- EA and MS are destructive analytical techniques, meaning that the sample gets destroyed (e.g., by burning or fragmentation) in the process. This requires sample in hand, some of which we can destroy.
- IR is nondestructive. This means that we can recover our sample after the experiment! In other words, IR spectroscopy can be run from afar.
- For example, consider the spectrum in Figure 1.15.
    - This is still an IR spectrum, even though the x-axis is in wavelength (λ) — measured in µm — and y-axis is in brightness.
    - The spectrum has a bad baseline, but we'll just forgive this.
    - A number of vibrational modes of CO_2, H_2O, and CO are recorded.
- What is this spectrum?
    - It is an IR spectrum of the atmosphere of Mars!
    - It was taken by the James Webb Telescope two years ago, in 2022.
    - We've had an IR spectrum of the moon since the 1940s, but this is new and cool!
- To generalize, here are some major applications of IR spectroscopy.
    - Space.
        - Just like the example in Figure 1.15, IR spectroscopy can be used to find new molecules in celestial bodies.
        - If you ever see a news story along the lines of "Amino acids found on an asteroid," the amino acids in question were probably detected using IR spectroscopy.
    - Climate science.
        - Example: Measuring the concentrations of methane (a potent greenhouse gas) over the arctic.
    - Art.
        - Example: Authenticating old paintings.
        - Indeed, we can use IR to look for diagnostic pigments.
        - A nondestructive method like IR is better in this context than a destructive method like EA or MS because you obviously don't want to chip off a bit of the paint just for an analysis!

- Why is CO_2 (a nonpolar molecule) IR active?

    - The stretching modes are IR silent.
    - However, some of the bending modes induce a dipole, and these are the IR active modes.

- Could we use IR to detect the presence of oxygen on Mars?

    - Oxygen is probably not IR active, so we could not use IR to detect its presence on Mars. There is probably another way, though!

1.4 Nuclear Magnetic Resonance - 1

9/11:
- Lecture 3 Recap.

    - Key regions of an IR spectrum from Figure 1.12.
    - A follow-up on C−H peaks.
        - See Steven's announcement on Canvas.

- Essentially, C−H peaks are typically (1) small and (2) not diagnostic.
    1. The reason why C−H peaks may be small is outside the scope of this class, but it has to do with the polarizability of the C−H bond.
    2. By not diagnostic, we mean that their presence or absence in an IR spectrum doesn't tell us very much since C−H bonds exist in almost every organic molecule. Indeed, the real power of IR spectroscopy is in identifying heteroatoms and their stretches.
- Takeaway / expectation for this course: If you are given a spectrum displaying a peak in the C−H region and there's nothing else to which you can assign this peak, you are expected to know that it's a C−H peak.

- A preview of what's to come in this course.

    - The remainder of this week: Rich in content, because there's a lot to talk about in NMR.
    - Next week: We'll begin putting all of the structure determination techniques together.

- Today: Nuclear magnetic resonance (NMR).

    - Reading: Clayden et al. (2012), Chapters 3 & 13.
    - Be sure to read this!!

- Lecture outline.

    - Theory.
    - Spectrometer schematic.
    - Spectrum elements.
    - Trends in identifying peaks.
    - Integration.
    - Coupling.

- **Nuclear magnetic resonance**: A method in which we measure the magnetic environment of the nucleus to learn about the chemical environment around atoms.

    - This is one of the most powerful and widely used techniques in modern, real-life Orgo research.
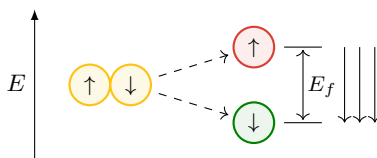
- NMR theory.

Figure 1.16: Nuclear magnetic resonance theory.

- Postulate: The nuclear spin has a small magnetic moment.
    - We won't be diving too deeply into the physics, but recall from Gen Chem that *spin* is one of the main quantum numbers of a nucleus.[7]
- Normally (i.e., in the absence of an external magnetic field), nuclei can be either spin up (↑) or spin down (↓) and have the same energy.
    - However, in an external magnetic field (↓↓↓), the nuclei split into different energy levels.
    - The level that is **parallel** to the magnetic field is stabilized, and the level that is **antiparallel** to the magnetic field is destabilized.

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[7] n, ℓ, m_ℓ, m_s.

- If we irradiate a nucleus in the spin down state, we can flip it to the spin up state.
  - However, we must irradiate it using a photon with the **resonance frequency** (E_f).
- A plot of the frequency required to flip each nucleus is called an NMR spectrum.
  - Example: If we only had one kind of nucleus in our sample, we would only see one peak in the spectrum. In particular, this peak would correspond to the frequency at which all of the (identical) nuclei present would flip.
- Another consideration is that for a nucleus to spin flip, its nuclear spin must not equal zero.
  - For example, the nuclei in ^{1}H and ^{13}C atoms have nonzero spin.
    - ➢ We'll look at NMR spectra of these nuclei extensively in this course.
  - However — and this is beyond the scope of this class — chemists can also look at spin-active nuclei like ^{11}B, ^{19}F, and ^{31}P.
- Lastly, note that the resonance frequency is not the same for all nuclei due to a phenomenon called **shielding**.

- **Resonance frequency** (of an atomic nucleus in a certain magnetic field): The frequency of radiation needed to flip the spin of the nucleus from spin down to spin up. *Denoted by* $\boldsymbol{E_f}$.

- **Shielding**: The chemical environment affects the frequency at which a nucleus flips.
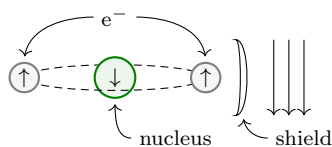

Figure 1.17: Shielding in NMR.

- Essentially, electrons have their own magnetic moments, which "shield" the nucleus they surround from the external field.
- More electron density — such as that from electron-donating groups (EDGs) — leads to more shielding.
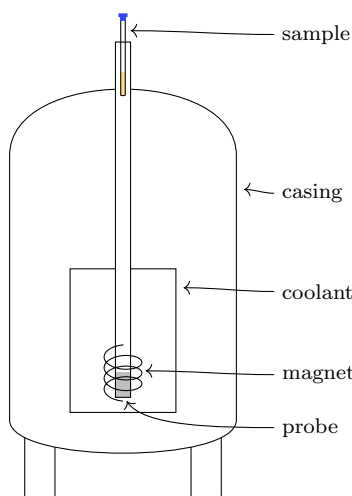
- A schematic of an NMR spectrometer.

Figure 1.18: NMR spectrometer schematic.

- – We have NMR spectrometers all over campus at MIT!
- – Basically, an NMR machine looks like a box with legs.
- – The "box" is a casing containing coolant.
- – The coolant keeps everything at the right temperature.
  - ■ Typically, the coolant is either liquid helium or liquid nitrogen.
  - ■ We use coolant because the magnet in an NMR spectrometer works more efficiently at lower temperatures.
- – The sample we are analyzing gets lowered into the magnet.
  - ■ The "sample" consists of a glass tube filled with the chemical we seek to analyze.
  - ■ Note that before we put the chemical in the tube, we usually dissolve it in a liquid solvent.
- – In the center of the magnet, there is a probe. The probe detects the frequencies that the nuclei absorb.
- – For scale, a typical NMR machines are about the size of a person, though some are smaller and some are as big as a shed!
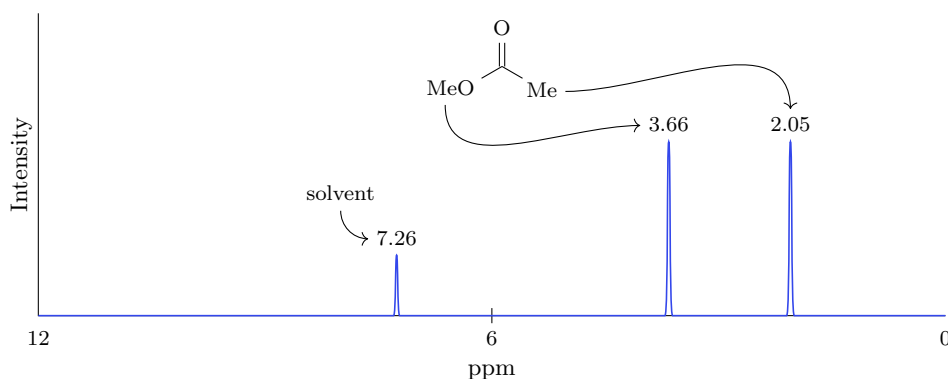
- Example NMR spectrum: Methyl acetate ($\sim_O \overset{O}{\overset{\|}{\diagdown}}$).

Figure 1.19: NMR spectrum of methyl acetate.

- – The y-axis is the intensity of the NMR peaks.
- – The x-axis is in parts per million (ppm).
  - ■ Raw NMR peaks are reported in hertz, but then we can divide by the magnet strength to get ppm (a uniform scale).[8]
- – We get two peaks at 3.66 and 2.05, corresponding to the two types of protons in the molecule.
- – We also get a third peak at 7.26, corresponding to the solvent in which the methyl acetate is dissolved.
  - ■ However, you can ignore this peak.
  - ■ We are discussing solvent peaks now so that if you ever look up an NMR spectrum online (or something) and see an extra peak, you know it probably corresponds to the solvent.

- We now discuss some common resonance frequencies, i.e., the resonance frequencies for protons in common functional groups. We call such resonance frequencies the **chemical shift**.

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[8]To elaborate: It is a fact of physics that the stronger the external magnetic field, the larger the energy level splitting E_f (see Figure 1.16). If the E_f of a nucleus increases, then we will need a higher frequency photon to flip it than we would have needed in the previous, weaker external magnetic field. Thus, to cancel out the influence of the external magnetic field strength on our raw data, we divide by the magnetic field strength. This division ensures that whether a specific NMR spectrometer's magnet is stronger or weaker, we can identify identical nuclei with an identical ppm value in our spectrum.

- **Chemical shift** (of a nucleus): The resonance frequency of the nucleus. *Denoted by δ. Units* **ppm**.
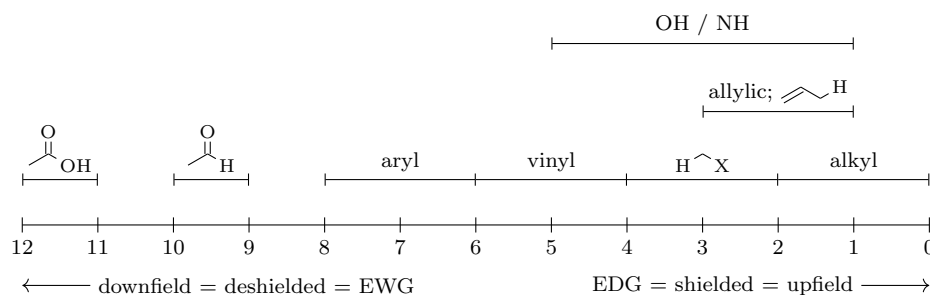

Figure 1.20: Chemical shifts of common proton types.

  - Tetramethylsilane (TMS / SiMe$_4$) has a chemical shift of 0 *by definition.*
    - In other words, TMS is used as an NMR reference compound, and we express the chemical shift of all other nuclei as the distance from TMS in ppm.
  - There are two directions: **Upfield** and **downfield**.
  - Peaks corresponding to carboxylic acid protons, alcohol protons, and amine protons are often broad due to chemical exchange.
    - This is exactly the same as exchangeable protons from IR spectroscopy!
  - OH and NH peaks are *often* broad, although they can appear as sharp peaks, including with coupling to neighboring protons.

- **Upfield** (chemical shift): A chemical shift that is more to the right side of an NMR spectrum. *Also known as* **shielded**.

  - Protons with upfield chemical shifts are often near electron donating groups (EDGs).

- **Downfield** (chemical shift): A chemical shift that is more to the left side of an NMR spectrum. *Also known as* **deshielded**.

  - Protons with downfield chemical shifts are often near electron withdrawing groups (EWGs).

- Important trend: More and stronger EWGs leads to a higher chemical shift.

- Example: $H_3C-F > H_3C-Cl > H_3C-Br$.

  - Sorted by electronegativity, fluorine is more electronegative than chlorine, which is more electronegative than bromine.
  - As such, the chemical shift of the protons in fluoromethane (4.10) is greater than the chemical shift of the protons in chloromethane (3.05), which is greater than the chemical shift of the protons in bromomethane (2.68).

- Example: Isopentane ( ).

  - The sole tertiary proton is surrounded by three EWGs (2 methyl and 1 ethyl), so it has the highest chemical shift at 1.46.
  - The secondary protons are surrounded by two EWGs (1 methyl and 1 isopropyl), so it has the second highest chemical shift at 1.20.
  - The primary protons then have the lowest chemical shifts. For example, the three protons at the right end of the molecule have a chemical shift of 0.86.

- Why are tertiary carbons more deshielded when adjacent methyl groups donate to a carbocation?

  - Prof. Elkin will not answer this question in full now because the answer comes from MO theory.
  - Simply, carbon is more electronegative than hydrogen, so carbon is a better EWG than hydrogen.

- Why does more electron density lead to a greater shielding effect and hence a lower resonance frequency?

    - Because they feel more of the external magnetic field, so it takes more energy to flip them to the higher spin state.

- **Integration** (of an NMR peak): The area under the peak.

    - The integration of a peak is equal to the number of nuclei in that chemical environment.

        ■ In other words, nuclei that are **chemically equivalent** help form the same peak in an NMR spectrum.

    - Only *relative* integrations matter; there is no use for *absolute* integration values.

- **Chemically equivalent** (protons): A set of protons within a molecule that are in the same chemical environment.
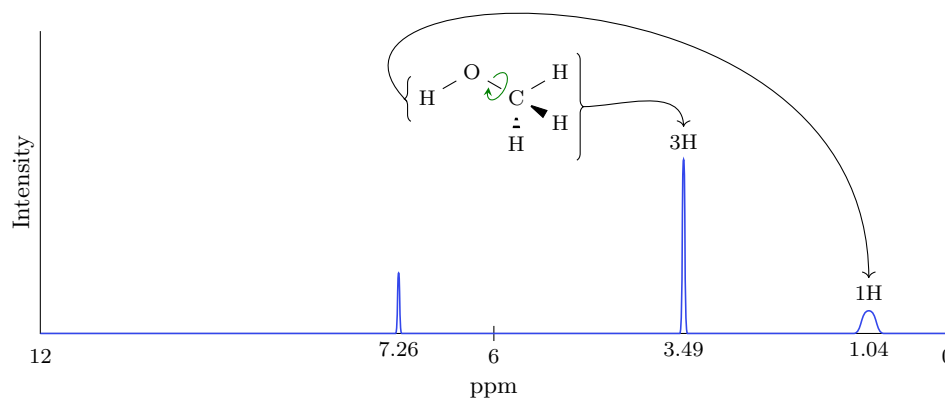
- Example NMR spectrum: Methanol (MeOH).

Figure 1.21: NMR spectrum of methanol.

    - In this example, there is free rotation around the C−O single bond. This rotation puts all of the methyl protons in the chemical environment, i.e., they are chemically equivalent. Thus, because they are chemically equivalent they all have the identical resonance frequency of 3.49 and all contribute to that peak.

        ■ Indeed, *any* single bond with unrestricted rotation makes protons chemically equivalent, leading to them resonating at the same frequency.

    - However, the alcohol proton is in a different chemical environment from the other protons, leading to a second peak.

        ■ Notice that this peak is broad because the alcohol proton is exchangeable!

    - Key takeaway: Chemical equivalence is why we see two peaks in Figure 1.21 (one for each *chemically nonequivalent* type of proton) instead of four (one for *every* proton).

        ■ It is also why one peak integrates to three times the area of the other peak.

        ■ These integrations are often denoted 1H and 3H.

    - Notice that once again, we have an extra peak at 7.26 due to our solvent.

- In our next example, we will see another way in which integration ratios can manifest themselves.

    - However, there will also be another feature (as of yet unmentioned).

    - We will discuss this feature subsequently.

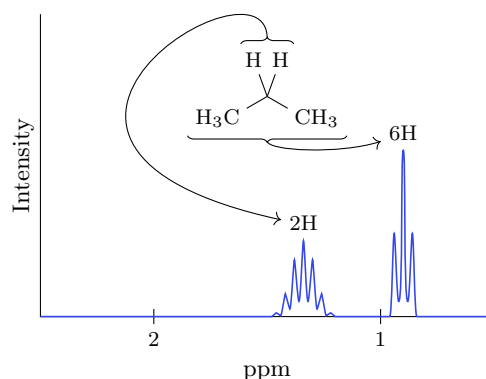- Example NMR spectrum: Propane ($\smile$).

Figure 1.22: NMR spectrum of propane.

- This NMR spectrum consists of two "funny-shaped" peaks.
- The ratio of their integrations is $1 : 3$. However, note that a $1 : 3$ ratio is equivalent to a $2 : 6$ ratio! (And a $3 : 9$ ratio, a $4 : 12$ ratio, etc.)
- Thus, based on the NMR spectrum alone, we do not have enough information to decide what exact ratio the peaks are showing.
  - Rather, we will need to know something else about the structure (such as the molecular formula!) in order to decide if it is $1 : 3$ or $2 : 6$!
  - Supposing we knew from EA and MS that the molecular formula was C_3H_8, we could then confirm that this is a $2 : 6$ ratio because $2 + 6 = 8$ total protons.

- Peaks have "funny shapes" due to an effect called **coupling**.

- **Coupling**: When nuclei are adjacent to each other, they alter one another's resonance frequency by inducing a ½ increase or ½ decrease. *Also known as* **proton coupling**, **peak splitting**, **multiplicity**.

  - Coupling is based on the same physical idea as shielding.
    - Indeed, just like electrons have magnetic moments that can interfere with their host nucleus, adjacent nuclei have magnetic moments that can interfere with their host nucleus.
  - When peaks split, they do so symmetrically about the original resonance frequency, and the new peaks have the same integration as the old peak.

- There are more kinds of coupling besides proton-proton coupling, but proton-proton is all we'll talk about today (and probably in this whole class).

- More on proton-proton splitting.

Adjacent Protons (n)	Peak Pattern ($n+1$)	Ratio of Peaks	Image
0	singlet (s)	1	
1	doublet (d)	$1 : 1$	
2	triplet (t)	$1 : 2 : 1$	
3	quartet (q)	$1 : 3 : 3 : 1$	

Table 1.3: Proton-proton coupling.

- Thus, in Figure 1.22, our peaks are a 2H septet and a 6H triplet.
- The ratio of peaks forms **Pascal's Triangle**! You can Google why, if you're interested!!
- Sometimes, these peak patterns are called **multiplets**.
  - ■ We tend to use the term "multiplet" when the splitting is either very complicated or low resolution, that is, when we cannot tell if the splitting is a triplet, quartet, septet, or something even more exotic (like what we'll discuss next class!).

- Note that identical protons do not couple themselves.[9]

  - This is why (for example) the septet in Figure 1.22 is not an octet: The two secondary protons do not couple to each other.

- **Coupling constant**: A measure of coupling. *Denoted by* **J**. *Units* **Hz**.

  - Protons that couple each other have identical J values.

- Coupled protons split via **roofing**.

- **Roofing**: A phenomenon in which coupled peaks slant towards each other.

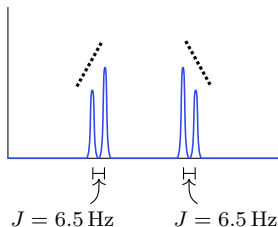$$J = 6.5\,\text{Hz} \qquad J = 6.5\,\text{Hz}$$

Figure 1.23: Roofing in NMR.

  - When you couple two doublets, they have this extra fun shape that helps hint toward coupling.

- Next time: Where J comes from, compounds coupling, carbon NMR, and more!

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[9]For a (heavily mathematical, quantum mechanical) explanation of why, see this resource.