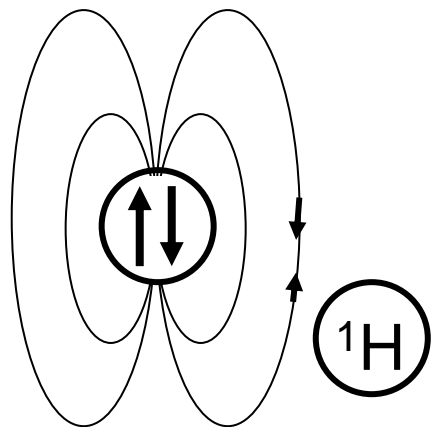
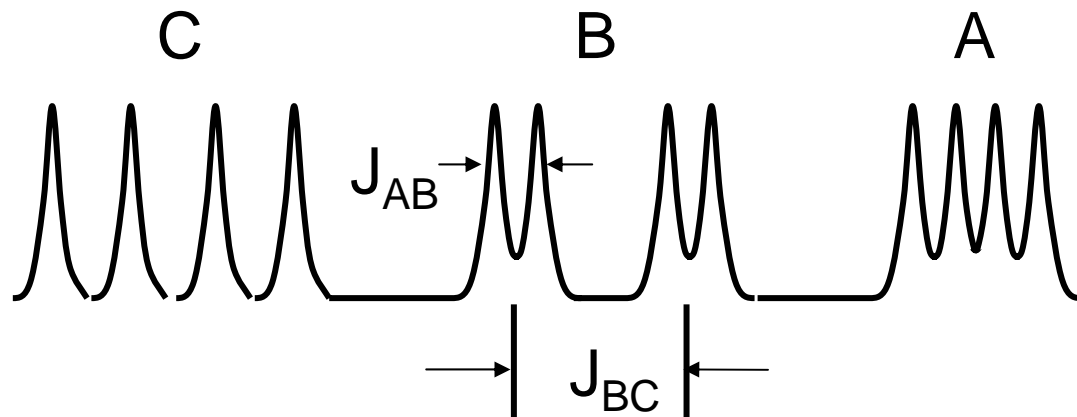
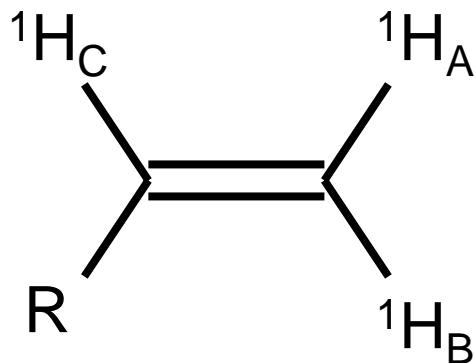


Origin of Scalar Couplings

BCMB/CHEM 8190

Traditional View of Scalar Coupling



Dipole Model: Two equal intensity lines from each interaction for each spin

Reasons to understand couplings:

- magnetization transfer (COSY, HSQC)
- structural information

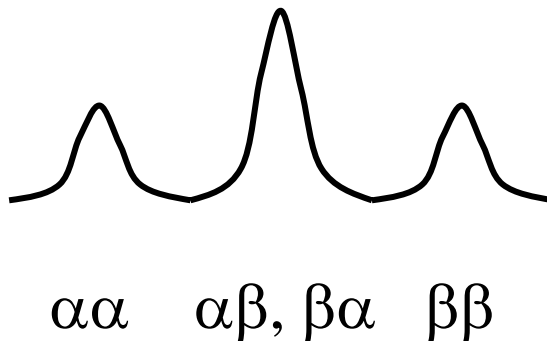
Measurement: directly as above,
2D J-resolved, intensity based

Problem: dipolar interactions average to zero in solution

Multiple sets of spins

Multiplet structure: as many as $n2^{(n-1)}$ lines in non-equivalent first order sets, $2^2 \times 3 = 12$ lines for previous example

Unequal intensities in equivalent cases; proton next to a methylene, has states $\alpha\alpha$, $\alpha\beta$, $\beta\alpha$, $\beta\beta$; a 1:2:1 triplet



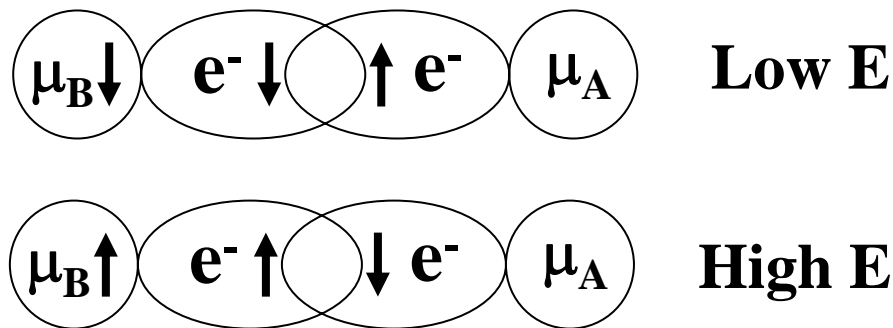
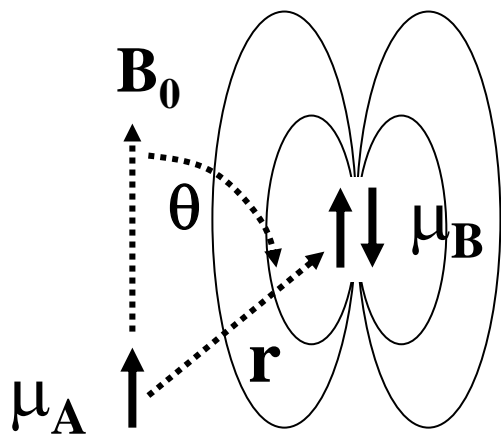
The Origin of Scalar Coupling Constants

$$E_J = \sum_{i \neq j} J_{ij} \mathbf{I}_i \cdot \mathbf{I}_j \approx \sum_{i \neq j} J_{ij} I_{zi} I_{zj} \quad \rightarrow \text{NMR spectrum with splitting } J$$

Mechanism:

not through space,
 $E \propto (3\cos^2\theta - 1) / r^3$

but Fermi contact
 $E \propto S_A \times S_B$



The Fermi-Contact Mechanism

- Electron-nucleus interaction:

$$\mathbf{H}_J = 4g\beta\gamma_N h/3 \sum_e \delta(r_N) \mathbf{I} \cdot \mathbf{S}$$

(only finite at $r_N = 0$)

- Interested in energy due to \mathbf{H}_J

$$E = \langle \psi_0 | \mathbf{H}_J | \psi_0 \rangle, \text{ but } \alpha \text{ and } \beta \text{ equally populated;}$$

equal to 0

- Second order expression

$$\text{replace } \psi_0 \text{ by } \psi_0 + \sum_i c_i \psi_i; \quad c_i = \langle \psi_0 | \mathbf{H}_J | \psi_i \rangle / (E_i - E_0)$$

- $E = (4g\beta\gamma_N h/3)^2 \sum_{jk} \langle \psi_0 | \delta(r_{kA}) \delta(r_{jB}) \mathbf{S}_{jz} \mathbf{S}_{kz} | \psi_0 \rangle \mathbf{I}_{zA} \mathbf{I}_{zB}$

Implications of Fermi-Contact Expression

- $I_{zA} I_{zX}$ dependence as expected for H_J
- $\gamma_A \gamma_X$ dependence as expected for H_J
- Depends on electron density at pair of nuclei ($\delta(r_{kA})\delta(r_{jB}) \mathbf{S}_{jz} \mathbf{S}_{kz}$) and spins must be correlated – hence bonded

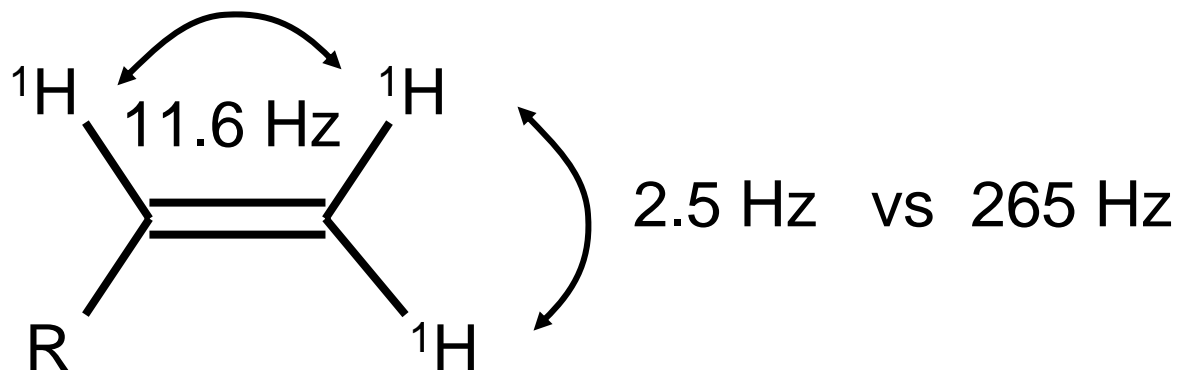
$$\left(\int \mathbf{S}_{jz} \mathbf{S}_{kz} = 0 \text{ if spins are uncorrelated} \right)$$

- Depends on “s” character of bond

$$\left(\delta(r_{kA}) \text{ is only finite for an s orbital} \right)$$

Predictions about Scalar Couplings

- Wave functions (electronic) for ^1H - ^1H can be calculated at a high level of theory – even at VB prediction of 200Hz is good.
- Experimental ^1H - ^2H is 44 Hz; correcting for γ_S , $J_{\text{H-H}} = \gamma_{^1\text{H}}/\gamma_{^2\text{H}} \times 44 = 6.5 \times 44 = 265\text{Hz}$
- Directly bonded pairs should have much larger couplings:



Some predictions for one-bond couplings

Couplings are short range and depend on electron densities at the coupled nuclei (ie, the product of “s characters”) as well as γ s.

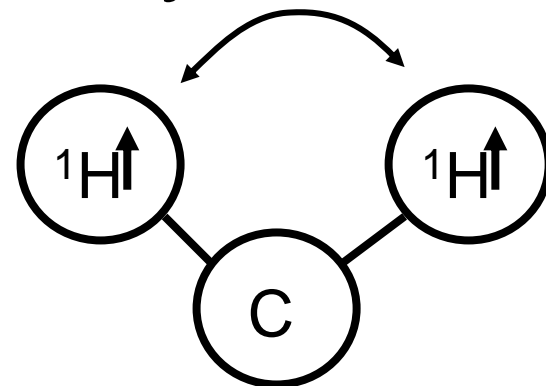
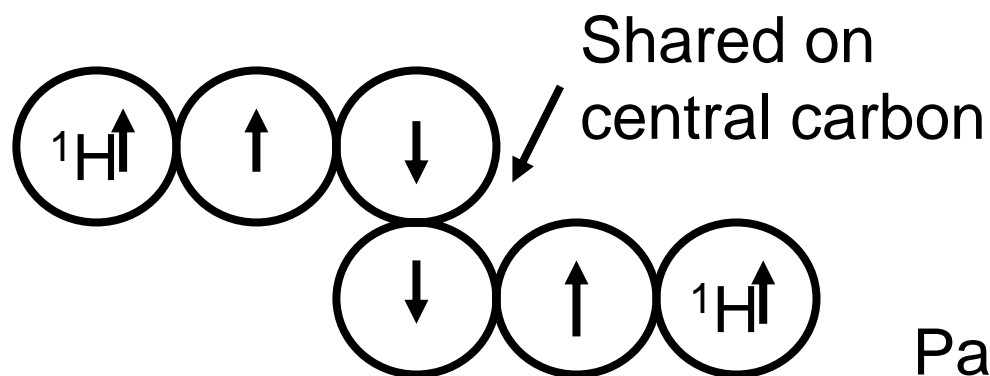
C-C

CH₃-CH₃	35 Hz	sp ³ - sp ³	1/4 x 1/4 = 1/16
CH₂=CH₂	67 Hz	sp ² - sp ²	1/3 x 1/3 = 1/9
C₆H₆	57 Hz	sp ² - sp ²	1/3 x 1/3 = 1/9
HC≡CH	171 Hz	sp-sp	1/2 x 1/2 = 1/4

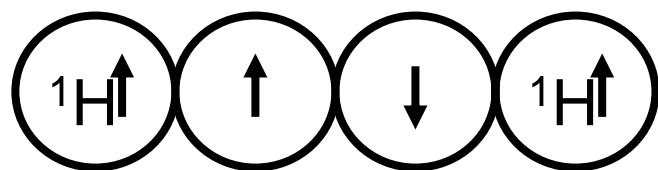
C-H

CH₃-CH₃	125 Hz	s - sp ³	1 x 1/4 = 1/4
CH₂=CH₂	156 Hz	s - sp ²	1 x 1/3 = 1/3
C₆H₆	158 Hz	s - sp ²	1 x 1/3 = 1/3
HC≡CH	249 Hz	s-sp	1 x 1/2 = 1/2

A two-bond coupling is small and sometimes negative – why?



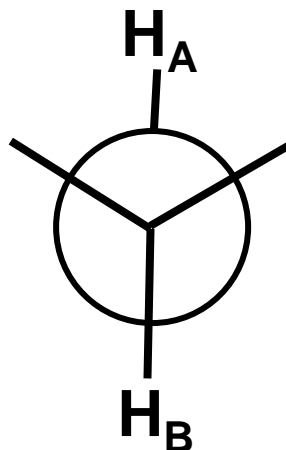
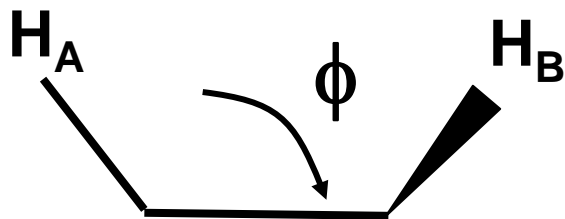
Parallel H and e contributes low energy



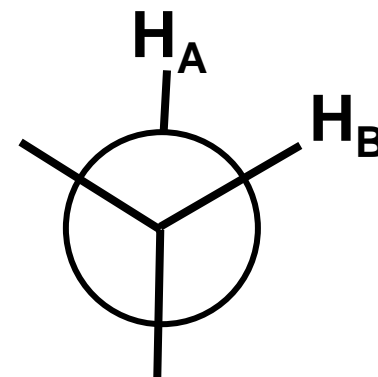
Anti parallel H and e contributes high energy
The two terms cancel

Coupling goes up again for a three-bond coupling

Vicinal Couplings (${}^3J_{\text{HH}}$)



9.2 Hz

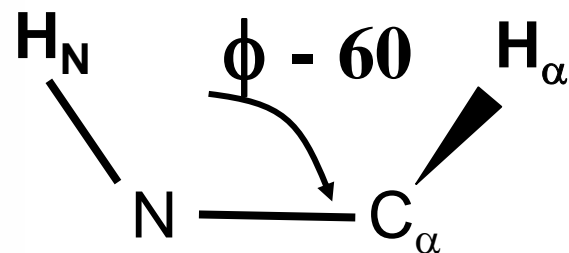
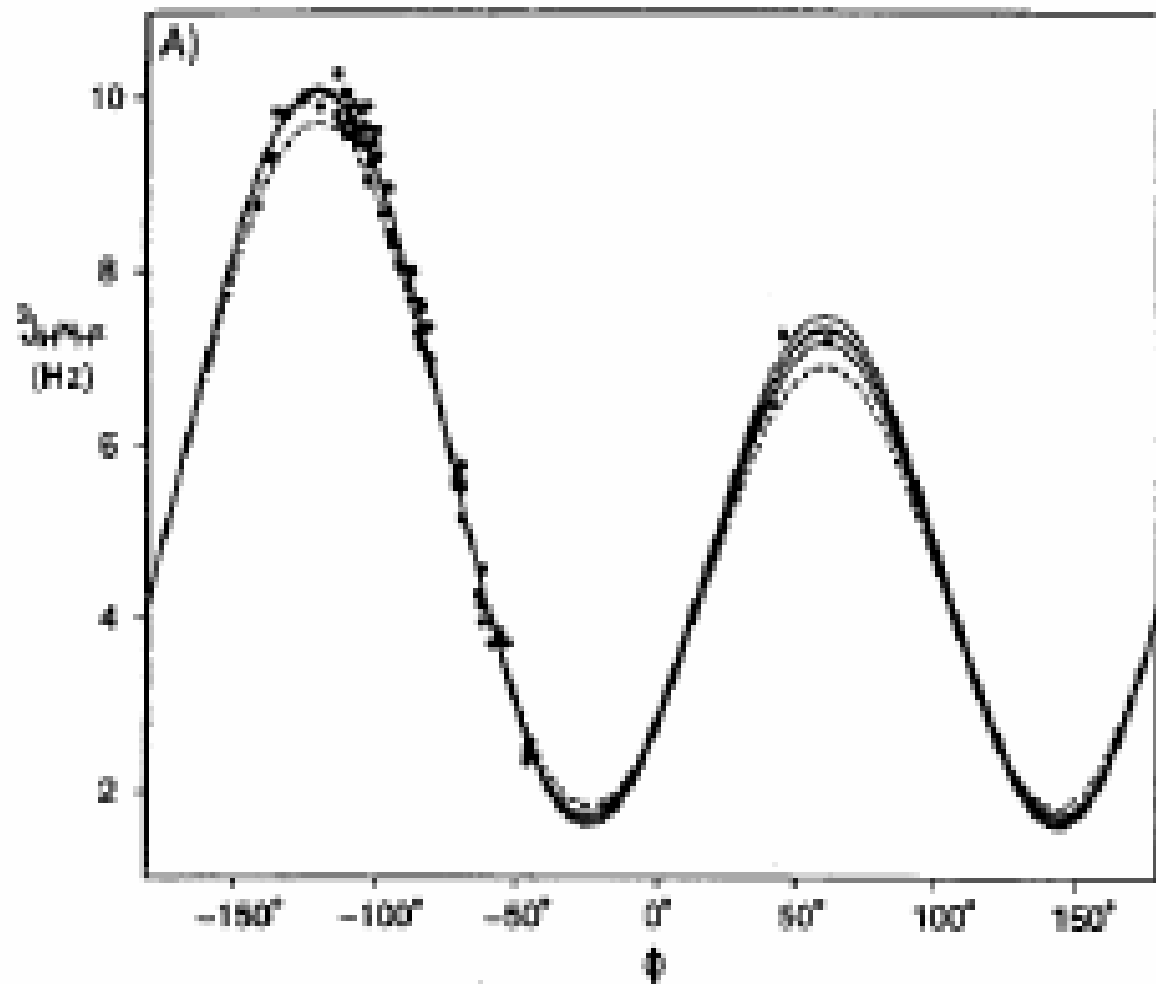


1.8 Hz

- Originally for H-C-C-H
- M. Karplus (1959) JCP **30** 11 - Karplus Equation
- $J_{\text{HNHA}} = 7.0 \cos^2(\phi) - 1.4 \cos(\phi) + 1.7$ for peptides
- (Bax and Wang (1996) JACS **118** 2492)

Wang-Bax Equation Compared to Ubiquitin Data

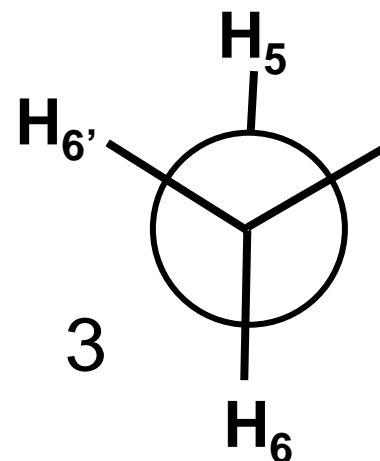
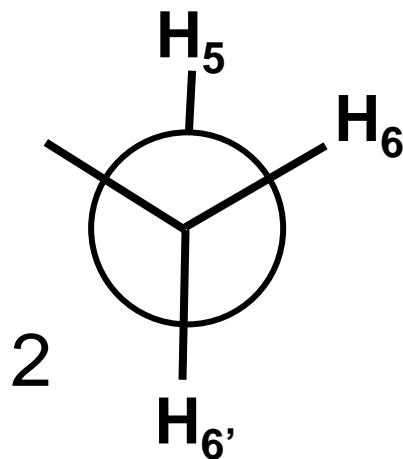
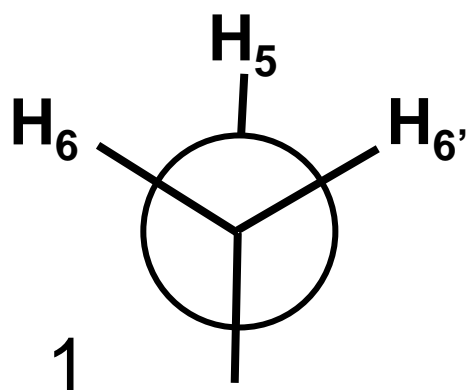
2492 *J. Am. Chem. Soc.*, Vol. 118, No. 10, 1996



ϕ measured as
C'-N-C _{α} -C''

Populations of Rotameric States from Couplings

An Application of the Karplus Equation



- Occurs in pyranosides, furanosides, and nucleosides
- Assume only minimum energy states populated
- $J_{56} = 1.8 F_1 + 1.8 F_2 + 9.2 F_3$
- $J_{56'} = 1.8 F_1 + 9.2 F_2 + 1.8 F_3$
- $F_1 + F_2 + F_3 = 1$

Application of Karplus Equations (cont)

Measure J_{65} and $J_{6'5}$ for α -Me-galactose

7.0 Hz, 3.0 Hz

Using averaging formula find:

0.15, 0.7, 0.15 for states 1, 2, and 3

Reference on scalar coupling in Levitt: 211-216

Scalar Couplings Can be Predicted Theoretically

- “Interpretation of chemical shifts and coupling constants in macromolecules” D.A. Case, *Curr. Opin. Struc. Biol.* 10, 197-203 (2000).
- “Density functional calculations on disaccharide minics: studies on molecular geometries and spin-couplings”, F. Cloran, I Carmichael, A.S. Serianni, *JACS*, 121, 9843-9851 (1999).

Couplings Across Hydrogen Bonds

- “Direct observation of hydrogen bonds in nucleic acid base pairs by internucleotide $^2J(\text{NN})$ couplings”, A.J. Dingley, S. Grzesiek, JACS, 120, 8293-8297 (1998).
- “NMR scalar couplings across Watson-Crick base pair hydrogen bonds in DNA ...”, K. Pervushin, ... K. Wuthrich, PNAS, 95, 14147-14151 (1998).

