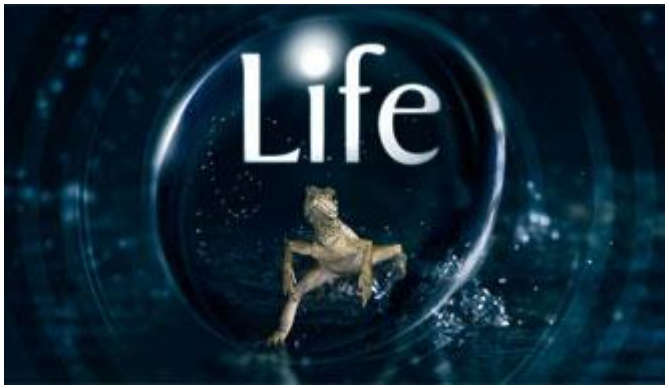

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CZ/FMP.17A/0436

STRATO-NANOBIOLAB

ASTROBIOLOGIE: Peptidy, bílkoviny a enzymy

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11. 02. 2015,
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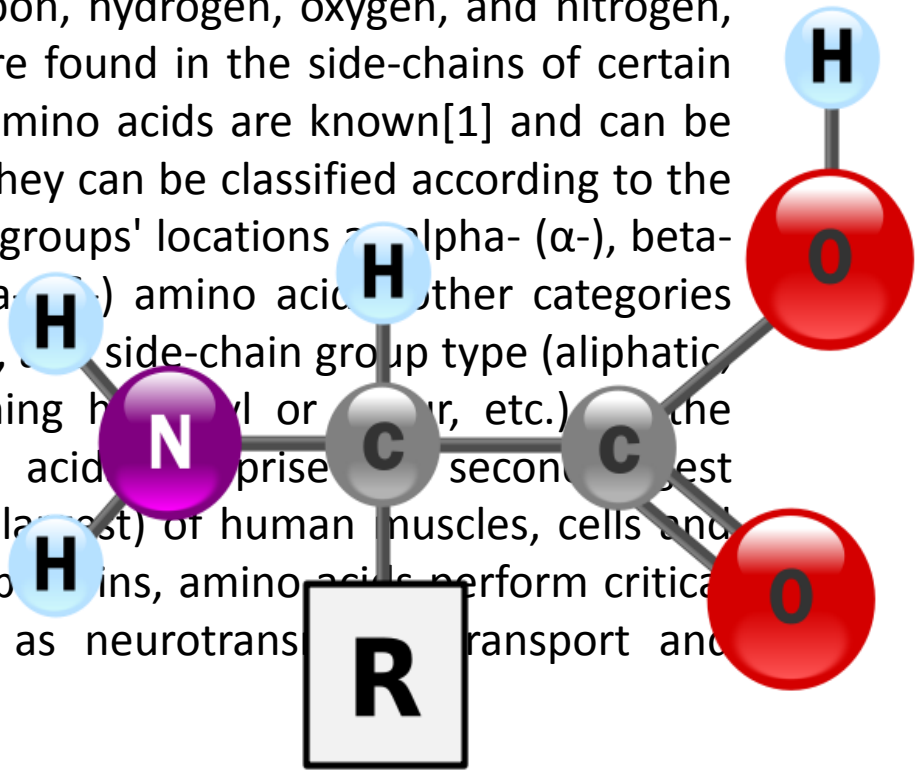
Amino acids (/əˈmiːnoʊ/, /əˈmaɪnoʊ/, or /ˈæmɪnoʊ/) are biologically important organic compounds composed of amine (-NH2) and carboxylic acid (-COOH) functional groups, along with a side-chain specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen, though other elements are found in the side-chains of certain amino acids. About 500 amino acids are known[1] and can be classified in many ways. They can be classified according to the core structural functional groups' locations as alpha- (α-), beta- (β-), gamma- (γ-) or delta- (δ-) amino acids; other categories relate to polarity, pH level, and side-chain group type (aliphatic, acyclic, aromatic, containing hydroxyl or sulfur, etc.). In the form of proteins, amino acid residues comprise the second-most abundant component (water is the most) of human muscles, cells and other tissues.[2] Outside proteins, amino acids perform critical roles in processes such as neurotransmission and transport and biosynthesis.



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In biochemistry, amino acids having both the amine and the carboxylic acid groups attached to the first (alpha-) carbon atom have particular importance. They are known as 2-, alpha-, or α-amino acids (generic formula H2NCHRCOOH in most cases[3] where R is an organic substituent known as a "side-chain");[4] often the term "amino acid" is used to refer specifically to these. They include the 23 proteinogenic ("protein-building") amino acids,[5][6][7] which combine into peptide chains ("polypeptides") to form the building-blocks of a vast array of proteins.[8] The all L-stereoisomers ("left-handed" isomers), although a f amino acids ("right-handed") occur in bacterial envelope some antibiotics.[9] Twenty of the proteinogenic amino aci encoded directly by triplet codons in the genetic code a known as "standard" amino acids. The other three ("non-sta or "non-canonical") are selenocysteine (present in noneukaryotes as well as most eukaryotes, but not coded d by DNA), pyrrolysine (found only in some archea an bacterium) and N-formylmethionine (which is often the amino acid of proteins in bacteria, mitochondria, and chloro Pyrrolysine and selenocysteine are encoded via variant codo example, selenocysteine is encoded by stop codon and element.[10][11][12] Codon–tRNA combinations not fou nature can also be used to "expand" the genetic code and novel proteins known as alloproteins incorporating non-proteinogenic amino acids.[

nonpolar polar basic acidic (stop codon)

Standard genetic code

1st base	2nd base U		2nd base C		2nd base A		2nd base G		3rd base
U	UUU	(Phe/F) Phenylalanine	UCU	(Ser/S) Serine	UAU	(Tyr/Y) Tyrosine	UGU	(Cys/C) Cysteine	U
	UUC		UCC		UAC		UGC		C
	UUA	(Leu/L) Leucine	UCA		UAA	Stop (*Ochre*)	UGA	Stop (*Opal*)	A
	UUG		UCG		UAG	Stop (*Amber*)	UGG	(Trp/W) Tryptophan	G
C	CUU		CCU	(Pro/P) Proline	CAU	(His/H) Histidine	CGU	(Arg/R) Arginine	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	(Gln/Q) Glutamine	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	(Ile/I) Isoleucine	ACU	(Thr/T) Threonine	AAU	(Asn/N) Asparagine	AGU	(Ser/S) Serine	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	(Lys/K) Lysine	AGA	(Arg/R) Arginine	A
	AUG[A]	(Met/M) Methionine	ACG		AAG		AGG		G
G	GUU	(Val/V) Valine	GCU	(Ala/A) Alanine	GAU	(Asp/D) Aspartic acid	GGU	(Gly/G) Glycine	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	(Glu/E) Glutamic acid	GGA		A
	GUG		GCG		GAG		GGG		G

[A] The codon AUG both codes for methionine and serves as an initiation site: the first AUG in an mRNA's coding region is where tra

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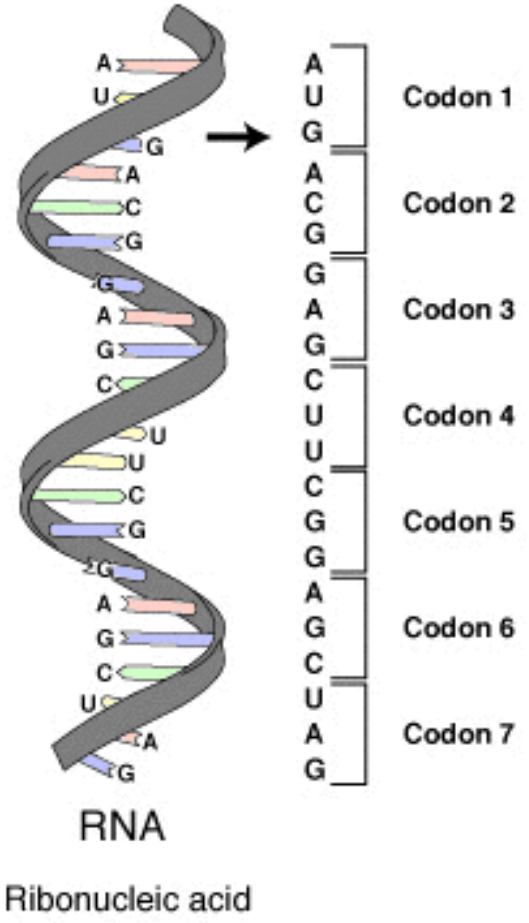
Many important proteinogenic and non-proteinogenic amino acids also play critical non-protein roles within the body. For example, in the human brain, glutamate (standard glutamic acid) and gamma-amino-butyric acid ("GABA", non-standard gamma-amino acid) are, respectively, the main excitatory and inhibitory neurotransmitters;[16] hydroxyproline (a major component of the connective tissue collagen) is synthesised from proline; the standard amino acid glycine is used to synthesise porphyrins used in red blood cells; and the non-standard carnitine is used in lipid transport.



Ribonucleic acid

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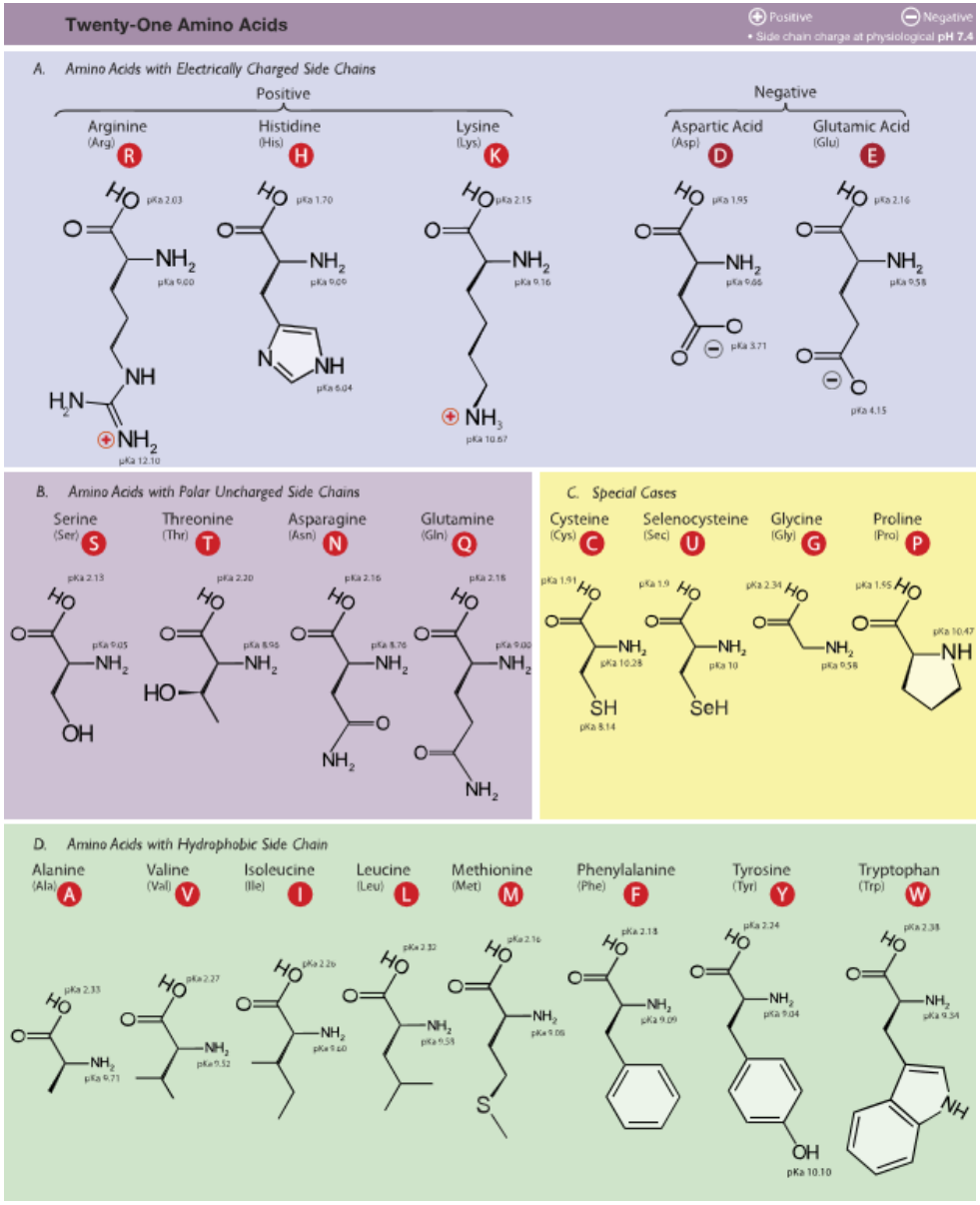

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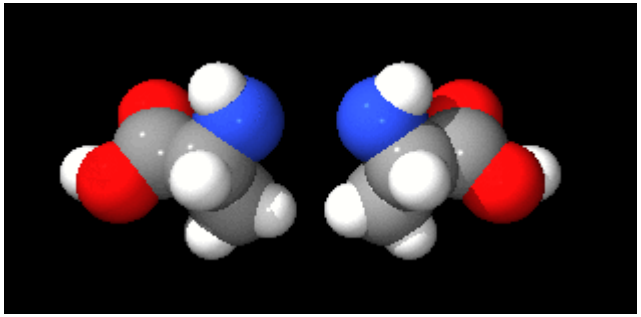
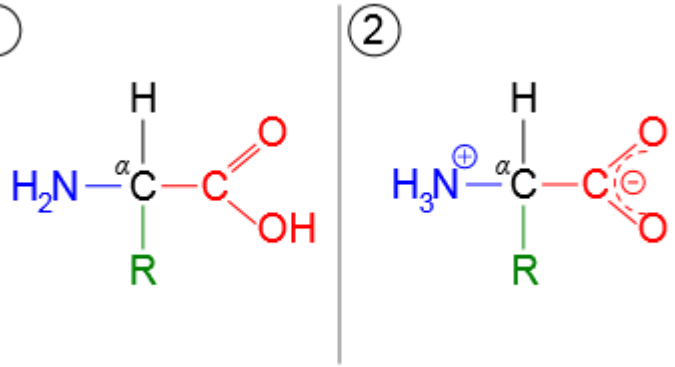
The alpha amino acids are the most common form found in nature, but only when occurring in the L-isomer. The alpha carbon is a chiral carbon atom, with the exception of glycine which has two indistinguishable hydrogen atoms on the alpha carbon.[29] Therefore, all alpha amino acids but glycine can exist in either of two enantiomers, called L or D amino acids, which are mirror images of each other (see also Chirality). While L-amino acids represent all of the amino acids found in proteins during translation in the ribosome, D-amino acids are found in some proteins produced by enzyme posttranslational modifications after translation and translocation to the endoplasmic reticulum, as in exotic sea-dwelling organisms such as cone snails.[30] They are also abundant components of the peptidoglycan cell walls of bacteria,[31] and D-serine may act as a neurotransmitter in the brain.[32] 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.[33] The L 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.[34] Cysteine is unusual since it has a sulfur atom at the second position in its side-chain, which has a larger atomic mass than the groups attached to the first carbon, which is attached to the α-carbon in the other standard amino acids, thus the (R) instead of (S).



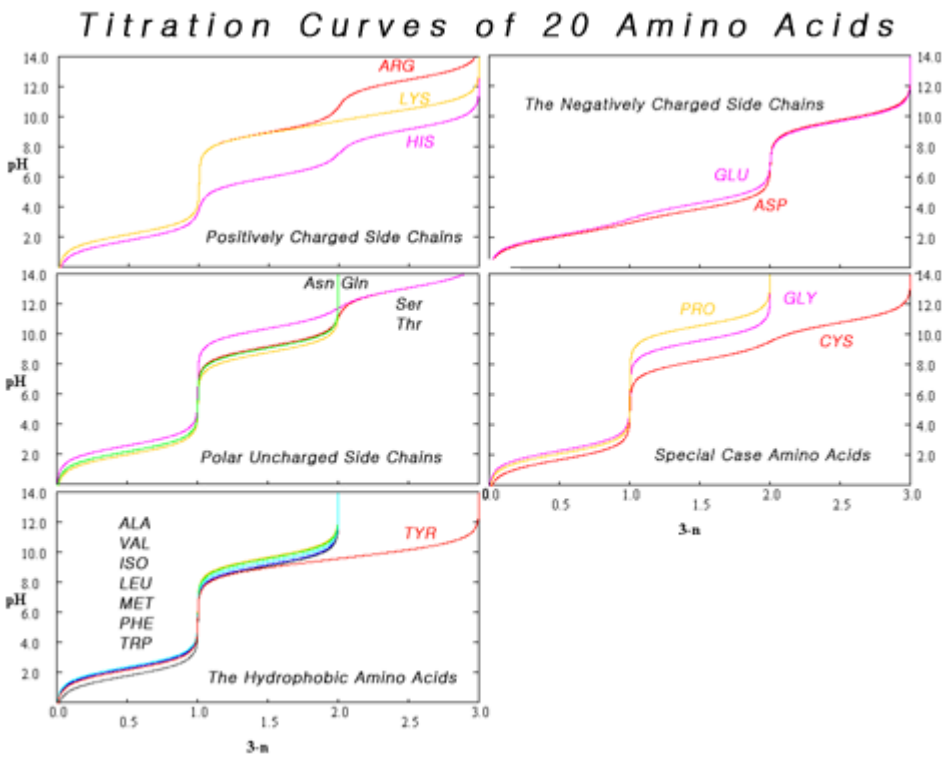
Zwitterions

The α-carboxylic acid group of amino acids is a weak acid, meaning that it releases a hydron (such as a proton) at moderate pH values. In other words, carboxylic acid groups (−CO2H) can be deprotonated to become negative carboxylates (−CO2−). The negatively charged carboxylate ion predominates at pH values greater than the pKa of the carboxylic acid group (mean for the 20 common amino acids is about 2.2, see the table of amino acid structures above). In a complementary fashion, the α-amine of amino acids is a weak base, meaning that it accepts a hydron at moderate pH values. In other words, α-amino groups (NH2−) can be protonated to become positive α-ammonium groups (+NH3−). The positively charged α-ammonium group predominates at pH values less than the pKa of the α-ammoniu group (mean for the 20 common α-amino acids is about 9.4).

Because all amino acids contain amine and carboxylic acid function groups, they share amphiprotic properties.[29] Below pH 2.2, th predominant form will have a neutral carboxylic acid group and positive α-ammonium ion (net charge +1), and above pH 9.4, negative carboxylate and neutral α-amino group (net charge −1). Bi at pH between 2.2 and 9.4, an amino acid usually contains both a negative carboxylate and a positive α-ammonium group, as shown in structure (2) on the right, so has net zero charge. This molecular state is known as a zwitterion, from the German Zwitter meaning hermaphrodite or hybrid.[39] The fully neutral form (structure (1) on the right) is a very minor species in aqueous solution throughout the pH range (less than 1 part in 107). Amino acids exist as zwitterions also in the solid phase, and crystallize with salt-like properties unlike typical organic acids or amines.

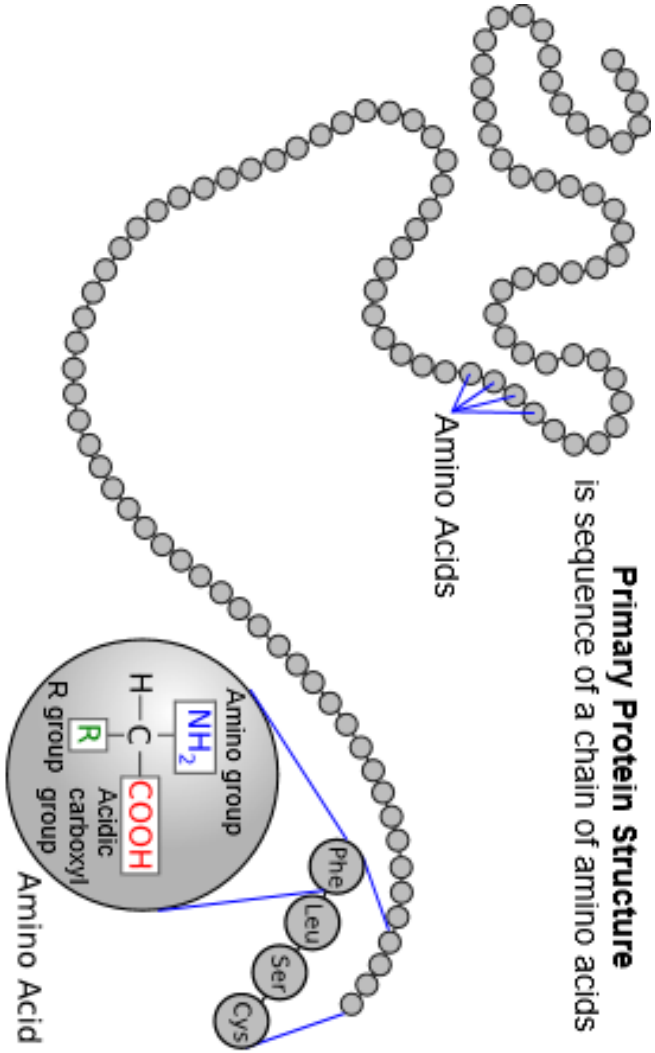


At pH values between the two pKa values, the zwitterion predominates, but coexists in dynamic equilibrium with small amounts of net negative and net positive ions. At the exact midpoint between the two pKa values, the trace amount of net negative and trace of net positive ions exactly balance, so that average net charge of all forms present is zero.[40] This pH is known as the isoelectric point pI, so pI = ½(pKa1 + pKa2). The individual amino acids all have slightly different pKa values, so have different isoelectric points. For amino acids with charged side-chains, the pKa of the side-chain is involved. Thus for Asp, Glu with negative side-chains, pI = ½(pKa1 + pKaR), where pKaR is the side-chain pKa. Cysteine also has potentially negative side-chain with pKaR = 8.14, so pI should be calculated as for Asp and Glu, even though the side-chain is not significantly charged at neutral pH. For His, Lys, and Arg with positive side-chains, pI = ½(pKaR + pKa2). Amino acids have zero mobility in electrophoresis at their isoelectric point, although this behaviour is more usually exploited for peptides and proteins than single amino acids. Zwitterions have minimum solubility at their isoelectric point and some amino acids (in particular, with non-polar side-chains) can be isolated by precipitation from water by adjusting the pH to the required isoelectric point.



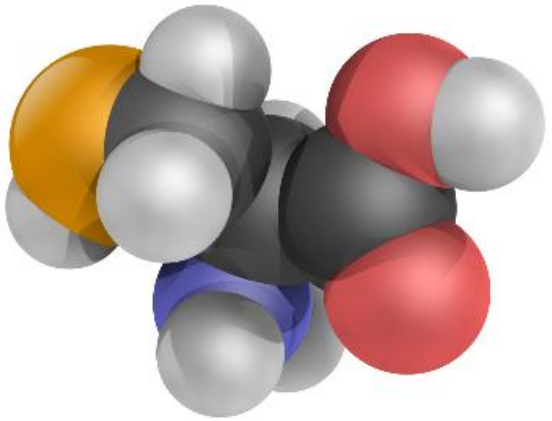
Amino acids are the structural units (monomers) that make up proteins. They join together to form short polymer chains called peptides or longer chains called either polypeptides or proteins. These polymers are linear and unbranched, with each amino acid within the chain attached to two neighboring amino acids. The process of making proteins is called translation and involves the step-by-step addition of amino acids to a growing protein chain by a ribozyme that is called a ribosome.[41] The order in which the amino acids are added is read through the genetic code from an mRNA template, which is a RNA copy of one of the organism's genes.

Twenty-three amino acids are naturally incorporated into polypeptides and are called proteinogenic or natural amino acids.[29] Of these, 21 are encoded by the universal genetic code. The remaining 2, selenocysteine and pyrrolysine, are incorporated into proteins by unique synthetic mechanisms. Selenocysteine is incorporated when the mRNA being translated includes a SECIS element, which causes the UGA codon to encode selenocysteine instead of a stop codon.[42] Pyrrolysine is used by some methanogenic archaea in enzymes that they use to produce methane. It is coded for with the codon UAG, which is normally a stop codon in other organisms.[43] This UAG codon is followed by a PYLIS downstream sequence.[44]

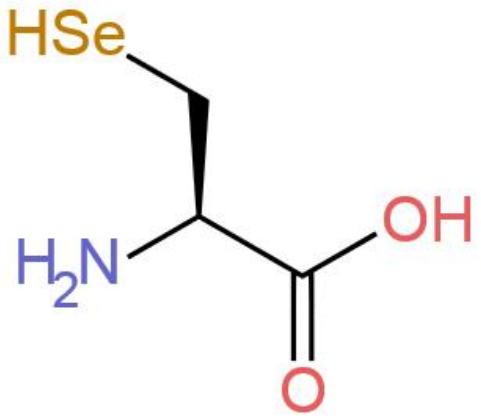


Non-proteinogenic amino acids

Aside from the 23 proteinogenic amino acids, there are many other amino acids that are called non-proteinogenic. Those either are not found in proteins (for example carnitine, GABA) or are not produced directly and in isolation by standard cellular machinery (for example, hydroxyproline and selenomethionine).



Non-proteinogenic amino acids that are found in proteins are formed by post-translational modification, which is modification after translation during protein synthesis. These modifications are often essential for the function or regulation of a protein; for example, the carboxylation of glutamate allows for better binding of calcium cations,[45] and the hydroxylation of proline is critical for maintaining connective tissues.[46] Another example is the formation of hypusine in the translation initiation factor EIF5A, through modification of a lysine residue.[47] Such modifications can also determine the localization of the protein, e.g., the addition of long hydrophobic groups can cause a protein to bind to a phospholipid membrane.[48]

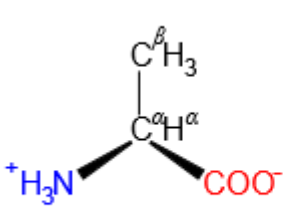


Some non-proteinogenic amino acids are not found in proteins. Examples include lanthionine, 2-aminoisobutyric acid, dehydroalanine, and the neurotransmitter gamma-aminobutyric acid. Non-proteinogenic amino acids often occur as intermediates in the metabolic pathways for standard amino acids – for example, ornithine and citrulline occur in the urea cycle, part of amino acid catabolism (see below).[49] A rare exception to the dominance of α-amino acids in biology is the β-amino acid beta alanine (3-aminopropanoic acid), which is used in plants and microorganisms in the synthesis of pantothenic acid (vitamin B5), a component of coenzyme A.[50]

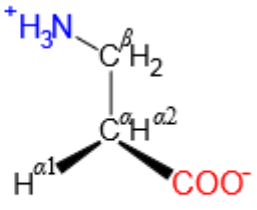
Non-standard amino acids[edit]

The 20 amino acids that are encoded directly by the codons of the universal genetic code are called standard or canonical amino acids. The others are called non-standard or non-canonical. Most of the non-standard amino acids are also non-proteinogenic (i.e. they cannot be used to build proteins), but three of them are proteinogenic, as they can be used to build proteins by exploiting information not encoded in the universal genetic code.

The three non-standard proteinogenic amino acids are selenocysteine (present in many noneukaryotes as well as most eukaryotes, but not coded directly by DNA), pyrrolysine (found only in some archea and one bacterium), and N-formylmethionine (which is often the initial amino acid of proteins in bacteria, mitochondria, and chloroplasts). For example, 25 human proteins include selenocysteine (Sec) in their primary structure,[51] and the structurally characterized enzymes (selenoenzymes) employ Sec as the catalytic moiety in their active sites.[52] Pyrrolysine and selenocysteine are encoded via variant codons. For example, selenocysteine is encoded by stop codon and SECIS element.[10][11][12]



L-α-alanine



β-alanine

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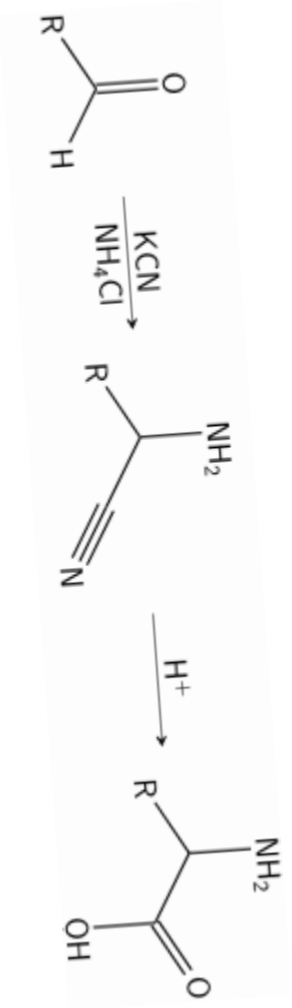
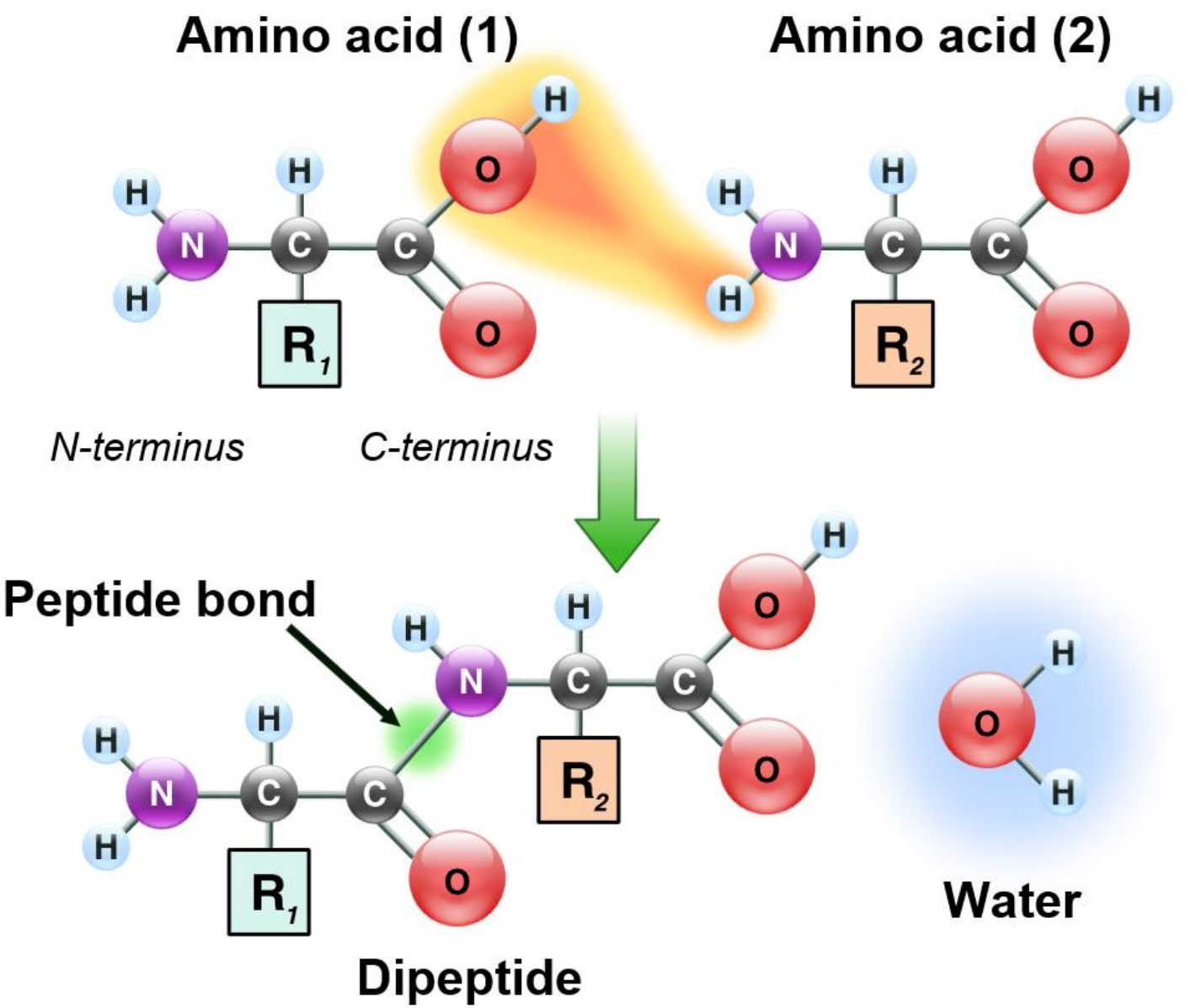
As both the amine and carboxylic acid groups of amino acids can react to form amide bonds, one amino acid molecule can react with another and become joined through an amide linkage. This polymerization of amino acids is what creates proteins. This condensation reaction yields the newly formed peptide bond and a molecule of water. In cells, this reaction does not occur directly; instead, the amino acid is first activated by attachment to a transfer RNA molecule through an ester bond. This aminoacyl-tRNA is produced in an ATP-dependent reaction carried out by an aminoacyl tRNA synthetase.[101] This aminoacyl-tRNA is then a substrate for the ribosome, which catalyzes the attack of the amino group of the elongating protein chain on the ester bond.[102] As a result of this mechanism, all proteins made by ribosomes are synthesized starting at their N-terminus and moving toward their C-terminus.





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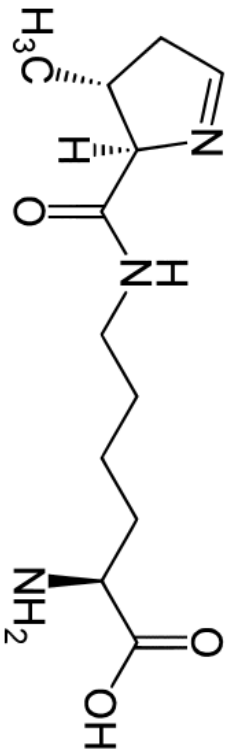
The pylT and pylS genes are part of an operon of Methanosarcina barkeri, with homologues in other sequenced members of the Methanosarcinaceae family: M. acetivorans, M. mazei, and M. thermophila. Pyrrolysine-containing genes are known to include monomethylamine methyltransferase (mtmB), dimethylamine methyltransferase (mtbB), and trimethylamine methyltransferase (mttB). Homologs of pylS and pylT have also been found in an Antarctic archaeon, Methanosarcina barkeri and a Gram-positive bacterium, Desulfitobacterium hafniense.[12][13]

The occurrence in Desulfitobacterium is of special interest, because bacteria and archaea are separate domains in the three-domain system by which living things are classified. When use of the amino acid appeared confined to the Methanosarcinaceae, the system was described as a "late archaeal invention" by which a 21st amino acid was added to the genetic code.[14] Afterward it was concluded that "PylRS was already present in the last universal common ancestor" some 3 billion years ago, but it only persisted in organisms using methylamines as energy sources.[15] Another possibility is that evolution of the system involved a horizontal gene transfer between unrelated microorganisms.[16] The other genes of the Pyl operon mediate pyrrolysine biosynthesis, leading to description of the operon as a "natural genetic code expansion cassette".[17]

Some differences exist between the bacterial and archaeal systems studied. Homology to pylS is broken into two separate proteins in D. hafniense. Most notably, the UAG codon appears to act as a stop codon in many of that organism's proteins, with only a single established use in coding pyrrolysine in that organism. By contrast, in methanogenic archaea it was not possible to identify any unambiguous UAG stop signal.[12] Because there was only one known site where pyrrolysine is added in D. hafniense it was not possible to determine whether some additional sequence feature, analogous to the SECIS element for selenocysteine incorporation, might control when pyrrolysine is added. It was previously proposed that a specific downstream sequence "PYLIS", forming a stem-loop in the mRNA, forced the incorporation of pyrrolysine instead of terminating translation in methanogenic archaea. However, the PYLIS model has lost favor in view of the lack of structural homology between PYLIS elements and the lack of UAG stops in those species.

Pyrrolysine (abbreviated as Pyl or O) is a naturally occurring, genetically coded amino acid used by some methanogenic archaea and one known bacterium in enzymes that are part of their methane-producing metabolism. It is similar to lysine, but with an added pyrroline ring linked to the end of the lysine side chain. It forms part of an unusual genetic code in these organisms, and is considered the 22nd proteinogenic amino acid.



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