

# Anisotropic Interactions and High-Resolution NMR in Solids

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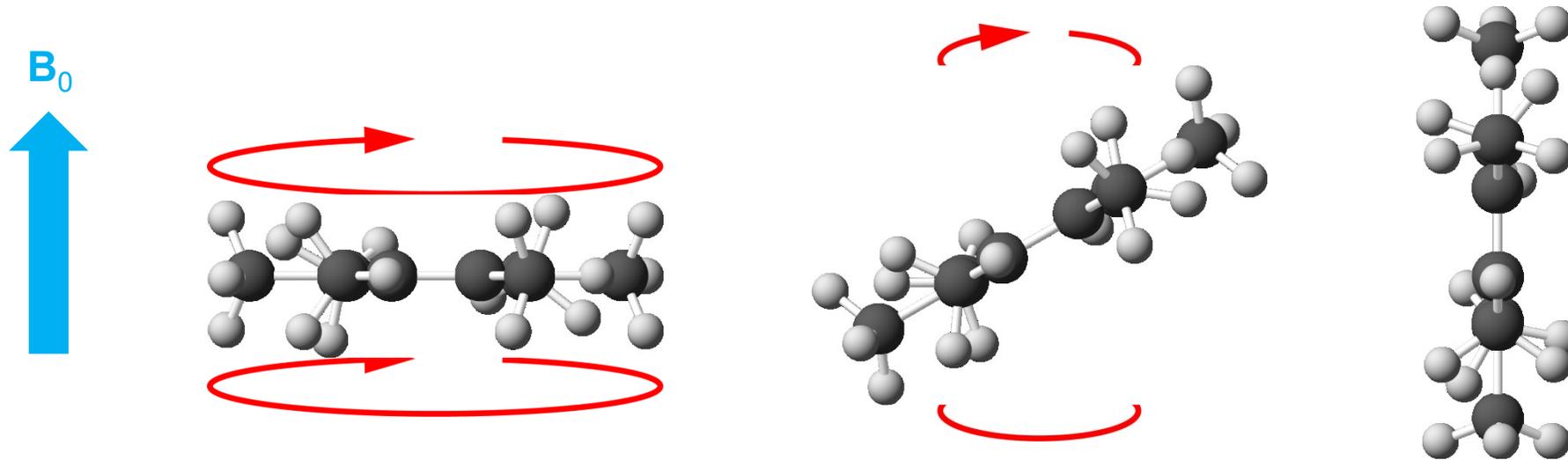
# Overview

- Introduction to anisotropy and why it matters
- The effects of anisotropic interactions
- Removing anisotropic interactions in solids
- Common types of solid-state NMR experiments
- Case study on metal-organic frameworks

# 1. Anisotropic Interactions in NMR

# Anisotropy

- “Anisotropic” means “not the same in all directions” and applies to many molecules



- We expect a different magnetic response, *i.e.*, shift, for the same  $^{13}\text{C}$  nucleus at the same  $B_0$  strength depending on the molecular orientation
- So why do we see sharp lines in solution for this anisotropic molecule?

# Liquids vs Solids

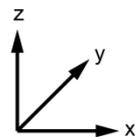
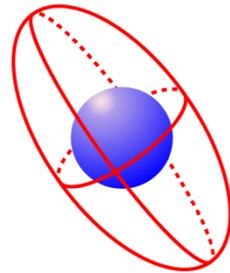
- In liquids, molecules tend to tumble rapidly compared to the Larmor frequency
  - $\tau_C$  around  $10^{-12}$  s (small molecules) to  $10^{-7}$  s (biomolecules)
  - $1/\nu_0$  around  $10^{-9}$  s (1 GHz) to  $10^{-8}$  s (100 MHz)
- Over the course of one nuclear oscillation, there is no memory of molecular orientation
  - caveat: this isn't always true for biomolecules, which have longer  $\tau_C$  and may behave more like small solid particles under certain conditions
- In a typical solid, motion is (nearly) absent owing to molecular packing, rigid ionic lattice potentials, *etc.*, so it matters which way up your crystallite is

# Some Maths

- We have seen chemical shifts reported as  $\delta$ , but this is the orientation-averaged isotropic value. In solids, we must represent the chemical shift as an interaction tensor.

lab frame

$$\delta^{\text{lab}} = \begin{pmatrix} \delta_{xx} & \delta_{xy} & \delta_{xz} \\ \delta_{yx} & \delta_{yy} & \delta_{yz} \\ \delta_{zx} & \delta_{zy} & \delta_{zz} \end{pmatrix}$$

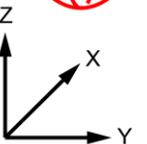
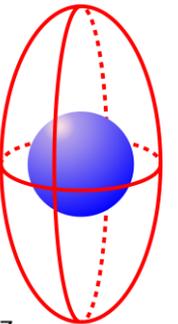


rotation transform  
between frames

principal axis system

$$\delta^{\text{PAS}} = \begin{pmatrix} \delta_{zz} & 0 & 0 \\ 0 & \delta_{yy} & 0 \\ 0 & 0 & \delta_{xx} \end{pmatrix}$$

$$\delta_{\text{iso}} = \frac{\delta_{zz} + \delta_{yy} + \delta_{xx}}{3}$$



axes fixed relative to the lab (and  $B_0$ )  
arbitrary orientation of the molecule

$$|\delta_{zz} - \delta_{\text{iso}}| \geq |\delta_{xx} - \delta_{\text{iso}}| \geq |\delta_{yy} - \delta_{\text{iso}}|$$

axes fixed relative to the molecule  
arbitrary relative orientation of  $B_0$

# Some Maths

- All shifts must be between  $\delta_{ZZ}$  and  $\delta_{XX}$ , and are distributed according to:

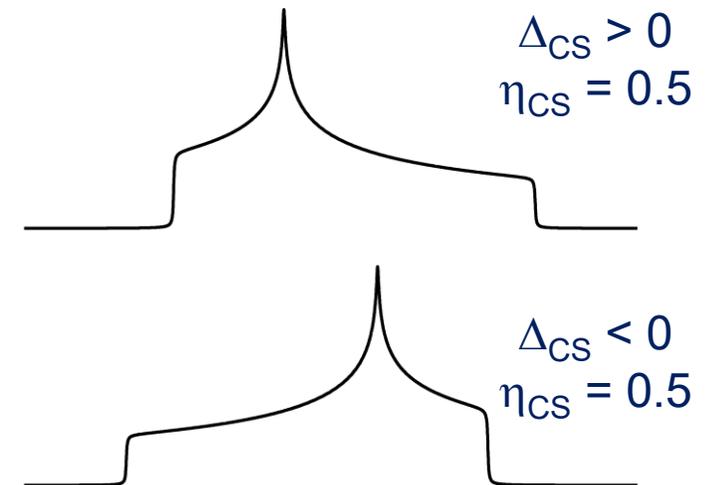
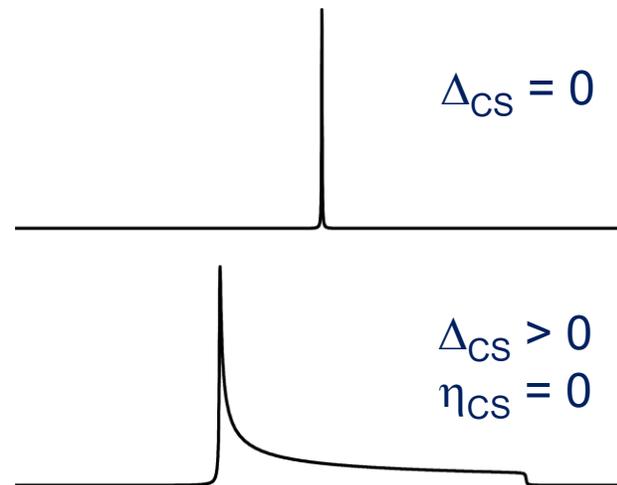
$$\delta = \delta_{\text{iso}} + \frac{\Delta_{\text{CS}}}{2} \left[ (3\cos^2\theta - 1) + \eta_{\text{CS}} (\sin^2\theta \cos 2\phi) \right]$$

orientation independent

orientation dependent

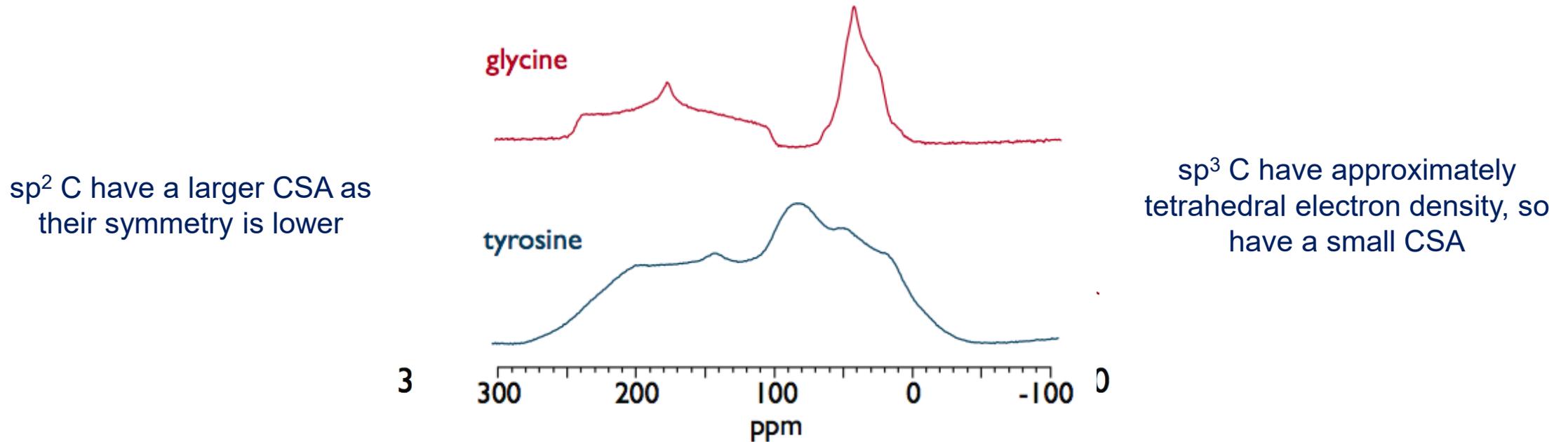
$$\Delta_{\text{CS}} = \delta_{\text{ZZ}} - \delta_{\text{iso}} \quad \text{“size”}$$

$$\eta_{\text{CS}} = \frac{\delta_{\text{YY}} - \delta_{\text{XX}}}{\Delta_{\text{CS}}} \quad \text{“shape”}$$



# The Problem with Anisotropy

- Having a spectrum where we can identify all three components of the shift tensor gives us more information than the average  $\delta_{iso}$  from solution, and more information is good, right?



- Broad signals are a problem when we have multiple resonances in the spectrum (*i.e.*, in most materials of interest)

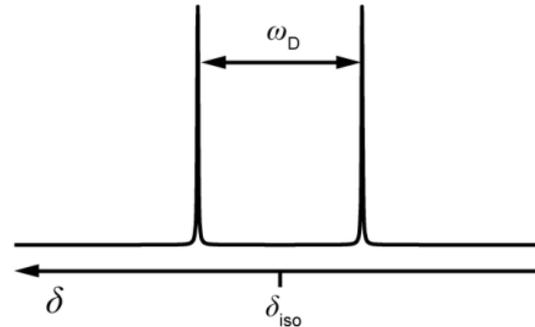
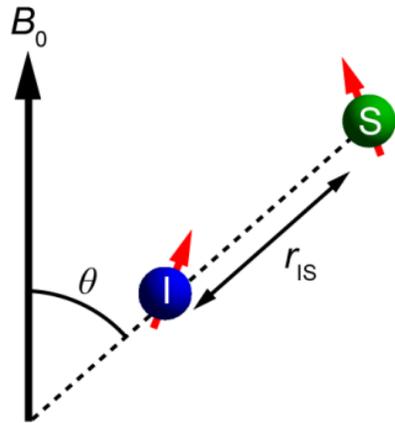
# Other Anisotropic Interactions

- If the molecule is anisotropic, all interactions present will be anisotropic

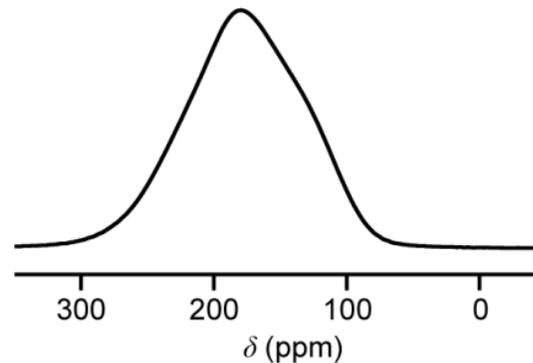
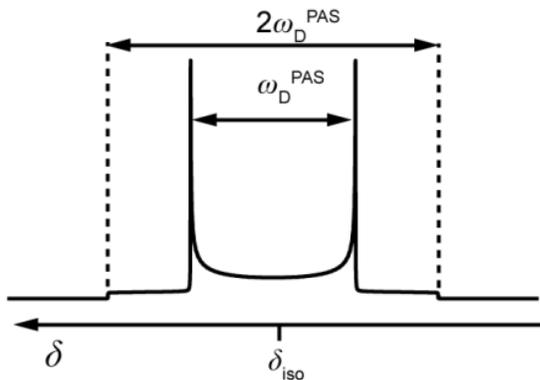
Interaction	Size	Liquids	Solids
Zeeman	$10^7 - 10^9$ Hz	yes	yes
RF pulses	$10^3 - 10^5$ Hz	yes	yes
chemical shift	$10^4 - 10^5$ Hz	isotropic	anisotropic
J coupling	$1 - 10^3$ Hz	isotropic	anisotropic
dipolar coupling	$10^3 - 10^5$ Hz	no	anisotropic
quadrupolar coupling	$10^3 - 10^7$ Hz	no	anisotropic

# Dipolar Couplings

- Nuclear spins generate a magnetic dipole, which can interact directly with other nuclear dipole moments through space



$$\omega_D = \frac{\omega_D^{PAS} (3\cos^2\theta - 1)}{2}$$



$$\omega_D^{PAS} = -\frac{\mu_0 \gamma_I \gamma_S \hbar}{4\pi r_{IS}^3}$$

# Quadrupolar Nuclei

- Nuclei with spin  $I > 1/2$  have a nuclear electric quadrupole moment  $Q$ , which interacts with an electric field gradient,  $\mathbf{V}$

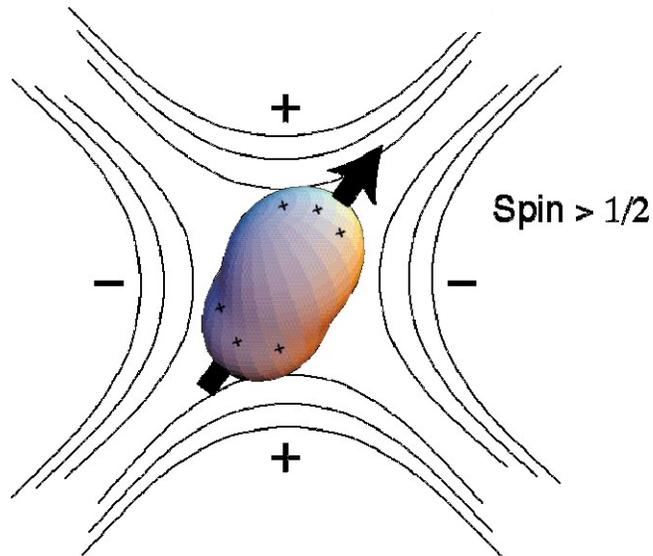
$$\mathbf{V}^{\text{PAS}} = \begin{pmatrix} V_{xx} & 0 & 0 \\ 0 & V_{yy} & 0 \\ 0 & 0 & V_{zz} \end{pmatrix}$$

$$C_Q = \frac{eQV_{zz}}{h}$$

$$\eta_Q = \frac{(V_{xx} - V_{yy})}{V_{zz}}$$

$$|V_{zz}| \geq |V_{yy}| \geq |V_{xx}|$$

$$P_Q = C_Q \left( 1 + \frac{\eta_Q^2}{3} \right)^{1/2}$$



# Nuclei with Integer Spins

- Only seven natural NMR-active nuclei have integer spins
  - $I = 1$ :  $^2\text{H}$ ,  $^6\text{Li}$ ,  $^{14}\text{N}$
  - $I = 3$ :  $^{10}\text{B}$
  - $I = 5$ :  $^{138}\text{La}$
  - $I = 6$ :  $^{50}\text{V}$
  - $I = 7$ :  $^{176}\text{Lu}$
- All exhibit combinations of very unfavourable properties
  - low abundance, low receptivity, large quadrupolar coupling...
- Can still be used to provide information, such as  $^2\text{H}$  for probing dynamics

# Quadrupolar Nuclei: $I = 1$

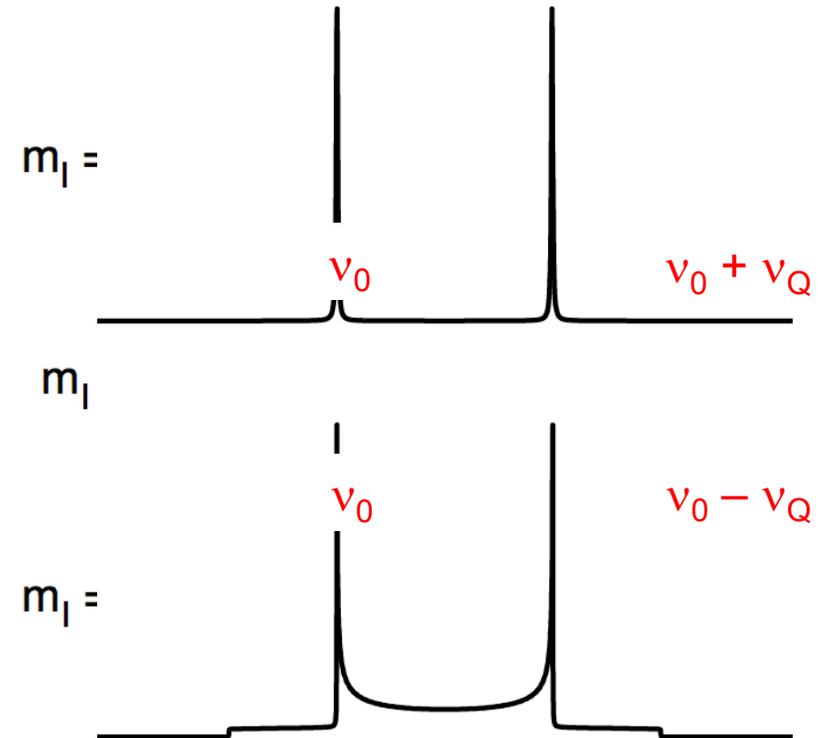
- for  $I = 1$ , three allowed Zeeman states give two allowed transitions

- these are degenerate when  $V_{zz} = 0$  but the quadrupolar interaction perturbs these energy levels, normally only to first order

$$v_Q = v_Q^{\text{PAS}} \frac{1}{2} \left[ (3\cos^2\theta - 1) + \eta_Q (\sin^2\theta \cos 2\phi) \right]$$

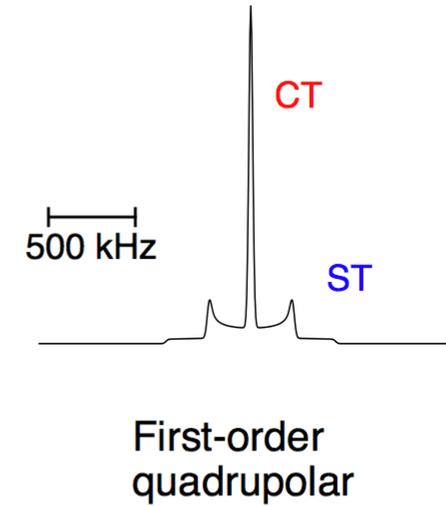
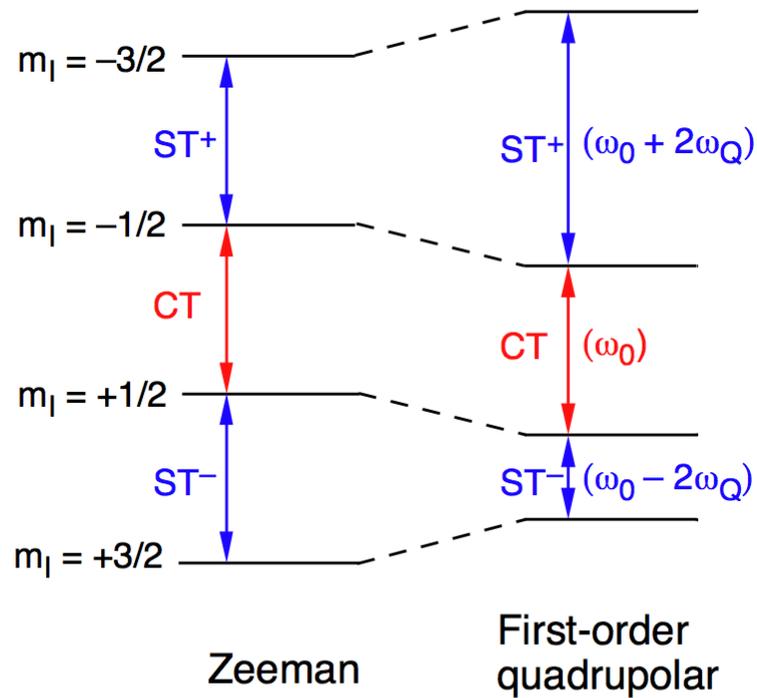
$$v_Q^{\text{PAS}} = \frac{3C_Q}{4I(2I-1)}$$

- two transitions observed in the spectrum



# Quadrupolar Nuclei: $I = 3/2$

- The same thing happens for half-integer spins...



# Quadrupolar Nuclei: $I = n/2$

- The second-order perturbation has a different orientation dependence

$$\nu_Q = \frac{(\nu_Q^{\text{PAS}})^2}{\nu_0} [A + B d_{00}^2(\theta) + C d_{00}^4(\theta)]$$

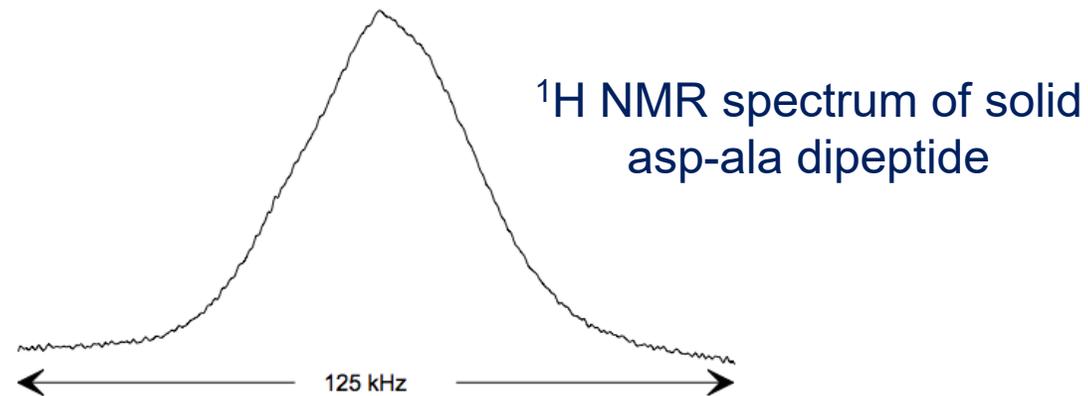
A: isotropic

B: first-order  $d_{00}^2(\theta) \propto 3\cos^2\theta - 1$

C: second-order  $d_{00}^4(\theta) \propto 35\cos^4\theta - 30\cos^2\theta + 3$

# Solid-State NMR: The Problem

- Typically, the width of lines in solid-state NMR spectra is greater than their separation
- Peaks overlap and the signal is typically spread out over hundreds of ppm

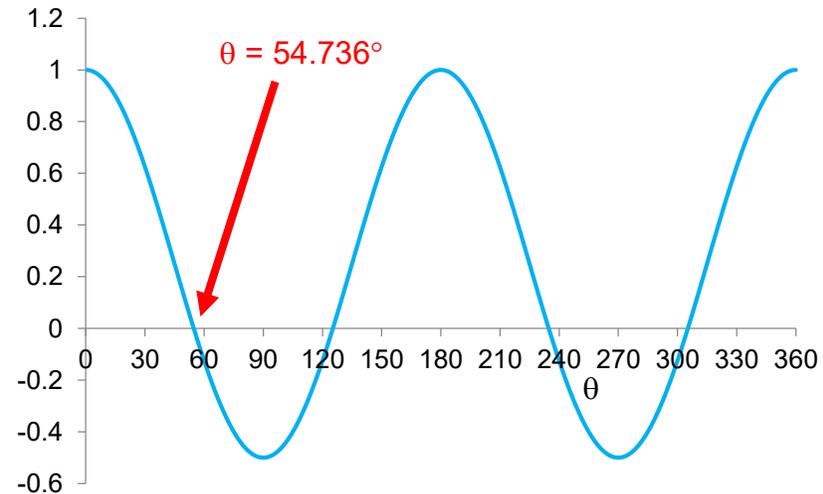


- The result is broad, featureless spectra that look like they contain no useful information
- They actually contain too much information!
  - chemistry, crystal and local symmetry, distances, bonds...

## 2. Improving Resolution and Sensitivity

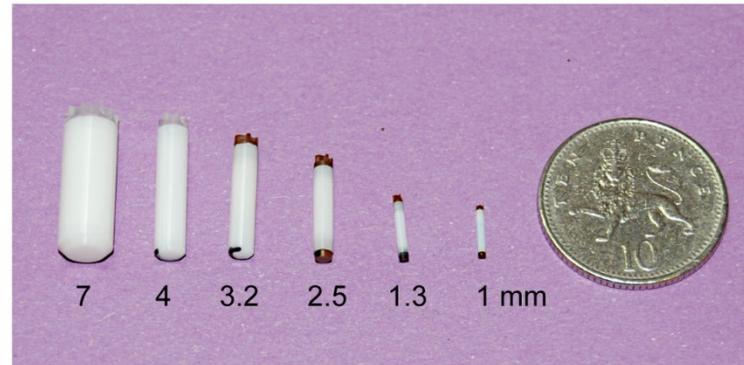
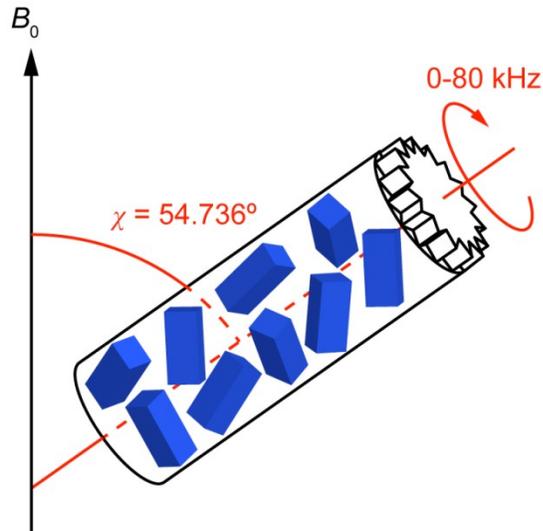
# Magic Angle Spinning

- Remember that most anisotropic contributions are proportional to  $(3\cos^2\theta - 1) / 2$
- This is zero at the “magic” angle of  $54.736^\circ$
- If we could align all crystallites at the magic angle, we would get an isotropic spectrum
  - This is not practical...
- If we could, instead, achieve an *average* crystallite orientation of the magic angle, we would still see the isotropic spectrum
- Rapid isotropic tumbling is why solution state NMR spectra have such high resolution



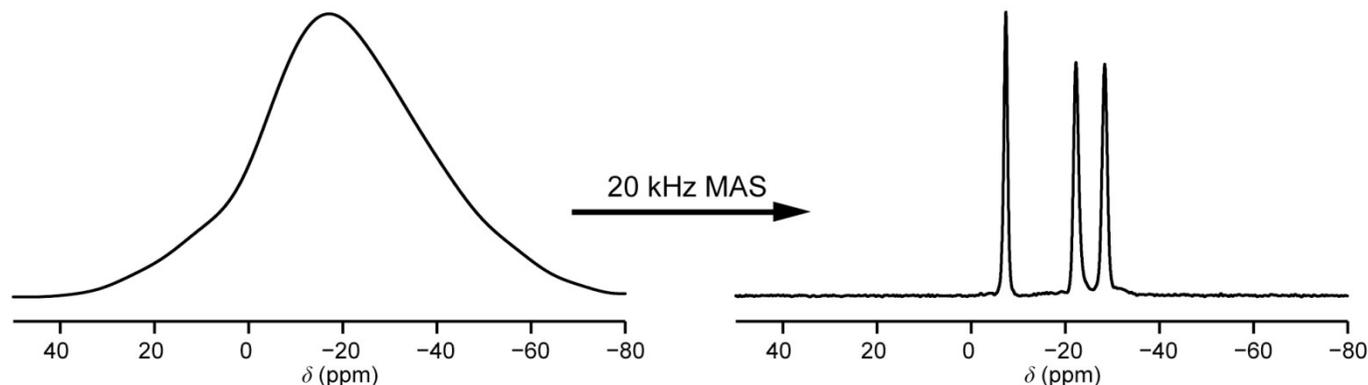
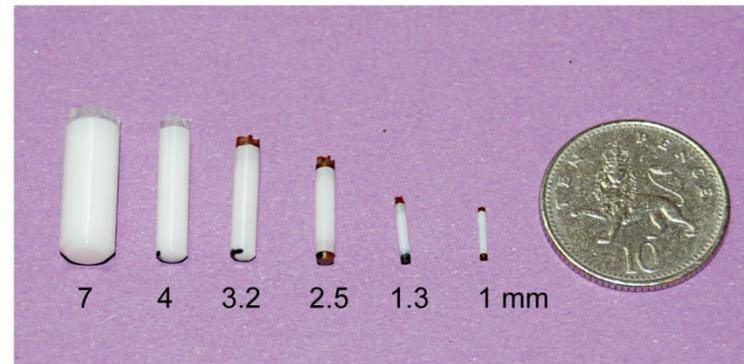
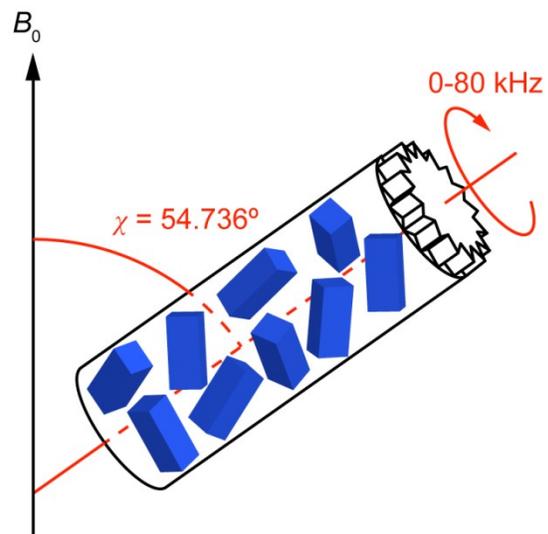
# Magic Angle Spinning

- In the magic angle spinning (MAS) experiment, the randomly oriented crystallites are packed into a rotor oriented at the magic angle



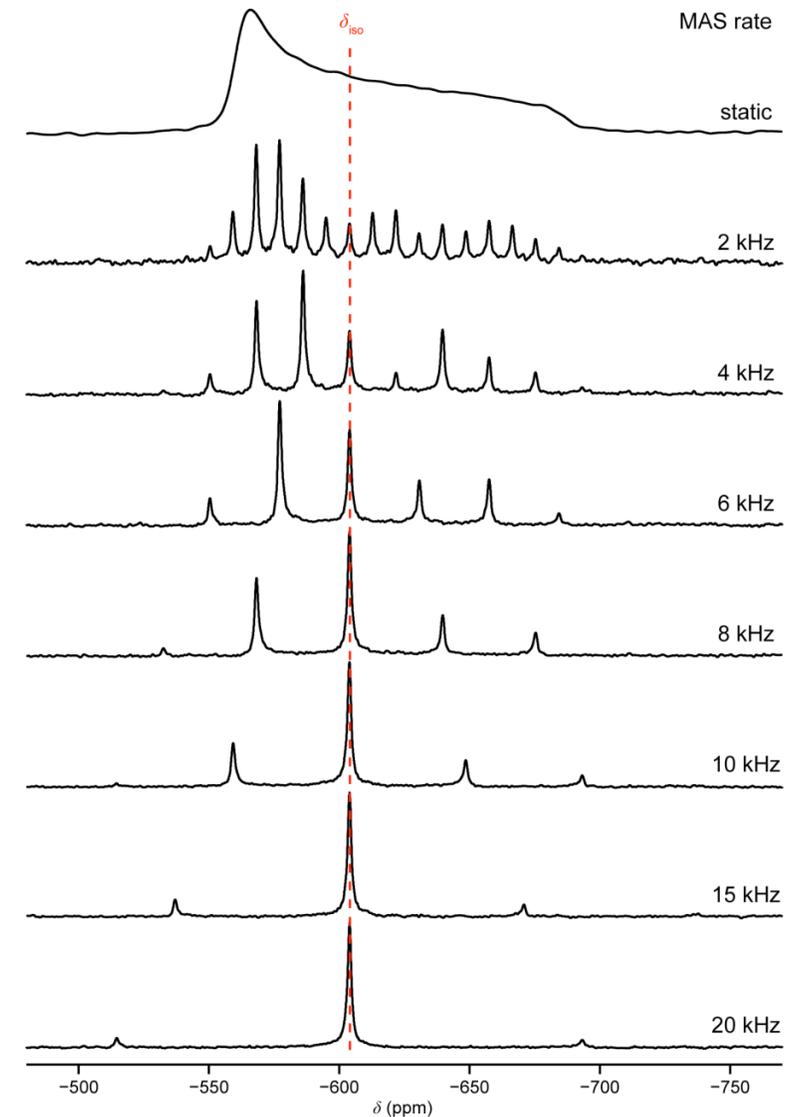
# Magic Angle Spinning

- Rapid rotation averages off-axis contributions to the crystallite orientation to zero, giving an orientation of  $54.736^\circ$
- The maximum rotation rate is limited by the speed of sound over the outer wall of the rotor
- Smaller rotors can rotate faster, but hold less sample
- Trade off between sensitivity (number of nuclei present) and resolution (MAS rate needed)



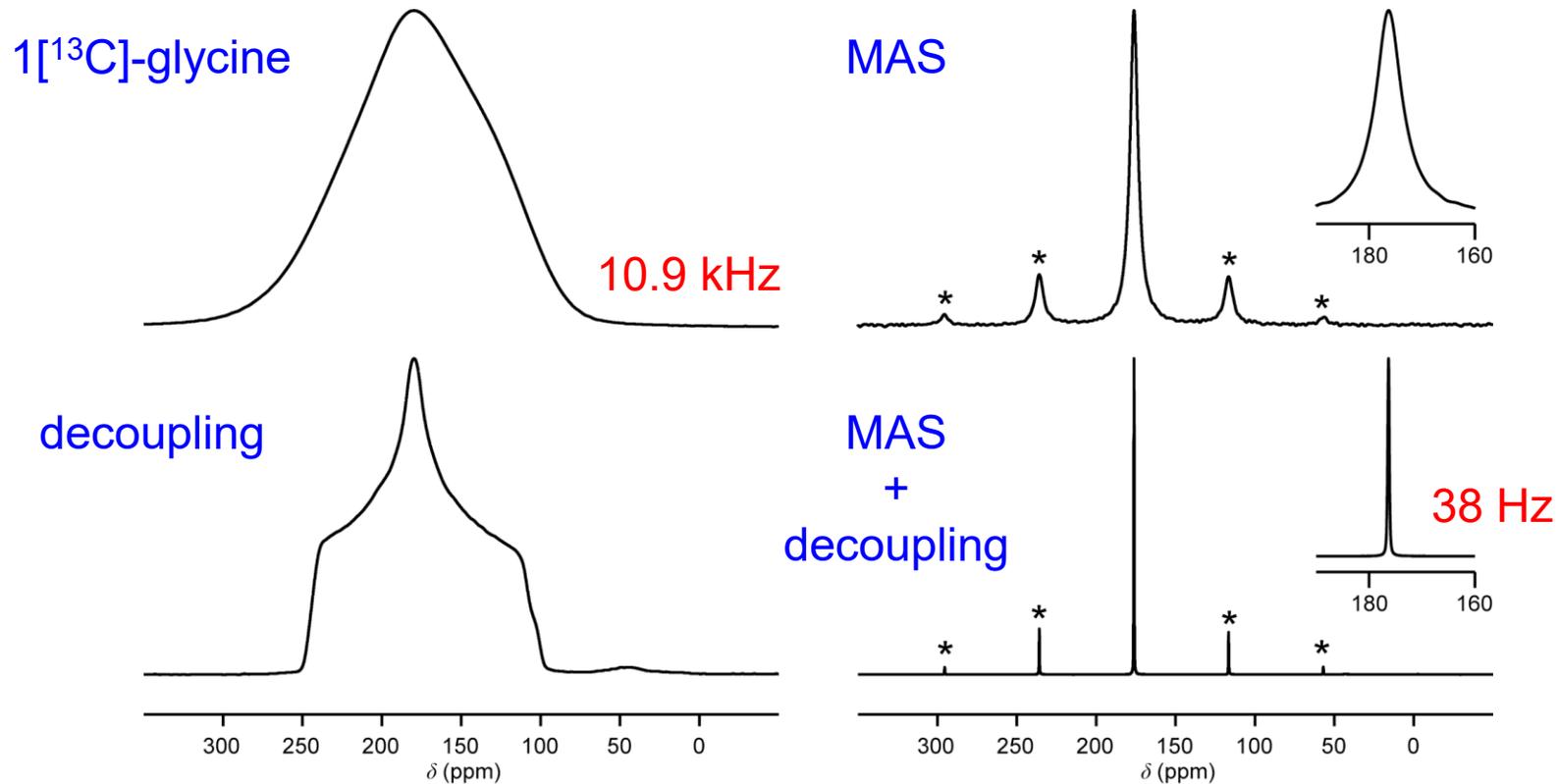
# Spinning Sidebands

- MAS works very well provided the rotation rate exceeds the broadening you are trying to remove
- At “slow” MAS rates, spinning sidebands are observed
- SSBs are still sharp and can provide information on anisotropic interactions (provided the manifolds from different resonances don't overlap)
- For some nuclei, (particularly  $^1\text{H}$  and  $^{19}\text{F}$ ), the homonuclear dipolar coupling still causes broad SSBs up to  $\sim 100$  kHz MAS



# Decoupling

- As in solution NMR, decoupling can remove the effects of spin-spin interactions (dipolar and J)

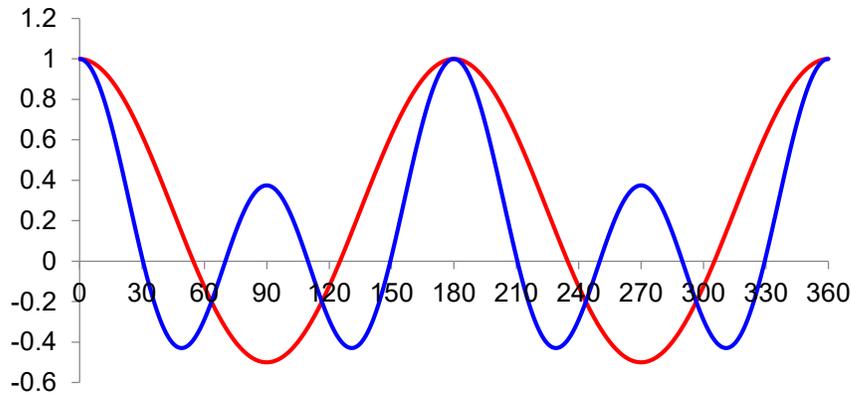


- Unlike solution-state NMR, 38 Hz counts as a narrow line!

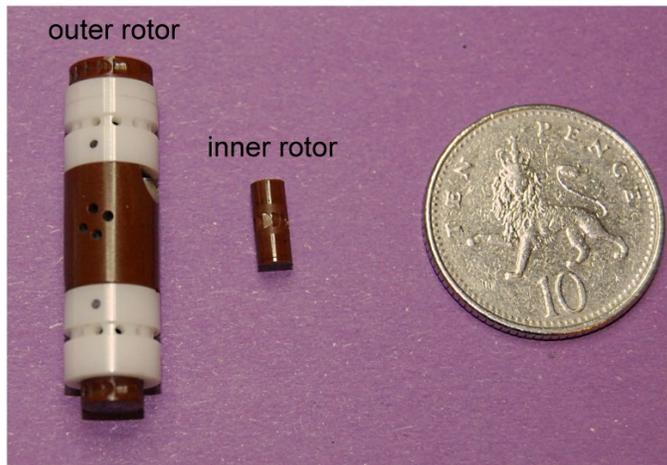
# MAS and Quadrupolar Nuclei

- The second-order quadrupolar perturbation has the orientation dependence

$$35\cos^4\theta - 30\cos^2\theta + 3$$



- Roots at  $30.56^\circ$  and  $70.12^\circ$
- Reduced to  $\sim 1/3$  by MAS but not removed
- Could be removed by spinning at  $30.56^\circ$  (or  $70.12^\circ$ )
- The Double Rotation (DOR) experiment spins the sample simultaneously at  $54.74^\circ$  and  $30.56^\circ$
- Specialist probe required, poor fill factor, top spinning rates  $\sim 2$  kHz (outer) and  $\sim 6$  kHz (inner) rotors...

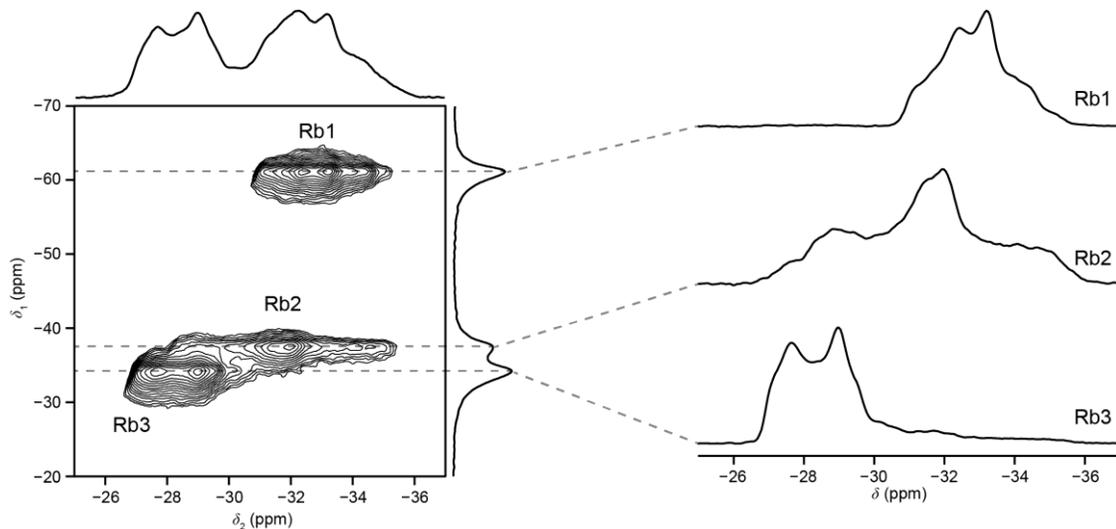


# The MQMAS Experiment

- Multiple-quantum (MQ) MAS has revolutionised high-resolution NMR of quadrupolar nuclei
- 2D experiment that exploits the different A, B and C coefficients for different transitions

$$\nu_Q = \frac{\left(\nu_Q^{\text{PAS}}\right)^2}{\nu_0} \left[ A + B d_{00}^2(\theta) + C d_{00}^4(\theta) \right]$$

- Correlates the isotropic MQ spectrum with the conventional MAS spectrum



- Individual lineshapes can be extracted to provide  $\delta_{\text{iso}}$ ,  $C_Q$ ,  $\eta_Q$
- If this is not possible, the centre of gravity can still give  $\delta_{\text{iso}}$  and  $P_Q$

# Cross Polarisation

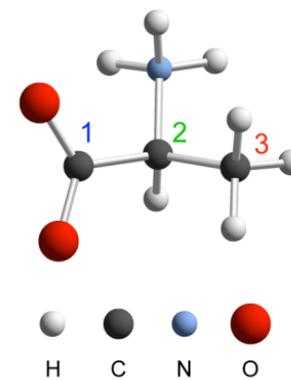
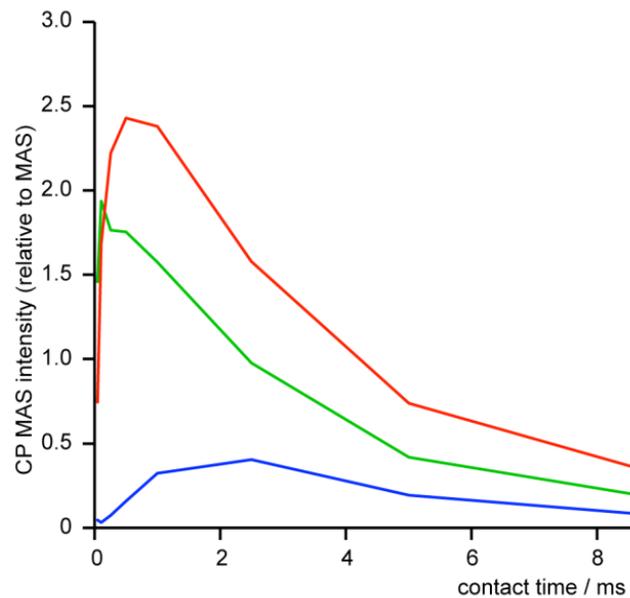
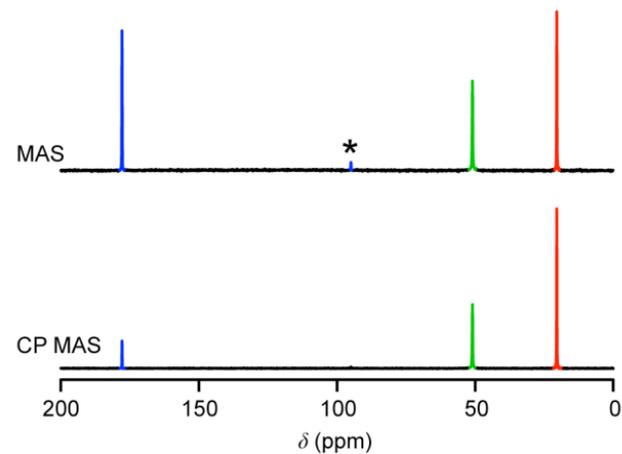
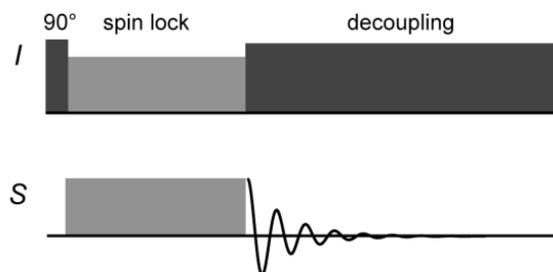
- Cross polarisation (CP) enhances the signal per transient by a theoretical maximum of  $\gamma_I/\gamma_S$ 
  - ~4 for  $^1\text{H}$ - $^{13}\text{C}$
  - ~6 for  $^1\text{H}$ - $^{29}\text{Si}$
  - ~10 for  $^1\text{H}$ - $^{15}\text{N}$

*in reality, this factor is rarely achieved due to relaxation effects, but factors of 2-3 for  $^{13}\text{C}$  are routine*

4-9× time saving
- CP also increases the signal per unit time since the magnetisation starts off on the higher- $\gamma$  nucleus, which typically relaxes faster
  - a factor of ~10 would be typical for  $^1\text{H}$ - $^{13}\text{C}$

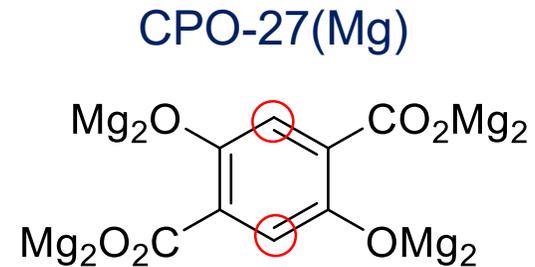
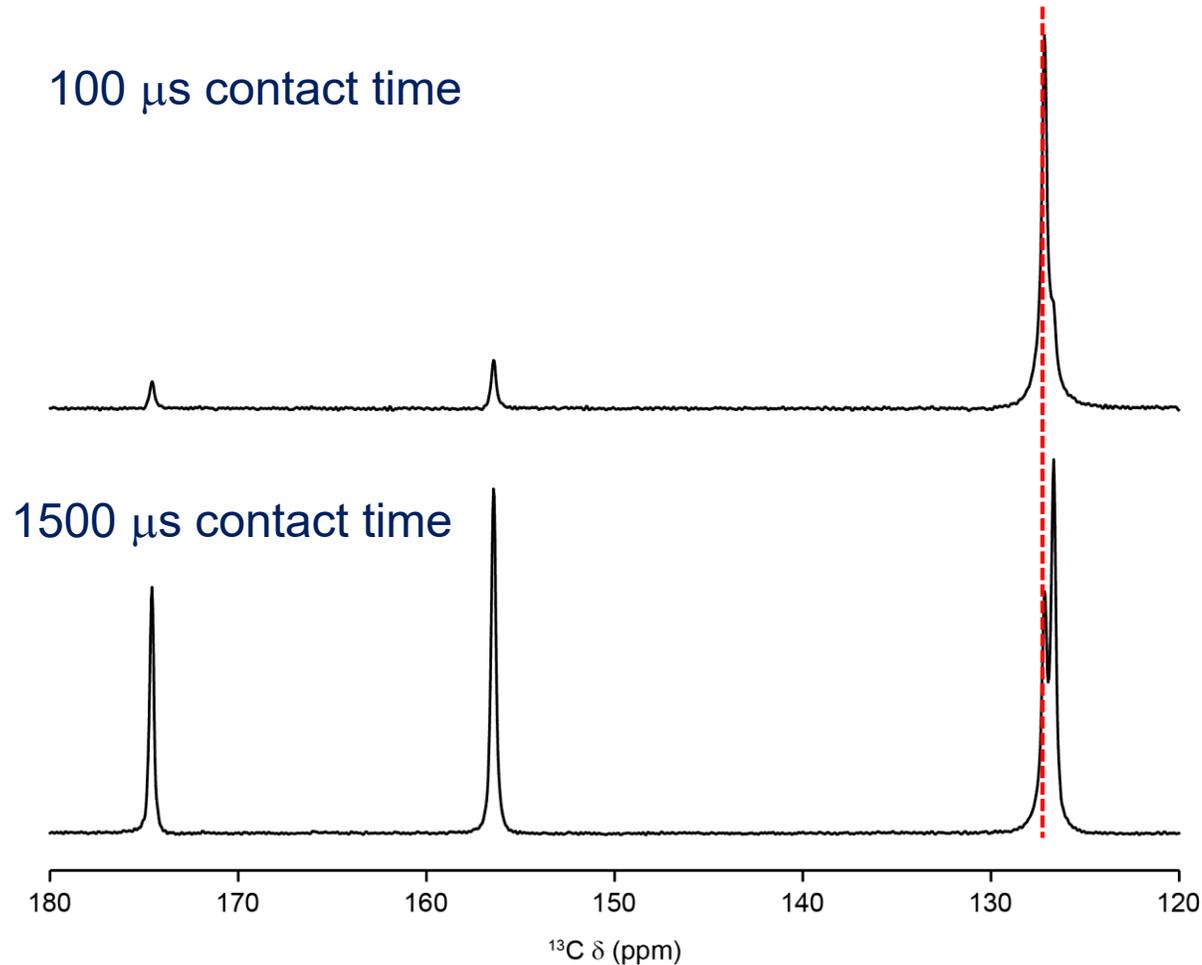
10× time saving
- A total time saving of a factor of ~50 is not uncommon
- CP is used routinely for  $^{13}\text{C}$ , but the technique is not quantitative and care must be taken when comparing signals from  $\text{C}_{\text{quat}}$  and  $\text{CH}_3$  or  $\text{Si}(\text{OSi})_3\text{OH}$  and  $\text{Si}(\text{OSi})_4$

# Cross Polarisation



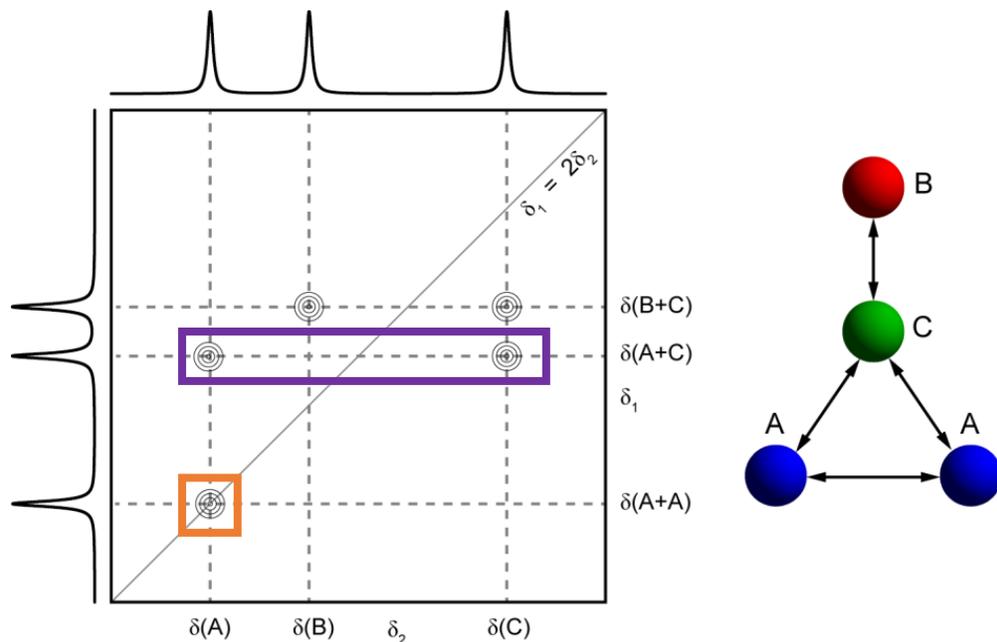
# Cross Polarisation

- The non-quantitative nature of CP can be used in “spectral editing” experiments, where a very short contact time is used to only show protonated species



# Other Common Solids Experiments

- Double-quantum (DQ) MAS is the solid-state equivalent of COSY
- Spectra look a bit different, since the experiment correlates DQ coherences with the MAS spectrum

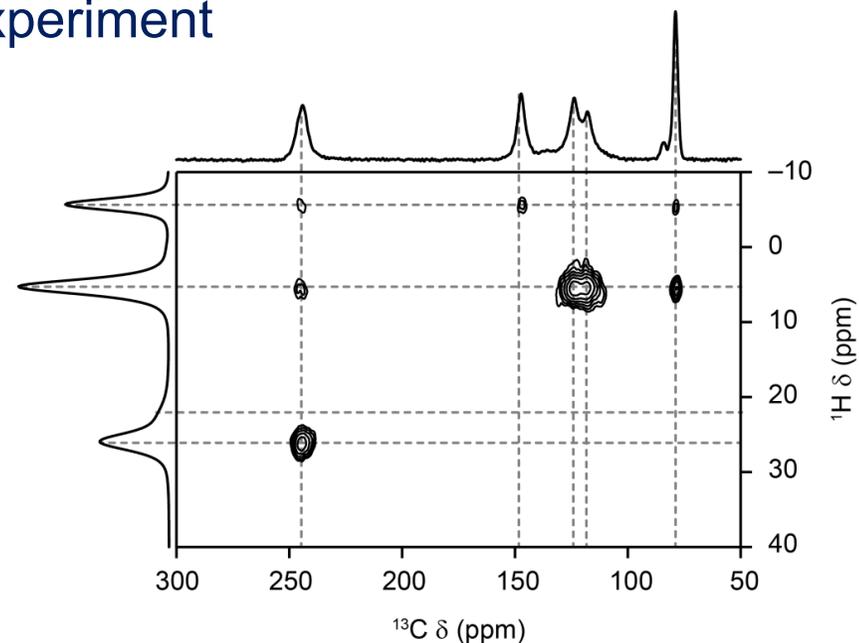
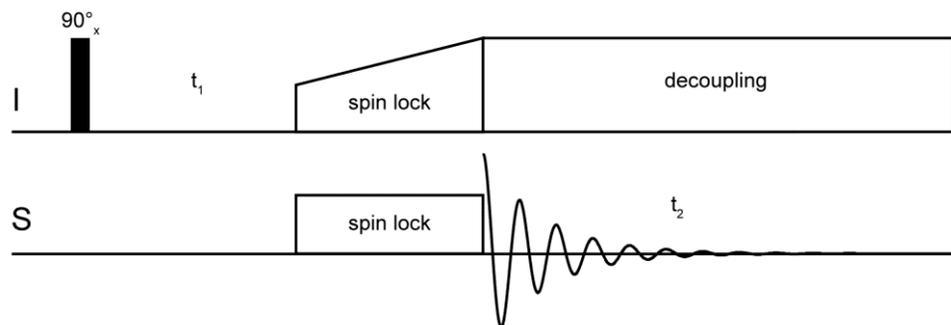


- pairs of peaks with the same DQ shift correspond to spatially close nuclei
- signals on the 2:1 diagonal correspond to pairs of spins with the same shift
- isolated spins (e.g.,  $O^{1H}$ ) may not be observed

- Many known DQ excitation schemes: BABA, POST-C7, R and C sequences...

# Other Common Solids Experiments

- HETCOR, or “HETeronuclear CORrelation” covers a wide range of 2D experiments where chemical shift information from spin I is correlated with chemical shift information of spin S
- The simplest sequence for solids is a CP-HETCOR experiment

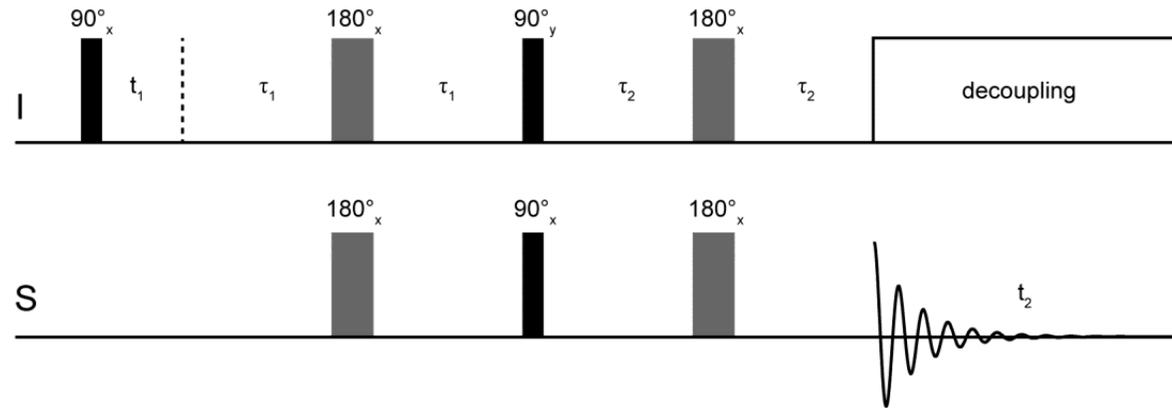


- A short contact time is normally used to show only spatially close pairs of nuclei (similar information to HSQC)

# Other Common Solids Experiments

- Other sequences such as INEPT and HMQC use the J coupling to transfer magnetisation

- At least, in theory...

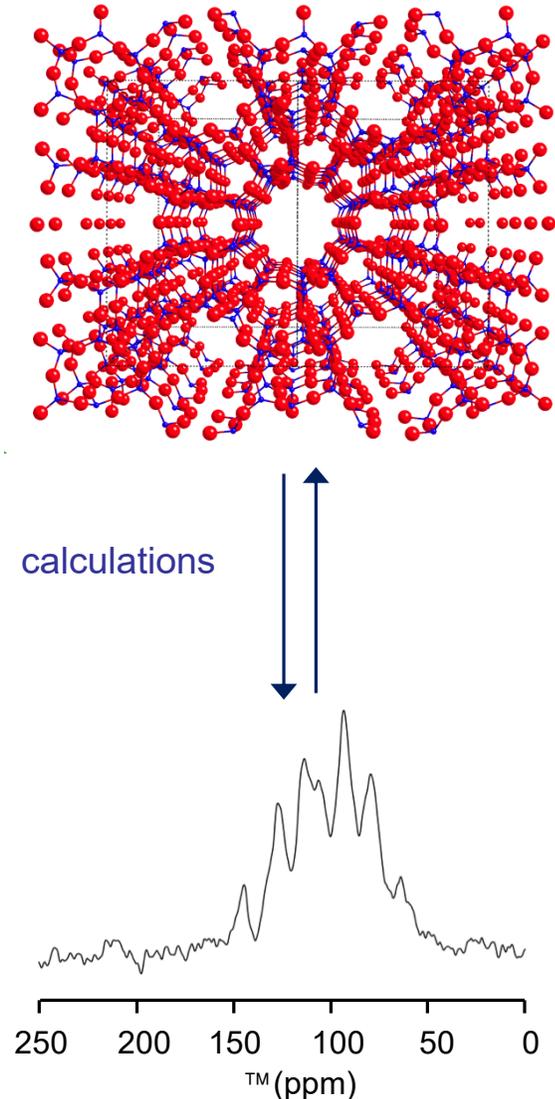


refocused INEPT

- In reality, there is generally still a contribution from the dipolar coupling

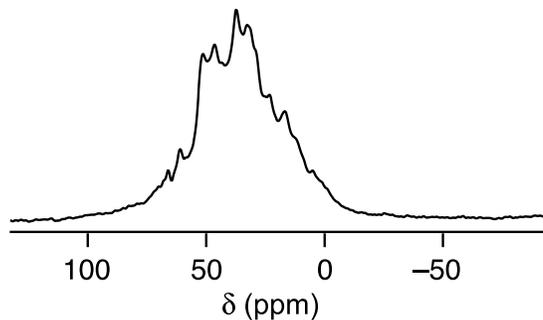
# First-Principles Calculations

- Calculation of NMR parameters from first principles can aid experimentalists
  - Spectral interpretation
  - Spectral assignment
  - Verification of NMR parameters
  - Additional information difficult to extract from experiment
  - Spectral prediction
  - Assessment of experimental feasibility
  - Flexible way to study the dependence of NMR parameters upon structure
  - Testing of structural models
  - For inorganic materials periodic calculations are most commonly used (density functional theory)



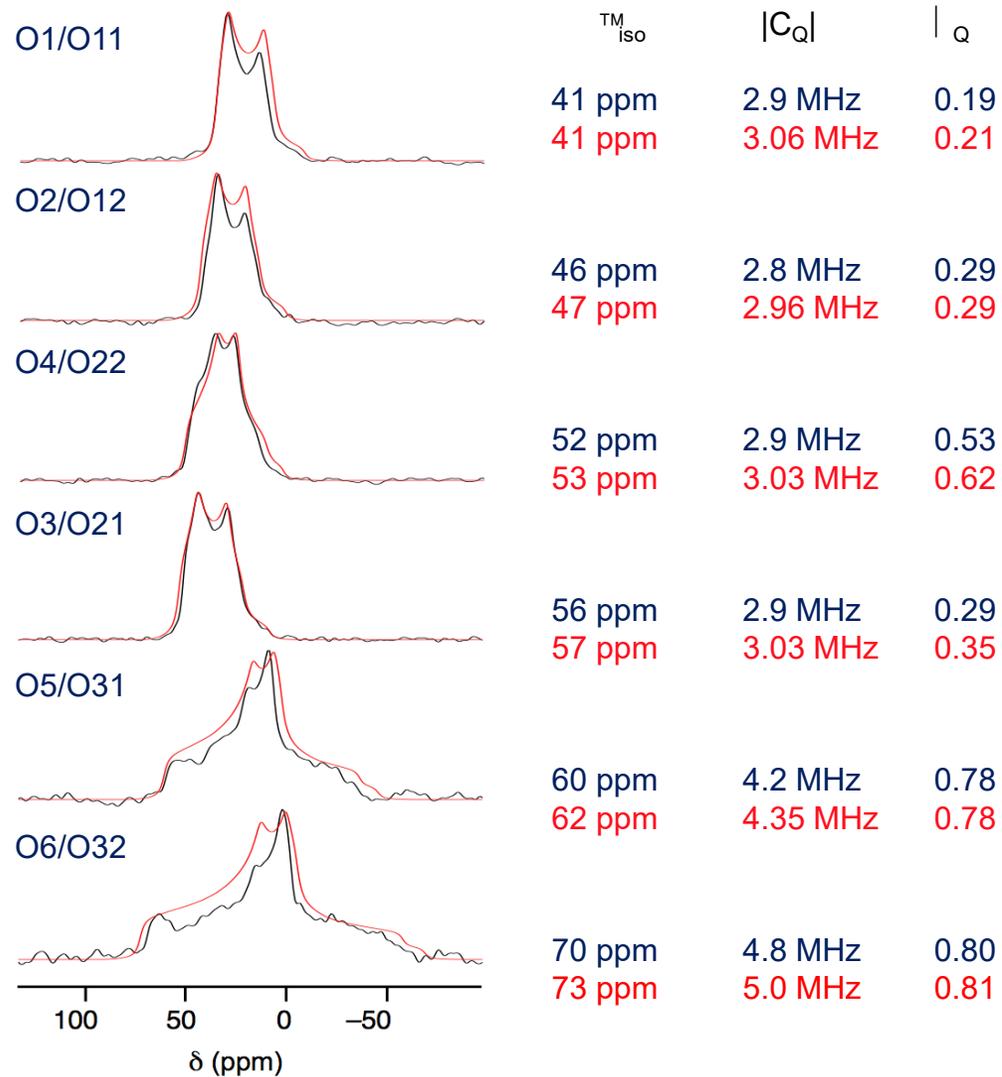
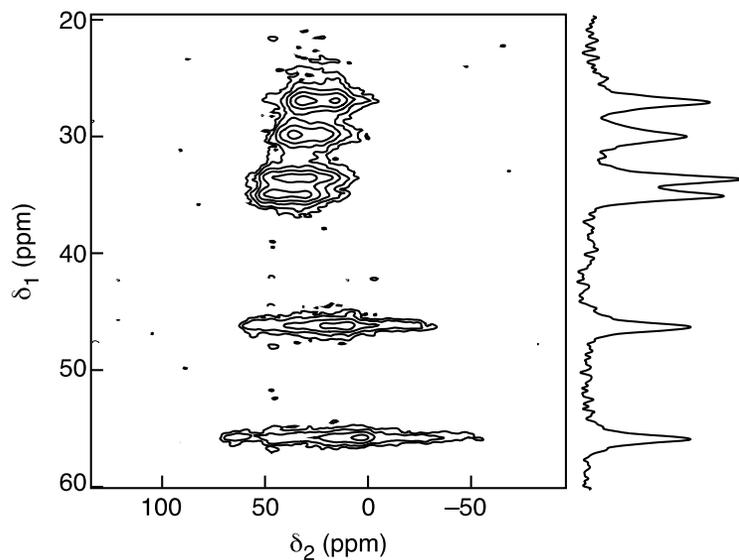
# First-Principles Calculations

9.4 T MAS



9.4 T MQMAS

6 O



## 3. Summary

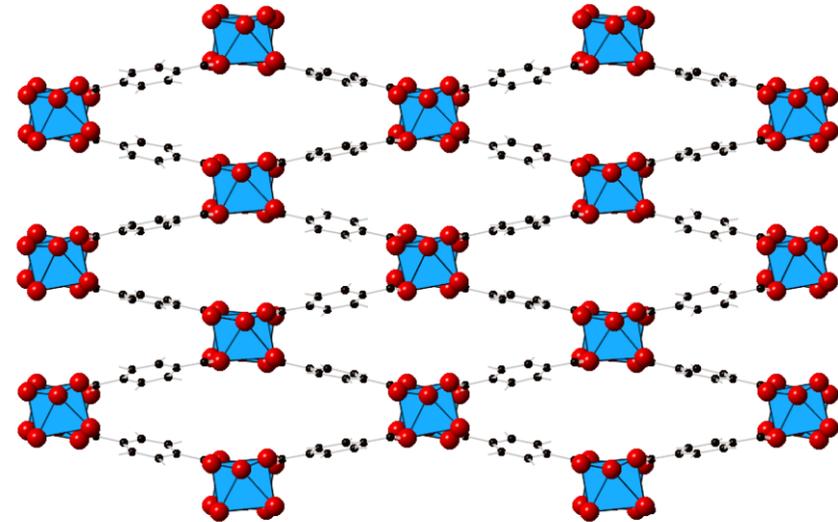
# Summary

- Interactions in NMR are anisotropic
  - molecules are always anisotropic, but rapid isotropic tumbling averages this in liquids
- Sometimes anisotropic broadening is useful
  - point symmetry/geometry information
- Most resonances in solids are broadened by multiple anisotropic interactions at once
  - broad, featureless, overlapping resonances are generally uninformative despite containing a lot of information!
- MAS can be used to improve resolution for  $I = 1/2$  nuclei
- Decoupling can remove spin-spin interactions but can't remove CSA or quadrupolar broadening
- More complicated experiments (most commonly MQMAS) are needed for quadrupolar nuclei

## 4. Case Study

# Metal-Organic Frameworks

- Metal-organic frameworks (MOFs) are a class of microporous material
- Porous structure results in a wide range of applications (e.g., gas adsorption, catalysis, and drug delivery)
- Increasing need to understand their structure-property relationships
  
- MIL-53 is composed of octahedrally coordinated metal nodes ( $\text{Al}^{3+}$ ,  $\text{Ga}^{3+}$ ,  $\text{Sc}^{3+}$ )
- The linker benzene-1,4-dicarboxylic acid (BDC) creates a “wine rack” like structure
- Bridging hydroxyl groups connect metal nodes together in rows



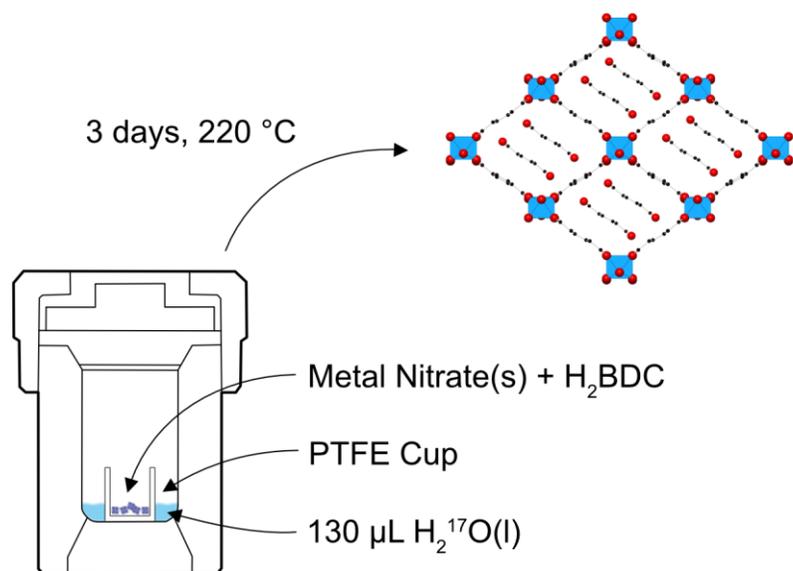
# Solid-State NMR of MOFs

- There are a range of NMR-active isotopes which can be studied in MOFs
- $^{13}\text{C}$  NMR spectra can be acquired using cross polarisation experiments to enhance sensitivity
- In order to acquire  $^{17}\text{O}$  NMR spectra on a reasonable timescale we must isotopically enrich these materials

Isotope	Natural Abundance	Spin	Quadrupolar Moment (Q) / fm <sup>2</sup>	Information
$^1\text{H}$	99.99%	1/2		Guest molecules present (e.g., water)
$^{13}\text{C}$	1.07%	1/2		Pore forms present (e.g., OP, CP, NP)
$^{17}\text{O}$	0.04%	5/2	-2.56	Metal distribution and pore forms present
$^{27}\text{Al}$	100%	5/2	14.66	
$^{71}\text{Ga}$	39.89%	3/2	10.7	

# $^{17}\text{O}$ Isotopic Enrichment

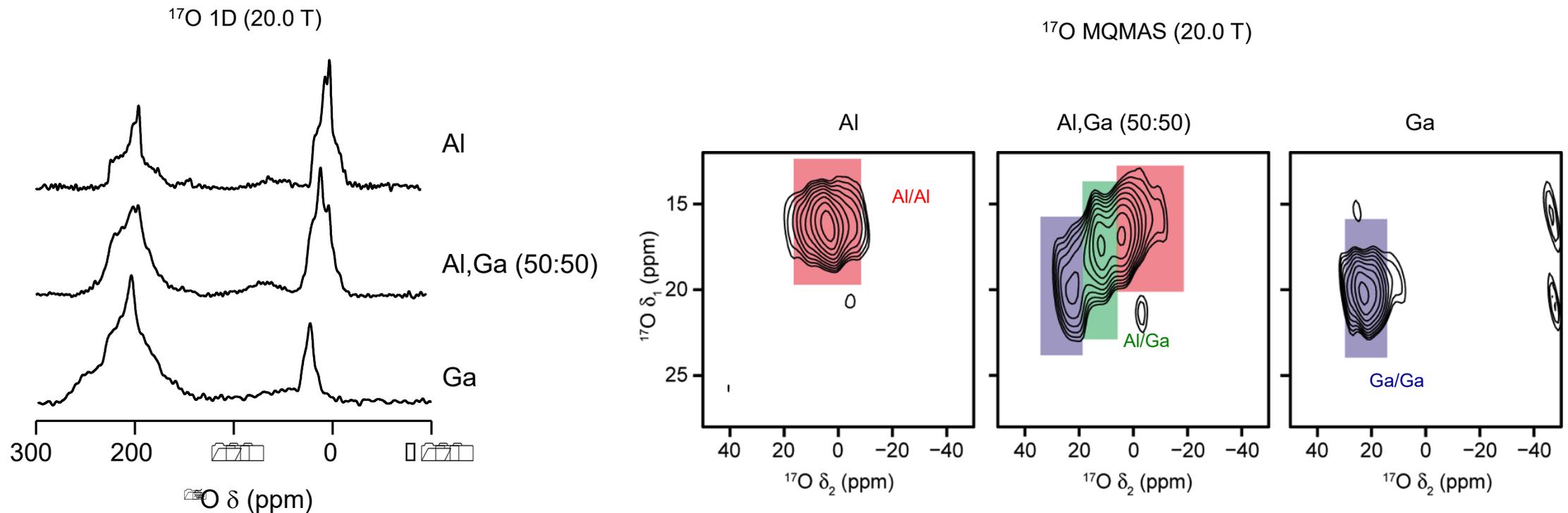
- Small solvent scale synthesis known as dry-gel conversion (DGC)
- Enables the use of isotopically enriched materials (90%  $\text{H}_2^{17}\text{O}$ , €1900 / mL) at a cost-effective level (130  $\mu\text{L}$ , ~ €250)



Compound	$\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ /mmol	$\text{Ga}(\text{NO}_3)_3 \cdot x\text{H}_2\text{O}$ /mmol	BDC /mmol
Al-MIL-53	1.38		1.81
Ga-MIL-53		1.38	1.81
Al,Ga-MIL-53 (80:20)	1.10	0.28	1.81
Al,Ga-MIL-53 (50:50)	0.69	0.69	1.81
Al,Ga-MIL-53 (20:80)	0.28	1.10	1.81

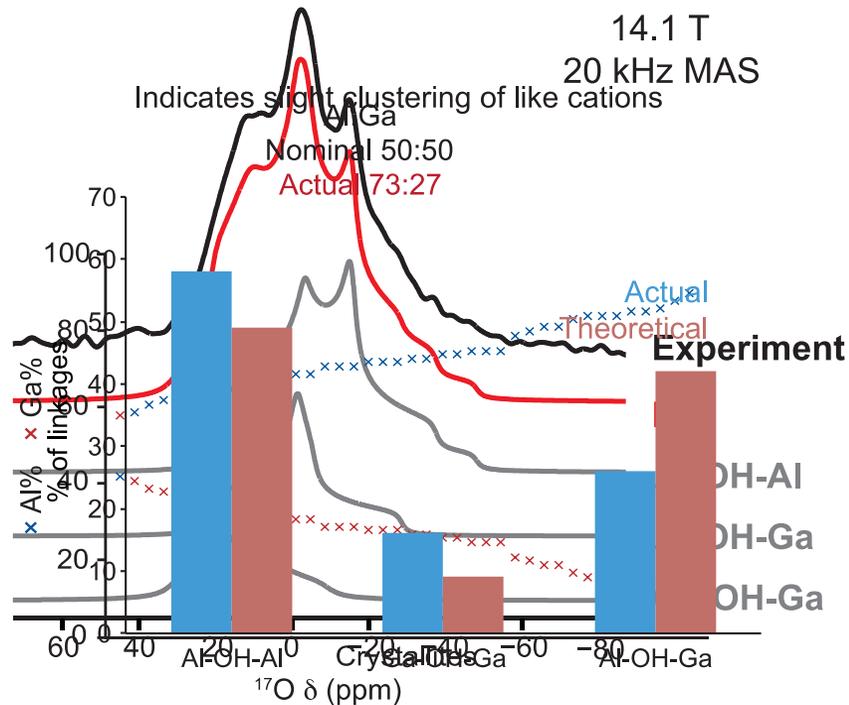
# $^{17}\text{O}$ NMR Spectroscopy

- Hydroxyl region in mixed-metal (Al,Ga)-MIL-53 (50:50) contains multiple resonances that are not simply the sum of the two end members



# Metal Distribution

- The hydroxyl region in the  $^{17}\text{O}$  MAS NMR spectrum provides information on the metal distribution
- More  $\text{Al}^{3+}$  containing linkages than expected for a Al:Ga 50:50 material

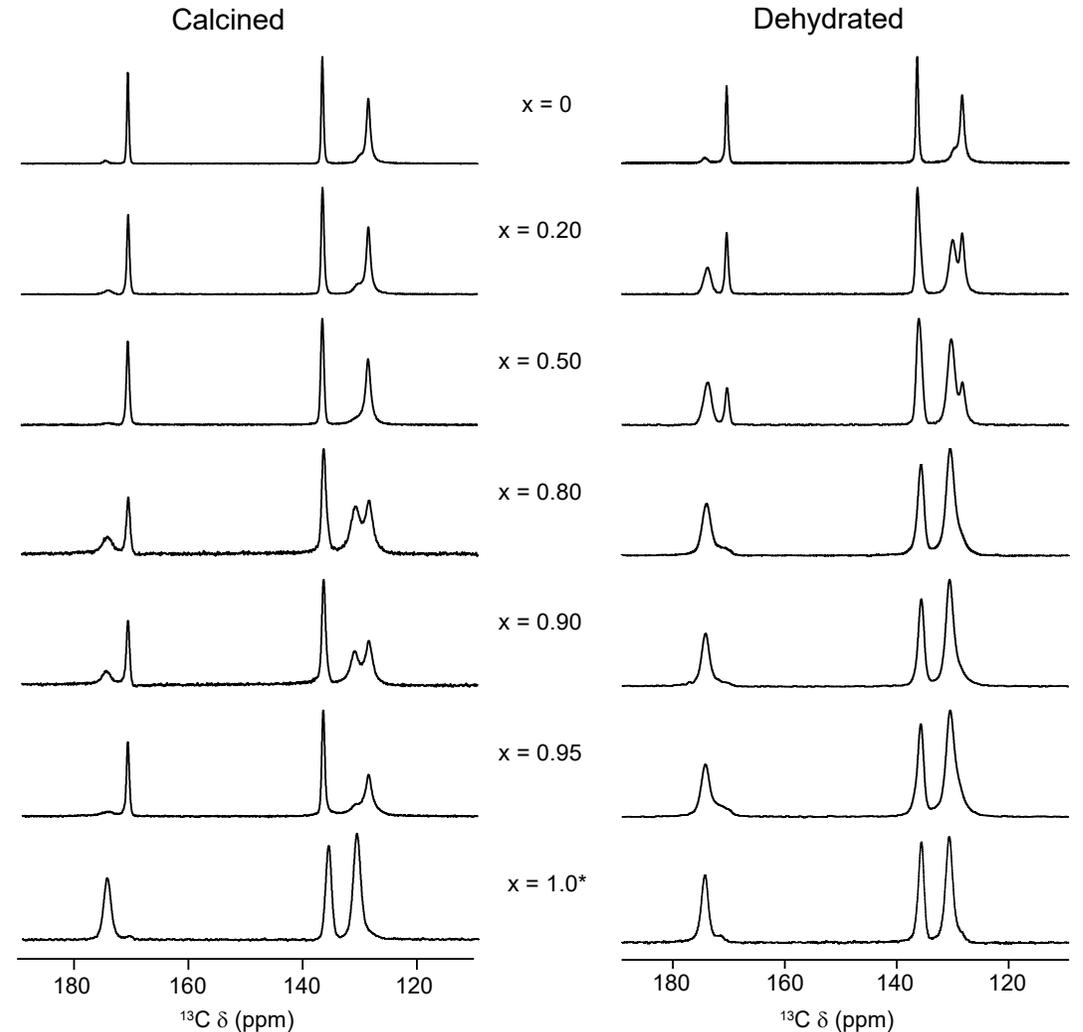


Hydroxyl	Al-OH-Al	Al-OH-Ga	Ga-OH-Ga
%	58(1)	26(1)	16(1)
$\delta_{\text{iso}}$ (ppm)	23(3)	25(3)	31(3)
$C_Q$ /MHz	5.4(2)	4.9(2)	3.9(2)
$\eta_Q$	0.7(1)	1.0(1)	1.0(1)

$^{17}\text{O}$  NMR fit indicates an actual Al:Ga of 70:30

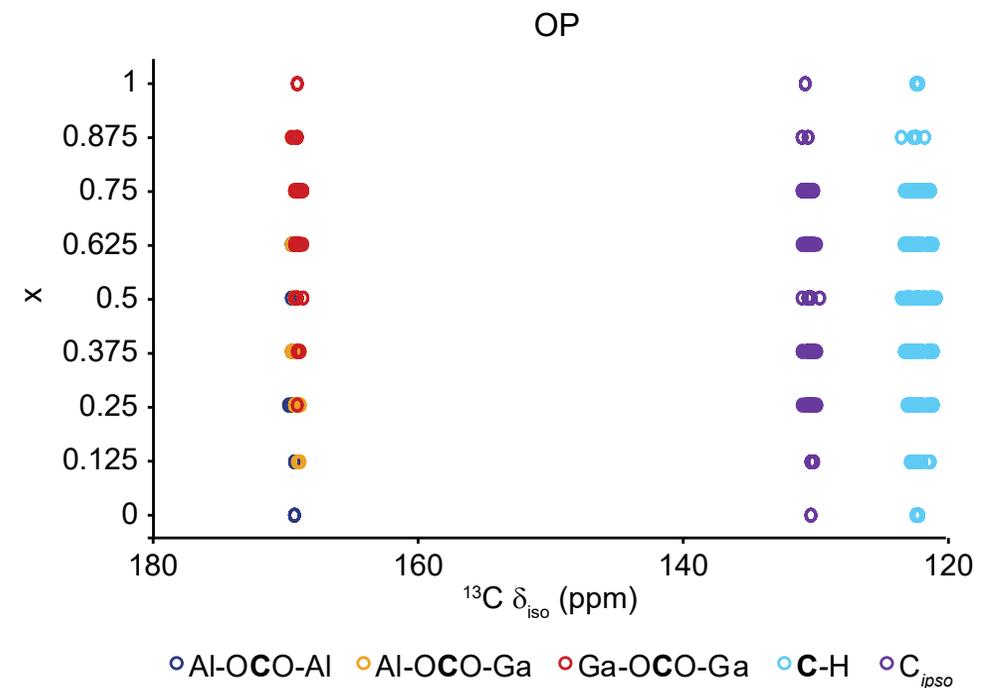
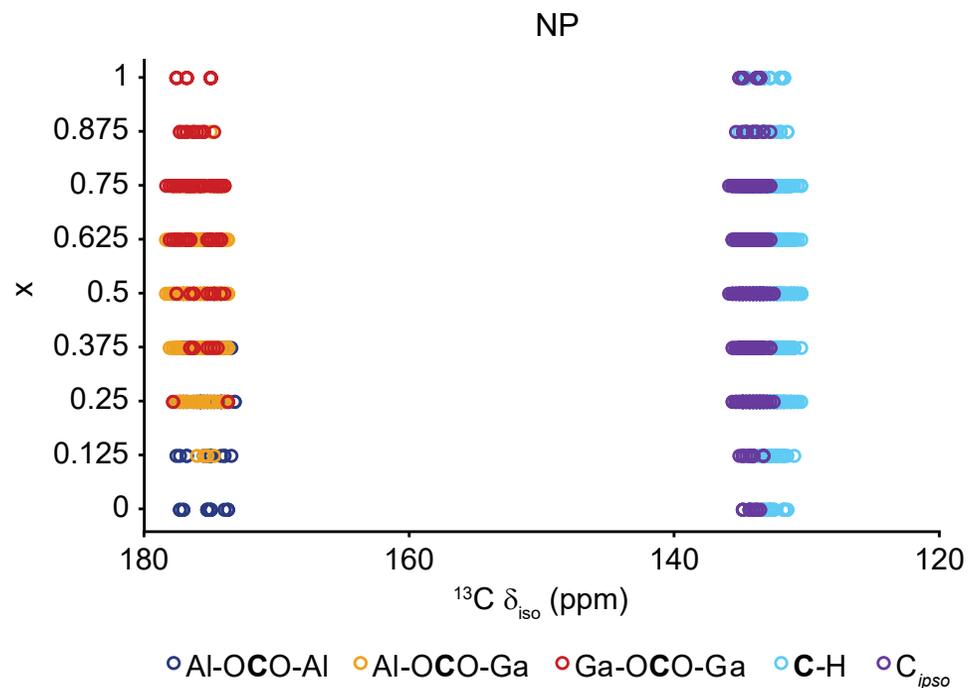
# Breathing Behaviour

- The  $^{13}\text{C}$  CP MAS NMR spectra can provide us with information on the breathing behaviour of (Al,Ga)-MIL-53
- Some  $^{13}\text{C}$  NMR spectra contain more than the three expected peaks
- We can use DFT calculations to help us assign these peaks



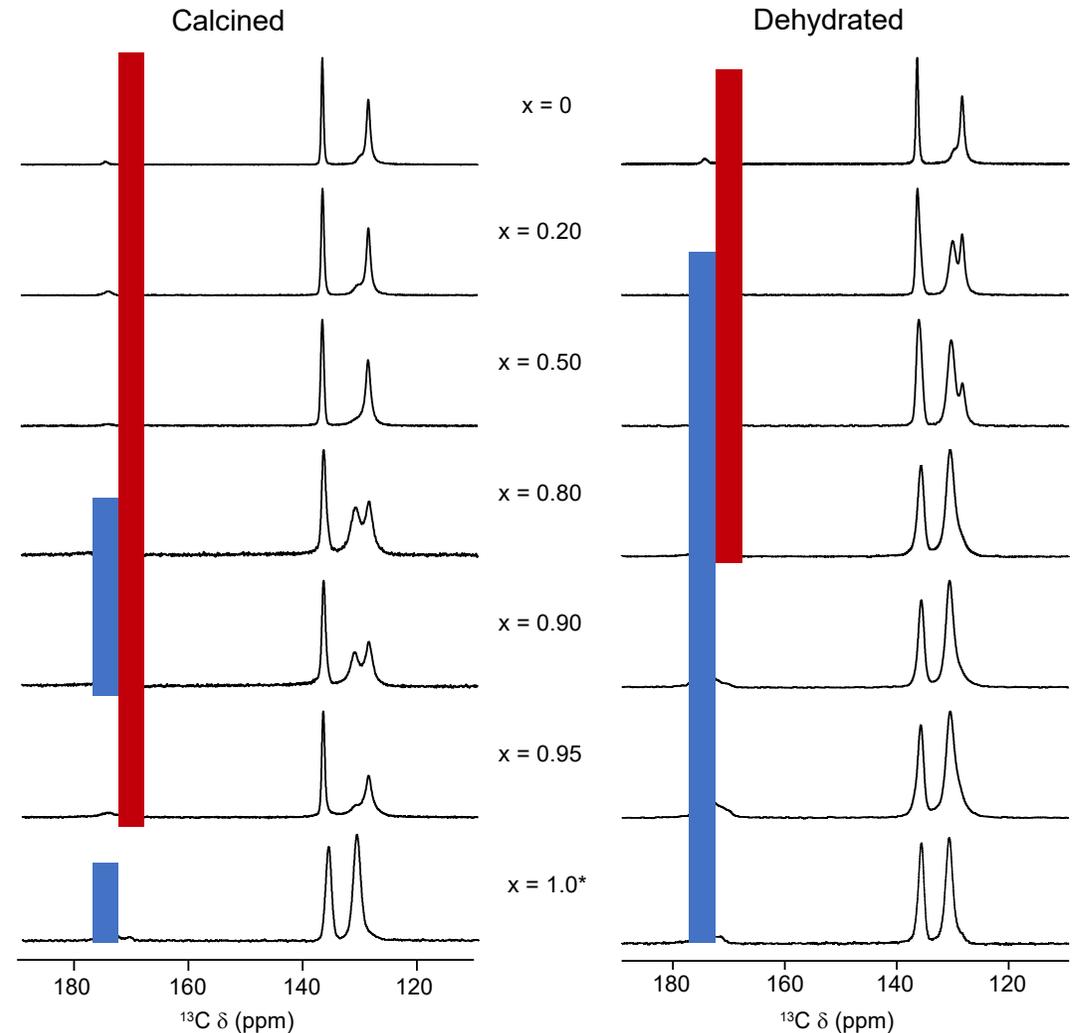
# DFT Calculations

- We can use DFT calculations to help us assign these peaks
- DFT predicts different  $^{13}\text{C}$  chemical shifts for the BDC linker depending on the pore form adopted by the framework



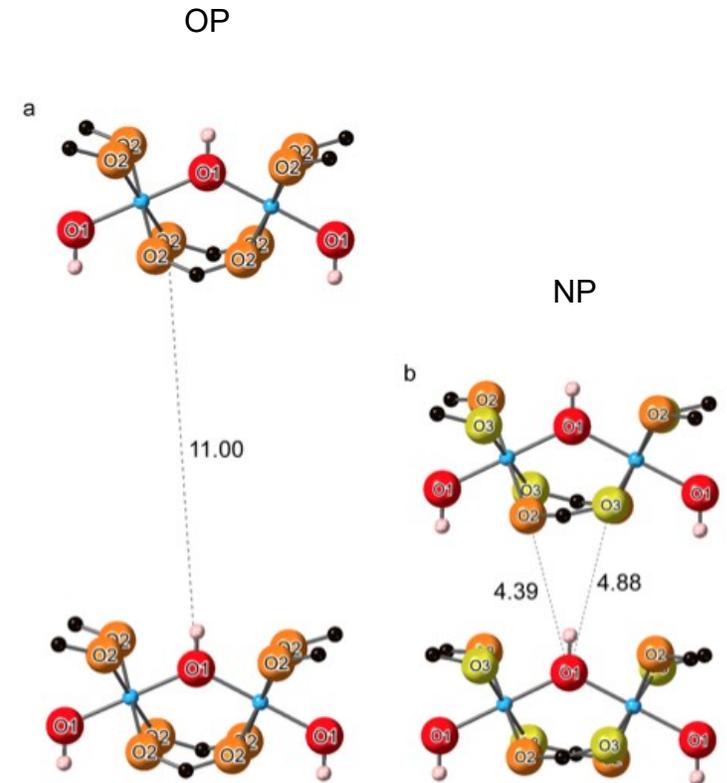
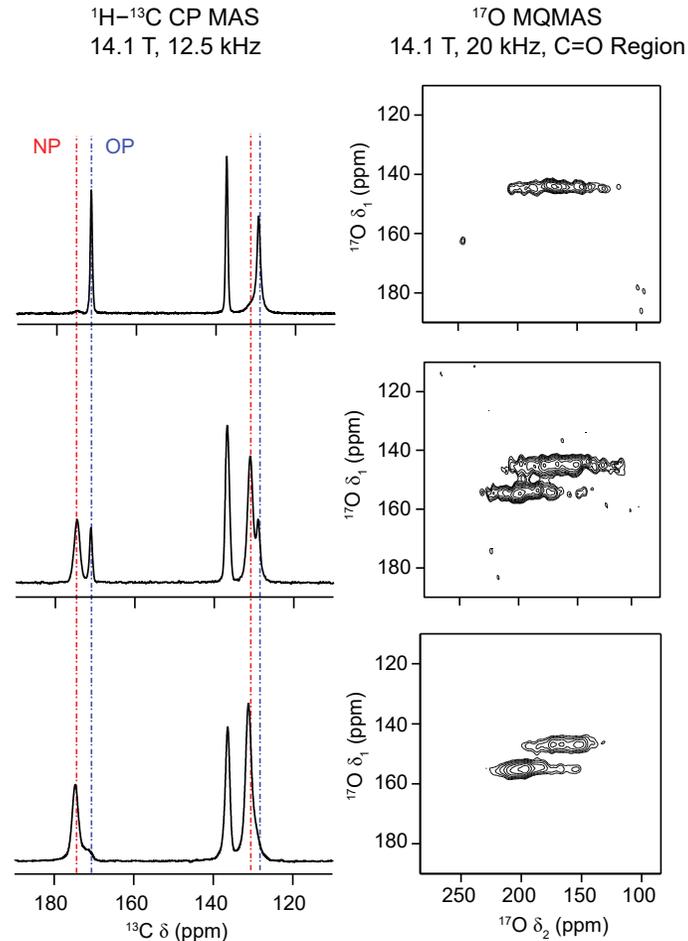
# Breathing Behaviour

- The  $^{13}\text{C}$  CP MAS NMR spectra can provide us with information on the breathing behaviour of (Al,Ga)-MIL-53
- Using information provided by DFT we can assign peaks to the two different pore forms
- Calcined structures show most materials adopt the OP form, with some adopting a mix of NP and OP forms ( $x = 0.8$  and  $0.9$ )
- Dehydrated structures show an increasing amount of NP form as the  $\text{Ga}^{3+}$  content increases



# Breathing Behaviour

- We can acquire further structural information from the  $^{17}\text{O}$  MQMAS spectra and DFT calculations
- $^{17}\text{O}$  MQMAS experiment contains only one resonance when the material is OP
- Unlike the NP form which contains two resonances
- DFT shows us these arise from inequivalent carboxyl oxygen environments



# Conclusions

- Solid-state NMR can provide us with a wealth of information
  - MAS is always used when acquiring NMR spectra
  - MQMAS experiments are essential for removing quadrupolar broadening
  - CP experiments can be used to improve sensitivity
  - Isotopic enrichment is sometimes necessary to acquire high sensitivity NMR spectra
- $^{17}\text{O}$  NMR spectra gives us information on the distribution of hydroxyl sites within mixed-metal MOFs
  - Preferential incorporation of  $\text{Al}^{3+}$ , small preference for clustering of like cations
- $^{13}\text{C}$  NMR experiments helps us to understand the breathing behaviour of these materials
  - Materials can adopt a mix of both the OP and NP forms depending on the metal ratio, calcined and dehydrated materials behave differently
- DFT calculations are helpful to assign resonances in solid-state NMR spectra

# Bibliography

- Many examples have been taken from the following reviews and references within:
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- G.P.M. Bignami, Z.H. Davis, D.M. Dawson, S.A. Morris, S.E. Morris, R.E. Morris and S.E. Ashbrook, *Chem. Sci.* **2018** 9 850-859.
- C.M. Rice, Z.H. Davis, D. McKay, G.P.M. Bignami, R.G. Chitac, D.M. Dawson, R.E. Morris and S.E. Ashbrook, *PCCP*, **2020** 22 14514-14526.