Computational analysis of amino acid helix-propensity

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Several experimental studies as well as theoretical evaluations have been performed to investigate helix stability. Stabilizing/destabilizing factors have been described in literature1-4, as resulted by studies on protein 3D structures or model peptides in solution. It has been reported that protein stability can be increased by stabilizing helices5. A specific search for helix stabilizing factors were recently carried out to verify their relevance in thermophilic proteins6. The classification of helix motifs 7 and their search within protein sequence has been also object of our interest 8 . Our work is currently aimed to provide a complete exploration of single amino acid tendencies at each helix position, in agreement to the possibility that specific amino acids at specific positions can improve helix stability 9-10.

We used computer-generated helix models to evaluate the effect of each amino acid at different helix positions. The starting helix model consists of a polyalanine. Each helix position has been modified by replacing alanine with each of the other amino acids. Side chains of Asp, Glu, Lys, Arg, and His, have been considered in both the charged and uncharged forms. The N- and C- termini have been examined in charged, uncharged and blocked states. Models were built by imposing the starting conformation, then optimizing geometry by energy minimization.

Results are in agreement with features of some amino acid, known by experimental observations. On the other hand, we have highlighted unknown preferences of some amino acid for specific positions within the helix. The final goal of this work is to develop a protocol useful to address protein engineering experiments.

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