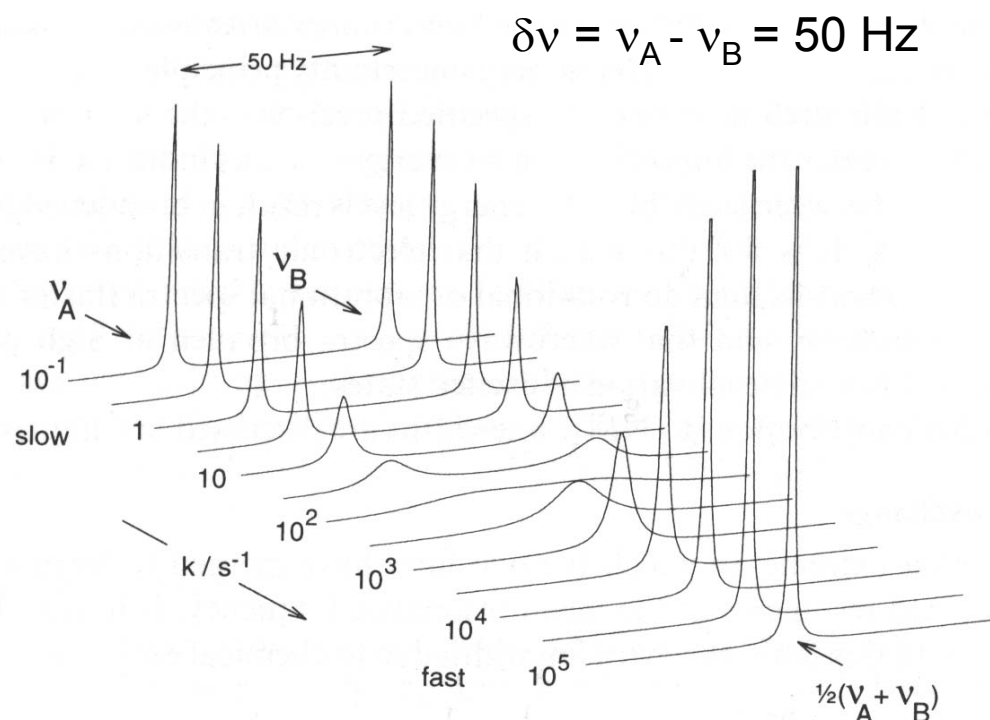
Dynamic equilibrium between two equal energy states - a symmetrical two-site exchange

Dimethylnitrosamine

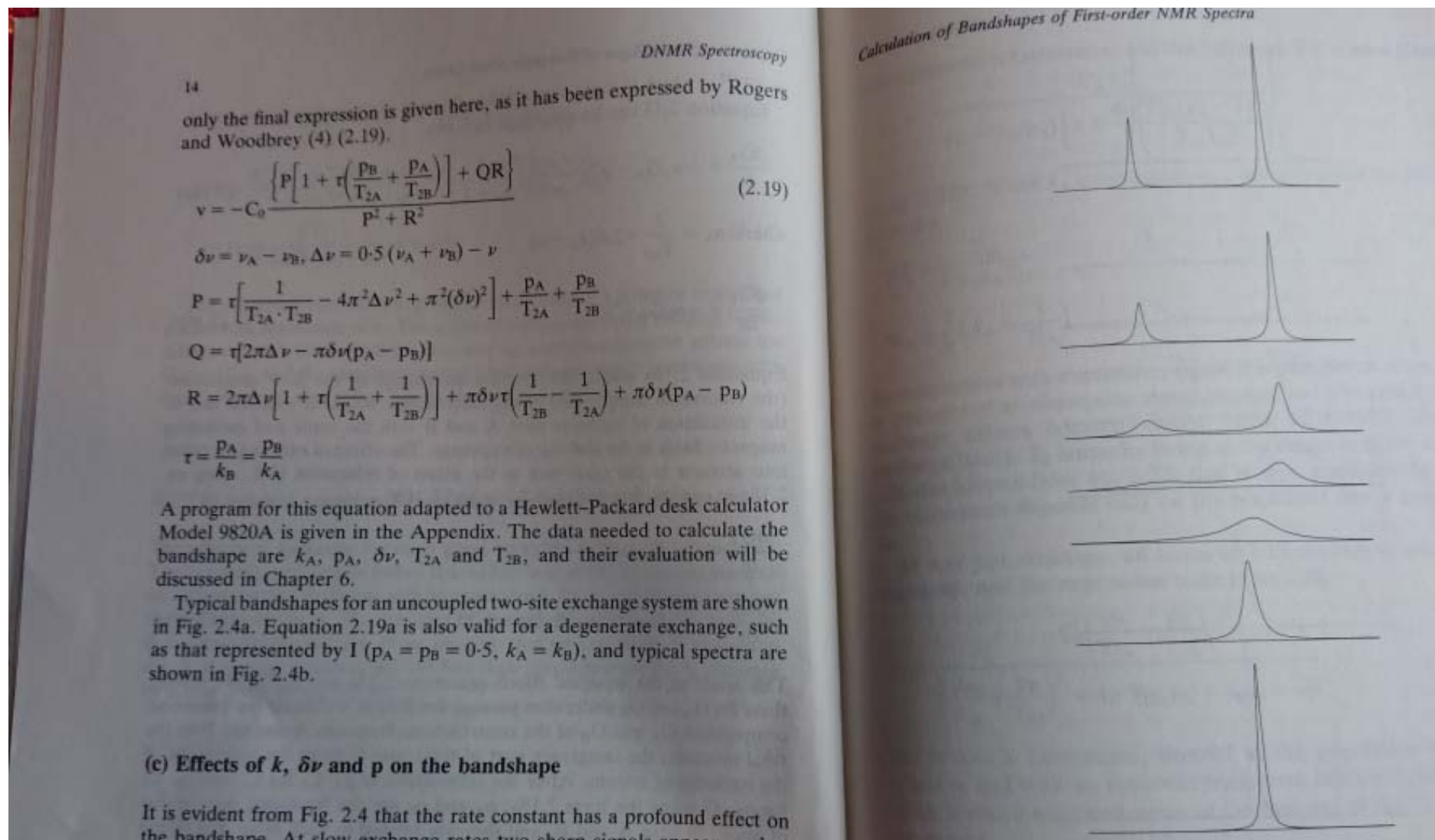


$$k_{\text{ex}} = k_{AB} + k_{BA} \text{ [s}^{-1}\text{]}$$

$$\text{Average lifetime } \tau = 1/k_{\text{ex}} \text{ [s]}$$



Can we simulate the chemical exchange spectra?



Rogers, M. T.; Woodbrey, J. C. *J. Phys. Chem.* **1962**, 66, 540.

Can we simulate the chemical exchange spectra?

$$\nu = -C_0 \frac{\left\{ P \left[1 + \tau \left(\frac{p_B}{T_{2A}} + \frac{p_A}{T_{2B}} \right) \right] + QR \right\}}{P^2 + R^2} \quad (2.19)$$

$$\delta\nu = \nu_A - \nu_B, \Delta\nu = 0.5 (\nu_A + \nu_B) - \nu$$

$$P = \tau \left[\frac{1}{T_{2A} \cdot T_{2B}} - 4\pi^2 \Delta\nu^2 + \pi^2 (\delta\nu)^2 \right] + \frac{p_A}{T_{2A}} + \frac{p_B}{T_{2B}}$$

$$Q = \tau [2\pi\Delta\nu - \pi\delta\nu(p_A - p_B)]$$

$$R = 2\pi\Delta\nu \left[1 + \tau \left(\frac{1}{T_{2A}} + \frac{1}{T_{2B}} \right) \right] + \pi\delta\nu\tau \left(\frac{1}{T_{2B}} - \frac{1}{T_{2A}} \right) + \pi\delta\nu(p_A - p_B)$$

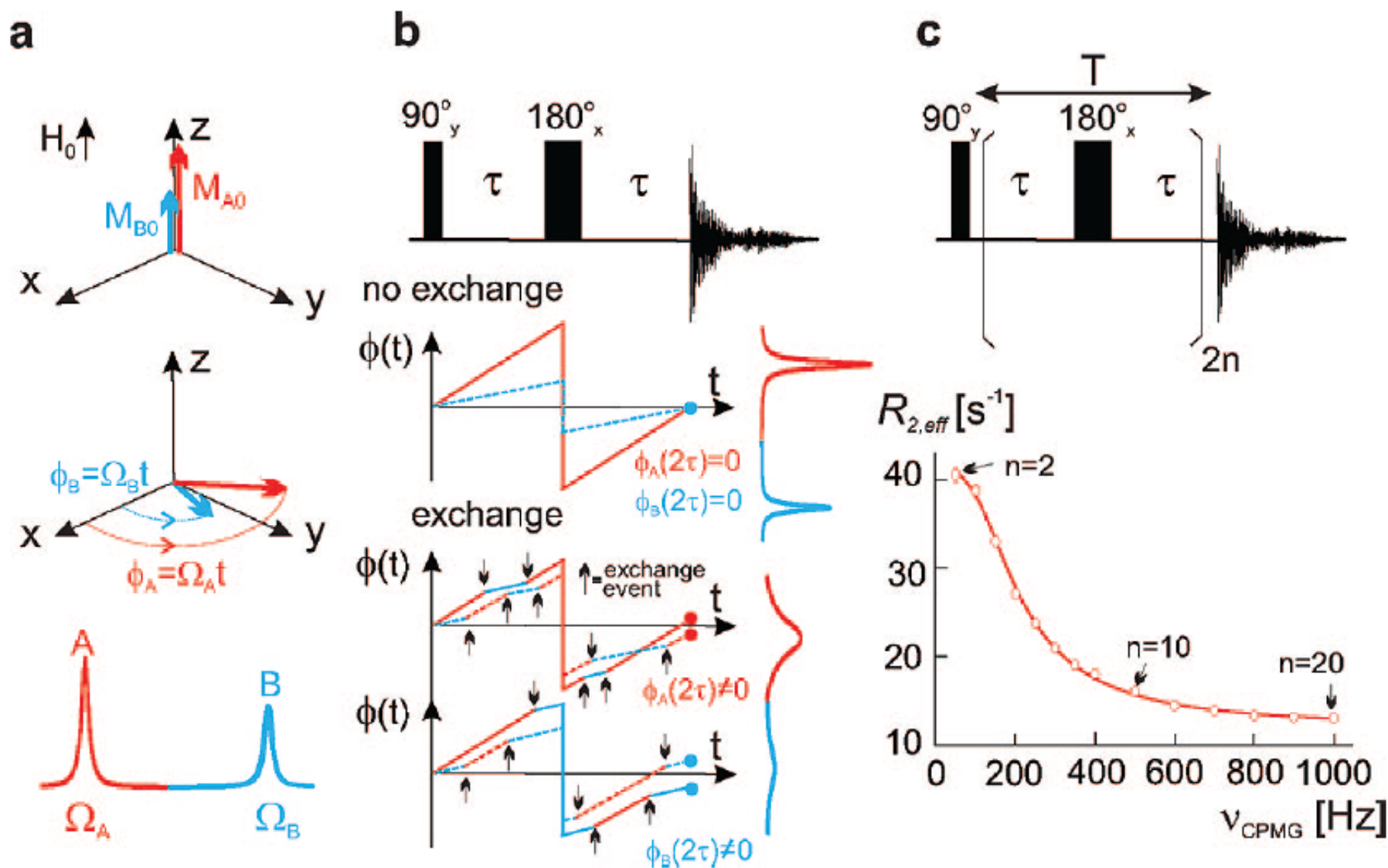
$$\tau = \frac{p_A}{k_B} = \frac{p_B}{k_A}$$

k_A, k_B - rates of transitions between states $\delta\Delta$ -
frequency differences between states

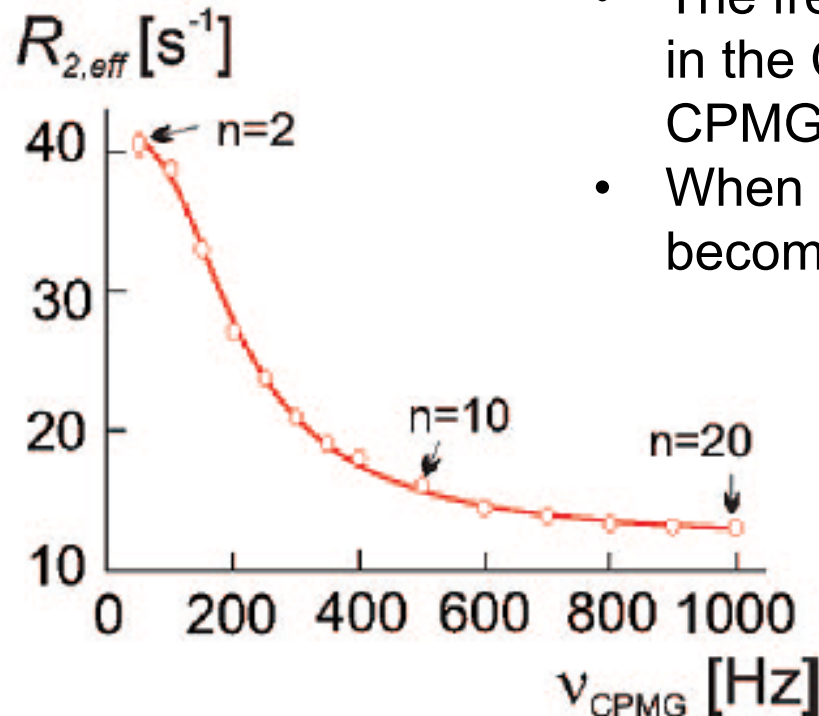
p_A, p_B - populations of exchanging states

T_{2A}, T_{2B} - relaxation in the absence of exchange

Relaxation dispersion



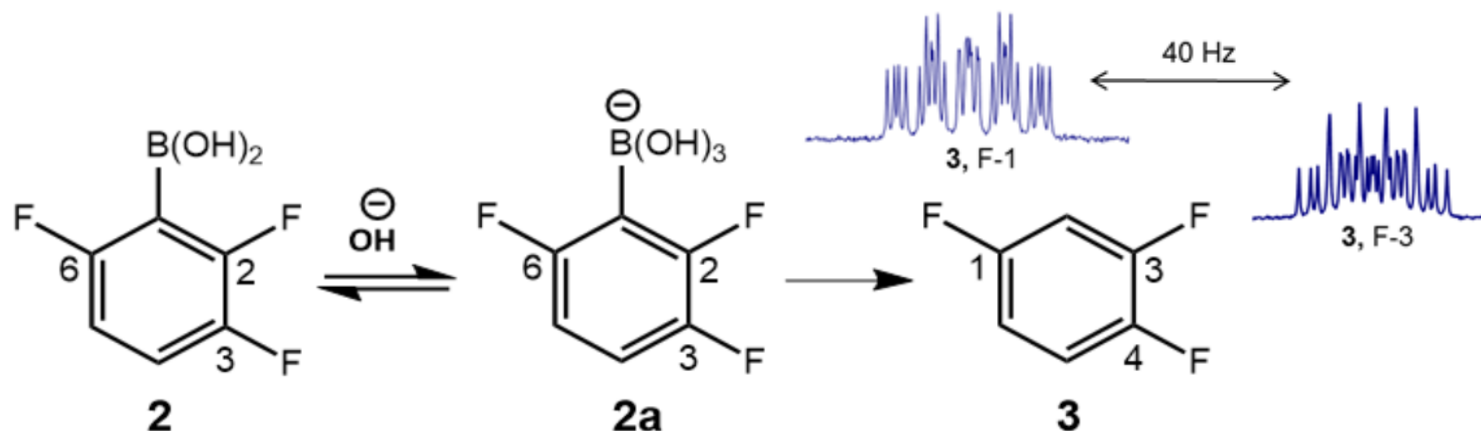
Relaxation dispersion



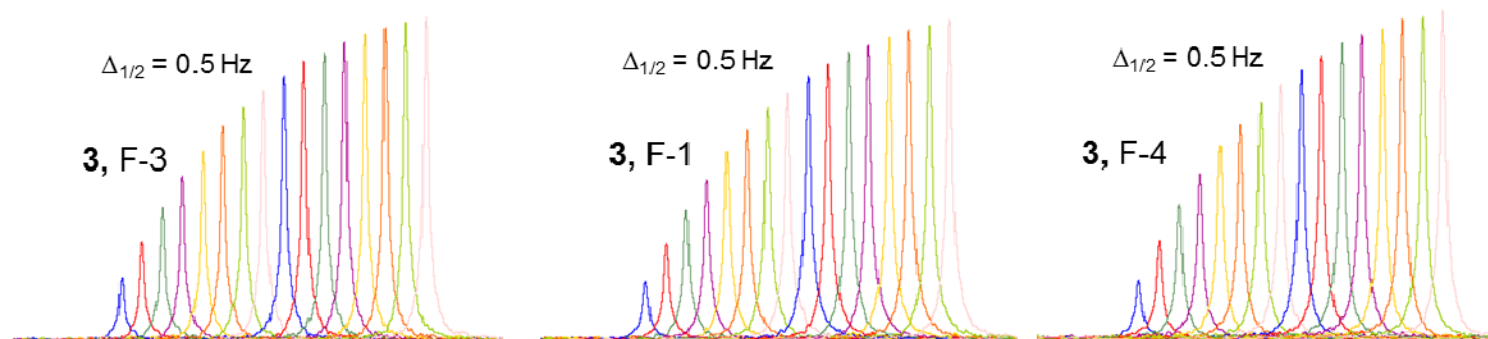
- The frequency of application of 180° pulses in the CPMG sequence, $1/(4\tau)$, is called the CPMG frequency, ν_{CPMG}
- When $\nu_{\text{CPMG}} \sim R_{2,\text{eff}}$, the CPMG sequence becomes less effective at refocusing

- NMR relaxation dispersion profiles $R_{2,\text{eff}}(\nu_{\text{CPMG}})$ provide sensitive measures of conformational/chemical exchange
- Fitting of $R_{2,\text{eff}}(\nu_{\text{CPMG}})$ allow determination of:
 - (i) rates of transitions between states
 - (ii) frequency differences between states
 - (iii) populations of exchanging states

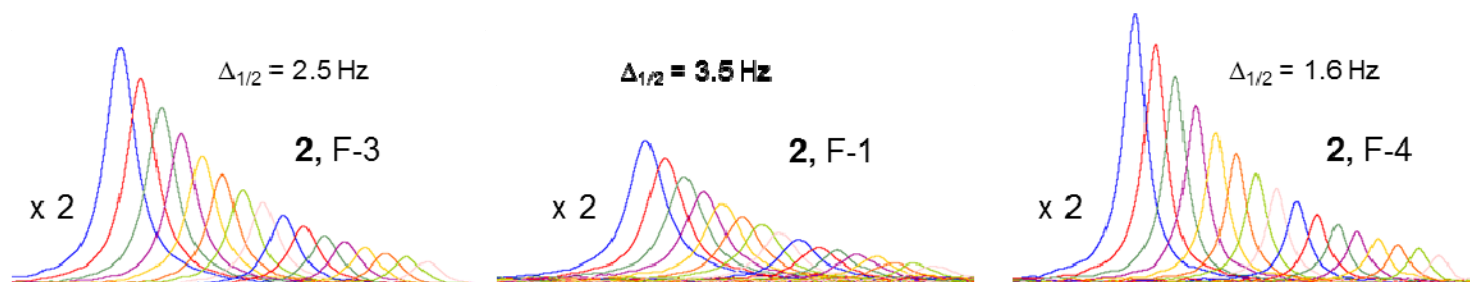
Protodeboronation dynamics



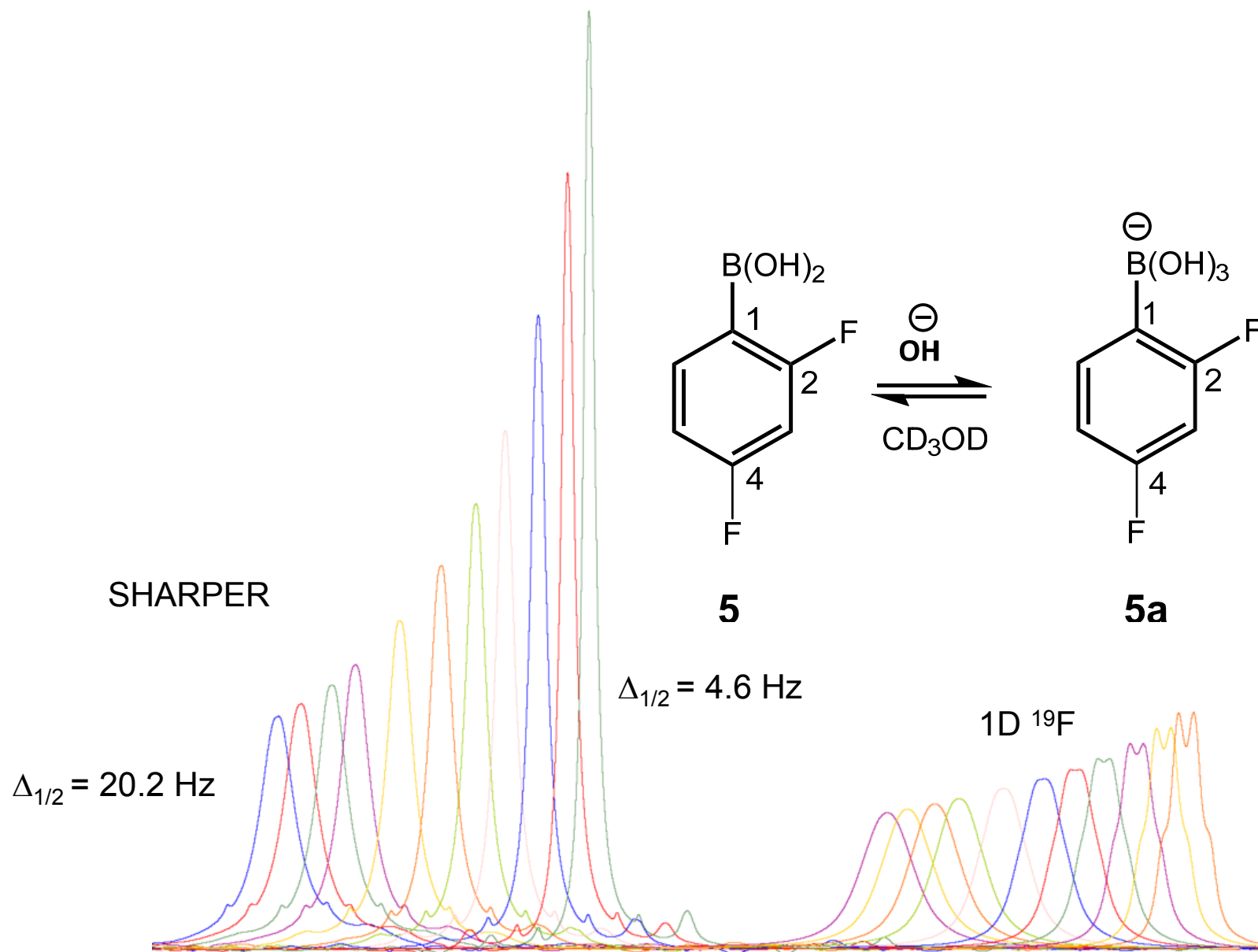
Products



Reactants



Protodeboronation dynamics



Boric acid – boronate equilibrium

