**Table S1: Rosetta loop modeling in comparative models with cyclic coordinate descent compared to kinematic loop closure.** Reported is the average RMSD and standard deviation for all comparative models of target receptors, calculated over C-alpha atoms in the loop regions compared to the corresponding experimental structure from the Protein Data Bank. Loop closure with KIC was only performed on a subset of the GPCR dataset.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Extracellular Loop 1 RMSD (Å) | | Extracellular Loop 2  RMSD (Å) | | Extracellular Loop 3  RMSD (Å) | | Full Receptor  RMSD (Å) | |
|  | CCD | KIC | CCD | KIC | CCD | KIC | CCD | KIC |
| bRh | 1.7±0.7\* | 2.0±0.8 | 7.3±1.4 | 7.3±4.2 | 2.6±0.6 | 2.6±0.8 | 4.7±0.6\* | 10.6±8.5 |
| B1Ar | 1.8±0.6\* | 2.5±0.8 | 6.0±1.2 | 5.7±3.3 | 1.9±0.7\* | 2.1±0.5 | 3.6±0.6\* | 4.3±3.4 |
| B2Ar | 1.5±0.7\* | 3.2±1.2 | 6.2±1.3\* | 6.7±3.8 | 1.7±0.5\* | 2.1±0.6 | 3.7±0.5\* | 4.9±3.4 |
| A2Ar | 1.4±0.5\* | 2.2±1.2 | n.d.a | n.d.a | 2.5±0.6\* | 2.7±1.4 | 3.4±0.5\* | 8.5±5.9 |
| CXCR4 | 1.6±0.4\* | 2.5±1.1 | 5.3±1.0\* | 6.2±3.3 | 2.8±0.7\* | 4.5±3.0 | 4.5±0.4\* | 9.3±8.7 |
| D3R | 2.1±0.6\* | 2.3±0.9 | 4.3±1.2\* | 5.3±3.0 | 2.1±0.5\* | 2.9±1.8 | 2.9±0.4\* | 4.0±3.1 |
| H1R | 1.5±0.6 | n.d. | n.d.a | n.d.a | 2.0±0.6 | n.d. | 2.5±0.6 | n.d. |
| S1P1R | 2.9±0.6 | n.d. | 5.9±0.8 | n.d. | 3.4±0.8 | n.d. | 4.2±0.9 | n.d. |
| M2R | 1.6±0.8 | n.d. | 4.8±0.8 | n.d. | 1.4±0.7 | n.d. | 2.6±0.4 | n.d. |
| M3R | 1.8±0.5 | n.d. | 5.1±0.9 | n.d. | 1.1±0.4 | n.d. | 2.8±0.4 | n.d. |
| MOR | 1.5±0.6 | n.d. | 5.6±1.4 | n.d. | 1.6±0.8 | n.d. | 3.2±0.9 | n.d. |
| KOR | 1.0±0.8 | n.d. | 5.3±1.0 | n.d. | n.d.a | n.d. | 3.5±0.4 | n.d. |
| NOP | 1.3±0.7 | n.d. | 5.5±1.1 | n.d. | 2.9±0.9 | n.d. | 3.1±0.6 | n.d. |
| DOR | 1.4±0.6 | n.d. | 5.7±1.1 | n.d. | 2.4±0.6 | n.d. | 3.2±0.5 | n.d. |

n.d. denotes not determined  
\* Indicated significant improvement using the CCD method over KIC for the given category, evaluated with the unpaired t-test, p < 0.05  
a Could not be evaluated because of unresolved structure in this region of the experimental structure in the Protein Data Bank.