More on coupling constants

Coupling constants can tell you a lot more about a proton’s neighbours.

**Geminal couplings** are couplings over 2 bonds. The $^2J$ coupling of protons attached to the same carbon is usually about 10 – 14 Hz. Note that geminal couplings are often negative, although chemists usually quote the absolute (positive) value $|^2J|$ for this coupling. While the sign makes no difference to a first-order spin system, it can drastically alter the appearance of higher-order ABX, ABC, AA'BB' etc. spin systems. Adjacent double bonds (C=C, C=O) increase the geminal coupling constant, whereas wide angles and heteroatoms decrease it considerably.

![Geminal couplings](image)

**Vicinal couplings** are couplings over 3 bonds. Here are some representative coupling constants:

\[
\begin{align*}
^3J_{	ext{ortho}} & = 8 \text{ Hz} \\
^3J_{	ext{para}} & = 12 \sim 18 \text{ Hz} \\
^3J_{	ext{ax}} & = 7 \sim 9 \text{ Hz} \\
^3J_{	ext{eq}} & = 2 \sim 5 \text{ Hz}
\end{align*}
\]

Vicinal coupling constants are sensitive to the angle between the coupling protons. The angle dependence is described by the Karplus equation. A dihedral angle of 0° gives a large coupling constant of about 8.5 Hz (in an alkyl chain) to 12 Hz (in an alkene). A dihedral angle of 180° between coupling protons results an even higher coupling of 9.5 – 16 Hz, whereas at a dihedral angle of 90° the coupling is close to zero.

![Karplus equation](image)

**Long-range couplings** over 4 or more bonds occur only when the protons are held in a fixed position suitable for coupling, usually following a perfect zig-zag or W-shaped path. Long-range couplings are often seen in rigid rings or for protons in an allylic position, as both double bonds and rings prevent bond rotation.

![Diastereotopic protons](image)

**Diastereotopic protons**

The two protons of a CH2 group can occasionally become non-equivalent. We call them **diastereotopic protons**. Diastereotopic protons have different chemical shifts and, because of this, they also couple to each other. The 1H NMR spectrum and multiplicities then become more complicated.

If a molecule has a **chiral centre**, the protons on a CH2 group anywhere in the molecule will be diastereotopic. The amino acid aspartic acid has a CH2 group next to a chiral centre (*). As a result, Hα and Hδ are diastereotopic; they have different chemical shifts and couple to each other with a characteristic large coupling constant greater than 10 Hz. Each diastereotopic proton also couples to another proton in the
vicinity (H_x) and each with a different coupling constant; in the preferred conformation shown, H_x is gauche to H_A but anti to H_B, so the coupling constant J_{AB} is larger than J_{AB} (Karplus equation).

The protons on a CH_2 next to a chiral centre are **diastereotopic**.

**Z-test**: Replace each of the CH_2 protons in turn with some other group (Z = D, Cl, R ...). If you end up with enantiomers, the CH_2 protons are magnetically equivalent and undistinguishable by NMR. If you get a pair of diastereoisomers, the two CH_2 protons are diastereotopic.

**Tip**: If your compound contains a chiral centre, each CH_2 group in it will have diastereotopic protons. No need to do the Z test in this case!

Another tip: An HSQC provides a nice way of identifying diastereotopic protons. A CH_2 carbon with diastereotopic protons will often show TWO crosspeaks in the CH correlation.

**Complex spin systems**

A welcome advantage of an expensive high-field NMR spectrometer (>400 MHz) is that signals that are hopelessly crowded and/or higher order at low field (e.g. 90 MHz) often become first order at a higher field.
However, some spin systems such as AA'BB' or AA'XX' will never become first order, no matter how large the NMR spectrometer frequency.

High-field spectra can also sometimes complicate things unnecessarily. The \(^1\)H NMR spectrum of 1-chloropropane looks straightforward at 90 MHz, showing a triplet, a sextet and a triplet for the ClCH\(_2\), CH\(_3\) and CH\(_2\) group, respectively. At 400 MHz, the splitting pattern of the middle signal changes noticeably; it becomes apparent that the coupling with the CH\(_2\) group is slightly different (7.4 Hz) to the coupling with the CH\(_2\)Cl protons (6.6 Hz), so the multiplicity is in fact a quartet of triplets with many lines overlapping. In such cases, a “splitting tree” helps to explain how more complex patterns arise.

### Higher-order spin systems

While the protons of a CH\(_3\) group are always chemically & magnetically equivalent, this is not necessarily the case when chemically equivalent protons are located on different carbons. In a \textit{para}-disubstituted benzene, H\(_A\) is chemically equivalent to H\(_X\), and indeed the two protons have the same chemical shift. However, the two protons are NOT magnetically equivalent because the \textit{ortho}-coupling between H\(_A\) and H\(_X\) (about 8 Hz) is different from the \textit{para}-coupling between H\(_A\) and H\(_X\) (usually very small, \(-0.5\) Hz). Spin systems of this type are called AA'XX' (say “A A dash X X dash”), or AA'BB', depending on whether the difference in chemical shift is large or small. A characteristic feature of higher-order spin systems is the appearance of small extra lines. The extra lines are NOT impurities, nor is the distance between neighbouring lines any more equal to a coupling constant. So, don’t be tempted to analyse an AA'XX' spin system as a pair of doublets — the distance in Hz between the big lines is NOT equal to the \textit{ortho} coupling constant.

You will also get higher-order effects when the chemical shifts of two mutually coupling protons move close to each other. The classic example is that of two doublets moving closer, resulting in an AB spectrum. This spin system soon becomes quite tricky when the two AB protons couple to one or more protons in the vicinity and give rise to an ABX or, worse, an ABC spin system.

### 2D NMR

2D NMR spectra reveal which signals couple to each other (COSY, HSQC), or are close in space (NOESY). They are important tools that can help you with the analysis of complicated NMR spectra. An HSQC (C-H correlation) takes about the same time as running a \(^{13}\)C NMR spectrum (ca. 15 minutes). However, while a single \(^1\)H NMR spectrum can be recorded in 3 – 4 minutes, a COSY will take several hours.
A COSY shows which protons are coupled to each other. The off-diagonal cross-peaks are the really important ones since these occur only when a proton on the horizontal axis and one on the vertical axis couple with each other. The NOESY spectrum looks at a first glance very similar to a COSY. However, its off-diagonal peaks show nuclei in a molecule that are close together in space — even if they don’t couple with each other. NOESY is a bit sensitive towards artifacts; for example, you often get stripes (called $T_1$ noise) parallel to the vertical axis for large singlets such as the water signal. Finally, the C-H correlation helps you in assigning non-querternary $^{13}$C NMR signals.

**Dynamic effects**

If a compound shows an NMR spectrum where some signals are unusually broad whereas most other signals remain sharp as usual, this is often an indication of a dynamic process that occurs at the NMR timescale. NMR spectroscopy is able to detect dynamic processes such as hindered rotation around an amide bond, slow ring inversions, dynamic equilibria between two stable species, and much more. The appearance of the NMR spectrum will become dependent on temperature. At low temperature, the NMR spectrum will show sharp signals of two species, whereas at elevated temperature the NMR spectrum will have just one set of signals which is an average of the two. We talk about **slow exchange** at low temperature and **fast exchange** at high temperature. In between the two extremes comes a point when the signals of the two components move closer together and finally merge — always accompanied by a characteristic **line broadening** of the NMR signals involved.

The temperature at which two signals merge is called **coalescence temperature**. The difference $\Delta \nu$ in Hz between the coalescing lines is then related to the rate $k$ of exchange at the coalescence temperature. The rate constant $k$ is linked to the free energy of activation ($\Delta G^\ddagger$) by the Eyring equation which you will encounter in your B19PC lectures; this allows NMR spectroscopists to determine the activation barrier of a dynamic process by simply looking at the temperature dependence of NMR lineshapes.

- At $T_c$:
  \[
  k = \frac{\pi}{\sqrt{2}} \Delta \nu
  \]

  From Eyring equation:
  \[
  \Delta G^\ddagger \text{[J mol}^{-1}] = 8.314 \times T_c \text{ (22.96 + ln } T_c \text{ − ln } \Delta \nu)
  \]

  ... then **coalesce** at $T_c$ ... and finally sharpen to one signal