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Reconstructing protein structure from solvent exposure using tabu search

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Abstract

Background: A new, promising solvent exposure measure, called *half-sphere-exposure* (HSE), has recently been proposed. Here, we study the reconstruction of a protein's C_α trace solely from structure-derived HSE information. This problem is of relevance for *de novo* structure prediction using predicted HSE measure. For comparison, we also consider the well-established contact number (CN) measure. We define energy functions based on the HSE- or CN-vectors and minimize them using two conformational search heuristics: *Monte Carlo simulation* (MCS) and *tabu search* (TS). While MCS has been the dominant conformational search heuristic in literature, TS has been applied only a few times. To discretize the conformational space, we use lattice models with various complexity.

Results: The proposed TS heuristic with a novel tabu definition generally performs better than MCS for this problem. Our experiments show that, at least for small proteins (up to 35 amino acids), it is possible to reconstruct the protein backbone solely from the HSE or CN information. In general, the HSE measure leads to better models than the CN measure, as judged by the RMSD and the angle correlation with the native structure. The angle correlation, a measure of structural similarity, evaluates whether equivalent residues in two structures have the same general orientation. Our results indicate that the HSE measure is potentially very useful to represent solvent exposure in protein structure prediction, design and simulation.

Background

The extent to which an amino acid in a protein is accessible to the surrounding solvent is highly dependent on the type of amino acid. In general, hydrophilic amino acids tend to be near the solvent accessible surface, while hydrophobic amino acids tend to be buried in the core of the protein. To measure this effect, several solvent exposure measures have been proposed [1-7], and one of these is the *contact number measure* (CN) [7]. The CN of a residue is the number of C_α atoms in a sphere centered at the C_α atom of the residue in question (Figure 1). The CN of all residues of a protein is called the *CN vector*. The CN vector is well conserved and can be predicted with high accuracy [8].

Recently, a new promising solvent exposure measure, called *half-sphere-exposure* (HSE), has been proposed [9]. While the CN measure uses a single sphere centered at the C_α atom, the HSE measure considers two hemispheres. Two values, an *up* and a *down* value, are associated with