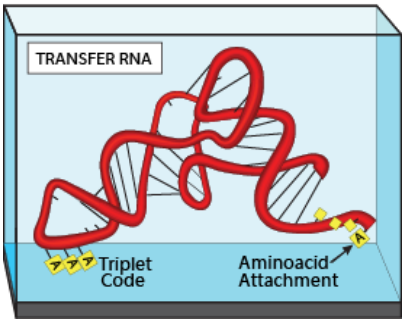
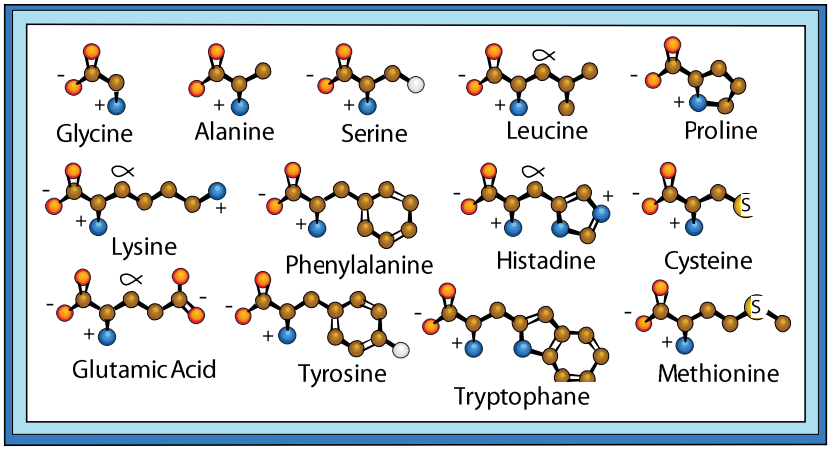
AMINO ACIDS, POLYPEPTIDES AND PROTEINS

Amino Acids and Coding

If it were not for transfer RNA molecules, protein synthesis would not be possible and there would be no coding of amino acids for polypeptide synthesis.

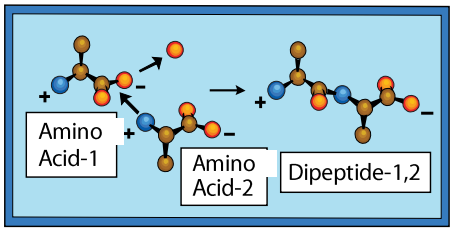


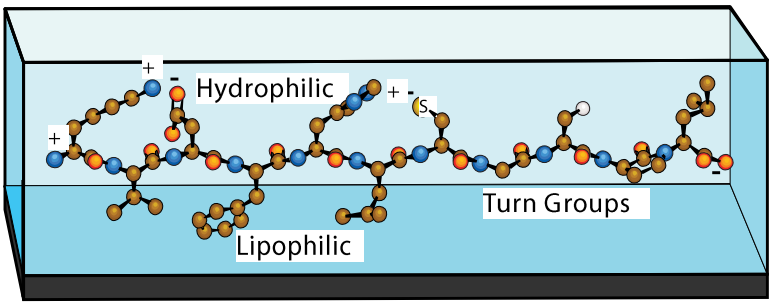
Every single cell in our bodies and in every other living organism contains about 20 t-RNAs with slightly different sequences of nucleotides but all with the same basic spatial structure.[48] Each one chemically-binds a specific amino acid on the terminal adenosine (A) end with a specific sequence of three nucleosides (a triplet code) on the loop at the other end. In other words, t-RNA molecules attach a specific three-letter nucleotide code (or word) to each amino acid so they can be positioned in a specific sequence in polypeptides as they are synthesized in ribosomes based on sequences of A, U, G and C nucleotides in long-chain messenger RNAs.



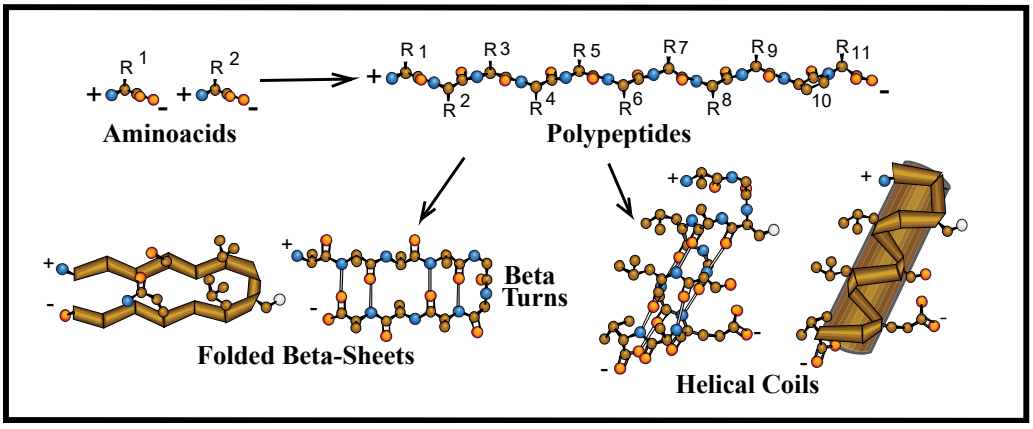
The code for phenylalanine is AAA, for serine, AGA, for leucine, GAG. As you can see in the chart above, each amino acid has a unique structure but they all contain the same CO_2 (acid) and N (amine) so they can be attached together to form amide bonds. As shown on the right below, long-chain polypeptides, sometimes composed of thousands of peptide units, are all arranged in specific sequences based on the specific sequences of triplet codes in linear messenger RNAs.

Polypeptides





Sequences of peptides serve unique roles in defining how polypeptides fold and assemble into proteins.[48] Series of peptides like alanine, phenylalanine, leucine and methionine, which have hydrophobic side chains and do not hydrogen-bond with surface water, induce the formation of adjacent unstable transient covalent linear elements of hydration. Since covalent bonding between water molecules is unstable above 0°C, water molecules in those elements spontaneously move into higher energy dielectric hydrogen-bonding, absorb quantized units of energy from the chains and move them into lower-energy coils.[49]



On the other hand, series of peptides with charged side-chains, like lysine, glutamic acid and histidine, form dielectric linear elements of hydration between their charged heads. Often they maintain chains in linear forms in beta sheets or in coils but, at times, highly-charged peptides like arginine, will produce so much random surface hydration that they break hydration order and initiate turns in chains.[48, 49] Small peptides like glycine, serine and proline continually form dynamic dielectric (point-charge) hydrogen-bonds with adjacent water. They disrupt the formation of linear elements and either cause chains to change direction in beta turns or form broad loops with the freedom to bend in space and fit hydration-ordering regions of beta-sheets and coils together to release ordered water and lower energy between the units.[5]

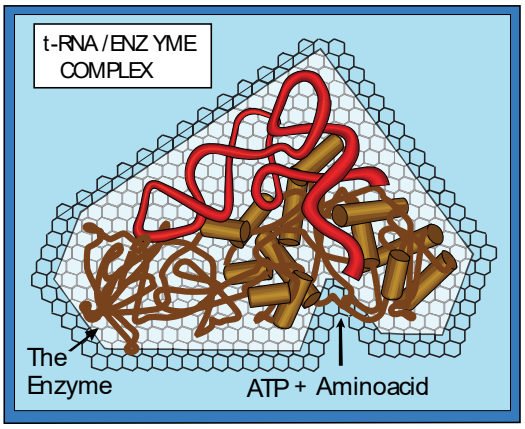
Although many of the amino acids involved in polypeptide syntheses today can be produced by subjecting ammonia and gaseous components in the atmosphere to electrical discharges,[50] we really do not know how they were formed originally - possibly on nucleic acids which no longer exist.[43,44] What we do know is that polypeptides of the type shown above were not formed simply by heating amino acids - heating converts

them into cyclic molecules, most of which are not found in nature.[19]

Thus, it is likely that the formation of natural molecules on the early earth proceeded through four stages: **Sugars and Polysaccharides**, **Nucleosides and Nucleic Acids**, **Polypeptides and Proteins** and, as we shall soon see, **Fatty Acids and Membranes**. As you can see, syntheses of functional polypeptides were much more complex than sugars and nucleic acids before them.

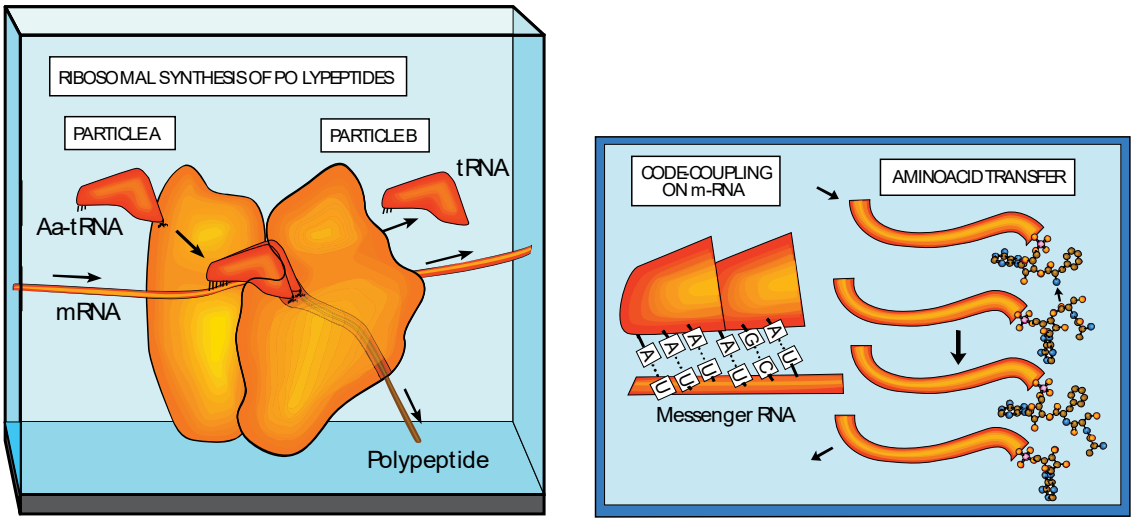
Polypeptide Synthesis

Random synthesis of polypeptides may have occurred prior to the development of functional nucleic acids but it was not until stable nucleic acids, like t-RNAs, were available that amino acids could be assembled into polypeptides with specific sequences of peptides.



Today, attachments of specific amino acids to specific t-RNAs are accomplished by specific enzymes, like the one shown above. A specific t-RNA molecule binds to the upper surface of an enzyme, as shown above, and, by bending the adenosine end of the t-RNA molecule into a groove on the lower right, permits a specific amino acid and a molecule of ATP to bind in the groove and catalytically attach the amino acid to the hydroxyl group of the terminal adenosine nucleoside to form an amino-acylated t-RNA (Aa-t-RNA) molecule. The triplet code on the other end of the t-RNA molecule, which corresponds to the amino acid that has been attached, binds to a complimentary polypeptide sequence on the other end of the enzyme. To increase stability, the t-RNA/enzyme complex conforms to the same cubic hydration patterning as the t-RNA molecule. Dielectric linear elements of hydration which radiate out from the groove most likely direct amino acids and ATP into the reaction binding site.[11] Of course, one question which one might ask is how this coding reaction could be performed before polypeptide enzymes of the sort shown above existed? The answer is that a small nucleic acid recently was isolated which catalyzes the same amino acid-attachment reaction.[46]

Although original ribosomes must have been extremely crude, sequences of nucleotides in those ribosomes which catalyzed the formation of polypeptides might have been the same as those in ribosomes today.



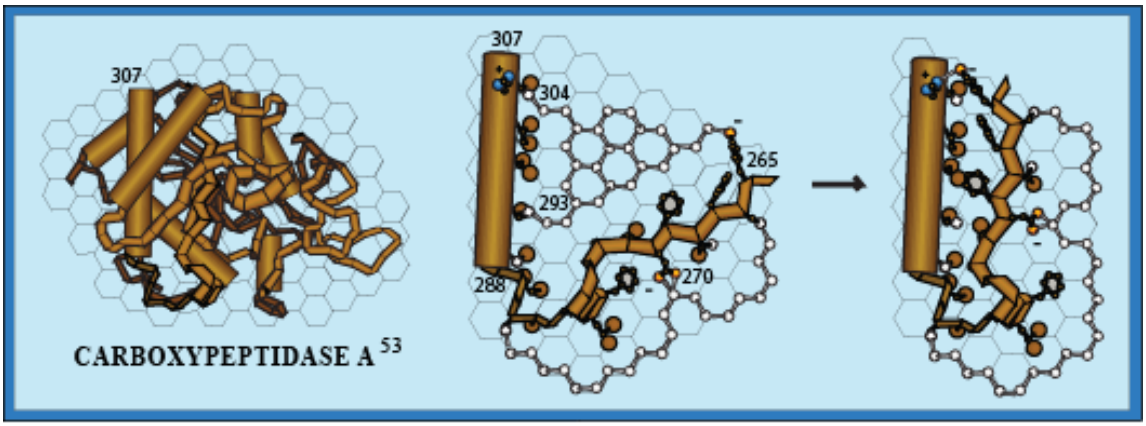
As you can see, ribosomes are extremely large and extremely complex today - containing three or more large nucleic acids and nine or more proteins - so large, in fact, that they can be seen microscopically as dots in cells. As shown on the right, the triplet-code loop of Aa-t-RNA molecules are flat so they can fit side-by-side on sequence codes of a messenger RNAs to position aminoacyl groups close enough together on particle B to form the polypeptide bonds.[51]

By selectively binding sequences of coded Aa-t-RNAs together, based on complimentary sequences of nucleotides in m-RNAs, specific polypeptides are produced extremely rapidly. Of course, as specific polypeptides began to be produced, some of them, undoubtedly, began binding to the ribosomes which produced them. Some proteins which bound increased stability, others provided a binding site for guanosine triphosphate (GTP) to drive m-RNA through the ribosome. Still others must have provided improved selectivity in binding aminoacyl-t-RNAs. Although little is known with regard to the role of surface water in the process of polypeptide formation, it must have been involved and must continue to be intimately involved. Once again, if a ribosome is heated in an aqueous environment, it separates into its parts - on cooling, it reassembles. As amazing as it may seem, if the parts of a ribosome were produced at random and at separate times, they would still have fit so perfectly together that they would have assembled spontaneously to produce the same complex ribosomal structures which exist today. Although water is ignored in terms of its involvement, without its surface ordering/disordering properties, there would be no ribosomes, no polypeptides and no life as we know it!

Proteins

As a linear polypeptide is released from particle B in a ribosome, it must immediately become coated with water (possibly, even before it is fully released). Some surface regions become coated with transient covalent linear elements of hydration, others hydrogen-bond directly with dynamic surface water and become mobile. The most highly-ordered regions rapidly release water and form coils, others remain as linear

elements and form beta sheets while others, by hydrogen-bonding with surface water, form bends and turns.[5] If natural polypeptides do not wrap and assemble properly, proteins called "chaperones" bind to them, rehydrate them and unwrap them to permit them to assemble more slowly into proper, low-energy forms.[52]

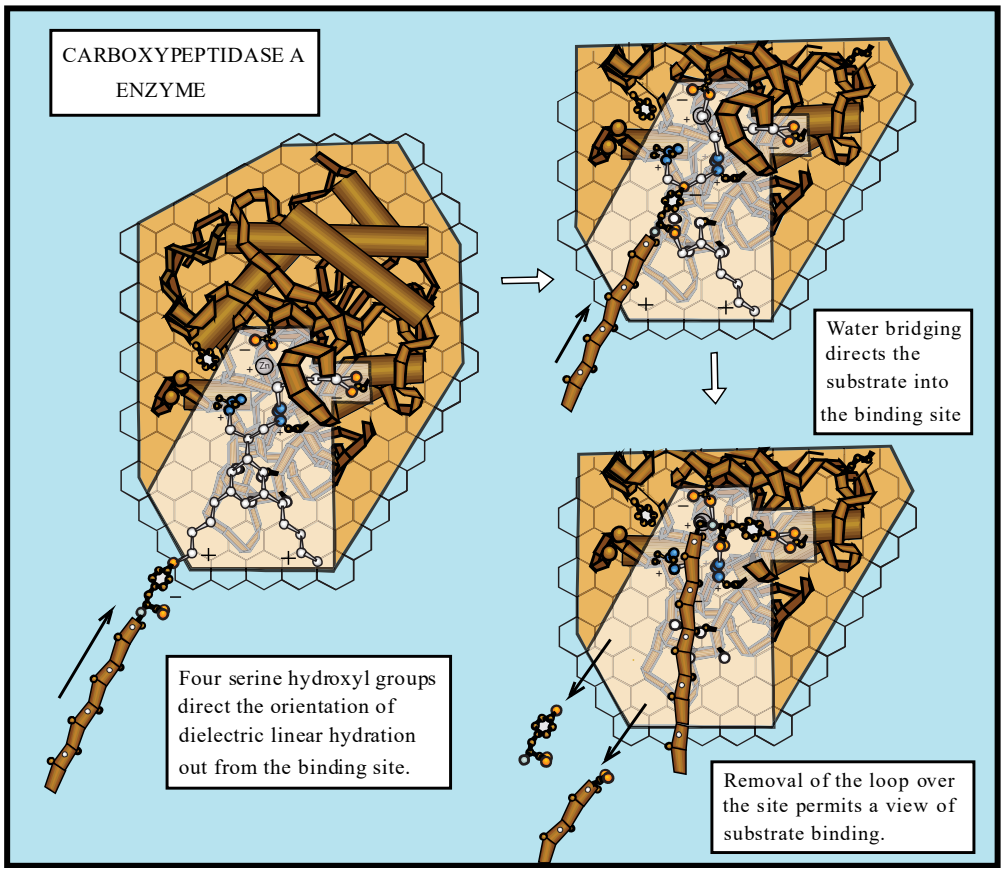


The complete polypeptide for the **Carboxypeptidase A Enzyme** is illustrated on the left.[53] Based on the TLH hypothesis, the long terminal coil of polypeptide ending with peptide 307, which is overlaid by three other coils in the finished protein, serves as one of the nucleating cores for hydration-directed folding and assembly. The middle figure illustrates how the hydroxyl groups of threonine peptides 304 and 293 on the right side of the 307-coil position a transient bridge of covalent linear elements of hydration around two leucine peptides; it is this transient linear element which defines the orientation and positioning of quantized cubic hydration patterning around the molecule. Remember, even though a number of ordered water molecules are pictured in quantized cubic-probability positions, only short linear elements of water are present in those positions at any instant. Most of time, water molecules are randomly distributed in clusters in that space. As water molecules spontaneously leave from ordering elements, the segment of polypeptide ending in tyrosine 265 is drawn into position next to the right side of the coil and the second stage of protein assembly has begun. By moving two hydration-ordering regions of polypeptide together, an anhydrous union is formed between them and the anionic phenol of tyrosine 265 can form an ionic hydrogen bond with the cationic ring of histidine 303. Once a quantized probability hydration patterning has been established around a core, it assists in directing, not only further folding and assembly, but the functional properties of the finished protein as well.

Enzymes

Although thousands of studies of polypeptides have provided convincing evidence that water serves a vital role in folding and assembly and nuclear magnetic resonance illustrates that water adjacent to lipophobic surfaces is "ice-like," [5,10] it has not been possible to define precisely how it performs that role.[3] Only by rigorously accepting the principle that water spontaneously forms dynamic **Quantized Transient Linear Elements of Hydration** adjacent to ordering surfaces and between charge centers and that a type of **Quantized Cubic Hydration Patterning** develops around molecules, has it been possible to realize that the same properties direct the functional properties of

finished proteins.[29]



For example, the schematic figures above illustrate how dielectric linear elements, which conform to established cubic hydration patterning, emanate from the enzymatic binding site of carboxypeptidase A to attract the anionic tyrosine end of a polypeptide chain into the site. A planar surface on the enzyme, with strategically-placed serine hydroxyls, permits multiple transient linear dielectric elements of hydration to radiate out from the central cationic binding site which is composed of two (blue) arginines, two (red) carboxylate groups and a (gray) zinc ion in the center. A single short transient covalent linear element of water continually forms in the site below a loop of enzyme to hold that region open for the side-chain of the terminal peptide. As the anionic tyrosine end of the reacting polypeptide is drawn toward the cationic binding site, water molecules continually form bridging dielectric linear elements between the charges. Once the terminal tyrosine peptide is bound firmly in the site with its phenolic ring below the loop, an oxygen atom of the (orange) acid group in the site reacts with the amide group of the second peptide, releases the terminal tyrosine as a free amino acid and then reacts with single water molecule above the zing ion to release the shortened polypeptide chain.

In order for the cleavage reaction to occur, all water within the binding site must be displaced by the terminal peptide. If the terminal peptide does not have an aromatic ring to displace all water below the loop (like the phenolic ring of tyrosine shown), residual water will destabilize the site and drive the peptide out before the reaction can occur.

Thus, the space below the loop must be precisely the size to permit only terminal peptides with aromatic rings, like tyrosine, phenylalanine and tryptophane, to bind and be cleaved by this enzyme. Usually, all water must be displaced from the binding sites in enzymes and receptor proteins for them to perform their normal functions. Quantized dimensional properties of ordered water are not only important in enzymes - they play a vital role in the binding sites of receptor proteins as well.[11, 29]

In fact, as we view the assembly of the enzyme shown above and its catalytic reaction properties, they seem so rational that we might suppose that the enzyme was specifically "designed" to perform the cleavage reaction. Perhaps it was but, more likely, this protein, as well as all other proteins in living cells, were assembled originally by a process of trial-and-error to achieve the **best fit for cooperative function**. In fact, molecular evolution and the process of trial and error are not complete and probably never will be. New nucleic acids, new proteins and new molecules are continually being produced as m-RNAs change, either by random or induced mutation. Remember, virus and bacteria - even the cells in our bodies - continually change to accommodate for changes in diet and surroundings.