Sequence and structural patterns detected in entangled proteins reveal the importance of co-translational folding

Marco Baiesi 1,2 , Enzo Orlandini 1,2 , Flavio Seno 1,2,* , and Antonio Trovato 1,2

¹Department of Physics and Astronomy, University of Padova, Via Marzolo 8, I-35131 Padova, Italy ²INFN, Sezione di Padova, Via Marzolo 8, I-35131 Padova, Italy

*seno@pd.infn.it

ABSTRACT

This Supplementary Information contains additional figures that complement those in the main text.



Figure S1. Enlarged view of the linking entanglement vs. the Gaussian entanglement. Each point represents a protein in the CATH database. Clusters of data are visible.



Figure S2. Amino acids ranked according to the average number of contacts (black dots) that they form with other amino acids in the protein structures of the CATH database. We recall that a contact between amino acids a and b is defined as a configuration where any of the heavy atoms of a is at distance lower than 4.5 from another heavy atom of b. The orange dots represent the average number of contacts of amino acids at the end of entangled loops. One can note that these are typically larger than the standard average values.

	TRP	PHE	TYR	CYS	ILE	VAL	LEU	MET	HIS	THR	ARG	PRO	GLN	ASN	ALA	SER	LYS	GLY	GLU	ASP
TRP	-31	-5	-29	-7	0	23	1	-20	-40	4	-29	-46	-40	-33	-16	3	-12	-25	-5	-23
PHE	-5	-9	-12	26	15	13	7	8	-10	3	-11	-39	-10	-11	11	11	-2	8	-18	-17
TYR	-29	-12	-21	36	4	4	4	-16	-32	-5	-21	-40	-20	-36	-16	-4	-20	-31	-34	-30
CYS	-7	26	36	130	49	56	52	15	-1	54	-9	-56	-11	6	42	25	49	52	6	54
ILE	0	15	4	49	50	49	37	21	11	32	8	-21	2	2	24	20	12	10	9	26
VAL	23	13	4	56	49	54	36	30	-1	34	14	-16	4	4	38	28	29	21	15	27
LEU	1	7	4	52	37	36	20	18	-10	16	-14	-21	0	-10	15	10	-12	-1	-2	-1
MET	-20	8	-16	15	21	30	18	21	-35	6	-22	-35	-23	-45	3	-1	-24	10	-35	-22
HIS	-40	-10	-32	-1	11	-1	-10	-35	9	-23	-3	-33	-29	-8	-10	-16	-2	-23	-21	-22
THR	4	3	-5	54	32	34	16	6	-23	17	-14	-32	-6	-9	15	6	10	12	-10	8
ARG	-29	-11	-21	-9	8	14	-14	-22	-3	-14	-42	-54	-23	-39	-22	-12	-21	-30	-29	-26
PRO	-46	-39	-40	-56	-21	-16	-21	-35	-33	-32	-54	-49	-46	-46	-20	-25	-32	-23	-42	-28
GLN	-40	-10	-20	-11	2	4	0	-23	-29	-6	-23	-46	-18	-35	-25	-23	-14	-30	-12	-10
ASN	-33	-11	-36	6	2	4	-10	-45	-8	-9	-39	-46	-35	-9	-16	-20	-28	-31	-41	-21
ALA	-16	11	-16	42	24	38	15	3	-10	15	-22	-20	-25	-16	-6	1	-3	-26	-12	3
SER	3	11	-4	25	20	28	10	-1	-16	6	-12	-25	-23	-20	1	12	2	-7	-15	-5
LYS	-12	-2	-20	49	12	29	-12	-24	-2	10	-21	-32	-14	-28	-3	2	-6	-20	-17	-22
GLY	-25	8	-31	52	10	21	-1	10	-23	12	-30	-23	-30	-31	-26	-7	-20	-29	-27	-6
GLU	-5	-18	-34	6	9	15	-2	-35	-21	-10	-29	-42	-12	-41	-12	-15	-17	-27	-37	-28
ASP	-23	-17	-30	54	26	27	-1	-22	-22	8	-26	-28	-10	-21	3	-5	-22	-6	-28	-38

Figure S3. Enrichment score ΔE_{enr} for entangled contacts, as in Fig. 7B of the main text but with a higher threshold $|G'_c(i)| > 1.2$ defining entangled loops.

	TRP	PHE	TYR	CYS	ILE	VAL	LEU	MET	HIS	THR	ARG	PRO	GLN	ASN	ALA	SER	LYS	GLY	GLU	ASP
TRP	-28	-12	-19	12	-5	20	-4	-13	-33	0	-17	-42	-29	-23	-10	-6	-22	-20	-13	-8
PHE	-12	-11	-12	25	14	18	-2	-7	-18	2	-14	-28	-12	-15	-1	10	-4	8	-16	-6
TYR	-19	-12	-5	29	5	8	-2	-11	-22	-2	-13	-32	-14	-22	-14	0	-10	-14	-26	-19
CYS	12	25	29	74	45	48	36	5	9	37	-17	-44	0	23	18	32	21	48	21	69
ILE	-5	14	5	45	35	37	18	7	12	20	3	-14	-4	1	9	19	8	7	9	34
VAL	20	18	8	48	37	50	22	11	6	28	17	-9	7	15	27	23	23	23	13	32
LEU	-4	-2	-2	36	18	22	4	-5	-8	1	-14	-26	-8	-5	0	-5	-12	0	-9	4
MET	-13	-7	-11	5	7	11	-5	-5	-18	-8	-25	-30	-26	-26	-10	-6	-20	-2	-28	0
HIS	-33	-18	-22	9	12	6	-8	-18	-5	-13	-8	-32	-22	0	-4	-9	3	-4	-12	-11
THR	0	2	-2	37	20	28	1	-8	-13	20	-4	-21	-1	-8	-3	6	13	13	2	15
ARG	-17	-14	-13	-17	3	17	-14	-25	-8	-4	-15	-37	-24	-20	-16	-10	-12	-22	-24	-14
PRO	-42	-28	-32	-44	-14	-9	-26	-30	-32	-21	-37	-43	-38	-32	-21	-28	-21	-10	-39	-15
GLN	-29	-12	-14	0	-4	7	-8	-26	-22	-1	-24	-38	-15	-17	-19	-11	-6	-14	-10	-13
ASN	-23	-15	-22	23	1	15	-5	-26	0	-8	-20	-32	-17	1	-9	-1	-16	-15	-23	-9
ALA	-10	-1	-14	18	9	27	0	-10	-4	-3	-16	-21	-19	-9	-13	-4	-3	-10	-15	15
SER	-6	10	0	32	19	23	-5	-6	-9	6	-10	-28	-11	-1	-4	11	-4	5	-8	-1
LYS	-22	-4	-10	21	8	23	-12	-20	3	13	-12	-21	-6	-16	-3	-4	4	-10	-17	-6
GLY	-20	8	-14	48	7	23	0	-2	-4	13	-22	-10	-14	-15	-10	5	-10	1	-15	14
GLU	-13	-16	-26	21	9	13	-9	-28	-12	2	-24	-39	-10	-23	-15	-8	-17	-15	-16	-13
ASP	-8	-6	-19	69	34	32	4	0	-11	15	-14	-15	-13	-9	15	-1	-6	14	-13	-2

Figure S4. Enrichment score ΔE_{enr} for entangled contacts, as in Fig. 7B of the main text but with a minimum separation of $s_0 = 5$ amino acid bonds between the thread and the loop.

	TRP	PHE	TYR	CYS	ILE	VAL	LEU	MET	HIS	THR	ARG	PRO	GLN	ASN	ALA	SER	LYS	GLY	GLU	ASP
TRP	-111	-111	-91	-98	-91	-79	-91	-88	-58	-33	-43	-46	-32	-14	-27	-22	-16	-2	-11	2
PHE	-111	-120	-89	-89	-106	-93	-102	-96	-39	-28	-22	-16	-9	6	-36	-4	5	7	21	32
TYR	-91	-89	-66	-66	-75	-64	-68	-67	-46	-19	-27	-30	-12	-1	-14	-2	-10	12	-3	2
CYS	-98	-89	-66	-194	-71	-66	-60	-60	-49	-21	-6	-7	6	4	-10	0	18	8	37	35
ILE	-91	-106	-75	-71	-113	-98	-102	-77	-18	-24	-1	9	6	27	-32	12	18	27	35	51
VAL	-79	-93	-64	-66	-98	-93	-86	-65	-13	-22	3	12	11	28	-25	14	16	29	35	51
LEU	-91	-102	-68	-60	-102	-86	-99	-71	-8	-10	4	13	16	36	-21	24	26	39	47	62
MET	-88	-96	-67	-60	-77	-65	-71	-72	-20	-10	6	5	11	21	-8	17	29	25	42	48
HIS	-58	-39	-46	-49	-18	-13	-8	-20	-53	-7	13	12	16	10	36	4	39	35	8	-3
THR	-33	-28	-19	-21	-24	-22	-10	-10	-7	1	16	32	20	23	33	27	29	47	42	44
ARG	-43	-22	-27	-6	-1	3	4	6	13	16	37	30	21	24	52	32	63	50	-19	-16
PRO	-46	-16	-30	-7	9	12	13	5	12	32	30	31	33	33	53	46	61	55	65	65
GLN	-32	-9	-12	6	6	11	16	11	16	20	21	33	29	29	61	40	39	59	59	59
ASN	-14	6	-1	4	27	28	36	21	10	23	24	33	29	12	63	35	42	46	54	41
ALA	-27	-36	-14	-10	-32	-25	-21	-8	36	33	52	53	61	63	37	61	69	73	90	95
SER	-22	-4	-2	0	12	14	24	17	4	27	32	46	40	35	61	45	51	61	60	54
LYS	-16	5	-10	18	18	16	26	29	39	29	63	61	39	42	69	51	76	66	2	3
GLY	-2	7	12	8	27	29	39	25	35	47	50	55	59	46	73	61	66	65	89	73
GLU	-11	21	-3	37	35	35	47	42	8	42	-19	65	59	54	90	60	2	89	113	114
ASP	2	32	2	35	51	51	62	48	-3	44	-16	65	59	41	95	54	3	73	114	95
	TOD	DUE	TVD	01/0				NACT	1110	TUD	400			ACN	A 1 A	050	1.1/0		0111	A 0 D
TDD	TRP	PHE	TYR	CYS	ILE	VAL	LEU	MET	HIS	THR	ARG	PRO	GLN	ASN	ALA	SER	LYS	GLY	GLU	ASP
TRP	TRP -34	PHE -15	TYR -21	CYS 11	ILE -3	VAL 21	LEU 0	MET -18	HIS -49	THR 0	ARG –19	PRO -42	GLN -33	ASN -22	ALA -12	SER -6	LYS -16	GLY -24	GLU -15	ASP -22
TRP PHE	TRP -34 -15	PHE -15 -9	TYR -21 -12	CYS 11 18	ILE -3 15	VAL 21 19	LEU 0 3	MET -18 -8	HIS -49 -18	THR 0 2	ARG -19 -14	PRO -42 -31	GLN -33 -16	ASN -22 -24	ALA -12 -1	SER -6 6	LYS -16 -5	GLY -24 -1	GLU -15 -10	ASP -22 -10
TRP PHE TYR	TRP -34 -15 -21	PHE -15 -9 -12	TYR -21 -12 -3	CYS 11 18 18	ILE -3 15 7	VAL 21 19 13	LEU 0 3 1	MET -18 -8 -9	HIS -49 -18 -22	THR 0 2 2	ARG -19 -14 -14	PRO -42 -31 -32	GLN -33 -16 -16	ASN -22 -24 -23	ALA -12 -1 -11	SER -6 6 0	LYS -16 -5 -8	GLY -24 -1 -20	GLU -15 -10 -19	ASP -22 -10 -18
TRP PHE TYR CYS	TRP -34 -15 -21 11	PHE -15 -9 -12 18	TYR -21 -12 -3 18	CYS 11 18 18 72	ILE -3 15 7 38	VAL 21 19 13 44	LEU 0 3 1 32	MET -18 -8 -9 14	HIS -49 -18 -22 12	THR 0 2 2 24	ARG -19 -14 -14 -10	PRO -42 -31 -32 -55	GLN -33 -16 -16 -2	ASN -22 -24 -23 29	ALA -12 -1 -11 21	SER -6 6 0 32	LYS -16 -5 -8 29	GLY -24 -1 -20 24	GLU -15 -10 -19 23	ASP -22 -10 -18 50
TRP PHE TYR CYS ILE	TRP -34 -15 -21 11 -3	PHE -15 -9 -12 18 15	TYR -21 -12 -3 18 7	CYS 11 18 18 72 38	ILE -3 15 7 38 38	VAL 21 19 13 44 40	LEU 0 3 1 32 22	MET -18 -9 14 9	HIS -49 -18 -22 12 9	THR 0 2 2 24 17	ARG -19 -14 -14 -10 9	PRO -42 -31 -32 -55 -21	GLN -33 -16 -16 -2 -2	ASN -22 -24 -23 29 -7	ALA -12 -1 -11 21 11	SER -6 0 32 19	LYS -16 -5 -8 29 14	GLY -24 -1 -20 24 7	GLU -15 -10 -19 23 17	ASP -22 -10 -18 50 33
TRP PHE TYR CYS ILE VAL	TRP -34 -15 -21 11 -3 21	PHE -15 -9 -12 18 15 19	TYR -21 -12 -3 18 7 13	CYS 11 18 18 72 38 44	ILE -3 15 7 38 38 40	VAL 21 19 13 44 40 55	LEU 0 3 1 32 22 28 10	MET -18 -8 -9 14 9 15	HIS -49 -18 -22 12 9 6	THR 0 2 2 24 17 28	ARG -19 -14 -14 -10 9 20	PRO -42 -31 -32 -55 -21 -9	GLN -33 -16 -16 -2 -2 -2 6	ASN -22 -24 -23 29 -7 10	ALA -12 -1 21 11 29	SER -6 0 32 19 26	LYS -16 -5 -8 29 14 29	GLY -24 -1 -20 24 7 18	GLU -15 -10 -19 23 17 23	ASP -22 -10 -18 50 33 28
TRP PHE TYR CYS ILE VAL LEU	TRP -34 -15 -21 11 -3 21 0	PHE -15 -9 -12 18 15 19 3 3	TYR -21 -12 -3 18 7 13 13	CYS 11 18 18 72 38 44 32 14	ILE -3 15 7 38 38 40 22	VAL 21 19 13 44 40 55 28 15	LEU 0 3 1 32 22 28 10	MET -18 -9 14 9 15 -1 11	HIS -49 -18 -22 12 9 6 -7	THR 0 2 2 24 17 28 4	ARG -19 -14 -14 -10 9 20 -9 26	PRO -42 -31 -32 -55 -21 -9 -25 21	GLN -33 -16 -16 -2 -2 -2 6 -6 28	ASN -22 -24 -23 29 -7 10 -5	ALA -12 -11 21 11 29 4	SER -6 0 32 19 26 1	LYS -16 -5 -8 29 14 29 -3 20	GLY -24 -1 24 24 7 18 -2	GLU -15 -10 -19 23 17 23 -1	ASP -22 -10 -18 50 33 28 5 5
TRP PHE TYR CYS ILE VAL LEU MET	TRP -34 -15 -21 11 -3 21 0 -18	PHE -15 -9 -12 18 15 19 3 -8 19	TYR -21 -12 -3 18 7 13 1 1 -9 22	CYS 11 18 18 72 38 44 32 14 12	ILE -3 15 7 38 38 40 22 9	VAL 21 19 13 44 40 55 28 15 6	LEU 0 3 1 32 22 28 10 -1	MET -18 -9 14 9 15 -1 -11 15	HIS -49 -18 -22 12 9 6 -7 -15	THR 0 2 2 24 17 28 4 4 -8	ARG -19 -14 -10 9 20 -9 -26 19	PRO -42 -31 -32 -55 -21 -9 -25 -31	GLN -33 -16 -16 -2 -2 6 -6 -28 27	ASN -22 -24 -23 29 -7 10 -5 -29 11	ALA -12 -11 21 11 29 4 -8	SER -6 0 32 19 26 1 -12	LYS -16 -5 -8 29 14 29 -3 -3 -20	GLY -24 -1 -20 24 7 18 -2 -11	GLU -15 -10 -19 23 17 23 -1 -23 -1	ASP -22 -10 -18 50 33 28 5 -6 17
TRP PHE TYR CYS ILE VAL LEU MET HIS THP	TRP -34 -15 -21 11 -3 21 0 -18 -49 0	PHE -15 -9 -12 18 15 19 3 -8 -8 -18 2	TYR -21 -12 -3 18 7 13 1 -9 -22 2	CYS 11 18 18 72 38 44 32 14 12 24	ILE -3 15 7 38 38 40 22 9 9 9	VAL 21 19 13 44 40 55 28 15 6 28	LEU 0 3 1 32 22 28 10 -1 -7	MET -18 -9 14 9 15 -1 -11 -15 -8	HIS -49 -18 -22 12 9 6 -7 -15 -7	THR 0 2 2 24 17 28 4 -8 -16 20	ARG -19 -14 -14 -10 9 20 -9 -26 -19	PRO -42 -31 -32 -55 -21 -9 -25 -31 -36 -21	GLN -33 -16 -16 -2 -2 -2 6 -6 -28 -27	ASN -22 -24 -23 29 -7 10 -5 -29 -11	ALA -12 -11 21 11 29 4 -8 -11	SER -6 0 32 19 26 1 -12 -15 7	LYS -16 -5 -8 29 14 29 -3 -3 -20 -5	GLY -24 -20 24 7 18 -2 -11 -12	GLU -15 -10 -19 23 17 23 -1 -23 -18 8	ASP -22 -10 -18 50 33 28 5 -6 -17
TRP PHE TYR CYS ILE VAL LEU MET HIS THR	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 10	PHE -15 -9 -12 18 15 19 3 -8 -8 -18 2 14	TYR -21 -12 -3 18 7 13 1 -9 -22 2	CYS 11 18 18 72 38 44 32 14 12 24	ILE -3 15 7 38 38 40 22 9 9 9 177	VAL 21 19 13 44 40 55 28 15 6 28 28 20	LEU 0 3 1 32 22 28 10 -1 -7 4	MET -18 -9 14 9 15 -1 -11 -15 -8 26	HIS -49 -18 -22 12 9 6 -7 -15 -7 -15 -7 -16	THR 0 2 2 4 17 28 4 -8 -16 20	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 16	PRO -42 -31 -32 -55 -21 -9 -25 -31 -36 -21	GLN -33 -16 -16 -2 -2 -2 6 -6 -28 -27 4 22	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 24	ALA -12 -1 21 11 29 4 -8 -11 -1 12	SER -6 0 32 19 26 1 -12 -15 7	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 12	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 21	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 8	ASP -22 -10 -18 50 33 28 5 -6 -17 13 20
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG DBO	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 42	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32	CYS 11 18 18 72 38 44 32 14 12 24 -10 55	ILE -3 15 7 38 38 40 22 9 9 9 9 17 9 21	VAL 21 19 13 44 40 55 28 15 6 28 28 20 20	LEU 0 3 1 22 28 10 -1 -7 4 -7 4 -9 -25	MET -18 -9 14 9 15 -1 -11 -15 -8 -26 -31	HIS -49 -18 -22 12 9 6 -7 -15 -7 -15 -7 -16 -19 26	THR 0 2 2 4 17 28 4 -8 -16 20 -6 -21	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 -16 -29	PRO -42 -31 -32 -55 -21 -9 -25 -31 -36 -21 -39 -40	GLN -33 -16 -16 -2 -2 -2 6 -6 -28 -27 4 -23 29	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 25	ALA -12 -11 21 11 29 4 -8 -11 -13 -24	SER -6 0 32 19 26 1 -12 -15 7 -10 -28	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 8 -20 -34	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 22	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 16	TYR -21 -12 -3 18 7 13 1 -9 -22 2 2 -14 -32 16	CYS 11 18 72 38 44 32 14 12 24 -10 -55	ILE -3 15 7 38 38 40 22 9 9 9 17 9 17 9 -21	VAL 21 19 13 44 40 55 28 15 6 28 15 6 28 20 -9 9 6	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 6	MET -18 -9 14 9 15 -11 -11 -15 -8 -26 -31 -28	HIS -49 -18 -22 12 9 6 -7 -15 -7 -15 -7 -16 -19 -36 27	THR 0 2 24 17 28 4 -8 -16 20 -6 -21	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 -16 -39 22	PRO -42 -31 -32 -55 -21 -9 -25 -31 -36 -21 -39 -40 20	GLN -33 -16 -16 -2 -2 6 -6 -28 -27 4 -23 -27 4 -23 -39 -12	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -24 -35 20	ALA -12 -11 21 11 29 4 -8 -11 -13 -24 14	SER -6 0 32 19 26 1 -12 -15 7 -10 -28	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 2	GLY -24 -1 24 7 18 -2 -11 -12 -6 -31 -25 26	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 -20 -34 -31	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20 16
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO GLN	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 -33 22	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 -16 24	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32 -16 22	CYS 11 18 72 38 44 32 14 12 24 -10 -55 -2	ILE -3 15 7 38 38 40 22 9 9 17 9 177 9 -21 -2 7	VAL 21 19 13 44 40 55 28 15 6 28 20 -9 6 10	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 -6 5	MET -18 -9 14 9 15 -11 -11 -15 -8 -26 -31 -28 20	HIS -49 -18 -22 12 9 6 -7 -15 -7 -15 -7 -16 -19 -36 -27 -11	THR 0 2 24 17 28 4 -8 -16 20 -6 -21 4	ARG -19 -14 -10 9 20 -9 -26 -19 -6 -16 -39 -23	PRO -42 -31 -32 -55 -21 -9 -25 -31 -36 -21 -39 -40 -39 25	GLN -33 -16 -16 -2 -2 -2 6 -6 -28 -27 4 -23 -27 4 -23 -39 -13	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -24 -35 -20	ALA -12 -11 21 11 29 4 -8 -11 -13 -24 -14 12	SER -6 0 32 19 26 1 -12 -15 7 -10 -28 -4	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 -3 -20	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25 -26 28	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 -20 -34 -11 -26	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20 -20 -16
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO GLN ASN	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 -33 -22 -12	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 -16 -24	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32 -16 -23 -11	CYS 11 18 72 38 44 32 14 12 24 -10 -55 -2 29 21	ILE -3 15 7 38 38 40 22 9 9 9 17 9 -21 -2 -7 11	VAL 21 19 13 44 40 55 28 15 6 28 20 -9 6 10 29	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 -6 -5	MET -18 -9 14 9 15 -1 -11 -15 -8 -26 -31 -28 -28 -29 o	HIS -49 -18 -22 12 9 6 -7 -15 -7 -15 -7 -16 -19 -36 -27 -11	THR 0 2 2 4 17 28 4 -8 -16 20 -6 -21 4 -21 4 -10	ARG -19 -14 -10 9 20 -9 -26 -19 -6 -16 -39 -23 -23 -23 -24 12	PRO -42 -31 -32 -55 -21 -9 -25 -31 -36 -21 -39 -40 -39 -39 -39 -32	GLN -33 -16 -16 -2 -2 -2 -2 -6 -6 -28 -27 4 -23 -23 -39 -13 -20 14	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -35 -20 -1 -12	ALA -12 -11 21 11 29 4 -8 -11 -13 -24 -14 -13 15	SER -6 0 32 19 26 1 -12 -15 7 -10 -28 -4 -6 5	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 -3 -20 1	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25 -26 -28 -22	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 -20 -34 -11 -26 -34 -11 -21 -21 -23 -1 -10 -19 -19 -19 -19 -19 -19 -19 -19	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20 -16 -17
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO GLN ASN ASN ASN	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 -33 -22 -12 -6	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 -16 -24 -1 6	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32 -16 -23 -16 -23 -10	CYS 11 18 18 72 38 44 32 14 12 24 -10 -55 -2 29 21 22	ILE -3 15 7 38 38 40 22 9 9 9 17 9 -21 -2 -7 11 19	VAL 21 19 13 44 40 55 28 15 6 28 20 -9 6 10 29 26	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 -6 -5 4 1	MET -18 -9 14 9 15 -1 -11 -15 -8 -26 -31 -28 -29 -8 -29 -8 -12	HIS -49 -18 -22 12 9 6 -7 -15 -7 -16 -19 -36 -27 -27 -11 -11 -15	THR 0 2 2 4 17 28 4 -8 -8 -16 20 -6 -6 -21 4 -10 -10 -7	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 -16 -39 -23 -24 -23 -24 -10	PRO -42 -31 -32 -55 -21 -9 -25 -31 -30 -21 -30 -21 -39 -40 -39 -35 -28	GLN -33 -16 -16 -2 -2 -2 -2 -6 -6 -28 -27 4 -23 -23 -39 -13 -20 -13 -20 -14 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -35 -20 -1 -1 -1 -3 -5 -20 -1 -1 -3 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	ALA -12 -1 21 11 29 4 -8 -11 -13 -24 -14 -13 -13 -24 5 5	SER -6 0 32 19 26 1 -12 -15 7 -10 -28 -4 -6 -5 15	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 -3 -20 -3 -20 -1 0	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25 -26 -28 -28 -28 -28	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 -20 -34 -11 -26 -10 -8 -8 -1 -23 -1 -23 -1 -1 -23 -1 -1 -23 -1 -1 -23 -23 -24 -24 -24 -25 -24 -24 -24 -25 -25 -25 -25 -25 -25 -25 -25	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20 -16 -17 9 4
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO GLN ASN ALA SER	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 -33 -22 -12 -6 16	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 -16 -24 -1 6 5	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32 -16 -23 -11 0 9	CYS 11 18 72 38 44 32 14 12 24 -10 -55 -2 29 21 32 29	ILE -3 15 7 38 38 40 22 9 9 9 17 9 -21 -2 -7 11 19 14	VAL 21 19 13 44 40 55 28 15 6 28 20 -9 6 10 29 6 10 29 26 20	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 -6 -5 4 1 2	MET -18 -9 14 9 15 -1 -11 -15 -8 -26 -31 -28 -29 -8 -8 -29 -8 -20	HIS -49 -18 -22 12 9 6 -7 -15 -7 -16 -19 -36 -27 -11 -11 -11 -15 5	THR 0 2 24 17 28 4 -8 -166 20 -66 -21 4 -100 -1 7 14	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 -16 -39 -23 -24 -13 -10 12	PRO -42 -31 -32 -55 -21 -9 -25 -31 -36 -21 -39 -40 -39 -40 -39 -35 -24 -24 -22	GLN -33 -16 -16 -2 -2 -2 -2 -6 -6 -28 -27 4 -23 -23 -13 -20 -13 -20 -14 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -35 -20 -1 -13 -6 -20	ALA -12 -1 21 11 29 4 -8 -11 -13 -24 -14 -13 -24 -14 -13 -25 -5 1	SER -6 0 32 19 26 1 -12 -15 7 -10 -28 -4 -6 -5 15 0	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 -3 -20 -1 0 2	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25 -26 -28 -28 -23 -23 -23 -17	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 -20 -34 -11 -26 -10 -10 -8 -10 -15 -10 -15 -10 -19 -19 -19 -19 -19 -19 -19 -19	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20 -16 -17 9 -4 -17 9 -4 -12
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO GLN ASN ALA SER LYS	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 -33 -22 -12 -6 -16 -24	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 -16 -24 -1 6 -5 -5 -1	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32 -16 -23 -11 0 -8 -8	CYS 11 18 72 38 44 32 14 12 24 -10 -55 -2 29 21 32 29 24	ILE -3 15 7 38 38 40 22 9 9 9 17 9 -21 -2 -7 11 19 14 7	VAL 21 19 13 44 40 55 28 15 6 28 20 -9 6 10 29 6 10 29 26 29 18	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 -6 -5 -5 4 1 -3 2	MET -18 -9 14 9 15 -1 -11 -15 -8 -26 -31 -28 -29 -8 -12 -8 -12 -1 -1 -1 -1 -1 -1 -1 -1 -1 -1	HIS -49 -18 -22 12 9 6 -7 -15 -7 -16 -19 -36 -27 -11 -11 -11 -15 -5 -12	THR 0 2 24 17 28 4 -8 -166 20 -66 -21 4 -100 -1 7 14 6	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 -16 -39 -23 -24 -13 -10 -12 -23 -24 -13 -10 -12 -23 -24 -13 -12 -23 -24 -13 -24 -23 -24 -23 -24 -23 -24 -23 -24 -23 -24 -23 -24 -24 -23 -24 -23 -24 -24 -24 -25 -26 -26 -26 -26 -27 -26 -26 -26 -26 -26 -27 -26 -26 -26 -26 -27 -26 -26 -26 -27 -26 -26 -26 -26 -27 -26 -22 -26 -22 -26 -24 -26 -24 -26 -24 -26 -24 -26 -24 -27 -26 -24 -27 -26 -24 -27 -26 -24 -24 -24 -24 -24 -24 -24 -24	PRO -42 -31 -32 -55 -21 -9 -25 -31 -30 -21 -39 -40 -39 -35 -24 -28 -28 -25	GLN -33 -16 -16 -2 -2 -2 -2 -6 -28 -27 4 -23 -23 -13 -20 -13 -20 -14 -4 -3 -26	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -20 -1 -13 -6 -20 28	ALA -12 -1 21 11 29 4 -8 -11 -13 -24 -14 -13 -24 -14 -13 -15 -5 -1 -22	SER -6 0 32 19 26 1 -12 -15 7 -10 -28 -4 -6 -5 15 0 4	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 -3 -20 -1 0 2 -1 0 2 -17	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25 -26 -28 -28 -23 -23 -4 -17 -10	GLU -15 -10 -19 23 17 23 -1 -23 -18 8 -20 -34 -11 -26 -10 -8 -10 -8 -11 -8 -11 -8 -12 -10 -19 -19 -19 -19 -19 -19 -19 -19	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20 -16 -17 9 -4 -4 -2 0
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO GLN ASN ALA SER LYS GLU	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 -33 -22 -12 -6 -16 -24 15	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 -16 -24 -1 6 -5 -1 10	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32 -16 -23 -11 0 -8 -8 -20 -12	CYS 11 18 72 38 44 32 14 12 24 -10 -55 -2 29 21 32 29 21 32 29 24 22	ILE -3 15 7 38 30 22 9 17 9 -21 -2 -7 11 19 14 7	VAL 21 19 13 44 40 55 28 15 6 28 20 -9 6 10 29 26 29 26 29 18 22	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 -6 -5 -6 -5 4 1 -3 -2 1	MET -18 -9 14 9 15 -1 -11 -15 -8 -26 -31 -28 -29 -8 -12 -20 -11 -22 -20 -11 -22	HIS -49 -18 -22 12 9 6 -7 -15 -7 -16 -19 -36 -27 -11 -11 -11 -15 -5 -5 -12	THR 0 2 2 4 17 28 4 -8 -8 -8 -0 20 -6 20 -6 -21 4 -10 -1 7 14 -10 -1 20 -1 20 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 -16 -39 -23 -24 -13 -10 -12 -12 -31 -22 -22 -23 -24 -13 -10 -22 -22 -22 -23 -24 -22 -22 -22 -22 -22 -22 -22	PRO -42 -31 -32 -55 -21 -9 -25 -31 -31 -36 -21 -39 -40 -39 -35 -24 -28 -23 -23 -24	GLN -33 -16 -16 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -20 -1 -13 -6 -20 -20 -20 -1 -35 -20 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	ALA -12 -1 -11 21 11 29 4 -8 -11 -13 -24 -14 -13 -24 -14 -13 -25 -5 -5 -1 -23 10	SER -6 0 32 19 26 1 -12 -15 7 -10 -28 -4 -6 -5 15 0 -4 -5 0 -4 -5 -5 -5 -5 -5 -5 -5 -5 -5 -5	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 -3 -20 -1 0 2 -17 15	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25 -26 -28 -28 -23 -23 -4 -17 -17 -10	GLU -15 -10 -19 23 17 23 -1 -23 -1 -23 -18 8 -20 -34 -11 -26 -10 -8 -15 -15 -14 -15 -10 -8 -15 -10 -8 -15 -10 -19 -19 -19 -19 -19 -19 -19 -19	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -20 -16 -17 9 -4 -12 0 10 -12 0 -12 -12 -12 -12 -12 -12 -12 -12
TRP PHE TYR CYS ILE VAL LEU MET HIS THR ARG PRO GLN ASN ALA SER LYS GLY GLY	TRP -34 -15 -21 11 -3 21 0 -18 -49 0 -19 -42 -33 -22 -12 -6 -16 -24 -15 22	PHE -15 -9 -12 18 15 19 3 -8 -18 2 -14 -31 -16 -24 -1 6 -5 -1 -10 10	TYR -21 -12 -3 18 7 13 1 -9 -22 2 -14 -32 -16 -23 -11 0 -8 -20 -19 18	CYS 11 18 72 38 44 32 14 12 24 -10 -55 -2 29 21 32 29 21 32 29 24 23 50	ILE -3 15 7 38 40 22 9 17 9 -21 -2 -7 11 19 14 7 17	VAL 21 19 13 44 40 55 28 15 6 28 20 -9 6 10 29 26 29 18 23 28	LEU 0 3 1 22 28 10 -1 -7 4 -9 -25 -6 -5 4 1 -3 -2 4 1 -3 -2 -1 5	MET -18 -9 14 9 15 -1 -11 -15 -8 -26 -31 -28 -29 -8 -29 -8 -12 -20 -11 -20 -11 -20 -11 -20 -12 -20 -12 -20 -12 -20 -3 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	HIS -49 -18 -22 12 9 6 -7 -15 -7 -16 -19 -36 -27 -11 -11 -11 -15 -5 -12 -12 -12 -13 -5 -12 -12 -13 -5 -12 -13 -15 -7 -7 -15 -7 -15 -7 -15 -7 -15 -7 -15 -7 -11 -11 -15 -5 -5 -12 -12 -12 -12 -12 -12 -12 -12	THR 0 2 2 4 17 28 4 -8 -8 -8 -0 20 -6 20 -6 -21 4 -10 -1 7 14 -6 8 8 12	ARG -19 -14 -14 -10 9 20 -9 -26 -19 -6 -16 -39 -23 -24 -13 -10 -12 -31 -20 20	PRO -42 -31 -32 -55 -21 -9 -25 -31 -31 -36 -21 -39 -40 -39 -40 -39 -35 -24 -28 -23 -25 -25 -25 -25 -25 -25 -25 -21 -21 -31 -31 -32 -31 -32 -25 -21 -31 -32 -21 -31 -32 -21 -31 -32 -21 -21 -31 -22 -21 -21 -21 -22 -21 -21 -22 -21 -21	GLN -33 -16 -16 -2 -2 -2 -2 -2 -2 -2 -2 -2 -2	ASN -22 -24 -23 29 -7 10 -5 -29 -11 -10 -24 -20 -1 -13 -6 -20 -28 -28 -28 -21 -17	ALA -12 -1 21 11 29 4 -8 -11 -13 -24 -14 -13 -24 -14 -13 -25 -5 -1 -23 -0 0	SER -6 0 32 19 26 1 -12 -15 7 -10 -28 -4 -6 -5 15 0 -4 -4 -5 15 0 -4 -4 -5 -4 -5 -5 -5 -5 -5 -5 -5 -5 -5 -5	LYS -16 -5 -8 29 14 29 -3 -20 -5 14 -12 -23 -3 -20 -1 0 2 -17 -15 12	GLY -24 -1 -20 24 7 18 -2 -11 -12 -6 -31 -25 -26 -28 -28 -23 -23 -23 -23 -23 -23 -21 -17 -10 -10 -10 -10 -10 -10 -10 -20 -24 -21 -20 -21 -20 -20 -20 -20 -20 -20 -20 -20 -20 -20	GLU -15 -10 -19 23 17 23 -1 -23 -1 -23 -18 8 -20 -34 -11 -26 -10 -34 -11 -26 -10 -34 -11 -21 -15 -10 -19 -19 -19 -19 -19 -19 -19 -19	ASP -22 -10 -18 50 33 28 5 -6 -17 13 -20 -16 -17 9 -4 -12 0 -12 0 -15 -12 -15 -15 -15 -15 -15 -15 -15 -15

Figure S5. Normal potential E_{norm} (top) and enrichment score ΔE_{enr} (bottom) for entangled contacts, with a minimum loop length $m_0 = 6$ instead of the value $m_0 = 10$ used in the main text (Fig. 7).