



Essential Techniques in Solid-state NMR

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Solid-state NMR

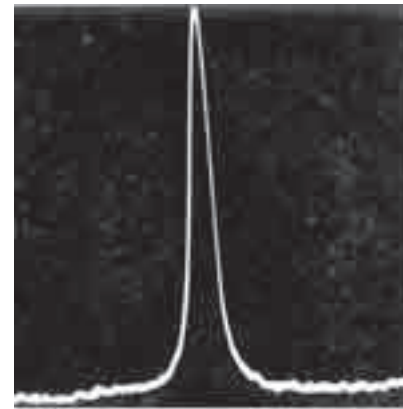
1945



Felix Bloch

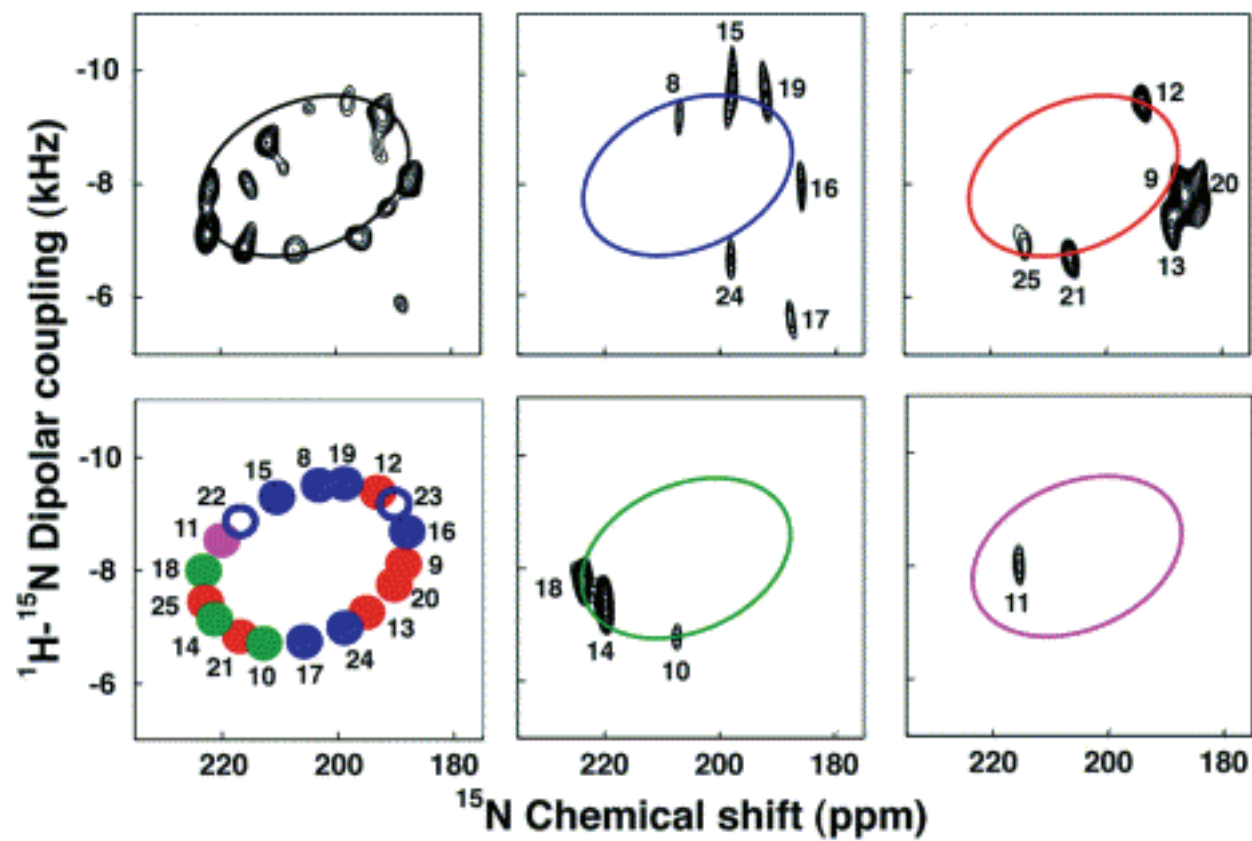


Ed Purcell

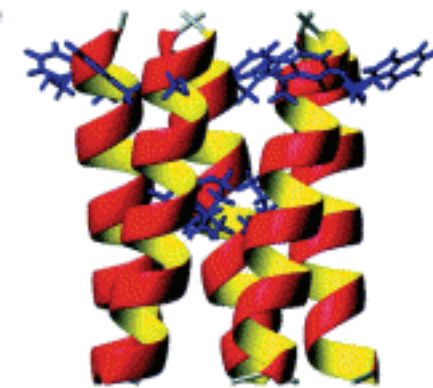
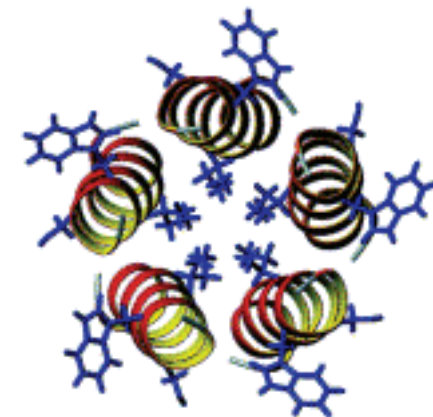


proton NMR of
paraffin wax

nitrogen-15 NMR of
VPU ion channel from HIV



2005



structure from
solid-state NMR

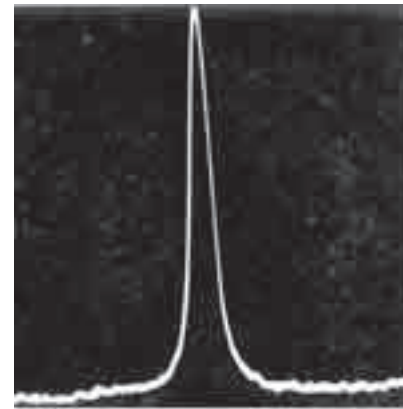
Solid-state NMR



Felix Bloch



Ed Purcell



proton NMR of
paraffin wax

“We were physicists. We knew all the answers; we just didn’t know what the questions were.”

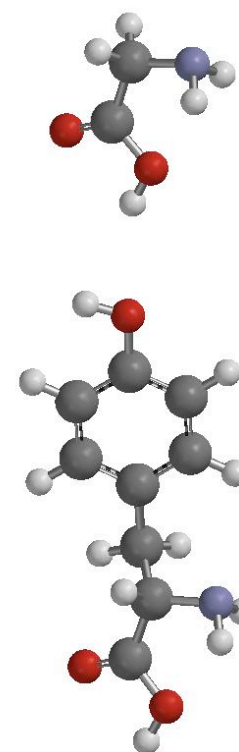
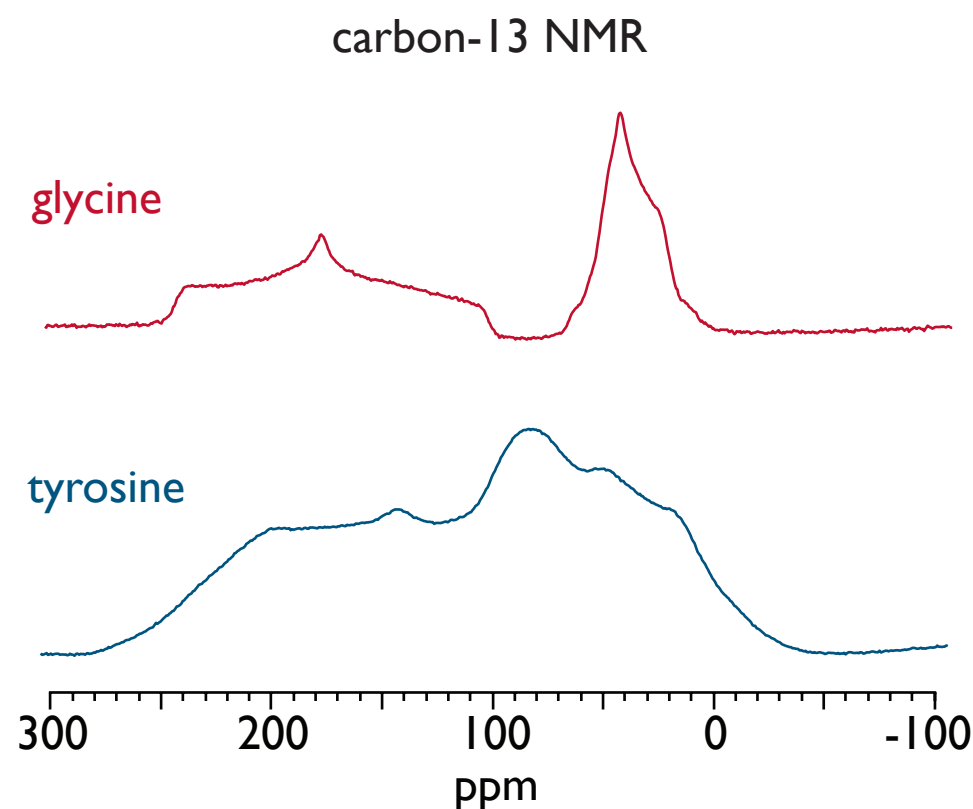
Problems with NMR of solids

Poor Resolution

- ★ Anisotropic nuclear spin interactions result in powder patterns.
- ★ Powder patterns from inequivalent sites overlap.
- ★ Multiple anisotropic interactions result in broad featureless lineshapes.

Low Sensitivity

- ★ NMR is inherently insensitive.
- ★ Many useful nuclei, such as carbon-13, nitrogen-15 etc, have low natural abundance.
- ★ Inefficient spin-lattice relaxation results in long experiment times.



Improving resolution

All internal Hamiltonians can be written as a product of two parts

- ★ A **spatial part** which contains the variation of the interaction with orientation with respect to the B_0 -field.
- ★ A **spin part** which (in the secular approximation) contains angular momentum operators which are parallel to the B_0 -field.

For example, the anisotropic part of the chemical shift Hamiltonian

$$H = \frac{I}{3} \left\{ \sum_{j=1}^3 \sigma_j + \sum_{j=1}^3 \left(3 \cos^2 \theta_j - 1 \right) \sigma_j \right\} \gamma I_z B_0$$

contains a **spatial** term proportional to $3 \cos^2 \theta - 1$ and a **spin** term proportional to I_z .

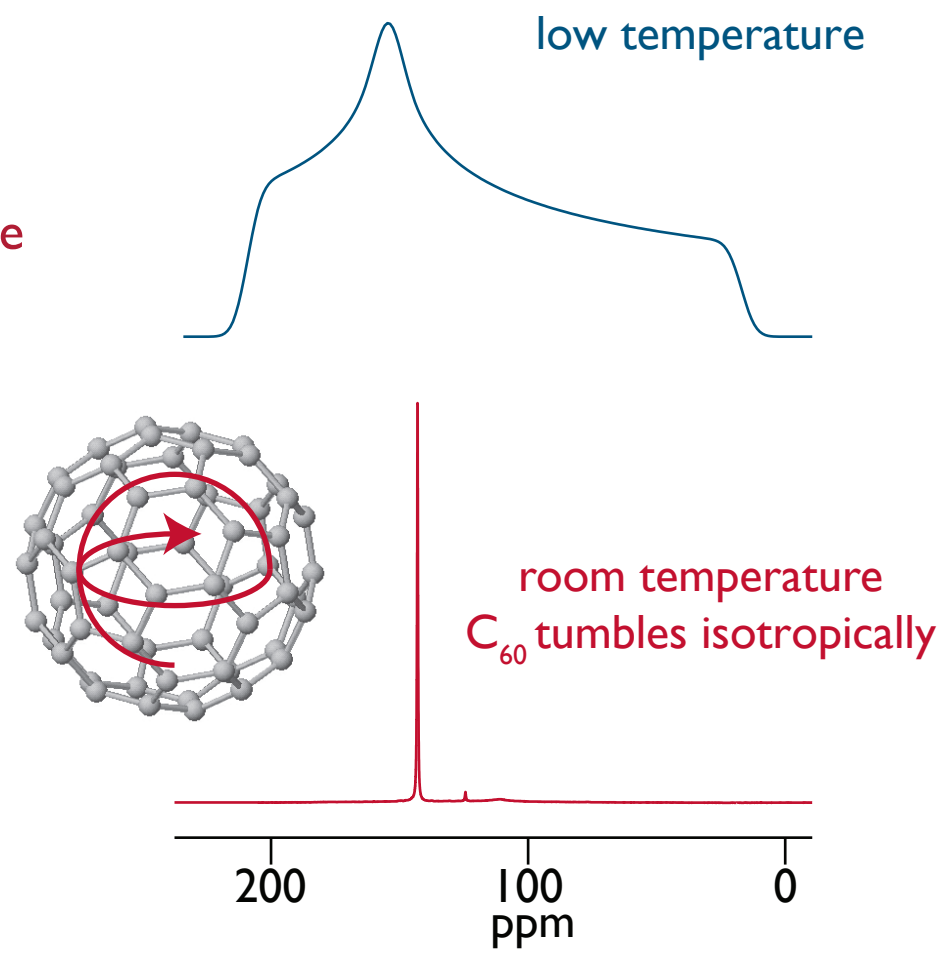
Motional averaging

Molecular motions can result in a **averaged** Hamiltonian which can be evaluated from the average over time for one spin or over orientation for many spins.

$$\bar{H}_{\text{int}} = \frac{1}{\tau} \int_0^{\tau} H_{\text{int}}(\theta(t)) dt$$
$$\bar{H}_{\text{int}} = \int_0^{\pi} H_{\text{int}}(\theta) \sin \theta d\theta$$

The techniques used to improve resolution in solid-state NMR subject the nuclear spins to some external motion in order to average interactions.

carbon-13 NMR of fullerene



Types of external motion

Two types of motions can be used:

- ★ **Motions in sample space.** These require a mechanical rotation of the sample itself. This changes the spatial part of the Hamiltonian. An example is magic angle spinning.
- ★ **Motions in spin space.** These require rotations of the magnetization by radiofrequency pulses. This changes the spin part of the Hamiltonian. An example is decoupling.

Note that in either case motional averaging is only effective when the motional frequency is greater than the broadening observed in the spectrum.

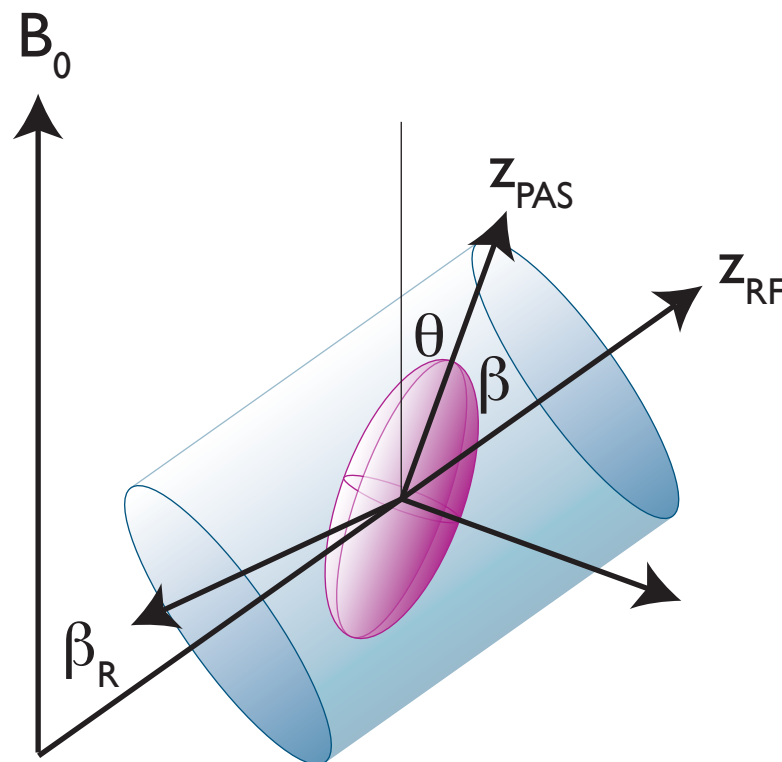
Magic angle spinning

Magic angle spinning simulates the rapid isotropic tumbling motion of a molecule in solution by rotation of the sample at a frequency ν_R (up to 70 kHz) around an axis inclined at β_R to the B_0 -field.

- ★ β_R is a constant which can be varied mechanically.
- ★ The axis z_{PAS} moves on the surface of a cone with a half angle β at the apex.
- ★ In a powder all values of the angles β and θ are present.

The motionally averaged Hamiltonian is

$$\bar{H} \propto \int_0^\pi (3\cos^2 \theta - 1) \sin \theta d\theta = \frac{1}{2} (3\cos^2 \beta_R - 1) (3\cos^2 \beta - 1)$$

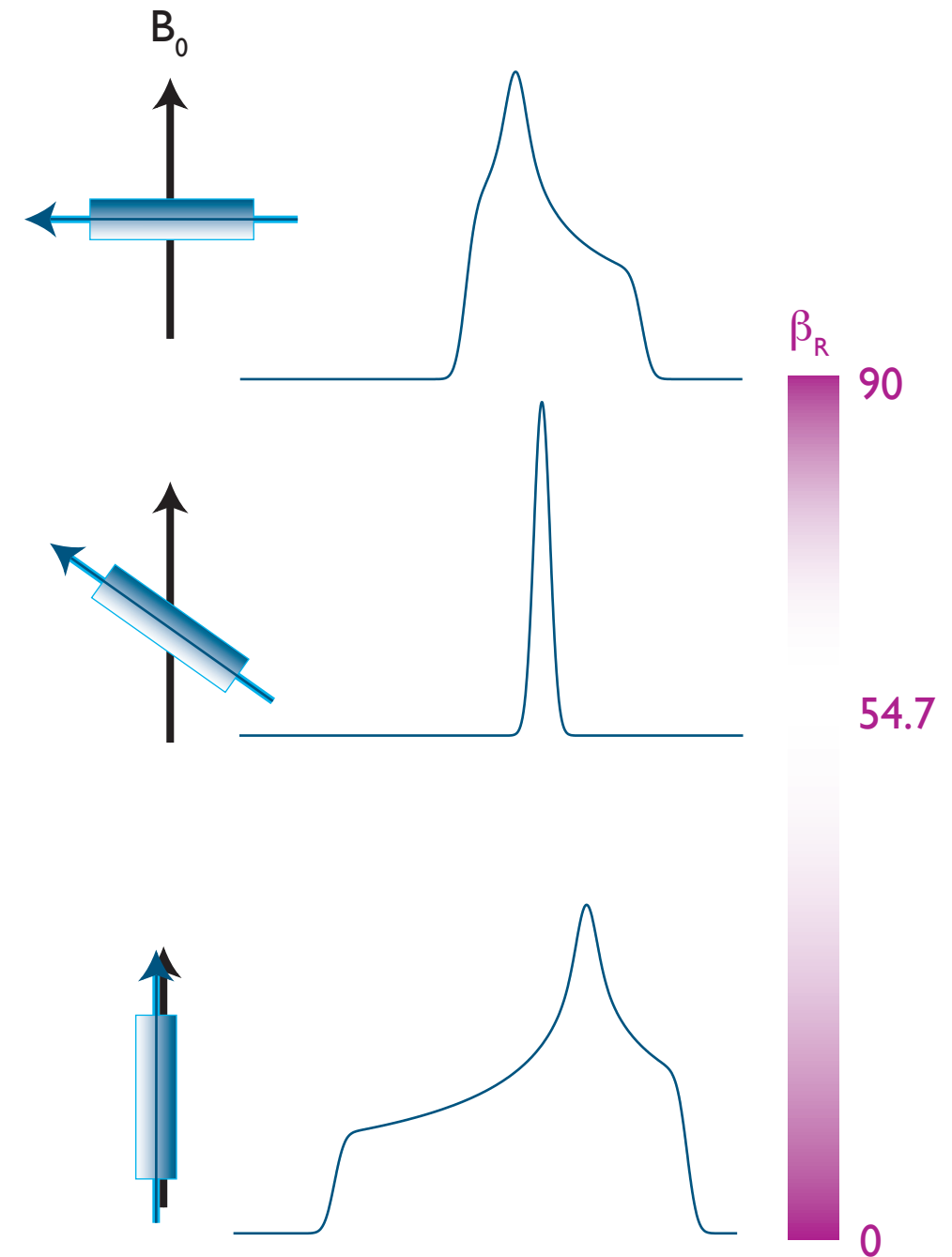


Scaling anisotropic interactions with MAS

$$\bar{H} \propto \int_0^\pi (3\cos^2 \theta - 1) \sin \theta d\theta = \frac{1}{2} (3\cos^2 \beta_R - 1) (3\cos^2 \beta - 1)$$

The term in β_R acts as a constant scaling factor on the powder pattern.

- ★ If $\beta_R = 0$ there is no effect on the spectrum.
- ★ If $\beta_R = 90^\circ$ the width of the powder pattern is scaled by a factor 1/2 and reversed in sign.
- ★ When $\beta_R = 54.7^\circ$ (known as the “**magic angle**”) the term in β is zero and MAS will scale the anisotropic part of the interaction to zero.



Magic angle spinning

1955

ν_R

1958

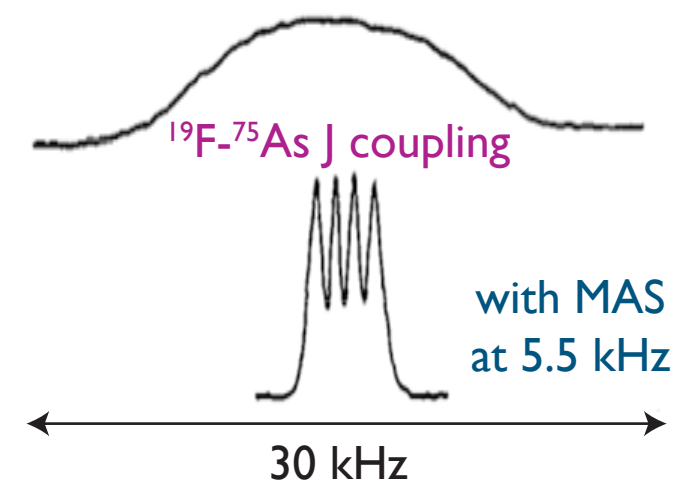
8 kHz



Raymond Andrew



Fluorine-19 MAS of KAsF_6



1990

15 KHz



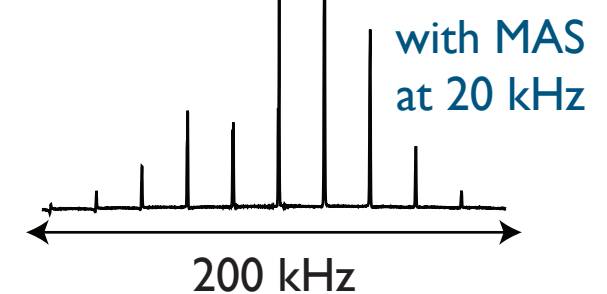
1996

35 kHz



Lithium-7 MAS of $\text{Li}_3\text{Eu}_3\text{Te}_2\text{O}_{12}$ garnet

Eu - ^7Li electron-nuclear dipolar coupling



2005

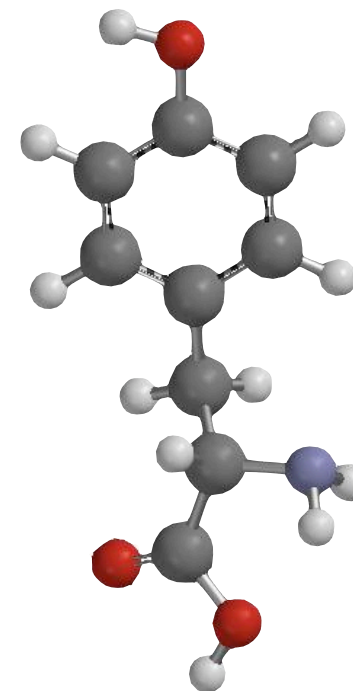
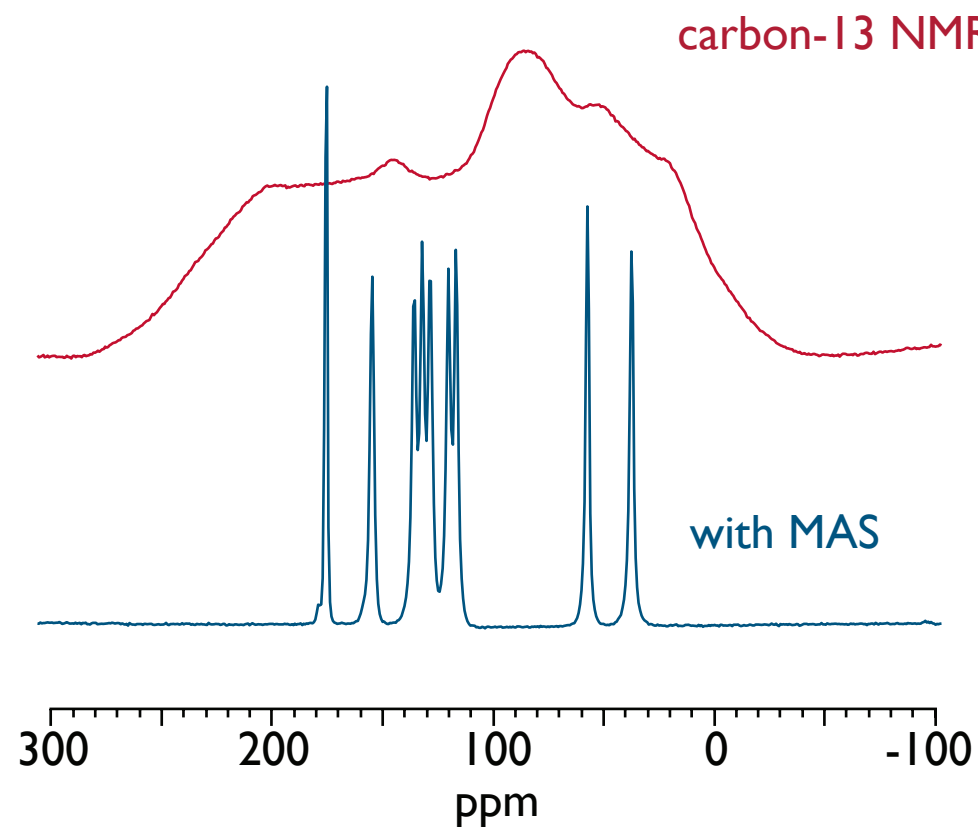
70 kHz

Fast spinning limit

When $\nu_R \gg \zeta$

- ★ the **anisotropic** part of the chemical shift is averaged to zero.
- ★ the **isotropic** part is retained.

$$H = \frac{1}{3} \left\{ \sum_{j=1}^3 \sigma_j + \sum_{j=1}^3 \left(3 \cos^2 \theta_j - 1 \right) \sigma_j \right\} \gamma I_z B_0$$



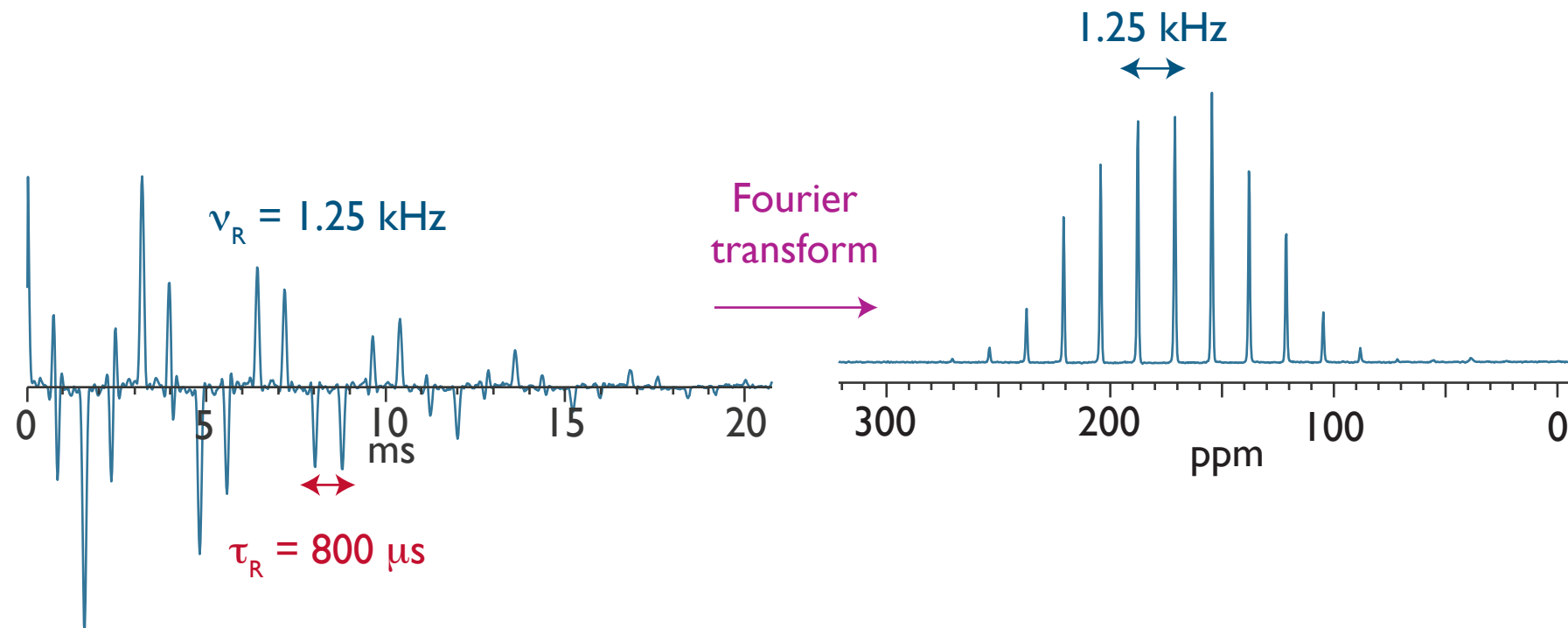
Slow spinning

When $\nu_R \ll \zeta$ the NMR precession frequency is modulated by the MAS

$$\nu(t; \Omega) = \sum_{m=-2}^2 \nu^{(m)}(\Omega) \exp(im\nu_R t)$$

As a consequence:

- ★ contributions from different orientations refocus after τ_R , resulting in “rotor echoes”.
- ★ rotational **sidebands** separated by ν_R appear in the spectrum.
- ★ sampling at the rotor echoes results in a spectrum of isotropic lines of restricted spectral width.



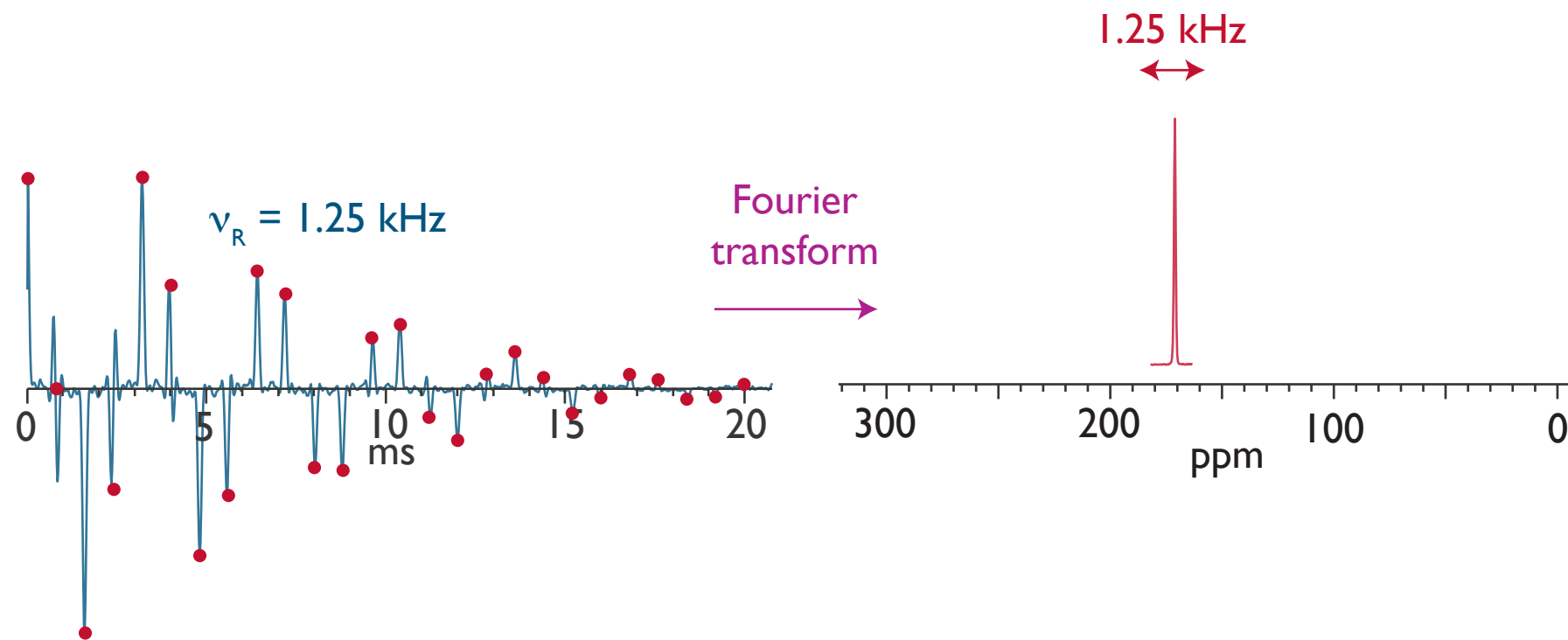
Synchronous sampling

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Spinning sidebands

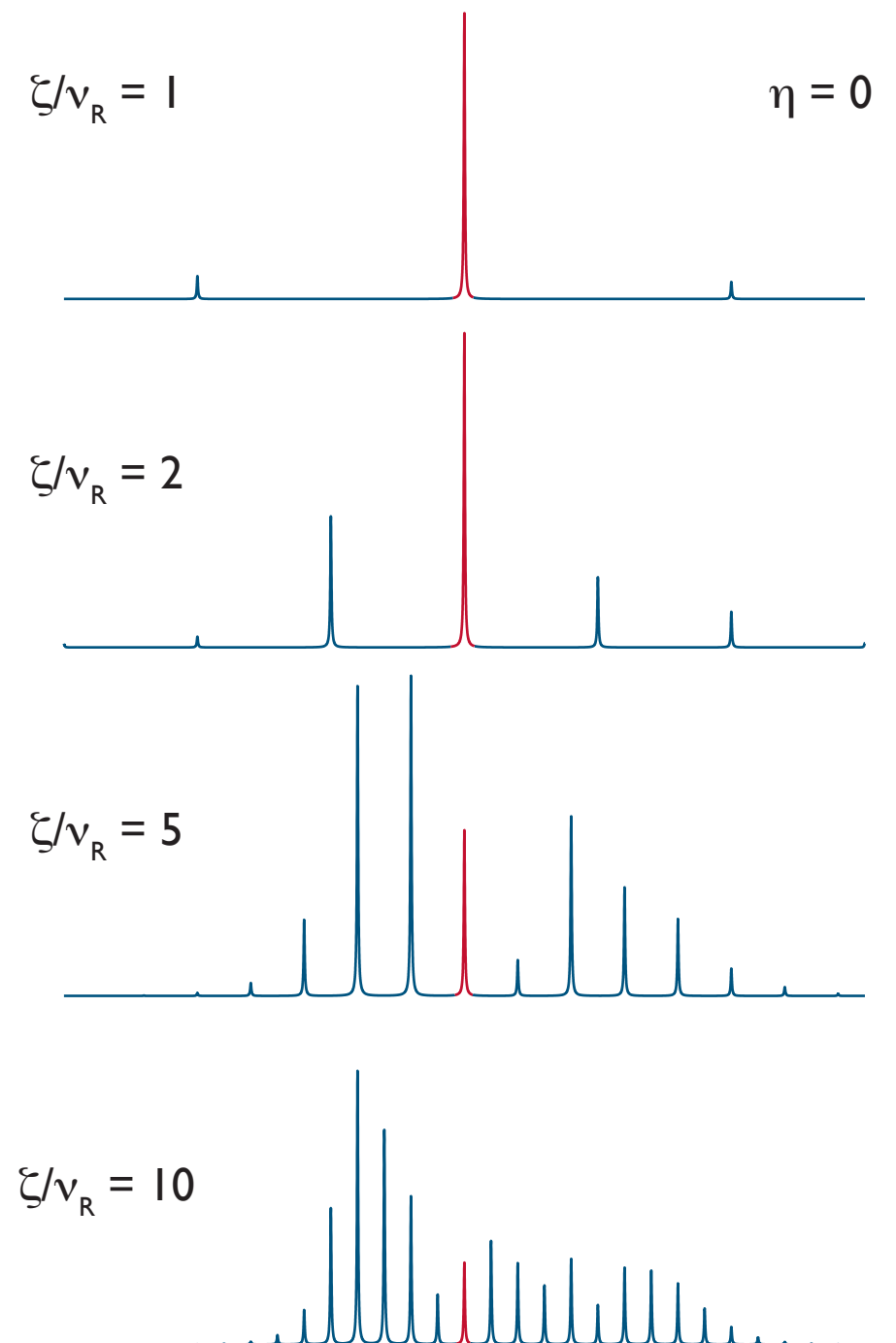
Measuring shift tensor parameters

- ★ The envelope of the sideband intensities depends on the anisotropy ζ and the asymmetry η .
- ★ This is the basis of the most common method for measuring these parameters.

Identifying the isotropic line

- ★ The **isotropic** line corresponds to the chemical shift observed in solution.
- ★ Note that the isotropic line is not always the most intense in the spectrum.
- ★ It can be identified as the sideband which does not change frequency when the MAS rate changes.

Simulated MAS sideband patterns



Choosing the MAS rate

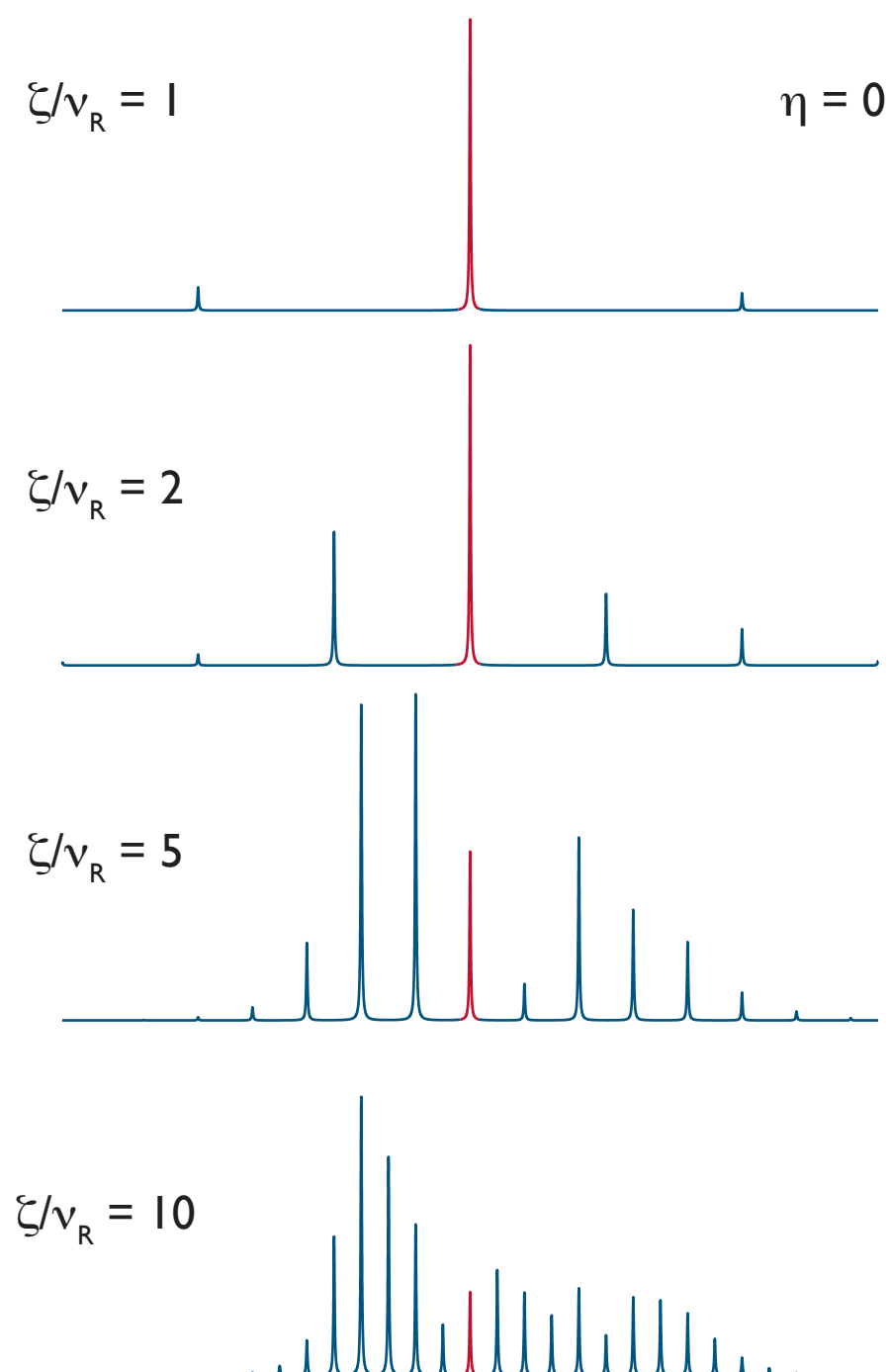
Measuring shift tensor parameters

- ★ To produce a solution-like spectrum with only isotropic lines the MAS rate must be greater than the largest shift anisotropy.
- ★ To measure the shift anisotropy from the sideband pattern with optimal precision approximately 7 sidebands are required.
- ★ To measure the asymmetry more than 10 sidebands are required.

Other considerations

- ★ Molecular motions in the sample on a kHz timescale will interfere with the MAS averaging and cause sidebands to broaden.
- ★ For abundant nuclei “rotational resonance conditions” where $\Delta\delta_{\text{iso}} = n\nu_{\text{R}}$ (n is a small integer) should be avoided.

Simulated MAS sideband patterns



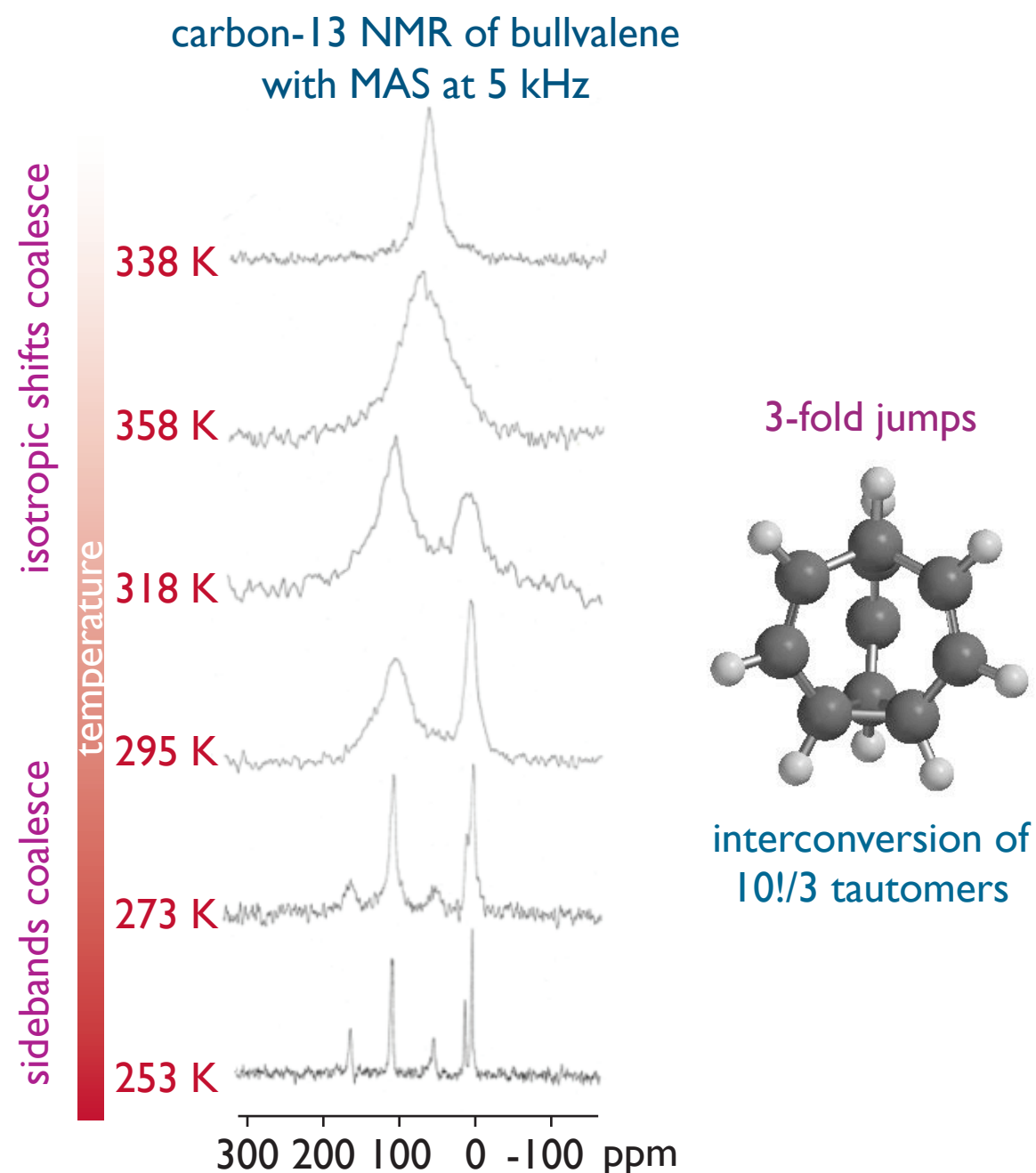
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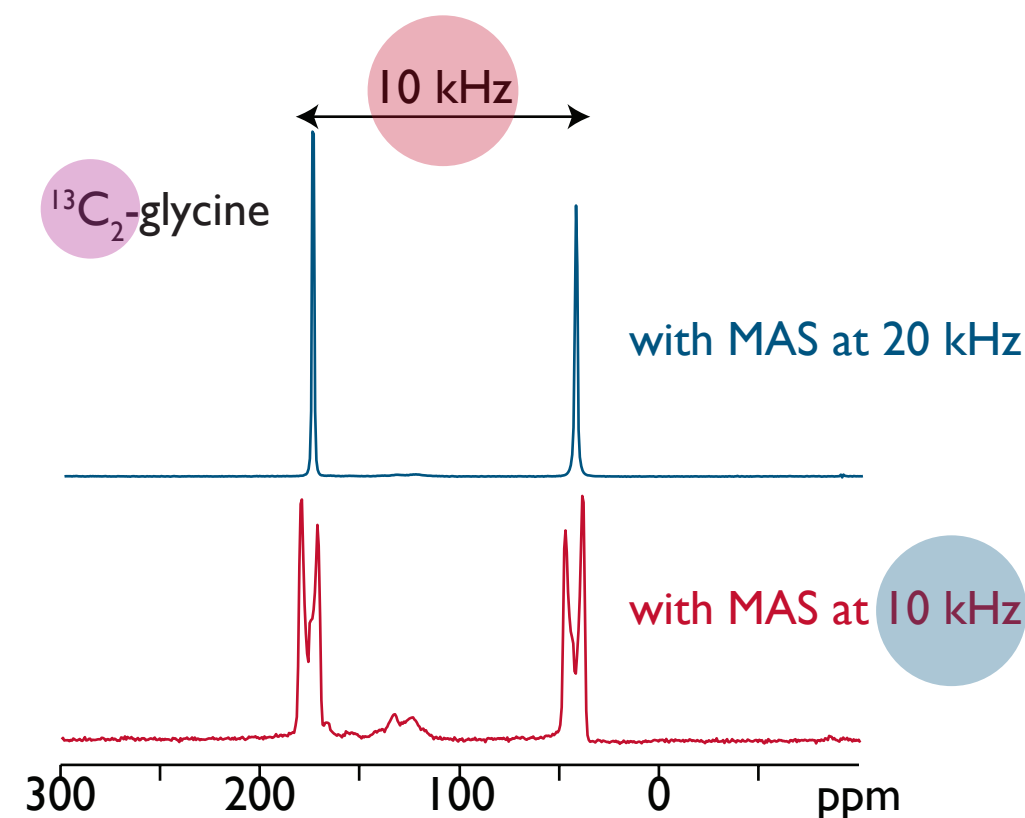
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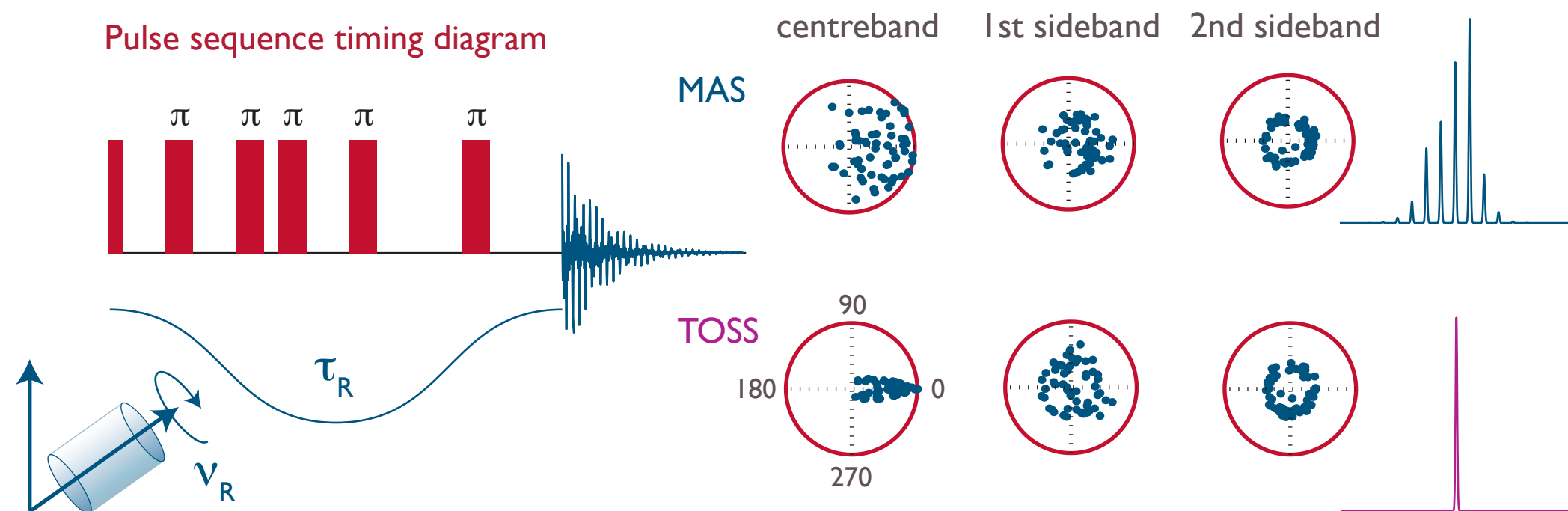
Sideband suppression with TOSS

TOSS (Total Suppression of Spinning Sidebands) uses a sequence of (five) carefully timed π pulses synchronized with the MAS rotor.

- ★ The phases of the sidebands depend in a new way on orientation.
- ★ For an isotropic sample the sidebands from different orientations interfere destructively and cancel.

Note:

- ★ The TOSS centreband is not quantitative.
- ★ For small ν_R/ζ the centreband can have negative intensity.



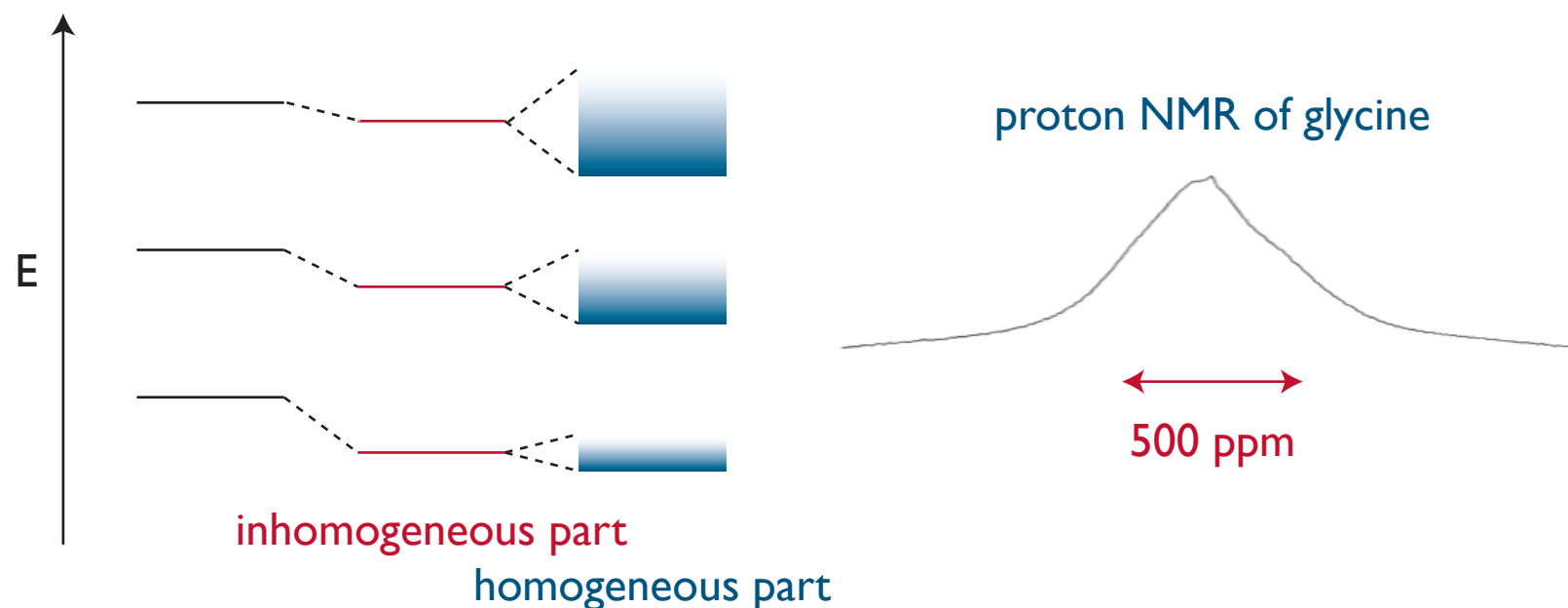
MAS and homonuclear dipolar couplings

$$H_D \propto 3I_{1z}I_{2z} - \mathbf{I}_1 \cdot \mathbf{I}_2 = 2I_{1z}I_{2z} - \frac{1}{2}(I_1^+I_2^- + I_1^-I_2^+)$$

There are two parts to the homonuclear dipolar Hamiltonian:

- ★ an **inhomogeneous** part which shifts the energies of the Zeeman eigenstates
- ★ a **homogeneous** part which mixes degenerate Zeeman states and causes line broadening

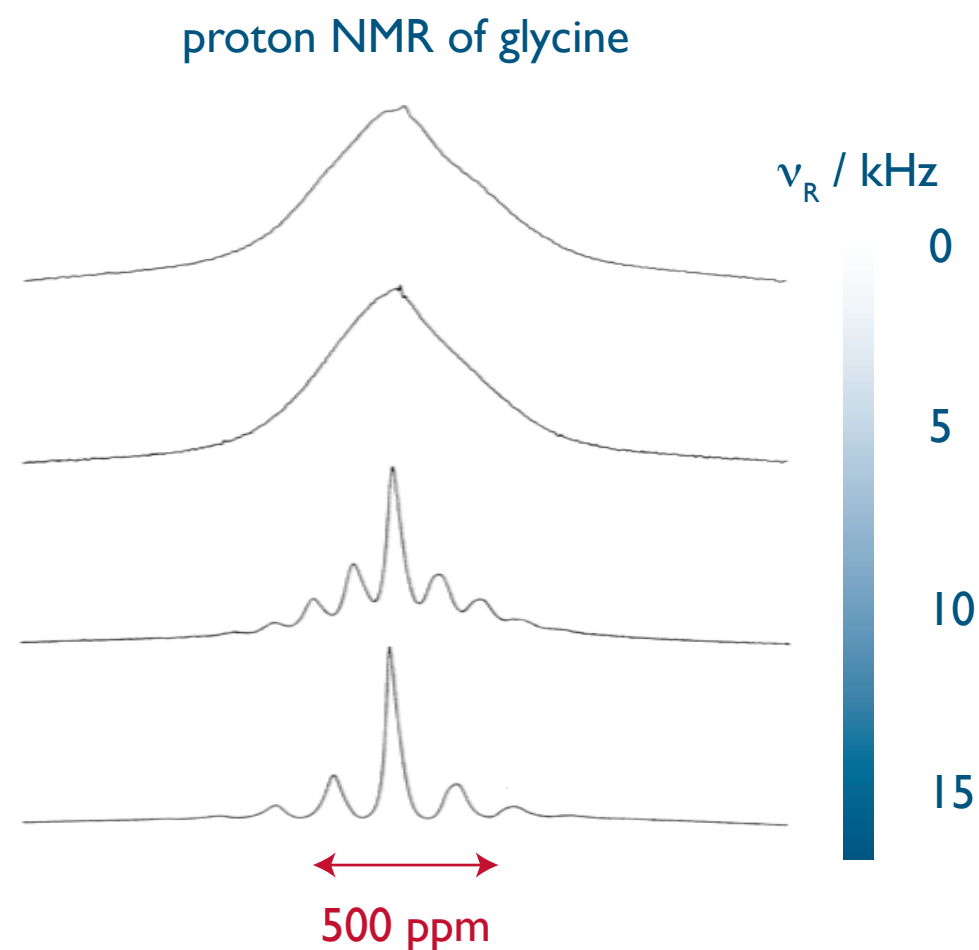
The homogeneous term also causes energy conserving “flip-flop” transitions between degenerate states at a rate which depends on the dipolar coupling.



MAS and homonuclear dipolar couplings

The flip-flop transitions mean that the state of the spin system fluctuates and when ν_R/d is small this interferes with the MAS averaging.

The spinning sidebands for a homogeneously broadened line behave very differently from those associated with an inhomogeneous interaction.



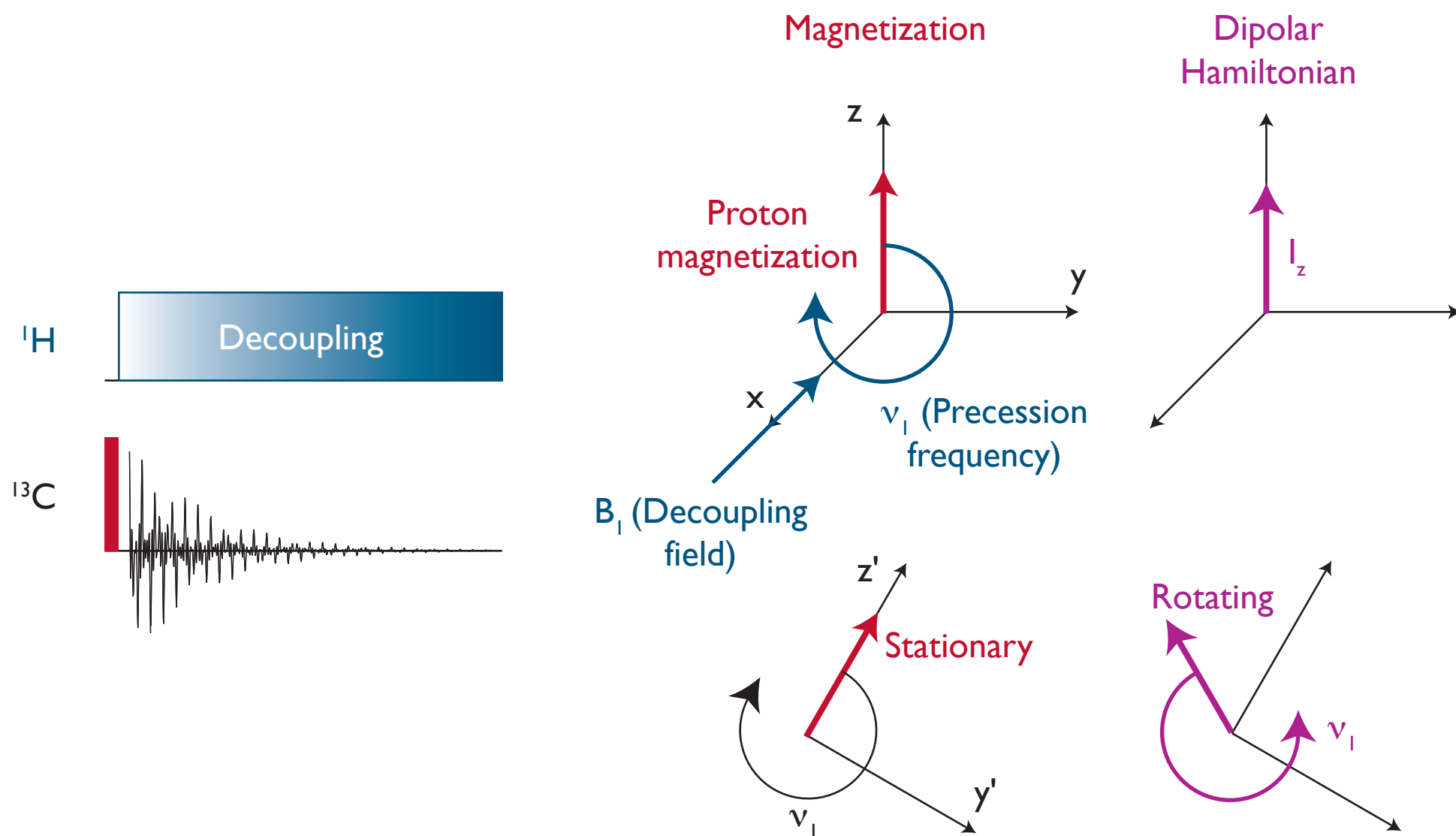
An isolated proton-carbon- 13 dipolar interaction is inhomogeneous, but if the proton is part of a homogeneous network then the overall behavior is homogeneous.

Decoupling

Decoupling uses an enforced motion in **spin space** to average heteronuclear dipolar couplings.

$$H_D = -\frac{d}{2}(3\cos^2\theta - 1)2I_zS_z$$

The spin part of the coupling Hamiltonian can be made to vary with time by continuous irradiation at the I-spin (proton) Larmor frequency while the S-spin (carbon-13) signal is observed.

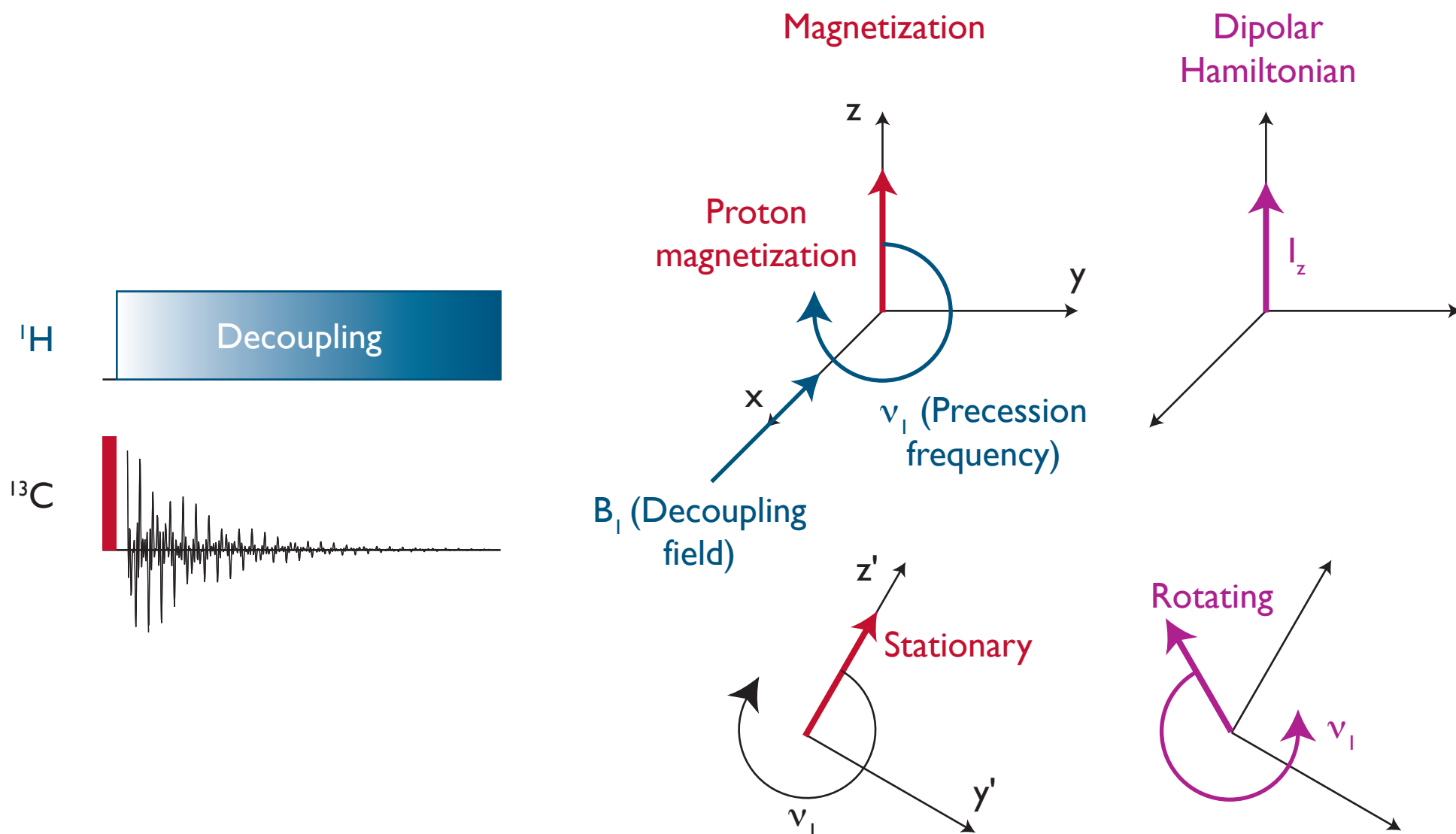


Decoupling

- ★ The radio-frequency radiation at the proton Larmor frequency causes the proton magnetization to precess at a rate in the yz-plane.
- ★ In a rotating frame which follows the precessing magnetization the I-spin operator appears to rotate, and the spin part of the dipolar Hamiltonian becomes

$$H_D(t) \propto (I_z \cos 2\pi\nu_1 t + I_y \sin 2\pi\nu_1 t) S_z$$

- ★ The oscillating I-spin operator terms cause the dipolar Hamiltonian to average to zero.



Setting the decoupler power

Hardware considerations

- ★ To be effective the B_1 field must cause the spins to precess at a rate ν_1 which is large compared to the IS dipolar coupling (about 20 kHz for ^1H - ^{13}C).
- ★ When the I spins are homogeneous the rate must be comparable to the I spin homonuclear dipolar coupling (about 60 kHz for ^1H).
- ★ The amplitude of the decoupler B_1 field is limited by the probe (60 kHz for 7.5 mm MAS probe; 140 kHz for 3.2 mm MAS probe). Note: an I-spin $\pi/2$ pulse of 2.5 μs corresponds to $B_1 = 100$ kHz.

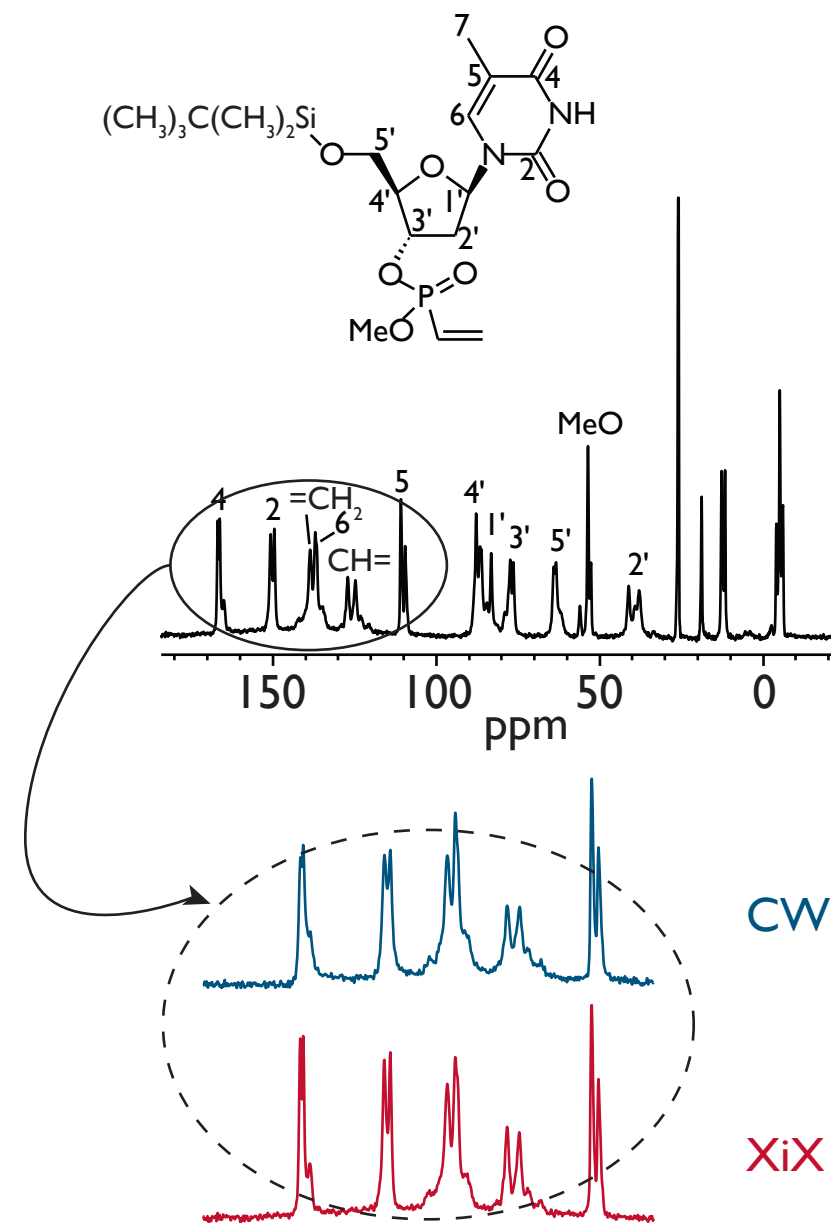
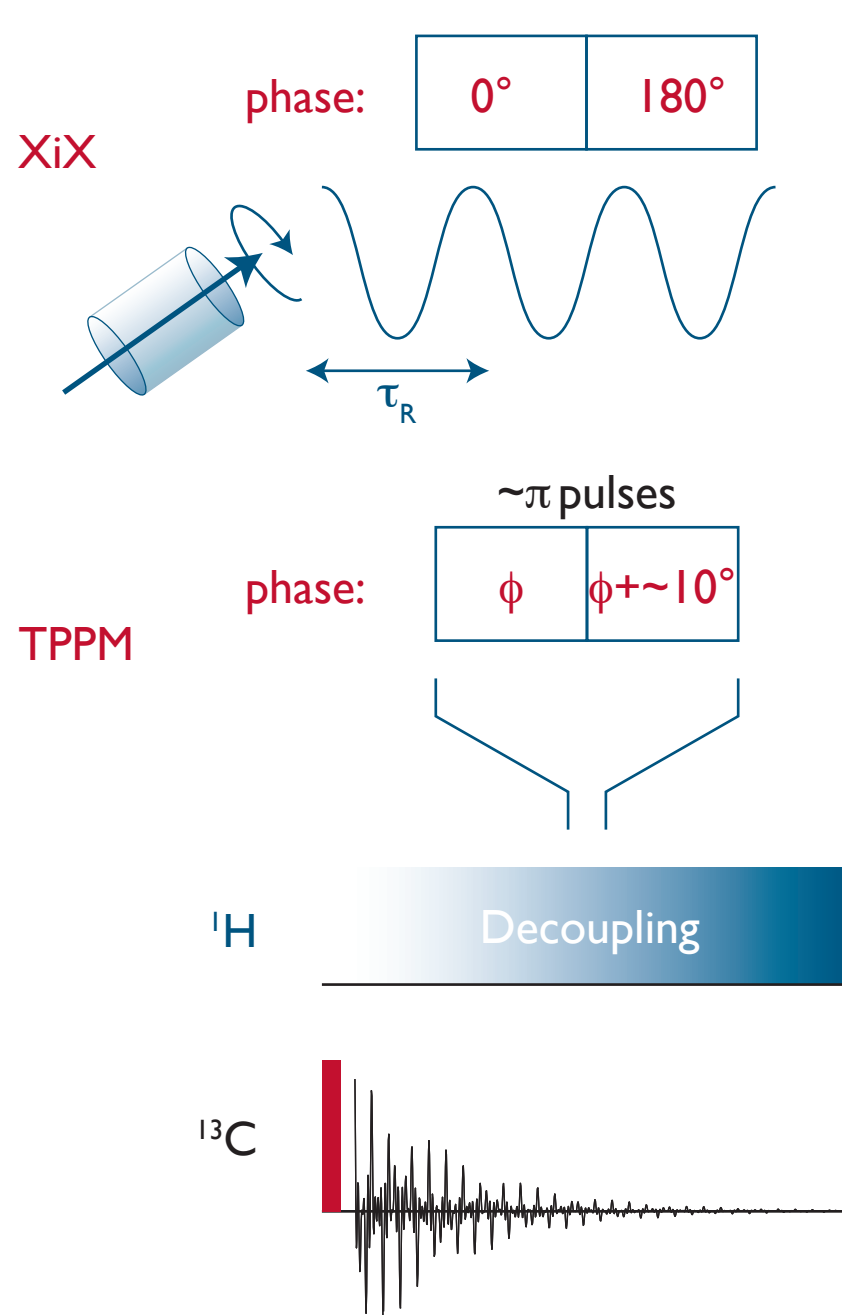
Sample considerations

- ★ Large B_1 will cause sample heating.
- ★ Molecular motions in the sample on a kHz timescale will interfere with the decoupling and cause lines to broaden.
- ★ At high MAS rates the averaging by MAS interferes with the averaging by decoupling and the decoupling efficiency can fall.

Improved decoupling schemes

A number of decoupling schemes have been proposed which give increased decoupling efficiency relative to CW for the same B_1 amplitude, especially at high ν_R .

These include **TPPM** (Two Pulse Phase Modulation) and **XiX**.



Problems with NMR of solids

Poor Resolution

- ★ Anisotropic nuclear spin interactions result in powder patterns.
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Low Sensitivity

- ★ NMR is inherently insensitive.
- ★ Many useful nuclei, such as carbon-13, nitrogen-15 etc, have low natural abundance.
- ★ Inefficient spin-lattice relaxation results in long experiment times.

Improving sensitivity

Sensitivity can be improved by:

- ★ increasing magnetization by polarization transfer from neighboring spins of **higher magnetogyric ratio**.
- ★ increasing the repetition rate of successive scans, so that more signal averaging can take place, by polarization transfer from neighboring spins with **more efficient spin-lattice relaxation**.

Communications

THE JOURNAL OF CHEMICAL PHYSICS VOLUME 56, NUMBER 4 15 FEBRUARY 1972

Proton-Enhanced Nuclear Induction Spectroscopy. A Method for High Resolution NMR of Dilute Spins in Solids*

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(Received 18 November 1971)

We report preliminary results of a general technique for high resolution NMR of isotopically rare (^{13}C , ^{15}N , ^2H , etc.) or chemically dilute spins in solids. The method combines established ideas of double resonance^{1,2} and spin decoupling³ in a novel way. It exploits abundant spins I , of abundance N_I and magnetic moment $\gamma_I \hbar$ (usually protons), present in the sample, as a reservoir of polarization for the rare spins S , to permit the accumulation of an adequately intense S -spin spectrum after a single polarization of the I spins to equilibrium. The general procedure is as follows: (1) Polarize I in high field. (2) Cool I to a low spin temperature in the rotating frame. (3) Establish I - S contact for a time τ . (4) Record the S free induction decay while decoupling I . Steps 3 and 4 are repeated $\sim N_I/N_S$ times during which the I polarization is depleted and the S signal accumulated. The spectrum is obtained by Fourier transformation. The repeated cross polarization (CP) of step 3 results in a gain in power sensitivity of $G_{CP} \sim (N_I/N_S)(\gamma_I/\gamma_S)^2$ over conventional Fourier transform spectroscopy. For $S = ^{13}\text{C}$ and $I = ^1\text{H}$ in typical organic compounds, $G_{CP} \approx 10^4$.

The expected gain has been verified in preliminary experiments using the natural abundance of ^{13}C in ~ 50 mg of solid adamantane, $\text{C}_{10}\text{H}_{16}$ (Fig. 1). The spectrum of Fig. 1(c), recorded in 0.8 sec, is severely limited by the nonideal probe and receiver employed, and by magnetic inhomogeneity, but nonetheless demonstrates the power of the cross-polarization procedure. In natural abundance ^{13}C spectra we expect a residual S - S linewidth of the order of 5 Hz.⁴

Many versions of this method are clearly possible since the cooling, cross polarization, and decoupling can each be accomplished in several ways. In the

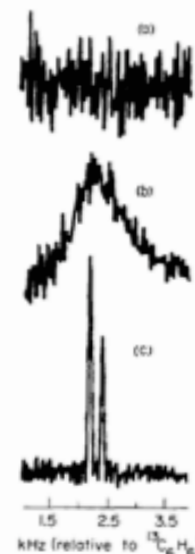


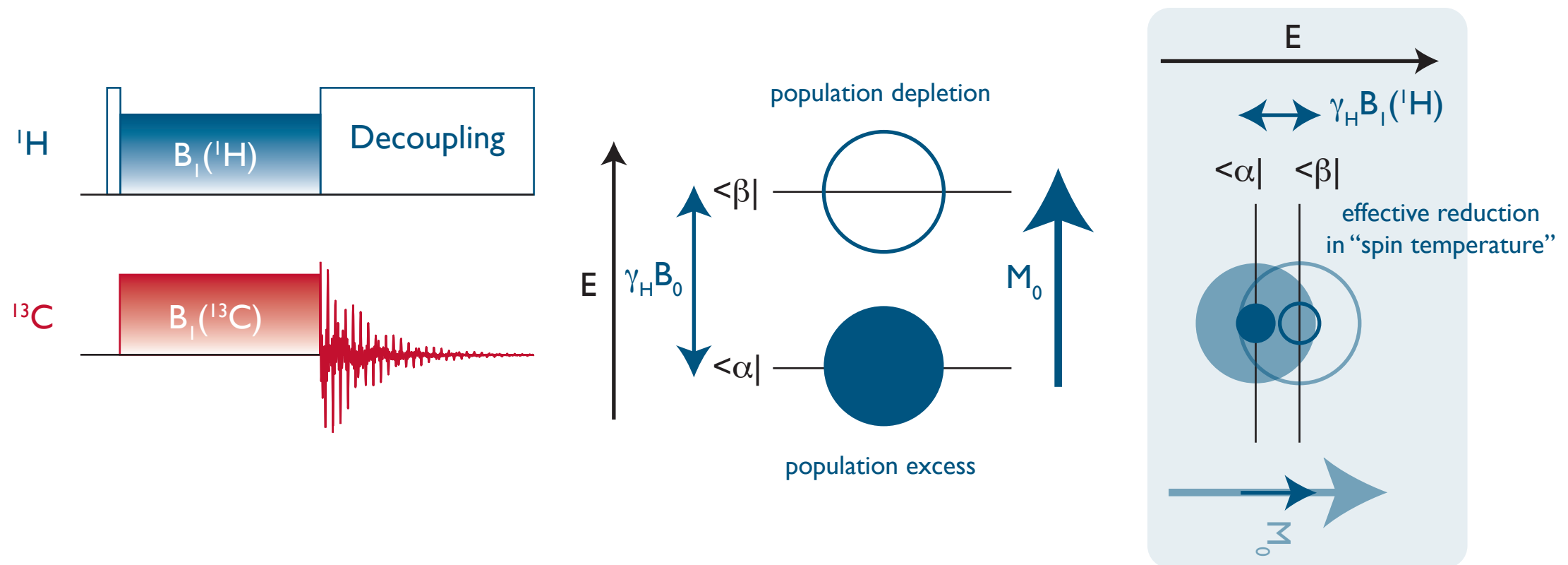
FIG. 1. Fourier transform NMR spectra of natural-abundance ^{13}C in polycrystalline adamantane at 24.46 MHz and room temperature. (a) Result of a single free induction decay. (b) Cross polarization spectrum without decoupling (50 I - S contacts). (c) Cross-polarization spectrum with proton decoupling (14 contacts) obtained in 0.8 sec. Resolution (40 Hz) is determined by magnet inhomogeneity. The two lines are 87.5 ± 1 ppm and 96.2 ± 1 ppm upfield from a neat external reference of liquid $^{13}\text{C}_6\text{H}_6$ (proton decoupled).



Alex Pines

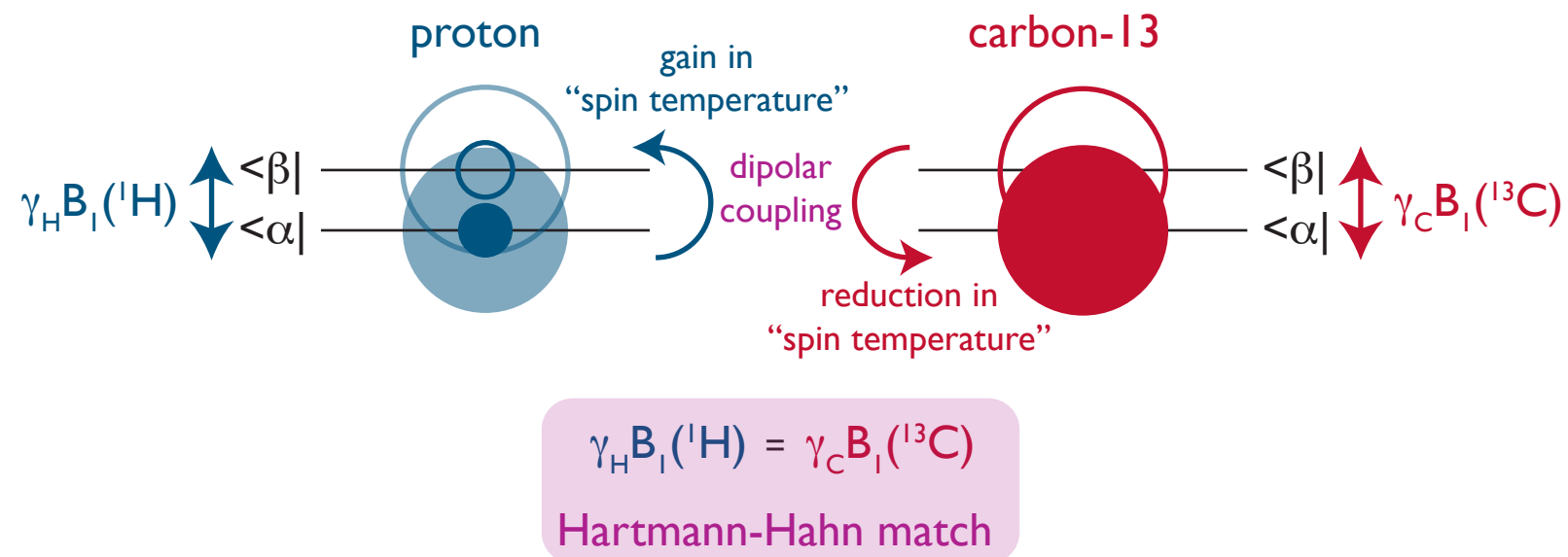
Cross polarization

- ★ Polarize the I spins at high field ($B_0 = \text{MHz}$).
- ★ Cool the I spins to a low “spin temperature” in the rotating frame ($B_1 = \text{kHz}$).



Hartmann-Hahn matching

- ★ Establish IS contact via the heteronuclear dipolar coupling and the [Hartmann-Hahn match](#).
- ★ Allow S spins to heat I spins and vice versa, resulting in a growth of an enhanced S-spin magnetization along B_I .



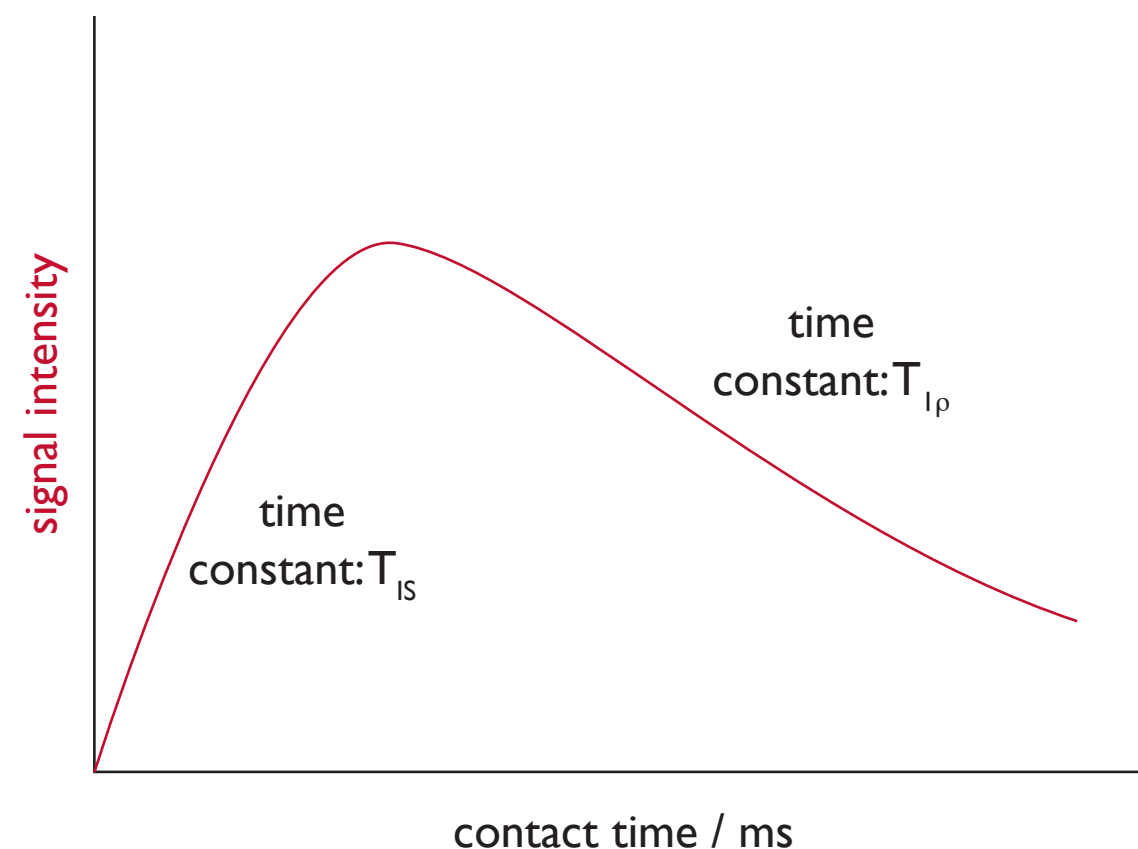
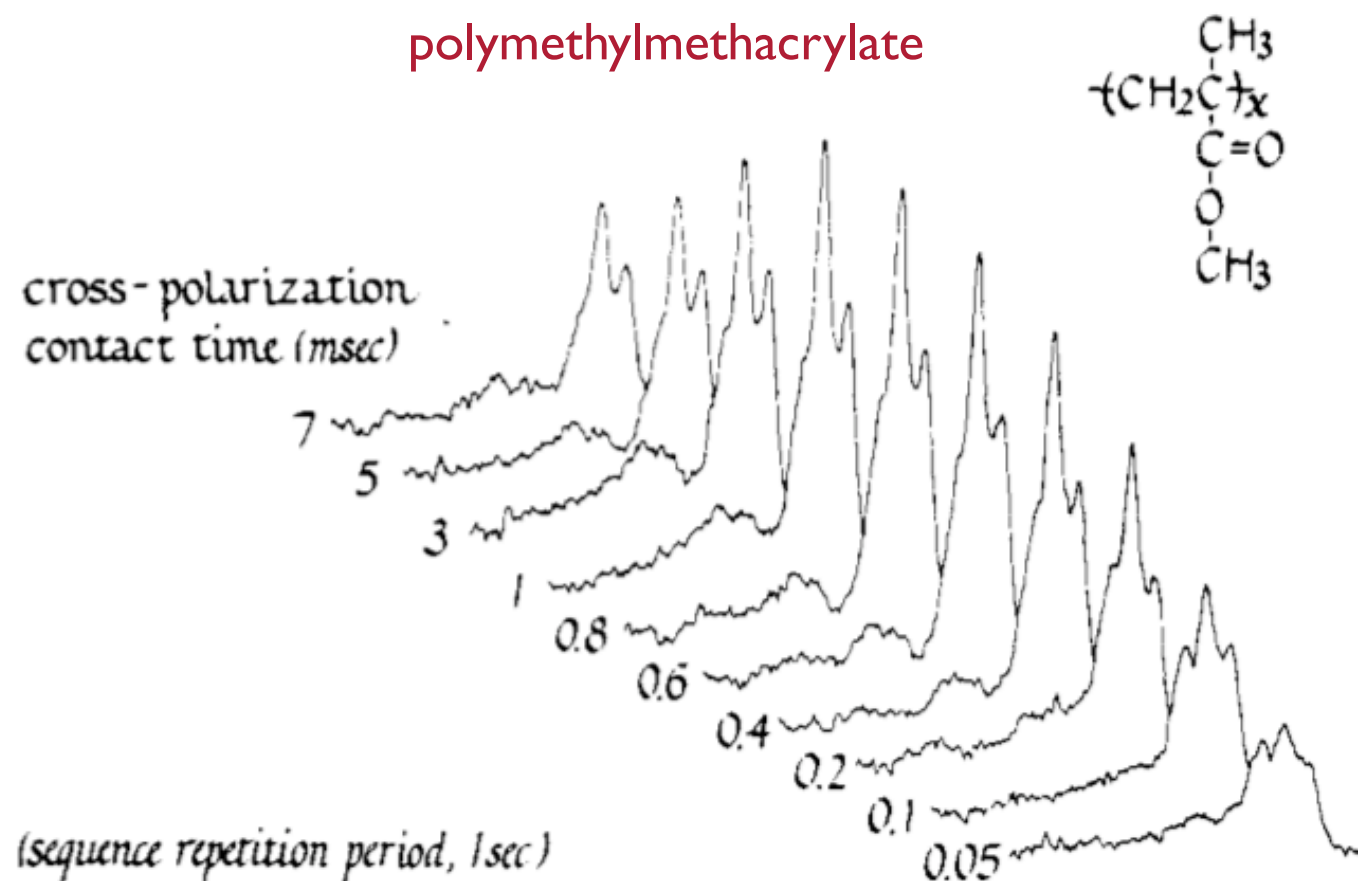
Choosing CP parameters

Experimental parameters

- ★ The I and S B_1 field are matched by observing maximum signal intensity for a suitable sample e.g. adamantane or hexamethylbenzene for carbon-13, kaolinite for silicon-29, glycine for nitrogen-15 etc.
- ★ Choose the contact time which gives the highest overall intensity, since different chemical sites have different T_{IS} and different I-spin T_{Ip} .

Sample considerations

- ★ Quarternary carbon sites require long contact times.
- ★ Mobile systems can have short I-spin T_{Ip} .



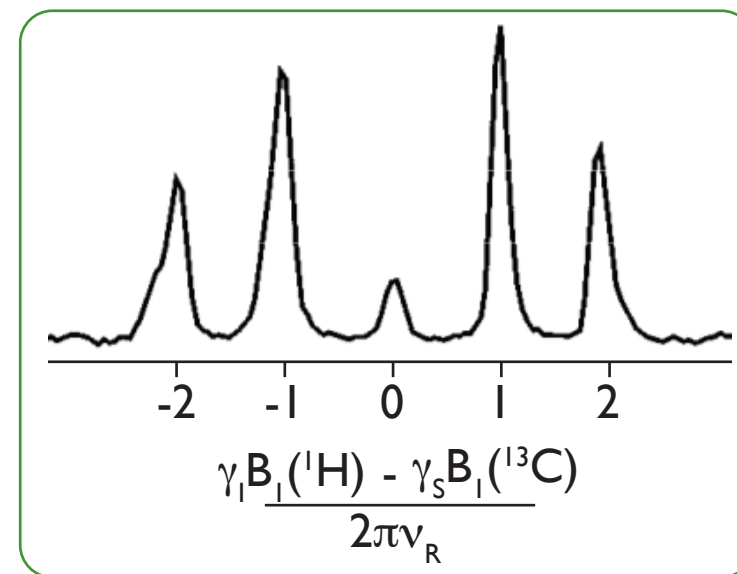
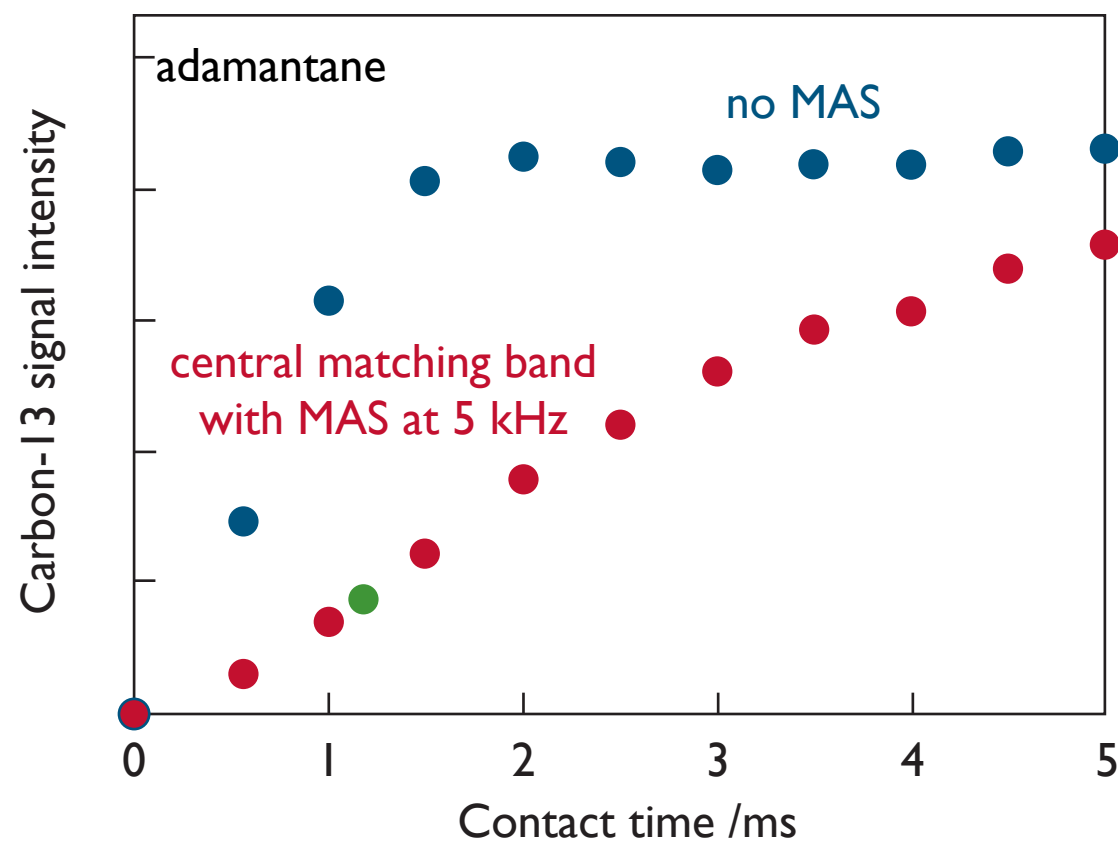
CPMAS

The combination of cross polarization, MAS and heteronuclear decoupling is now the routine experimental method for recording high resolution NMR spectra of spin- $I/2$ nuclei.

Cross polarization and rapid MAS

MAS averages the heteronuclear dipolar coupling.

- ★ When ν_R is rapid compared to d_{IS} the Hartmann-Hahn matching condition splits into a set of spinning sidebands.
- ★ The central matching condition has a slower T_{IS} than the sideband matches.

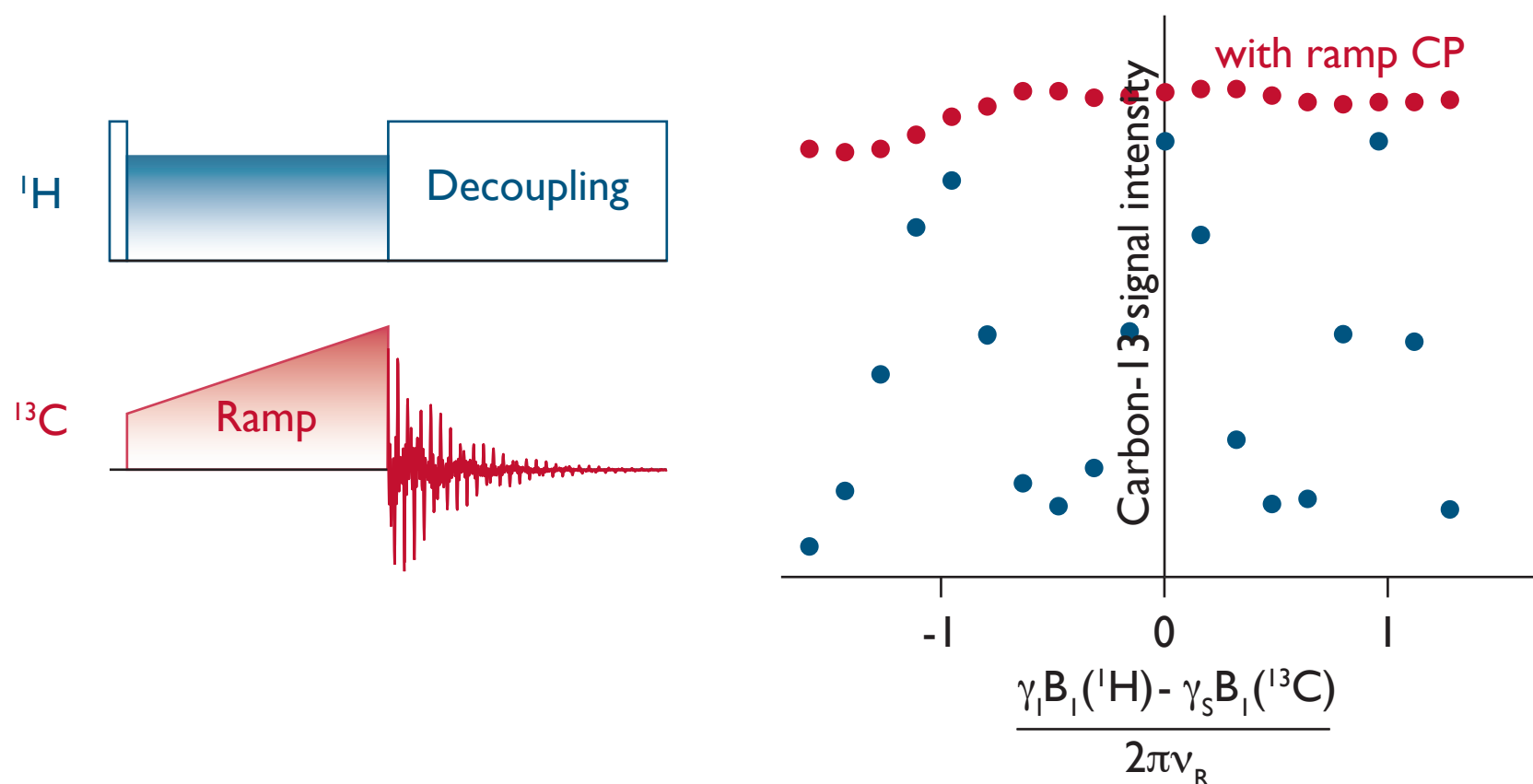


Variable amplitude CP

This problem can be overcome by ramping the amplitude of the cross polarization B_1 field.

For optimal signal:

- ★ the ramp size should be approximately twice ν_R
- ★ the step size should be as small as possible



Summary

Anisotropic nuclear spin interactions cause loss of resolution in NMR spectra of solids.

Magic angle spinning can be used to average inhomogeneously broadened interactions, such as the chemical shift anisotropy. MAS uses a mechanical rotation in sample space to average the interaction.

For homogeneous interactions, averaging is best achieved by rotations in spin space using radiofrequency pulses. For example to remove the heteronuclear dipolar interaction between carbon-13 and a proton which is itself part of a dipolar-coupled network **heteronuclear decoupling** is required.

Solid-state NMR spectroscopy is insensitive because of long spin-lattice relaxation times.

Cross polarization can be used to enhance sensitivity by transferring polarization from neighboring spins with higher magnetogyric ratio and more efficient spin-lattice relaxation.