Peptides

Summer 2023

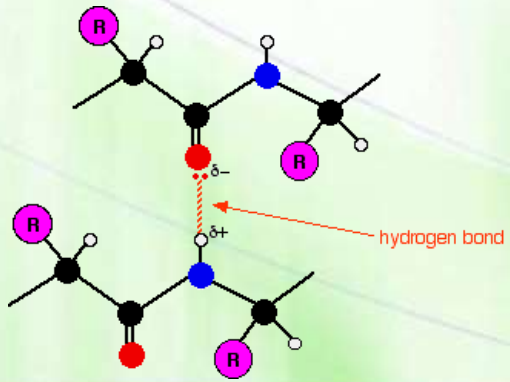
Formation of a polypeptide

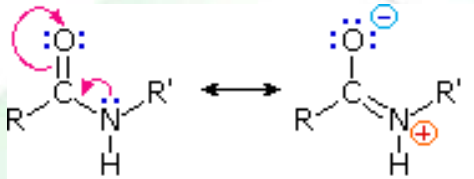
Definitions and concepts

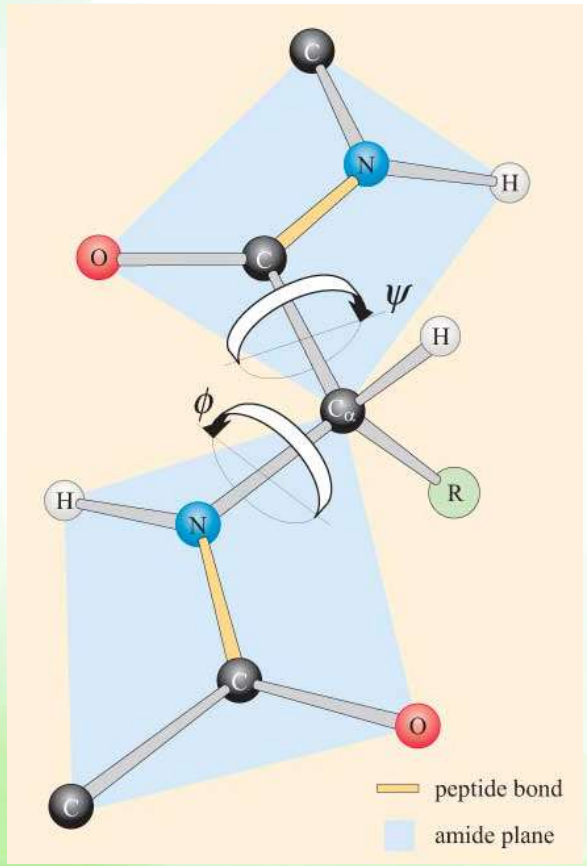
- A residue: each amino acid in a (poly)peptide
- Dipeptide, tripeptide, tetrapeptide, etc.
- Oligopeptide (peptide): a short chain of 20-30 amino acids
- Polypeptide: a longer peptide with no particular structure
- Protein: a polypeptide chains with an organized 3D structures
- The average molecular 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)

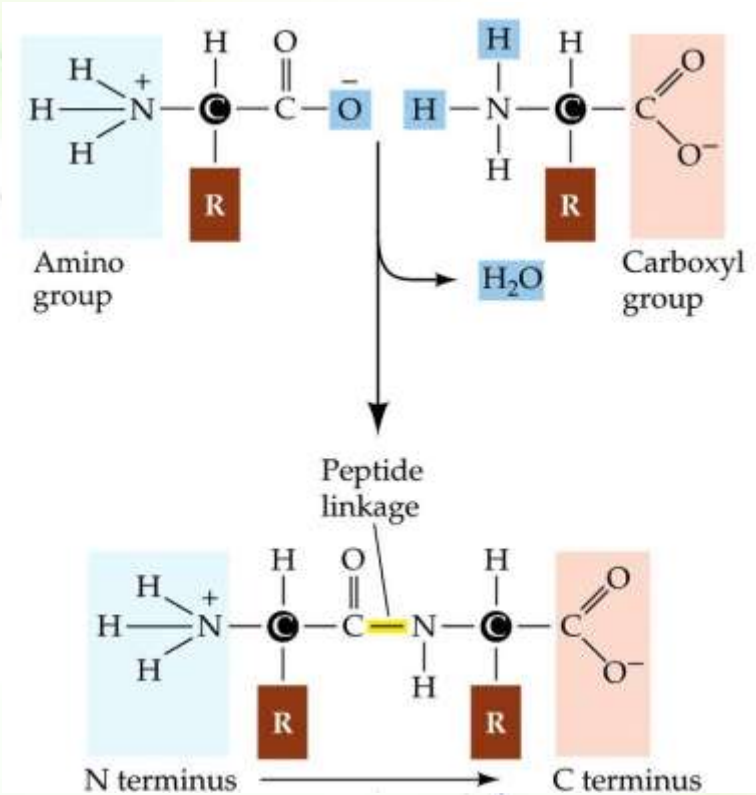
Peptide bond

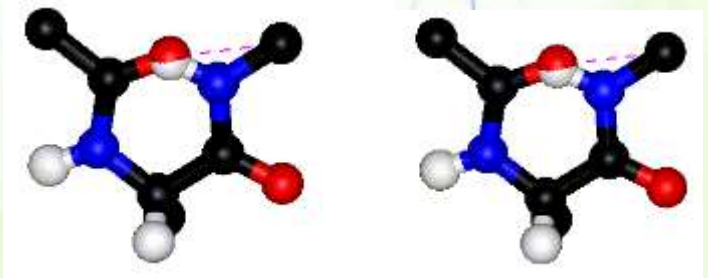
- It is called an amide bond formed via a condensation reaction.
- Features
  - It has a resonance structure
  - Zigzag structure
  - Double bond
    - Planar, charged, Rigid, Un-rotatable
  - Hydrogen bonding
    - Except proline





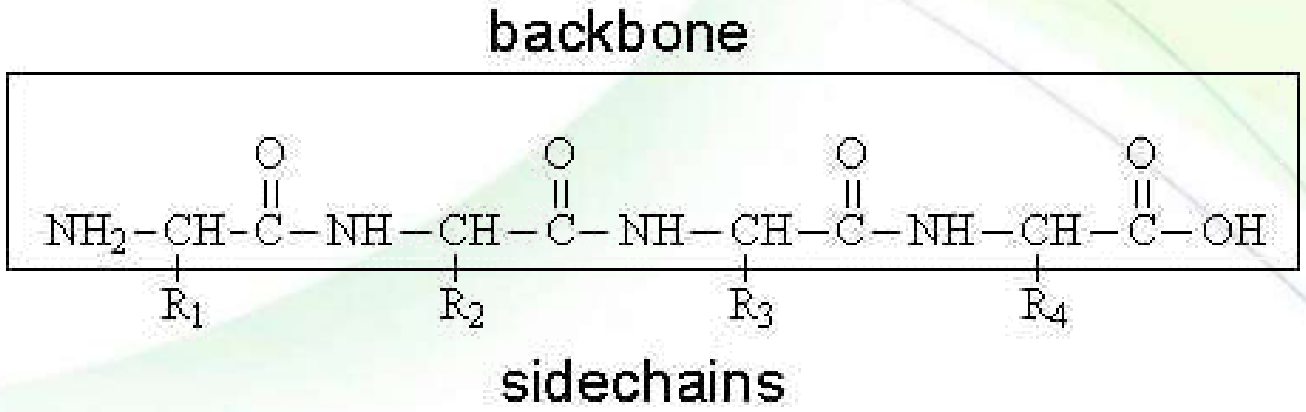


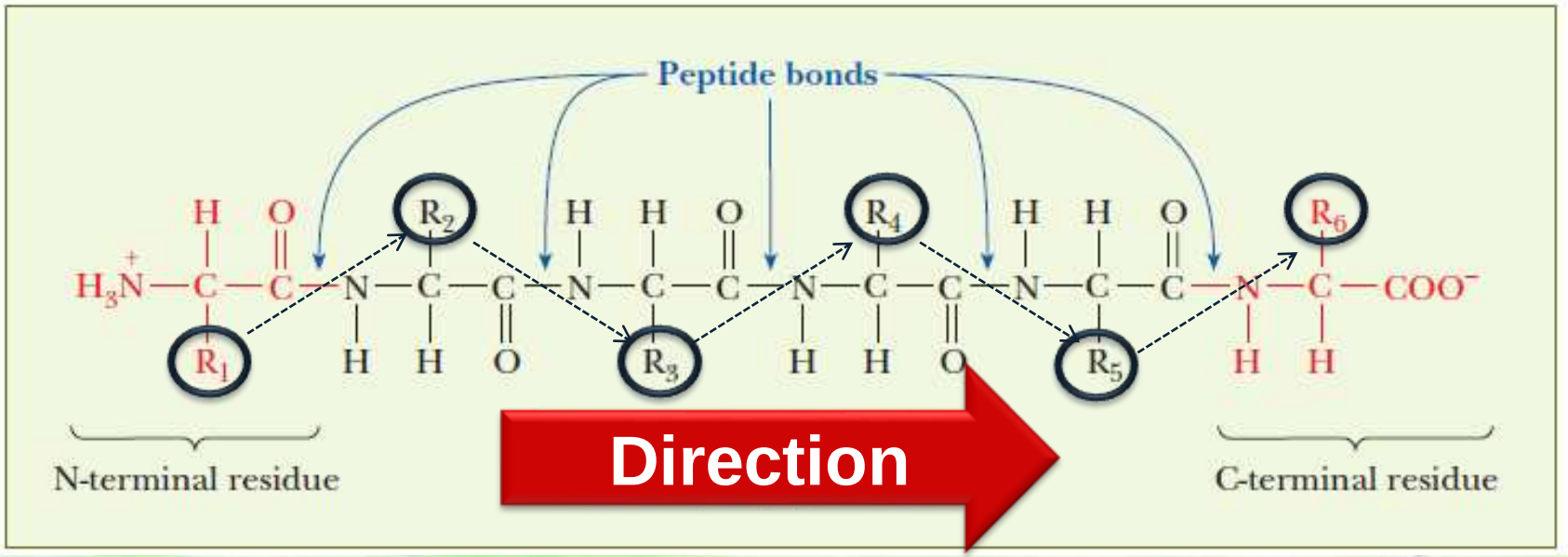




Backbone, orientation and directionality

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

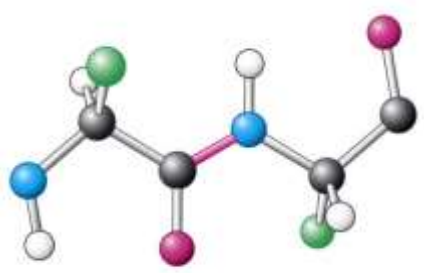




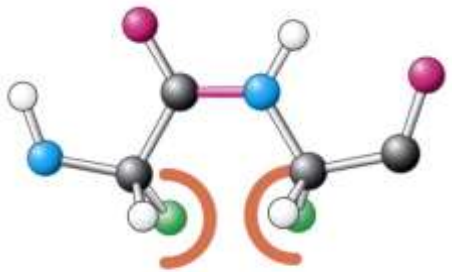
Except for proline

- Steric hindrance between the functional groups attached to the Cα 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.

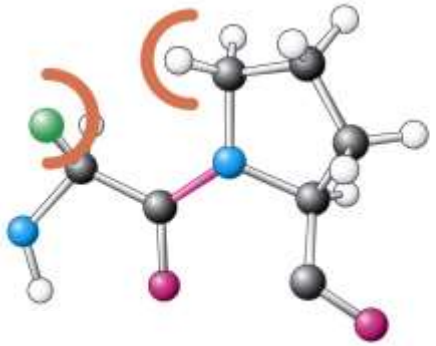
All other amino acids



Trans

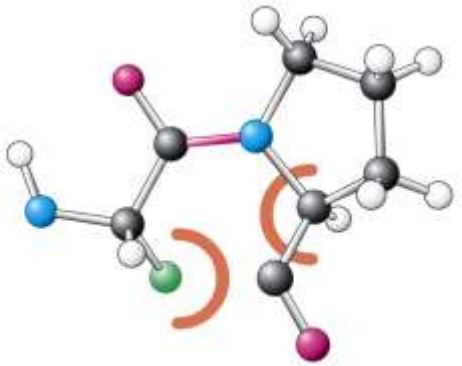


Cis



Trans

Proline

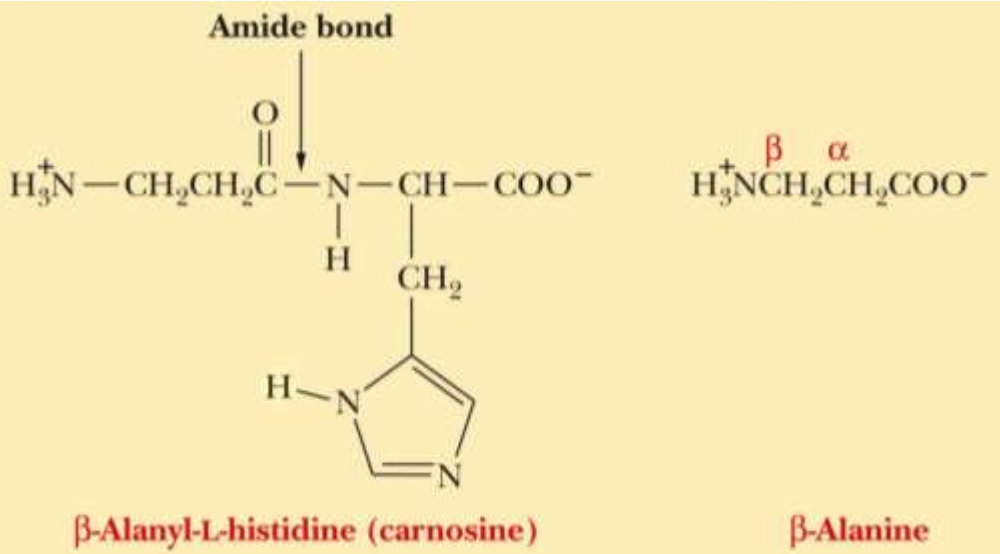


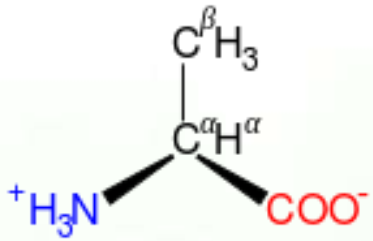
Cis

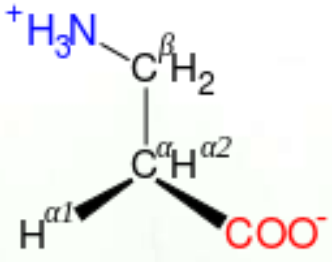
Examples of functional and exceptional peptides

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

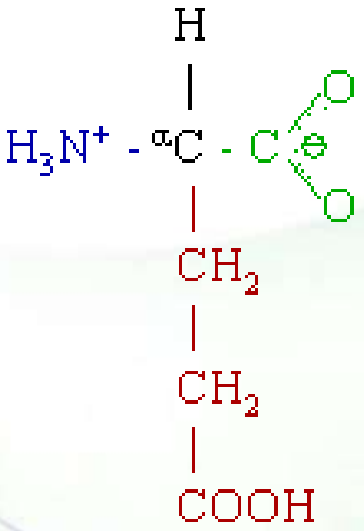




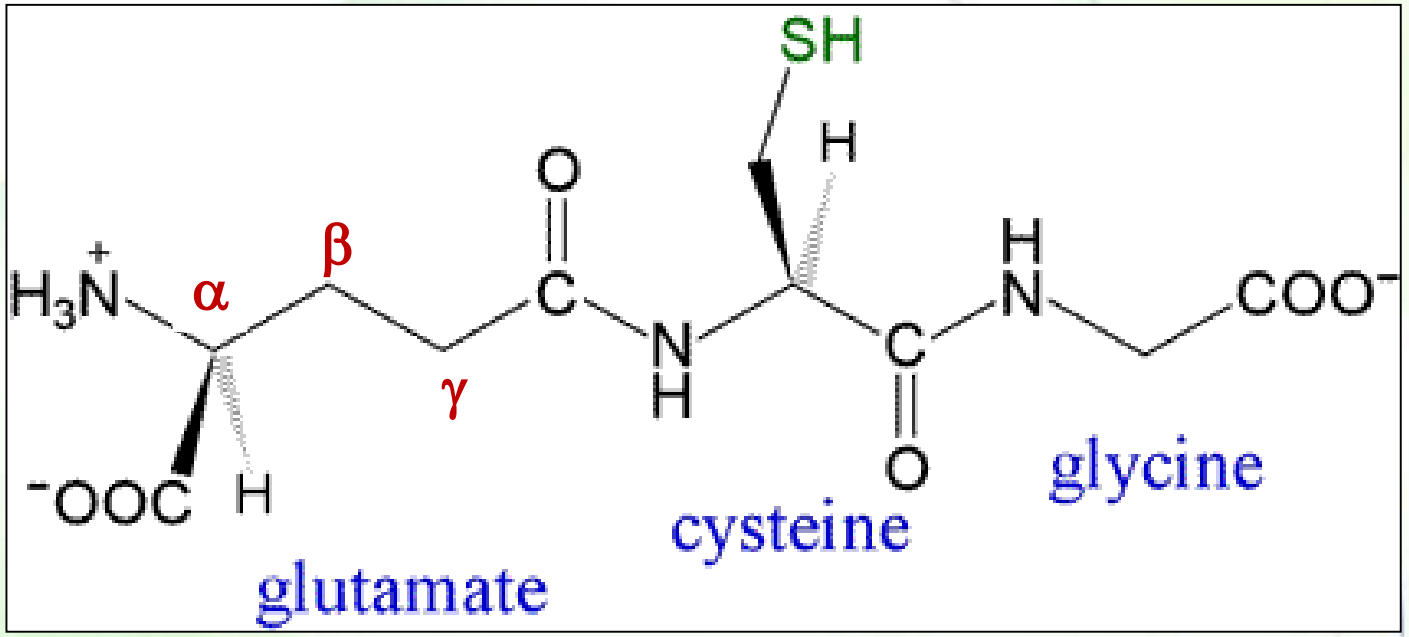


Glutathione

(γ-glutamyl-L-cysteinylglycine)



Glutamic Acid
(Glu / E)

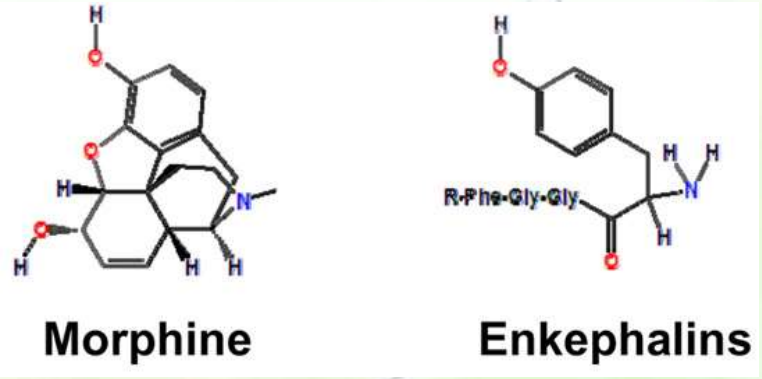


Function of glutathione

- 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.

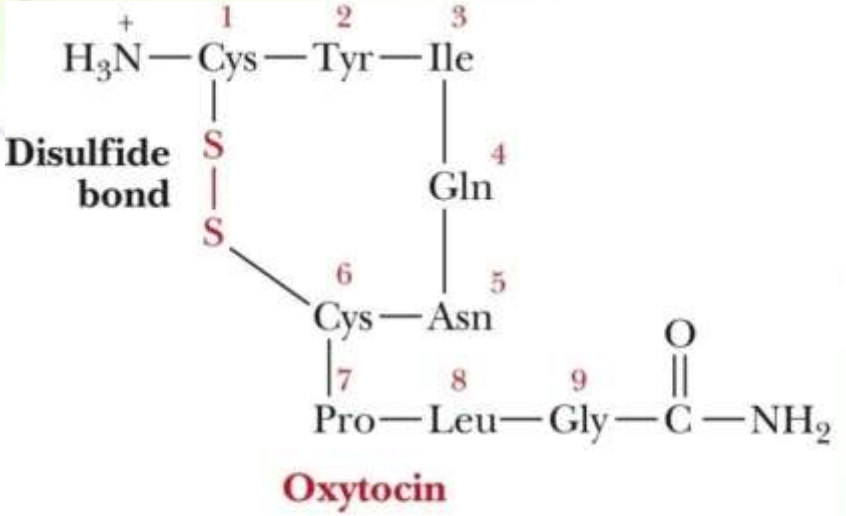
Enkephalins

- 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.

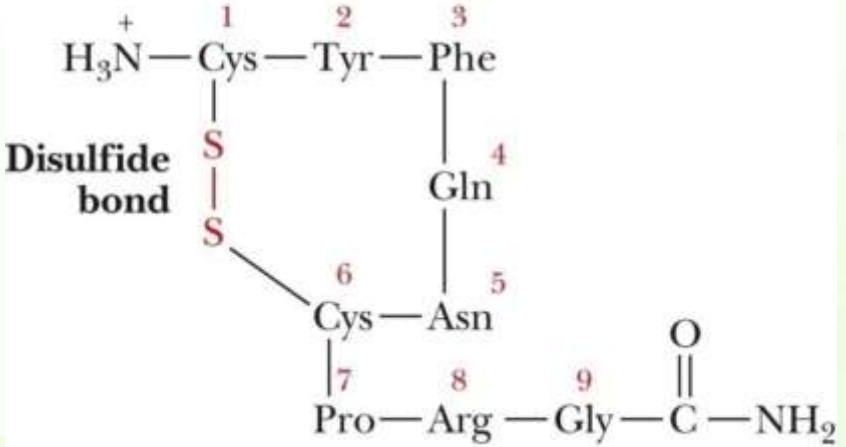


Oxytocin and vasopressin

- 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.



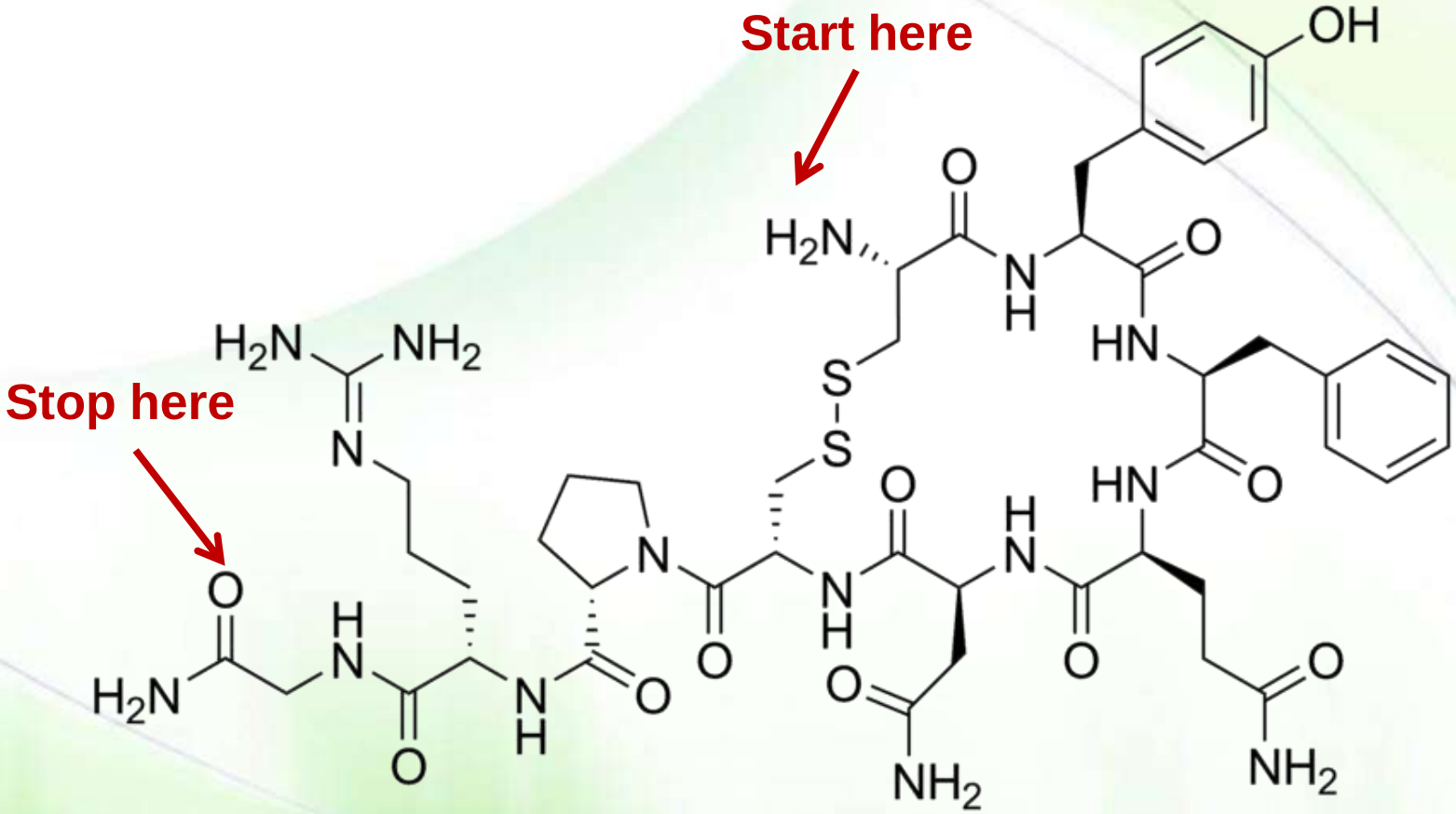
Oxytocin



Vasopressin

Vasopressin

Practice: what is the primary structure?

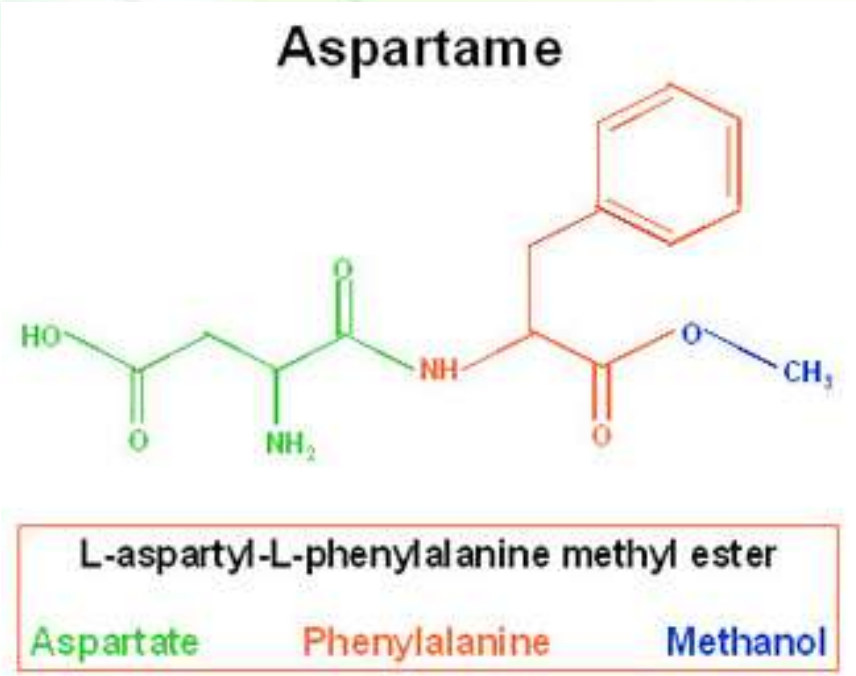


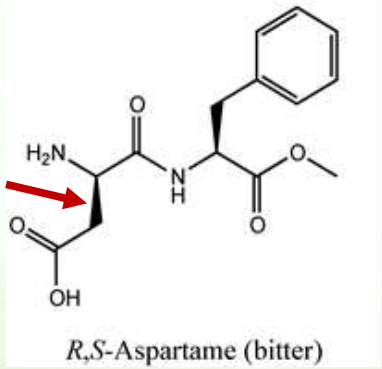
Note: the structure ends with NH2

Aspartame

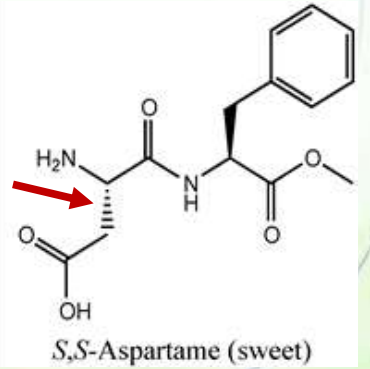
L-Aspartyl-L-phenylalanine (methyl ester)

- 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.





R,S-Aspartame (bitter)



S,S-Aspartame (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 causes mental retardation.
- Sources of phenylalanine such as aspartame must be limited.
- A substitute for aspartame, known as alitame, contains alanine rather than phenylalanine.