Analysis of β-helix proteins using the STACK toolkit

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Introduction

β-helix proteins contain a solenoid domain of parallel β-strands folded into a large prism. Each turn of the solenoid, called a *β-coil*, consists of a succession of a few (usually three) β-strands. β-strands from adjacent coils stack to form parallel β-sheets that make up the faces of the prism. These faces are linked by loop regions that protrude from the helix and, in many cases, form the binding site of the helix. The cross section of this prism is typically L-shaped in right-handed parallel β-helices and triangular in left-handed parallel β-helices, as shown in Fig. 1.

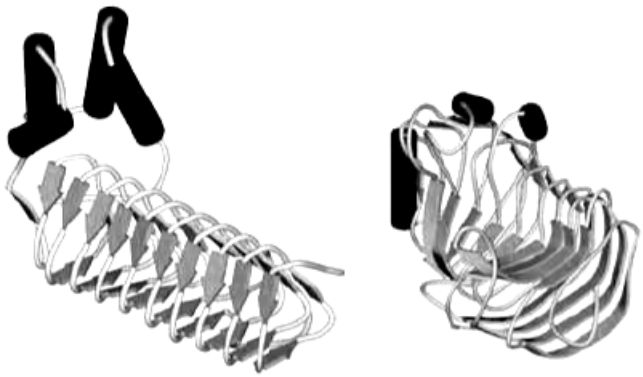

Fig. 1 Left-handed and right-handed β-helices have a different cross section

The stability of the domain is mainly obtained by the stacking of similar residue side-chains at equivalent positions in successive coils, both inside and outside the helix. The inward side chains are mainly hydrophobic and, when not, maximal hydrogen bonding or electrostatic interactions neutralise their polar or charged groups.
We have formalised the intuitive notion of a β-helix in a set of objective algorithms that recognize automatically the basic structural elements of β-helices: residue stacks, β-coils, cores and β-helices. We define the core of a β-helix as the helical domain of the protein, as distinguished from the protruding loop regions (Fig. 2).

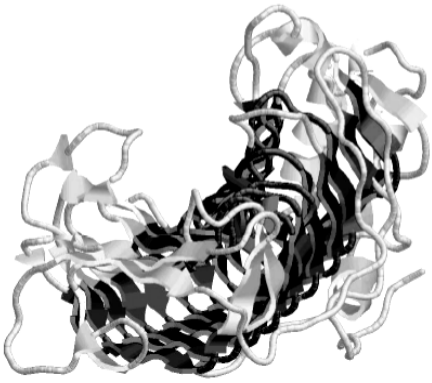

Fig. 2 The core of a β-helical protein (dark regions) distinguished from the loop regions

Methods

Our algorithms have been implemented within STACK, a toolkit for analysing β-helix proteins. Our approach is based on first identifying residues stacks – linear spatial arrangements of residues with similar conformations. STACK identifies aromatic, aliphatic and amidic stacks, such as asparagine ladders, and then combines these elementary patterns to form β-coils, β-core, and β-helices. β-helices identified in this way are consistent with those defined in the literature [1]. STACK also provides a set of tools to calculate a number of geometrical features including the orientation of side chains, the packing index of a β-coil, its cross-sectional shape and area, the pitch and twist between adjacent β-coils and the axis of the β-helix.

Implementation

STACK is implemented in Java and runs on Unix and Windows. An interface between STACK and RasMol enables structural features to be highlighted automatically. The geometric values derived by STACK are stored in a relational database, and can be queried by users to compare and tabulate geometric features of different β-helix structures.

Results

We have used STACK to analyse over twenty β-helix proteins taken from the Protein Data Bank [2], including both left-handed and right-handed β-helix structures. The results of these studies will be presented.

References

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