Drugs & Disease – Fall 2024

Course Overview:

1. Introductory Biochemistry
2. DNA, RNA, protein synthesis, biotechnology
3. Immunology & Immunotherapy
4. Drug Discovery – Enzyme Inhibitors
5. Genome Editing – CRISPR
6. Final presentations

Expectations:

- 6 Problem sets
- One mid-class exam
- Presentation (10 min, topic of choice)
- Short paper (Same topic as presentation)

Course materials:
https://www.andrew.cmu.edu/user/rule/Drugs_Disease/

My Story

- Born in Ottawa Canada
- Undergraduate: University of Waterloo, largely physics
- MS: Penn State University
- PhD: Carnegie Mellon
- Post-doc: Stanford University
- Faculty: University of Virginia, Carnegie Mellon

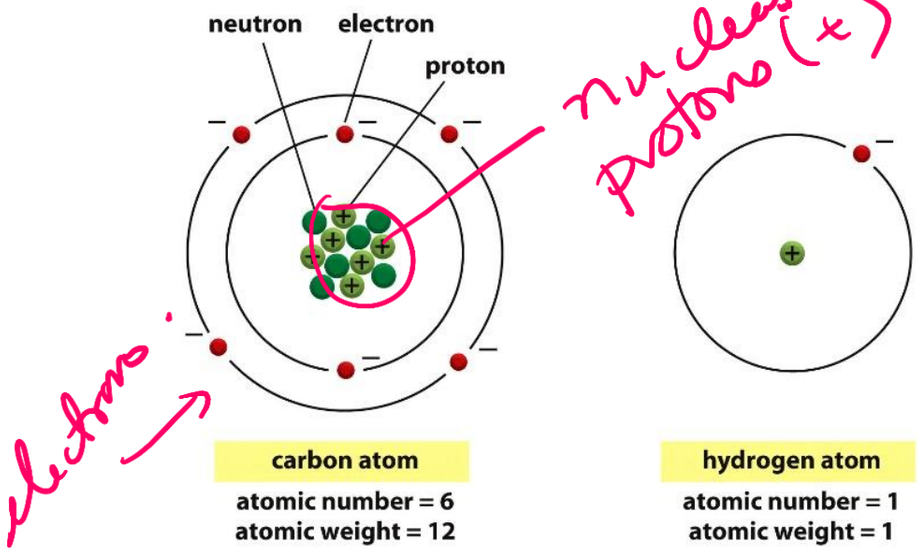
Research area:

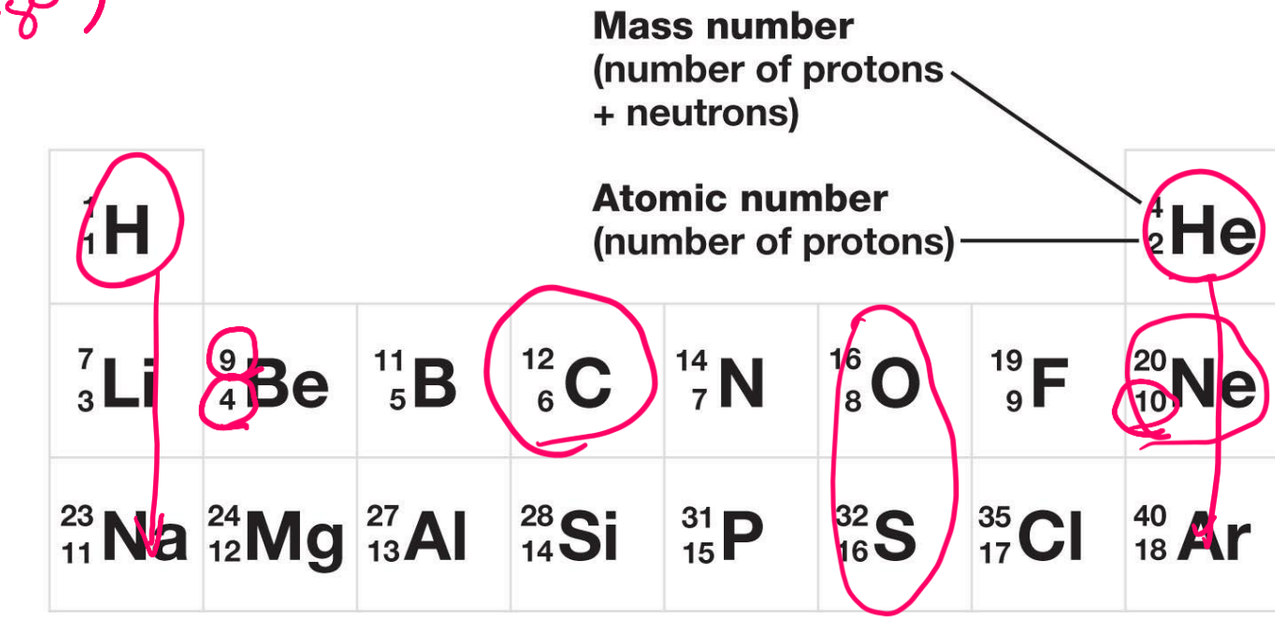
- Protein structure and dynamics
- Drug discovery

Take-home exercise:
Send me an email with a short paragraph describing why you took the course and what you hope to take away from the course.

Chemistry and Biology Fundamentals

- Chemical Bonding
- Functional Groups

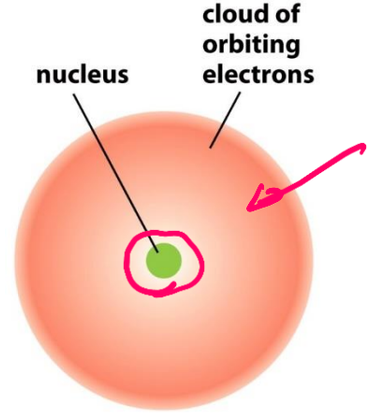




- Atoms are composed of:
  - Protons – positively charged particles
  - Neutrons – neutral particles
  - Electrons – negatively charged particles
- Protons and neutrons are located in the nucleus.
- Electrons are found in **orbitals** surrounding the nucleus.
- The overall charge on an element is neutral (#electrons = # protons).

Atomic number = # of protons = # electrons in element

Isotope = different # of neutrons = same bonding capability

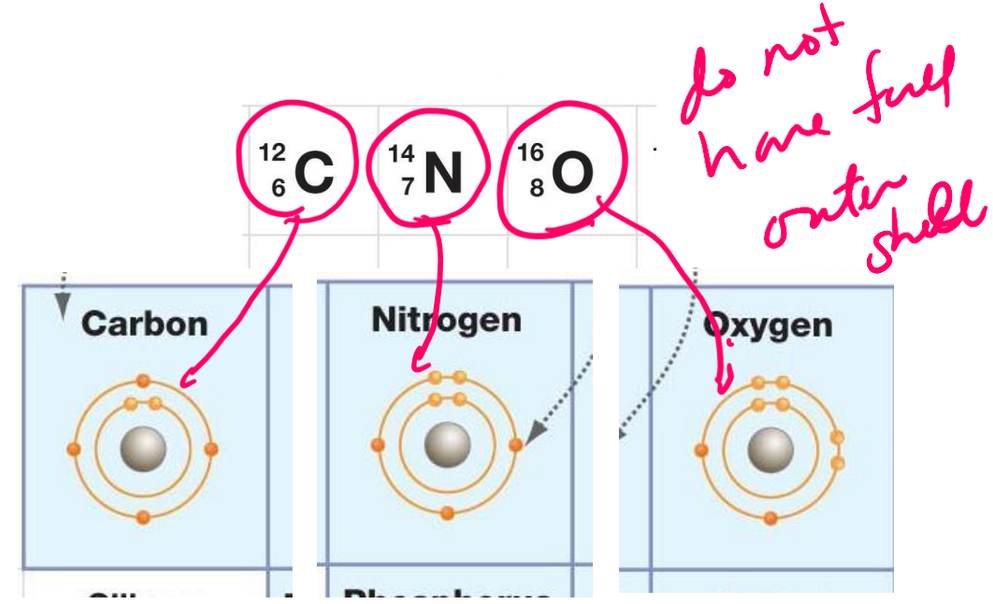


Electron Orbitals

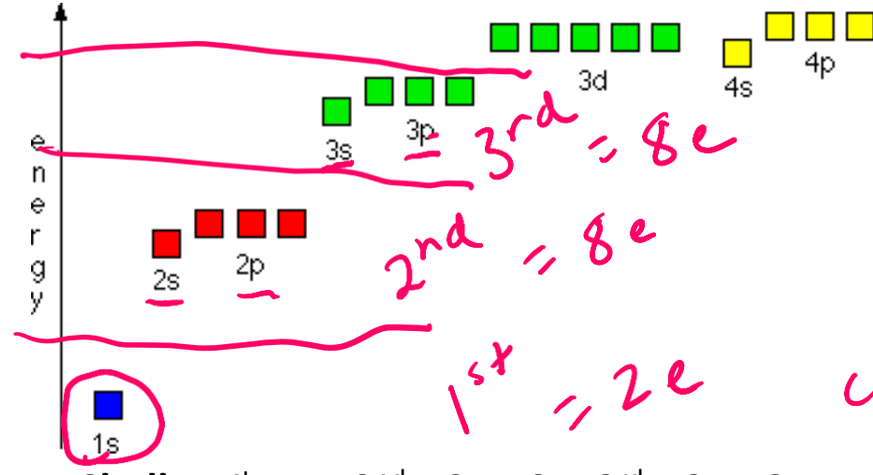
- Electrons arranged around the nucleus in specific regions called orbitals.
  - Each orbital can only hold two electrons
- Orbitals are grouped into electron shells
  - Numbered 1,2,3…
  - Lower numbers = shells closer to the nucleus
  - First shell can hold a maximum of 2 electrons
  - Second shell can hold up to 8
  - Third shell can also hold 8
- Orbitals are usually filled from lowest energy (inner shell) to highest energy (outer shell)
- Outer shell is the ***valence shell*** and is used for forming bonds with other elements.
- The most stable configuration is a complete (full) outer shell.

2e orbital.

fill lowest energy



do not have full outer shell.

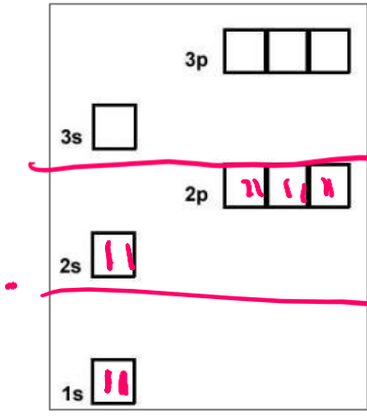


3rd = 8e

2nd = 8e

1st = 2e

Electron Configuration of Ne – an inert gas (10e)



completely full shell.

3

2

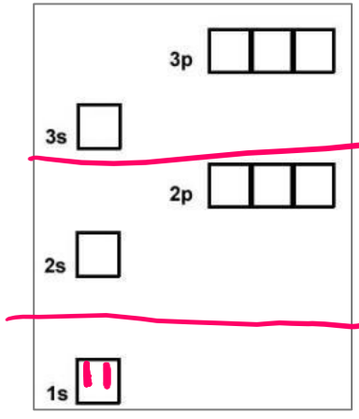
1

Shells: 1st = 1s, 2nd = 2s + 2p, 3rd = 3s + 3p

Shell is a collection of orbitals with similar energy

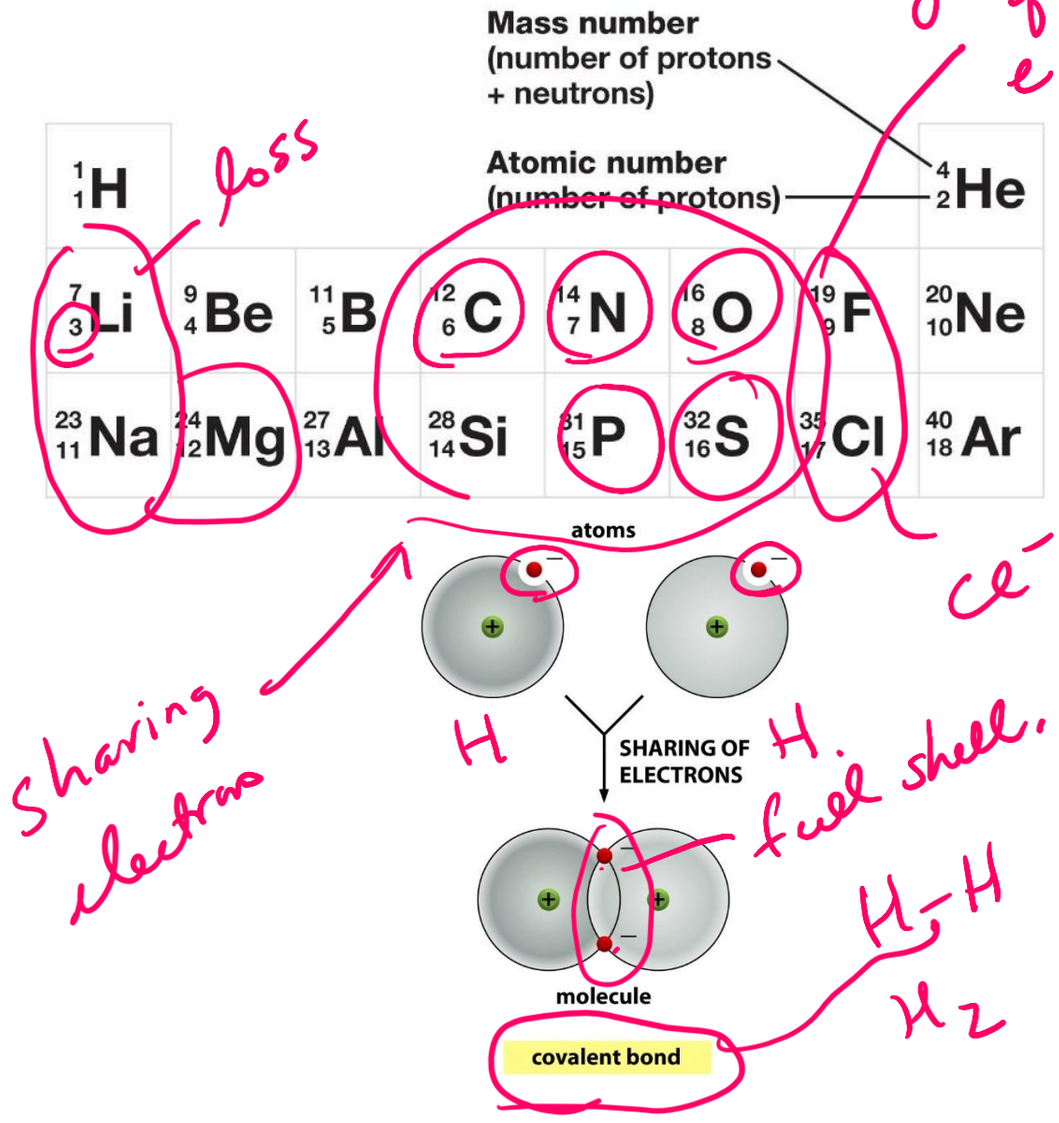
Ions or Covalent Chemical Bonds – What's an Element going to do?

- Elements like Li, Na, F, Cl, Mg, readily form ions to generate a complete outer shell.



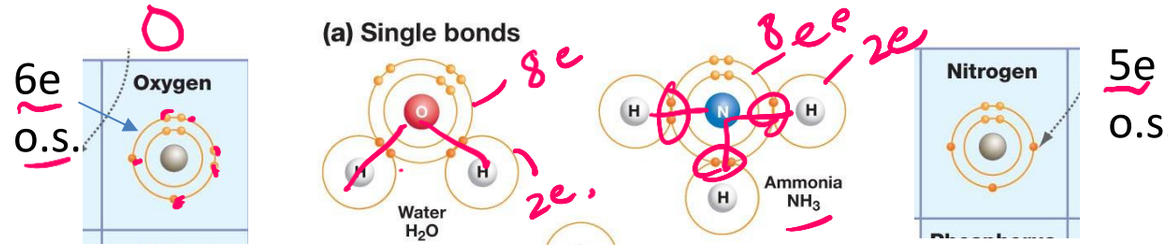
Example:
Li with 3 electrons

- Some elements cannot form stable ions because it would involve the loss or gain of too many electrons. This includes C, N, and O – which are common in biological systems.
- Unfilled electron orbitals on elements like C, N, and O allow for the formation of ***covalent bonds***, and atoms are most stable when each electron orbital is filled.
  - Each atom's unpaired *valence* electrons are shared by both nuclei to fill their orbitals.
  - Substances held together by covalent bonds are called molecules

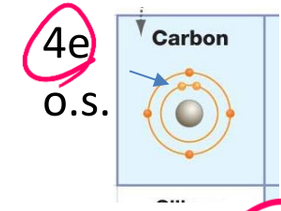


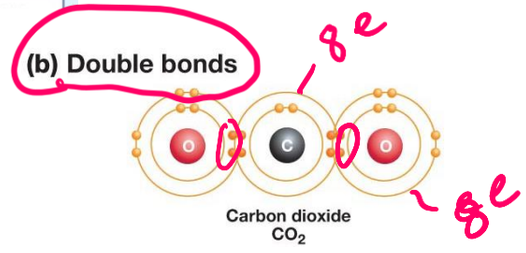
Covalent Bonds – Filling the Outer Shell by Sharing

- The number of unpaired electrons in the outer shell determines the number of bonds an atom can make.
- Multiple bonds form when atoms share multiple electrons.



How many bonds will carbon form?





O=C=O

The number of covalent bonds (valence) formed by common elements.

- Oxygen = 2 bonds
- Nitrogen = 3 bonds
- Carbon = 4
- Sulfur = 2 bonds (in biological systems)
- Hydrogen = 1 bond
- Phosphorous = 5 bonds in biological molecules

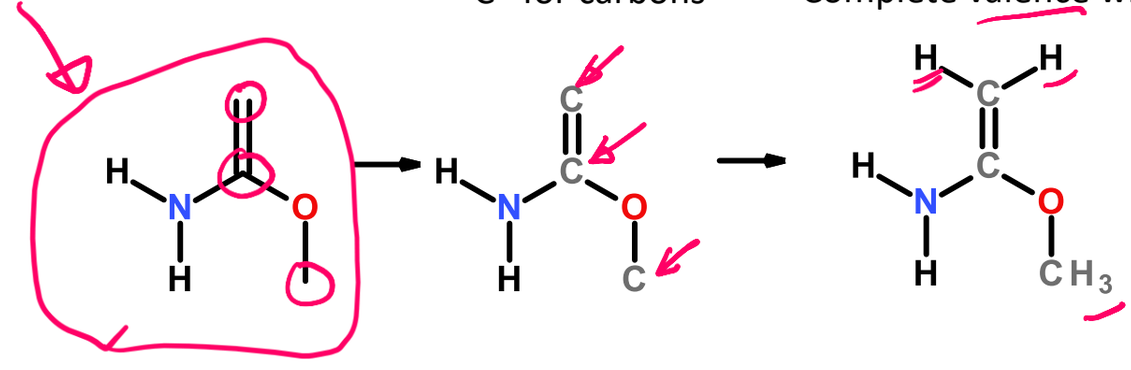
You must know these numbers.

Abbreviated Chemical Drawings:

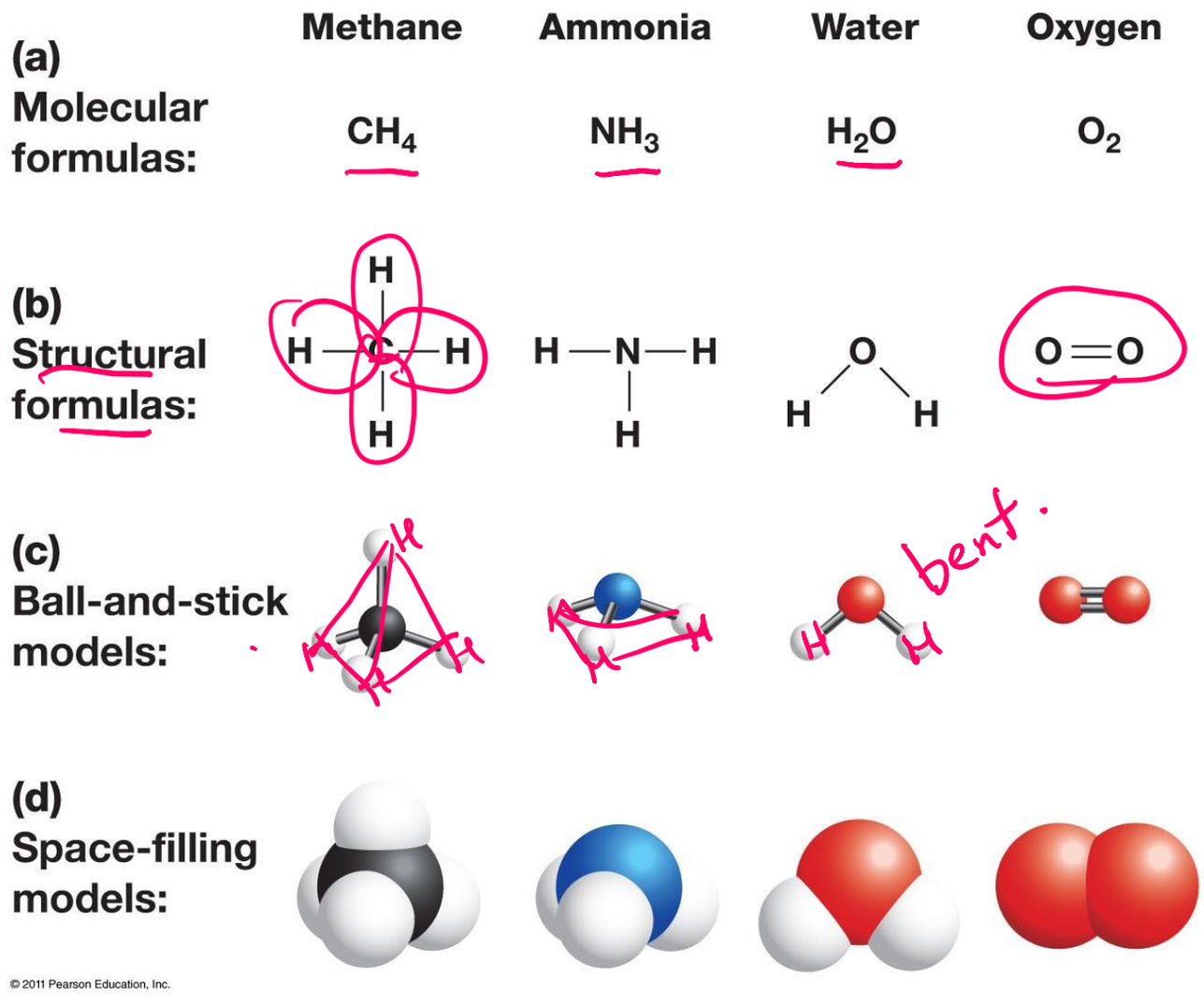
- "C" for carbon is not drawn, but carbons are found at the ends of lines and when lines join or "kink"
- Hydrogens attached to carbon are not shown, you need to add them to complete to complete the valence of the carbon atoms.

You must know how to do this.

"C" for carbons Complete valence with H



Representation of Molecules



types of bonds.

direction in space for atoms.

electron cloud.

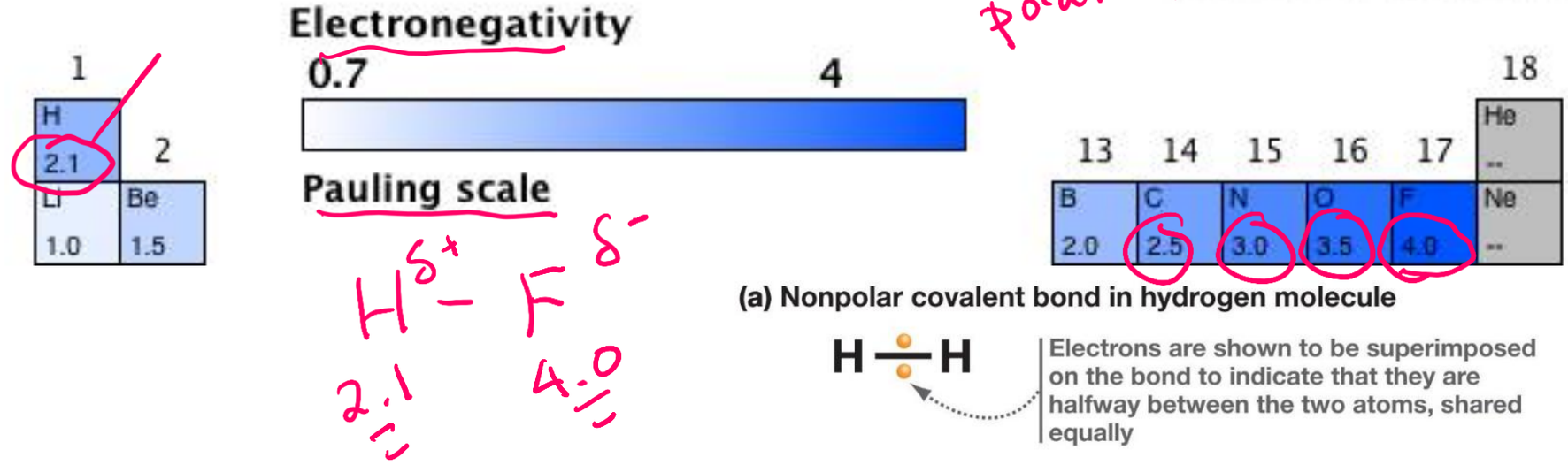
Space occupied by atom.

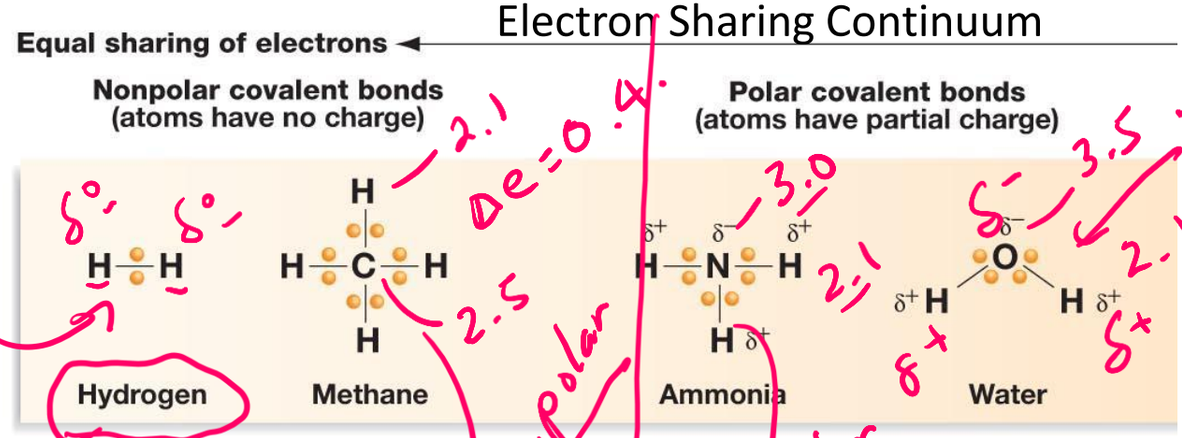
Electron Sharing and Bond Polarity – Are All Bonds Equal?

- Polar bonds = different electron density of each atom.
- The polarity of a bond depends on the electronegativity of the atoms.
- Electronegativity - ability of atoms to pull electrons from other atoms.
- Atoms with higher electronegativity will develop a partial negative charge, the atom they are bonded will have a partial positive charge.
- The order of electronegativity is:

  H ~ C < N < O

Increased pos. charge of nucleus.



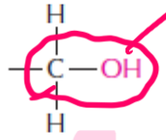


Functional Groups – You should Become Familiar with These

C–O COMPOUNDS

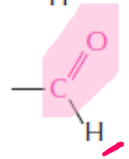
Many biological compounds contain a carbon bonded to an oxygen. For example,

alcohol

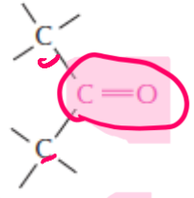


The –OH is called a hydroxyl group.

aldehyde

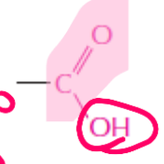


ketone



The C=O is called a carbonyl group.

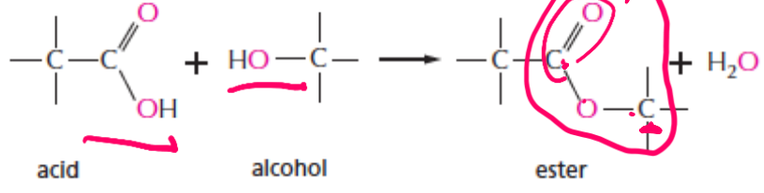
carboxylic acid



The –COOH is called a carboxyl group. In water this loses an H^+ ion to become $-COO^-$.

esters

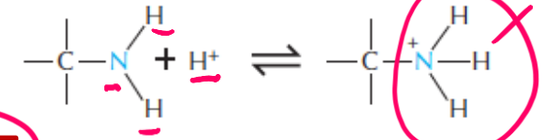
Esters are formed by combining an acid and an alcohol.



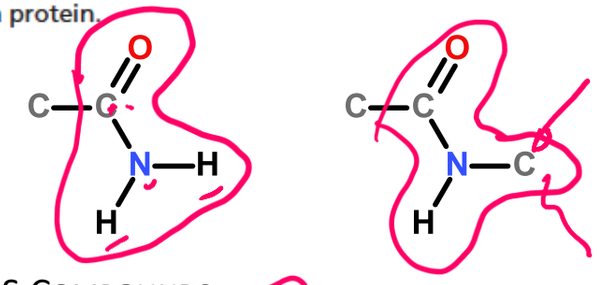
C–N COMPOUNDS

Amines and amides are two important examples of compounds containing a carbon linked to a nitrogen.

Amines in water combine with an H^+ ion to become positively charged.

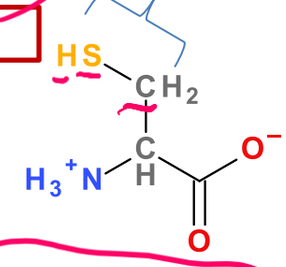


Amides are formed by combining an acid and an amine. Unlike amines, amides are uncharged in water. An example is the peptide bond that joins amino acids in a protein.



C–S COMPOUNDS

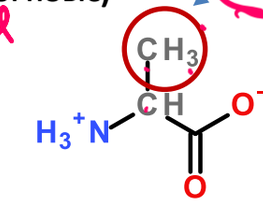
thiol



Cysteine (amino acid)

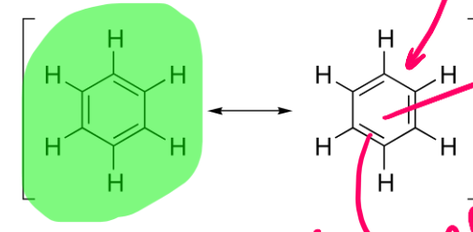
C–H GROUPS (HYDROPHOBIC)

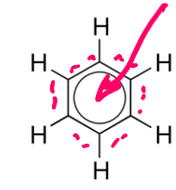
Methyl



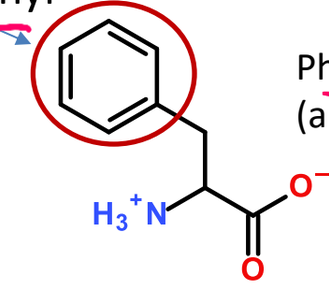
Alanine (amino acid)

Aromatic – planer rings, alt double bonds





Phenyl



Phenylalanine (amino acid)

Key Points & Expectations

Chemistry

- Number of bonds formed by common elements:
  (N=3, C=4, O=2, S=2, H=1).
- You should be able to complete chemical structures by adding hydrogens to carbons.
- Predict degree of bond polarity based on electronegativies, N-H and O-H and C=O are polar, C-H is not.

- Be able to draw the following functional groups & identify them on larger molecules.
  - Non-polar:
    - Methyl
    - Phenyl
  - Polar:
    - Alcohol (C-OH)
    - Thiol (C-SH)
    - Carboxylate (ketone, aldehyde) (C=O)
    - Ester
    - Carboxylic acid
    - Amide
    - Amino

A. Give the names of the functional groups on these two amino acids.
B. Which functional groups are common?