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 |