

Week 1

Project 1 Presentations

1.1 Introduction to Proton, Carbon, Nitrogen, and Phosphorus

1/11:

- Our presentation.
- ^{13}C NMR presentation (Angel, Nate).
 - Broadband decoupled ^{13}C NMR gives no coupling with protons, so the number of peaks is the number of distinct carbons.
 - Low abundance of ^{13}C gives 100 times weaker signal than ^1H .
 - Gyromagnetic ratio γ is 1/4 that of ^1H .
 - The signal intensity is proportional to γ^3 , so overall, proton signal is about 6400 times stronger than ^{13}C .
 - Solution: Increase sample concentration, longer relaxation delay (d1), higher field strength NMR (600 MHz), DEPT, 2D NMR.
 - Chemical shifts: 0-220 ppm.
 - Two regions: Above and below 100 ppm.
 - Aliphatic: 0-50 ppm.
 - EWG-substituted aliphatic: 50-100 ppm.
 - Aromatic: 100-150 ppm.
 - Since carbon is more electronegative than hydrogen, adding carbon substituents shifts signals downfield.
 - Resonance structures and partial charges can help predict shifts.
 - Steric effects: Up to 10 ppm shifts from van der Waals interactions of atoms being near each other, especially in rigid molecules.
 - Impurities.
 - CDCl_3 has an equally heighted triplet at 77 ppm due to the spin 1 deuteron splitting the carbon peak into 3 peaks of equal height.
 - Functional groups (shifts and couplings).
 - Alkenes: 100-150 ppm.
 - One-bond coupling of about 150 Hz.
 - Alkynes: 70-90 ppm.
 - Results from differences in electronic configuration around the carbon nuclei.
 - One-bond coupling to proton in acetylene of about 249 Hz (*sp*-hybridized carbons have huge couplings; shorter bonds!).
 - Two-bond coupling to other proton of about 49 Hz.

- Aldehydes.
- Halides.
 - Big bulky electron density on iodine pushes shift for alkyl iodides to -20 to -40 ppm.
- Why isn't ^{13}C NMR quantitative?
 - We'll talk about it, but it might have something to do with NOESY.
 - Polarization transfer can amplify signals *and* decouple.
 - Turning off NOE, very long relaxation delay, and can make ^{13}C NMR quantitative!
- For ^1H , we don't have an issue with chemical shift anisotropy. For almost any heteroatom (and carbon), we will have this issue. And it increases with the square of the field strength, so there's an ideal field strength range for carbon NMR whereas for proton, you can go as high as they make them.
- ^{15}N and ^{31}P NMR (Natalie, Rosalind).
 - For both nuclei: Typical chemical shifts, proton-heteroatom coupling constants, and what this can look like in biomolecular NMR.
 - ^{15}N .
 - Spin $1/2$.
 - 0.37% abundant.
 - Low γ .
 - > 1000 ppm range of chemical shifts.
 - Most groups fall within 0-500 ppm. Metal nitrosyl (M-NO) complexes are roughly 300-1200 ppm, but this is helpful for identifying metal complexes (such as iron sulfur complexes, i.e., metalloproteins which store or transport NO)!
 - Proton-nitrogen couplings are difficult to detect. Magnitude affected by solvent used as well as intermolecular interactions (e.g., hydrogen bonding).
 - A variety of techniques be used to study biomolecules (e.g., at MIT in Mei Hong's lab). HSQC experiments, solid-state, isotopic labeling, and many more.
 - DNA is only made of four simple nitrogen-containing heterocycles, so looking at isolated nucleotides can be very helpful.
 - Shifts affected by post-translational modifications, DNA shape, protonation, etc.
 - 100-130 ppm for backbone nitrogens in proteins, varies drastically for side chains (30-220 ppm).
 - HSQC is a protein fingerprint, as well as the gateway into deuterium exchange experiments. Can be used to study the folding of proteins.
 - ^{31}P .
 - Spin $1/2$ and 100% isotopic abundance. Thus, very easy to measure!
 - 2000 ppm shift range.
 - Upfield defined by P_4 at -527 ppm.
 - Downfield defined by...
 - Proton-phosphorus J -coupling allows us to tell how far part phosphorus and hydrogen atoms are. Very useful tool!
 - Great examples in the slides.
 - Chirality determination with a chiral phosphorus reagent and ^{31}P NMR.
 - ^{31}P NMR in DNA.
 - Gives information about backbone conformation (e.g., A vs. B vs. Z).
 - Dickerson dodecamer backbone; researchers were able to correlate ^{31}P NMR shift with the percent of a certain conformation in the sample.
 - Cummins and Radosevich labs will have a lot to say on ^{31}P - ^{31}P couplings!
 - These nuclei are also not often studied at higher fields; you lose stuff even at 600 MHz.