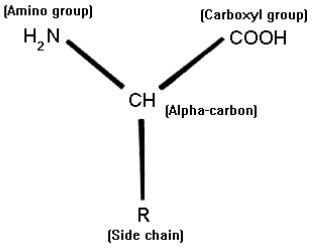
UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
Bioinformatics Tutorials

Protein Modeling

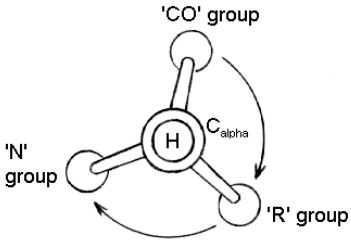
Iosif Vaisman

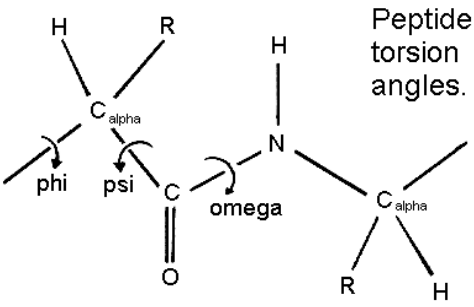
2000

Amino Acid Residue

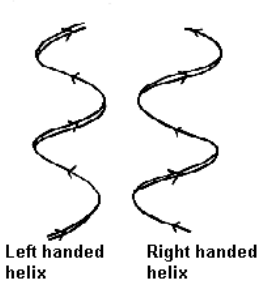


Amino Acid Residue

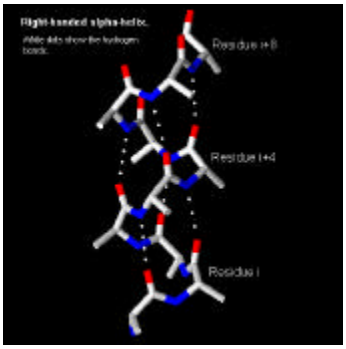




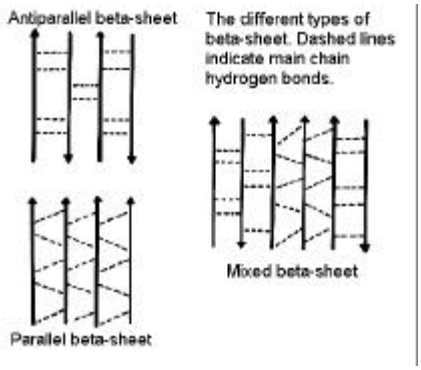
Secondary Structure (Helices)

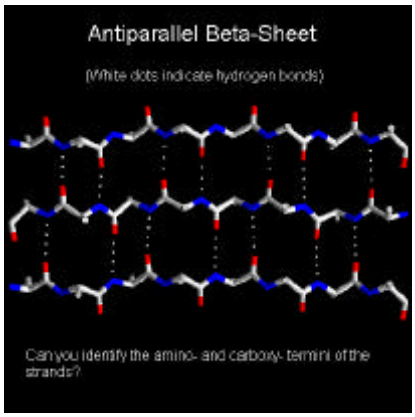


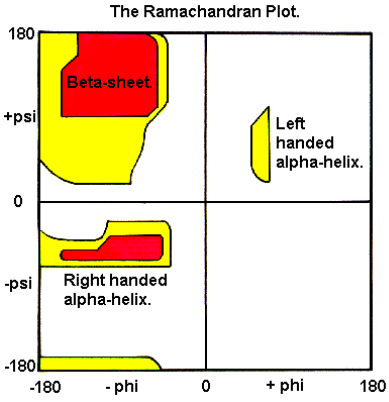
Helix

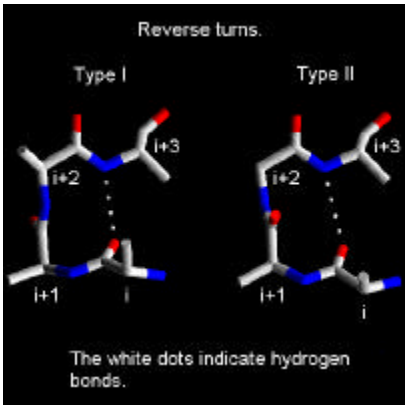


Secondary Structure (Beta-sheets)

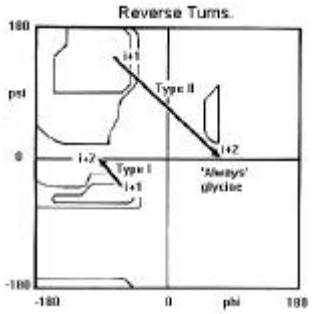


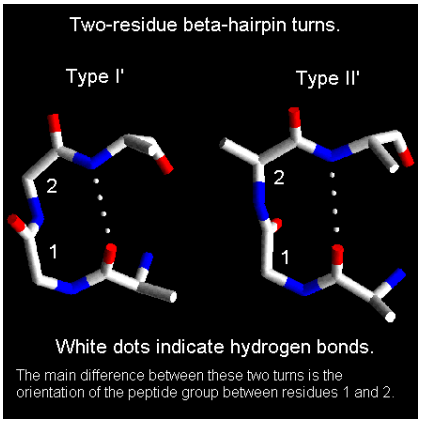




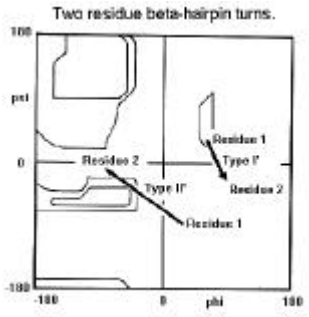


Reverse Turns on a Ramachandran Plot

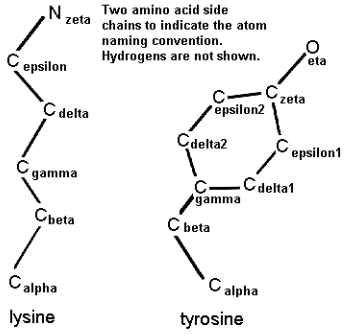




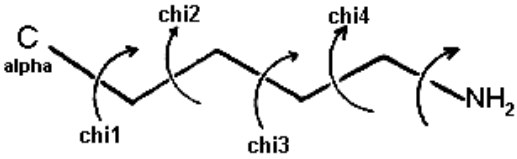
Beta-hairpin Turns on a Ramachandran Plot



Side-Chain Atom Nomenclature



Side-Chain Torsional Angles



Secondary Structure Prediction

Three-state model: helix, strand, coil

Given a protein sequence:

- `NWVLSTAADMQGVVTDGMASGLDKD...`

Predict a secondary structure sequence:

- `LLEEEELLLLHHHHHHHHHHLHHHL...`

Methods:

- statistical
- stereochemical

Accuracy: 50-85%

Statistical Methods

Residue conformational preferences:

Glu, Ala, Leu, Met, Gln, Lys, Arg - helix
Val, Ile, Tyr, Cys, Trp, Phe, Thr - strand
Gly, Asn, Pro, Ser, Asp - turn

Chou-Fasman algorithm:

Identification of helix and sheet "nuclei"
Propagation until termination criteria met

Chou-Fasman Parameters

Name	P(a)	P(b)	P(turn)	f(i)	f(i+1)	f(i+2)	f(i+3)
Alanine	142	83	66	0.06	0.076	0.035	0.058
Arginine	98	93	95	0.070	0.106	0.099	0.085
Aspartic Acid	101	54	146	0.147	0.110	0.179	0.081
Asparagine	67	89	156	0.161	0.083	0.191	0.091
Cysteine	70	119	119	0.149	0.050	0.117	0.128
Glutamic Acid	151	37	74	0.056	0.060	0.077	0.064
Glutamine	111	110	98	0.074	0.098	0.037	0.098
Glycine	57	75	156	0.102	0.085	0.190	0.152
Histidine	100	87	95	0.140	0.047	0.093	0.054
Isoleucine	108	160	47	0.043	0.034	0.013	0.056
Leucine	121	130	59	0.061	0.025	0.036	0.070
Lysine	114	74	101	0.055	0.115	0.072	0.095
Methionine	145	105	60	0.068	0.082	0.014	0.055
Phenylalanine	113	138	60	0.059	0.041	0.065	0.065
Proline	57	55	152	0.102	0.301	0.034	0.068
Serine	77	75	143	0.120	0.139	0.125	0.106
Threonine	83	119	96	0.086	0.108	0.065	0.079
Tryptophan	108	137	96	0.077	0.013	0.064	0.167
Tyrosine	69	147	114	0.082	0.065	0.114	0.125
Valine	106	170	50	0.062	0.048	0.028	0.053

Chou-Fasman Algorithm

Identification of helix and sheet "nuclei"

- helix - 4 out of 6 residues with high helix propensity (P > 100)
- sheet - 3 out of 5 residues with high sheet propensity (P > 100)

Propagation until termination criteria met

Turn prediction

1) `p(t) > 0.000075`
2) `P(turn) > 1.00`
3) `P(a) < P(turn) > P(b)`

where `p(t) = f(j)f(j+1)f(j+2)f(j+3)`

Garnier - Osguthorpe - Robson (GOR) Algorithm

Likelihood of a secondary structure state depends on the neighboring residues:

$$L(S_j) = \Sigma\ (S_j;R_{j+m})$$

Window size - [j-8; j+8] residues

Accuracy for a single sequence - 60%
Accuracy for an alignment - 65%

Evolutionary Methods

Taking into account related sequences helps in identification of “structurally important” residues.

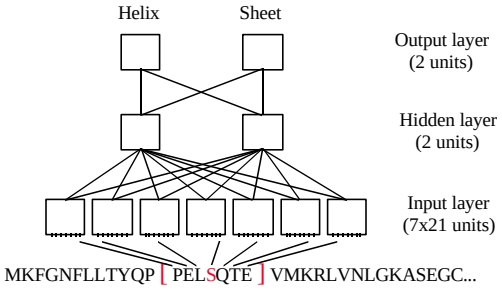
Algorithm:

- find similar sequences
- construct multiple alignment
- use alignment profile for secondary structure prediction

Additional information used for prediction

- mutation statistics
- residue position in sequence
- sequence length

Neural Networks Methods



Stereochemical Methods

Patterns of hydrophobic and hydrophilic residues in secondary structure elements:

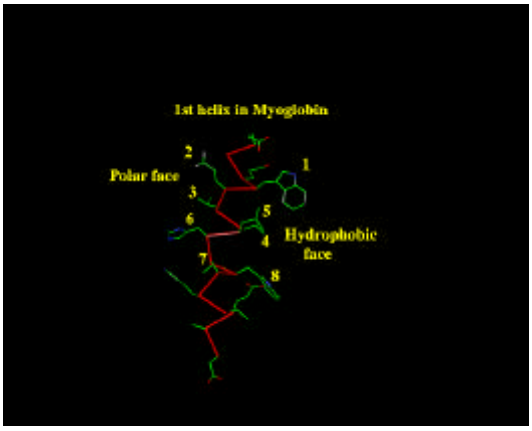
- segregation of hydrophobic and hydrophilic residues
- hydrophobic residues in the positions 1-2-5 and 1-4-5
- oppositely charged polar residues in the positions 1-5 and 1-4 (e.g. Glu (i), Lys (i+4))

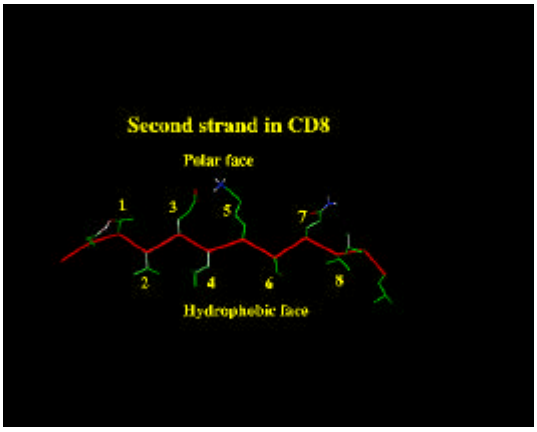
Definitions of hydrophobic and hydrophilic residues (hydrophobicity scales) are ambiguous

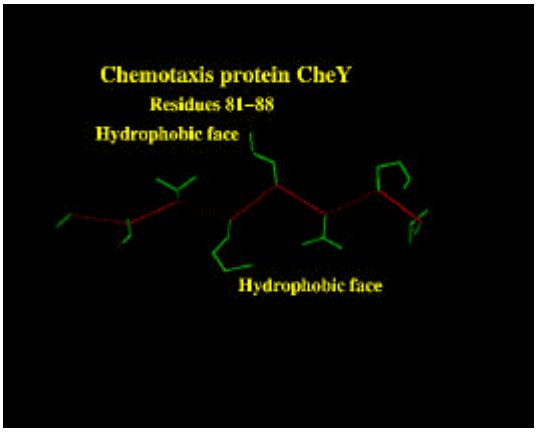
Stereochemical Methods

Hydropathic correlations in helices and sheets

		F-F	F-L	L-F	L-L
a	*i, i+2*	-	+	+	-
	i, i+3	+	-	-	+
	i, i+4	+	-	-	+
	i, i+5	-	+	+	-
b	*i, i+1*	-	+	+	-
	i, i+2	+	-	-	+
	i, i+3	-	+	+	-


1st helix in Myoglobin
Polar face
Hydrophobic face
1
2
3
4
5
6
7
8


Second strand in CD8
Polar face
Hydrophobic face
1
2
3
4
5
6
7
8


Chemotaxis protein CheY
Residues 81–88
Hydrophobic face
Hydrophobic face