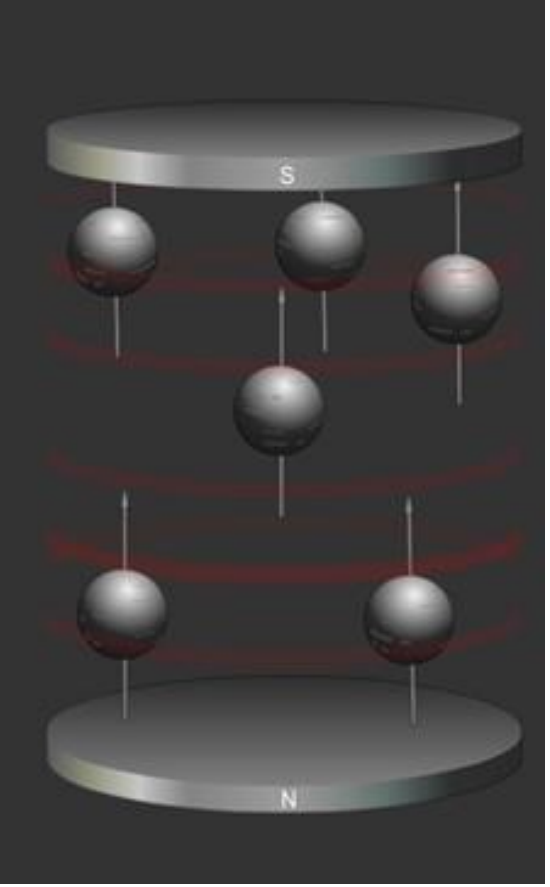


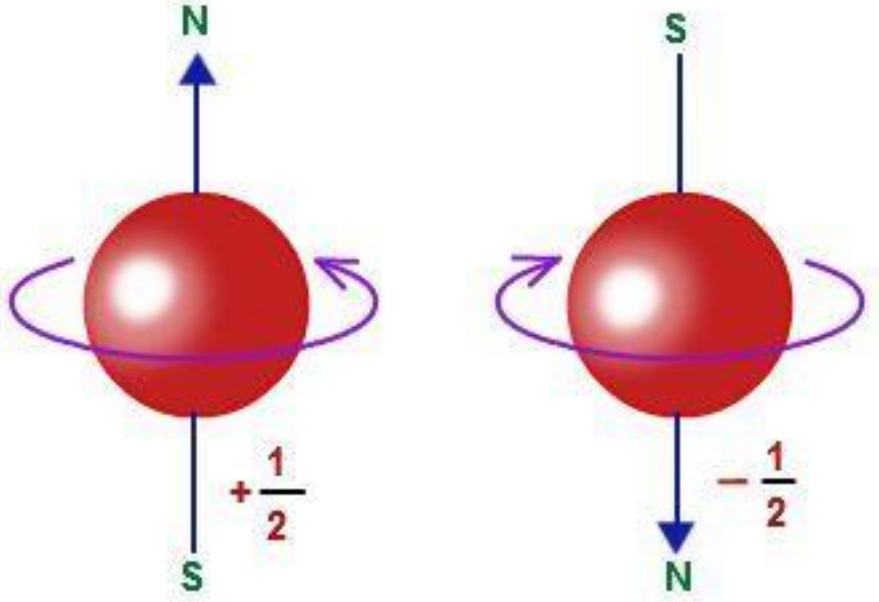
Nuclear Magnetic Resonance (NMR) Spectroscopy

Nuclear Spin

- Electrons have the tendency to spin, with a fixed spin number of -1/2 and +1/2

- The nuclei of some atoms also have a property to spin

- is given



All nucleus are not active (or show spin)

No. of protons	No. of neutrons	Spin quantum no. (I)	Example
even	even	0	^{12}C, ^{16}O
odd	even	1/2, 3/2, 5/2….	^{1}H, ^{19}F, ^{31}P
even	odd	1/2, 3/2, 5/2….	^{13}C
odd	odd	1, 2, 3….	^{2}H, ^{14}N

Ex: 1

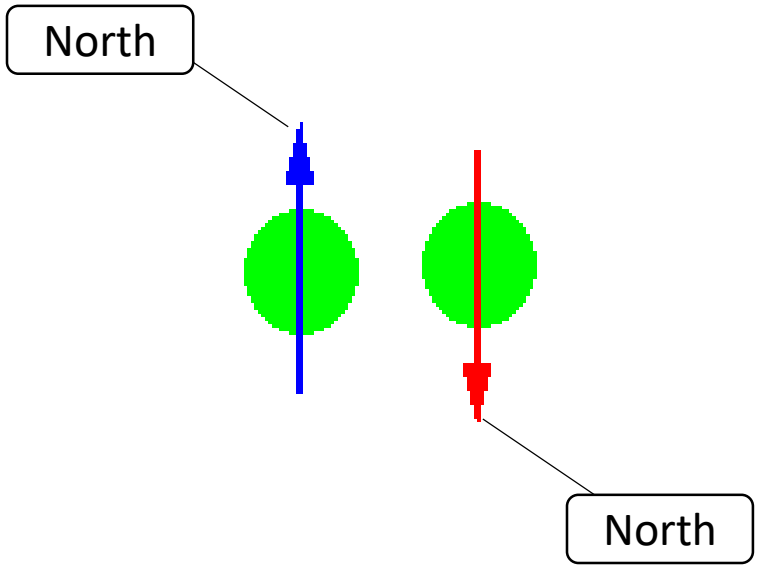
^{12}C → No. of protons = 6 → 3 x +1/2 and 3 x -1/2 = 0

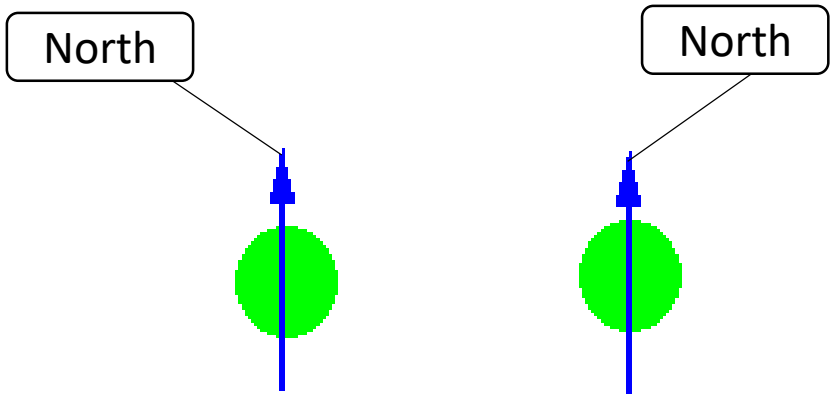
No. of neutrons = 6 → 3 x +1/2 and 3 x -1/2 = 0 therefore, I = 0

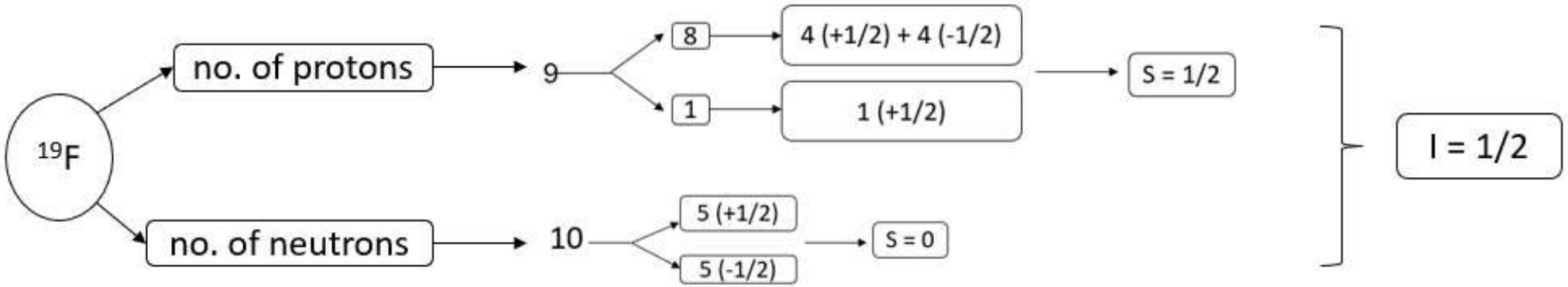
Ex: 2

^{2}H → No. of protons = 1 → 1/2

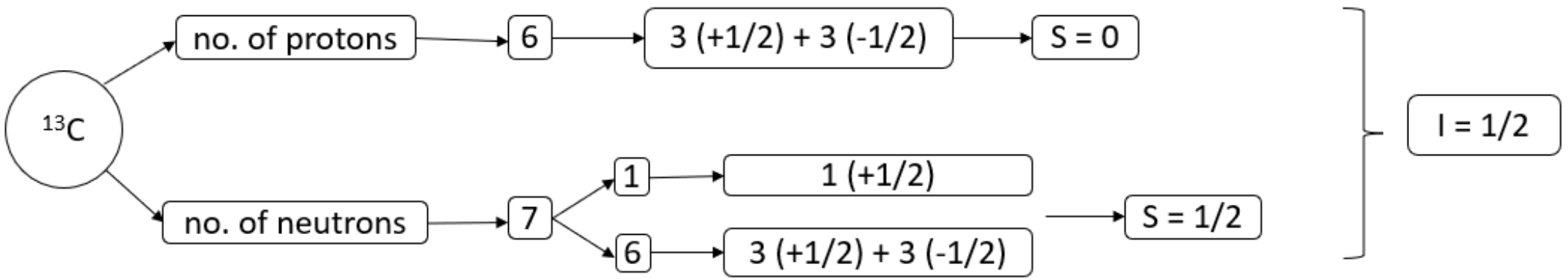
No. of neutrons = 1 → 1/2 therefore, I = 1/2 + 1/2 = 1


North
North


North
North

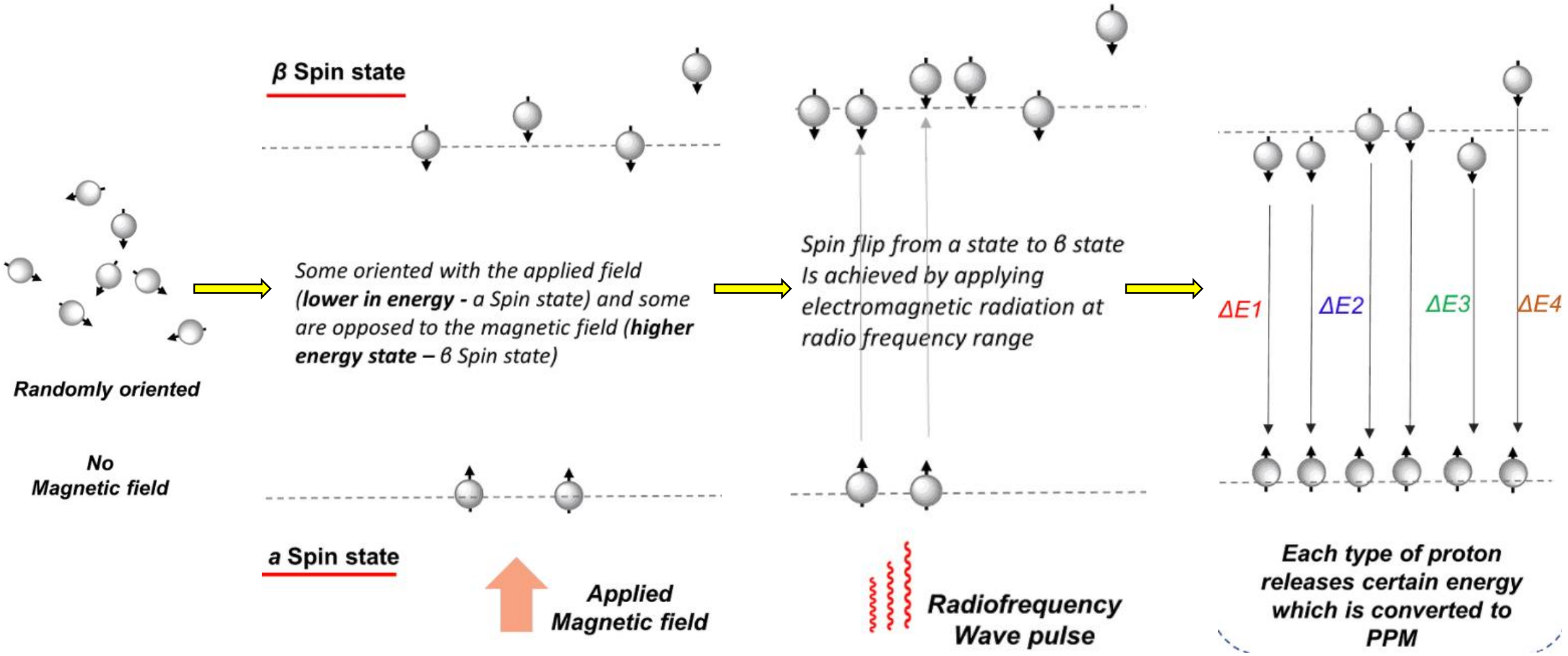

^{19}F
no. of protons
9
8
4 (+1/2) + 4 (-1/2)
1
1 (+1/2)
S = 1/2
no. of neutrons
10
5 (+1/2)
5 (-1/2)
S = 0
I = 1/2

Ex: 3


^{13}C
no. of protons
6
3 (+1/2) + 3 (-1/2)
S = 0
no. of neutrons
7
1
1 (+1/2)
6
3 (+1/2) + 3 (-1/2)
S = 1/2
I = 1/2

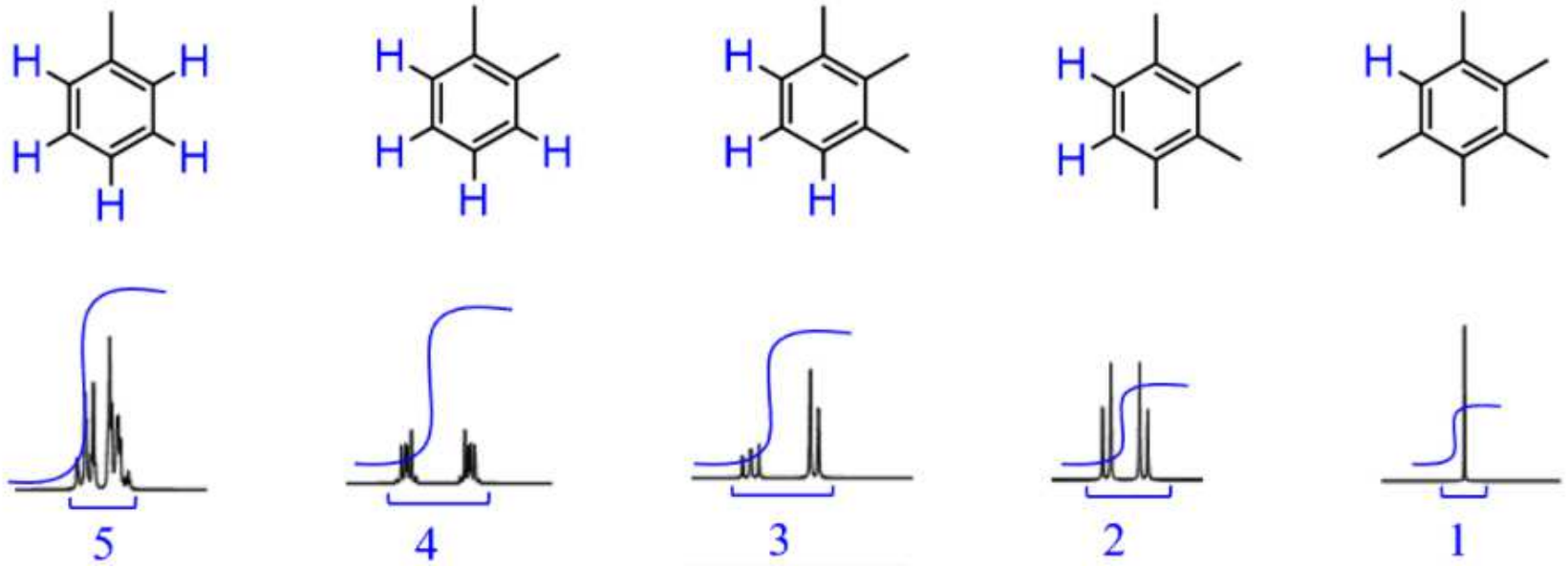
Ex: 4

NMR Principle



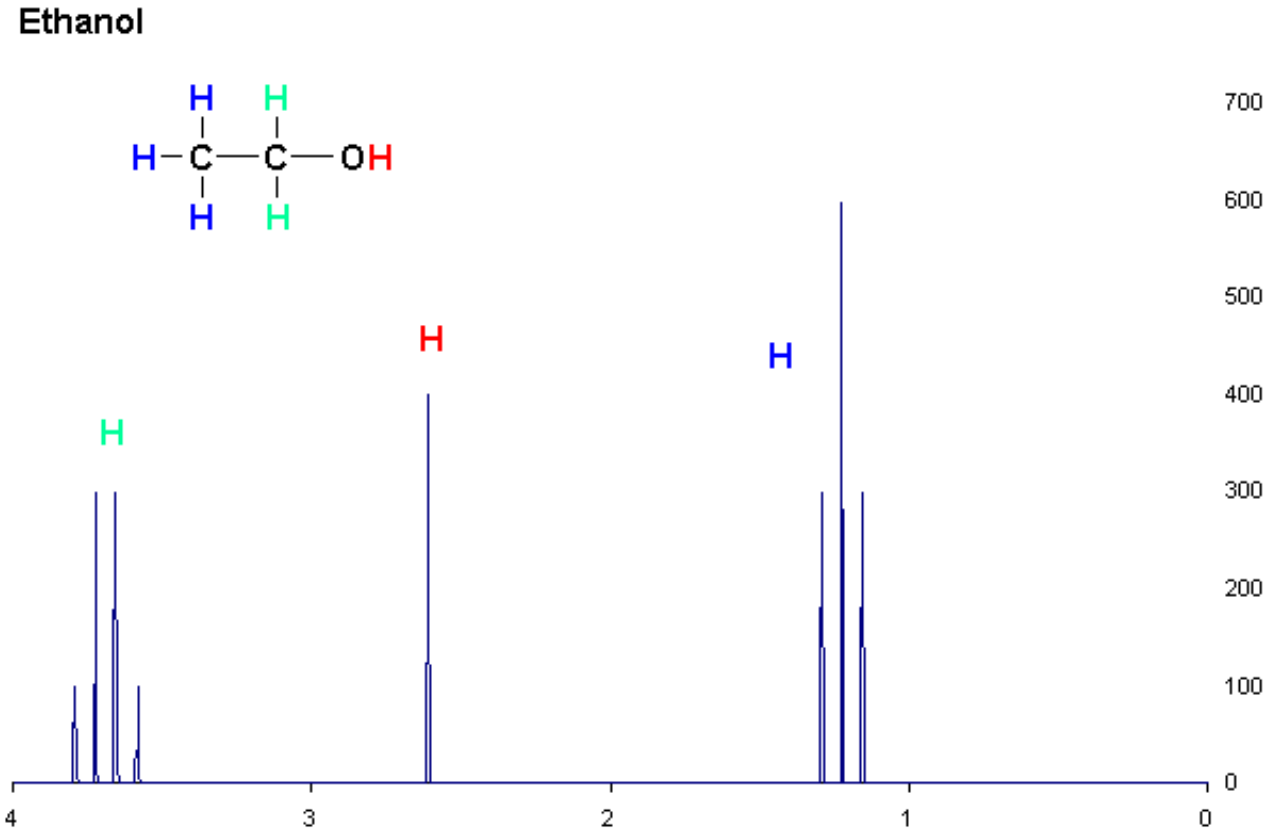
Main information we obtain from an ^{1}H NMR Spectrum

1. The Number of Protons – NMR Integrals



- How many protons you have for the given signal?
- The number of protons (it is the relative number) is given right under the **integral** sign
- The **height** of the integral is proportional to the **number** of the protons.

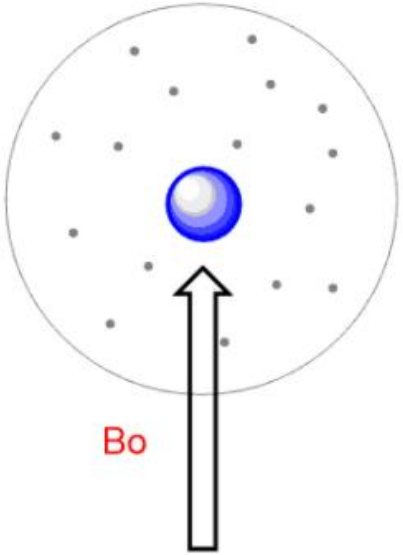
2. Chemical Shift



Protons should resonate at the same frequency then **why they give a signal at different energy or frequency?**

2.1 Shielding effect

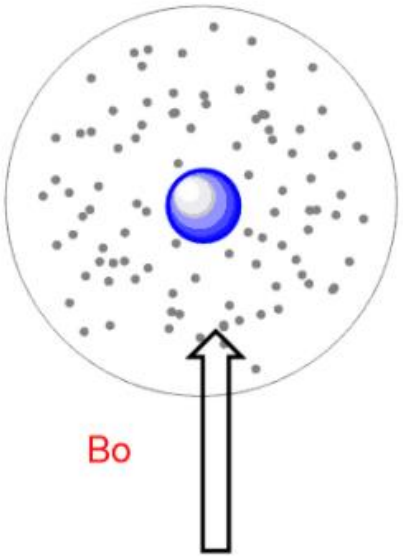
low electron density



This nucleus experiences **stronger magnetic field** because it is not shielded as much.

Electron cloud shields the **nucleus** from the magnetic field

high electron density

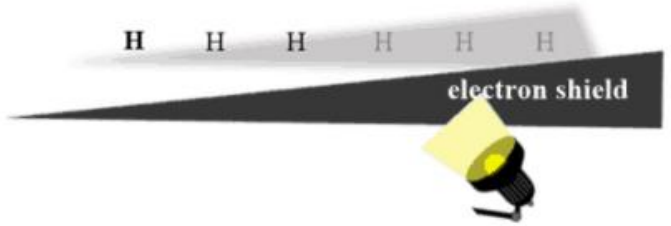


This nucleus is shielded and experiences **weaker magnetic field** - will appear upfield (low energy).

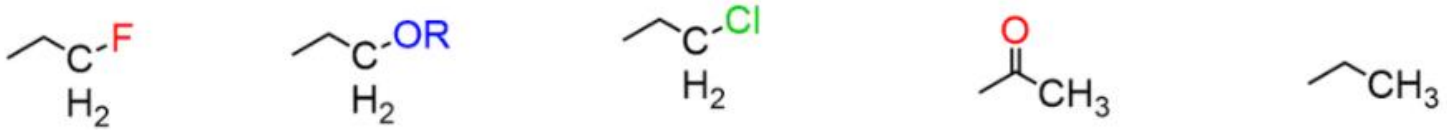
2.2 Downfield and Upfield

Increasing electron-withdrawing power

Downfield
high frequency
electron deshielded



Upfield
low frequency
electron shielded



~ 4.5 ~ 4 ~ 3.5 ~ 2.5 ~ 1

ppm

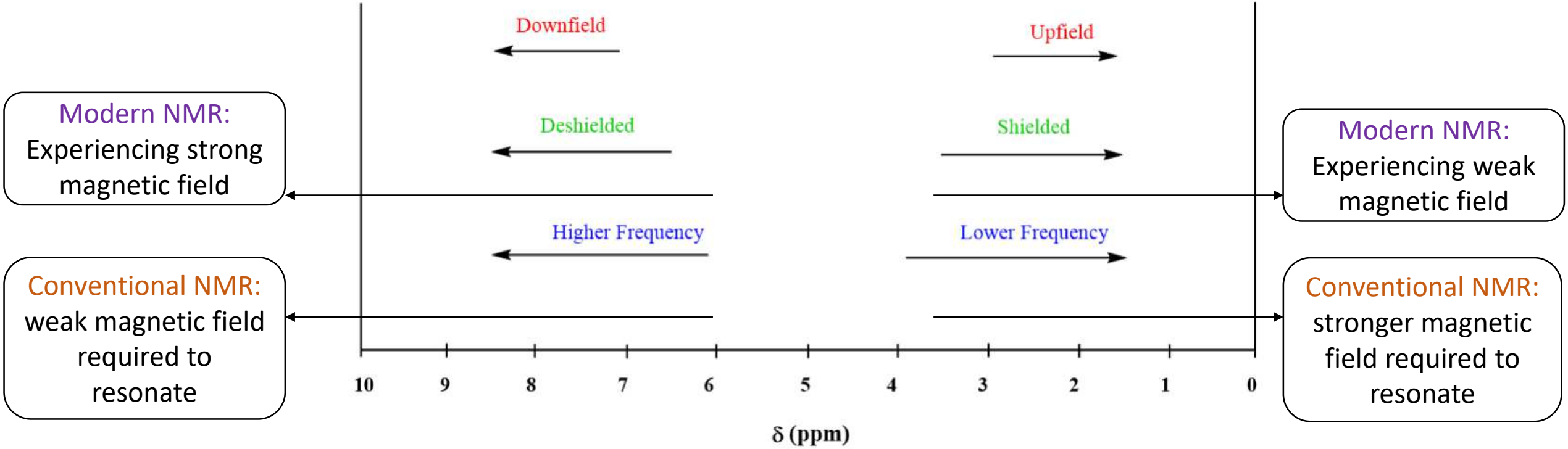
Fluorine, as the **most electronegative element, deshields and shifts** the signal of adjacent protons to ~ 4 ppm.

The **oxygen and chlorine are not as electronegative** and the ppm value is less downfield. I, Br, and some other groups also shift the signal to this region.

The **carbonyl group is electron-withdrawing** and the frequency of H's next to are shifted downfield by ~ 1.5 and found at 2.5 ppm.

This is t**he typical region of alkyl protons**. Increasing the number of alkyl groups shifts the signal downfield.

2.3 Shielding and Frequency relation



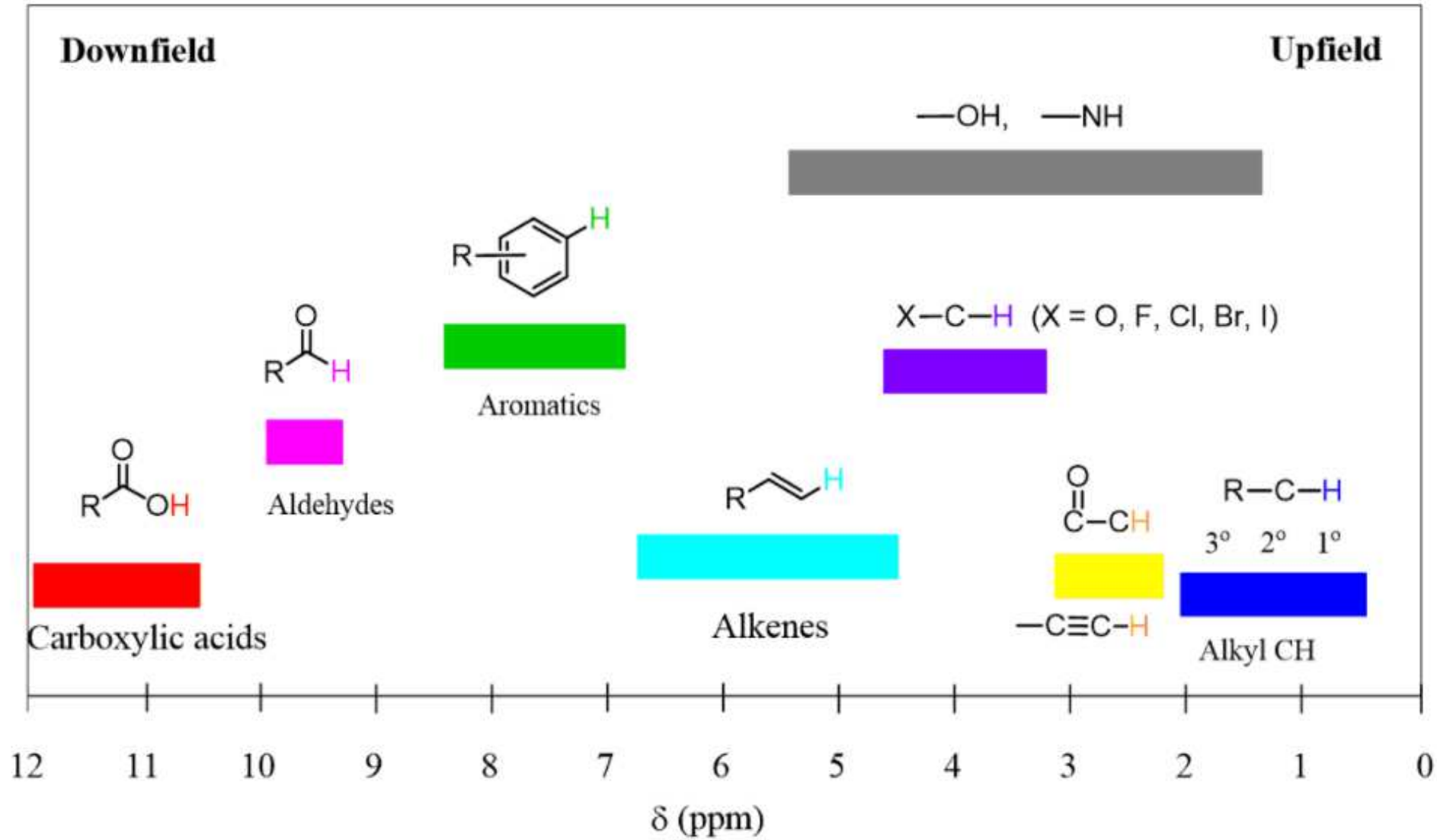
Modern NMR: Experiencing strong magnetic field

Conventional NMR: weak magnetic field required to resonate

Modern NMR: Experiencing weak magnetic field

Conventional NMR: stronger magnetic field required to resonate

Remember the terminology **upfield** and **downfield** with respect to **shielding** experienced by the protons


Downfield
Upfield
—OH, —NH
X—C—H (X = O, F, Cl, Br, I)
Aromatics
Aldehydes
Carboxylic acids
Alkenes
—C≡C—H
R—C—H
3° 2° 1°
Alkyl CH
12 11 10 9 8 7 6 5 4 3 2 1 0
δ (ppm)

Question 1

^{1}H and ^{13}C are two of the most common nuclides studied by high-field NMR spectroscopy due to their abundance in human tissues. Other isotopes that have been studied include ^{14}N, ^{17}O, ^{31}P, ^{79}Br, and ^{127}I. Based on this information, which of the following nuclides will NOT be considered suitable for use with NMR spectroscopy?

Choose 1 answer:

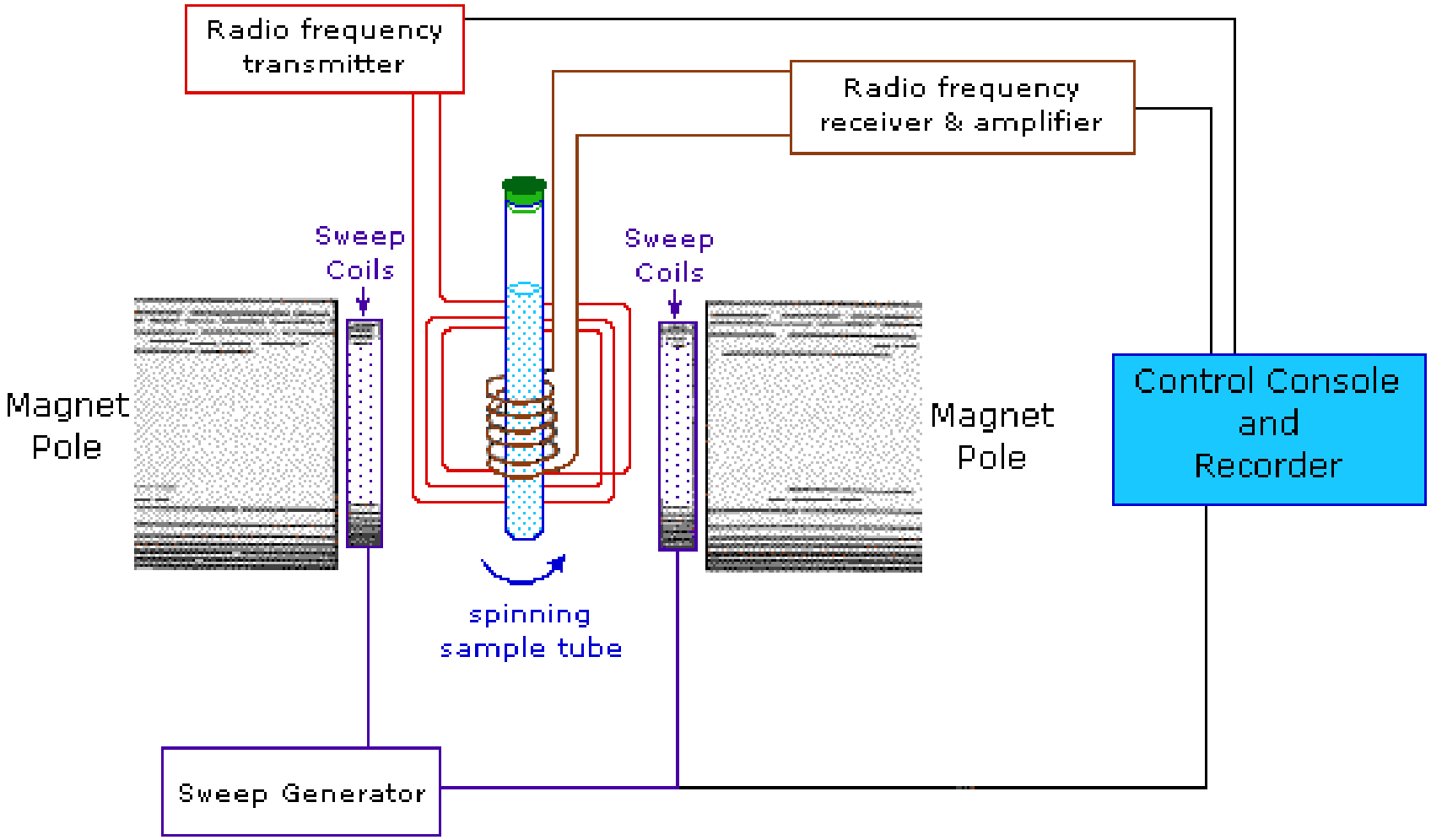
(A) ^{19}F

(B) ^{2}H

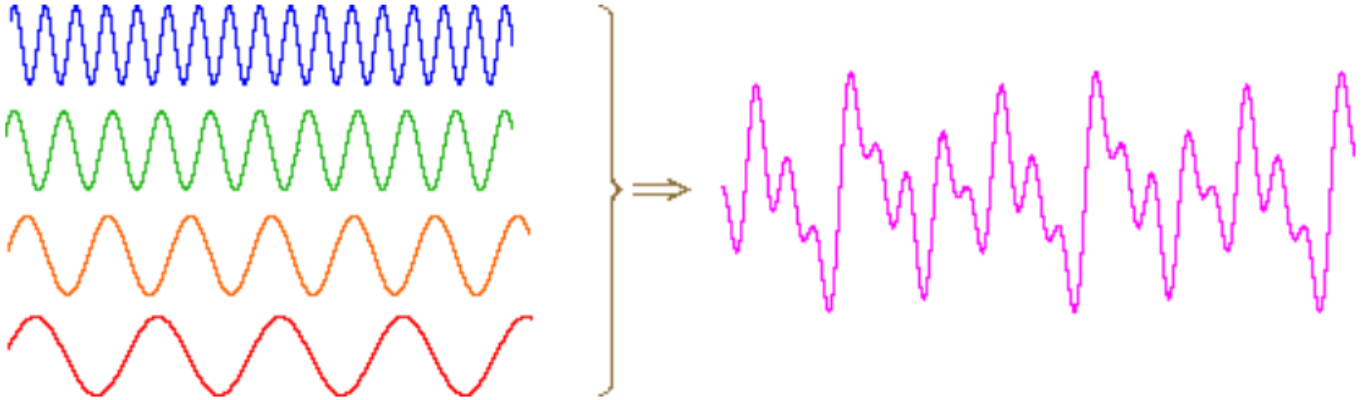
(C) ^{20}Ne

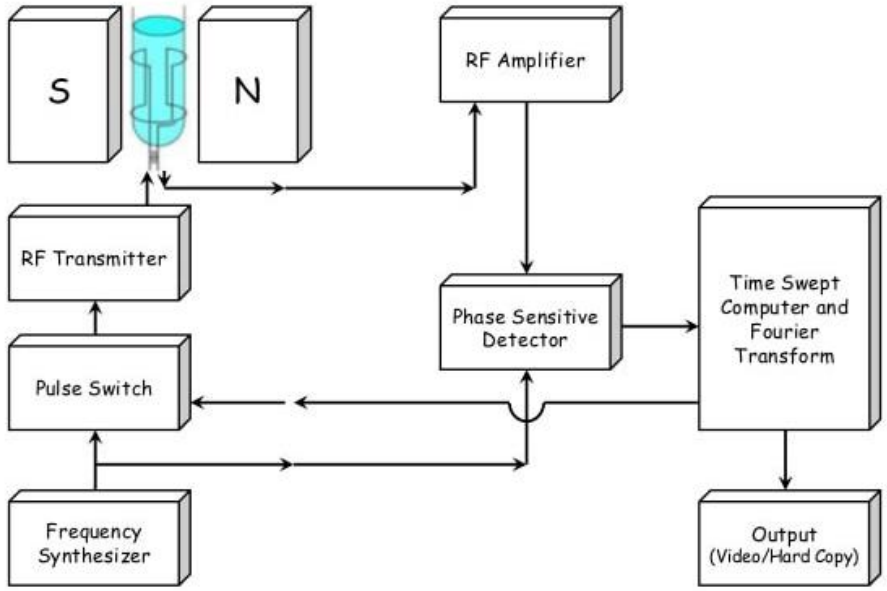
(D) ^{35}Cl

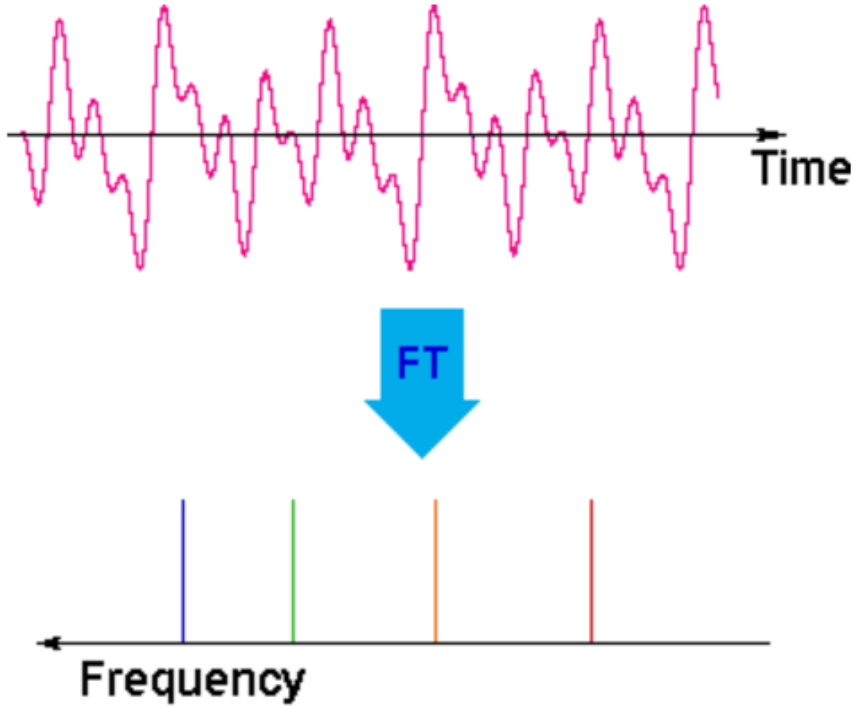
NMR Instrumentation (continuous wave field sweep)



NMR Instrumentation (Fourier-transform NMR)

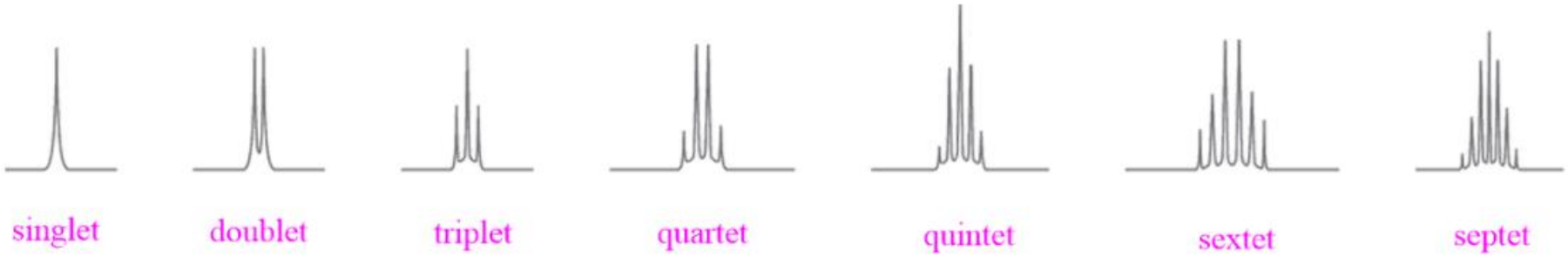




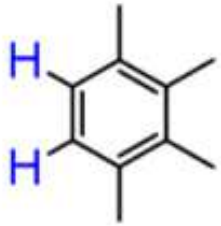


3. Splitting

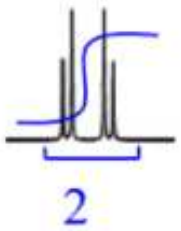
NMR signals may have **different number of peaks** (the number of lines). This is called the **splitting** of the signal or the **multiplicity**



*There is **no correlation** between the multiplicity (**number of peaks**) and the **number of protons**.*

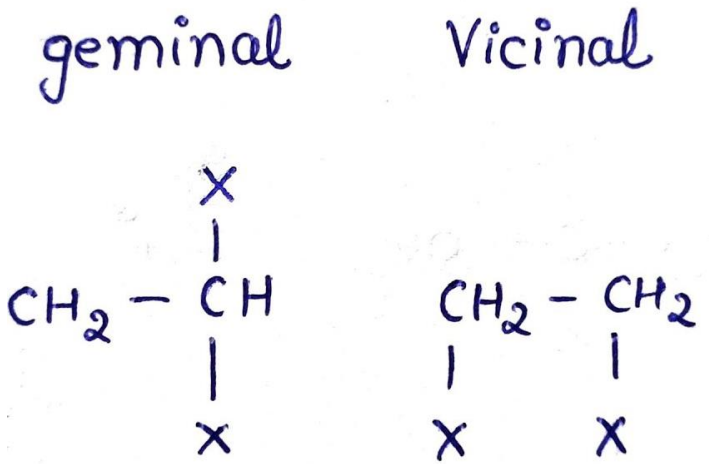


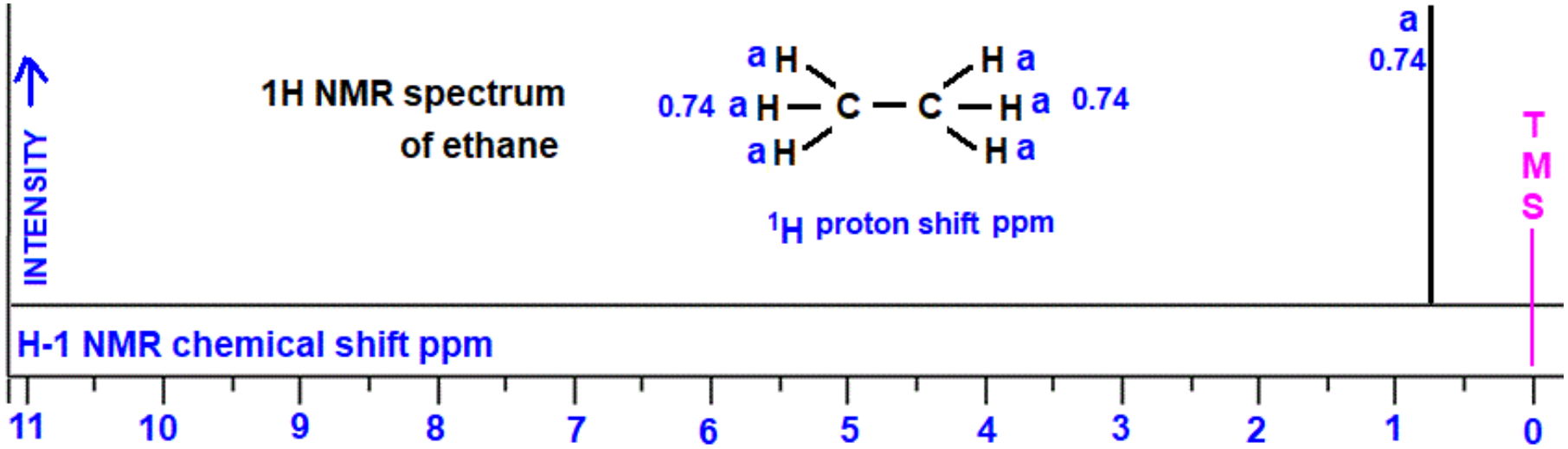
Do not confuse **splitting** with the **integration,** these two are **not related**



3.1 The Origin of Splitting

- The **splitting is caused** by the hydrogens on the **same** (geminal hydrogens) or on the **neighboring carbons** (vicinal hydrogens)
- Only **non-equivalent protons split the signal** of the given proton(s)





1,2-dichloroethane

$Cl\text{-}CH_2\text{-}CH_2\text{-}Cl$

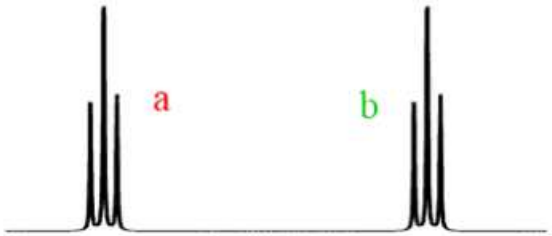
a

All the ***protons are equivalent*** *(H_a), so there is* ***no splitting*** *and the NMR signal is one* ***singlet****.*

$Cl\text{-}CH_2\text{-}CH_2\text{-}Br$

a b

Ha protons are nonequivalent to Hb but they are equivalent to themselves. . That's why the signal is split only by Hb.



Hb protons are nonequivalent to Ha but they are equivalent to themselves. That's why the signal is split only by Ha.

1-chloro-2-bromoethane

3.2 Splitting of the signal

For example: Ha and Hb are nonequivalent protons so they split each other's NMR signals.

The H_a [illegible] **no adjacent hydrogen** has **two**

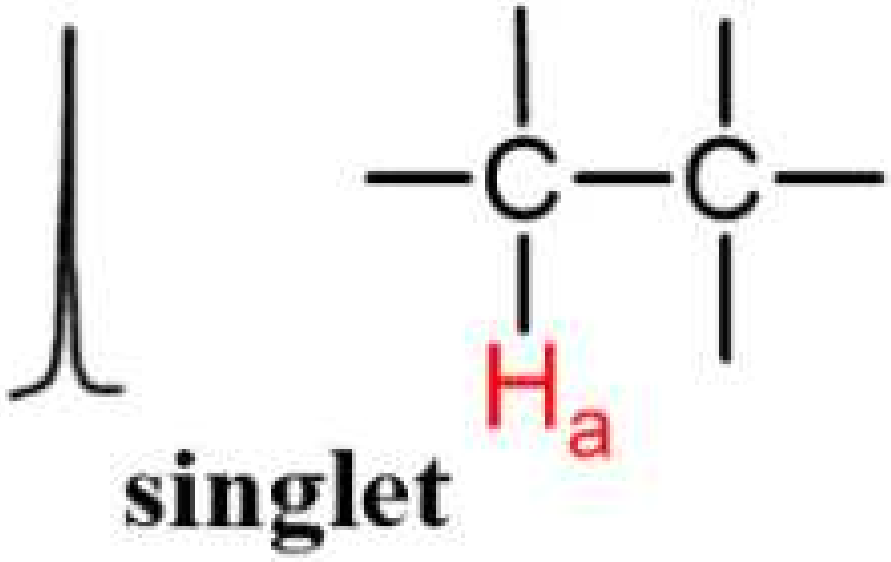
neighbo [illegible] efore its

signal is [illegible] o a **triplet** .

.

The Ha signal is spl [illegible] H_b signal is split into a

doublet by the H_b p [illegible] t by the two Ha protons.

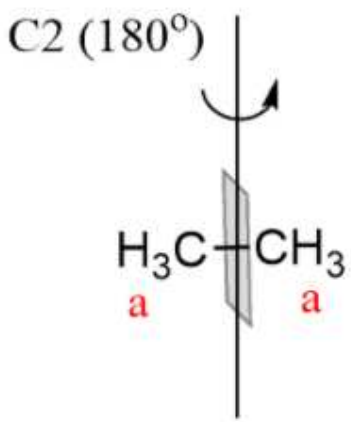


singlet

Symmetry element - one signal, equivalent protons.

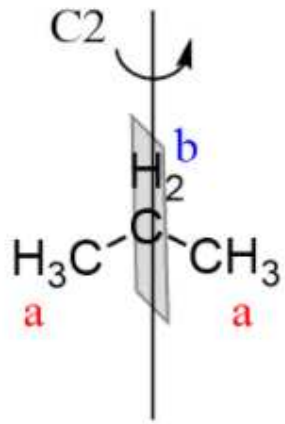
No symmetry element - different signals, not equivalent protons.

These protons are exchangeable by both a symmetry plane and an axis:



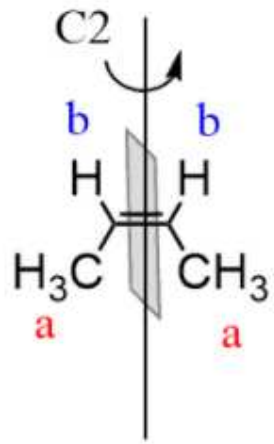
6 protons but

1 signal



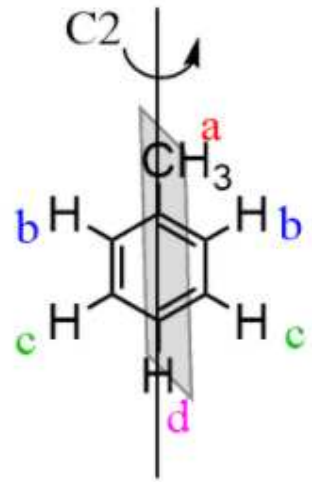
8 protons but

2 signals



8 protons but

2 signals



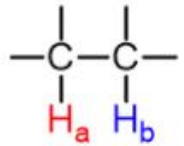
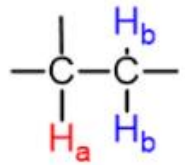
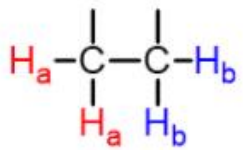
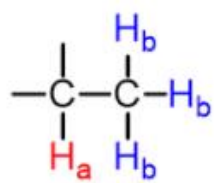
8 protons but

4 signals

3.3 Spin multiplicity (n + 1 rule)

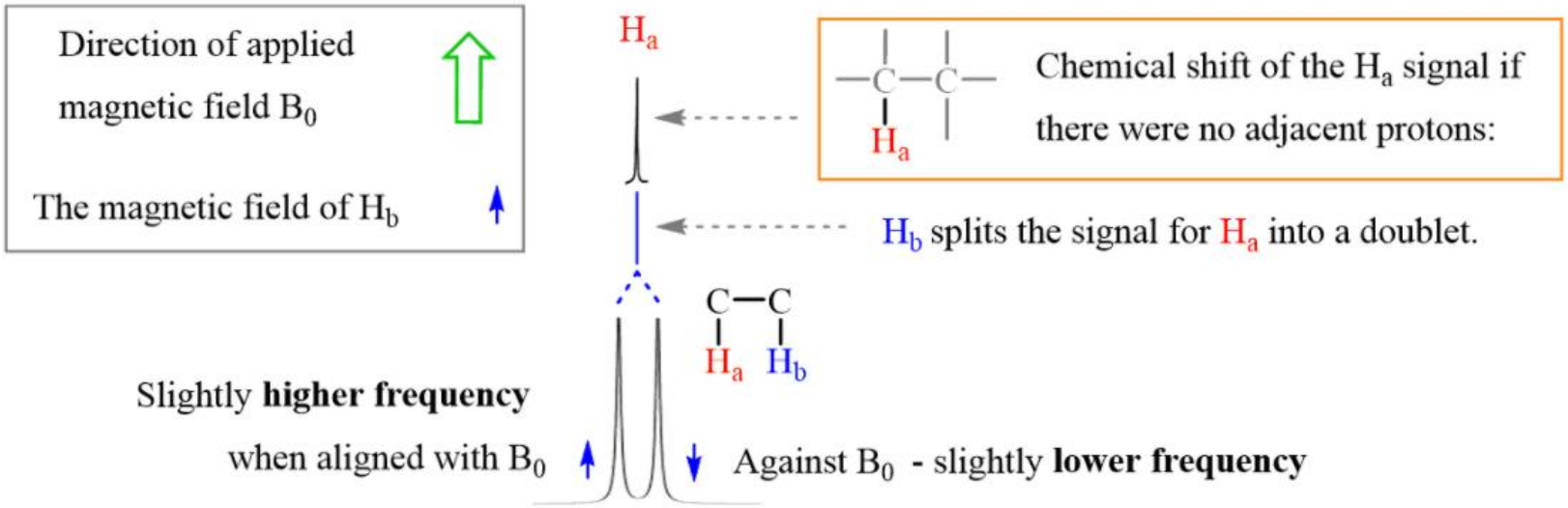
- The formula for predicating the number of peaks base on the neighboring hydrogens is given as the ***n + 1 rule***, where **n** is the number of neighboring protons
- The more general formula for this is ***2nI + 1,*** where ***I* is the magnetic spin number** of the given nucleus
- And since it is equal to 1/2 for hydrogen, the formula that we use in ^{1}H NMR is n + 1

The pattern is that n protons split the signal into n+1 peaks, which is known as the **n+1 rule**.

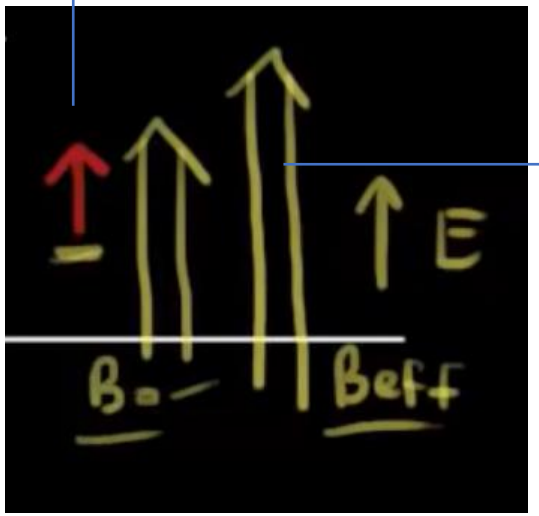
Multiplicity	N +1	H_a	Signal	H_b	N +1	Multiplicity
Doublet	1+1 = 2				1+1 = 2	Doublet
Triplet	2+1 = 3				1+1 = 2	Doublet
Triplet	2+1 = 3				2+1 = 3	Triplet
Quartet	3+1 = 4				1+1 = 2	Doublet

Number of equivalent adjacent protons	Multiplicity		Ratio of Intensities
0	singlet		1
1	doublet		1:1
2	triplet		1:2:1
3	quartet		1:3:3:1
4	quintet		1:4:6:4:1
5	hextet		1:5:10:10:5:1
6	septet		1:6:15:20:15:6:1

3.4 Why peaks of different frequency?



H_b spin aligned with B_0

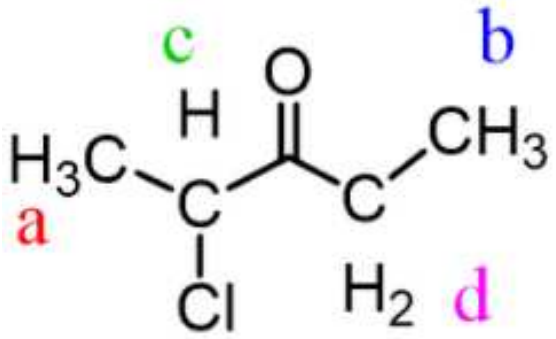


Magnetic field experienced by H_a is more, high energy, high frequency

H_b spin aligned against B_0

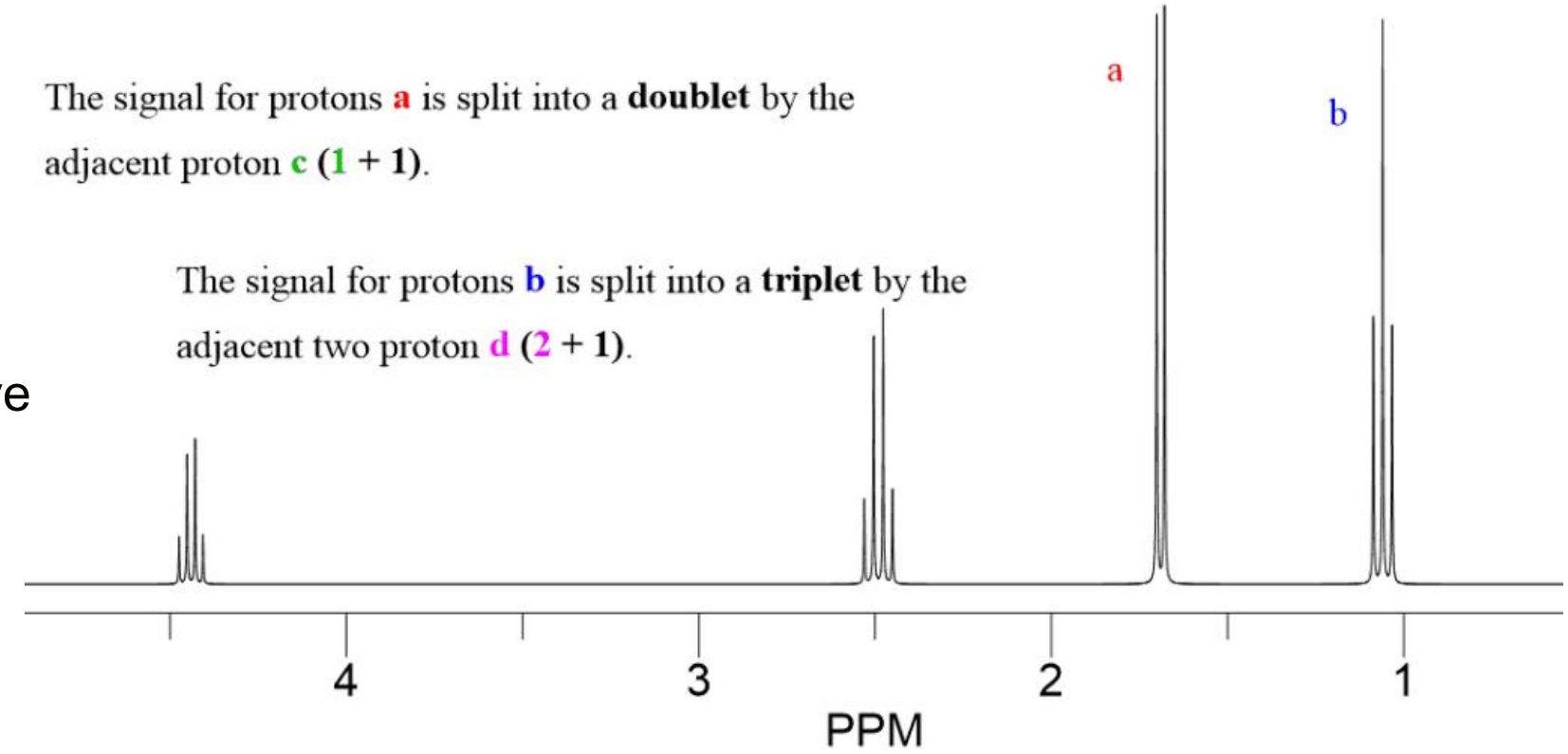
Magnetic field experienced by H_a is less, low energy, low frequency

3.5 Importance of Spin splitting

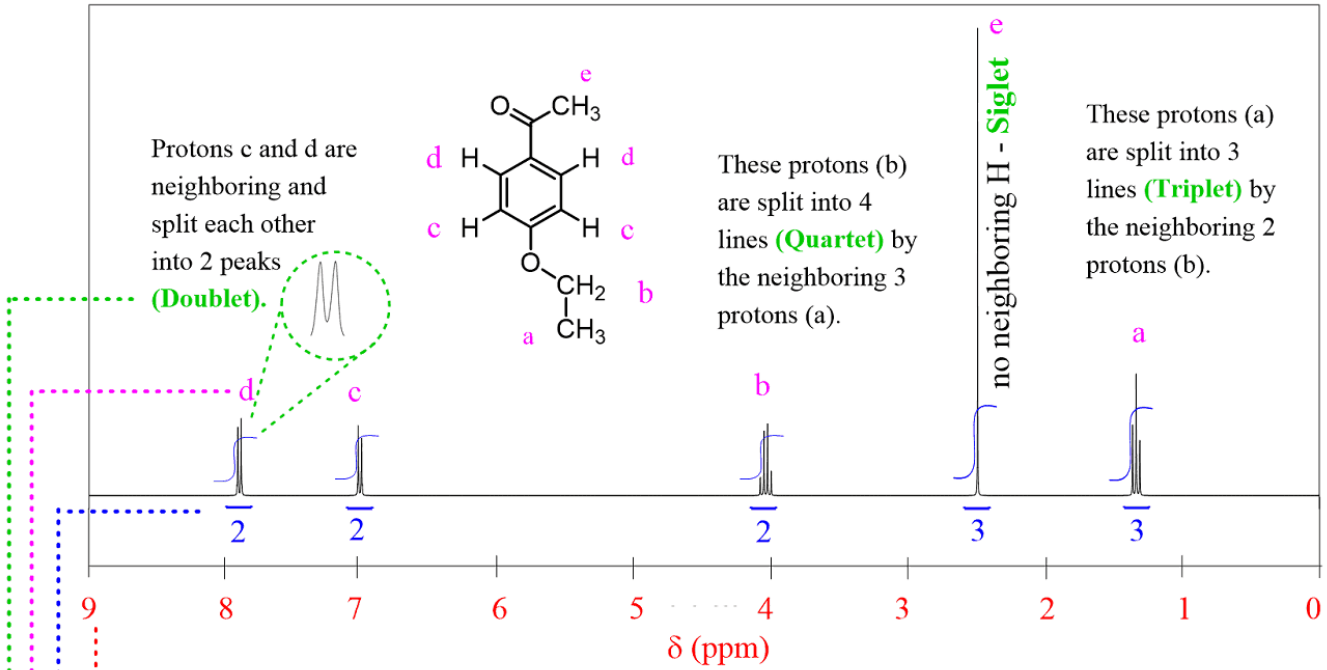


How do we distinguish between the two methyl groups in the following molecule?

They are both next to electron-withdrawing groups with comparable power & they will both have the same integration



The Summary of Main Information we obtain from an ^{1}H NMR spectrum



1. The **functional groups** that are present in the molecule. This is determined based on the **positions (ppm)** of the signals on the spectrum. Most often the scale goes from 0-12 ppm.

2. The **number of protons** represented by each signal. This measured by the **integration** which is the surface area under each signal peak(s).

3. The **number of different types of protons** in the molecule. This is determined by the **number of NMR signals**. Only non-equivalent protons give different signals. Chemically equivalent protons give one NMR signal regardless of their number.

4. The **spin-spin splitting** tells **how many protons are connected to the neighboring carbons**. This is determined by the **number of the peaks (signal multiplicity)** within the signal based on the **n+1 rule**, n being the number of neighboring protons.

Question 2

Which of the following compounds produces a ^{1}H-NMR spectrum with a singlet?

Choose 1 answer:

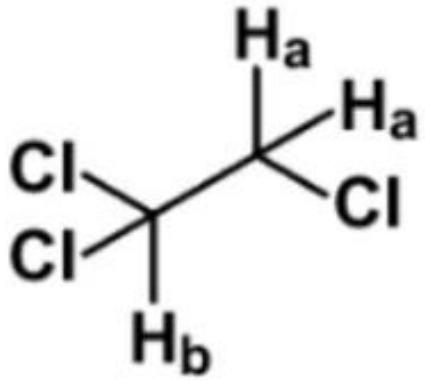
(A) 1-chloro-2-bromoethane

(B) 1,1,2,2-tetraiodoethane

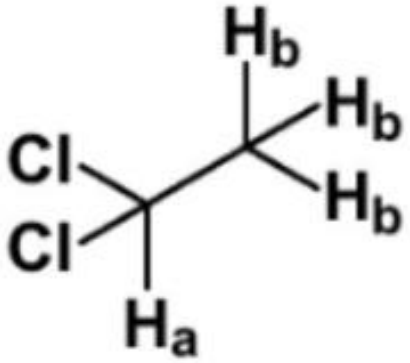
(C) 1,1,2-trichloroethane

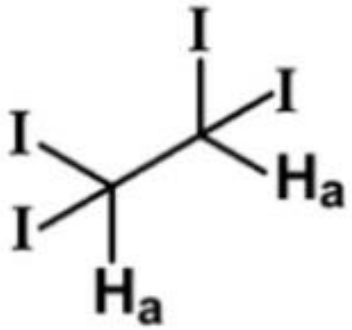
(D) 1,1-dichloroethane

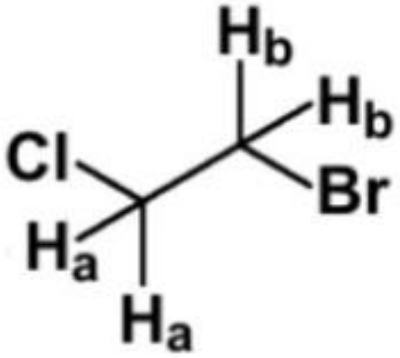
1,1,2-trichloroethane



1,1-dichloroethane





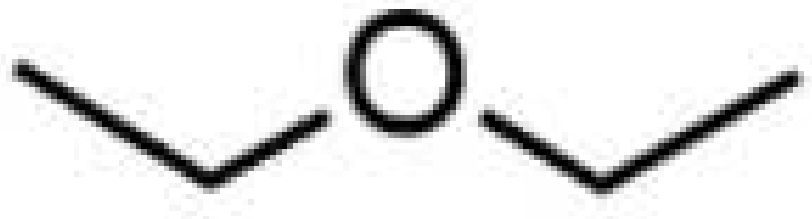


1,1,2,2-tetraiodoethane

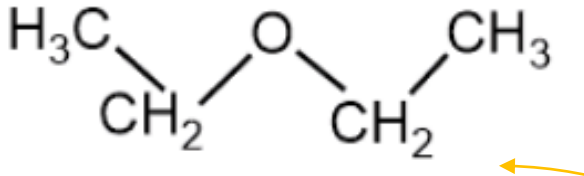
1-chloro-2-bromoethane

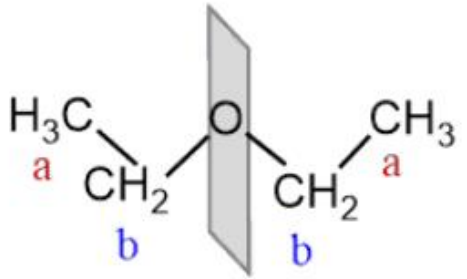
Question 3

Indicate the **number of signals and the multiplicity** of each signal in the 1H NMR spectrum for the following compound:



1) Number of signals

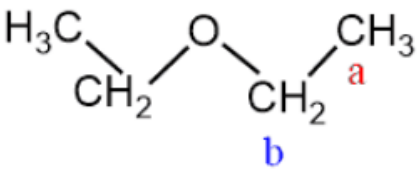




Protons reflected through the mirror are equivalent -one signal.

2 Signals

2) The multiplicity

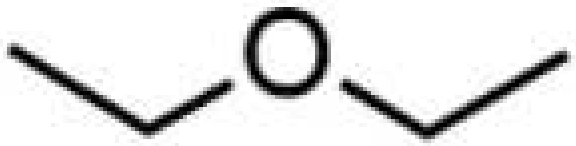


2 neighbors, $n + 1 = 3$

Triplet

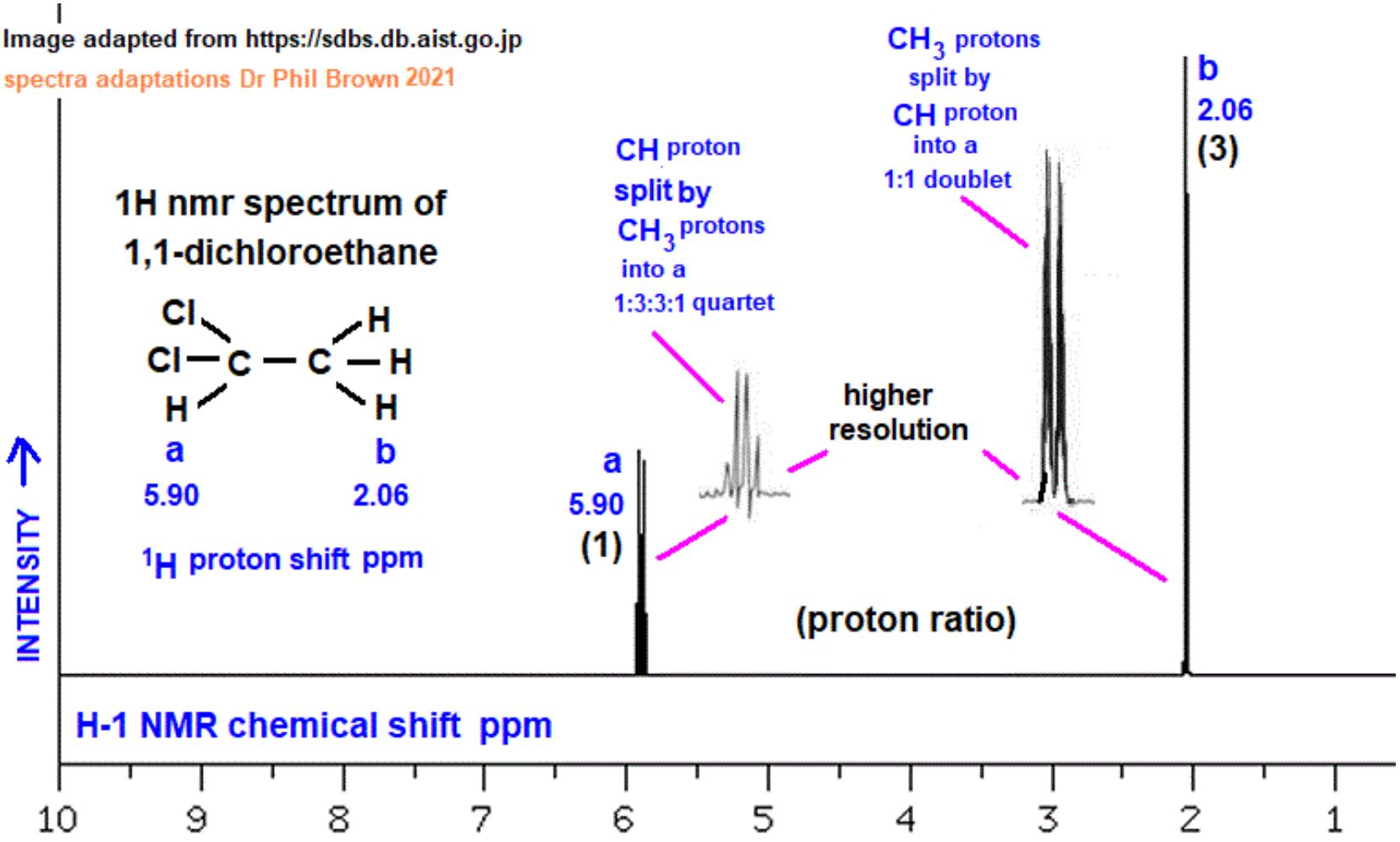
3 neighbors, $n + 1 = 4$

Quartet



Major application

- **Molecular structure determination:**



Structural Element	Information Gained	Analytical Technique
Primary	The specific sequence of amino acids in polypeptides	Mass Spectrometry (MS)
Secondary	Coiling and folding of polypeptide chain e.g. α-helix, β-sheets, and random coils	Circular Dichroism (CD) **Infrared Spectroscopy (IR)**
Tertiary	Overall 3D shape or form of a single polypeptide	X-Ray Diffraction Christallography (XRD) Nuclear Magnetic Resonance (NMR)
Quarternary	Overall 3D structure of proteins composed of two or more polypeptide chains	Size Exclusion Chromatography (SEC) Dynamic Light Scattering (DSC) Analytical Ultra Centrifugation (AUC)

Learning shouldn't be hard,
it should be fun....