MIAX: A System for Assessment of Macromolecular Interaction. 4) Interaction Site Inference by Molecular Hydrophobic and Electrostatic Analysis

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Keywords: interaction sites, electrostatic complementarity, hydrophobicity

1 Introduction

Specific recognition of the interaction site in protein-protein interactions is the most relevant requirement to predict biochemical function of proteins. The role played by electrophysical complementarity as a determinant of protein-protein interaction is important.

In the present study we have focused on the distribution of these forces on the protein surface. the distribution is evaluated by means of a self organizing map (SOM) [5] which renders a nonlinear projection of the high dimensional configuration of the electrophysical forces on the surface of the monomers into a lower dimensional map of neurons.

In the analysis of these map, we undertake the problem of reduction of the huge configuration search space for the complex in order to improve processing times of the system for automatic assessment of macromolecular interaction system (MIAX) [2, 3].

We evaluate the algorithm predicting plausible interaction sites for several complexes whose coordinates are found in the PDB,and comparing them with inferred candidate interaction regions.

2 Methodology

To examine hydrophobic and electrostatic interaction regions among two interacting macromolecules, a probe (M) is placed on every point of a grid on the surface of each molecule.

The Molecular Hydorophobicity Potential (MHP) [1] was calculated by

$$\mathrm{MHP} = \sum E_{tri} exp(r_i - d_i) \tag{1}$$

where E_{tri} is the transfer energy of the atom i, r_i is the radius of the atom i, and d_i is the distance between atom i and a probe M. The transfer energy E_{tri} represents the energy of transfer from a hydrophobic to hydrophilic phase for an atom i.

The electrostatic energy was calculated by the Coulomb law:

$$Eelc = 332 \sum_j \frac{q_j}{\epsilon r_{ij}} \tag{2}$$

where $Eelc$ represents the electrostatic energy on the molecular surface at a probe M. q_j is the atomic charge and r_{ij} is the distance between the atomic center and the probe M on the molecular surface. ϵ is the sigmoidal distance dependent dielectric function [4].

The calculation is performed for both monomers composing the complex.

3 Results and Discussion

Validation of the algorithm proposed was carried out by comparing inferred interaction regions for monomers composing complexes whose structures are recorded in the PDB. Here we show results for the Potato Inhibitor complex of carboxypeptidease (PDB:4CPA).

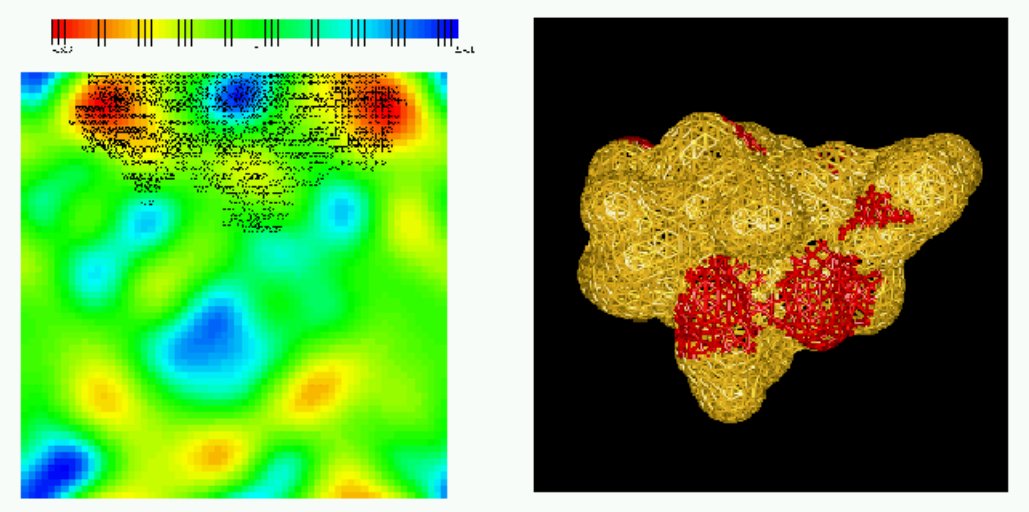

Figure 1: Hydrophobicity Map (left), Prediction of Hydrophobic Interaction Site (right).

Inferred interaction sites are in high agreement with the crystal structure, yielding in this way appropriate starting positions for the optimization process in MIAX, reducing the configurational serch-space for the complexes.

References

[1] Brasseur, R., Differentiation of lipid-associating helices by use of threedimensional molecular hydrophobicity potential calculations, *J. Biol. Chem.*, 266:16120–16127, 1991.

[2] Del Carpio, C.A. and Yoshimori, A., MIAX: a novel system for assessment of macromolecular interaction in condensed phases. 1) description of the interaction model and simulation algorithm, *Genome Informatics*, 10:3–12, 1999.

[3] Del Carpio, C.A. and Yoshimori, A., MIAX: a system for assessment of macromolecular interaction. 3) a parallel hybrid ga for flexible protein docking, *Genome Informatics*, 11, 2000.

[4] Okamoto,Y., *Biopolymers*, 34:529, 1994.

[5] Kohonen, T., The self-organizing map, *Proc. IEEE*, 78:1464–1480, 1990.