Binding Pocket Shape Analysis for Protein Function Prediction

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We present a novel method for the comparison of protein binding pockets and ligands. An increasing number of protein structures are being determined for which no biochemical characterisation is available. The analysis of protein structure and function assignment is becoming an unexpected challenge and major bottleneck towards the goal of well-annotated genomes. As shape plays a crucial role in biomolecular recognition and function, shape techniques are likely to be of prime importance for understanding protein structure-function relationships.

A highly efficient shape comparison technique based on a real spherical harmonics expansion is presented for protein function prediction from structure. Our approach identifies the active site by a geometrical surface analysis method combined with an evolutionary trace technique. The binding pocket is then placed into a standard frame of reference using a heuristic that employs the first three moments of the spatial extent of the shape to find the orientation. The method uses the coefficients of a real spherical harmonics expansion to describe the shape of a protein's binding pocket. Shape similarity is computed as the Euclidean distance in coefficient space and is therefore extremely fast, enabling thousands of comparisons to the carried out per second on a standard PC.

[1] Morris R.J., Najmanovich R.J., Kahraman A., Thornton J.M., *Bioinformatics*, 2005, *in press*.

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