



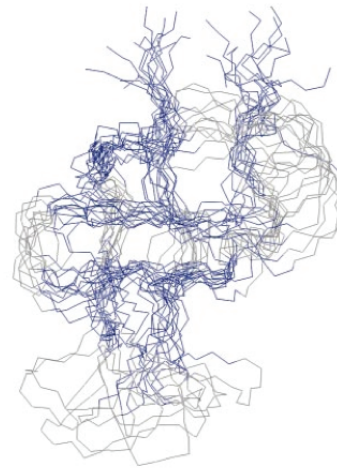
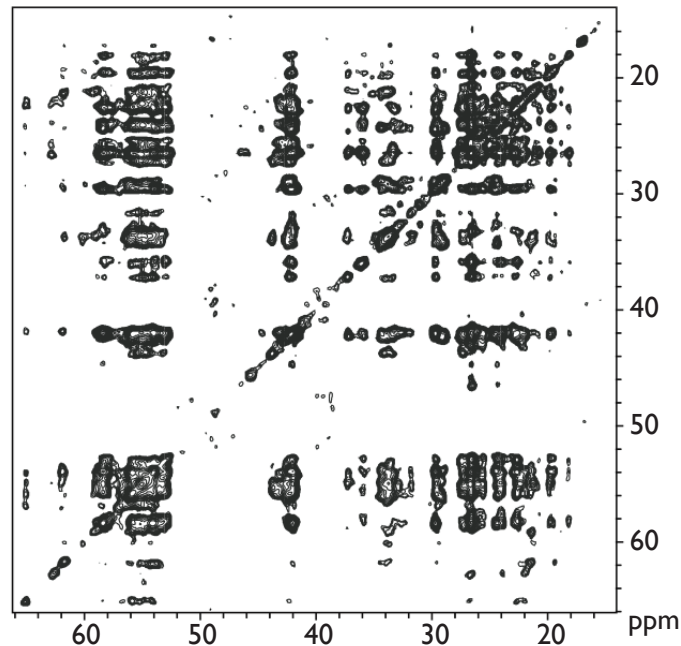
Introduction to solid-state NMR: anisotropic interactions

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Solid-state NMR

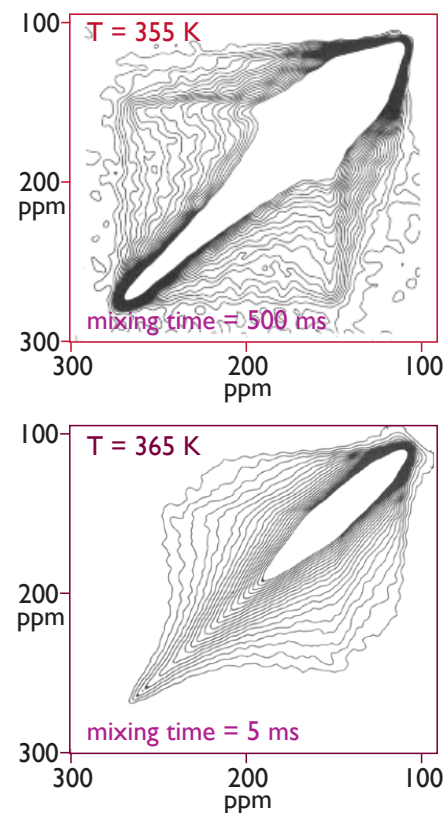
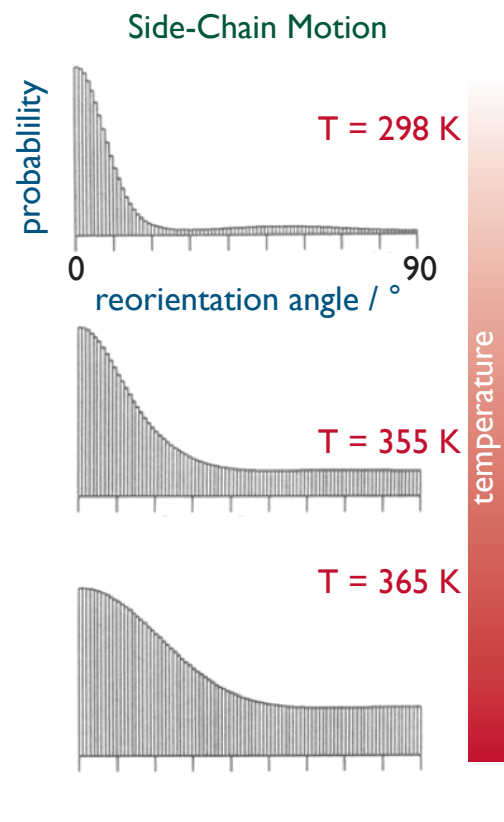
Protein structures

carbon-13 PDSD spectrum

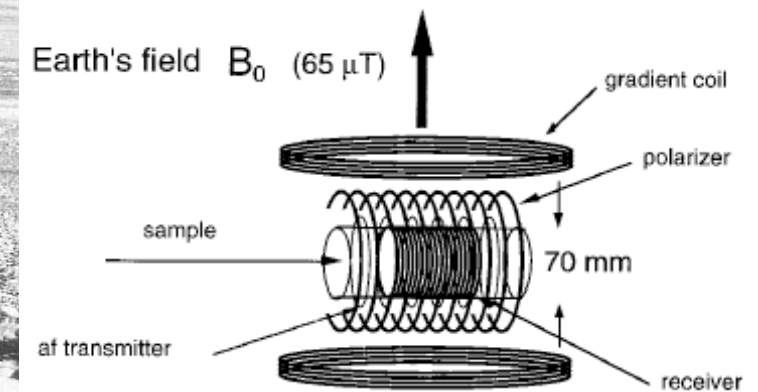


structure by
solid-state NMR

Polymer dynamics

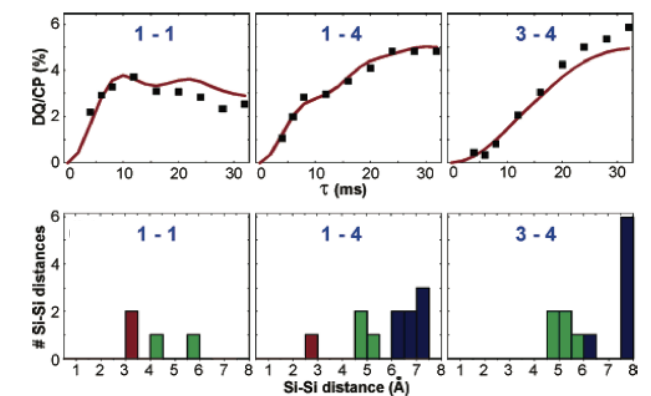
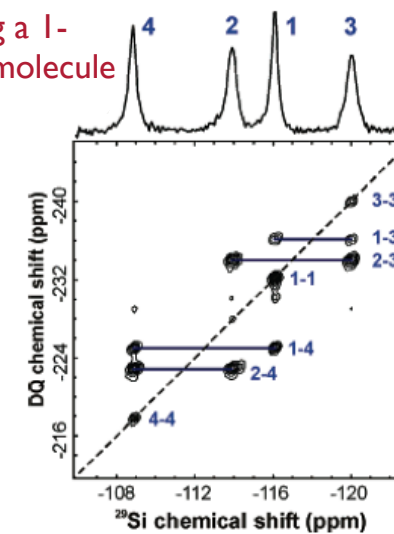
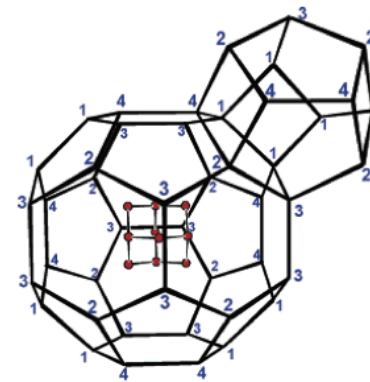


Environmental science



Zeolite structures

Clathrasil Sigma-2 hosting a 1-
aminoadamantane template molecule



Spider silk



“what did solid-state NMR ever do for us?”

Conformation: local structure; interatomic distances; dihedral angles; proteins; carbohydrates; biological systems

Crystallography: unit cell contents; polymorphism; heterogeneous phases; lattice parameters; space groups; pharmaceutical molecules; zeolites; minerals

Disordered solids: molecular structure; orientational order; zeolites; polymers; glasses; liquid crystals

Heterogeneity: amorphous and crystalline domains; phase separation; domain sizes; polymer blends; block copolymers; nano-composites; supramolecular systems

Dynamics: molecular rotations; diffusion; τ_c from s to ps; model-free; plastic crystals; liquid crystals; polymers; superionic conductors; intercalates



Nuclear spin Hamiltonian

$$H = -\sum_j \gamma_j I_{jz} B_0 - \sum_j \gamma_j \frac{B_{rf}}{2} \left[I_{jx} \cos(\omega_{rf} t + \varphi) + I_{jy} \sin(\omega_{rf} t + \varphi) \right] +$$

$$\sum_j \gamma_j \mathbf{I}_j \cdot \boldsymbol{\sigma}_j \mathbf{B}_0 + 2\pi \sum_{j < k} \mathbf{I}_j \mathbf{J}_{jk} \mathbf{I}_k + \sum_{j < k} \mathbf{I}_j \mathbf{D}_{jk} \mathbf{I}_k + \sum_j \mathbf{I}_j \mathbf{Q}_j + \sum_j \mathbf{I}_j \mathbf{A}_j \mathbf{S}$$

External terms: static magnetic field B_0 and radiofrequency field B_{rf}

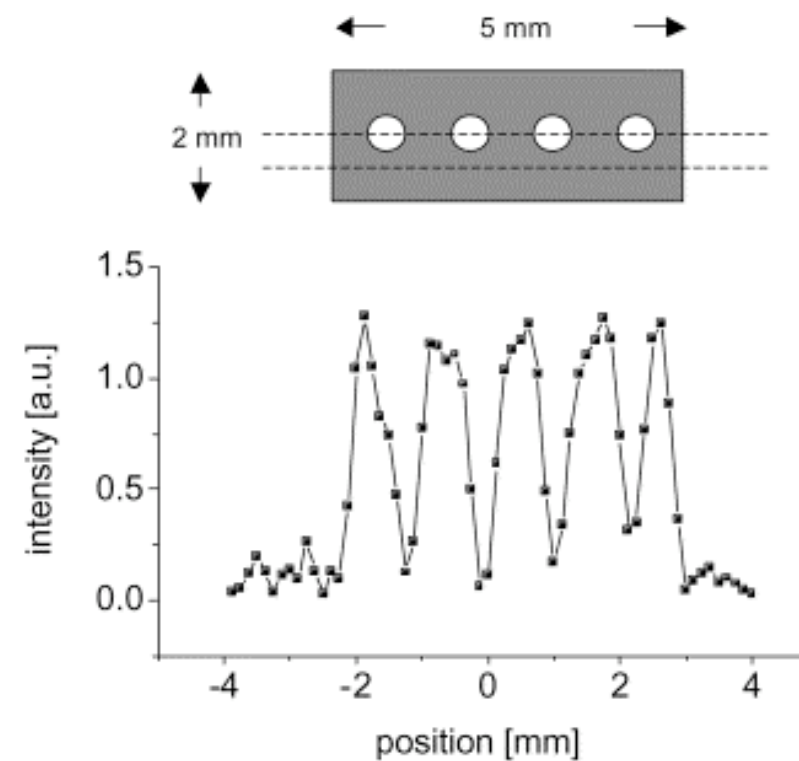
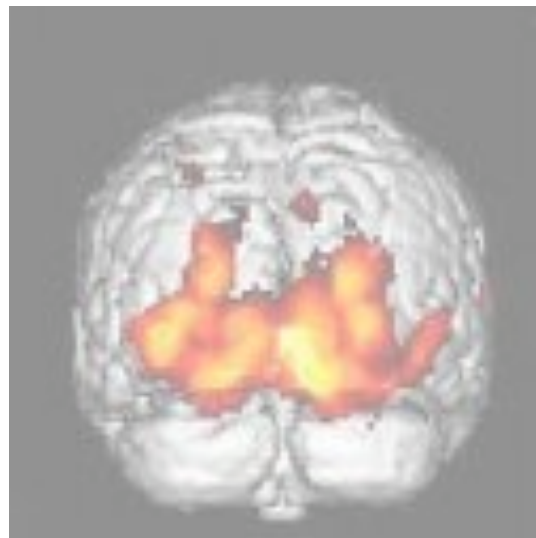
Internal terms: which contain information about the molecule

Nuclear spin Hamiltonian

$$H = - \sum_j \gamma_j I_{jz} B_0 - \sum_j \gamma_j \frac{B_{rf}}{2} \left[I_{jx} \cos(\omega_{rf} t + \varphi) + I_{jy} \sin(\omega_{rf} t + \varphi) \right] +$$

Zeeman interaction

$$\sum_j \gamma_j \mathbf{I}_j \cdot \boldsymbol{\sigma}_j \mathbf{B}_0 + 2\pi \sum_{j < k} \mathbf{I}_j \mathbf{J}_{jk} \mathbf{I}_k + \sum_{j < k} \mathbf{I}_j \mathbf{D}_{jk} \mathbf{I}_k + \sum_j \mathbf{I}_j \mathbf{Q}_j \mathbf{I}_j + \sum_j \mathbf{I}_j \mathbf{A}_j \mathbf{S}$$



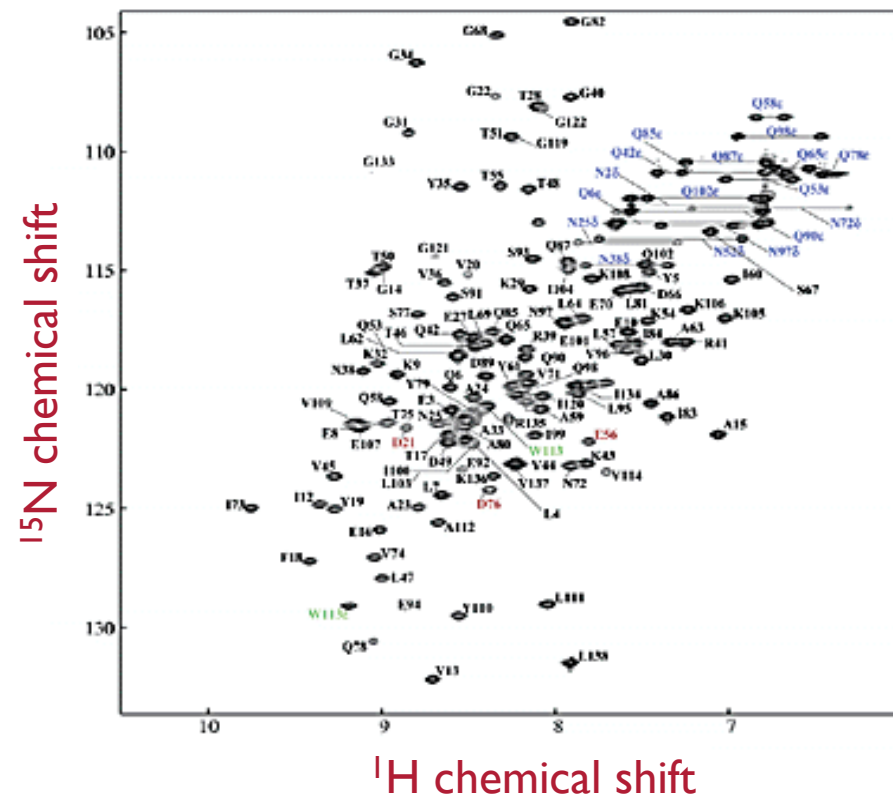
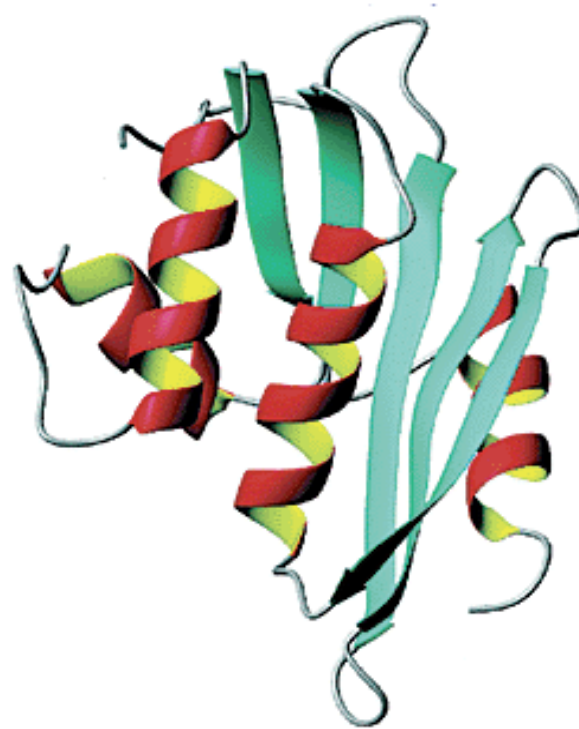
MR Imaging - the magnetic field depends on position

Nuclear spin Hamiltonian

$$H = -\sum_j \gamma_j I_{jz} B_0 - \sum_j \gamma_j \frac{B_{rf}}{2} \left[I_{jx} \cos(\omega_{rf} t + \varphi) + I_{jy} \sin(\omega_{rf} t + \varphi) \right] +$$

chemical shifts; scalar couplings

$$\sum_j \gamma_j \mathbf{I}_j \sigma_j \mathbf{B}_0 + 2\pi \sum_{j < k} \mathbf{I}_j J_{jk} \mathbf{I}_k + \sum_{j < k} \mathbf{I}_j \mathbf{D}_{jk} \mathbf{I}_k + \sum_j \mathbf{I}_j \mathbf{Q}_j \mathbf{I}_j + \sum_j \mathbf{I}_j \mathbf{A}_j \mathbf{S}$$



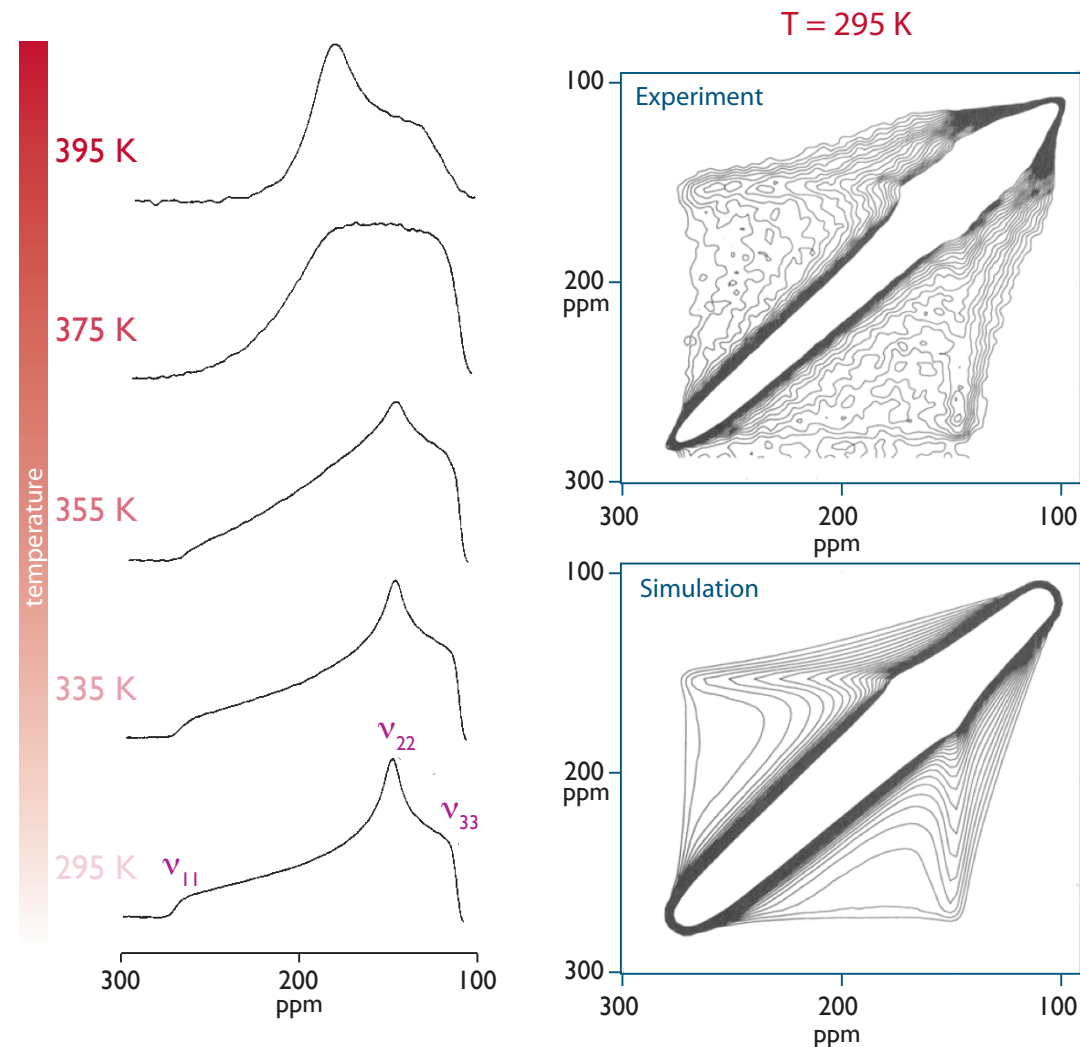
Solution-state NMR - the NMR frequency is very sensitive to environment

Nuclear spin Hamiltonian

$$H = -\sum_j \gamma_j I_{jz} B_0 - \sum_j \gamma_j \frac{B_{rf}}{2} \left[I_{jx} \cos(\omega_{rf} t + \varphi) + I_{jy} \sin(\omega_{rf} t + \varphi) \right] +$$

chemical shifts; scalar couplings;
dipolar and quadrupolar interactions

$$\sum_j \gamma_j \mathbf{I}_j \cdot \boldsymbol{\sigma}_j \mathbf{B}_0 + 2\pi \sum_{j < k} \mathbf{I}_j \mathbf{J}_{jk} \mathbf{I}_k + \sum_{j < k} \mathbf{I}_j \mathbf{D}_{jk} \mathbf{I}_k + \sum_j \mathbf{I}_j \mathbf{Q}_j \mathbf{I}_j + \sum_j \mathbf{I}_j \mathbf{A}_j \mathbf{S}$$



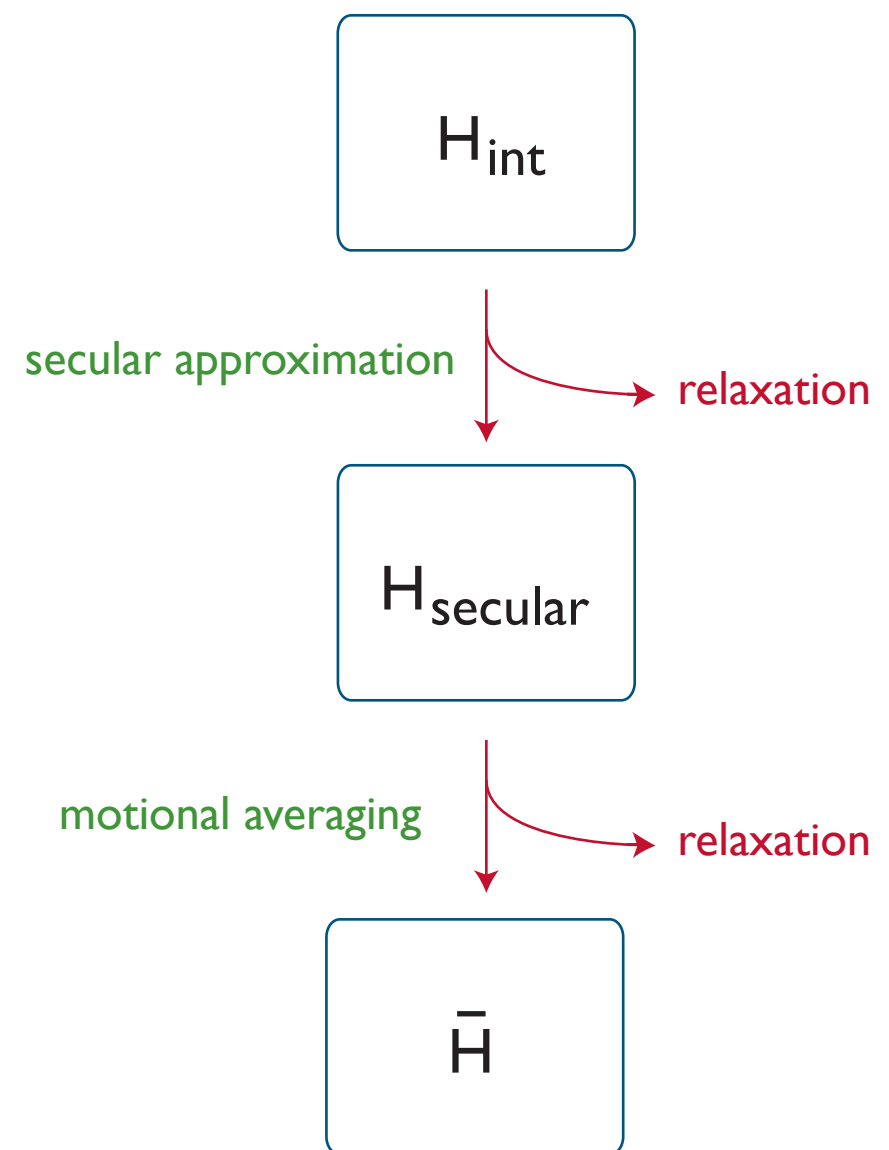
Solid-state NMR - the NMR frequency is also sensitive to orientation

Secular approximation

Even for a simple molecule the full nuclear spin Hamiltonian is complicated. It is usually possible to use a simplified form when:

- ★ the Zeeman interaction is **large**. This is usually the case because the external magnetic field used in modern NMR spectrometers is very strong. This simplification is called the **secular approximation** and the form of the spectrum is determined by the components of the internal Hamiltonian which are **parallel to the external magnetic field**.
- ★ there is rapid molecular motion.

Terms from the internal Hamiltonian which are omitted by these simplifications are responsible for relaxation.



Chemical shift

The **chemical shift** measures the extent to which the nuclear spin is shielded from the external field by electrons in the surrounding bonds.

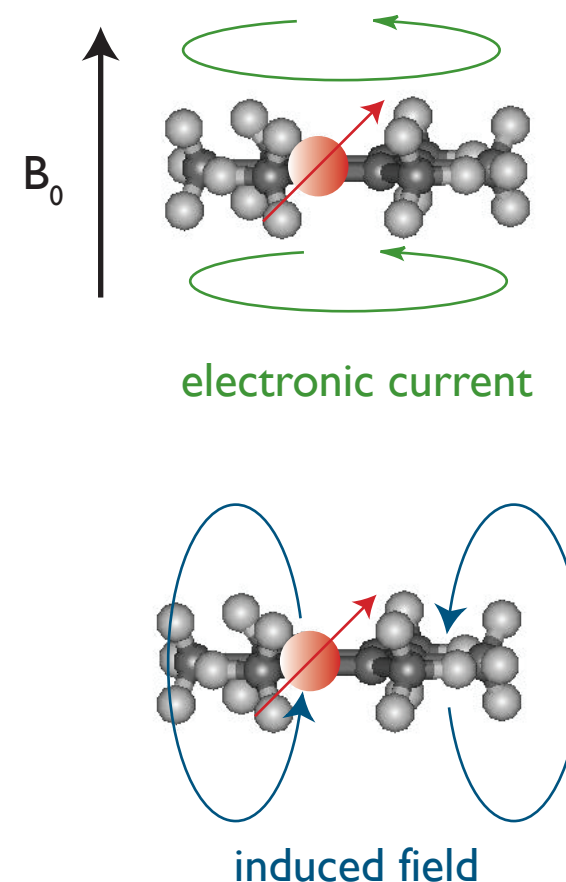
The shielding occurs by a two-step process:

- ★ the external magnetic field B_0 induces an **electronic current** in the bonds surrounding the nucleus
- ★ the circulating electrons in turn generate a **magnetic field** B_i which subtracts from or adds to (shields or “deshields”) B_0 .

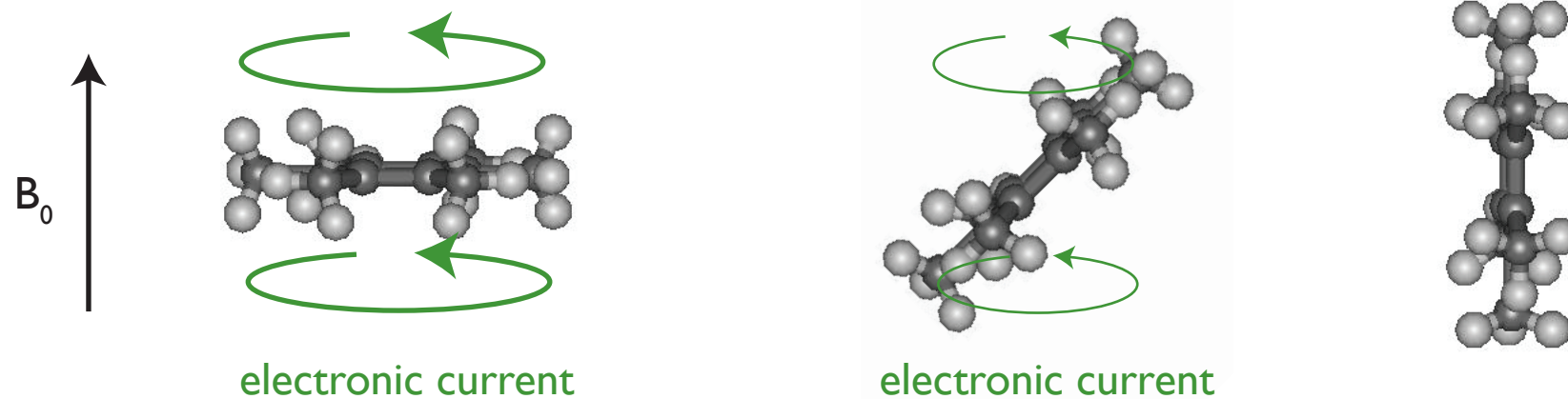
The nuclear spins precess with frequencies which are determined by the local field B_{loc} which is given by

$$\mathbf{B}_{\text{loc}} = \mathbf{B}_0 + \mathbf{B}_i$$

and nuclei in different chemical environments precess at different frequencies.



Chemical shielding tensor



The components of the induced field are given by

$$\begin{pmatrix} B_{i,x} \\ B_{i,y} \\ B_{i,z} \end{pmatrix} = - \begin{pmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{pmatrix} \begin{pmatrix} 0 \\ 0 \\ B_0 \end{pmatrix}$$

The matrix (called the **shielding tensor**) is required because the induced field is not necessarily parallel to the external field.

The nuclear spin interacts with the induced magnetic field according to the Zeeman interaction so that the chemical shift Hamiltonian is

$$H_{CS} = \gamma \sigma_{xz} I_x B_0 + \gamma \sigma_{yz} I_y B_0 + \gamma \sigma_{zz} I_z B_0$$

In the secular approximation only the **last term** is retained.

Principal axis system

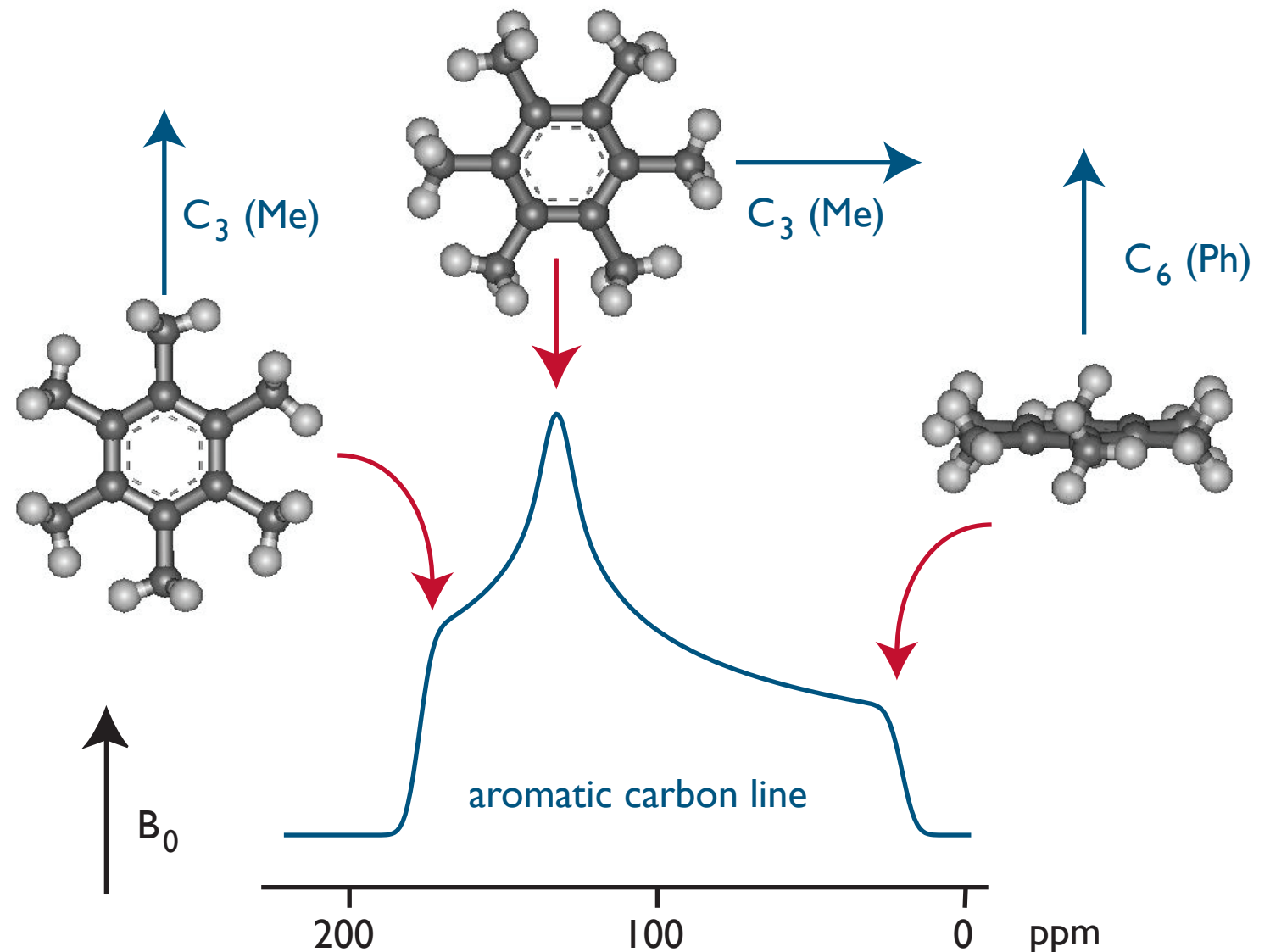
The elements of the shielding tensor depend on the orientation of the molecule with respect to the external magnetic field.

$$\sigma_{zz} = \frac{1}{3} \left\{ \sum_{j=x,y,z} \sigma_j + \sum_{j=x,y,z} (3\cos^2 \theta_j - 1) \sigma_j \right\}$$

The σ_j are three limiting shielding values called the **principal components** of the shielding tensor.

Each principal component is associated with a local symmetry axis of the molecule, and these three axes are known as the **principal axes**.

The angles θ_j represent the orientation of these axes with respect to B_0 for a particular molecule.



Chemical shift parameters: anisotropy, asymmetry

In the **principal axis system** the shielding tensor is diagonal

$$\sigma^{\text{PAS}} = \begin{pmatrix} \sigma_x & 0 & 0 \\ 0 & \sigma_y & 0 \\ 0 & 0 & \sigma_z \end{pmatrix}$$

Often the **chemical shift tensor** (remember δ measures deshielding) is used instead where

$$\delta^{\text{PAS}} = -\sigma^{\text{PAS}}$$

and the isotropic shift, shift anisotropy and asymmetry are defined

$$\delta_{\text{iso}} = \frac{1}{3}(\delta_x + \delta_y + \delta_z)$$

$$\zeta = \delta_z - \delta_{\text{iso}}$$

$$\eta = \frac{\delta_x - \delta_y}{\zeta}$$

Note: alternative definitions for these parameters exist!

Powder lineshape

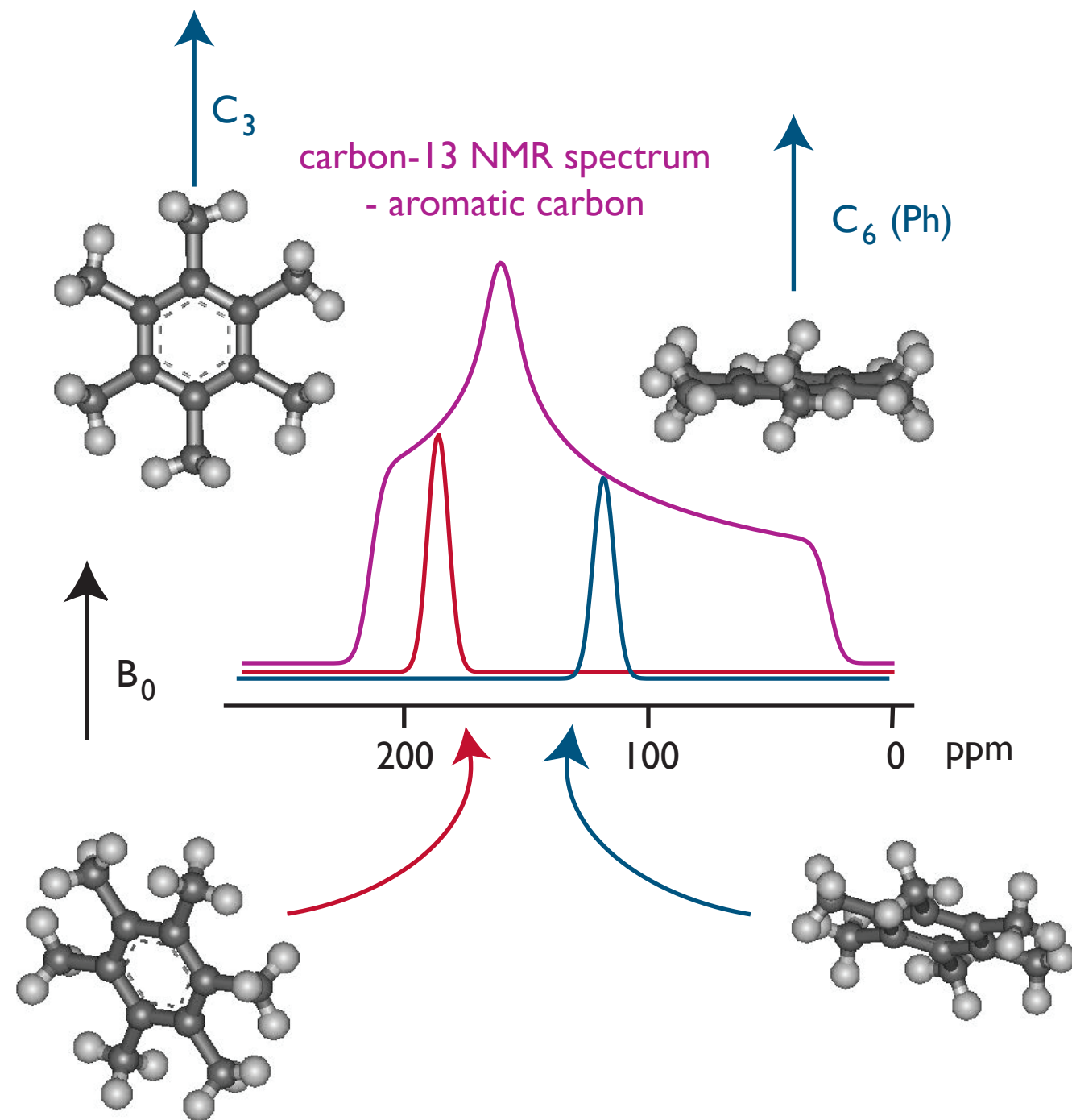
For a **single crystal sample** in which all molecules have the same orientation each chemical site results in a line at a frequency which depends on orientation.

In a **powder sample** molecules are in all possible orientations in the magnet and all possible values of the precession frequency are observed.

The lineshape observed in the spectrum is a sum of individual lines for all possible molecular orientations with a characteristic shape called a **powder pattern**.

The principal values of the chemical shift tensor can be measured directly from the **singularities** in the powder lineshape.

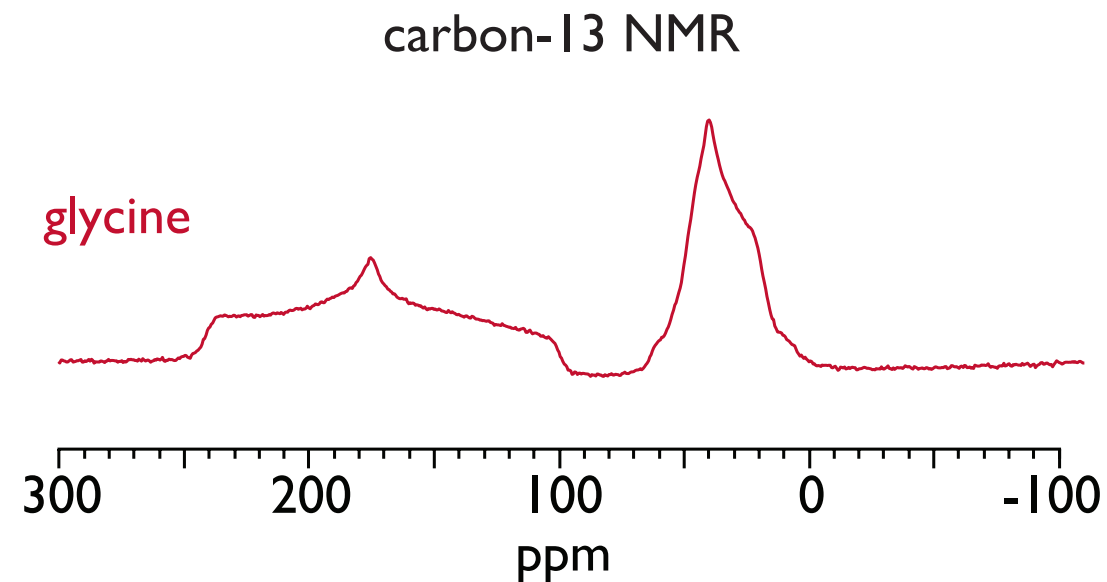
By convention δ_z is always the furthest principal value from δ_{iso} so that ζ can change sign.



CSA tensor and local environment

Example: carbon-13 CSA

- ★ Carbon atoms in olefinic environments have relatively small anisotropies of about 40 ppm, because they are sp^3 hybridized and the bonding electrons have approximately tetrahedral symmetry.
- ★ Aromatic carbons and carbons with double bonds are sp^2 hybridized and show larger anisotropies of up to 200 ppm because the arrangement of the bonding electrons is much less symmetrical.

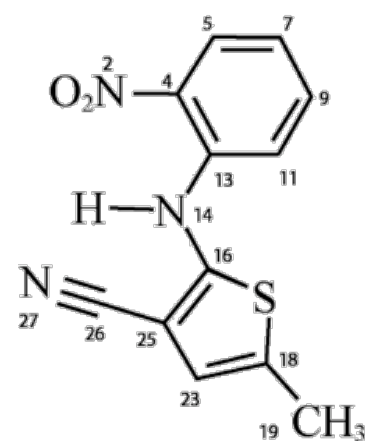


Polymorphism in pharmaceutical molecules

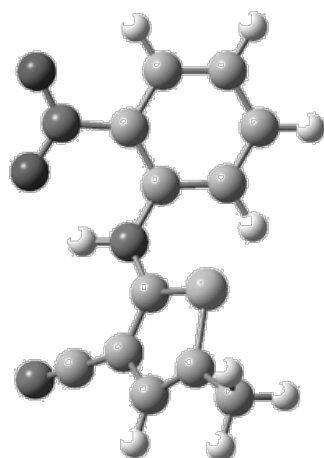
The three polymorphs of 5-methyl-2-[(2-nitrophenyl)amino]-3-thiophenecarbonitrile have a similar molecular structure with the exception of the dihedral angle between the phenyl and thiophene rings.

5-methyl-2-[(2-nitrophenyl)amino]

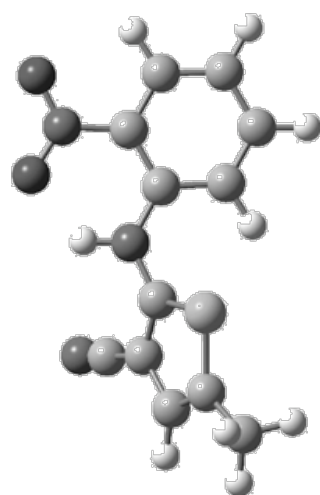
-3-thiophenecarbonitrile



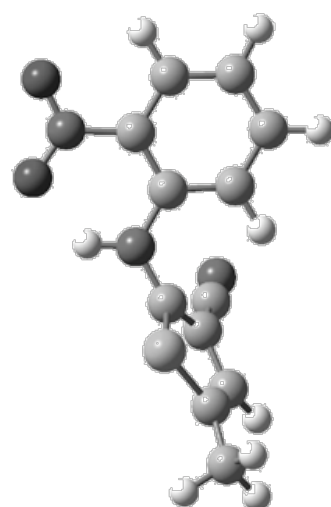
red



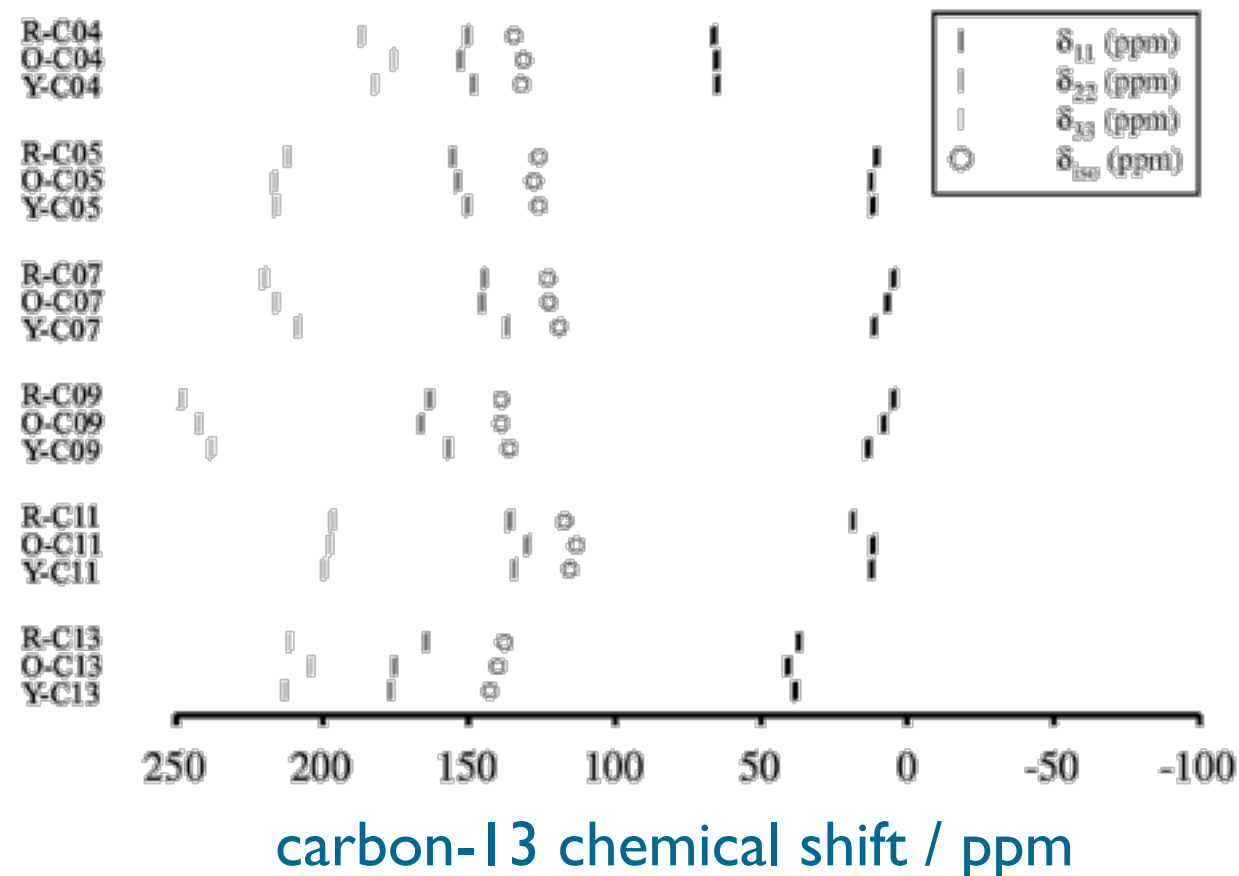
orange



yellow



Differences in chemical shift tensor principal components for different polymorphs



Orientation of the chemical shift tensor

The relationship between the principal components and the directions of individual bonds is not always easy to establish.

- ★ **For aromatic groups** the most shielded principal component corresponds to the chemical shift when the benzene ring is perpendicular to the magnetic field.
- ★ **For methylene groups** the most shielded principal value corresponds to the chemical shift when the plane containing the two hydrogen atoms is perpendicular to the magnetic field.

Couplings

The NMR precession frequency is also affected by the magnetic moments of neighboring nuclei (or electrons). Since (for spin-1/2) the magnetic moments are aligned either parallel or anti-parallel to the B_0 field they either increase or decrease the local field splitting the line into a doublet.

Dipolar coupling

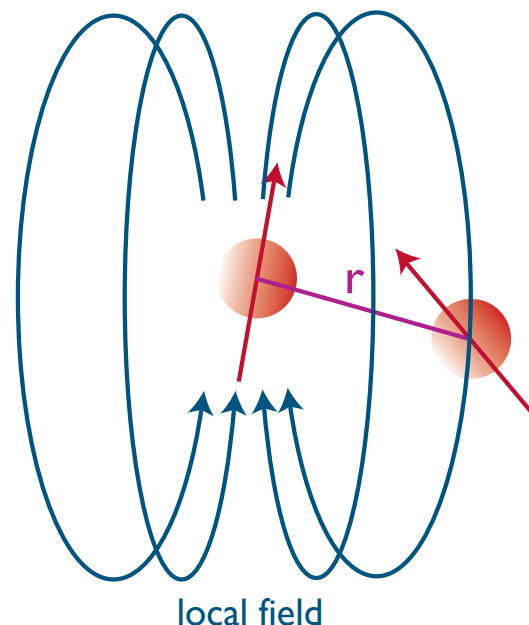
- ★ The direct through-space interaction between the magnetic moments of two nuclei ($d \sim \text{kHz}$)

Scalar coupling

- ★ The indirect through-bond interaction between the magnetic moments of two nuclei ($J \sim \text{Hz}$)
- ★ The J anisotropy is usually neglected even in solids.

Hyperfine coupling

- ★ A term given to all electron-nucleus interactions, including the Fermi contact interaction and the electron-nucleus through-space dipolar interaction ($A \sim \text{MHz}$)



Dipolar coupling

The magnitude of the local field depends the **internuclear distance**. The Hamiltonian is

$$H_D = \mathbf{I}_j \mathbf{D}_{jk} \mathbf{I}_k$$

where **D** is the dipolar tensor which is symmetric and traceless in the principal axis system. Note that the z axis of the principal axis system is always parallel to the internuclear vector.

$$\mathbf{D}^{\text{PAS}} = \begin{pmatrix} -d/2 & 0 & 0 \\ 0 & -d/2 & 0 \\ 0 & 0 & d \end{pmatrix}$$

The **dipolar coupling constant** in Hz is

$$d = \frac{1}{2\pi} \left(\frac{\mu_0}{4\pi} \right) \frac{\hbar \gamma^2}{r^3}$$

The dipolar interaction is always several orders of magnitude smaller than the B_0 field, so the secular approximation applies to the corresponding Hamiltonian.

The **secular** form of the dipolar Hamiltonian for a pair of like spins (the **homonuclear** dipolar coupling) is

$$H_D = \frac{d}{2} (1 - 3 \cos^2 \theta) (3 I_{1z} I_{2z} - \mathbf{I}_1 \cdot \mathbf{I}_2)$$

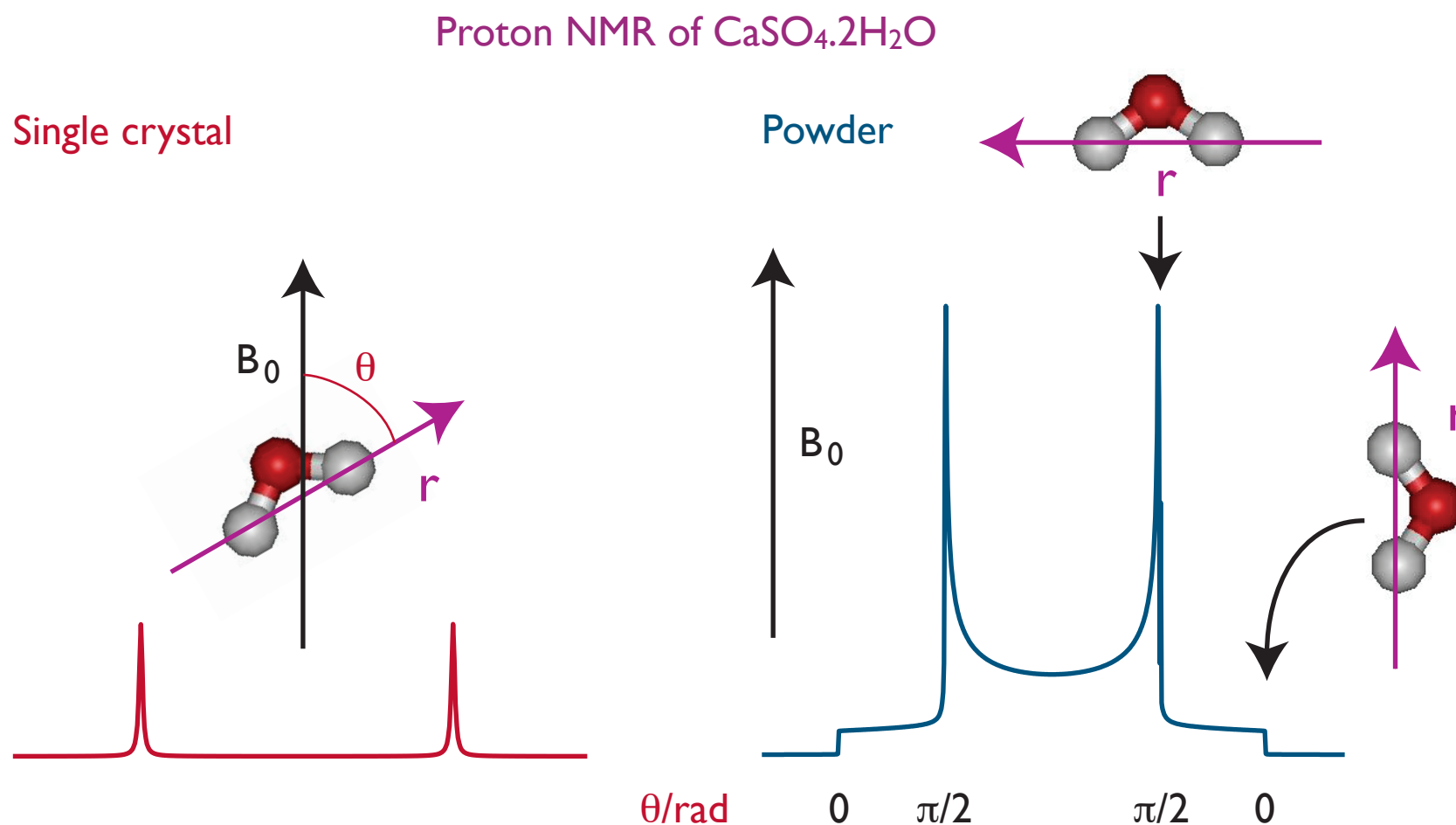
where θ is the angle describing the orientation of the internuclear vector relative to B_0 .

Pake pattern

A **single crystal** of a material containing isolated pairs of nuclei gives a doublet spectrum with a splitting in Hz which depends on molecular orientation.

$$\delta\nu = \frac{3d}{2} \left(3\cos^2 \theta - 1 \right)$$

In a **powdered sample** all possible orientations of the internuclear vector are present, resulting in a characteristic double powder pattern known as a **Pake doublet**. The Pake lineshape can be used to measure internuclear distances, since the splitting (in Hz) between the two maxima of the pattern is $3d/2$.



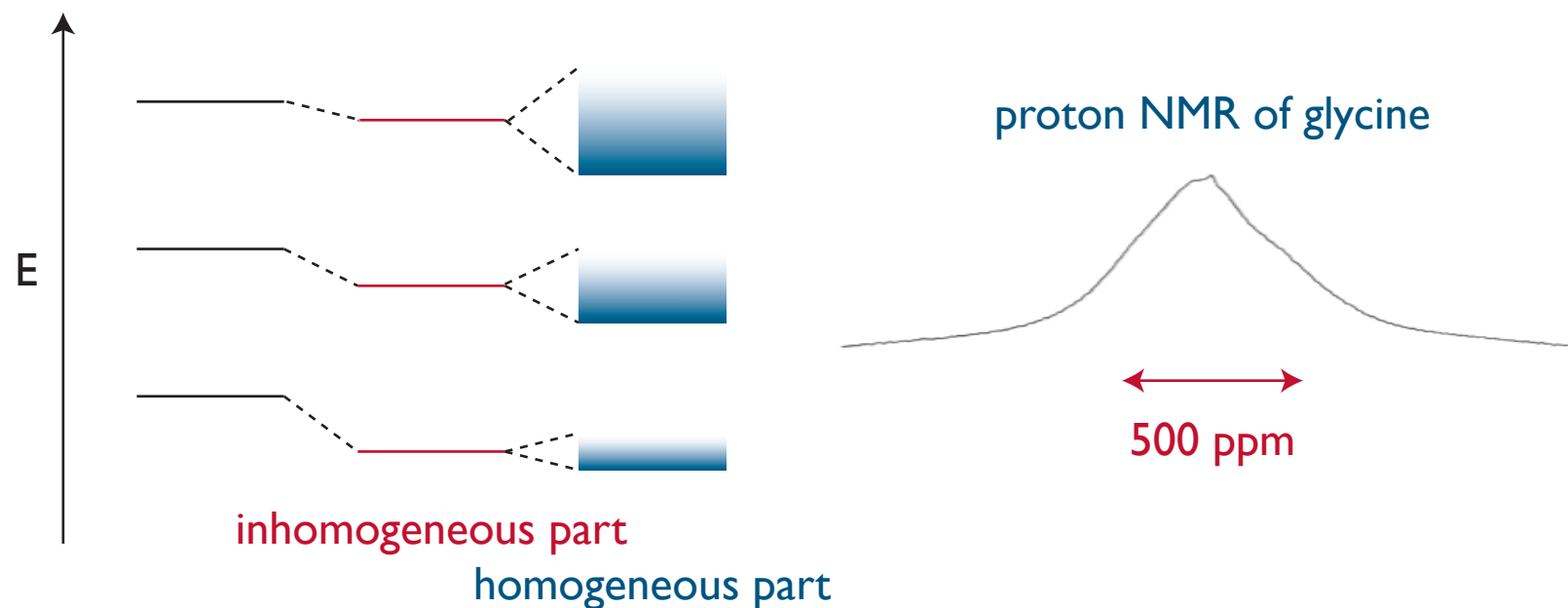
Multi-spin systems

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

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.



Note the homogeneous part can be **neglected** when the two spins have different magnetogyric ratios (**heteronuclear** couplings).

Motional averaging

If the interactions fluctuate at a rate which is sufficiently fast the spectrum arises from a motionally averaged Hamiltonian.

Molecular motions which occur on the right timescale to cause motional averaging include translations and rotations.

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

If τ is long enough, this time average can be replaced by an **orientational average**

$$\bar{H}_{\text{int}} = \int_0^{\pi} d\theta \sin \theta H_{\text{int}}(\theta)$$

This integral is called the **isotropic average** of the internal Hamiltonian.

In solution the molecular tumbling is rapid and the internal spin interactions are averaged to their isotropic values. Hence, the effects of the anisotropy of the interactions are not observed in the spectrum.

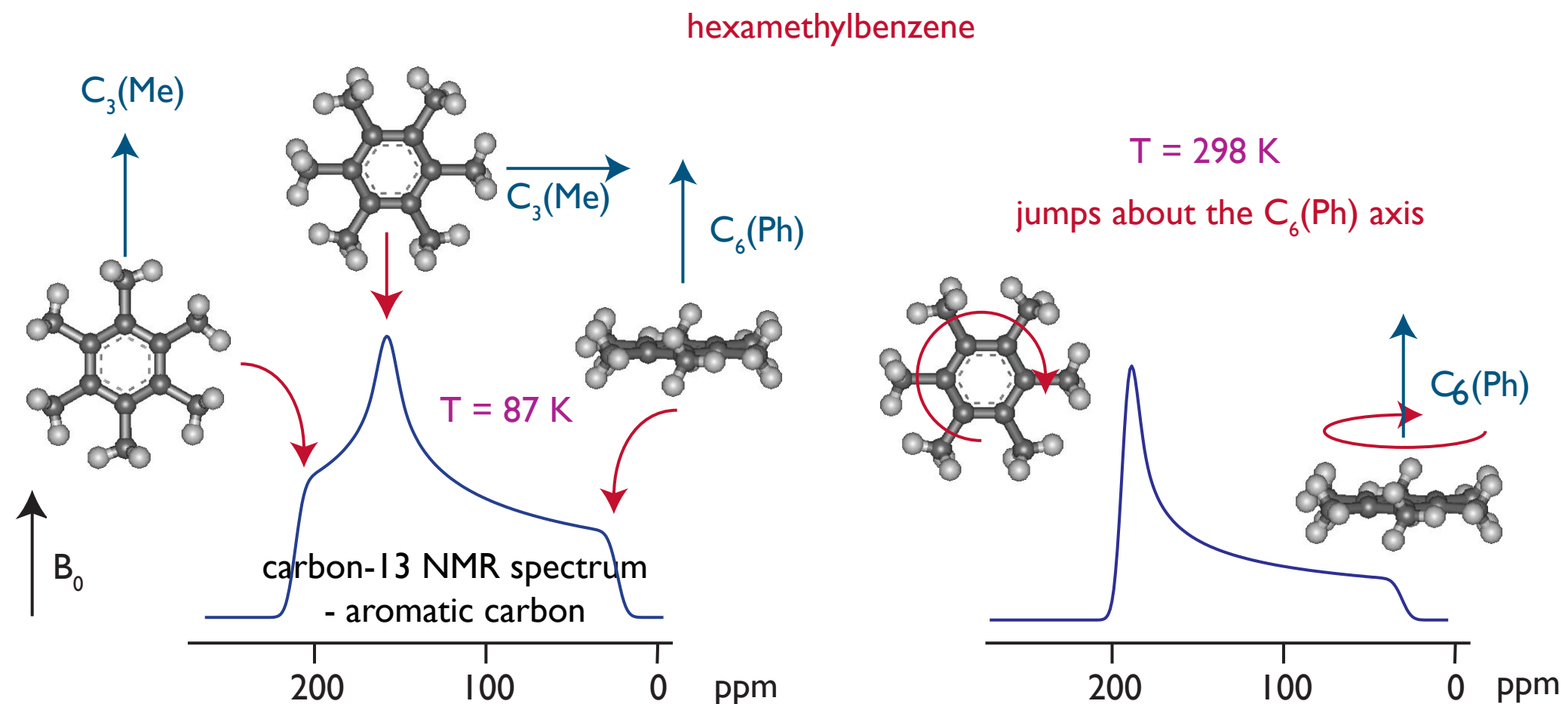
Motion in solids

In **plastic crystals**, such as hexamethylbenzene, adamantane and C_{60} , the molecules tumble rapidly on their lattice sites. If these motions are isotropic intramolecular spin interactions are averaged while intermolecular interactions survive as there is no relative motion of the molecules.

If the motions are **anisotropic** they can be studied via lineshape analysis.

Example: hexamethylbenzene

- ★ At 298 K the molecules jump about the C_6 local symmetry axis and hence the principal component of the carbon-13 chemical shift tensor δ_z which is parallel to that axis remains invariant.
- ★ The six-fold jumps occur at a rate which is faster than 3.3 kHz, the frequency separation of δ_x and δ_y .

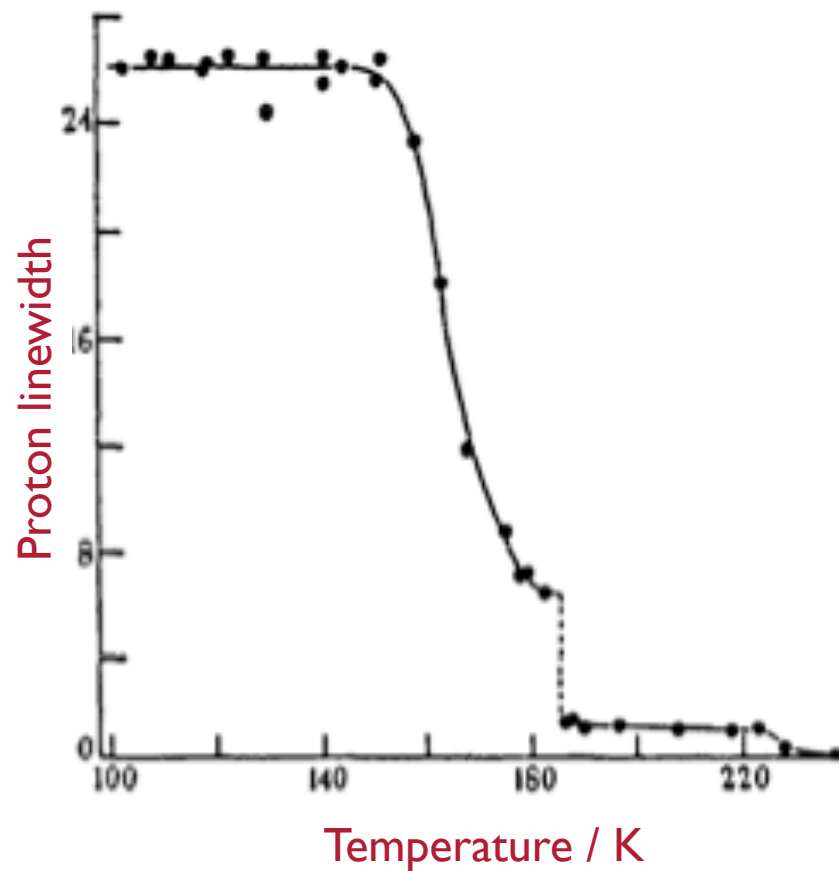


Motion in solids

Example: cyclohexane

As the temperature is raised three distinct motional narrowing modes are observed in the proton spectrum:

- ★ jumps about the C_3 symmetry axis
- ★ isotropic reorientation
- ★ molecular self-diffusion



Summary

Nuclear spin interactions are **anisotropic**.

In solids where molecular motions are normally very restricted this results in **loss of resolution** due to powder broadening. Much effort has been expended designing methods for averaging the powder lineshape to obtain solution-like spectra of solids (as described in the following lecture).

However, measurement of the **whole tensor** rather than its isotropic average provides additional information, particularly about dynamics.