A scoring framework for predicting protein structures

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We have developed a statistical mechanics-based iterative method to extract statistical atomic interaction potentials from known, non-redundant protein structures. Our method circumvents the long-standing reference state problem in deriving traditional knowledge-based scoring functions, by using rapid iterations through a physical, global convergence function. The rapid convergence of this physics-based method, unlike other parameter optimization methods, warrants the feasibility of deriving distance-dependent, all-atom statistical potentials to keep the scoring accuracy. The derived potentials, referred to as ITScore/Pro, have been validated using three diverse benchmarks: the high-resolution decoy set, the AMBER benchmark decoy set, and the CASP8 decoy set. Significant improvement in performance has been achieved. Finally, comparisons between the potentials of our model and potentials of a knowledge-based scoring function with a randomized reference state have revealed the reason for the better performance of our scoring function, which could provide useful insight into the development of other physical scoring functions. The potentials developed in the present study are generally applicable for structural selection in protein structure prediction.