

MINOR PROJECT 2: Protein Structure Prediction Using SWISS-MODEL

Abstract:

This project involves predicting the 3D structure of a protein using homology modeling. Based on the provided or selected amino acid sequence, tools like SWISS-MODEL identify a known structural template with high sequence similarity and build a model structure. Structural predictions are essential when experimental structures (X-ray, NMR) are not available and help in studying protein function, active sites, or drug binding regions.

Step-by-Step Explanation

Step 1: Select and Retrieve the Target Protein Sequence

- **What You Do:**
Choose a protein of interest, preferably one without a known 3D structure, and retrieve its amino acid sequence in FASTA format from UniProt.
 - **Why It's Important:**
The FASTA sequence serves as input for homology modeling.
 - **How To Do It:**
 - Visit <https://www.uniprot.org/>
 - Search for a protein (e.g., "Zika virus envelope protein")
 - Click on the relevant entry, go to the "Sequence" section
 - Click "FASTA" to download
 - Save as: zika_env.fasta
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Step 2: Submit the Sequence to SWISS-MODEL

- **What You Do:**
Upload the FASTA file to SWISS-MODEL for template search and model building.
- **Why It's Important:**
SWISS-MODEL uses sequence homology to build accurate protein structure models.
- **How To Do It:**
 - Go to: <https://swissmodel.expasy.org/interactive>
 - Paste the FASTA sequence or upload the file
 - Choose "Automated Mode" to let the tool find the best template
 - Click "Start Modelling"

Step 3: Select the Best Template

- **What You Do:**
Review the templates suggested by SWISS-MODEL based on sequence identity and coverage.
- **Why It's Important:**
A good template (usually >30% identity) ensures a more reliable model.
- **How To Do It:**
 - Choose the model with:
 - Highest sequence identity
 - Best coverage
 - GMQE and QMEAN scores (closer to 1.0 is better)
- Click "Build Model" for your selected template.

Step 4: Download the 3D Model File

- **What You Do:**
Once the modeling is complete, download the predicted structure in PDB format.
- **Why It's Important:**
You'll use this file for visualization and validation.
- **How To Do It:**
 - Click "Download PDB File"
 - Save as zika_model.pdb

Step 5: Visualize the Predicted Structure

- **What You Do:**
Open the predicted protein structure using 3D visualization software like PyMOL or UCSF Chimera.
- **Why It's Important:**
Helps explore structure: alpha helices, beta sheets, active sites, disulfide bonds, etc.
- **How To Do It:**
 - Open PyMOL:

bash

CopyEdit

pymol zika_model.pdb

- Use commands like:

bash

CopyEdit

show cartoon

color chainbow

Step 6: Validate the Model

- **What You Do:**
Check the stereochemical quality of the predicted structure using Ramachandran Plot and other quality metrics.
- **Why It's Important:**
Ensures the reliability of the predicted 3D conformation.
- **How To Do It:**
 - **Use:**
 - SAVES server <http://servicesn.mbi.ucla.edu/SAVES/>
 - PROCHECK (via PDBsum or online servers)
 - Upload the .pdb file and get a Ramachandran plot

Step 7: Write a Mini-Report Summarizing the Results

- **What You Do:**
Summarize each step, provide figures/screenshots of your predicted structure, and interpret what the structure reveals.
- **Why It's Important:**
Clearly documents your approach, findings, and insights from structure prediction.
- **What To Include:**
 - UniProt ID of protein
 - Template used
 - Sequence identity and GMQE score
 - Visualizations (PyMOL images)
 - Ramachandran plot and structural quality stats
 - Biological relevance (e.g., active site, potential function)



Tools Required:

Tool	Purpose
UniProt	Retrieve protein sequence
SWISS-MODEL	Homology modeling
PyMOL / Chimera	3D structure visualization
PROCHECK / SAVES	Structural validation

Summary Table:

Step	Tool	Output
1	UniProt	FASTA sequence file
2	SWISS-MODEL	Predicted model
3	SWISS-MODEL	Template selection
4	SWISS-MODEL	PDB file
5	PyMOL / Chimera	3D visual output
6	SAVES / PROCHECK	Validation reports
7	Word / PDF	Mini-project report