Electronic Supplementary Information for

RBD spatial orientation of the spike protein and its binding to ACE2: insight into high infectivity of SARS-CoV-2 Delta variant from MD simulations

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1. Estimation of the binding free energy by MM/GBSA

The molecular mechanics generalized Born surface area (MM/GBSA) approach has been widely used in prediction of the binding free energy for the protein folding, protein-ligand binding, protein-protein interaction.[1,2] A variety of GB models are available in Amber software for MM/GBSA calculations.[3] Generally, the first modification model developed by Onufriev et al is the best for the protein-small molecule and protein-protein systems,[4] and thus this model is used to calculate the binding free energy here.

It is worth mentioning that when calculating the interaction of C-RBD with A-RBD, the receptor is the entire complex of protomer A and ACE2, and the ligands are protomers B and C. Since the interaction of protomer B/C with protomer A is not restricted to the B-NTD/C-RBD domain, in calculation of the binding free energy of C-RBD and A-RBD, only the total energy of residues in the range of 402-409, 415-419, 444-458, 471-505 of progenitor C was counted. Similarly, when calculating the binding free energy of B-NTD and A-RBD, only the total energy of residues in the range of 164-171, 229-233 of progenitor B was counted.

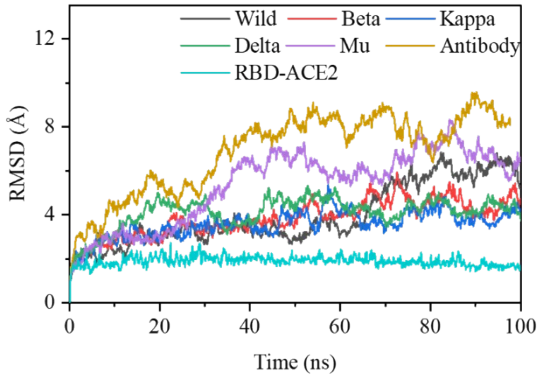

Figure S1. The RMSDs from molecular dynamics trajectories for all the systems.

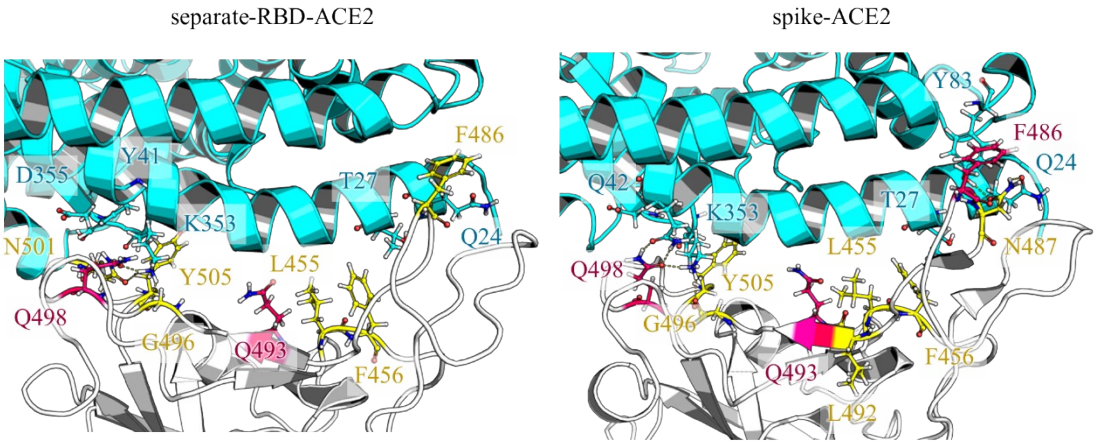

Figure S2. Schematic diagram of the residue interaction patterns of separate-RBD-ACE2 (Model 1) and spike-ACE2 (Model 2). The key residues in RBD with the energy contribution greater than 4 kcal/mol are colored red, and those with the energy contribution greater than 2 kcal/mol are colored yellow. The key residues in ACE2 are colored cyan, and there are no key residues in ACE2 with the energy contribution greater than 4 kcal/mol in both models.

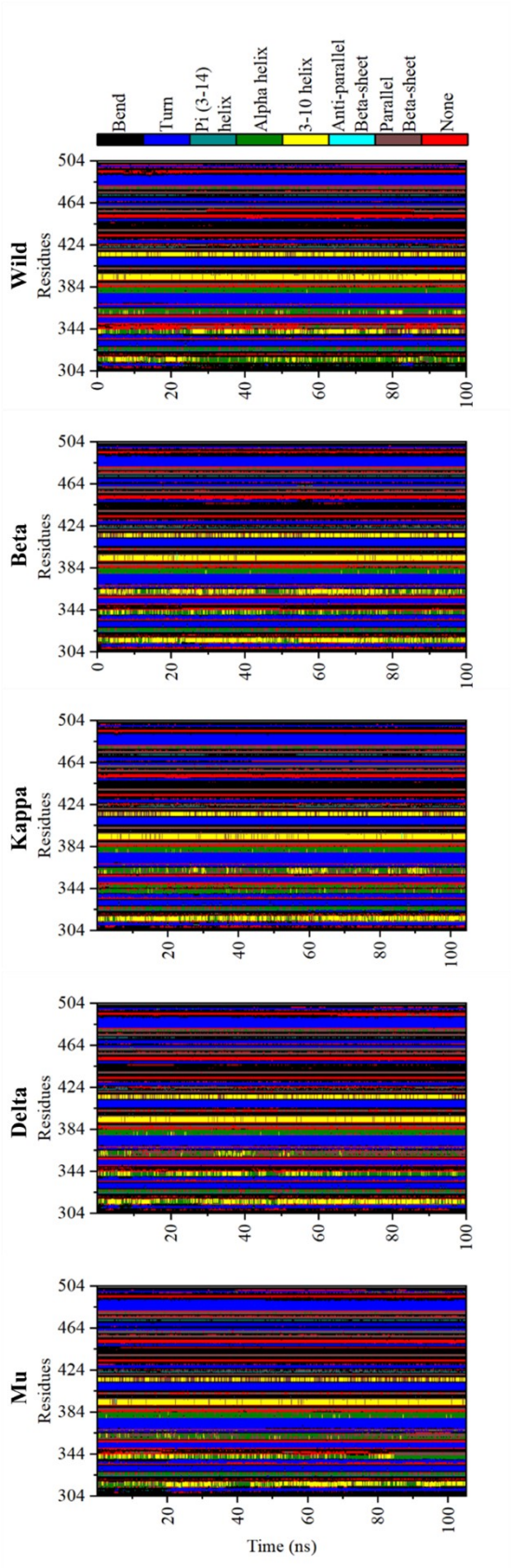

Figure S3. DSSP analysis of the RBD domain for all models.

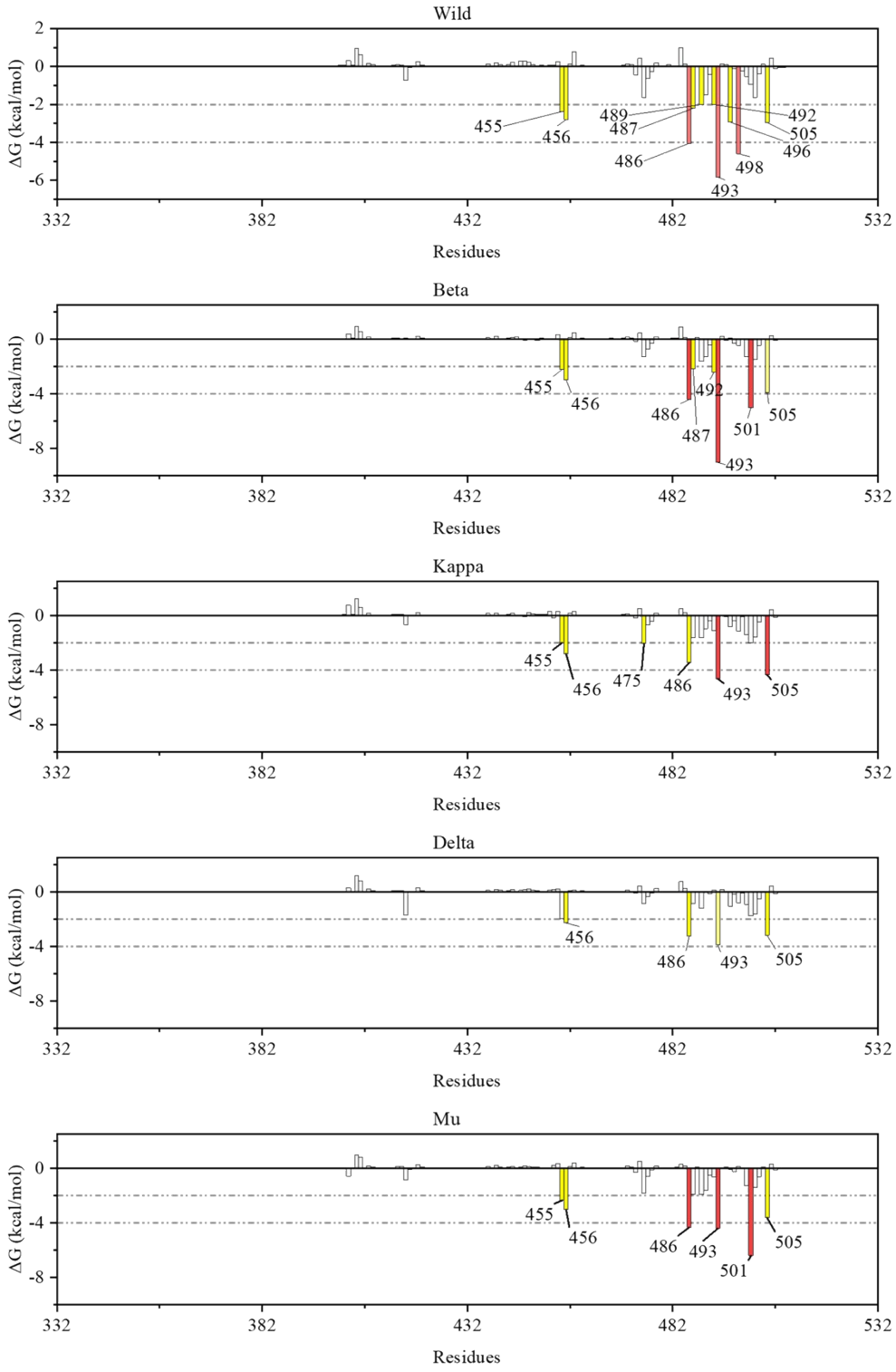

Figure S4. Per-residue energy decomposition diagrams of the spike (wild/mutant) RBD-ACE2 complex. A schematic of the protein surface is shown on the right. Residues with the energy contribution below -4 kcal/mol are colored red and those below –2 kcal/mol are colored yellow.

Table S1. Missing residues in the crystal structure

PDB ID	Missing residues
6lzg	None
7a94	71-75, 625-632, 677-688, 828-852, 941-943

Table S2. Hydrogen bonding analysis of separate-RBD-ACE2 complex (Model 1) and the spike-ACE2 complex (Model 2).

Model	Acceptor[a]	Donor[a]	Frequency
spike-ACE2	r-ASN_487@OD1	a-TYR_83@OH	0.96
	a-LYS_353@O	r-GLY_502@N	0.85
	r-GLN_498@OE1	a-LYS_353@NZ	0.81
	a-ASP_355@OD2	r-THR_500@OG1	0.80
	a-TYR_83@OH[b]	r-TYR_489@OH	0.78
	r-GLN_493@OE1	a-LYS_31@NZ	0.74
	a-GLU_35@OE1(2)	r-GLN_493@NE2	0.72
	r-GLY_496@O	a-LYS_353@NZ	0.56
	a-GLN_42@OE1	r-GLN_498@NE2	0.50
	r-GLN_498@OE1	a-GLN_42@NE2	0.49
	a-GLN_24@OE1	r-ASN_487@ND2	0.42
	a-ALA_386@O	r-TYR_505@OH	0.31
separate-RBD-ACE2	r-ASN_487@OD1	a-TYR_83@OH	0.81
	a-LYS_353@O	r-GLY_502@N	0.81
	a-GLU_35@OE1(2)	r-GLN_493@NE2	0.83
	r-GLN_498@OE1	a-LYS_353@NZ	0.69
	a-ASP_355@OD1	r-THR_500@OG1	0.68
	a-ASP_38@OD2	r-GLN_498@NE2	0.42
	r-GLY_496@O	a-LYS_353@NZ	0.41
	r-GLN_493@OE1	a-LYS_31@NZ	0.39

	r-ALA_475@O	a-SER_19@OG	0.35
	a-GLU_37@OE2	r-TYR_505@OH	0.34

[a] "r-" represents the residues of the RBD domain, "a-" represents the residues of the ACE2 protein.
[b] Hydrogen bonds that are not present in both models are marked in red.

Table S3. Energy decomposition of key residues in the RBD domain

Model	Serial	van der Waals	Electrostatic	Polar Solvation	Non-Polar Solv.	Total
WT	493	-2.21	-18.84	15.84	-0.61	-5.82
	498	-1.88	-9.72	7.52	-0.51	-4.60
	486	-4.50	-3.31	4.58	-0.81	-4.04
	505	-4.17	-5.48	7.52	-0.82	-2.95
	496	-0.68	-4.52	2.45	-0.18	-2.94
	456	-2.73	-0.58	0.90	-0.38	-2.79
	455	-2.83	1.46	-0.74	-0.27	-2.37
	487	-1.48	-6.82	6.32	-0.23	-2.21
	489	-4.04	-2.91	5.58	-0.64	-2.01
	492	0.06	-5.40	3.35	-0.01	-2.00
Beta	493	-2.60	-25.77	20.02	-0.67	-9.03
	501	-5.02	-3.24	3.72	-0.48	-5.03
	486	-4.90	-2.94	4.25	-0.83	-4.42
	505	-4.34	-5.58	6.76	-0.75	-3.91
	456	-2.98	-0.91	1.37	-0.45	-2.96
	492	0.13	-5.91	3.34	0.00	-2.44
	455	-2.74	1.22	-0.39	-0.32	-2.22
	487	-1.69	-6.17	5.94	-0.25	-2.17
Kappa	493	-2.04	-18.17	16.17	-0.61	-4.64
	505	-5.21	-6.87	8.62	-0.88	-4.33
	486	-4.10	-3.13	4.59	-0.81	-3.44
	456	-2.80	-1.10	1.48	-0.38	-2.80
	475	-1.84	-6.69	6.87	-0.38	-2.05

	501	-3.12	0.08	1.23	-0.19	-2.00
Delta	493	-1.87	-18.00	16.60	-0.60	-3.88
	486	-3.98	-2.51	4.09	-0.85	-3.25
	505	-4.49	-4.87	7.00	-0.82	-3.17
	456	-2.26	-0.68	1.03	-0.35	-2.26
Mu	501	-4.98	-4.92	3.97	-0.47	-6.40
	493	-2.01	-15.93	14.06	-0.54	-4.41
	486	-4.83	-2.91	4.25	-0.84	-4.33
	505	-3.26	-10.39	10.66	-0.63	-3.62
	456	-2.85	-0.50	0.68	-0.36	-3.04
	455	-2.78	1.03	-0.35	-0.26	-2.35

Table S4. The per-residue energy contribution for all system RBD domains

	Single RBD	WT	Beta	Kappa	Delta	Mu	Antibody
residue number	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)
331	——	-3.81E-04	-9.52E-05	-2.86E-04	-1.43E-04	1.43E-04	-2.11E-04
332	——	-1.43E-04	-2.38E-04	-1.90E-04	-4.76E-04	-2.38E-04	-1.58E-04
333	-0.00145	-1.43E-04	4.76E-05	-4.76E-05	-2.38E-04	-9.52E-05	-2.63E-04
334	-2.89E-04	-1.90E-04	-1.43E-04	-3.33E-04	-1.90E-04	-4.76E-05	-4.21E-04
335	-5.77E-04	-3.33E-04	-5.71E-04	-1.43E-04	-2.86E-04	-5.24E-04	-4.47E-04
336	-2.99E-04	-9.52E-05	-6.19E-04	-4.29E-04	-1.90E-04	-4.76E-04	-2.37E-04
337	-4.63E-04	-7.14E-04	-6.67E-04	-2.86E-04	-2.38E-04	-2.86E-04	-9.47E-04
338	-1.28E-03	-8.57E-04	-1.00E-03	-7.62E-04	-5.71E-04	-0.00114	-0.00197
339	-2.99E-05	-2.85E-15	3.33E-04	2.86E-04	9.52E-05	2.86E-04	-0.00108
340	0.0051	0.00738	0.00781	0.00867	0.00781	0.00857	-0.00408
341	0.00124	8.10E-04	0.0019	0.00219	0.00105	0.00195	0.00303
342	-0.00193	-0.0019	-0.00219	-0.00248	-0.00186	-0.00162	6.05E-04
343	-4.03E-04	-3.81E-04	-3.33E-04	1.90E-04	-3.33E-04	-8.57E-04	0.00566
344	7.61E-04	-3.33E-04	4.29E-04	0.00119	5.71E-04	0.00152	0.01608
345	0.00158	-4.29E-04	0.00186	0.00224	0.0019	0.00333	0.06845
346	-0.00712	-0.01043	-0.00948	-0.01443	-0.01676	-0.01629	0.31231
347	0.00802	0.00386	0.00676	0.00638	0.00467	0.00562	0.06355
348	0.00962	0.01586	0.01071	0.012	0.00886	0.00895	0.05253
349	0.01172	0.01105	0.01476	0.00929	0.00743	0.004	0.02889
350	0.02977	0.01581	0.01671	0.02067	0.00562	0.00514	0.01889

351	0.00139	-0.007	-0.03876	-0.00986	-9.05E-04	-0.00986	-0.03795
352	0.00249	0.0029	0.00276	0.00105	0.00186	0.00333	0.02426
353	-0.0089	-0.00667	-0.01029	-0.0099	-0.00671	-0.00814	-0.00574
354	-0.00175	-0.00129	-0.00171	-0.0021	-0.00167	-0.00129	0.02918
355	-0.00603	-0.01143	-0.01181	-0.01095	-0.01267	-0.01443	0.01134
356	-0.00589	-0.00986	-0.00905	-0.00857	-0.00895	-0.00933	0.00924
357	-0.00264	-0.00352	-0.00457	-0.00405	-0.00471	-0.00467	0.00403
358	-7.16E-04	-6.67E-04	-5.24E-04	-4.76E-04	-4.76E-04	-3.81E-04	-0.00108
359	-8.46E-05	-1.43E-04	-1.43E-04	-1.43E-04	-4.76E-05	1.43E-04	-4.21E-04
360	-2.19E-04	-1.43E-04	-4.29E-04	3.38E-16	4.76E-05	-3.33E-04	-3.42E-04
361	-2.89E-04	-2.86E-04	4.76E-05	-1.43E-04	-1.90E-04	-1.43E-04	-2.63E-04
362	-2.54E-04	4.76E-05	4.76E-05	-5.24E-04	-5.24E-04	-2.38E-04	-2.11E-04
363	-4.03E-04	-7.62E-04	-5.24E-04	-5.24E-04	-6.67E-04	-4.29E-04	-2.63E-04
364	0.00351	0.00524	0.00505	0.00495	0.00476	0.0059	-0.00247
365	-1.48E-03	-5.71E-04	-5.71E-04	-5.24E-04	-3.33E-04	-3.33E-04	-8.42E-04
366	-3.73E-04	-1.90E-04	1.43E-04	-1.90E-04	2.86E-04	4.76E-05	-4.21E-04
367	-3.68E-04	4.76E-05	2.86E-04	-4.76E-05	1.43E-04	3.81E-04	-2.89E-04
368	2.64E-04	4.29E-04	-6.67E-04	-7.62E-04	-7.62E-04	-5.24E-04	-5.26E-04
369	-8.66E-04	-0.00214	-0.00143	-0.00129	-0.00129	-0.00157	-6.05E-04
370	5.82E-04	0.00267	-1.90E-04	9.52E-05	-2.86E-04	-9.52E-05	-3.95E-04
371	0.00296	0.013	0.00129	0.0041	2.38E-04	0.00329	-3.95E-04
372	0.01277	0.007	0.00267	0.00986	4.29E-04	0.0061	-3.16E-04
373	0.01713	0.00424	0.02143	0.01119	0.026	0.0359	-4.74E-04
374	0.01238	0.01243	0.0099	0.01543	0.01381	0.00967	-7.11E-04
375	0.04083	0.05057	0.049	0.06829	0.04529	0.05414	-0.00103
376	0.02839	0.024	0.02319	0.03667	0.02929	0.0231	-0.00121
377	-7.16E-04	-0.00105	-4.29E-04	-9.52E-05	-1.43E-04	-6.19E-04	-8.16E-04
378	0.00821	0.01448	0.01557	0.01576	0.02462	0.00729	0.00492
379	-1.16E-03	-3.33E-04	-7.14E-04	-3.81E-04	-4.76E-04	-2.38E-04	-2.89E-04
380	-0.00339	-0.00676	-0.005	-0.00471	-0.00562	-0.00724	-7.89E-04
381	-6.82E-04	-0.00119	-0.00129	-0.00129	-0.00119	-0.00124	-2.63E-05
382	-5.32E-04	-3.81E-04	-4.76E-04	-4.76E-04	-4.76E-05	-2.38E-04	-3.68E-04
383	-6.62E-04	-3.33E-04	-4.76E-04	-4.76E-04	-4.76E-04	-5.24E-04	-1.32E-04
384	-0.00155	-0.00233	-0.00214	-0.00171	-0.0019	-0.00238	-2.11E-04
385	-6.87E-04	-9.05E-04	-5.71E-04	-0.00124	-6.67E-04	-0.00105	5.26E-05
386	-0.00346	-0.00443	-0.00467	-0.00395	-0.00452	-0.00519	7.63E-04
387	-6.27E-04	-0.00129	-0.00114	-8.57E-04	-5.71E-04	-0.00114	-5.26E-05
388	-4.68E-04	-6.67E-04	-9.52E-04	-5.71E-04	-1.43E-04	-4.29E-04	-1.05E-04
389	0.00153	0.00224	0.00257	0.00233	0.00238	0.00267	-8.16E-04
390	-4.33E-04	-8.57E-04	-4.29E-04	-5.24E-04	-5.24E-04	-5.71E-04	-2.89E-04
391	-2.29E-04	-4.29E-04	-4.76E-04	-3.81E-04	9.52E-05	-2.38E-04	-1.05E-04
392	-6.32E-04	-5.24E-04	-9.52E-04	-4.76E-04	-3.81E-04	-9.05E-04	-1.84E-04
393	-3.53E-04	-4.29E-04	-5.71E-04	-3.81E-04	-6.67E-04	-3.33E-04	-7.89E-05
394	-4.48E-04	-6.19E-04	-1.43E-04	-3.81E-04	-3.81E-04	-3.81E-04	1.05E-04

395	-3.03E-04	-3.33E-04	4.76E-05	-9.52E-05	4.76E-05	-3.33E-04	-5.26E-05
396	-9.20E-04	-8.10E-04	-9.05E-04	-1.00E-03	-8.10E-04	-9.05E-04	-5.79E-04
397	6.02E-04	5.71E-04	2.38E-04	8.57E-04	4.76E-04	4.29E-04	8.68E-04
398	0.0052	0.01271	0.01319	0.01105	0.01362	0.01629	-0.00968
399	0.003	0.00219	0.00271	0.00329	0.00129	0.00176	0.00766
400	-0.00286	-0.00462	-0.01071	-0.00443	-0.00657	-0.01005	0.00979
401	0.05866	0.06695	0.03648	0.05771	0.04476	0.0329	0.03279
402	0.07432	0.07652	0.0351	0.06476	0.051	0.026	0.01505
403	0.45037	0.30701	0.39639	0.69759	0.30305	-0.58279	0.09095
404	0.05991	0.063	0.07476	0.10271	0.07233	0.06543	1.58E-04
405	0.90471	0.9595	0.94895	1.01716	1.2023	0.99475	-0.01674
406	0.55624	0.61	0.57386	0.70131	0.80164	0.81976	0.01032
407	0.01802	0.02281	0.02224	0.01548	0.01976	0.02948	-6.84E-04
408	0.2231	0.18017	0.18393	0.14728	0.23819	0.19433	0.01882
409	0.08149	0.09462	0.05533	0.07652	0.08905	0.09148	0.00221
410	2.94E-04	-2.38E-04	7.62E-04	0.00176	0.00248	0.0011	-0.00161
411	4.98E-04	0.00119	0.00352	2.38E-04	0.00281	0.00414	-0.00142
412	-4.63E-04	0.00167	6.67E-04	0.00271	0.00314	0.0039	-0.00105
413	0.01513	0.01614	0.01157	0.01348	0.00533	0.01157	-2.37E-04
414	0.08052	0.06657	0.0879	0.08048	0.09124	0.05457	-6.84E-04
415	0.098	0.09819	0.10757	0.10819	0.10714	0.12	0.00163
416	0.11474	0.07343	0.05576	0.09243	0.09619	0.12533	0.00424
417	-0.83729	-0.7188	0.11343	-1.26789	-1.71191	-0.8434	0.11553
418	-0.05745	-0.05919	-0.03857	-0.03757	-0.04433	-0.0601	-0.01205
419	0.00264	0.00729	0.01157	0.00276	9.05E-04	0.00967	2.63E-05
420	0.17511	0.25943	0.23729	0.2349	0.30033	0.27776	-0.01513
421	0.09132	0.07574	0.11471	0.07505	0.08489	0.07958	0.01132
422	0.03863	0.04638	0.05143	0.03886	0.0349	0.04562	0.01484
423	7.06E-04	0.00362	0.00243	6.67E-04	0.0051	0.00571	-0.00579
424	0.05381	0.04795	0.04129	0.04238	0.04252	0.05062	0.01405
425	5.57E-04	0.00157	0.00119	0.00233	0.00214	0.00281	-0.00124
426	-0.00519	-0.00524	-0.00557	-0.00552	-0.0049	-0.00557	-0.00211
427	0.00623	0.01238	0.02038	0.0189	0.02524	0.02981	-0.00689
428	0.00147	0.00529	0.00629	0.00505	0.00695	0.00738	-0.00358
429	-0.0042	-0.00414	-0.005	-0.00505	-0.00538	-0.00519	-0.00108
430	-6.62E-04	-4.29E-04	-6.67E-04	-4.29E-04	-3.81E-04	-3.33E-04	-2.37E-04
431	9.45E-05	1.43E-04	1.43E-04	3.33E-04	3.33E-04	1.90E-04	2.63E-04
432	8.86E-04	0.00114	0.00148	0.00214	8.57E-04	0.0011	2.63E-04
433	0.00342	0.00462	0.00457	0.005	0.00295	0.00348	0.00155
434	3.08E-04	4.76E-04	0.00105	0.00248	4.29E-04	7.62E-04	-0.00179
435	0.00942	0.00629	0.00757	0.00943	0.00705	0.006	0.00232
436	0.00928	0.00876	0.00371	0.01233	0.00533	0.00638	-0.001
437	0.16653	0.13966	0.13218	0.17586	0.13671	0.15705	0.01666
438	0.0041	0.0071	-1.90E-04	0.00919	0.01105	0.00838	-0.01274

439	0.23023	0.20405	0.21558	0.1951	0.19829	0.22843	0.04466
440	0.10398	0.10852	0.05405	0.08481	0.12829	0.10905	0.06561
441	0.04552	0.04043	0.03552	0.04376	0.03852	0.03186	0.04982
442	0.09082	0.08986	0.07876	0.10138	0.09343	0.09519	-2.89E-04
443	0.12358	0.24086	0.11814	0.20048	0.17295	0.11743	0.15016
444	0.13756	0.0369	0.18662	0.04852	0.05381	0.06967	-0.76003
445	0.16505	0.29673	0.0625	0.00746	0.12944	0.11515	0.04848
446	0.09335	0.27919	-0.05646	-0.09429	0.16062	0.19422	0.24869
447	0.23644	0.21855	0.04138	0.23333	0.22436	0.12843	-1.05371
448	0.0541	0.10924	0.07257	0.144	0.12986	0.0869	-1.58152
449	-0.86713	0.00501	-0.0786	0.04848	0.08228	0.11011	-5.04708
450	0.1019	0.08314	0.08162	0.07943	0.06486	0.06371	-2.15832
451	0.01259	0.04143	0.03095	0.07186	0.06324	0.04276	0.01279
452	0.05424	0.08881	0.06852	0.30233	0.14453	0.04433	-1.1207
453	-0.17113	0.08467	-0.03864	0.15071	0.17155	0.23863	-0.08074
454	0.28249	0.24519	0.35048	0.30776	0.22367	0.36281	0.28239
455	-2.06835	-2.3712	-2.22481	-2.15846	-1.97899	-2.35446	0.02663
456	-2.15825	-2.79249	-2.96262	-2.71346	-2.25838	-3.03773	0.01997
457	0.17328	0.14862	0.15313	0.17208	0.10671	0.15581	0.07139
458	0.2844	0.78084	0.49215	0.14909	0.14003	0.40044	0.06958
459	0.02312	0.0211	0.02138	0.02581	0.01648	0.01605	-0.00321
460	0.06685	0.08557	0.09324	0.06776	0.11038	0.111	0.00576
461	0.00549	0.00619	0.01062	0.00919	0.00633	0.0091	0.00329
462	0.00363	0.00129	-0.00186	-9.52E-05	-0.00738	0.00143	0.00982
463	-0.00148	-0.0021	-0.00233	-0.00167	-0.00205	-0.00195	-3.95E-04
464	-0.00186	-0.0031	-0.00386	-0.0031	-0.00352	-0.00414	-9.00E-16
465	0.00865	0.0271	0.02595	0.02214	0.03148	0.03157	-0.01013
466	1.40E-02	-0.00119	-1.43E-04	0.00548	-0.00519	-0.006	0.08808
467	0.01426	-0.00381	0.07681	0.02819	0.02462	-0.01581	0.00332
468	0.00929	0.003	0.0109	0.00824	0.002	0.00467	0.04503
469	5.07E-04	0.05081	0.01771	0.04281	0.02943	0.0399	0.05216
470	0.06337	0.06276	0.093	0.0719	0.05652	0.06005	0.0209
471	0.09064	0.14486	0.16724	0.1249	0.12352	0.17557	0.25834
472	0.04129	0.09995	0.07586	0.05871	0.03943	0.10324	-0.4397
473	-0.00246	-0.44322	-0.14582	-0.13398	-0.09603	-0.30304	-0.00474
474	0.5292	0.43366	0.45705	0.59041	0.43548	0.52043	0.08511
475	-1.63128	-1.63942	-1.2897	-2.23954	-0.85374	-1.83257	0.02482
476	-0.48078	-0.61331	-0.71309	-0.63403	-0.32161	-0.58074	0.02647
477	-0.29646	-0.2504	-0.27601	-0.2132	-0.05655	-0.11257	0.03718
478	0.21845	0.192	0.18973	0.21567	0.26247	0.1739	0.10792
479	0.04004	0.03967	0.06243	0.05029	0.04667	0.05557	0.12013
480	0.02303	0.01524	0.01629	0.0049	0.00838	0.01043	0.14716
481	0.08901	0.09714	0.07081	0.06043	0.05395	0.06081	0.3813
482	0.05747	0.05567	0.07848	0.05638	0.05148	0.06857	0.25918

483	0.05807	0.05781	0.08452	0.07067	0.04505	0.08876	-2.76312
484	0.84614	0.98955	0.90444	0.43575	0.75958	0.29329	-3.32576
485	0.20292	0.14607	0.15317	0.23565	0.27234	0.18347	-0.08542
486	-3.82353	-4.04292	-4.41666	-3.50107	-3.24633	-4.32962	-0.32485
487	-1.32597	-2.20791	-2.16618	-1.66864	-0.85287	-1.93459	0.13108
488	0.0612	0.02962	0.11833	0.0669	0.03957	0.09981	0.03384
489	-1.14687	-2.00862	-1.62646	-1.42674	-1.18843	-1.90161	0.13078
490	0.05713	-1.48937	-1.28474	-0.63079	0.02413	-1.60536	-3.43542
491	-0.13328	-0.41257	-0.42671	-0.31505	-0.1359	-0.50224	-0.22034
492	0.1139	-2.00086	-2.44256	-0.88666	0.11674	-0.62813	-0.19071
493	-4.55598	-5.82158	-9.02663	-4.57771	-3.875	-4.40987	0.17209
494	0.39998	0.1494	0.22559	0.14706	0.18532	0.06539	-0.17651
495	-0.19028	0.10741	-0.09059	-0.02281	-0.02176	0.07531	0.02474
496	-2.07595	-2.93525	0.09558	-0.92229	-1.04068	-0.06571	0.06732
497	-0.38087	-0.10462	-0.29376	-0.35371	-0.16938	-0.238	-0.23303
498	-6.17336	-4.59987	-0.44085	-1.12713	-0.7749	0.13703	0.22182
499	-0.19581	-0.2297	-0.03515	-0.07735	-0.07623	0.00654	-0.01589
500	-0.80882	-0.52327	-1.26204	-1.41992	-0.90678	-1.28147	0.04789
501	-3.88672	-0.95696	-5.02587	-1.98487	-1.75762	-6.40497	0.08655
502	-1.71101	-1.63859	-1.49097	-1.55511	-1.60407	-1.38979	-0.01334
503	-0.36386	-0.38541	-0.44956	-0.40696	-0.49907	-0.62477	-2.89E-04
504	0.12245	0.13058	0.05435	0.03402	0.06969	0.10209	0.00363
505	-3.68303	-2.95146	-3.90673	-4.36109	-3.17128	-3.61858	0.04774
506	0.43987	0.45429	0.2647	0.45069	0.43375	0.3215	0.05692
507	-0.15616	-0.12414	-0.09029	-0.13205	-0.11219	-0.10267	-0.01518
508	-0.04436	-0.03405	-0.0231	-0.0511	-0.02681	-0.01776	-0.01371
509	-0.0255	-0.0351	-0.03167	-0.039	-0.03729	-0.03324	0.05989
510	7.41E-04	0.002	5.24E-04	0.0021	4.76E-04	7.62E-04	-1.84E-04
511	-7.31E-04	-2.86E-04	-5.24E-04	-8.10E-04	-8.10E-04	8.57E-04	-2.63E-04
512	-2.44E-04	-4.29E-04	-2.38E-04	1.43E-04	1.43E-04	2.86E-04	-4.21E-04
513	-0.00194	-0.00143	-0.00133	-0.00138	-0.00162	-0.00138	-0.00121
514	-0.0011	-0.00157	-0.00162	-0.00148	-0.00157	-0.00138	-7.11E-04
515	-0.00103	-0.00114	-0.00114	-0.00129	-0.00162	-0.00143	-7.63E-04
516	0.00129	0.003	0.00338	0.00333	0.00448	0.00505	-0.00505
517	-8.86E-04	-3.81E-04	-5.71E-04	-3.33E-04	-1.90E-04	-5.71E-04	-3.95E-04
518	-4.43E-04	-2.38E-04	-3.33E-04	-3.33E-04	-2.86E-04	-4.76E-04	-1.05E-04
519	-2.89E-04	-9.52E-05	-2.38E-04	-1.90E-04	-3.33E-04	-2.86E-04	-7.89E-05
520	-8.46E-05	-1.43E-04	-4.76E-05	9.52E-05	-2.45E-15	-4.29E-04	8.88E-16
521	-2.09E-04	-2.38E-04	-1.43E-04	-4.76E-05	-1.43E-04	4.76E-05	-3.16E-04
522	-1.04E-04	-2.38E-04	-3.33E-04	-3.33E-04	-4.29E-04	-3.81E-04	1.05E-04
523	-2.14E-04	-3.81E-04	-2.86E-04	-1.69E-16	-2.86E-04	-9.52E-05	-1.05E-04
524	-3.53E-04	-2.38E-04	-4.76E-04	-3.81E-04	-5.24E-04	-3.33E-04	-2.89E-04
525	-2.34E-04	-2.86E-04	-1.43E-04	-9.52E-05	-4.29E-04	-9.52E-05	-3.42E-04
526	-3.53E-04	-9.52E-05	-1.90E-04	1.43E-04	9.52E-05	1.14E-15	-2.11E-04

527	0.0016	-3.38E-16	-1.18E-15	-2.38E-04	-6.77E-16	1.90E-04	-2.89E-04
528	——	-0.00205	-0.00252	-0.002	-0.0019	-0.00262	6.05E-04

Table S5. The per-residue energy contribution for all system C-RBD domains

	WT	Beta	Kappa	Delta	Mu
residue number	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)	energy (kcal/mol)
402	0.03195	0.03052	0.05286	0.07457	0.03557
403	-5.53673	0.85896	1.35894	-2.04619	0.72956
404	0.01962	0.04738	0.02267	0.02176	0.01571
405	0.96976	0.92569	0.70666	0.4481	1.26026
406	0.47264	0.5243	0.25911	0.94725	0.7246
407	0.01919	0.0271	0.02719	-0.00157	0.02676
408	0.07494	0.30909	0.27062	0.14552	0.0162
409	0.10376	0.1299	0.15301	0.12238	0.10748
415	0.14914	0.24962	0.24074	0.21933	0.1831
416	0.08705	0.2893	0.16012	0.15387	0.15171
417	0.92864	-0.16809	1.69502	-0.66698	2.35013
418	-0.08757	-0.07457	-0.08405	-0.11281	-0.06024
419	0.05195	0.05305	0.03014	0.05171	0.04576
444	0.24367	0.27229	0.12524	0.31919	0.47167
445	0.10607	0.17213	0.38101	0.29355	0.29043
446	0.16891	0.16459	0.01222	-0.36297	0.06932
447	0.12759	0.13119	0.17369	0.01311	0.1376
448	0.08095	0.07571	0.1279	0.08086	0.0979
449	0.13031	0.33975	0.24612	-0.10042	0.16399
450	0.09052	0.12129	0.12824	0.14281	0.14038
451	0.02152	0.00105	0.05305	0.01676	0.02329
452	0.04462	0.04986	0.3306	0.37343	0.05181
453	0.11217	0.06275	-0.0821	-0.85307	0.05935
454	0.69619	0.45957	0.35029	0.77862	0.47076
455	-2.30363	-1.42396	-1.55756	-3.83302	-1.63082
456	-2.14709	-1.57019	-1.43812	-1.94566	-1.50439
457	0.56106	0.58204	0.53662	0.54594	0.59283
458	0.41259	0.43529	0.30162	0.33365	0.32964
471	0.40403	0.3379	0.05395	0.35143	0.34371
472	0.024	0.00948	0.01133	-0.01129	0.000286
473	0.13267	0.1533	0.01308	-0.44993	-0.29068
474	0.45505	0.23971	0.24657	0.27329	0.21508
475	-0.2596	-0.12924	-0.17086	-0.74436	-0.13053
476	-0.40245	0.11961	0.10185	-0.69249	0.02591
477	-0.65452	0.1883	0.14933	-0.06888	0.20126

478	0.06372	0.18738	0.15186	-0.35899	0.1191
479	0.03948	0.04995	0.0479	0.04978	0.04176
480	0.04357	0.02424	0.02395	0.02119	0.0191
481	0.15952	0.06114	0.06519	0.10581	0.05395
482	0.0799	0.04671	0.0839	0.08557	0.04838
483	0.05556	0.04052	0.02758	0.04395	0.04767
484	0.7172	0.62586	-0.56797	1.42527	0.59095
485	0.20453	0.1264	-0.84582	0.08196	0.16676
486	-3.68562	-4.2962	-3.73149	-7.38799	-4.89712
487	-0.97351	-0.26955	-0.84214	-3.90715	-0.16126
488	-0.00992	-0.04948	-0.25514	-0.2171	-0.02457
489	-0.61668	-0.57251	-1.81155	-2.18944	-1.50791
490	0.13314	0.16638	0.1089	0.17235	0.14533
491	0.013	-0.09957	-0.09086	-0.28123	-0.13843
492	0.12181	0.15333	0.20316	0.27645	0.1749
493	0.27998	0.31931	-0.19615	-1.46042	-0.07288
494	0.19566	0.04614	0.26847	0.23334	0.07983
495	0.0379	0.04367	0.00644	0.0306	0.09055
496	0.11348	0.11656	0.17648	-0.0856	0.04792
497	-0.13814	-0.12329	-0.23886	-0.24257	-0.112
498	-0.39508	-0.52632	-0.62009	-2.51056	-0.39359
499	-0.01637	-0.03342	-0.09789	-0.13414	-0.01181
500	0.44582	-0.64586	-0.03415	-0.3094	-1.93851
501	0.21633	-1.10418	-3.07494	-1.41866	-2.68668
502	-0.18966	-0.83751	-1.78131	-0.96858	-1.10453
503	-0.01114	-0.23627	-0.14048	0.02519	-0.05019
504	-0.18764	-0.37097	-0.06568	-0.07086	0.03107
505	-2.00305	-2.04549	-3.33076	-1.89596	-1.93892

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