Amino Acid

Amino Acid	One-Letter Code	Three-Letter Code	Chemical Properties
Alanine	A	Ala	nonpolar
Arginine	R	Arg	basic, polar
Asparagine	N	Asn	polar, uncharged
Aspartic Acid	D	Asp	acidic, polar
Cysteine	C	Cys	polar, uncharged
Glutamine	Q	Gln	polar, uncharged
Glutamic Acid	E	Glu	acidic, polar
Glycine	G	Gly	nonpolar
Histidine	H	His	basic, polar
Isoleucine	I	Ile	nonpolar
Leucine	L	Leu	nonpolar
Lysine	K	Lys	basic, polar
Methionine	M	Met	nonpolar
Phenylalanine	F	Phe	nonpolar
Proline	P	Pro	nonpolar
Serine	S	Ser	polar, uncharged
Threonine	T	Thr	polar, uncharged
Tryptophan	W	Trp	nonpolar
Tyrosine	Y	Tyr	polar
Valine	V	Val	nonpolar

Dynorphin

Dynorphin is a neuropeptide that belongs to the opioid family of peptides. It is a 17 amino acid long peptide that is known to play a role in pain modulation and addiction. Like other neuropeptides, dynorphin has a unique sequence of amino acids and specific properties.

Dynorphin contains a disulfide bond between amino acids 5 and 11. This bond is crucial for maintaining the structure and stability of the peptide. The bond angle between these two amino acids is around 105 degrees, which is important for the proper folding of the peptide. Additionally, dynorphin has several side chains, including a phenylalanine at position 3, an arginine at position 7, and a tyrosine at position 13.

The amino acids 7 and 10 of dynorphin are similar to those of Substance P. Like Substance P, amino acid 7 of dynorphin is an arginine residue, which is positively charged and can interact with negatively charged molecules. Amino acid 10 of dynorphin is a phenylalanine residue, which is non-polar and hydrophobic. This residue is important for forming hydrophobic interactions within the peptide or with other molecules.

Like other amino acids, dynorphin amino acids have a chiral center, which means they can exist in two possible stereoisomers, L or D. The natural form of dynorphin is composed of L-amino acids, which are the most common type found in biological systems.

Overall, dynorphin is a complex neuropeptide with a unique sequence of amino acids and specific properties that contribute to its function in the body. Its similarity to Substance P in terms of amino acid composition underscores the importance of these amino acids in neuropeptide function and structure.

Properties:

1. Molecular weight: 2110.3 g/mol
2. Chemical formula: C93H147N25O20S2
3. Three-dimensional structure: Dynorphin has a helix-turn-helix motif, which consists of two alpha-helices connected by a short turn region.
4. Bond angle: The peptide bond angle is approximately 120 degrees, and the bond length is approximately 1.3 angstroms.

5. Chirality: Dynorphin is a chiral molecule, meaning that it has a non-superimposable mirror image.
6. Side chains: Dynorphin has several side chains that contribute to its biological activity, including the aromatic ring of phenylalanine, the basic side chains of arginine and lysine, and the acidic side chain of aspartic acid.

No. of Amino Acid	Peptide	3-Letter Code	1-Letter Code	Molecular Weight	Sequence	Structure	Side Chain	Ground State Energy (kJ/mol)	Physiological Function	Nature (Hydrophobic or Not)	CHIRAL	BOND ANGLE	BOND LENGTH
17	Dynorphin	Dyn	Y	1972.2	Tyr-Gly-Gly-Phe-Leu-Arg-Arg-Ile-Arg-Pro-Lys-Leu-Lys-Trp-Asp-Asn-Gln	Alpha helix and beta sheet	Both polar and nonpolar, aromatic and aliphatic	-46.6	Pain modulation, stress response, and addiction	Both hydrophobic and hydrophilic	Yes	109.5°	1.46 Å
7	Amino acids 7	APRLRFY	APRFLY	833.9	Ala-Pro-Arg-Leu-Arg-Phe-Tyr	Alpha helix	Both polar and nonpolar, aromatic and aliphatic	-5.5	None	Both hydrophobic and hydrophilic	Yes	109.5°	1.46 Å
10	Amino acids 10	TRVYIHPFHL	TRVYIHPFHL	1177.4	Thr-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu	Alpha helix	Both polar and nonpolar, aromatic and aliphatic	-18.3	None	Both hydrophobic and hydrophilic	Yes	109.5°	1.46 Å

Dynorphin is a neuropeptide composed of 17 amino acids. It is known to act as an endogenous opioid peptide that binds to kappa-opioid receptors in the central nervous system. Dynorphin is characterized by its unique structural features, including a disulfide bond between cysteine residues at positions 2 and 13, and a C-terminal amidation.

Amino acid 7 is proline, which is a cyclic amino acid with a rigid structure. Proline is often found in turns or loops in protein structures due to its unique geometry. It has a secondary amine group that is part of the cyclic structure, which causes it to have a lower reactivity than other amino acids.

Amino acid 10 is phenylalanine, which is an aromatic amino acid with a bulky side chain. It is often involved in hydrophobic interactions due to its nonpolar nature. Phenylalanine is important for protein stability and can also participate in various protein-protein interactions.

In terms of **similarities** between dynorphin, amino acid 7, and amino acid 10, all three molecules contain chiral centers. Dynorphin contains several chiral centers due to the presence of multiple amino acids, including proline and phenylalanine. Amino acid 7 (proline) is also chiral, while amino acid 10 (phenylalanine) contains a chiral center in its side chain.

All three molecules also have unique bond angles and bond lengths due to their specific chemical structures. Dynorphin contains a disulfide bond between cysteine residues, while proline has a cyclic structure that affects its bond angles. Phenylalanine contains a benzene ring in its side chain, which affects its bond lengths and angles.

Overall, while dynorphin, amino acid 7 (proline), and amino acid 10 (phenylalanine) have some similarities, they also have distinct structural features that make them unique**.**

Levinthal's paradox

Levinthal's paradox is a thought experiment in biochemistry and biophysics that highlights the fundamental problem of protein folding. It was proposed by the American biophysicist Cyrus Levinthal in 1969.

The paradox is based on the assumption that a protein can sample all possible conformations before finding its final, most stable state. If each amino acid in a protein chain has two possible states (cis and trans), there would be 2^N possible conformations for a protein with N amino acids. For example, a protein with just 100 amino acids would have 2^100, or approximately 10^30, possible conformations.

If a protein could randomly sample all these conformations, it would take an extremely long time to find the correct one. However, proteins can fold into their native conformations in a fraction of a second or less, which is too short a time for the protein to sample all possible conformations.

This paradox led to the proposal of the idea of folding pathways, which suggests that proteins follow a set of intermediate states on their way to the native state, rather than sampling all possible conformations. This concept has been supported by experimental evidence and computational simulations. The folding pathway hypothesis also implies that the protein folding process is highly cooperative, with the different regions of the protein folding simultaneously.

Constraint term

H_{gc} (geometrical constraint term) : H_gc (geometrical constraint term) refers to the restriction on the growth of the primary sequence of amino acids without branching or bifurcation. It is one of the factors that limit the number of possible conformations a protein can adopt during the folding process.
Proteins are linear polymers of amino acids that fold into specific three-dimensional structures to perform their biological functions. However, the number of possible conformations that a protein can adopt is astronomically large, making it impossible for a protein to explore all the possible conformations and find the native, functional state by random search alone.
H_gc acts as a constraint that limits the possible paths that a protein can take during the folding process. It dictates that the growth of the protein chain must proceed in a linear, non-branching fashion, with each amino acid residue being added to the growing chain in a specific sequence. This constraint reduces the conformational space available to the protein during folding, making it easier for the protein to find the native state.

Overall, the geometrical constraint term H_gc is a crucial factor in protein folding, as it limits the number of possible conformations that a protein can adopt during the folding process and helps guide the protein to its native state.

In molecular biology, chirality is a property of a molecule that is non-superimposable on its mirror image, which means that it is asymmetric. In the context of protein structure, chirality is important because amino acids have chiral centers in their side chains, and the right stereochemistry is crucial for the proper folding and function of the protein.

Chirality Constraint : H_{ch}, the chirality constraint term in protein folding, enforces the correct stereochemistry of the system. This term penalizes conformations that violate the right-handedness of the peptide bond, ensuring that only peptides with the correct stereochemistry are allowed in the protein structure. This is important because if the wrong stereochemistry is allowed, it could lead to non-functional proteins or even harmful effects in living organisms.

The Nearest Neighbor Interactions : In the context of protein folding simulations, H_{in} represents the interaction energy between neighboring amino acids in the protein chain. The energy of interaction between two amino acids depends on their specific side chain properties and their spatial arrangement relative to each other.

The nearest neighbor interactions refer to the interactions between amino acids that are in direct contact with each other in the protein chain, that is, the amino acids that are next to each other in the sequence. The energy of interaction between neighboring amino acids is a function of their distance, orientation, and the nature of their side chains.

The H_{in} term in the energy function takes into account the interactions between all pairs of neighboring amino acids in the protein chain. By considering only the nearest neighbor interactions, the computational complexity of the protein folding simulation can be significantly reduced, while still capturing the essential features of protein folding. This simplification allows for a more efficient exploration of the conformational space and can lead to faster convergence towards the native state of the protein.

Other Constraint

Van der Waals interactions: These are the attractive and repulsive forces between atoms that arise due to fluctuations in electron density. In protein folding, van der Waals interactions play a major role in determining the relative positions of atoms within the protein.

Electrostatic interactions: These are the attractive and repulsive forces between charged particles. In proteins, electrostatic interactions between charged amino acid side chains can play an important role in determining the stability and conformation of the protein.

Hydrogen bonds: These are weak bonds between hydrogen atoms and electronegative atoms (such as oxygen or nitrogen). In protein folding, hydrogen bonds play a critical role in stabilizing the secondary structure of the protein (such as alpha helices and beta sheets).

Torsional energy: This refers to the energy required to bend or twist the protein backbone. Torsional energy can play a significant role in determining the overall shape of the protein.

Entropic effects: These refer to the changes in entropy that occur during protein folding. Entropic effects can have a significant impact on the folding process and the stability of the protein.

Steric constraints: These are constraints that arise due to the physical size and shape of amino acid side chains. Steric constraints can limit the conformational space available to the protein and can impact the folding process.

Solvent effects: The presence of water molecules and other solvents can also impact protein folding. Solvent molecules can interact with the protein and influence its conformational stability.

All of these terms and constraints must be considered when modeling protein folding. By accounting for these factors, researchers can develop accurate models of protein folding and gain insights into the molecular mechanisms underlying this process.

How a van der waal's interaction occur in 7 amino acid , 10 amino acid and dynorphin ?

Van der Waals interactions occur in all proteins, including 7 amino acid, 10 amino acid, and Dynorphin. These interactions arise due to temporary or induced dipoles in nonpolar molecules that attract each other, resulting in weak intermolecular forces.

In proteins, van der Waals interactions occur between nonpolar amino acid side chains, such as those of alanine, valine, leucine, isoleucine, phenylalanine, and tryptophan. These side chains are typically found in the hydrophobic interior of proteins, where they help stabilize the protein's three-dimensional structure.

The strength of van der Waals interactions depends on the distance between the atoms involved and the size of the atoms. At very short distances, the electron clouds of the atoms begin to repel each other, resulting in a rapid decrease in the attractive force. At larger distances, the attractive force decreases more slowly, eventually reaching zero.
The effect of van der Waals interactions on the minimum energy of a protein fold depends on the specific arrangement of atoms in the protein. In some cases, van der Waals interactions can stabilize a protein fold by bringing nonpolar amino acid side chains into close proximity and minimizing the surface area exposed to water. In other cases, van der Waals interactions can destabilize a protein fold by causing nonpolar side chains to cluster together and interfere with the proper packing of the protein.

Overall, van der Waals interactions play an important role in the folding and stability of proteins, including 7 amino acid, 10 amino acid, and Dynorphin.
The folding of a protein is a complex process that involves many factors, including the interactions between amino acids and the environment. In a protein consisting of 17 amino acids, the folding process will be guided by various factors, such as the hydrophobicity and polarity of the amino acids, as well as the formation of hydrogen bonds and van der Waals interactions.

The folding process begins with the linear chain of amino acids, known as the primary structure. This structure can be thought of as a string of beads, with each bead representing an amino acid. The next step is the formation of local structures, such as alpha helices and beta sheets, which are stabilized by hydrogen bonds between the amino acid residues. These local structures can then fold further to form larger structures, such as domains and subunits.

The folding process is driven by the search for the lowest energy state, or the most stable conformation, of the protein. This search is guided by various interactions between amino acids, such as hydrophobic interactions, which cause non-polar amino acids to cluster together, and electrostatic interactions, which occur between charged amino acids.

In the case of a 17 amino acid protein, the folding process will be much simpler than in larger proteins, due to the smaller number of amino acids involved. However, the principles of protein folding remain the same, and the folding process will still be guided by the interactions between amino acids and the environment.

In order to predict the conformation of a protein consisting of 17 amino acids, computational methods can be used. These methods simulate the folding process and predict the most stable conformation based on various physical and chemical parameters. However, even with these methods, predicting the conformation of a protein can still be challenging, due to the complexity of the folding process and the many factors that can influence it.

The Miyazawa-Jernigan potentials

Miyazawa and Jernigan introduced knowledge-based potentials for protein inter-residue contacts in their paper "Estimation of effective inter-residue contact energies from protein crystal structures: quasi-chemical approximation" published in Macromolecules in 1985.

The quasi-chemical approximation assumes that the presence of a residue at a certain position in a protein chain affects the energy of the residues in its vicinity. The potential energy between two residues is therefore proportional to the frequency of their contact in a database of protein structures.

Miyazawa and Jernigan's potentials were derived from a set of 65 non-redundant protein structures using a simple Lennard-Jones potential. They calculated the frequency of contact between all pairs of amino acids and used this information to generate a matrix of contact energies. This matrix provides an estimate of the energy required to bring two residues into contact in a folded protein structure.
The Miyazawa-Jernigan potentials have been widely used in protein structure prediction and design. They provide a useful tool for evaluating the quality of protein structures and for guiding the design of new proteins with desired properties.

We can use Miyazawa-Jernigan (MJ) potential to calculate the energy of inter-residue contacts for a protein consisting of 17 amino acids. The MJ potential is derived based on the statistical analysis of inter-residue contacts in a large set of known protein structures, and it provides a way to estimate the stability of protein structures based on the types and distances of contacts between amino acid residues.

To use the MJ potential, we would need to calculate the distances and types of contacts between all pairs of amino acids in our 17-amino acid protein, and then use the MJ potential to calculate the energy associated with each contact. The total energy of the protein would be the sum of all contact energies.

Keep in mind that the MJ potential is a simplified model of protein interactions, and it does not capture all of the complexities of protein folding and stability. However, it can be a useful tool for predicting the relative stability of different protein structures and for guiding protein engineering efforts.

Penalty

1. Penalty_chiral: A penalty parameter used to impose the correct chirality in the peptide chain. The amino acids in the peptide chain have a specific stereochemistry, and a penalty is applied if the model generates incorrect stereochemistry for an amino acid. This penalty term ensures that the peptide chain generated by the model has the correct chirality.

2. Penalty_back: A penalty parameter used to penalize turns along the same axis in the peptide chain. If the model generates a sequence where the same axis is chosen twice in a row, it is eliminated. This constraint ensures that the peptide chain generated by the model does not fold back into itself, which would be a physically unrealistic configuration.

3. Penalty_1: A penalty parameter used to penalize local overlap between beads within a nearest neighbor contact. This penalty term ensures that there are no steric clashes or overlaps between amino acids in close proximity to each other in the peptide chain. The model penalizes configurations where the beads overlap, ensuring that the peptide chain has a physically realistic structure.

The penalty functions mentioned are related to the conformation of a protein and can be applied to any protein or peptide including 7 amino acid, 10 amino acid, and dynorphin. These penalties are used to ensure that the physical constraints on the protein are respected during the folding process.

Penalty_chiral: In the case of 7 amino acid, 10 amino acid, and dynorphin, this penalty ensures that the amino acids are in the correct orientation to form the proper backbone structure.

Penalty_back: This penalty helps to maintain the proper protein backbone structure in 7 amino acid, 10 amino acid, and dynorphin, which is important for its overall stability and function.

Penalty_1: It helps to avoid steric clashes between amino acids that are close to each other. Steric clashes can lead to an increase in the minimum energy of the protein structure, making it less stable. By avoiding these steric clashes, the protein can maintain its proper structure and function, which is critical for biological activity.

Overall, these penalties help to reduce the minimum energy of the protein by ensuring that the amino acids are in the correct orientation and that the protein structure is stable and free from steric clashes.

We can try these peptides of Dynorphin

Peptide	**Peptide Sequence**	**One-Letter Code**
Dynorphin A	YGGFLRRIRPKLKWDNQ	YFLRIPKWDNQ
Dynorphin B	YGGFLRRQFKVVT	YFLRFKVVT
Dynorphin B-29	YGGFLRRQFKVVTG	YFLRFKVVTG
Dynorphin B-30	YGGFLRRQFKVVTH	YFLRFKVVTH
Dynorphin A-(1-8)	YGGFLRRQ	YFLRRQ