

Supplementary Information

Binding properties of the anti-TB drugs bedaquiline and TBAJ-876 to a mycobacterial F-ATP synthase

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Table S1: Number of heavy-atom contacts between each drug and the protein (cut-off 5 Å). Average and standard deviations for each system were obtained over the whole triplicate simulation sampling (300 ns).

a) drug and E65 charged		
Number of contacts		
	BDQ	TBAJ-876
Lagging	64.4 ± 4.1	72.5 ± 4.2
Leading	74.4 ± 5.6	81.2 ± 6.4
c-ring	50.7 ± 5.1	52.5 ± 4.3

b) drug and E65 neutral		
Number of contacts		
	BDQ	TBAJ-876
Lagging	60.7 ± 4.3	65.5 ± 4.6
Leading	74.6 ± 5.5	76.6 ± 10.2
c-ring	44.8 ± 4.5	45.7 ± 5.3

Table S2: Minimum distances of protein residues to BDQ and TBAJ-876. Distances are shown for both drugs bound to each site (leading, lagging and *c*-ring only) when drug and key-glutamate are neutral. Averages and standard deviations were derived from merging all data over all simulated trajectories (300 ns each).

	BDQ (protonated)			TBAJ-876 (protonated)		
	<i>c</i> -ring	Lagging	Leading	<i>c</i> -ring	Lagging	Leading
A28	5.8 ± 0.9	4.7 ± 0.5	5.4 ± 0.5	5.7 ± 1.1	5.0 ± 0.5	5.1 ± 0.6
V61	5.2 ± 0.7	5.7 ± 0.5	5.4 ± 0.5	5.4 ± 0.7	5.2 ± 0.5	5.6 ± 0.5
G62	4.4 ± 0.4	4.5 ± 0.4	4.4 ± 0.3	4.4 ± 0.4	4.2 ± 0.3	4.4 ± 0.4
L63	4.3 ± 0.6	4.6 ± 0.5	4.3 ± 0.5	4.4 ± 0.6	4.5 ± 0.5	4.4 ± 0.6
E65	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.3	3.6 ± 0.2	3.6 ± 0.3
A66	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.3	3.6 ± 0.2	3.6 ± 0.2
A67	4.4 ± 1.0	3.8 ± 0.2	3.8 ± 0.2	4.2 ± 1.1	3.8 ± 0.2	3.9 ± 0.3
Y68	3.7 ± 0.3	3.6 ± 0.2	3.8 ± 0.3	4.0 ± 1.0	3.6 ± 0.2	3.7 ± 0.2
F69	3.5 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.5 ± 0.1	3.4 ± 0.2	3.4 ± 0.2
I70	3.7 ± 0.3	3.7 ± 0.2	3.6 ± 0.2	3.8 ± 0.2	3.7 ± 0.2	3.6 ± 0.2
L72	4.6 ± 1.1	3.8 ± 0.3	4.5 ± 0.6	4.6 ± 1.7	3.8 ± 0.4	3.8 ± 0.6
F74	6.8 ± 1.2	5.0 ± 0.8	7.2 ± 1.2	6.2 ± 2.3	4.3 ± 0.7	4.9 ± 1.1
E65:Oε2 - LIG:N^{neutral}	3.5 ± 1.3	2.8 ± 0.1	2.8 ± 0.2	3.2 ± 0.2	2.8 ± 0.1	2.8 ± 0.2
F169	N/A	5.17 ± 1.14	N/A	N/A	4.5 ± 0.8	N/A
L170	N/A	4.41 ± 0.54	N/A	N/A	4.0 ± 0.4	N/A
P172	N/A	3.98 ± 0.31	N/A	N/A	3.6 ± 0.3	N/A
I173	N/A	3.62 ± 0.18	N/A	N/A	3.6 ± 0.2	N/A
V176	N/A	3.68 ± 0.29	N/A	N/A	3.8 ± 0.3	N/A
L199	N/A	N/A	5.7 ± 0.7	N/A	N/A	6.3 ± 2.0
F206	N/A	N/A	8.3 ± 1.2	N/A	N/A	5.6 ± 2.4
F213	N/A	N/A	3.8 ± 0.3	N/A	N/A	3.9 ± 0.5
P214	N/A	N/A	4.8 ± 0.7	N/A	N/A	4.6 ± 1.2
V217	N/A	N/A	3.7 ± 0.3	N/A	N/A	4.2 ± 0.8
W218	N/A	N/A	2.3 ± 0.5	N/A	N/A	3.6 ± 1.9
F221	N/A	N/A	2.9 ± 0.4	N/A	N/A	2.6 ± 0.6

Table S3: Block analysis of the minimum distances for both drugs. The minimum distances for windows of 10 – 70 ns, 40 – 70 ns and 70 – 100 ns are shown for all three sites. In a) and b) the BDQ bound state is shown in its charged and neutral state, respectively. In c) and d) the minimum distances for the TBAJ-876 bound state are shown when drug and key-glutamate are charged or neutral, respectively.

a) BDQ (deprotonated)	c-ring			Lagging			Leading		
	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns
cA28	4.9 ± 0.6	4.8 ± 0.6	4.7 ± 0.6	4.9 ± 0.6	4.8 ± 0.5	4.8 ± 0.6	5.4 ± 0.6	5.2 ± 0.7	5.6 ± 0.8
cV61	4.2 ± 0.3	4.2 ± 0.4	4.1 ± 0.5	5.0 ± 0.5	5.4 ± 0.7	5.5 ± 0.7	4.8 ± 0.6	5.3 ± 0.8	5.5 ± 1.0
cG62	4.0 ± 0.4	4.0 ± 0.4	3.9 ± 0.3	4.2 ± 0.3	4.4 ± 0.4	4.5 ± 0.5	4.4 ± 0.3	4.4 ± 0.4	4.6 ± 0.6
cL63	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	4.2 ± 0.3	4.3 ± 0.4	4.8 ± 0.7	4.0 ± 0.3	4.2 ± 0.4	4.4 ± 0.8
cE65	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.3	3.5 ± 0.1	3.5 ± 0.1	3.6 ± 0.2	3.5 ± 0.1	3.5 ± 0.1	3.6 ± 0.2
cA66	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.3	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2
cA67	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.7 ± 0.3	3.7 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.9 ± 0.3	4.2 ± 0.4
cY68	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.7 ± 0.1	3.7 ± 0.2	3.7 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.7 ± 0.2
cF69	3.7 ± 0.3	3.7 ± 0.3	3.7 ± 0.3	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2
cI70	5.0 ± 1.2	5.1 ± 1.3	5.2 ± 1.4	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.9 ± 0.5
cL72	7.1 ± 1.2	7.1 ± 1.2	7.1 ± 1.3	3.9 ± 0.3	3.8 ± 0.3	3.6 ± 0.2	4.7 ± 0.7	4.5 ± 0.7	5.1 ± 1.5
cF74	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	5.5 ± 0.6	5.0 ± 0.7	5.0 ± 0.7	7.1 ± 0.8	6.9 ± 0.9	7.1 ± 1.5
cE65:Oex-LIG:N	4.9 ± 0.6	4.8 ± 0.6	4.7 ± 0.6	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.8 ± 0.1
aF169	N/A	N/A	N/A	5.9 ± 1.5	5.6 ± 1.4	5.1 ± 1.4	N/A	N/A	N/A
aL170	N/A	N/A	N/A	4.3 ± 0.5	4.3 ± 0.5	4.5 ± 0.6	N/A	N/A	N/A
aP172	N/A	N/A	N/A	3.9 ± 0.3	3.9 ± 0.3	3.9 ± 0.3	N/A	N/A	N/A
aI173	N/A	N/A	N/A	3.7 ± 0.2	3.6 ± 0.2	3.7 ± 0.2	N/A	N/A	N/A
aV176	N/A	N/A	N/A	3.8 ± 0.3	3.8 ± 0.3	3.7 ± 0.3	N/A	N/A	N/A
aL199	N/A	N/A	N/A	N/A	N/A	N/A	4.9 ± 0.8	5.4 ± 0.9	5.8 ± 1.1
aF213	N/A	N/A	N/A	N/A	N/A	N/A	4.0 ± 0.4	4.1 ± 0.5	4.1 ± 0.6
aP214	N/A	N/A	N/A	N/A	N/A	N/A	5.4 ± 0.6	5.2 ± 0.7	6.0 ± 1.2
aV217	N/A	N/A	N/A	N/A	N/A	N/A	3.8 ± 0.3	3.8 ± 0.3	3.9 ± 0.3
aW218	N/A	N/A	N/A	N/A	N/A	N/A	2.1 ± 0.3	2.2 ± 0.5	2.4 ± 0.5
aF221	N/A	N/A	N/A	N/A	N/A	N/A	3.2 ± 0.4	3.3 ± 0.4	3.5 ± 0.5

b) BDQ (protonated)	c-ring			Lagging			Leading		
	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns
cA28	5.7 ± 0.8	6.0 ± 0.9	6.0 ± 0.9	4.6 ± 0.5	4.8 ± 0.5	4.9 ± 0.5	5.4 ± 0.5	5.4 ± 0.5	5.5 ± 0.5
cV61	5.4 ± 0.7	5.1 ± 0.8	5.1 ± 0.8	5.7 ± 0.5	5.6 ± 0.5	5.8 ± 0.5	5.4 ± 0.5	5.4 ± 0.5	5.3 ± 0.5
cG62	4.4 ± 0.4	4.3 ± 0.4	4.3 ± 0.4	4.5 ± 0.4	4.4 ± 0.3	4.5 ± 0.4	4.4 ± 0.3	4.4 ± 0.3	4.4 ± 0.3
cL63	4.3 ± 0.5	4.4 ± 0.7	4.4 ± 0.7	4.5 ± 0.5	4.6 ± 0.6	4.6 ± 0.6	4.2 ± 0.4	4.3 ± 0.4	4.3 ± 0.5
cE65	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2
cA66	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2
cA67	4.1 ± 0.8	4.6 ± 1.2	4.6 ± 1.2	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.9 ± 0.3	3.9 ± 0.2	3.8 ± 0.3
cY68	3.8 ± 0.3	3.7 ± 0.3	3.7 ± 0.3	3.6 ± 0.2	3.7 ± 0.2	3.7 ± 0.2	3.7 ± 0.3	3.8 ± 0.3	3.8 ± 0.3
cF69	3.5 ± 0.2	3.5 ± 0.2	3.5 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.5 ± 0.2
cI70	3.6 ± 0.3	3.7 ± 0.3	3.7 ± 0.3	3.7 ± 0.2	3.7 ± 0.2	3.7 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.7 ± 0.2
cL72	4.5 ± 1.0	4.7 ± 1.2	4.7 ± 1.2	3.8 ± 0.2	3.8 ± 0.3	3.9 ± 0.3	4.5 ± 0.6	4.4 ± 0.6	4.6 ± 0.7
cF74	6.4 ± 1.1	7.1 ± 1.2	7.1 ± 1.2	4.9 ± 0.8	4.9 ± 0.8	5.2 ± 0.8	6.9 ± 1.0	7.4 ± 1.1	7.8 ± 1.3
cE65:O _{Ex} -LIG:N	3.2 ± 1.0	3.8 ± 1.5	3.9 ± 1.6	2.8 ± 0.1	2.8 ± 0.1	2.8 ± 0.1	2.8 ± 0.1	2.9 ± 0.4	2.8 ± 0.1
αF169	N/A	N/A	N/A	5.6 ± 1.2	5.5 ± 1.2	4.3 ± 0.6	N/A	N/A	N/A
αL170	N/A	N/A	N/A	4.3 ± 0.5	4.5 ± 0.5	4.5 ± 0.6	N/A	N/A	N/A
αP172	N/A	N/A	N/A	3.9 ± 0.3	4.0 ± 0.3	4.1 ± 0.3	N/A	N/A	N/A
αI173	N/A	N/A	N/A	3.6 ± 0.2	3.6 ± 0.2	3.7 ± 0.2	N/A	N/A	N/A
αV176	N/A	N/A	N/A	3.8 ± 0.3	3.7 ± 0.3	3.6 ± 0.3	N/A	N/A	N/A
αL199	N/A	N/A	N/A	N/A	N/A	N/A	5.6 ± 0.7	5.9 ± 0.8	5.7 ± 0.7
αF213	N/A	N/A	N/A	N/A	N/A	N/A	3.8 ± 0.3	3.7 ± 0.3	3.8 ± 0.4
αP214	N/A	N/A	N/A	N/A	N/A	N/A	4.6 ± 0.5	4.8 ± 0.6	5.0 ± 0.9
αV217	N/A	N/A	N/A	N/A	N/A	N/A	3.7 ± 0.3	3.6 ± 0.3	3.6 ± 0.2
αW218	N/A	N/A	N/A	N/A	N/A	N/A	2.3 ± 0.4	2.4 ± 0.6	2.3 ± 0.4
αF221	N/A	N/A	N/A	N/A	N/A	N/A	2.9 ± 0.4	2.9 ± 0.4	2.9 ± 0.4

c) TBAJ-876 (deprotonated)	c-ring			Lagging			Leading		
	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns
cA28	5.0 ± 0.5	5.0 ± 0.5	5.0 ± 0.5	5.0 ± 0.5	5.0 ± 0.5	5.0 ± 0.5	5.2 ± 0.6	5.0 ± 0.7	5.5 ± 0.6
cV61	5.0 ± 0.5	4.9 ± 0.6	4.8 ± 0.6	4.5 ± 0.5	4.6 ± 0.5	4.7 ± 0.5	5.0 ± 0.8	5.2 ± 1.0	5.1 ± 0.9
cG62	4.1 ± 0.3	4.1 ± 0.3	4.1 ± 0.4	4.0 ± 0.2	4.1 ± 0.2	4.1 ± 0.3	4.4 ± 0.3	4.6 ± 0.4	4.5 ± 0.4
cL63	4.0 ± 0.3	4.0 ± 0.3	4.0 ± 0.3	4.0 ± 0.3	4.0 ± 0.3	4.0 ± 0.3	4.3 ± 0.8	4.5 ± 0.9	4.5 ± 0.9
cE65	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.2	3.5 ± 0.2	3.5 ± 0.2
cA66	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2
cA67	3.8 ± 0.2	3.9 ± 0.3	3.9 ± 0.3	3.6 ± 0.2	3.6 ± 0.2	3.7 ± 0.2	3.9 ± 0.3	4.0 ± 0.3	3.9 ± 0.3
cY68	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.3	3.8 ± 0.3
cF69	3.4 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.5 ± 0.2	3.4 ± 0.2	3.4 ± 0.2
cI70	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.7 ± 0.3	3.6 ± 0.2	3.6 ± 0.3	3.7 ± 0.3
cL72	3.8 ± 0.7	3.8 ± 0.7	3.9 ± 0.8	3.5 ± 0.3	3.5 ± 0.3	3.4 ± 0.3	4.4 ± 0.9	4.5 ± 0.9	4.7 ± 0.9
cF74	5.3 ± 1.1	5.6 ± 1.2	6.0 ± 1.4	4.8 ± 0.7	5.2 ± 1.2	5.4 ± 1.2	6.7 ± 1.8	7.0 ± 2.2	7.0 ± 2.2
cE65:OEx-LIG:N	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1
αF169	N/A	N/A	N/A	4.4 ± 0.8	4.9 ± 1.0	4.3 ± 0.8	N/A	N/A	N/A
αL170	N/A	N/A	N/A	4.0 ± 0.4	4.0 ± 0.4	4.1 ± 0.5	N/A	N/A	N/A
αP172	N/A	N/A	N/A	3.5 ± 0.3	3.6 ± 0.3	3.6 ± 0.3	N/A	N/A	N/A
αI173	N/A	N/A	N/A	3.6 ± 0.2	3.5 ± 0.2	3.6 ± 0.2	N/A	N/A	N/A
αV176	N/A	N/A	N/A	3.7 ± 0.3	3.8 ± 0.3	3.8 ± 0.3	N/A	N/A	N/A
αL199	N/A	N/A	N/A	N/A	N/A	N/A	5.2 ± 0.9	5.0 ± 1.3	4.4 ± 1.4
αF213	N/A	N/A	N/A	N/A	N/A	N/A	3.6 ± 0.3	3.7 ± 0.4	4.0 ± 0.7
αP214	N/A	N/A	N/A	N/A	N/A	N/A	4.2 ± 0.5	4.5 ± 0.7	4.3 ± 0.5
αV217	N/A	N/A	N/A	N/A	N/A	N/A	3.8 ± 0.3	3.8 ± 0.3	3.9 ± 0.5
αW218	N/A	N/A	N/A	N/A	N/A	N/A	2.3 ± 0.4	2.4 ± 0.5	2.5 ± 0.6
αF221	N/A	N/A	N/A	N/A	N/A	N/A	3.1 ± 0.4	3.1 ± 0.5	3.2 ± 0.5

d) TBAJ-876 (protonated)	c-ring			Lagging			Leading		
	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns	10-40 ns	40-70 ns	70-100 ns
cA28	5.1 ± 0.5	5.1 ± 0.6	5.2 ± 0.7	4.9 ± 0.6	4.8 ± 0.5	4.8 ± 0.6	5.2 ± 0.5	5.2 ± 0.7	5.6 ± 0.8
cV61	4.9 ± 0.6	4.8 ± 0.6	4.7 ± 0.6	5.0 ± 0.5	5.4 ± 0.7	5.5 ± 0.7	5.7 ± 0.5	5.3 ± 0.8	5.5 ± 1.0
cG62	4.2 ± 0.3	4.2 ± 0.4	4.1 ± 0.5	4.2 ± 0.3	4.4 ± 0.4	4.5 ± 0.5	4.4 ± 0.3	4.4 ± 0.4	4.6 ± 0.6
cL63	4.0 ± 0.4	4.0 ± 0.4	3.9 ± 0.3	4.2 ± 0.3	4.3 ± 0.4	4.8 ± 0.7	4.4 ± 0.5	4.2 ± 0.4	4.4 ± 0.8
cE65	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	3.5 ± 0.1	3.6 ± 0.2	3.6 ± 0.2	3.5 ± 0.1	3.6 ± 0.2
cA66	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.3	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2
cA67	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.7 ± 0.2	3.7 ± 0.2	3.8 ± 0.2	3.9 ± 0.3	3.9 ± 0.3	4.2 ± 0.4
cY68	3.8 ± 0.2	3.8 ± 0.2	3.8 ± 0.2	3.7 ± 0.2	3.7 ± 0.2	3.7 ± 0.2	3.7 ± 0.2	3.8 ± 0.2	3.7 ± 0.2
cF69	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.4 ± 0.2	3.6 ± 0.2	3.6 ± 0.2
cI70	3.7 ± 0.3	3.7 ± 0.3	3.7 ± 0.3	3.6 ± 0.2	3.6 ± 0.2	3.6 ± 0.2	3.5 ± 0.2	3.6 ± 0.2	3.9 ± 0.5
cL72	5.0 ± 1.2	5.1 ± 1.3	5.2 ± 1.4	3.9 ± 0.3	3.8 ± 0.3	3.9 ± 0.3	3.9 ± 0.6	4.5 ± 0.7	5.1 ± 1.5
cF74	7.1 ± 1.2	7.1 ± 1.2	7.1 ± 1.3	5.5 ± 0.6	5.0 ± 0.7	5.0 ± 0.6	4.9 ± 1.1	6.9 ± 0.8	7.1 ± 1.5
cE65:OEx-LIG:N	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	2.8 ± 0.1	2.7 ± 0.1	2.8 ± 0.1
αF169	N/A	N/A	N/A	3.6 ± 0.2	5.6 ± 1.4	5.1 ± 1.4	N/A	N/A	N/A
αL170	N/A	N/A	N/A	4.3 ± 0.5	4.3 ± 0.5	4.5 ± 0.6	N/A	N/A	N/A
αP172	N/A	N/A	N/A	3.9 ± 0.3	3.9 ± 0.3	3.9 ± 0.3	N/A	N/A	N/A
αI173	N/A	N/A	N/A	3.7 ± 0.2	3.6 ± 0.2	3.7 ± 0.2	N/A	N/A	N/A
αV176	N/A	N/A	N/A	3.8 ± 0.3	3.8 ± 0.3	3.7 ± 0.3	N/A	N/A	N/A
αL199	N/A	N/A	N/A	N/A	N/A	N/A	5.1 ± 1.3	5.4 ± 0.9	5.8 ± 1.1
αF213	N/A	N/A	N/A	N/A	N/A	N/A	3.9 ± 0.5	4.1 ± 0.5	4.1 ± 0.6
αP214	N/A	N/A	N/A	N/A	N/A	N/A	4.1 ± 0.4	5.2 ± 0.7	5.9 ± 1.2
αV217	N/A	N/A	N/A	N/A	N/A	N/A	4.3 ± 0.7	3.8 ± 0.3	3.8 ± 0.3
αW218	N/A	N/A	N/A	N/A	N/A	N/A	2.9 ± 1.1	2.2 ± 0.5	2.4 ± 0.5
αF221	N/A	N/A	N/A	N/A	N/A	N/A	2.9 ± 0.5	3.3 ± 0.4	3.5 ± 0.5

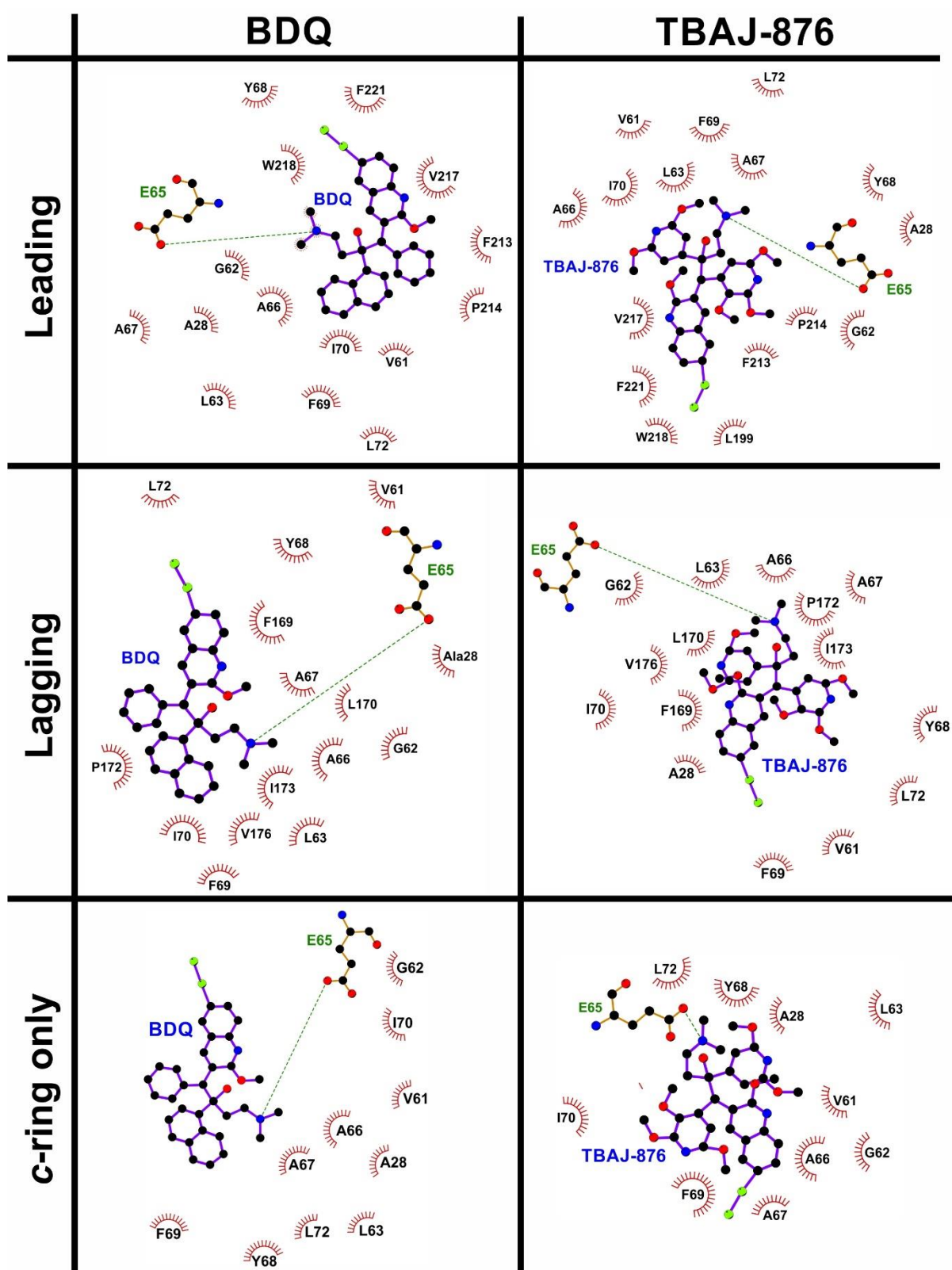


Figure S1: Protein drug interactions. LigPlot+ representations of protein-drug interactions for both drugs bound, when E65 and the drugs are charged, to all three sites. Carbon, nitrogen, oxygen and bromine (also lone pair) atoms of the drug are shown in *black, blue, red* and *green*, respectively.