**Knots in protein structures**

**.1 Knots**

Knots in proteins are very rare and they should be avoided in the protein folding process. Proteins are considered knotted if their backbone is entangled to form a knot. Imagine pulling a protein by holding both its termini (N and the C terminals), if the sequence ends up having a loop which goes through itself, then we consider it as a knotted protein[1]. Knots in protein chains occur in much lesser frequency than would be expected from the polymers of the same length. In many cases the knots are formed near the terminals, these knots disappear when the short sections near the terminals of the polypeptide chain are trimmed. Deep knots in protein chain however occur very far from the terminals and are not often observed. Nearly 2% of the proteins deposited in the PDB are discovered to be knotted.

**.2 Discovery of knots in protein structures**

Relationship between folding pathways and it the native structure of the protein has led to the development of measures to predict the folding rates of a protein[2]. According to these measures proteins may not fold easily to its native states if their pathways have strange and unlikely configurations. These can happen particularly if the proteins have complex topological features such as knots. Although they are rare, a few of them have been found. Computational, structural, and biophysical investigations of these unusual proteins should lead to valuable insight into how proteins fold and how they maintain their folded configurations, often under extreme conditions[2].

Crippen in 1974[3] considered the case of how likely a linear protein chain would fold into a knot. None of the known structures back then had knotted protein backbones. Twenty years later Mansfield considered the situation computationally by taking the database of known protein structures and checking them for knots. In a mathematical sense, only a closed curve can get knotted, but ideas with open curves such as proteins were introduced which were considered knotted practically. The chain termini were extended from the body of the protein and joined them virtually[4]. In the first computational survey, approximately 400 known protein structures were examined and no deep knots were found. The concept of protein knots again changed in the year 2000 when Taylor[5] discovered a deeply knotted protein structure. This led to the reopening of the questions related to how unlikely knots are in proteins and emphasized on the importance of using computational methods to examine proteins with such topological features. Recent investigations have identified five or six distinct protein having knots with significant depth[1][6]and experiments to understand the effects of proteins have started.

**.3 Effects of knots in proteins.**

In general a protein with no knots should get disentangled and it should not have any loops in it. Knots in proteins are tough to understand as the complexity to reach its native state becomes tougher and complicated to determine its function and proteins with knots are less efficient than the unknotted proteins. Structure Prediction methods do not model the protein folding process itself but rather try to seek only the native state. Consequently, the knot prediction mechanisms are not relevant to the protein modeling process, which means the possibility of finding knots are high in protein models.

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