

Supplementary Information for Sahai and Biggin.

Table SI-1. Basis Set Superimposition Error (BSSE) energies for water and ligand fragments in each QM system kcal mol⁻¹. Fragments are defined as follows: WX; waters where X is 1-5 or A or G as described in Figure 2 of the main manuscript. Ws; all other waters (eg. for the W1-Ws cell for 1FTJ-Glu, Ws would mean W2, W3, W4, W5 and WG), L; ligand (AMPA or Glu), P; protein, LP; ligand and protein, WsL; waters and ligand, WsP; waters and protein, WsLP; waters and ligand and protein.

Fragment	Ws	L	P	LP	WsL	WsP	WsLP
1FTJ-GLU							
W1	0.00	0.61	6.47	6.53	0.60	6.48	15.47
W2	2.28	0.12	8.05	9.35	3.17	8.66	9.41
W3	0.73	0.14	8.86	9.16	0.86	9.06	8.92
W4	0.00	0.77	9.33	8.72	0.72	9.28	8.67
W5	0.08	1.97	8.06	8.12	1.81	7.88	8.11
WG	1.75	4.51	6.18	6.07	6.15	7.16	7.53
L	-	-	-	-	-	32.18	-
1FTJ-AMPA							
W1	-	-	-	-	-	-	-
W2	2.21	1.09	6.63	7.60	2.87	7.77	8.71
W3	0.65	1.49	6.58	7.63	2.03	8.10	7.95
W4	0.00	0.55	10.22	9.32	0.53	10.01	9.28
W5	0.03	2.24	7.77	8.31	2.06	7.69	8.17
WG	1.59	1.49	4.26	5.39	3.02	4.31	6.67
L	-	-	-	-	-	89.40	-
1FTM-AMPA							
W1	0.00	0.59	16.42	3.24	0.40	-15.17	10.76
W2	0.00	0.68	8.39	9.64	0.61	8.79	9.72
W3	0.12	3.09	7.32	7.94	2.57	12.24	7.62
W4	0.00	0.14	8.41	7.24	0.13	8.24	7.16
W5	1.57	0.14	7.17	7.27	2.49	7.84	8.01
WG	1.74	5.72	6.55	8.85	6.54	7.40	9.46
L	-	-	-	-	-	38.97	-
1FTM-GLU							
W1	0.01	0.35	5.98	5.91	0.33	8.90	13.85
W2	0.05	0.29	7.55	7.95	0.32	8.10	8.04
W3	0.20	2.78	7.32	8.13	2.37	7.39	7.95
W4	0.01	1.13	8.51	7.63	0.94	8.24	7.60
W5	1.57	0.09	7.71	7.69	2.51	11.86	8.57
WG	1.78	5.07	6.35	8.28	6.28	7.20	9.08
L	-	-	-	-	-	41.79	-