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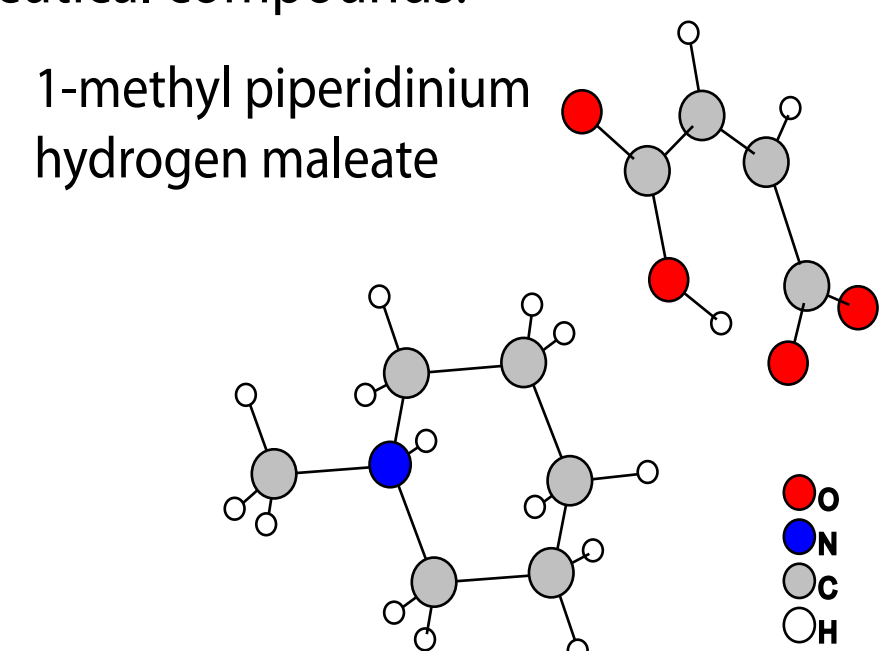
## Objectives

The objective of the project was to use solid-state magic angle spinning proton NMR to investigate pharmaceutical compounds.

Aims.

1. Use proton NMR techniques to study chemical environment of 1-methyl piperidinium hydrogen maleate

2. Compare experimental data with computer simulated system



Calculations were carried out using the CASTEP software package, which uses density functional theory to calculate atomic level data for a given crystal structure<sup>[2]</sup> including NMR chemical shifts.

CASTEP data provided input parameters for Spinevolution, a density matrix simulator, which was used to model the double quantum buildup of the 7 nearest protons to the -OH proton. The pulse sequence modelled used up to 7 POST-C7 elements.

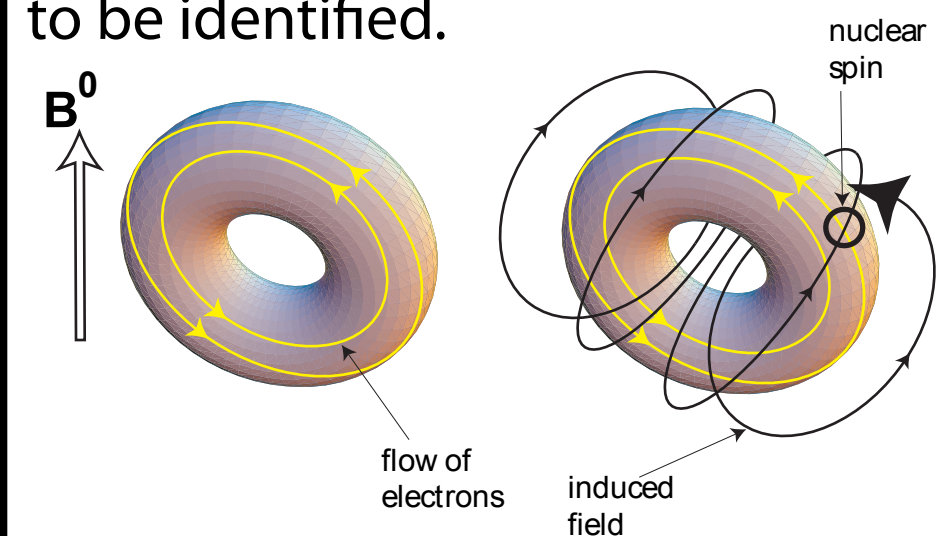
## Solid-state NMR

NMR can be used to identify chemical environments and give spatial information within molecules<sup>[1]</sup>.

A sample is placed in a large magnetic field,  $B_0$ , causing nuclei to precess about the direction of the field with a characteristic frequency,  $\omega_0$ .

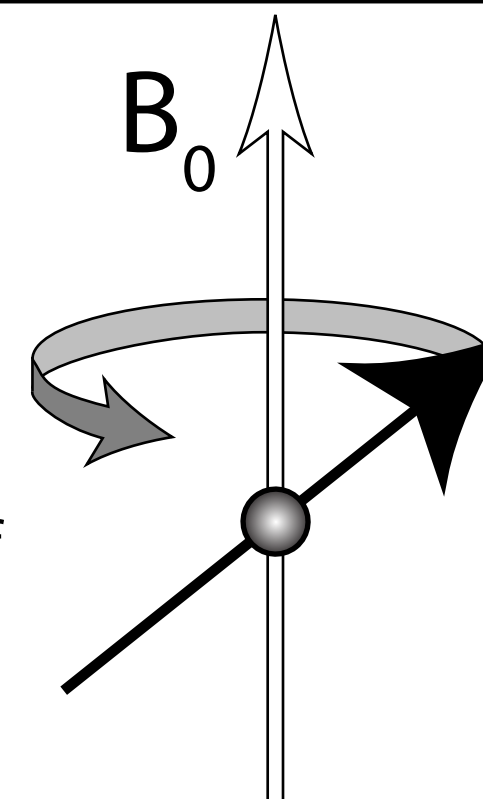
A pulsed field is then applied to the sample.

Electrons from nearby nuclei shield a given nucleus from  $B_0$  and cause a shift,  $\sigma$ , in the precession frequency. Detection of this altered frequency allows nuclei in different chemical environments to be identified.



This shifted frequency is given by:

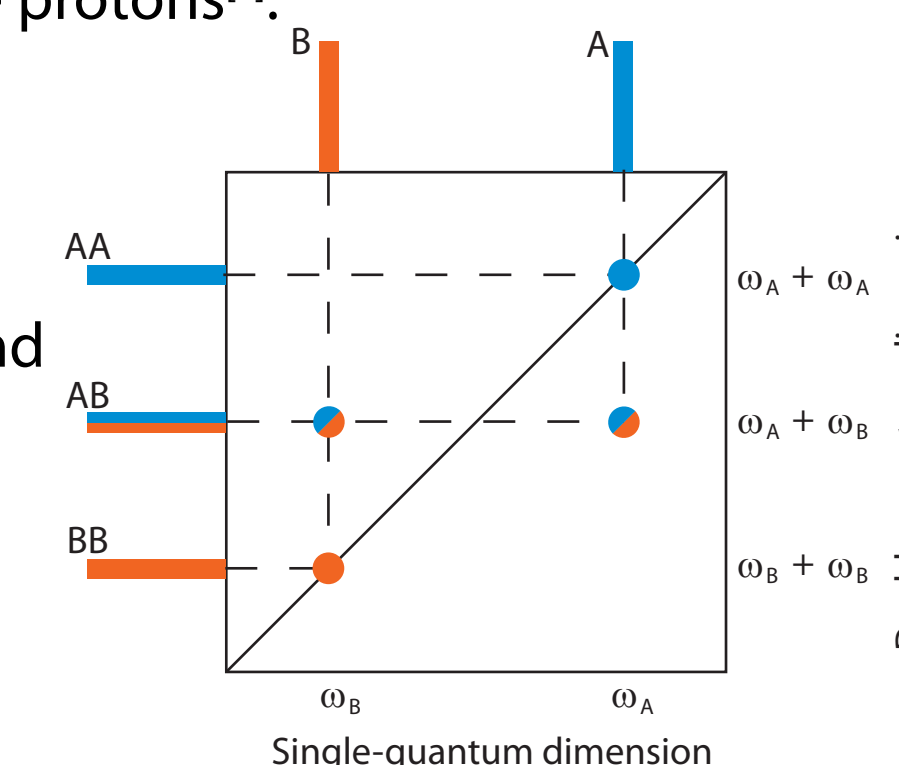
$$\delta(\text{ppm}) = \frac{\omega^0 - \omega_{\text{ref}}^0}{\omega_{\text{ref}}^0}$$



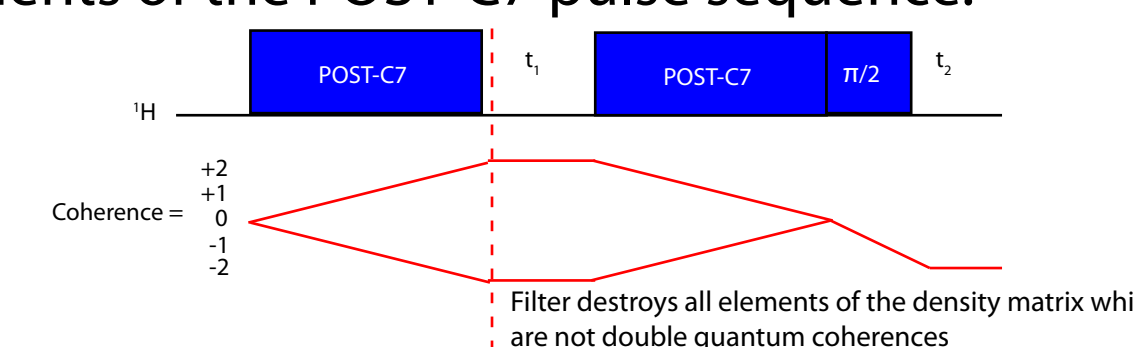
## 2D Double Quantum Correlation Experiments

The dipolar interaction between nuclei in a compound is dependent upon their spatial proximity and can be used to detect distances ( $< 3\text{\AA}$ ) between nuclei via a two dimensional double quantum spectrum, in this case on the protons<sup>[2]</sup>.

On diagonal peaks coincide with an interaction between two like protons in close proximity, and off diagonal peaks of an interaction between two unlike protons.

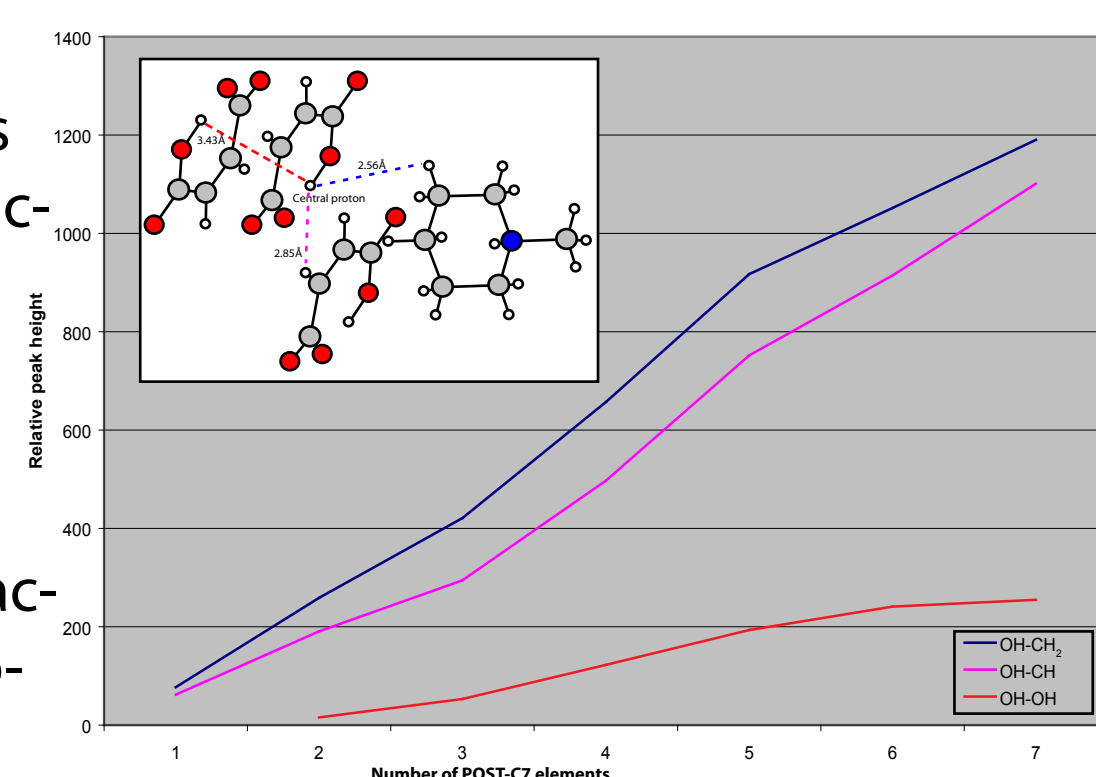


The pulse sequence used for both experiment and simulation uses elements of the POST-C7 pulse sequence.



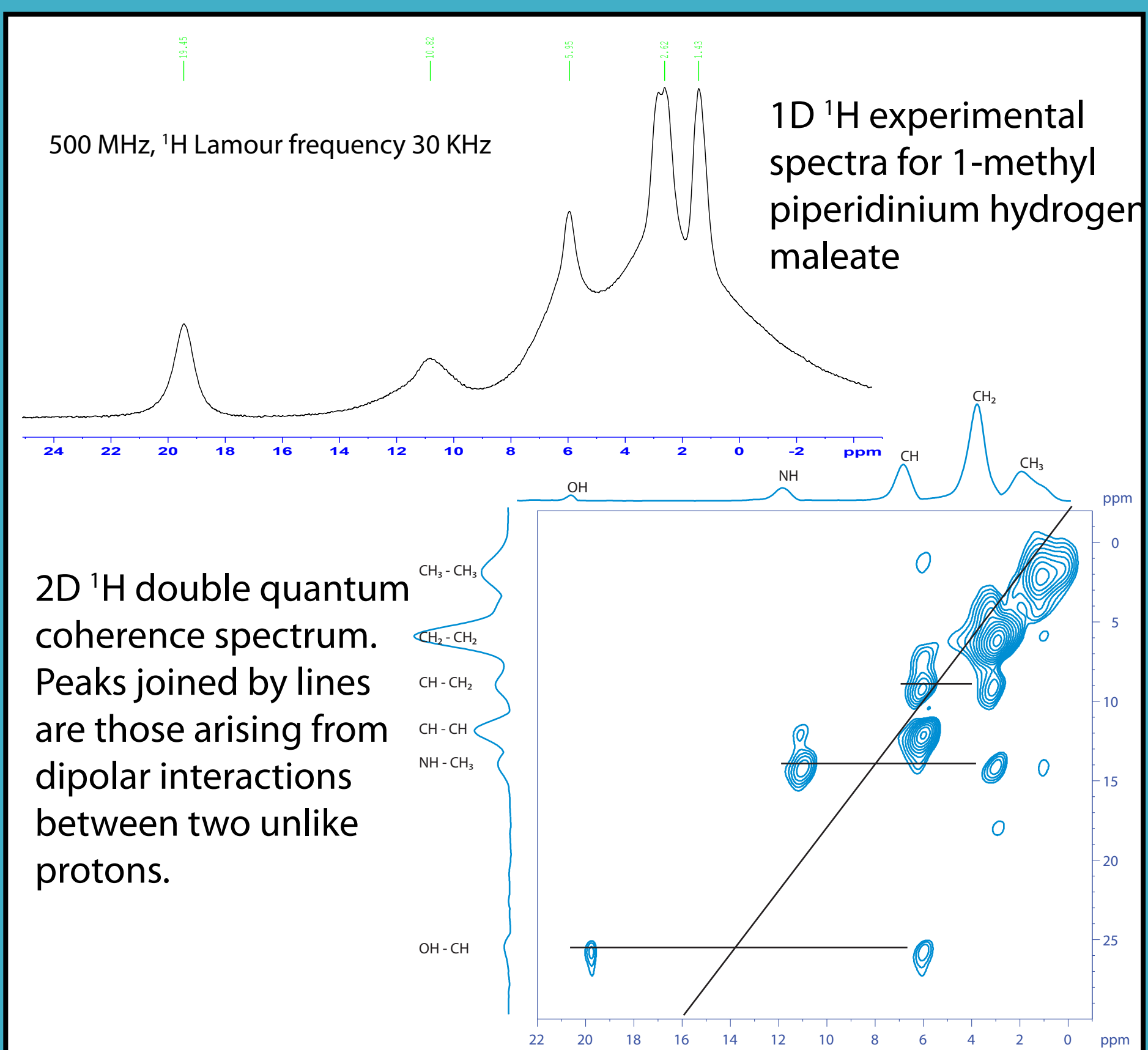
## CASTEP and Simulations

The steeper buildup curves show intermolecular interactions between OH-CH<sub>2</sub> (2.56Å) and OH-CH (2.85Å). The slower buildup corresponds to the longer distance OH-OH (3.43Å) interaction, calculated by Spinevolution.



Chemical Group	Chemical Shift (ppm)	
	CASTEP	Experiment
CH <sub>3</sub>	0.64	1.43
CH <sub>2</sub>	2.62	2.62
CH	6.14	5.95
NH	8.38	10.82
OH	22.15	19.45

The calculated chemical shift values differ to the experimental data, but retain the same general trend.



## Results

Solid-state NMR was used to experimentally resolve different proton chemical sites within 1-methyl piperidinium hydrogen maleate. The close proximities of these protons was illustrated through the use of proton double quantum coherence experiments using the POST-C7 pulse sequence.

Agreement was seen between the experimental data, and first principles calculations carried out by CASTEP. These were used to produce density matrix simulations using Spinevolution.

The buildup curves produced by Spinevolution indicated the difference in proximities between different chemical groups within the molecule.

### Acknowledgements

I would like to thank Dr. Steven Brown and Jonathan Bradley for their support and guidance throughout this project.

[1] Spin dynamics: Basic principles of NMR spectroscopy. Malcolm Levitt. Wiley, 2001

[2] Introduction to NMR spectroscopy. Melinda J. Duer. Blackwell, 2004

[3] All-electron magnetic response with pseudopotentials: NMR chemical shifts. Pickard, Mauri. Physical Review B, vol 63, 2001