SWISS-MODEL Homology Modelling Report

Model Building Report

This document lists the results for the homology modelling project "Untitled Project" submitted to SWISS-MODEL workspace on April 8, 2025, 8:27 p.m..The submitted primary amino acid sequence is given in Table T1.

If you use any results in your research, please cite the relevant publications:

- Waterhouse A, Bertoni M, Bienert S, Studer G, Tauriello G, Gumienny R, Heer FT, de Beer TAP, Rempfer C, Bordoli L, Lepore R, Schwede T
  SWISS-MODEL: homology modelling of protein structures and complexes.
  Nucleic Acids Res 46, W296-W303. (2018) 29788355 10.1093/nar/gky427
- Bienert S, Waterhouse A, de Beer TAP, Tauriello G, Studer G, Bordoli L, Schwede T
  The SWISS-MODEL Repository - new features and functionality.
  Nucleic Acids Res 45, D313-D319. (2017) 27899672 10.1093/nar/gkw1132
- Studer G, Tauriello G, Bienert S, Biasini M, Johner N, Schwede T
  ProMod3 - A versatile homology modelling toolbox.
  PLOS Comp Biol 17(1), e1008667. (2021) 33507980 10.1371/journal.pcbi.1008667
- Studer G, Rempfer C, Waterhouse AM, Gumienny R, Haas J, Schwede T
  QMEANDisCo - distance constraints applied on model quality estimation.
  Bioinformatics 36, 1765-1771. (2020) 31697312 10.1093/bioinformatics/btz828
- Bertoni M, Kiefer F, Biasini M, Bordoli L, Schwede T
  Modeling protein quaternary structure of homo- and hetero-oligomers beyond binary interactions by homology.
  Scientific Reports 7. (2017) 28874689 10.1038/s41598-017-09654-8

Results

The SWISS-MODEL template library (SMTL version 2025-04-02, PDB release 2025-03-28) was searched with BLAST (Camacho et al.) and HHblits (Steinegger et al.) for evolutionary related structures matching the target sequence in Table T1. For details on the template search, see Materials and Methods. Overall 46 templates were found (Table T2).

Models

The following model was built (see Materials and Methods "Model Building"):

Model #03	File	Built with	Oligo-State	Ligands	GMQE	QMEANDisCo Global
	PDB	ProMod3 3.4.1	monomer (matching prediction)	None	0.26	0.46 ± 0.07

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Range	Coverage	Description
8wcm.1.A	16.11	homo-dimer	0.00	HHblits	EM	-	0.27	46 - 202	0.50	Non-structural protein NS-S

The template contained no ligands.

```
Target    MSLSKASQPSVKSACVRLPIVVLEPNLAELSTSYVGLVSCKCSVLTCSMMRKMKAFTNTVWLFGNP-----NNPLHALEP
8wcm.1.A  -----------------------------------------------RFSDFYNVGEFPYR-VGLGDFASNVAPPPAKPFQR

Target    AVEQLLDEYSGDLGSYSQQEKSALRWPSGKPSVHFLQAAHLFFSLKNTWAVETGQENWRGFFHRITSGKKYKFEGDMVID
8wcm.1.A  LIDLIGHMTLSDFTRF-PNLKEAISWPLGEPSLAFFDLSSTRVH-RNDDIRR---DQIATLAMRSCKIT--NDLEDSFVG

Target    SCYKIDERRRRMGLPDTFITGLNPIMDVALLQIESLLRVRGLTLNYHLFTSSFLDKPLLDSLYFAIWRDKKKDDGSYSQD
8wcm.1.A  LHRMIVTEAILRGIDLCLLPGFDLMYEVAHVQCVRLLQAAKEDISNA--------------------------------
```

```
Target    EGARQDDPLNPLDELLYLSDLPKPLAHYLNKCPLHNIIMHDEEVREAYLNPIWGKDWPALSSSP
8wcm.1.A  ------------------------------------------------------------
```

Materials and Methods

Template Search

Template search with BLAST and HHblits has been performed against the SWISS-MODEL template library (SMTL, last update: 2025-04-02, last included PDB release: 2025-03-28).

The target sequence was searched with BLAST against the primary amino acid sequence contained in the SMTL.

An initial HHblits profile has been built using the procedure outlined in (Steinegger et al.), followed by 1 iteration of HHblits against Uniclust30 (Mirdita, von den Driesch et al.). The obtained profile has then be searched against all profiles of the SMTL. A total of 46 templates were found.

Template Selection

For each identified template, the template's quality has been predicted from features of the target-template alignment. The templates with the highest quality have then been selected for model building.

Model Building

Models are built based on the target-template alignment using ProMod3 (Studer et al.). Coordinates which are conserved between the target and the template are copied from the template to the model. Insertions and deletions are remodelled using a fragment library. Side chains are then rebuilt. Finally, the geometry of the resulting model is regularized by using a force field.

Model Quality Estimation

The global and per-residue model quality has been assessed using the QMEAN scoring function (Studer et al.).

Ligand Modelling

Ligands present in the template structure are transferred by homology to the model when the following criteria are met: (a) The ligands are annotated as biologically relevant in the template library, (b) the ligand is in contact with the model, (c) the ligand is not clashing with the protein, (d) the residues in contact with the ligand are conserved between the target and the template. If any of these four criteria is not satisfied, a certain ligand will not be included in the model. The model summary includes information on why and which ligand has not been included.

Oligomeric State Conservation

The quaternary structure annotation of the template is used to model the target sequence in its oligomeric form. The method (Bertoni et al.) is based on a supervised machine learning algorithm, Support Vector Machines (SVM), which combines interface conservation, structural clustering, and other template features to provide a quaternary structure quality estimate (QSQE). The QSQE score is a number between 0 and 1, reflecting the expected accuracy of the interchain contacts for a model built based a given alignment and template. Higher numbers indicate higher reliability. This complements the GMQE score which estimates the accuracy of the tertiary structure of the resulting model.

References

- Camacho C, Coulouris G, Avagyan V, Ma N, Papadopoulos J, Bealer K, Madden TL
  BLAST+: architecture and applications.
  BMC Bioinformatics, 10, 421-430. (2009) 20003500 10.1186/1471-2105-10-421
- Steinegger M, Meier M, Mirdita M, Vöhringer H, Haunsberger SJ, Söding J
  HH-suite3 for fast remote homology detection and deep protein annotation.
  BMC Bioinformatics 20, 473. (2019) 31521110 10.1186/s12859-019-3019-7
- Mirdita M, von den Driesch L, Galiez C, Martin MJ, Söding J, Steinegger M
  Uniclust databases of clustered and deeply annotated protein sequences and alignments.
  Nucleic Acids Res, 45, D170–D176. (2016) 27899574 10.1093/nar/gkw1081

Table T1:

Primary amino acid sequence for which templates were searched and models were built.

```
MSLSKASQPSVKSACVRLPIVVLEPNLAELSTSYVGLVSCKCSVLTCSMMRKMKAFTNTVWLFGNPNNPLHALEPAVEQLLDEYSGDLGSYSQQEKSALR
WPSGKPSVHFLQAAHLFFSLKNTWAVETGQENWRGFFHRITSGKKYKFEGDMVIDSCYKIDERRRRMGLPDTFITGLNPIMDVALLQIESLLRVRGLTLN
YHLFTSSFLDKPLLDSLYFAIWRDKKKDDGSYSQDEGARQDDPLNPLDELLYLSDLPKPLAHYLNKCPLHNIIMHDEEVREAYLNPIWGKDWPALSSSP
```

Table T2:

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Coverage	Description
7rlo.1.K	13.50	monomer	-	HHblits	EM	NA	0.27	0.55	Non-structural protein NS-S
7f67.1.K	14.20	monomer	-	HHblits	EM	NA	0.27	0.54	Non-structural protein NS-S
7f64.1.L	14.20	monomer	-	HHblits	EM	NA	0.27	0.54	Non-structural protein NS-S
7f64.1.K	14.20	monomer	-	HHblits	EM	NA	0.27	0.54	Non-structural protein NS-S
7f66.1.L	14.20	monomer	-	HHblits	EM	NA	0.27	0.54	Non-structural protein NS-S
8wcm.1.A	16.11	homo-dimer	-	HHblits	EM	NA	0.27	0.50	Non-structural protein NS-S
7f67.1.L	14.20	monomer	-	HHblits	EM	NA	0.27	0.54	Non-structural protein NS-S
5ooo.1.A	20.79	monomer	-	HHblits	X-ray	2.20Å	0.29	0.34	Non-structural protein NS-S
7k02.1.B	13.51	homo-dimer	-	HHblits	X-ray	3.40Å	0.27	0.25	Bcl-2 homologous antagonist/killer
7k02.2.A	13.51	homo-dimer	-	HHblits	X-ray	3.40Å	0.27	0.25	Bcl-2 homologous antagonist/killer
7k02.2.B	13.51	homo-dimer	-	HHblits	X-ray	3.40Å	0.27	0.25	Bcl-2 homologous antagonist/killer
7k02.3.A	13.51	homo-dimer	-	HHblits	X-ray	3.40Å	0.27	0.25	Bcl-2 homologous antagonist/killer
7k02.3.B	13.51	homo-dimer	-	HHblits	X-ray	3.40Å	0.27	0.25	Bcl-2 homologous antagonist/killer
7k02.1.A	13.51	homo-dimer	-	HHblits	X-ray	3.40Å	0.27	0.25	Bcl-2 homologous antagonist/killer
6stj.1.A	8.93	homo-tetramer	-	HHblits	X-ray	2.20Å	0.22	0.19	Induced myeloid leukemia cell differentiation protein Mcl-1
5c3f.1.A	8.93	monomer	-	HHblits	X-ray	1.43Å	0.22	0.19	Induced myeloid leukemia cell differentiation protein Mcl-1
6o4u.1.A	10.71	monomer	-	HHblits	X-ray	1.70Å	0.24	0.19	Induced myeloid leukemia cell differentiation protein Mcl-1
6stj.1.D	8.93	homo-tetramer	-	HHblits	X-ray	2.20Å	0.22	0.19	Induced myeloid leukemia cell differentiation protein Mcl-1
6o6g.1.A	10.71	monomer	-	HHblits	X-ray	2.40Å	0.24	0.19	Induced myeloid leukemia cell differentiation protein Mcl-1
7ado.1.H	26.92	monomer	-	HHblits	EM	NA	0.34	0.09	ER membrane protein complex subunit 8
6stj.1.C	8.93	homo-tetramer	-	HHblits	X-ray	2.20Å	0.22	0.19	Induced myeloid leukemia cell differentiation protein Mcl-1
8eoi.1.G	25.93	monomer	-	HHblits	EM	NA	0.33	0.09	ER membrane protein complex subunit 8
6z3w.1.H	25.93	monomer	-	HHblits	EM	NA	0.32	0.09	ER membrane protein complex subunit 9
9c7v.1.I	26.92	monomer	-	HHblits	EM	NA	0.34	0.09	ER membrane protein complex subunit 8

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Coverage	Description
8j0n.1.H	26.92	monomer	-	HHblits	EM	NA	0.34	0.09	ER membrane protein complex subunit 8
6ww7.1.H	26.92	monomer	-	HHblits	EM	NA	0.34	0.09	ER membrane protein complex subunit 8
8j0o.1.H	26.92	monomer	-	HHblits	EM	NA	0.34	0.09	ER membrane protein complex subunit 8
7adp.1.G	26.92	monomer	-	HHblits	EM	NA	0.34	0.09	ER membrane protein complex subunit 8
6qfi.1.A	12.50	monomer	-	HHblits	X-ray	2.40Å	0.21	0.05	Induced myeloid leukemia cell differentiation protein Mcl-1
4hw3.2.A	13.33	monomer	-	HHblits	X-ray	2.40Å	0.22	0.05	Induced myeloid leukemia cell differentiation protein Mcl-1

The table above shows the top 30 filtered templates. A further 16 templates were found which were considered to be less suitable for modelling than the filtered list.
4hw2.1.A, 4hw2.2.A, 4hw2.3.A, 4hw2.4.A, 4hw2.5.A, 4hw2.6.A, 4hw3.1.A, 4hw3.10.A, 4hw3.11.A, 4hw3.12.A, 4hw3.4.A, 4hw3.5.A, 4hw3.6.A, 4hw3.7.A, 4hw3.8.A, 4hw3.9.A