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Prediction of Protein-Ligand Binding Sites for Cisplatin and Transplatin based on Hydrogen Bonds

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ABSTRACT

Platinum compounds are very important to treatment of various malignant tumors. However, prediction of platinum-binding sites is very hard to be made. Nevertheless, hydrolysis of leaving groups bounded to platinum compounds plays an important role in delivering platinum to a target molecule. Herein, a study in silico provides an understanding of the molecular surface in atomic level of three-dimensional structure of cisplatin and transplatin and their binding-sites in order to offer some insights in drug designing. The goal of this work was to implement a new approach based on geometric and physicochemical parameters to find platinum-binding sites using parallel computing algorithms for graphics processing units (GPUs). These algorithms were tested and validated by analysing platinum-binding sites in five known proteins. The results indicated that these binding sites were predicted with significant success. In our analysis HexServer and PatchDock server did not find putative binding-sites for cisplatin and transplatin as we found for the five chosen proteins. Herein, we have shown that the present method have had a better prediction of platinum-binding site than HexServer and PatchDock methodsThree-dimensional structures (3D) of proteins and ligands reveal a significant geometrical correspondence between their contact regions [1], i.e., shape complementarity and other physicochemical characteristics of protein surfaces determine the nature of interaction between the protein's binding-site and the ligand [2]. It is reasonable that analysis of protein's binding-sites are crucial in order to provide a better understanding of their structure and function, which are important parameters to drug discovery field. As binding-sites contains amino acid residues involved in interactions that require a well-defined arrangement [2], a challenge is to identify groups of interaction between protein and its ligandIn our method we first decide which atoms are important to calculate the vector v, which is used to limit the acceptor and donor areas of each residue. As MSProt is still in development, in future work our method will take into account all hydrogen bonds and interaction forces that hold cofactors seen as HETATM, and we are going to use that approach to increase the range of proteins that could be submitted to our method. The ranking analysis was speeded up by discarding sequences through the employment of four parameters. The first parameter is the geodesic value among points of greatest electrostatic potential between the protein and the ligand. For protein analysis in relation to a chosen ligand, same process of permutation created several sequences, which had not exceeded the maximum number of six elements for the reason described in geodesic of ligands. In order to calculate the shortest path among these points, a virtual sphere was used to select the points that falls within That virtual sphere represents the ligand (cisplatin or transplatin) whose measured distance between two internal atoms in the optimized ligand structure was measured as 4.94 Å, which was considered to be the diameter

Keywords: **Binding sites; Hydrogen bonds; Cisplatin; Transplatin; Molecular surface; GPU computing**