

Quiz on Friday:

Need to know ALL amino acids and their basic properties
 No multiple choices question: all Q&As

3. Amino Acids (Chapter 4)

Jianhan Chen

Office Hour: M 1:30-2:30PM, Chalmers 034

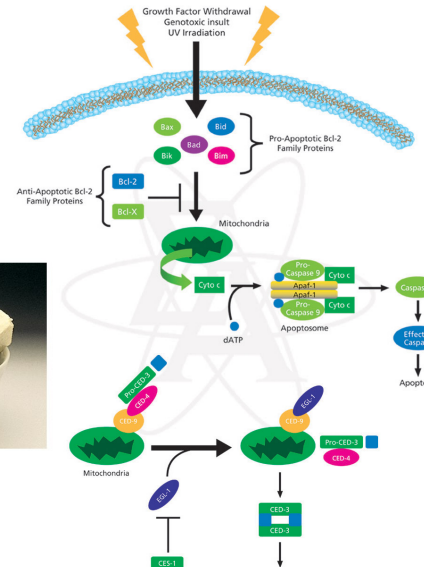
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Proteins and Protein Functions

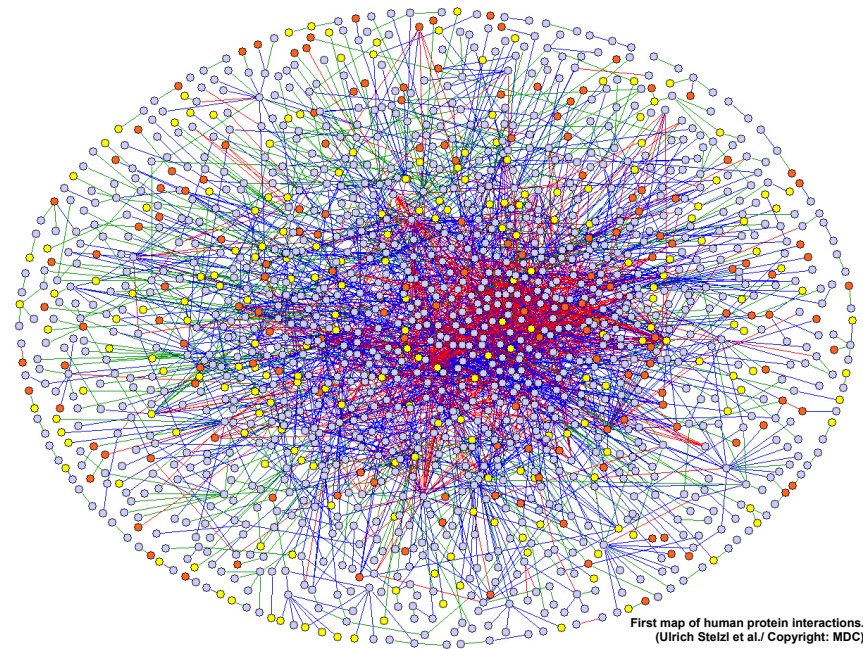


Programmed Cell Death



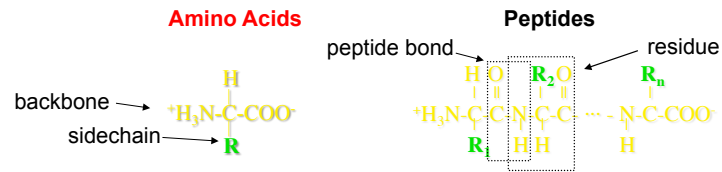
Which of the following is NOT made of protein?

- A. rhino horn
- B. human toe nails
- C. sheep wool
- D. bacterial cell walls
- E. jello

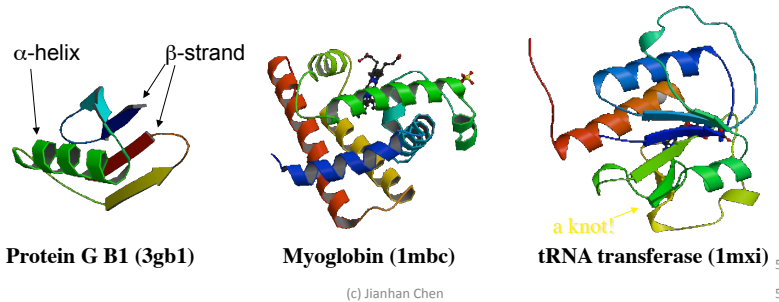


First map of human protein interactions. (Ulrich Steizl et al./ Copyright: MDC)

Hierarchical Organization of Proteins



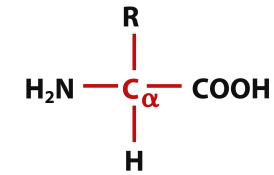
Primary Sequence: MTYKLILNGK TLKGETTTEA VDAATAEKVF
 KQYANDNGVD GEWTYDDATK TFTVTE



4.1 Amino Acid (Chemical) Structure

Key Concepts 4.1

- The 20 standard amino acids share a common structure but differ in their side chains.
- Peptide bonds link amino acid residues in a polypeptide.
- Some amino acid side chains contain ionizable groups whose pK values may vary.

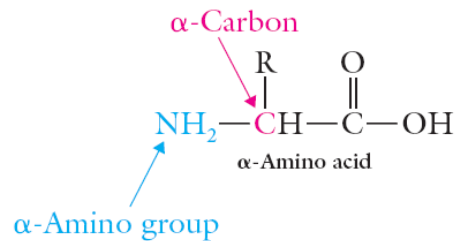


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α -Amino Acids

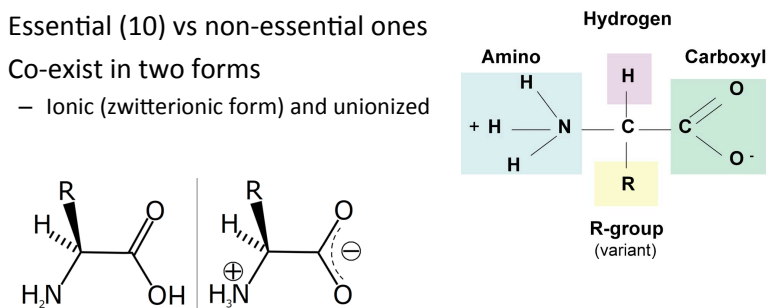
- An **amino acid** is an organic compound that contains both an **amino** ($-\text{NH}_2$) group and a **carboxyl** ($-\text{COOH}$) group bound to the same carbon (α carbon).



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Natural Amino Acids

- Nearly all polypeptides from animals and plants are constructed from the 20 standard α -amino acids
- All α -amino acids in L-configuration (except gly)
- Side chains vary
- Essential (10) vs non-essential ones
- Co-exist in two forms
 - Ionic (zwitterionic form) and unionized

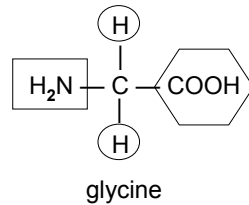
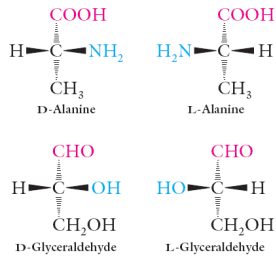


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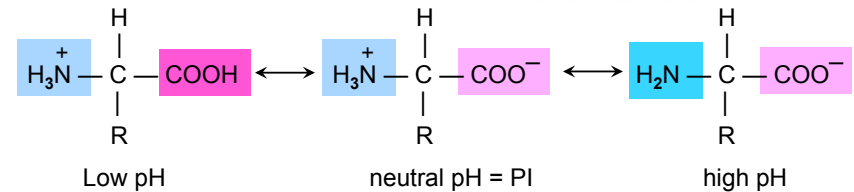
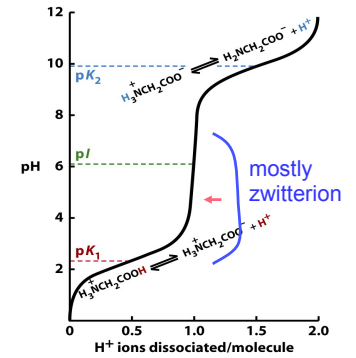
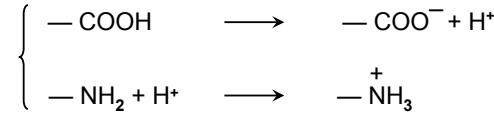
Chirality of α -Amino Acids

- α -carbon is a tetrahedral stereocenter (except glycine)
 - Pair of enantiomers
- Only L- α -amino acids exist in the proteins of animals and plants (with very few exceptions)
 - Amino acids refer to L- α -enantiomers



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Acid-Base Properties: Dipolar/Zwitterion

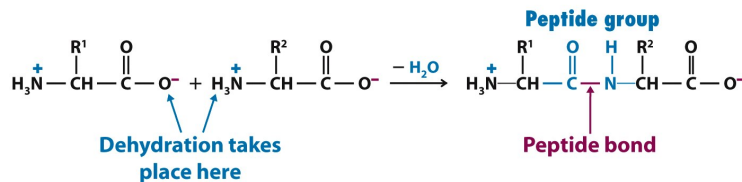


Isoelectric point (pI): *zwitterion*

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Basic Chemical Reactions

- Backbone: common to all amino acids
 - Amines and carboxylic acids undergo dehydration to form amides
 - Peptides are polyamides formed by α -amino acids

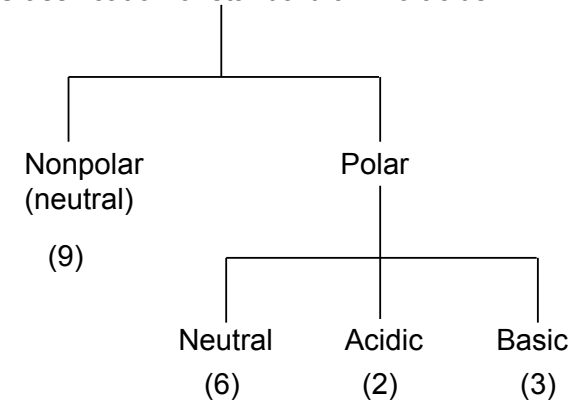


- Side chains: amino acid specific
 - Often occurred as “post-translational” modifications (signaling, natural modification, oxidation/damage etc)
 - Disulfide bond formation: between cysteines, an important structural feature

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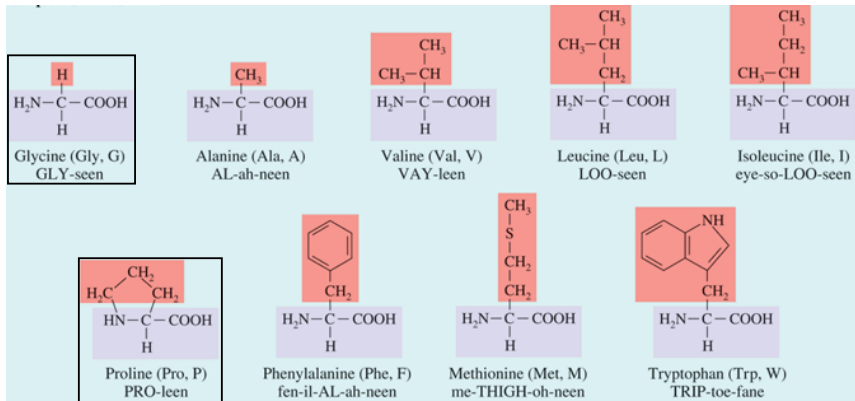
Classification of α -Amino Acids

Classification of standard amino acids



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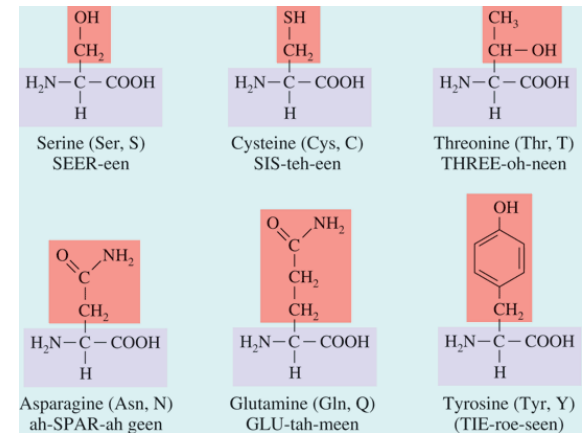
Nonpolar α -Amino Acids



A *nonpolar amino acid* is an amino acid that contains one amino group, one carboxyl group, and a *nonpolar hydrophobic* side chain.

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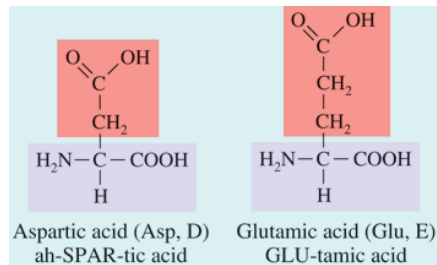
Polar Neutral α -Amino Acids



A *polar neutral amino acid* contains a side chain that is polar but neutral at physiological pH (side chain can form H-bonds).

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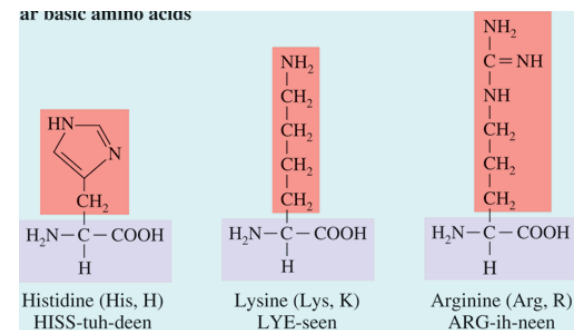
Polar Acidic α -Amino Acids



A *polar acidic amino acid* is an amino acid that contains one amino group and 2 carboxyl groups, the second carboxyl group being part of the side chain.

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Polar Basic α -Amino Acids



A *polar basic amino acid* is an amino acid that contains ≥ 2 amino groups and one carboxyl group, the second amino group being part of the side chain.

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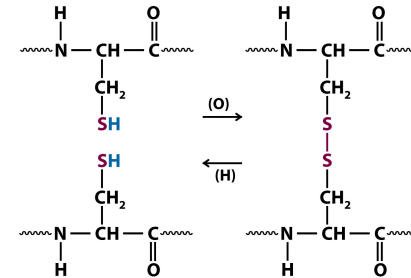
Three-Letter and Single-Letter Codes

Amino Acid	3-Letter	1-Letter	Amino Acid	3-Letter	1-Letter
Alanine	Ala	A	Leucine	Leu	L
Arginine	Arg	R	Lysine	Lys	K
Asparagine	Asn	N	Methionine	Met	M
Aspartate	Asp	D	Phenylalanine	Phe	F
Cysteine	Cys	C	Proline	Pro	P
Histidine	His	H	Serine	Ser	S
Isoleucine	Ile	I	Threonine	Thr	T
Glutamine	Gln	Q	Tryptophan	Trp	W
Glutamate	Glu	E	Tyrosine	Tyr	Y
Glycine	Gly	G	Valine	Val	V

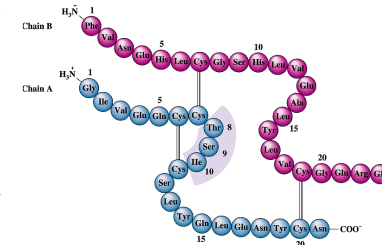
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Disulfide Bonds



The small protein insulin has two polypeptide chains connected by two interchain disulfide bonds. There is also one intrachain disulfide.



- The amino acid cysteine contains a **thiol** group, -SH. Pairs of cysteine residues often link two peptide chains or two parts of one peptide chain through **disulfide bridges**.
- Formation of disulfide is an oxidation reaction and the reverse involves disulfide reduction.

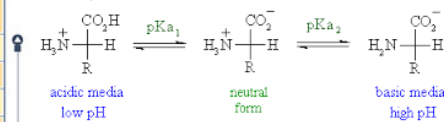
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Isoelectric Point

- The pH at which the net charge is zero.
- For amino acids: $pI = (pK_i + pK_j)/2$
 - K_i and K_j are the dissociation constants of two charged species
- Slight side chain dependence; also dependent on structure

Isoelectric points of alpha-amino acids

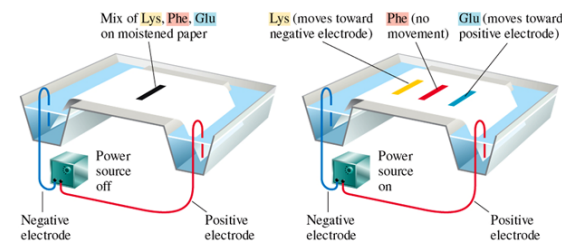
Amino acid	Isoelectric point (pI)	Amino acid	Isoelectric point (pI)
alanine	6.11	leucine	6.04
arginine	10.76	lysine	9.74
asparagine	5.41	methionine	5.74
aspartic acid	2.98	phenylalanine	5.91
cysteine	5.02	proline	6.30
glutamic acid	3.08	serine	5.68
glutamine	5.65	threonine	5.60
glycine	6.06	tryptophan	5.88



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Electrophoresis

- Analyze a mixture of α -amino acids
- Identify substances in an electrical field by separation
 - Cations (1+) move to the negative electrode
 - Anions (1-) move to the positive electrode
 - Neutral α -amino acids does not migrate

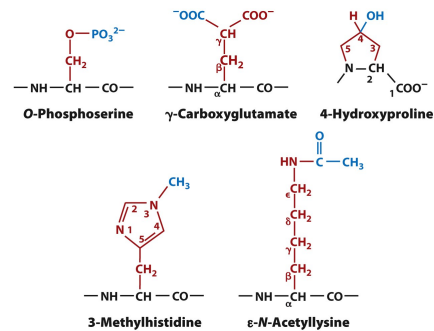


Lys: positively charged
Glu: negatively charged
Phe: neutral

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4.3 Amino Acid Derivatives

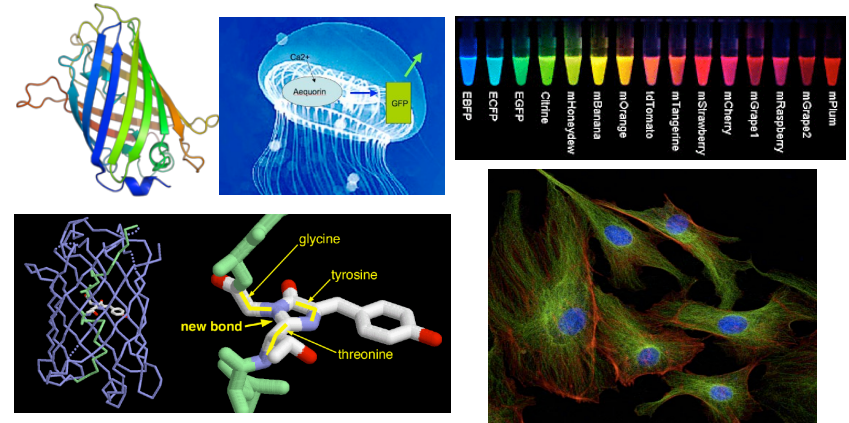
- Post-translational modifications
 - The side chains of amino acid residues in proteins are often modified.
 - Adding small groups: Hydroxylation, methylation, acetylation, carboxylation, phosphorylation
 - Attaching large tails: lipids, carbohydrates etc
- A key signaling and regulatory mechanism



(c) Figure 4-14
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Green Fluorescent Protein

The light emitting group: Ser-Tyr-Gly under go spontaneous cyclization and oxidation and form conjugated double bond system!

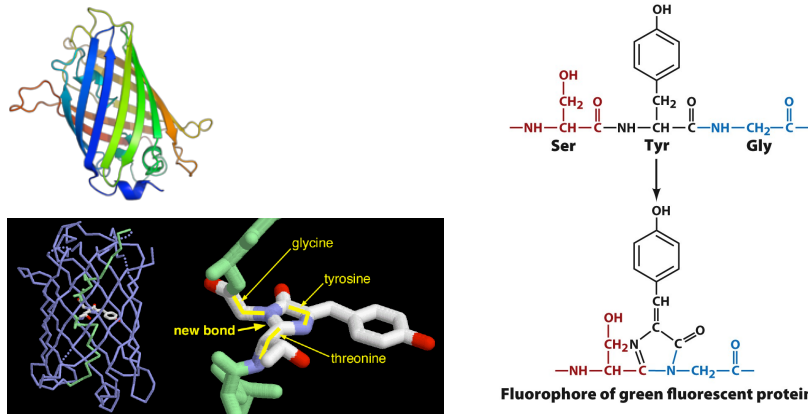


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Green Fluorescent Protein

The light emitting group: Ser-Tyr-Gly under go spontaneous cyclization and oxidation and form conjugated double bond system!



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Box 4-3b
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Biological Active Amino Acid Derivatives

- Complex pathways of amino acid metabolic transformations
- Beyond AA synthesis and energy generation

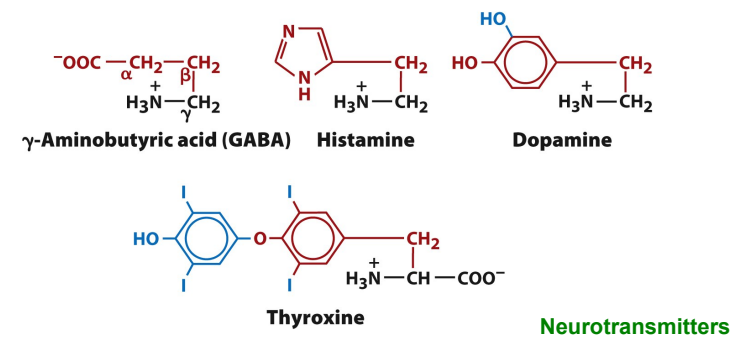


Figure 4-15
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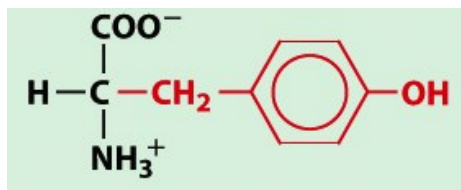
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Neurotransmitters

Which amino acid is this?

- A. Phe
- B. His
- C. Tyr
- D. Trp



Which of the following pairs of amino acids might form a salt bridge?

- A. Thr, Glu
- B. Tyr, Ser
- C. Glu, Asp
- D. Lys, Arg
- E. Lys, Asp

Which of the following amino acid side chains is polar and uncharged?

- A. Glu
- B. Trp
- C. Tyr
- D. Phe
- E. Ile

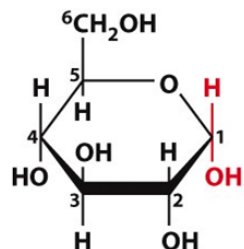
How many charged functional groups are present on the peptide below at physiological pH ?

- A. 1
- B. 2
- C. 3
- D. 4
- E. 5

Arg-Asp-Cys-Tyr-Gln-Val-Glu

Which of the following groups of amino acid side chains is MOST LIKELY to be positioned into the active site of an enzyme that binds glucose as a substrate?

- A. Gln, Asn, Ser
- B. Val, Leu, Ile
- C. Trp, Phe, Ile
- D. Val, Glu, Lys
- E. Cys, Met, Pro



Glucose

Which of the following amino acids has a side chain that can form covalent cross-links in proteins?

- A. Ser
- B. Met
- C. Trp
- D. Cys
- E. Thr

Which of the following statements regarding amino acids is/are false?

- A. Thr and Cys may be phosphorylated.
- B. The side chain of the amino acid histidine usually acts as a base at pH 7.0.
- C. Arg contains four nitrogens.
- D. A and B
- E. All of the above statements are false.

Which of the following statements regarding amino acids is/are false?

- A. Ala, Val, Leu and Ile play an important role in establishing and maintaining the 3-D structures of proteins.
- B. Every amino acid has at least two pKa values.
- C. When the pH of a solution is below the pKa value of an ionizable group, the unprotonated form of that group predominates.
- D. Statements A and B are false.
- E. All of the above statements are false.

Which of the following does NOT contain a carboxamide functional group?

- A. The amino acid Asn.
- B. The amino acid Asp.
- C. The dipeptide Gln-His.
- D. All of these contain a carboxamide group.
- E. None of these contain a carboxamide group.

How many chiral carbons does Thr contain?

- A. 0
- B. 1
- C. 2
- D. 3

Which of the following net charge best represents aspartate at pH 12?

- A. -2
- B. -1
- C. 0
- D. +1
- E. +2

There are several amino acid side chains that are always charged at physiological pH. These are:

- A. Gln, Asn, Lys, and Arg.
- B. Glu, Asp, Lys, and Arg.
- C. Lys, His, and Arg.
- D. Glu, Asp, Lys, Arg, and His.

Which L amino acid has the *R*- configuration for C_{α} ?

- A. C
- B. A
- C. R
- D. T
- E. S

Which of the following amino acids could form a hydrogen-bonding interaction between their sidechains?

- A. Q and A
- B. Q and V
- C. Q and F
- D. Q and I
- E. Q and W

How many charged R groups are present on the peptide below at physiological pH ?

- A. 1
- B. 2
- C. 3
- D. 4
- E. 5

Asn-Asp-Cys-Tyr-Lys-Val-Glu

What is the net charge of the peptide below at physiological pH?

- A. -2
- B. -1
- C. 0
- D. +1
- E. +2

Ala-Arg-Asn-Asp-Glu-Ser-Gly