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A Novel Volumetric Criterion for Optimal Shape Matching of Surfaces for Protein-Protein Docking

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Abstract

The problem of molecular docking is to predict whether two given molecules *bind* together to interact. A shape-based algorithm is proposed for predictive docking by noting that shape complementarity between their outer surfaces is necessary for two molecules to bind. A methodology with five stages has been developed to find the *pose* in which the shape complementarity is maximum. It involves surface generation, segmentation, parameterization, shape matching, and filtering and scoring. The most significant contribution of this paper is the novel scoring function called 'Normalized Volume Mismatch' which evaluates the matching between a pair of surface patches efficiently by measuring the gap or solid volume entrapped between two patches of a pair of proteins when they are placed one against the other at a contact point. After the evaluation, it is found that, with local shape complementarity as the only criterion, the algorithm is able to predict a conformation close to the exact one, in case of known docking conformations, and also rank the same among the top 40 solutions. This is remarkable considering the fact that many existing docking methods fail to rank a near-native conformation among top 50 solutions. The shape-based approaches are used for the initial stage of docking to identify a small set of candidate solutions to be investigated further with exhaustive energy studies etc. The ability of capturing the correct conformation as highly ranked among top few candidate solutions is the most valuable facet of this new predictive docking algorithm.

Keywords: Scoring function, Shape matching, Normalized volume mismatch, Protein docking

1. Introduction

Proteins are a class of biomolecules. They are essential to all living organisms because of their structural, catalytic and transportation properties. Many biochemical processes within a cell involve some kind of mole-

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