بسم الله الرحمن الرحيم

BIOCHEMISTRY

Lecture 11

Amino Acids

استحضر – رعاك الله – عظمة الطريق وأخلص النية:

﴿وَمَنْ أَحْيَاهَا فَكَأَنَّمَآ أَحْيَا ٱلنَّاسَ جَمِيعًا﴾

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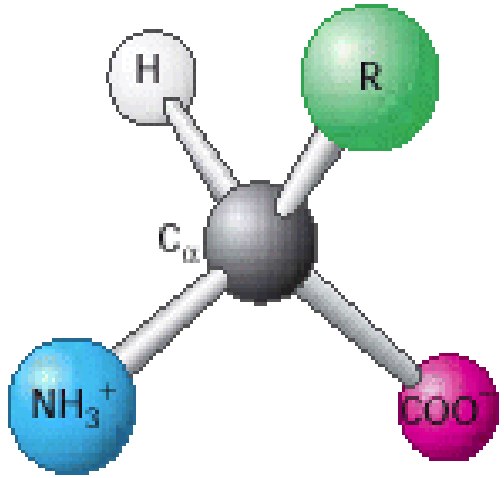
General structure

- Proteins are polymers of α-amino acids (or amino acids).
- An amino acid consists of:
  - a central carbon atom, called the α carbon, linked to four groups
  - an amino group (-NH2),
  - a carboxylic acid group (-COOH)
  - a hydrogen atom
  - a specific R group (side chain)



They are the Monomers that builds up a protein.

Amino acids differ in the R group, which gives the amino acid its characteristics.

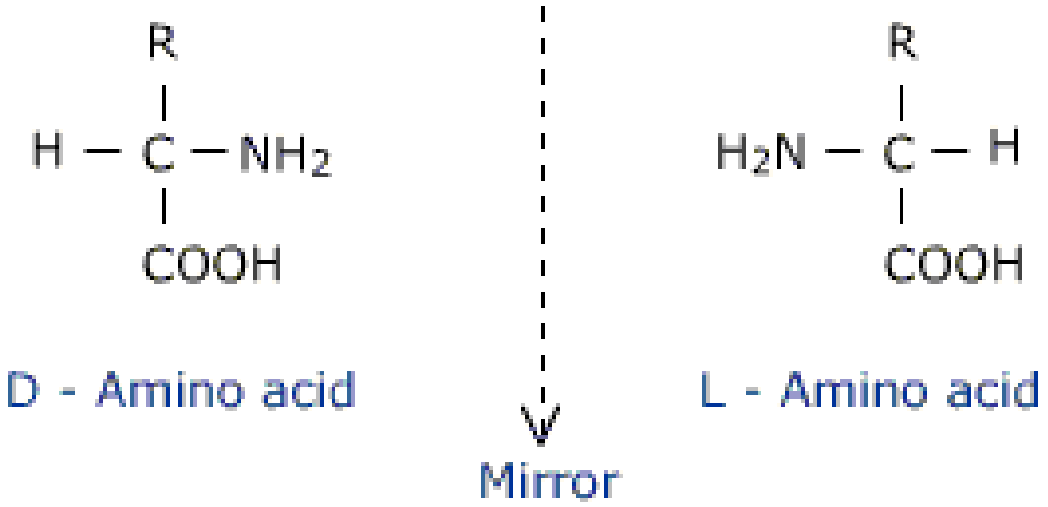
At physiological pH, the amino group and the carboxyl group are ionized with the amino group having a positive charge and the carboxylic group having a negative charge, so the overall amino acid is neutral (supposing that the R group is not charged) – for more about the overall charge, see Lecture 12.

L and D isomers

In our body, all amino acids are in the L configuration.

- The α-carbon atom is chiral and, thus, amino acids are chiral and can be present in two forms, L and D isomers, that are mirror-images of each other (they are enantiomers).
- Only L amino acids naturally make up proteins.

Note that the amino and carboxylic groups of all amino acids are ionized at neutral pH



To determine if the amino acid is in the D or L configuration, we draw a fisher projection of the amino acid with the carboxylic group on the bottom and the R group on the top then we look at the position of the amino group, if it is on the left the amino acid is in the L form and vice versa.

Types of amino acids

How many amino acids we have in our body?

We have many amino acids but only twenty of them are involved in protein synthesizing.

Citrulline is an amino acid which does not form proteins

- There are twenty kinds of amino acids *depending on the side chains* varying in
  - Size (Small and large)
  - Shape (aliphatic or aromatic), (branched and non-branched)
  - Charge (+ or - or neutral)
  - Hydrogen-bonding capacity (polar or non-polar)
  - Hydrophobic character (hydrophobic or hydrophilic)
  - Chemical reactivity (reactive or non-reactive)

The R group is considered reactive if it has electronegative atoms such as oxygen, nitrogen, phosphorus and sulfur.

Classification (according to R group)

The figures used in the next slides emphasize on the R group, don't forget that the carboxylic and amino groups are ionized at physiological PH. You also should know the **name** and the **abbreviation** of every amino acid and be able to recognize their **structure and R group.**

Non-polar	Polar	Charged (positive)	Charged (negative)
Alanine	Serine	Lysine	Glutamate
Valine	Threonine	Arginine	Aspartate
Leucine	Glutamine	Histidine	
Isoleucine	Asparagine		
Methionine	Cysteine		
Tryptophan	Tyrosine		
Phenylalanine			
Proline			
Glycine			

The classification takes into consideration the characteristics of the R group and not the whole molecule.

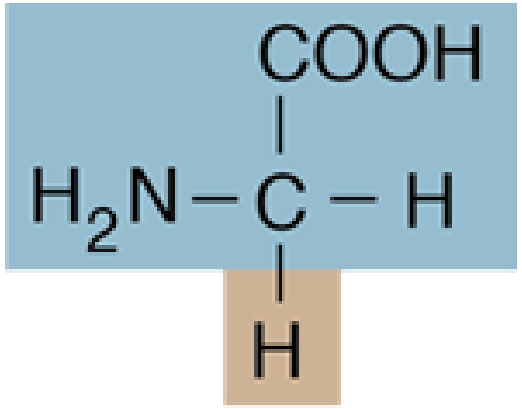
For example:
Glycine (a small amino acid which has a carboxylic end and an amino end) is overall polar, but because the hydrogen atom as an R group is considered non-polar, glycine is placed conventionally under the non-polar category.

Glycine (Gly)

The simplest and smallest amino acid; since R is substituted by a hydrogen atom.

The α-carbon of glycine is connected to two hydrogens (the general H present in all amino acids + the special H which is the R group of glycine).

So, it is achiral and therefore glycine doesn't have an enantiomer.
It is essentially the only achiral amino acid.



Glycine (gly)

- Glycine is a derivative of acetic acid.

Note that the amino and carboxylic groups are normally ionized at physiological pH

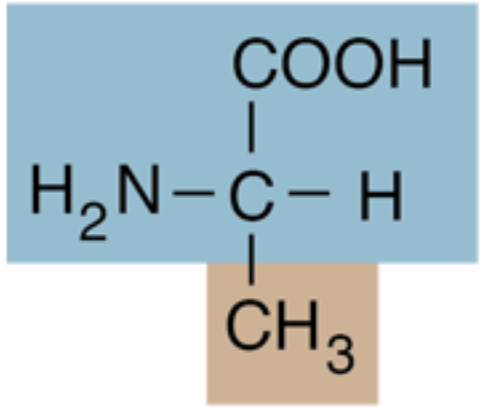
Is it chiral?

Non-polar, Aliphatic Amino Acids

(R group is a hydrocarbon chain)

Alanine (Ala)

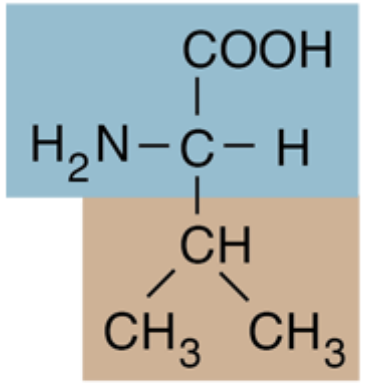
- Alanine, the next simplest amino acid, has a methyl group ($-CH_3$) as its side chain.



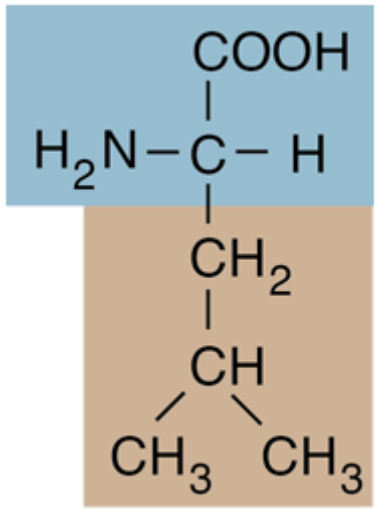
Alanine (ala)

Valine (Val), leucine (Leu), and isoleucine (Ile)

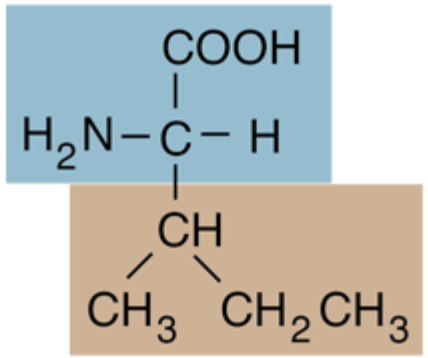
Leu and Ile have the same molecular formula.
They are constitutional isomers.



Valine (val)*



Leucine (leu)*



Isoleucine (ile)*

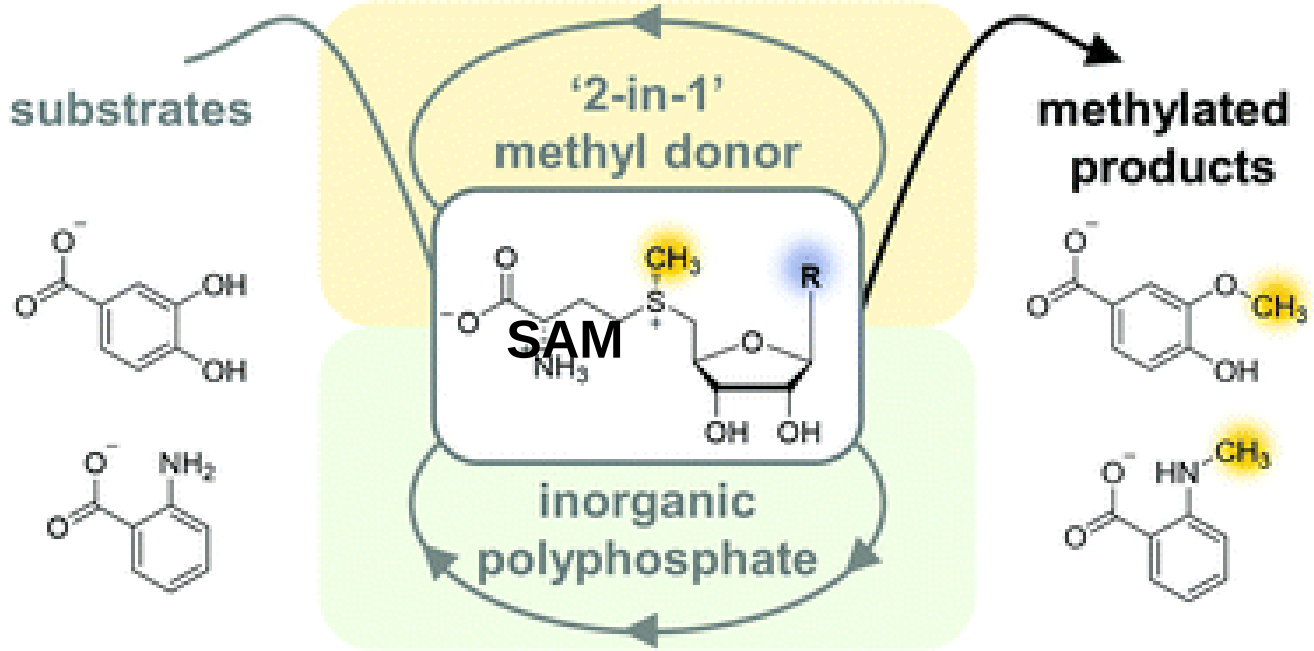
They are branched amino acids.
These are *essential amino acids since the body* cannot synthesize them.

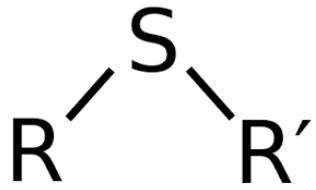
Our body can't synthesize essential amino acids, we can only get them from our diet.

Methionine (Met)

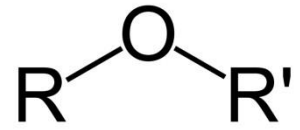
Methionine is one of the two amino acids that have sulfur In their R group.
The R group in Methionine is a thioether (-S-), (thio = sulfur) group and it isn't considered reactive since the sulfur atom is **internal**.

It can form **S-Adenosyl-L-Methionine (SAM)** which serves as a **methyl donor** in

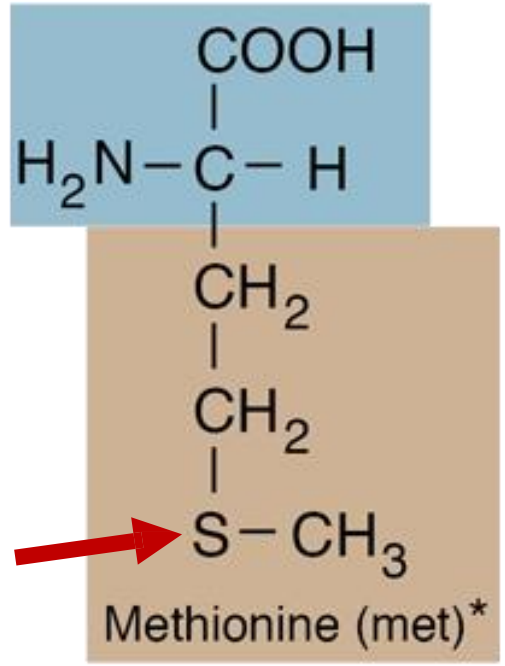




Thioether



Ether



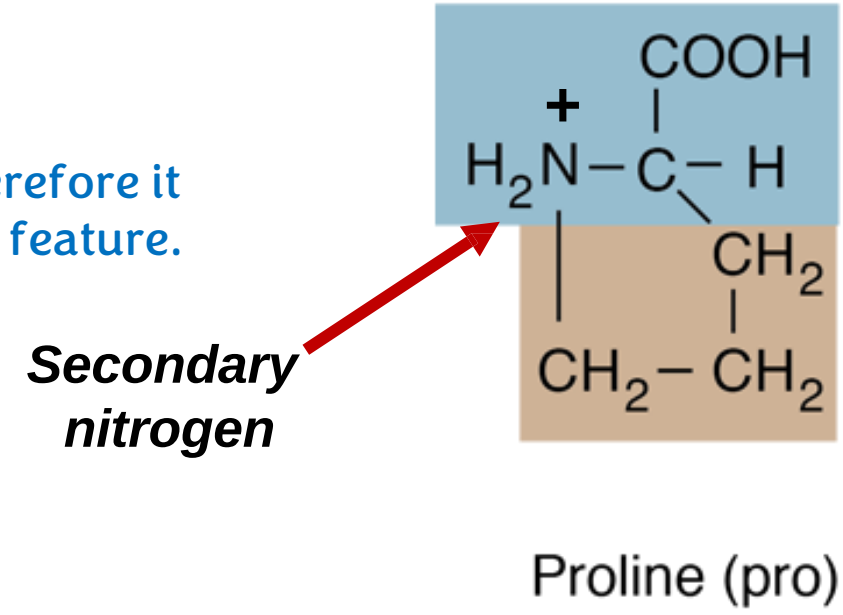
Proline (Pro)

(the only cyclic amino acid)

The amino acid itself is cyclic, not the R group.

It is a **rigid** molecule since it is packed and small.

The nitrogen in the amino group is connected to two carbons therefore it is a secondary amine, proline is the only amino acid that has this feature.

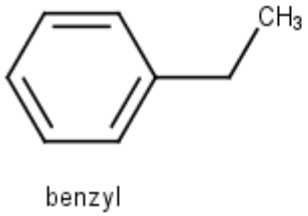


Proline (pro)

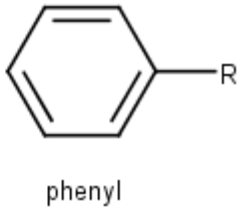
Non-polar, Aromatic Amino Acids

Phenylalanine (Phe) and Tryptophan (Trp)

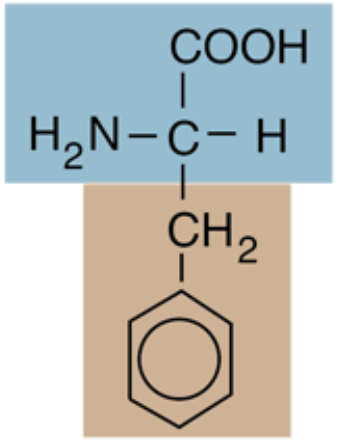
- Phenylalanine contains a phenyl ring. → Large and hydrophobic
- Tryptophan has an indole ring; the indole group consists of two fused rings and an NH group. (the largest amino acid since its R has two fused rings)



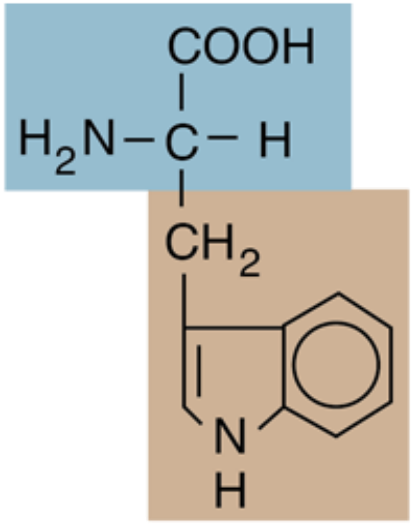
benzyl



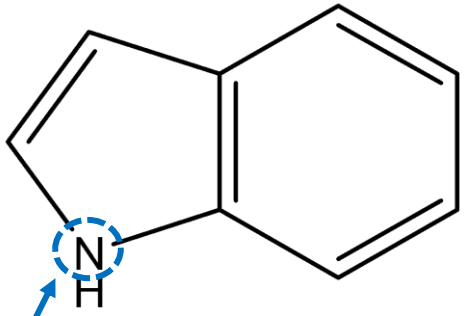
phenyl



Phenylalanine (phe)*



Tryptophan (trp)*



Indole

Even though we have a nitrogen atom in the indole ring, tryptophan is non-polar (hydrophobic).

Positively-Charged Amino Acids

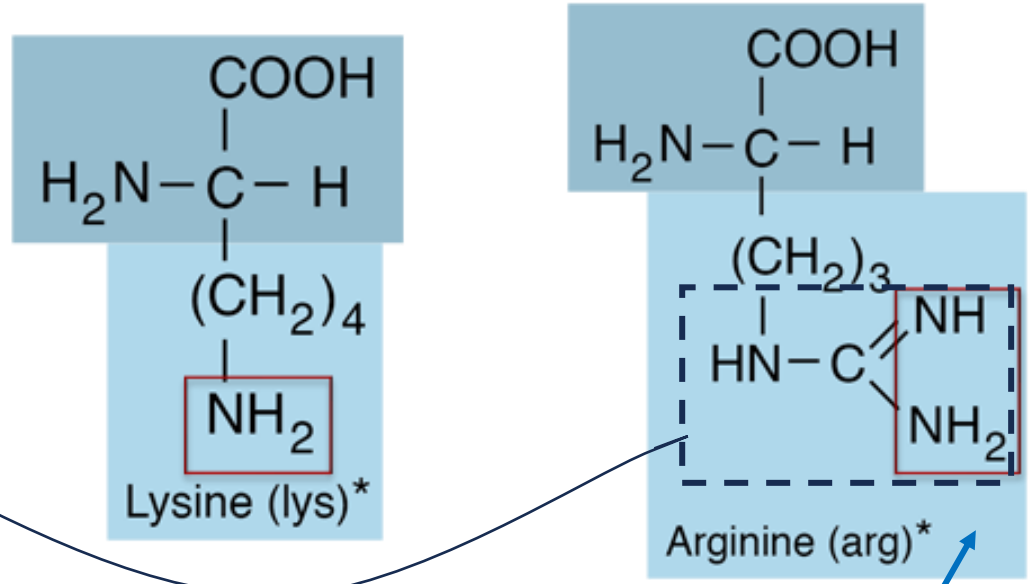
Lysine (Lys) and arginine (Arg)

They are aliphatic because their R groups are chains.

Their R groups terminate with amine groups that carry a positive charge under physiological PH.

- Lysine and arginine have relatively long side chains that terminate with groups that are positively charged at a neutral pH.

- Lysine ends with a primary amino group and arginine by a guanidinium group.



In lysine, the R group ends with a primary amino group that has a positive charge when protonated under physiological PH.

In arginine, the R group ends with a guanidinum group (3 nitrogen atoms attached to one carbon with the presence of a double bond).

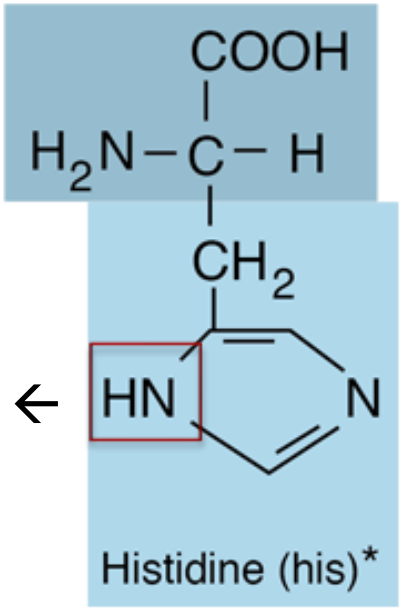
The double bond is delocalized by resonance as well as the positive charge.

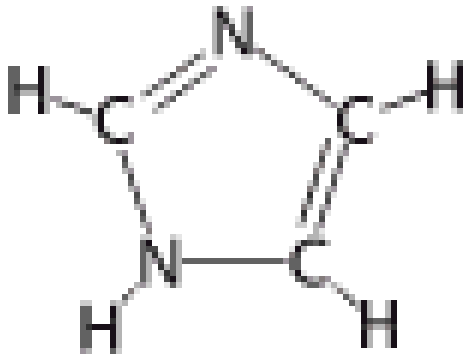
Histidine (His)

It is aromatic since R has a ring structure.

- Histidine contains an **imidazole** group, an aromatic ring that also can be positively charged.

Usually carries a (+) charge ←





Imidazole

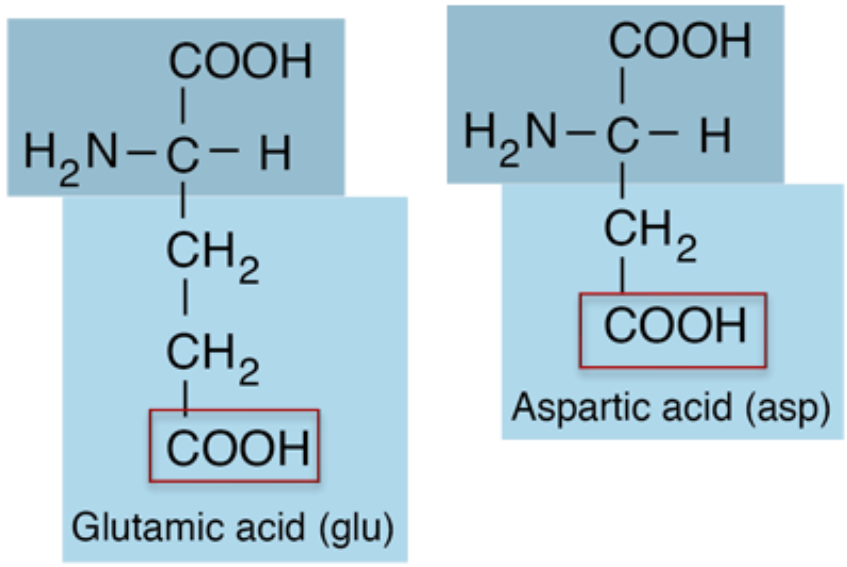
Negatively-Charged Amino Acids

Aspartic acid (Asp) and glutamic acid (Glu)

- Two amino acids contain acidic side chains: aspartic acid and glutamic acid.
- These amino acids are often called **aspartate** and **glutamate** when they are charged.

They are negatively charged because their R groups contain a carboxylic group which is ionized (unprotonated) under physiological PH.

When you see (glut) you should know that the molecule is **five** carbon molecule. (notice glutamic acid)



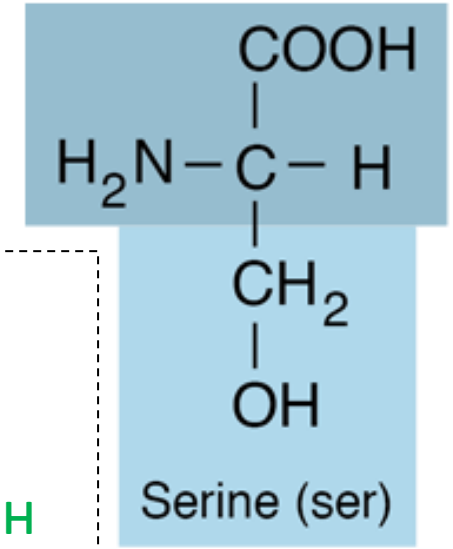
Same as Asp but with an extra CH_2

Polar, Hydrophilic, Neutral Amino Acids

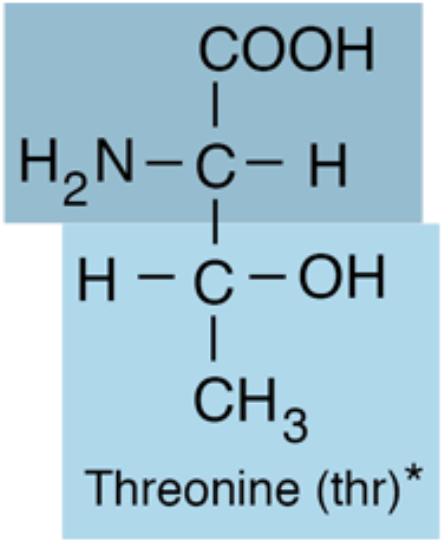
They are **not** charged, but their R groups are considered polar

Serine (Ser) and threonine (Thr)

- Serine and threonine, contain aliphatic hydroxyl groups (polar and reactive).
- The hydroxyl groups on serine and threonine make them hydrophilic and reactive.



Serine (ser)



Threonine (thr)*

Serine =

Alanine + OH

or

Phenylalanine – phenyl + OH

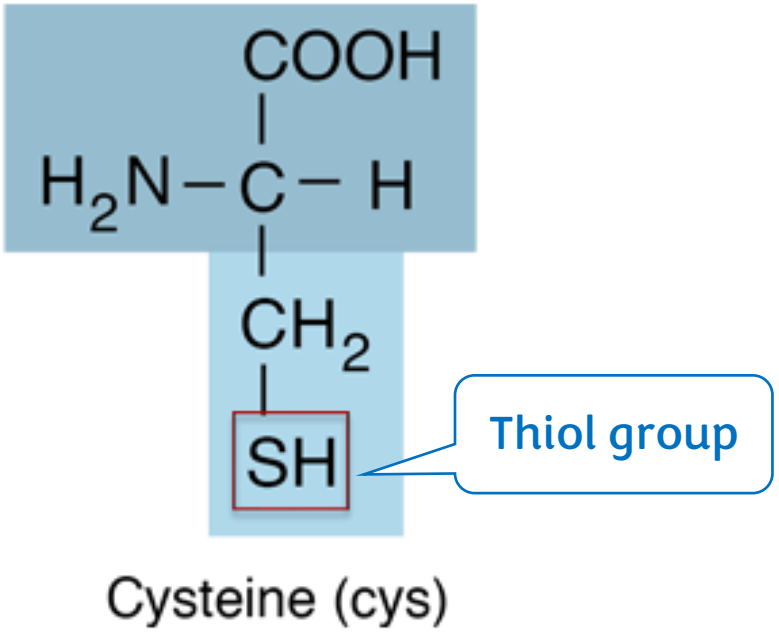
Threonine =

Serine + CH3 on the last carbon

Cysteine (Cys)

- Cysteine contains a sulfhydryl or thiol (-SH), group.
- The sulfhydryl group is reactive.

Amino Acid	Has Sulfur group?	Group name	Location	Reactive and Hydrophilic?
Met	Yes	Thioether (-S-)	Internal	No
Cys	Yes	Thiol (-SH)	Terminal	Yes

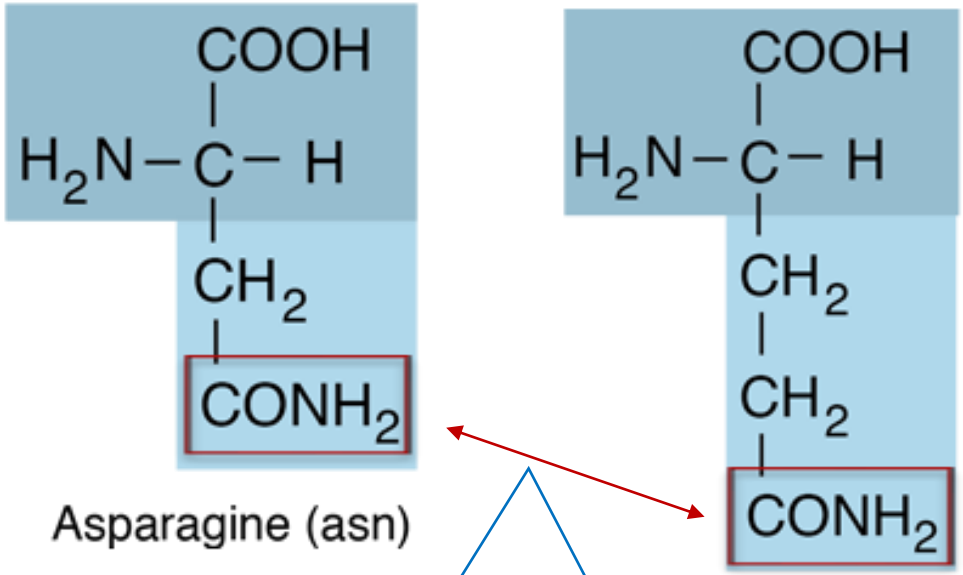


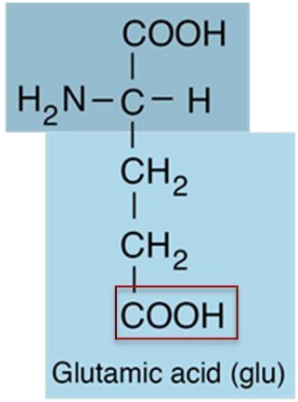
Cysteine (cys)

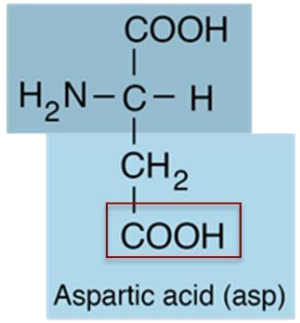
Asparagine (Asn) and glutamine (Gln)

They are polar amino acids, but they carry no charge – they are neutral; **unlike** Asp and Glu.

- Asparagine and glutamine are **uncharged derivatives** of aspartate and glutamate, respectively.
- Each contains a terminal carboxamide in place of a carboxylic acid.







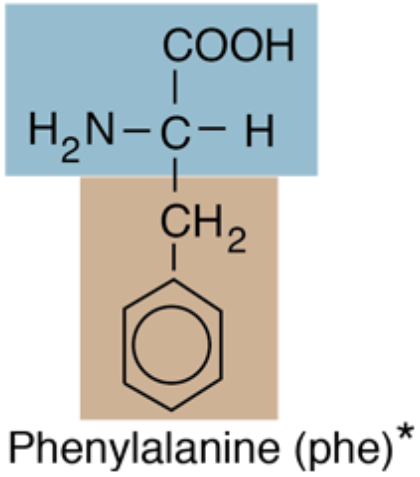
Carboxamide (CONH2) in Asn & Gln instead of (COOH) in their (–)ly charged counterparts Asp and Glu

Tyrosine (Tyr)

Think about the tires (wheels), so tyrosine has an aromatic ring.
Similar to phenylalanine but with an extra OH.

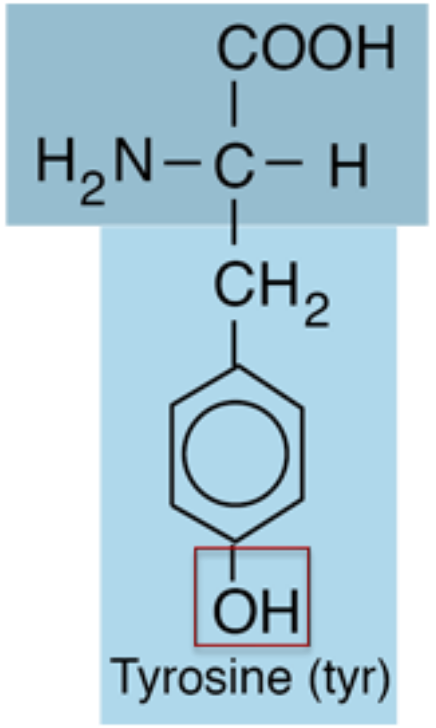
So, tyrosine (tires) → aromatic ring + OH.

- The aromatic ring of tyrosine contains a hydroxyl group.
  - It is derived from phenylalanine.
- This hydroxyl group is reactive.



Phenylalanine (phe)*

Not reactive, non-polar.



Reactive, Polar (it has OH).

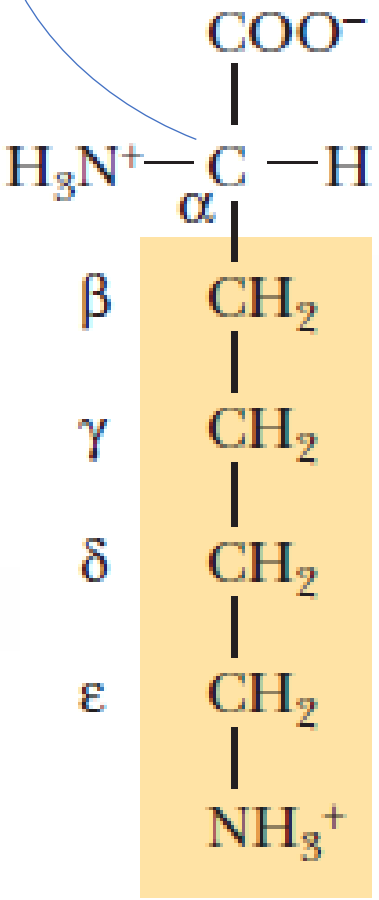
Designation of carbons

An alpha carbon is the carbon atom directly attached to a carboxylic group

- Side-chain carbon atoms are designated with letters of the Greek alphabet, counting from the α-carbon. These carbon atoms are, in turn, the β-, γ-, δ-, and ε- carbons.

  Beta, Gamma, Delta, and Epsilon

- If a carbon atom is terminal, it is referred to as the ω-carbon (as seen in fatty acids).



Questions

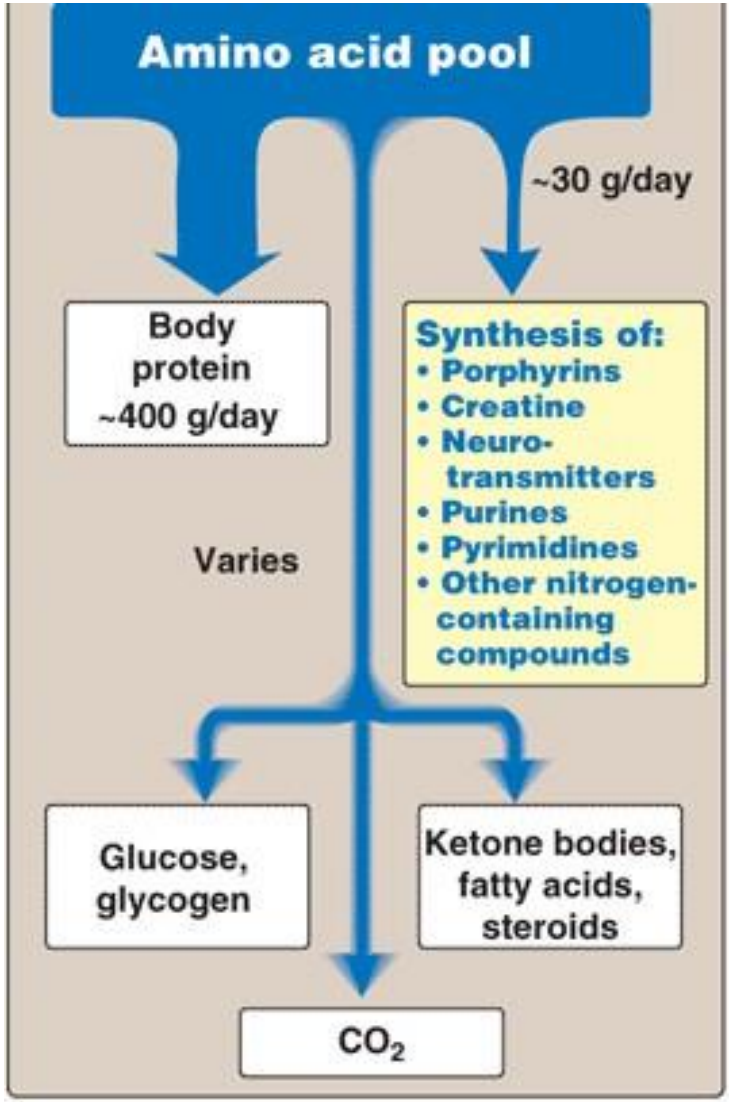
- Two amino acids are negatively-charged: **Glutamate and Aspartate**
- The following amino acid is achiral: **Glycine**
- …etc.

Specialized and Uncommon Amino Acids

Other functions besides being the building blocks of proteins:

Biological significance of amino acids

- α-nitrogen atom of amino acids is a primary source for many nitrogenous compounds:
  - Hormones
  - Neurotransmitters
  - Biologically active peptides



An amino acid itself, such as glycine or aspartate, can act as a neurotransmitter.

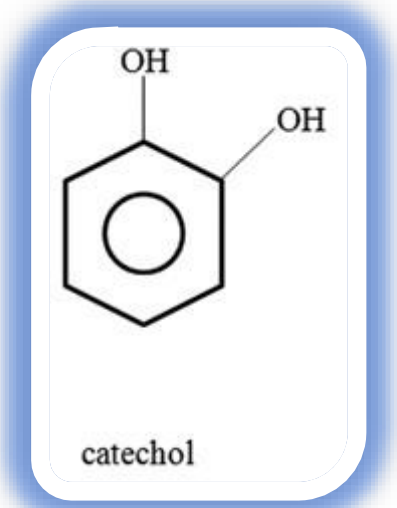
Amino acids can be used to make other biological molecules (see next slides).

Amino acids' carbon atoms can be used to synthesize glucose, CO_2, fatty acids, etc....

Tyrosine (1)

- It is converted into catecholamine neurotransmitters (3 amines below).
  - Dopamine
  - Norepinephrine (or Noradrenaline)
  - Epinephrine (or Adrenaline)
    - Fight or Flight response

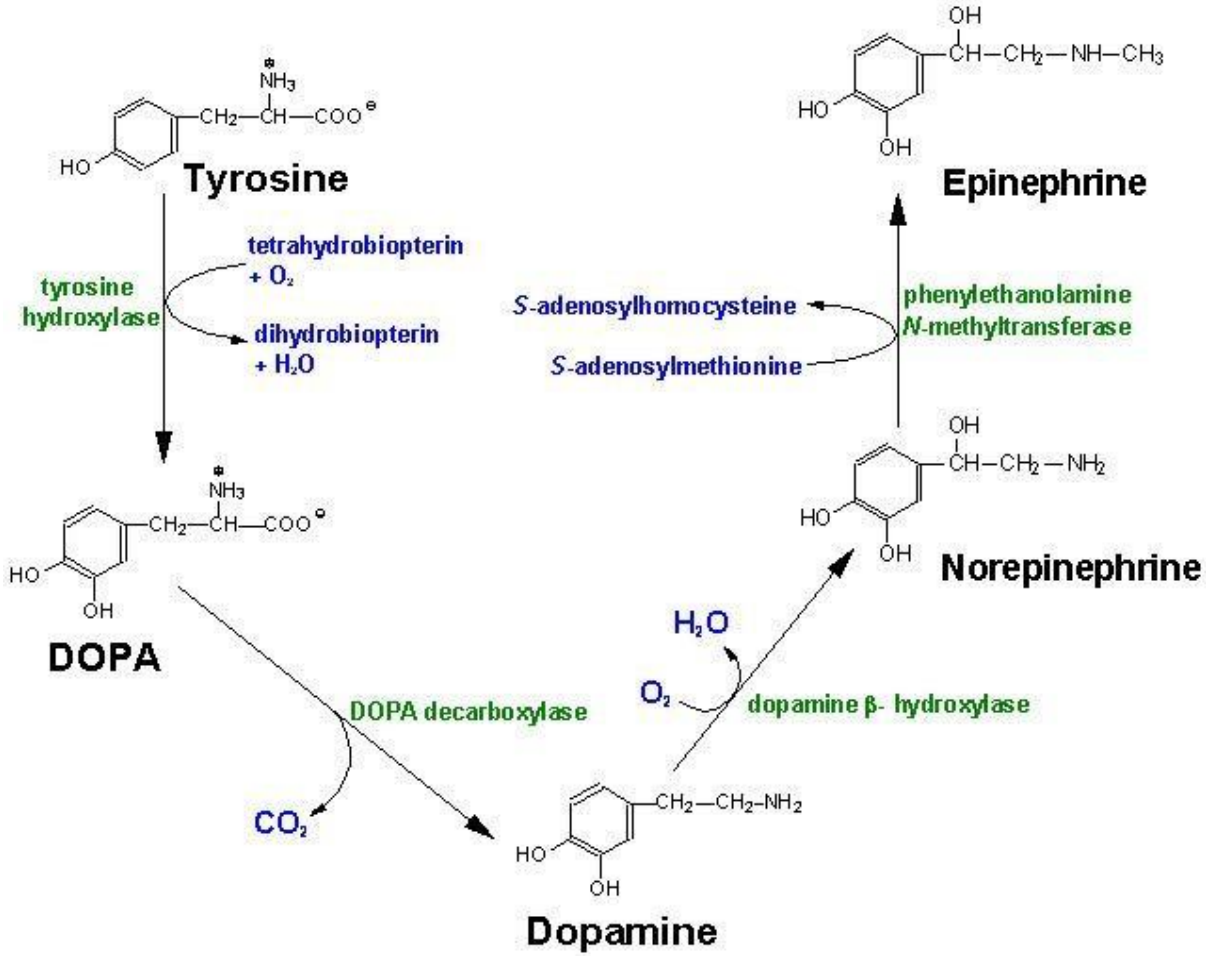
In order



We don't need – for now – to know the reactions and enzymes which convert tyrosine into the 3 catecholamines listed above.

We need to know that those 3 are called catecholamines because they contain the catechol group (see left figure).

Catecholamines are tyrosine derivatives

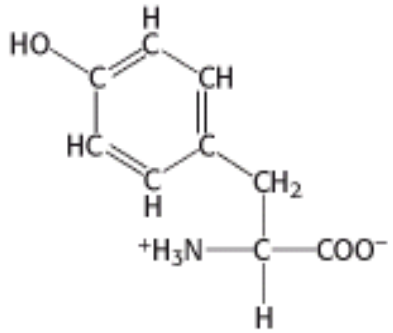


The catechol group is (recall O-Chem class!):

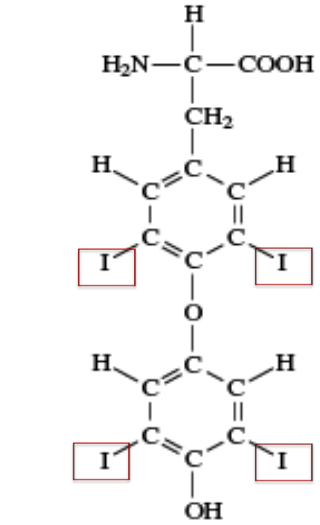
1,2-dihydroxybenzene Or ortho-hydroxyphenol

Tyrosine (2)

- Tyrosine is converted into:
  - Thyroxine (hormone): thyroid gland hormone which gives us energy.
  - Melanin (skin color)
    - **UV light protection**



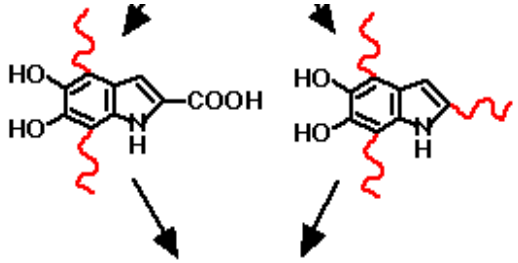
Tyrosine
(Tyr, Y)



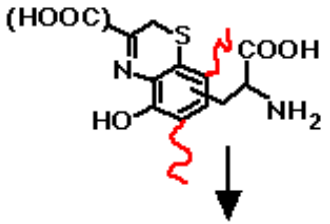
thyroxine (Thy)
occurs only in the hormone protein
thyroglobulin: I=iodine

Thyroxine is composed of 2 connected "tyrosines" with iodine atoms attached.

This is why iodine is important to our bodies – it is used to make thyroxine.



EUMELANINS



PHEOMELANINS

Eumelanin gives skin its dark color; it is abundant in the skin of Africans, and scarce in the skin of Scandinavians.
This is why Africans can withstand sunlight while Scandinavians can easily develop skin cancer if they are exposed to UV light.

Pheomelanin is the component that gives skin, hair and other features their red color.

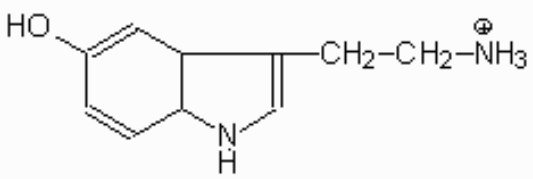
Both melanin types are tyrosine derivatives.

We don't need to know the structural difference between the 2.

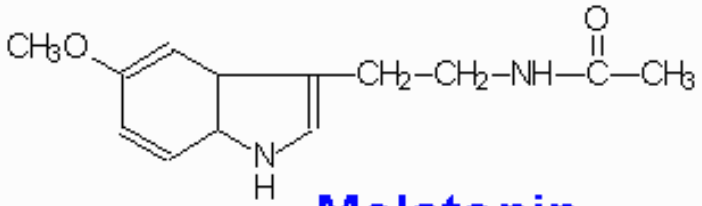
Tryptophan

- Tryptophan serves as the precursor for the synthesis of 2 Neurotransmitters
  - Serotonin (neurotransmitter-sedative)
  - Melatonin (day-night cycle)

Circadian rhythm;
also deals with season changes



Serotonin
(5-hydroxytryptamine)

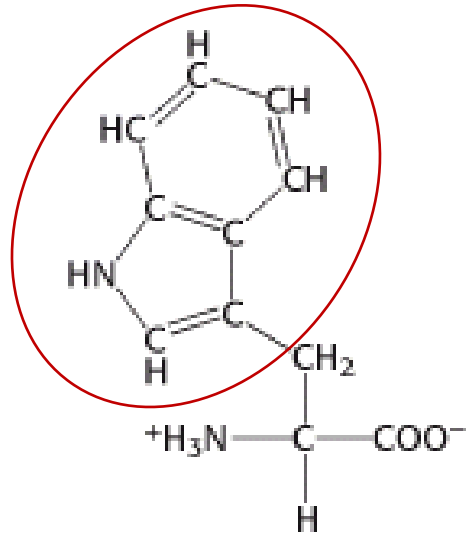


Melatonin

Serotonin is kept active by preventing its reuptake.

Selective Serotonin Reuptake Inhibitors (SSRI) are drugs that prevent the reuptake of serotonin prolonging its anti-depressive effects; people suffering from depression are advised to take such drugs.

People changing time zones, such as in transcontinental flights, use melatonin to help them fix their sleep schedule; day-night cycle.



Tryptophan
(Trp, W)

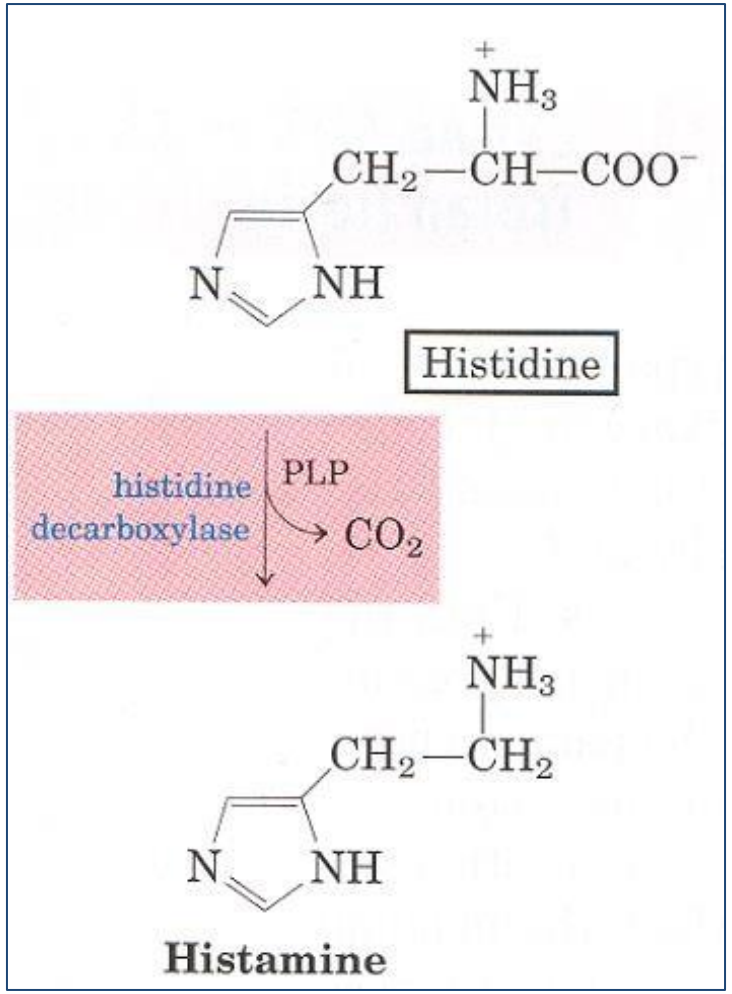
Recall this indole ring.
Recall that Tryptophan is the largest amino acid.

Melatonin presence decreases with age:
infants > children > teenagers > adults > old people

Histamine (histidine derivative)

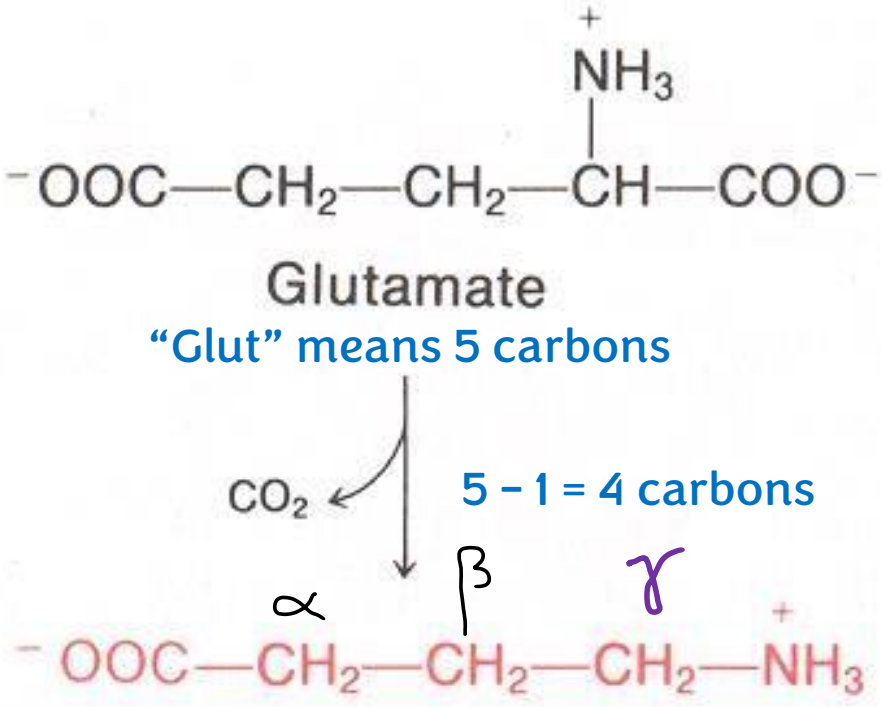
- Acts as a neurotransmitter
- Causes allergic symptoms (a major causes for asthma)

This is why antihistamines are used to treat allergies.



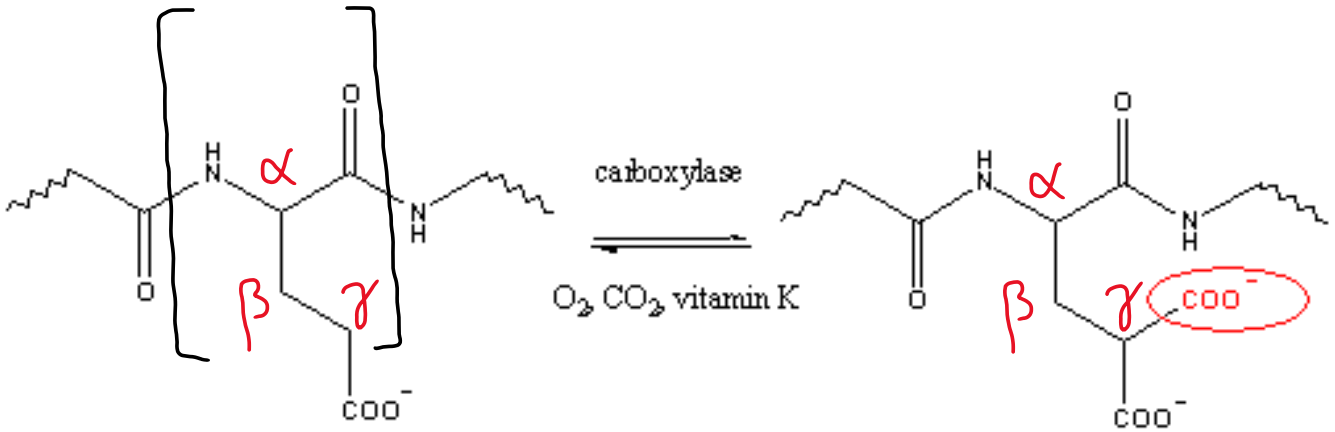
Glutamate

- It is a precursor of γ-aminobutyric acid (GABA), an inhibitory neurotransmitter.
- It has relaxing, anti-anxiety and anti-convulsive effects.



γ- carboxyglutamate (Gla)

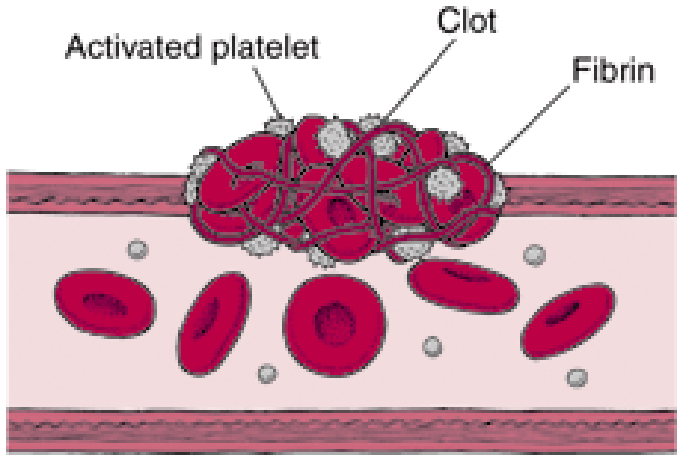
- The glutamate residues of some blood proteins factors are carboxylated to form γ- carboxyglutamate (Gla) residues.
  - Vitamin **K** (coagulation; "Koagulation") is essential for the process
- This carboxylation is essential for blood clotting; which helps repair injuries and fight pathogens.



Glu

Gla

The second carboxyl group (shown in red) is attached to the gamma carbon

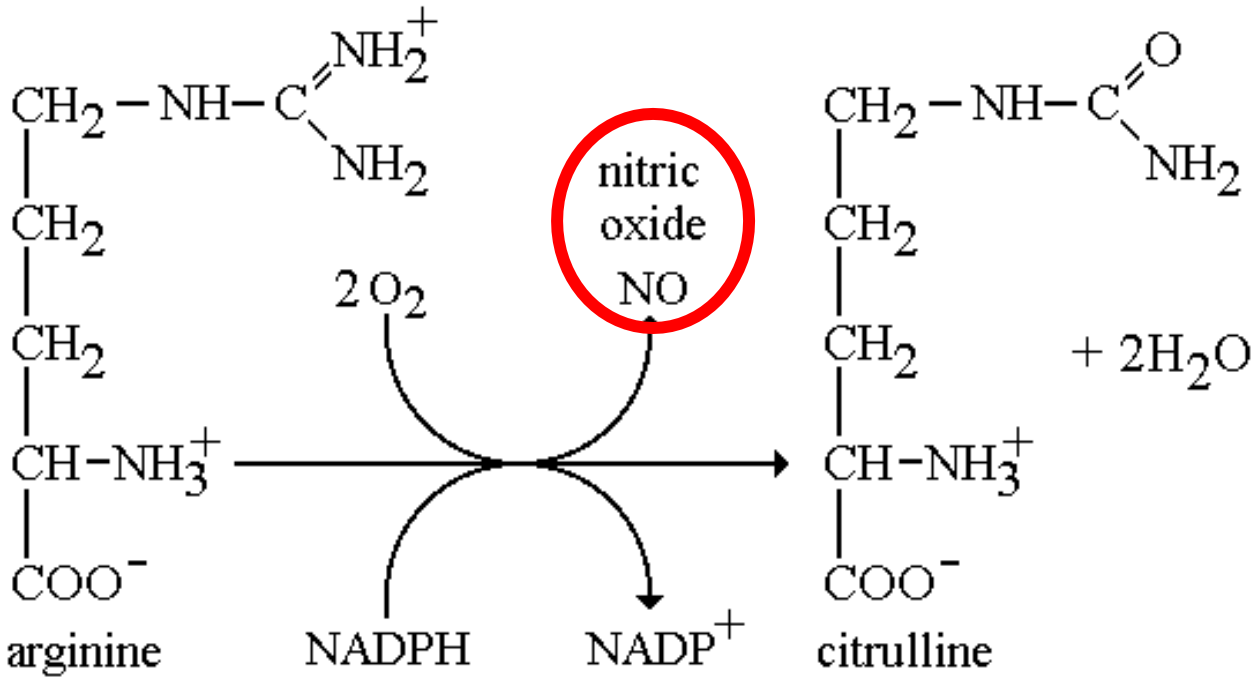


Arginine

Recall that NO is a gas

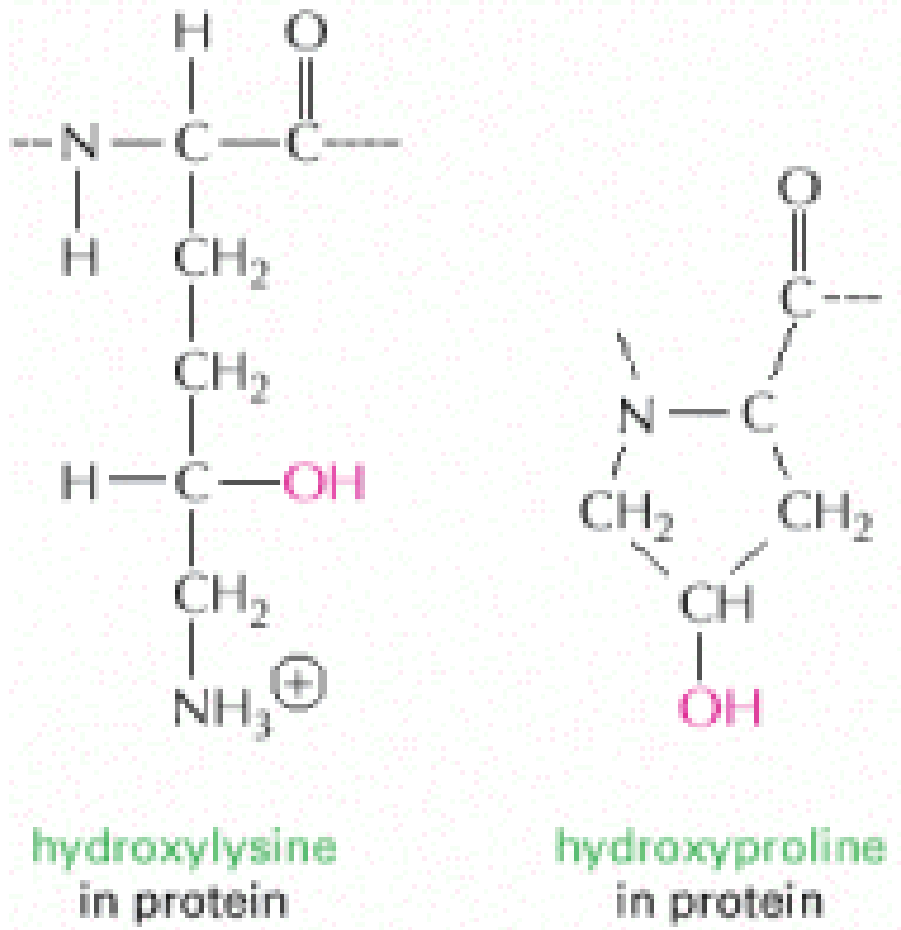
- L-arginine is the precursor of nitric oxide (NO)
- NO functions:
  - Vasodilation (relaxing), inhibition of platelet adhesion, anti-inflammatory

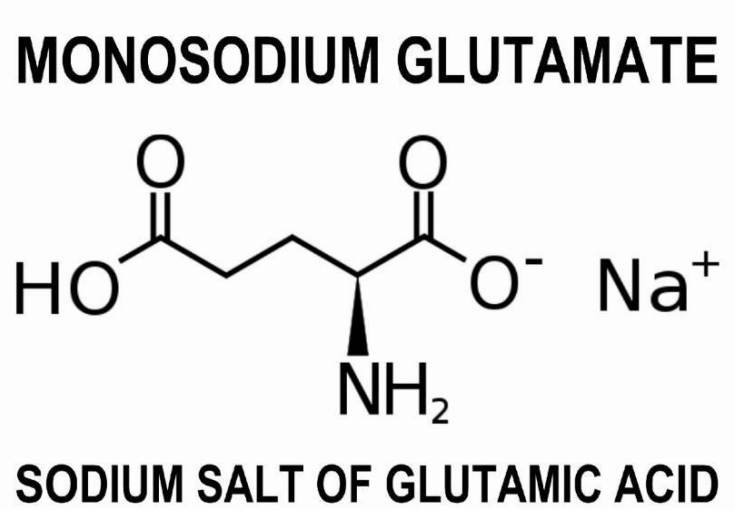
NO has a very short half life, about half a second, but it has very important effects.



Hydroxylysine and hydroxyproline

- Lysine and proline are hydroxylated and are part of collagen structure.
- Both are modified after protein synthesis.





A lot of studies were conducted to find whether MSG is carcinogenic, but it is not proven to be so.

Biochemical applications: Monosodium glutamate (MSG) – meat tenderizer

Glutamic acid derivative

Flavor enhancer, Asian food.

MSG causes a physiological reaction in some people (chills, headaches, and dizziness)

Chinese restaurant syndrome.

Symptoms: shivering, fever, headache, dizziness

QUIZ

- What is special about (example: proline)?
  Only cyclic amino acid + It has a secondary (N) instead of primary
- An acidic amino acid is Negatively charged at physiological conditions.
- Name 2 amino acids that share a functional group in their side chain.
  Many answers: e.g., serine and threonine / glutamine and asparagine

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V1 → V2	2; the text at the bottom	-	*Added the line in Purple*

V2 → V3	28	• Dopamine
		• Epinephrine (or Adrenaline)
		  • Fight or Flight response
		• Norepinephrine (or Noradrenaline)
			In order
			• Dopamine
			• Norepinephrine (or Noradrenaline)
			• Epinephrine (or Adrenaline)
			  • Fight or Flight response

Additional Resources Used:

1. Campbell Textbook:
   sec. 3.1 (Amino Acids Exist in a Three-Dimensional World)
   sec. 3.2 (Individual Amino Acids: Their structures and Properties)

2. YouTube link for easier memorization of amino acid:

رسالة من الفريق العلمي:

صلوا على خير الأنام محمد

اللهم صل وسلم وبارك على سيدنا محمد

وعلى آله وصحبه أجمعين