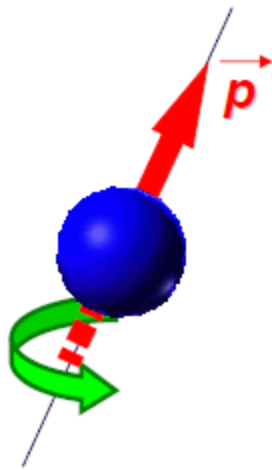


# What is a spin?



A difficult question... but we may use a picture:



If the nucleus has a *spin* („rotation“), the *angular momentum*  $\vec{p}$  is a vector parallel to the axis of rotation

The magnitude of the angular momentum is given by the *spin quantum number*  $I$ :

$$|p| = h/2\pi * \sqrt{I(I+1)}$$

# Nucleus and spin quantum number $I$



$$M = Z + N$$

$M$  = mass number

$Z$  = number of protons (atomic number)

$N$  = number of neutrons

$M$  even  $\Rightarrow I$  (spin quantum number) is an even number

-  $Z$  even,  $N$  even  $\Rightarrow I = 0$

Ex.:  $^{16}\text{O}$ ,  $^{12}\text{C}$ : not NMR observable!

-  $Z$  uneven,  $N$  uneven  $\Rightarrow I = 1, 2, 3, \dots$

Ex.:  $^2\text{H}$ ,  $^{14}\text{N}$ : quadrupolar moment results in broad lines!

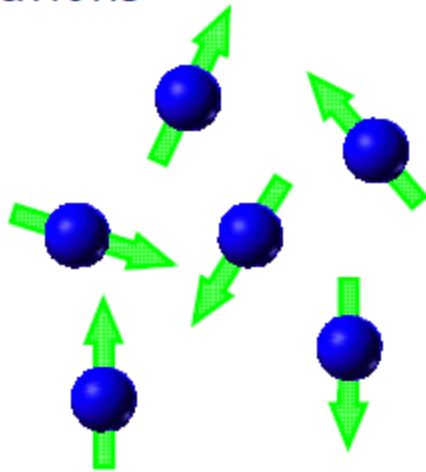
$M$  uneven  $\Rightarrow I = 1/2, 3/2, 5/2, \dots$

Ex.:  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{15}\text{N}$ ,  $^{19}\text{F}$ ,  $^{31}\text{P}$  ( $I = 1/2$ ): sharp lines, good for NMR;

$^{27}\text{Al}$ ,  $^{11}\text{B}$  ( $I > 1/2$ ): quadrupolar moment!

# Magnetic moment ( $I=1/2$ ) & external field

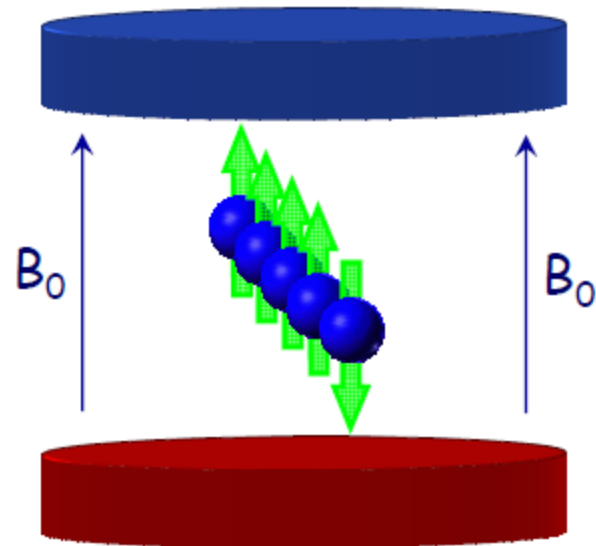
Without external magnetic field: magnetic moments are distributed over all orientations



Sum of magnetic moments (macroscopic magnetization):

is zero !

With external magnetic field: alignment

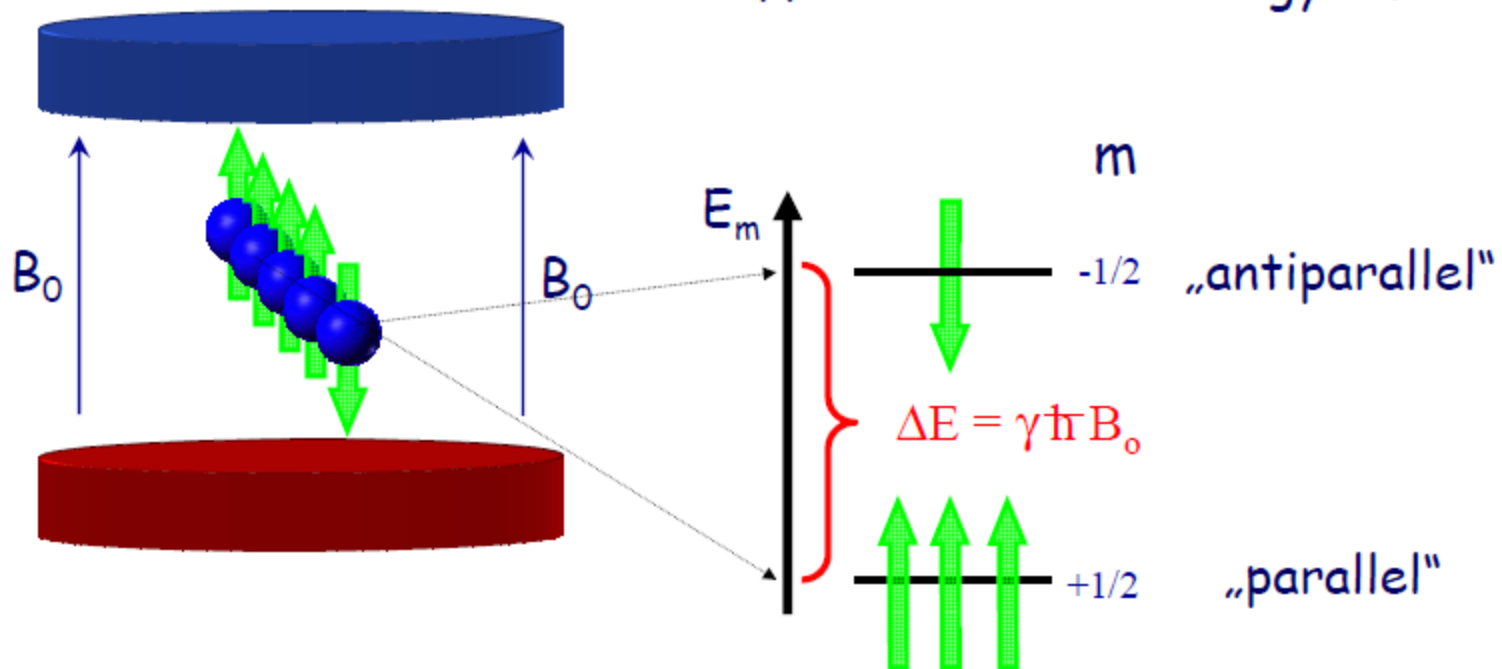


we have a net magnetization !

# Energy levels ( $I=1/2$ )



Due to „hyperfine interaction“ we observe for  $I = 1/2$  two different Zeeman energy levels:



# Intensity of net magnetization $M_0$



The sensitivity (intensity of net magnetization  $M_0$ ) depends on:

## A) the natural abundance of the nucleus

natural abundance of $^1\text{H}$ :	99.989 %
natural abundance of $^{13}\text{C}$ :	1.108 %
natural abundance of $^{15}\text{N}$ :	0.368 %

⇒ sensitivity of nuclei with low natural abundance can be enhanced by isotopic labeling, for example for protein-NMR or for detection of  $^{15}\text{N}$  in coordination compounds

$$\gamma(^1\text{H}) = 26.75$$

$$\gamma(^{13}\text{C}) = 6.73$$

# Inductive effects on chemical shifts

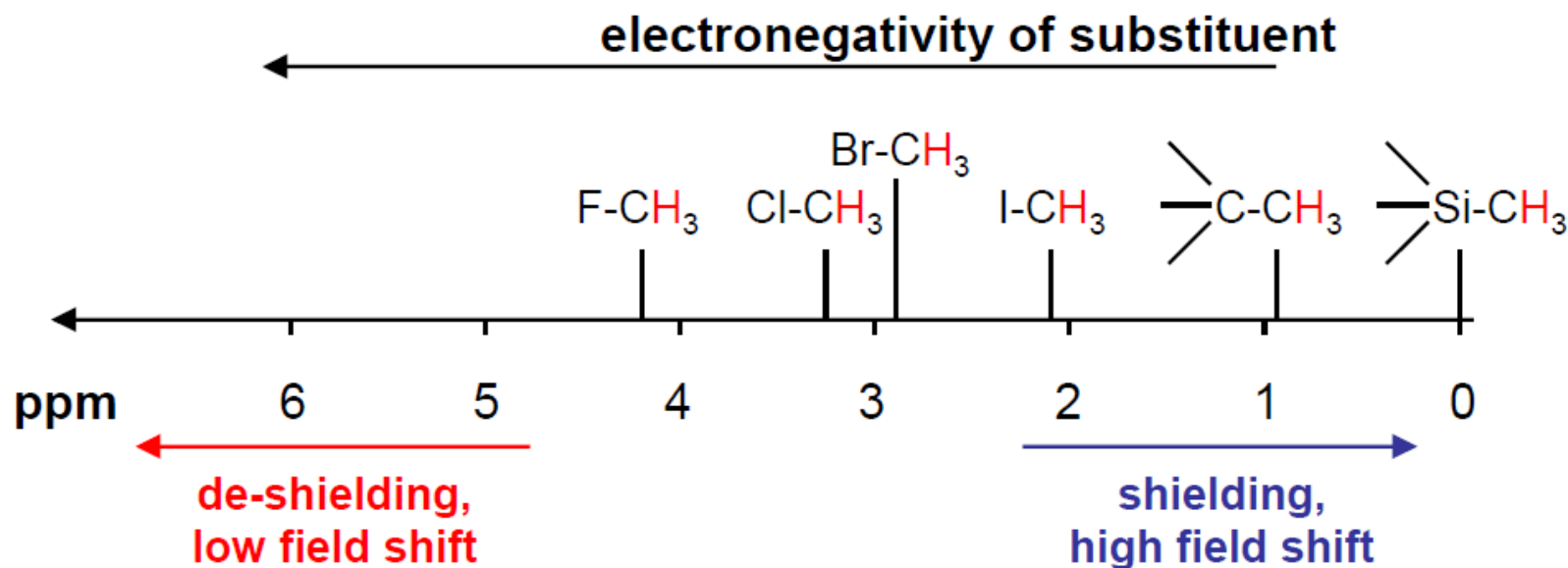


For better comparison of data: Hz  $\rightarrow$  ppm

$$1 \text{ ppm} = \text{Spectrometer Frequency in Hz} / 10^6$$

The chemical environment around an observed nucleus (e.g.  $^1\text{H}$ ) influences the chemical shift ( $\delta$ )

- High electron density around the nucleus shields the nucleus  $\rightarrow$  low resonance frequency = high (magnetic) field
- Low electron density around the nucleus de-shields the nucleus  $\rightarrow$  high resonance frequency = low (magnetic) field

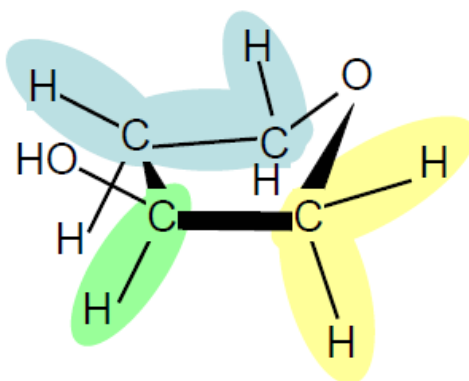


# Signal multiplicity and coupling



## Coupling between Nuclei give rise to line splitting often in a certain multiplicity pattern

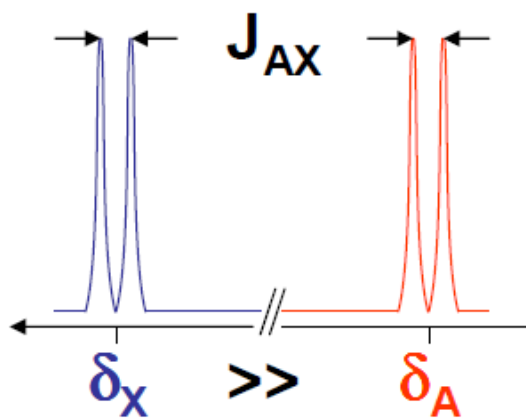
- Coupling constant  $J$  = distance between lines in Hz (in 1st order spectra)
- Coupling constant is independent of the field strength
- Scalar coupling can be observed between 1 or more bonds:  
 $^1J$  (one bond-),  $^2J$  (geminal-),  $^3J$  (vicinal-) or  $^nJ$  (multiple bond-)



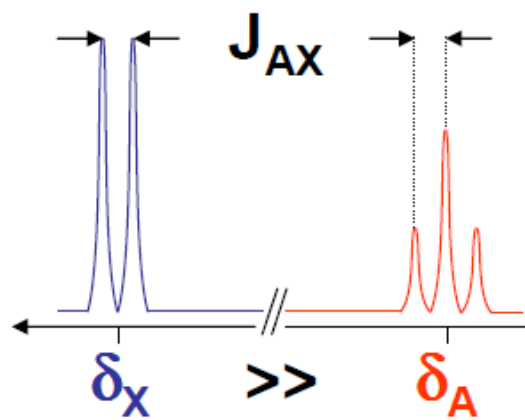
Observable couplings:  $^2J_{HH}$  and  $^3J_{HH}$  sometimes  $^4J_{HH}$

$^1J_{CH} \gg ^2J_{CH}, ^3J_{CH}$

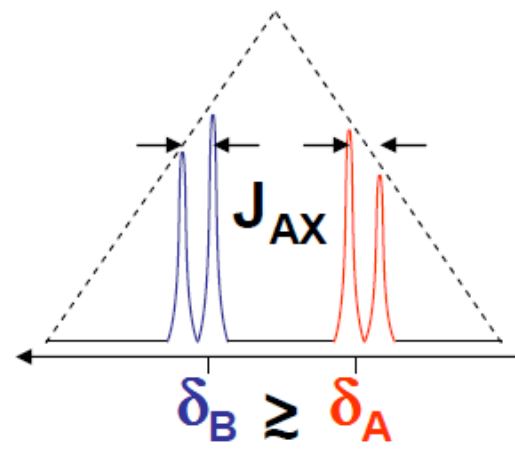
**AX** spin system



**AX<sub>2</sub>** spin system



**AB** spin system



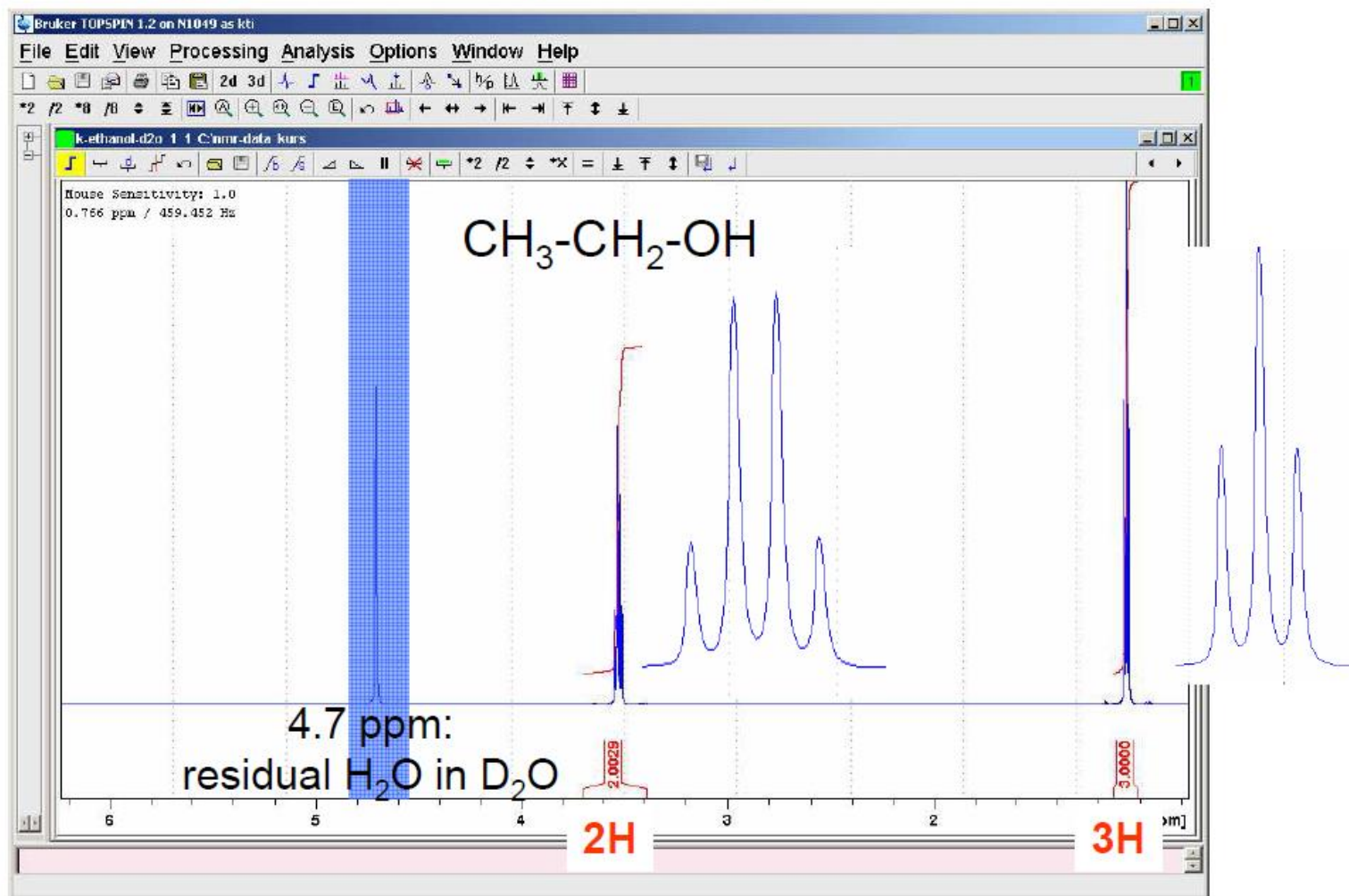


# Exchange phenomena

## Chemical exchange with solvent $^2\text{H}$

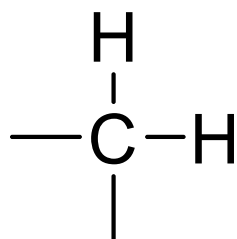


Ethanol in  $\text{D}_2\text{O}$ :  $-\text{OH}$  exchanges with  $\text{D}_2\text{O} \Rightarrow \text{OH}$  line not observed

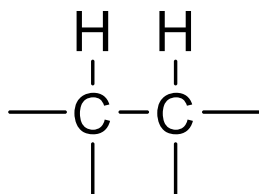


# Factors influencing coupling constant “J”

Number of bonds intervening between nuclei is important, since the coupling is transmitted via the electrons. Direct coupling  $^{13}\text{C}$ - $^1\text{H}$  is a one bond coupling.



$^2\text{J}$  varies from 10-18 Hz

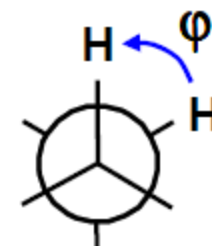


$^3\text{J}$  varies from 0 to 12 Hz

## Factors influencing geminal coupling

- The electronegativity of an attached substituent alters the value of geminal coupling. In  $\text{CH}_2\text{-X}$ , the gem coupling will range from 12 to 9 Hz as the electronegativity of X is increased.

## Factors influencing vicinal coupling

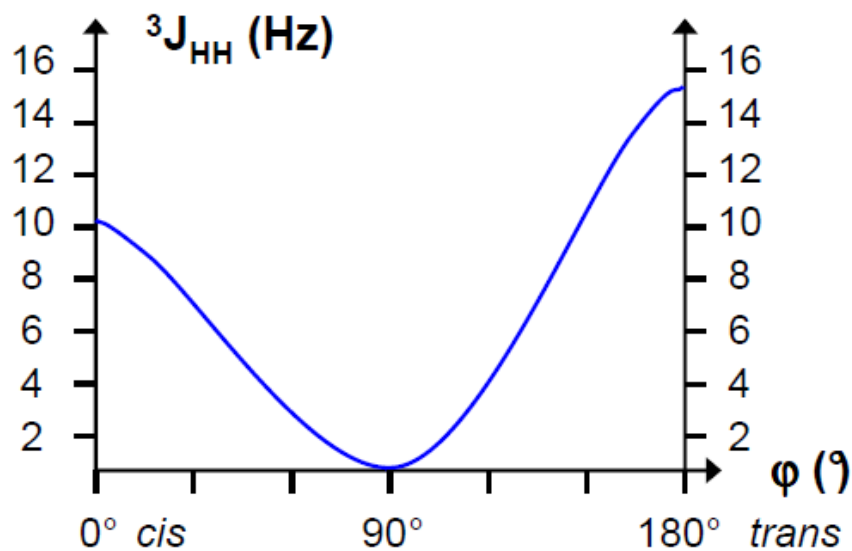


Electronegativity of attached substituents alters the value of vicinal coupling. The more electronegative the substituent, the smaller the value of  $J_{vic}$ . In ethane  $J = 8 \text{ Hz}$ ; halogen substituted ethane it is lowered to **6-7 Hz**.

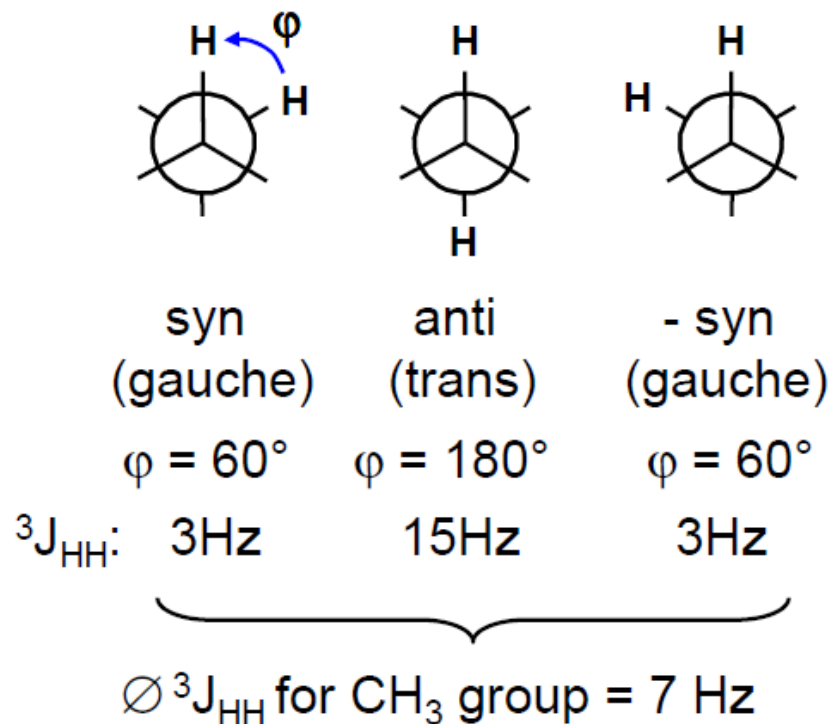
### Karplus equation

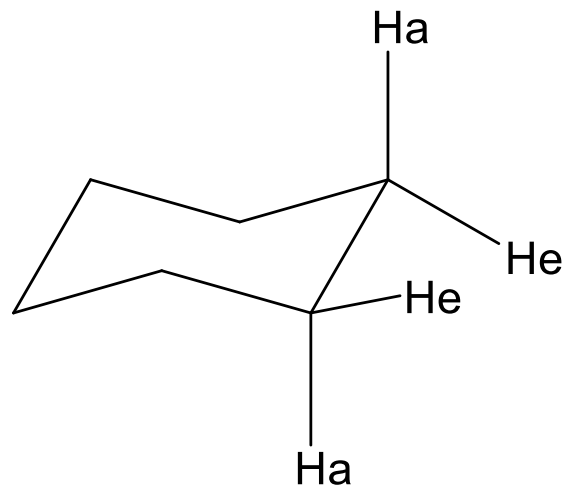
When  $\phi$  is between  $0^\circ$  and  $90^\circ$ ;  $J_{vic} = 8.5 \cos^2 \phi - 0.28$

When  $\phi$  is between  $90^\circ$  and  $180^\circ$ ;  $J_{vic} = 9.5 \cos^2 \phi - 0.28$



It also works on double bonds  
for cis / trans distinction



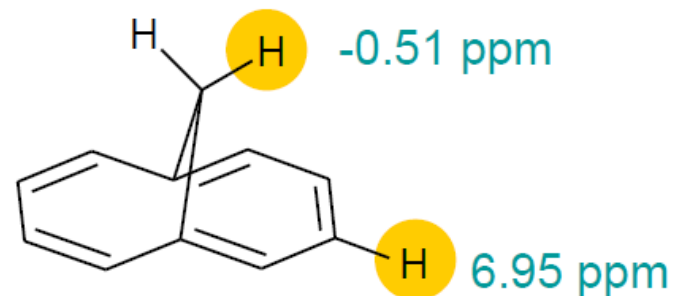
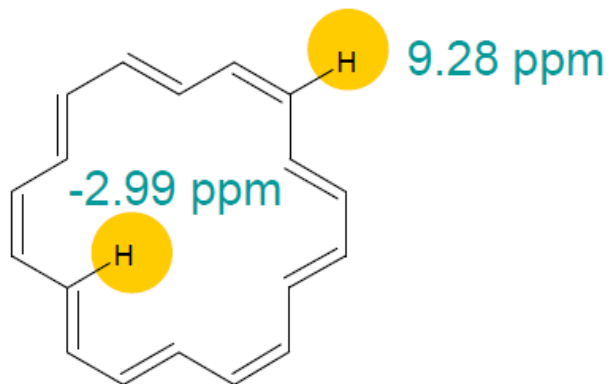
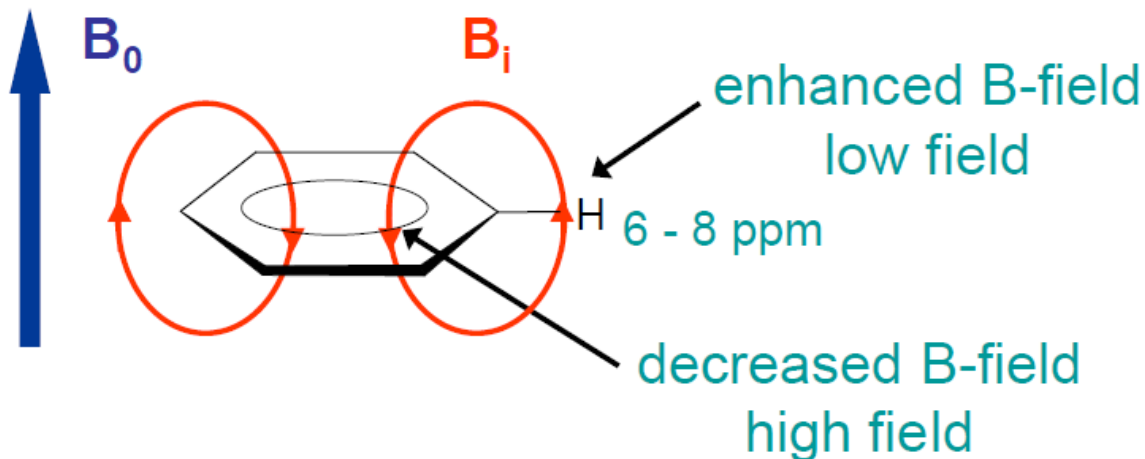


Di axial protons have coupling constants around 10-13 Hz

# Anisotropic effects on chemical shifts



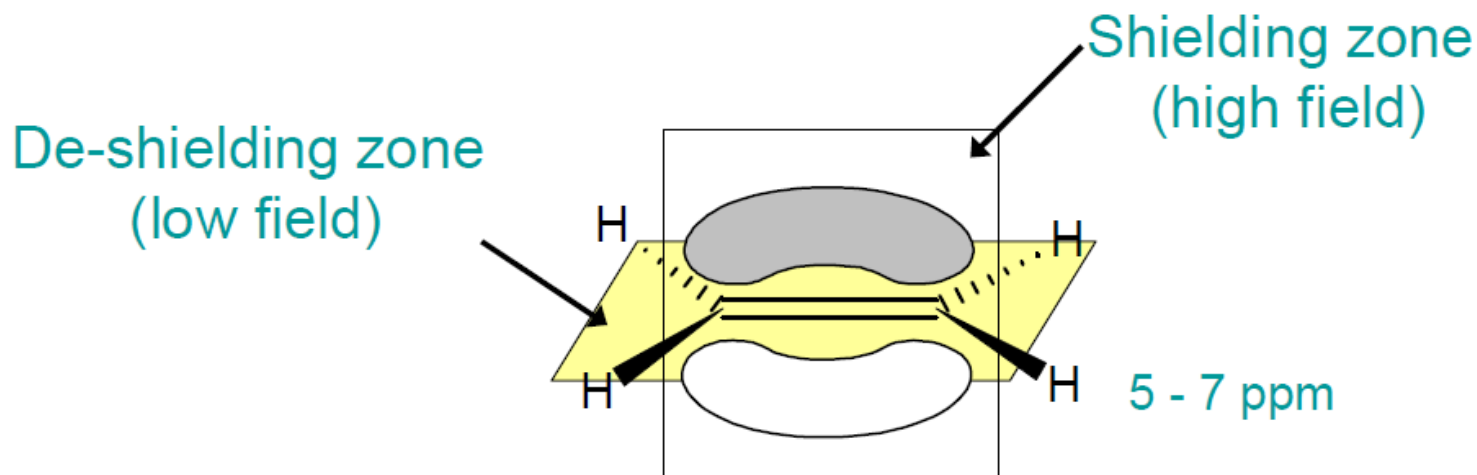
Shielding / De-shielding due to ring current effects:  
de-shielding in the plane of a double bond, shielding above the bond



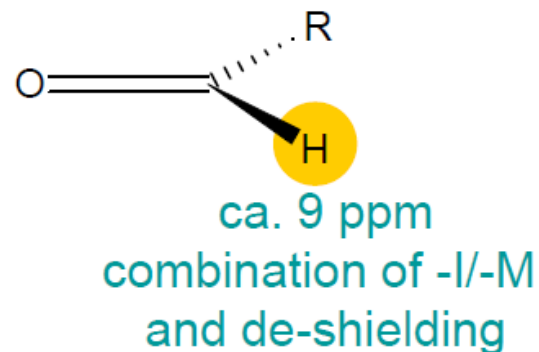
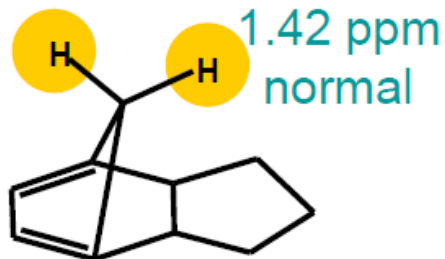
# Anisotropic effects on chemical shifts



Shielding / De-shielding due to double bond anisotropy:  
de-shielding in the plane of a double bond, shielding above the bond



0.42 ppm  
shielded

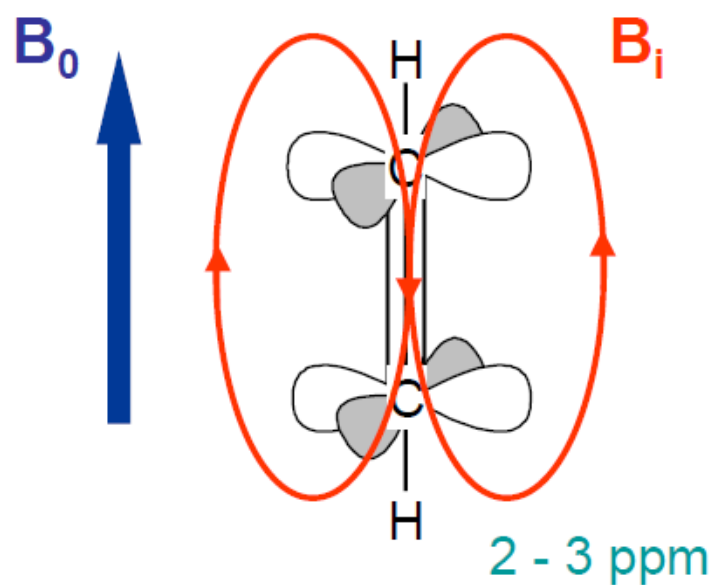


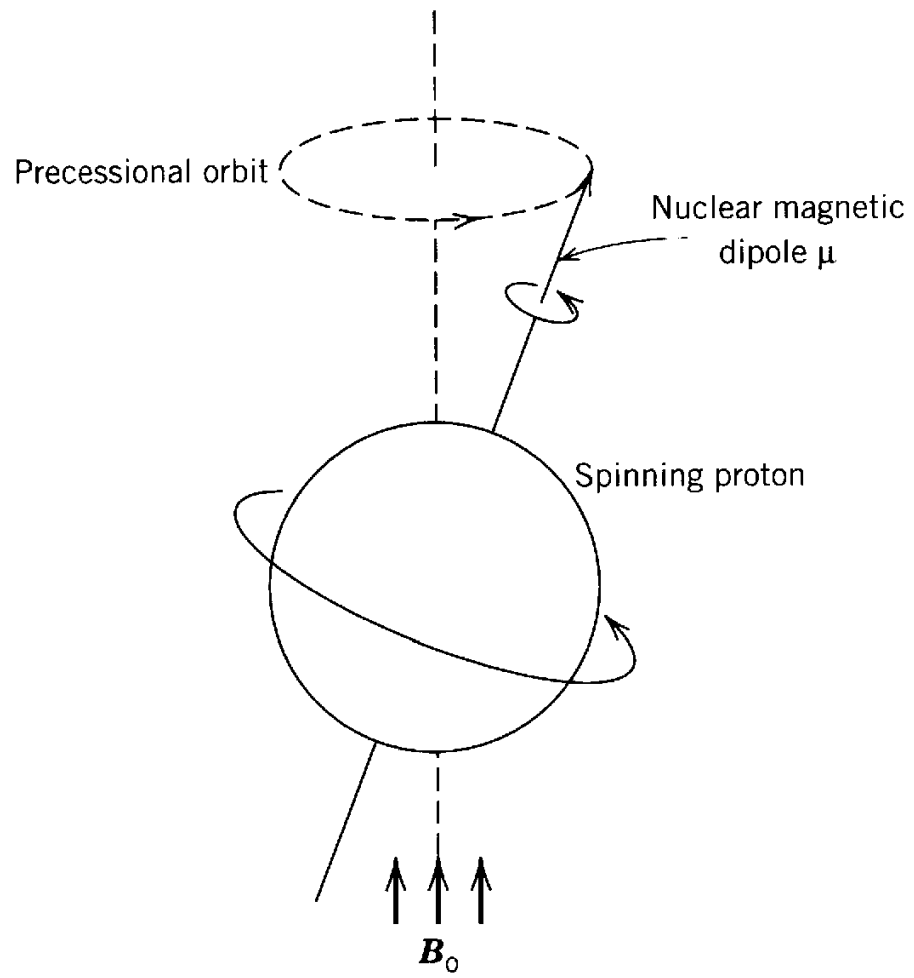


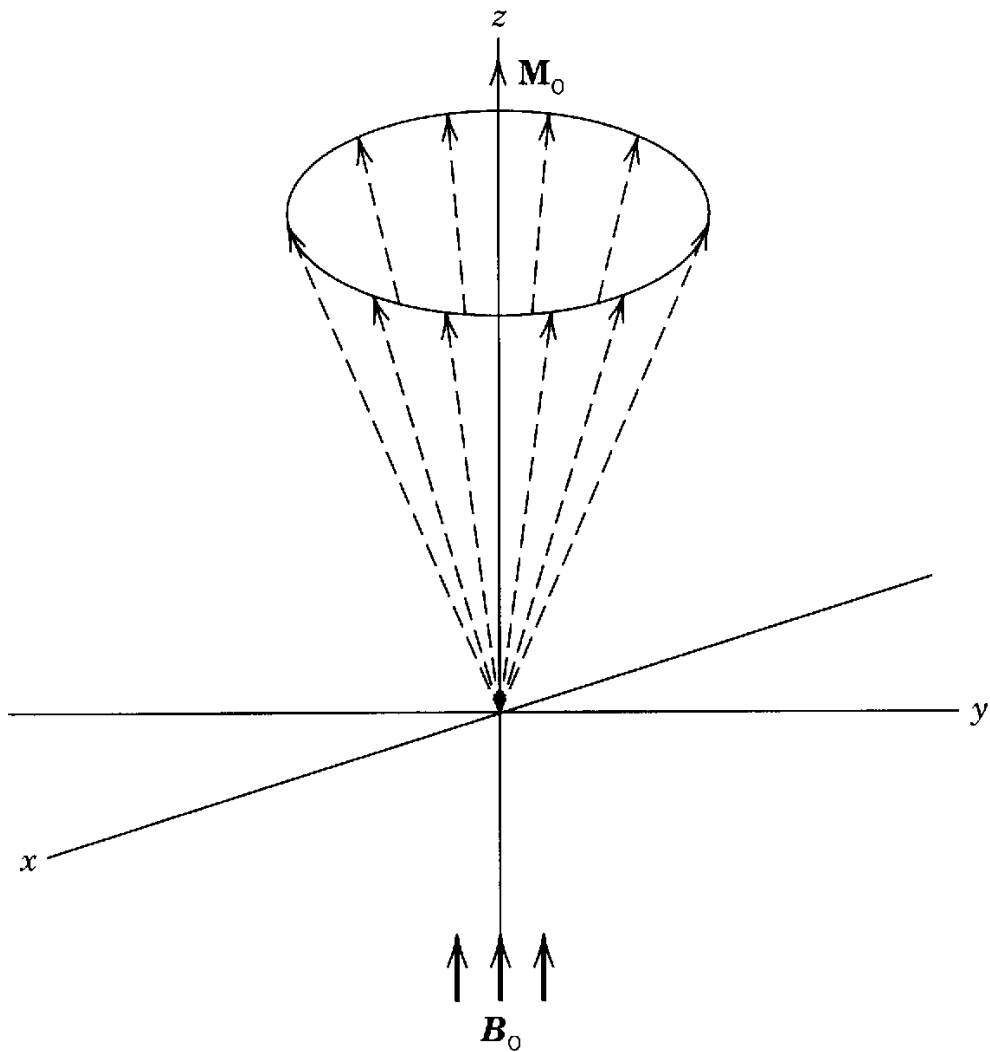
# Anisotropic effects on chemical shifts



Shielding / De-shielding due to triple bond anisotropy:  
shielding along the axis of a triple bond



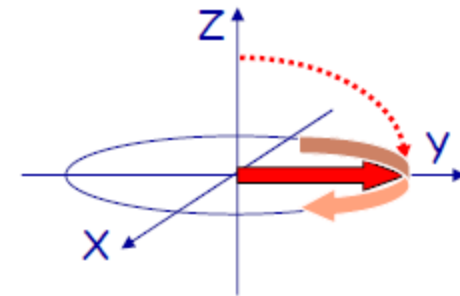
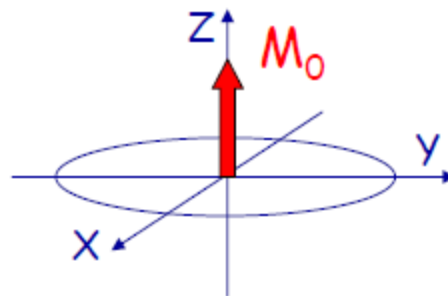
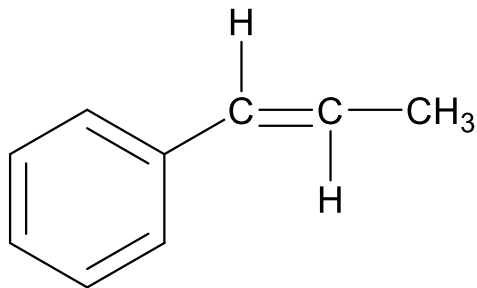




**FIGURE 4.4.** Assemblage of precessing nuclei with net macroscopic magnetization  $\mathbf{M}_0$  in the direction of the stationary magnetic field  $\mathbf{B}_0$ .

# CW NMR

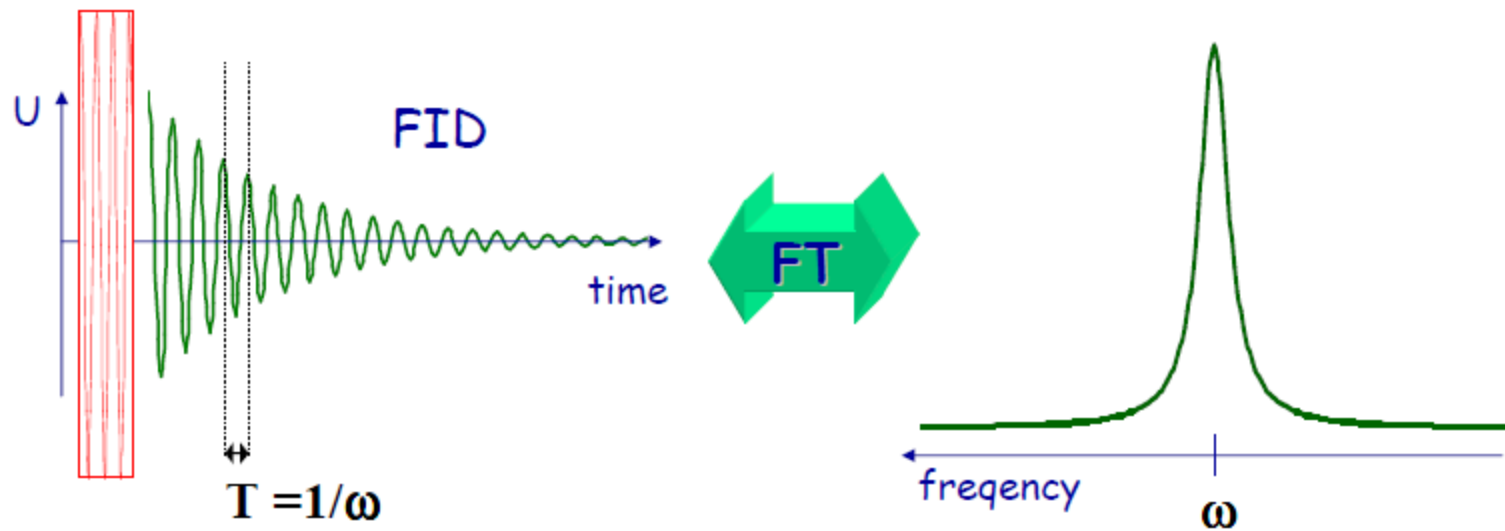
Continuous Wave (CW) method operates by exciting the nuclei under observation one at a time. In case of  $^1\text{H}$  nuclei each distinct type is excited individually and NMR is recorded independently of all others.



# FT NMR

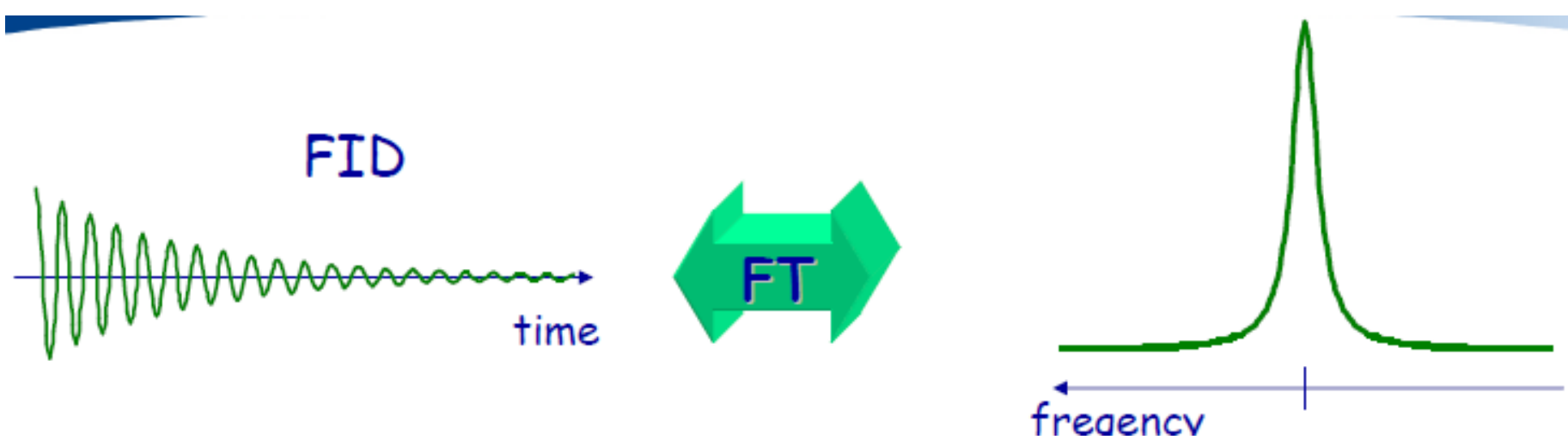
Alternative approach adopted in modern NMR instruments is to use a powerful and short burst of energy called a pulse that excites all of the magnetic nuclei in the molecule simultaneously. Pulse actually contains a range of frequencies centered about the fundamental frequency.

# NMR signal: Free Induction Decay



The mathematical operation of the Fourier Transform allows to display the same information either in the time domain (left, FID) or in the frequency domain (right, spectrum displaying a Lorentz Line)

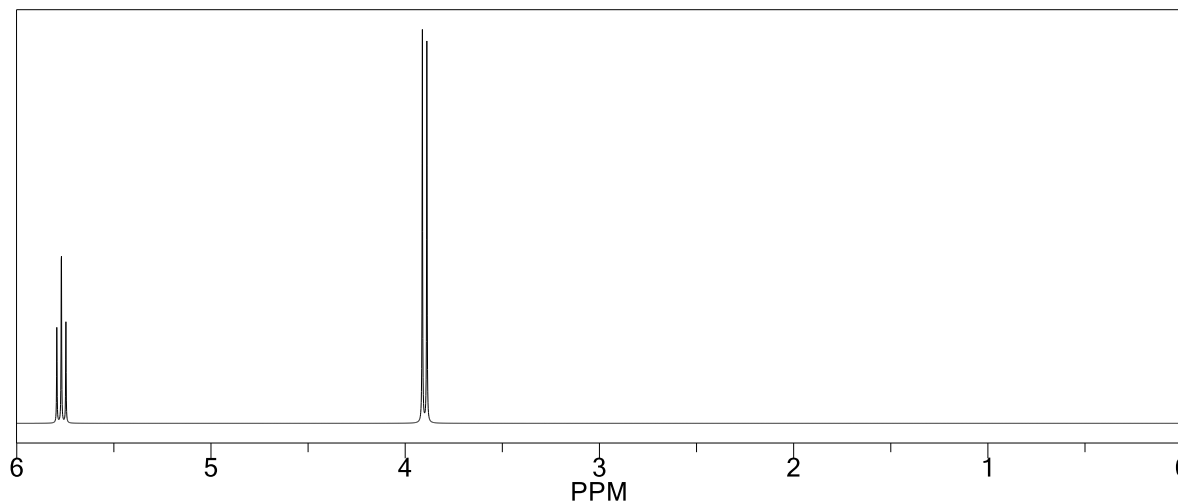
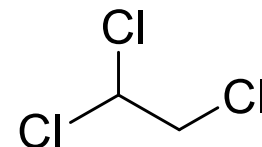
When the pulse is discontinued, the excited nuclei begin to lose their excitation energy and return to the original spin state or relax. As each excited nucleus relaxes, it emits electromagnetic radiation. Molecule consists of many different nuclei, many different frequencies of electromagnetic radiation are emitted simultaneously. This emission is called a free induction (FID) decay.



**Conversion of time domain signal to frequency domain, which is the format for a CW instrument is called Fourier transform (FT). FT is a mathematical operation which breaks the FID into separate sine or cosine wave components. Best signal/noise ratio can be achieved by pulsed FT technique.**

## **Second order effects on spectra**

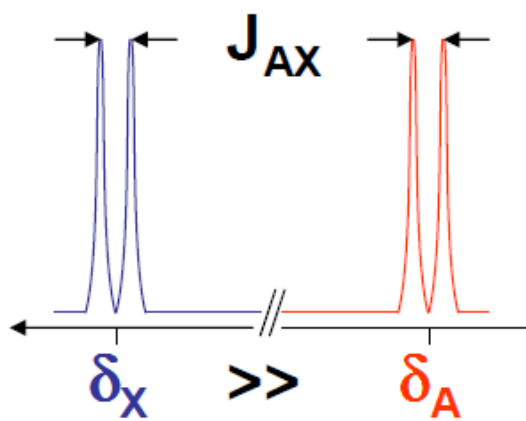
**In the AX<sub>2</sub> case of 1,1,2 trichloro ethane only five lines appear as predicted by first order rules.**



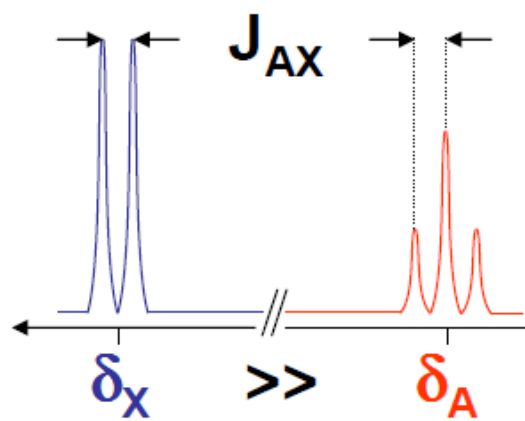
- If the chemical shift values of A and X are closer together, the spectrum is non first order ( $AB_2$ ); altogether nine lines may appear. Precise appearance of the spectrum depends on the ratio of  $\Delta\Upsilon/J$ .



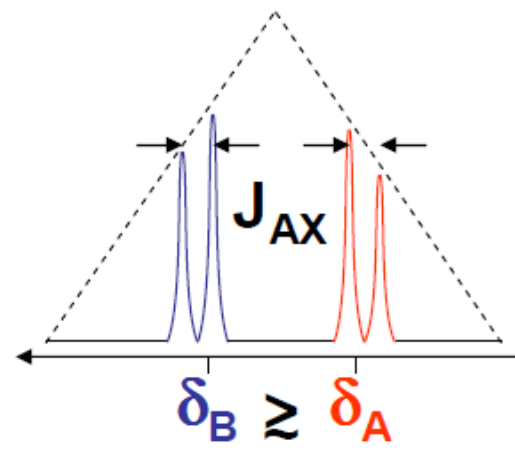
**AX** spin system



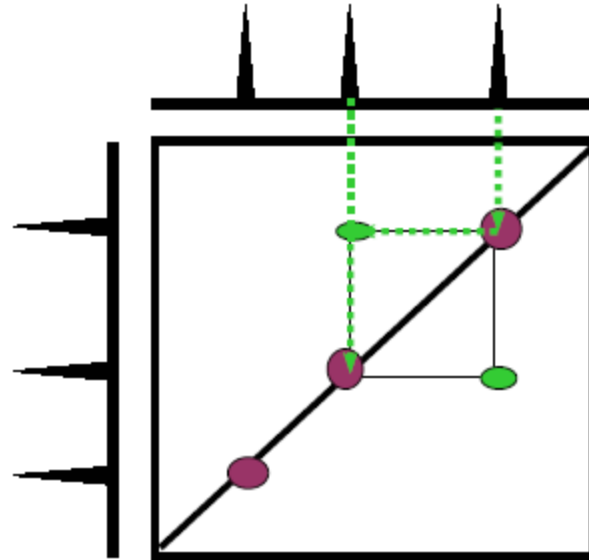
**AX<sub>2</sub>** spin system



**AB** spin system



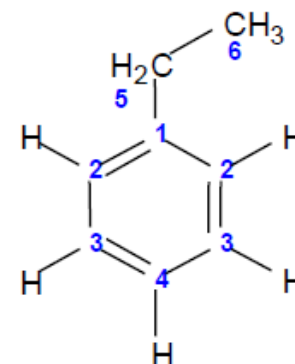
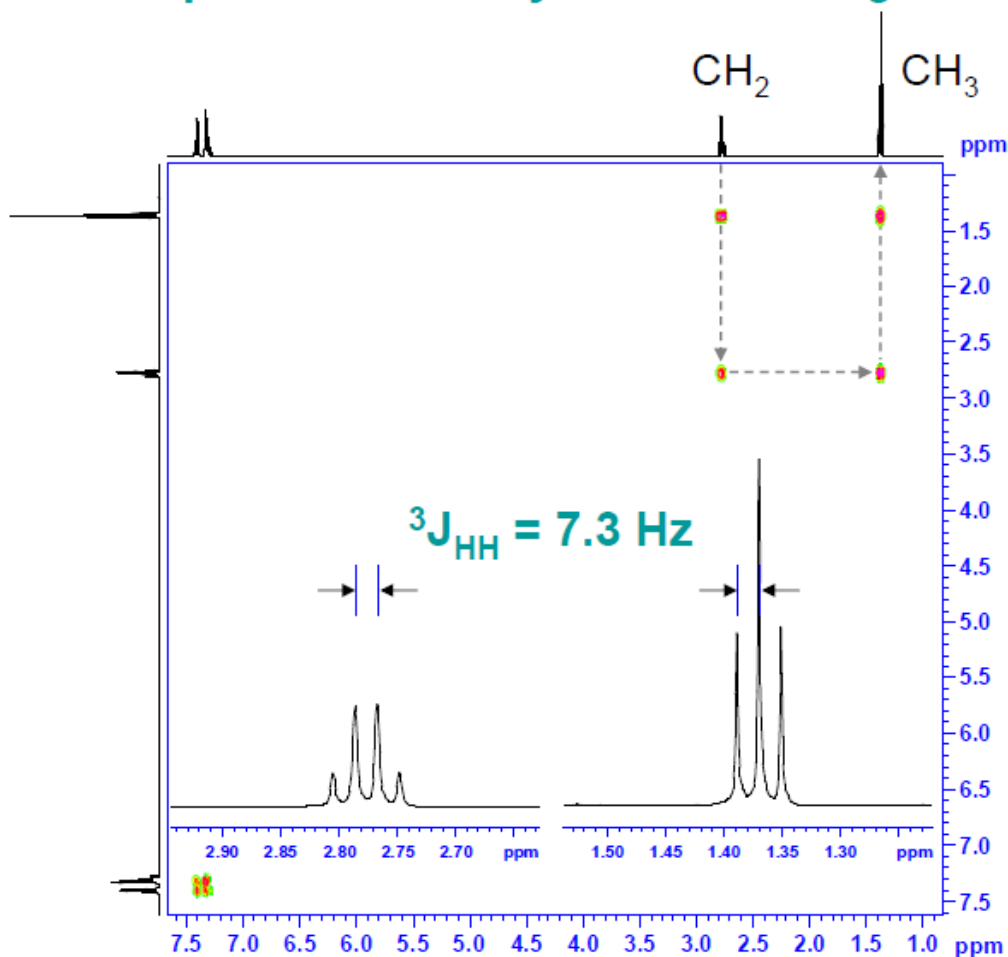
# 2D-NMR, COSY



# Direct HH correlations through bonds



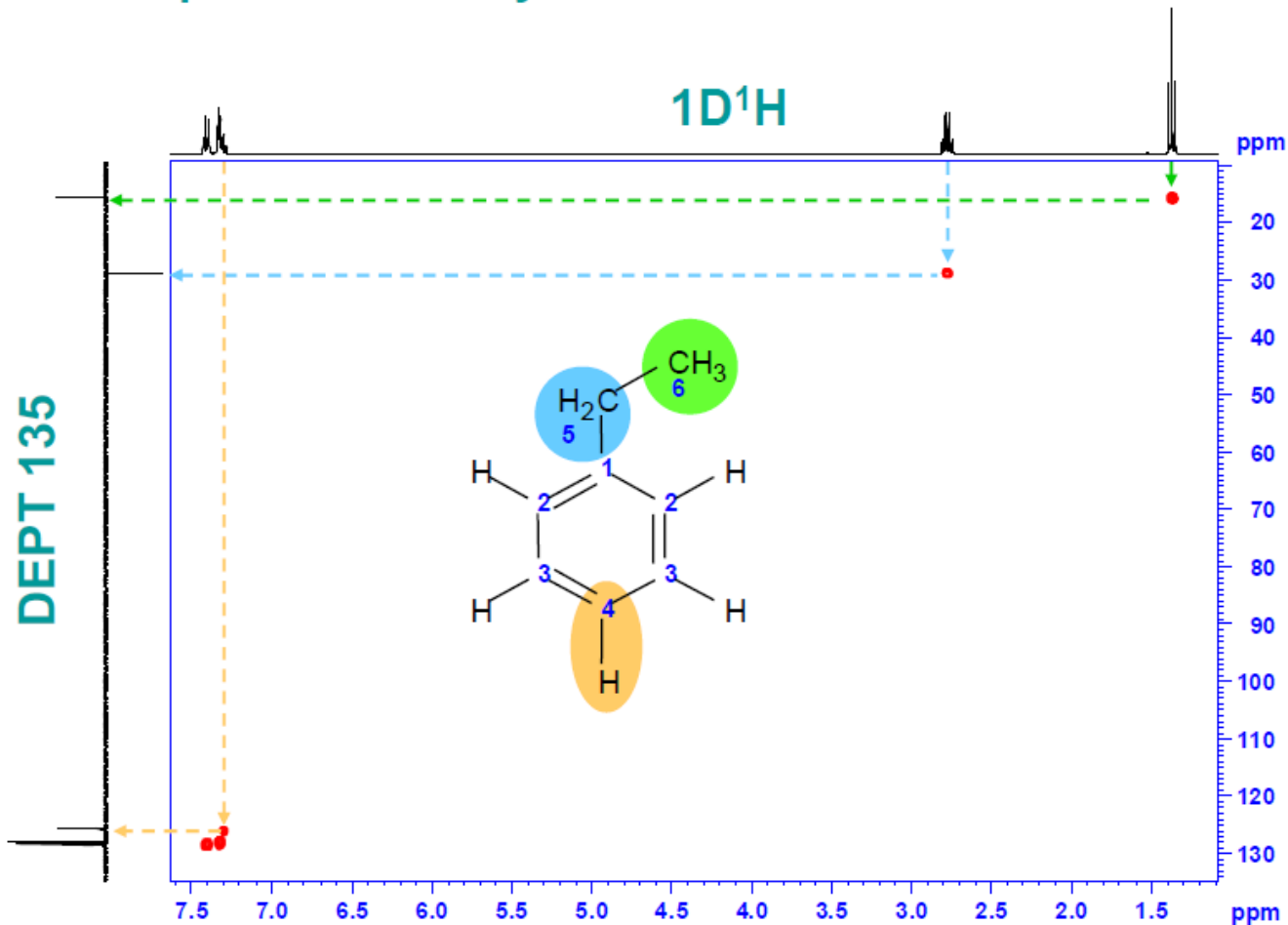
## COSY spectrum of ethylbenzene: neighboring protons



# Direct CH correlations



HSQC spectrum of ethylbenzene: 1 bond CH correlations





# Carbohydrates in Chemical biology

Dr. Franklin John  
Dept. of Chemistry  
Wayne State University  
Detroit, USA 48202

June 9, 2011

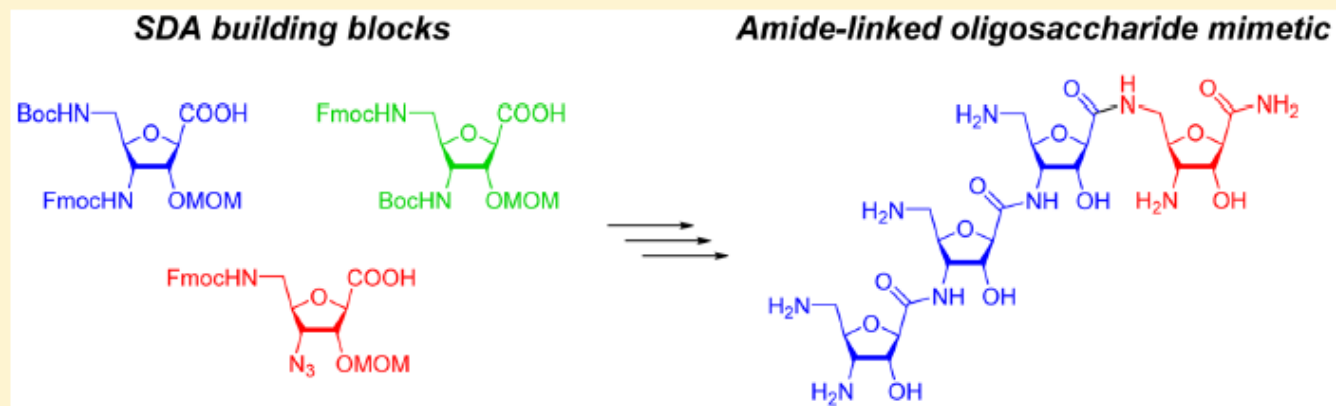
# Orthogonally Protected Furanoid Sugar Diamino Acids for Solid-Phase Synthesis of Oligosaccharide Mimetics

Franklin John<sup>†,‡</sup> and Valentin Wittmann<sup>\*,†</sup>

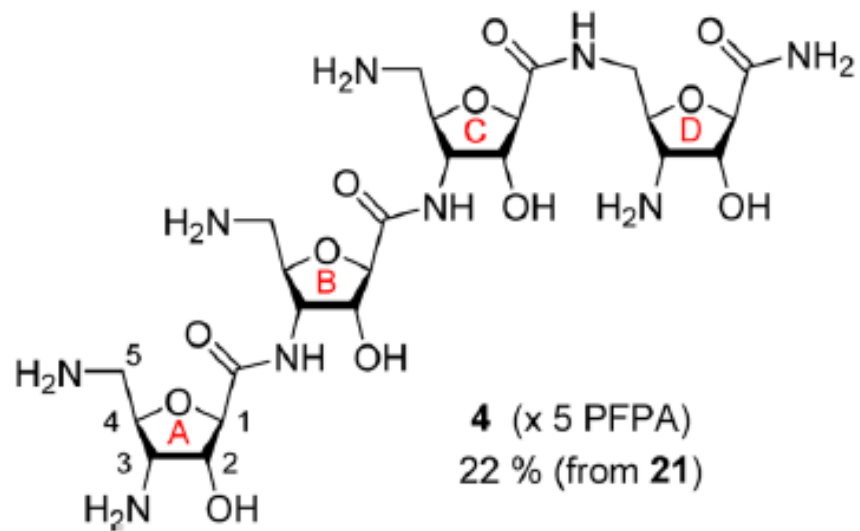
<sup>†</sup>Fachbereich Chemie and Konstanz Research School Chemical Biology (KoRS-CB), Universität Konstanz, 78457 Konstanz, Germany

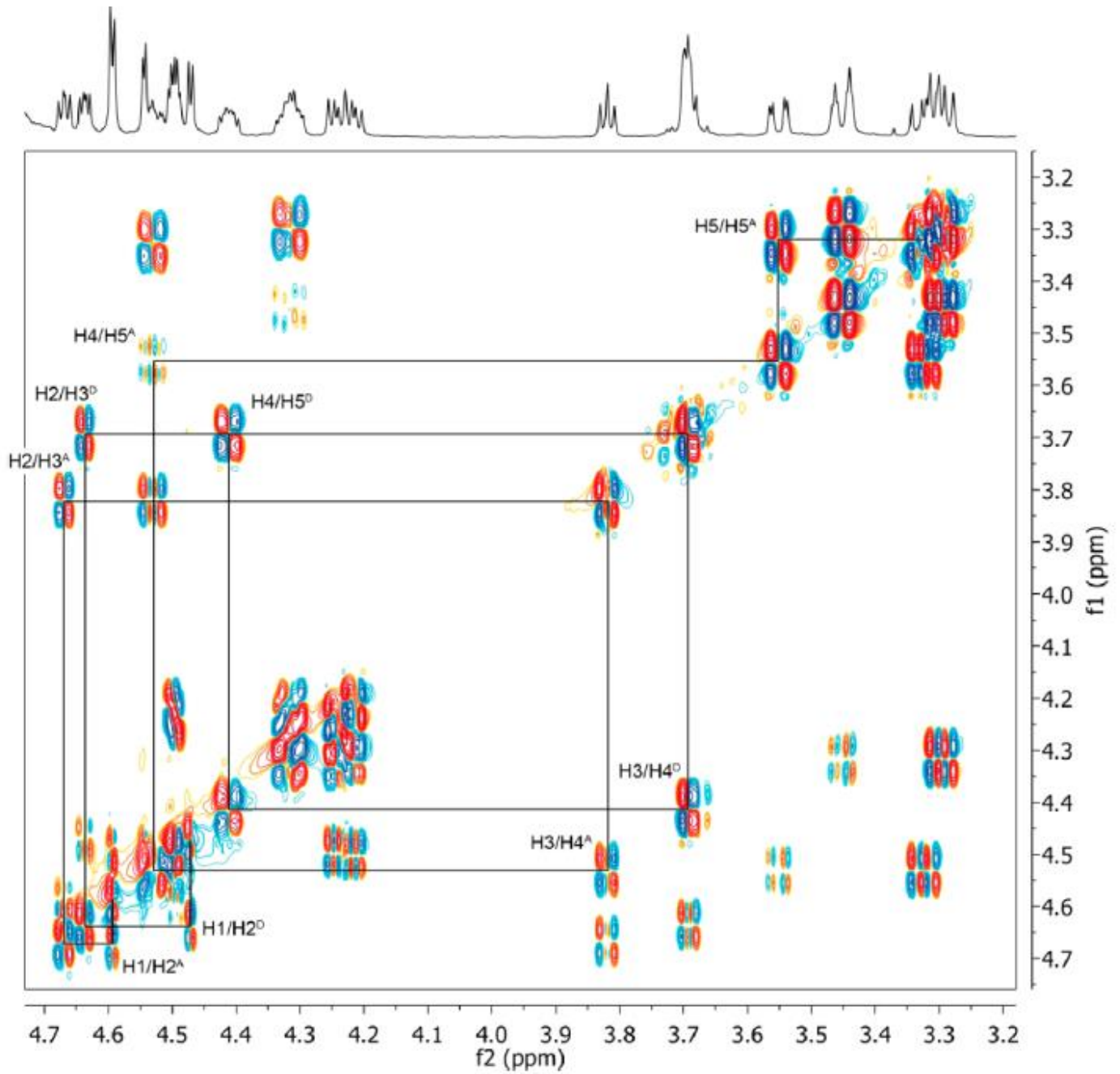
<sup>‡</sup>Department of Chemistry, Sacred Heart College (M. G. University), Kochi 682013, India

**S** Supporting Information



**ABSTRACT:** Sugar diamino acids (SDAs), which differ from the widely used sugar amino acids in the presence of a second amino group connected to the carbohydrate core, share structural features of both amino acids and carbohydrates. They can be used for the preparation of linear and branched amide-linked oligosaccharide mimetics. Such oligomers carry free amino groups, which are positively charged at neutral pH, in a spatially defined way and, thus, represent a potential class of aminoglycoside mimetics. We report here the first examples of orthogonally protected furanoid SDAs and their use in solid-phase synthesis. Starting from D-glucose, we developed a divergent synthetic route to three derivatives of 3,5-diamino-3,5-dideoxy-D-ribofuranose. These building blocks are compatible with solid-phase peptide synthesis following the 9-fluorenylmethoxycarbonyl (Fmoc) strategy, which we demonstrate by the synthesis of an SDA tetramer.



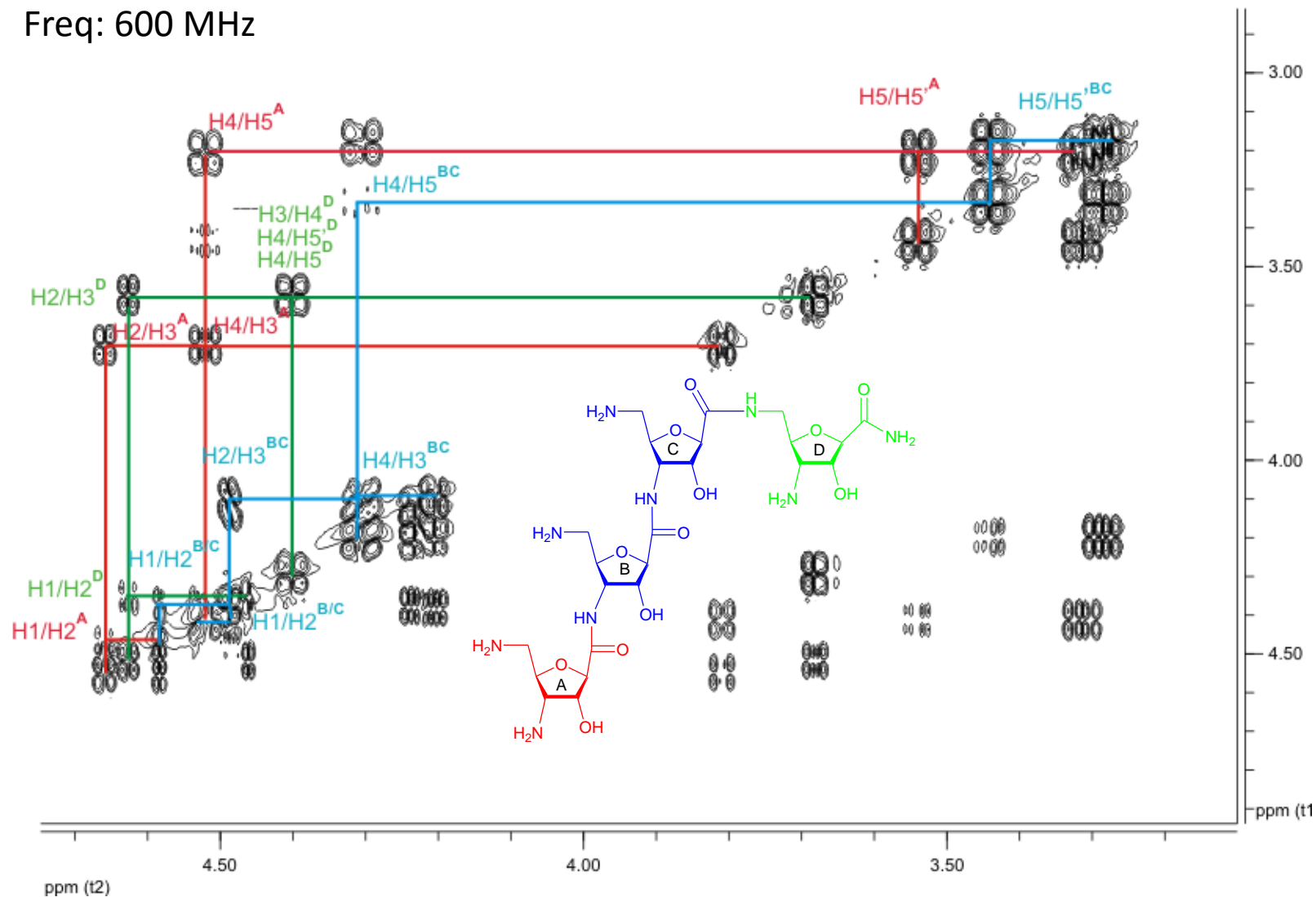




# COSY Spectrum

Solvent: D<sub>2</sub>O

Freq: 600 MHz





## Acknowledgements

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Dr. Frank Sicherl (Roche, Germany)

Dr. Marco Worch (Aldrich, Switzerland)

#### **Collaboration:**

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Prof. Dr. J. Hartig (Uni Konstanz, Germany)

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Dr. Rachel Morissette (NIH, Baltimore, USA)

Yug Varma, Megan Ehrenwerth (Wayne State University)

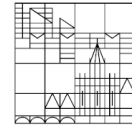
#### **Collaboration:**

Prof. Dr. A. Conzelmann (Switzerland)

#### **Funding**

American Cancer Society

Universität  
Konstanz

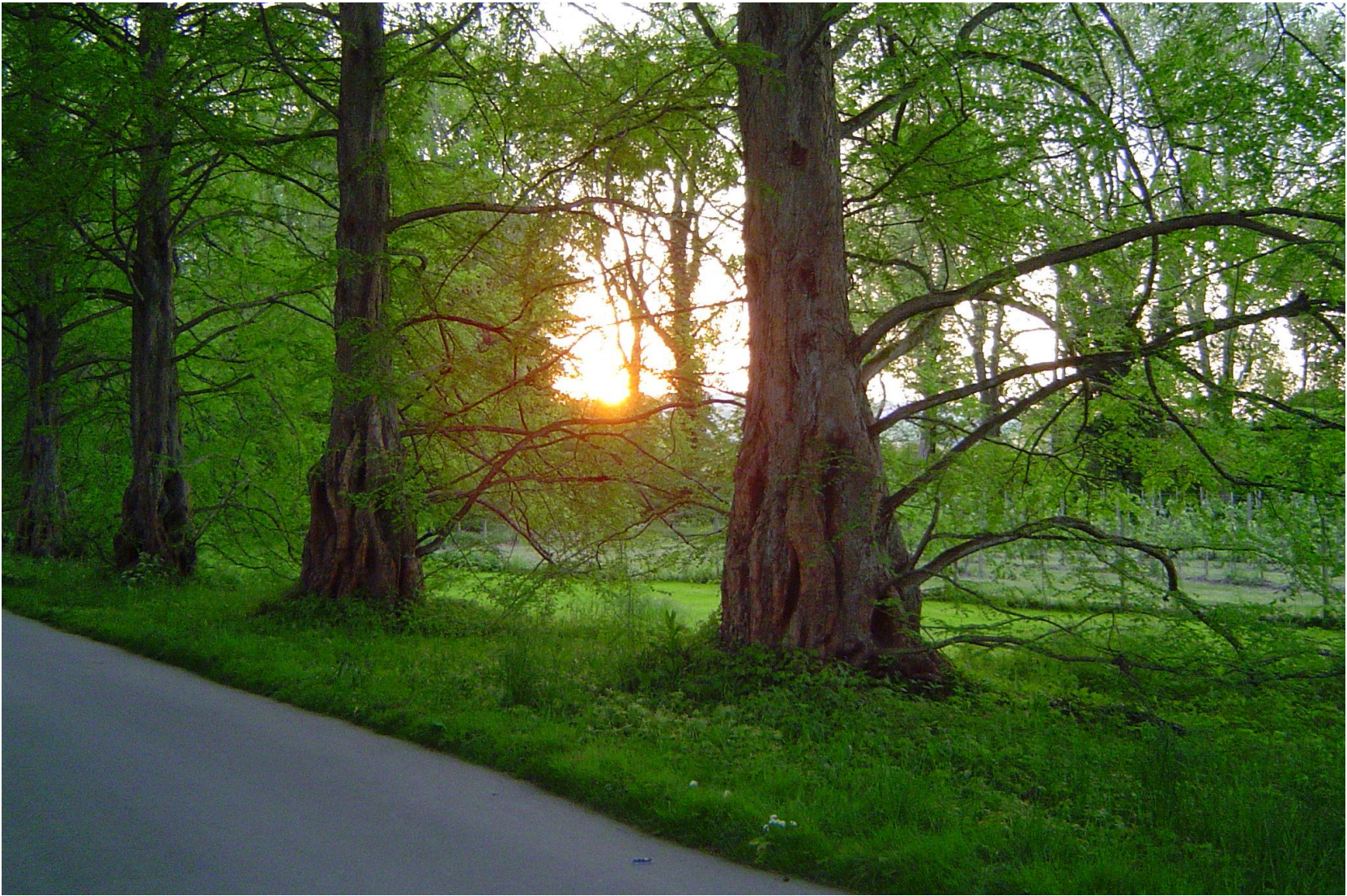


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