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Topics: Chemical and physical properties of amino acids

Ribosomes are assembly lines found in humans, plants, algae and bacteria alike. Polymerases are natural copy machines. They do not make mistakes often. They make 1 mistake per billion copying process.

Proteases and proteosomes are for protein destruction, which is equally important for normal functioning of cells and all living systems. Uncontrolled growth of organs could result in tumors otherwise. 2002 and 2004 Nobel Prizes in Medicine have gone to research in programmed cell death and controlled protein degradation.

Ligases are chain couplers for DNA that joins short double helical DNA fragments into single long one. It joins faster when the DNA fragments have complementary overlap ends which can sometimes find each other without external help. Ligase can still couple DNA fragments without the overlapping ends, also called blunt ends, but at a slow rate with low efficiency because the ligase must first find the ends and hold them together, and before it can couple them enzymatically.

One mystery unsolved in biology so far is: Size of cell is 5~10 microns but the molecules inside are 2-10s of nanometer. The transport of the molecules within the cell is rapid. The transport mechanism is not by diffusion and it is not understood well yet. The network in the cell is very dense (30% substances and 70% water)

Like postal and UPS and postal mail deliveries, protein sorting makes no mistake. If a mistake is made, it results in disaster for the cell.

The cell membrane is differentially charged and has a definite potential. The charge potential is used for making nerve impulses.

Single neuron can simultaneously connect to 1,000-5,000 other cells.

Different colors of stones pack in the same place. 2-D Packing of stones in the same place is remarkably similar to protein folding. Shape determines function. This is similar to proteins folding also.

Potala palace in Lhasa, Tibet, constructed in ~700 AD. The palace is made with a lot of straws and stones, assembled by men. This process is called programmed assembly, namely, programmed and hand assembled by human.

Proteins are made of many individual amino acids, assembled by ribosomes. A single amino acid cannot do much. If you put 20 different kinds of amino acids together in various forms, from few tens, few hundreds to thousands, you can create a remarkable machine, a protein. The protein that performs photosynthesis that converts solar energy to chemical energy has only 20 kinds of amino acids.

Sizes of single amino acids is a few Ås in 3-D with a few atoms.

There are 4 hemes in a haemoglobin molecule. Haemoglobin molecules transport oxygen. People living in high altitudes have high haemoglobin content in their blood. Nature self-assembles molecules through weak forces of attraction. Why it requires 4 chains in haemoglobin to be fully functional is not well understood yet. It is common in proteins that require multi-units to be functional. Some people suggest for the coordinated action and high efficiency. The real reason remains unknown.

Molecular orbital sp^3 hybridization results in tetrahedral structure. That occurs in several atoms. Methane has tetrahedral structure. If we replace one hydrogen with some other molecule, the structure changes, thus the functions.

The side chains determine the handedness of a molecule. Handedness of molecule is important to determine function. L- form reads CORN in clockwise direction. L-form is ubiquitous in nature. It is not well understood why it is so commonly prevalent. Barry Sharpless who was a former MIT chemistry professor won Nobel Prize for asymmetrical synthesis.

L-form enzyme cannot chew D-form substrate and vice-versa. Ribosomes can discriminate the amino acids. Fungi can make antibiotics containing D-form. So we can take in these antibiotics without fear of destroying our own proteins. If we make material with D-form will be stable for a very long time.

Memory: L- to the left, D- to the right. It is important in chemistry and material science as to make a material more stable, we have to make it using D-form amino acids.

pKa is the dissociation constant for the hydrogen in the side-chains. Lysine and Arginine are highly positively charged. Histidine can be protonated or deprotonated. Cysteine can bind to metals such as gold, silver very well. Serine, Threonine and Histidine coordinate to metals through H-bonds.

Classification:
Hydrophobic groups. Different sizes of side chains.

Glycine is the simplest amino acid known. It is the most commonly prevalent amino acid. Most structural material like collagens, silk, spider silk and bioadhesives have abundance of Glycine and Alanine. Glycine has been discovered in the intergalactic dust.

Influence of side chains: Serine and Threonine, Tyrosine can form 2 more hydrogen bonds. Asparagine can form 4 H-bonds, 2 donors on -NH2 and 2 acceptors on =O.

Arginine is extremely soluble in water. Additionally it can get protonated at < pH 12. Lysine can get protonated at < pH 10.

Non-polar residues are folded on the inside of the protein. It is easy to study globular proteins while it is difficult to study membrane proteins. There are > 35,000 globular proteins known so far in PDB. However only 106 unique membrane proteins are known out of 204 containing slight changes (April 2006).

Once primary structure is specified, some proteins will likely fold on its own because of the force of water. But some others need the assistant called chaperons for the correct folding.

β- branch amino acids tend to form β-sheets. Isoleucine and Valine are beta-branched while Leucine is not. With leucine we get alpha-helical structure. With Valine and Isoleucine, we get a beta-sheet structure. But there is always exception to the rule in biology.

In Phenylalanine, it has a ring structure like benzene. In Tyrosine there is phenol group which makes it more soluble in water. Sugar is soluble in water because it has a lot of OH groups, which can form many H-bonds. Tryptophan has 2 rings but can only make single hydrogen bond. It is very important in function. Phe is less soluble and hydrophobic. Trp is more soluble and less hydrophobic. These can be detected under UV light of 214 nm for the backbone and at 260 nm for Phe and Tyr and 280 nm for Trp. Most proteins have high Trp content. If Trp is not present, it is difficult to detect the protein. These amino acids contain aromatic rings which can form additional hydrogen bond through it rings which has an electron cloud that acts as hydro acceptor. This type of hydrogen bond has been observed in proteins including haemoglobins.

Amino acids have some similar and different shapes. For example, Serine and Cysteine look identical in shape. Cysteine smells bad but Serine has no smell. Methionine also smells bad because of the thiol group. If a protein becomes oxidized it becomes a bad protein. Likewise, Threonine and Valine look alike but have very different chemical properties.

Proline has a ring structure with fully saturated hydrogen and is hydrophobic. Collagens in animals and in our body have a lot of prolines and modified hydroxyprolines, i.e. proline with an extra –OH group.

Both Aspartic acid and glutamic acid have two oxygen groups, Asn and Gln have one oxygen and one amine group. Asp and Glu have 4 hydrogen acceptors. Asn and Gln have 2 hydrogen acceptors and 2 donors. Glu and Gln have similar structure as Asp and Asn, except an additional carbon atom is added in Glu and Gln increases the side chain ~1.5 Å.

Ala, Gly, Cys, Thr, Ser have small side-chains. Solubility in water determines if an amino acid is polar and non-polar.

The genetic code, in nucleic acids, Purines have larger rings. Pyrimidines have smaller rings. Uracil, Cytosine, Thymine are pyrimidines, Adenine, Guanine are purines. The second codon in the genetic code is critical. This way of writing genetic code is crucial in designing new material. It is curios to note that nature has some special preference for the 2nd codon for particular amino acid properties. When the 2nd codon is pyrimidine, the amino acids are hydrophobic with different degree hydrophobicity. On the other hand, when the 2nd codon is purine, the amino acids are often hydrophilic.

Protein folding or protein-protein interactions are through weak interactions. Van der Waals interaction is one which has no charges. Leucine-Leucine interactions are through van der Waals forces. Water mediated interactions are called water-mediated hydrogen bonds. We need to understand both inter-molecular structure and intra-molecular structure for collagen formation.

The hydrogen bonds of Arginine are in the same plane. Nine consecutive Arg molecules in a peptide facilitate cellular transport for gene delivery or drug delivery.

Weak interactions are individually weak, but collectively they are very strong and result in self-assembly in biological systems. One penny is not worth very much, but 1billion pennies are worth a lot of money.

The dipole interactions occur in water, amino acids, peptides and proteins. Asymmetric molecule has a dipole moment.

Salt plays a crucial role in protein precipitation and protein salvation. Ions once surrounded by charged molecules have weaker interactions.