BHAGEERATH-H: A Homology *ab-intio* Hybrid Web server for Protein Tertiary Structure Prediction

Theory

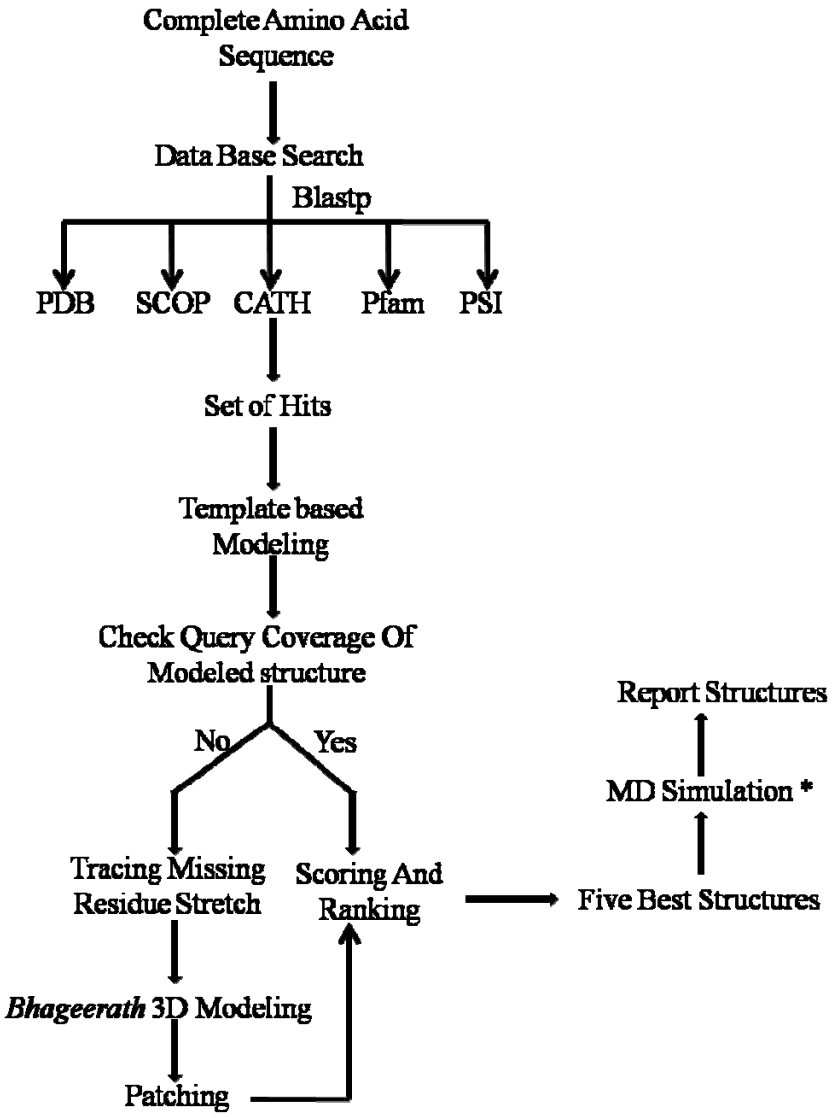
The term "protein homology modeling", also called comparative modeling, refers to modeling a protein structure using a known experimentally determined structure of a homologous protein as a modeling template. In this tutorial we will discuss the basics of homology modeling techniques, questions like: basic steps involved in Bhageerath-H, the need of Bhageerah-H and the accuracy. Two cases are discussed, the first one is relatively easy for modeling, while the second contains modeling of a multi-domain protein with 2 or 3 templates followed by patching of fragments finally fitting the domains to the final structure (will be finished soon!).

Introduction

The term "homology modeling", also called comparative modeling, or protein homology modeling, refers to modeling a 3D (tertiary) structure of a protein using a known experimentally determined (x-ray or NMR) structure of a homologous protein as a template. Homology modeling can provide the molecular biologists and biochemists with "low-resolution" structures, which will contain sufficient information about the spatial arrangement of important residues in the protein and which may guide the design of new experiments. The use of this method is based on the observation that two proteins belonging to the same family and sharing highly similar amino acid sequences will have similar three-dimensional structures.

Provided that you know that a protein homologous to your protein with a known tertiary structure is available, it is a good idea before starting the modeling project, to make a multiple sequence alignment of your protein with homologous sequences. This will give you an idea on the general features of the protein family, degree of conservation, the consensus sequence, etc. Features like insertions and deletions, the location of the active site residues are very important to have in mind when making a homology model. This information will help you in the later stages of the modeling process to decide on the feasibility of modeling and to correct an automatically generated sequence alignment. After an initial sequence analysis, we may proceed to the modeling as such. An outline of the process in shown below and explained in Figure 1.

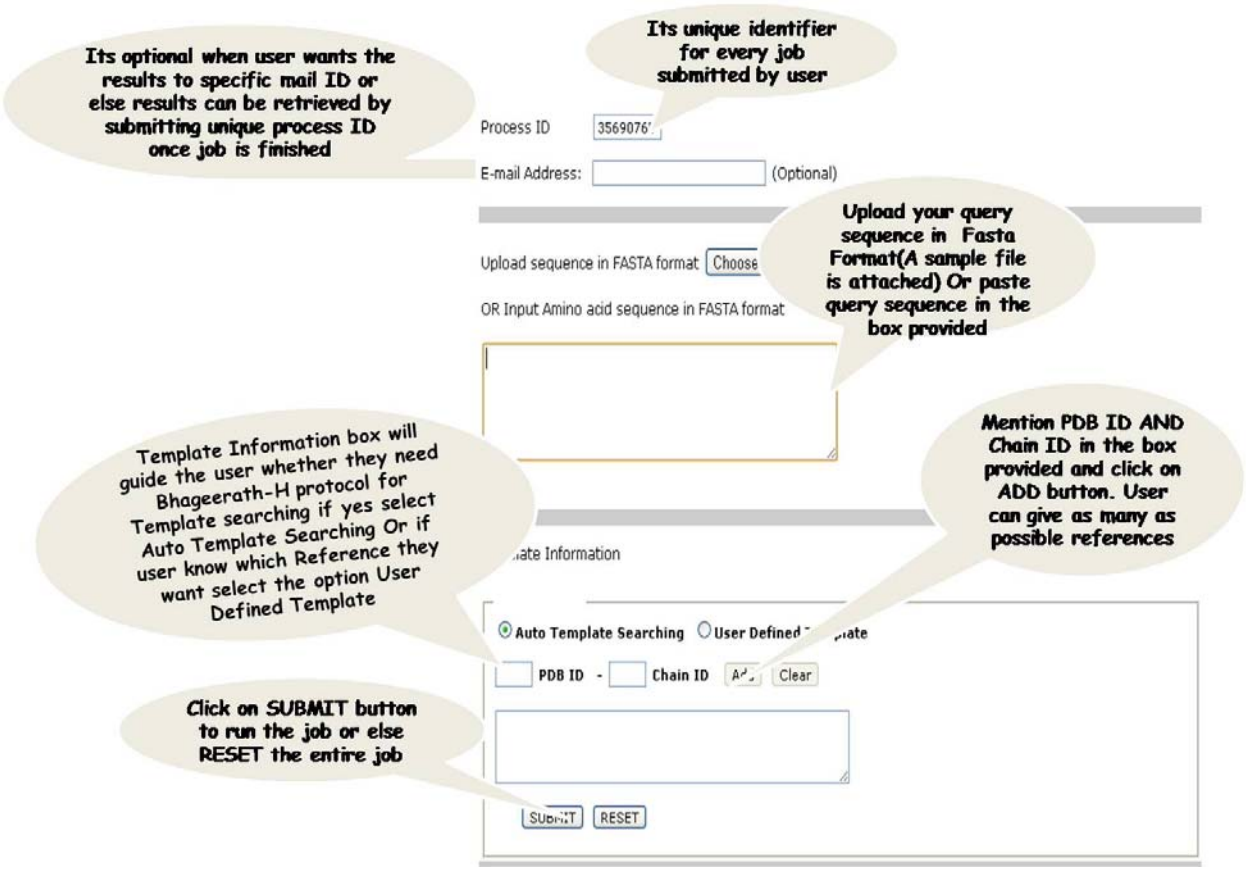
- template identification;
- amino acid sequence alignment;
- Template based modeling and backbone generation;
- *ab-initio* loop building and end repair (if required);
- MD Simulation(optional);



* MD Simulation is optional

Figure 1: Basic Protocol for Bhageerath-H

Bhageerath-H web-utility



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