Singapore-MIT Alliance for Research and Technology

BIOSYSTEMS AND MICROMECHANICS

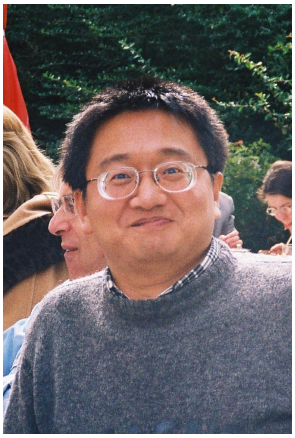
Focused Seminar Series on Computational Techniques

15 Feb — 4 Apr 2016, Level 5 Seminar Room, Enterprise Wing @ UTown, S'138602

Seminar 1: Reduce false positive through multiple conformations docking

Professor Mu Yuguang

Nanyang Technological University



Date: 15 Feb 2016, Monday

Time: 4pm to 5pm

Venue: Perseverance Room, Enterprise Wing Level 5 @ UTown

Abstract

Structure-based virtual screening for selecting potential drug candidates is usually challenged by how to exclude numerous false positives in a molecule library when receptor plasticity is considered. In this study, based on the binding energy landscape theory, a hypothesis that a true inhibitor can bind to different conformations of the binding site favorably was brought out and the related strategies were devised to defeat this challenge: reducing false positives while considering receptor plasticity. The receptor in study is the influenza A nucleoprotein, whose oligomerization is a requirement for RNA binding. The structure flexibility of influenza A nucleoprotein was explored by molecular dynamics simulations. The resultant distinctive structures and the crystal structure were used as the receptor models and two binding sites, one from protein-protein interface and the other from RNA binding site, were targeted by docking the Otava PrimScreen1 diversity-molecule library using GOLD software. The intersection ligands that were listed in all the top-ranked molecules from the different conformations docking were selected. Such selection strategy successfully distinguished the high-affinity and the low-affinity control molecules added to the molecule library. This work provides an applicable approach for reducing false positives and selecting true binders from molecule libraries.

Biography

Dr. Mu yuguang is currently an associate professor at Nanyang Technological University. He obtained his PhD degree from Shandong University (China) in 1997. His research mainly focuses on molecular dynamics simulation on peptide/protein folding and assembly, DNA/RNA folding and protein-DNA/RNA/ligand recognition as well as advanced simulation method development.