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Supplemental information

Differences in local anaesthetic and antiepileptic binding in the inactivated state of human sodium channel Nav1.4

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Supplementary Information for:

Differences in the binding of Local Anaesthetics and Anti-Epileptics in the inactivated state of the human sodium channel Nav1.4

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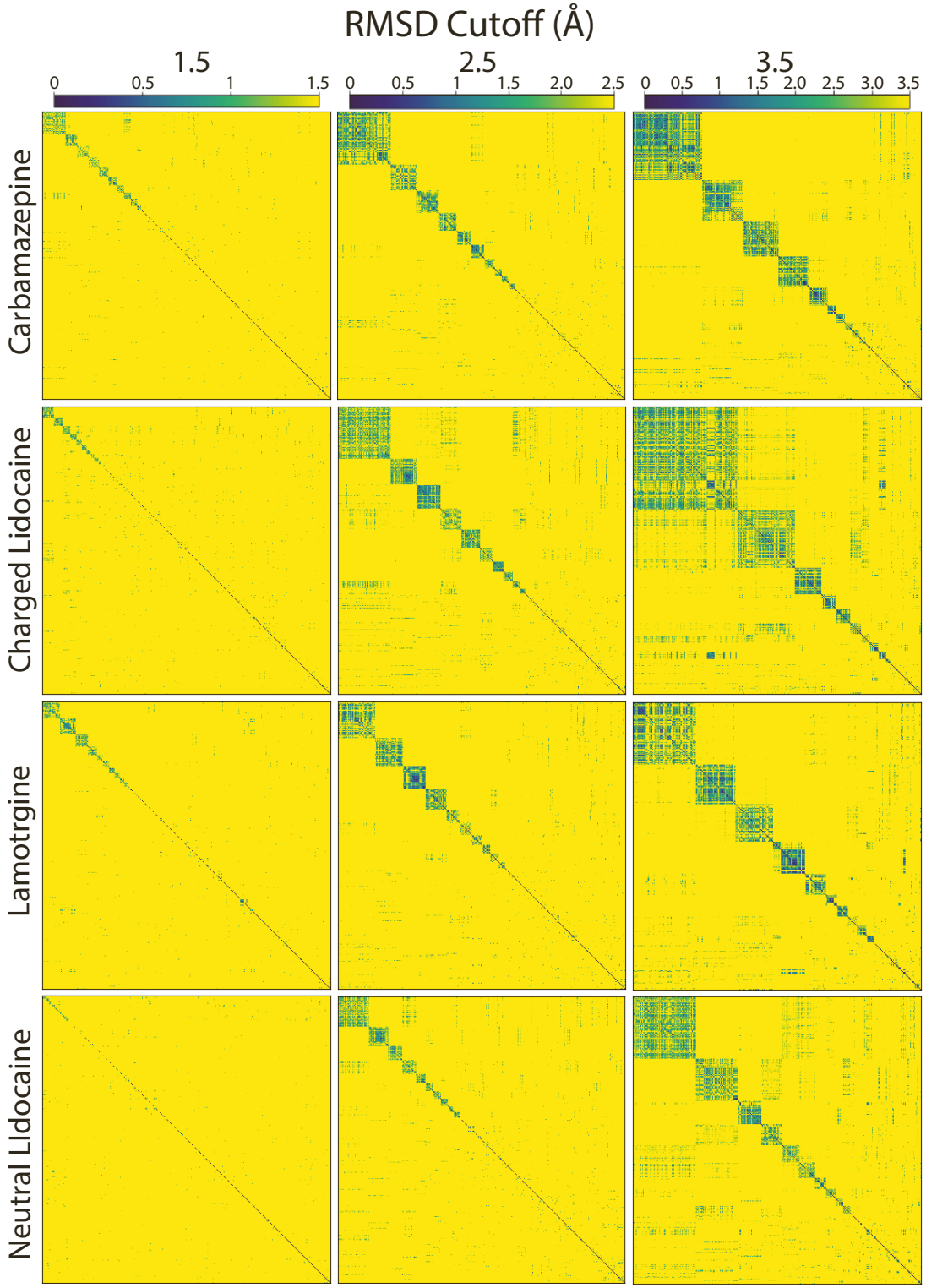

Figure S1. Clustering tendency of the dug poses. RMSD matrices of every frame with every other frame, with frames ordered by cluster membership. Results are shown for each drug using 1.5, 2.5 and 3.5Å cut offs for each compound. The number of frames on the x and y axes is 12,500.

Figure S2. Visualisation of the top 4 clusters of carbamazepine for four different clustering cut offs. Carbamazepine is in varying shades of yellow licorice, and the protein backbone is represented in grey cartoon.

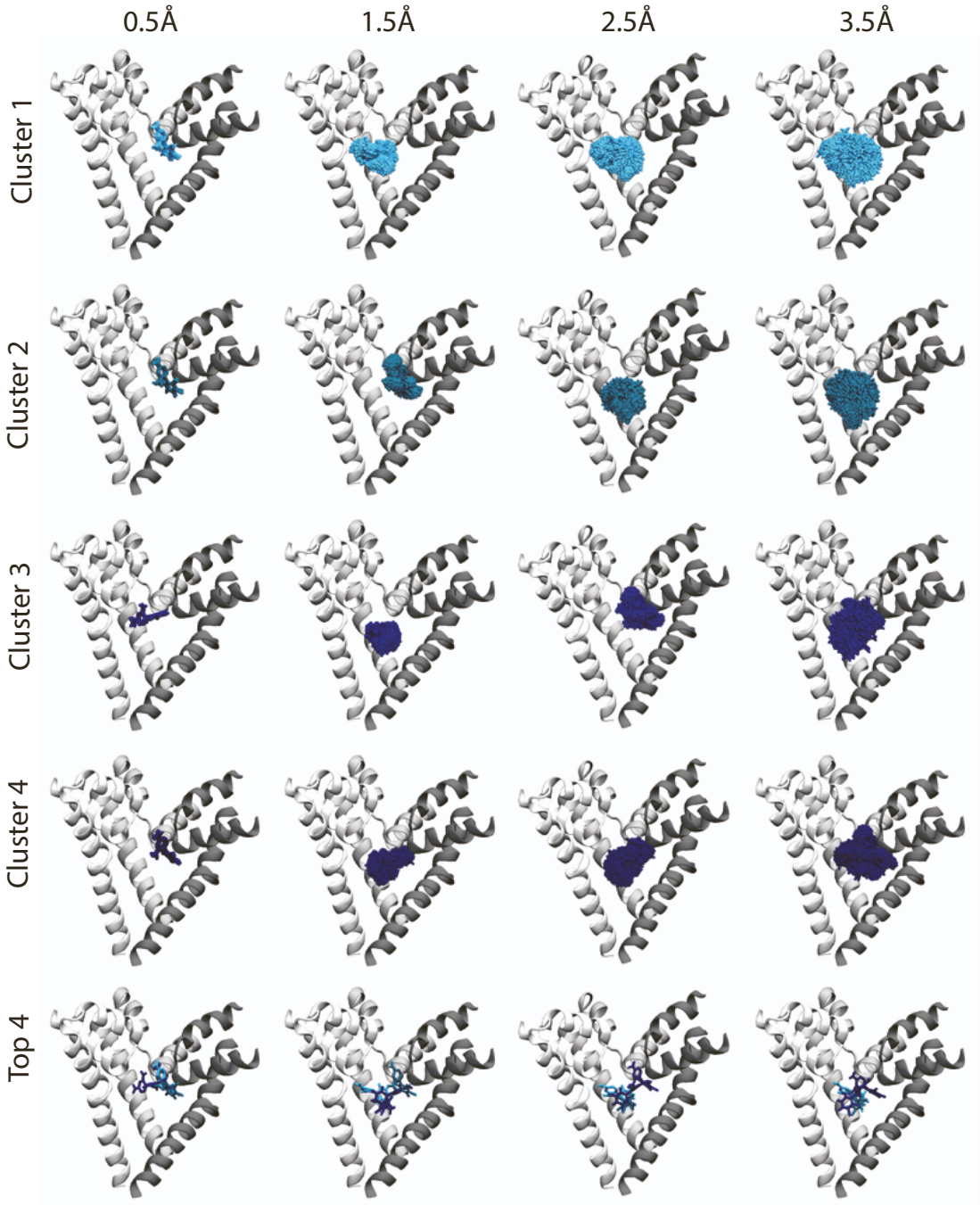

Figure S3. Visualisation of the top 4 clusters of lamotrigine for four different clustering cut offs. Lamotrigine is in varying shades of blue licorice, and the protein backbone is represented in grey cartoon.

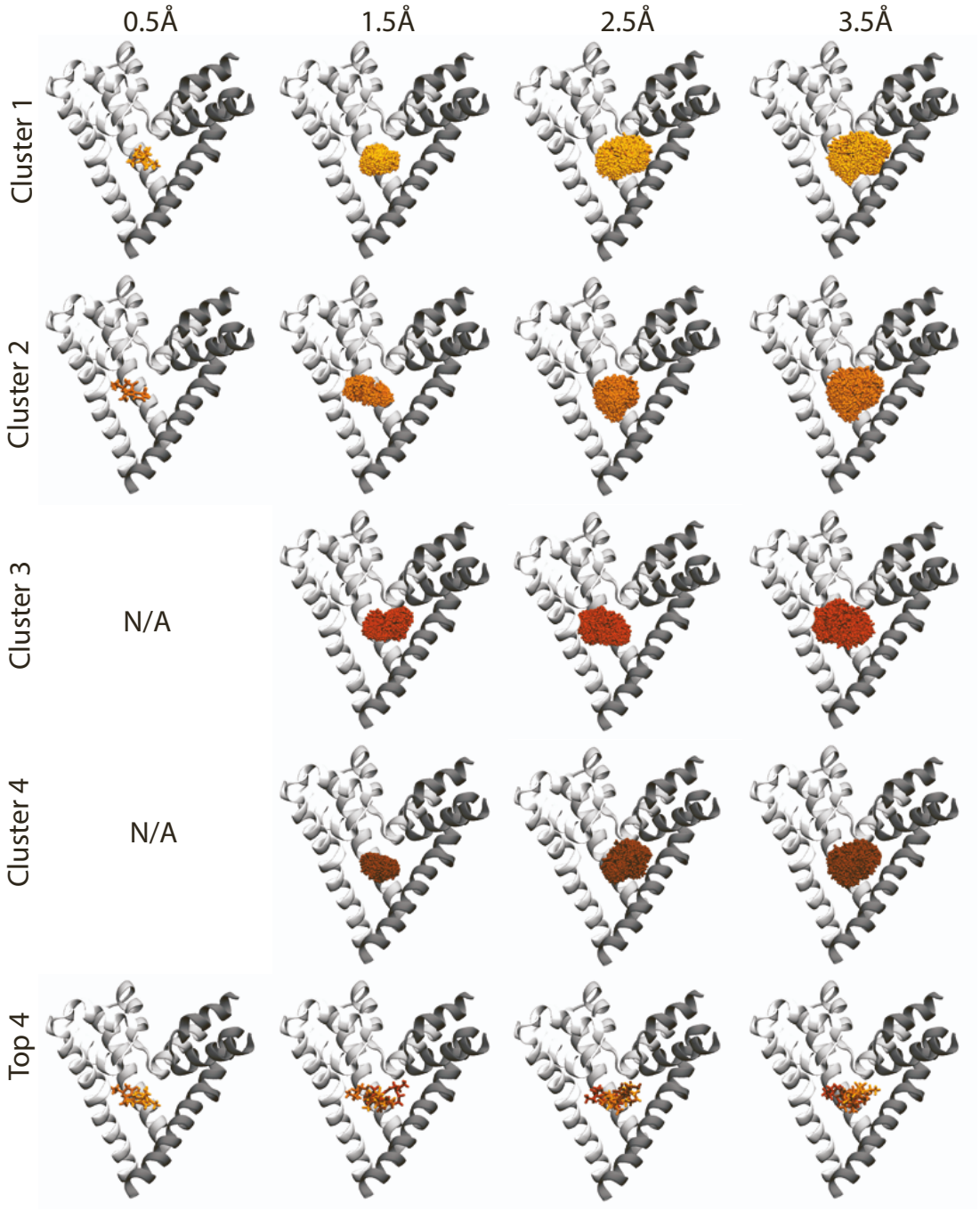

Figure S4. Visualisation of the top 4 clusters of neutral lidocaine for four different clustering cut offs. Neutral lidocaine is in varying shades of orange licorice, and the protein backbone is represented in grey cartoon.

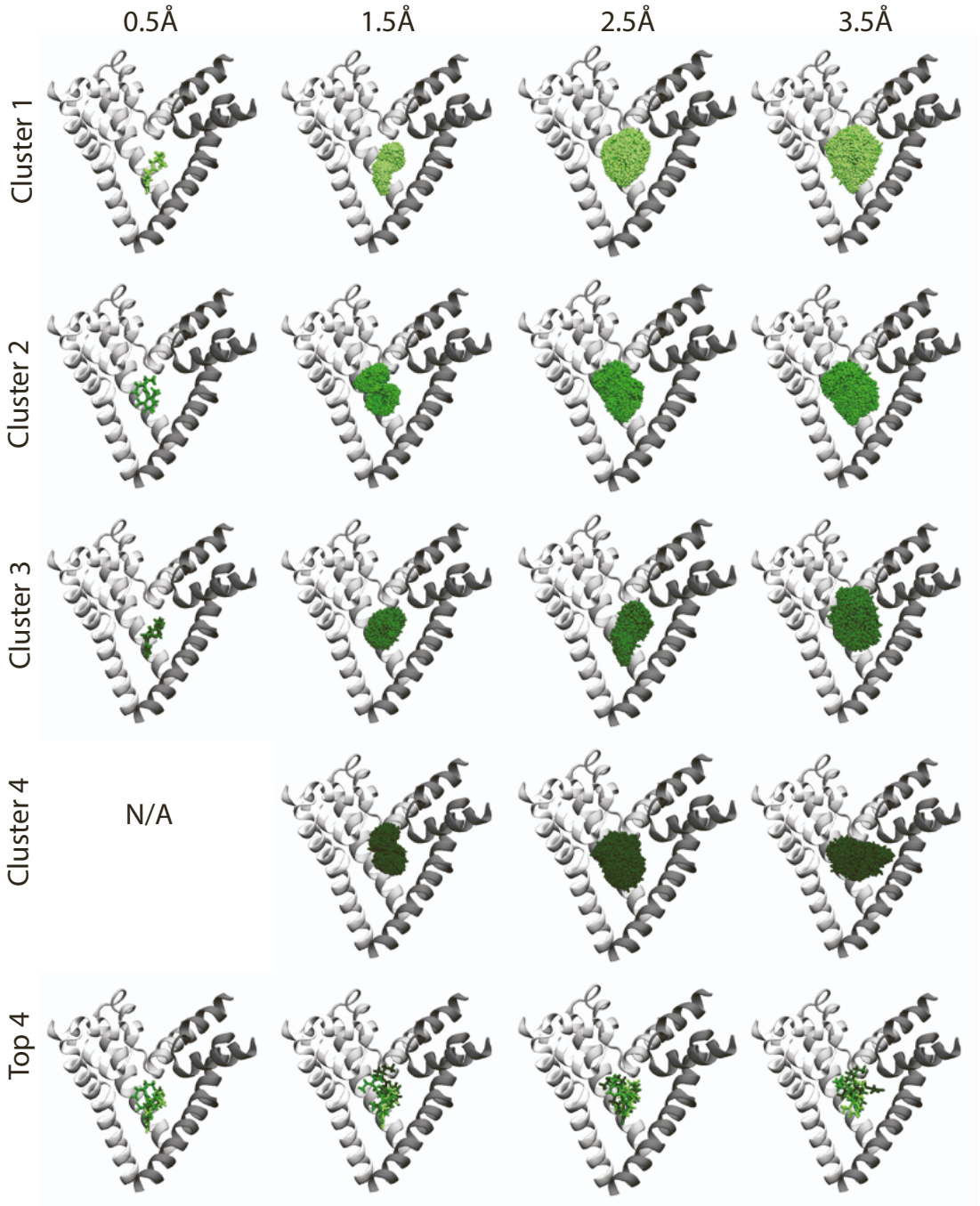

Figure S5. Visualisation of the top 4 clusters of charged lidocaine for four different clustering cutoffs. Charged lidocaine is in varying shades of orange licorice, and the protein backbone is represented in grey cartoon.

Cluster	1	2	3	4	5	6	7	8	9	10	5 to 10	LO
1	1.00	0.98	0.38	0.57	0.46	0.87	0.56	0.16	0.08	0.28	0.69	0.71
2		1.00	0.36	0.55	0.41	0.86	0.54	0.18	0.05	0.25	0.67	0.70
3			1.00	0.89	0.51	0.26	0.84	0.08	0.14	0.89	0.61	0.71
4				1.00	0.68	0.40	0.97	0.28	0.20	0.82	0.82	0.89
5					1.00	0.31	0.75	0.12	0.60	0.46	0.84	0.70
6						1.00	0.42	0.01	0.03	0.19	0.59	0.53
7							1.00	0.25	0.26	0.79	0.86	0.88
8								1.00	-0.03	0.09	0.44	0.51
9									1.00	0.08	0.47	0.32
10										1.00	0.57	0.64
5 to 10											1.00	0.94
LO												1.00

Table S1. Pearson correlation coefficients determined from the average per residue interaction energy for each of 10 clusters and leftover frames (LO) determined from the carbamazepine simulation.

Cluster	1	2	3	4	5	6	7	8	9	10	5 to 10	LO
1	1.00	0.37	0.37	-0.07	0.51	0.80	0.27	0.34	0.02	0.10	0.60	0.65
2		1.00	0.01	0.32	0.42	0.43	0.11	0.16	0.13	0.10	0.40	0.60
3			1.00	-0.23	0.48	0.35	0.51	-0.04	-0.19	0.15	0.41	0.53
4				1.00	-0.05	-0.12	0.26	-0.03	0.77	0.62	0.39	0.36
5					1.00	0.68	0.31	0.05	-0.02	0.04	0.65	0.73
6						1.00	0.24	0.38	-0.10	0.00	0.66	0.66
7							1.00	-0.06	0.34	0.37	0.66	0.61
8								1.00	-0.02	-0.04	0.34	0.19
9									1.00	0.76	0.53	0.35
10										1.00	0.60	0.40
5 to 10											1.00	0.88
LO												1.00

Table S2. Pearson correlation coefficients determined from the average per residue interaction energy for each of 10 clusters and leftover frames (LO) determined from the lamotrigine simulation.

Cluster	1	2	3	4	5	6	7	8	9	10	5 to 10	LO
1	1.00	0.85	0.59	0.93	0.80	0.91	0.83	0.83	0.88	0.88	0.93	0.93
2		1.00	0.71	0.80	0.95	0.89	0.92	0.83	0.67	0.93	0.96	0.91
3			1.00	0.49	0.67	0.53	0.60	0.54	0.64	0.78	0.69	0.71
4				1.00	0.74	0.91	0.76	0.84	0.74	0.79	0.87	0.91
5					1.00	0.77	0.96	0.87	0.58	0.87	0.95	0.87
6						1.00	0.79	0.77	0.76	0.85	0.90	0.90
7							1.00	0.88	0.57	0.87	0.95	0.87
8								1.00	0.59	0.76	0.91	0.89
9									1.00	0.75	0.75	0.80
10										1.00	0.94	0.90
5 to 10											1.00	0.96
LO												1.00

Table S3. Pearson correlation coefficients determined from the average per residue interaction energy for each of 10 clusters and leftover frames (LO) determined from the neutral lidocaine simulation.

Cluster	1	2	3	4	5	6	7	8	9	10	5 to 10	LO
1	1.00	0.85	0.92	0.87	0.75	0.83	0.85	0.64	0.93	0.85	0.89	0.18
2		1.00	0.82	0.95	0.71	0.98	0.65	0.72	0.70	0.89	0.88	0.07
3			1.00	0.79	0.61	0.79	0.81	0.56	0.82	0.76	0.78	0.28
4				1.00	0.78	0.97	0.69	0.78	0.79	0.91	0.94	0.14
5					1.00	0.74	0.60	0.36	0.59	0.94	0.93	0.04
6						1.00	0.68	0.72	0.69	0.90	0.91	0.10
7							1.00	0.49	0.81	0.67	0.75	0.23
8								1.00	0.72	0.53	0.62	0.15
9									1.00	0.68	0.77	0.25
10										1.00	0.98	0.04
5 to 10											1.00	0.10
LO												1.00

Table S4. Pearson correlation coefficients determined from the average per residue interaction energy for each of 10 clusters and leftover frames (LO) determined from the charged lidocaine simulation.