



Peptides

Summer semester 2024



Formation of a polypeptide

Definitions and concepts



- A residue: each amino acid in a (poly)peptide
- Dipeptide, tripeptide, tetrapeptide, etc.
- Oligopeptide (peptide): a short chain of 20-30 amino acids
- Polypeptide: a longer peptide with no particular structure
- Protein: a polypeptide chains with an organized 3D structures
- The average molecular weight of an amino acid residue is about 110
 - The molecular weights of most proteins are between 5500 and 220,000 (calculate how many amino acids)
- We refer to the mass of a polypeptide in units of Daltons
 - A 10,000-MW protein has a mass of 10,000 Daltons (Da) or 10 kilodaltons (kDa)

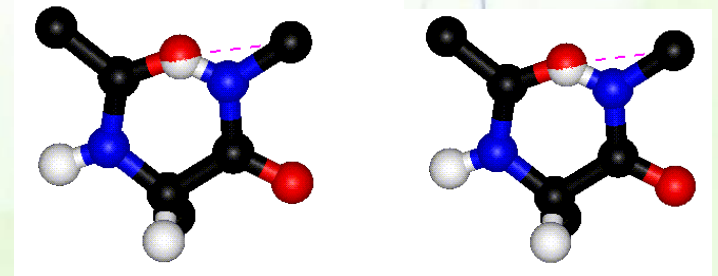
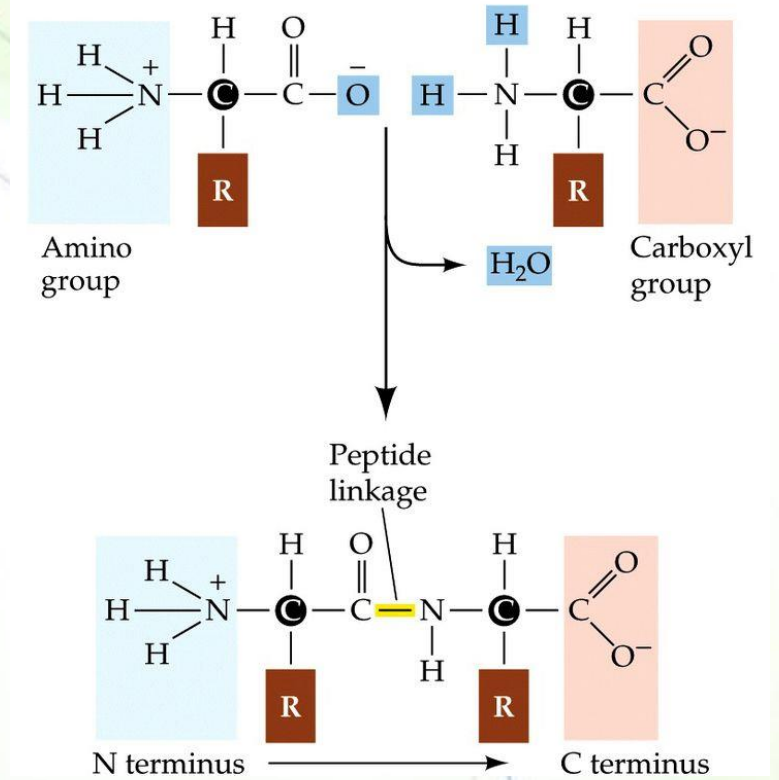
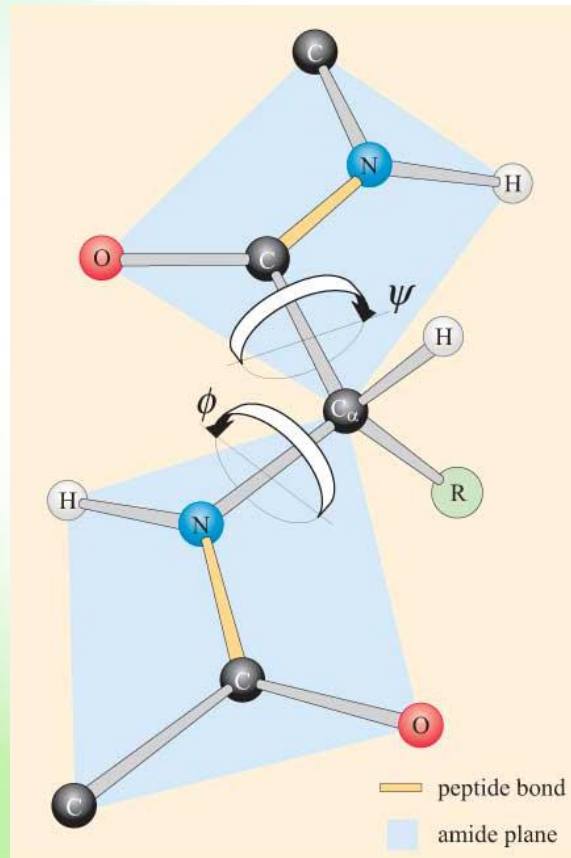
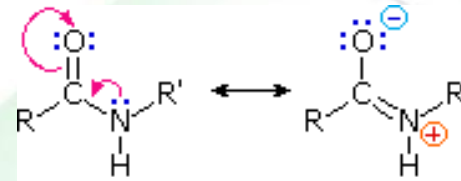
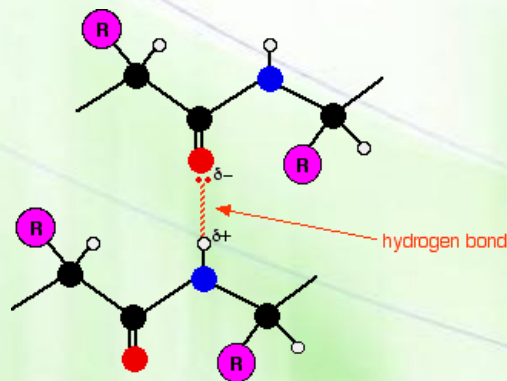
Peptide bond

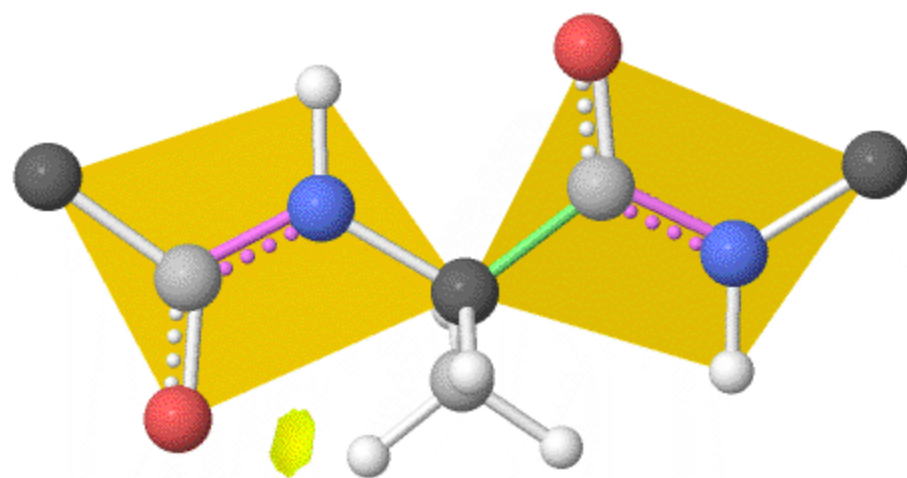


- It is called an amide bond formed via a condensation reaction.

- Features

- It has a resonance structure
- Zigzag structure
- Double bond
 - Planar, charged, Rigid, Un-rotatable
- Hydrogen bonding
 - Except proline



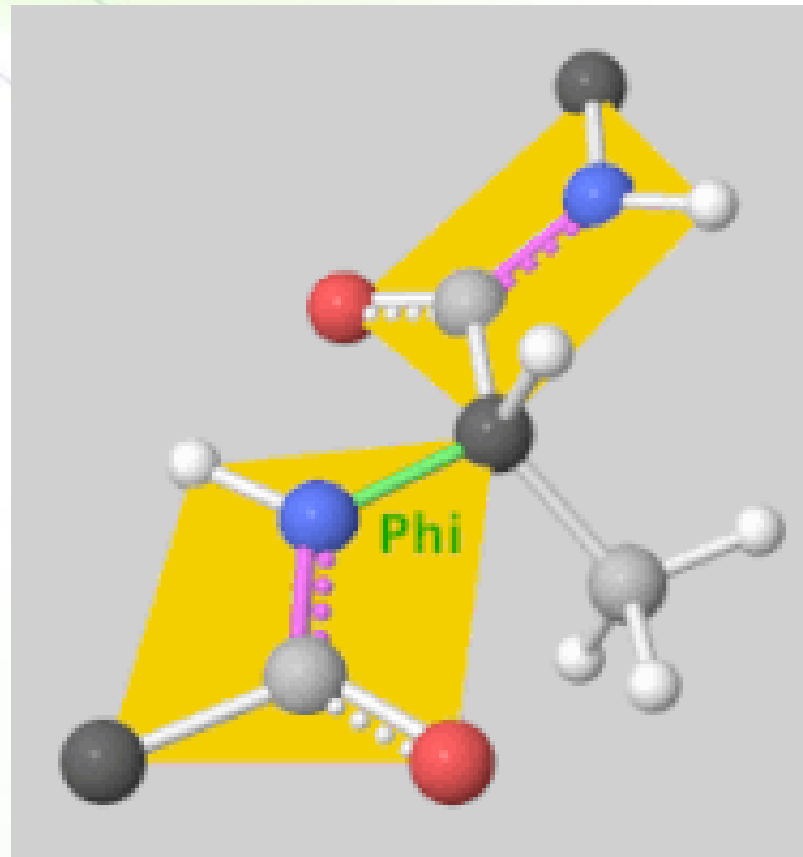


C α C H N O

○ Phi ϕ ● Psi ψ
-175° -175°

-20° +20°

- Alanine
- Peptide Bonds
- Planes
- van der Waals⁴
- Show Clashes

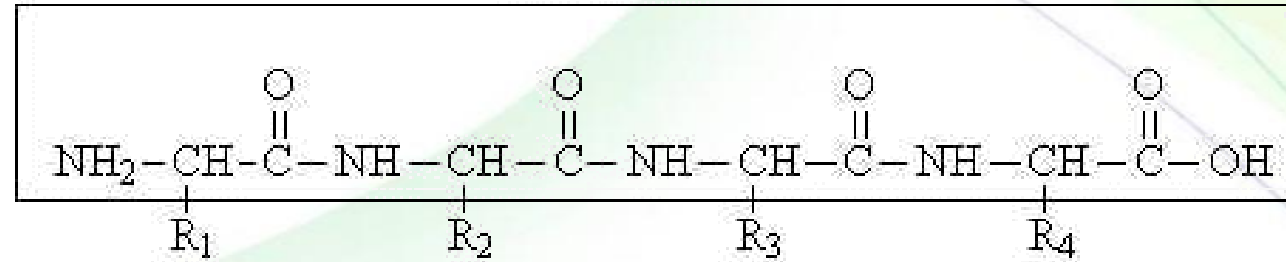


Backbone, orientation and directionality

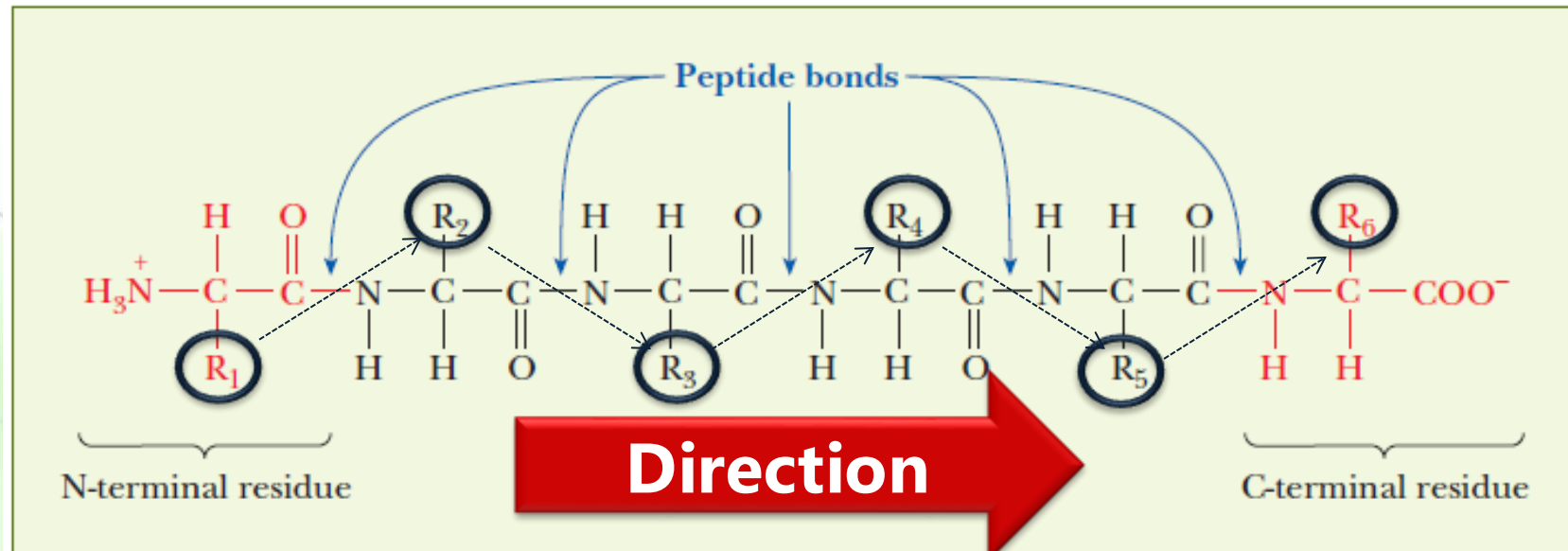


α -amide N, the α -C, and the α carbonyl C atom

backbone



sidechains

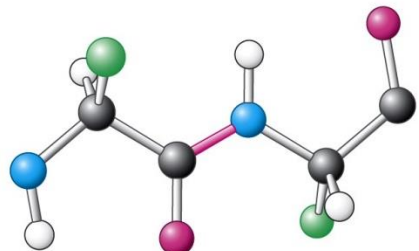


Except for proline

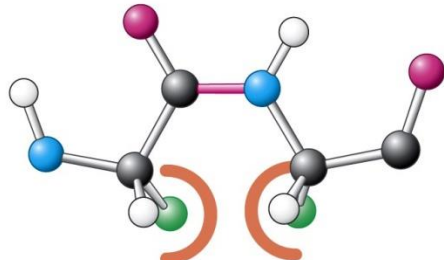


- Steric hindrance between the functional groups attached to the C α atoms will be greater in the cis configuration.
- In proline, both cis and trans conformations have about equivalent energies.
- Proline is thus found in the cis configuration more frequently than other amino acid residues.

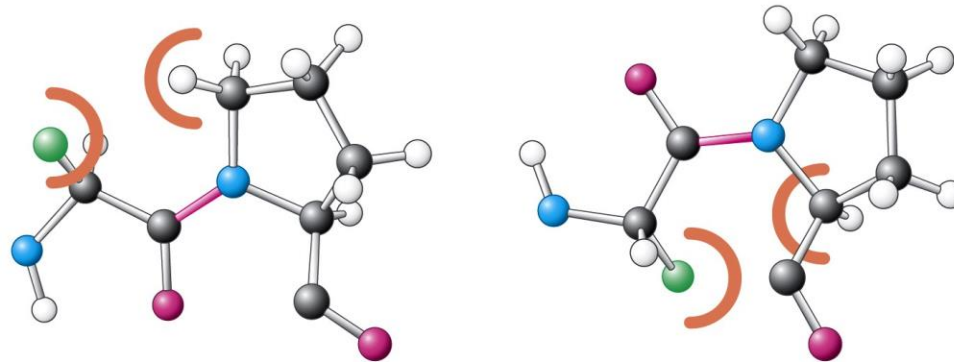
All other amino acids



Trans



Cis

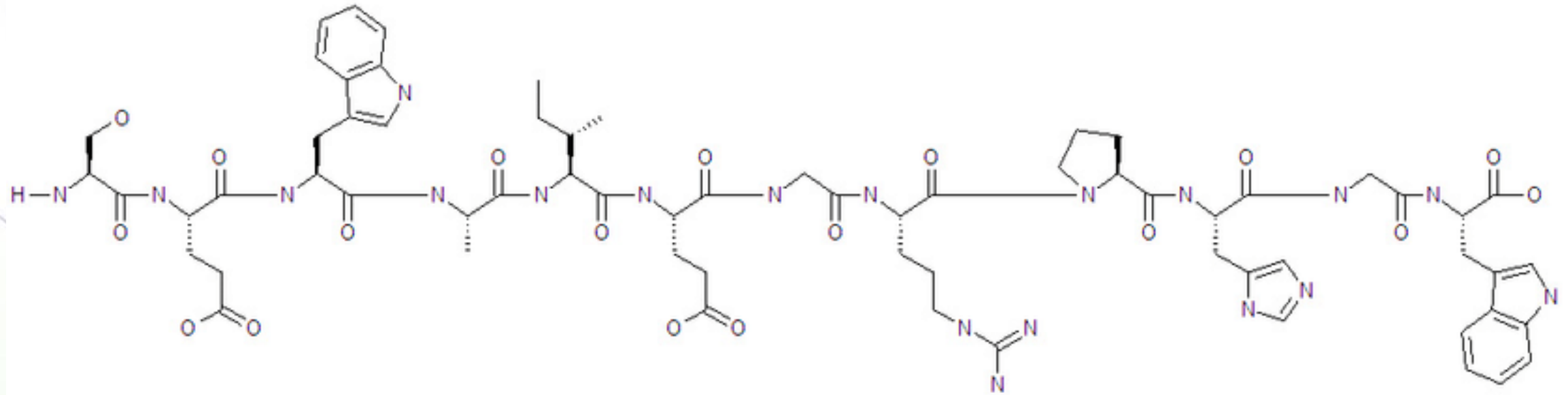


Trans

Proline

Cis

Practice: *name the amino acid residues*



NH_2 —S E W A I E G R P H G W— COOH

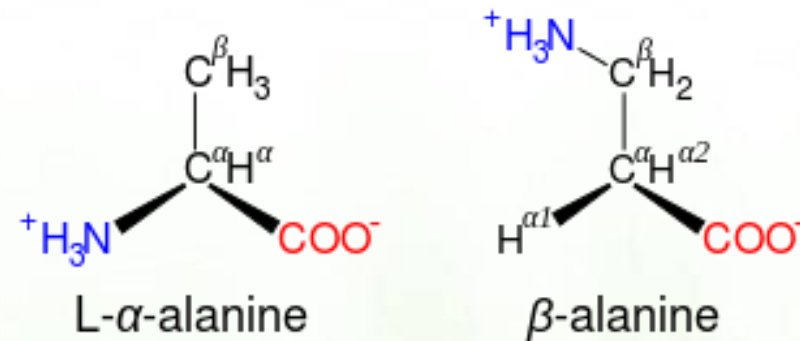
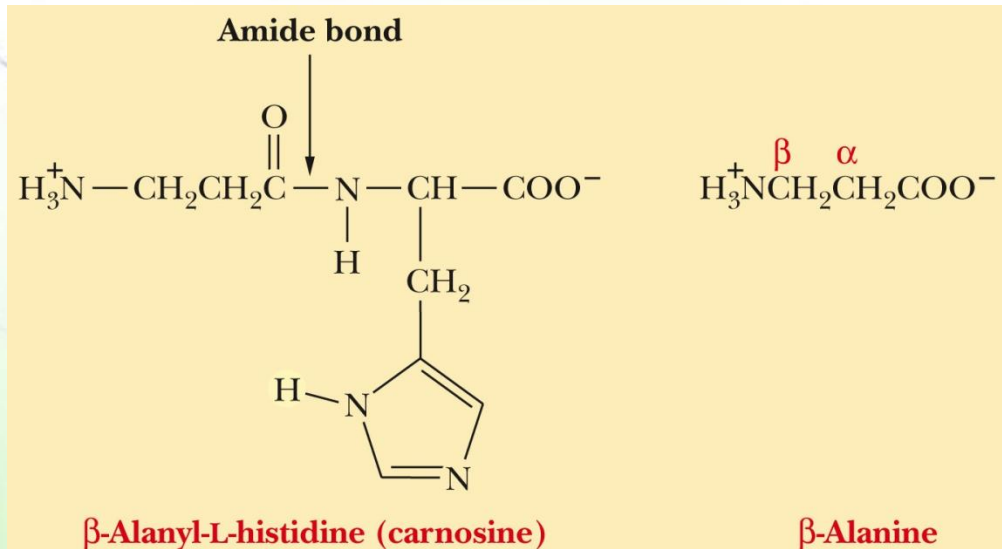


Examples of functional and exceptional peptides

Carnosine (β -alanyl-L-histidine)



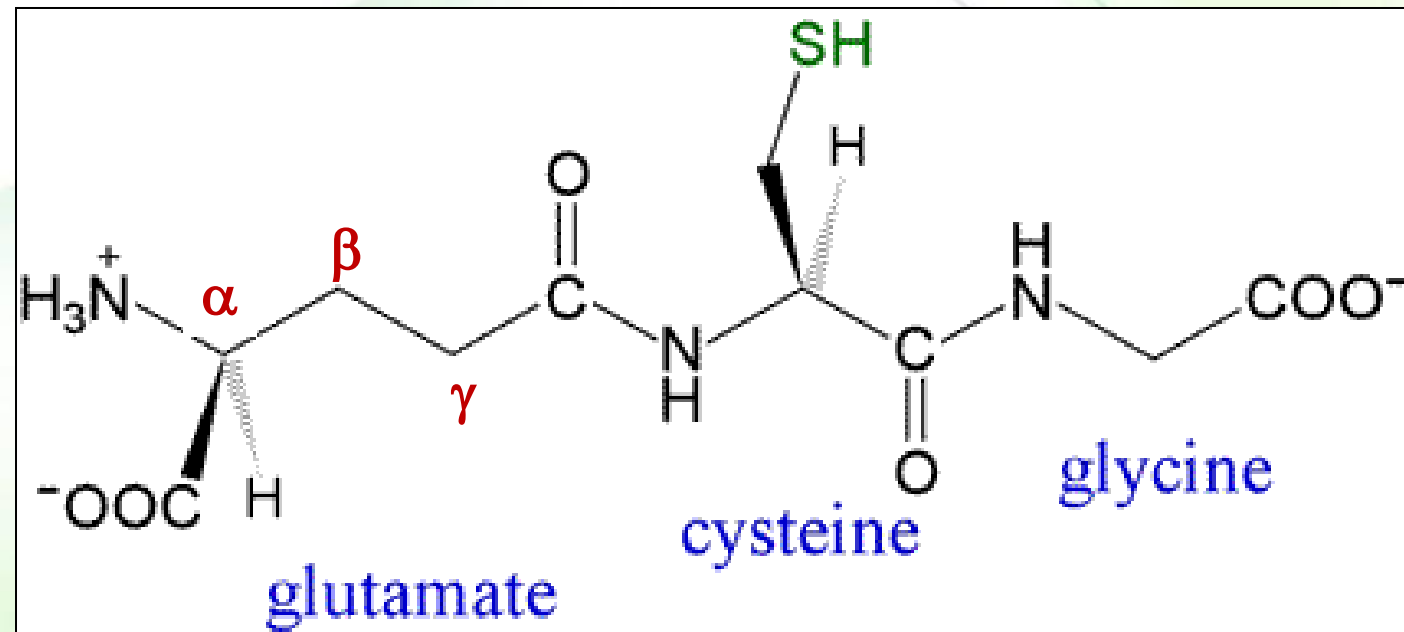
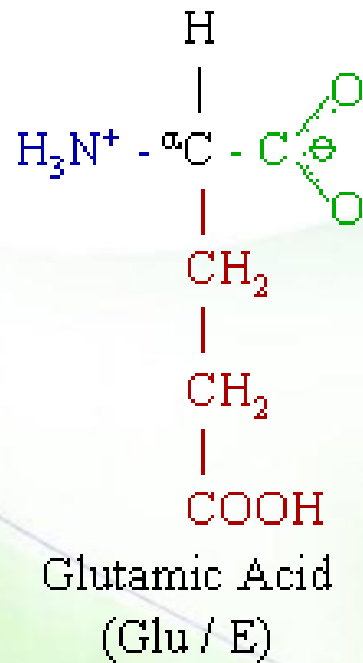
- A dipeptide of β -alanine and histidine
- The amino group is bonded to the β -carbon of alanine
- It is highly concentrated in muscle and brain tissues
 - Protection of cells from ROS (radical oxygen species) and peroxides
 - Contraction of muscle



Glutathione



(γ -glutamyl-L-cysteinylglycine)



Function of glutathione



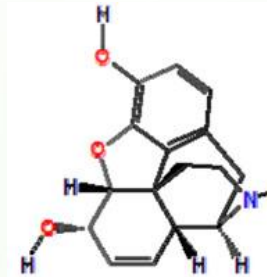
- It scavenges oxidizing agents by reacting with them.
- Two molecules of the reduced glutathione molecules form the oxidized form of glutathione by forming a disulfide bond between the —SH groups of the two cysteine residues.



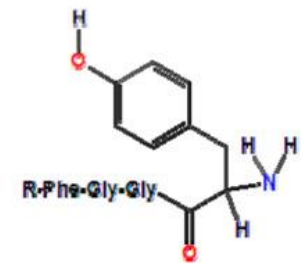
Enkephalins



- Two pentapeptides found in the brain known as enkephalins, and function as analgesics (pain relievers).
 - They differ only in their C-terminal amino acids.
 - Met-enkephalin: Tyr-Gly-Gly-Phe-Met
 - Leu-enkephalin: Tyr-Gly-Gly-Phe-Leu
 - The aromatic side chains of tyrosine and phenylalanine play a role in their activities.
- There are similarities between the three-dimensional structures of opiates, such as morphine, and enkephalins.



Morphine

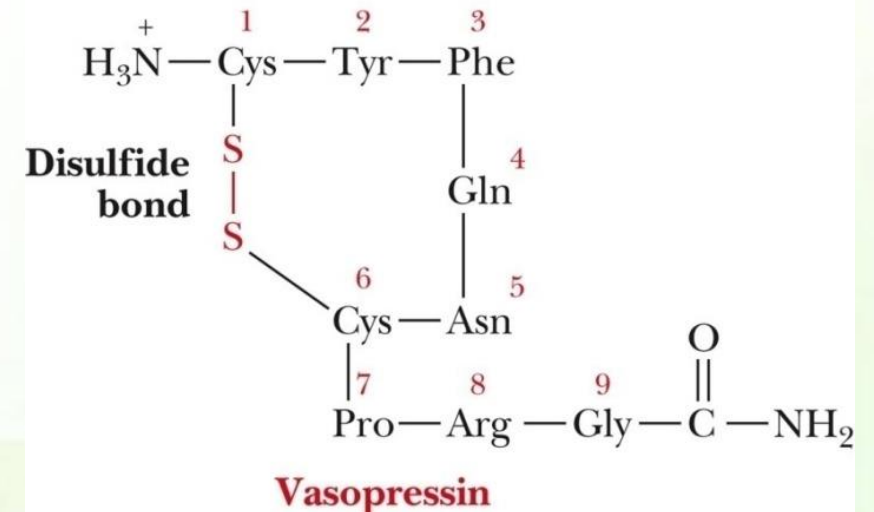
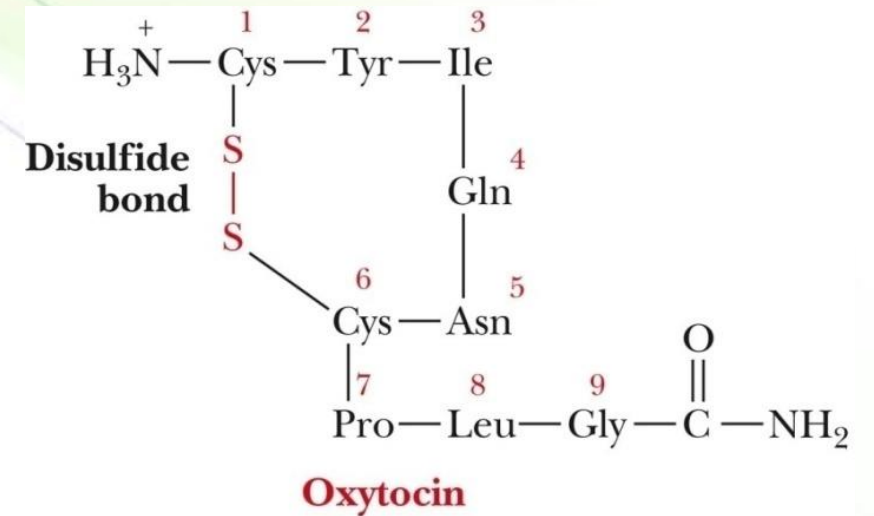


Enkephalins

Oxytocin and vasopressin



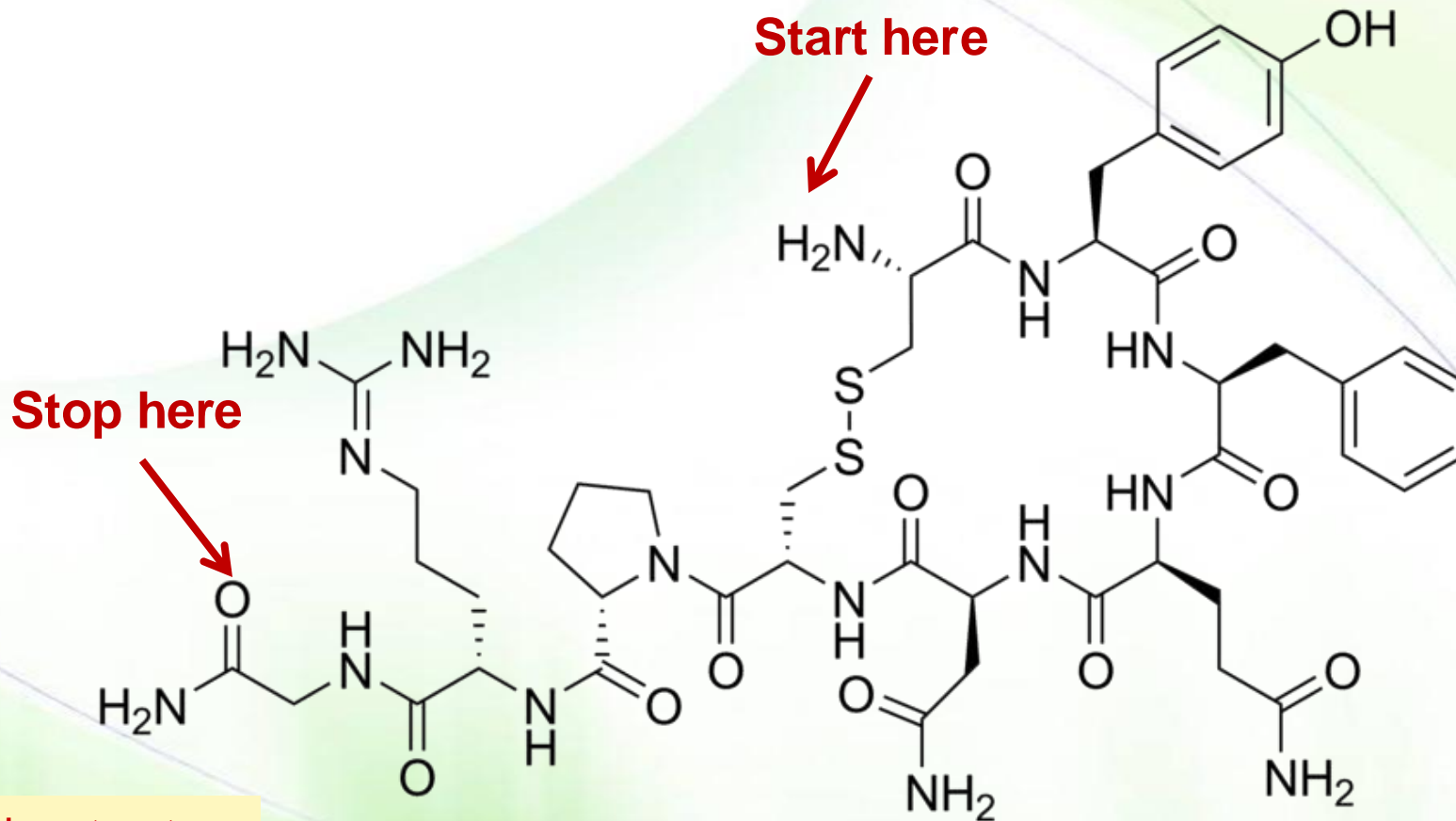
- Hormones with cyclic structures due to S-S link between Cys.
- Both have amide group at the C-terminus.
- Both contain nine residues, but:
 - Oxytocin has isoleucine and leucine.
 - Vasopressin has phenylalanine and arginine .
- Oxytocin regulates contraction of uterine muscle (labor contraction).
- Vasopressin regulates contraction of smooth muscle, increases water retention, and increases blood pressure.



Vasopressin



Practice: what is the primary structure?



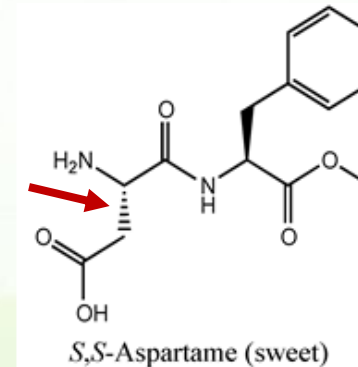
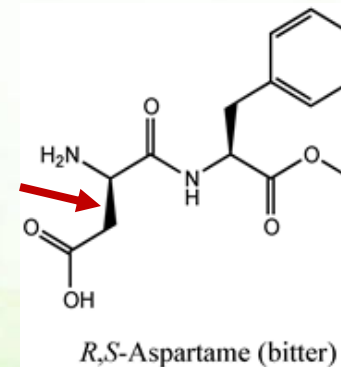
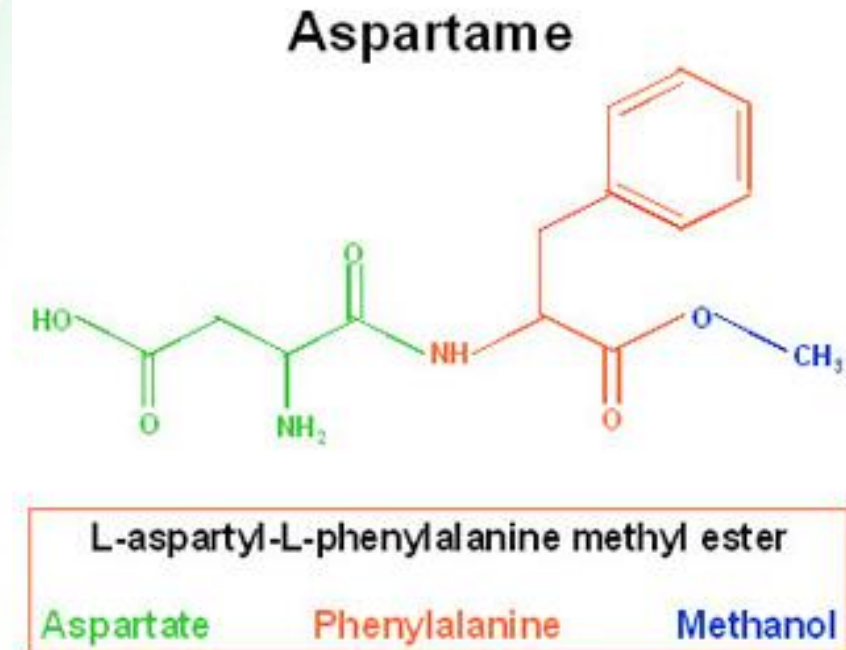
Note: the structure ends with NH₂

Aspartame



L-Aspartyl-L-phenylalanine (methyl ester)

- A dipeptide that is 200 times sweeter than sugar.
- If a D-amino acid is substituted for either amino acid or for both of them, the resulting derivative is bitter rather than sweet.



Aspartame and cancer



REUTERS®

World ▾

Business ▾

Markets ▾

Sustainability ▾

Legal ▾

Breakingviews

Technology ▾

Invest

Government Health Policy

Exclusive: WHO's cancer research agency to say aspartame sweetener a possible carcinogen -sources

By Jennifer Rigby and Richa Naidu

June 29, 2023 10:17 PM GMT+3 · Updated 7 days ago



Phenylketonuria (PKU)



- PKU is a hereditary “inborn error of metabolism” caused by defective enzyme, phenylalanine hydroxylase.
- It causes accumulation of phenylpruvate, which causes mental retardation.
- Sources of phenylalanine such as aspartame must be limited.
- A substitute for aspartame, known as alitame, contains alanine rather than phenylalanine.

