

針對結構生物學家的蛋白質-蛋白質交互作用應用實例

利用生物信息, ZDOCK取樣技術, 及以DFIRE統計能量函數導引之叢集所作的對位預測

Authors entered the CAPRI experiment during the middle of Round 4 and have submitted predictions for all 6 targets released since then. They used the following procedures for docking prediction: (1) the identification of possible binding region(s) of a target based on known biological information, (2) rigid-body sampling around the binding regions(2) by using the docking program ZDOCK, (3) ranking of the sampled complex conformations by employing the DFIRE-based statistical energy function, (4) clustering based on pairwise RMSD and the DFIRE energy, and (5) manual inspection and relaxation of the side-chain conformations of the top-ranked structures by geometric constraint. Reasonable predictions were made for 4 of the 6 targets. The best fraction of native contacts within the top 10 models are 89.1% for Target 12, 54.3% for Target 13, 29.3% for Target 14, and 94.1% for Target 18.

Docking Prediction Using Biological Information, ZDOCK Sampling Technique, and Clustering Guided by the DFIRE Statistical Energy Function

Reference: Chi Zhang et al, *PROTEINS: Structure, Function, and Bioinformatics* 60 (2005), 314;

Used Module: ZDOCK, RDOCK



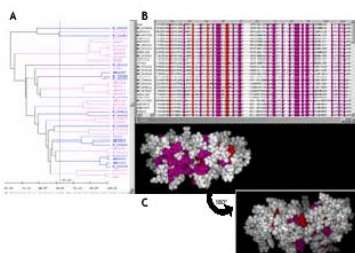
用蛋白質-蛋白質對位方法來作的複雜蛋白質互動關係分析

There are 1400 known protein-protein interactions in humans (DIP, <http://dip.doe-mbi.ucla.edu/>). Understanding these interactions is necessary in order to gain insight into molecular recognition and networks such as signal transduction pathways in cells. One key interaction is between regulator of G-protein signaling (RGS) proteins and alpha subunit of G-proteins. The RGS family proteins are involved in accelerating GTP hydrolysis of the G-protein alpha subunit, which leads to rapid recovery of signaling transduction cascades. To analyze and validate the G-protein regulating system, we used ZDOCKpro for protein-protein docking and a complementary tool Evolutionary Trace for protein family analysis. Results indicate that Evolutionary Trace identified a cluster of residues in the RGS domain that includes the RGS/G-protein alpha subunit binding interface. These residues were then used to guide the protein-protein docking experiment. Out of 3600 docked complexes, ZDOCKpro predicted a good complex structure within the top 10 ranked complexes. Results improved with the addition of the Evolutionary Trace data with the best ranked ZDOCKpro complex having an interface RMSD of 4Å. Overall, we find that protein-protein docking and complementary tools are useful to study protein-protein interactions of unknown complex assemblies.

Protein-Protein Docking Method Used to Study Complex Protein Interactions

Reference: Glennon and Dana Haley-VicenteAsano, *Accelrys World* 2005;

Used Module: ZDOCKpro, Evolutionary Trace



ZDOCK和RDOCK在CAPRI第3, 4和5回合之表現

Authors present an evaluation of the results of their original ZDOCK and RDOCK algorithms in Rounds 3, 4 and 5 of the protein docking challenge CAPRI. ZDOCK is a Fast Fourier Transform (FFT)-based, initial-stage rigid-stage rigid-body docking algorithm, and RDOCK is an energy minimization algorithm for refining and reranking ZDOCK results. Of the 9 targets for which they submitted predictions, they attained at least acceptable accuracy for 7, at least medium accuracy for 6, and high accuracy for 3. These results are evidence that ZDOCK in combination with RDOCK is capable of making accurate predictions on a diverse set of protein complexes.

ZDOCK and RDOCK Performance in CAPRI Rounds 3, 4 and 5

Reference: Kevin Wiehe, Zhiping Weng et al, *PROTEINS: Structure, Function, and Bioinformatics* 60 (2005), 207;

Used Module: ZDOCK, RDOCK

TABLE I Overall Performance of ZDOCK and RDOCK

Target	Protein complexes	Accuracy ^a	I RMS (Å) ^b	L RMS (Å) ^c	Contact % ^d	Ranked ^e
8	Nidogen-laminin	Medium	1.09	10.38	47	1
9	LicT homodimer	Incorrect	9.77	14.68	8	2
10	TBEV trimer	Incorrect	5.05	11.98	11	3
11	Cohesin-dockerin	Acceptable	2.17	9.15	13	1
12	Cohesin-dockerin	High	0.49	1.02	84	1 ^f
13	SAG1-FAB	High	0.64	2.57	87	1
14	MYPT1-PP1	High	0.95	3.83	53	8
18	GH11 Xylanase-TAXI	Medium	1.86	5.54	91	1
19	Ovine prion-FAB	Medium	1.26	4.67	57	8

^aAccuracy is determined by the CAPRI evaluation team based on interface RMSD, ligand RMSD, and percentage of correct contacts predicted.²

^bInterface RMSD.

^cLigand RMSD.

^dPercentage of correct interface residue contact pairs predicted.

^eRank of best prediction out of the 10 submissions for that target unless noted otherwise.

^fFor Target 12 our best prediction was ranked 9th, but our first ranked prediction also achieved high accuracy.

抗體抗原結合點靜電特性的差異：特異性和交叉反應性

The significance of this work is the observed variations in electrostatic interactions among the three antibody-antigen complexes. Their work demonstrates that higher electrostatics, both as a number of short-range electrostatic interactions and their contributions, lead to higher binding specificity. Strong salt bridges, their networking, and electrostatically driven binding, limit flexibility through geometric constraints. In contrast, hydrophobic driven binding and low levels of electrostatic interactions are associated with conformational flexibility and cross-reactivity.

Differences in Electrostatic Properties at Antibody-Antigen Binding Sites: Implications for Specificity and Cross-Reactivity

Reference: Neeti Sinha et al *Biophysical Journal* 83 (2002) 2946;

Module: InsightII, Dephi

