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Using Mathematics to Predict Protein Interactions

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120 Ingraham Hall

Abstract:

The human genome contains instructions for encoding thousands of different proteins, and these proteins perform many important biological functions. A protein is a linear sequence of amino acids that folds into a distinctive three-dimensional structure. Once the protein has folded, it can perform its intended function(s) through interaction with proteins, DNA, small molecules or ions. For two molecules to interact, they must bind to form a single unit, called a "bound complex." The lecture will discuss mathematical approaches to predicting the bound complex between a pair of proteins or other macromolecules. Two important factors determining how molecules can interact are their electrostatic and shape properties, and the Docking Mesh Evaluator and Fast Atomic Density Evaluation programs were developed in order to study these properties.

The Docking Mesh Evaluator (DoME) program uses adaptive mesh solutions to the Poisson-Boltzmann equation to model electrostatic interactions. The Poisson-Boltzmann equation is a nonlinear partial differential equation that treats water and solvent as a continuum. This time-averaged "implicit solvent" approach is more computationally efficient than direct electrostatic calculation with solvent ions and water molecules. DoME is presently in development, and initial results for its parallel scanning and optimization capabilities will be given.

The Fast Atomic Density Evaluation (FADE) program calculates molecular shape features of an individual protein or shape complementarity for bound complexes. FADE is based on atomic density methodology, and it uses Fast Fourier Transforms and convolution integrals for rapid calculation. FADE has been successfully used in the prediction of bound protein complexes, and the complementarity markers found by FADE correlate well with experimental mutation data for several studied examples.

(Molecular Biometry Cluster Candidate)