

Protein structure prediction



INDRAPRASTHA INSTITUTE *of*
INFORMATION TECHNOLOGY **DELHI**

Dr. Jaspreet Kaur Dhanjal

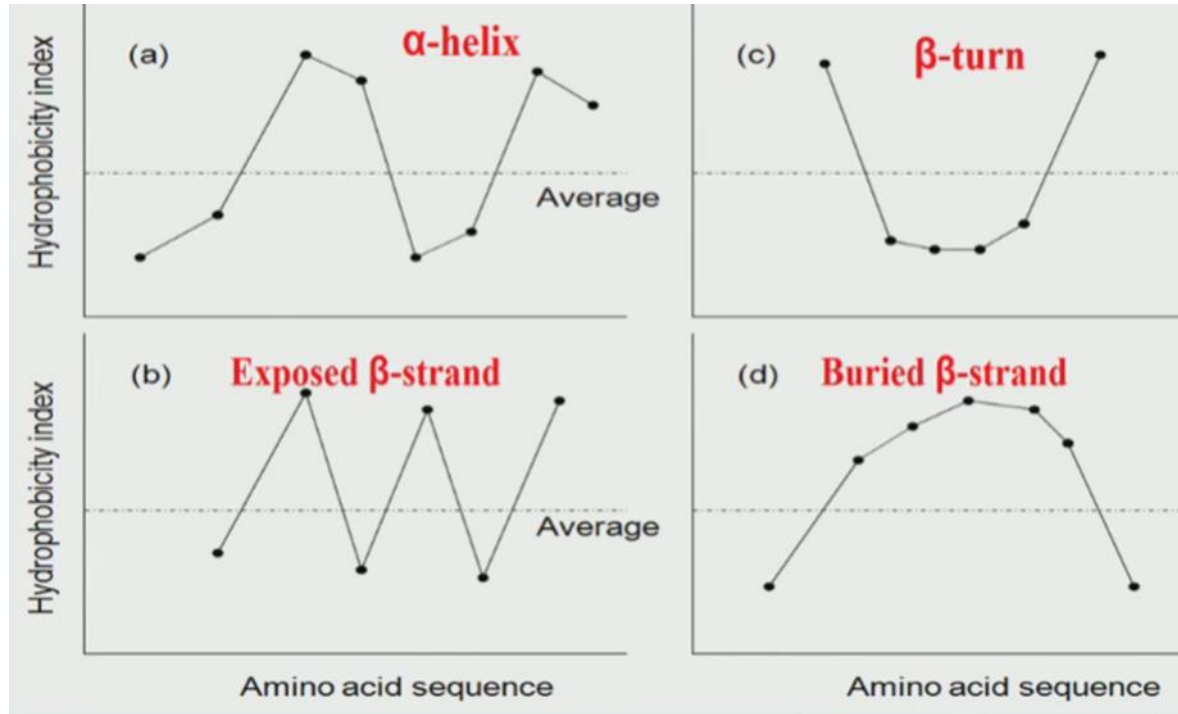
Assistant Professor, Department of Computational Biology

Email ID: jaspreet@iiitd.ac.in

५

October 07, 2025

Hydrophobicity Profile



Multiple sequence alignment

- Average of helix, strand, coil and turn parameters (GOR) for all the aligned residues at each position
- Insertion is given a value of zero
- Confidence of the prediction is related to the conservation score (0-1) at the position
- Zpred – First SS predictor using MSA

Jpred 4
Incorporating Jnet

A Protein Secondary Structure Prediction Server

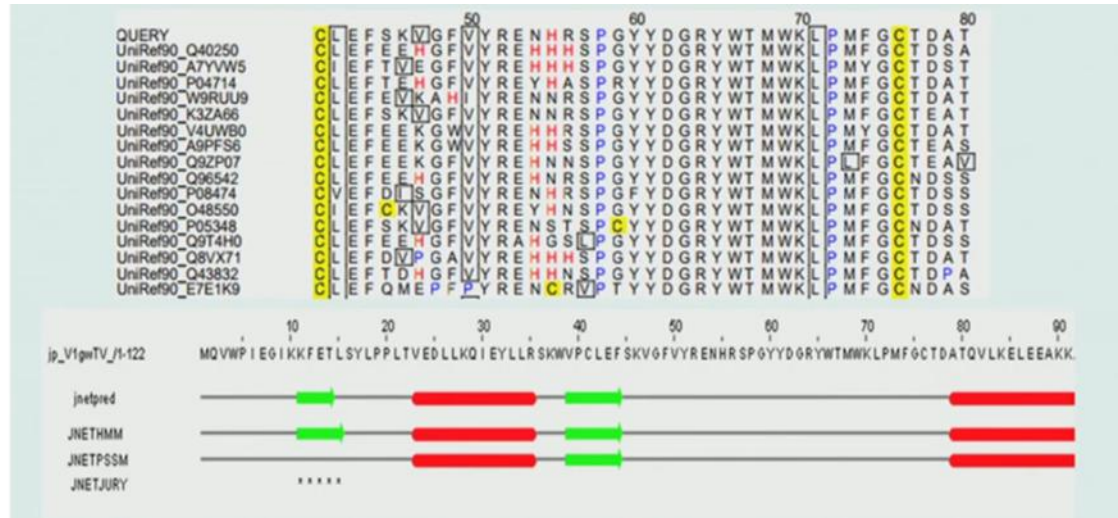
Home RESOURCES About News FAQ Help & Tutorial Webinars Contact Publications

IMPORTANT MESSAGE: Do you use JPred and/or our other resources?
We are applying to renew funding for the next 5 years, so please help keep the services available for your use by writing us a support letter.
THANK YOU to those who have already written, but it is not too late for others to help us! Please write us a support letter by **Friday Night (22nd September)**.
In your letter please say how you use our services and how important they are to you in your research/teaching.
Please send the letter as a PDF, ideally on headed paper to: support_jpred@cam.ac.uk.
Thank you in advance for your help
Geoff Barton

Input sequence:

Advanced options click to show/hide

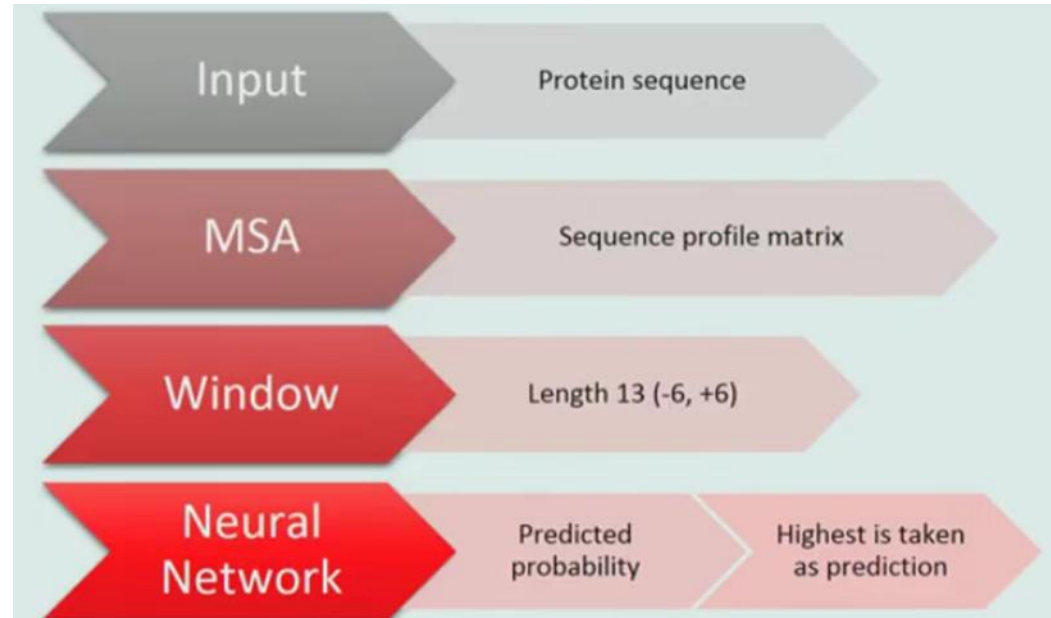
Make Prediction Reset Form



Machine learning techniques

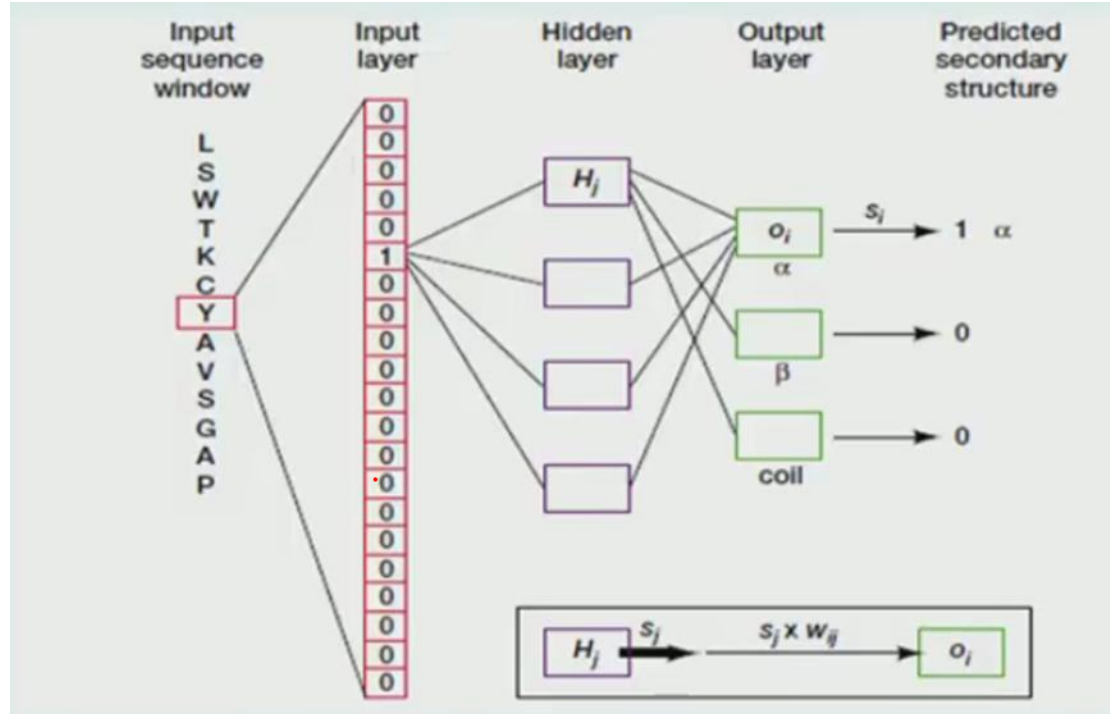
Profile neural network systems from HeiDelberg (PHD)

- Aspects:
 - Multiple sequence alignment
→ Evolutionary information
 - Neural networks →
Learning secondary structure
– amino acid residue
pattern/information
 - Window approximation →
Captures effect of
neighboring residues



Machine learning techniques

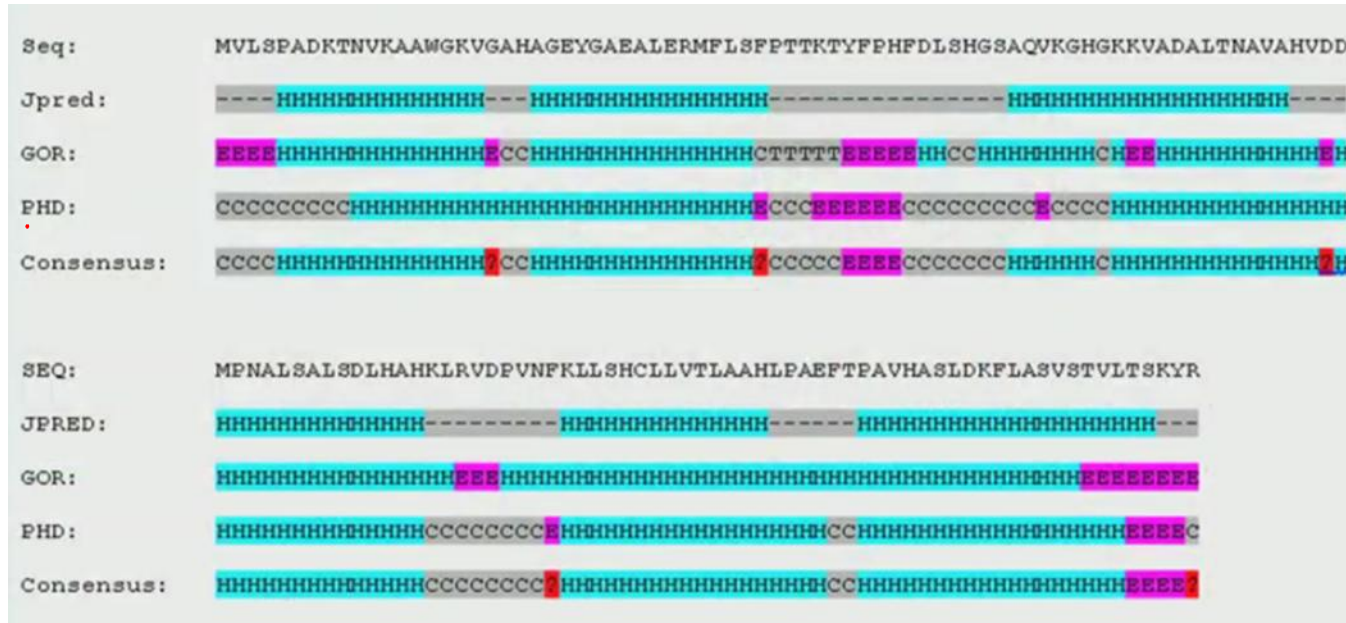
Profile neural network systems from HeiDelberg (PHD)



Consensus (joint) prediction methods

1. Consensus

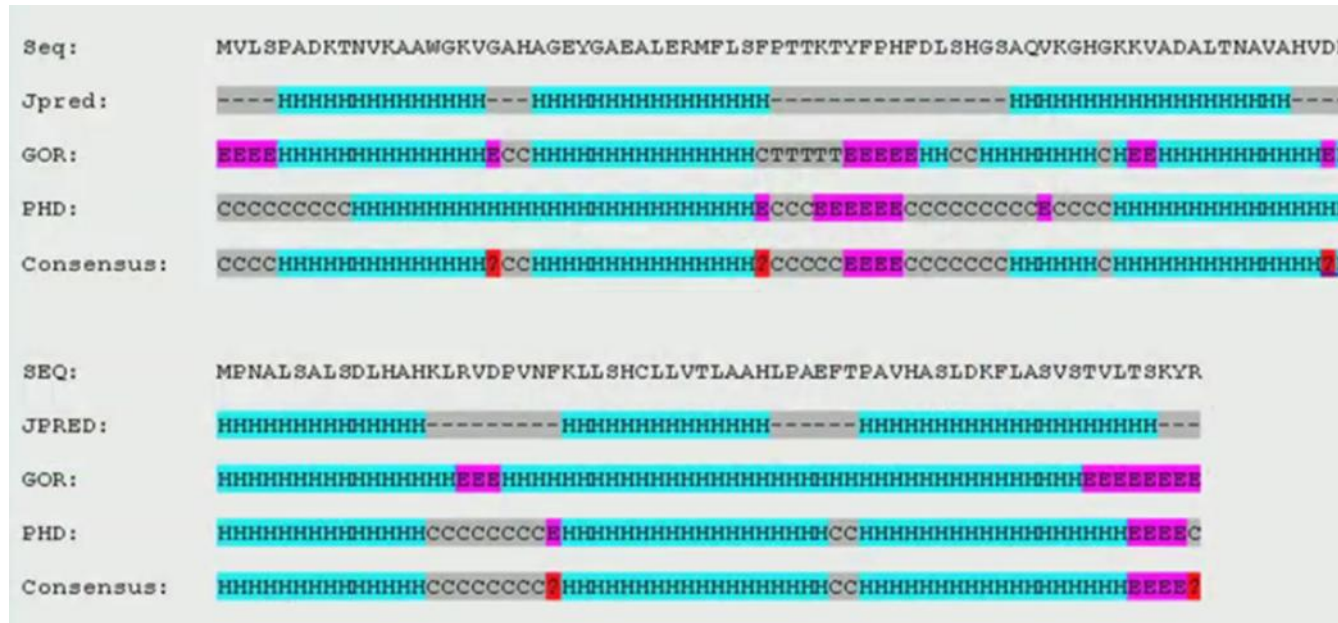
- Input: Prediction results from other methods
- Strategy: Majority of voting
- Output: Based on high vote



Consensus (joint) prediction methods

1. Meta prediction

- Input: Prediction results from other methods
- Strategy: Train on machine learning methods
- Output: Improved outcome



Summary of secondary structure prediction methods

Methods:

1. Statistical analysis
(Preference of residues, by Chou and Fasman in 1974)
2. Information theory (GOR method, by Garnier, Osguthorpe, and Robson in 1978)
3. Hydrophobicity Profile
4. Multiple sequence alignment
5. Machine learning techniques
(Neural networks, support vector machines, etc.)
6. Consensus (Joint)

Knowledge based prediction of protein tertiary structure

Homology Modeling

- Need homologues of known protein structure
- Backbone modelling
- Side chain modelling
- Fails in absence of similarity with other proteins

Threading Based Methods

- New way of fold recognition
- Sequence is tried to fit in known structures
- Motif recognition
- Loop & Side chain modelling
- Fails in absence of known example

Homology modeling of proteins

- Structure of a protein is uniquely determined by its amino acid sequence. Therefore, knowing the sequence should, at least in theory, suffice to obtain the structure.
- During evolution, a structure is more stable and changes at a slower rate as compared to its sequence, so that similar sequences adopt practically identical structures, and distantly related sequences still fold into similar structures.
- If the percentage of similarity or homology is 40%, two sequences are practically guaranteed to adopt a similar structure.

Step 1- Finding the best template

<i>Homo sapiens</i>	GUTMPGTLWCGVGDSAGNSSSELGVFQGPDLCCREHDCPQNISPLOQYNYGI	51
<i>Bos taurus</i>	GUTVPGTLWCGVGDSAGNSSSELGVFQGPDLCCREHDCPHNVSPFQYNYGI	51
<i>Mus musculus</i>	GUTIPGTLWCGVGNSAENASELGVFHGPDLCCEHDCPQTISPLOQYNYGI	51
<i>Heloderma suspectum</i>	AFIMPGLTWCGAGNAASDYSQLGTEKDTDMCCRDHDCENWISALEYKHGM	51
<i>Apis mellifera</i>	-IIYPGTLWCGHGNKSSGPNELGRFKHTDACERTHDCPDVMSAGESKHGL	50

<i>Homo sapiens</i>	RNYRFHTISHCDTRFQQCLQNQHDSIS-DIVGVAFFNVLEIPCFVLEE	100
<i>Bos taurus</i>	RNYRFHTISHCNDARFQQCLQDQRDSVS-DIMGVAFFNVLAIPCFVLEE	100
<i>Mus musculus</i>	RNFRFHTISHCDVRFQQCLRSQGDSIS-DIMGVAFFNVLEIPCFVLKE	100
<i>Heloderma suspectum</i>	RNYYPSTISHCDNQRSCLMKLKDGTADYVGQTYFNVLKIPCFELEE	100
<i>Apis mellifera</i>	TNTASHTRLSCDDDKFYDCLKNSADTISSYFVGKMYFNLDTKCYKLEH	100

			Identity	Acc. No.
<i>Homo sapiens</i>	QEACVAWYWUGGCRMYGTVPPLARLQPRTFYNASWSSRATSPT-	142	--	Q9NZ20
<i>Bos taurus</i>	QEACVEWYWUGGCRRYGSVPFARLQPRTFYNASWSSPATSLT-	142	88%	Q1JPB9
<i>Mus musculus</i>	QEACVAUNWUGGCRAYGSTPLAHLRPRIYNASWKAETSPT-	142	81%	Q6AXHO
<i>Heloderma suspectum</i>	GEGCVDWNFULECTESKIMPVAKLVSAAPYQAQAEQSGEGR.	141	50%	P16354
<i>Apis mellifera</i>	PVTGCGERTEGRCLHYTVDKSKPKVYQWFDLRKY.....	135	44%	P00630

Step 1- Finding the best template

BLAST® » blastp suite » results for RID-5V06HD4V013

Job Title O15393:RecName: Full=Transmembrane protease...

Filter Results

RID
Pro
Dat
Que
Des
Mol
Que
Oth

Descriptions

Graphic Summary

Alignments

Taxonomy

Sequences producing significant alignments

Download

New

Select columns

Show

100

?

☒ select all 100 sequences selected

GenPept

Graphics

Distance tree of results

Multiple alignment

New

MSA Viewer

	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
50% 50% D1 D2	<input checked="" type="checkbox"/> human lysosomal protease domain in complex with active site directed inhibitor [Homo sapiens]	Homo sapiens	213	213	47%	7e-66	42.92%	242	6T7P_A
	<input checked="" type="checkbox"/> Crystal structure of extracellular domain of MSPL in complex with furin inhibitor [Homo sapiens]	Homo sapiens	214	214	47%	8e-66	45.38%	261	6KD5_B
	<input checked="" type="checkbox"/> Structure of human plasma kallikrein [Homo sapiens]	Homo sapiens	211	211	48%	1e-64	42.56%	263	5TJX_A
	<input checked="" type="checkbox"/> The crystal structure of human Plasma Kallikrein in complex with its peptide inhibitor pkalin-2 [Homo sapiens]	Homo sapiens	209	209	47%	2e-64	42.50%	239	5F8T_A
	<input checked="" type="checkbox"/> Expression, crystallization and three-dimensional structure of the catalytic domain of human plasma kallikrein: Implic...	Homo sapiens	209	209	47%	2e-64	42.50%	241	2ANW_A
	<input checked="" type="checkbox"/> Expression, Crystallization and the Three-dimensional Structure of the Catalytic Domain of Human Plasma Kallikrein:...	Homo sapiens	209	209	47%	4e-64	42.50%	241	2ANY_A
	<input checked="" type="checkbox"/> Crystal structure of the extracellular region of the transmembrane serine protease hepsin with covalently bound prefe...	Homo sapiens	211	211	67%	2e-63	34.10%	372	1Z8G_A
	<input checked="" type="checkbox"/> Human hepsin protease in complex with the Fab fragment of an inhibitory antibody [Homo sapiens]	Homo sapiens	211	211	67%	2e-63	34.10%	372	3T2N_A
	<input checked="" type="checkbox"/> Full length human plasma kallikrein with inhibitor [Homo sapiens]	Homo sapiens	217	217	51%	6e-63	41.92%	638	6O1G_A
	<input checked="" type="checkbox"/> The Serine Protease Domain Of Enteropeptidase Bound To Inhibitor Val- Asp-asp-asp-asp-lys-chloromethane [Bos t...	Bos taurus	202	202	46%	1e-61	42.31%	235	1EKB_B
	<input checked="" type="checkbox"/> Dissecting and Designing Inhibitor Selectivity Determinants at the S1 site Using an Artificial Ala190 Protease (Ala190...	Homo sapiens	202	202	47%	1e-61	40.98%	255	1O5E_H
	<input checked="" type="checkbox"/> Crystal Structure of the Catalytic Domain of Coagulation Factor XIa in Complex with Double Bridged Peptide F19 [Ho...	Homo sapiens	202	202	47%	2e-61	42.21%	262	6TWB_A

human plasmakallikrein protease domain in complex with active site directed inhibitor [Homo sapiens]

Sequence ID: [6T7P_A](#) Length: 242 Number of Matches: 1

Range 1: 1 to 237 [GenPept](#) [Graphics](#)

▼ [Next Match](#) ▲ [Previous Match](#)

Score	Expect	Identities	Positives	Gaps
213 bits(543)	7e-66	103/240(43%)	149/240(62%)	8/240(3%)

Query 25 **Crystal structure of the extracellular region of the transmembrane serine protease hepsin with covalently bound preferred substrate. [Homo sapiens]**

Sbjct 1 Sequence ID: [1Z8G_A](#) Length: 372 Number of Matches: 1

Query 31 Range 1: 18 to 360 [GenPept](#) [Graphics](#)

▼ [Next Match](#) ▲ [Previous Match](#)

Related Information

[Structure](#) - 3D structure displays

Query	Score	Expect	Identities	Positives	Gaps
37	211 bits(537)	2e-63	118/346(34%)	174/346(50%)	17/346(4%)
Sbjct	11	Query 158	LQVYSSQRKSWHPVCQDDWNNENYGRAACRDMGYKNNFYSSQGIVDDSGSTSFMKLN-TSA	216	
			L V+ +W +C N +C +MG+ S+ V +G+		
Query	43	Sbjct 18	LMVFDKTEGTWRLLCSSRSNARVAGLSCEEMGFLRALTHSELDVRTAGAAAGTSGFFCVDE	77	
Sbjct	17	Query 217	GNVDIYKKLYHSDA---CSSKAVVSLRCIACGVNLNSSRQSRIVGGESALPGAWPWQVSL	273	
			G + ++L + C ++ C CG RIVGG G WPWQVSL		
		Sbjct 78	GRLPHTQRLLEIVSVCDCPRGRFLAAICQDCG--RRKLPVDRIVGGRTSLGRWPWQVSL	135	
		Query 274	HVQNVHVCGGSIITPEWIVTAAHCVEKPLNNPWHWTAFAGILRQSFMYGAGYQVEKVIS	333	
			H+CGGS+++ +W++TAAHC + W FAG + Q+ +G V+ V+		
		Sbjct 136	RYDGAHLCCGGSLLSGDWVLTAAHCFPERNRVLSRWVFAGAVAQASP-HGLQLGVQAVVY	194	
		Query 334	HPNY-----DSKTKNNDIALMKLQKPLTFNDLVKPVCLPNPGMMLQPEQLCWISGWGAT	387	
			H Y +S+ +NDIAL+ L PL + ++PVCLP G L ++C ++GWG T		
		Sbjct 195	HGGYLPFRDPNSENSENNDIALVHLSSPLPLTEYIQPVCLPAAGQALVDGKICTVTGWGNT	254	
		Query 388	EEKGKTSEVLNAAKVLLIETQRCNSRYVDNLITPAMICAGFLQGNVDSQGDSCGGPLV-	446	
			+ G+ + VL A+V +I CN Y N I P M CAG+ +G +D+CQGDSCGGP V		
		Sbjct 255	QYYGQQAGVLQEARVPIISNDVCGADFYGNQIKPKMFCAGYPEGGIDACQGDSCGGPVC	314	
		Query 447	---TSKNNIWWLIGDTSWGSACAKAYRPGVYGNVMVFTDWIYRQMR	489	
			S+ W L G SWG+GCA A +PGVY V F +WI++ ++		
		Sbjct 315	EDSISRTPRWRLCGIVSWGTCALAQKPGVYTKVSDFREWIFQAIK	360	



Crystal structure of the extracellular region of the transmembrane serine protease hepsin with covalently bound preferred substrate. [Homo sapiens]

Sequence ID: [1Z8G_A](#) Length: 372 Number of Matches: 1

Range 1: 18 to 360 [GenPept](#) [Graphics](#)

[Next Match](#) [Previous Match](#)

Related Information

[Structure](#) - 3D structure displays

Score	Expect	Identities	Positives	Gaps
211 bits(537)	2e-63	118/346(34%)	174/346(50%)	17/346(4%)
Query 158	LQVYSSQQRKSWHPVCQDDWNNENYGRAACRDMGYKNNFYSSQGIIVDDSGSTSFMKLN-TSA	216		
Sbjct 18	L V+ +W +C N +C +MG+ S+ V +G+ LMVFDKTEGTWRLCCSSRSNARVAGLSCEEMGFLRALTHSELDVRTAGAAAGTSGFFCVD E 77			
Query 217	GNVDIYKKLYHSDA---CSSKAVVSLRCIACGVNLSSRQSRIVGGESALPGAWPWQVSL	273		
Sbjct 78	G + ++L + C ++ C CG RIVGG G W P W Q V S L GRLPHTQRLLEVISVCDPCRGRFLAAICQDCG--RRKLPVDRIVGGRDTS LGRWPWQVSL 135			
Query 274	HVQNVHVCGGSIITPEWIVTAAHCVEKPLNNPWHWTAFAGILRQSFMYGAGYQVEKVIS	333		
Sbjct 136	H+CGGS+++ +W++TAAHC + W FAG + Q+ +G V+ V+ RYDGAHLCGGSLLSGDWVLTAAHCFPERNRVLSRWRVFAGAVAQASP-HGLQLGVQAVVY 194			
Query 334	HPNY-----DSKTKNNDIALMKLQKPLTFNDLVKPVCLPNPGMMLQPEQLCWIISGWGAT	387		
Sbjct 195	H Y +S+ +NDIAL+ L PL + ++PVCLP G L ++C ++GWG T HGGYLPFRDPNPEENSNDIALVHLSPLPLTEYIQPVCLPAAGQALVDGKICTVTGWGNT 254			
Query 388	EEKGKTSEVLNAAKVLLIETQRCNSRYVDNLITPAMICAGFLQGNVDSQGDGSGGPLYV-	446		
Sbjct 255	+ G+ + VL A+V +I CN Y N I P M CAG+ +G +D+CQGDGSGGP V QYYGQQAQVLQEARVPIISNDVNCNADFYGNQIKPKMFCAGYPEGGIDACQGDGSGGPFVC 314			
Query 447	---TSKNNIWNLIGDTSWGS GCAYRPGVYGNVMVFTDWIYRQMR	489		
Sbjct 315	S+ W L G SWG+GCA A +PGVY V F +WI++ ++ EDSISRTPRWRLCGIVSWGTGCALAQKPGVYTKVSDFREWI FQA I K 360			

Human hepsin protease in complex with the Fab fragment of an inhibitory antibody [Homo sapiens]

Sequence ID: [3T2N_A](#) Length: 372 Number of Matches: 1

[See 2 more title\(s\)](#) [See all Identical Proteins \(IPG\)](#)

Range 1: 18 to 360 [GenPept](#) [Graphics](#)

[Next Match](#) [Previous Match](#)

Related Information

[Structure](#) - 3D structure displays

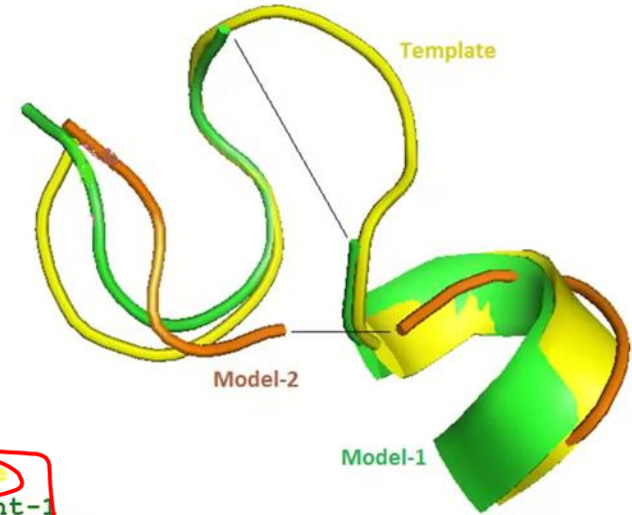
[Identical Proteins](#) - Identical proteins to 3T2N_A

Score	Expect	Identities	Positives	Gaps
211 bits(537)	2e-63	118/346(34%)	174/346(50%)	17/346(4%)
Query 158	LQVYSSQQRKSWHPVCQDDWNNENYGRAACRDMGYKNNFYSSQGIIVDDSGSTSFMKLN-TSA	216		
Sbjct 18	L V+ +W +C N +C +MG+ S+ V +G+ LMVFDKTEGTWRLCCSSRSNARVAGLSCEEMGFLRALTHSELDVRTAGANGTSGFFCVD E 77			
Query 217	GNVDIYKKLYHSDA---CSSKAVVSLRCIACGVNLSSRQSRIVGGESALPGAWPWQVSL	273		
Sbjct 78	G + ++L + C ++ C CG RIVGG G W P W Q V S L GRLPHTQRLLEVISVCDPCRGRFLAAICQDCG--RRKLPVDRIVGGRDTS LGRWPWQVSL 135			
Query 274	HVQNVHVCGGSIITPEWIVTAAHCVEKPLNNPWHWTAFAGILRQSFMYGAGYQVEKVIS	333		
Sbjct 136	H+CGGS+++ +W++TAAHC + W FAG + Q+ +G V+ V+ RYDGAHLCGGSLLSGDWVLTAAHCFPERNRVLSRWRVFAGAVAQASP-HGLQLGVQAVVY 194			
Query 334	HPNY-----DSKTKNNDIALMKLQKPLTFNDLVKPVCLPNPGMMLQPEQLCWIISGWGAT	387		
Sbjct 195	H Y +S+ +NDIAL+ L PL + ++PVCLP G L ++C ++GWG T HGGYLPFRDPNPEENSNDIALVHLSPLPLTEYIQPVCLPAAGQALVDGKICTVTGWGNT 254			
Query 388	EEKGKTSEVLNAAKVLLIETQRCNSRYVDNLITPAMICAGFLQGNVDSQGDGSGGPLYV-	446		
Sbjct 255	+ G+ + VL A+V +I CN Y N I P M CAG+ +G +D+CQGDGSGGP V QYYGQQAQVLQEARVPIISNDVNCNADFYGNQIKPKMFCAGYPEGGIDACQGDGSGGPFVC 314			
Query 447	---TSKNNIWNLIGDTSWGS GCAYRPGVYGNVMVFTDWIYRQMR	489		
Sbjct 315	S+ W L G SWG+GCA A +PGVY V F +WI++ ++ EDSISRTPRWRLCGIVSWGTGCALAQKPGVYTKVSDFREWI FQA I K 360			

Step2- Correct sequence alignment

- Sometimes it may be difficult to align two sequences in a region where the percentage sequence identity is very low.
- A simple sequence alignment gives the higher score based on matching/pairing of residues on the two sequences

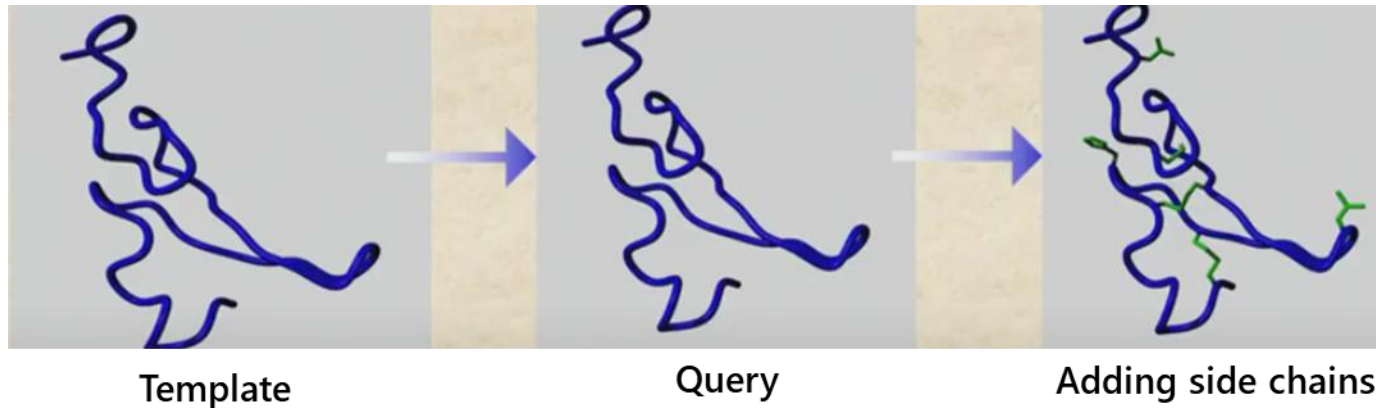
1	2	3	4	5	6	7	8	9	10	11	12	13	14	
ALA	SER	ILE	CYS	ARG	LEU	PRO	GLY	SER	ALA	GLU	GLY	VAL	CYS	Template
ALA	ASN	VAL	CYS	ARG	THR	PRO	---	---	---	GLU	GLY	ILE	CYS	Alignment-1
ALA	ASN	VAL	CYS	ARG	---	---	---	THR	PRO	GLU	GLY	ILE	CYS	Alignment-2



- Model-2 for alignment-2 is correct, because it leads to a small gap and can be corrected by small backbone shifts.

Step3- Generating the backbone

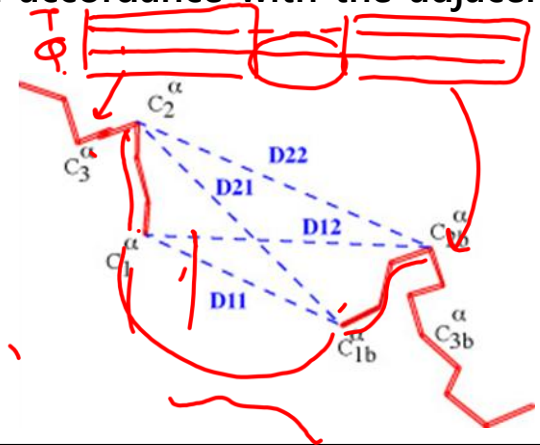
- Generate backbone coordinates from the template for the aligned regions.
- If most of aligned residues are identical, back bone too will be identical
- Template that generates a back bone with least errors is chosen.
- Back bone of secondary structural elements like helices and beta sheets are usually maintained, while variations may be seen in the loops and turns,



Step4- Loop modeling

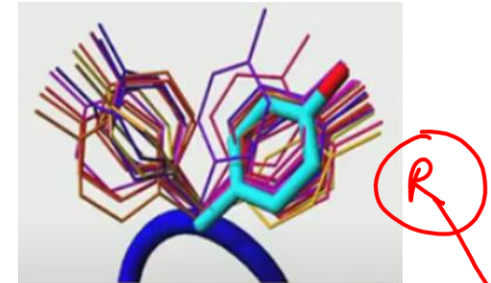
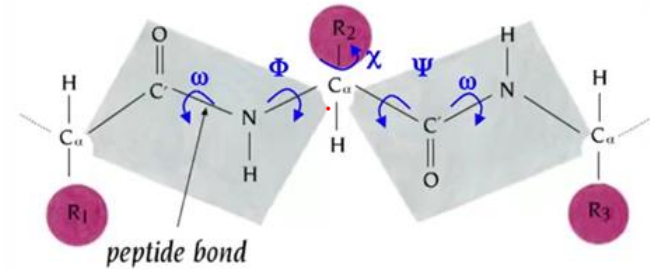
- Region of query sequence that is not aligned to template is modeled as a loop.
- Loop modeling is done by knowledge-based method where PDB is searched for known loops, or by Energy based method where long chains are built by sampling Ramachandran conformations randomly.
- For deletions, residues from the template is omitted, creating a void in the model that is filled by bringing together the adjacent residues' coordinates.
- For insertions, the coordinates for the missing residues is given a loop conformation in most cases and simulated for it to take up a secondary structure in accordance with the adjacent structures in the template.

Selecting protein fragments for loop modelling: In the example shown here, the gap in the framework is characterized by 4 distances (D11, D12, D21 and D22) between the 2 C α preceding the gap and the 2 C α following the gaps. The library of protein structure fragments of appropriate size (i.e. Ngap + 4, where Ngap is the number of residues in the gap and 4 corresponds to the 2 anchoring residues on each side of the gap) is scanned and the fragments with the proper geometry (i.e. such that the distances between the 2 first and last residues match the 4 characteristic distances of the gap) are retained has potential loops to fill in the gap.



Step5- Side chain modeling

- Involves placing side chains coordinates either obtained from a template structure or generated from *ab initio* modeling simulations or both.
- Side chain remains more flexible on the surface and tend to adopt multiple conformations as compared to the core where residues have restricted environment and limited conformational liberty.
- At high levels of sequence identity χ 1-angles adopt positions from template structure and for sequence identity <35% combinatorial approach using rotamer libraries are used.
- Wrong backbone will affect the side chain building process.
- Prediction accuracy is highly dependent on scoring functions.



TYR

Step6- Model optimization and structure refinement

- Model optimization tries to bring it closer to real in-vivo conformation.
- Commonly achieved by Molecular Dynamics Simulation.
- Simulation follows the motions of the protein on a femto-second timescale and mimics true folding process.
- This helps to get a true structural model having minimum energy configuration

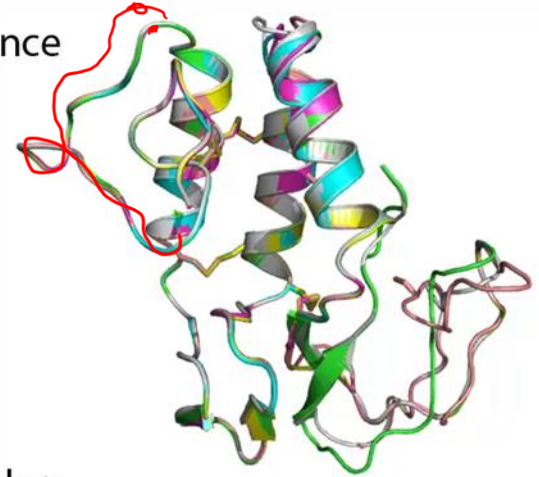
Step6- Validation of the developed model

Root mean square deviation (RMSD)

- Root mean square deviation is the measure of the average distance between the atoms of two superimposed proteins.

$$RMSD = \sqrt{\frac{1}{N} \sum_{i=1}^{i=N} \delta_i^2}$$

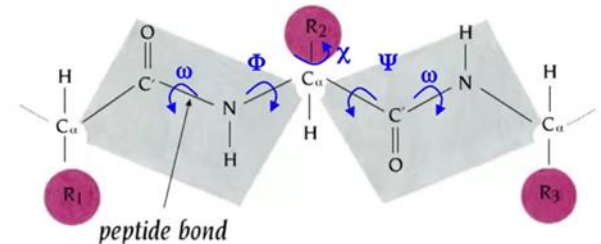
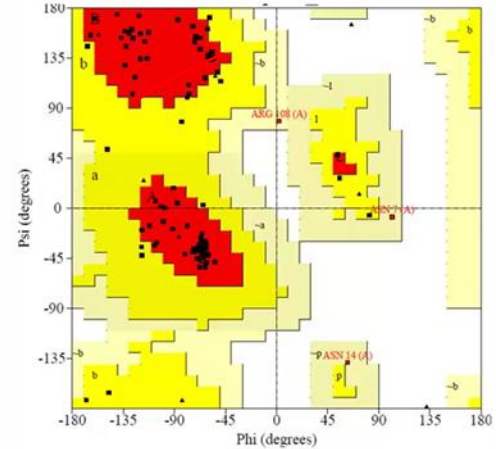
- δ is the distance between number of pairs of equivalent atoms
- 0.0-0.5Å : Essentially Identical; <1.5 Å: Very good fit; < 5.0 Å: Moderately > 7.0 Å: Dubious; > 12.0 Å: Completely unrelated



Step6- Validation of the developed model

Ramachandran Plot

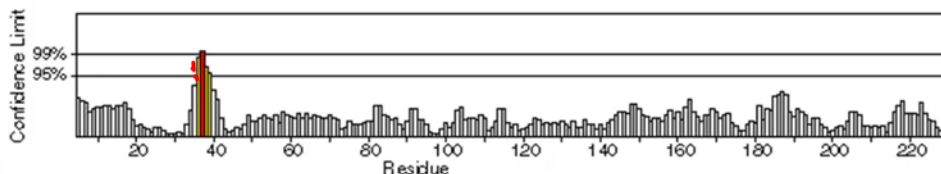
- Atoms are treated as hard spheres with dimensions corresponding to their van der Waals radii
- Residues with phi and psi angles which cause atoms to collide are considered to be in sterically disallowed conformations
- Most allowed region occupied by residues with no steric clashes
- Dis-allowed region with residues whose atoms come closer than their van der Waals radii.
- Additionally allowed region with residues have atoms with inter-atomic distance slightly shorter than van der Waals radii.



Step6- Validation of the developed model

ERRAT Plot

- Of three heavy atoms carbon, nitrogen, and oxygen, there exist six different combinations of pairwise non-covalently bonded interactions (CC, CN, CO, NN, NO, and OO).
- In a database of 96 reliable protein structures, these set of pairwise interactions are characterized; ERRAT finds regions of model structures that have incorrect pattern of non-bonded interactions that result in incorrectly folded regions

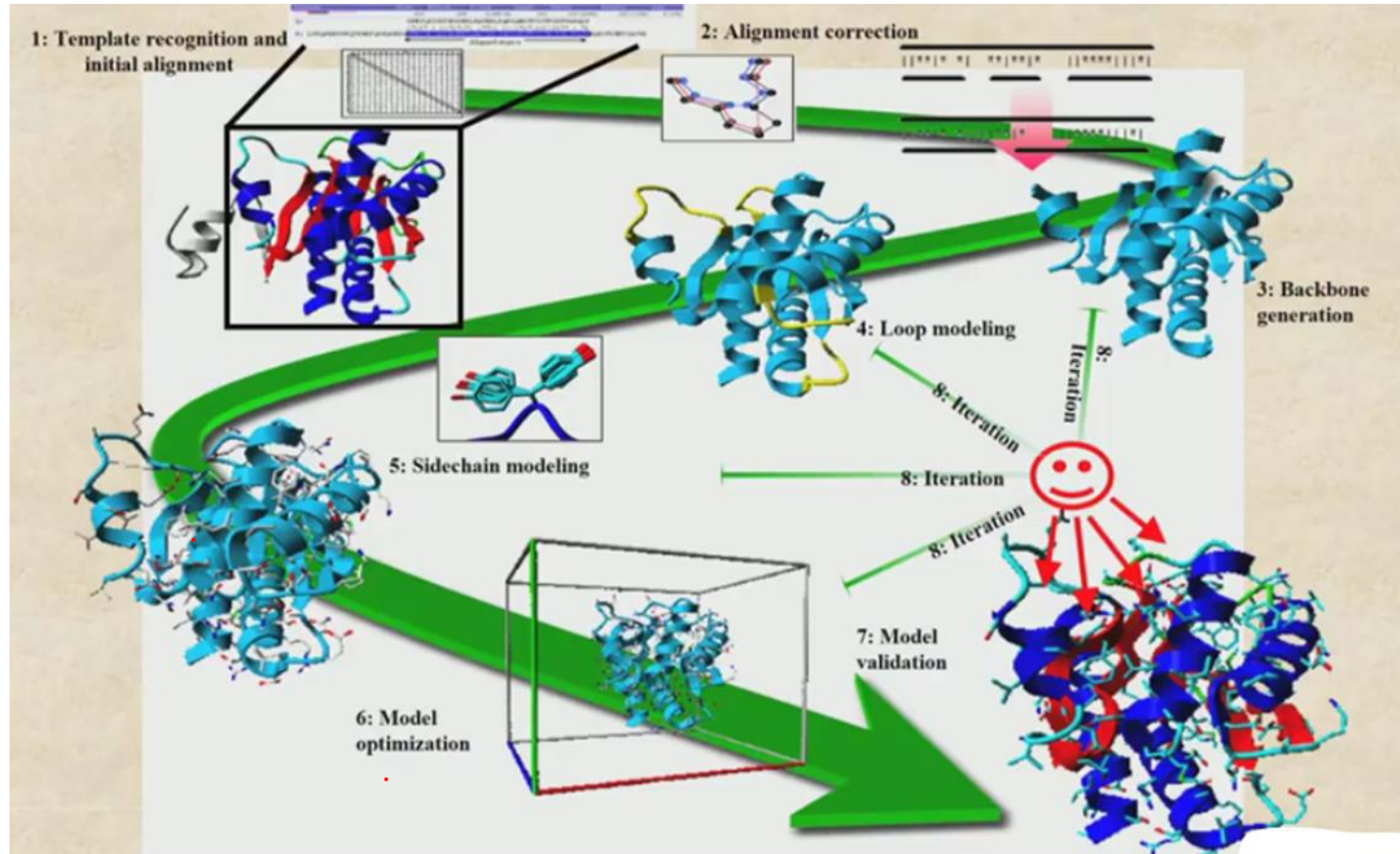


Regions of the structure that can be rejected at the 95% confidence level are shown in yellow and regions that can be rejected at the 99% level are shown in red.

Step6- Validation of the developed model

- WHAT IF <http://www.cmbi.kun.nl/gv/servers/WIWWWI/>
- SOV <http://predictioncenter.llnl.gov/local/sov/sov.html>
- PROVE <http://www.ucmb.ulb.ac.be/UCMB/PROVE/>
- ANOLEA <http://www.fundp.ac.be/pub/ANOLEA.html>
- ERRAT <http://www.doe-mpi.ucla.edu/Services/ERRATv2/>
- VERIFY3D http://shannon.mpi.ucla.edu/DOE/Services/Verify_3D/
- BIOTECH <http://biotech.embl-ebi.ac.uk:8400/>
- ProsaII <http://www.came.sbg.ac.at>
- WHATCHECK <http://www.sander.embl-heidelberg.de/whatcheck/>

Revisiting the protocol for homology modeling



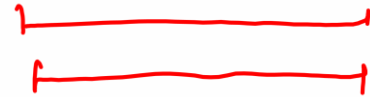
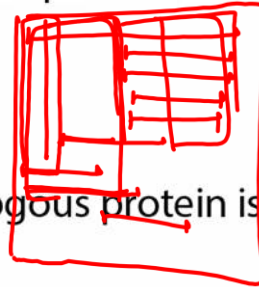
Advantages and disadvantages of homology modeling

Advantages

- Requires amino acid sequence and a 3D structure of a similar protein
- Does not involve any bench work or consumables
- Less time consuming and less costly
- Most of the softwares are freely available online
- Most promising method among the three computational methods

Disadvantages

- Loop regions are difficult to model
- Experimentally derived structure for homologous protein is essential
- Does not explain aspects of protein folding.



Programs available for homology modeling of proteins

- SWISS Model : <http://www.expasy.org/swissmod/SWISS-MODEL.html>
- WHAT IF : <http://www.cmbi.kun.nl/swift/servers/>
- The CPHModels Server : <http://www.cbs.dtu.dk/services/CPHmodels/>
- 3D Jigsaw : <http://www.bmm.icnet.uk/~3djigsaw/>
- SDSC1 : <http://cl.sdsc.edu/hm.html>
- EsyPred3D : <http://www.fundp.ac.be/urbm/bioinfo/esypred/>

- COMPOSER
<http://www.tripos.com/sciTech/inSilicoDisc/bioInformatics/matchmaker.html>
- MODELER <http://salilab.org/modeler>
- InsightII <http://www.msi.com/>
- SYBYL <http://www.tripos.com/>