Dr. Ratna Singh

Structural Bioinformatics tutorial

Basic principle-- Evolutionary related protein tend to have similar structure

→ Predicts the three-dimensional structure of a given protein sequence (TARGET) based on an alignment to one or more known protein structures (TEMPLATES)

→ If similarity between the TARGET sequence and the TEMPLATE sequence is detected, structural similarity can be assumed.

Basic steps in Homology modeling :

i) Model building

ii) Refinement

ii) Evaluation

Model-building (Swiss model)--> Model-refinement (Galaxy webserver)--> model evaluation (Molprobity)

HOMOLOGY MODELING

1) Identify the homologous structures of your query sequence from pdb BLAST.

Check the quality of the pdb and disorderd region

Hints: query sequence --> pdb blast, take the pdb code, search the pdb data bank and check the sequence information, resolution of the structure.

2) Build the model using swiss-pdb automated and alignment mode? Compares the results and check the quality of the models? (http://swissmodel.expasy.org/)

3) Check the quality of the model using molprobity, identify the residues with errors

(http://molprobity.biochem.duke.edu/)

Molprobity

i) Without adding the hydrogen

Upload the structure→continue→ Analyze geometry without all atom contacts→ result

ii) Adding the hydrogen

Upload the structure→continue→ add hydrogens→continue→ Analyze all atom contact and geometry→ result

4) Improve the quality of the model

Hint : Use Kobamin server and after refinement recheck the quality of the model using

http://csb.stanford.edu/kobamin/ or

http://chopra-modules.science.purdue.edu/modules/kobamin/html/

5) Improve the quality of the model

GalaxyWEB (http://galaxy.seoklab.org/cgi-bin/submit.cgi?type=REFINE)

MODLOOP –identify the loop region which you want to optimize→

Modeller license key – MODELIRANJE—upolad pdb→ enter loop segments in following format 15::22:: or 15:A:22:A:

After any optimization recheck with molprobity

For using multiple template for generating a model use HHPRED

HHpred--> paste sequence--> select templates--> click model using selection-->this give alignment (please copy paste alignment somewhere for your record)---> Enter key MODELIRANJE--> Submit-->3D structure download pdb

Go to the swissmodel access https://swissmodel.expasy.org/assess, compare your generated structures (by different methods) compare their qmean, Gmqe , molprobity score, also go to pymol and also look for RMS value. Based on the values select a model for further galaxyweb optimization.