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Fold helical proteins by energy minimization in dihedral space and a DFIRE-based statistical energy function.
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Summary: Statistical energy functions are discrete (or stepwise) energy functions that lack van der Waals repulsion. As a result, they are often applied directly to a given structure (native or decoy) without further energy minimization being performed to the structure. However, the full benefit (or hidden defect) of an energy function cannot be revealed without energy minimization. This paper tests a recently developed, all-atom statistical energy function by energy minimization with a fixed secondary helical structure in dihedral space. This is accomplished by combining the statistical energy function based on a distance-scaled finite ideal-gas reference (DFIRE) state with a simple repulsive interaction and an improper torsion energy function. The energy function was used to minimize 2000 random initial structures of 41 small and medium-sized helical proteins in a dihedral space with a fixed helical region. Results indicate that near-native structures for most studied proteins can be obtained by minimization alone. The average minimum root-mean-squared distance (rmsd) from the native structure for all 41 proteins is 4.1 . The energy function (together with a simple clustering of similar structures) also makes a reasonable selection of near-native structures from minimized structures. The average rmsd value and the average rank for the best structure in the top five is 6.8 and 2.4, respectively. The accuracy of the structures sampled and the structure selections can be improved significantly with the removal of flexible terminal regions in rmsd calculations and in minimization and with the increase in the number of minimizations. The minimized structures form an excellent decoy set for testing other energy functions because most structures are well-packed with minimum hard-core overlaps with correct hydrophobic/hydrophilic partitioning. They are available online at `http://theory.med.buffalo.edu`.

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