DOI 10.18699/SBB-2022-147

β-turns parameters refinement using neutron diffraction data

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Key words: β-turn, conformation, polypeptide chain, β-hairpin

Motivation and Aim: Beta-turns are an insufficiently studied object in proteins, since the stabilization mechanism of energetically unfavorable conformation still remains unclear. Classification of beta-turns usually carried out according to conformational angles φ and ψ of amino acid residues i + 1 and i + 2. However, analysis of the Ramachandran map of amino acid residues i + 1 and i + 2 indicates a high conformational stress arising in the turn, which should be compensated by additional interactions. We assume that in order to stabilize the beta-turn, an additional hydrogen bond must exist, the energy of which compensates for the stress of the Beta-turn. This additional hydrogen bond couldn't be taken into account because of X-ray methods of protein analysis used to determine prior beta-turns classifications. Our main aim was to analyze protein structures determined by neutron diffraction and cluster beta-turns conformational angles with satisfying criteria for hydrogen bond.

Methods and Algorithms: We used PDB database to collect all protein structures which were determined by neutron diffraction (as of November 2020). To calculate hydrogen bonds in protein structures and β-turns HBPLUS software was used [2]. The turns were selected according to the Venkatachalam's criteria for a β-turns of the presence of a closing hydrogen bond between the oxygen of the main chain of the i-th amino acid residue and the nitrogen of the main chain of the i+3 residue [6]. This is a more rigorous and unambiguous approach to identifying β-turns than estimating the distance between Cα atoms. In addition to the four amino acid residues that form the turn itself, two flanking residues were also considered to the right and left of the turn. Thus, fragments of eight amino acid residues containing a kink with a closing hydrogen bond in the middle were selected. A total of 3717 such fragments were found, i.e. an average of 22 turns in one structure. The conformational angles phi, psi, and omega of the six central residues were determined in the fragment structure.

Results: It was found that all 3717 turns can be easily classified by ϕ, ψ angles of i + 1 and i + 2 residues of the turn into eight classes only. 4 of them correspond to classical beta turn types, so the central values ϕ, ψ of type I, type I ', type II and type II ' have been refined. The other four classes of peptides have corresponding classes in Shapovalov [5] and de Brevern [1] classifications. We did not find additional stabilizing bifurcated hydrogen bond formed between the CO oxygen atom of the i-th residue group and the nitrogen atom of the i-th residue + 2.

Conclusion: These results indicate the absence of additional stabilization of the strained conformation of the beta-turn at the level of the protein secondary structure by the bifurcated hydrogen bond. Forced-conformation segments, taken by themselves, must be conformationally labile. Indeed, they cannot have a preferred conformation that is the same as the one they should adopt in the protein, since this conformation is met with

stereochemical obstacles, but it is better if this segment has a whole set of conformations (with favorable energy, of course). The most unfavorable case is when the fragment has one conformation, moreover, with a favorable energy. Then it is especially difficult for external factors to give this part of the protein chain the required shape. Based on the foregoing, one can expect increased conformational freedom from beta-turns.

Acknowledgements: This research has been supported by Russian Science Foundation Grant No. 22-24-00936.

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