Beta-Bends As An Example Of Conformationally Predetermined Segments Of Protein. Conditions Of Stabilization Of The Structure And Role Of Context

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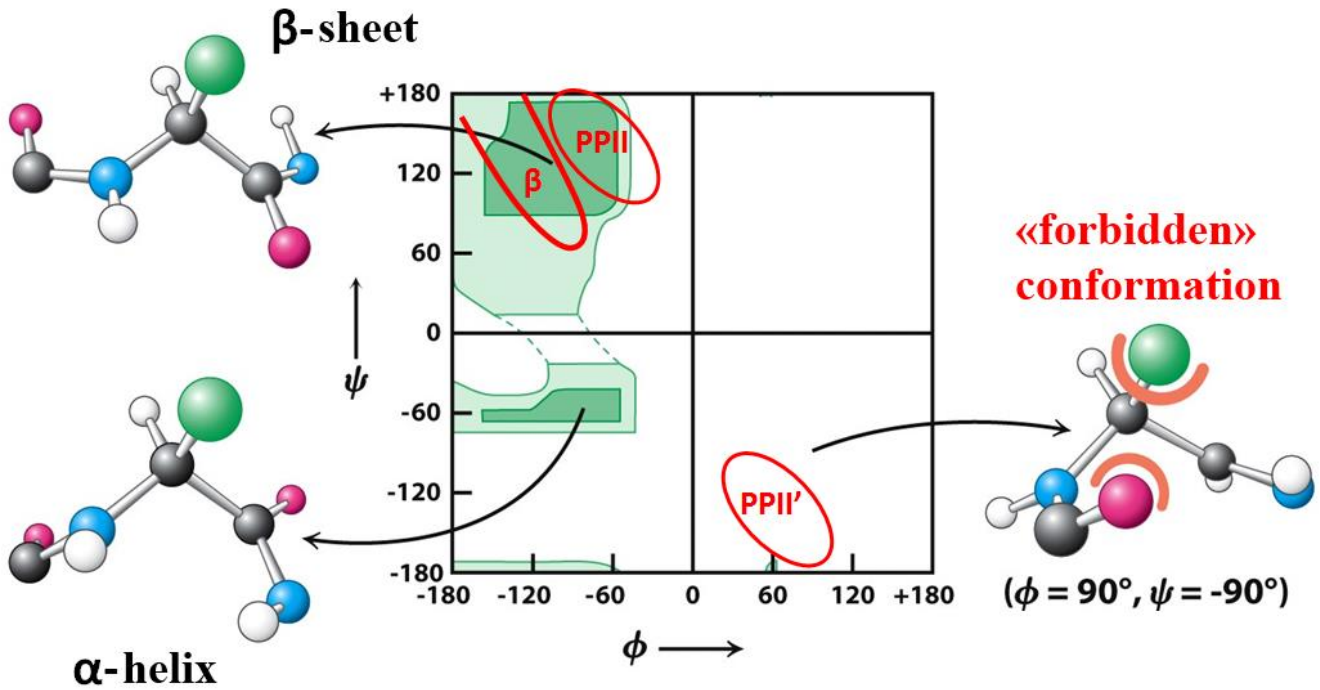
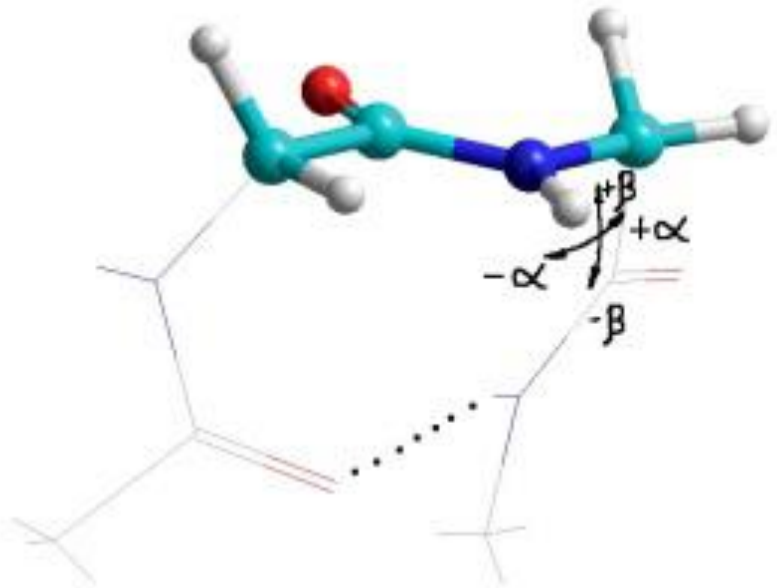
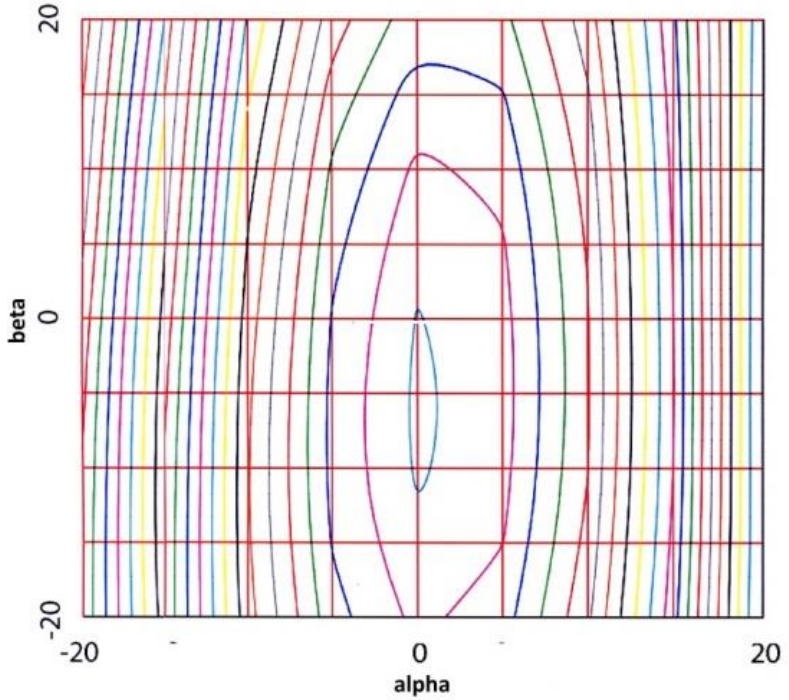
Type	φ_{i+1}	ψ_{i+1}	φ_{i+2}	ψ_{i+2}
I	−60°	−30°	−90°	0°
II	−60°	120°	80°	0°
I′	60°	30°	90°	0°
II′	60°	−120°	−80°	0°



A β-hairpin included β-bend can be treated as an example of composite local structure which components (β-bend and fragment of β-structure) play different structural, energetic and geometric role. In accord to our conception, the fragment of antiparallel β-structure characterized by increased stability imposes to the linker (β-bend) the definite set of conformations. Wherein, the number of independence conformational variables reduces due to pseudo-cycle formation across hydrogen bonds. As a result the overall number of conformations in this system does not exceed two for main types of β-bends. Thus the conformation of β-bend (linker) is determined by context, namely assigning β-structural part of the whole structure. It must be underline that definite conformation is enforced to β-bend independently to the primary structure of β-bend itself even if this conformation encounters sterically hinders (so called ‘disallowed’ conformations). In current study the primary and three-dimensional structures of both parts of the composite structure have been studied. On the basis of representative sample it can be found that the sequence and the structure provide enlarge stability of the context part. In spite to predetermined character of the β-bend part of the whole structure some peculiarities in amino acid composition rather than in sequence take place. Contacts within β-hairpin and its part as well as long-distance contacts were estimated by Voronoi-Delaunay tessellation (the non-parametric approach). Degree of conservation of residues in β-structural part and in β-bend separately was determined by multiple-alignments of homologous structures and sequences of corresponded protein domains using various matrices of amino acid similarities. Possible biological implementations are discussed.

The hydrogen bond characteristic of beta bends, in which the CO group of the ***i***-th residue is used as an acceptor

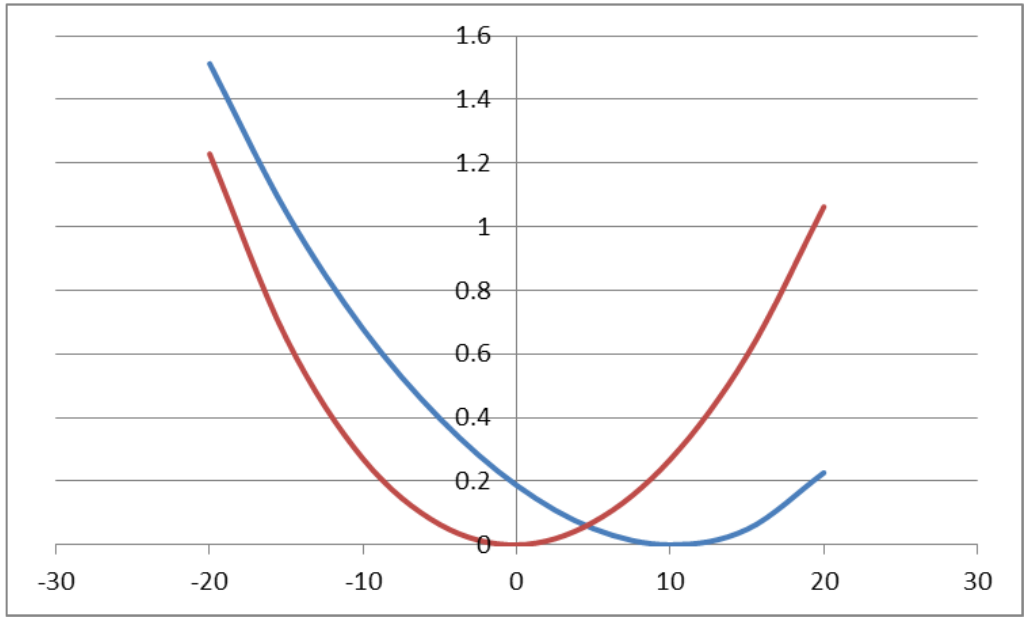




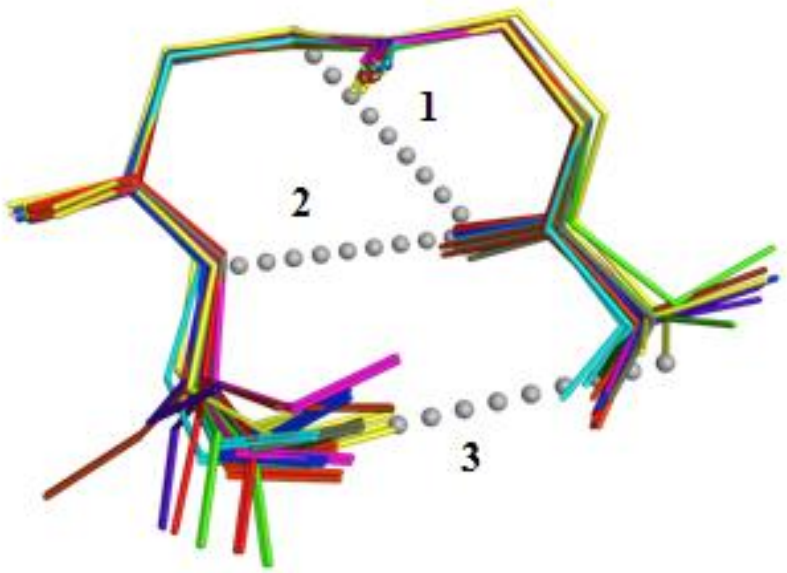
Typical dependence of fragment energy on alpha and beta angles. Level lines drawn through 0.5 kcal / mol

The dependence of the energy of the molecule on the angle beta at a fixed angle alpha.

Using the ab initio method 6-31 ++ G * taking into account the MP2 correlation, calculations of the beta-type variant II type were performed. Quantum-chemical methods studied the possibility of the formation of an additional hydrogen bond in beta bending between the NH group of the selected fragment and the CO group of the ith residue (see Figure top left). The figure shows the main hydrogen bond characteristic of beta bends, in which the CO group of the ith residue is also used as an acceptor. In the course of calculations, in order to investigate the possibility of the formation of an additional hydrogen bond, the change in the total energy of the molecule is determined depending on the orientation in the space of the NH bond by the peptide group highlighted in color, connecting ***i + 1*** and ***i + 2*** bending residues.



Possible hydrogen bonds in the structure of beta bend type II ’



Hydrogen bond 1 is formed between the oxygen of the main chain of the residue preceding the turn and the nitrogen atom of the second residue in the bend, bond 2 between the oxygen of the main chain of the residue preceding the turn and the nitrogen atom of the third residue in the bend, bond 3 between the nitrogen atom of the main chain of the preceding bend, and the oxygen atom of the third residue in the bend. Hydrogen bond 1 was found in 98.2% of structures of this type, bond 2 in 98.4%, and bond 3 in 29.4% (see the Table).

Bend’s type	Number of structures	Hydrogen bonds, number and share (%)					
		1		2		3	
I	162262	153500	94.6	155285	95.7	9736	0.6
I’	7024	6923	98.6	6792	96.7	4121	58.7
II	13747	13594	98.9	13477	98.0	530	3.9
II’	4351	4272	98.2	4280	98,4	1279	29.4

Three types of hydrogen bonds in bends were analyzed (see the Figure). Hydrogen bond 1 is formed between the oxygen of the main chain of the residue preceding the turn and the nitrogen atom of the second residue in the bend, bond 2 between the oxygen of the main chain of the residue preceding the turn and the nitrogen atom of the third residue in the bend, bond 3 between the nitrogen atom of the main chain of the preceding bend, and the oxygen atom of the third residue in the bend. It was found that hydrogen bonds of the first and second types are present in all types of beta bends, in the amount of 94.6-98.9%. The question of the existence of a hydrogen bond was solved by estimating the nitrogen-oxygen distance (about 3 Å), which is a necessary condition for the existence of a hydrogen bond, but is not a sufficient condition. The hydrogen bond of the third type was found in the bend of I ’type in 58.7% of structures, and II’ type in 29.4% of structures.

The WKVEVND peptide is the N-terminal fragment of the “twisted” beta hairpin of the sh3 domain (1SHG, fragment 42-53 of WKVEVNDRQGFV), which is interesting in that it retains the forbidden conformation of asparagine-47 despite mutagenesis. Our assessments of conformational stability showed that the 42–45 WKVE tetrapeptide is the most stable in the entire structure of the SH3 domain (4 out of 5 stability criteria developed in this project are met) and, to some extent, the KVEV peptide (2 out of 5 criteria). It is also important to note that all tetrapeptides after the asparagine-47 residue and to the end of the beta hairpin sequence are conformationally labile (0 out of 5 criteria are met).

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