

Figure S1: Root Mean Square Deviation (RMSD) graph of hesperidin and RBD S protein (Hes + RBD S protein) on Global and Local docking

Simulation time (nanosecond, ns)	Root-mean square deviation, RMSD (Å)	
	Local simulation	Global simulation
0.00	0.58	0.55
0.25	2.90	1.65
0.5	2.44	1.92
0.75	2.32	2.69
1.00	2.55	2.71
1.25	2.69	3.05
1.50	2.40	2.42
1.75	1.64	2.76
2.00	1.44	2.55
2.25	1.77	2.80
2.50	1.47	2.03
2.75	1.97	3.95
3.00	1.91	4.45
3.25	1.58	4.66
3.50	1.72	5.12
3.75	1.41	5.89
4.00	1.86	5.58
4.25	2.29	4.61
4.50	1.70	4.92
4.75	1.43	5.29
5.00	1.64	3.59
5.25	1.96	5.42
5.50	1.19	5.20
5.75	1.33	4.96
6.00	1.89	2.39
6.25	1.81	3.40
6.50	2.34	2.79
6.75	1.94	2.81
7.00	1.94	2.40

7.25	2.23	2.76
7.50	1.86	2.77
7.75	2.07	2.73
8.00	1.95	2.61
8.25	2.27	2.25
8.5	1.97	2.48
8.75	2.01	2.76
9.00	2.97	2.91
9.25	3.50	3.84
9.50	2.16	4.79
9.75	2.06	5.64
10.0	2.24	4.52
10.25	2.57	4.53
10.50	3.49	2.88
10.75	2.89	4.38
11.00	3.11	5.32
11.25	2.73	5.03
11.50	2.86	4.88
11.75	2.84	4.97
12.00	3.28	4.02
12.25	3.36	4.66
12.50	3.19	4.04
12.75	3.33	4.18
13.00	3.07	4.84
13.25	3.67	3.28
13.50	3.27	3.09
13.75	3.43	3.33
14.00	3.15	2.31
14.25	3.23	3.46
14.50	3.17	3.17
14.75	3.18	3.95
15.00	2.46	4.32
15.25	1.95	4.43
15.50	2.39	5.04
15.75	2.54	5.05
16.00	2.99	5.93
16.25	2.81	4.64
16.50	2.91	5.21
16.75	2.53	5.17
17.00	2.63	5.16
17.25	2.64	5.98
17.50	3.51	5.67
17.75	2.97	5.64
18.00	3.31	5.58
18.25	3.22	5.41
18.50	2.80	5.54
18.75	2.59	5.34
19.00	3.16	5.96
19.25	3.31	5.32
19.50	3.08	5.94
19.75	3.38	5.86
20.00	3.22	5.79
20.25	3.38	6.31
20.50	3.36	6.59
20.75	3.35	6.23
21.00	3.34	6.18
21.25	3.58	6.75
21.50	3.71	5.48
21.75	3.52	5.36

22.00	3.82	4.89
22.25	3.59	5.08
22.50	3.94	5.97
22.75	3.58	5.48
23.00	3.43	4.73
23.25	3.52	4.94
23.50	3.16	5.36
23.75	3.75	5.66
24.00	4.15	4.83
24.25	3.92	5.64
24.50	3.51	5.38
24.75	2.98	5.39
25.00	3.10	5.85
25.25	4.21	5.86
25.50	3.79	5.56
25.75	3.14	5.31
26.00	3.49	5.86
26.25	3.41	5.79
26.50	3.34	5.75
26.75	3.76	5.53
27.00	3.59	6.01
27.25	3.11	5.65
27.50	3.26	5.53
27.75	3.58	5.52
28.00	3.39	5.58
28.25	3.60	5.76
28.50	3.38	5.87
28.75	3.43	5.19
29.00	3.47	5.54
29.25	3.59	5.88
29.50	3.42	5.29
29.75	3.29	5.56
30.00	3.17	4.83
30.25	3.08	5.06
30.50	3.39	5.09
30.75	3.63	5.35
31.00	3.37	5.49
31.25	3.19	5.58
31.50	3.38	5.94
31.75	3.39	6.22
32.00	3.06	4.94
32.25	2.73	4.63
32.50	3.35	5.19
32.75	2.84	5.49
33.00	3.14	5.65
33.25	3.13	5.58
33.50	3.11	5.35
33.75	3.26	5.18
34.00	3.29	4.91
34.25	3.41	5.73
34.50	3.44	5.01
34.75	3.17	5.35
35.00	3.68	4.95
35.25	3.93	5.04
35.50	3.38	5.66
35.75	3.78	4.92
36.00	3.58	5.44
36.25	3.21	4.74
36.50	3.01	5.58

36.75	3.95	5.88
37.00	3.23	5.67
37.25	3.09	5.10
37.50	3.30	5.27
37.75	3.45	5.51
38.00	3.45	5.29
38.25	3.15	5.22
38.50	3.36	5.33
38.75	3.16	5.56
39.00	3.42	5.31
39.25	2.58	5.05
39.50	3.80	5.53
39.75	2.68	5.39
40.00	3.22	5.67
40.25	3.17	6.15
40.50	3.34	6.14
40.75	3.28	6.62
41.00	3.24	6.42
41.25	3.07	6.48
41.50	2.95	6.57
41.75	2.86	6.55
42.00	3.53	6.41
42.25	2.68	6.61
42.50	2.59	6.43
42.75	2.70	6.12
43.00	3.52	6.01
43.25	2.81	6.45
43.50	2.91	6.12
43.75	2.77	6.28
44.00	2.66	6.41
44.25	3.00	6.47
44.50	2.76	6.57
44.75	2.92	6.49
45.00	3.07	5.73
45.25	3.22	5.17
45.50	3.25	5.54
45.75	2.87	5.47
46.00	3.32	4.50
46.25	2.67	4.99
46.50	2.47	6.27
46.75	3.56	5.49
47.00	3.40	5.46
47.25	3.58	4.62
47.50	4.07	3.00
47.75	3.83	2.74
48.00	3.93	2.89
48.25	3.84	3.03
48.50	3.63	3.97
48.75	3.27	4.19
49.00	3.73	4.16
49.25	3.37	4.25
49.50	3.11	3.98
49.75	2.78	3.63
50.00	2.92	2.70

Table S1: The Root-mean square deviation (RMSD) values of Global and Local simulation between hesperidin and RBD S protein (Hes + RBD S protein) of SARS-CoV-2

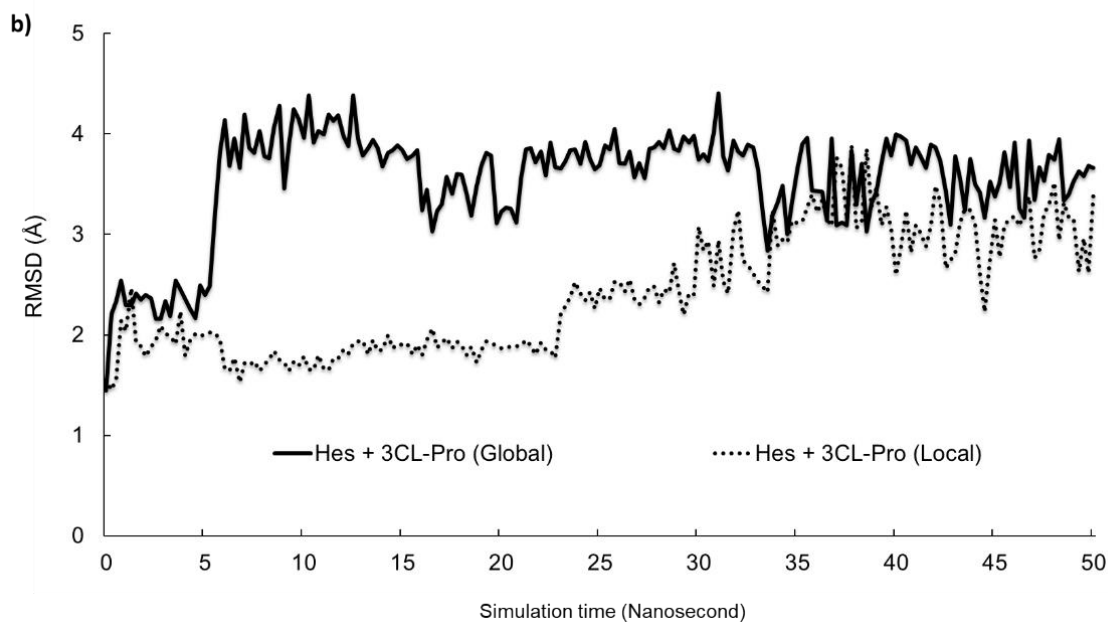


Figure S2: Root Mean Square Deviation (RMSD) of hesperidin and 3CL-Pro (Hes + 3CL-Pro) on Global and Local docking

Simulation time (nanosecond, ns)	Root-mean square deviation, RMSD (Å)	
	Local simulation	Global simulation
0.00	1.55	1.45
0.25	1.45	2.21
0.5	1.57	2.34
0.75	2.14	2.54
1.00	2.04	2.29
1.25	2.46	2.29
1.50	1.92	2.42
1.75	1.89	2.34
2.00	1.79	2.39
2.25	1.88	2.36
2.50	1.95	2.16
2.75	2.09	2.16
3.00	2.01	2.34
3.25	1.99	2.19
3.50	1.91	2.54
3.75	2.25	2.45
4.00	1.79	2.36
4.25	1.94	2.26
4.50	2.01	2.16
4.75	1.99	2.49
5.00	2.00	2.39
5.25	2.02	2.48
5.50	2.02	3.23
5.75	1.95	3.82
6.00	1.66	4.14
6.25	1.64	3.68
6.50	1.78	3.95
6.75	1.53	3.66
7.00	1.72	4.19
7.25	1.69	3.86
7.50	1.74	3.81

7.75	1.64	4.03
8.00	1.70	3.77
8.25	1.75	3.75
8.5	1.84	4.06
8.75	1.75	4.28
9.00	1.72	3.46
9.25	1.64	3.90
9.50	1.73	4.24
9.75	1.69	4.15
10.0	1.79	3.96
10.25	1.66	4.38
10.50	1.65	3.91
10.75	1.79	4.03
11.00	1.66	3.99
11.25	1.65	4.19
11.50	1.77	4.13
11.75	1.77	4.18
12.00	1.85	3.97
12.25	1.81	3.88
12.50	1.92	4.38
12.75	1.95	3.95
13.00	1.94	3.78
13.25	1.81	3.86
13.50	1.98	3.94
13.75	1.84	3.85
14.00	1.85	3.68
14.25	1.99	3.81
14.5	1.87	3.84
14.75	1.91	3.89
15.00	1.90	3.84
15.25	1.92	3.74
15.50	1.82	3.78
15.75	1.90	3.84
16.00	1.79	3.24
16.25	1.95	3.44
16.50	2.06	3.03
16.75	1.88	3.27
17.00	1.92	3.30
17.25	1.97	3.57
17.50	1.87	3.41
17.75	1.93	3.60
18.00	1.89	3.59
18.25	1.79	3.41
18.50	1.88	3.19
18.75	1.72	3.49
19.00	1.85	3.69
19.25	1.93	3.82
19.50	1.91	3.78
19.75	1.89	3.11
20.00	1.87	3.22
20.25	1.87	3.27
20.50	1.88	3.26
20.75	1.88	3.12
21.00	1.89	3.56
21.25	1.94	3.85
21.50	1.89	3.86
21.75	1.81	3.72
22.00	1.92	3.83
22.25	1.85	3.58

22.50	1.84	3.91
22.75	1.78	3.67
23.00	2.21	3.65
23.25	2.28	3.73
23.50	2.38	3.84
23.75	2.52	3.85
24.00	2.41	3.70
24.25	2.34	3.92
24.50	2.42	3.75
24.75	2.26	3.65
25.00	2.47	3.68
25.25	2.35	3.88
25.50	2.36	3.84
25.75	2.52	4.05
26.00	2.53	3.71
26.25	2.43	3.71
26.50	2.56	3.83
26.75	2.36	3.57
27.00	2.31	3.71
27.25	2.37	3.56
27.50	2.48	3.85
27.75	2.48	3.87
28.00	2.32	3.92
28.25	2.45	3.86
28.50	2.42	4.04
28.75	2.72	3.86
29.00	2.44	3.83
29.25	2.20	3.98
29.50	2.42	3.92
29.75	2.41	3.97
30.00	3.08	3.74
30.25	2.84	3.79
30.50	2.94	3.73
30.75	2.48	4.01
31.00	2.94	4.41
31.25	2.53	3.77
31.50	2.41	3.64
31.75	3.04	3.93
32.00	3.24	3.83
32.25	2.74	3.78
32.50	2.70	3.89
32.75	2.61	3.87
33.00	2.54	3.65
33.25	2.48	3.21
33.50	2.43	2.84
33.75	3.24	3.18
34.00	2.89	3.32
34.25	2.95	3.49
34.50	2.92	3.00
34.75	3.14	3.33
35.00	3.11	3.66
35.25	3.14	3.90
35.50	3.27	3.96
35.75	3.39	3.44
36.00	3.22	3.43
36.25	3.34	3.42
36.50	3.15	3.14
36.75	3.09	3.95
37.00	3.76	3.09

37.25	3.66	3.12
37.50	3.15	3.09
37.75	3.88	3.83
38.00	3.06	3.29
38.25	3.14	3.73
38.50	3.85	3.02
38.75	3.28	3.31
39.00	3.46	3.41
39.25	3.08	3.71
39.50	3.27	3.95
39.75	3.06	3.78
40.00	2.59	3.99
40.25	2.86	3.97
40.50	3.24	3.93
40.75	2.82	3.69
41.00	3.09	3.86
41.25	3.02	3.77
41.50	2.88	3.66
41.75	3.08	3.89
42.00	3.48	3.87
42.25	3.32	3.73
42.50	2.66	3.44
42.75	2.75	3.07
43.00	2.82	3.78
43.25	3.12	3.56
43.50	3.26	3.24
43.75	3.24	3.75
44.00	3.09	3.49
44.25	2.61	3.42
44.50	2.22	3.17
44.75	2.76	3.53
45.00	3.14	3.38
45.25	2.77	3.52
45.50	3.09	3.82
45.75	3.16	3.47
46.00	3.18	3.91
46.25	3.08	3.26
46.50	3.25	3.16
46.75	3.37	3.93
47.00	2.77	3.34
47.25	2.84	3.66
47.50	3.21	3.53
47.75	3.29	3.79
48.00	3.52	3.74
48.25	2.94	3.94
48.50	3.32	3.33
48.75	3.17	3.4
49.00	3.15	3.53
49.25	2.63	3.63
49.50	2.96	3.58
49.75	2.62	3.68
50.00	3.38	3.67

Table S2: The Root-mean square deviation (RMSD) values of Global and Local simulation between hesperidin and 3CL-Pro (Hes + 3CL-Pro) of SARS-CoV-2

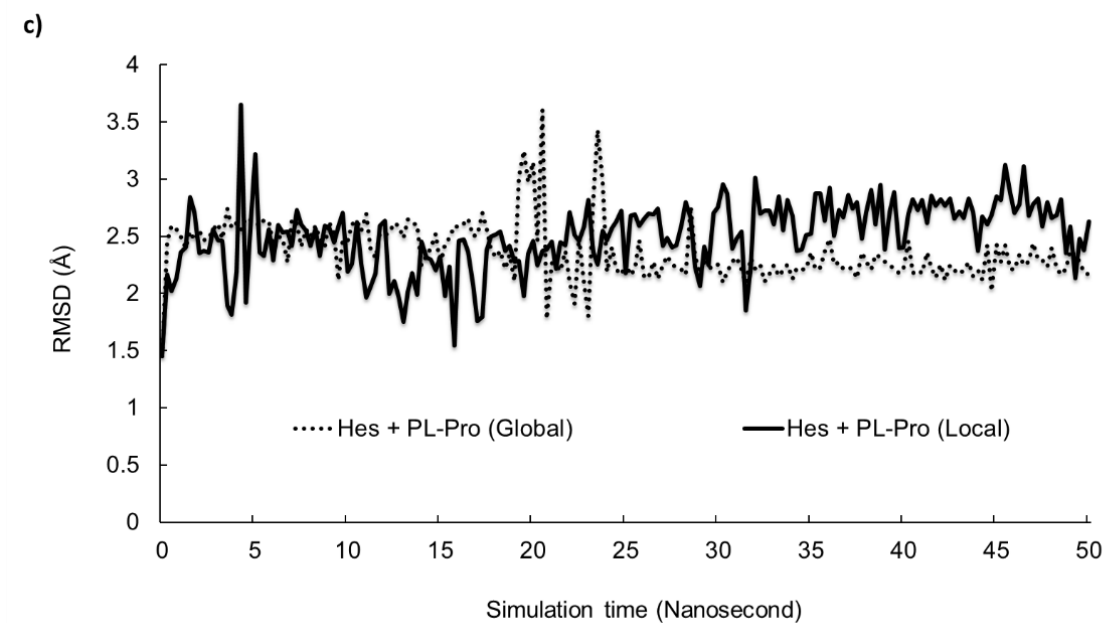


Figure S3: The Root Mean Square Deviation (RMSD) of hesperidin and PL-Pro (Hes + PL-Pro) on Global and Local docking

Simulation time (nanosecond, ns)	Root-mean square deviation, RMSD (Å)	
	Local simulation	Global simulation
0.00	1.47	1.45
0.25	2.17	2.45
0.5	2.02	2.59
0.75	2.14	2.56
1.00	2.36	2.49
1.25	2.41	2.39
1.50	2.84	2.54
1.75	2.71	2.46
2.00	2.35	2.55
2.25	2.37	2.46
2.50	2.36	2.48
2.75	2.56	2.56
3.00	2.47	2.61
3.25	2.46	2.47
3.50	1.89	2.74
3.75	1.82	2.57
4.00	2.19	2.62
4.25	3.65	2.56
4.50	1.92	2.66
4.75	2.55	2.64
5.00	3.22	2.62
5.25	2.36	2.59
5.50	2.33	2.65
5.75	2.56	2.63
6.00	2.29	2.41
6.25	2.60	2.50
6.50	2.54	2.48
6.75	2.54	2.27
7.00	2.42	2.65

7.25	2.72	2.61
7.50	2.60	2.41
7.75	2.54	2.56
8.00	2.41	2.49
8.25	2.56	2.59
8.50	2.33	2.48
8.75	2.59	2.41
9.00	2.57	2.63
9.25	2.44	2.53
9.50	2.58	2.12
9.75	2.70	2.47
10.00	2.19	2.46
10.25	2.25	2.60
10.50	2.65	2.64
10.75	2.26	2.55
11.00	1.96	2.69
11.25	2.06	2.38
11.50	2.18	2.31
11.75	2.59	2.52
12.00	2.64	2.51
12.25	1.99	2.53
12.50	2.11	2.62
12.75	1.98	2.59
13.00	1.75	2.48
13.25	2.02	2.64
13.50	2.18	2.61
13.75	1.99	2.60
14.00	2.46	2.25
14.25	2.31	2.33
14.50	2.29	2.39
14.75	2.20	2.52
15.00	2.32	2.25
15.25	1.98	2.44
15.50	2.24	2.48
15.75	1.55	2.59
16.00	2.46	2.58
16.25	2.47	2.60
16.50	2.37	2.65
16.75	2.08	2.50
17.00	1.76	2.51
17.25	1.79	2.71
17.50	2.38	2.56
17.75	2.49	2.38
18.00	2.52	2.32
18.25	2.54	2.32
18.50	2.37	2.22
18.75	2.42	2.34
19.00	2.28	2.11
19.25	2.29	3.01
19.50	1.98	3.25
19.75	2.35	2.97
20.00	2.46	3.14
20.25	2.25	2.46
20.50	2.37	3.61
20.75	2.39	1.78
21.00	2.46	2.26
21.25	2.22	2.25
21.50	2.45	2.19
21.75	2.42	2.37

22.00	2.71	2.09
22.25	2.50	1.91
22.50	2.46	2.49
22.75	2.58	2.09
23.00	2.81	1.80
23.25	2.36	2.83
23.5	2.25	3.43
23.75	2.55	2.98
24.00	2.47	2.19
24.25	2.57	2.41
24.50	2.63	2.21
24.75	2.72	2.17
25.00	2.18	2.27
25.25	2.68	2.16
25.50	2.69	2.22
25.75	2.59	2.47
26.00	2.65	2.14
26.25	2.70	2.14
26.50	2.69	2.28
26.75	2.75	2.13
27.00	2.42	2.25
27.25	2.48	2.33
27.50	2.40	2.25
27.75	2.42	2.23
28.00	2.59	2.21
28.25	2.79	2.17
28.50	2.66	2.76
28.75	2.24	2.33
29.00	2.07	2.17
29.25	2.41	2.27
29.50	2.25	2.23
29.75	2.70	2.22
30.00	2.75	2.26
30.25	2.95	2.10
30.50	2.87	2.19
30.75	2.39	2.28
31.00	2.48	2.32
31.25	2.54	2.21
31.50	1.85	2.09
31.75	2.24	2.31
32.00	3.01	2.21
32.25	2.69	2.26
32.50	2.72	2.10
32.75	2.72	2.17
33.00	2.60	2.25
33.25	2.85	2.16
33.50	2.55	2.20
33.75	2.82	2.25
34.00	2.68	2.13
34.25	2.37	2.22
34.50	2.37	2.21
34.75	2.51	2.22
35.00	2.53	2.36
35.25	2.87	2.21
35.50	2.87	2.23
35.75	2.63	2.37
36.00	2.92	2.48
36.25	2.50	2.25
36.50	2.73	2.27

36.75	2.67	2.22
37.00	2.86	2.23
37.25	2.74	2.22
37.50	2.79	2.13
37.75	2.48	2.36
38.00	2.71	2.28
38.25	2.91	2.21
38.50	2.60	2.34
38.75	2.95	2.31
39.00	2.39	2.28
39.25	2.72	2.25
39.50	2.89	2.22
39.75	2.39	2.18
40.00	2.41	2.22
40.25	2.70	2.46
40.50	2.83	2.18
40.75	2.73	2.20
41.00	2.82	2.18
41.25	2.62	2.36
41.50	2.86	2.22
41.75	2.77	2.14
42.00	2.83	2.26
42.25	2.77	2.11
42.50	2.83	2.25
42.75	2.66	2.21
43.00	2.72	2.17
43.25	2.66	2.20
43.50	2.83	2.21
43.75	2.72	2.15
44.00	2.37	2.20
44.25	2.68	2.12
44.50	2.60	2.42
44.75	2.68	2.02
45.00	2.85	2.43
45.25	2.82	2.27
45.50	3.13	2.43
45.75	2.88	2.22
46.00	2.71	2.21
46.25	2.78	2.34
46.50	3.11	2.24
46.75	2.68	2.27
47.00	2.78	2.42
47.25	2.83	2.29
47.50	2.58	2.29
47.75	2.79	2.23
48.00	2.65	2.39
48.25	2.63	2.22
48.50	2.82	2.17
48.75	2.35	2.22
49.00	2.58	2.38
49.25	2.12	2.33
49.50	2.48	2.28
49.75	2.38	2.18
50.00	2.63	2.16

Table S3: The Root-mean square deviation (RMSD) values of Global and Local simulation between hesperidin and PL-Pro (Hes + PL-Pro) of SARS-CoV-2

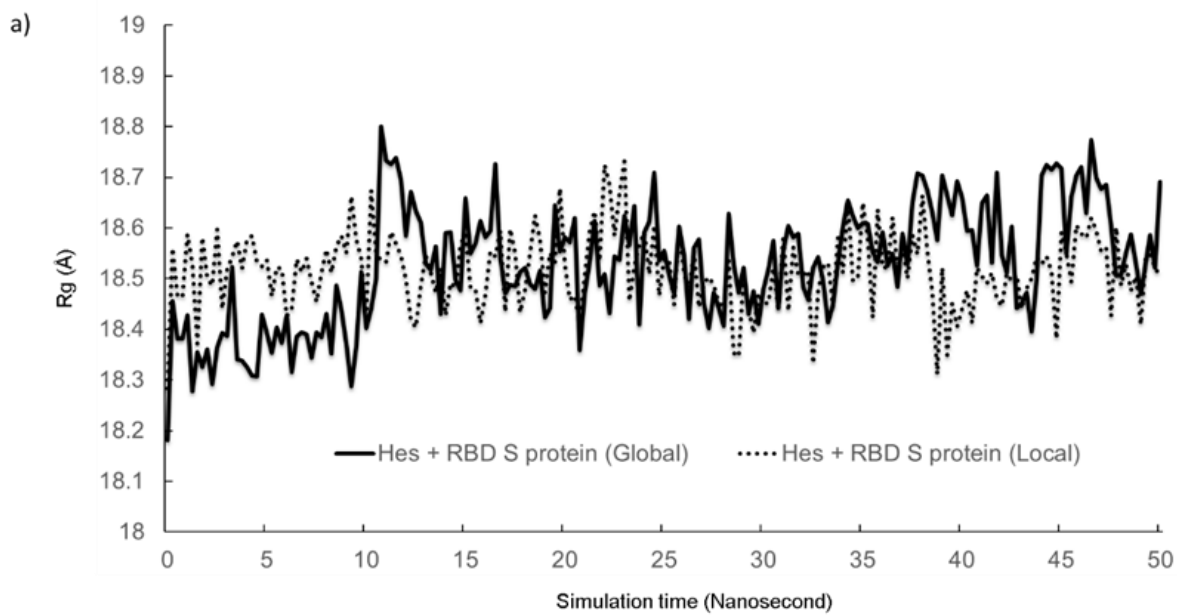


Figure S4: Radius of gyration (R_g) of hesperidin and RBD S protein (Hes + RBD S protein) on Global and Local docking

Simulation time (nanosecond, ns)	Radius of gyration, R_g (Å)	
	Local simulation	Global simulation
0.00	18.28	18.18
0.25	18.56	18.56
0.5	18.47	18.38
0.75	18.46	18.38
1.00	18.59	18.43
1.25	18.53	18.28
1.50	18.37	18.36
1.75	18.58	18.33
2.00	18.50	18.36
2.25	18.49	18.29
2.50	18.59	18.37
2.75	18.44	18.39
3.00	18.52	18.39
3.25	18.54	18.52
3.50	18.57	18.34
3.75	18.52	18.34
4.00	18.58	18.33
4.25	18.59	18.31
4.50	18.53	18.31
4.75	18.52	18.43
5.00	18.54	18.39
5.25	18.47	18.35
5.50	18.52	18.40
5.75	18.52	18.37
6.00	18.43	18.43
6.25	18.44	18.32
6.50	18.54	18.39
6.75	18.51	18.39
7.00	18.54	18.39
7.25	18.49	18.34

7.50	18.45	18.39
7.75	18.51	18.38
8.00	18.56	18.43
8.25	18.51	18.35
8.5	18.56	18.49
8.75	18.59	18.44
9.00	18.55	18.37
9.25	18.66	18.28
9.50	18.58	18.36
9.75	18.54	18.51
10.0	18.42	18.40
10.25	18.67	18.44
10.50	18.55	18.50
10.75	18.54	18.80
11.00	18.53	18.73
11.25	18.59	18.77
11.50	18.57	18.74
11.75	18.55	18.69
12.00	18.49	18.58
12.25	18.42	18.67
12.50	18.40	18.63
12.75	18.49	18.61
13.00	18.55	18.53
13.25	18.51	18.52
13.50	18.47	18.56
13.75	18.52	18.43
14.00	18.43	18.59
14.25	18.49	18.59
14.5	18.48	18.49
14.75	18.57	18.48
15.00	18.59	18.66
15.25	18.48	18.55
15.50	18.48	18.57
15.75	18.41	18.61
16.00	18.47	18.58
16.25	18.55	18.59
16.50	18.54	18.73
16.75	18.59	18.54
17.00	18.44	18.47
17.25	18.59	18.49
17.50	18.55	18.49
17.75	18.43	18.51
18.00	18.48	18.52
18.25	18.55	18.49
18.50	18.63	18.48
18.75	18.58	18.52
19.00	18.47	18.42
19.25	18.55	18.44
19.50	18.53	18.65
19.75	18.68	18.55
20.00	18.53	18.58
20.25	18.46	18.57
20.50	18.47	18.62
20.75	18.41	18.36
21.00	18.51	18.47
21.25	18.59	18.53
21.50	18.63	18.61
21.75	18.53	18.49
22.00	18.73	18.51

22.25	18.69	18.43
22.50	18.58	18.54
22.75	18.67	18.54
23.00	18.73	18.62
23.25	18.46	18.57
23.50	18.52	18.64
23.75	18.57	18.41
24.00	18.59	18.59
24.25	18.51	18.61
24.50	18.61	18.71
24.75	18.47	18.54
25.00	18.54	18.56
25.25	18.54	18.51
25.50	18.45	18.47
25.75	18.60	18.60
26.00	18.51	18.55
26.25	18.47	18.42
26.50	18.56	18.56
26.75	18.44	18.58
27.00	18.49	18.45
27.25	18.50	18.40
27.50	18.49	18.47
27.75	18.45	18.44
28.00	18.44	18.41
28.25	18.54	18.63
28.50	18.35	18.53
28.75	18.35	18.47
29.00	18.50	18.52
29.25	18.44	18.43
29.50	18.39	18.48
29.75	18.47	18.41
30.00	18.45	18.48
30.25	18.45	18.52
30.50	18.52	18.57
30.75	18.44	18.44
31.00	18.59	18.56
31.25	18.44	18.60
31.50	18.56	18.58
31.75	18.51	18.59
32.00	18.51	18.48
32.25	18.52	18.46
32.50	18.33	18.52
32.75	18.48	18.54
33.00	18.52	18.49
33.25	18.53	18.41
33.50	18.44	18.45
33.75	18.58	18.53
34.00	18.51	18.60
34.25	18.66	18.65
34.50	18.49	18.62
34.75	18.50	18.60
35.00	18.65	18.61
35.25	18.58	18.61
35.50	18.42	18.55
35.75	18.64	18.53
36.00	18.52	18.59
36.25	18.52	18.52
36.50	18.62	18.55
36.75	18.52	18.48

37.00	18.56	18.50
37.25	18.50	18.53
37.50	18.59	18.65
37.75	18.55	18.71
38.00	18.66	18.70
38.25	18.55	18.67
38.50	18.47	18.63
38.75	18.31	18.58
39.00	18.52	18.70
39.25	18.35	18.67
39.50	18.45	18.63
39.75	18.41	18.69
40.00	18.44	18.66
40.25	18.48	18.59
40.50	18.41	18.59
40.75	18.52	18.53
41.00	18.50	18.65
41.25	18.49	18.67
41.50	18.51	18.53
41.75	18.46	18.71
42.00	18.45	18.55
42.25	18.51	18.51
42.50	18.49	18.60
42.75	18.51	18.44
43.00	18.44	18.45
43.25	18.48	18.47
43.50	18.50	18.39
43.75	18.54	18.49
44.00	18.53	18.70
44.25	18.54	18.72
44.50	18.52	18.72
44.75	18.38	18.73
45.00	18.59	18.72
45.25	18.55	18.55
45.50	18.49	18.66
45.75	18.61	18.70
46.00	18.59	18.72
46.25	18.58	18.63
46.50	18.62	18.77
46.75	18.59	18.70
47.00	18.55	18.68
47.25	18.56	18.69
47.50	18.43	18.60
47.75	18.60	18.51
48.00	18.49	18.51
48.25	18.53	18.55
48.50	18.48	18.59
48.75	18.50	18.53
49.00	18.41	18.47
49.25	18.55	18.53
49.50	18.55	18.59
49.75	18.52	18.52
50.00	18.50	18.69

Table S4: The Radius of gyration (Rg) values of Global and Local simulation between hesperidin and RBD S protein (Hes + RBD S protein) of SARS-CoV-2

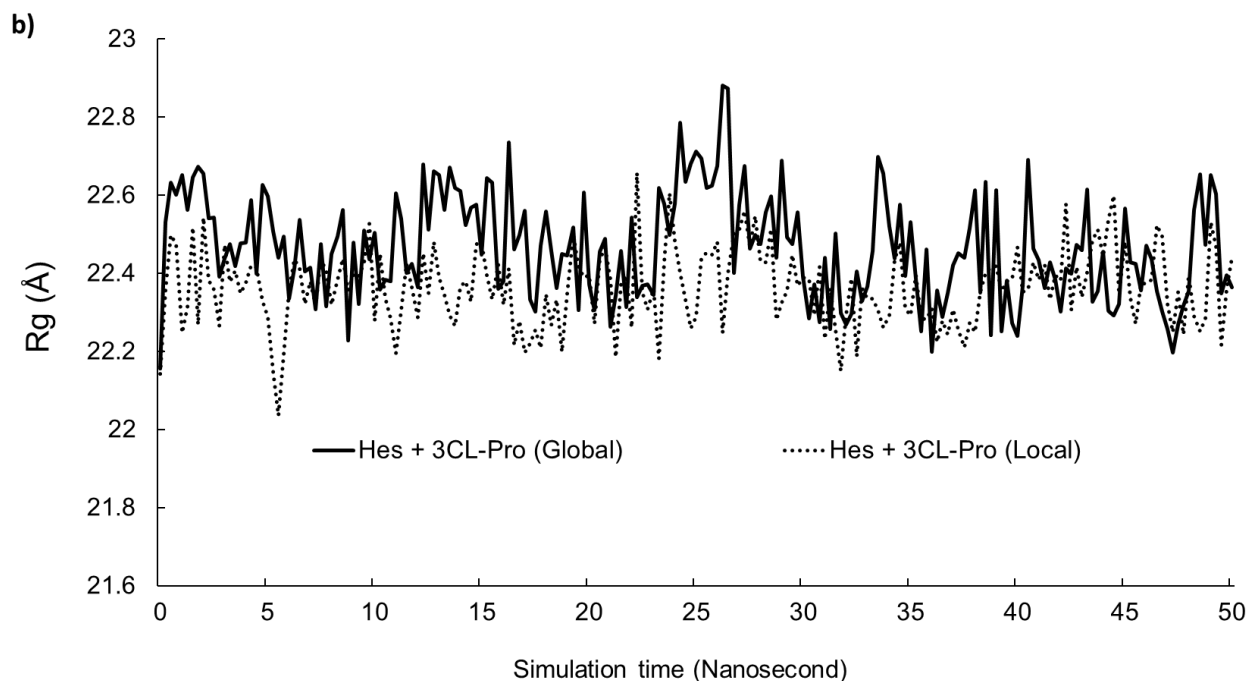


Figure S5: Radius of gyration (Rg) of hesperidin and 3CL-Pro (Hes + 3CL-Pro) on Global and Local docking of SARS-CoV-2

Simulation time (nanosecond, ns)	Radius of gyration, Rg (Å)	
	Local simulation	Global simulation
0.00	22.14	22.15
0.25	22.35	22.53
0.5	22.49	22.63
0.75	22.47	22.60
1.00	22.24	22.65
1.25	22.31	22.56
1.50	22.51	22.64
1.75	22.26	22.67
2.00	22.54	22.65
2.25	22.38	22.54
2.50	22.35	22.54
2.75	22.26	22.39
3.00	22.47	22.44
3.25	22.37	22.47
3.50	22.41	22.42
3.75	22.35	22.48
4.00	22.38	22.48
4.25	22.42	22.58
4.50	22.41	22.39
4.75	22.33	22.63
5.00	22.29	22.59
5.25	22.14	22.51
5.50	22.03	22.44
5.75	22.19	22.49
6.00	22.35	22.33
6.25	22.43	22.41
6.50	22.41	22.53
6.75	22.32	22.40
7.00	22.3	22.41
7.25	22.38	22.30
7.50	22.43	22.47
7.75	22.40	22.31
8.00	22.31	22.45

8.25	22.38	22.49
08.5	22.43	22.56
8.75	22.35	22.23
9.00	22.39	22.47
9.25	22.39	22.32
9.50	22.42	22.51
9.75	22.52	22.43
10.0	22.27	22.50
10.25	22.45	22.35
10.50	22.33	22.38
10.75	22.28	22.38
11.00	22.19	22.60
11.25	22.30	22.53
11.50	22.45	22.40
11.75	22.36	22.43
12.00	22.28	22.36
12.25	22.45	22.67
12.50	22.34	22.51
12.75	22.48	22.66
13.00	22.38	22.65
13.25	22.34	22.56
13.50	22.29	22.67
13.75	22.26	22.61
14.00	22.36	22.61
14.25	22.37	22.52
14.5	22.32	22.56
14.75	22.47	22.57
15.00	22.47	22.44
15.25	22.39	22.64
15.50	22.33	22.63
15.75	22.42	22.36
16.00	22.31	22.37
16.25	22.41	22.73
16.50	22.21	22.46
16.75	22.27	22.49
17.00	22.19	22.56
17.25	22.22	22.33
17.50	22.25	22.30
17.75	22.20	22.47
18.00	22.34	22.55
18.25	22.26	22.45
18.50	22.33	22.36
18.75	22.19	22.45
19.00	22.34	22.44
19.25	22.49	22.52
19.50	22.41	22.31
19.75	22.38	22.61
20.00	22.39	22.37
20.25	22.27	22.31
20.50	22.43	22.45
20.75	22.46	22.48
21.00	22.38	22.26
21.25	22.18	22.34
21.50	22.37	22.45
21.75	22.39	22.31
22.00	22.26	22.54
22.25	22.65	22.33
22.50	22.35	22.36
22.75	22.30	22.37

23.00	22.3	22.34
23.25	22.18	22.61
23.5	22.43	22.57
23.75	22.60	22.49
24.00	22.48	22.57
24.25	22.40	22.78
24.50	22.33	22.63
24.75	22.25	22.68
25.00	22.28	22.71
25.25	22.43	22.69
25.50	22.45	22.61
25.75	22.44	22.62
26.00	22.48	22.67
26.25	22.24	22.88
26.50	22.39	22.87
26.75	22.50	22.40
27.00	22.51	22.57
27.25	22.56	22.67
27.50	22.46	22.46
27.75	22.54	22.49
28.00	22.43	22.47
28.25	22.42	22.55
28.50	22.51	22.59
28.75	22.28	22.44
29.00	22.32	22.68
29.25	22.35	22.49
29.50	22.44	22.47
29.75	22.36	22.55
30.00	22.3	22.39
30.25	22.38	22.28
30.50	22.29	22.37
30.75	22.42	22.27
31.00	22.23	22.44
31.25	22.36	22.25
31.50	22.25	22.50
31.75	22.15	22.29
32.00	22.29	22.26
32.25	22.38	22.29
32.50	22.18	22.40
32.75	22.36	22.32
33.00	22.33	22.36
33.25	22.33	22.45
33.50	22.31	22.69
33.75	22.21	22.65
34.00	22.29	22.52
34.25	22.43	22.43
34.50	22.48	22.57
34.75	22.31	22.39
35.00	22.29	22.53
35.25	22.39	22.38
35.50	22.28	22.25
35.75	22.28	22.46
36.00	22.30	22.19
36.25	22.22	22.35
36.50	22.28	22.28
36.75	22.24	22.34
37.00	22.30	22.42
37.25	22.25	22.45
37.50	22.21	22.43

37.75	22.27	22.51
38.00	22.24	22.61
38.25	22.35	22.35
38.50	22.40	22.63
38.75	22.41	22.24
39.00	22.41	22.61
39.25	22.35	22.25
39.50	22.37	22.38
39.75	22.38	22.27
40.00	22.46	22.23
40.25	22.35	22.36
40.50	22.35	22.69
40.75	22.42	22.46
41.00	22.38	22.43
41.25	22.42	22.36
41.50	22.33	22.42
41.75	22.39	22.38
42.00	22.38	22.30
42.25	22.58	22.41
42.50	22.31	22.39
42.75	22.41	22.47
43.00	22.33	22.46
43.25	22.40	22.61
43.50	22.48	22.32
43.75	22.51	22.36
44.00	22.44	22.46
44.25	22.53	22.30
44.50	22.59	22.29
44.75	22.35	22.32
45.00	22.48	22.57
45.25	22.34	22.43
45.50	22.27	22.43
45.75	22.37	22.36
46.00	22.37	22.47
46.25	22.38	22.44
46.50	22.52	22.35
46.75	22.49	22.30
47.00	22.32	22.25
47.25	22.25	22.19
47.50	22.35	22.26
47.75	22.24	22.31
48.00	22.39	22.35
48.25	22.29	22.56
48.50	22.25	22.65
48.75	22.29	22.47
49.00	22.53	22.65
49.25	22.47	22.60
49.50	22.22	22.34
49.75	22.36	22.39
50.00	22.44	22.36

Table S5: The Radius of gyration (Rg) values of Global and Local simulation between hesperidin and 3CL-Pro (Hes + 3CL-Pro) of SARS-CoV-2

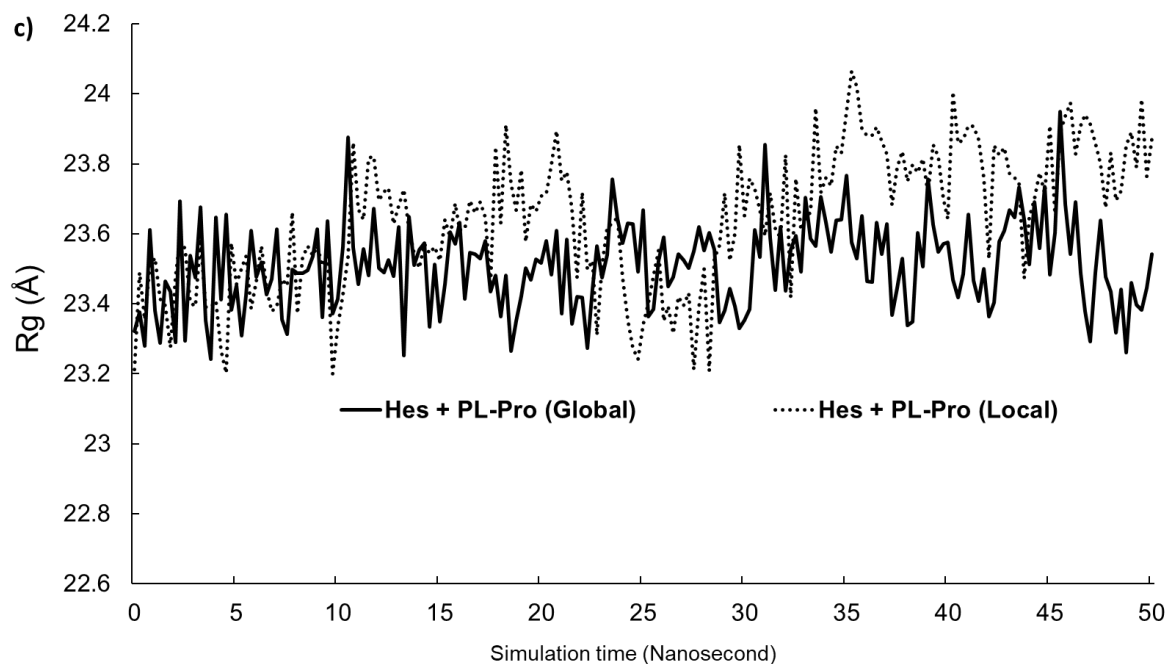


Figure S6: Radius of gyration (Rg) of hesperidin and PL-Pro (Hes + PL-Pro) on Global and Local docking of SARS-CoV-2

Simulation time (nanosecond, ns)	Radius of gyration, Rg (Å)	
	Local simulation	Global simulation
0.00	23.21	23.32
0.25	23.49	23.38
0.5	23.36	23.28
0.75	23.51	23.61
1.00	23.53	23.38
1.25	23.41	23.29
1.50	23.39	23.47
1.75	23.28	23.43
2.00	23.48	23.29
2.25	23.59	23.69
2.50	23.56	23.29
2.75	23.40	23.54
3.00	23.39	23.47
3.25	23.59	23.67
3.50	23.39	23.35
3.75	23.39	23.24
4.00	23.42	23.65
4.25	23.27	23.41
4.50	23.20	23.66
4.75	23.57	23.38
5.00	23.46	23.45
5.25	23.50	23.31
5.50	23.54	23.42
5.75	23.39	23.61
6.00	23.46	23.48
6.25	23.57	23.52
6.50	23.44	23.43
6.75	23.38	23.47
7.00	23.39	23.61
7.25	23.47	23.35
7.50	23.45	23.31
7.75	23.66	23.49
8.00	23.37	23.48
8.25	23.53	23.48

08.5	23.56	23.49
8.75	23.54	23.54
9.00	23.56	23.62
9.25	23.51	23.36
9.50	23.55	23.64
9.75	23.19	23.37
10.0	23.34	23.41
10.25	23.43	23.56
10.50	23.53	23.88
10.75	23.86	23.56
11.00	23.67	23.46
11.25	23.64	23.56
11.50	23.82	23.48
11.75	23.82	23.67
12.00	23.69	23.50
12.25	23.72	23.49
12.50	23.73	23.53
12.75	23.63	23.48
13.00	23.68	23.62
13.25	23.73	23.25
13.50	23.61	23.65
13.75	23.54	23.51
14.00	23.50	23.55
14.25	23.57	23.57
14.5	23.55	23.33
14.75	23.56	23.51
15.00	23.52	23.35
15.25	23.64	23.46
15.50	23.59	23.60
15.75	23.69	23.57
16.00	23.61	23.63
16.25	23.61	23.41
16.50	23.69	23.55
16.75	23.66	23.54
17.00	23.69	23.53
17.25	23.65	23.58
17.50	23.45	23.43
17.75	23.85	23.48
18.00	23.63	23.36
18.25	23.91	23.48
18.50	23.74	23.27
18.75	23.67	23.35
19.00	23.78	23.42
19.25	23.57	23.50
19.50	23.68	23.46
19.75	23.66	23.52
20.00	23.71	23.52
20.25	23.71	23.58
20.50	23.79	23.48
20.75	23.89	23.61
21.00	23.75	23.37
21.25	23.77	23.58
21.50	23.66	23.34
21.75	23.47	23.42
22.00	23.72	23.42
22.25	23.49	23.27
22.50	23.52	23.45
22.75	23.31	23.57
23.00	23.51	23.47

23.25	23.62	23.54
23.5	23.63	23.70
23.75	23.65	23.64
24.00	23.47	23.57
24.25	23.36	23.63
24.50	23.27	23.63
24.75	23.24	23.49
25.00	23.34	23.67
25.25	23.40	23.36
25.50	23.48	23.39
25.75	23.55	23.52
26.00	23.35	23.59
26.25	23.39	23.45
26.50	23.32	23.48
26.75	23.42	23.54
27.00	23.39	23.53
27.25	23.43	23.50
27.50	23.21	23.55
27.75	23.39	23.62
28.00	23.50	23.55
28.25	23.21	23.60
28.50	23.53	23.55
28.75	23.57	23.35
29.00	23.72	23.38
29.25	23.52	23.44
29.50	23.60	23.39
29.75	23.85	23.33
30.00	23.65	23.35
30.25	23.76	23.39
30.50	23.73	23.61
30.75	23.66	23.53
31.00	23.59	23.86
31.25	23.72	23.59
31.50	23.62	23.44
31.75	23.58	23.62
32.00	23.82	23.44
32.25	23.42	23.55
32.50	23.76	23.59
32.75	23.61	23.49
33.00	23.65	23.70
33.25	23.66	23.59
33.50	23.96	23.56
33.75	23.72	23.71
34.00	23.76	23.63
34.25	23.74	23.55
34.50	23.85	23.64
34.75	23.83	23.64
35.00	23.95	23.77
35.25	24.07	23.58
35.50	24.02	23.53
35.75	23.90	23.65
36.00	23.88	23.47
36.25	23.88	23.46
36.50	23.91	23.63
36.75	23.87	23.54
37.00	23.82	23.63
37.25	23.68	23.37
37.50	23.79	23.46
37.75	23.84	23.53

38.00	23.75	23.34
38.25	23.79	23.34
38.50	23.78	23.60
38.75	23.82	23.51
39.00	23.72	23.76
39.25	23.86	23.63
39.50	23.82	23.55
39.75	23.70	23.57
40.00	23.64	23.57
40.25	24.01	23.47
40.50	23.86	23.42
40.75	23.86	23.48
41.00	23.91	23.65
41.25	23.91	23.46
41.50	23.81	23.40
41.75	23.76	23.49
42.00	23.53	23.36
42.25	23.85	23.40
42.50	23.83	23.57
42.75	23.85	23.61
43.00	23.77	23.67
43.25	23.76	23.65
43.50	23.75	23.73
43.75	23.47	23.64
44.00	23.64	23.51
44.25	23.69	23.69
44.50	23.77	23.55
44.75	23.72	23.73
45.00	23.91	23.48
45.25	23.66	23.60
45.50	23.88	23.95
45.75	23.93	23.68
46.00	23.97	23.54
46.25	23.83	23.69
46.50	23.91	23.48
46.75	23.94	23.37
47.00	23.91	23.29
47.25	23.88	23.49
47.50	23.80	23.64
47.75	23.67	23.47
48.00	23.83	23.43
48.25	23.69	23.32
48.50	23.72	23.44
48.75	23.85	23.26
49.00	23.89	23.46
49.25	23.79	23.39
49.50	23.99	23.38
49.75	23.76	23.45
50.00	23.87	23.54

Table S6: The Radius of gyration (Rg) values of Global and Local simulation between hesperidin and PL-Pro (Hes + PL-Pro) of SARS-CoV-2

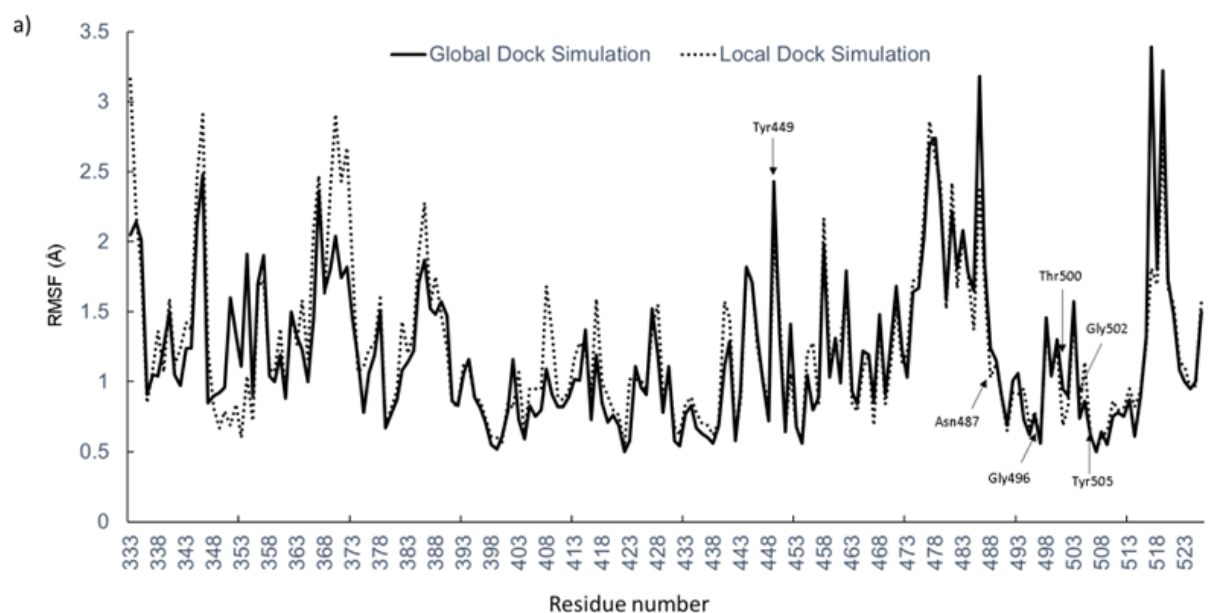


Figure S7: Root Mean Square Fluctuation (RMSF) of hesperidin and RBD S protein (Hes + RBD S protein) on Global and Local docking of SARS-CoV-2

Residue number		Root-mean square fluctuation, RMSF (Å)	
		Local simulation	Global simulation
THR	333	3.16	2.05
ASN	334	2.19	2.14
LEU	335	1.80	2.01
CYS	336	0.85	0.91
PRO	337	1.09	1.05
PHE	338	1.36	1.04
GLY	339	1.07	1.25
GLU	340	1.59	1.50
VAL	341	1.12	1.05
PHE	342	1.24	0.97
ASN	343	1.42	1.24
ALA	344	1.37	1.24
THR	345	2.45	2.13
ARG	346	2.91	2.48
PHE	347	1.24	0.85
ALA	348	0.81	0.90
SER	349	0.67	0.92
VAL	350	0.79	0.96
TYR	351	0.69	1.60
ALA	352	0.84	1.33
TRP	353	0.60	1.11
ASN	354	1.04	1.91
ARG	355	0.72	0.90
LYS	356	1.67	1.7
ARG	357	1.73	1.9
ILE	358	1.09	1.04
SER	359	1.07	1.00
ASN	360	1.38	1.19
CYS	361	0.88	0.88

VAL	362	1.50	1.5
ALA	363	1.27	1.32
ASP	364	1.58	1.23
TYR	365	1.16	1.00
SER	366	2.10	1.46
VAL	367	2.47	2.36
LEU	368	1.62	1.65
TYR	369	2.37	1.8
ASN	370	2.91	2.04
SER	371	2.43	1.74
ALA	372	2.67	1.82
SER	373	1.88	1.47
PHE	374	1.07	1.17
SER	375	1.11	0.78
THR	376	1.23	1.06
PHE	377	1.27	1.19
LYS	378	1.60	1.50
CYS	379	0.69	0.67
TYR	380	0.81	0.77
GLY	381	0.94	0.87
VAL	382	1.43	1.08
SER	383	1.20	1.14
PRO	384	1.35	1.22
THR	385	1.92	1.71
LYS	386	2.28	1.87
LEU	387	1.55	1.52
ASN	388	1.75	1.48
ASP	389	1.48	1.57
LEU	390	1.24	1.47
CYS	391	0.85	0.86
PHE	392	0.82	0.83
THR	393	1.13	1.06
ASN	394	1.12	1.16
VAL	395	0.89	0.89
TYR	396	0.86	0.81
ALA	397	0.74	0.71
ASP	398	0.61	0.55
SER	399	0.60	0.52
PHE	400	0.57	0.61
VAL	401	0.85	0.79
ILE	402	0.81	1.16
ARG	403	1.07	0.73
GLY	404	0.62	0.59
ASP	405	0.95	0.83
GLU	406	0.95	0.75
VAL	407	0.95	0.80
ARG	408	1.68	1.09
GLN	409	1.35	0.91
ILE	410	0.89	0.82
ALA	411	0.87	0.82
PRO	412	0.93	0.89
GLY	413	1.17	1.02
GLN	414	1.28	1.01
THR	415	1.23	1.37
GLY	416	0.92	0.73
LYS	417	1.59	1.19
ILE	418	0.99	0.85
ALA	419	0.90	0.71
ASP	420	0.80	0.76

TYR	421	0.76	0.69
ASN	422	0.53	0.50
TYR	423	1.02	0.58
LYS	424	1.02	1.11
LEU	425	1.01	0.96
PRO	426	0.94	0.91
ASP	427	1.39	1.52
ASP	428	1.55	1.19
PHE	429	0.90	0.78
THR	430	1.03	1.11
GLY	431	0.68	0.58
CYS	432	0.62	0.54
VAL	433	0.84	0.77
ILE	434	0.89	0.83
ALA	435	0.78	0.67
TRP	436	0.70	0.63
ASN	437	0.69	0.60
SER	438	0.62	0.56
ASN	439	0.71	0.69
ASN	440	1.57	1.11
LEU	441	1.46	1.29
ASP	442	0.61	0.58
SER	443	0.86	0.93
LYS	444	1.79	1.82
VAL	445	1.73	1.71
GLY	446	1.26	1.33
GLY	447	1.02	1.00
ASN	448	0.84	0.72
TYR	449	2.02	2.43
ASN	450	1.47	1.35
TYR	451	0.66	0.64
LEU	452	1.06	1.41
TYR	453	0.68	0.68
ARG	454	0.58	0.56
LEU	455	1.20	1.05
PHE	456	1.28	0.80
ARG	457	0.85	0.89
LYS	458	2.17	1.98
SER	459	1.19	1.03
ASN	460	1.25	1.31
LEU	461	1.28	0.99
LYS	462	1.64	1.79
PRO	463	0.85	0.93
PHE	464	0.79	0.84
GLU	465	1.09	1.22
ARG	466	1.19	1.19
ASP	467	0.69	0.86
ILE	468	1.41	1.48
SER	469	0.84	0.91
THR	470	1.11	1.25
GLU	471	1.54	1.68
ILE	472	1.14	1.23
TYR	473	1.2	1.03
GLN	474	1.72	1.64
ALA	475	1.74	1.67
GLY	476	2.17	2.02
SER	477	2.86	2.70
THR	478	2.59	2.74
PRO	479	2.42	2.3

CYS	480	1.52	1.58
ASN	481	2.42	2.22
GLY	482	1.67	1.81
VAL	483	2.03	2.08
GLU	484	1.78	1.78
GLY	485	1.37	1.65
PHE	486	2.37	3.18
ASN	487	1.70	1.84
CYS	488	1.03	1.24
TYR	489	1.13	1.15
PHE	490	0.90	0.91
PRO	491	0.65	0.69
LEU	492	0.92	1.01
GLN	493	0.91	1.06
SER	494	0.95	0.73
TYR	495	0.68	0.62
GLY	496	0.79	0.76
PHE	497	0.58	0.56
GLN	498	1.39	1.46
PRO	499	1.04	1.04
THR	500	1.23	1.30
ASN	501	0.69	0.95
GLY	502	0.82	0.90
VAL	503	1.47	1.57
GLY	504	0.79	0.74
TYR	505	1.14	0.86
GLN	506	0.62	0.62
PRO	507	0.50	0.50
TYR	508	0.61	0.64
ARG	509	0.64	0.55
VAL	510	0.86	0.75
VAL	511	0.80	0.78
VAL	512	0.81	0.75
LEU	513	0.95	0.87
SER	514	0.82	0.61
PHE	515	0.93	0.89
GLU	516	1.28	1.32
LEU	517	1.81	3.39
LEU	518	1.69	1.80
HIS	519	2.72	3.22
ALA	520	1.67	1.73
PRO	521	1.55	1.47
ALA	522	1.14	1.08
THR	523	1.11	1.00
VAL	524	0.95	0.95
CYS	525	0.97	1.00
GLY	526	1.57	1.50

Table S7: The Root-mean square fluctuation (RMSF) values of Global and Local simulation between hesperidin and RBD S protein (Hes + RBD S protein) of SARS-CoV-2

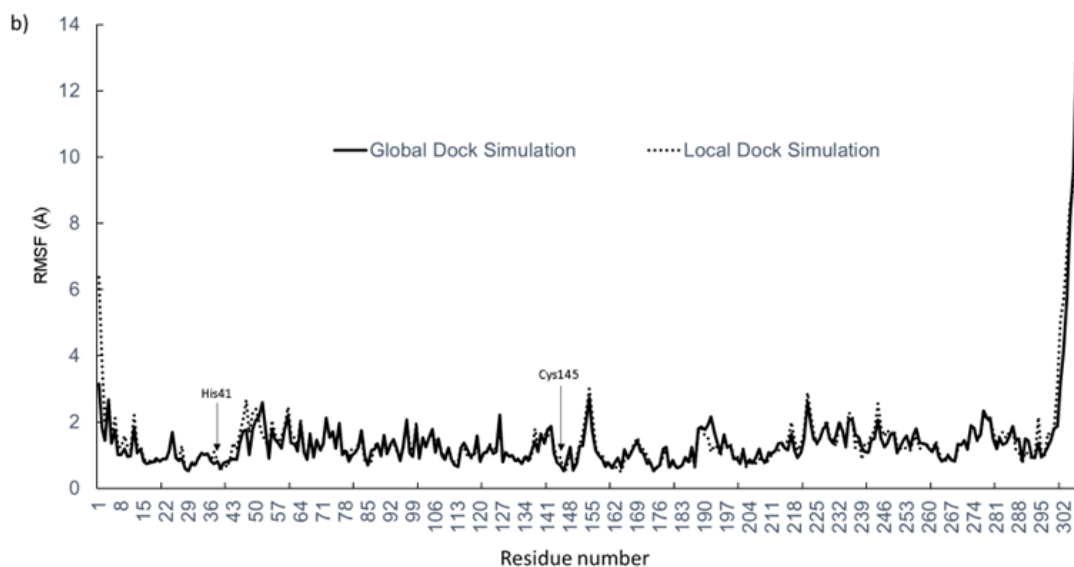


Figure S8: Root Mean Square Fluctuation (RMSF) of hesperidin and 3CL-Pro (Hes + 3CL-Pro) on Global and Local docking of SARS-CoV-2

Residue number		Root-mean square fluctuation, RMSF (Å)	
		Local simulation	Global simulation
SER	1	6.38	3.15
GLY	2	3.84	1.84
PHE	3	1.96	1.45
ARG	4	2.72	2.66
LYS	5	1.61	1.35
MET	6	2.13	1.76
ALA	7	1.29	1.01
PHE	8	1.22	1.02
PRO	9	1.58	1.20
SER	10	1.25	0.96
GLY	11	1.15	0.97
LYS	12	2.22	1.85
VAL	13	1.32	1.07
GLU	14	1.26	1.20
GLY	15	0.91	0.81
CYS	16	0.80	0.75
MET	17	0.83	0.78
VAL	18	0.80	0.80
GLN	19	0.81	0.91
VAL	20	0.82	0.81
THR	21	0.87	0.88
CYS	22	0.91	0.88
GLY	23	1.12	1.15
THR	24	1.66	1.69
THR	25	1.00	0.92
THR	26	0.87	0.83
LEU	27	1.29	0.91
ASN	28	0.55	0.58
GLY	29	0.54	0.53
LEU	30	0.79	0.77
TRP	31	0.65	0.71

LEU	32	0.93	0.89
ASP	33	1.05	1.07
ASP	34	1.01	1.01
VAL	35	1.05	1.04
VAL	36	0.81	0.82
TYR	37	1.11	0.74
CYS	38	0.82	0.82
PRO	39	0.50	0.60
ARG	40	0.79	0.76
HIS	41	0.63	0.82
VAL	42	0.89	0.85
ILE	43	1.38	0.89
CYS	44	1.17	0.87
THR	45	1.66	1.36
SER	46	2.09	1.73
GLU	47	2.66	1.77
ASP	48	1.67	1.01
MET	49	2.29	1.80
LEU	50	2.40	2.06
ASN	51	2.03	2.15
PRO	52	1.57	2.60
ASN	53	1.48	1.82
TYR	54	1.14	0.90
GLU	55	2.05	1.80
ASP	56	1.66	1.48
LEU	57	1.38	1.36
LEU	58	1.56	1.21
ILE	59	1.82	1.74
ARG	60	2.45	2.20
LYS	61	1.65	1.38
SER	62	1.51	1.34
ASN	63	1.30	1.12
HIS	64	2.08	1.96
ASN	65	1.13	1.09
PHE	66	0.96	0.87
LEU	67	1.65	1.60
VAL	68	0.91	0.94
GLN	69	1.48	1.46
ALA	70	1.11	1.16
GLY	71	1.36	1.34
ASN	72	2.06	2.12
VAL	73	1.50	1.54
GLN	74	1.68	1.71
LEU	75	1.20	1.21
ARG	76	1.92	1.96
VAL	77	1.03	1.01
ILE	78	1.19	1.12
GLY	79	0.95	0.81
HIS	80	1.20	0.99
SER	81	1.12	1.08
MET	82	1.36	1.24
GLN	83	1.61	1.75
ASN	84	0.80	0.95
CYS	85	0.69	0.71
VAL	86	0.83	1.15
LEU	87	1.32	1.17
LYS	88	1.30	1.36
LEU	89	1.06	0.98
LYS	90	1.51	1.60

VAL	91	1.02	1.04
ASP	92	1.33	1.33
THR	93	1.37	1.48
ALA	94	1.10	1.15
ASN	95	0.83	0.84
PRO	96	1.23	1.27
LYS	97	2.00	2.07
THR	98	1.34	1.06
PRO	99	1.03	0.96
LYS	100	1.98	1.87
TYR	101	0.93	0.91
LYS	102	1.54	1.53
PHE	103	1.28	1.25
VAL	104	1.48	1.52
ARG	105	1.69	1.78
ILE	106	1.43	1.08
GLN	107	1.41	1.49
PRO	108	1.11	1.00
GLY	109	0.89	0.86
GLN	110	1.20	1.23
THR	111	0.88	0.87
PHE	112	0.78	0.71
SER	113	0.82	0.65
VAL	114	1.25	1.23
LEU	115	1.21	1.38
ALA	116	0.97	1.15
CYS	117	0.91	0.96
TYR	118	0.95	1.04
ASN	119	1.33	1.59
GLY	120	0.78	0.82
SER	121	1.10	1.06
PRO	122	1.09	1.08
SER	123	1.35	1.29
GLY	124	1.11	1.04
VAL	125	1.24	1.10
TYR	126	1.70	2.22
GLN	127	1.07	0.80
CYS	128	1.08	1.08
ALA	129	0.97	0.96
MET	130	1.00	0.99
ARG	131	0.81	0.83
PRO	132	0.92	0.85
ASN	133	0.78	0.74
PHE	134	1.01	0.95
THR	135	0.85	0.83
ILE	136	0.92	1.10
LYS	137	1.80	1.43
GLY	138	1.21	1.11
SER	139	1.68	1.64
PHE	140	1.65	1.35
LEU	141	1.54	1.77
ASN	142	1.79	1.88
GLY	143	1.24	1.07
SER	144	0.86	0.78
CYS	145	0.94	0.68
GLY	146	0.50	0.52
SER	147	0.58	0.82
VAL	148	1.22	1.25
GLY	149	0.60	0.55

PHE	150	0.94	0.76
ASN	151	1.33	1.28
ILE	152	1.62	1.28
ASP	153	2.33	2.05
TYR	154	3.00	2.74
ASP	155	2.21	1.73
CYS	156	1.23	1.13
VAL	157	1.05	0.99
SER	158	1.00	0.87
PHE	159	0.71	0.66
CYS	160	0.81	0.78
TYR	161	0.58	0.61
MET	162	0.70	0.77
HIS	163	0.55	0.93
HIS	164	0.51	0.62
MET	165	0.86	1.17
GLU	166	0.97	0.91
LEU	167	1.11	1.07
PRO	168	1.35	1.27
THR	169	1.54	1.42
GLY	170	1.19	1.12
VAL	171	1.18	1.05
HIS	172	1.00	0.75
ALA	173	0.77	0.80
GLY	174	0.51	0.53
THR	175	0.62	0.64
ASP	176	0.67	0.69
LEU	177	0.98	1.19
GLU	178	1.25	1.25
GLY	179	0.59	0.63
ASN	180	0.77	0.85
PHE	181	0.62	0.65
TYR	182	0.61	0.63
GLY	183	0.71	0.70
PRO	184	0.93	0.94
PHE	185	0.75	0.79
VAL	186	1.09	1.25
ASP	187	0.64	0.68
ARG	188	1.70	1.80
GLN	189	1.82	1.85
THR	190	1.58	1.77
ALA	191	1.53	1.91
GLN	192	1.11	2.16
ALA	193	1.30	1.67
ALA	194	1.23	1.35
GLY	195	0.98	1.09
THR	196	1.57	1.62
ASP	197	1.23	1.24
THR	198	1.33	1.29
THR	199	0.95	0.89
ILE	200	1.02	0.90
THR	201	0.81	0.74
VAL	202	1.20	1.16
ASN	203	0.65	0.73
VAL	204	0.77	0.86
LEU	205	0.75	0.76
ALA	206	0.76	0.95
TRP	207	0.88	1.20
LEU	208	0.83	0.87

TYR	209	0.72	0.8
ALA	210	0.88	1.09
ALA	211	1.01	1.04
VAL	212	1.17	1.14
ILE	213	1.13	1.35
ASN	214	1.27	1.37
GLY	215	1.37	1.21
ASP	216	1.42	1.15
ARG	217	2.00	1.64
TRP	218	1.48	1.16
PHE	219	1.14	0.93
LEU	220	1.34	1.08
ASN	221	1.66	1.48
ARG	222	2.89	2.59
PHE	223	2.25	2.00
THR	224	1.69	1.49
THR	225	1.31	1.38
THR	226	1.54	1.52
LEU	227	1.78	1.78
ASN	228	2.05	1.93
ASP	229	1.55	1.50
PHE	230	1.42	1.35
ASN	231	1.29	1.63
LEU	232	2.03	1.99
VAL	233	1.69	1.71
ALA	234	1.25	1.28
MET	235	2.28	2.07
LYS	236	2.18	2.08
TYR	237	1.23	1.63
ASN	238	1.53	1.54
TYR	239	0.86	1.23
GLU	240	1.35	1.11
PRO	241	1.33	1.08
LEU	242	1.64	1.46
THR	243	1.72	1.50
GLN	244	2.56	2.08
ASP	245	1.85	1.51
HIS	246	1.56	1.25
VAL	247	1.74	1.38
ASP	248	1.63	1.63
ILE	249	1.75	1.66
LEU	250	1.30	1.06
GLY	251	1.19	1.24
PRO	252	1.27	1.47
LEU	253	1.19	1.59
SER	254	1.14	1.23
ALA	255	1.44	1.58
GLN	256	1.58	1.80
THR	257	1.19	1.38
GLY	258	1.29	1.35
ILE	259	1.39	1.33
ALA	260	1.22	1.19
VAL	261	1.16	1.11
LEU	262	1.42	1.33
ASP	263	1.11	0.96
MET	264	0.86	0.82
CYS	265	0.80	0.89
ALA	266	1.05	0.98
SER	267	0.85	0.85

LEU	268	0.81	0.83
LYS	269	1.21	1.34
GLU	270	1.34	1.32
LEU	271	1.46	1.45
LEU	272	1.15	1.18
GLN	273	1.87	1.89
ASN	274	1.87	1.82
GLY	275	1.42	1.46
MET	276	1.65	1.63
ASN	277	2.24	2.34
GLY	278	2.05	2.10
ARG	279	2.08	2.12
THR	280	1.73	1.50
ILE	281	1.32	1.20
LEU	282	1.63	1.52
GLY	283	1.70	1.32
SER	284	1.51	1.38
ALA	285	1.70	1.55
LEU	286	1.84	1.87
LEU	287	1.17	1.44
GLU	288	1.11	1.49
ASP	289	0.76	0.81
GLU	290	1.11	1.50
PHE	291	1.03	1.44
THR	292	0.90	0.94
PRO	293	0.91	0.93
PHE	294	2.14	1.38
ASP	295	0.96	0.94
VAL	296	0.96	1.04
VAL	297	1.68	1.27
ARG	298	1.55	1.47
GLN	299	1.74	1.81
CYS	300	3.13	1.88
SER	301	5.11	3.19
GLY	302	5.66	4.12
VAL	303	7.18	5.82
THR	304	8.58	8.17
PHE	305	9.04	9.64
GLN	306	11.11	12.84

Table S8: The Root-mean square fluctuation (RMSF) values of Global and Local simulation between hesperidin and 3CL-Pro (Hes + 3CL-Pro) of SARS-CoV-2

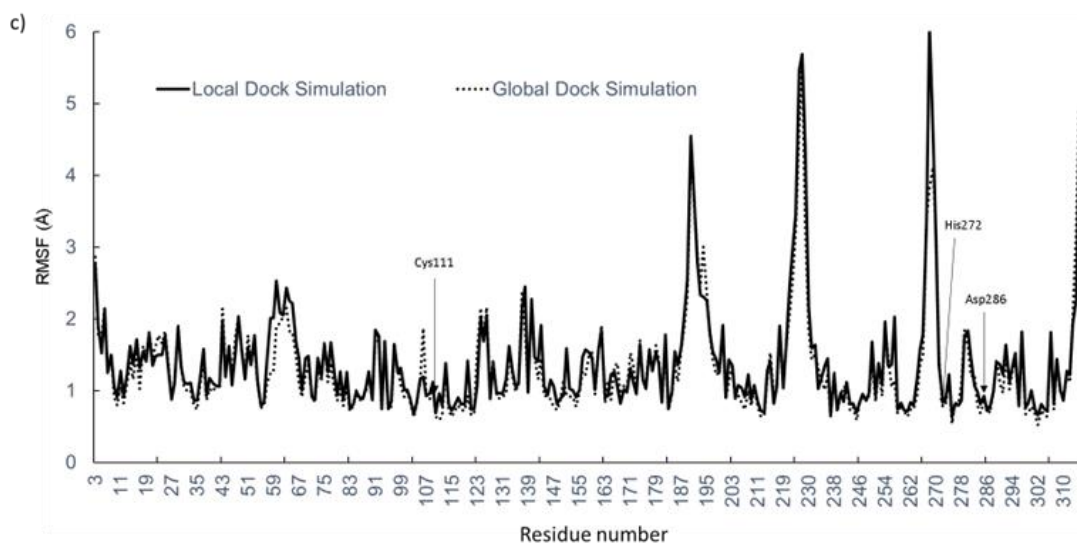


Figure S9: Root Mean Square Fluctuation (RMSF) of hesperidin and PL-Pro (Hes + PL-Pro) on Global and Local docking of SARS-CoV-2

Residue number		Root-mean square fluctuation, RMSF (Å)	
		Local simulation	Global simulation
ARG	3	2.77	2.86
THR	4	1.90	1.79
ILE	5	1.52	1.78
LYS	6	2.14	2.16
VAL	7	1.25	1.25
PHE	8	1.50	1.51
THR	9	1.05	0.92
THR	10	0.91	0.80
VAL	11	1.28	1.05
ASP	12	0.92	0.83
ASN	13	1.24	1.12
ILE	14	1.62	1.39
ASN	15	1.37	1.16
LEU	16	1.71	1.56
HIS	17	1.32	1.03
THR	18	1.55	1.62
GLN	19	1.41	1.44
VAL	20	1.80	1.81
VAL	21	1.35	1.48
ASP	22	1.48	1.62
MET	23	1.50	1.77
SER	24	1.50	1.66
MET	25	1.76	1.83
THR	26	1.27	1.33
TYR	27	0.88	0.91
GLY	28	1.11	1.09
GLN	29	1.88	1.92
GLN	30	1.34	1.35
PHE	31	1.12	1.05
GLY	32	1.09	0.99
PRO	33	1.11	1.00
THR	34	0.86	0.79
TYR	35	0.86	0.74
LEU	36	1.16	1.08
ASP	37	1.58	1.40

GLY	38	0.93	0.87
ALA	39	1.18	1.03
ASP	40	1.10	0.99
VAL	41	1.07	1.08
THR	42	1.06	1.03
LYS	43	1.97	2.14
ILE	44	1.19	1.28
LYS	45	1.62	1.62
PRO	46	1.08	1.19
HIS	47	1.55	1.76
ASN	48	2.04	2.04
SER	49	1.60	1.58
HIS	50	1.16	1.21
GLU	51	1.61	1.77
GLY	52	1.36	1.37
LYS	53	1.77	1.63
THR	54	1.14	1.10
PHE	55	0.79	0.76
TYR	56	0.84	0.79
VAL	57	1.42	1.10
LEU	58	2.01	1.24
PRO	59	2.01	1.26
ASN	60	2.53	1.90
ASP	61	2.09	1.94
ASP	62	2.05	2.03
THR	63	2.43	2.15
LEU	64	2.25	1.83
ARG	65	2.22	1.82
VAL	66	1.68	1.49
GLU	67	1.46	1.11
ALA	68	1.00	0.91
PHE	69	1.45	1.22
GLU	70	1.48	1.35
TYR	71	0.91	0.92
TYR	72	0.87	0.84
HIS	73	1.46	1.32
THR	74	1.20	1.13
THR	75	1.64	1.68
ASP	76	1.26	1.12
PRO	77	1.67	1.39
SER	78	1.31	1.06
PHE	79	0.94	0.86
LEU	80	1.27	1.03
GLY	81	0.87	0.79
ARG	82	1.26	1.05
TYR	83	0.75	0.71
MET	84	0.81	0.79
SER	85	0.99	1.00
ALA	86	0.91	0.86
LEU	87	0.89	0.90
ASN	88	1.04	0.98
HIS	89	1.27	1.19
THR	90	0.87	0.88
LYS	91	1.85	1.77
LYS	92	1.76	1.67
TRP	93	0.75	0.75
LYS	94	1.69	1.68
TYR	95	0.75	0.73
PRO	96	0.85	0.78

GLN	97	1.65	1.54
VAL	98	1.25	1.32
ASN	99	1.32	1.08
GLY	100	1.01	0.91
LEU	101	1.01	0.99
THR	102	0.89	0.84
SER	103	0.67	0.63
ILE	104	0.84	0.81
LYS	105	1.17	1.15
TRP	106	1.19	1.87
ALA	107	0.93	0.93
ASP	108	0.96	0.88
ASN	109	1.10	1.13
ASN	110	0.69	0.64
CYS	111	0.96	0.59
TYR	112	0.79	0.66
LEU	113	1.38	1.34
ALA	114	0.81	0.73
THR	115	0.72	0.64
ALA	116	0.81	0.73
LEU	117	0.90	0.80
LEU	118	0.81	0.73
THR	119	0.81	0.72
LEU	120	1.42	0.93
GLN	121	0.74	0.66
GLN	122	0.75	0.70
ILE	123	1.07	1.54
GLU	124	2.03	2.15
LEU	125	1.69	1.70
LYS	126	2.05	2.16
PHE	127	0.89	0.99
ASN	128	1.38	1.43
PRO	129	0.95	0.94
PRO	130	0.97	0.89
ALA	131	0.95	0.92
LEU	132	1.16	0.95
GLN	133	1.62	1.54
ASP	134	1.26	1.19
ALA	135	1.06	0.99
TYR	136	1.09	1.09
TYR	137	2.17	2.39
ARG	138	2.45	1.84
ALA	139	0.98	1.01
ARG	140	2.28	2.23
ALA	141	1.47	1.48
GLY	142	1.41	1.16
GLU	143	1.91	1.45
ALA	144	1.07	0.93
ALA	145	0.94	0.93
ASN	146	1.15	0.88
PHE	147	1.07	0.78
CYS	148	0.81	0.73
ALA	149	0.89	0.84
LEU	150	0.94	1.16
ILE	151	1.59	0.94
LEU	152	1.03	0.92
ALA	153	1.00	0.91
TYR	154	0.91	0.78
CYS	155	1.01	0.99

ASN	156	1.47	1.28
LYS	157	1.57	1.23
THR	158	1.53	1.48
VAL	159	1.47	1.53
GLY	160	1.01	0.95
GLU	161	1.57	1.56
LEU	162	1.85	1.91
GLY	163	0.91	0.83
ASP	164	0.93	1.14
VAL	165	1.23	0.87
ARG	166	1.26	1.34
GLU	167	1.05	1.38
THR	168	0.82	0.91
MET	169	1.02	1.08
SER	170	0.98	1.04
TYR	171	1.32	1.52
LEU	172	1.11	1.35
PHE	173	0.95	0.99
GLN	174	1.65	1.70
HIS	175	1.15	1.13
ALA	176	1.03	1.11
ASN	177	1.57	1.59
LEU	178	1.28	1.25
ASP	179	1.54	1.63
SER	180	1.37	1.43
CYS	181	0.84	0.83
LYS	182	1.78	1.62
ARG	183	0.76	0.72
VAL	184	0.98	0.95
LEU	185	1.55	1.35
ASN	186	1.36	1.13
VAL	187	1.62	1.61
VAL	188	2.06	1.90
CYS	189	2.54	2.33
LYS	190	4.55	4.30
THR	191	3.76	3.65
CYS	192	2.79	2.91
GLY	193	2.33	2.47
GLN	194	2.31	3.00
GLN	195	2.26	2.34
GLN	196	1.81	1.78
THR	197	1.54	1.44
THR	198	1.43	1.22
LEU	199	1.25	1.26
LYS	200	1.91	1.86
GLY	201	0.90	0.89
VAL	202	1.43	1.12
GLU	203	1.35	1.36
ALA	204	0.90	0.89
VAL	205	1.08	0.94
MET	206	1.04	0.83
TYR	207	0.91	0.74
MET	208	1.23	1.00
GLY	209	0.87	0.79
THR	210	1.08	1.03
LEU	211	0.85	0.78
SER	212	0.72	0.65
TYR	213	0.70	0.65
GLU	214	1.28	1.17

GLN	215	1.42	1.52
PHE	216	0.82	0.95
LYS	217	1.05	1.03
LYS	218	1.90	1.87
GLY	219	1.04	1.04
VAL	220	1.64	1.62
GLN	221	2.48	2.09
ILE	222	2.99	2.55
PRO	223	3.45	3.23
CYS	224	5.47	4.64
LYS	228	5.69	5.56
GLN	229	4.43	3.36
ALA	230	2.18	1.84
THR	231	1.59	1.43
LYS	232	1.64	1.51
TYR	233	1.03	1.32
LEU	234	1.16	1.16
VAL	235	1.34	1.01
GLN	236	1.45	1.22
GLN	237	0.67	0.64
GLU	238	1.23	1.27
SER	239	0.73	0.71
PRO	240	0.97	0.92
PHE	241	0.85	1.06
VAL	242	1.12	1.03
MET	243	0.81	0.72
MET	244	0.82	0.77
SER	245	0.70	0.59
ALA	246	0.84	0.83
PRO	247	0.95	0.92
PRO	248	0.86	0.87
ALA	249	0.97	0.93
GLN	250	1.68	1.39
TYR	251	0.92	0.85
GLU	252	1.38	1.29
LEU	253	1.08	0.93
LYS	254	1.96	1.90
HIS	255	1.35	1.48
GLY	256	1.36	1.05
THR	257	2.03	1.14
PHE	258	0.74	0.69
THR	259	0.83	0.80
CYS	260	0.73	0.71
ALA	261	0.71	0.64
SER	262	0.84	0.74
GLU	263	0.80	0.74
TYR	264	1.16	0.94
THR	265	1.57	1.36
GLY	266	1.79	1.50
ASN	267	3.35	3.39
TYR	268	6.10	3.82
GLN	269	4.58	4.12
CYS	270	3.13	3.15
GLY	271	1.36	1.46
HIS	272	0.90	0.79
TYR	273	0.87	0.79
LYS	274	1.23	1.19
HIS	275	0.63	0.54
ILE	276	0.81	0.83

THR	277	0.80	0.82
SER	278	0.86	1.10
LYS	279	1.75	1.85
GLU	280	1.84	1.62
THR	281	1.46	1.20
LEU	282	1.07	1.23
TYR	283	0.99	0.80
CYS	284	0.81	0.69
ILE	285	0.93	0.85
ASP	286	0.72	0.78
GLY	287	0.77	0.69
ALA	288	0.99	0.99
LEU	289	1.40	1.44
LEU	290	1.37	1.10
THR	291	1.23	0.97
LYS	292	1.64	1.48
SER	293	1.12	1.02
SER	294	1.33	1.26
GLU	295	1.52	1.44
TYR	296	0.79	0.77
LYS	297	1.82	1.78
GLY	298	0.76	0.67
PRO	299	0.83	0.70
ILE	300	1.00	0.78
THR	301	0.75	0.68
ASP	302	0.66	0.52
VAL	303	0.81	0.73
PHE	304	0.75	0.66
TYR	305	0.71	0.64
LYS	306	1.81	1.72
GLU	307	0.81	0.74
ASN	308	1.44	1.44
SER	309	1.01	0.95
TYR	310	0.86	0.90
THR	311	1.28	1.22
THR	312	1.22	1.12
THR	313	1.94	2.03
ILE	314	2.27	3.29
LYS	315	4.25	4.96

Table S9: The Root-mean square fluctuation (RMSF) values of Global and Local simulation between hesperidin and PL-Pro (Hes + PL-Pro) of SARS-CoV-2

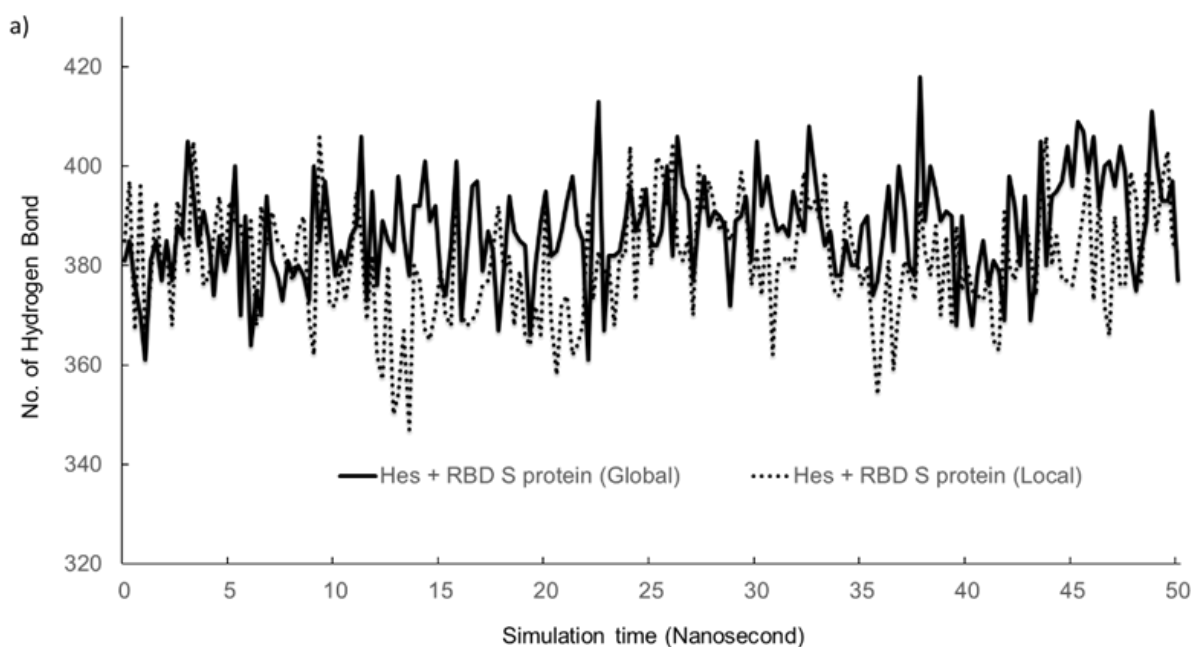


Figure S10: Number of Hydrogen Bond between solute and solvent of Hes + RBD S protein on Local and Global Docking

Simulation time (nanosecond, ns)	Number of Hydrogen Bond	
	Local simulation	Global simulation
0.00	385	381
0.25	397	385
0.50	367	376
0.75	396	370
1.00	366	361
1.25	377	381
1.50	393	385
1.75	378	377
2.00	384	385
2.25	368	377
2.50	393	388
2.75	388	386
3.00	379	405
3.25	405	395
3.50	395	384
3.75	376	391
4.00	378	385
4.25	386	374
4.50	394	386
4.75	380	379
5.00	393	384
5.25	389	400
5.50	388	370
5.75	382	390
6.00	389	364
6.25	368	375
6.50	392	370
6.75	384	394
7.00	391	381
7.25	385	378
7.50	384	373

7.75	379	381
8.00	377	378
8.25	387	380
8.5	390	378
8.75	369	373
9.00	362	400
9.25	406	385
9.50	391	397
9.75	372	388
10.00	372	378
10.25	380	383
10.50	373	380
10.75	381	386
11.00	395	388
11.25	386	406
11.50	369	373
11.75	382	395
12.00	362	376
12.25	357	389
12.50	380	385
12.75	350	383
13.00	354	398
13.25	367	386
13.50	347	378
13.75	380	392
14.00	377	392
14.25	367	401
14.50	365	389
14.75	371	392
15.00	379	377
15.25	370	374
15.50	368	384
15.75	400	401
16.00	370	369
16.25	368	383
16.50	369	396
16.75	371	397
17.00	376	379
17.25	377	387
17.50	383	383
17.75	392	367
18.00	379	379
18.25	382	394
18.50	368	387
18.75	379	385
19.00	366	384
19.25	364	366
19.50	372	380
19.75	366	389
20.00	393	395
20.25	369	382
20.50	358	383
20.75	372	387
21.00	374	393
21.25	362	398
21.50	364	388
21.75	368	385
22.00	391	361
22.25	373	393

22.50	383	413
22.75	378	367
23.00	380	382
23.25	368	382
23.50	382	383
23.75	382	389
24.00	404	396
24.25	373	387
24.50	395	390
24.75	396	395
25.00	380	384
25.25	402	384
25.50	400	387
25.75	392	400
26.00	404	382
26.25	384	406
26.50	381	396
26.75	386	393
27.00	370	377
27.25	400	389
27.50	391	398
27.75	397	388
28.00	392	391
28.25	387	390
28.50	389	388
28.75	385	372
29.00	388	389
29.25	399	390
29.50	392	394
29.75	376	381
30.00	383	405
30.25	374	392
30.50	389	398
30.75	362	391
31.00	380	387
31.25	381	388
31.50	382	386
31.75	379	395
32.00	389	390
32.25	399	387
32.50	391	408
32.75	393	399
33.00	389	390
33.25	399	384
33.50	379	387
33.75	374	378
34.00	374	378
34.25	393	385
34.50	385	380
34.75	381	380
35.00	376	388
35.25	380	390
35.50	366	374
35.75	354	377
36.00	369	386
36.25	381	396
36.50	359	383
36.75	372	400
37.00	381	392

37.25	378	380
37.50	373	378
37.75	393	418
38.00	383	389
38.25	378	400
38.50	388	395
38.75	370	389
39.00	386	391
39.25	368	390
39.50	388	368
39.75	375	390
40.00	380	375
40.25	375	368
40.50	374	379
40.75	373	385
41.00	379	376
41.25	365	381
41.50	363	379
41.75	391	369
42.00	380	398
42.25	377	392
42.50	385	380
42.75	390	394
43.00	382	369
43.25	374	379
43.50	398	405
43.75	406	380
44.00	380	394
44.25	386	395
44.50	377	397
44.75	377	404
45.00	376	396
45.25	383	409
45.50	391	407
45.75	399	399
46.00	373	406
46.25	394	392
46.50	372	400
46.75	366	401
47.00	390	396
47.25	376	404
47.50	376	399
47.75	399	382
48.00	394	375
48.25	376	383
48.50	399	389
48.75	397	411
49.00	387	401
49.25	397	393
49.50	403	393
49.75	385	397
50.00	382	377

Table S10: Number of Hydrogen Bonds between solute and solvent per simulation time of Hes + RBD S protein

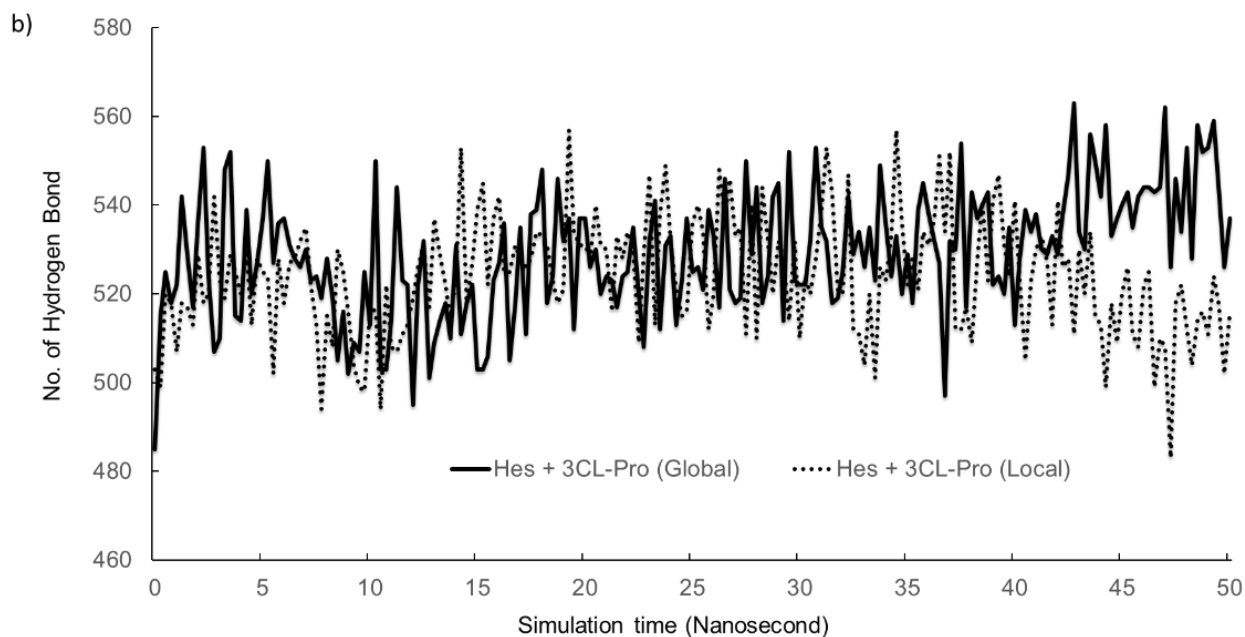


Figure S11: Number of Hydrogen Bond between solute and solvent of Hes + 3CL-Pro on Local and Global Docking

Simulation time (nanosecond, ns)	Number of Hydrogen Bond	
	Local simulation	Global simulation
0.00	503	485
0.25	499	515
0.50	520	525
0.75	518	518
1.00	507	522
1.25	518	542
1.50	517	529
1.75	513	517
2.00	529	536
2.25	518	553
2.50	520	524
2.75	542	507
3.00	523	510
3.25	519	548
3.50	529	552
3.75	525	515
4.00	520	514
4.25	530	539
4.50	513	520
4.75	528	527
5.00	525	537
5.25	524	550
5.50	502	527
5.75	528	536
6.00	518	537
6.25	527	531
6.50	528	528
6.75	532	526
7.00	535	530
7.25	522	523
7.50	513	524
7.75	494	519
8.00	515	528

8.25	508	519
08.5	530	505
8.75	525	516
9.00	516	502
9.25	504	509
9.50	499	507
9.75	498	525
10.00	517	513
10.25	516	550
10.50	494	503
10.75	522	503
11.00	508	514
11.25	507	544
11.50	511	523
11.75	513	522
12.00	519	495
12.25	526	522
12.50	531	532
12.75	517	501
13.00	537	509
13.25	529	514
13.50	522	518
13.75	514	510
14.00	524	531
14.25	553	511
14.50	518	518
14.75	527	522
15.00	539	503
15.25	545	503
15.50	522	506
15.75	537	523
16.00	542	527
16.25	525	536
16.50	525	505
16.75	531	518
17.00	528	535
17.25	526	511
17.50	528	538
17.75	534	539
18.00	533	548
18.25	531	518
18.50	523	524
18.75	518	546
19.00	521	532
19.25	557	537
19.50	534	512
19.75	531	537
20.00	531	537
20.25	528	526
20.50	540	530
20.75	531	520
21.00	530	524
21.25	516	523
21.50	533	517
21.75	528	524
22.00	534	525
22.25	530	535
22.50	509	520
22.75	529	508

23.00	547	532
23.25	513	541
23.50	538	512
23.75	549	531
24.00	532	533
24.25	521	513
24.50	515	523
24.75	516	537
25.00	536	525
25.25	540	526
25.50	534	521
25.75	512	539
26.00	520	533
26.25	548	517
26.50	537	546
26.75	546	521
27.00	533	518
27.25	535	519
27.50	511	550
27.75	540	529
28.00	510	544
28.25	544	518
28.50	532	524
28.75	520	542
29.00	532	545
29.25	528	514
29.50	514	552
29.75	532	523
30.00	510	522
30.25	524	522
30.50	520	532
30.75	528	553
31.00	539	535
31.25	553	532
31.50	543	518
31.75	521	519
32.00	520	525
32.25	547	542
32.50	512	529
32.75	511	534
33.00	504	526
33.25	520	535
33.50	501	523
33.75	526	549
34.00	523	536
34.25	533	524
34.50	557	533
34.75	536	520
35.00	522	529
35.25	528	518
35.50	521	539
35.75	534	545
36.00	531	538
36.25	537	532
36.50	551	527
36.75	534	497
37.00	552	532
37.25	512	530
37.50	512	554

37.75	517	517
38.00	509	543
38.25	528	537
38.50	541	540
38.75	523	543
39.00	541	522
39.25	547	524
39.50	531	520
39.75	524	535
40.00	541	513
40.25	523	528
40.50	505	539
40.75	523	534
41.00	530	538
41.25	533	530
41.50	527	529
41.75	513	533
42.00	541	529
42.25	526	538
42.50	528	547
42.75	511	563
43.00	530	534
43.25	520	530
43.50	534	556
43.75	515	550
44.00	513	542
44.25	499	558
44.50	518	533
44.75	509	537
45.00	520	540
45.25	526	543
45.50	511	535
45.75	508	542
46.00	522	544
46.25	525	544
46.50	499	543
46.75	510	544
47.00	508	562
47.25	483	526
47.50	518	546
47.75	522	534
48.00	512	553
48.25	504	528
48.50	514	558
48.75	516	552
49.00	511	553
49.25	524	559
49.50	518	544
49.75	502	526
50.00	516	537

Table S11: Number of Hydrogen Bonds between solute and solvent per simulation time of Hes + 3CL-Pro

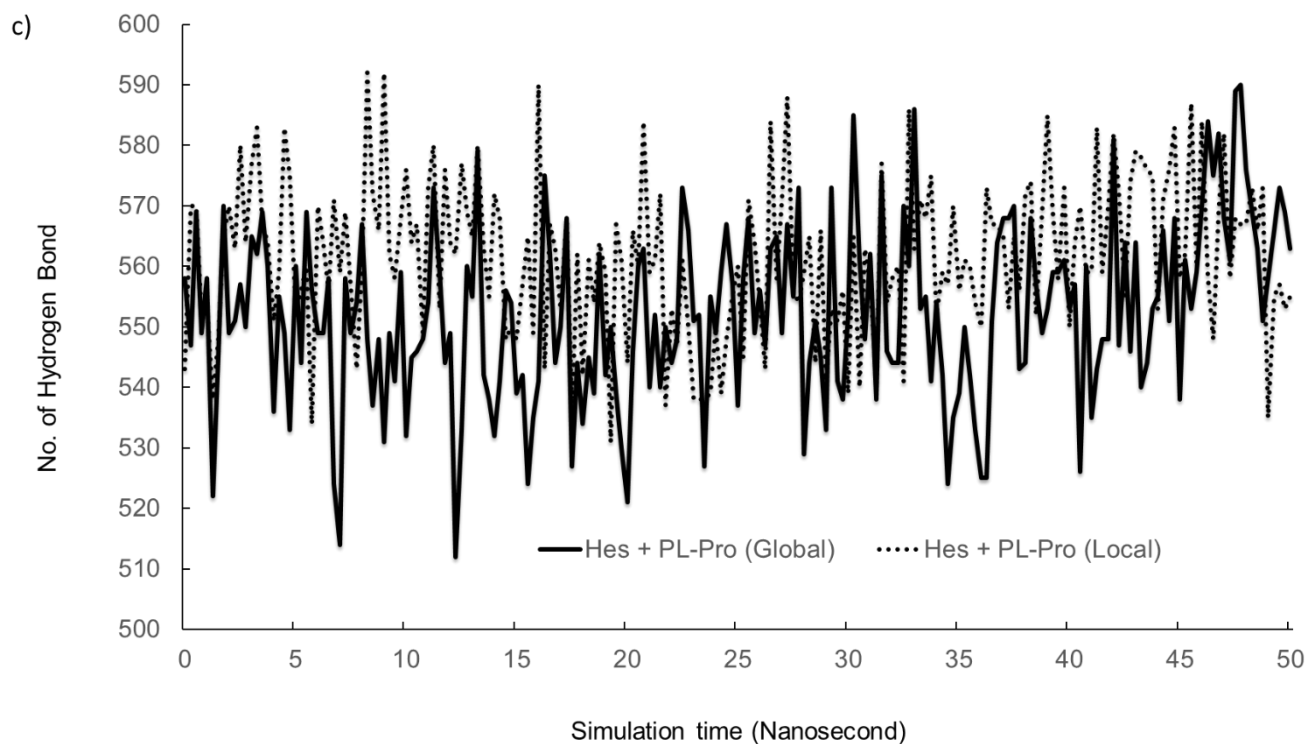


Figure S12: Number of Hydrogen Bond between solute and solvent of Hes + PL-Pro on Local and Global Docking

Simulation time (nanosecond, ns)	Number of Hydrogen Bond	
	Local simulation	Global simulation
0.00	543	558
0.25	570	547
0.50	570	569
0.75	552	549
1.00	554	558
1.25	538	522
1.50	548	545
1.75	565	570
2.00	570	549
2.25	563	551
2.50	580	557
2.75	564	550
3.00	577	565
3.25	583	562
3.50	567	569
3.75	564	560
4.00	551	536
4.25	559	555
4.50	583	549
4.75	575	533
5.00	552	560
5.25	556	544
5.50	560	569
5.75	534	556
6.00	570	549
6.25	564	549
6.50	556	558
6.75	571	524

7.00	559	514
7.25	569	558
7.50	557	549
7.75	543	554
8.00	560	567
8.25	592	548
8.50	572	537
8.75	566	548
9.00	592	531
9.25	562	549
9.50	558	541
9.75	568	559
10.00	576	532
10.25	564	545
10.50	567	546
10.75	549	548
11.00	573	554
11.25	580	573
11.50	553	559
11.75	576	544
12.00	564	549
12.25	562	512
12.50	577	533
12.75	569	560
13.00	565	555
13.25	580	579
13.50	563	542
13.75	555	538
14.00	572	532
14.25	568	541
14.50	548	556
14.75	550	554
15.00	548	539
15.25	557	542
15.50	565	524
15.75	549	535
16.00	590	541
16.25	543	575
16.50	567	562
16.75	563	544
17.00	553	550
17.25	568	568
17.50	535	527
17.75	562	544
18.00	542	534
18.25	561	545
18.50	554	539
18.75	564	562
19.00	559	542
19.25	531	550
19.50	567	539
19.75	561	530
20.00	544	521
20.25	566	546
20.50	560	560
20.75	584	563
21.00	559	540
21.25	561	552
21.50	572	540

21.75	537	550
22.00	553	544
22.25	547	548
22.50	561	573
22.75	550	566
23.00	538	551
23.25	538	552
23.50	538	527
23.75	539	555
24.00	550	549
24.25	539	559
24.50	548	567
24.75	555	557
25.00	560	537
25.25	545	558
25.50	571	568
25.75	564	549
26.00	554	556
26.25	543	547
26.50	584	563
26.75	558	565
27.00	571	549
27.25	588	567
27.50	556	555
27.75	554	573
28.00	559	529
28.25	565	544
28.50	544	551
28.75	566	545
29.00	541	533
29.25	553	573
29.50	551	541
29.75	556	538
30.00	539	552
30.25	565	585
30.50	540	561
30.75	563	548
31.00	557	562
31.25	541	538
31.50	577	575
31.75	554	546
32.00	558	544
32.25	560	544
32.50	541	570
32.75	586	560
33.00	563	586
33.25	571	553
33.50	568	555
33.75	575	541
34.00	552	554
34.25	559	542
34.50	557	524
34.75	570	535
35.00	556	539
35.25	561	550
35.50	560	542
35.75	554	533
36.00	550	525
36.25	573	525

36.50	567	551
36.75	567	564
37.00	565	568
37.25	553	568
37.50	565	570
37.75	556	543
38.00	572	544
38.25	574	568
38.50	552	557
38.75	569	549
39.00	585	553
39.25	569	559
39.50	558	559
39.75	573	561
40.00	550	553
40.25	564	557
40.50	570	526
40.75	559	560
41.00	559	535
41.25	583	543
41.50	559	548
41.75	570	548
42.00	582	581
42.25	572	547
42.50	555	564
42.75	574	546
43.00	579	564
43.25	578	540
43.50	576	544
43.75	575	553
44.00	553	555
44.25	571	566
44.50	576	551
44.75	583	568
45.00	558	538
45.25	562	561
45.50	587	553
45.75	560	559
46.00	584	570
46.25	558	584
46.50	548	575
46.75	569	582
47.00	582	568
47.25	558	561
47.50	568	589
47.75	567	590
48.00	567	576
48.25	573	569
48.50	566	563
48.75	573	551
49.00	535	558
49.25	555	566
49.50	557	573
49.75	553	569
50.00	555	563

Table S12: Number of Hydrogen Bonds between solute and solvent per simulation time of Hes + PL-Pro