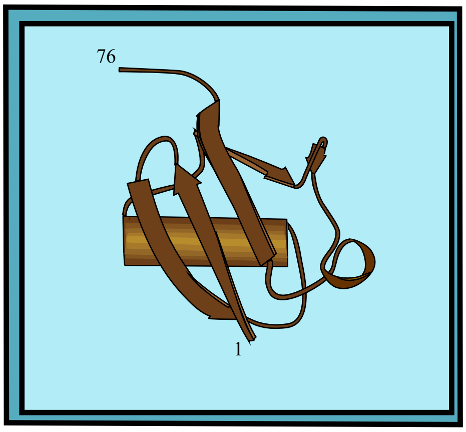
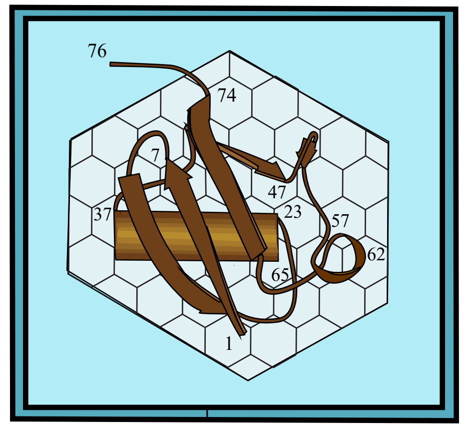
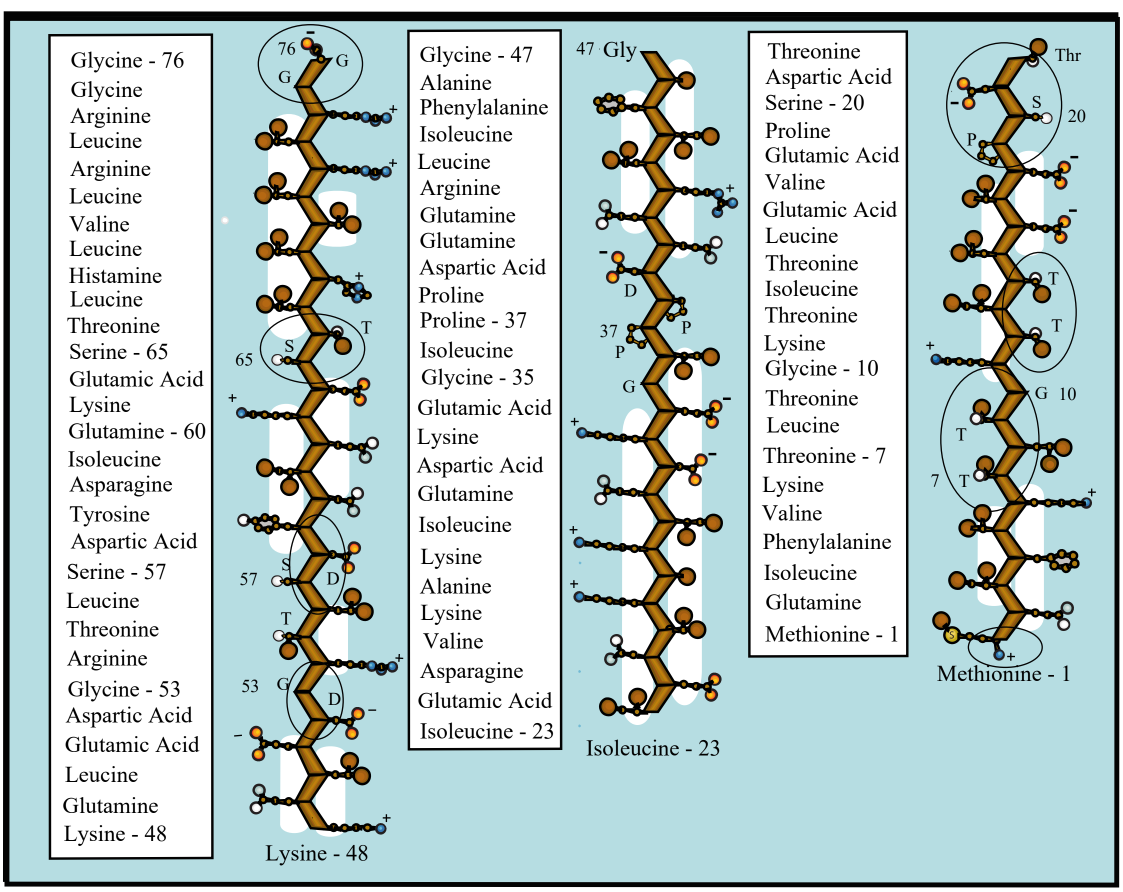
Ubiquitin

Ubiquitins are members of a family of proteins which are present in almost every living cell. By attaching the 76 gycine ends of their flexible tails to proteins, they take them to enzymes where they are degraded back to amino-acids. Ubiquitins are so prevalent that they are considered to be fundamental proteins of life.[1]



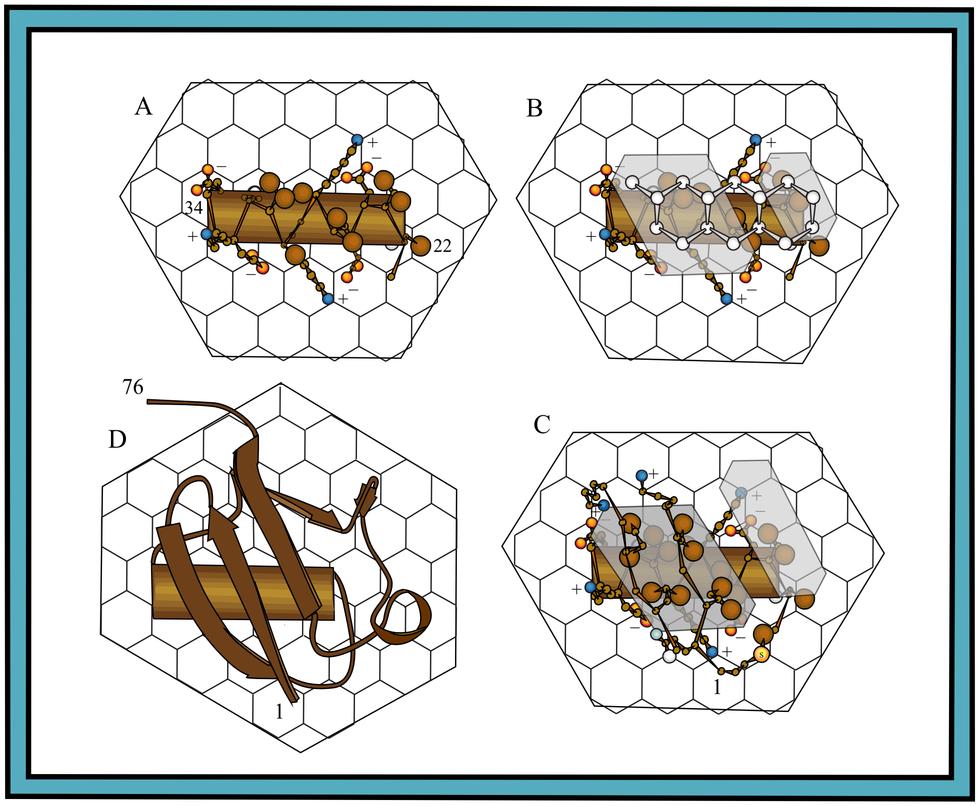


When viewed in the orientation shown above,[2] the linear segments tend to follow the basic cubic patterning established by transient linear elements of hydration around the coiled core.[3] Regions of the polypeptide which do not hydrogen-bond with surface water and induce covalent bonding between water molecules are given a white background below. Those that hydrogen bond with surface water are circled. The region starting with isoleucine 23, orders hydration on both sides, rapidly loses energy and forms the coil.



Five other regions which induce transient linear hydration order on one side, remove enough energy to straighten the segments. Three of them pass over the coil, one follows the diagonal ordering of water and one follows verticle elements. Peptides which hydrogen-bond directly with surface water, exchange energy with that water, maintain flexibility and permit hydration-ordering regions to assemble, release surface water and be driven from randomness toward order. Segment 57 to 65 forms a coil to permit the amides on glutamine 62 and asparagine 60 to hydrogen bond with water on the corner.

Ubiquitin is an interesting protein because it contains a number of external lysine side-chains which attach them together to form linear aggregates. Even the coil, which serves as the core as illustrated in A below, has three cationic lysines and four anionic glutamates extending from the sides.



The upper surface of the coil is highly lipophylic with two isoleucines and a valine providing a flat upper face to induce the formation of dynamic covalent linear elements on an upper level, as shown in B. Isoleucines, leucines and valines of two linear beta-sheet elements, as shown in C, bind in the shaded space to release unstable water. A third linear beta-sheet segment displaces ordered water over isoleucine on the end of the coil with its flexible end passing out of the cubically-patterned region, as shown in D, to permit terminal glycine at 76 to bind with the amines of lysines in other proteins.[1]

It is amazing that prolines, threonines, glycines and serines, are in specific positions in the chains of natural polypeptides, such as this, to permit lipophylic regions to form such firm complimntaty unions that all water between them can be released. When the earliest phases of random polypeptde synthesis began, it was sequences of amino-acids that could spontaneous assemble by bringing oppositely-charged ions and non-hydrogen-bonding surfaces together to release ordered water which survived. Those that retained destabilizing internal water were returned to the amino-acids from which they came by lytic enzymes and ribozymes.[3]

References

1. C. M. Pickart and M.J. Eddins, *Biochemica et Biophysica Acta* **1695**(1-3): 55-77 (2004). Ubiquitin: structure, function, mechanisms.
2. W.J. Cook, L.C. Jeffery, L.C. Carson, Z. Chen and C.M. Pickart, J. Biol. Chem. **267**: 16467-16471 (1992). Structure 1AAR in the Protein Data-Base.
3. J. C. Collins, *The Matrix of Life* (Molecular Presentations Inc., 1991). www.cubichydration.com.