A Simulated Annealing Algorithm for Geometrical Assessment of Macromolecular Hydrophobic Interaction

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1 Introduction

Macromolecular interaction is critical to many biological and biochemical processes and phenomena in living systems. Its assessment would lead to a deeper understanding of many relevant phenomena at the molecular level such as molecular and cellular recognition, signal transmission, and many other processes in life systems, as well as in drug and protein engineering.

It is widely recognized that one of the primary organizing principles in structural biochemistry and biology is the so called hydrophobic effect. The hydrophobic effect is the tendency of apolar molecular species to associate spontaneously in aqueous solutions. The hydrophobic effect at the molecular level involves contact interactions among apolar groups which are stabilized by entropic effects originated in the solvent.

In the present work we approach the problem firstly from a geometrical point of view. This consists in the evaluation of the changes in solvent accessible surface area (SASA) of proteins or any other macromolecules at interaction with other molecular species. We propose a methodology to assess hydrophobic interaction as a function of the decrement of SASA and the optimal accommodation of the interacting surfaces of macromolecules so as to maximize this decrement.

Finally we apply our methodology and attempt to assess the best configurations at interaction of macromolecular complexes in aqueous solutions.

2 Methodology

Estimation of interaction energies of solutes based on the solvent accessible surface area combined with experimental data was attempted by Eisenberg *et al.* [1]. In general, and in Eisenberg's model in particular, the interaction energy among molecules in solution is composed by four terms: van der Waals interactions (repulsion term) E_{vdw}, the cavity formation energy or void term E_{cav}, the electrostatic interaction $E_{coulomb}$, and the hydrophobic interaction E_h; i.e.:

$$E_{interaction} = E_{vdw} + E_{cav} + E_{coulomb} + E_h$$

The electrostatic term can be computed by the classical Coulomb law (0 por apolar or neutral solutes), the vdW interaction is well characterized, while the cavity formation energy is that arriving from the exclusion of solvent molecules initially attached to the interacting molecules.

Here we concentrate on the hydrophobic interaction energy which can be expressed as:

$$E_h = \sum_{i=1}^{m} \sigma_i SASA_i$$