Week 1

1D NMR Principles and Practices

1.1 Underlying Principles of NMR

1/4:
- Philosophy: NMR is a complicated and useful set of tool for chemists.
- Background on Walt.
  - Training: Masters, PhD, Postdoc, and 5 jobs in NMR.
  - 20 years industry experience, 10 years academia experience, some small company experience.
  - Considers himself somewhere in the middle between knowing nothing and everything about NMR.
  - Experience in natural products discovery, drug discovery, biological NMR, etc.
- Goal of the class: Distill what's most important for us to know.
- Announcements.
  - Syllabus now posted on Canvas!
  - Everything important will be posted on Canvas.
  - MestReNova is what we should use; TopSpin is what Walt is more comfortable with.
  - Slides posted to Canvas at the end of the day.
- This week: The fundamentals.
  - Chemical shift, coupling constants, correlations (new), NMR relaxation
- The NMR periodic table.
  - ^{1}H has almost 100% spin 1/2.
  - ^{12}C is 99% abundant and has spin 0.
    - Thus, we can only do NMR with ^{13}C.
- The resonant frequency depends on an absolutely fundamental physical property called the **gyromagnetic ratio** (γ).
  - Highest gyromagnetic ratio is tritium (^{3}H), then fluorine, then a whole bunch, then phosphorus, carbon, nitrogen (with a bunch in between these three as well).
- Higher magnetic field gives more signal.
  - But 1/4 as much for ^{13}C as for ^{1}H, because γ for ^{13}C is 1/4 what it is for ^{1}H.
- The highest field NMR systems commercially available are at 1.2 GHz.
  - Walt will typically only go up to 600 MHz in this class, corresponding to a 14.1 T magnet.

- Range of chemical shifts.

Figure 1.1: Chemical shift ranges of common nuclei.

  - The range of chemical signals we'll see is tiny, though; only about 6000 Hz if we're talking about a 10 ppm window.
  - Different nuclei appear in different windows and with different ranges (think of how carbon is 0-200 ppm vs. proton -5-15!!).
  - Note that the ranges in Figure 1.1 are to scale relative to each other, but have been scaled up absolutely by 10 times.
- All atoms' spins are active as soon as we magnetize the sample in the magnet bore. Differentiating between them is now an electronics problem.
- α- and β-D-glucose's anomeric protons have significantly different chemical shifts (4.6 ppm vs. 5.1 ppm, roughly).
- Oxygen is virtually all spin 0 ^{16}O, but protons will couple to each other and to ^{13}C (giving carbon satellites).
  - 1% of the time, the proton is coupled to ^{13}C, and gets massively split.
  - All couplings exist; it's just a question of whether we can see them!
    - 170 Hz coupling for the 1-bond carbon-to-proton coupling.
    - 2-bond connection is then expected to be much smaller, maybe 25-30 Hz.
  - Protons are present in much higher concentration, though, so we see their splitting much more (but it's also smaller because they're farther away!). This is why vicinal protons couple in 4-8 Hz instead of 200 Hz.
- Sergei: Why no coupling to the alcohol protons?
  - Because the sample is in D_2O, we get exchange everywhere to OD.
  - Since deuterium is spin 1, it should split the spin 1/2 nucleus into a triplet. But it also has 1/6 the gyromagnetic ratio. Additionally, fast exchange prevents any meaningful coupling from developing.
  - Dissolving the sample in (very dry) DMSO-d_6 will *not* lead to proton exchange, and we *can* observe the couplings to the hydroxyl protons!
- Equations.
  - 5/2 exponent for gyromagnetic ratio means it *really* matters for sensitivity.
- 600 MHz denotes the resonance for protons at the set magnetic field.
  - Carbon would be at 150 MHz in this case (because 1/4 gyromagnetic ratio)!
  - 140-150 A of current in the magnetic.
- A 4 Hz coupling is on the order of parts per billion, so to discern it, we need parts per billion homogeneity in the magnetic field. This is why we need shimming.
  - Shimming is done with additional coils that impart additional magnetism to parts of the sample.

  - Shimming is done for all of the few dozen coils every once in a while, and then with some of the coils for each particular sample.
  - To shim, you measure the deuterium lock signal and how broad or narrow/high the peak is and then you fiddle with the coils!
  - All you really have to look at is the height because the area is the same, so the height of the lock signal correlates to how good the shimming is.
  - Today, we do **radian shimming**, which tells us how to change the current in the coils to make the shimming better.
  - Shim coils can only be adjusted so far; if there's no sample below the coil, the shimming likely can't compensate enough to get a good spectrum.

- Administrivia.
  - There will be some kind of group project.
  - Final project is for us to use our skills to do something useful.
  - Write up our PSets independently, but we can work together on them.