Chapter 3

Scoring Functions in Docking Experiments

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ABSTRACT

Molecular docking is a computational technique used to predict the binding orientation of a molecule while interacting with other molecule and finally quantify the inter-molecular interactions in terms of a binding score or binding affinity. In general, every docking algorithm comprises one or more “scoring function(s)” which is/are responsible for finding a precise binding pose as well as for predicting the binding affinity. In the last two decades, a significant development has been found in the field of scoring functions. In this chapter, the authors will discuss in detail about various types of scoring functions used in the docking experiments. This chapter will get the readers acquainted with different types of scoring functions available, their theoretical background, essential components, desired properties, and the important task performed by the scoring functions. The authors will also discuss the challenges faced by the scoring functions and their recent progress.

INTRODUCTION

Molecular docking is a computational technique used to predict the binding orientation or native pose of a molecule while interacting with another molecule to form a stable complex. This technique is routinely carried out to study various kinds of inter-molecular interactions between ligand and protein, ligand and DNA, protein and protein, protein and DNA. In the pharmaceutical field, it is often used to find out the binding orientation of a lead molecule (ligand) to its target protein so as to understand the mechanism of action as well as to predict the binding affinity that plays a vital role in the rational drug designing (RDD). Each docking algorithm comprises one or more ‘scoring function(s)’, which plays the central role in exploring the correct binding orientation and understanding the outcome of the docking experiment. In docking, scoring function can be defined as a mathematical function that is used to compute
Scoring Functions in Docking Experiments

Figure 1. Hydrogen bonding
Snapshot taken in Discovery Studio software (DiscoveryStudio, 2007) for demonstration purpose only.

a representative score and to decide a binding pose, by evaluating the favorable (rewarding term) and unfavorable (penalty term) inter-molecular interactions found in a docked complex. The typical components of scoring functions are hydrogen bonding (illustrated in Figure 1), electrostatic interaction, van der Waals interaction (Figure 2), desolvation effect (Figure 3) and loss of torsional entropy upon binding (Figure 4).

BACKGROUND

The basic aim of a scoring function is to find a docking score that should somehow represent the experimentally-determined binding affinity of the docked ligand.

The scoring functions are intended to accomplish the following mentioned tasks:

1. To predict the absolute binding affinity between a ligand and a protein or at least the relative binding affinities among the multiple ligands and a protein.

Figure 2. van der Waal interactions
Snapshot taken in Discovery Studio software for demonstration purpose only.