# Supporting Information

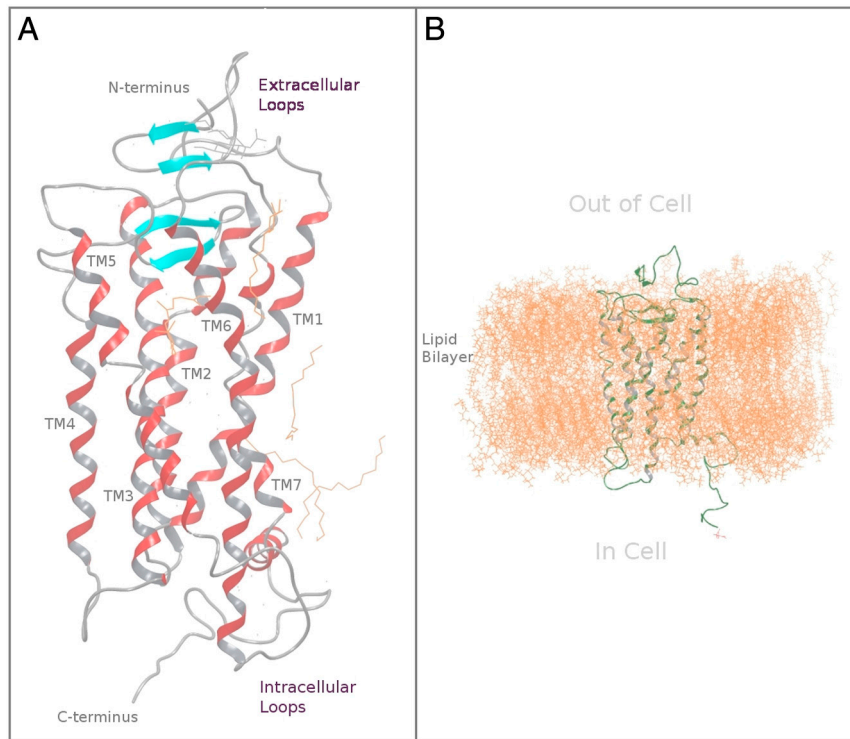## Goldfeld et al. 10.1073/pnas.1016951108



**Fig. S1.** Pictorial representations of G-protein-coupled receptors (GPCRs). (*A*) A cartoon of bovine rhodopsin. The red sections are the seven transmembrane helices (labeled TM1 through TM7), which are connected by gray, alternating intra- and extracellular loops. The N and C termini are also labeled. (*B*) A cartoon of bovine rhodopsin embedded within a lipid bilayer. When a ligand binds to the extracellular loops, it induces a conformational shift of the receptor, which triggers the intercellular domain to couple with a G-protein.

**Fig. S2.** The first extracellular loop of the four representative GPCRs. In each case the native loop is gray, and the predicted loop is purple. The numbers denote the starting and ending points of each loop. (*A*) The native and predicted structures of ECL1 of bRh; the backbone rmsd is 0.17 Å. (*B*) The native and predicted structures of the first extracellular loop (ECL1) of A2Ar; the backbone rmsd is 0.18 Å. (*C*) The native and predicted structures of ECL1 of β1AR; the backbone rmsd is 0.27 Å. (*D*) The native and predicted structures of ECL1 of β2AR; the backbone rmsd is 0.12 Å.

**Table S1. Crystal contacts**

| GPCR | Loop | Residue 1, name_number: atom name | Residue 2, name_number: atom type | Distance, Å |
|---|---|---|---|---|
| β2AR | 171–196 | ASN_1053: OD1 | ILE_177: O | 2.91 |
| | | THR_1109: CG2 | GLU_187: OE1 | 3.56 |
| | 299–304 | LYS_1035: O | ASN_301: CB | 3.14 |
| | | PRO_1037: CG | GLN_299: NE2 | 3.4 |
| bRh | 224–241 | THR_242: OG1 | GLN_237: NE2 | 2.95 |
| | | GLN_237: O | GLN_238: CB | 2.83 |
| | | GLN_236: OE1 | GLN_238: OE1 | 2.33 |
| | | GLN_238: O | GLN_238: OE1 | 2.92 |
| | 173–199 | GLU_196: OE2 | PRO_194: CG | 3.02 |
| A2Ar | 107–117 | LYS_292: CE | ASN_113: ND2 | 3.34 |
| | 142–173 | GLN_207: NE2 | GLN_157: O | 2.83 |
| | | ARG_369: NH2 | GLY_158: O | 3.05 |
| | | ASN_247: OD1 | GLU_161: N | 3.26 |
| | | LYS_250: CB | GLU_161: OE1 | 3.07 |
| | | SER_251: OG | GLU_161: CB | 3.73 |
| | | ASN_260: OD1 | GLY_147: OE2 | 3.13 |
| | | ASN_262: OD1 | GLY_162: CA | 3.05 |
| | 259–266 | GLU_161: OE2 | ASN_260: OD1 | 3.13 |
| | 34–40 | THR_316: OG1 | SER_35: CB | 3.41 |
| | | GLU_315: CB | SER_35: OG | 3.64 |
| | | ASN_288: ND2 | GLN_38: OE1 | 2.75 |
| | 67–73 | LEU_202: CD2 | PHE_70: CG | 3.54 |
| | | ARG_205: O | CYS_71: N | 2.72 |

All loop predictions that did not include an explicit membrane were performed using crystal neighbors in the calculations. All the copies of the asymmetric unit are predicted simultaneously, rather than the entire structures of the neighbors being used to guide the prediction of the central asymmetric unit. Listed above are the crystal contacts (defined as being within 4 Å) that exist in the 21 loops that we predicted for this paper.