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Protein Designability in the 2-D Triangular Lattice

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Short Abstract: Using a lattice model with relatively higher coordination number than that of many studies, we explore the question of protein designability. Our definition of designability is based on the uniqueness of conformations that a sequence folds to with lowest energy. We identify and classify designable conformations for different shapes.

Long Abstract:
Understanding the relationship between protein sequence and protein structure continues to be a basic, yet only partially resolved, question of science. Better computational models coincide with an
explosion of experimentally obtained data on structure, dynamics, and protein-protein interactions. Much work has been done using reduced models of proteins that attempt to mimic aspects of folding while making the computational costs more affordable. Here we avail ourselves of a lattice hydrophobic/polar (HP) model. Each residue
in a protein is represented by a point on a regular lattice. Amino acids are taken to be either hydrophobic or polar (H or P) which is a binary representation. There is a considerable body of work which suggests that this representation, simplified as it is, still manages to capture many of the important characteristics of folding [1-5].

We concern ourselves with the issue of protein designability, that is, the relation between the structure and sequence space of real proteins that has allowed them to be "found" by evolution. The
majority of work done in this area using lattice models has focused on the 2-D square and 3-D cubic lattice. Much theoretical groundwork on these lattices is available for extending the lattice
models to real protein systems. However, the square and cubic lattices suffer from at least one major drawback, that of parity. It is impossible for any two residues to be in contact unless there is
an even number of residues between them on the polypeptide chain. Is this shortcoming responsible for arbitrary artifacts in studies done using the model? We propose a foray into a different lattice model, the 2-D triangular/3-D FCC lattice. With these lattices the coordination numbers are 6 and 12, respectively, as opposed to 4 and 6 for the square and cubic lattice. There is some work supporting
the assertion that, among reduced lattice models, the fcc lattice model comes closest to approximating the packing of amino acids in real proteins [6-8].

We propose a study of designability using the 2-D triangular and/or 3-D fcc lattice model. Designability studies have been done for several small lattices of size 5x5 and 6x6 for the

square lattice and 3x3x3 for the cubic lattice. The definition of designability we use, proposed in [3], uses the number of sequences that fold to a unique conformation with lowest energy as a measure of
designability. Our studies suggest that the triangular and fcc lattices are superior in mimicking certain aspects of real proteins, such as residue packing or the mimicking of surface irregularities,
and that important insights can be gained from approaching design studies with this lattice.

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