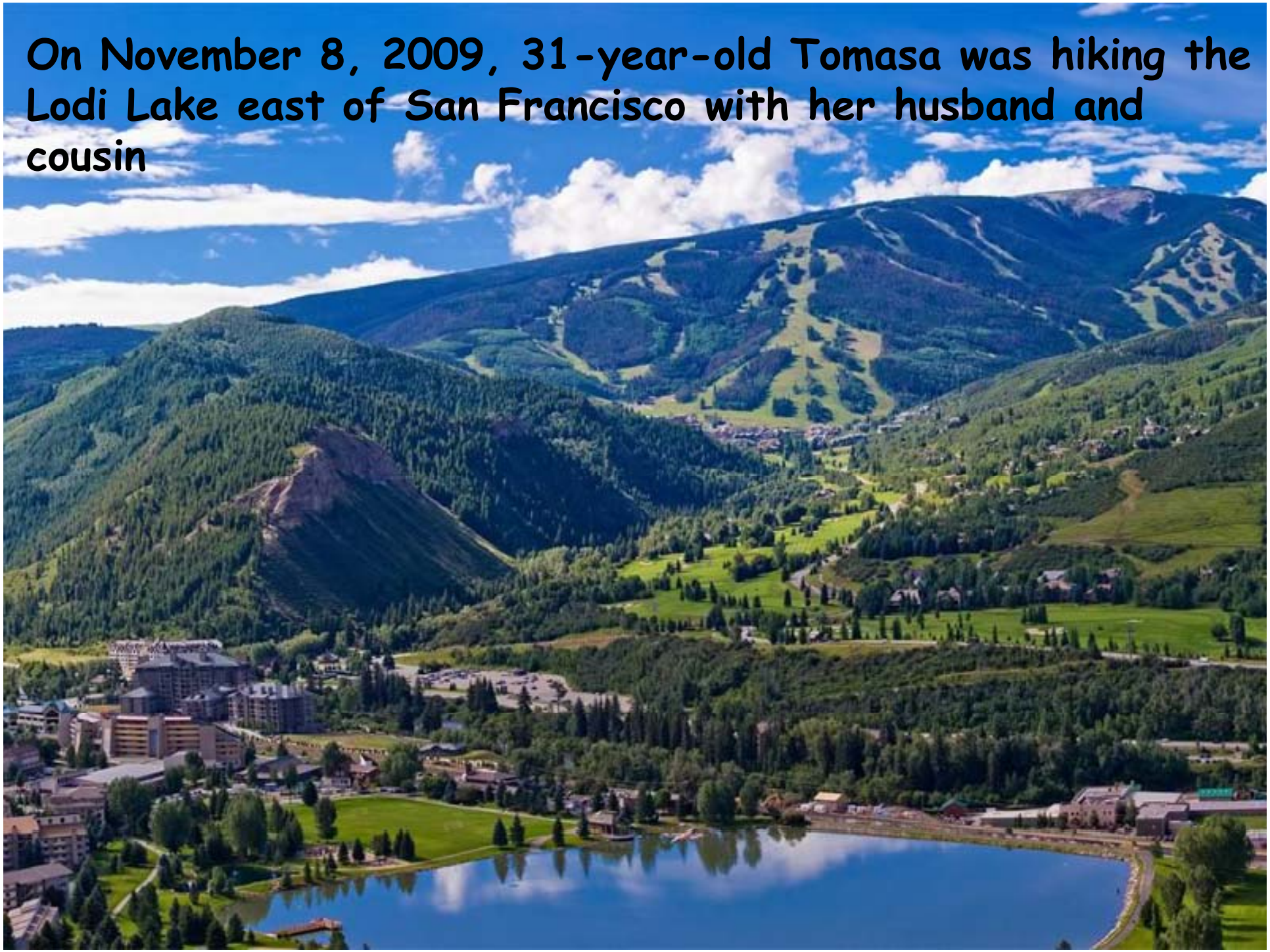
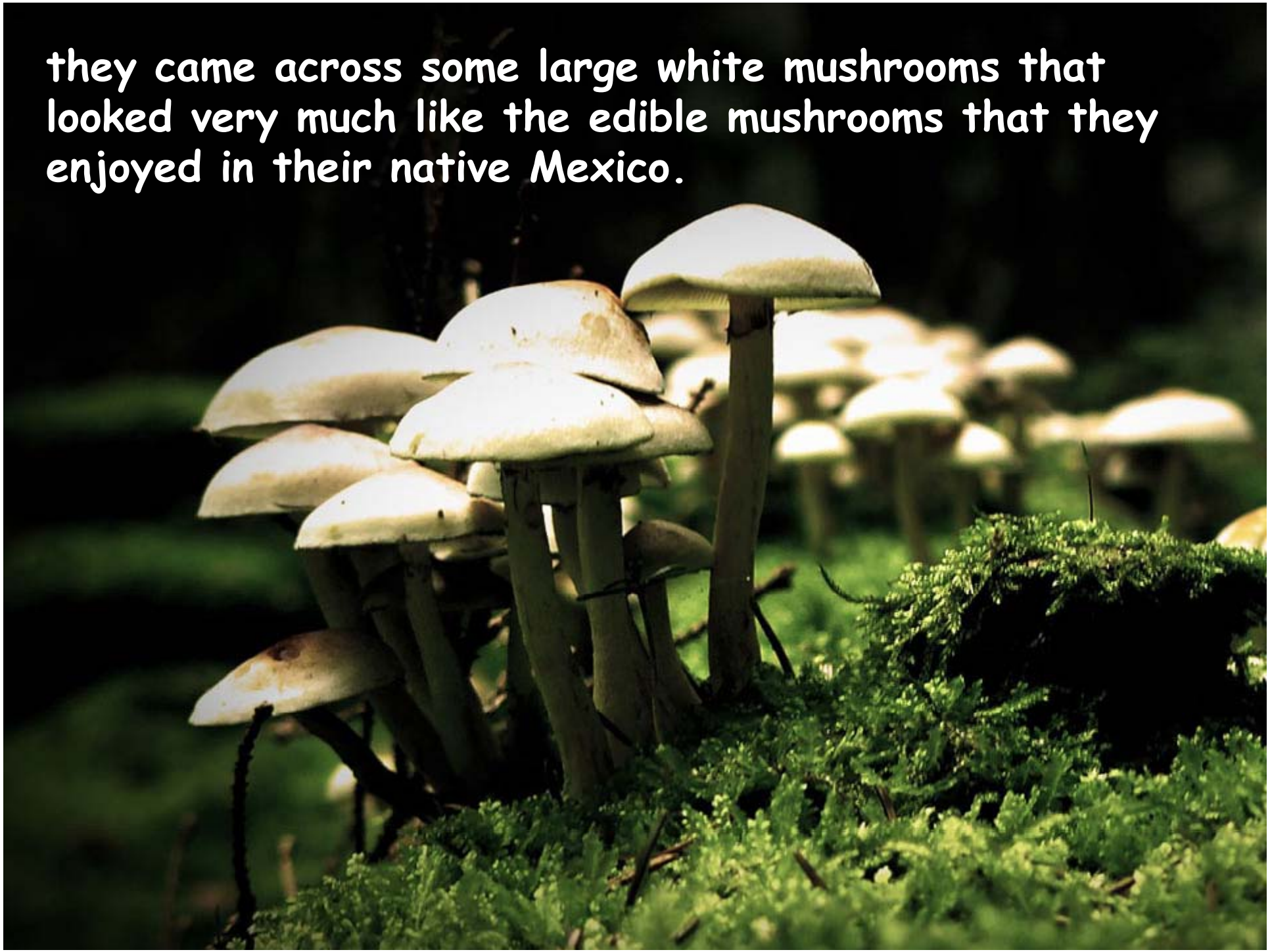

phillipmartin.info
MARTIN


On November 8, 2009, 31-year-old Tomasa was hiking the Lodi Lake east of San Francisco with her husband and cousin

they came across some large white mushrooms that looked very much like the edible mushrooms that they enjoyed in their native Mexico.

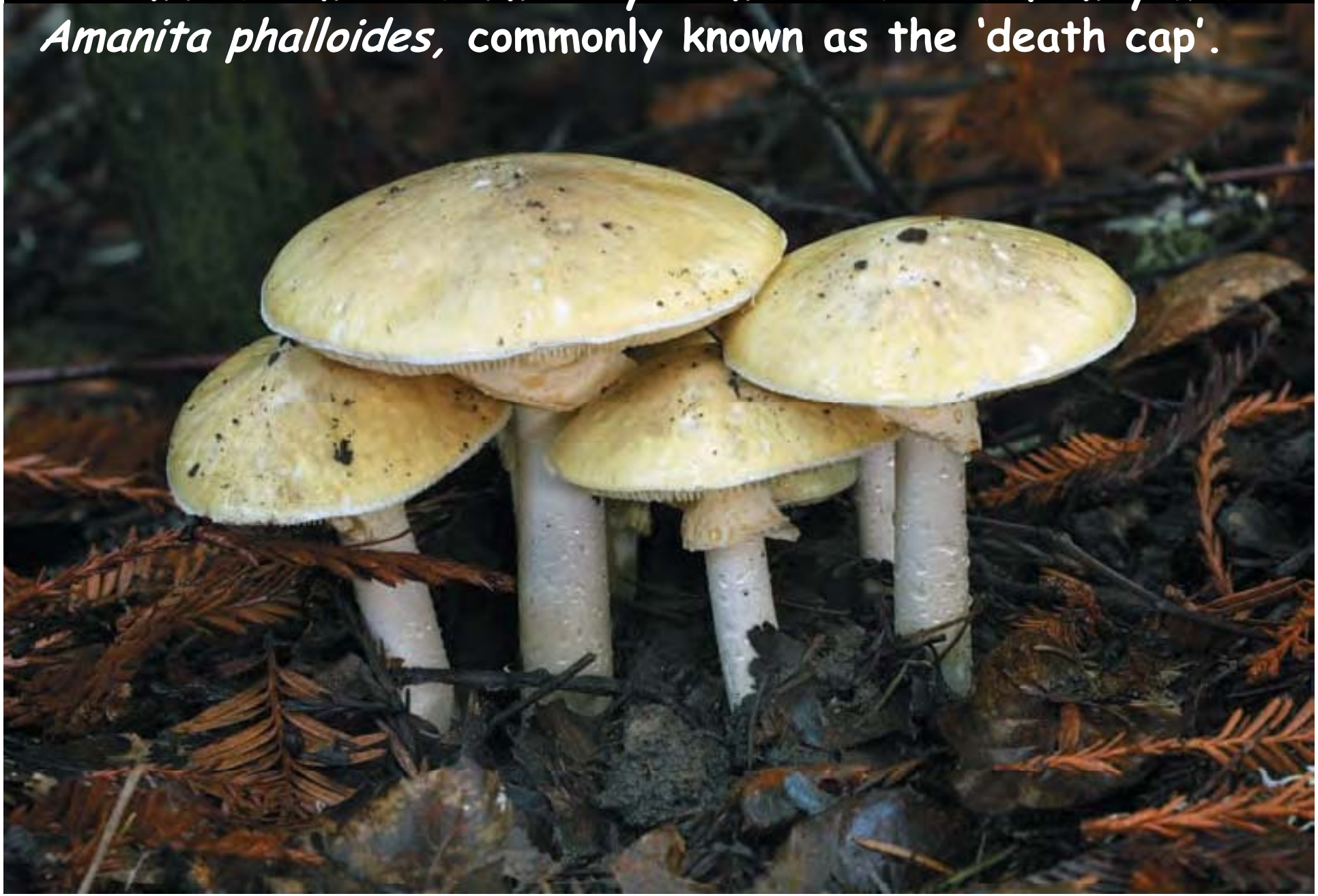


They picked the mushrooms and took them home, cooking and consuming them for dinner.

Within hours, Tomasa and her family were sick and went to the hospital.

They were later transferred to the critical care unit at California Pacific Medical Center in San Francisco, where Tomasa died of liver failure 3 weeks later. Her husband eventually recovered after a lengthy hospitalization; her cousin required a liver transplant to survive.

The mushrooms consumed by Tomasa and her family were *Amanita phalloides,* commonly known as the 'death cap'.



A single death cap mushroom contains enough toxin to kill an adult human.

The death rate among those who consume death caps is 22%; among children under the age of 10, it's more than 50%.

Death cap mushrooms appear to be spreading in California, leading to a recent surge in the number of mushroom poisonings.

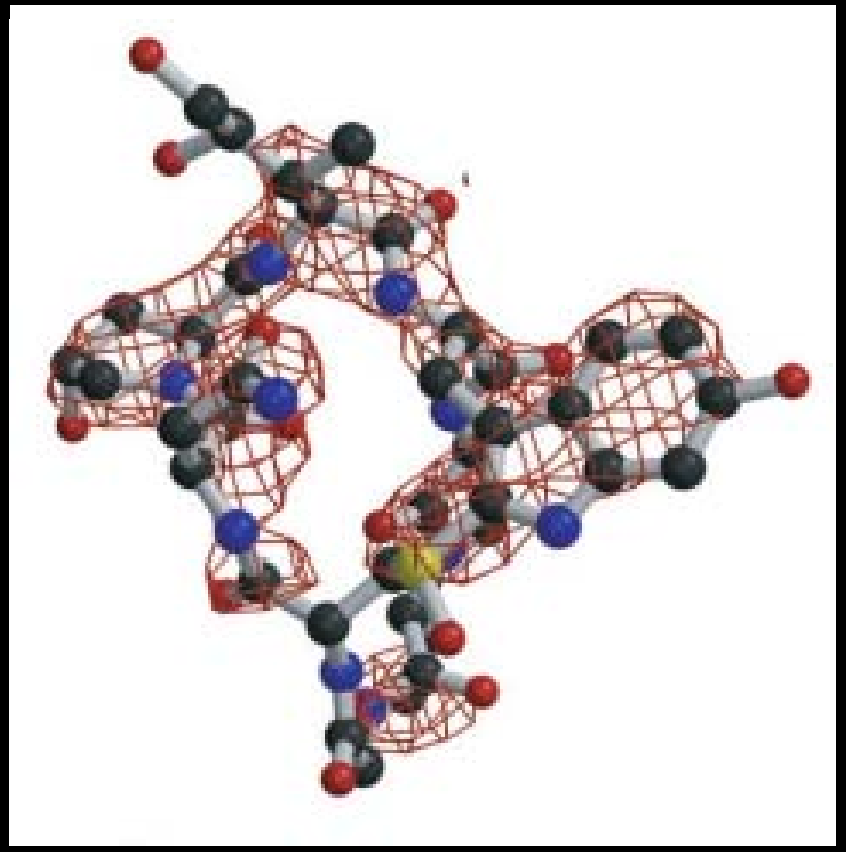
Death cap poisoning is insidious. Gastrointestinal symptoms (abdominal pain, cramping, vomiting, diarrhea) begin within 6 to 12 hours of consuming the mushrooms, but these symptoms usually subside within a few hours and the patient seems to recover.

Because of this initial remission, the poisoning is often not taken seriously until it's too late to pump the stomach and remove the toxin from the body.

After a day or two, serious symptoms begin. Cells in the liver die, often causing permanent liver damage and death within a few days. There is no effective treatment, other than a liver transplant to replace the damaged organ.

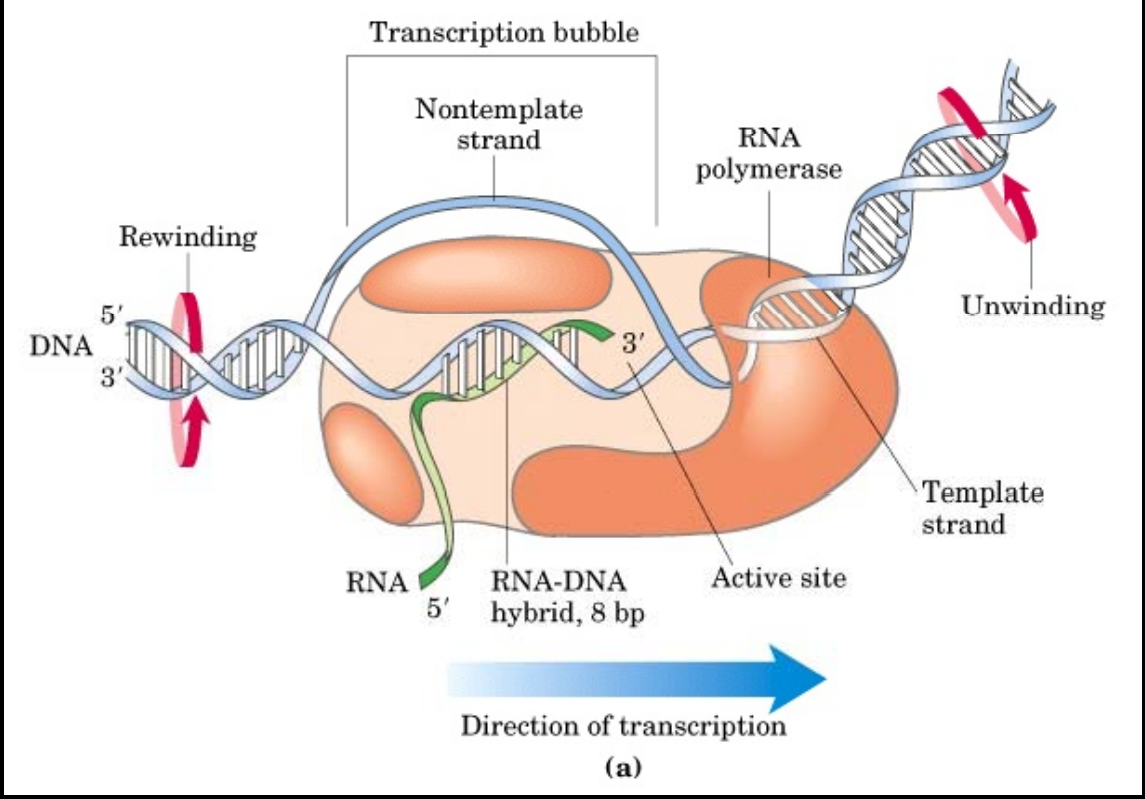
How do the death caps kill?

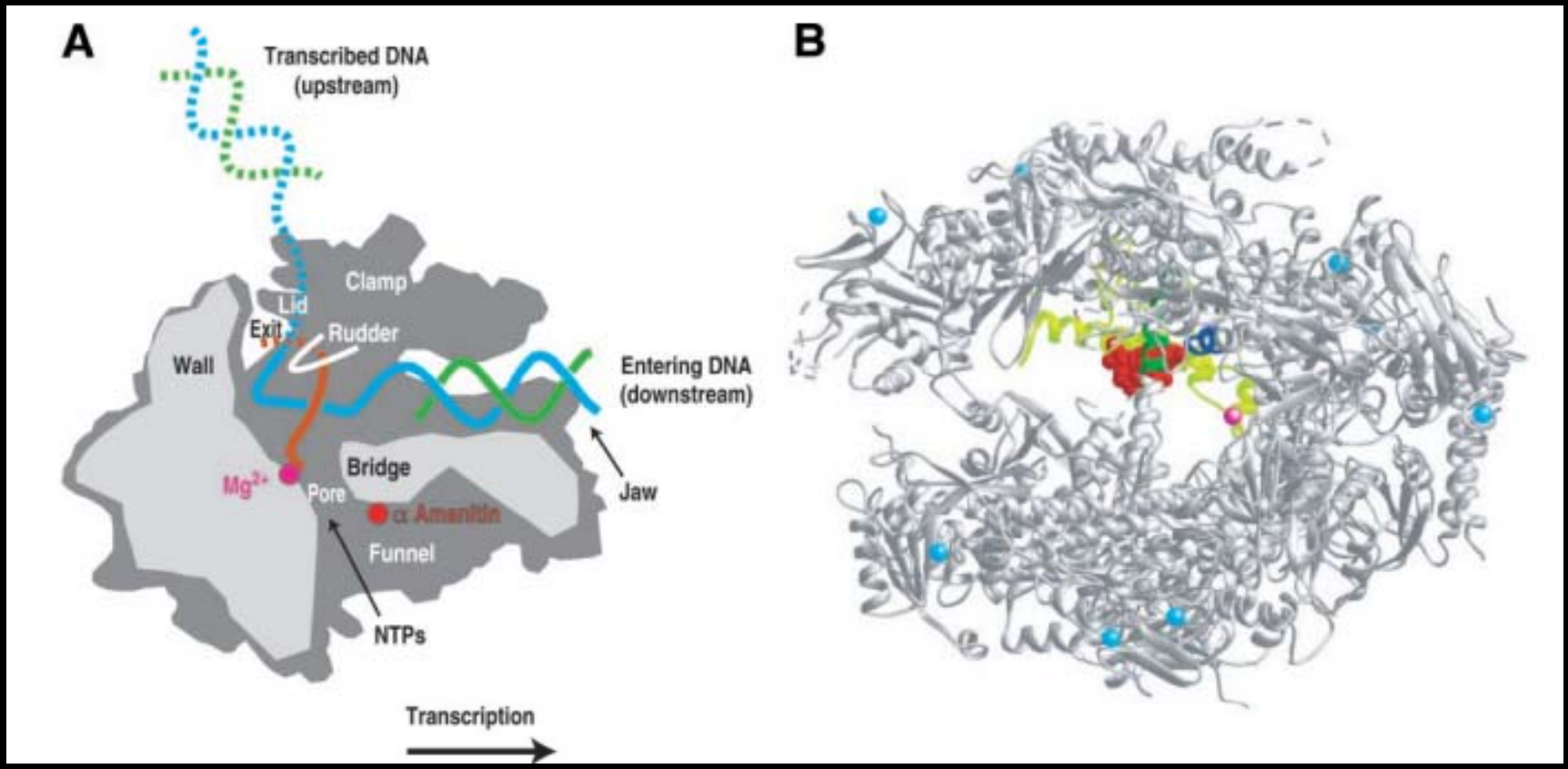
Their deadly toxin, contained within the fruiting bodies, is the protein "α-amanitin", which consists of a short peptide of eight amino acids that forms a circular loop.



a-Amanitin is a potent inhibitor of RNA polymerase II, the enzyme that transcribes protein-encoding genes in eukaryotes.

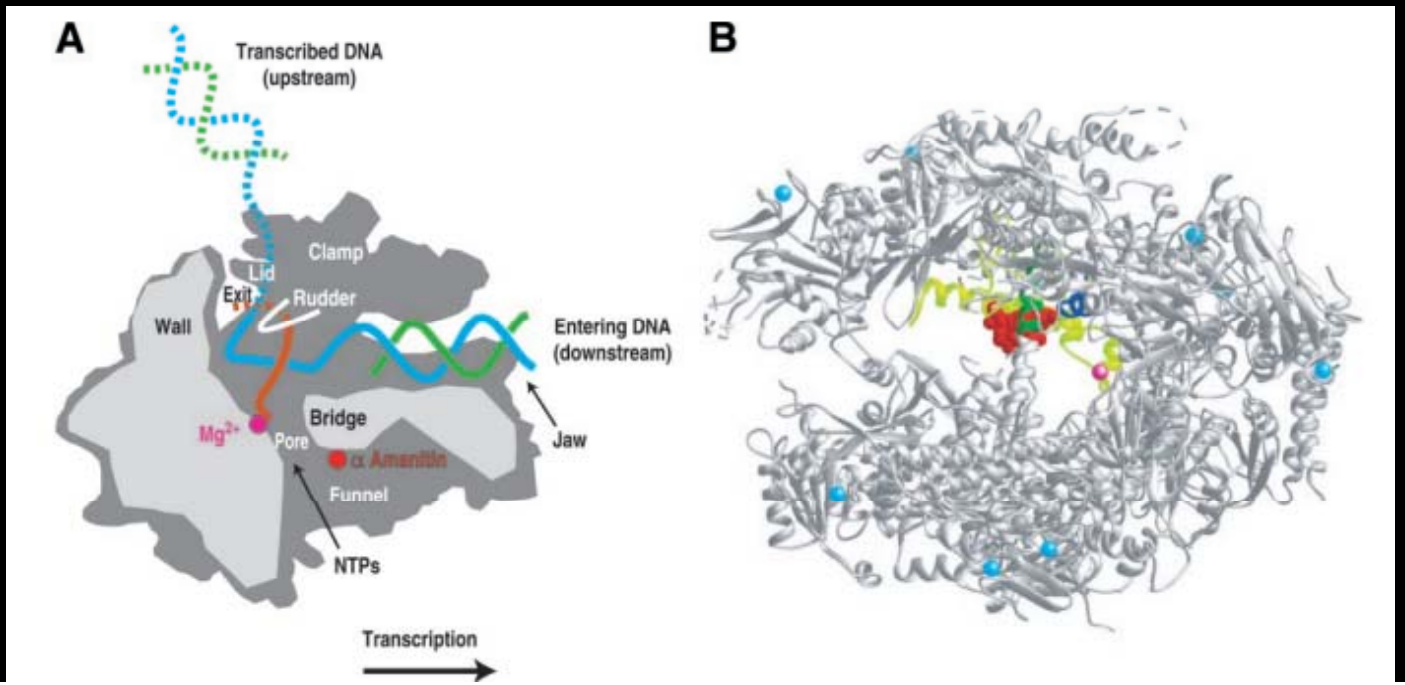
RNA polymerase II binds to genes and synthesizes RNA molecules that are complementary to the DNA template.




A
Transcribed DNA
(upstream)
Clamp
Lid
Exit
Rudder
Wall
Entering DNA
(downstream)
Bridge
Mg2+
Pore
α Amanitin
Jaw
Funnel
NTPs
Transcription
B

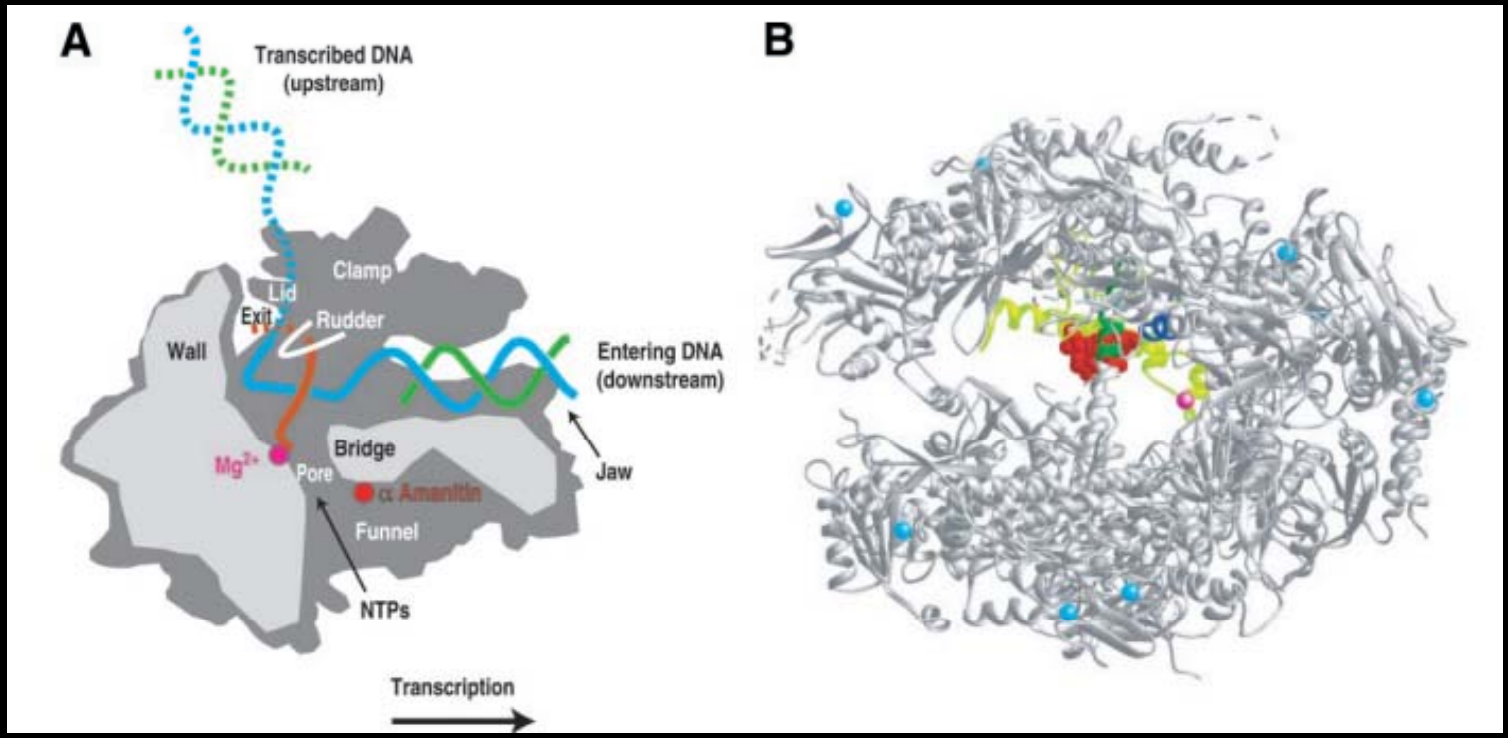
In the process of transcription, the RNA polymerase moves down the DNA template, adding one nucleotide at a time to the growing RNA chain.

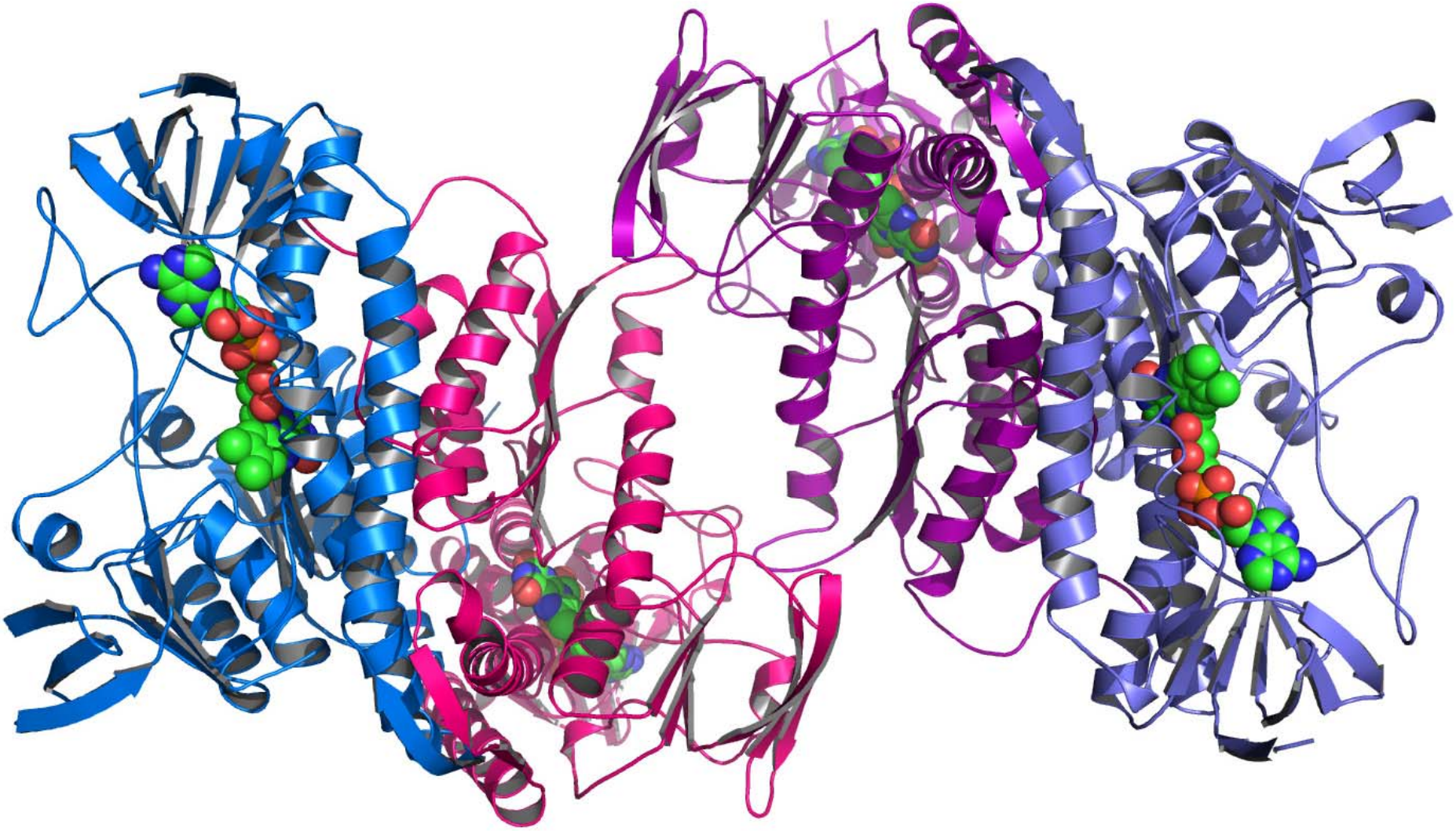
a-Amanitin binds to RNA polymerase and jams the moving parts of the enzyme, interfering with its ability to move along the DNA template. In the presence of a-amanitin, RNA synthesis slows from its normal rate of several thousand nucleotides per minute to just a few nucleotides per minute.



The results are catastrophic. Without transcription, protein synthesis - required for cellular function - ceases and cells die.

The liver, where the toxin accumulates, is irreparably damaged and stops functioning. In severe cases, the patient dies.



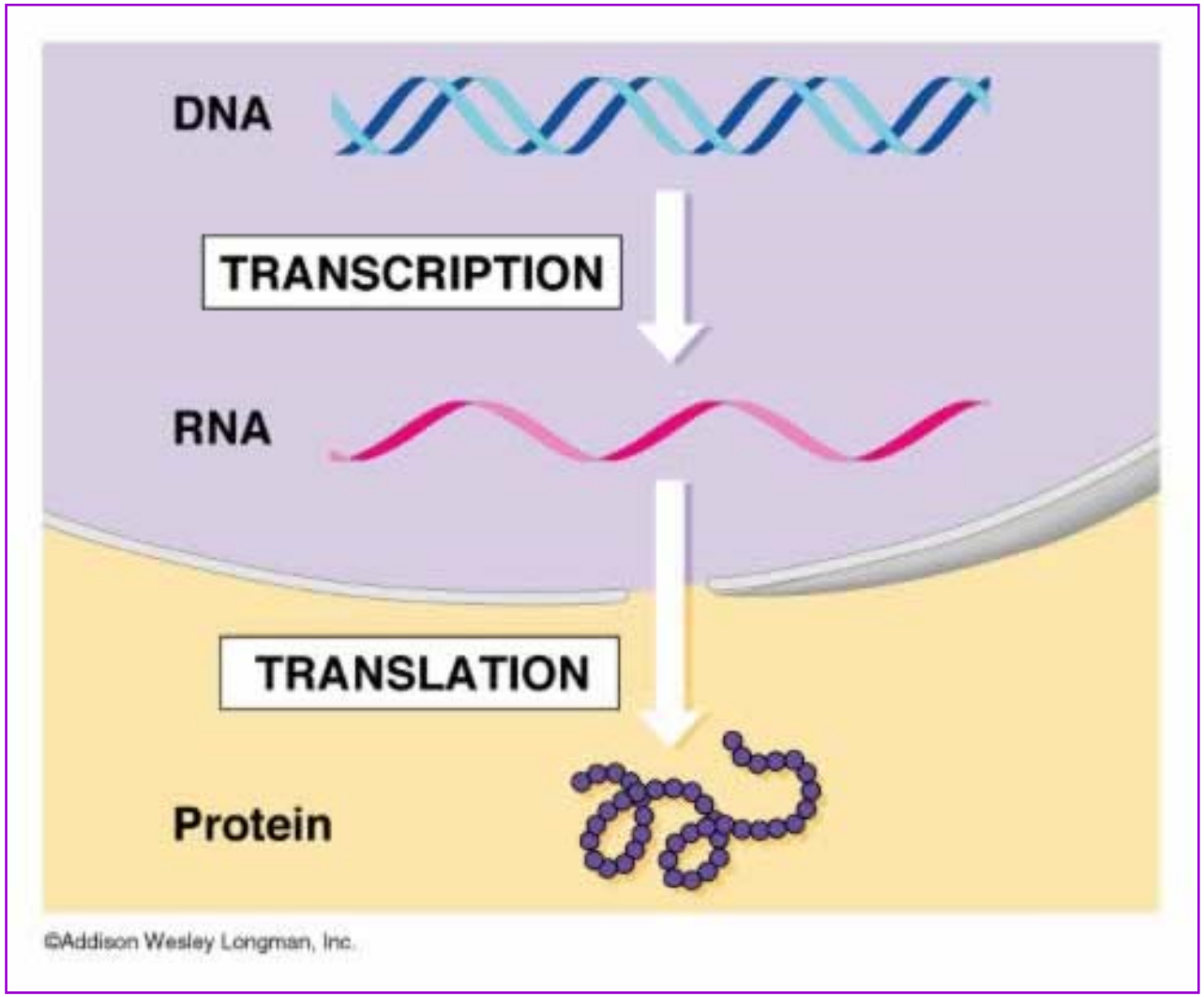


PROTEINS

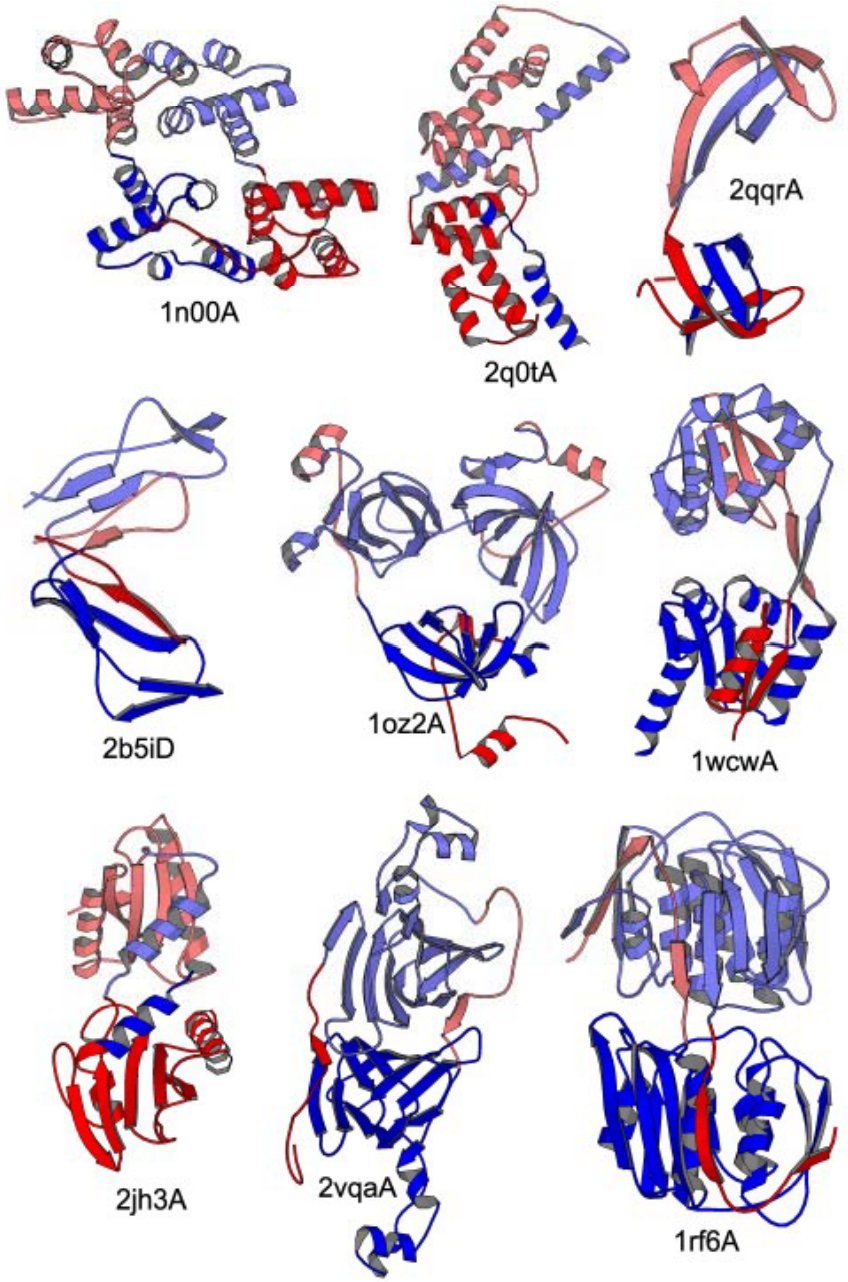
Most versatile, Most abundant, biomolecule on earth

Occurs in all cells, and in all parts of cells

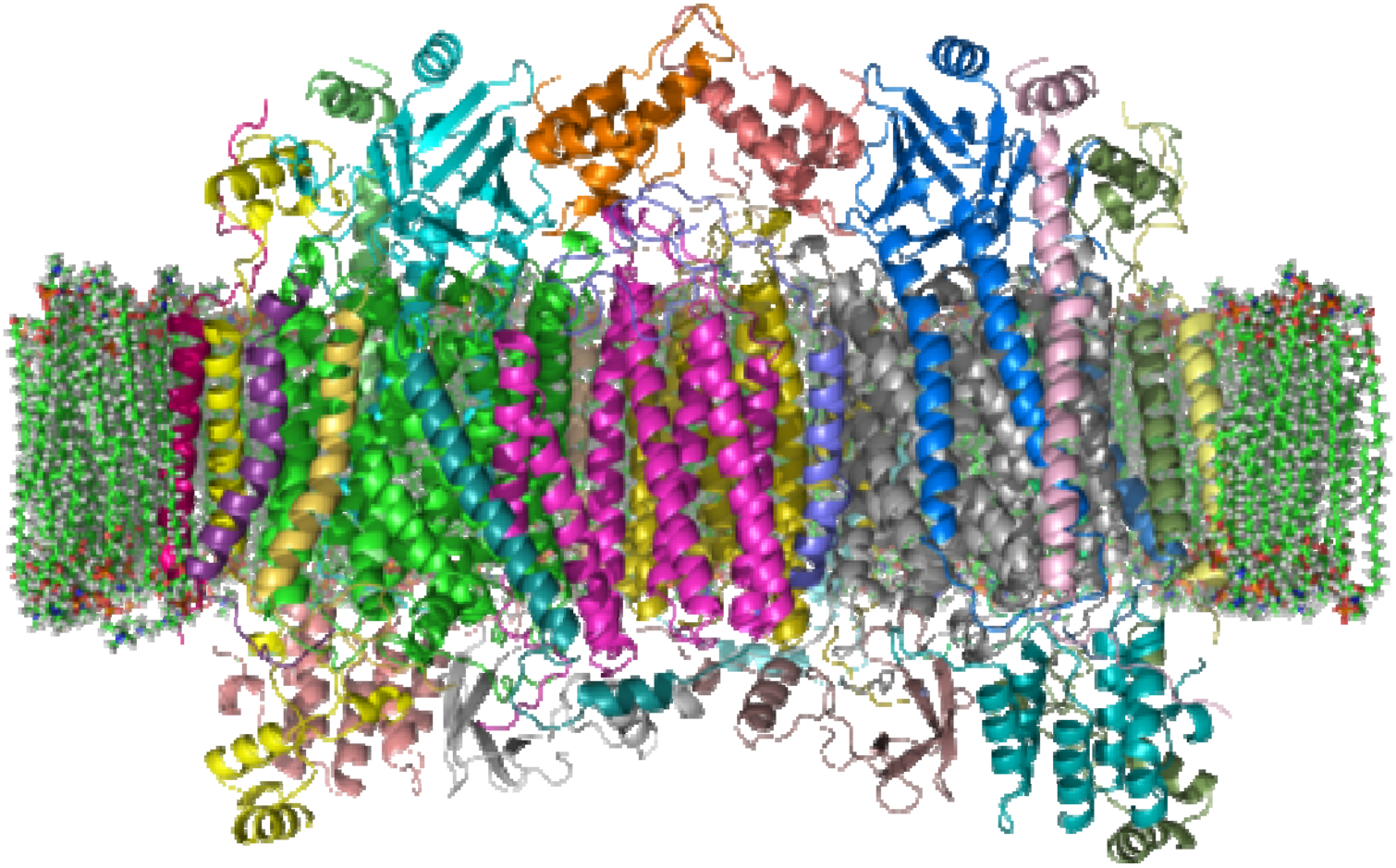
Proteins are the instruments through which genetic information is expressed



Proteins occur in great variety; thousands of different kinds, ranging in size from relatively small peptides to huge polymers with molecular weights in the millions, may be found in a single cell.



Proteins exhibit enormous diversity of biological function and are the most important final products of the information pathway.



Gr. Proteios

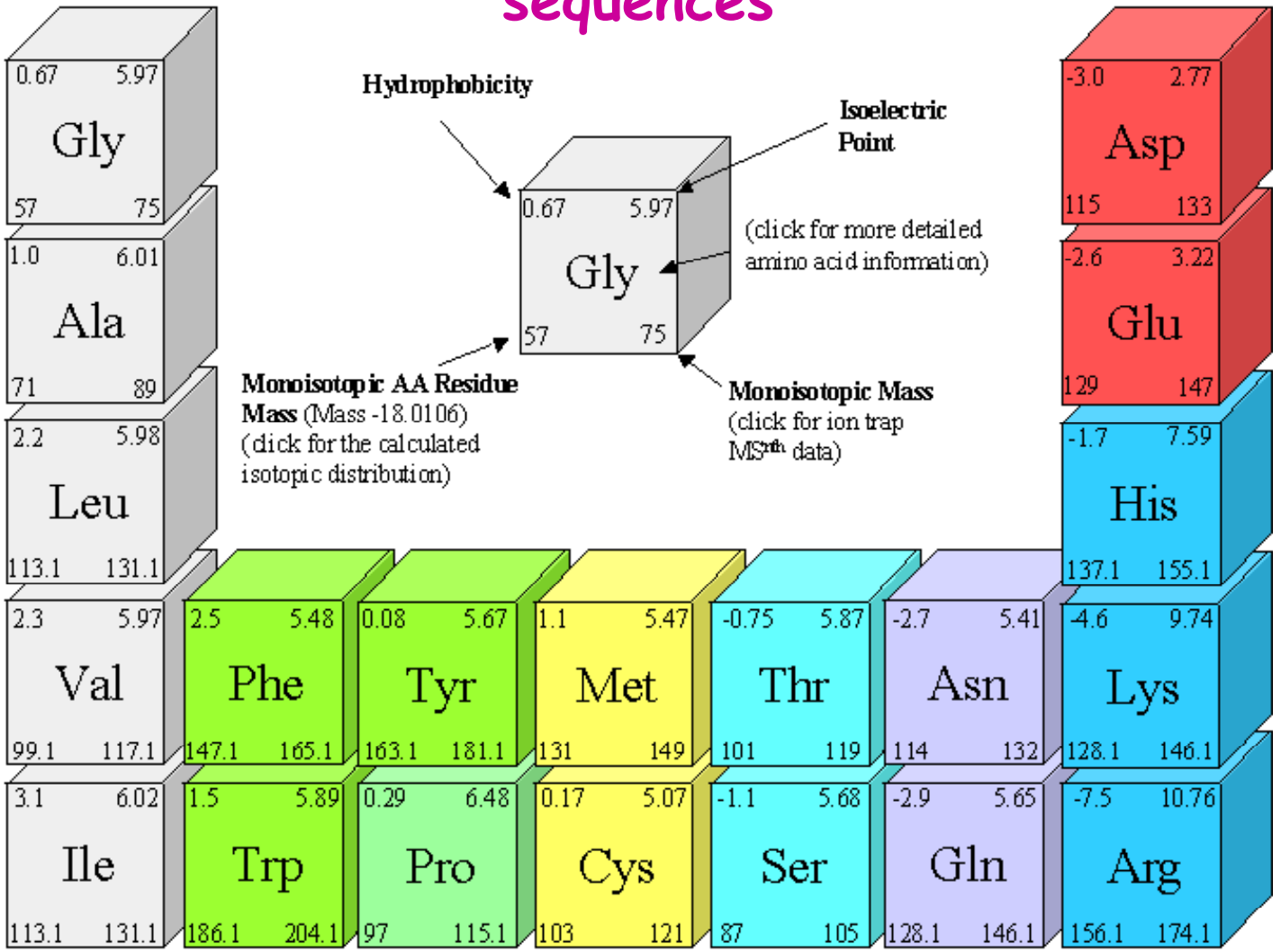
= primary

= in the lead

= standing in front

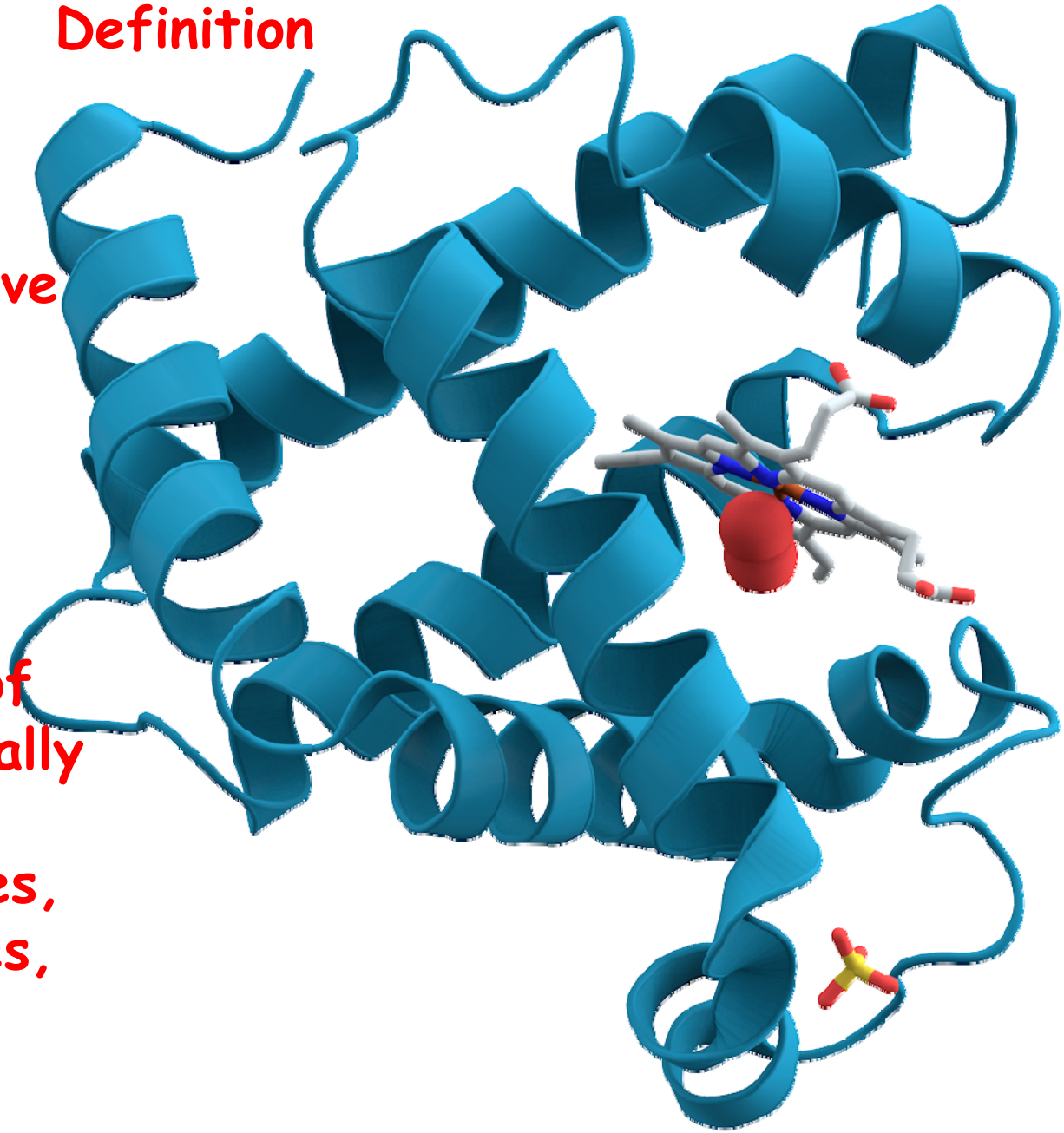
= of the I rank

Proteins are built from a repertoire of 20 amino acids joining in many different combinations and sequences

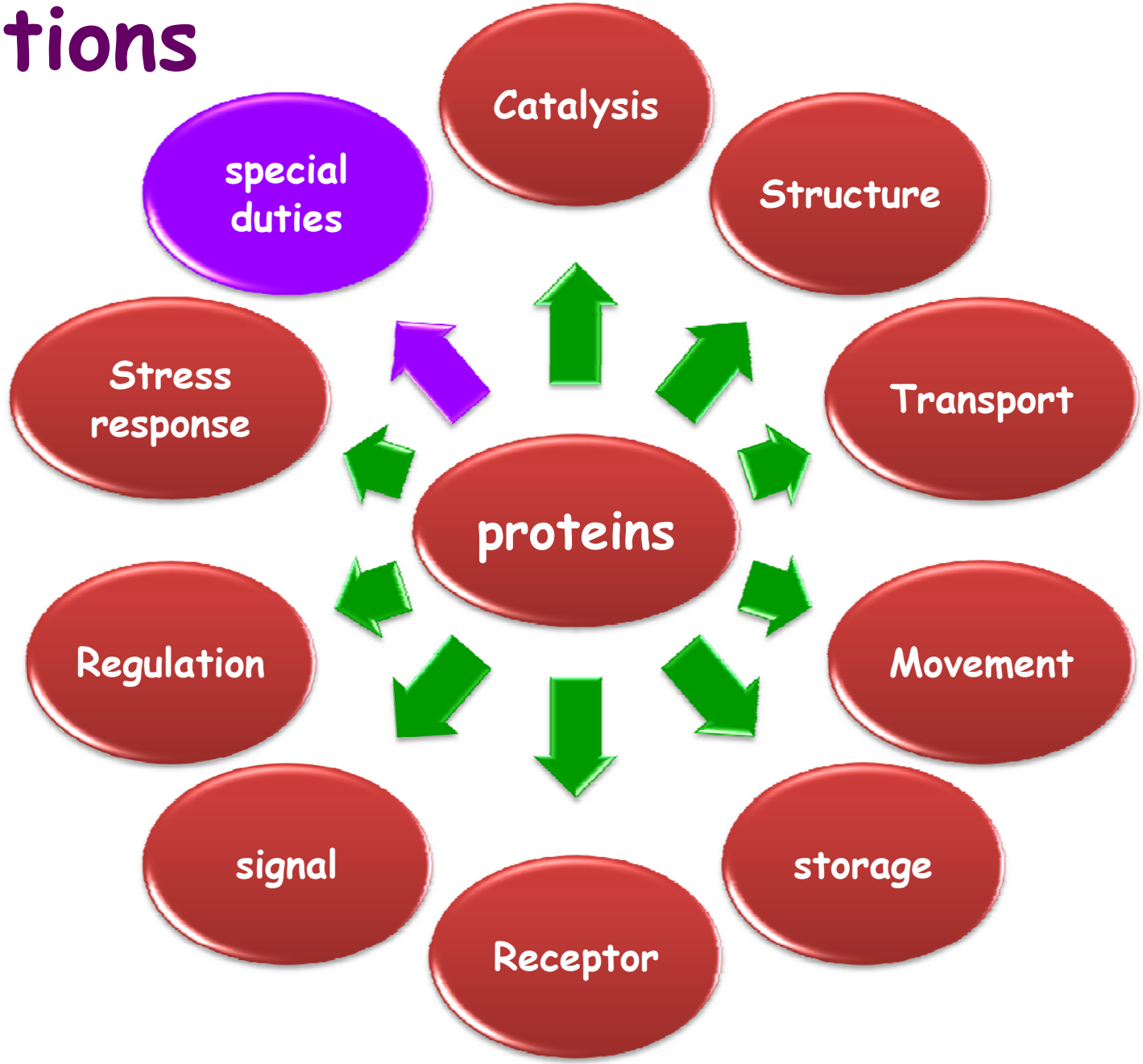


Definition

Any of a class of nitrogenous organic compounds which have large molecules composed of one or more long chains of amino acids and are necessary for the proper functioning of an organism, especially as structural components, enzymes, hormones, antibodies, carriers, receptors, etc

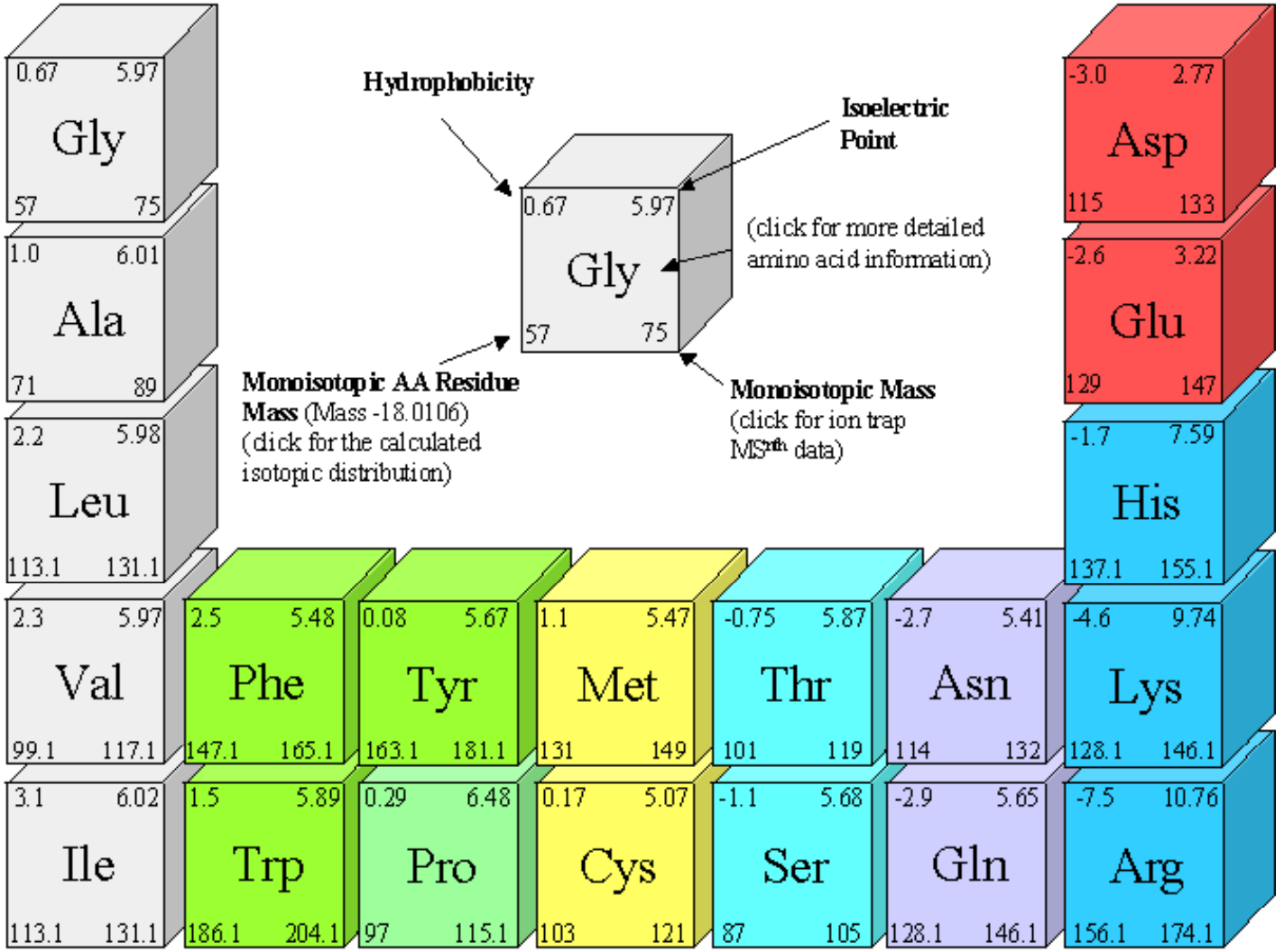


Functions

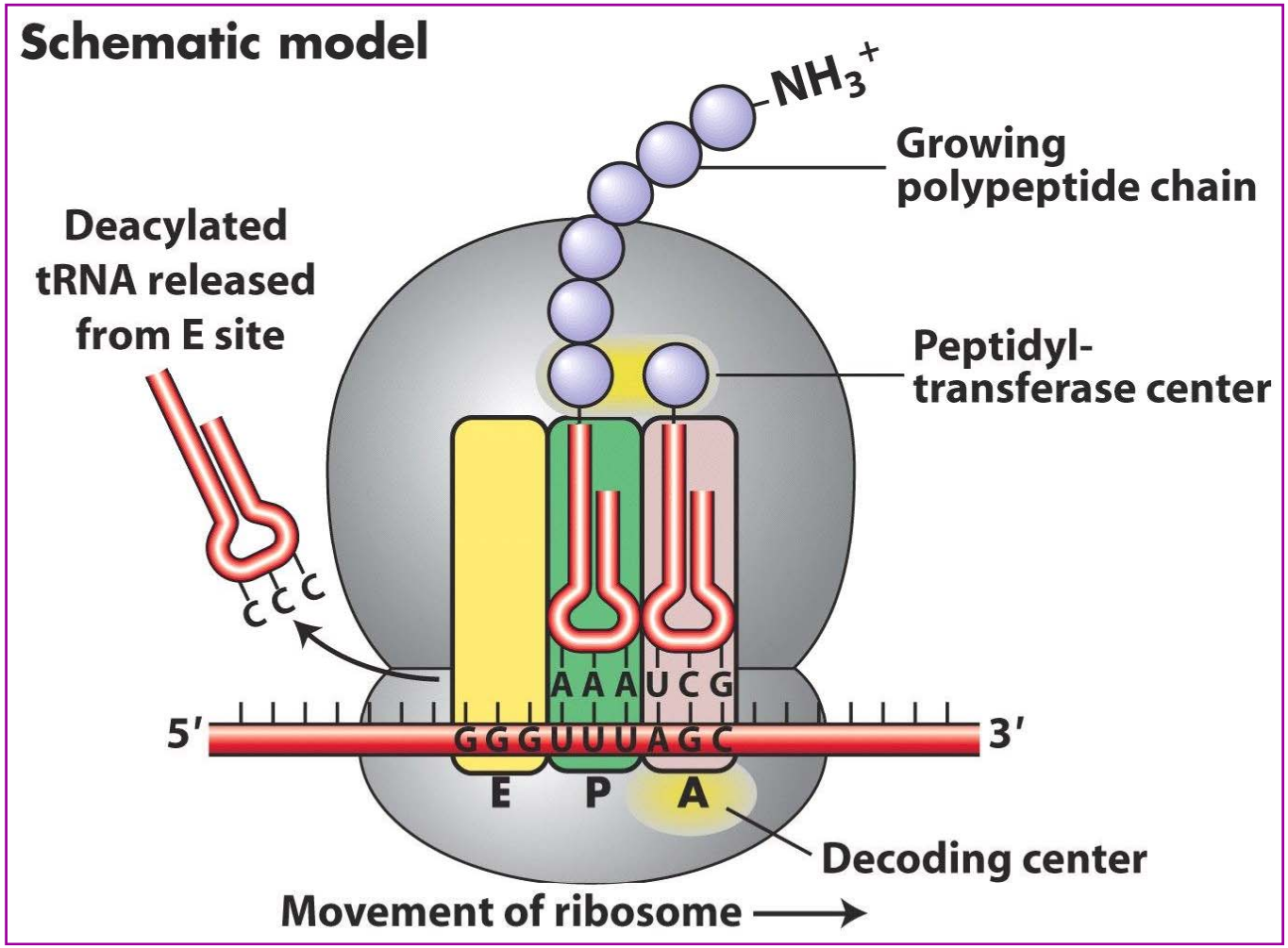

Catalysis
Structure
special duties
Stress response
Transport
proteins
Regulation
Movement
signal
storage
Receptor

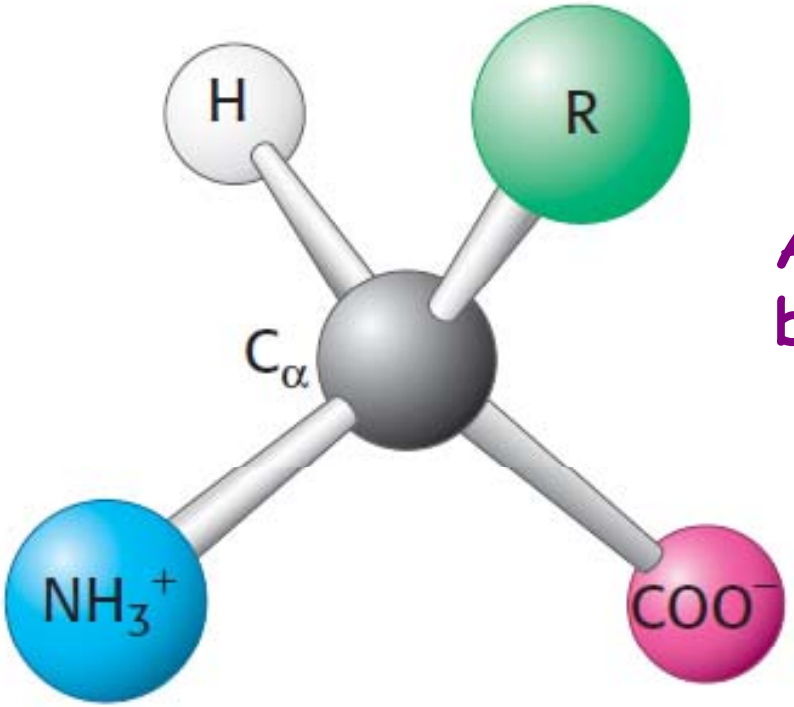
Amino acids: the building blocks of proteins

Built from a repertoire of 20 amino acids joining in many different combinations and sequences

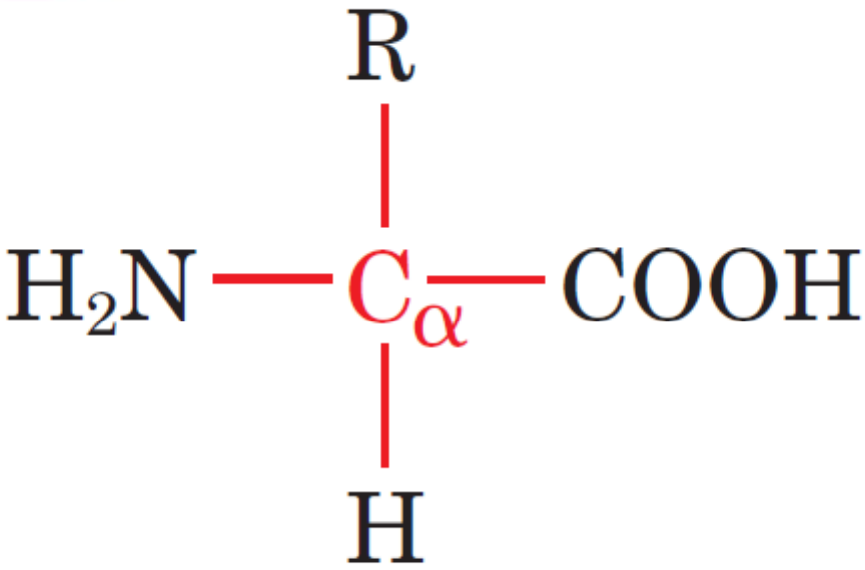


Polymerization of amino acids in the cell is catalyzed by ribosome during translation





Amino acids are the building blocks of proteins.



Are constructed from the set of 20 amino acids, covalently linked in characteristic linear sequences.

The most remarkable fact is that cells can produce proteins with strikingly different properties and activities by joining the same 20 amino acids in many different combinations and sequences.

From these building blocks different organisms can make such widely diverse products as enzymes, hormones, antibodies, transporters, muscle fibers, the lens protein of the eye, feathers, spider webs, rhinoceros horn, milk proteins, antibiotics, mushroom poisons, and other substances having distinct biological activities

Proteins are polymers of amino acids, with each amino acid residue joined to its neighbor by a specific type of covalent bond.

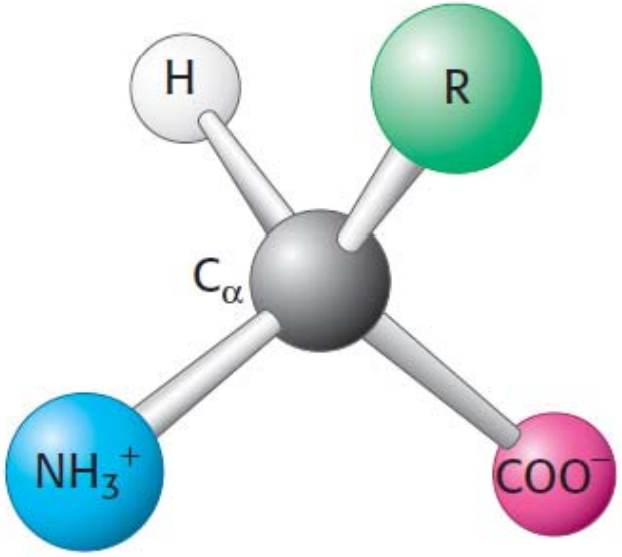
Twenty different amino acids are commonly found in proteins

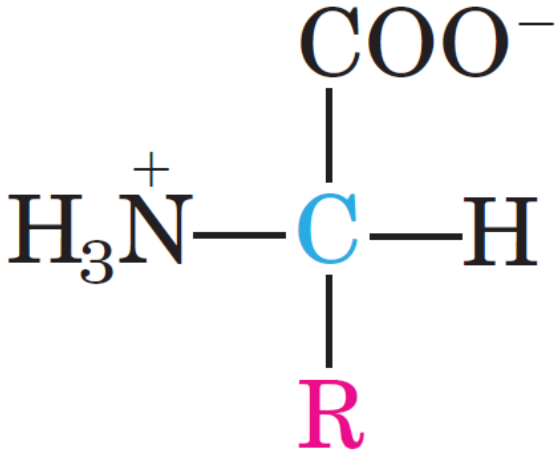
The first to be discovered was asparagine, in 1806. The last of the 20 to be found, threonine, was not identified until 1938.

All 20 of the common amino acids are α-amino acids

An α-amino acids consists of a central carbon atom, called the α carbon, linked to an amino group, a carboxylic acid group, a hydrogen atom, and a distinctive R group. The R group is often referred to as the side chain.

With four different groups connected to the tetrahedral α-carbon atom, α-amino acids are chiral and α-carbon atom is thus a chiral center

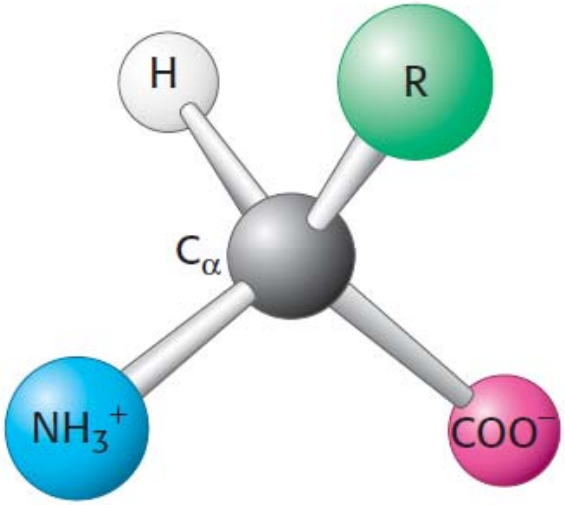




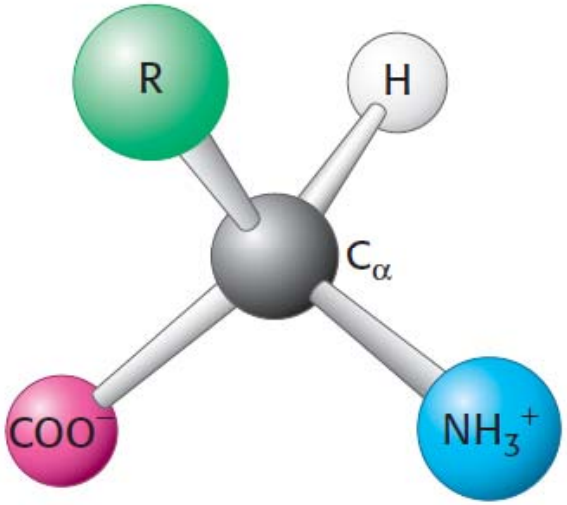
The molecules with a chiral center are also optically active ie., they rotate under plane-polarized light.

L for levorotatory (rotating light to the left) and
D for dextrorotatory (rotating light to the right)

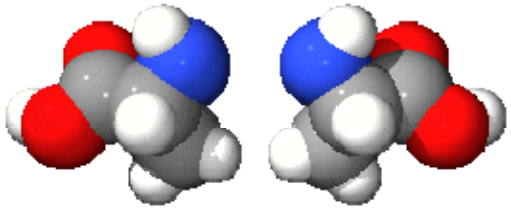
They may exist in one or the other of two mirror-image forms, called the L isomer and the D isomer



L isomer



D isomer



L & D alanine

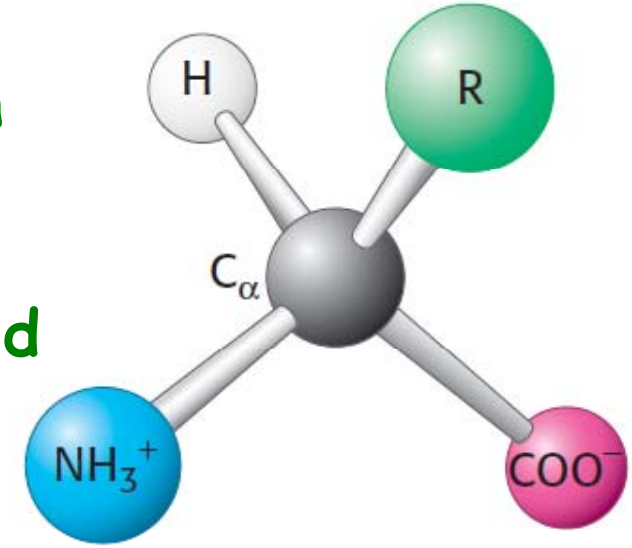
Only L amino acids are most abundant constituents of proteins.

What is the basis for the preference for L amino acids?

answer is not completely known....

but evidence shows that L amino acids are slightly more soluble than D. D-amino acids usually tend to form crystals.

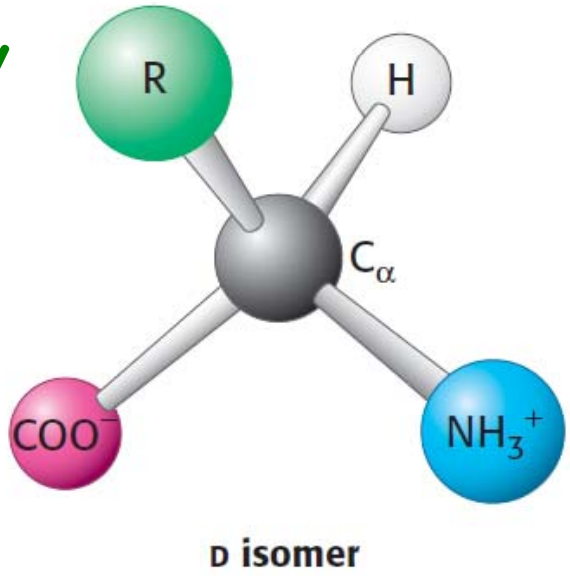
This small solubility difference could have been amplified over time so that the L isomer became dominant in solution.



L isomer

Why D-A.a exists...?

D-Amino acid residues are components of many of the short (20 a.a residues) bacterial polypeptides that are enzymatically rather than ribosomally synthesized.



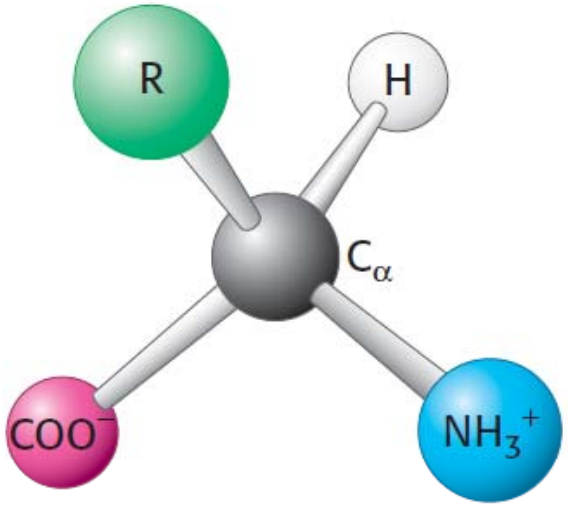
These polypeptides are usually the components of peptidoglycan cell walls of bacteria.

D-amino acids render less susceptible to attack by the peptidases (enzymes that hydrolyze peptide bonds).

D-amino acids are components of many bacterially produced peptide antibiotics including valinomycin, gramicidin A, and actinomycin D.

D-serine may act as a neurotransmitter in the brain

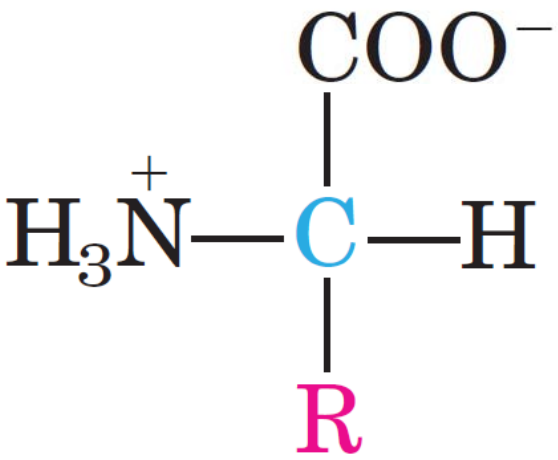
D-amino acids are found in some proteins produced by enzyme posttranslational modifications after translation and translocation to the endoplasmic reticulum, as in sea-dwelling organisms such as cone snails.



D isomer

These D-amino acid residues are posttranslationally formed, through the enzymatically mediated inversion of the preexisting L-amino acid residues.

D-serine may act as a neurotransmitter in the brain.[37] D-amino acids are used in racemic crystallography to create centrosymmetric crystals, which (depending on the protein) may allow for easier and more robust protein structure determination.[38] TheL and D convention for amino acid configuration refers not to the optical activity of the amino acid itself but rather to the optical activity of the isomer of glyceraldehyde from which that amino acid can, in theory, be synthesized (D-glyceraldehyde is dextrorotatory; L-glyceraldehyde is levorotatory). In alternative fashion, the (S) and (R) designators are used to indicate the absolute stereochemistry. Almost all of the amino acids in proteins are (S) at the α carbon, with cysteine being (R) and glycine non-chiral.[39] Cysteine has its side-chain in the same geometric position as the other amino acids, but the R/S terminology is reversed because of the higher atomic number of sulfur compared to the carboxyl oxygen gives the side-chain a higher priority, whereas the atoms in most other side-chains give them lower priority.



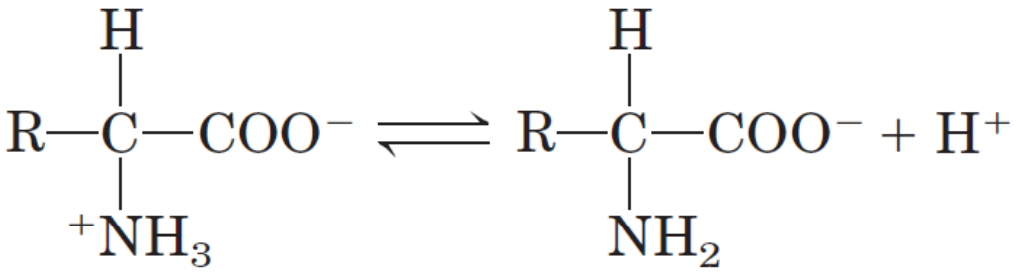
Side chains or R groups, which vary in structure, size, and electric charge, and which influence the solubility of the amino acids in water.

Because each of these amino acids has a side chain with distinctive chemical properties, this group of 20 precursor molecules may be regarded as the alphabet in which the language of protein structure is written.

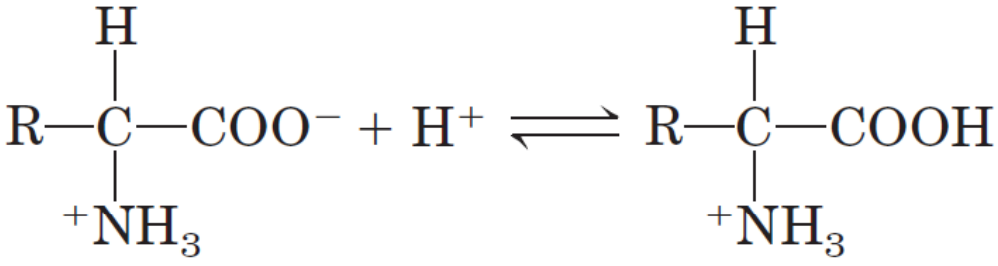
Amino Acids Can Act as Acids and Bases

When an amino acid is dissolved in water, it exists in solution as the dipolar ion, or Zwitterion (German for "hybrid ion") at pH 7.

A zwitterion can act as either an acid (proton donor) or a base (proton acceptor)

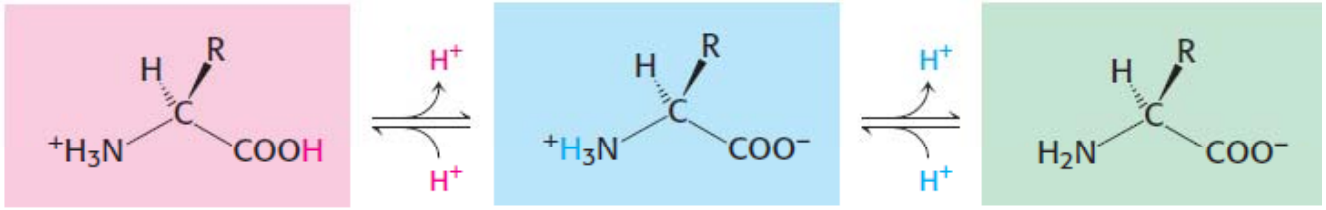


Zwitterion



Zwitterion

Amino acids in solution at neutral pH exist predominantly as dipolar ions (also called zwitterions). In the dipolar form, the amino group is protonated (-NH3+) and the carboxyl group is deprotonated (-COO-).
The ionization state of an amino acid varies with pH.
In acid solution, the amino group is protonated (-NH3+) and the carboxyl group is not dissociated (-COOH).



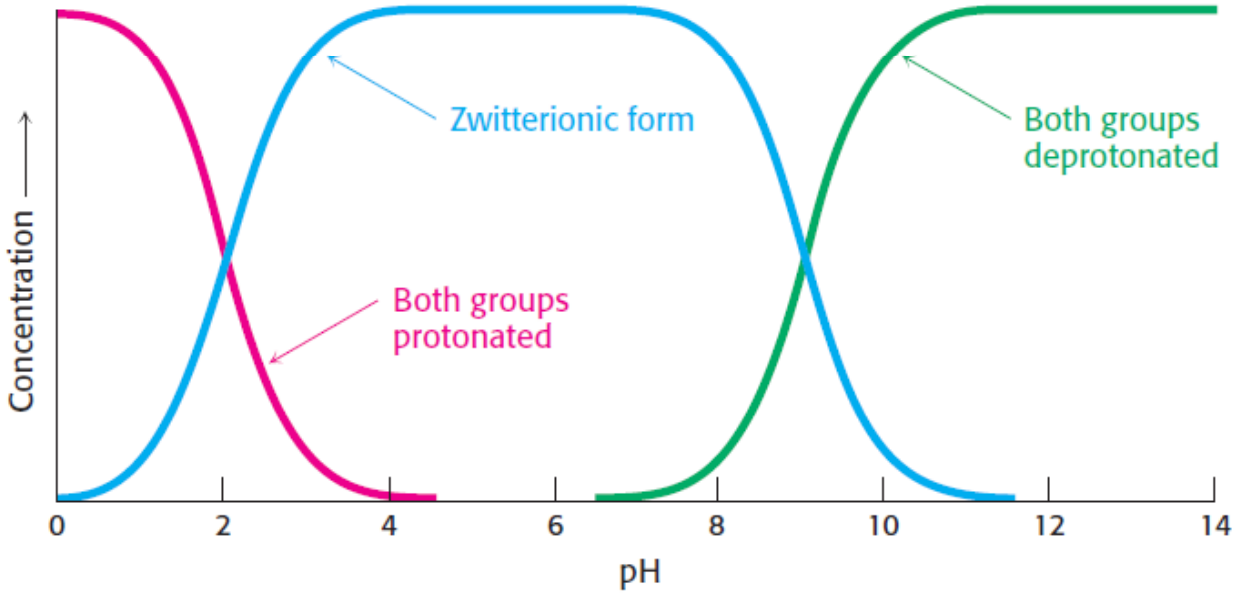


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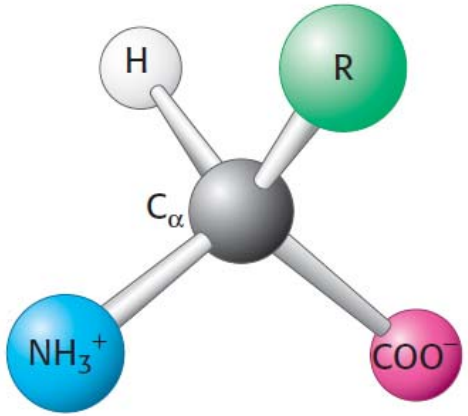
Table 2.2 Abbreviations for amino acids

Amino acid	Three-letter abbreviation	One-letter abbreviation	Amino acid	Three-letter abbreviation	One-letter abbreviation
Alanine	Ala	A	Methionine	Met	M
Arginine	Arg	R	Phenylalanine	Phe	F
Asparagine	Asn	N	Proline	Pro	P
Aspartic acid	Asp	D	Serine	Ser	S
Cysteine	Cys	C	Threonine	Thr	T
Glutamine	Gln	Q	Tryptophan	Trp	W
Glutamic acid	Glu	E	Tyrosine	Tyr	Y
Glycine	Gly	G	Valine	Val	V
Histidine	His	H	Asparagine or aspartic acid	Asx	B
Isoleucine	Ile	I	Glutamine or glutamic acid	Glx	Z
Leucine	Leu	L			
Lysine	Lys	K			

Classification

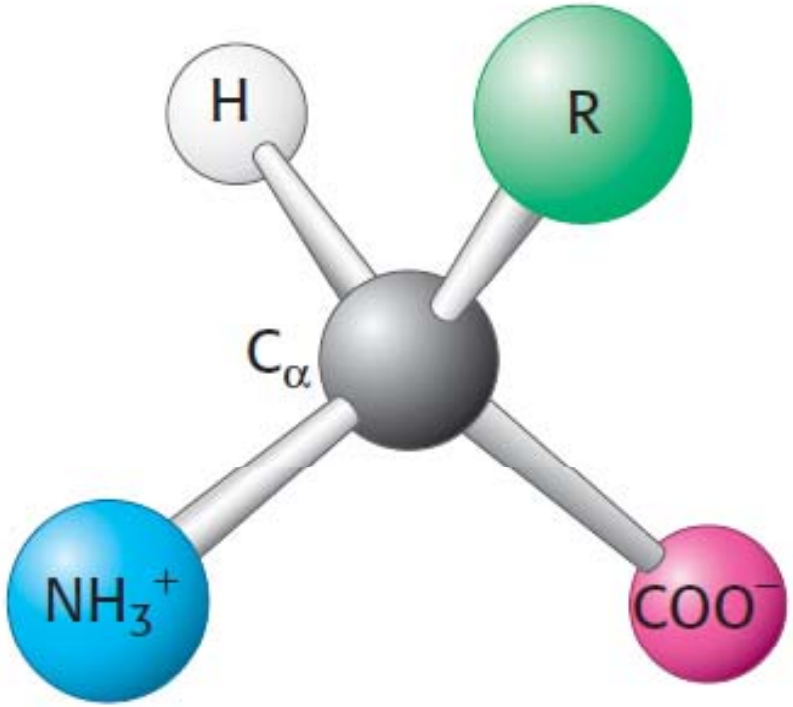


Amino acids can be classified by R group

Chemical properties of the common amino acids is determined by the R group.

Twenty kinds of side chains varying in size, shape, charge, hydrogen bonding capacity, hydrophobic character, and chemical reactivity.

Amino acids are divided into five main classes based on the properties of their R groups; mostly base on their polarity, or tendency to interact with water at biological pH (near ph 7.0).

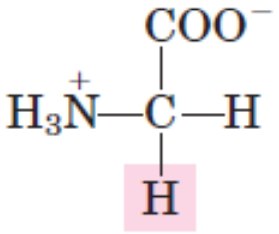


The polarity of the R groups varies widely, from non polar and hydrophobic (water-insoluble) to highly polar and hydrophilic (water-soluble).

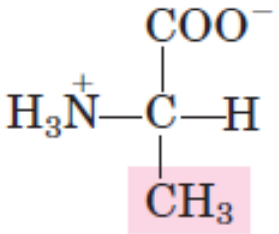
Within each class there are gradations of polarity, size, and shape of the R groups

1. Nonpolar Aliphatic R Groups

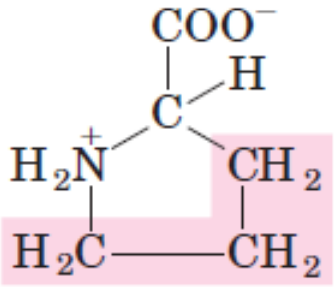
The R groups are nonpolar and hydrophobic.



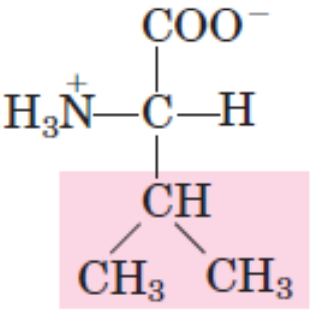
Glycine



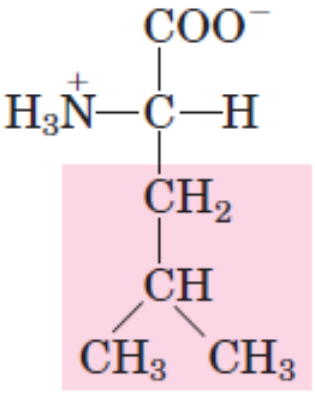
Alanine



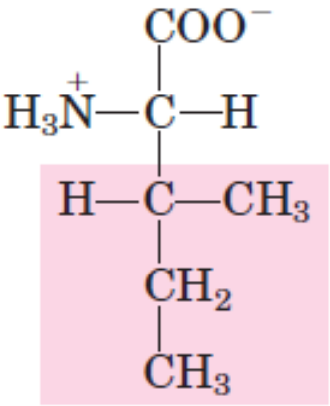
Proline



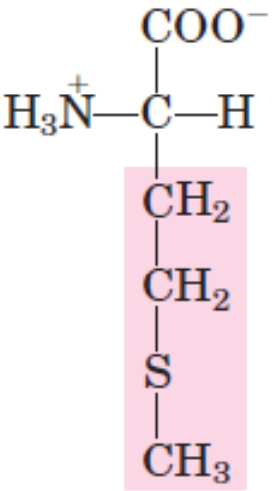
Valine



Leucine



Isoleucine



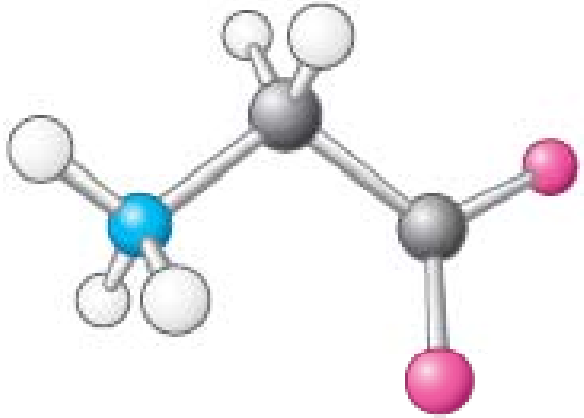
Methionine

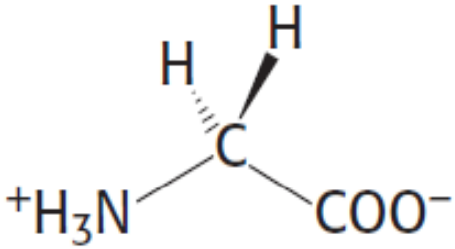
Glycine is the simplest amino acid.

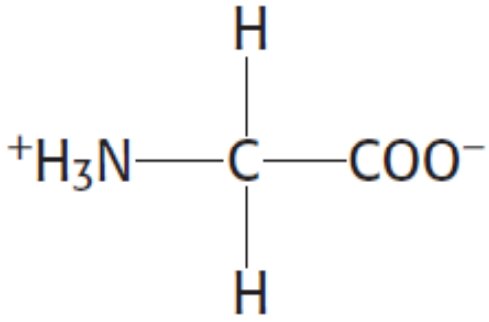
has a single hydrogen atom as its side chain.

With two hydrogen atoms bonded to the a-carbon atom, glycine is unique in being achiral.

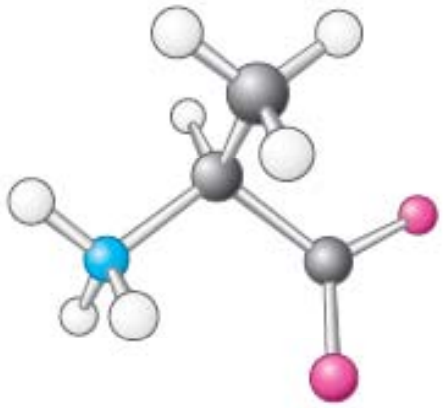
its very small side chain makes no real contribution to hydrophobic interactions

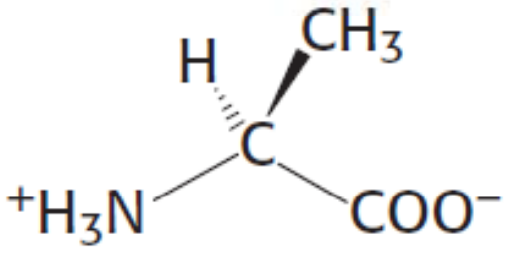






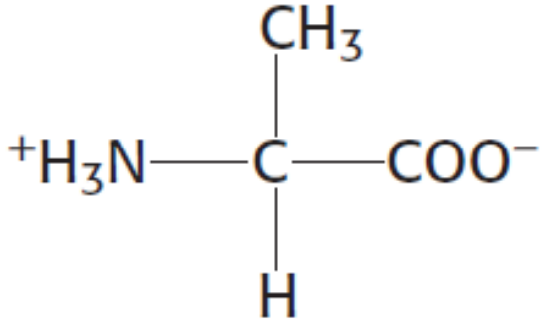
Glycine
(Gly, G)





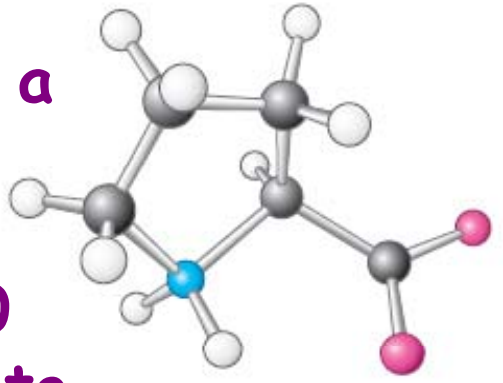
Alanine, the next simplest amino acid

has a methyl group (-CH3) as its side chain

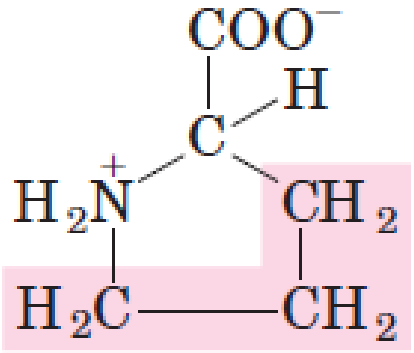


Alanine
(Ala, A)

Proline has an aliphatic side chain with a distinctive cyclic structure.

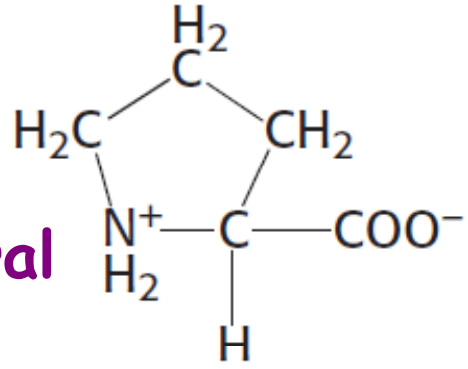


It completely differs from other of 20 a.as in its side chain, which is bonded to both the nitrogen and the a-carbon atoms.

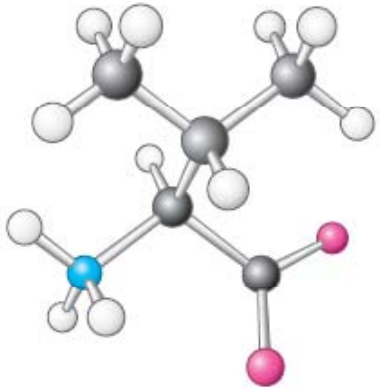


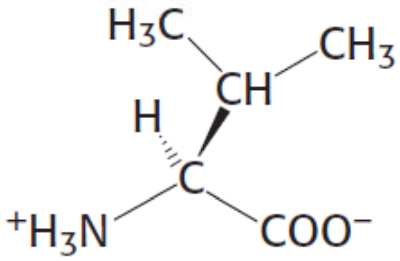
Proline markedly influences protein secondary structure because its ring structure makes it more conformationally restricted than the other amino acids.

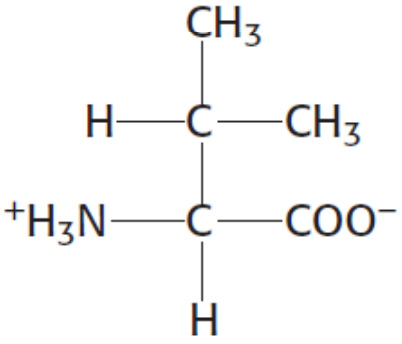
Proline residues is held in a rigid conformation that reduces the structural flexibility of polypeptide regions containing proline.



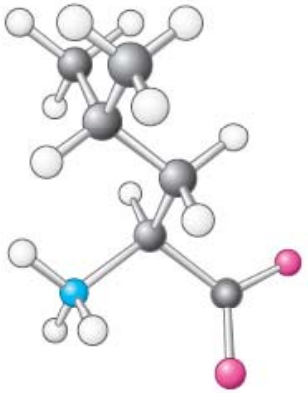
Proline (Pro, P)

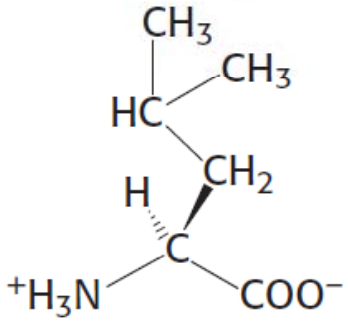


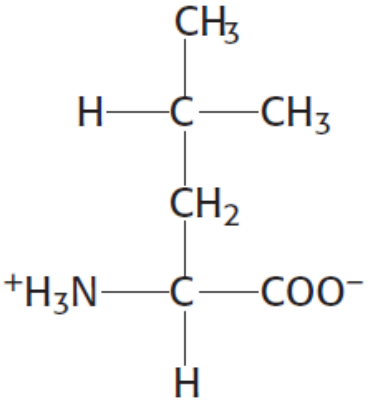




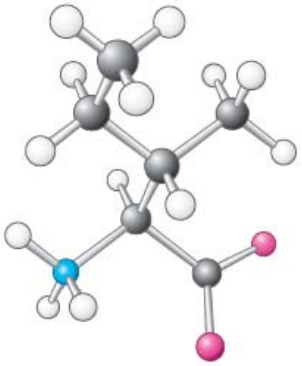
Valine
(Val, V)

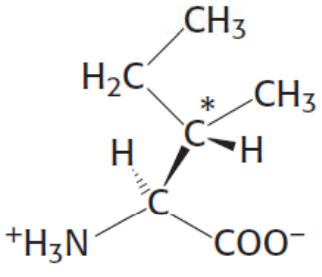


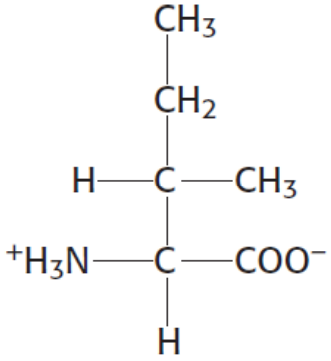




Leucine
(Leu, L)



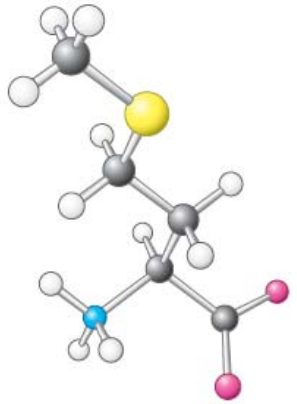


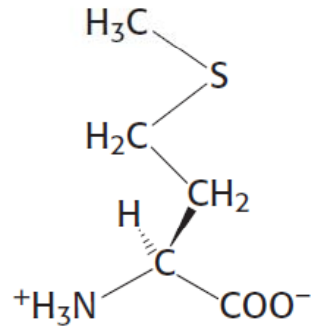


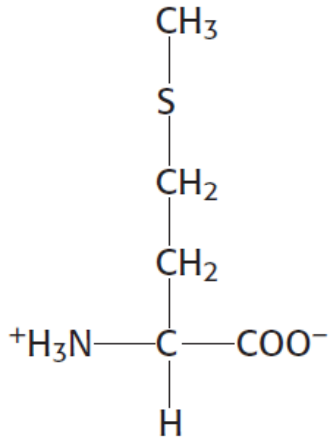
Isoleucine
(Ile, I)

Larger hydrocarbon side chains are found in valine, leucine, and isoleucine.

Methionine, one of the two sulfur containing amino acids, has a nonpolar thioether (-S-) group in its side chain.





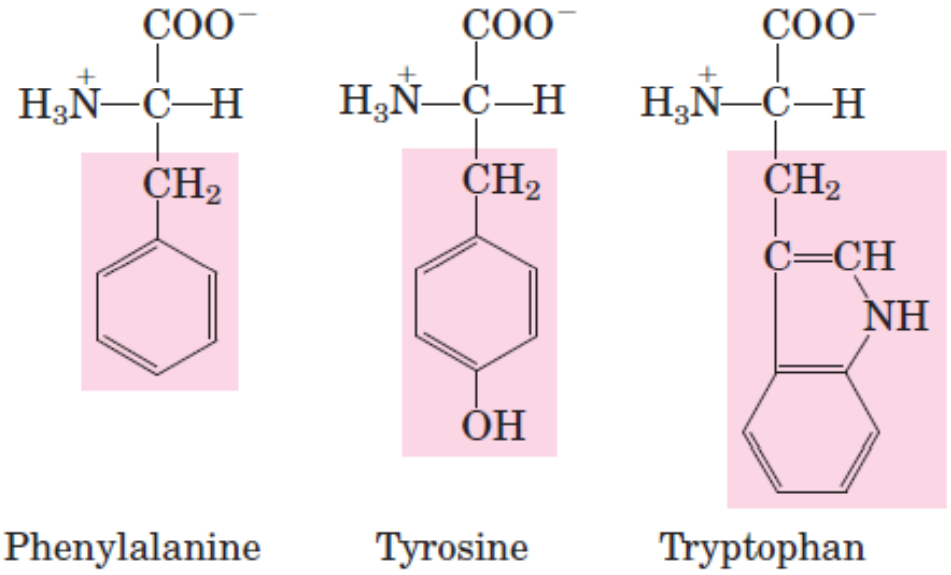


Methionine
(Met, M)

2. Aromatic R Groups

With their aromatic side chains and are relatively nonpolar (hydrophobic).

All can participate in hydrophobic interactions.



Phenylalanine Tyrosine Tryptophan

Tryptophan and tyrosine, and to a much lesser extent phenylalanine, absorb ultraviolet light.

This accounts for the characteristic strong absorbance of light by most proteins at a wavelength of 280 nm, a property exploited in the characterization of proteins.

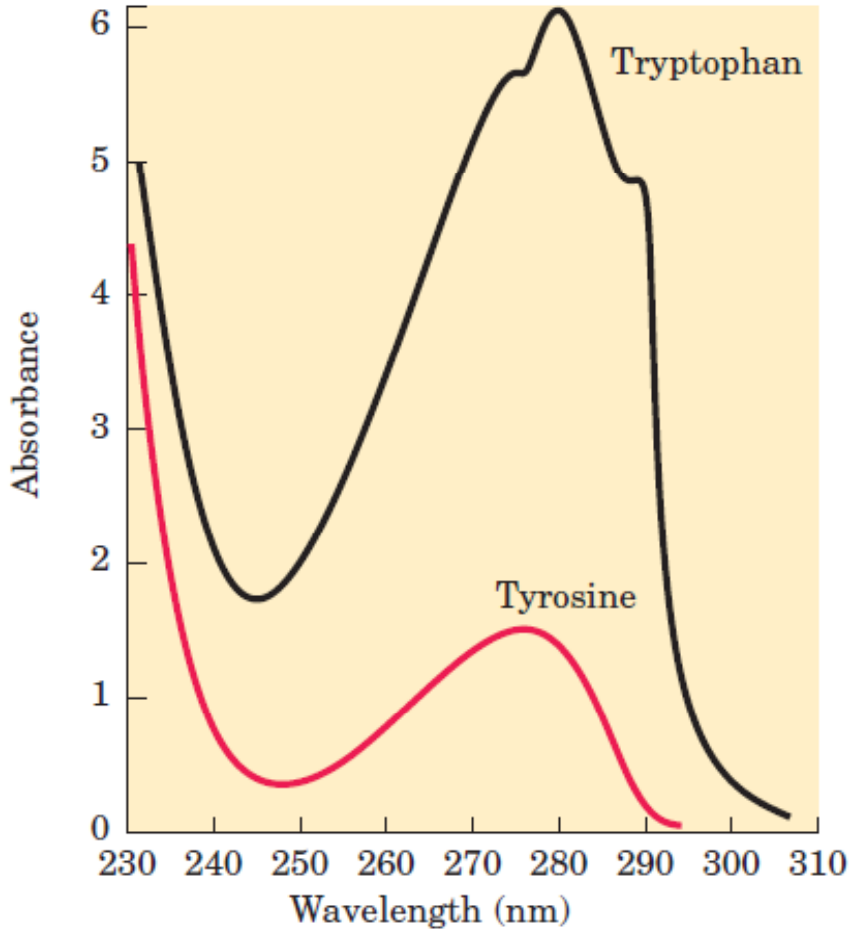
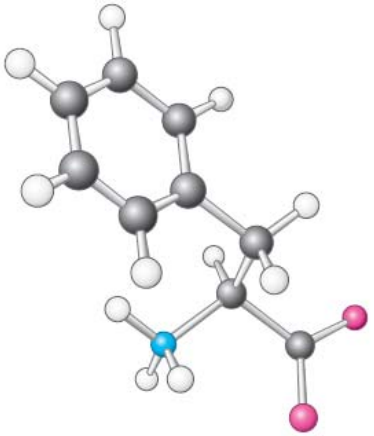
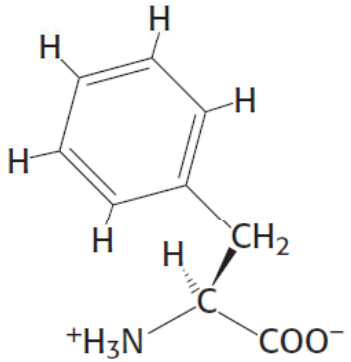
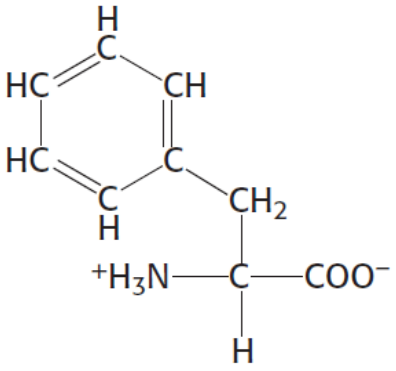


FIGURE 3–6 Absorption of ultraviolet light by aromatic amino acids. Comparison of the light absorption spectra of the aromatic amino acids tryptophan and tyrosine at pH 6.0. The amino acids are present in equimolar amounts (10^{-3} M) under identical conditions. The measured absorbance of tryptophan is as much as four times that of tyrosine. Note that the maximum light absorption for both tryptophan and tyrosine occurs near a wavelength of 280 nm. Light absorption by the third aromatic amino acid, phenylalanine (not shown), generally contributes little to the spectroscopic properties of proteins.



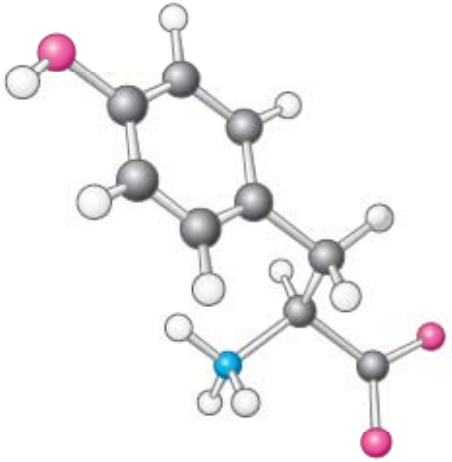


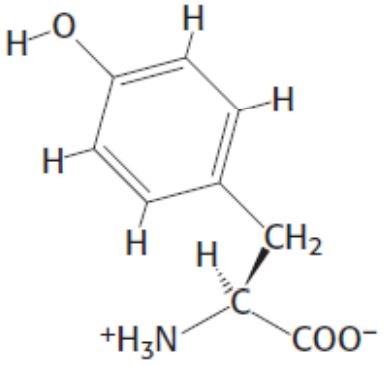


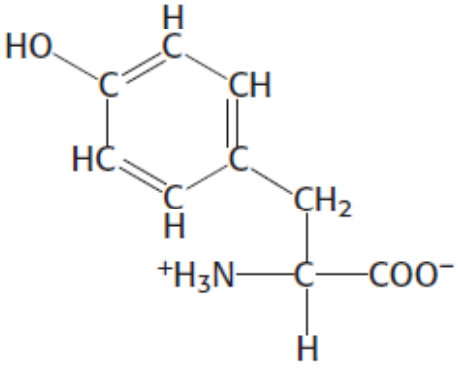
Phenylalanine
(Phe, F)

Phenylalanine, is purely hydrophobic

Tyrosine
(Tyr, Y)



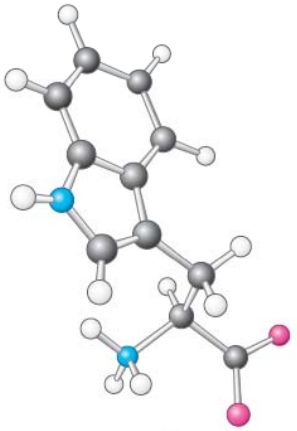


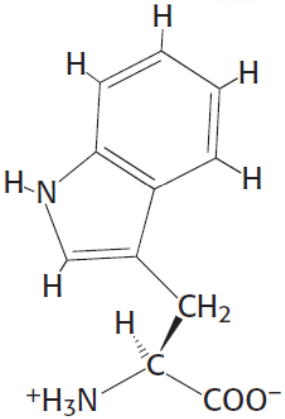


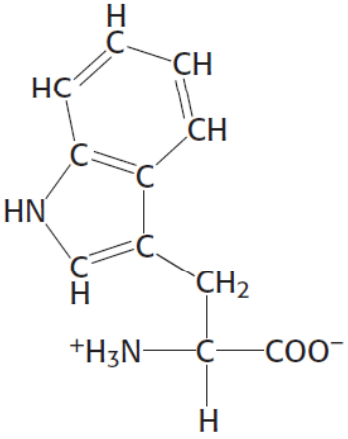
The hydroxyl group of tyrosine can form hydrogen bonds, and it is an important functional group in some enzymes.

Tyrosine and tryptophan are significantly more polar than phenylalanine, because of the tyrosine hydroxyl group and the nitrogen of the tryptophan indole ring.

Tryptophan
(Trp, W)

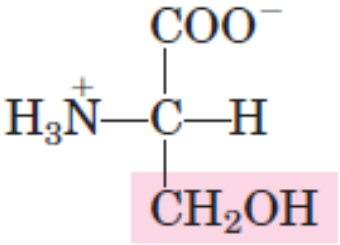




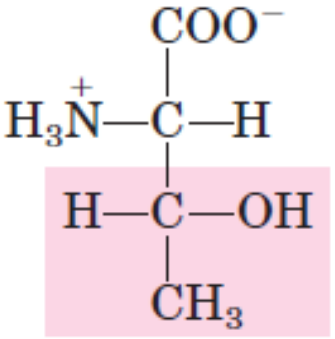


3. Polar, Uncharged R Groups

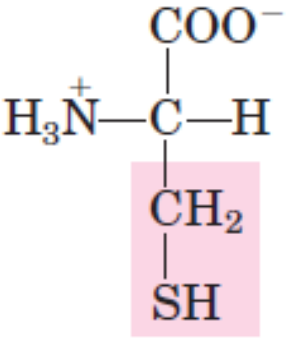
The R groups of these amino acids are more soluble in water & hydrophilic



Serine



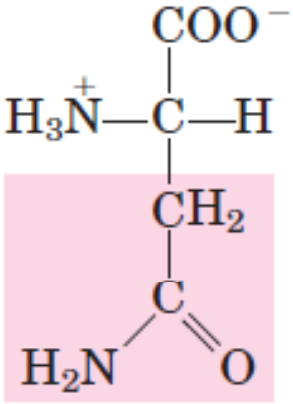
Threonine



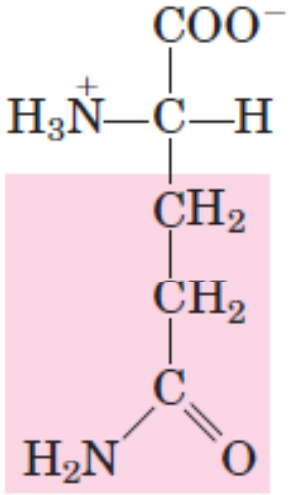
Cysteine

They contain functional groups that form hydrogen bonds with water.

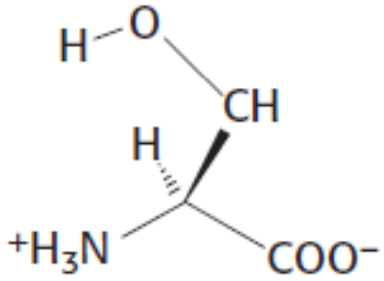
The hydroxyl group makes these amino acids much more hydrophilic (water loving) and reactive

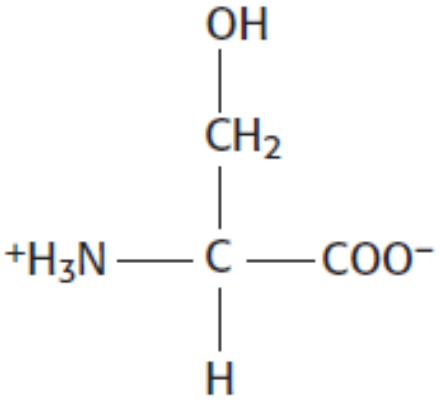


Asparagine



Glutamine



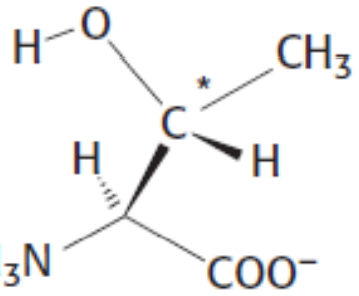


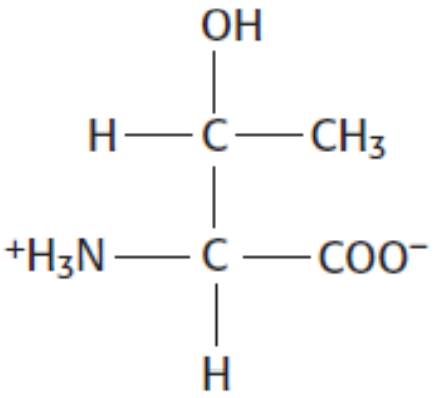
Serine
(Ser, S)

The polarity of serine is contributed by its hydroxyl group

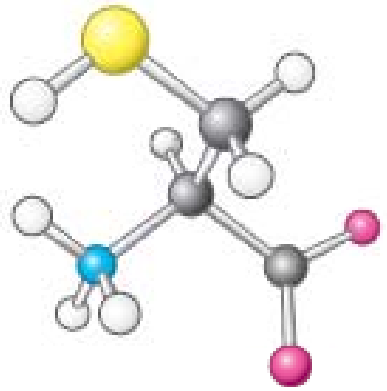
Serine can be thought of as a version of alanine with a hydroxyl group attached

The polarity of threonine is also contributed by its hydroxyl group





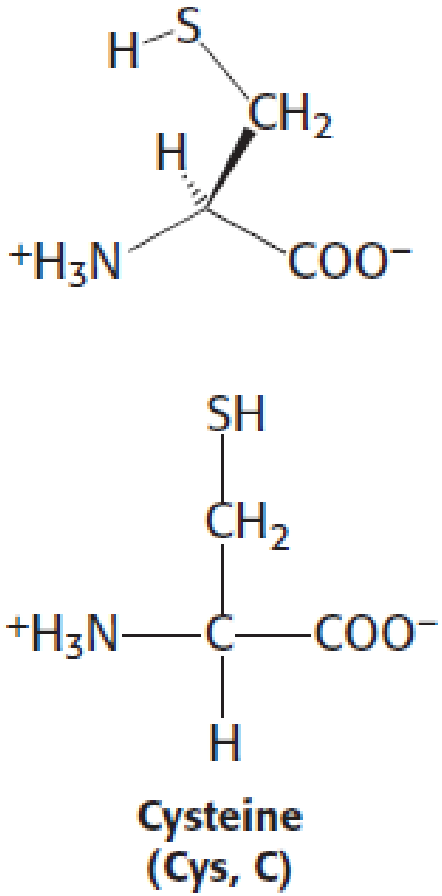
Threonine
(Thr, T)



The polarity of cysteine is contributed by the sulfhydryl group

The sulfhydryl group is much more reactive.

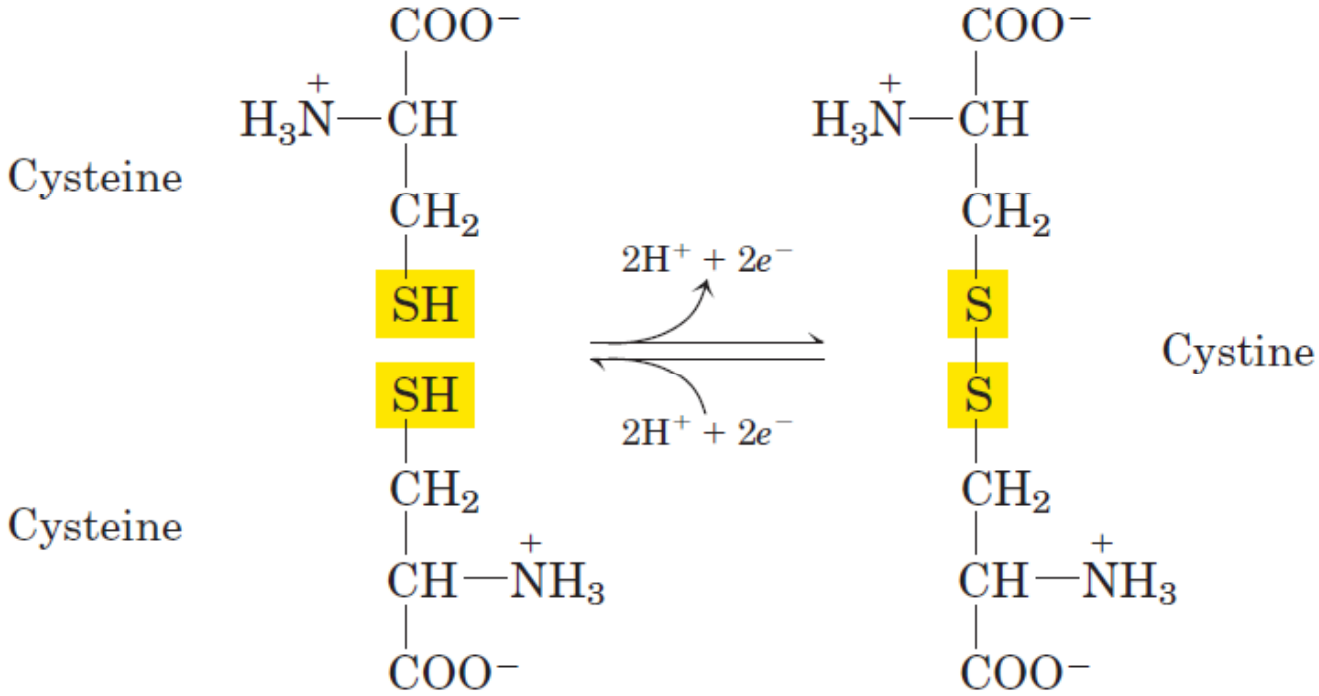
Pairs of sulfhydryl groups may come together to form disulfide bonds, which are particularly important in stabilizing some proteins,



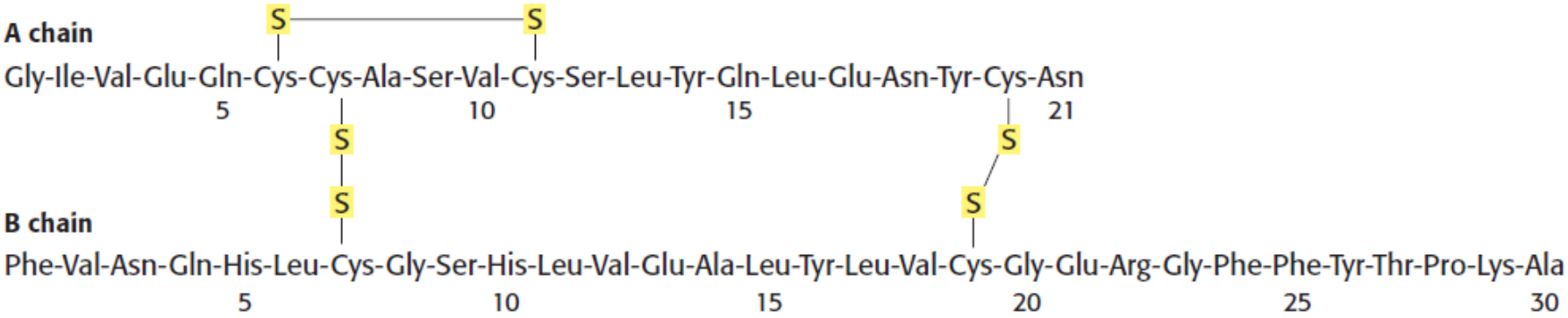
Cysteine (Cys, C)

Cysteine is readily oxidized to form a covalently linked dimeric amino acid called cystine, in which two cysteine molecules are joined by a disulfide bond.

Disulfide bonds play a special role in the structures of many proteins by forming covalent links between parts of a protein molecule or between two different polypeptide chains.

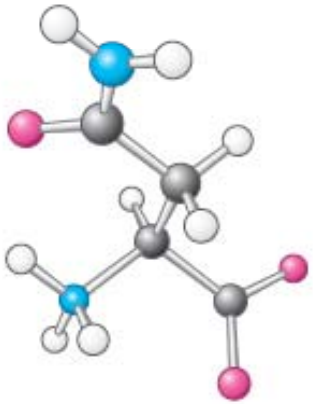


E.g., Insulin A and B chains are connected by two –S-S- bond

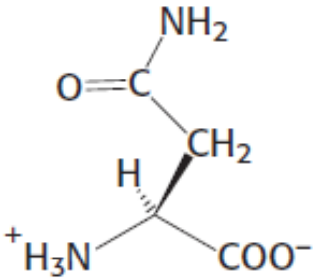


Extracellular proteins often have several disulfide bonds, whereas intracellular proteins usually lack them.

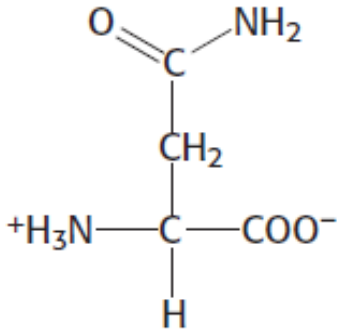
Asparagine
(Asn, N)



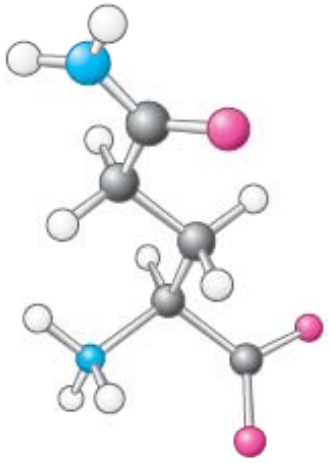
asparagine and glutamine, are derivatives of the acidic amino acids aspartate and glutamate

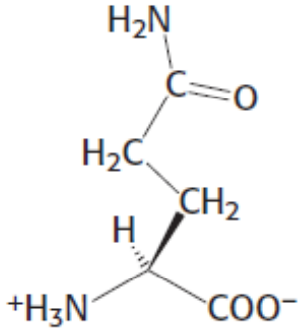


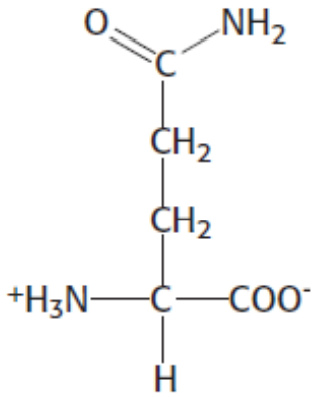
the polarity is contributed by its amide (carboxamide) group



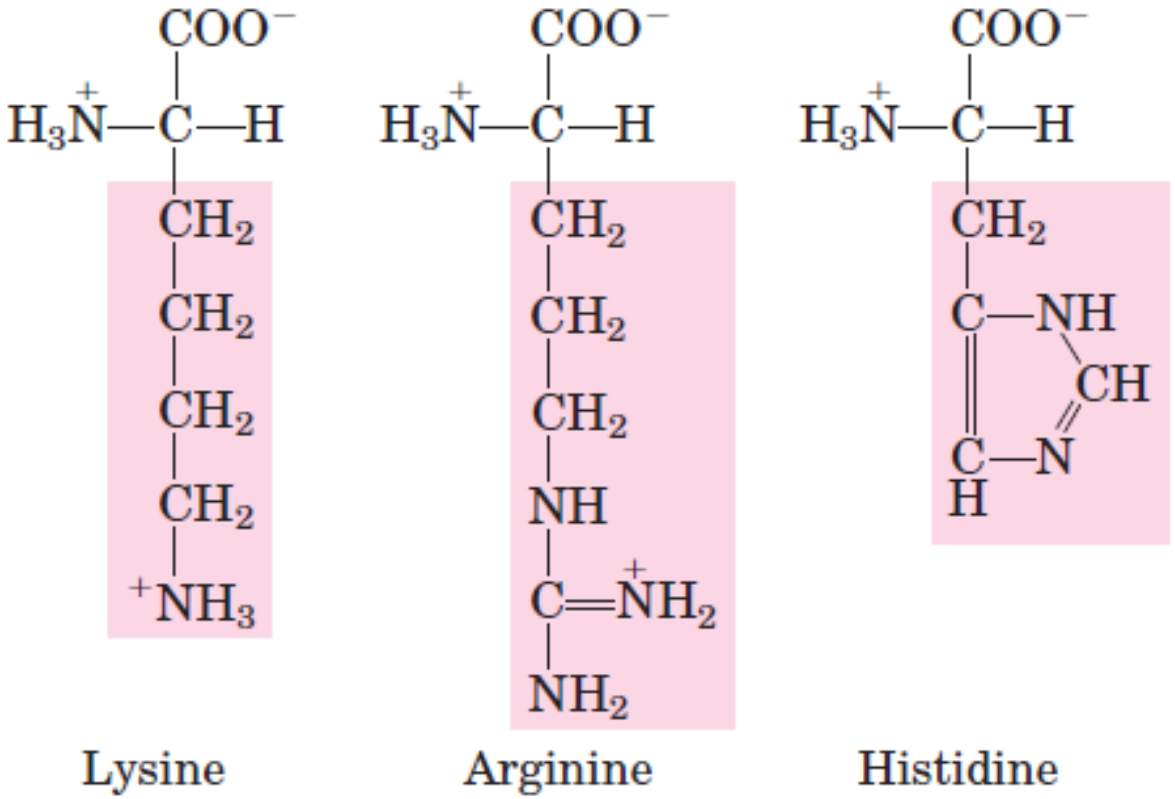
Glutamine
(Gln, Q)





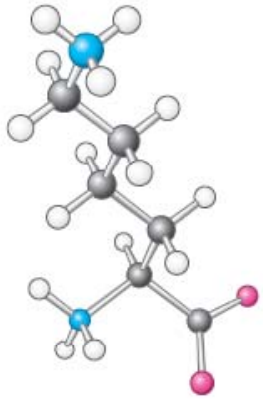


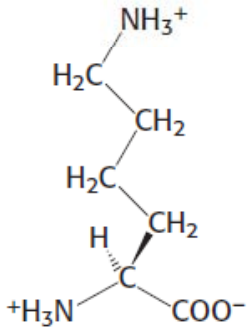
4. Positively Charged (Basic) R Groups

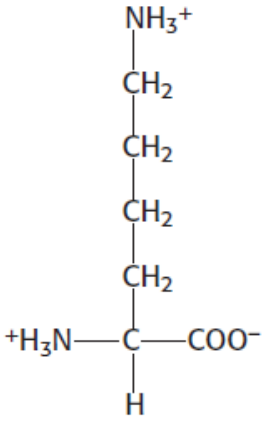


Lysine Arginine Histidine

The R groups have significant positive charge at pH 7.0; and are highly hydrophilic

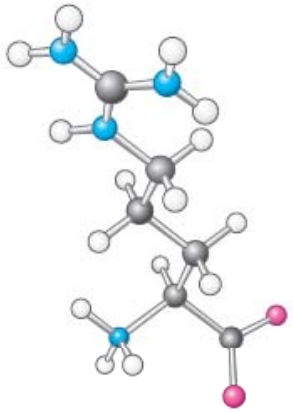


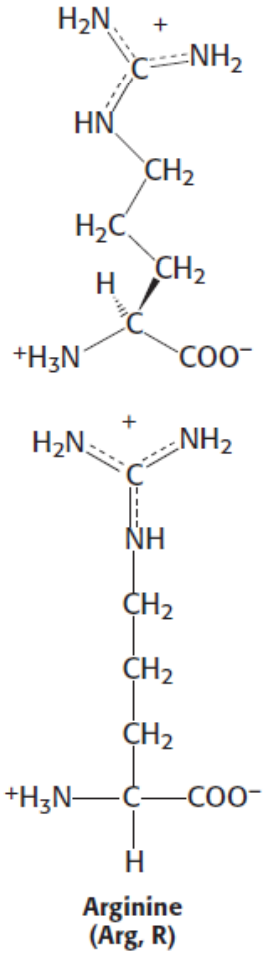




Lysine
(Lys, K)

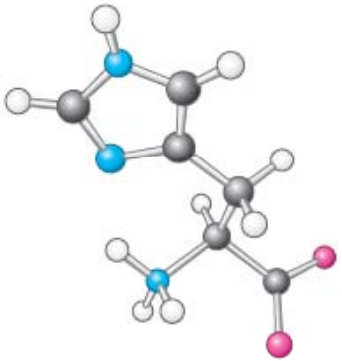
lysine, has a second amino group at the position on its aliphatic chain

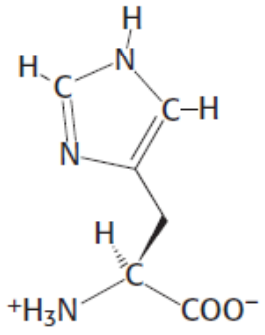




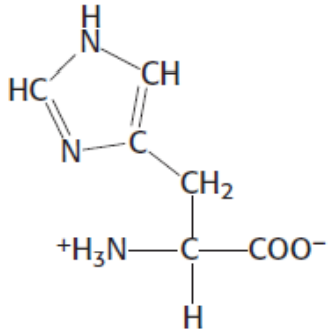
Arginine
(Arg, R)

arginine, has a positively charged guanidino group



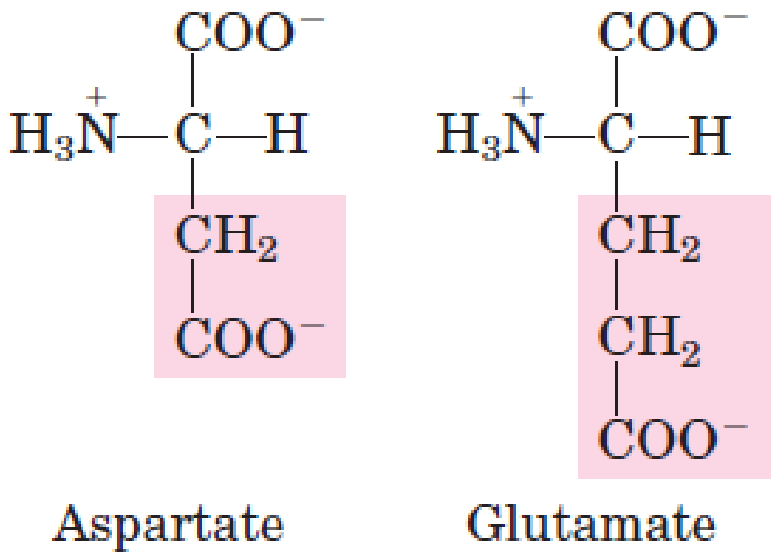


histidine, has an imidazole group. In many enzyme-catalyzed reactions, a His residue facilitates the reaction by serving as a proton donor/acceptor.



Histidine
(His, H)

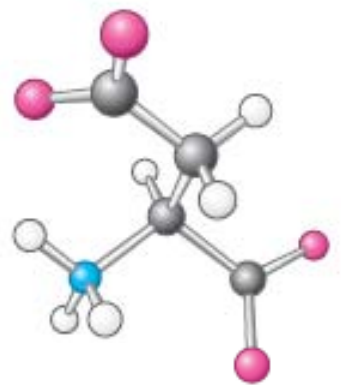
5. Negatively Charged (Acidic) R Groups

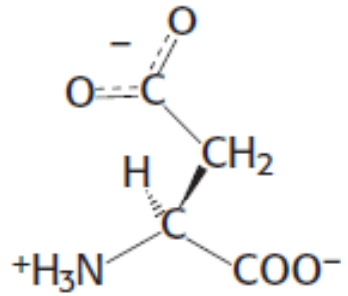


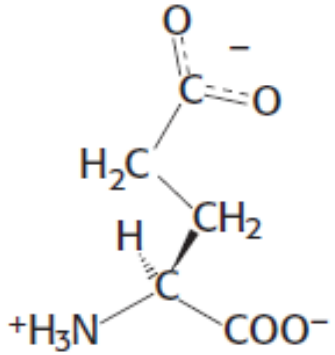
Aspartate Glutamate

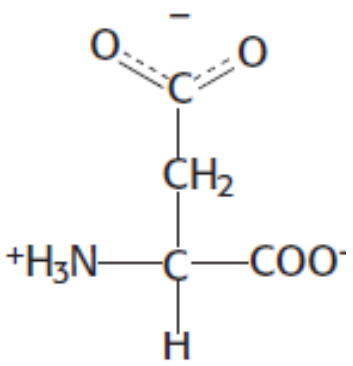
The two amino acids having R groups with a net negative charge at pH 7.0; has a second carboxyl group.

These amino acids (Aspartic acid and Glutamic acid) are often called aspartate and glutamate; because, at physiological pH, their side chains usually lack a proton that is present in the acid form and hence are negatively charged

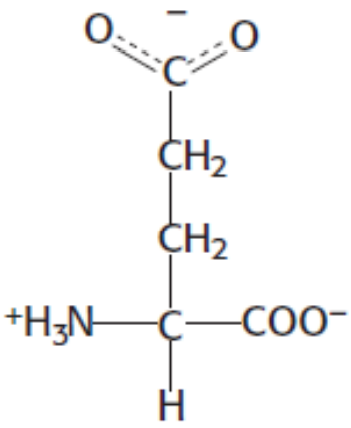








Aspartate
(Asp, D)



Glutamate
(Glu, E)

"NONSTANDARD" AMINO ACIDS

The 20 standard amino acids are not the only occurring in biological systems.

Uncommon amino acids also have important functions

"Nonstandard" amino acid residues are often important constituents of proteins and biologically active polypeptides.

All are derived from common amino acids; extra functional groups added by modification.

"NONSTANDARD" AMINO ACIDS

Amino Acids as part of Proteins

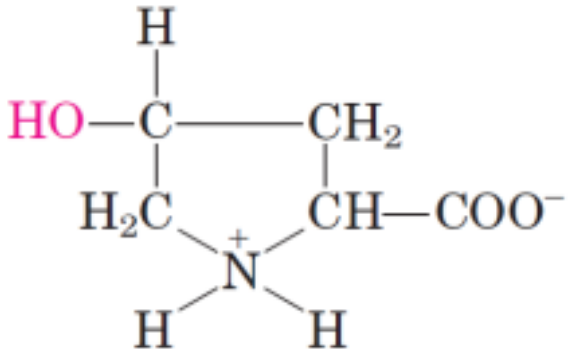
Non-Protein Functions

Amino Acids as part of Proteins

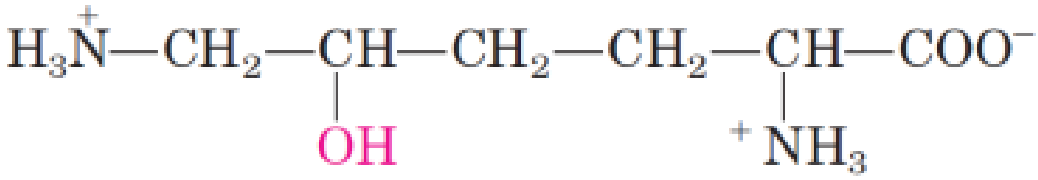
- ✓ **4-hydroxyproline**
  a derivative of proline
  found in plant cell wall proteins

- ✓ **5-hydroxylysine**
  derived from lysine

both are found in collagen, a fibrous protein of connective tissues.

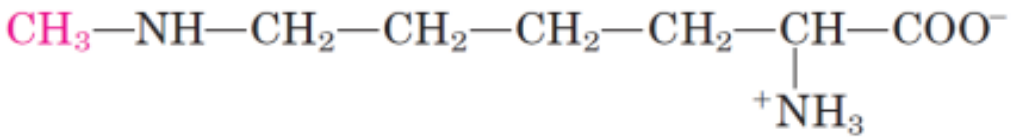


4-Hydroxyproline



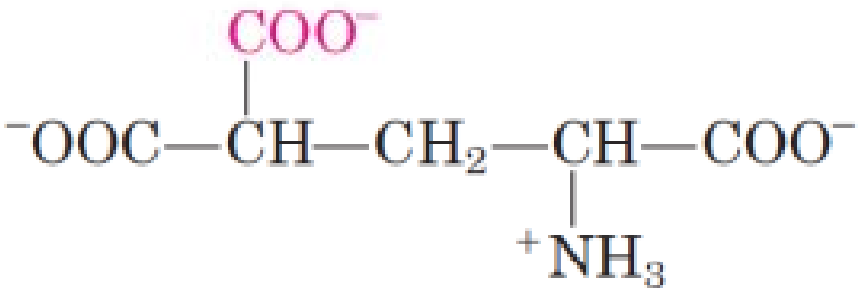
5-Hydroxylysine

- ✓ **6-N Methyl lysine**
  constituent of myosin (a contractile protein of muscle)



6-*N*-Methyllysine

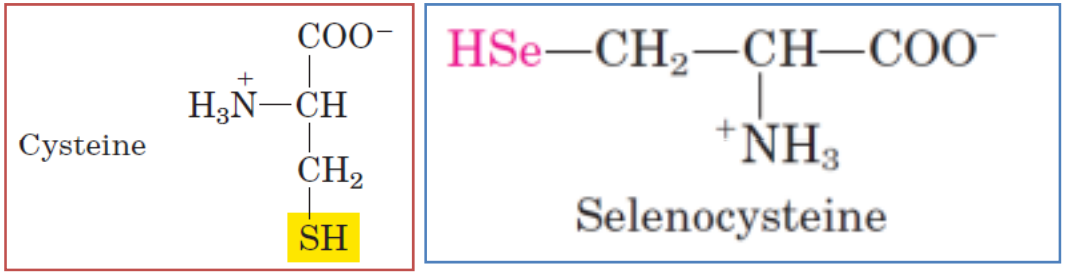
- ✓ **γ-carboxyglutamate**
  found in the blood clotting protein prothrombin and in certain calcium binding proteins



γ-Carboxyglutamate

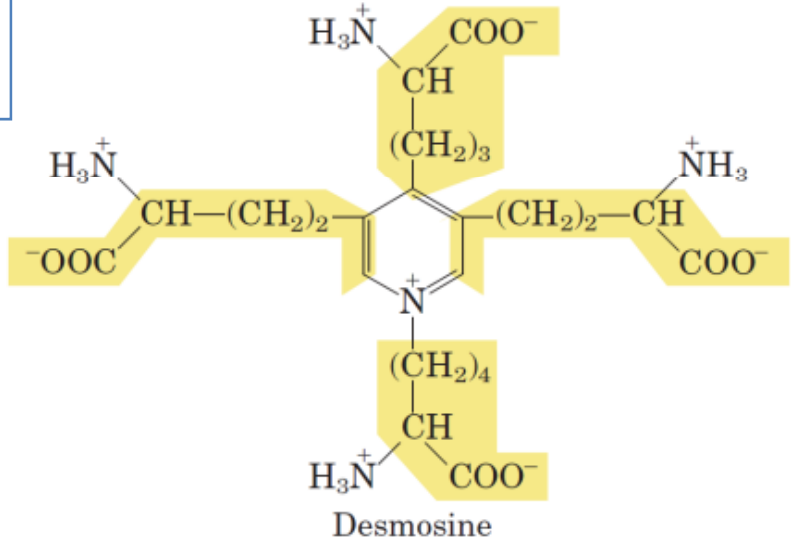
✓Selenocysteine

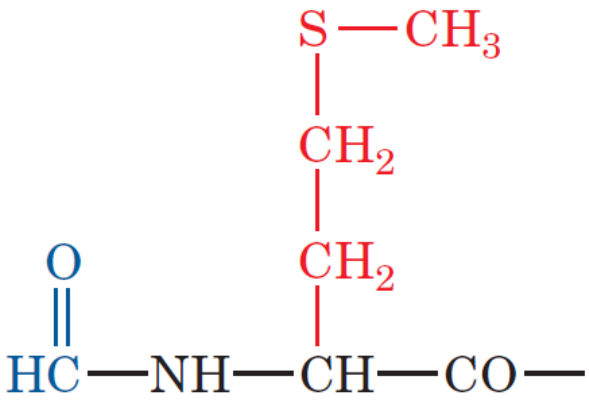
It is a special case.
This rare amino acid residue is introduced during protein synthesis rather than created through a post-synthetic modification.
It contains selenium rather than the sulfur of cysteine. Actually derived from serine, selenocysteine is a constituent of just a few known proteins.



✓ Desmosine

a derivative of four Lys
found in the fibrous protein elastin





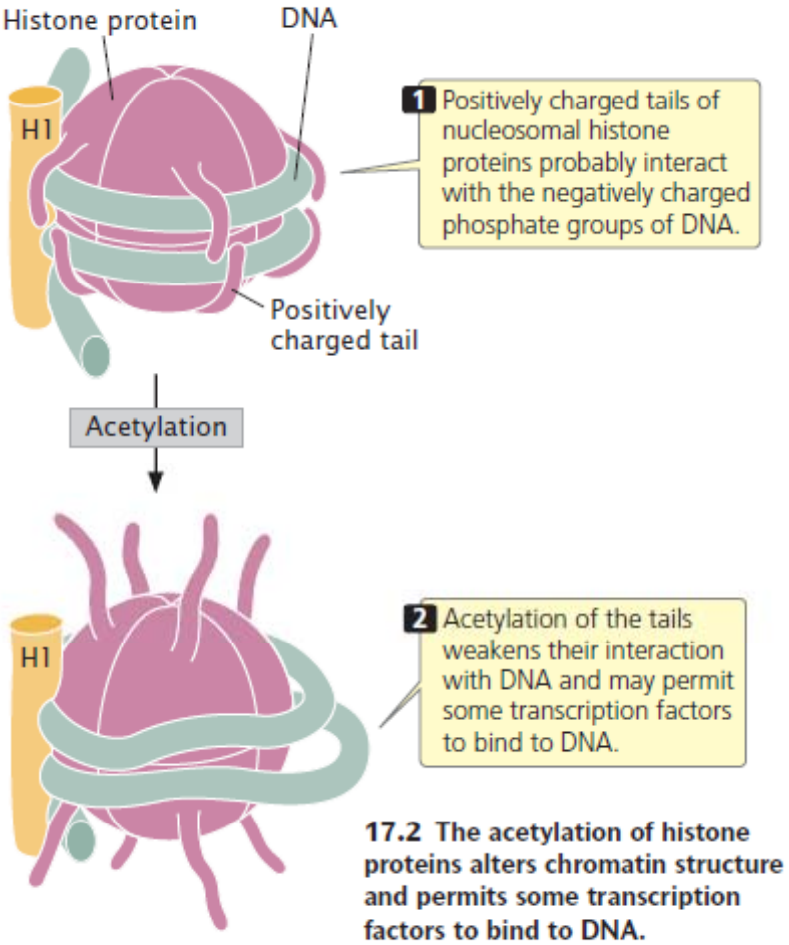
***N*-Formylmethionine**

✓ **N-Formylmethionine**

It is initially the N-terminal residue of all prokaryotic proteins,

but is usually removed as part of the protein maturation process

Modification of amino acids of histone proteins



17.2 The acetylation of histone proteins alters chromatin structure and permits some transcription factors to bind to DNA.

Amino acids of proteins that form complexes with nucleic acids are often modified.

For example, the chromosomal proteins known as histones may be mspecifically methylated, acetylated, and/or phosphorylated at specific Lys, Arg, and Ser residues.

Over 700 different amino acids have been found in various plants, animals, fungi, and bacteria.

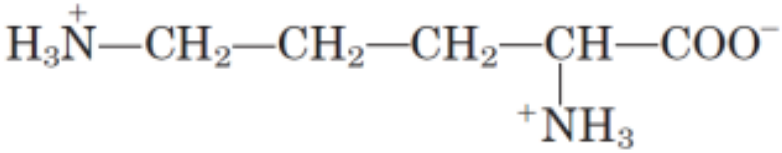
But many amino acids are not constituents of proteins; with their derivatives, they play a variety of biologically important functions.

Non-Protein Functions

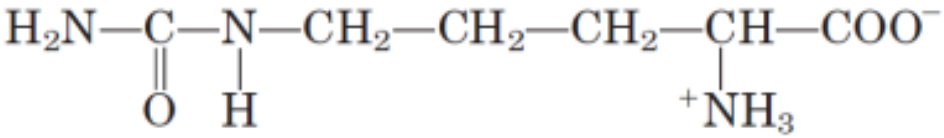
Certain amino acids are important intermediates in various metabolic processes

Ornithine & Citrulline

they are the key intermediates (metabolites) in the biosynthesis of arginine and in the urea cycle.



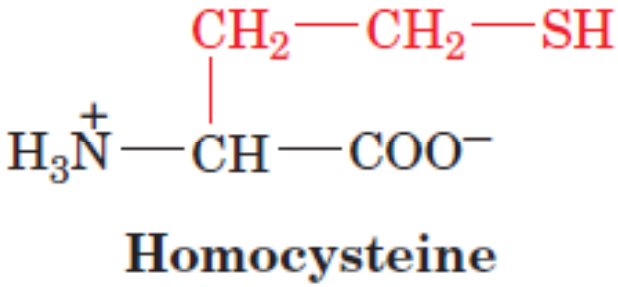
Ornithine



Citrulline

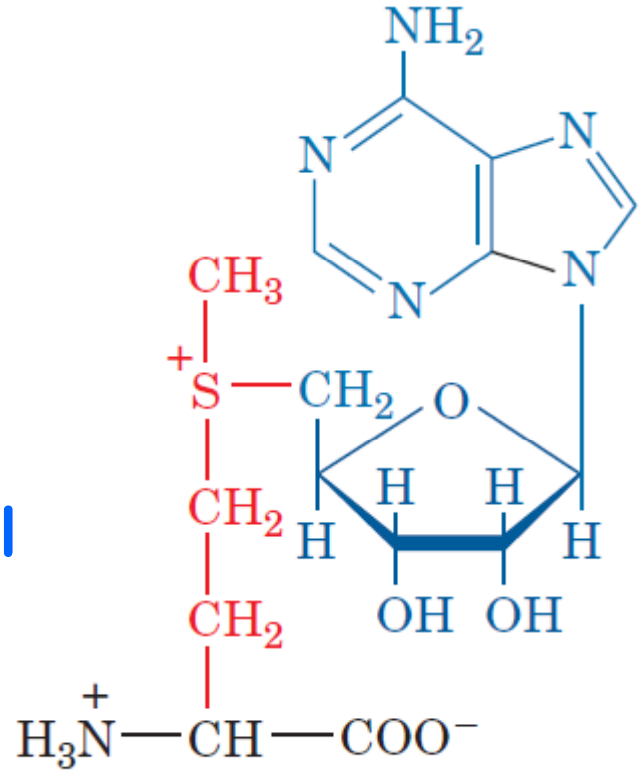
Certain amino acids are important intermediates in various metabolic processes

homocysteine, an intermediate in amino acid metabolism.



Homocysteine

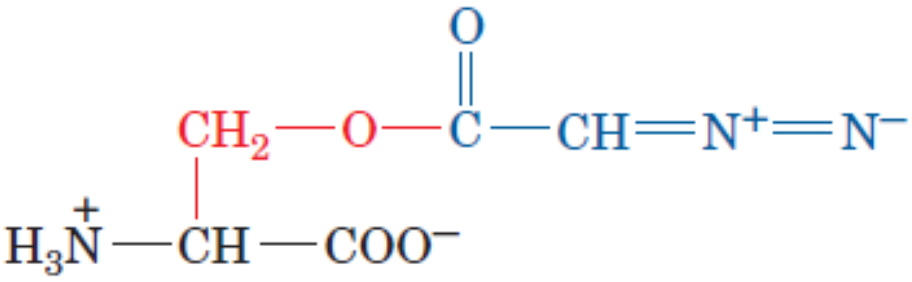
S-adenosylmethionine, a biological methylating reagent.



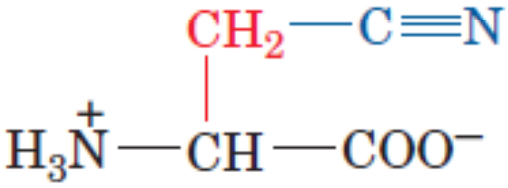
***S*-Adenosylmethionine**

Some amino acids are protective in function

Azaserine and β-cyanoalanine are medically useful antibiotics



Azaserine

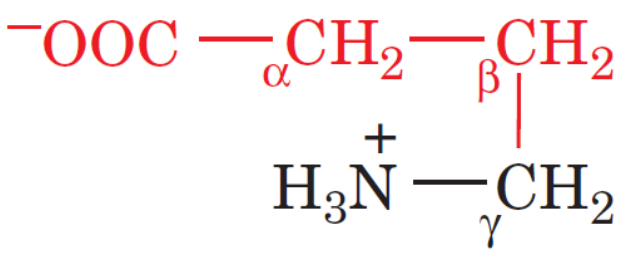


β-Cyanoalanine

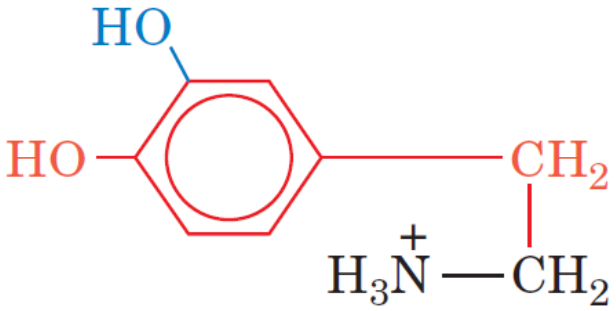
Amino acids and their derivatives often function as chemical messengers in the communications between cells.

Glycine γ-aminobutyric acid (GABA): a decarboxylation product glutamate

Dopamine: a tyrosine derivative



γ-Aminobutyric acid (GABA)

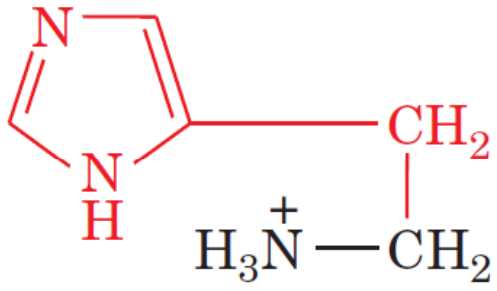


Dopamine

Both are neurotransmitters (substances released by nerve cells to alter the behaviour of their neighbours)

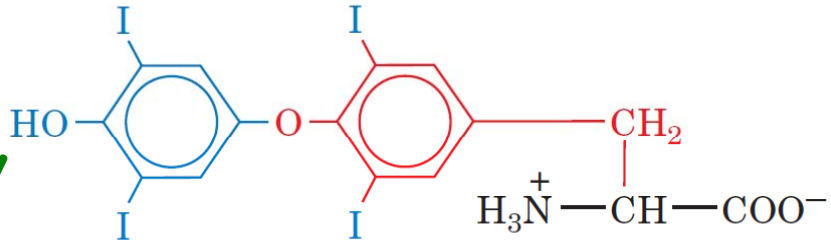
Amino acids and their derivatives often function as chemical messengers in the communications between cells.

Histamine: the decarboxylation product of histidine)
It is a potent local mediator of allergic reactions.



Histamine

Thyroxine: a tyrosine derivative
It is an iodine-containing thyroid hormone that generally stimulates vertebrate metabolism.



Thyroxine

Essential and Nonessential Amino acids

Most microorganisms, such as *E. coli*, can synthesize the entire basic set of 20 amino acids, whereas human beings cannot make 9 of them.

The amino acids that must be supplied in the diet are called essential amino acids, whereas the others are termed nonessential amino acids

Table 24.1 Basic set of 20 amino acids

Nonessential	Essential
Alanine	Histidine
Arginine	Isoleucine
Asparagine	Leucine
Aspartate	Lysine
Cysteine	Methionine
Glutamate	Phenylalanine
Glutamine	Threonine
Glycine	Tryptophan
Proline	Valine
Serine	
Tyrosine	


BREAK...

amino acids are the building blocks of proteins and the nitrogen source for many other important molecules, including nucleotides, neurotransmitters, and prosthetic, etc.

cannot make 9 of them

Many higher organisms, including human beings, have lost the ability to synthesize some amino acids and must therefore obtain adequate quantities of these essential amino acids in their diets.

Most microorganisms a entire basic set of 20 amino acids, wher ke 9 of them. The amino acids that mu called essential amino acids, whereas th ntial amino acids.

A deficiency of even one tive nitrogen balance. In this state, m s synthesized, and so more nitrogen is

Table 24.1 Basic set of 20 amino acids

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Alanine	Histidine
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Cysteine	Methionine
Glutamate	Phenylalanine
Glutamine	Threonine
Glycine	Tryptophan
Proline	Valine
Serine	
Tyrosine	

The nonessential amino acids are synthesized by quite simple reactions, whereas the pathways for the formation of the essential amino acids are quite complex.

For example, the nonessential amino acids alanine and aspartate are synthesized in a sin[illegible]acetate, respectively.

In contrast, the path[illegible]s require from 5 to 16 steps.

The sole exception t[illegible]ch as the synthesis of this nor[illegible]quires 10 steps.

Tyrosine, classified [illegible]ause it can be synthesized in 1 ste[illegible]

Table 24.1 Basic set of 20 amino acids

Nonessential	Essential
Alanine	Histidine
Arginine	Isoleucine
Asparagine	Leucine
Aspartate	Lysine
Cysteine	Methionine
Glutamate	Phenylalanine
Glutamine	Threonine
Glycine	Tryptophan
Proline	Valine
Serine	
Tyrosine	

Biosynthesis of Amino acids

Ref.
Biochemistry- Robert Horton (V) P.514
Biochemistry- Stryer (VII) P.705
Plant Physiology(V)-Taiz and Zeiger P.343

keep in mind...

Nitrogen fixation

- ✓ Breaking of stable triple covalent bond between two nitrogen atoms (N_2) to produce ammonia or nitrate
- ✓ By both industrial and natural processes

Industrial (Haber–Bosch process): about 200°C temperature and high pressure (200 atm) N_2 combines with hydrogen to form ammonia.

Natural processes

a. **Lightning**: Lightning converts water vapor and oxygen into highly reactive hydroxyl free radicals, free hydrogen atoms, and free oxygen atoms that attack molecular nitrogen (N_2) to form nitric acid (HNO_3). This nitric acid subsequently falls to Earth with rain.
b. **Photochemical reactions**: reactions between gaseous nitric oxide (NO) and ozone (O_3) that produce nitric acid (HNO_3).
c. **Biological nitrogen fixation**: bacteria or blue-green algae (cyanobacteria) fix N_2 into ammonium (NH_4^+).

keep in mind...

Nitrate Assimilation

Plants assimilate most of the nitrate absorbed by their roots into organic nitrogen compounds.

Step I: the reduction of nitrate to nitrite by nitrate reductase enzyme in the cytosol

$$NO_3^- + NAD(P)H + H^+ + 2\,e^- \rightarrow NO_2^- + NAD(P)^+ + H_2O$$

Step II: the enzyme nitrite reductase converts nitrite to ammonium

$$NO_2^- + 6\,Fd_{red} + 8\,H^+ + 6\,e^- \rightarrow NH_4^+ + 6\,Fd_{ox} + 2\,H_2O$$

keep in mind...

Formation of Ammonia by Biological Nitrogen Fixation

In biological nitrogen fixation, the nitrogenase enzyme complex fixes N_2 into ammonia

$$N_2 + 8\,e^- + 8\,H^+ + 16\,ATP \rightarrow 2\,NH_3 + H_2 + 16\,ADP + 16\,P_i$$

Examples of organisms that can carry out nitrogen fixation

Symbiotic nitrogen fixation	
Host plant	**N-fixing symbionts**
Leguminous: legumes, *Parasponia*	*Azorhizobium*, *Bradyrhizobium*, *Photorhizobium*, *Rhizobium*, *Sinorhizobium*
Actinorhizal: alder (tree), *Ceanothus* (shrub), *Casuarina* (tree), *Datisca* (shrub)	*Frankia*
Gunnera	*Nostoc*
Azolla (water fern)	*Anabaena*
Sugarcane	*Acetobacter*
Free-living nitrogen fixation	
Type	**N-fixing genera**
Cyanobacteria (blue-green algae)	*Anabaena*, *Calothrix*, *Nostoc*
Other bacteria	
Aerobic	*Azospirillum*, *Azotobacter*, *Beijerinckia*, *Derxia*
Facultative	*Bacillus*, *Klebsiella*
Anaerobic	
Nonphotosynthetic	*Clostridium*, *Methanococcus* (archaebacterium)
Photosynthetic	*Chromatium*, *Rhodospirillum*

keep in mind...

Nitrogen uptake from the Symbiotic Partner

The symbiotic nitrogen-fixing prokaryotes release ammonia; to avoid toxicity, it is rapidly converted into organic forms in the root nodules before being transported to the shoot via the xylem.

Nitrogen-fixing legumes can be divided into amide exporters or ureide exporters on the basis of the composition of the xylem sap.

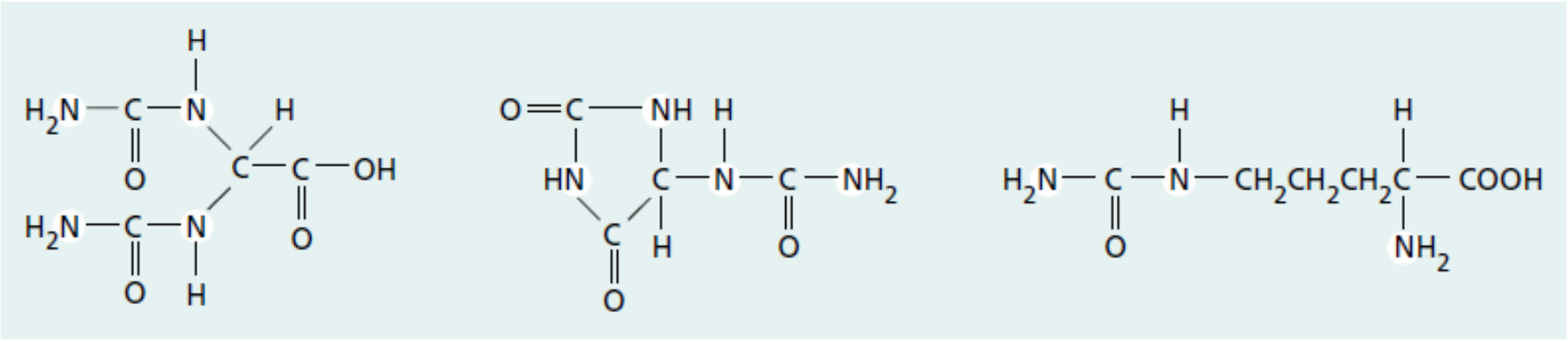
keep in mind...

Amides and Ureides are the Transported Forms of Nitrogen

- ✓ Amides (asparagine or glutamine) are exported by temperate-region legumes (Pisum,Trifolium, broad bean, etc)
- ✓ Ureides are exported by legumes of tropical origin (soybean, kidney bean, peanut, etc)
- ✓ The three major ureides are allantoin, allantoic acid, and citrulline.
- ✓ All three compounds are ultimately released into the xylem and transported to the shoot, where they are rapidly catabolized to ammonium.
- ✓ This ammonium enters the assimilation pathway.

keep in mind...

the three major ureides



Allantoic acid

Allantoin

Citrulline

keep in mind...

Ammonium Assimilation

Plant cells avoid ammonium toxicity by rapidly converting the ammonium generated from nitrate assimilation into amino acids

Glutamate and glutamine are the primarily formed amino acids

Two Pathways:

(a) glutamate dehydrogenase pathway

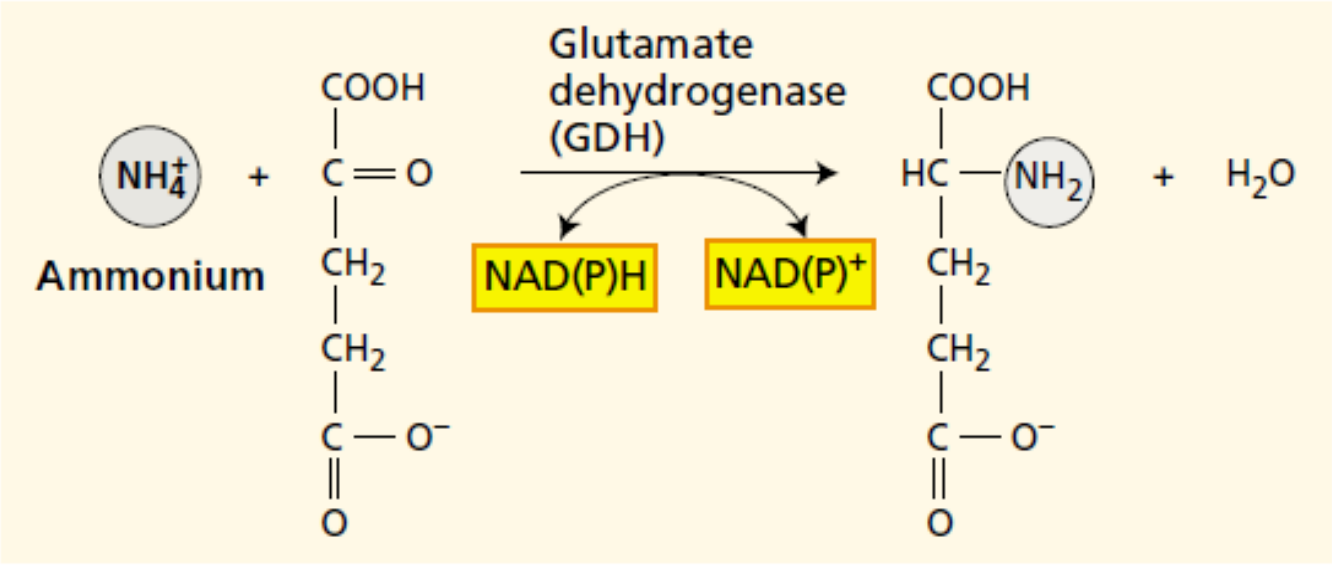
(b) Combined action of glutamine synthetase and glutamate synthase under conditions of low NH_4^+ concentration

keep in mind...

Glutamate Dehydrogenase Pathway

Ammonium can be assimilated via an alternative pathway

Glutamate dehydrogenase (GDH) catalyzes a synthesis of glutamate from 2-Oxoglutarate by the addition of ammonium

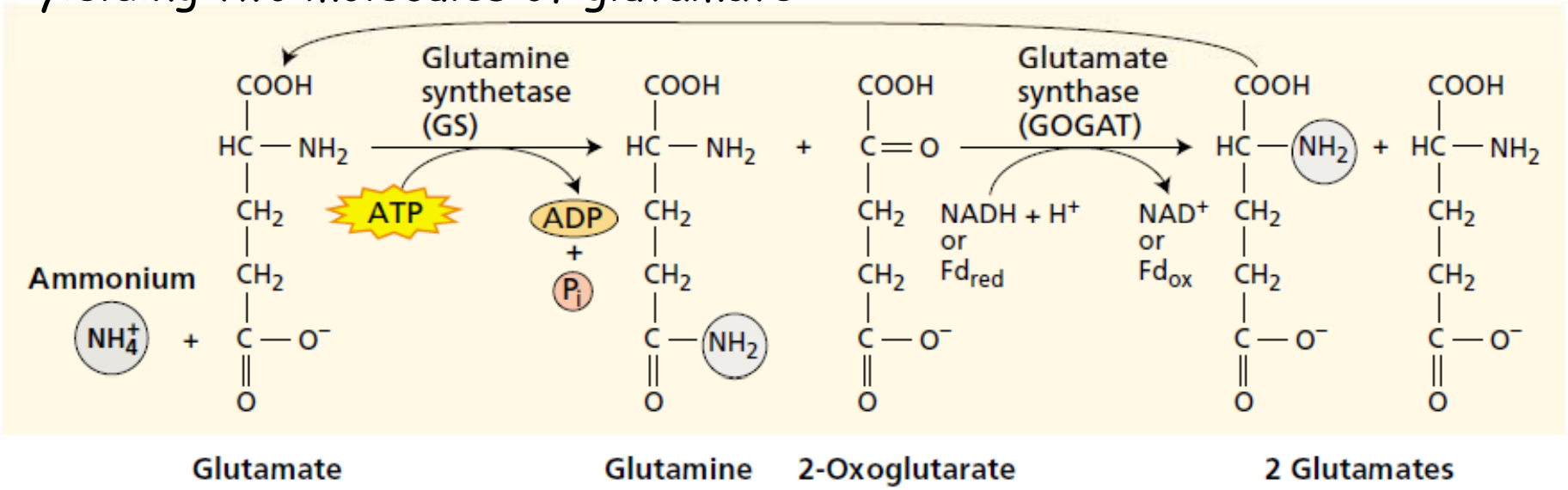


2-Oxoglutarate = α-Ketoglutarate

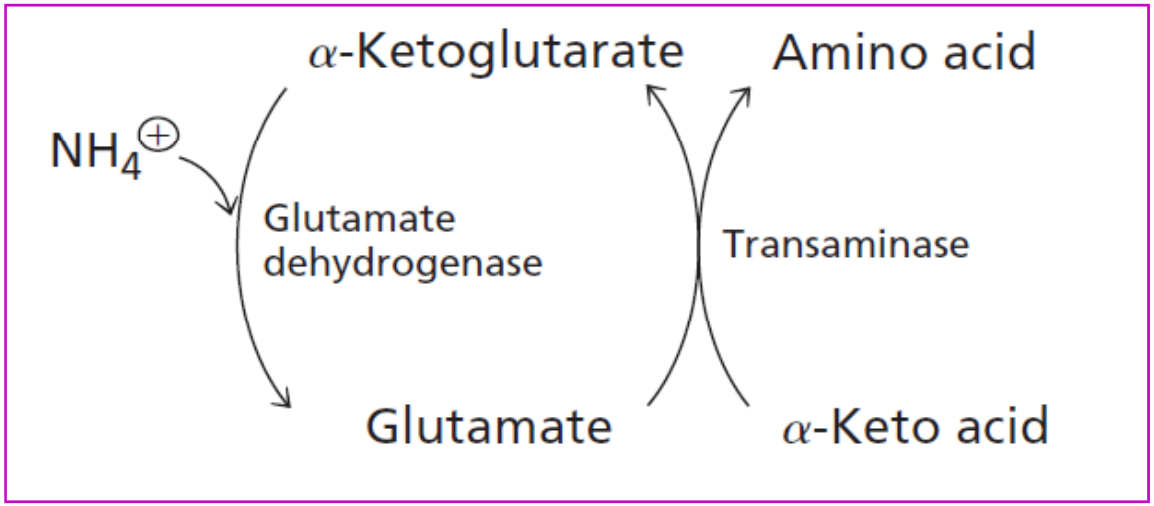
keep in mind...

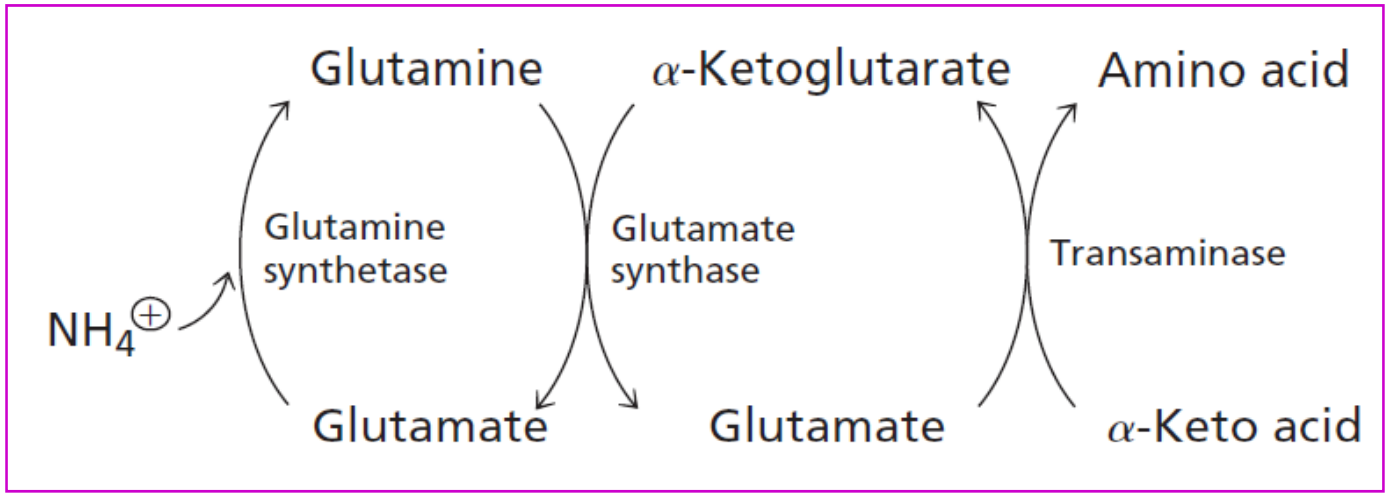
Glutamine Synthetase and Glutamate Synthase pathway

- ✓ requires two enzymes
- ✓ Glutamine synthetase (GS) combines ammonium with glutamate to form glutamine
- ✓ Elevated levels of glutamine stimulate the activity of glutamate synthase (glutamine:2-oxoglutarate aminotransferase, or GOGAT).
- ✓ This enzyme transfers the amide group of glutamine to 2- xoglutarate, yielding two molecules of glutamate



keep in mind...


α-Ketoglutarate
Amino acid
NH4+
Glutamate dehydrogenase
Transaminase
Glutamate
α-Keto acid


Glutamine
α-Ketoglutarate
Amino acid
Glutamine synthetase
Glutamate synthase
Transaminase
NH4+
Glutamate
Glutamate
α-Keto acid

keep in mind…

Once N is fixed into ammonium, it enters various metabolic pathways and passes through several organic forms…

Biosynthesis of Amino acids

Amino acids are made from intermediates of the Citric acid cycle and other major pathways.

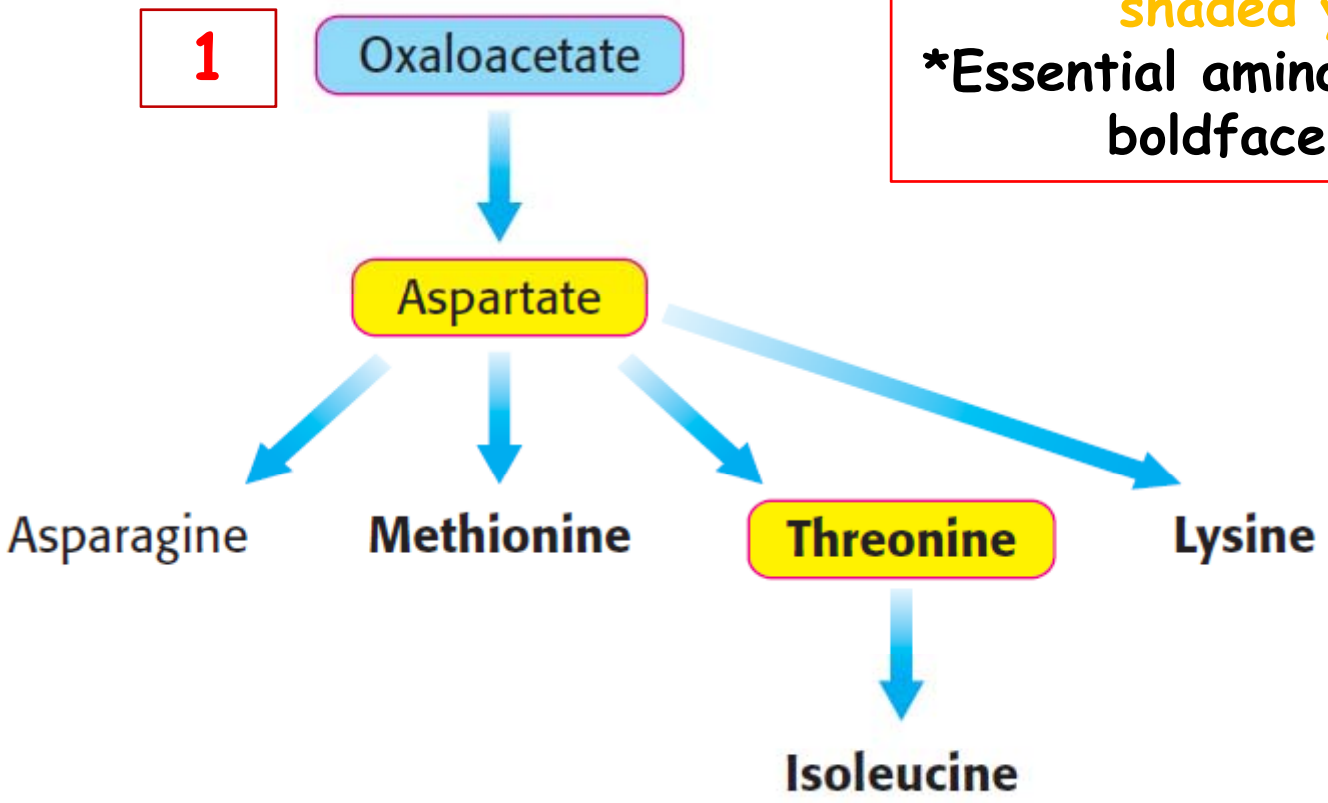
the majority of amino acids obtain their nitrogen from glutamate or glutamine

&

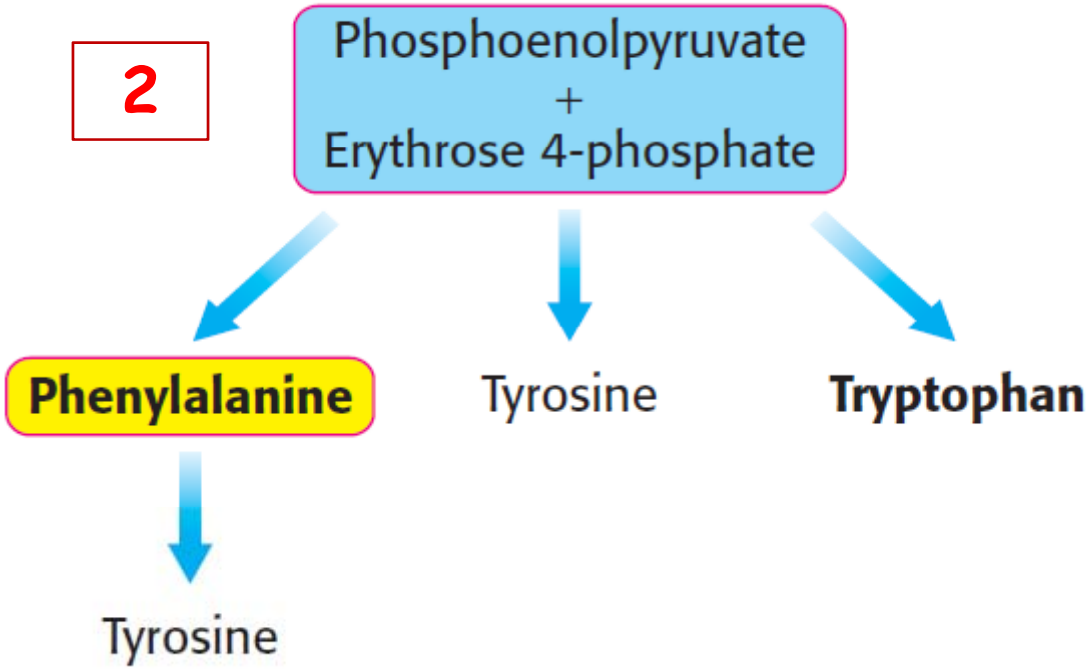
carbon skeletons come from intermediates of glycolysis, the pentose phosphate pathway, or the citric acid cycle.

On the basis of the starting material, amino acids can be grouped into six biosynthetic families;

*Major metabolic precursors are shaded blue.
*Amino acids that give rise to other amino acids are shaded yellow
*Essential amino acids are in boldface type.



On the basis of these starting materials, amino acids can be grouped into six biosynthetic families;



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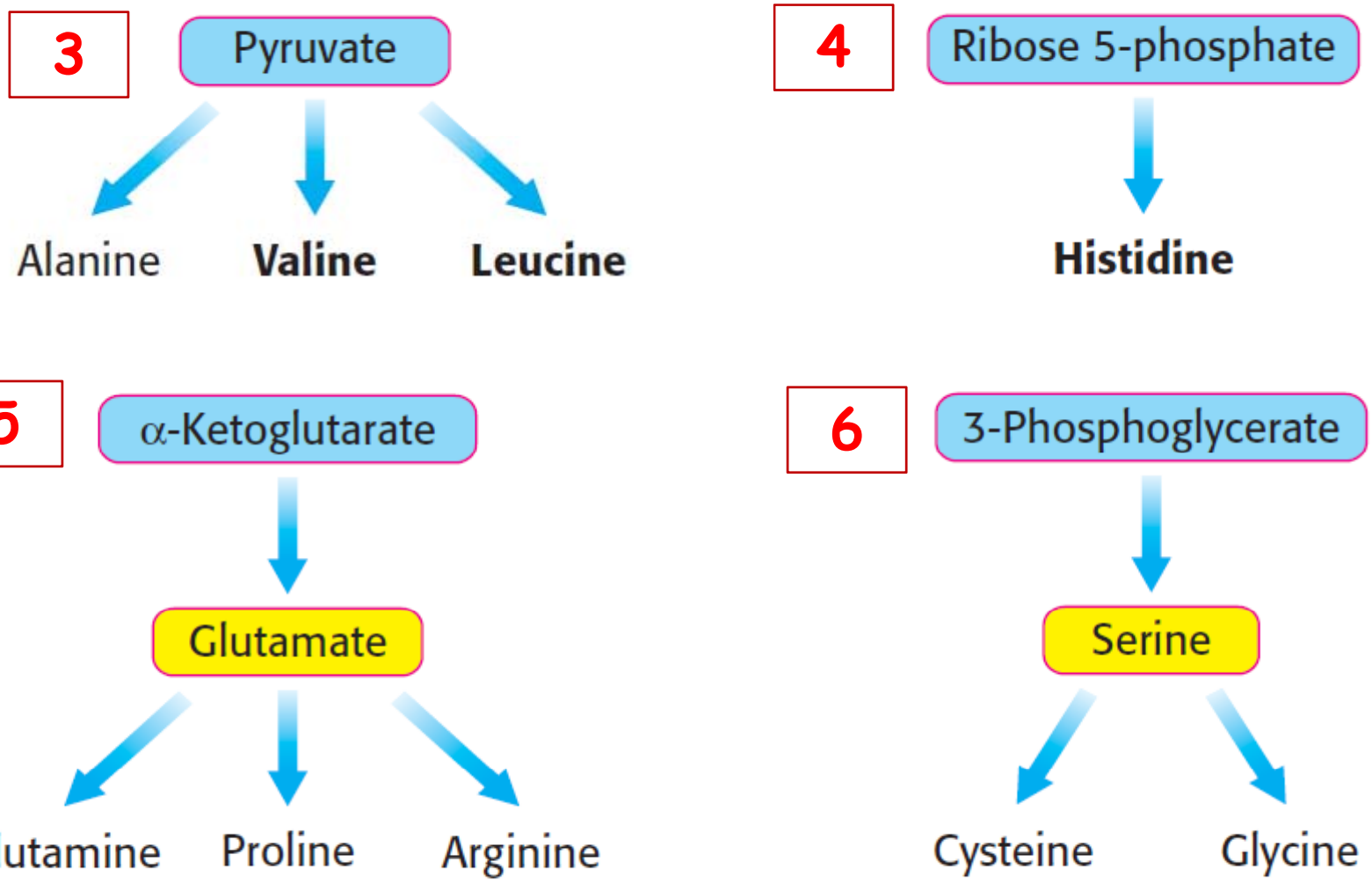


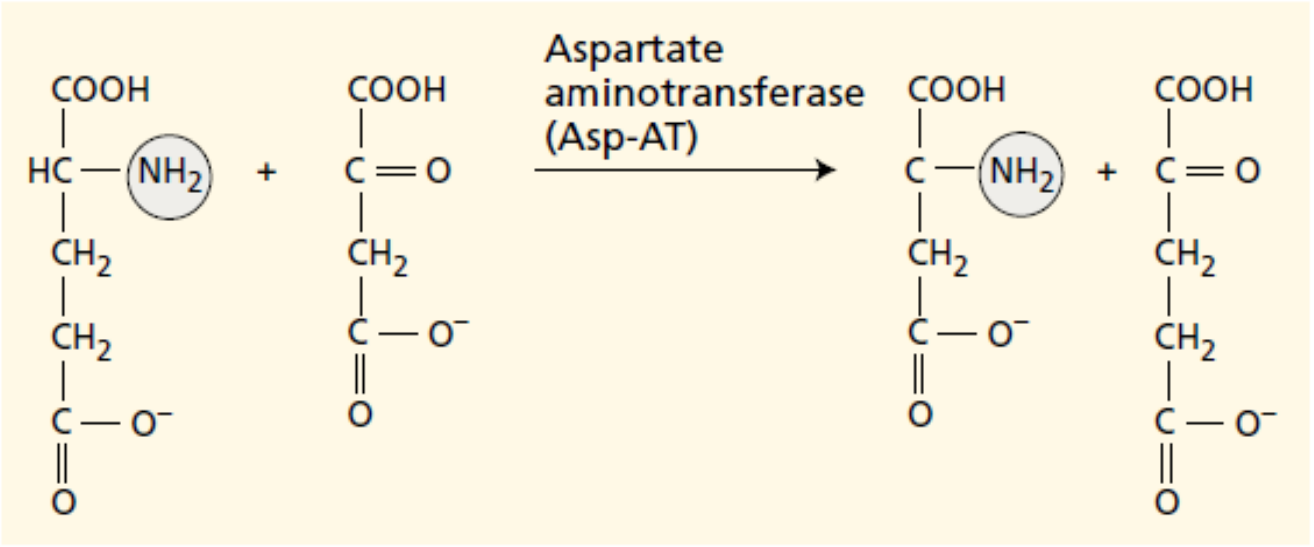
Aspartate, alanine, and glutamate are formed by the addition of an amino group to an alpha-ketoacids (α-ketoglutarate, oxaloacetate, and pyruvate)

1. Glutamate

$$NH_4^+ + \alpha\text{-ketoglutarate} + NADPH + H^+ \rightleftharpoons glutamate + NADP^+ + H_2O$$

Glutamate dehydrogenase

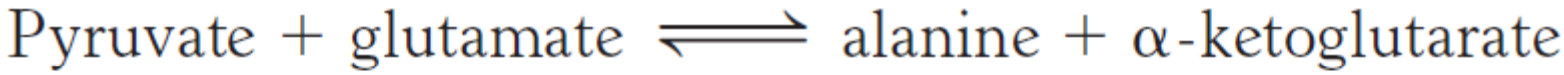
2. Aspartate



Aspartate aminotransferase (Asp-AT)

The amino group from glutamate can be transferred to α-ketoacids by transamination reactions

3. Alanine



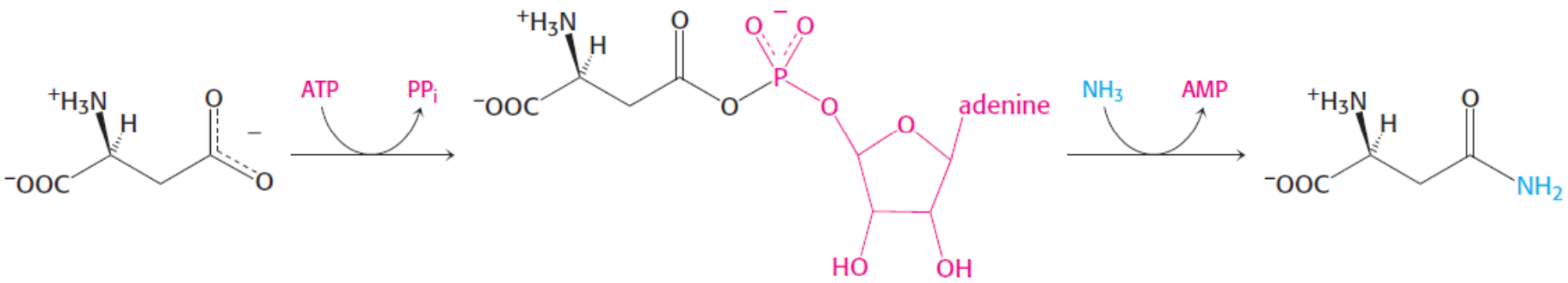
pyridoxal phosphate-dependent transaminases

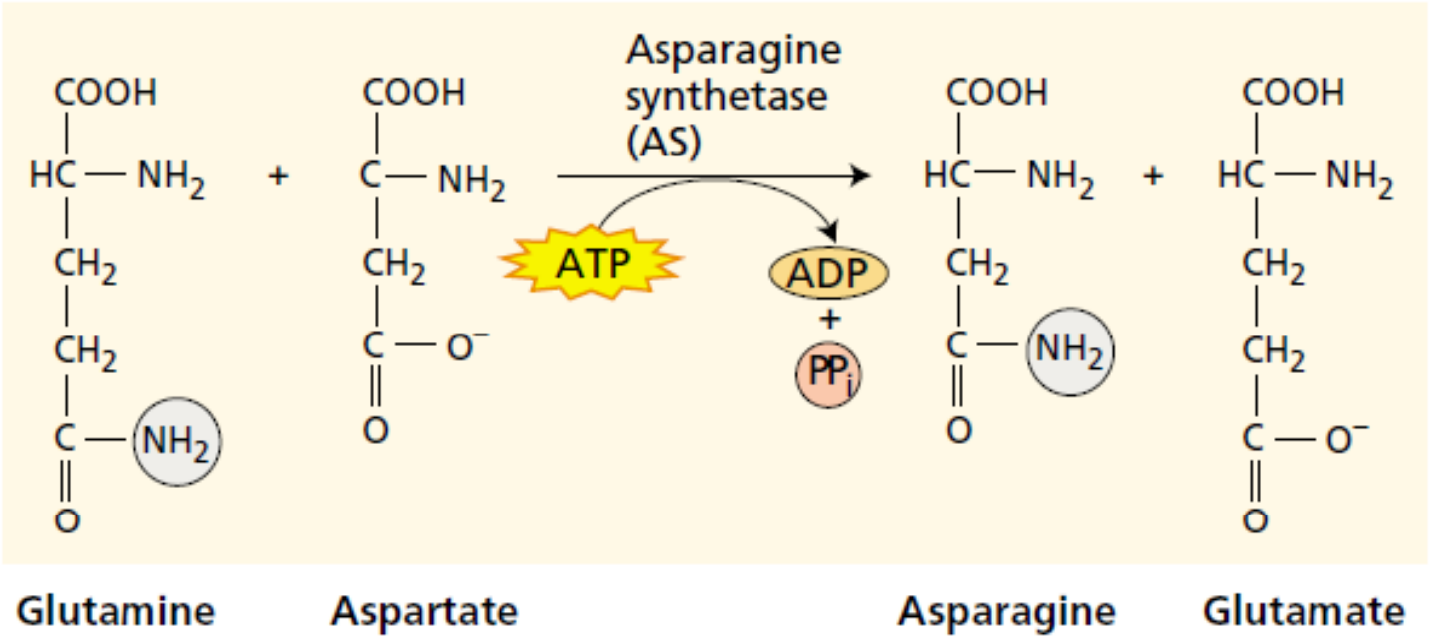
The amino group from glutamate can be transferred to α-ketoacids by transamination reactions

4. Asparagine

Asparagine is formed from aspartate through an adenylated intermediate

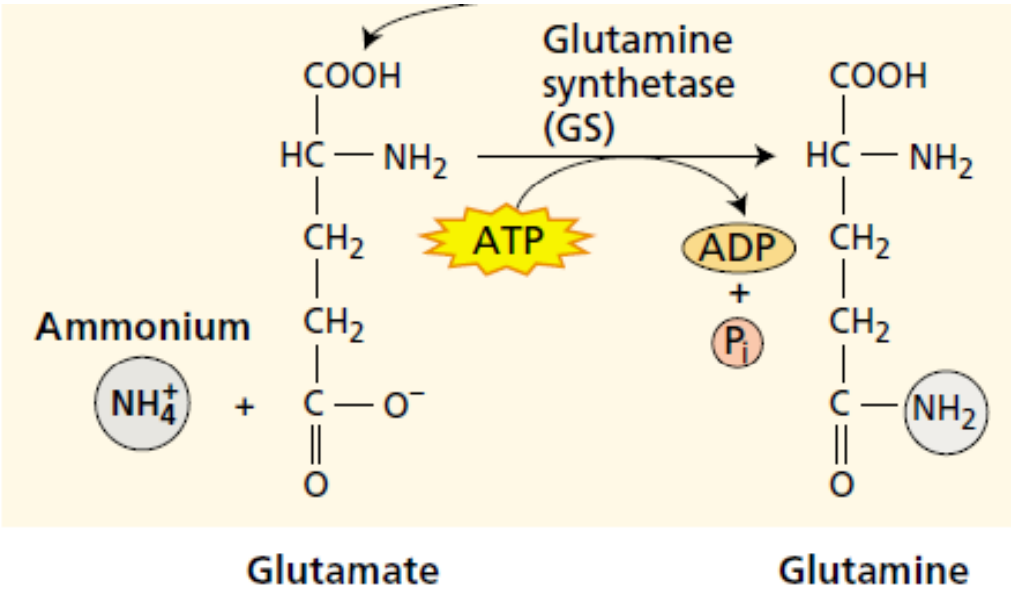
asparagine synthetase




Asparagine synthetase (AS)
ATP
ADP
+
PPi
Glutamine
Aspartate
Asparagine
Glutamate

Glutamate is the precursor of glutamine, proline, and arginine

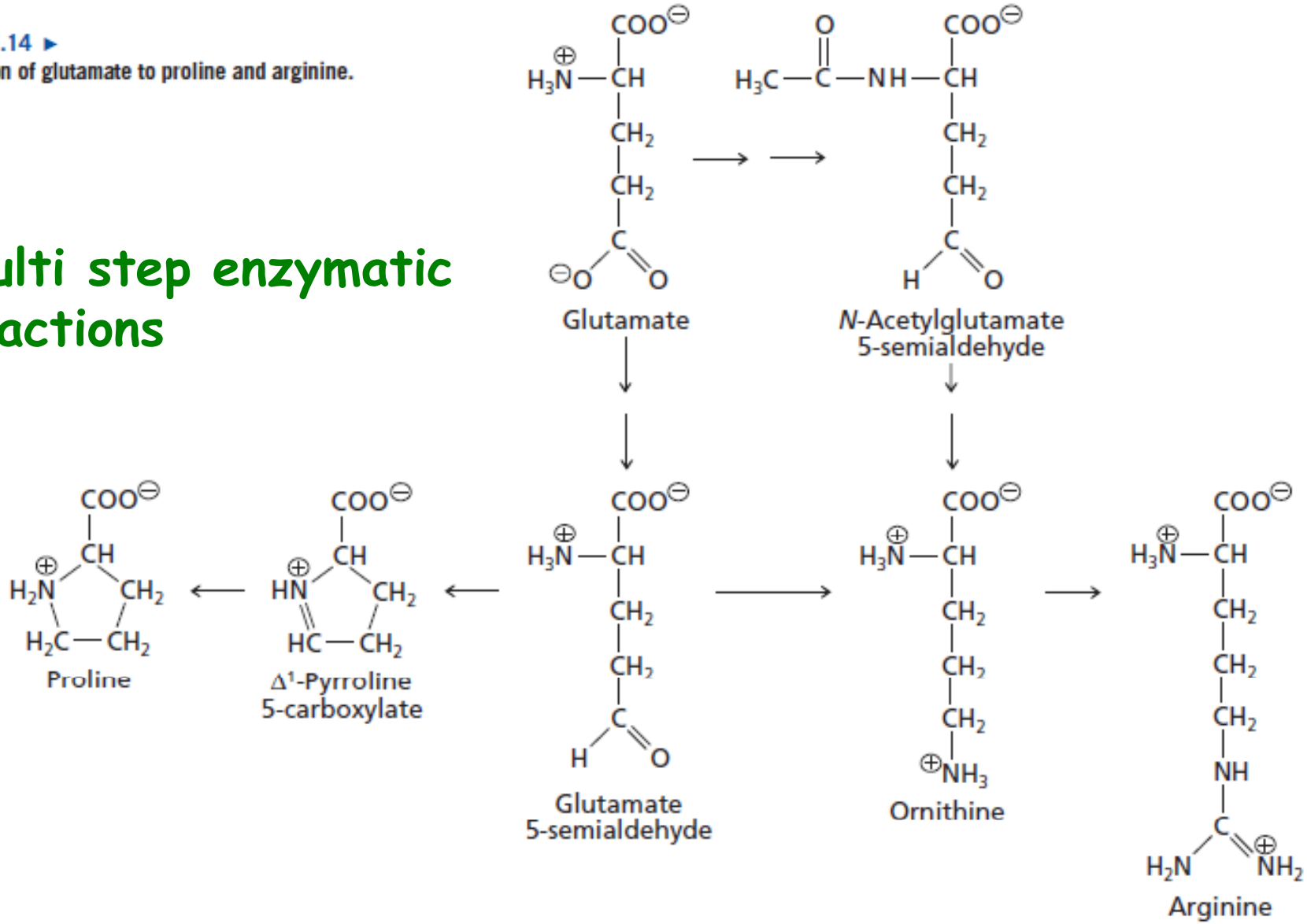
5. Glutamine



glutamine synthetase

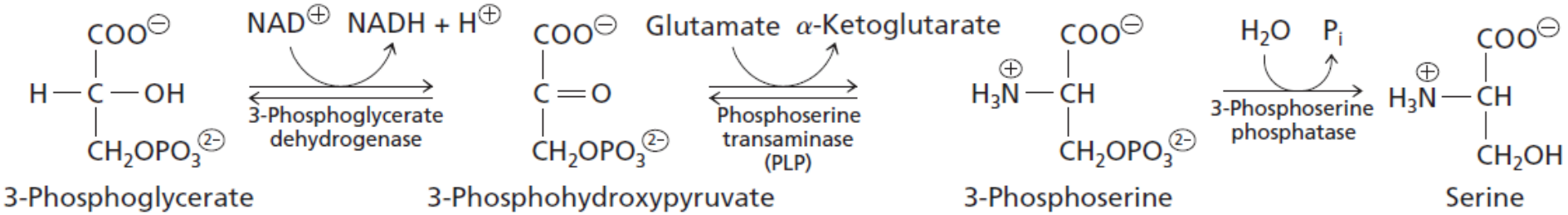
6. Proline & 7. Arginine

Figure 17.14 ▶
Conversion of glutamate to proline and arginine.



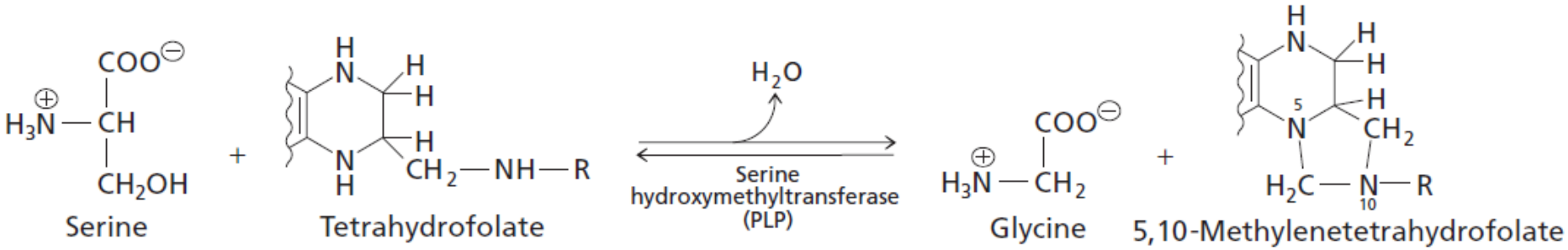
8. Serine

Serine is synthesized from 3-phosphoglycerate (3-PGA; an intermediate in glycolysis)



Serine is the precursor of cysteine and glycine

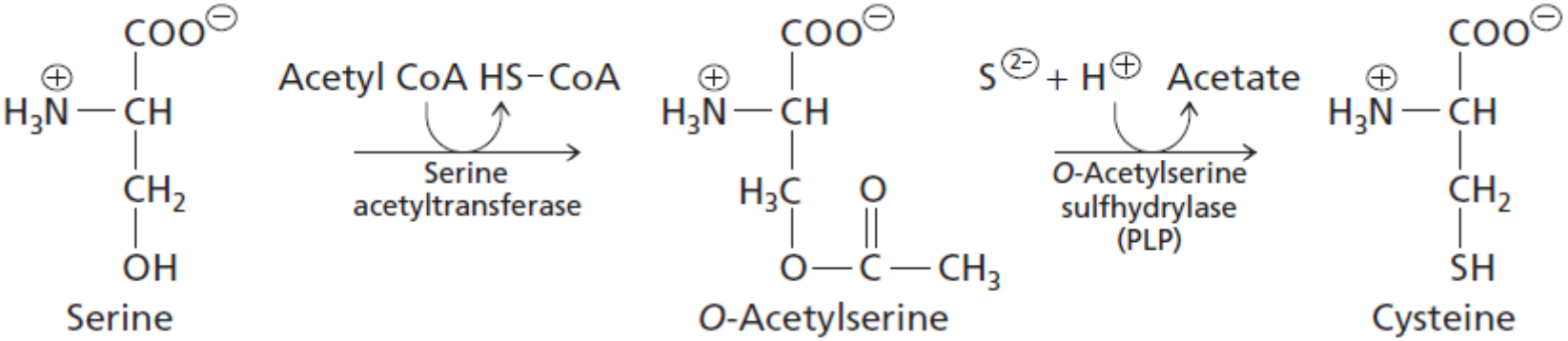
9. glycine



serine hydroxymethyltransferase

10. Cysteine

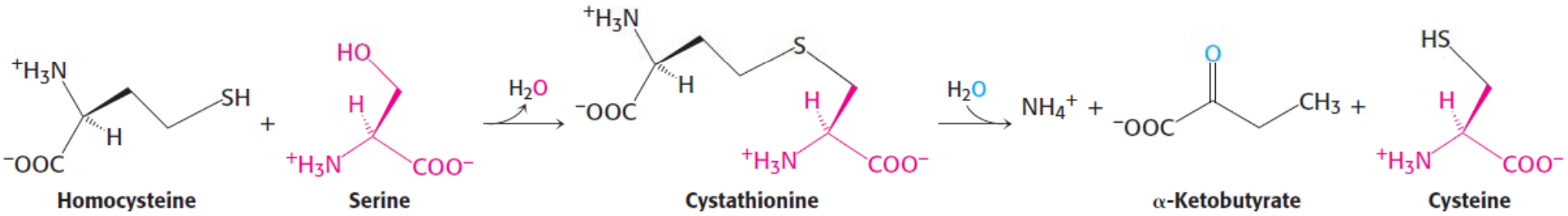
Plants & Bacteria



10. Cysteine

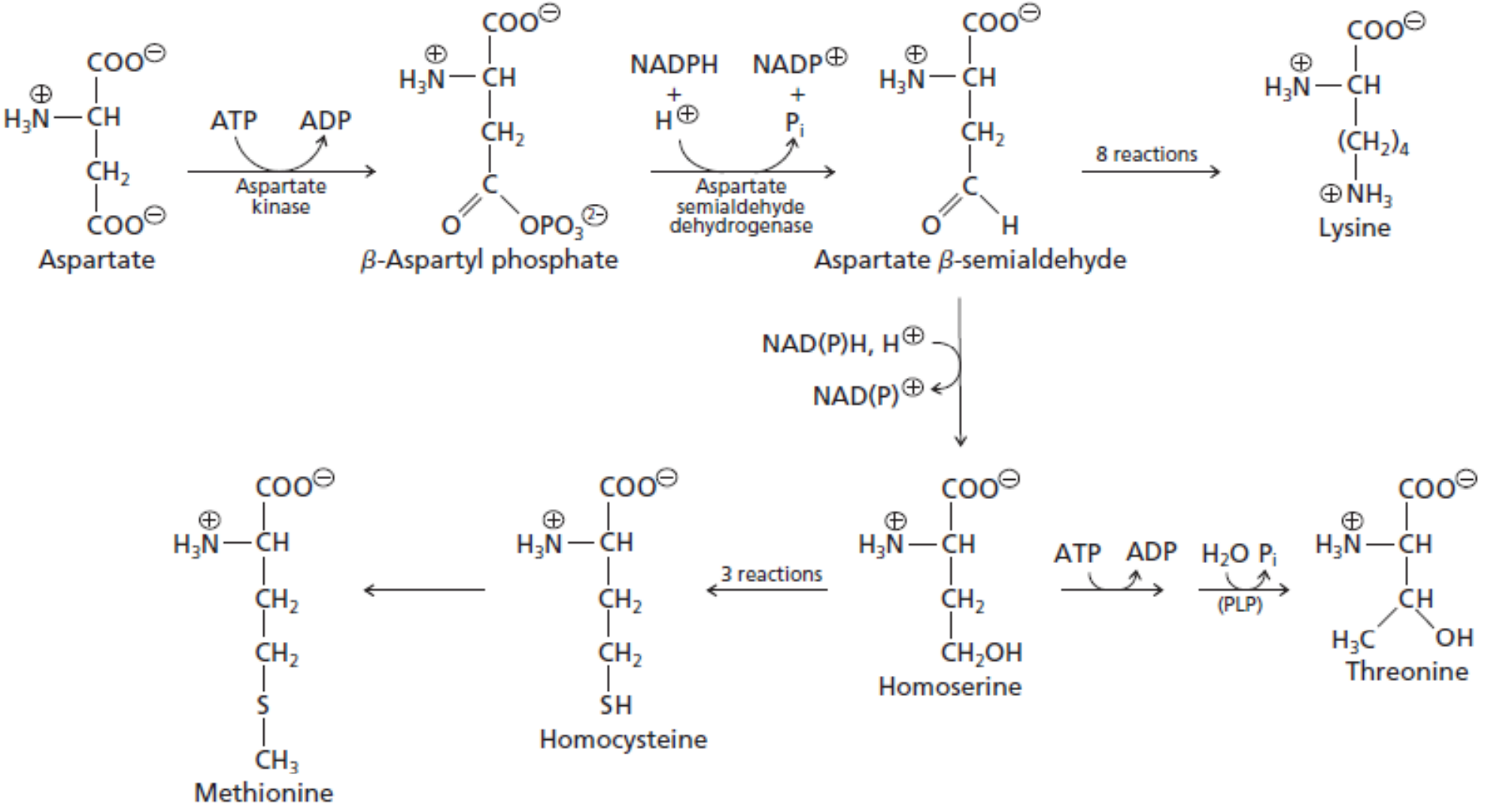
In Animals, Cysteine is synthesized from serine and homocysteine

Homocysteine + serine $\rightleftharpoons$ cysteine + α-ketobutyrate + NH_4^+



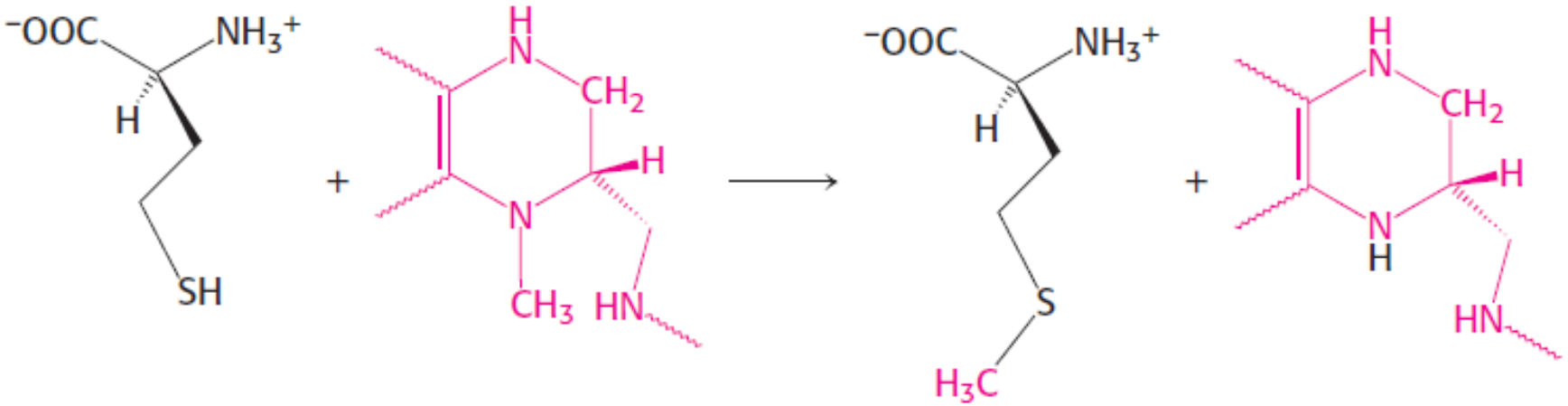
Cystathionine γ-lyase or cystathionase

Aspartate is the precursor for synthesis of 11. lysine, 12. methionine, and 13. threonine



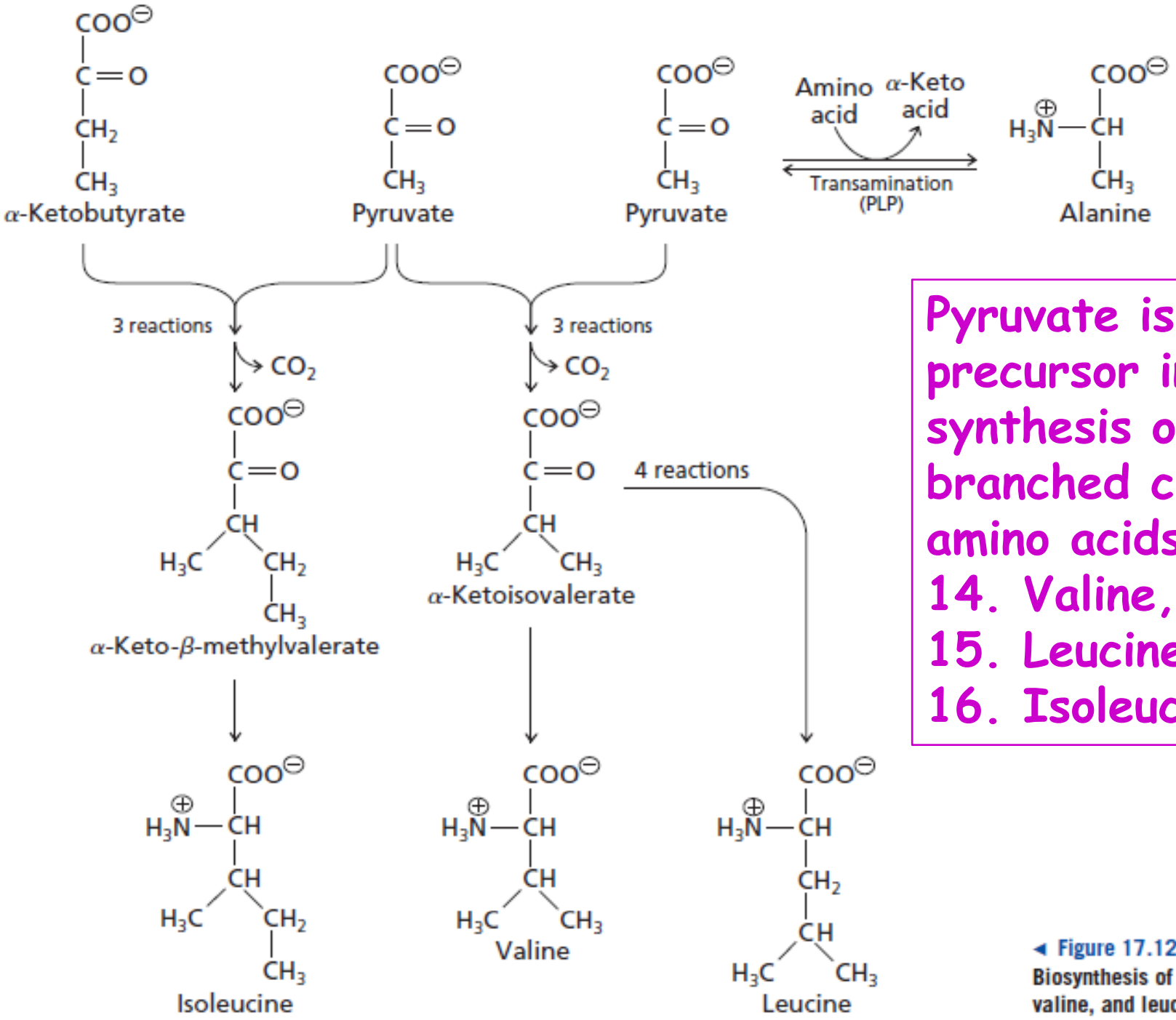
▲ Figure 17.11
Biosynthesis of lysine, threonine, and methionine from aspartate.

13. Methionine



Homocysteine + **N^5-Methyl-tetrahydrofolate** → **Methionine** + **Tetrahydrofolate**

Methionine synthase (homocysteine methyltransferase)

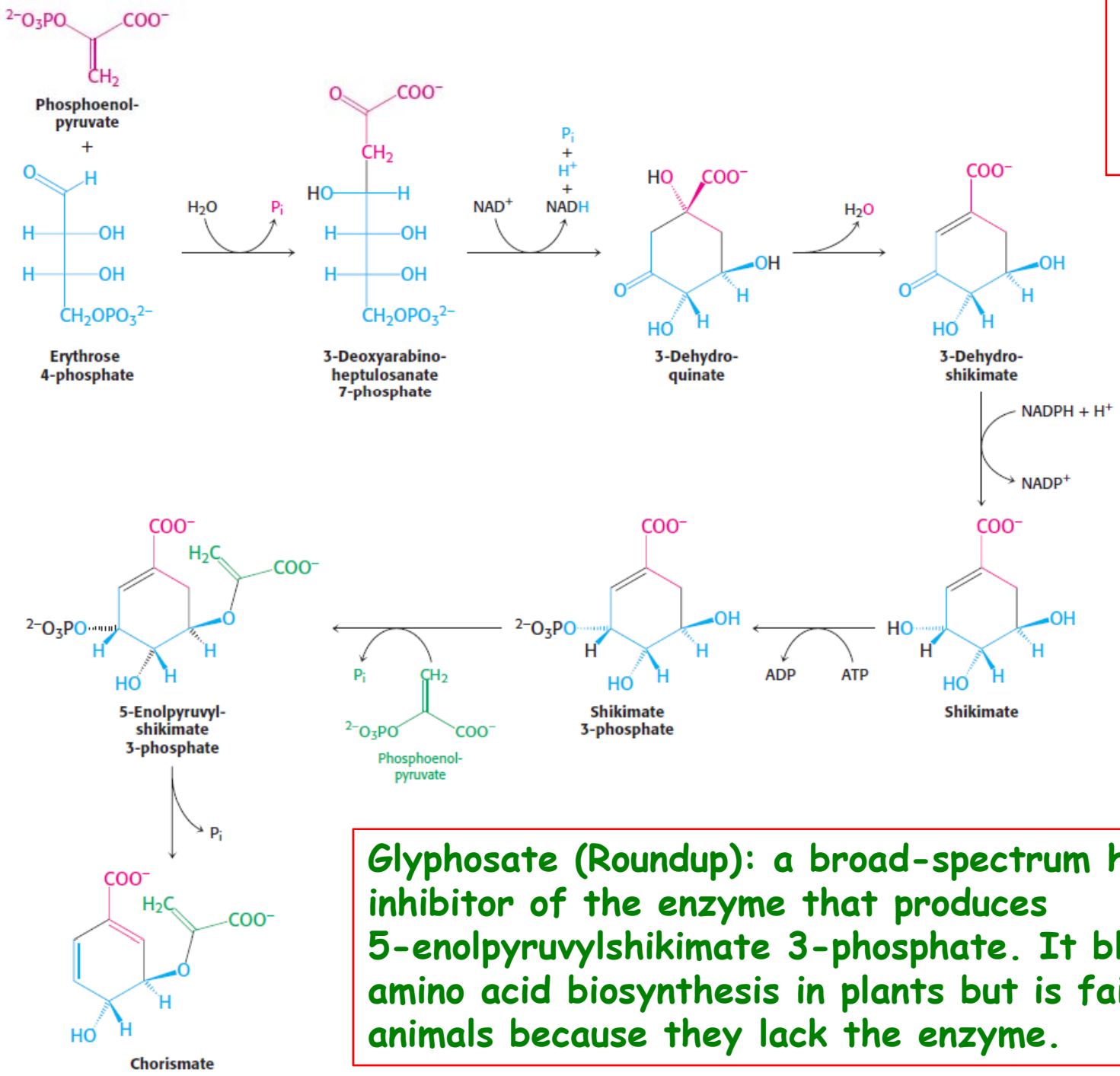


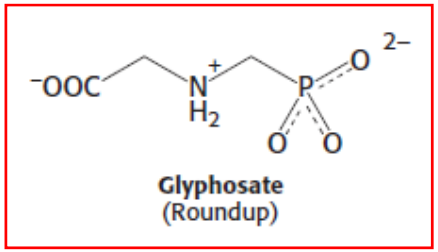
Pyruvate is a precursor in the synthesis of the branched chain amino acids;
14. Valine,
15. Leucine, and
16. Isoleucine

◀ Figure 17.12
Biosynthesis of alanine, isoleucine, valine, and leucine.

17. Phenylalanine, 18. tyrosine, and 19. tryptophan are synthesized by a common pathway

Shikimate and chorismate are intermediates in the biosynthesis of aromatic amino acids





Glyphosate (Roundup): a broad-spectrum herbicide, is an inhibitor of the enzyme that produces 5-enolpyruvylshikimate 3-phosphate. It blocks aromatic amino acid biosynthesis in plants but is fairly nontoxic in animals because they lack the enzyme.

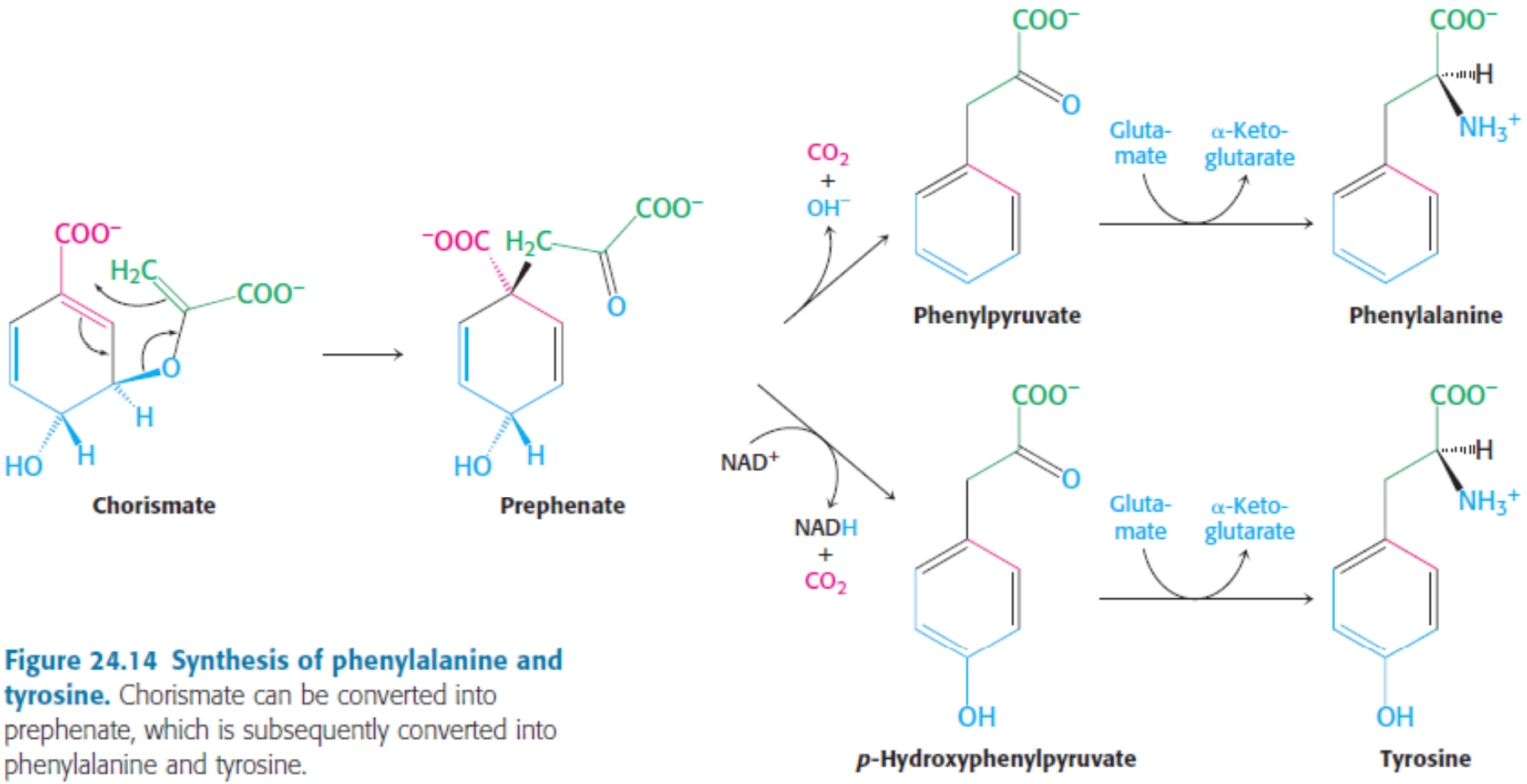


Figure 24.14 Synthesis of phenylalanine and tyrosine. Chorismate can be converted into prephenate, which is subsequently converted into phenylalanine and tyrosine.

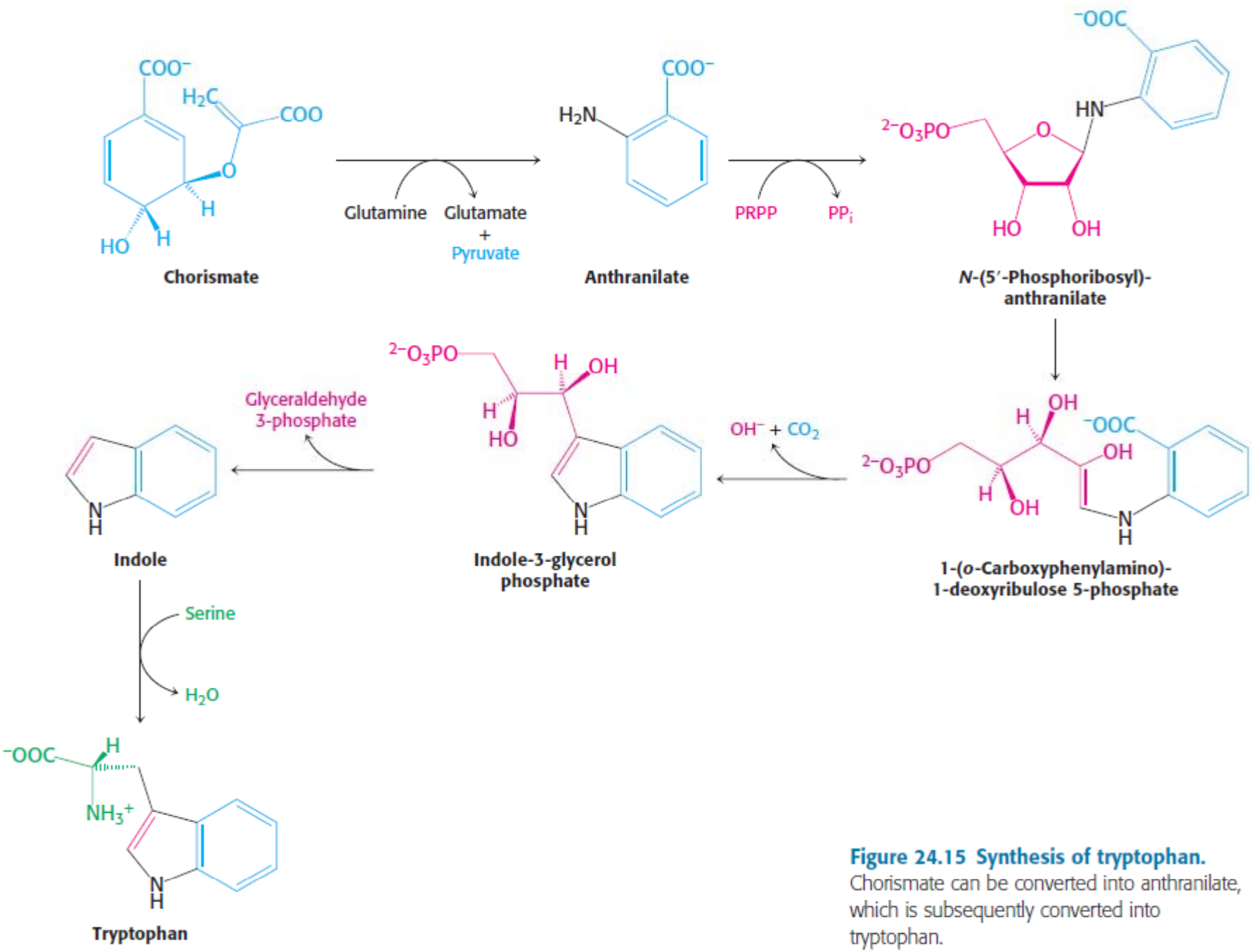


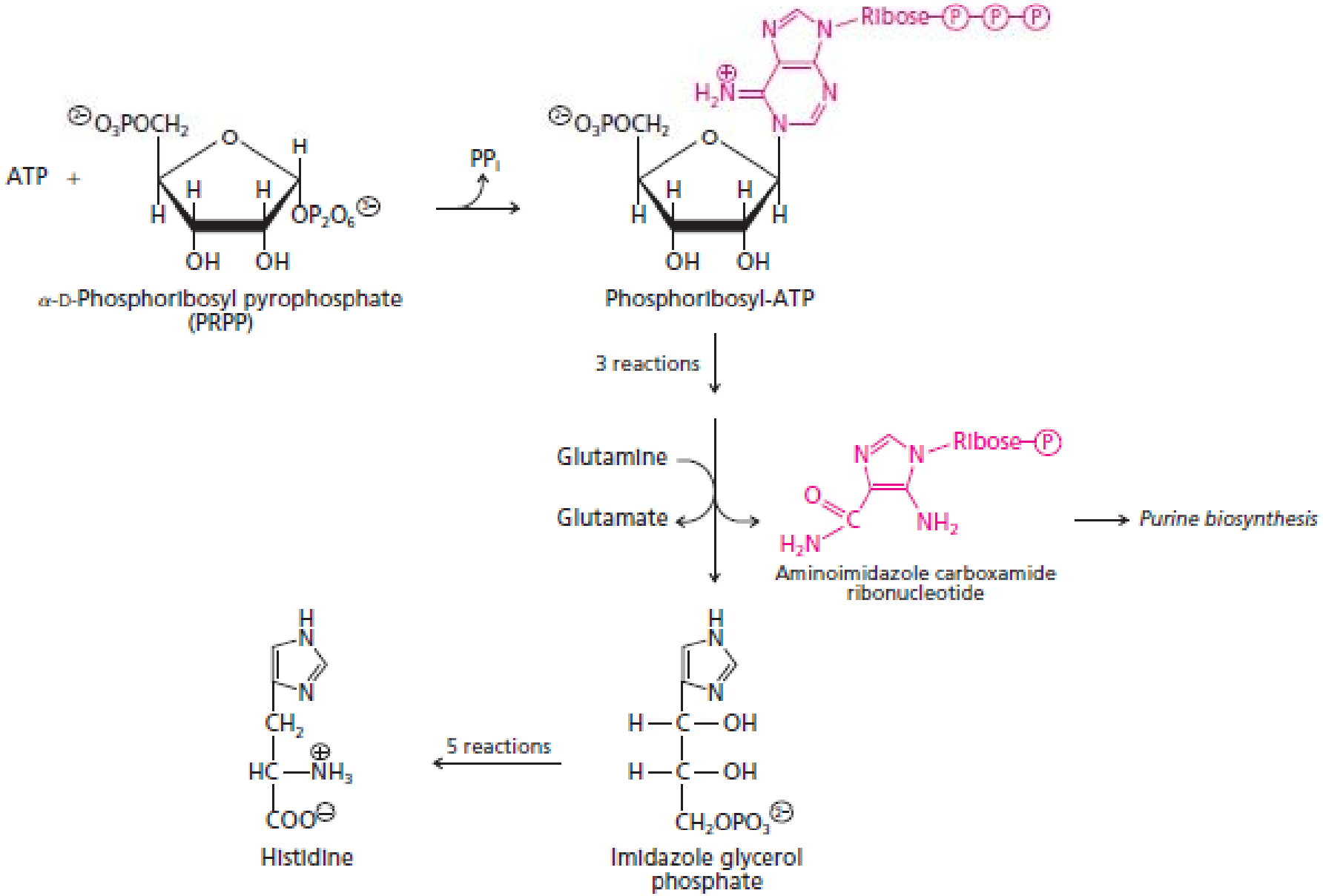
Figure 24.15 Synthesis of tryptophan.
Chorismate can be converted into anthranilate, which is subsequently converted into tryptophan.

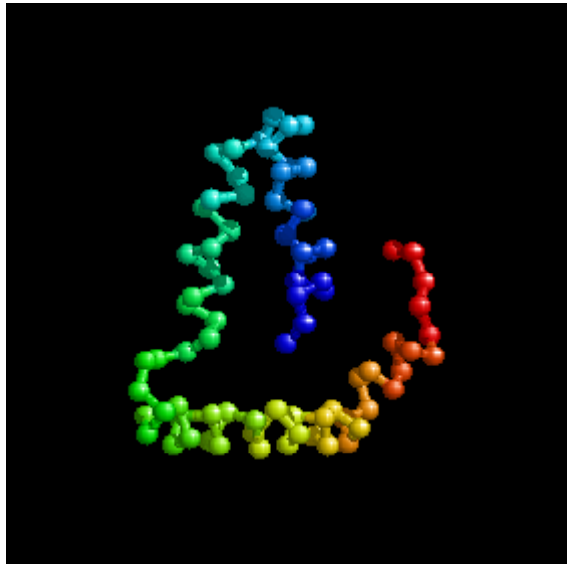
20. Histidine

The ten-step pathway for the biosynthesis of histidine in bacteria begins with a condensation between the six-membered ring of ATP and a ribose derivative, phosphoribosyl pyrophosphate (PRPP)

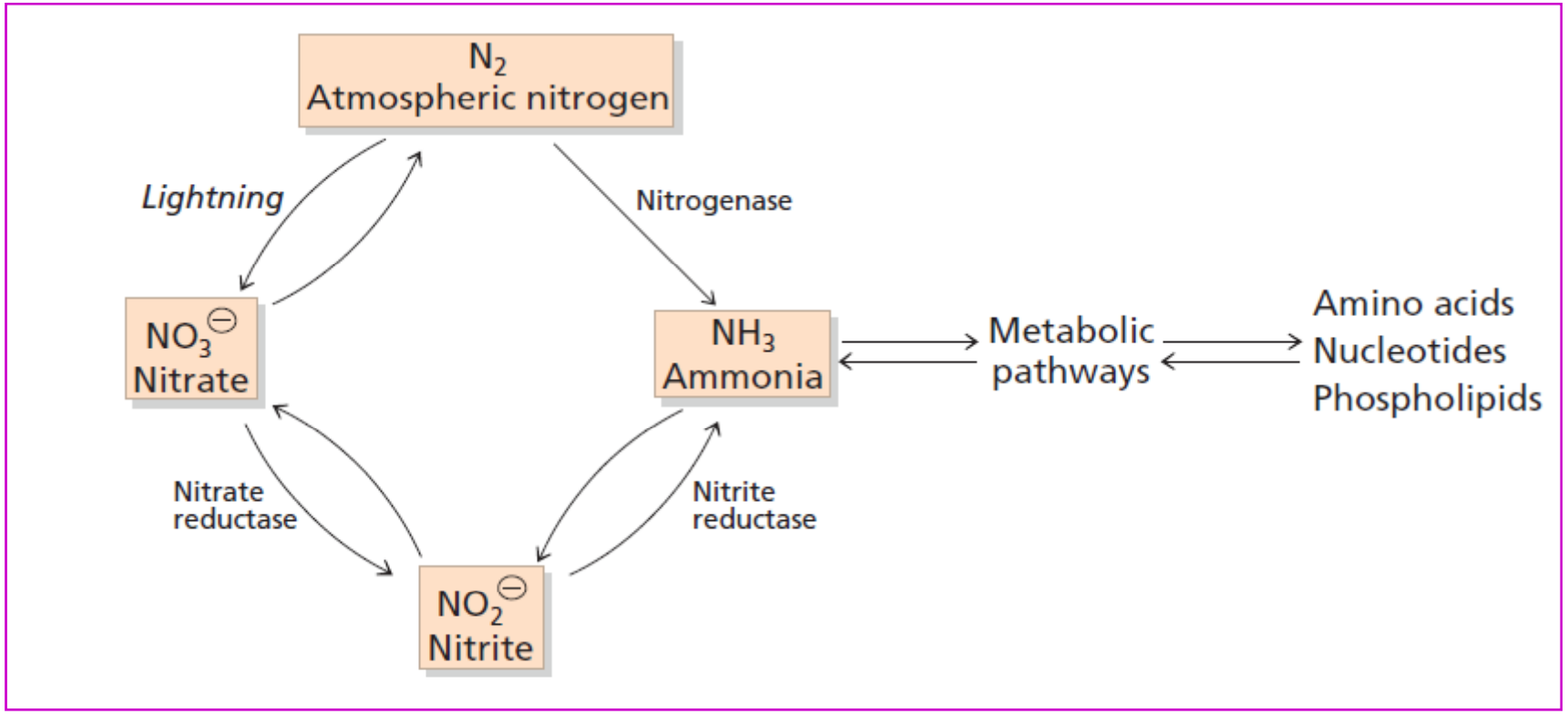
▼ **Figure 17.23**

Synthesis of histidine from phosphoribosyl pyrophosphate (PRPP) and ATP.
Histidine is derived from PRPP (5 C atoms), the purine ring of ATP (1 N and 1 C), glutamine (1 N), and glutamate (1 N).





reduction of N_2 to ammonia in a process called nitrogen fixation




BREAK...