Homology modeling

upload.wikimedia.org

Homology modeling, also known as comparative modeling, is a computational technique used in structural biology to predict the three-dimensional (3D) structure of a protein or other macromolecule based on its amino acid sequence and the known structure of a related protein1. Here are the key steps involved in homology modeling:

Identification and Selection of Template Structures:

The first step is to identify and select appropriate template structures from the Protein Data Bank (PDB).

Pair-wise sequence alignment methods like BLAST help identify proteins with high sequence homology to the query protein in the PDB.

Multiple sequence alignments or automated iterative methods (e.g., PSI-BLAST) can be used for more sensitive template identification.

Factors such as sequence identity, alignment scores, phylogenetic relationships, biological function, and environmental context guide template selection.

Alignment of the Query Sequence with the Template:

Achieving a high-quality sequence alignment is crucial for accurate modeling.

Multiple sequence alignment programs (e.g., Proline, T-Coffee) are recommended to incorporate evolutionary information.

Visual examination of the alignment ensures proper alignment of conserved residues.

Model Building:

Based on the aligned sequences, a 3D model is built for the query protein using the template’s known structure.

The model is constructed by aligning corresponding residues in the query and template sequences.

Loop Modeling:

Loops or missing segments in the template structure are modeled to complete the full protein structure.

Various algorithms and tools are available for loop modeling.

Model Optimization:

Energy minimization and refinement techniques are applied to optimize the model.

Molecular dynamics simulations and other methods improve the model’s accuracy.

Applications of Homology Modeling:

Drug Discovery: Homology models aid in understanding protein-ligand interactions, guiding drug design.

Functional Annotation: Predicting protein function based on structure.

Enzyme Mechanism Studies: Investigating active site residues and catalytic mechanisms.

Protein Engineering: Designing mutations for improved properties.

References:

Microbe Notes: Homology Modeling2

SpringerLink: Homology Modeling3

Wikipedia: Homology Modeling4

Learn more:

1. microbiologynote.com

2. microbenotes.com

3. link.springer.com

4. en.wikipedia.org

5. en.wikipedia.org