Chiral, Biological Nanostructures: Conformational Changes and Elasticity

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Introduction

Numerous studies of synthetic D,L-alternating peptides provide information about the influence that various structural factors, such as the length of the peptide chain, the nature of the lateral substituents and of the end groups, and the specific pattern of configuration (DLD… or LDL) may have on the conformational properties of syndiotactic peptides. From this results the characterization of different type of single- and double stranded β-helix was obtained. A lot of attention has been paid to this β-helical conformation in view of its peculiar property of forming specific ion conducting channels across natural or synthetic membranes. Elastic proteins are characterized by being able to undergo significant deformation, without rupture, before returning to their original state when the stress is removed. The sequence of elastic proteins contains elastomeric domains, which comprise repeated sequences, which in many cases appear to form β-turns. In addition, the majority also contains domains that form intermolecular cross-link, which may be covalent or non-covalent. The mechanism of elasticity varies between the different proteins and appears to be related to the biological role of the proteins. Elastin consists of putative repeats of VPGVG that mainly impart rubber-like property to the protein. Previous study revealed the presence of two different types of conformers: folded or semi-folded, consisting of β-turn and extended conformation such as polyproline-II. The presence of folded and extended conformers giving rise to dynamic β-turns that slide along the chain. Here we observe the sliding in D,L-alternating peptide chains and the conformational changes after the insertion of an sequence homologue of that present in elastic proteins.

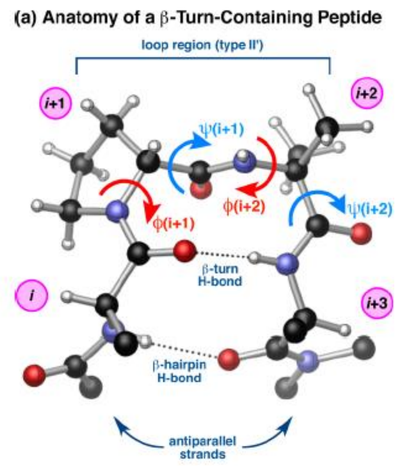

Figure 1. Pertinent features of a β-turn-containing peptide.

Molecular Model: Boc-(L-Val-D-Val)$_4$-OMe

Single-crystal X-ray analysis, it was found that this octapeptide exist in the crystals in the form of double-stranded β-helical dimers with antiparallel chains. NMR analysis in $CDCl_3$ solution, the results show that (*i*) there are different ways of maximizing the number of interturn hydrogen bonds in ↓↑$\beta^{5.6}$ helices with either sense of twist (*ii*) the highest number (14) of these bonds is exhibited by two left-handed ↓↑ $\beta^{5.6}$ helices. The hydrogen-bonding characteristics of these two structures are illustrated in Figure 2 . In one of these helices (helix **A**), the hydrogen bonds connect three pairs of D residues and four pairs of L residues, and the only free NH group per chain belongs to the residue no.2 . In the other left-handed ↓↑ β5.6 helix (helix **B**), the hydrogen bonds connect four pairs of D residues and three pairs of L residues, and the only free NH group per chain belongs to the residue no.7. **Note that helix A can be converted into helix B (or vice versa) simply by transposing one strand by two residues with respect to the other.**

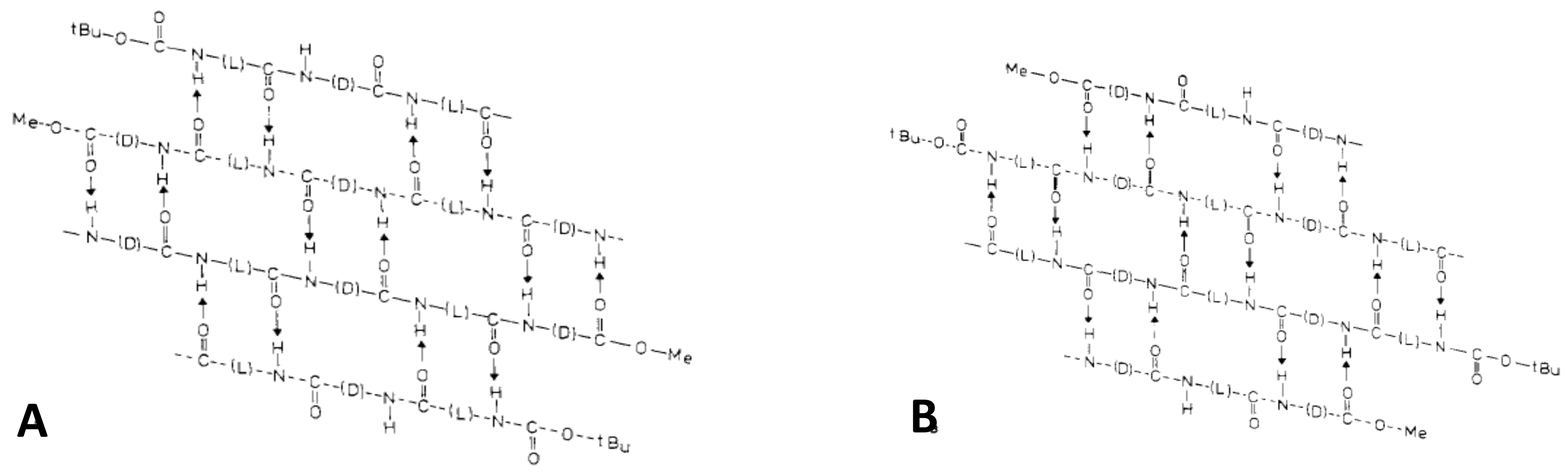

Figure 2. Hydrogen-bonding pattern of the two left-handed ↓↑ $\beta^{5,6}$-helical structure of Boc-(L-Val-D-Val)$_4$-OMe with 14 interturn hydrogen bonds.

Thermodynamic analysis

For a synthetic alternating D,L-oligopeptide with ten norleucines, N-methylated at the residue 7 and having HCO- and –OMe as terminal groups a thermodynamic analysis of the equilibrium between both conformations has been carried out by one-dimensional NMR measurements at ten different temperatures. The temperature at which 50% of dimer conformation is dissociated is 319°K..

Figure 3. HCO-XNle-OMe conformational changes on raising the temperature from↑↓ $\beta^{5.6}$-helix to $\beta^{4.4}$-helix

Drug delivery applications

A variety of drug delivery platforms such as nano/micro particles, hydrogels, and films have been developed from synthetic block copolymers for the purpose of local and controlled delivery of bioactive molecule. Synthetic block copolymers with distinct block polarity, can self-assemble into a range of supramolecular structures that facilitate the loading of hydrophobic drugs into local hydrophobic microenvironments. During the study of elastin like polypeptides has been shown that one repeat unit of VPGVG is sufficient to allow the transition of random conformation into an ordered β-turn, although higher molecular weight polymers are required for useful material properties. On these basis we studied D,L-oligopeptides containing a β-turn forming sequence.

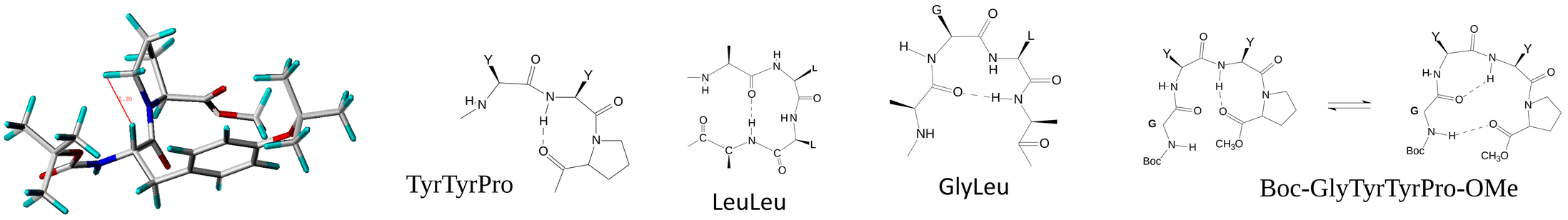

Figure 4. Boc-Tyr(tBu)^1-Pro^2-OMe *trans* distance $H_\alpha(Y^1)$-$H_\delta(P^2)$

Conclusions

The increasing amount of knowledge acquired from recent studies on elastomeric proteins has inspired the design and synthesis of biopolymers with interesting mechanical and biological properties. Results obtained suggest an optimistic vision for the production of efficient elastomeric biomaterials.

References

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