# A Quick Guide To SWISS-MODEL Homology Modeling Server and Repository

http://swissmodel.expasy.org

This is an introduction to the SWISS-MODEL homology-modeling server and Repository of annotated 3-dimensional protein structure homology models.
This guide is intended as a quick tour. Basic knowledge of protein structure and homology modeling methods is assumed.

## HOMOLOGY MODELING

Homology modeling (comparative modeling) is currently the only computational method that can reliably generate a 3D model of a protein structure from its amino acid sequence (target).

Successful model building requires at least one experimentally determined 3D structure (template) that shows significant amino acid sequence similarity with the target sequence. The template is used as a scaffold to model the structure of the target sequence following a four step procedure: template selection, target template alignment, model building, and evaluation. These steps can be iteratively repeated, until a satisfying model structure is achieved.

## SWISS-MODEL: SUBMISSION MODES

SWISS-MODEL is a server for automated comparative protein modeling. It is freely accessible via its web interface on the ExPASy web server:

http://swissmodel.expasy.org

or from the program DeepView (Swiss Pdb-Viewer), an integrated tool for viewing and analyzing protein structures and models (http://www.expasy.org/spdbv).

The server gives the user the choice between three main interaction modes:

**First approach mode:** The amino acid sequence of a protein to be modeled or the Swiss-Prot/TrEMBL (http://www.expasy.org/sprot) accession code can be directly submitted via the web interface. The server will create models for the target sequence in a fully automated modeling procedure.
Optionally the user can specify template structures, either from an internal template library (ExPDB) extracted from the PDB database (http://www.pdb.org), or by uploading coordinate files in PDB format.

**Alignment mode:** The prerequisite for this mode is a multiple sequence alignment containing (at least) target and template sequences. The server will build the model based on the given alignment. The user specifies which sequence corresponds to the target and which to the template.

**Project mode:** This mode allows the user to submit a manually optimized request to the server. DeepView is used to create a project file containing the template structure(s) and the alignment between the target and the template(s), which is then uploaded to the server. This mode offers detailed control over the modeling process, e.g. by selecting different template(s) and manually editing the target template alignment to correctly place insertions and deletions. The project mode can also be used to iteratively improve the output of the first approach mode.

Modeling of multimeric proteins with SWISS-MODEL can be done in Project mode. A multimeric template structure (with different chain IDs) is loaded into DeepView. The target sequence is imported into DeepView in FASTA format containing the sequences in the same order as the protomer templates separated by semicolons:

```
>ModelName
PROTOMERSEQUENCE;PROTOMERSEQUENCE
```

After aligning target and template in DeepView and manually editing the initial alignment, the complete project file is submitted to the server.

## SWISS-MODEL: RESULTS AND EVALUATION

SWISS-MODEL returns a log file tracing all actions taken by the server, and the model coordinates via e-mail. Two output options can be specified:

**DeepView (Swiss Pdb-Viewer) mode:** returns the model and the template(s) as a DeepView project file;

**Normal mode:** returns the model coordinates file in PDB format (for viewing with other applications, e.g. Rasmol).

The accuracy of a model can vary significantly, even within different regions of the same protein. Several tools are provided to evaluate the reliability of the model:

A C-score (similar to B-factors in crystal structures) is included in the result file giving an estimate of the variability of the template structures at this position. Those parts of the model where no template information could be used for model building (insertions/deletions) are assigned a C-score of 99. Furthermore, the log file includes force field energies for the overall structure and for each individual residue. This helps identifying regions with obvious conformational or electrostatic problems.

Optionally a report from the protein verification tool WhatCheck (http://www.cmbi.kun.nl/gv/whatcheck) can be included in the results. Additionally the quality of the model can be checked by using the ANOLEA atomic mean force potential web interface on the server (http://swissmodel.expasy.org/anolea).

Inaccurate target template alignments are the most frequent source of errors in models. DeepView allows to manually adjusting the alignment while visually verifying the structural implications, e.g. the placement of gaps in the correct structural context.

Fine-tuning of the model, such as energy checks, loop re-building and site chain rotamer search can be performed with DeepView on the project files returned from the server.

## SWISS-MODEL REPOSITORY: ACCESSION

The SWISS-MODEL Repository is a database of annotated 3D comparative protein structure models generated by the fully automated homology-modeling pipeline of SWISS-MODEL.

The Repository contains 3D models for sequences from the Swiss-Prot and TrEMBL databases for which suitable templates are available. Annotation and cross-linking of the models with other databases, e.g. Swiss-Prot and InterPro allow for seamless navigation between protein sequence and structure information.

The SWISS-MODEL Repository can be queried via an interactive web site:

`http://swissmodel.expasy.org/repository`

**A Quick search** for the models in the repository can be done by submitting a Swiss-Prot/TrEMBL protein `accession number (AC)` or `identification (ID)`.

**The Advanced Search** interface allows complex queries combining different keywords, e.g. protein name, gene name, biological description or organism.

## SWISS-MODEL REPOSITORY: SECTIONS

The `model navigator` allows the access to the target sequence information and the navigation between the models available for a given protein sequence entry.

For each model the following information is provided:

**Model info section:** This section gives access to display the model and download its coordinates. Information about the template used for modeling is provided with cross references to structural information databases;

**Alignment section:** displays the `target template` sequence alignment used in the modeling procedure and the assigned secondary structure;

**ANOLEA and GROMOS section:** contains a GROMOS empirical force field and ANOLEA mean force potential plots to evaluate the quality of the model;

**Modeling log section:** The modeling log gives a detailed description of the individual modeling steps, e.g. template selection and loop building;

For each target sequence various biological information, e.g. gene name, taxonomy, protein description is provided in the `target` sequence info section.

**InterPro mapping:** InterPro descriptors are mapped onto the target sequence and the available models to identify individual domains and specific biological features in the `target` protein; (`http://www.ebi.ac.uk/interpro`)

## REFERENCES


1. N. Guex and M.C. Peitsch (1997) SWISS-MODEL and the Swiss-PdbViewer: An environment for comparative protein modeling, *Electrophoresis* **18**: 2714-2723.

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3. J. Kopp and T. Schwede, (2004). The SWISS-MODEL Repository of annotated 3-dimensional protein structure homology models, *Nucleic Acids Research* **32**: D230-D234.



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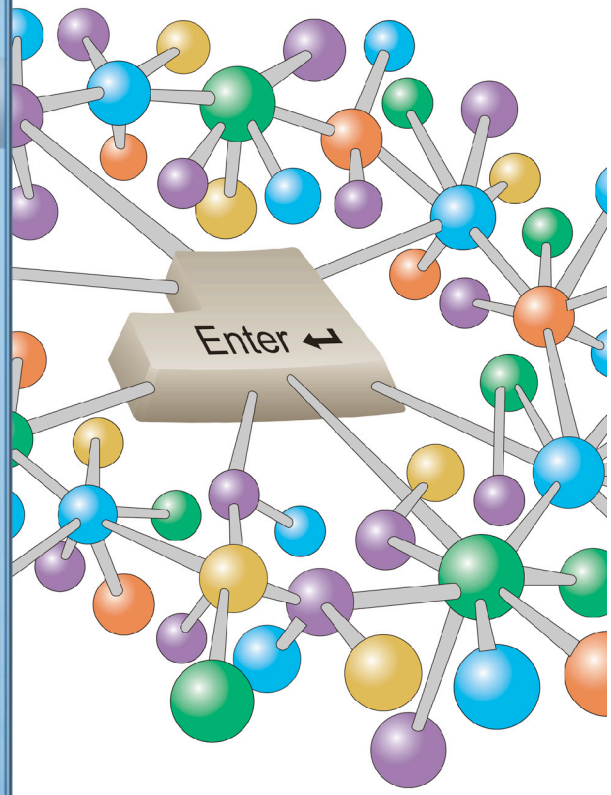


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