Certain nuclei such as ^1H nuclei have a quantum mechanical property called spin that comes with an associated magnetic field.

^1H nuclei can exist in two different spin states, $+1/2$ and $-1/2$.

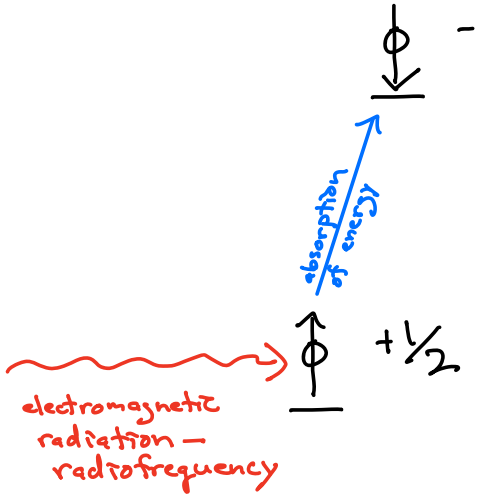
In a strong magnetic field, the nuclei with spin line up with ($+1/2$) and against ($-1/2$) the magnetic field.

Nuclei in the $+1/2$ spin state are of lower energy and nuclei in the $-1/2$ spin state are of higher energy in a magnetic field.

The difference in energy between the $+1/2$ and $-1/2$ spin states is directly proportional to the strength of the magnetic field experienced by the nuclei

Radiofrequency electromagnetic radiation of exactly the right energy (i.e. frequency) is absorbed by $+1/2$ spin state nuclei causing them to "flip" to the $-1/2$ spin state. $\Rightarrow$ A process called "resonance"

NMR experiment → place sample of a molecule in a very strong magnetic field

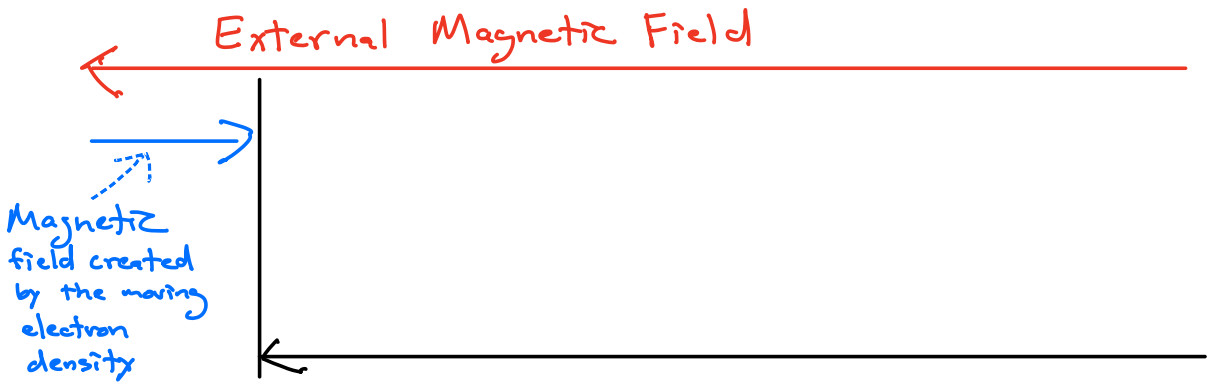


The energy absorption/nuclear spin flipping phenomenon is called "Resonance"

The ^1H nucleus of spin state $+\frac{1}{2}$ absorbs a quanta of energy of precisely the correct frequency and the nucleus is "excited" to the $-\frac{1}{2}$ spin state

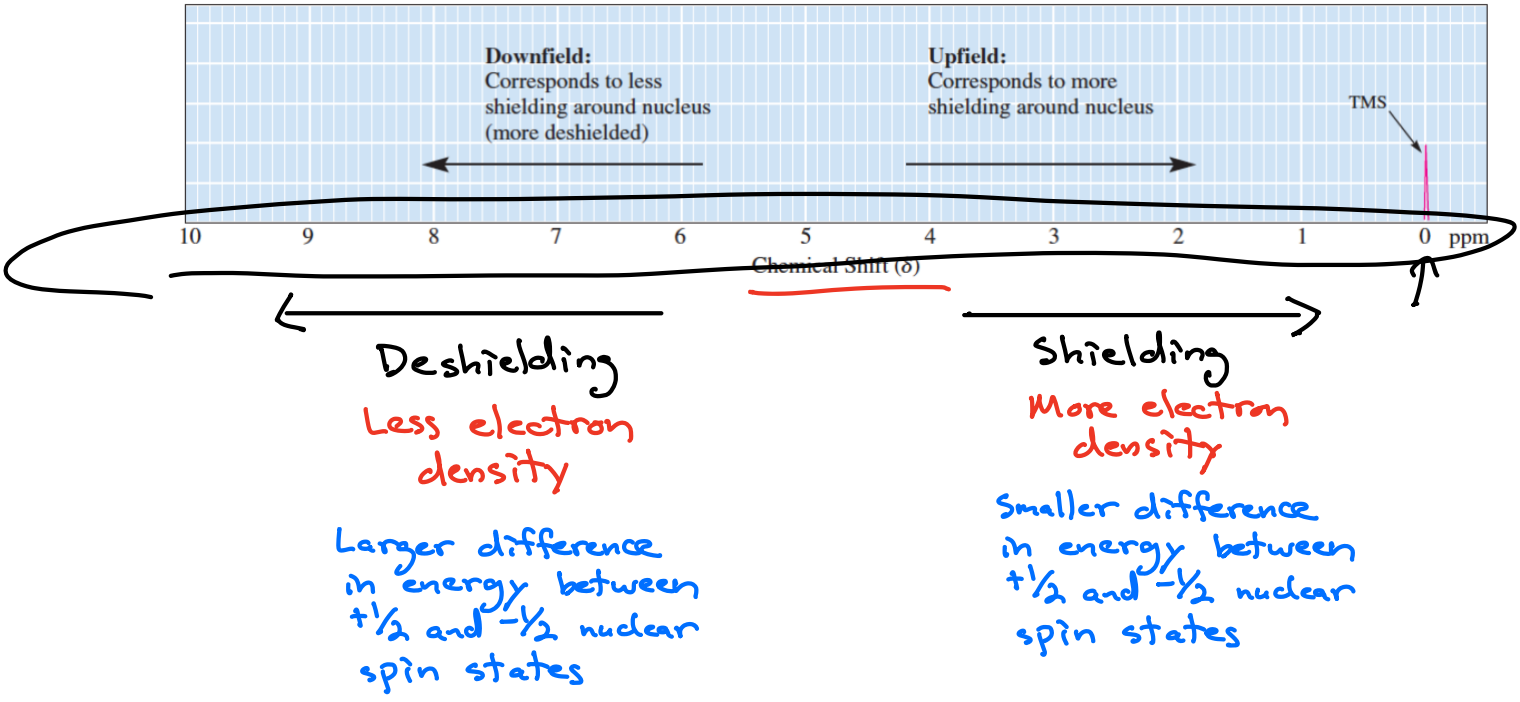
Shielding → explanation

The external magnetic field induces electron density to circulate, which creates its own small magnetic field that will always directly oppose the external magnetic field.



The magnitude of the magnetic field experienced by a nucleus under the electron density.

Plot is backwards → larger values to the left!



J. The hybridization state of carbon atoms attached to an H atom influences shielding in predictable ways by removing differing amounts of electron density around adjacent nuclei.

K. Electron density in pi bonds also has a large effect on H atom shielding because pi electrons are more free to circulate in an a magnetic field compared to electron density in sigma bonds. Geometry of the pi bond is important.

Table 13.3 The Effect of Hybridization on Chemical Shift

Type of Hydrogen (R = alkyl)	Name of Hydrogen	Chemical Shift δ
RCH_3, R_2CH_2, R_3CH	Alkyl	0.8–1.7
$R_2C{=}C(R)CHR_2$	Allylic	1.6–2.6
$RC{\equiv}CH$	Acetylenic	2.0–3.0
$R_2C{=}CHR$, $R_2C{=}CH_2$	Vinylic	4.6–5.7
RCHO	Aldehydic	9.5–10.1

Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*	Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*
		RCH_2OH	3.4-4.0
R_2NH	0.5-5.0	RCH_2Br	3.4-3.6
ROH	0.5-6.0	RCH_2Cl	3.6-3.8
RCH_3	0.8-1.0	$RCOCH_3$	3.7-3.9
RCH_2R	1.2-1.4	$RCOCH_2R$	4.1-4.7
R_3CH	1.4-1.7	RCH_2F	4.4-4.5
$R_2C{=}CRCHR_2$	1.6-2.6	$ArOH$	4.5-4.7
$RC{\equiv}CH$	2.0-3.0	$R_2C{=}CH_2$	4.6-5.0
$RCCH_3$	2.1-2.3	$R_2C{=}CHR$	5.0-5.7
$RCCH_2R$	2.2-2.6	$H_2C(O)CH_2$	3.3-4.0
$ArCH_3$	2.2-2.5	RCH	9.5-10.1
RCH_2NR_2	2.3-2.8	$RCOH$	10-13
RCH_2I	3.1-3.3		
RCH_2OR	3.3-4.0		

* Values are relative to tetramethylsilane. Other atoms within the molecule may cause the signal to appear outside these ranges.

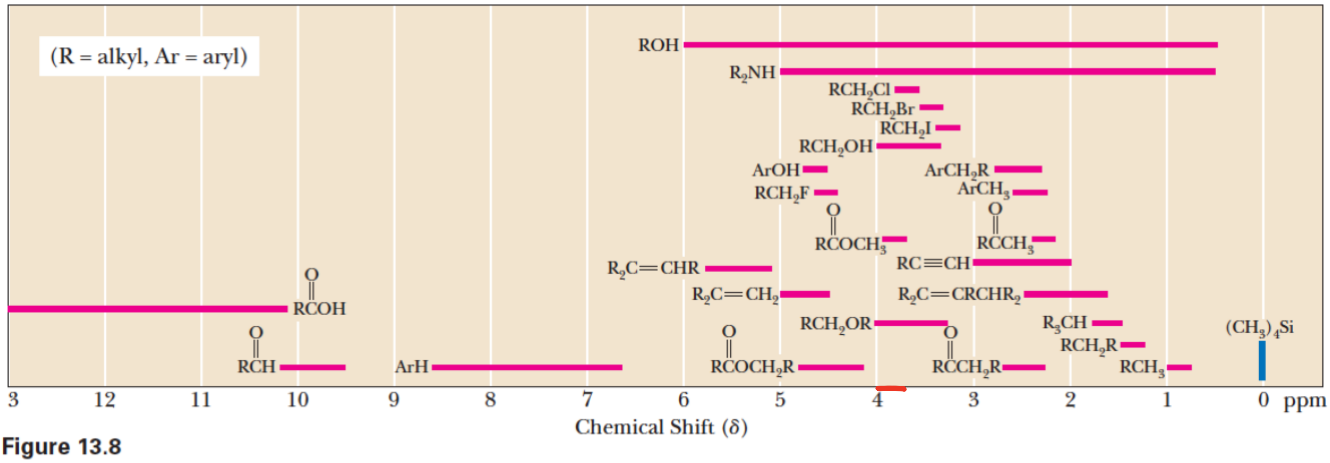
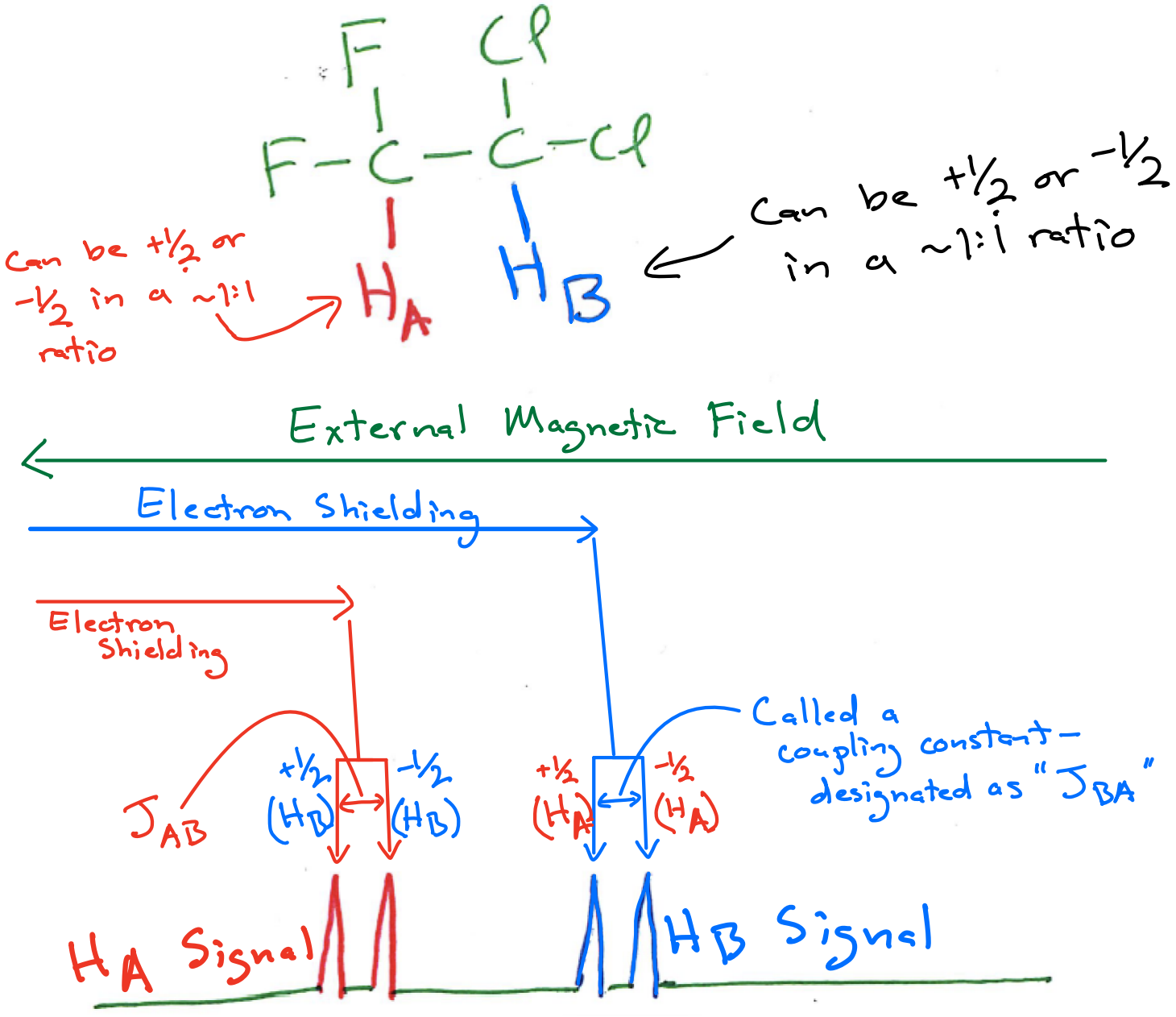


Figure 13.8
Average values of chemical shifts of representative types of hydrogens. These values are approximate. Other atoms or groups in the molecules may cause signals to appear outside of these ranges.

N. Adjacent nuclei have magnetic fields associated with their spins. The spins of equivalent adjacent nuclei can be either +1/2 or -1/2, and at room temperature they are found in about a 50:50 mixture at any given nucleus (very slight excess of lower energy +1/2). These can add to give n+1 different spin **combinations** in the proportions predicted by Pascal's triangle. Each different spin combination produces a different magnetic field, which leads to n+1 splittings in the peaks of the NMR spectra of the adjacent (no more than three bonds away) nuclei.



$J_{AB} = J_{BA}$ → Coupling constants between H_A and H_B are the same in both directions

General case → For "n" equivalent adjacent H atoms a signal is split into "n+1" peaks

As long as the H atom is on a C that is freely rotating

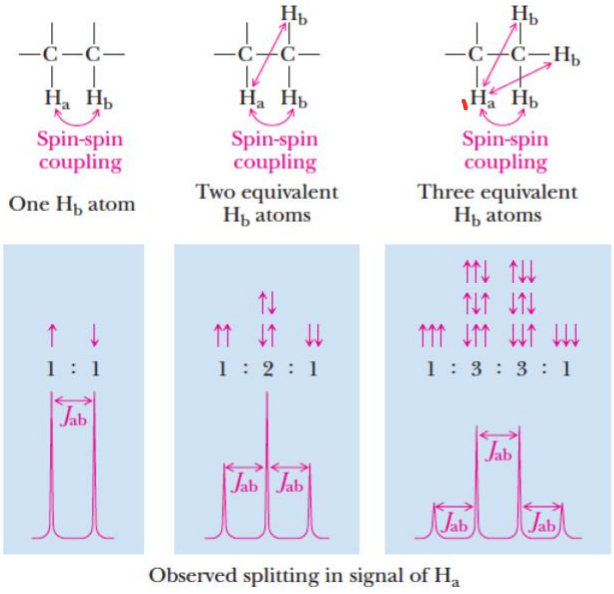


Figure 13.15
The origins of signal splitting patterns. Each arrow represents an H_b nuclear spin orientation.

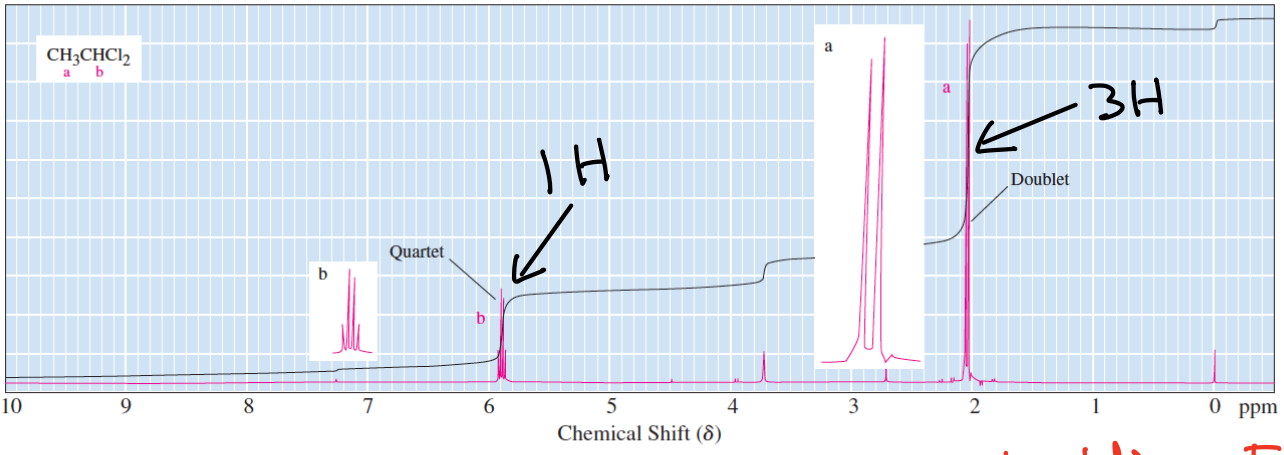
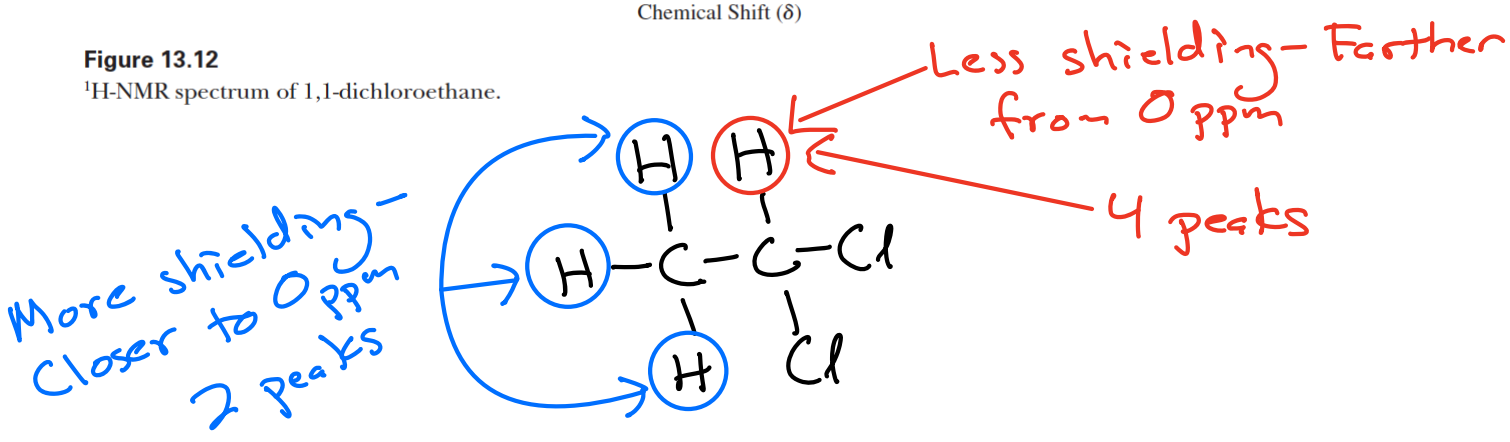
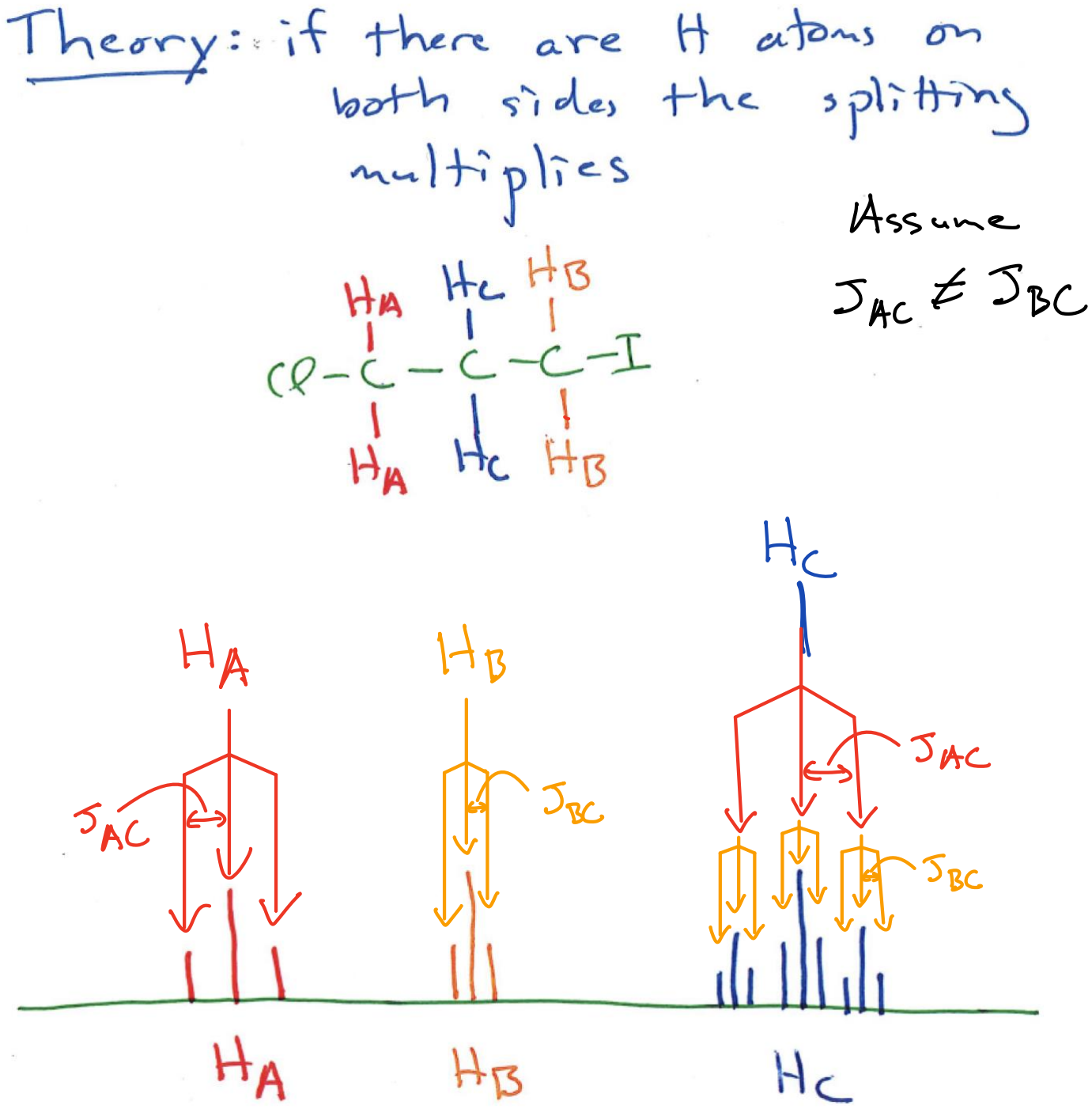


Figure 13.12
^{1}H-NMR spectrum of 1,1-dichloroethane.



O. THEORY: When there are two sets of adjacent H atoms, the number of peaks multiply. For example, a CH_2 group with a CH_2 group and a CH_3group on either side should show 3 x 4 = 12 splittings! You can say this group is a "triplet of quartets" (or a "quartet of triplets").

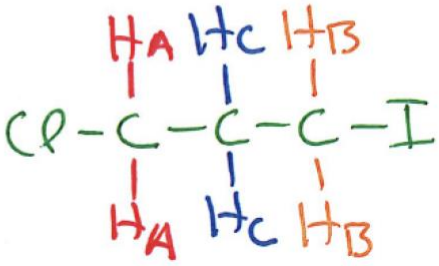
P. WHAT YOU WILL SEE IN REALITY : For alkyl groups complex splittings simplify because coupling constants ("J") are all about the same. In practice, if there are n adjacent H atoms, equivalent or not, you will see n+1 peaks. This is an approximation, but almost always true on spectra taken with all but the most sophisticated NMR spectrometers.

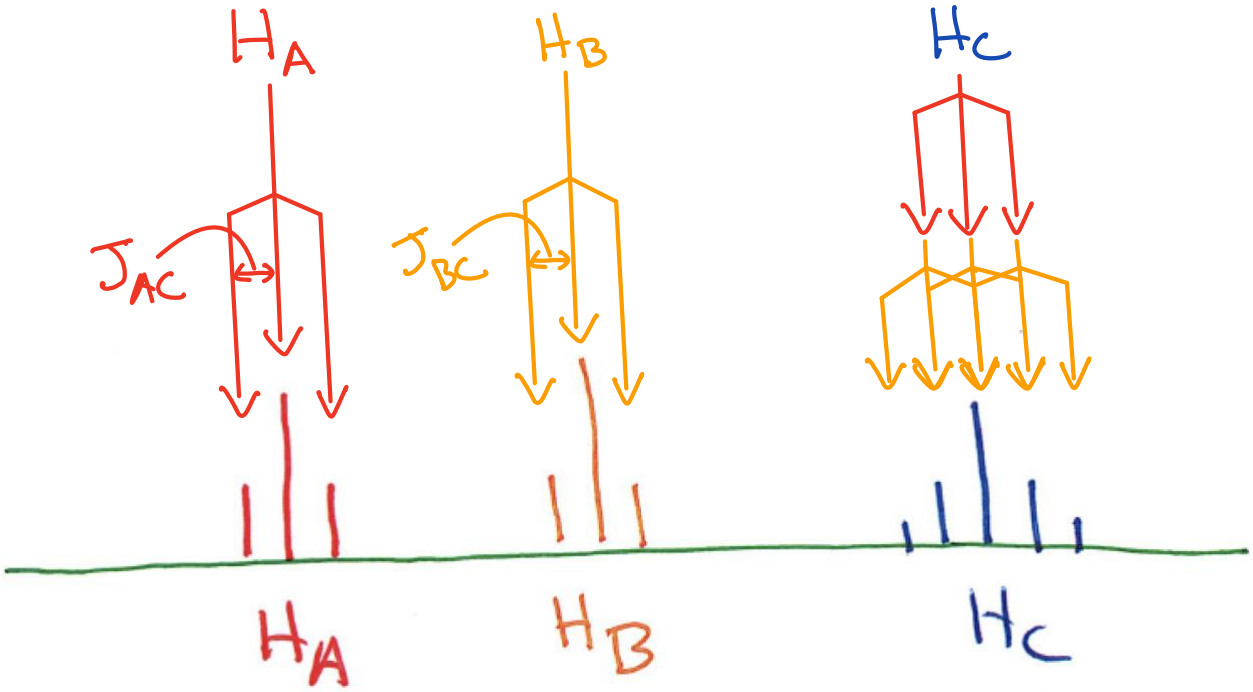


Reality: The splitting does multiply, but $J_{AC} = J_{BC}$ causing overlap of peaks

$\Rightarrow$ we observe $n+1$ peaks

(n = total # of adjacent H atoms)





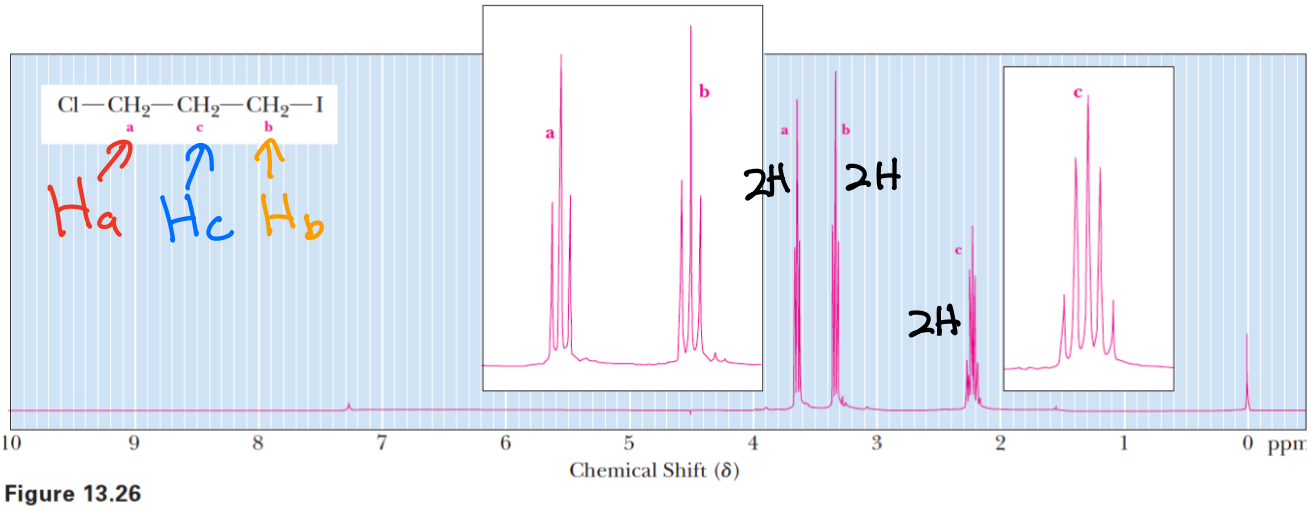


Figure 13.26
300 MHz ^{1}H-NMR spectrum of 1-chloro-3-iodopropane

Recap:

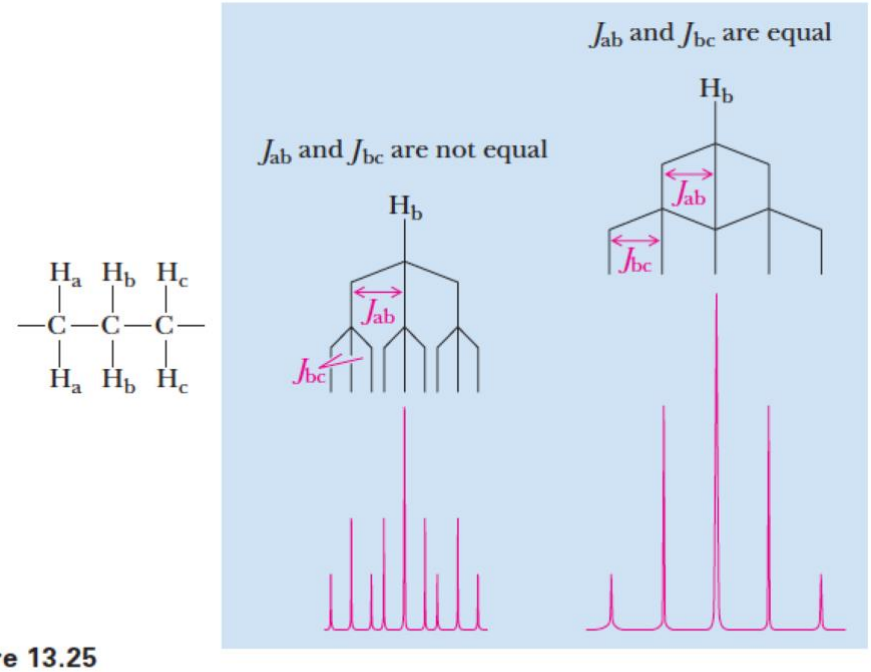
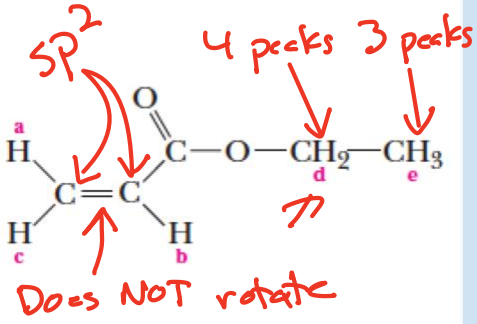


Figure 13.25
Simplification of signal splitting that occurs when coupling constants are the same.

Q. Non-equivalent H atoms on the same C atom can split each other (called geminal coupling), for example on alkenes or small rings. This coupling usually has very small coupling constants, so is difficult to see on some spectra.

H_a, H_c and H_b are all different



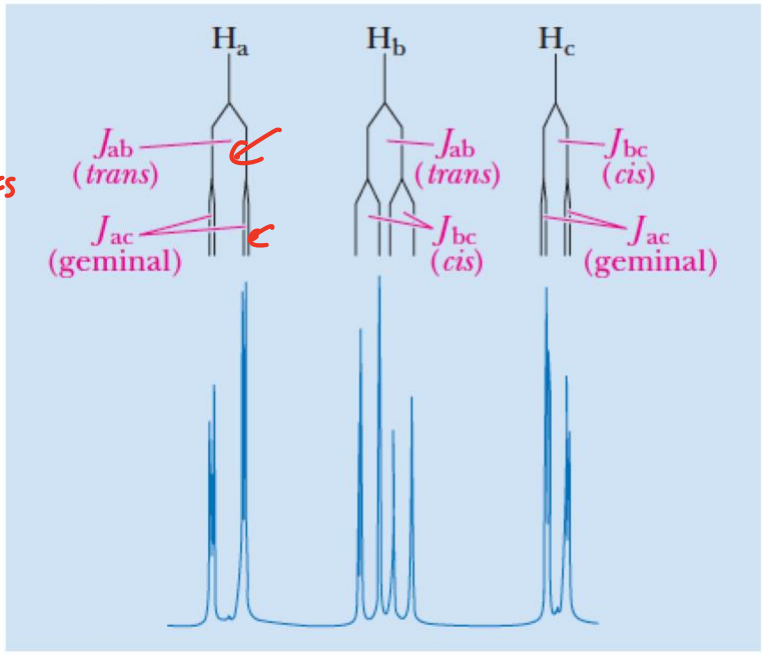


Figure 13.22
Tree diagrams for the complex coupling seen for the alkenyl H atoms in the ^{1}H-NMR spectrum of ethyl propenoate.

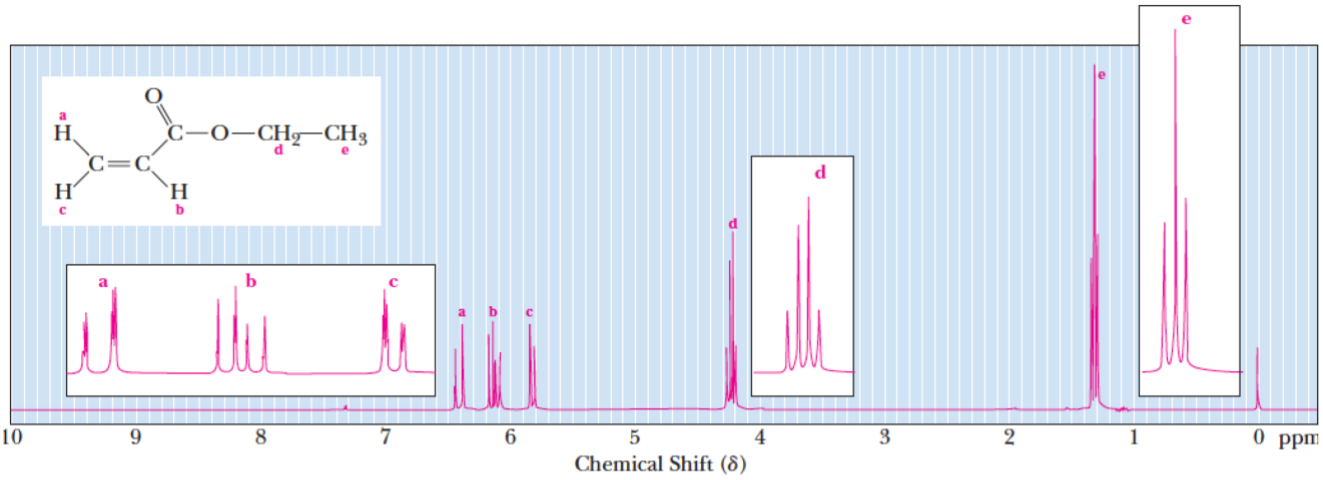


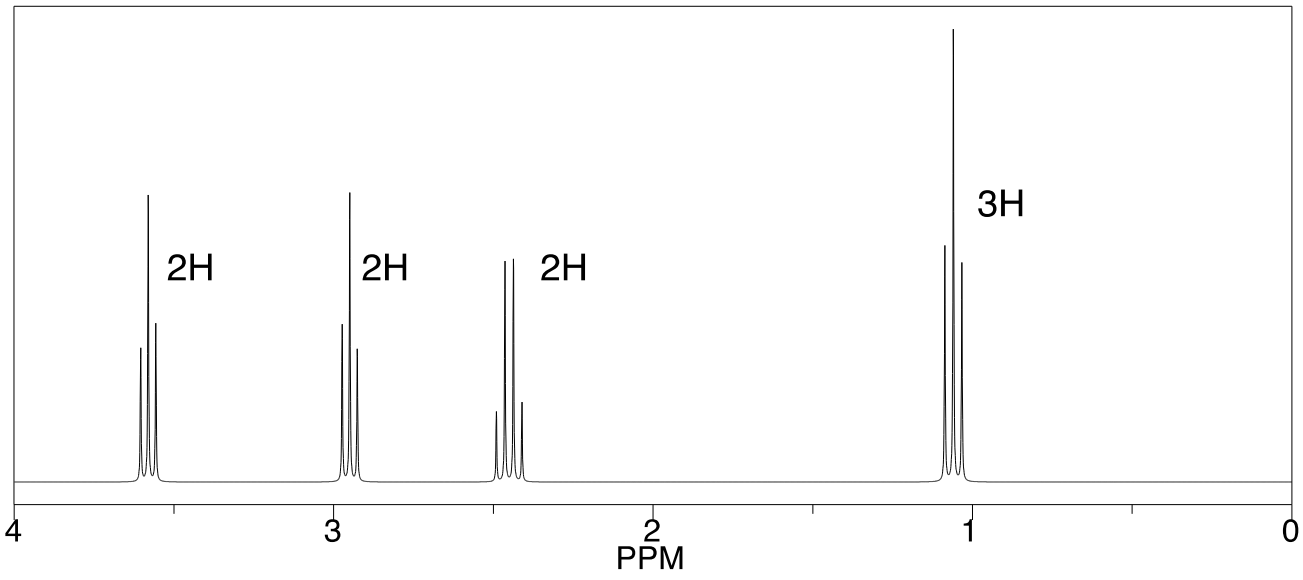
Figure 13.21
300 MHz ^{1}H-NMR spectrum of ethyl propenoate.

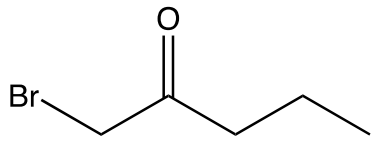
On the same C atom ⇒ "Geminal" coupling constants for H atoms on the same sp^2 C atom are very small

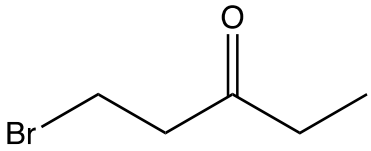
Trans coupling constants are larger than cis coupling constants

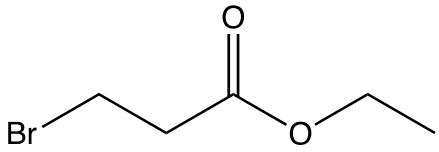
V. When solving NMR spectra problems:

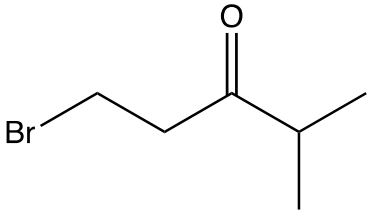
1) **Determine number and relative integrations of signals predicted for a given structure**
2) **Make sure the splitting pattern matches with the spectrum for each signal and**
3) **If the number and relative integrations as well as splitting patterns match with the spectra, compare expected chemical shifts with those of the signals in the spectra.**

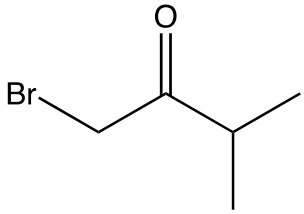


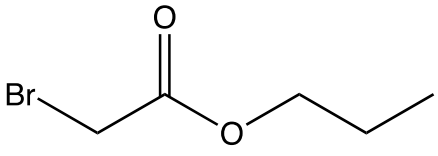






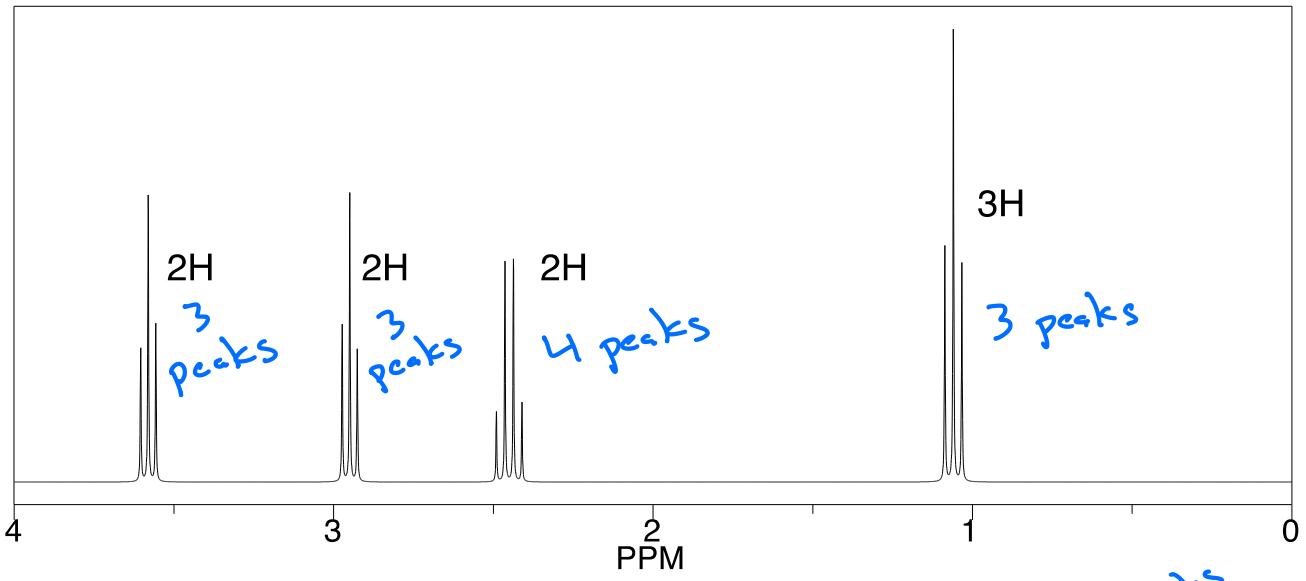


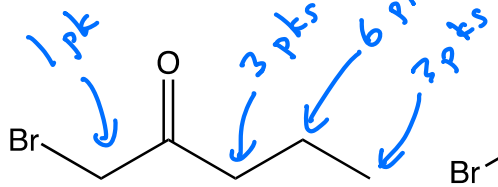




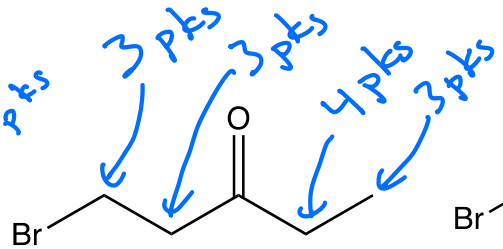
V. When solving NMR spectra problems:

1) **Determine number and relative integrations of signals predicted for a given structure**
2) **Make sure the splitting pattern matches with the spectrum for each signal and**
3) **If the number and relative integrations as well as splitting patterns match with the spectra, compare expected chemical shifts with those of the signals in the spectra.**

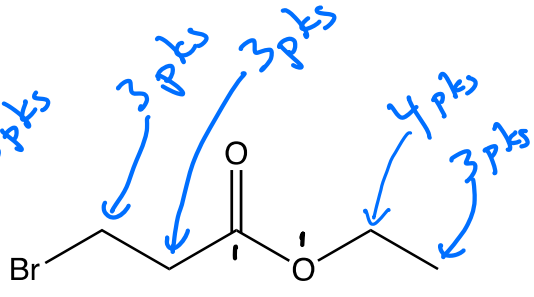




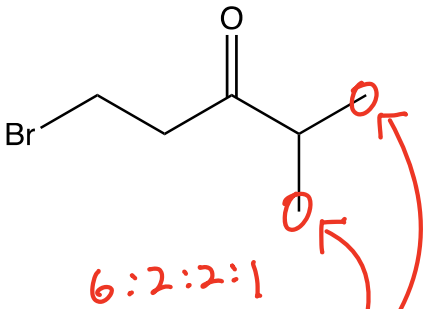
3 : 2 : 2 : 2



3 : 2 : 2 : 2

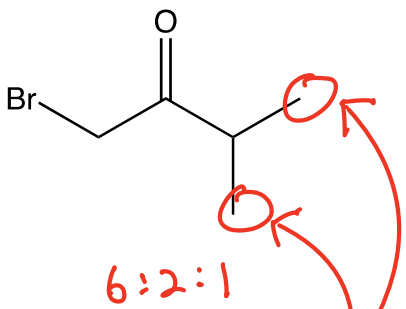


3 : 2 : 2 : 2



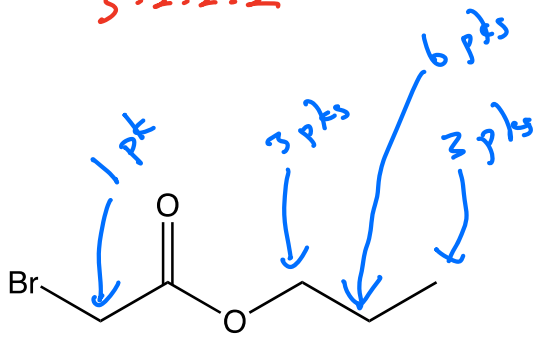
6 : 2 : 2 : 1

All 6 H atoms on the 2 methyl groups are equivalent due to symmetry



6 : 2 : 1

All 6 H atoms on the 2 methyl groups are equivalent due to symmetry



3 : 2 : 2 : 2

Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*	Type of Hydrogen (R = alkyl, Ar = aryl)	Chemical Shift (δ)*
		RCH_2OH	3.4-4.0
R_2NH	0.5-5.0	RCH_2Br	3.4-3.6
ROH	0.5-6.0	RCH_2Cl	3.6-3.8
RCH_3	0.8-1.0	$RCOCH_3$	3.7-3.9
RCH_2R	1.2-1.4	$RCOCH_2R$	4.1-4.7
R_3CH	1.4-1.7	RCH_2F	4.4-4.5
$R_2C{=}CRCHR_2$	1.6-2.6	$ArOH$	4.5-4.7
$RC{\equiv}CH$	2.0-3.0	$R_2C{=}CH_2$	4.6-5.0
$RCCH_3$	2.1-2.3	$R_2C{=}CHR$	5.0-5.7
$RCCH_2R$	2.2-2.6	$H_2C{-}CH_2$	3.3-4.0
$ArCH_3$	2.2-2.5	RCH	9.5-10.1
RCH_2NR_2	2.3-2.8	$RCOH$	10-13
RCH_2I	3.1-3.3		
RCH_2OR	3.3-4.0		

* Values are relative to tetramethylsilane. Other atoms within the molecule may cause the signal to appear outside these ranges.

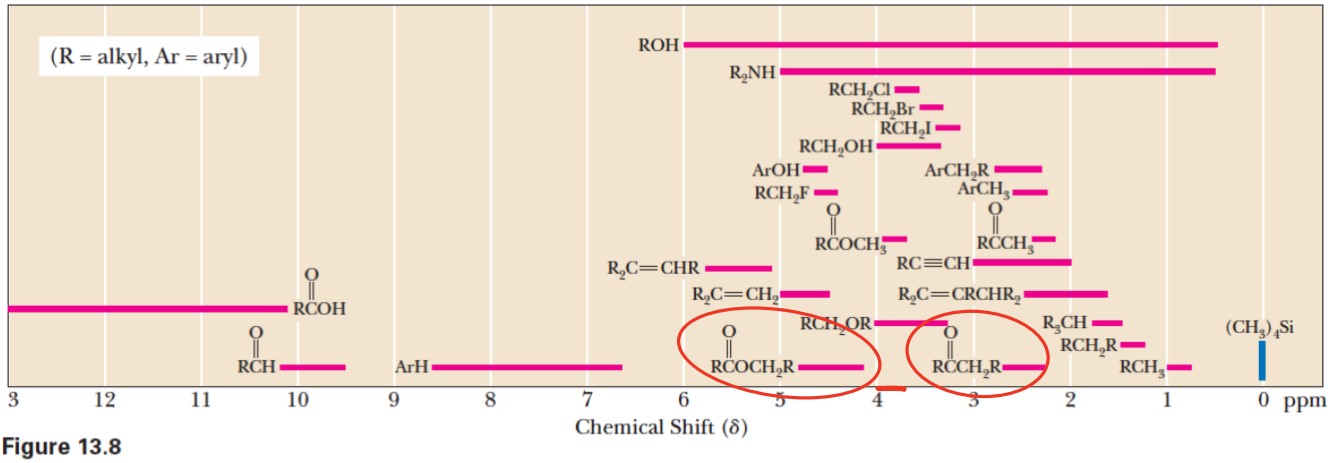
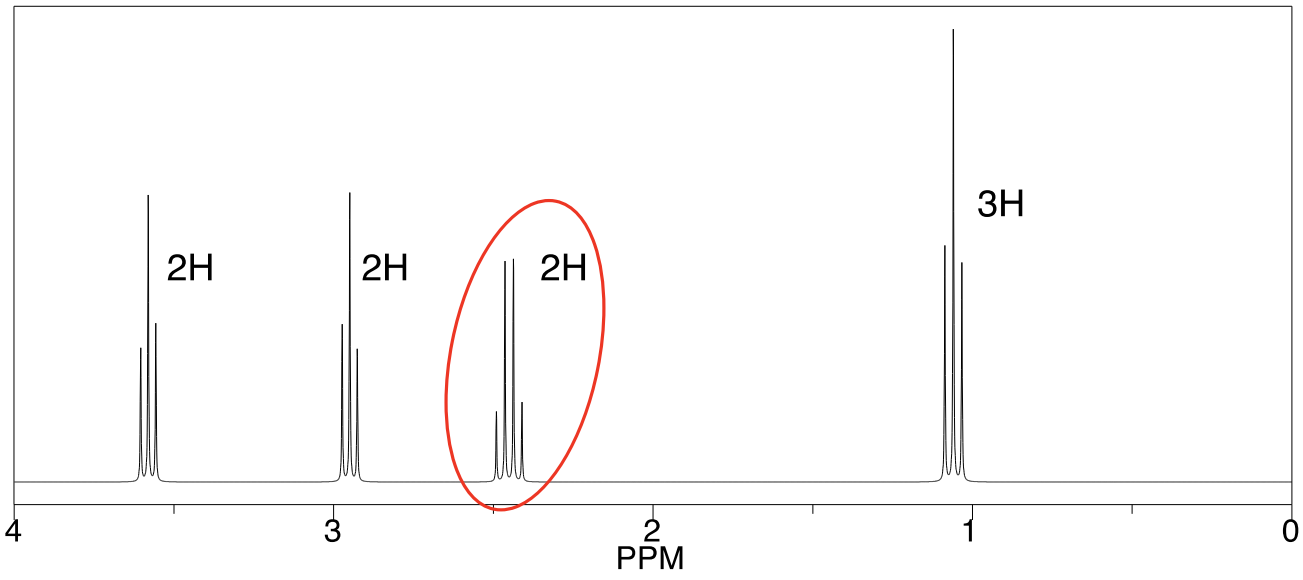
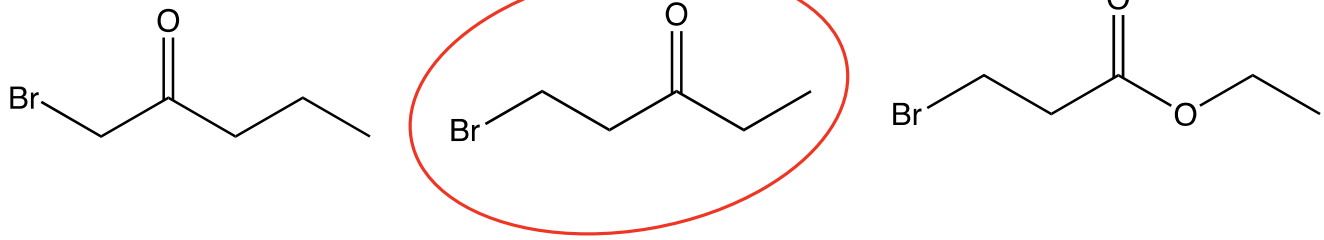


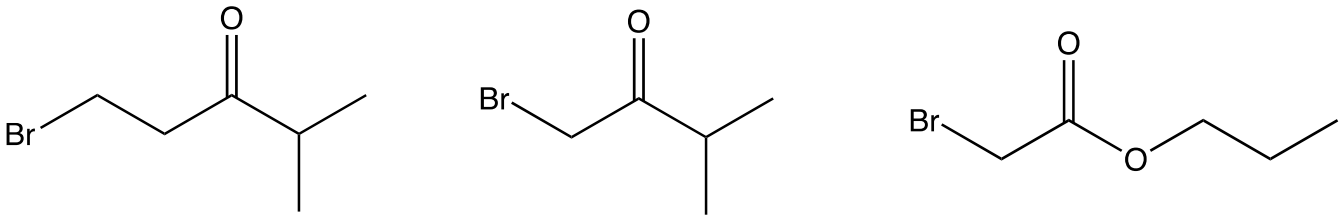
Figure 13.8
Average values of chemical shifts of representative types of hydrogens. These values are approximate. Other atoms or groups in the molecules may cause signals to appear outside of these ranges.

V. When solving NMR spectra problems:

1) **Determine number and relative integrations of signals predicted for a given structure**
2) **Make sure the splitting pattern matches with the spectrum for each signal and**
3) **If the number and relative integrations as well as splitting patterns match with the spectra, compare expected chemical shifts with those of the signals in the spectra.**





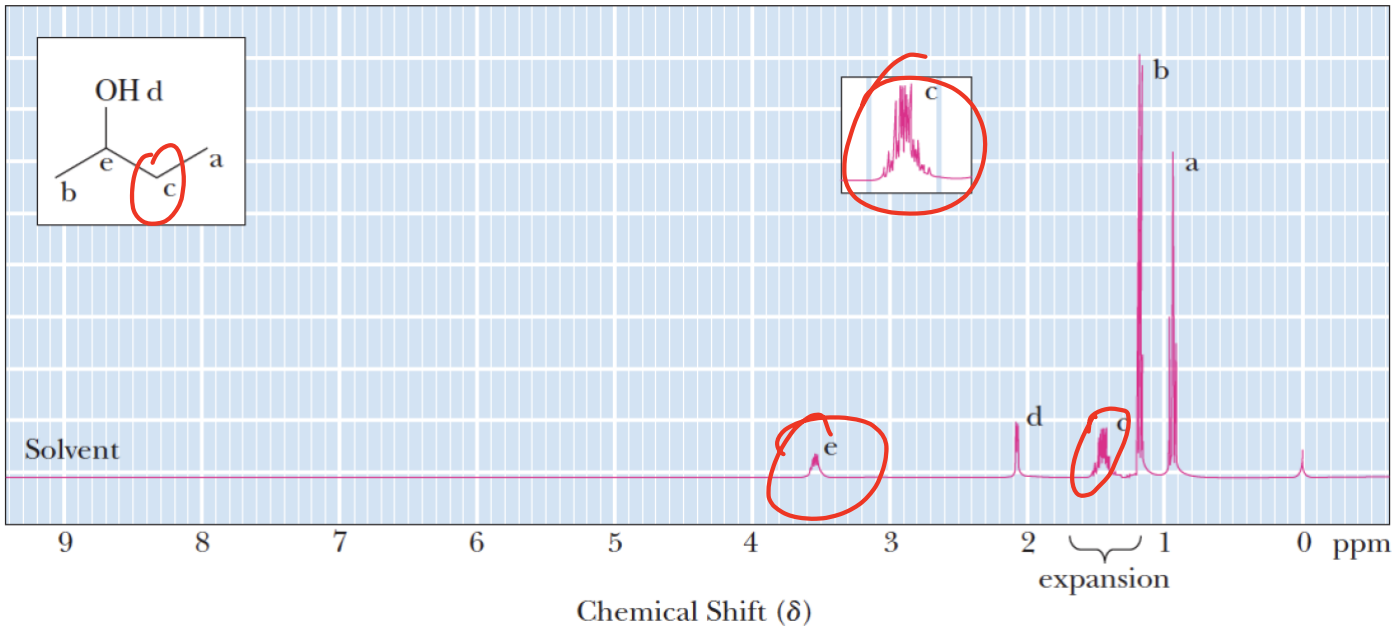


R. Deuterium atoms do not show up in ^{1}H-NMR spectra, so deuerated solvents are used to dissolve NMR samples.

S. The H atoms of relatively acidic functional groups (alcohols, carboxylic acids, amines) exchange rapidly, so they often do not split adjacent protons, and they can be replaced (signal disappears) with deuterium by adding a drop of D_2O to the NMR sample.

T. H-bonding changes the location of a signal for H-bonding groups in a concentration dependent manner explaining why -OH and -NH_2 group signals can vary so much in location.

U. The splitting of a -CH_2- group adjacent to a chiral center will be "messed up", that is split into many peaks. This is useful for identifying chiral centers in molecules.



W. The old way to carry out an NMR experiment: Scan wavelengths (ex. High to low ppm) of radiofrequency electromagnetic radiation then measure absorbance during the scan. This is NOT used any more.

X. What we did not tell you: After a nuclear spin is flipped back from +1/2 to -1/2, it will relax back to the +1/2 spin state and EMIT a photon of the same wavelength it absorbed in the first place.

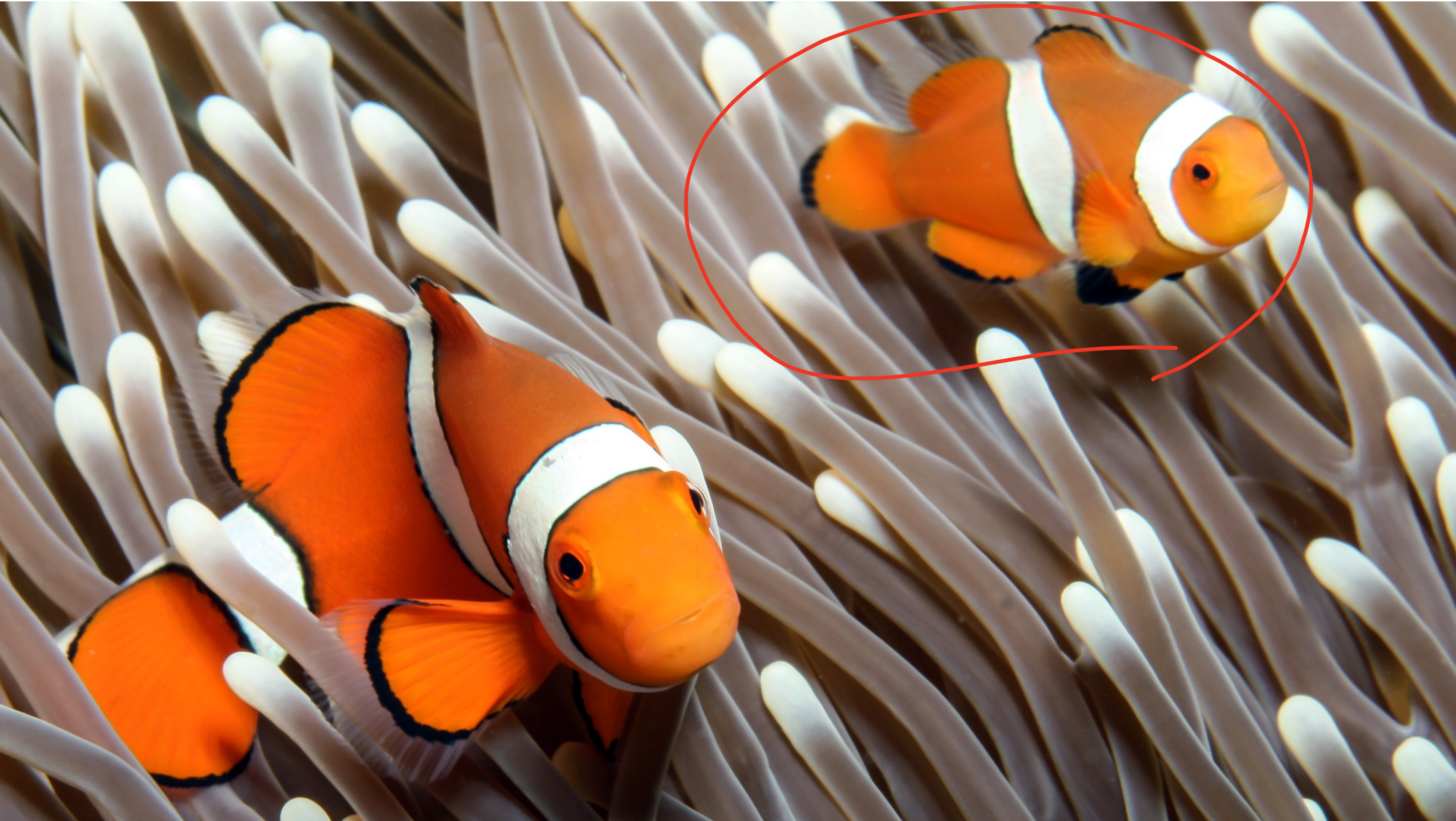
Y. How modern NMR works:

The sample is irradiated with all wavelengths simultaneously in a short blast → → All ^{1}H nuclear spins are now $-\frac{1}{2}$ ← Then the sample is monitored for emitted photons as the nuclear spins "relax" back to $+\frac{1}{2}$ spin states. The emitted photons are analyzed using a mathematical technique called Fourier Transform (FT) to extract frequency and intensity information. The frequency and intensity information is used to plot the spectrum on the ppm scale.

Z. The Fourier transform converts the emitted photon data into component wavelength and intensity information that is plotted on the ppm scale.

Allows measurement of an NMR spectrum 100's or 1,000's of times very quickly

→ DRAMATICALLY improving signal-to-noise



MRI – ~~Nuclear~~ Magnetic Resonance Imaging – Produces a 3-d image inside the body.

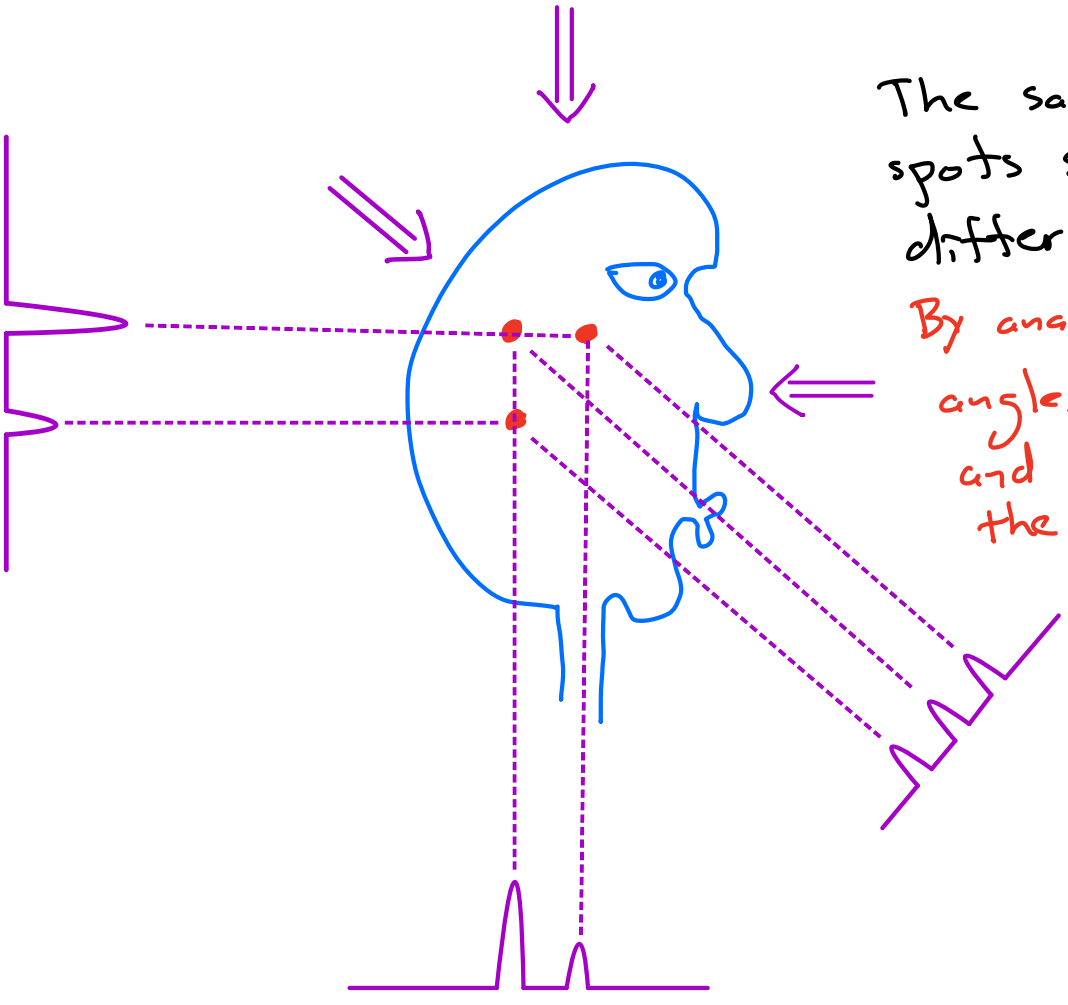
MRI is similar in approach, but complementary to, a CAT scan, which uses X-rays for imaging.

MRI is therefore safer than a CAT scan (no X-rays or other damaging radiation is used). Radiofrequency electromagnetic radiation does not cause DNA damage or any other kind of damage.

MRI primarily visualizes soft-tissue and especially cancer tumors while a CAT scan primarily visualizes bones or Calcium based dyes drunk to visualize the digestive tract.

MRI uses the same principles and NMR.

1) The patient is placed in a very strong magnetic field. Creating this very strong magnetic field is technically very demanding, explaining MRI machines are so expensive (~ 0.5 – 1.5 $ million)
2) The patient is irradiated with radiofrequency electromagnetic radiation.
3) The flipping (resonance) of 1H nuclear spins is monitored – Actually emitted photons are measured using the FT method.
4) Magnetic field gradients are used to gain imaging information. The magnetic field gradients are rotated around a central point and measurements are taken at each angle around 360° to gain 2-dimensional information. This technique is called **tomography**.



The same three spots seen from different angles—

By analyzing all angles the locations and intensities of the 3 objects can be calculated

The overall MRI imaging approach involves looking at each 2-dimensional slice.

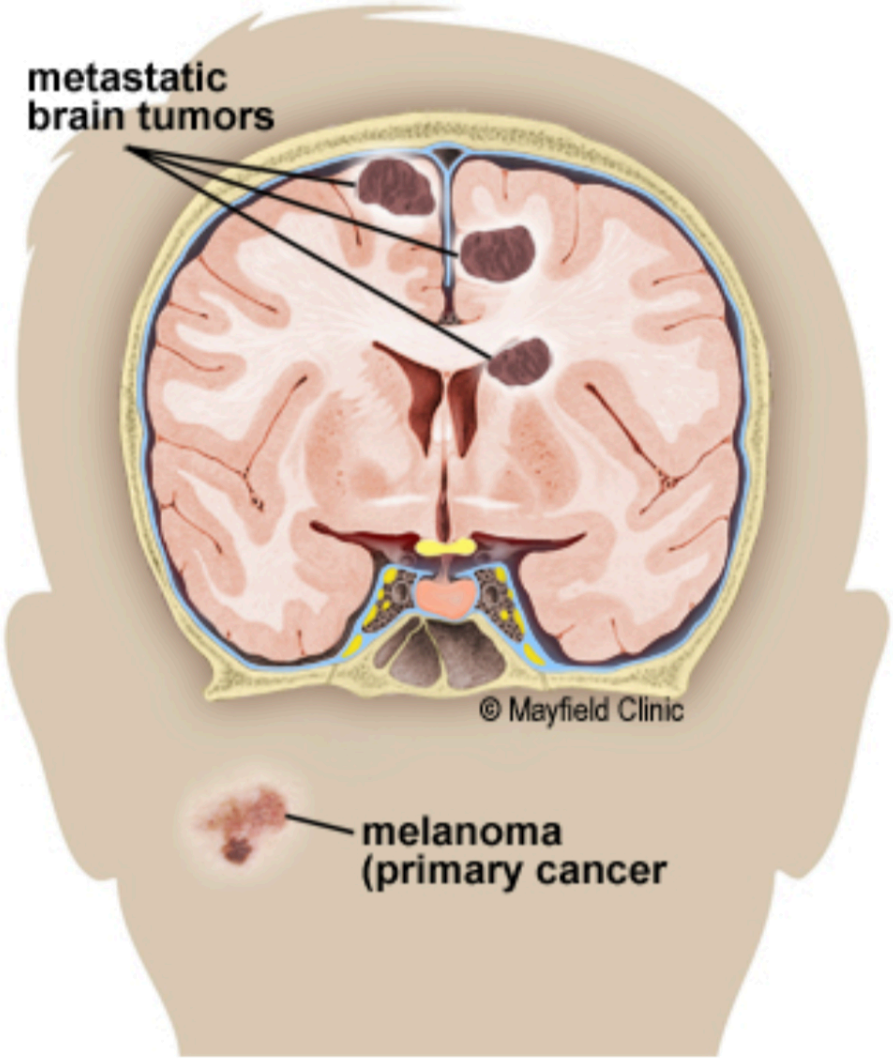
Each slice is added to give a 3-dimensional stack (analogous to stacking DVD's or CD's).

Each slice is shaded to indicate differences in the amount of ^{1}H atoms in different areas/tissues.

Water and fat have the highest density of ^{1}H atoms, so these are primarily being monitored in an MRI image.

The popular medical diagnostic technique of magnetic resonance imaging (MRI) is based on the same principles as NMR, namely the flipping (i.e. resonance) of nuclear spins of H atoms by radio frequency irradiation when a patient is placed in a strong magnetic field. Magnetic field gradients are used to gain imaging information, and rotation of the gradient around the center of the object gives imaging in an entire plane (i.e. slice inside patient). In an MRI image, you are looking at individual slices that when stacked make up the three-dimensional image of relative amounts of H atoms, especially the H atoms from water and fat, in the different tissues [Memorize the preceding passage, as it will be worth 14 points on the final. No I am not kidding, 14 points right there.]

Yep, you must memorize this for the final ↓



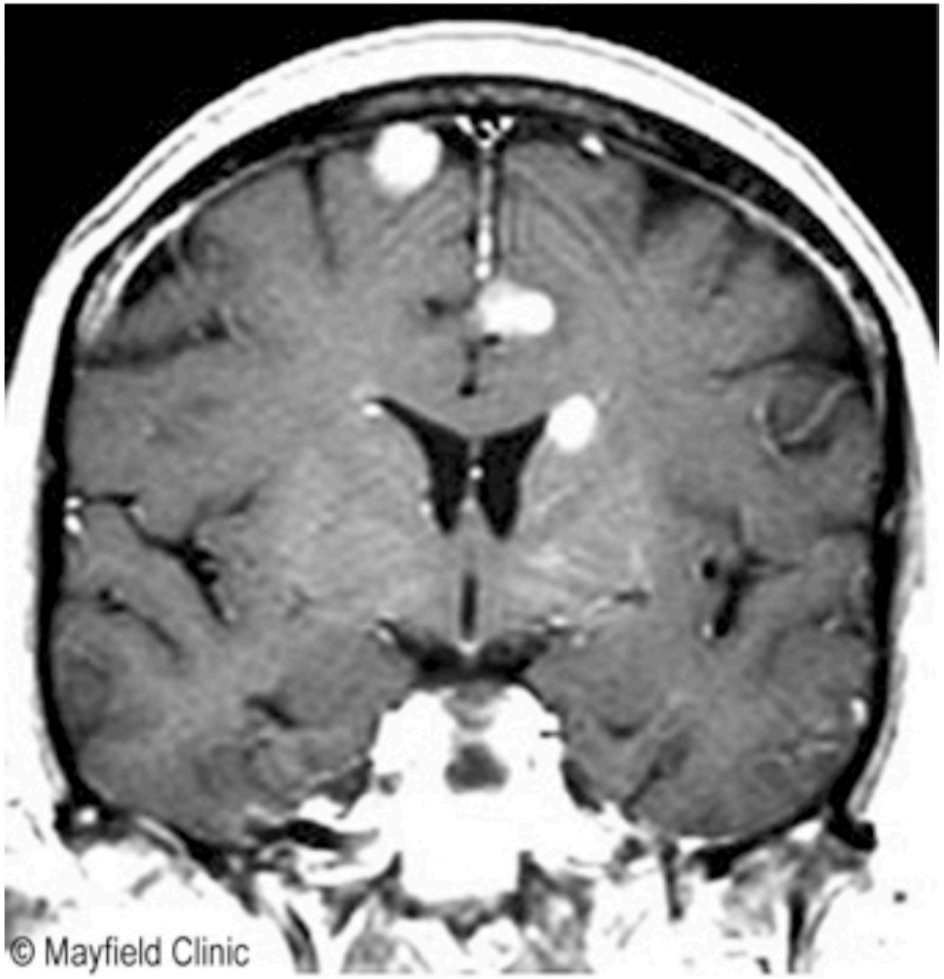
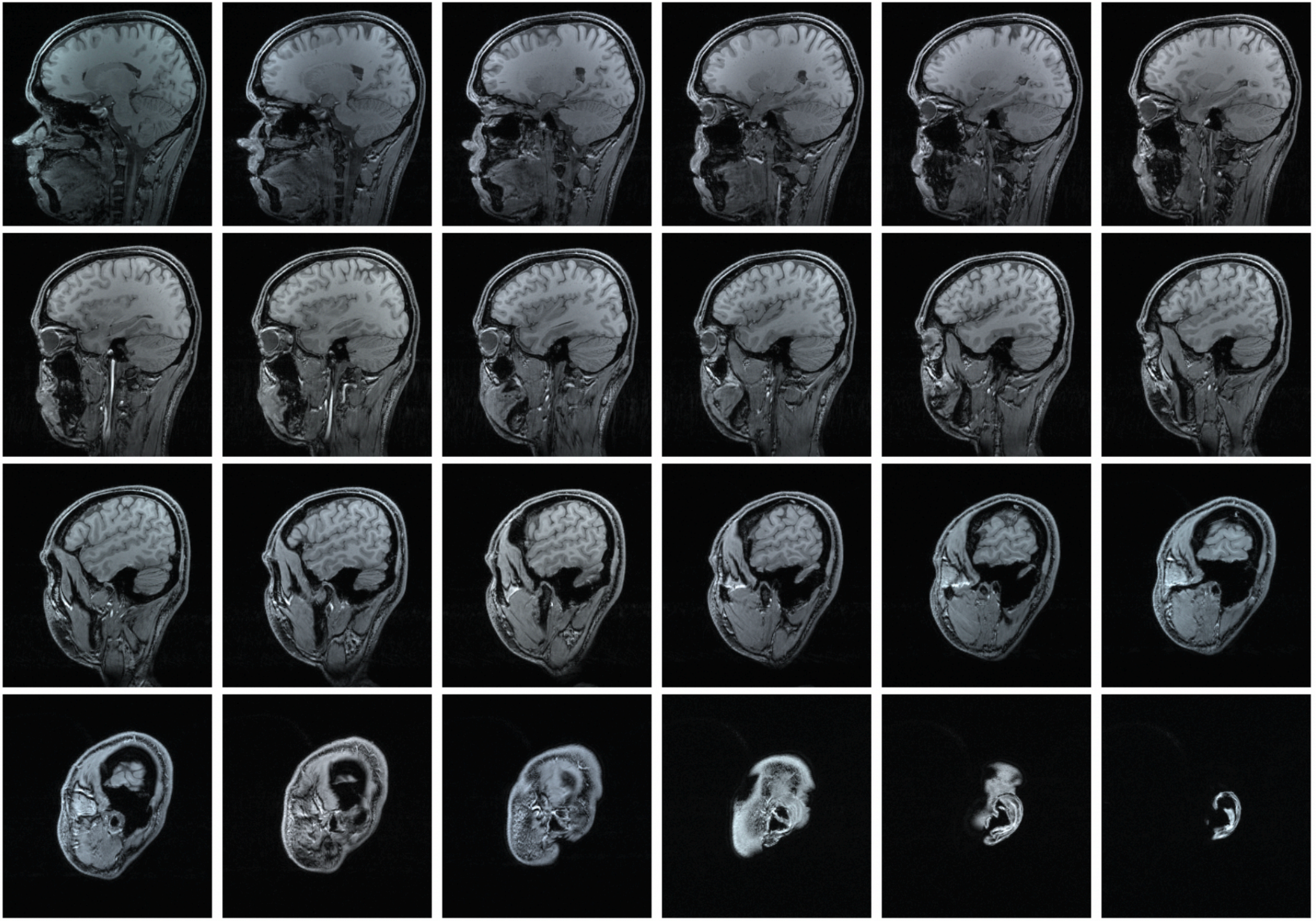


Figure 1. Illustration and MRI of multiple metastatic brain tumors that have spread from the melanoma skin cancer on the face.



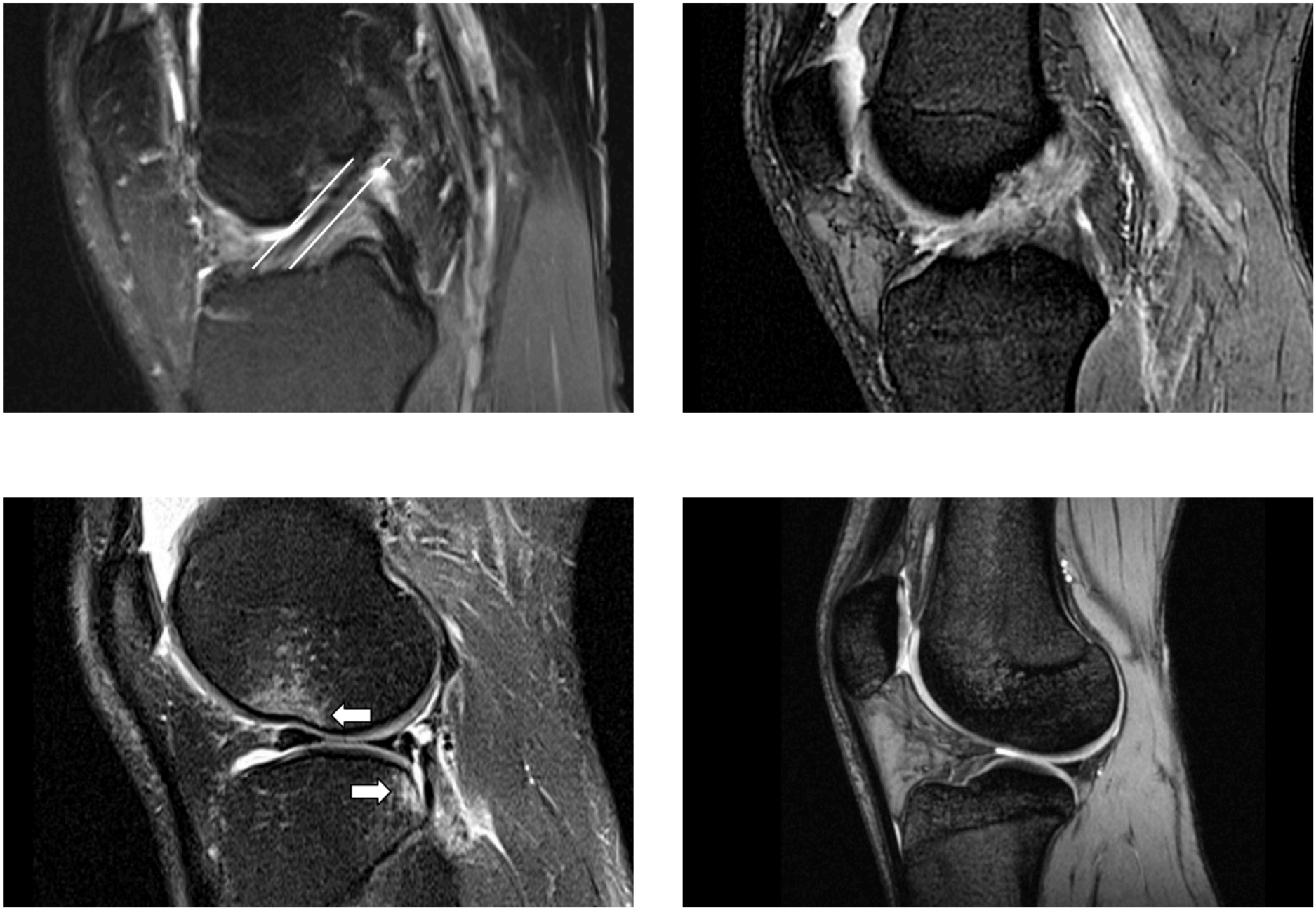


Image 13-16: MRI images of a normal ACL (between white lines), ruptured ACL (ligament not clearly visible), bone marrow oedema (white arrows) and anterior tibial translation.

<u>Organic Chemistry</u> is the study of carbon-containing molecules.

This class has two points.

The first point of the class is to understand the organic chemistry of living systems. We will teach you how to think about and understand the most amazing things on the planet!!

Water is essential for life, you will learn why water has such special properties. 8/25/2022

You will learn the secret structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life. 9/6/22

You will learn why when you take Advil for pain, exactly half of what you take works, and the other half does nothing. 9/20/22

You will learn how toothpaste works. 9/29/22

You will learn how a single chlorofluorocarbon refrigerant molecule released into the atmosphere can destroy many, many ozone molecules, leading to an enlargement of the ozone hole. 10/27/22

You will learn how medicines like Benadryl, Seldane, and Lipitor work. 11/10/22

You will learn how Naloxone is an antidote for an opioid overdose.

You will learn why Magic Johnson is still alive, decades after contracting HIV.

You will learn how MRI scans work. 11/29/22

The second point of organic chemistry is the synthesis of complex molecules from simpler ones by making and breaking specific bonds.

You will learn how to understand movies of reaction mechanisms like alkene hydration. 10/4/22

You will learn reactions that once begun, will continue reacting such that each product molecule created starts a new reaction until all the starting material is used up. 10/27/22

You will learn reactions that can make antifreeze from vodka. 11/10/22

You will learn a reaction that can make nail polish remover from rubbing alcohol. 11/15/22

You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions. 11/16/22

You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex starting molecules.