
MD simulation combined to fragment based approach for protein-peptide complex structure prediction

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Abstract

Protein-protein interactions play a key role in almost all cellular functions. The modulation of these interactions has many therapeutic applications, but the physical characteristics of these interfaces make the rational design of inhibitors difficult. The rational design of peptide inhibitors is an explored strategy for modulating protein-protein interactions. Numerical prediction of the binding modes and affinity of a peptide on a protein presents many difficulties.

We use molecular dynamics simulations of protein in the presence of small peptides to identify binding sites and key *hot-spots*. Binding affinity of small peptides being weak, these simulations intend to sample extensively peptide binding around a target protein.

Our method has been tested on a set of nine proteins-peptide complexes which structure have been solved in free and complexed forms. In all cases we were able to identify at least one binding site overlapping with the crystal peptide binding site. Different metrics have been used to characterize each binding site and in particular their peptide sequence specificity and affinity.

The proposed method aims at a better prediction of peptide-protein structure prediction and ultimately to optimize the peptide sequence or predict de novo optimal peptide composition.

Keywords: Protein Peptide interactions, MD simulation

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