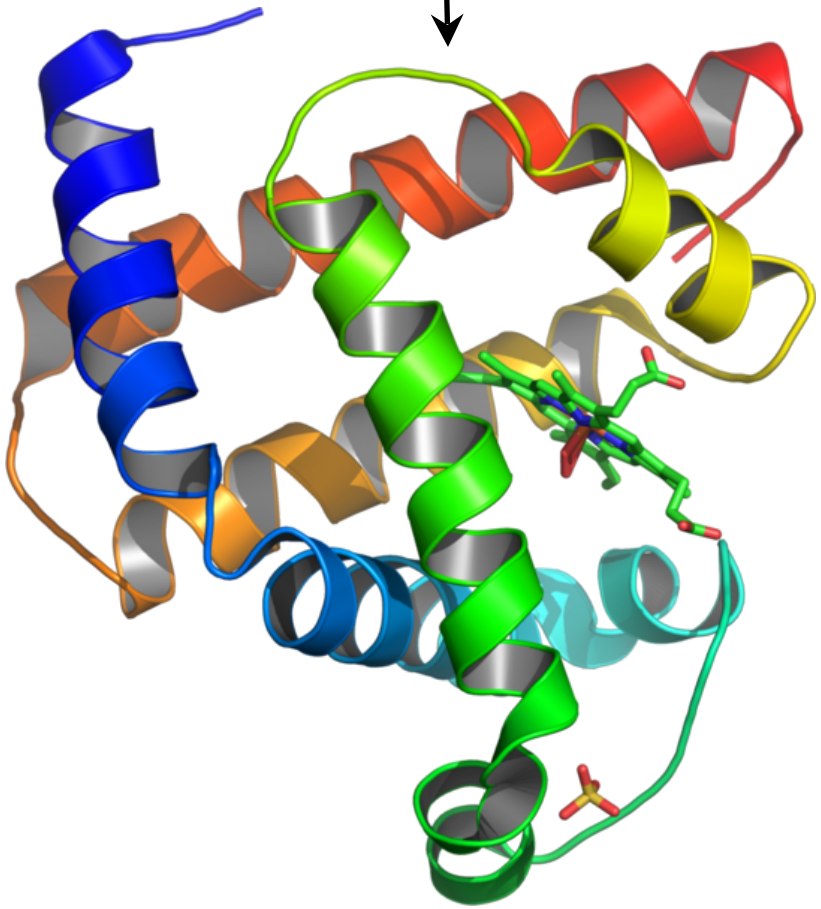
Application of Logistic Regression

Protein Contact Map Prediction

Protein Structure Prediction (1D →3D)

EAEASICSEPKKVGRCKGYFPRFYFDSETGKCTPFIYGGCGGNGNNFETLHQCRAICRALG

Primary Sequence



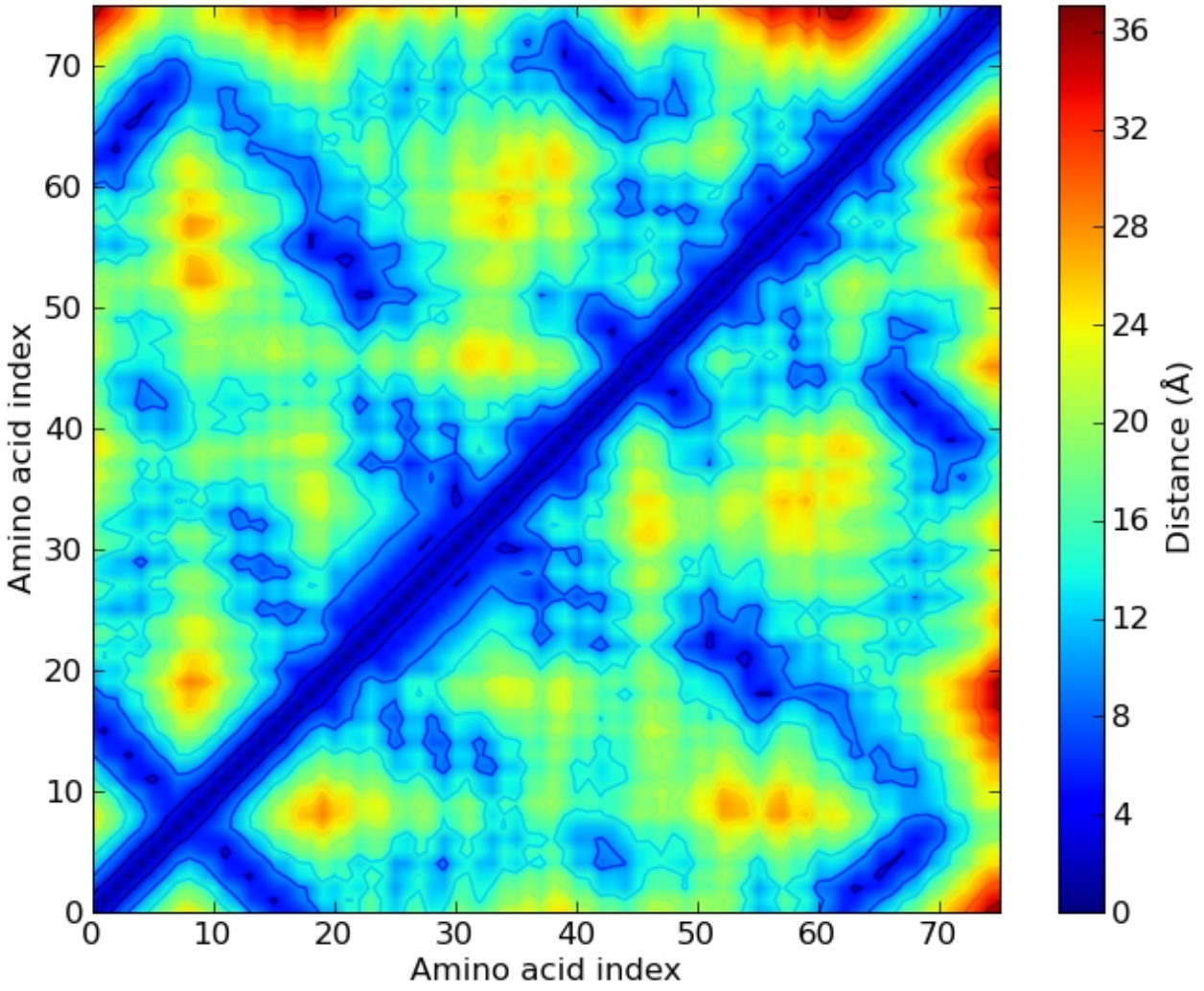
Tertiary Structure

Secondary Structure

Solvent Accessibility

Can we directly predict
the tertiary structure of a protein?

Protein 3D Structure = Distance Matrix (D_{ij})



Can we apply learning
to predict the distance matrix?

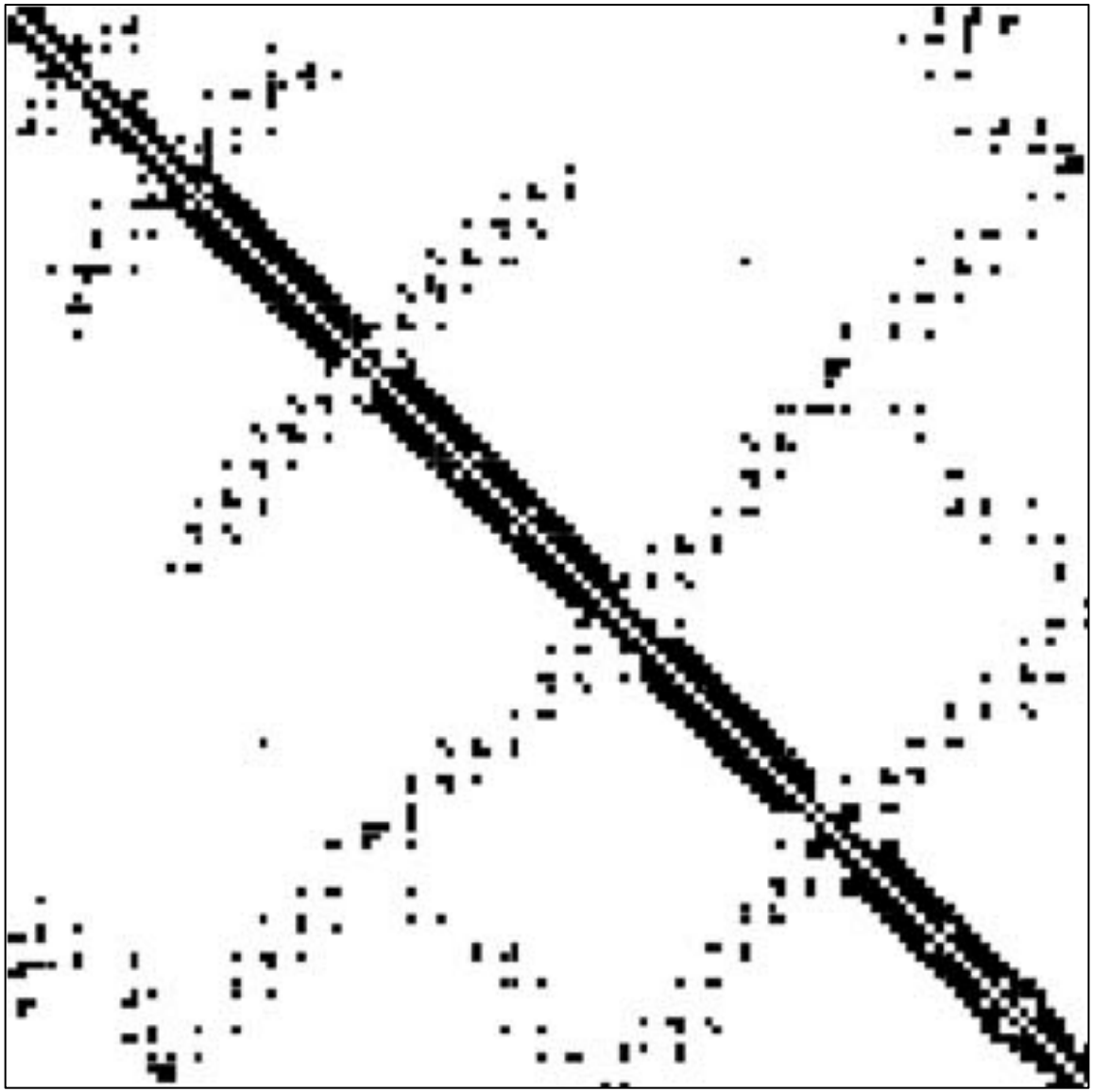
But distance is real-valued…

Use a cutoff to make it binary…

Protein “Contact”

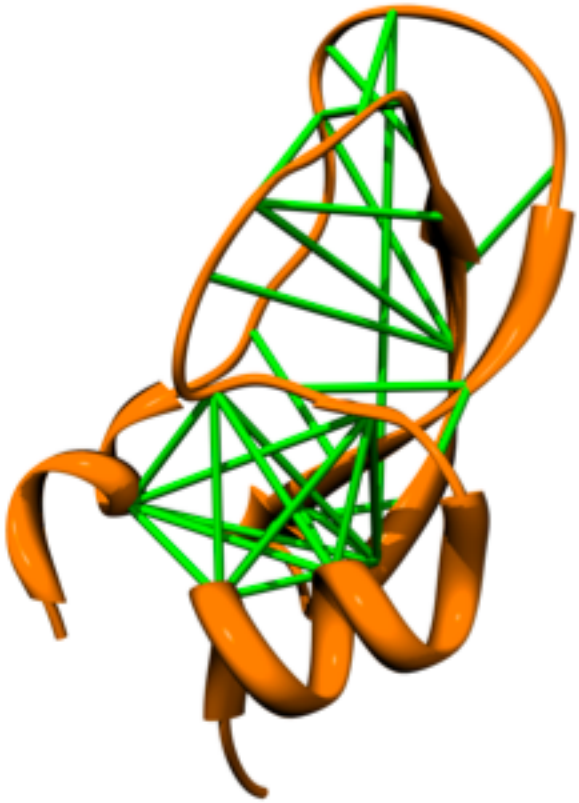
$$C_{ij} = \begin{cases} 1 & \text{if } D_{ij} < Dcutoff \\ 0 & \text{otherwise} \end{cases}$$

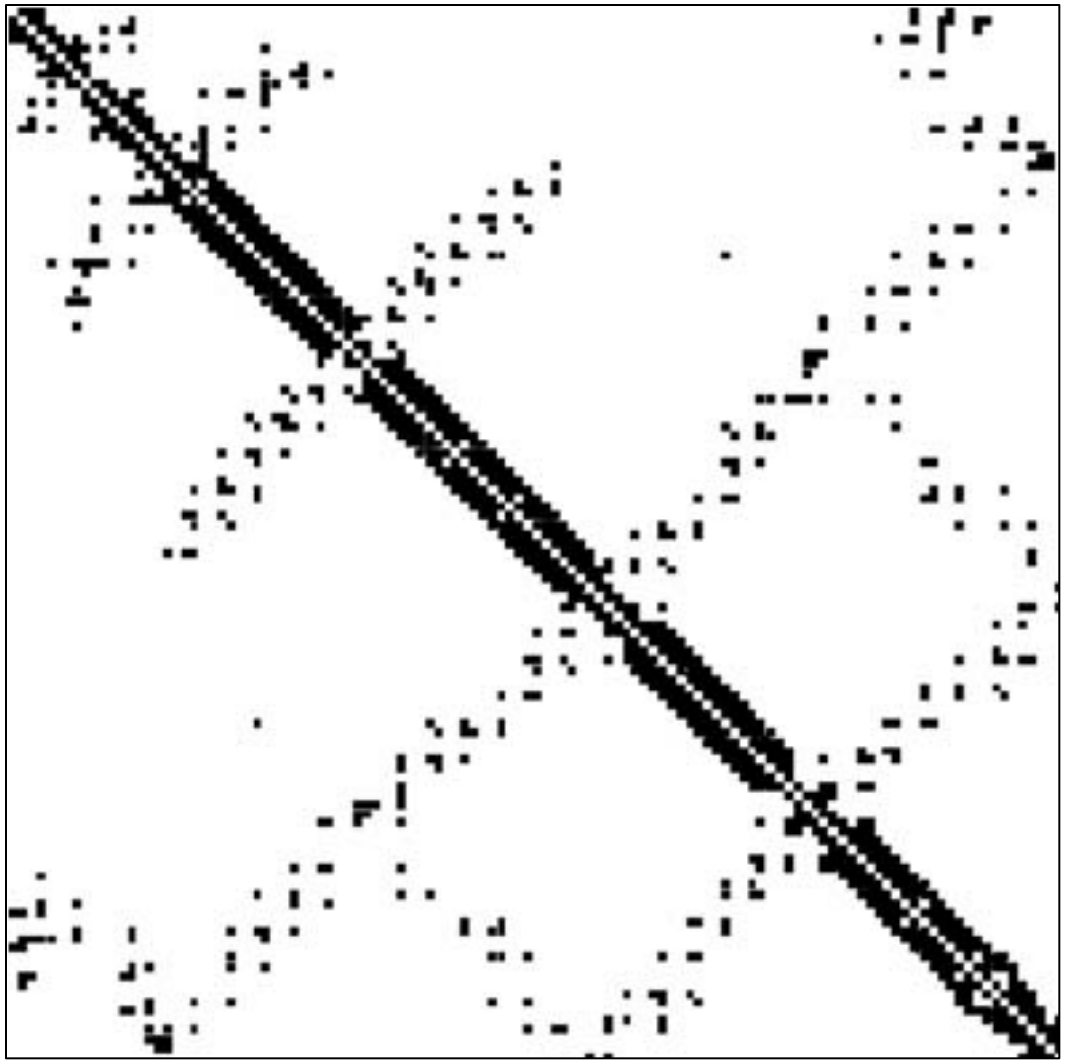
Protein “Contact” Matrix



PyMOL demo
1AIL

Tertiary Structure → Contact Maps





Protein Contact Prediction

using Logistic Regression…

Protein Contact Map Prediction

- We have two classes: Contact (**1**), noncontact (**0**)
  - Discrete labels (Y)

- What about features (X)?
  - We can use the sequence profile using PSSM

Position Specific Scoring Matrix (PSSM)

Run psiblast against non redundant (nr) sequence database

blastpgp -d <nr_db> -j 3 -b 1 -a 80 –i <protein.seq> -Q <protein.pssm>

Last position-specific scoring matrix computed, weighted observed percentages rounded down, information per position, and relative weight of gapless real matches to pseudocounts

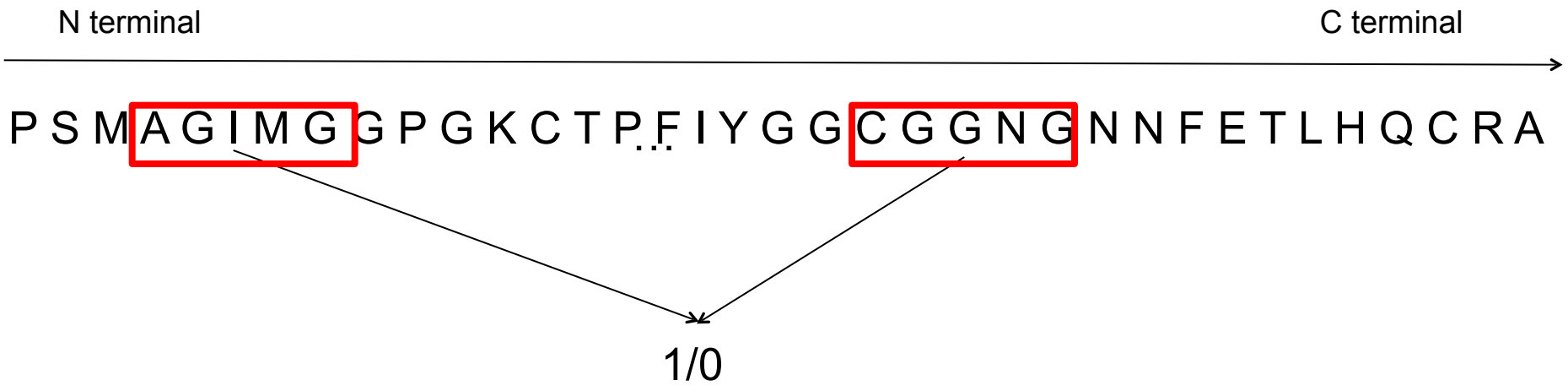
		A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V		
1	S	2	-2	2	-3	-3	-2	-2	-3	-3	-4	-4	2	-3	-5	-3	4	4	-5	-4	-3	16	0	12	0	0	0	0	0	0	0	0	13	0	0	0	33	26	0	0	0	0.70	0.31
2	K	-1	4	3	-3	-6	2	-1	-4	-1	-6	-6	6	-4	-4	-3	-2	-2	-6	-5	-5	5	18	13	0	0	8	3	1	1	0	0	47	0	1	1	1	1	0	0	0	1.04	0.44
3	R	2	4	-2	-4	-2	-1	-3	4	1	-5	-4	0	-4	-5	-4	2	0	-5	-5	-4	16	22	1	0	1	2	0	27	3	0	1	5	0	0	0	15	6	0	0	0	0.62	0.34
4	Y	-5	-6	-7	-7	1	-6	-7	-7	-4	1	2	-6	-1	6	-7	-6	-5	5	5	-1	0	0	0	0	2	0	0	0	0	8	21	0	1	36	0	0	0	7	22	3	1.40	0.52
5	F	-7	-8	-8	-9	-8	-8	-8	-8	-6	-4	-3	-8	-5	10	-9	-8	-7	-1	0	-6	0	0	0	0	0	0	0	0	0	1	1	0	0	96	0	0	0	1	1	0	3.33	0.99
6	V	-5	-7	-7	-8	-5	-7	-7	-8	-8	6	-2	-7	-3	-5	-7	-6	-5	-7	-6	6	0	0	0	0	0	0	0	0	0	41	2	0	0	0	0	0	0	0	0	56	1.95	0.69
7	T	1	-6	-5	-6	-6	-6	-6	-7	-3	-5	-6	-5	-7	-6	-3	8	-7	-7	-3		10	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	87	0	0	1	2.35	0.90
8	G	-2	-7	-5	-6	-7	-7	-7	8	-7	-9	-9	-6	-8	-8	-7	-5	-6	-8	-8	-8	3	0	0	0	0	0	0	97	0	0	0	0	0	0	0	0	0	0	0	0	2.75	0.90
9	T	-5	-6	-5	-6	-6	-6	-6	-7	-7	-4	-6	-6	-6	-7	-6	-3	8	-8	-7	-5	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	98	0	0	0	2.89	1.03
10	D	-7	-7	-3	9	-9	-5	-3	-3	-6	-8	-9	-6	-8	-9	-7	-5	-6	-10	-8	-8	0	0	0	97	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	3.05	0.99
11	T	-4	-6	-5	-6	-6	-6	-6	-7	-7	-6	-6	-6	-6	-7	-6	-2	8	-8	-7	-5	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	98	0	0	0	2.85	1.02
12	E	-1	-2	2	5	-7	-3	4	3	-3	-7	-7	-4	-6	-7	-5	-2	-4	-7	-6	-6	6	2	11	29	0	0	28	23	0	0	0	0	0	0	0	0	2	0	0	0	1.08	0.49
13	V	0	-7	-7	-7	1	-6	-6	-7	-7	4	-3	-6	-2	-5	-6	-2	-4	-7	-5	7	8	0	0	0	3	0	0	0	0	17	0	0	0	0	0	3	0	0	0	68	1.62	0.63
14	G	-5	-8	-6	-7	-8	-7	-7	8	-7	-9	-9	-7	-8	-8	-7	-5	-7	-8	-8	-9	0	0	0	0	0	0	0	100	0	0	0	0	0	0	0	0	0	0	0	0	2.96	0.99
15	K	-6	-3	-5	-6	-9	-4	-4	-7	-6	-8	-8	8	-7	-9	-6	-6	-6	-9	-7	-8	0	0	0	0	0	0	0	0	0	0	100	0	0	0	0	0	0	0	0	0	3.03	1.07
16	T	-5	-7	-5	-6	-6	-6	-6	-7	-7	-6	-7	-6	-6	-8	-7	-2	8	-8	-7	-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	99	0	0	0	2.96	1.09
17	V	-2	-3	-5	-6	-1	-5	-4	-6	1	2	1	-5	0	3	-6	-4	1	2	2	5	2	2	0	0	1	0	1	0	3	10	13	0	2	10	0	0	8	3	8	37	0.69	0.37
18	A	2	-6	-6	-7	1	-6	-6	-5	-7	3	-3	-6	-4	-4	-6	-1	-4	-7	-4	6	19	0	0	0	2	0	0	1	0	14	1	0	0	0	0	5	0	0	0	57	1.32	0.60
19	S	3	-5	-4	-5	-1	-5	-5	-4	-6	-6	-6	-5	-7	-5	6	4	-7	-6	-4		20	0	0	0	1	0	0	0	0	0	0	0	0	0	0	52	25	0	0	1	1.44	0.71
20	C	3	4	-3	-5	6	-2	-4	-1	-5	-3	-2	-1	-3	-5	-5	1	1	-6	-5	-1	24	20	0	0	19	1	0	5	0	1	4	3	0	0	0	11	7	0	0	4	0.72	0.41
21	A	6	-2	-4	-6	-1	-3	-5	2	-4	-3	-2	-3	-3	-4	-5	-2	0	-6	-6	-3	63	2	1	0	1	1	0	16	0	2	5	1	0	0	0	2	5	0	0	2	1.12	0.57
22	L	-6	-7	-8	-8	-6	-7	-8	-8	-7	3	6	-7	1	-3	-7	-7	-6	-6	-6	-2	0	0	0	0	0	0	0	0	0	0	17	79	0	2	1	0	0	0	0	0	1	1.89	0.74
23	L	2	-6	-7	-7	-1	-6	-4	-6	-6	2	5	-6	2	-4	-6	-5	-3	-6	-5	0	15	0	0	0	1	0	1	0	0	11	62	0	4	0	0	0	1	0	0	5	1.19	0.55
24	Q	1	2	-1	-2	-3	6	-1	-2	6	-5	-4	0	-2	-6	-5	-2	-2	-6	-2	-5	11	12	2	1	1	37	3	3	16	0	1	5	1	0	0	3	2	0	1	0	0.96	0.52
25	A	5	-2	-3	-5	0	-3	-3	0	0	-2	0	-1	-2	-1	-4	-1	-1	-1	1	0	48	2	1	0	2	1	1	5	2	1	10	4	1	2	0	4	4	1	5	5	0.55	0.36
26	A	3	-6	-6	-7	0	-5	-6	-6	-4	0	4	-6	1	4	-6	-5	-5	-2	-1	-2	25	0	0	0	2	0	0	0	0	4	45	0	2	18	0	0	0	1	1	1	1.02	0.50
27	K	3	4	2	-4	-4	2	-2	-2	0	-1	-2	1	-2	-5	-3	0	0	-5	-4	-1	23	21	11	0	0	10	1	3	2	4	3	8	1	0	1	5	4	0	0	4	0.42	0.31
28	A	2	3	0	-1	-4	3	1	-2	0	-4	-2	2	-2	-5	-3	0	-1	-5	-4	-4	20	16	4	3	0	16	9	3	2	1	5	12	1	0	0	5	2	0	0	0	0.42	0.29
29	A	2	2	-1	-2	-3	4	0	-2	4	-3	-1	1	0	-4	-4	0	-1	-5	-1	-2	18	13	3	1	1	19	5	2	9	1	7	6	2	0	0	7	3	0	2	2	0.37	0.28
30	G	-4	-4	1	-2	-7	-2	-5	7	1	-7	-7	-2	-4	-7	-6	-3	-6	-7	-4	-6	1	1	6	3	0	2	1	78	3	0	0	2	0	0	0	1	0	0	1	0	1.90	0.73
31	Y	-2	1	-3	-4	-1	0	-2	-4	2	1	2	1	1	1	-4	-3	-2	1	3	1	2	8	1	0	1	4	1	1	6	8	23	10	2	5	1	1	1	1	12	10	0.30	0.22
32	R	-2	4	1	0	-1	2	-2	-4	1	-4	-4	2	-4	-6	-2	3	2	-6	-5	-3	2	25	7	6	2	8	1	0	3	1	1	11	0	0	1	20	11	0	0	2	0.59	0.37
33	T	3	-5	-5	-6	0	-5	-5	-5	-6	1	-4	-5	-2	-4	-5	0	4	-6	-3	4	25	0	0	0	2	0	0	0	0	8	0	0	1	1	0	5	27	0	1	31	0.96	0.51

Position Specific Scoring Matrix (PSSM)

Last position-specific scoring matrix computed, weighted observed perce

		A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V
1	S	2	-2	2	-3	-3	-2	-2	-3	-3	-4	-4	2	-3	-5	-3	4	4	-5	-4	-3
2	K	-1	4	3	-3	-6	2	-1	-4	-1	-6	-6	6	-4	-4	-3	-2	-2	-6	-5	-5
3	R	2	4	-2	-4	-2	-1	-3	4	1	-5	-4	0	-4	-5	-4	2	0	-5	-5	-4
4	Y	-5	-6	-7	-7	1	-6	-7	-7	-4	1	2	-6	-1	6	-7	-6	-5	5	5	-1
5	F	-7	-8	-8	-9	-8	-8	-8	-8	-6	-4	-3	-8	-5	10	-9	-8	-7	-1	0	-6
6	V	-5	-7	-7	-8	-5	-7	-7	-8	-8	6	-2	-7	-3	-5	-7	-6	-5	-7	-6	6
7	T	1	-6	-5	-6	-6	-6	-6	-6	-7	-3	-5	-6	-5	-7	-6	-3	8	-7	-7	-3
8	G	-2	-7	-5	-6	-7	-7	-7	8	-7	-9	-9	-6	-8	-8	-7	-5	-6	-8	-8	-8
9	T	-5	-6	-5	-6	-6	-6	-6	-7	-7	-4	-6	-6	-6	-7	-6	-3	8	-8	-7	-5
10	D	-7	-7	-3	9	-9	-5	-3	-3	-6	-8	-9	-6	-8	-9	-7	-5	-6	-10	-8	-8
11	T	-4	-6	-5	-6	-6	-6	-6	-7	-7	-6	-6	-6	-6	-7	-6	-2	8	-8	-7	-5
12	E	-1	-2	2	5	-7	-3	4	3	-3	-7	-7	-4	-6	-7	-5	-2	-4	-7	-6	-6
13	V	0	-7	-7	-7	1	-6	-6	-7	-7	4	-3	-6	-2	-5	-6	-2	-4	-7	-5	7
14	G	-5	-8	-6	-7	-8	-7	-7	8	-7	-9	-9	-7	-8	-8	-7	-5	-7	-8	-8	-9
15	K	-6	-3	-5	-6	-9	-4	-4	-7	-6	-8	-8	8	-7	-9	-6	-6	-6	-9	-7	-8
16	T	-5	-7	-5	-6	-6	-6	-6	-7	-7	-6	-7	-6	-6	-8	-7	-2	8	-8	-7	-5
17	V	-2	-3	-5	-6	-1	-5	-4	-6	1	2	1	-5	0	3	-6	-4	1	2	2	5
18	A	2	-6	-6	-7	1	-6	-6	-5	-7	3	-3	-6	-4	-4	-6	-1	-4	-7	-4	6
19	S	3	-5	-4	-5	-1	-5	-5	-4	-6	-6	-6	-5	-5	-7	-5	6	4	-7	-6	-4
20	C	3	4	-3	-5	6	-2	-4	-1	-5	-3	-2	-1	-3	-5	-5	1	1	-6	-5	-1
21	A	6	-2	-4	-6	-1	-3	-5	2	-4	-3	-2	-3	-3	-4	-5	-2	0	-6	-6	-3
22	L	-6	-7	-8	-8	-6	-7	-8	-8	-7	3	6	-7	1	-3	-7	-7	-6	-6	-6	-2
23	L	2	-6	-7	-7	-1	-6	-4	-6	-6	2	5	-6	2	-4	-6	-5	-3	-6	-5	0
24	Q	1	2	-1	-2	-3	6	-1	-2	6	-5	-4	0	-2	-6	-5	-2	-2	-6	-2	-5
25	A	5	-2	-3	-5	0	-3	-3	0	0	-2	0	-1	-2	-1	-4	-1	-1	-1	1	0
26	A	3	-6	-6	-7	0	-5	-6	-6	-4	0	4	-6	1	4	-6	-5	-5	-2	-1	-2
27	K	3	4	2	-4	-4	2	-2	-2	0	-1	-2	1	-2	-5	-3	0	0	-5	-4	-1
28	A	2	3	0	-1	-4	3	1	-2	0	-4	-2	2	-2	-5	-3	0	-1	-5	-4	-4
29	A	2	2	-1	-2	-3	4	0	-2	4	-3	-1	1	0	-4	-4	0	-1	-5	-1	-2
30	G	-4	-4	1	-2	-7	-2	-5	7	1	-7	-7	-2	-4	-7	-6	-3	-6	-7	-4	-6
31	Y	-2	1	-3	-4	-1	0	-2	-4	2	1	2	1	1	1	-4	-3	-2	1	3	1
32	R	-2	4	1	0	-1	2	-2	-4	1	-4	-4	2	-4	-6	-2	3	2	-6	-5	-3
33	T	3	-5	-5	-6	0	-5	-5	-5	-6	1	-4	-5	-2	-4	-5	0	4	-6	-3	4

Use a Sliding Window for residue pair



Considering a sliding window of 5 around the central residue for each pair (i, j)
Number of features = 20 x 5 x 2 = 200

We can assume they follow Gaussian distribution

Use minimum sequence separation of 6 residues. i.e. $|i - j| > 5$

Noncontacts vastly outnumber contacts. May need to balance training data.

Protein Contact Map Prediction using LR

- We have two classes: contact (**1**), non contact (**0**)
  - Discrete labels (Y)
- We can use PSSM (X) with sliding window strategy for each residue pair
- We can train LR to predict whether a residue pair is in contact or not
  - Estimate w's
  - Gradient ascent algorithm to maximize MCLE
- Calculate accuracy to estimate performance
  - Calculate accuracy of **TOP CONTACTS ONLY** (20, 100, L/5, L/2, etc.)
  - No need to balance test data