



Peptides and Polypeptides

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**Campbell and Farrell's Biochemistry, Chapters 3
(pp.72-78) and 4**



Formation of a polypeptide

Definitions and concepts

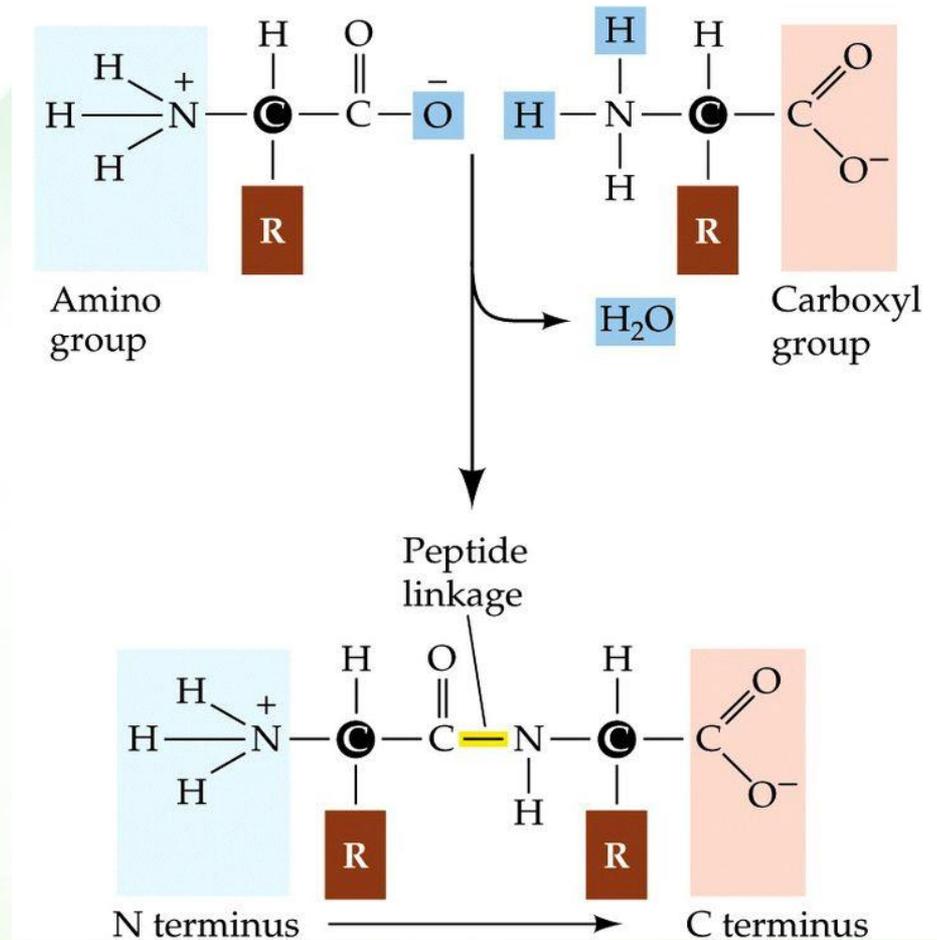


- A residue: each amino acid in a (poly)peptide
- Dipeptide, tripeptide, tetrapeptide, etc.
- Oligopeptide (peptide): a short chain of 20-30 amino acids
- Polypeptide: a longer peptide with no particular structure
- Protein: a polypeptide chains with an organized 3D structures
- The average molecular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



- Chemically, it is an amide bond.
- A condensation reaction

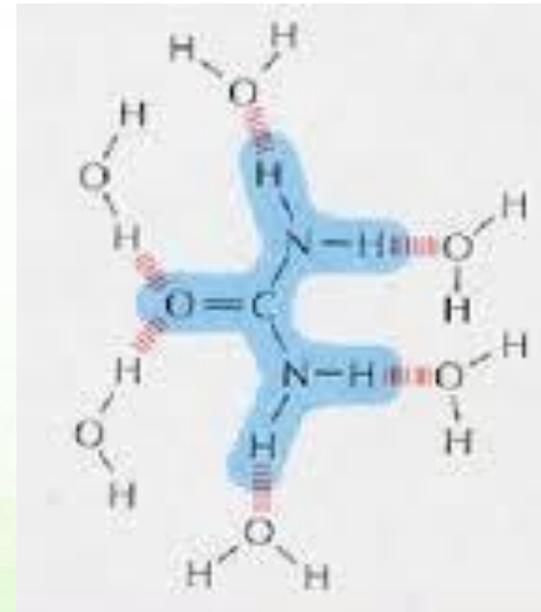
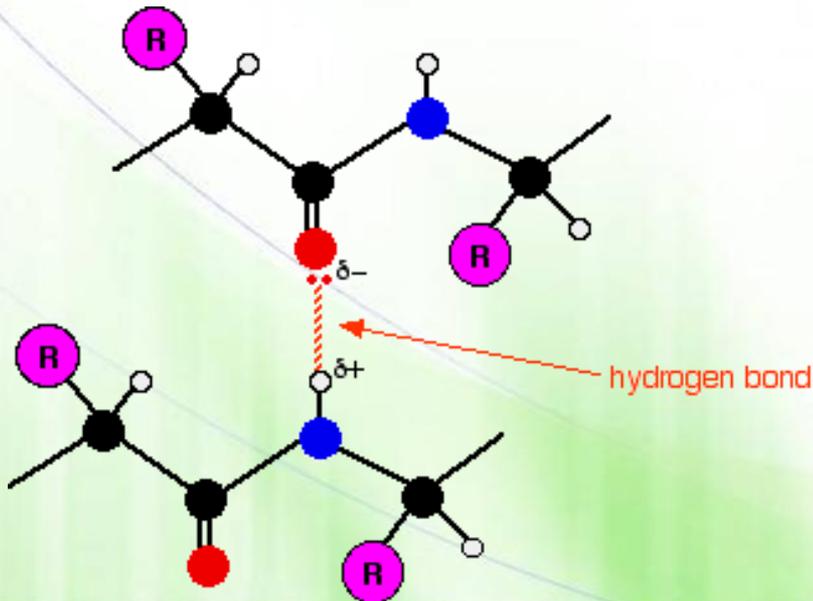
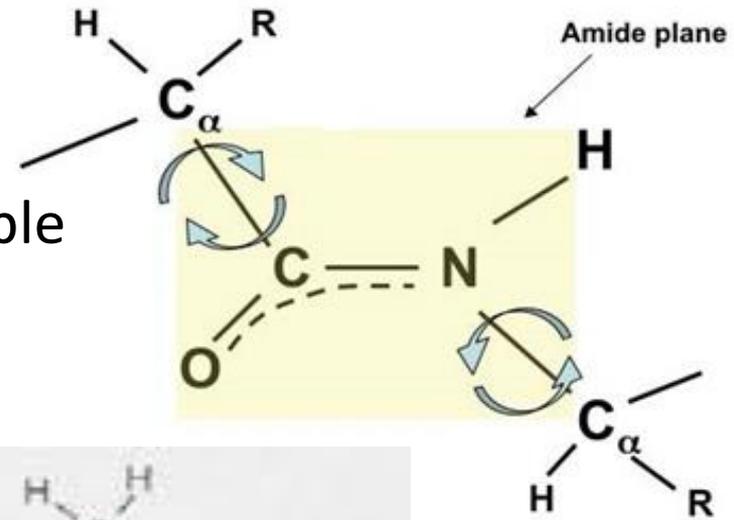


Features of the peptide bond



- Resonance structure makes peptide bond

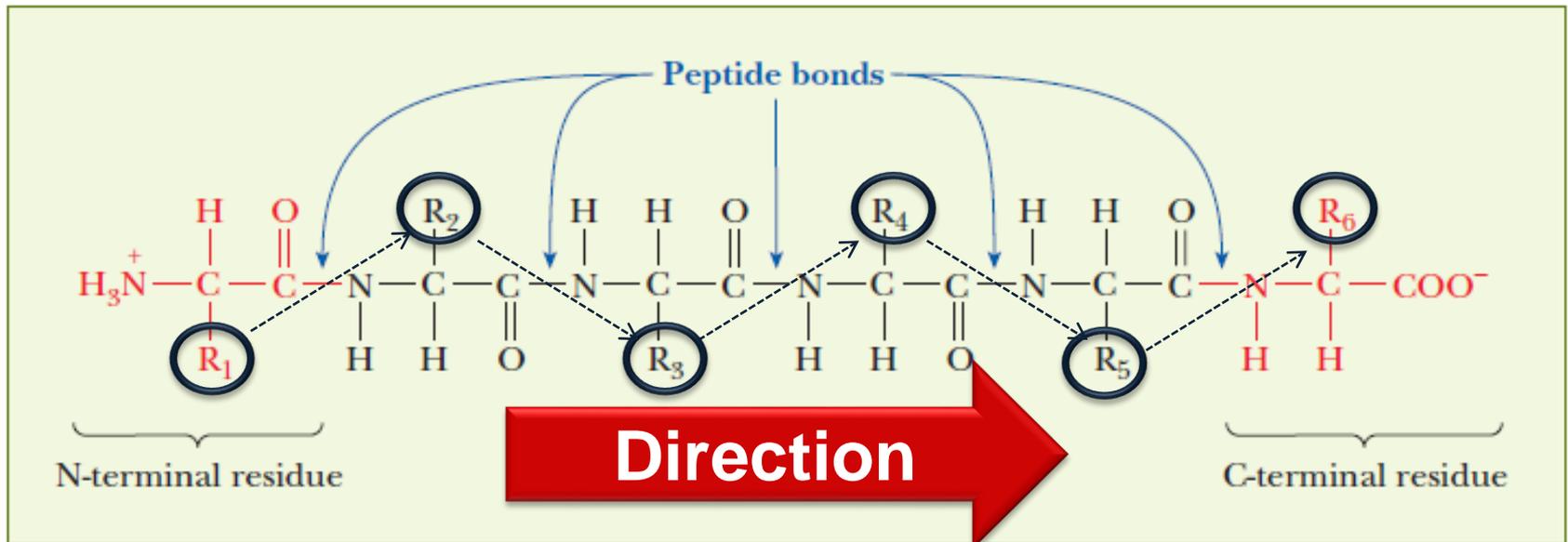
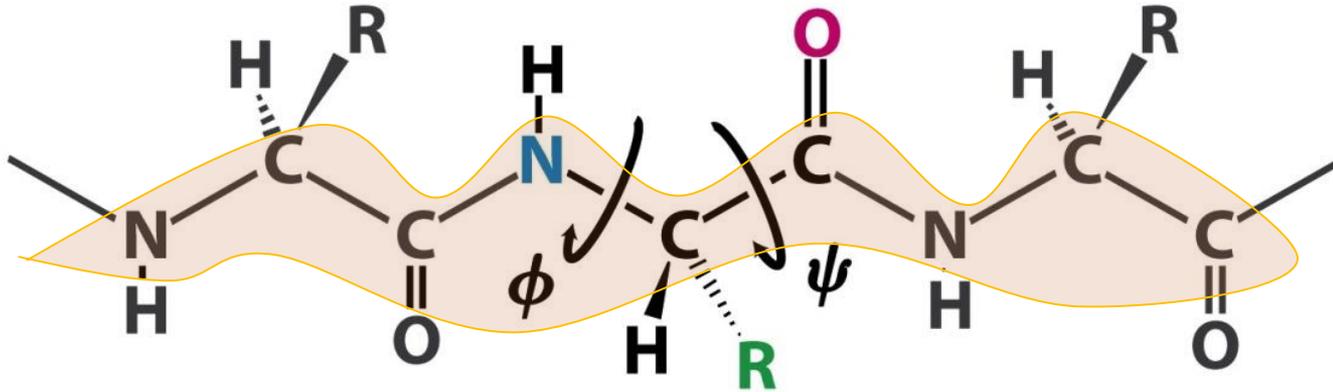
- Zigzag structure
- Double bond
 - Planar, Charged, Rigid, Un-rotatable
- Hydrogen bonding
 - Except proline



Backbone, orientation and directionality



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

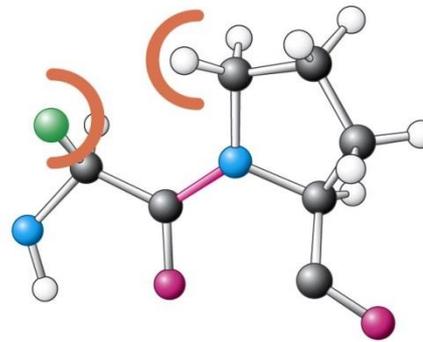
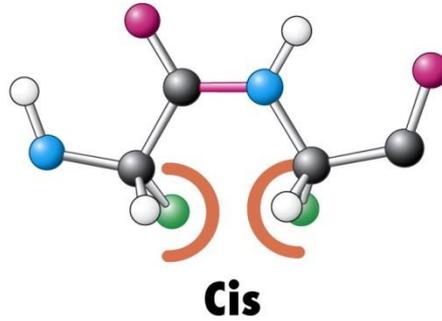
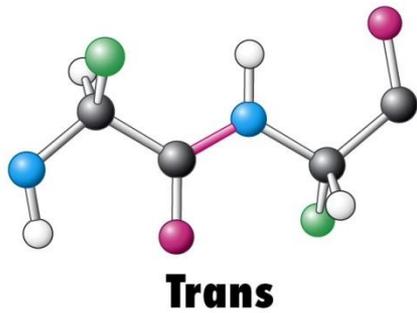


Except for proline

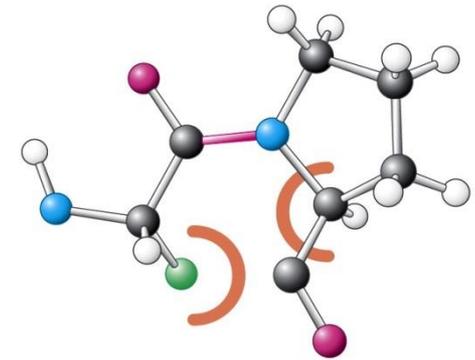


- Steric hindrance between the functional groups attached to the C α atoms will be greater in the *cis* configuration.
- In proline, both *cis* and *trans* conformations have about equivalent energies.
- Proline is thus found in the *cis* configuration more frequently than other amino acid residues.

All other amino acids



Proline



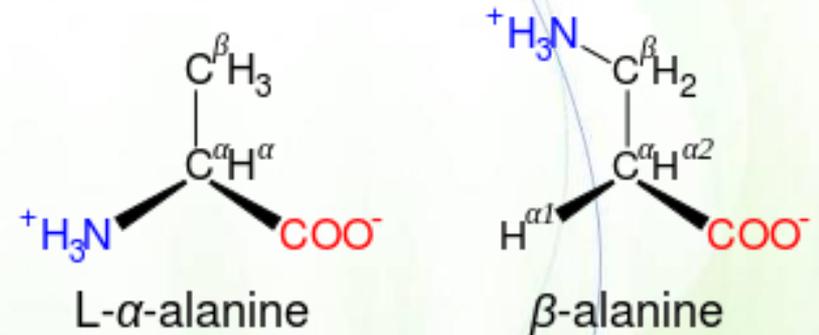
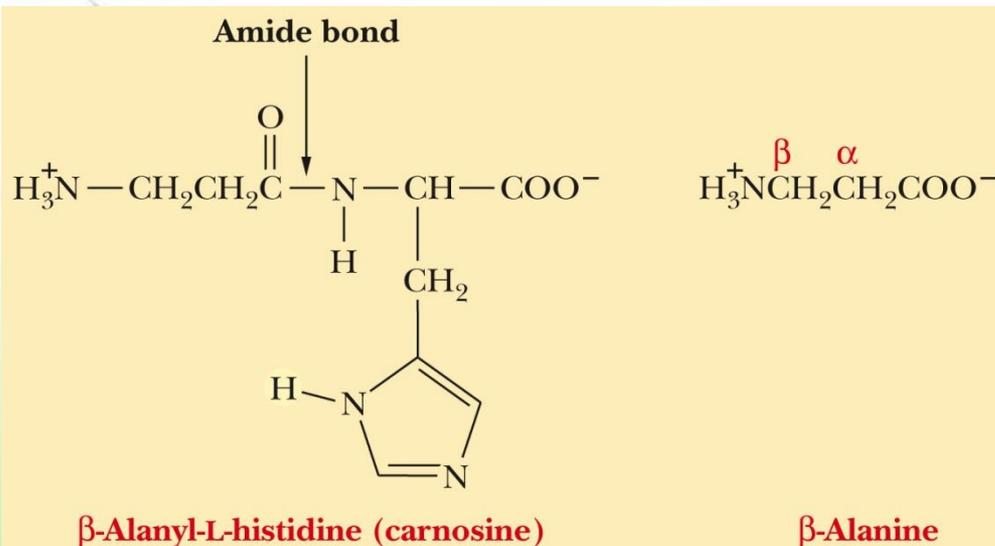


Examples of Functional and Exceptional Peptides

Carnosine (β -alanyl-L-histidine)



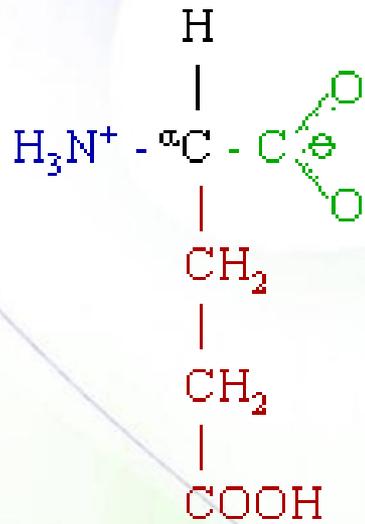
- A dipeptide of β -alanine and histidine
- The amino group is bonded to the β -carbon of alanine
- It is highly concentrated in muscle and brain tissues
 - Protection of cells from ROS (radical oxygen species) and peroxides
 - Contraction of muscle



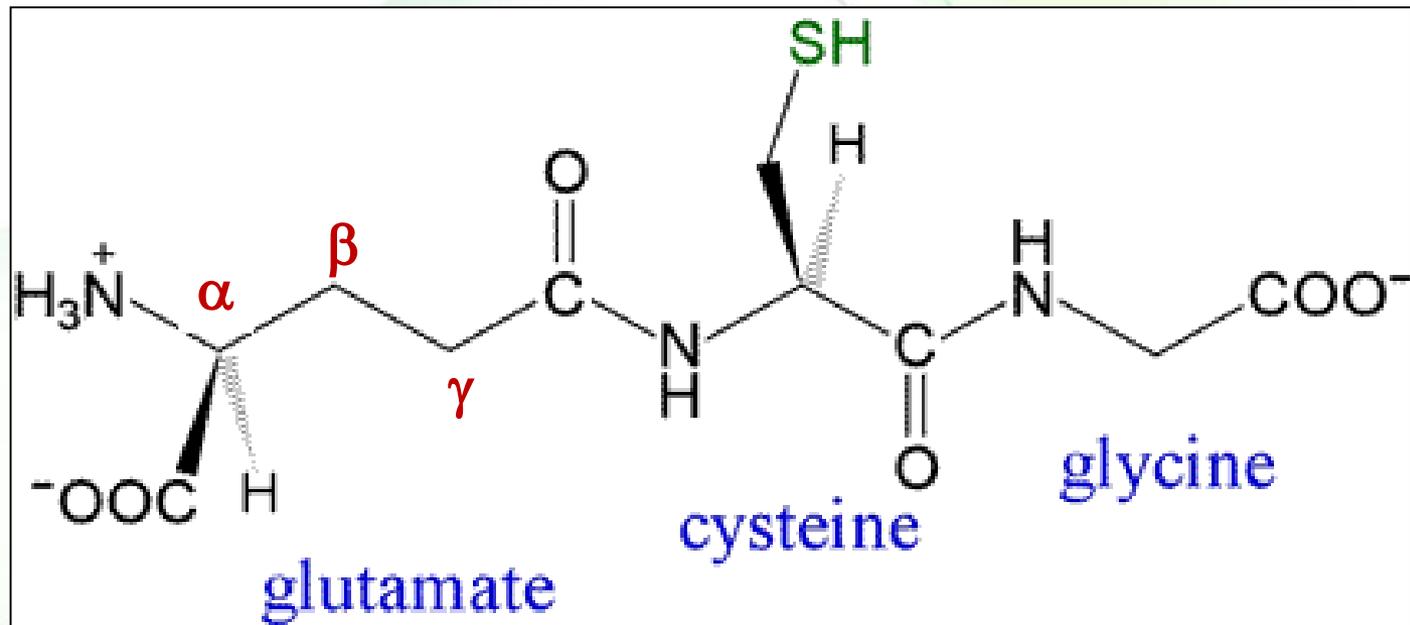
Glutathione



(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

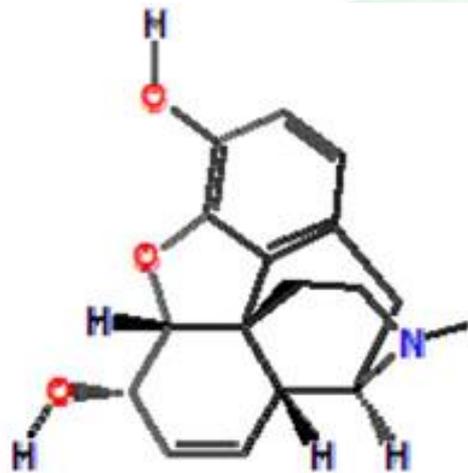


- Two pentapeptides found in the brain known as enkephalins, and function as analgesics (pain relievers).
- They differ only in their C-terminal amino acids
Met-enkephalin: **Tyr-Gly-Gly-Phe-Met**
Leu-enkephalin: **Tyr-Gly-Gly-Phe-Leu**
- The aromatic side chains of tyrosine and phenylalanine play a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

Enkephalins and morphine



- There are similarities between the three-dimensional structures of opiates, such as morphine, and enkephalins.



Morphine

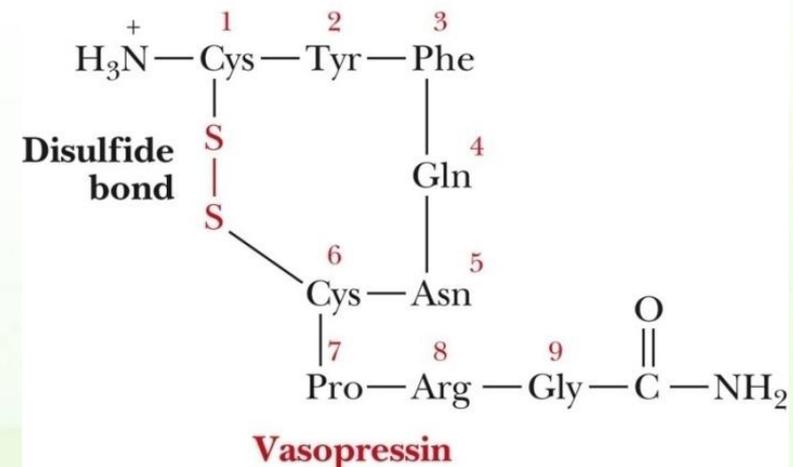
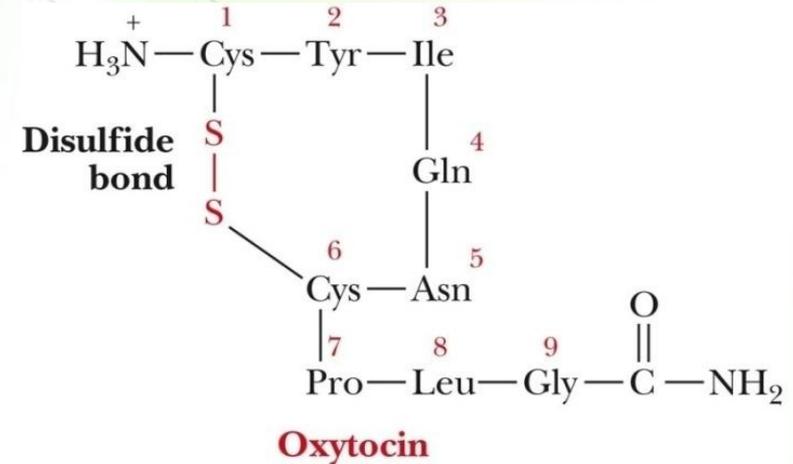


Enkephalins

Oxytocin and vasopressin



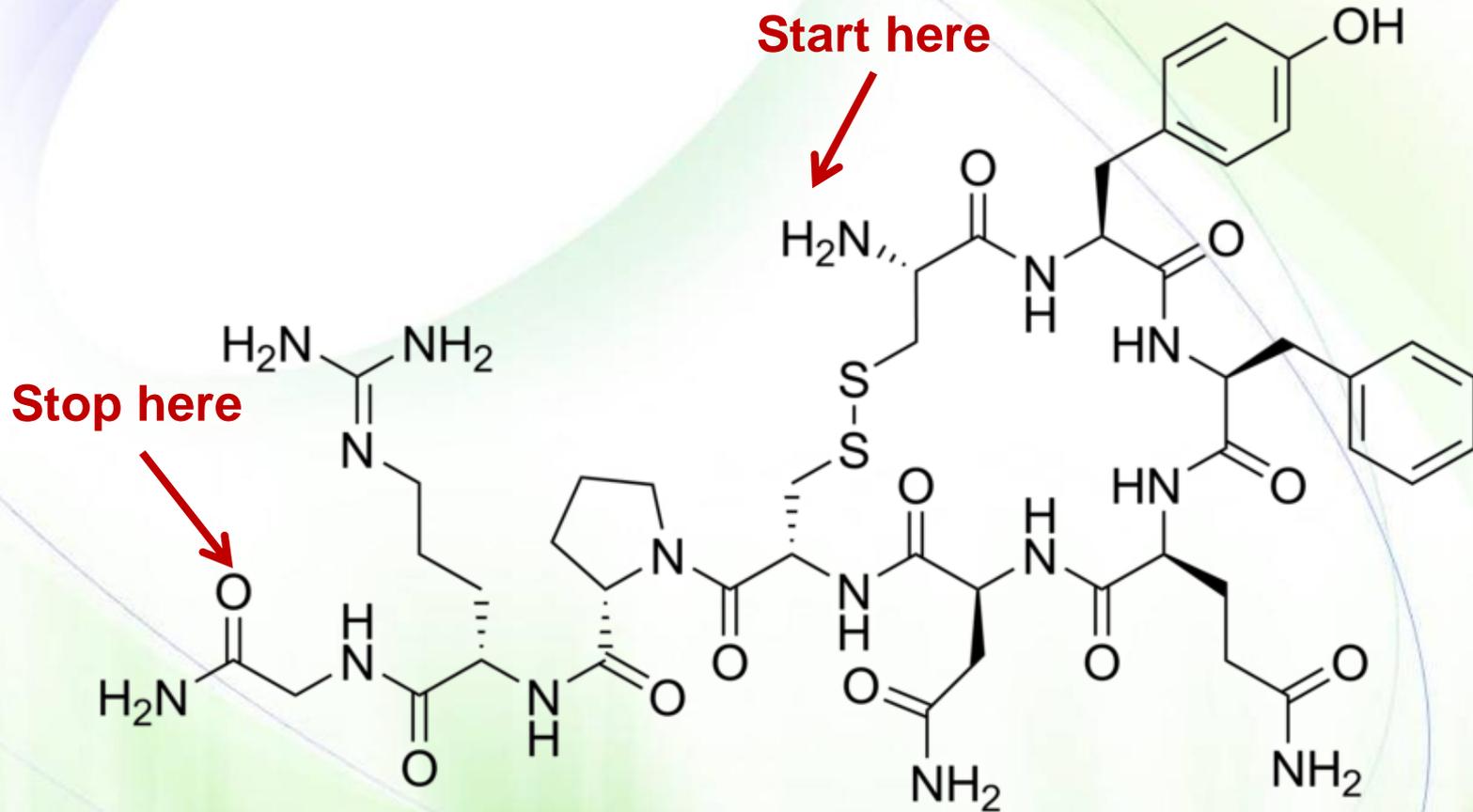
- Hormones with cyclic structures due to S-S link between Cys.
- Both have amide group at the C-terminus.
- Both contain nine residues, but:
 - Oxytocin has isoleucine and leucine.
 - Vasopressin has phenylalanine and arginine.
- Oxytocin regulates contraction of uterine muscle (labor contraction).
-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



Vasopressin



Practice: what is the primary structure?

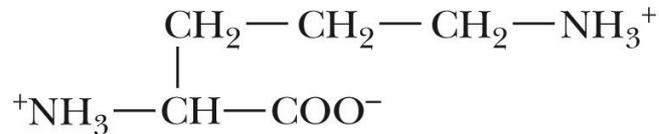


Note: the structure ends with NH₂

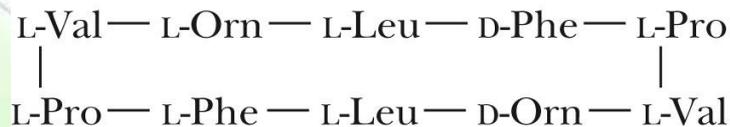
Gramicidin S and tyrocidine A



- They are cyclic decapeptides formed by the peptide bonds.
- They are produced by the bacterium *Bacillus brevis* and act as antibiotics.
- Both contain D- and L-amino acids.
- Both contain the amino acid ornithine (Orn), which does not occur in proteins.

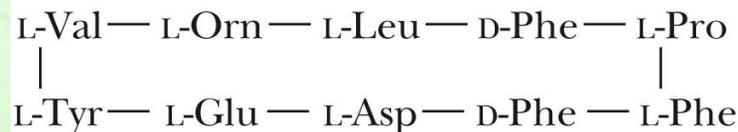


Ornithine (Orn)



Gramicidin S

Direction of peptide bond



Tyrocidine A

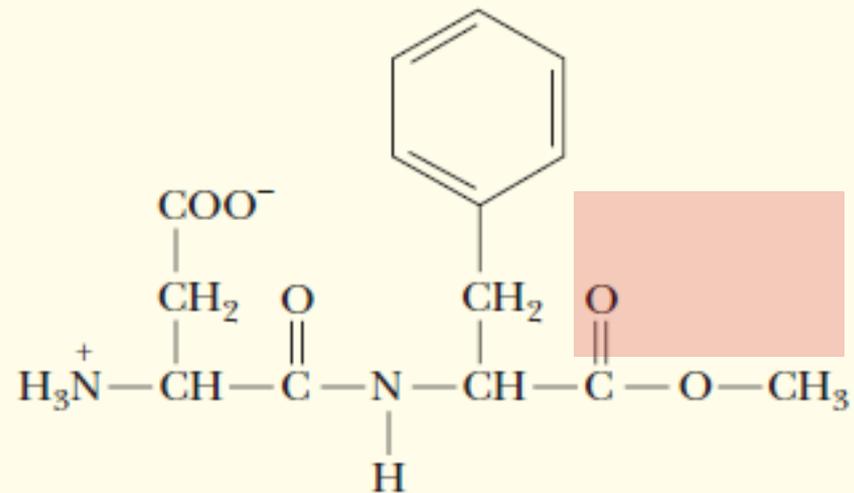
Direction of peptide bond

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.



L-Aspartyl-L-phenylalanine (methyl ester)

Phenylketonuria (PKU)



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

