Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Origin of the Tight Binding Mode to ACE2 triggered by Multi-point Mutations in Omicron Variant: a Dynamic Insight

*Xiaoyu Zhao, Danyang Xiong, Song Luo, Lili Duan**

School of Physics and Electronics, Shandong Normal University, Jinan, 250014, China

Corresponding author (duanll@sdnu.edu.cn)

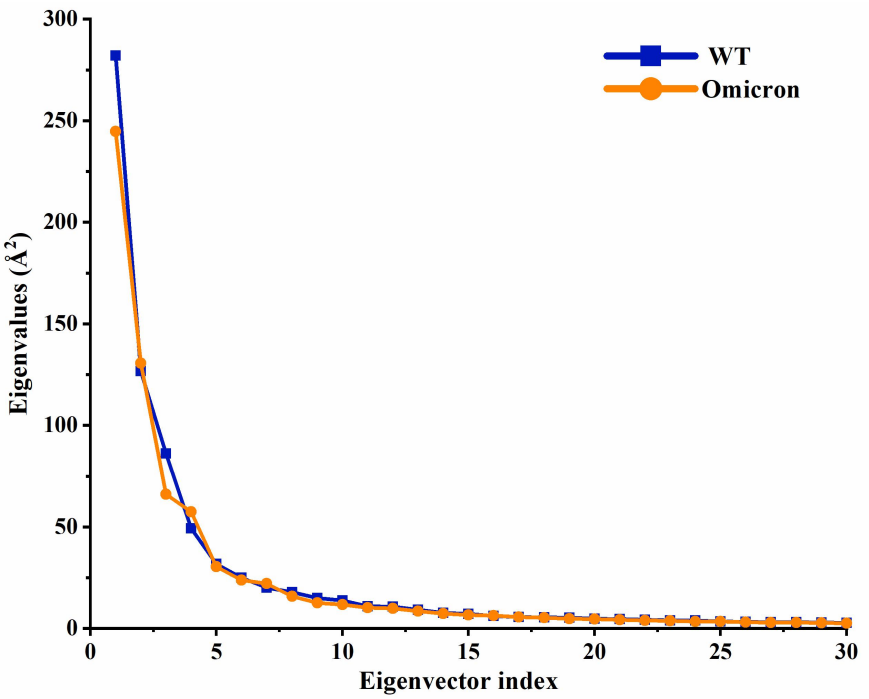

Figure S1. The eigenvalues of the top 30 eigenvectors for WT and Omicron variant, respectively.

Table S1. The energy contribution for all residues of RBD for WT within 10 Å from the binding interface obtained by the ASIE method. All values are in kcal/mol.

Systems	Residues	$\Delta\Delta E_{vdW}$	$\Delta\Delta E_{ele}$	$\Delta\Delta G_{GB}$	$\Delta\Delta G_{SA}$	$\Delta\Delta H$	$-T\Delta\Delta S$	$\Delta\Delta G_{bind}$
	G339	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	S371	0.00	0.01	-0.01	0.00	0.00	0.03	0.03
	S373	0.00	0.06	-0.06	0.00	0.00	0.07	0.08
	S375	0.00	-0.24	0.23	0.00	-0.01	0.03	0.03
	R403	-1.41	-55.75	52.32	-0.13	-4.98	0.94	-4.04
	D405	-0.16	52.13	-48.74	0.00	3.23	0.57	3.79
	E406	-0.14	50.19	-46.97	0.00	3.09	0.46	3.55
	R408	-0.13	-47.87	44.90	0.00	-3.10	0.59	-2.50
	Q409	-0.05	-1.14	1.11	0.00	-0.07	0.11	0.04
	K417	0.18	-59.05	54.54	-0.38	-4.71	2.96	-1.74
	I418	-0.05	-0.12	0.13	0.00	-0.04	0.02	-0.02
	D420	-0.02	41.50	-38.88	0.00	2.60	0.35	2.95
	Y421	-0.20	0.00	0.09	0.00	-0.11	0.30	0.19
	N422	-0.03	-0.43	0.41	0.00	-0.05	0.03	-0.02
	N437	-0.05	-0.41	0.40	0.00	-0.06	0.04	-0.02
	N439	-0.11	-0.26	0.27	0.00	-0.10	0.10	0.00
	N440	-0.02	0.56	-0.50	0.00	0.04	0.43	0.47
	D442	-0.01	41.57	-38.97	0.00	2.59	0.14	2.73
	S443	-0.02	0.28	-0.27	0.00	-0.02	0.04	0.02
	K444	-0.05	-44.12	41.40	0.00	-2.77	0.60	-2.18
	V445	-0.19	-0.06	0.18	0.00	-0.08	0.06	-0.02
	G446	0.00	0.00	0.00	0.00	0.00	0.00	0.00
WT	**N448**	-0.03	-0.33	0.32	0.00	-0.04	0.02	-0.01
	Y449	-0.67	-5.59	5.07	-0.51	-1.71	1.94	0.24
	Y451	-0.04	-0.38	0.37	0.00	-0.05	0.01	-0.04
	L452	-0.07	0.13	-0.10	0.00	-0.04	0.04	0.00
	Y453	-1.57	-1.50	1.70	-0.20	-1.56	0.89	-0.66
	R454	-0.05	-38.27	35.88	0.00	-2.44	0.15	-2.29
	L455	-3.41	-0.63	1.10	-0.40	-3.35	0.23	-3.11
	F456	-4.44	-1.23	2.29	-0.58	-3.96	1.73	-2.23
	R457	-0.03	-36.04	33.79	0.00	-2.28	0.13	-2.15
	K458	-0.11	-35.19	33.04	-0.01	-2.28	0.70	-1.58
	I472	-0.05	0.03	-0.02	0.00	-0.05	0.00	-0.05
	Y473	-1.30	-0.84	1.07	-0.16	-1.23	0.59	-0.63
	Q474	-0.13	-0.16	0.18	0.00	-0.11	0.08	-0.04
	S477	-0.11	-0.30	0.29	-0.05	-0.16	0.37	0.22
	T478	-0.12	-0.01	0.01	-0.01	-0.13	0.10	-0.03
	C480	-0.03	0.65	-0.63	0.00	-0.02	0.00	-0.02
	V483	-0.02	0.02	-0.01	0.00	-0.01	0.01	0.00
	E484	-0.21	41.29	-38.59	-0.03	2.45	0.88	3.34
	F486	-6.14	-1.32	3.17	-0.92	-5.22	1.89	-3.33
	N487	-1.77	-1.12	1.07	-0.36	-2.18	1.49	-0.70
	C488	-0.05	-0.82	0.82	0.00	-0.05	0.00	-0.05
	Y489	-6.29	0.11	0.67	-0.81	-6.32	0.98	-5.34
	F490	-0.15	0.35	-0.24	0.00	-0.04	-0.02	-0.06

P491	-0.04	0.42	-0.41	0.00	-0.03	0.01	-0.02
L492	-0.04	0.38	-0.38	0.00	-0.04	0.05	0.01
Q493	-2.87	-8.11	6.14	-0.77	-5.62	3.15	-2.47
S494	-0.11	0.24	-0.14	-0.01	-0.02	0.14	0.12
Y495	-0.65	-0.72	0.81	-0.02	-0.58	0.07	-0.50
G496	0.00	0.00	0.00	0.00	0.00	0.00	0.00
F497	-0.26	-0.04	-0.07	0.00	-0.38	0.07	-0.31
Q498	-3.02	-3.55	2.44	-0.51	-4.65	1.78	-2.87
P499	-0.23	0.20	-0.23	0.00	-0.25	0.08	-0.17
T500	-0.45	-3.68	3.36	-0.30	-1.06	1.49	0.42
N501	-3.48	-5.20	4.57	-0.27	-4.38	1.05	-3.34
V503	-0.54	0.26	-0.02	-0.06	-0.36	0.15	-0.22
Y505	-5.88	-4.54	4.22	-0.89	-7.09	2.23	-4.86
Q506	-0.38	-2.38	2.35	-0.01	-0.42	0.08	-0.34
P507	-0.05	0.07	-0.10	0.00	-0.08	0.00	-0.08
Y508	-0.08	0.18	-0.16	0.00	-0.06	0.09	0.03

Table S2. The energy contribution for all residues of RBD for Omicron variant within 10 Å from the binding interface obtained by the ASIE method. All values are in kcal/mol.

Systems	Residues	$\Delta\Delta E_{vdW}$	$\Delta\Delta E_{ele}$	$\Delta\Delta G_{GB}$	$\Delta\Delta G_{SA}$	$\Delta\Delta H$	$-T\Delta\Delta S$	$\Delta\Delta G_{bind}$
	D339	0.00	30.34	-28.44	0.00	1.90	0.08	1.97
	L371	0.00	0.08	-0.08	0.00	0.00	0.01	0.01
	P373	0.00	-0.05	0.05	0.00	0.00	0.03	0.03
	F375	-0.04	-0.25	0.32	0.00	0.02	0.00	0.02
	R403	-1.10	-54.71	51.37	-0.09	-4.53	1.12	-3.41
	D405	-0.21	52.05	-48.67	-0.01	3.16	0.56	3.72
	E406	-0.16	49.12	-45.96	0.00	3.00	0.50	3.50
	R408	-0.15	-47.26	44.34	0.00	-3.07	0.58	-2.49
	Q409	-0.05	-1.08	1.06	0.00	-0.08	0.06	-0.02
	N417	-0.38	-0.38	0.57	-0.05	-0.24	0.23	-0.01
	I418	-0.05	-0.09	0.10	0.00	-0.04	0.01	-0.02
	D420	-0.02	40.66	-38.09	0.00	2.54	0.32	2.86
	Y421	-0.19	-0.01	0.11	0.00	-0.08	0.24	0.16
	N422	-0.03	-0.20	0.19	0.00	-0.04	0.03	-0.01
	N437	-0.04	-0.31	0.30	0.00	-0.05	0.03	-0.01
	N439	-0.10	-0.08	0.10	0.00	-0.07	0.09	0.02
	K440	-0.04	-45.53	42.72	0.00	-2.85	1.78	-1.08
	D442	-0.01	42.26	-39.62	0.00	2.63	0.14	2.77
	S443	-0.02	0.26	-0.25	0.00	-0.01	0.06	0.04
	K444	-0.04	-44.92	42.14	0.00	-2.83	0.50	-2.33
	V445	-0.24	-0.01	0.12	-0.02	-0.16	0.08	-0.08
	S446	-0.06	0.16	-0.08	0.00	0.01	0.15	0.17
Omicron	**N448**	-0.02	-0.35	0.34	0.00	-0.04	0.06	0.03
	Y449	-0.95	-0.82	0.87	-0.13	-1.02	0.63	-0.40
	Y451	-0.03	-0.41	0.40	0.00	-0.04	0.02	-0.02
	L452	-0.04	0.18	-0.16	0.00	-0.03	0.04	0.02
	Y453	-1.37	-0.81	1.10	-0.24	-1.33	0.90	-0.43
	R454	-0.05	-38.37	35.98	0.00	-2.44	0.16	-2.28
	L455	-3.21	-0.61	1.43	-0.43	-2.82	0.51	-2.31
	F456	-4.31	-0.82	2.14	-0.59	-3.59	1.43	-2.15
	R457	-0.03	-35.87	33.63	0.00	-2.26	0.13	-2.13
	K458	-0.12	-34.79	32.67	-0.01	-2.24	0.72	-1.52
	I472	-0.05	0.04	-0.01	0.00	-0.03	0.00	-0.02
	Y473	-1.06	-0.93	1.20	-0.14	-0.92	0.46	-0.46
	Q474	-0.15	-0.10	0.12	0.00	-0.12	0.07	-0.05
	N477	-0.80	-6.14	5.24	-0.38	-2.08	3.04	0.96
	K478	-0.09	-37.99	35.67	0.00	-2.42	1.24	-1.17
	C480	-0.04	0.58	-0.56	0.00	-0.02	0.00	-0.02
	V483	-0.02	0.01	0.01	0.00	-0.01	0.01	0.00
	A484	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	F486	-6.16	-1.48	3.42	-0.93	-5.15	1.58	-3.56
	N487	-1.64	-1.69	1.41	-0.37	-2.28	1.87	-0.42
	C488	-0.05	-0.87	0.86	0.00	-0.05	0.01	-0.04
	Y489	-6.14	0.46	0.39	-0.85	-6.15	0.70	-5.44
	F490	-0.12	0.18	-0.06	0.00	-0.01	-0.01	-0.01

P491	-0.04	0.44	-0.42	0.00	-0.02	0.01	-0.01
L492	-0.03	0.50	-0.48	0.00	-0.02	0.05	0.03
R493	-2.26	-72.68	64.53	-1.20	-11.62	4.82	-6.80
S494	-0.06	-0.13	0.19	-0.01	-0.01	0.24	0.23
Y495	-0.22	-0.39	0.44	0.00	-0.17	0.02	-0.15
S496	0.73	-3.35	2.33	-0.11	-0.39	1.44	1.05
F497	-0.18	0.33	-0.28	0.00	-0.13	0.04	-0.09
R498	-4.60	-60.37	56.41	-0.75	-9.31	2.80	-6.51
P499	-0.17	0.19	-0.19	0.00	-0.17	0.11	-0.06
T500	-0.58	-3.58	3.33	-0.30	-1.13	1.48	0.35
Y501	-6.46	-0.10	0.35	-0.69	-6.90	1.11	-5.79
V503	-0.29	0.26	-0.10	-0.01	-0.14	0.05	-0.10
H505	-4.72	-2.35	2.51	-0.48	-5.04	1.04	-4.00
Q506	-0.30	-2.31	2.26	0.00	-0.35	0.04	-0.31
P507	-0.04	0.03	-0.06	0.00	-0.07	0.00	-0.07
Y508	-0.08	-0.23	0.23	0.00	-0.07	0.07	0.00

Table S3. The occupancy of hydrogen bonds and salt bridges between RBD and ACE2.

	Residues		WT			Omicron variant		
	RBD residues	**ACE2 residues**	**Distance (Å)**	**Average Angle (°)**	**Occupancy (%)**	**Distance (Å)**	**Average Angle (°)**	**Occupancy (%)**
Hydrogen bonding	G502	K353	2.84	161.10	84.11	2.86	163.50	73.05
	T500	D355	2.72	161.52	71.85	2.71	161.80	89.69
	N487	Y83	2.76	161.10	68.15	2.75	158.81	88.33
	Q493(R)	D38	-	-	-	2.79	156.22	60.02
	A475	S19	-	-	-	2.75	158.81	88.22
Salt bridge	K417(N)	D30	3.57	-	99.59	-	-	-
	R403	E37	6.69	-	23.04	6.07	-	57.25
	E484(A)	K31	7.77	-	24.14	-	-	-
	Q493(R)	E35	-	-	-	4.88	-	99.59
	Q493(R)	D38	-	-	-	4.11	-	99.90