Supplementary Materials

Table S1. Comparison of Galaxy7TM with AutoDock Vina applied to input GPCR structures (Input-Vina) and to GPCR structures refined by MPrelax (MPrelax-Vina), and AutoDock Vina with flexible sidechains (VinaFlex) in terms of docking accuracy on a test set of 125 GPCR structure–ligand inputs when the best of ten predictions are considered.

Uniprot ID	PDB ID	Template PDB ID[a]	Seq ID (%)[b]	Model building method[c]	Input structure GDT-HA[d]	Ligand RMSD (Å)				Contact ratio (%)			
						Galaxy 7TM	Input-Vina	MP relax-Vina	Vina Flex[e]	Galaxy 7TM	Input-Vina	MP relax-Vina	Vina Flex
O43614	4s0v	4buo	22.5	Galaxy	61.9	4.6	4.7	2.7	3.6	14.8	13.0	33.3	13.0
P07550	2rh1	4iaq	35.5	Galaxy	55.0	2.3	4.5	10.5	4.7	43.5	21.7	1.5	18.8
P07550	3ny8	4iaq	35.5	Galaxy	54.5	1.6	3.5	11.1	4.6	43.4	24.5	0.0	15.1
P07550	3sn6	4iaq	35.5	Galaxy	56.2	2.3	3.2	10.5	4.4	36.0	17.3	5.3	9.3
P07550	4lde	4iaq	35.5	Galaxy	55.4	2.3	2.7	10.5	5.1	31.1	22.2	2.2	11.1
P07550	3d4s	4iaq	35.5	Galaxy	54.4	2.6	4.1	11.1	5.7	37.7	18.8	4.4	15.9
P07700	3zpr	4gbr	59.9	Galaxy	80.6	0.8	3.4	7.5	4.1	49.1	18.2	1.8	18.2
P07700	4amj	4gbr	59.9	Galaxy	80.9	1.7	1.4	2.3	1.0	42.2	42.2	25.3	42.2
P07700	4bvn	4gbr	59.9	Galaxy	77.8	1.4	1.5	1.9	1.0	34.3	41.8	32.8	38.8
P07700	3zpq	4gbr	59.9	Galaxy	79.3	0.7	2.3	1.4	2.4	50.0	27.3	50.0	20.5
P07700	5a8e	4gbr	59.9	Galaxy	76.2	0.9	2.1	3.4	3.1	57.0	26.6	21.5	22.8
P07700	2y00	4gbr	59.9	Galaxy	79.0	2.3	3.3	3.6	3.0	33.9	20.3	33.9	18.6
P08172	4mqs	4ldl	28.0	Galaxy	58.8	4.1	5.4	5.9	6.5	12.7	4.2	9.9	7.0
P08172	3uon	4ldl	28.0	Galaxy	46.5	3.2	5.7	13.3	5.5	21.2	6.1	1.5	4.6
P08483	4u15	3pds	34.0	Galaxy	60.3	7.2	9.4	12.3	6.3	5.8	2.3	1.2	11.5
P21453	3v2w	3rfm	26.6	Galaxy	54.4	5.7	7.1	5.5	5.8	17.7	4.8	8.1	12.9
P25116	3vw7	4phu	21.1	Galaxy	45.8	6.9	6.7	7.6	7.2	12.4	2.5	2.5	4.9
P28222	4iaq	2rh1	36.2	Galaxy	59.0	4.4	4.9	3.9	4.4	28.6	14.3	23.8	17.9
P28222	4iar	2rh1	36.2	Galaxy	55.9	4.6	5.1	3.7	4.1	19.1	11.2	23.6	18.0
P29274	2ydo	3zev	19.5	Galaxy	36.6	5.8	4.2	4.1	3.3	9.5	6.4	4.8	6.4
P29274	2ydv	3zev	19.5	Galaxy	36.7	5.9	4.6	4.7	4.6	3.8	8.9	3.8	11.4
P29274	4ug2	3zev	19.5	Galaxy	37.5	8.6	7.9	6.6	9.3	5.4	3.6	6.3	2.7
P29274	3qak	3zev	19.5	Galaxy	36.9	10.0	9.3	8.5	10.2	11.9	4.5	6.7	3.7
P29274	3eml	3zev	19.5	Galaxy	48.6	7.5	9.3	5.7	8.6	6.7	2.7	6.7	4.0
P32300	4n6h	4ea3	59.2	Galaxy	64.0	3.9	4.4	5.7	4.4	22.6	11.3	4.8	14.5
P34998	4k5y	4l6r	33.5	Galaxy	45.7	17.4	18.7	19.1	18.5	0.0	1.7	0.0	1.7
P35367	3rze	4iaq	36.7	Galaxy	57.8	5.3	7.2	7.5	7.6	11.8	15.8	9.2	14.5
P35462	3pbl	2ycw	37.9	Galaxy	62.0	1.9	3.2	3.2	3.3	31.6	15.8	7.0	8.8
P41145	4djh	4s0v	27.7	Galaxy	51.1	6.3	4.8	7.4	6.4	11.4	16.5	2.5	19.0
P41146	4ea3	4dkl	58.9	Galaxy	72.8	4.3	2.4	3.2	4.2	17.9	16.1	7.1	7.1
P41146	5dhg	4dkl	58.9	Galaxy	72.7	3.2	4.4	3.2	3.5	20.6	17.8	15.1	13.7
P41146	5dhh	4dkl	58.9	Galaxy	71.8	2.0	2.5	2.8	2.9	18.2	10.9	9.1	9.1
P41594	4oo9	4daj	9.2	Galaxy	23.8	8.8	6.4	8.5	6.7	1.2	1.2	3.7	2.5
P41594	5cgd	4daj	9.2	Galaxy	23.8	7.7	7.2	7.4	7.8	3.2	6.5	3.2	5.4
P41595	4ib4	4iaq	31.1	Galaxy	54.1	1.8	1.3	3.1	1.4	36.2	33.0	23.4	24.5
P42866	5c1m	4ea3	59.2	Galaxy	47.2	1.1	2.0	1.6	2.2	54.6	45.5	21.2	24.2
P51681	4mbs	4rwd	25.8	Galaxy	52.4	5.1	5.1	5.2	4.1	13.3	4.0	8.0	6.7
P61073	3odu	4mbs	32.4	Galaxy	54.1	3.3	4.2	3.4	5.1	23.3	14.0	14.0	11.6
Q13255	4or2	4daj	9.4	Galaxy	22.4	5.7	5.9	7.1	5.1	4.9	1.6	3.3	1.6
Q99835	4jkv	2hpy	11.5	Galaxy	27.5	12.3	7.7	14.1	12.5	2.2	3.2	0.0	0.0
Q99835	4qim	2hpy	11.5	Galaxy	27.7	8.0	8.9	12.9	9.8	3.7	2.5	0.0	2.5
Q99835	4o9r	2hpy	11.5	Galaxy	28.5	15.7	10.8	14.7	13.3	2.6	10.3	5.1	10.3
Q99835	4qin	2hpy	11.5	Galaxy	27.8	8.1	14.2	17.9	15.2	5.4	1.1	2.2	1.1
Q99835	4n4w	2hpy	11.5	Galaxy	27.9	6.1	4.9	7.1	5.4	11.3	10.0	5.0	6.3
Q9H244	4pxz	4n6h	22.2	Galaxy	38.9	6.4	6.5	4.5	5.8	7.0	3.5	2.6	3.5
Q9H244	4ntj	4n6h	22.2	Galaxy	37.9	7.3	8.6	7.5	8.4	6.9	3.5	3.5	9.2
O43614	4s0v	4buo	22.5	Modeller	60.9	0.7	4.0	5.2	3.4	40.7	22.2	5.6	24.1
P07550	2rh1	4iaq	35.5	Modeller	55.2	3.1	6.7	3.5	2.5	24.6	8.7	36.2	20.3
P07550	3ny8	4iaq	35.5	Modeller	54.1	1.4	2.8	2.6	1.4	50.9	20.8	26.4	60.4
P07550	3sn6	4iaq	35.5	Modeller	57.2	6.6	1.9	3.0	1.8	8.0	28.0	25.3	21.3
P07550	4lde	4iaq	35.5	Modeller	56.9	6.4	1.5	2.6	1.6	11.1	32.2	27.8	27.8
P07550	3d4s	4iaq	35.5	Modeller	54.3	1.9	3.5	3.1	2.0	33.3	11.6	24.6	26.1
P07700	3zpr	4gbr	59.9	Modeller	80.8	1.0	1.0	0.9	3.1	52.7	38.2	43.6	9.1
P07700	4amj	4gbr	59.9	Modeller	80.7	2.4	1.1	2.2	1.5	21.7	50.6	39.8	41.0
P07700	4bvn	4gbr	59.9	Modeller	75.9	0.8	1.5	1.6	1.1	58.2	44.8	32.8	34.3
P07700	3zpq	4gbr	59.9	Modeller	79.5	1.1	1.3	1.3	1.7	52.3	25.0	31.8	29.6
P07700	5a8e	4gbr	59.9	Modeller	75.6	1.3	1.3	2.7	2.8	44.3	44.3	24.1	15.2
P07700	2y00	4gbr	59.9	Modeller	79.4	1.7	1.7	4.0	3.5	39.0	22.0	20.3	13.6
P08172	4mqs	4ldl	28.0	Modeller	58.4	4.1	5.2	4.8	4.6	12.7	5.6	29.6	7.0
P08172	3uon	4ldl	28.0	Modeller	46.1	4.1	10.1	4.2	5.1	9.1	1.5	16.7	16.7
P08483	4u15	3pds	34.0	Modeller	60.3	5.6	5.7	11.9	8.1	16.1	12.6	0.0	8.1
P21453	3v2w	3rfm	26.6	Modeller	53.3	7.0	4.4	4.9	5.9	8.1	9.7	14.5	8.1

P25116	3vw7	4phu	21.1	Modeller	45.8	8.9	6.7	9.2	7.9	8.6	11.1	4.9	11.1
P28222	4iaq	2rh1	36.2	Modeller	57.1	4.4	3.3	8.3	4.4	25.0	17.9	4.8	13.1
P28222	4iar	2rh1	36.2	Modeller	54.4	5.0	3.2	5.3	3.8	12.4	16.9	14.6	20.2
P29274	2ydo	3zev	19.5	Modeller	37.6	6.0	3.6	3.7	3.7	11.1	4.8	11.1	4.8
P29274	2ydv	3zev	19.5	Modeller	37.3	5.8	4.4	4.6	4.3	5.1	5.1	3.8	3.8
P29274	4ug2	3zev	19.5	Modeller	37.9	8.6	8.2	8.3	7.3	5.4	6.3	5.4	8.0
P29274	3qak	3zev	19.5	Modeller	37.7	8.3	8.3	7.7	8.5	6.7	0.1	0.0	0.1
P29274	3eml	3zev	19.5	Modeller	49.0	8.0	6.3	8.1	7.6	1.3	4.0	8.0	2.7
P32300	4n6h	4ea3	59.2	Modeller	64.9	4.4	4.4	4.3	4.4	14.5	21.0	6.5	11.3
P34998	4k5y	4l6r	33.5	Modeller	46.0	16.6	19.0	17.4	18.5	3.3	0.0	1.7	0.0
P35367	3rze	4iaq	36.7	Modeller	58.8	2.9	5.8	5.3	4.3	17.1	13.2	14.5	15.8
P35462	3pbl	2ycw	37.9	Modeller	59.9	2.1	3.2	7.1	3.2	28.1	8.8	5.3	8.8
P41145	4djh	4s0v	27.7	Modeller	51.6	7.0	6.1	6.1	4.3	24.1	20.3	10.1	30.4
P41146	4ea3	4dkl	58.9	Modeller	74.2	4.8	3.3	4.2	2.8	16.1	7.1	12.5	14.3
P41146	5dhg	4dkl	58.9	Modeller	73.8	2.6	3.5	5.5	2.5	26.0	11.0	4.1	16.4
P41146	5dhh	4dkl	58.9	Modeller	73.8	2.4	2.7	5.1	2.6	29.1	18.2	5.5	12.7
P41594	4oo9	4daj	9.2	Modeller	23.2	8.4	7.6	8.7	4.9	2.5	3.7	1.2	6.2
P41594	5cgd	4daj	9.2	Modeller	23.3	9.5	7.4	8.7	8.2	1.1	7.5	3.2	11.8
P41595	4ib4	4iaq	31.1	Modeller	52.2	1.6	1.5	2.4	1.4	44.7	30.9	19.2	26.6
P42866	5c1m	4ea3	59.2	Modeller	46.9	1.3	1.9	4.1	1.0	30.3	57.6	12.1	57.6
P51681	4mbs	4rwd	25.8	Modeller	52.2	5.3	5.7	4.0	5.0	16.0	5.3	13.3	8.0
P61073	3odu	4mbs	32.4	Modeller	54.4	4.5	4.0	6.7	3.6	11.6	7.0	14.0	27.9
Q13255	4or2	4daj	9.4	Modeller	21.0	6.5	4.1	5.6	3.8	3.3	1.6	4.9	1.6
Q99835	4jkv	2hpy	11.5	Modeller	28.1	13.0	13.2	13.3	13.3	0.0	5.4	0.0	3.2
Q99835	4qim	2hpy	11.5	Modeller	27.5	12.8	8.6	9.6	12.4	1.2	2.5	3.7	3.7
Q99835	4o9r	2hpy	11.5	Modeller	28.6	16.1	16.1	3.9	15.6	0.0	0.0	7.7	5.1
Q99835	4qin	2hpy	11.5	Modeller	28.6	17.2	17.4	15.8	13.7	0.0	0.0	0.0	2.2
Q99835	4n4w	2hpy	11.5	Modeller	28.3	8.1	7.7	7.2	6.0	12.5	5.0	3.8	13.8
Q9H244	4pxz	4n6h	22.2	Modeller	38.4	5.2	7.0	7.0	5.3	8.8	2.6	1.8	0.9
Q9H244	4ntj	4n6h	22.2	Modeller	37.8	6.4	8.9	10.7	9.0	5.8	2.3	0.0	1.2
O43614	4s0v	4buo	-	I-TSSR	64.1	2.6	4.5	4.8	4.8	22.2	16.7	9.3	18.5
P07550	2rh1	4iaq	-	I-TSSR	95.0	0.7	1.0	2.1	0.8	68.1	53.6	27.5	56.5
P07550	3ny8	4iaq	-	I-TSSR	86.4	1.6	2.4	3.0	2.3	43.4	34.0	17.0	28.3
P07550	3sn6	4iaq	-	I-TSSR	54.4	1.8	1.5	2.8	1.6	46.7	38.7	9.3	34.7
P07550	4lde	4iaq	-	I-TSSR	60.5	1.4	1.5	2.7	1.6	48.9	35.6	10.0	28.9
P07550	3d4s	4iaq	-	I-TSSR	88.9	1.0	1.2	2.6	0.7	58.0	53.6	17.4	55.1
P08172	4mqs	4ldl	-	I-TSSR	56.9	4.5	10.5	5.4	2.5	14.1	2.8	2.8	12.7
P08172	3uon	4ldl	-	I-TSSR	91.5	2.5	11.1	2.3	0.8	21.2	1.5	15.2	68.2
P21453	3v2w	3rfm	-	I-TSSR	92.3	3.1	5.9	5.7	2.7	25.0	7.4	10.3	36.8
P25116	3vw7	4phu	-	I-TSSR	97.4	10.7	11.9	8.5	10.1	6.2	2.5	1.2	22.2
P28222	4iaq	2rh1	-	I-TSSR	90.1	4.3	4.3	2.7	3.7	17.9	17.9	26.2	33.3
P28222	4iar	2rh1	-	I-TSSR	94.8	4.2	4.2	2.4	3.6	18.0	14.6	18.0	32.6
P29274	2ydo	3zev	-	I-TSSR	56.9	3.1	3.7	2.4	0.0	27.0	31.8	36.5	0.0
P29274	2ydv	3zev	-	I-TSSR	56.5	3.4	4.9	2.0	3.0	22.8	17.7	31.7	38.0
P29274	4ug2	3zev	-	I-TSSR	59.9	4.2	2.7	3.7	3.0	13.4	28.6	15.2	30.4
P29274	3qak	3zev	-	I-TSSR	59.0	3.1	4.0	2.5	6.1	27.6	18.7	39.6	14.2
P29274	3eml	3zev	-	I-TSSR	81.1	3.9	3.0	2.5	2.0	33.3	16.0	30.7	36.0
P35367	3rze	4iaq	-	I-TSSR	98.5	2.9	2.6	0.8	3.0	21.1	27.6	39.5	18.4
P35462	3pbl	2ycw	-	I-TSSR	97.8	8.1	10.8	9.7	3.8	5.3	3.5	1.8	21.1
P41145	4djh	4s0v	-	I-TSSR	91.6	6.1	5.1	3.7	5.3	24.4	16.7	11.5	14.1
P41146	4ea3	4dkl	-	I-TSSR	88.4	5.8	5.9	5.9	4.3	7.1	5.4	3.6	3.6
P41146	5dhg	4dkl	-	I-TSSR	86.9	3.7	5.4	5.5	4.9	8.2	4.1	8.2	5.5
P41146	5dhh	4dkl	-	I-TSSR	85.6	3.2	5.1	6.7	5.1	12.7	9.1	10.9	7.3
P41595	4ib4	4iaq	-	I-TSSR	89.5	1.7	1.6	2.7	1.1	28.7	33.0	14.9	39.4
P51681	4mbs	4rwd	-	I-TSSR	97.5	5.4	2.6	6.5	2.4	20.0	28.0	6.7	17.3
P61073	3odu	4mbs	-	I-TSSR	91.3	7.5	8.7	6.8	8.6	6.7	4.4	17.8	20.0
Q99835	4jkv	2hpy	-	I-TSSR	90.2	5.8	1.5	8.6	2.6	18.9	53.3	17.8	34.4
Q99835	4qim	2hpy	-	I-TSSR	85.7	8.4	5.3	5.7	6.4	17.5	20.0	18.8	22.5
Q99835	4o9r	2hpy	-	I-TSSR	81.9	10.5	8.4	10.5	7.0	0.0	5.1	12.8	15.4
Q99835	4qin	2hpy	-	I-TSSR	84.4	9.6	8.0	9.8	8.0	5.4	6.5	7.5	5.4
Q99835	4n4w	2hpy	-	I-TSSR	94.8	7.7	6.7	6.1	3.8	3.9	3.9	6.4	20.5
Q9H244	4pxz	4n6h	-	I-TSSR	87.6	1.3	2.5	1.4	2.2	56.1	29.0	54.4	35.1
Q9H244	4ntj	4n6h	-	I-TSSR	69.1	6.2	6.6	6.9	6.8	8.1	8.1	17.2	18.4
Mean	-	-	33.0	-	59.7	5.2	5.4	6.1	5.1	20.4	15.5	13.0	16.8
Median	-	-	31.8	-	56.9	4.5	4.6	5.3	4.3	16.1	11.2	9.1	13.8

[a] PDB ID of the template GPCR used for model building with GalaxyTBM and MODELLER

[b] Sequence identity of the input GPCR and the selected template

[c] Model building method used for each input structure; ‘Galaxy’ for GalaxyTBM (1), ‘Modeller’ for MODELLER (2), and ‘I-TSSR’ for GPCR-I-TASSER (3).

[d] GDT-HA of the input GPCR structure

[e] AutoDock Vina (4) applied to input GPCR structures with manually assigned flexible sidechains. Among the predicted binding pocket residues, sidechains placed inside the grid box were selected as flexible sidechains with restraints on the sum of the number of side chain torsion angles $\leq$ 32.

Table S2. Comparison of Galaxy7TM with GalaxyRefine and MPrelax in terms of improvement in receptor structure quality for full structure on a test set of 125 GPCR structure–ligand inputs when the best of ten predictions are considered.

Uniprot ID	PDB ID	Template PDB ID[a]	Seq ID (%)[b]	Model building method[c]	Input Str GDT-HA[d]	ΔGDT-HA[e]			ΔGDC-SC[f]			-ΔCα-RMSD[g]		
						Galaxy 7TM	Galaxy Refine[h]	MP relax[i]	Galaxy 7TM	Galaxy Refine	MP relax	Galaxy 7TM	Galaxy Refine	MP relax
O43614	4s0v	4buo	22.5	Galaxy	61.88	1.24	0.98	2.13	14.05	11.82	14.51	0.05	0.04	0.02
P07550	2rh1	4iaq	35.5	Galaxy	54.96	1.51	1.96	3.46	11.77	10.47	13.00	0.06	0.05	-0.03
P07550	3ny8	4iaq	35.5	Galaxy	54.5	0.99	1.53	1.08	12.16	12.07	11.31	0.07	0.06	-0.06
P07550	3sn6	4iaq	35.5	Galaxy	56.22	1.29	1.10	-2.83	12.61	11.87	8.24	0.05	0.05	0.03
P07550	4lde	4iaq	35.5	Galaxy	55.37	2.34	2.24	-0.89	12.19	11.28	8.59	0.05	0.06	0.02
P07550	3d4s	4iaq	35.5	Galaxy	54.41	1.53	1.44	1.79	12.51	11.71	11.59	0.06	0.05	-0.06
P07700	3zpr	4gbr	59.9	Galaxy	80.55	1.35	0.45	-1.52	12.57	8.14	10.18	-0.01	-0.02	0.2
P07700	4amj	4gbr	59.9	Galaxy	80.85	0.44	0.27	-3.02	12.48	9.70	10.18	0.00	-0.01	0.16
P07700	4bvn	4gbr	59.9	Galaxy	77.78	1.21	0.61	-4.26	11.46	7.88	7.95	0.05	0.03	0.03
P07700	3zpq	4gbr	59.9	Galaxy	79.26	0.88	0.35	-1.87	12.50	9.52	11.34	0.00	-0.01	0.17
P07700	5a8e	4gbr	59.9	Galaxy	76.24	1.50	1.68	-2.48	11.14	6.55	7.85	0.03	0.01	0.31
P07700	2y00	4gbr	59.9	Galaxy	78.99	1.95	0.80	-1.33	10.68	7.88	8.83	-0.01	-0.01	0.16
P08172	4mqs	4ldl	28.0	Galaxy	58.76	1.53	1.62	4.78	8.27	7.68	12.42	0.05	0.06	0.13
P08172	3uon	4ldl	28.0	Galaxy	46.49	1.08	1.08	0.09	4.85	3.44	4.82	0.04	0.06	0.18
P08483	4u15	3pds	34.0	Galaxy	60.26	1.77	2.52	-2.14	9.68	8.98	9.44	0.07	0.02	-0.05
P21453	3v2w	3rfm	26.6	Galaxy	54.44	1.93	1.74	2.9	11.76	9.73	9.61	0.03	0.04	0.15
P25116	3vw7	4phu	21.1	Galaxy	45.82	1.45	1.46	5.00	9.44	10.77	11.28	0.03	0.03	0.35
P28222	4iaq	2rh1	36.2	Galaxy	59	2.11	1.92	2.20	10.1	7.88	7.85	0.05	0.05	0.03
P28222	4iar	2rh1	36.2	Galaxy	55.85	1.79	1.88	3.58	9.45	6.66	8.31	0.01	0.02	0.05
P29274	2ydo	3zev	19.5	Galaxy	36.62	1.41	1.41	1.76	8.17	7.95	7.24	0.02	0.03	0.02
P29274	2ydv	3zev	19.5	Galaxy	36.67	0.96	0.96	1.49	8.66	8.10	6.47	0.02	0.03	0.06
P29274	4ug2	3zev	19.5	Galaxy	37.46	1.05	0.87	1.05	8.37	7.98	6.38	0.04	0.03	0.02
P29274	3qak	3zev	19.5	Galaxy	36.88	1.15	1.24	3.00	9.73	8.34	6.87	0.05	0.03	0.05
P29274	3eml	3zev	19.5	Galaxy	48.6	2.19	2.19	-0.26	8.22	9.19	9.28	0.02	0.03	-0.02
P32300	4n6h	4ea3	59.2	Galaxy	64.04	0.60	0.34	-1.45	9.63	4.69	7.31	0.06	0.05	0.49
P34998	4k5y	4l6r	33.5	Galaxy	45.65	1.41	1.31	-1.73	7.09	6.29	6.17	0.07	0.03	0.08
P35367	3rze	4iaq	36.7	Galaxy	57.84	1.58	0.74	0.56	9.24	4.9	6.33	0.03	0.02	-0.07
P35462	3pbl	2ycw	37.9	Galaxy	61.95	2.21	1.28	1.65	9.34	5.66	8.14	0.02	0.02	0.12
P41145	4djh	4s0v	27.7	Galaxy	51.05	2.09	1.91	1.39	14.5	10.11	13.75	0.04	0.03	0.07
P41146	4ea3	4dkl	58.9	Galaxy	72.84	1.44	1.26	0.00	8.20	5.29	8.64	0.07	0.06	0.04
P41146	5dhg	4dkl	58.9	Galaxy	72.69	1.42	0.97	-0.54	7.88	5.60	8.42	0.06	0.06	0.04
P41146	5dhh	4dkl	58.9	Galaxy	71.77	2.15	1.98	0.90	9.10	5.68	8.51	0.06	0.06	0.05
P41594	4oo9	4daj	9.2	Galaxy	23.81	1.08	0.97	2.60	1.40	1.79	2.48	0.09	0.11	0.21
P41594	5cgd	4daj	9.2	Galaxy	23.83	1.17	1.39	2.13	1.18	2.08	3.48	0.10	0.1	0.21
P41595	4ib4	4iaq	31.1	Galaxy	54.06	-0.09	0.00	-3.43	8.43	6.39	4.68	0.04	0.04	0.1
P42866	5c1m	4ea3	59.2	Galaxy	47.2	1.18	0.91	1.18	5.63	4.11	6.08	0.04	0.02	-0.28
P51681	4mbs	4rwd	25.8	Galaxy	52.35	1.05	1.22	4.45	11.61	8.01	12.65	0.05	0.01	0.19
P61073	3odu	4mbs	32.4	Galaxy	54.1	1.15	1.44	2.01	7.69	6.73	5.71	0.07	0.09	0.12
Q13255	4or2	4daj	9.4	Galaxy	22.36	0.91	0.91	2.03	2.35	0.62	0.95	0.05	0.04	0.28
Q99835	4jkv	2hpy	11.5	Galaxy	27.52	1.63	0.9	0.98	2.2	2.57	3.1	0.08	0.05	0.12
Q99835	4qim	2hpy	11.5	Galaxy	27.7	1.50	1.11	0.63	2.55	2.98	2.98	0.05	0.04	0.06
Q99835	4o9r	2hpy	11.5	Galaxy	28.46	1.16	0.75	0.25	0.76	1.73	1.17	0.07	0.06	0.05
Q99835	4qin	2hpy	11.5	Galaxy	27.75	1.29	1.05	0.32	1.43	2.04	2.05	0.07	0.06	0.1
Q99835	4n4w	2hpy	11.5	Galaxy	27.85	0.98	0.82	1.14	2.96	2.62	3.34	0.07	0.05	0.05
Q9H244	4pxz	4n6h	22.2	Galaxy	38.88	1.33	1.24	0.62	6.26	5.57	4.10	0.08	0.07	0.18
Q9H244	4ntj	4n6h	22.2	Galaxy	37.92	1.49	1.39	1.11	7.24	5.70	4.10	0.03	0.04	-0.12
O43614	4s0v	4buo	22.5	Modeller	60.91	2.48	1.06	1.68	9.12	5.42	9.07	0.05	0.03	-0.02
P07550	2rh1	4iaq	35.5	Modeller	55.23	1.33	0.89	1.6	5.98	6.76	7.3	0.04	0.03	0.13
P07550	3ny8	4iaq	35.5	Modeller	54.14	1.44	1.35	0.81	6.71	7.46	5.53	0.04	0.04	0.1
P07550	3sn6	4iaq	35.5	Modeller	57.23	1.93	0.83	-3.39	9.57	7.94	5.18	0.04	0.04	0.14
P07550	4lde	4iaq	35.5	Modeller	56.9	2.24	2.06	-1.88	8.65	6.26	5.71	0.03	0.04	0.19
P07550	3d4s	4iaq	35.5	Modeller	54.32	1.53	1.44	2.79	8.49	8.08	6.91	0.04	0.04	0.1
P07700	3zpr	4gbr	59.9	Modeller	80.82	0.99	0.90	-4.48	4.33	3.27	4.04	0.01	-0.01	-0.14
P07700	4amj	4gbr	59.9	Modeller	80.67	0.27	0.71	-5.67	5.36	4.36	4.00	-0.01	0.00	-0.1
P07700	4bvn	4gbr	59.9	Modeller	75.87	1.3	1.82	-5.64	5.35	4.96	4.74	0.02	0.02	0.02
P07700	3zpq	4gbr	59.9	Modeller	79.52	1.16	1.51	-4.17	4.43	3.70	4.46	-0.01	0.00	-0.08
P07700	5a8e	4gbr	59.9	Modeller	75.62	1.59	1.50	-5.56	4.83	3.92	3.69	0.01	0.01	-0.05
P07700	2y00	4gbr	59.9	Modeller	79.43	0.98	1.07	-4.7	4.54	3.23	4.34	-0.01	0.00	-0.09
P08172	4mqs	4ldl	28.0	Modeller	58.39	1.54	1.36	3.97	7.48	5.22	9.82	0.04	0.05	-0.09
P08172	3uon	4ldl	28.0	Modeller	46.13	0.45	0.90	1.8	3.21	2.15	6.17	0.05	0.07	0.24
P08483	4u15	3pds	34.0	Modeller	60.26	2.61	1.68	-3.82	7.76	4.09	1.47	0.04	0.02	-0.04
P21453	3v2w	3rfm	26.6	Modeller	53.28	1.16	1.35	1.45	7.46	6.37	7.02	0.05	0.03	0.27
P25116	3vw7	4phu	21.1	Modeller	45.82	1.54	2.00	2.09	3.43	1.95	1.87	0.00	-0.01	0.08
P28222	4iaq	2rh1	36.2	Modeller	57.09	2.01	1.43	0.57	6.2	5.81	4.87	0.06	0.05	0.03
P28222	4iar	2rh1	36.2	Modeller	54.43	1.98	1.13	1.14	6.19	5.43	4.86	0.02	0.01	0.03
P29274	2ydo	3zev	19.5	Modeller	37.59	0.35	0.61	7.39	7.57	6.24	10.81	0.00	0.01	0.23
P29274	2ydv	3zev	19.5	Modeller	37.28	0.44	0.18	7.32	7.22	6.77	10.51	0.02	0.01	0.25
P29274	4ug2	3zev	19.5	Modeller	37.89	1.14	1.15	7.2	7.15	5.35	12.1	0.01	0.01	0.22
P29274	3qak	3zev	19.5	Modeller	37.67	0.71	0.80	8.55	6.64	5.73	11.4	0.02	0.01	0.22

P29274	3eml	3zev	19.5	Modeller	49.04	1.22	1.31	3.93	7.00	7.57	10.47	0.01	0.01	0.14
P32300	4n6h	4ea3	59.2	Modeller	64.9	1.02	-0.26	-2.4	7.23	2.04	4.52	0.05	0.02	-0.35
P34998	4k5y	4l6r	33.5	Modeller	45.95	1.22	0.71	-1.42	6.04	2.70	4.04	0.03	0.06	0.15
P35367	3rze	4iaq	36.7	Modeller	58.77	0.93	0.65	-1.49	6.71	4.32	6.1	0.05	0.05	-0.04
P35462	3pbl	2ycw	37.9	Modeller	59.93	2.11	1.29	3.03	7.14	3.46	7.31	0.02	0.03	-0.01
P41145	4djh	4s0v	27.7	Modeller	51.57	1.92	1.48	-0.44	8.57	3.29	5.82	0.05	0.05	0.11
P41146	4ea3	4dkl	58.9	Modeller	74.19	2.43	2.25	-2.7	7.44	3.91	6.03	0.04	0.05	0.04
P41146	5dhg	4dkl	58.9	Modeller	73.84	1.96	1.87	-3.46	6.41	2.16	4.69	0.04	0.04	0.01
P41146	5dhh	4dkl	58.9	Modeller	73.84	2.24	2.14	-3.05	7.99	3.34	5.25	0.04	0.06	0.02
P41594	4oo9	4daj	9.2	Modeller	23.16	1.19	0.97	1.41	2.49	2.25	2.65	0.06	0.05	0.31
P41594	5cgd	4daj	9.2	Modeller	23.3	1.06	0.85	1.27	2.49	2.28	2.94	0.04	0.02	0.33
P41595	4ib4	4iaq	31.1	Modeller	52.17	1.08	1.53	0.00	8.67	6.92	7.26	0.03	0.01	0.28
P42866	5c1m	4ea3	59.2	Modeller	46.93	1.27	0.99	-0.36	5.17	2.60	3.57	0.02	0.00	0.19
P51681	4mbs	4rwd	25.8	Modeller	52.18	1.04	0.34	5.75	10.33	7.13	13.04	0.04	0.05	0.25
P61073	3odu	4mbs	32.4	Modeller	54.39	0.95	0.57	0.67	5.61	5.21	5.08	0.05	0.05	0.05
Q13255	4or2	4daj	9.4	Modeller	21.04	0.71	0.4	0.6	2.32	2.09	1.12	0.03	0.01	0.58
Q99835	4jkv	2hpy	11.5	Modeller	28.09	1.31	1.39	0.09	2.98	2.61	3.36	0.04	0.02	0.30
Q99835	4qim	2hpy	11.5	Modeller	27.46	1.27	1.35	0.48	2.34	2.08	2.05	0.04	0.01	0.37
Q99835	4o9r	2hpy	11.5	Modeller	28.55	1.4	1.07	-0.42	2.82	2.3	2.66	0.05	0.01	0.46
Q99835	4qin	2hpy	11.5	Modeller	28.64	0.97	0.97	-0.24	1.66	1.62	2.23	0.04	0.03	0.47
Q99835	4n4w	2hpy	11.5	Modeller	28.26	1.55	1.38	0.16	2.42	1.32	2.07	0.03	0.02	0.42
Q9H244	4pxz	4n6h	22.2	Modeller	38.43	1.52	1.52	-0.18	4.05	2.94	2.11	0.07	0.04	0.52
Q9H244	4ntj	4n6h	22.2	Modeller	37.83	2.13	1.86	2.78	5.19	3.24	3.46	0.08	0.07	0.26
O43614	4s0v	4buo	-	I-TSSR	64.06	0.26	1.24	0.44	7.19	7.64	7.92	0.03	0.05	-0.13
P07550	2rh1	4iaq	-	I-TSSR	95.02	-1.55	-2.24	-19.33	1.33	-8.89	-8.33	-0.02	-0.02	-0.03
P07550	3ny8	4iaq	-	I-TSSR	86.41	-1.04	-2.00	-15.5	1.65	-7.84	-6.59	-0.02	-0.02	0.02
P07550	3sn6	4iaq	-	I-TSSR	54.44	0.35	0.26	-5.4	0.20	-4.42	-3.00	-0.04	-0.05	0.02
P07550	4lde	4iaq	-	I-TSSR	60.53	0.00	0.00	-5.44	-0.02	-4.09	-1.44	-0.02	-0.03	0.1
P07550	3d4s	4iaq	-	I-TSSR	88.94	-0.70	-0.70	-17.34	2.22	-5.9	-5.96	-0.01	-0.02	-0.01
P08172	4mqs	4ldl	-	I-TSSR	56.86	1.44	1.26	-3.52	2.86	-0.27	-1.47	0.06	0.04	-0.28
P08172	3uon	4ldl	-	I-TSSR	91.48	-1.25	-1.25	-20.53	4.20	0.91	-2.93	0.02	0.01	0.07
P21453	3v2w	3rfm	-	I-TSSR	92.31	-2.91	-1.76	-14.31	2.51	-0.76	-2.05	0.00	0.01	-0.32
P25116	3vw7	4phu	-	I-TSSR	97.41	-1.79	-2.05	-14.02	13.1	10.04	6.98	0.01	0.01	-0.03
P28222	4iaq	2rh1	-	I-TSSR	90.07	-1.74	-2.26	-12.54	-0.79	-5.86	-6.36	-0.06	-0.04	-0.63
P28222	4iar	2rh1	-	I-TSSR	94.76	-2.76	-2.57	-13.14	0.67	-6.11	-5.69	-0.07	-0.06	-0.38
P29274	2ydo	3zev	-	I-TSSR	56.9	0.76	0.17	0.42	5.38	5.76	5.53	0.02	0.02	-0.23
P29274	2ydv	3zev	-	I-TSSR	56.54	0.33	0.00	-0.50	4.95	6.22	5.44	0.02	0.00	-0.16
P29274	4ug2	3zev	-	I-TSSR	59.93	-0.08	0.09	-0.09	5.19	6.62	4.94	0.02	0.01	0.04
P29274	3qak	3zev	-	I-TSSR	59.03	0.45	0.09	-2.19	7.46	8.26	7.39	0.01	-0.01	-0.19
P29274	3eml	3zev	-	I-TSSR	81.14	-2.08	-1.21	-9.26	10.2	10.31	4.62	-0.02	-0.02	-0.3
P35367	3rze	4iaq	-	I-TSSR	98.51	-4.48	-3.64	-14.84	-0.12	-5.88	-3.03	-0.14	-0.13	-0.54
P35462	3pbl	2ycw	-	I-TSSR	97.78	-2.03	-1.47	-22.13	3.94	-4.42	-11.72	-0.14	-0.13	-1.19
P41145	4djh	4s0v	-	I-TSSR	91.61	-2.36	-1.49	-9.7	8.47	0.03	2.4	-0.06	-0.05	-0.18
P41146	4ea3	4dkl	-	I-TSSR	88.4	-1.44	-1.53	-5.94	4.06	-1.27	2.97	-0.05	-0.04	-0.17
P41146	5dhg	4dkl	-	I-TSSR	86.92	-0.8	-0.62	-6.58	4.64	-0.06	2.01	-0.04	-0.03	-0.15
P41146	5dhh	4dkl	-	I-TSSR	85.55	0.53	0.27	-5.58	5.43	-0.62	1.59	-0.02	-0.01	-0.17
P41595	4ib4	4iaq	-	I-TSSR	89.53	-0.18	-1.06	-8.98	13.37	10.72	9.04	-0.01	-0.02	-0.2
P51681	4mbs	4rwd	-	I-TSSR	97.48	-3.56	-2.95	-13.71	1.46	-2.68	-4.39	-0.14	-0.11	-0.50
P61073	3odu	4mbs	-	I-TSSR	91.27	-4.58	-4.41	-26.61	6.35	2.54	-6.70	-0.04	-0.04	-3.08
Q99835	4jkv	2hpy	-	I-TSSR	90.24	-1.22	-1.06	-10.81	-4.68	-8.80	-7.23	-0.03	-0.03	-0.23
Q99835	4qim	2hpy	-	I-TSSR	85.69	-0.48	-0.48	-3.94	-3.10	-6.54	-4.6	-0.01	-0.02	-0.14
Q99835	4o9r	2hpy	-	I-TSSR	81.9	-0.42	-0.92	-7.24	-6.83	-8.94	-6.61	-0.03	-0.03	-0.10
Q99835	4qin	2hpy	-	I-TSSR	84.41	0.00	-0.33	-9.00	-6.50	-9.72	-6.47	-0.01	-0.02	-0.09
Q99835	4n4w	2hpy	-	I-TSSR	94.79	-1.63	-1.71	-9.37	-6.20	-7.18	-6.96	-0.01	-0.03	-0.50
Q9H244	4pxz	4n6h	-	I-TSSR	87.63	-2.54	-1.75	-7.72	4.20	4.55	1.39	-0.06	-0.03	-0.19
Q9H244	4ntj	4n6h	-	I-TSSR	69.12	-1.02	-1.20	-5.51	2.02	1.22	0.49	0.00	-0.01	-0.15
Mean	-	-	33.0	-	59.7	0.71	0.59	-2.21	6.04	3.91	4.50	0.02	0.02	0.00
Median	-	-	31.8	-	56.9	1.16	0.97	-0.24	6.41	4.69	4.94	0.03	0.02	0.04

[a]PDB ID of the template GPCR used for model building with GalaxyTBM and MODELLER

[b]Sequence identity of the input GPCR and the selected template

[c]Model building method used for each input structure; 'Galaxy' for GalaxyTBM (1), 'Modeller' for MODELLER (2), and 'I-TSSR' for GPCR-I-TASSER (3).

[d] GDT-HA of the input GPCR structure

[e-g] The results were evaluated by applying the LGA method as used in CASP (5,6)

[h] Results of applying GalaxyRefine (7,8). The number of conformations generated was 120 for each target and the 10 lowest refinement energy structures were selected for evaluation.

[i] Results of applying MPrelax (9). The number of conformations generated was 120 for each target and the 10 lowest score structures were selected for evaluation. In addition to the given Rosetta protocol to run MPrelax, atom-pair constraints with weight 1.0 were applied to prevent drift-away from the input structure.

Table S3. Comparison of Galaxy7TM with GalaxyRefine and MPrelax in terms of improvement in receptor structure quality for binding pocket residues on a test set of 125 GPCR structure–ligand inputs when the best of ten predictions are considered.

Uniprot ID	PDB ID	Template PDB ID[a]	Seq ID (%)[b]	Model building method[c]	Input str GDT-HA[d]	ΔGDT-HA[e]			ΔGDC-SC[f]			-ΔCα-RMSD[g]		
						Galaxy 7TM	Galaxy Refine[h]	MP relax[i]	Galaxy 7TM	Galaxy Refine	MP relax	Galaxy 7TM	Galaxy Refine	MP relax
O43614	4s0v	4buo	22.5	Galaxy	71.1	3.95	3.95	9.21	18.68	15.55	23.64	0.05	0.20	0.28
P07550	2rh1	4iaq	35.5	Galaxy	80.9	1.47	1.47	1.48	13.79	3.42	18.18	0.24	0.20	0.39
P07550	3ny8	4iaq	35.5	Galaxy	76.9	1.92	1.92	3.85	15.25	3.78	15.81	0.19	0.01	0.45
P07550	3sn6	4iaq	35.5	Galaxy	73.5	5.88	4.41	7.35	7.92	2.86	9.09	0.06	-0.10	0.55
P07550	4lde	4iaq	35.5	Galaxy	76.4	1.39	2.77	4.16	8.99	-0.11	7.17	0.14	0.05	0.42
P07550	3d4s	4iaq	35.5	Galaxy	79.4	2.94	2.94	1.47	13.15	3.74	13.37	0.04	-0.01	0.32
P07700	3zpr	4gbr	59.9	Galaxy	96.7	1.66	0.00	0.00	10.52	-7.54	-1.69	0.05	-0.01	-0.12
P07700	4amj	4gbr	59.9	Galaxy	100.0	0.00	-1.67	-6.67	8.97	-11.64	-4.61	0.05	-0.04	-0.17
P07700	4bvn	4gbr	59.9	Galaxy	95.3	0.00	-1.56	-3.12	8.12	-5.33	-2.06	0.02	0.02	-0.09
P07700	3zpq	4gbr	59.9	Galaxy	97.2	2.78	2.78	-2.78	8.48	-0.20	7.47	0.09	0.02	-0.14
P07700	5a8e	4gbr	59.9	Galaxy	95.6	0.00	0.00	-5.88	7.61	-7.16	-3.87	0.06	0.05	-0.08
P07700	2y00	4gbr	59.9	Galaxy	88.2	7.36	2.95	2.95	16.57	-2.68	7.16	0.11	0.02	0.06
P08172	4mqs	4ldl	28.0	Galaxy	85.7	3.58	7.15	7.15	24.62	19.17	36.23	0.13	0.09	0.36
P08172	3uon	4ldl	28.0	Galaxy	70.6	1.47	2.94	2.94	16.48	7.39	16.24	-0.01	-0.02	-0.19
P08483	4u15	3pds	34.0	Galaxy	78.1	3.13	4.69	3.13	8.70	2.86	15.07	0.13	0.16	0.46
P21453	3v2w	3rfm	26.6	Galaxy	67.2	1.56	0.00	0.00	7.27	2.38	8.52	0.11	0.17	-0.17
P25116	3vw7	4phu	21.1	Galaxy	35.7	2.37	2.37	2.38	4.34	5.15	3.33	0.09	0.03	-0.14
P28222	4iaq	2rh1	36.2	Galaxy	72.5	2.50	2.50	3.75	13.50	3.26	5.94	0.13	0.14	0.60
P28222	4iar	2rh1	36.2	Galaxy	72.6	4.76	2.38	3.57	10.54	1.18	5.18	-0.02	0.01	0.47
P29274	2ydo	3zev	19.5	Galaxy	57.7	3.85	1.93	1.93	14.97	9.93	9.79	-0.77	-0.01	-0.41
P29274	2ydv	3zev	19.5	Galaxy	58.3	3.33	3.33	1.66	5.70	6.79	1.82	-1.13	-0.03	-1.14
P29274	4ug2	3zev	19.5	Galaxy	47.4	3.94	2.63	3.94	8.99	8.28	2.43	0.04	-0.05	-0.80
P29274	3qak	3zev	19.5	Galaxy	47.8	4.34	4.34	5.43	10.28	11.54	8.06	0.03	0.14	-0.08
P29274	3eml	3zev	19.5	Galaxy	58.3	2.08	2.08	0.00	12.88	13.03	7.12	0.45	0.35	0.32
P32300	4n6h	4ea3	59.2	Galaxy	82.7	5.77	1.93	-1.92	8.49	-6.06	1.36	0.04	0.04	-1.54
P34998	4k5y	4l6r	33.5	Galaxy	75.0	4.17	4.17	2.09	14.05	14.21	15.86	-0.05	-0.01	0.53
P35367	3rze	4iaq	36.7	Galaxy	76.8	3.58	1.79	5.36	4.55	-9.22	5.20	0.45	0.26	0.73
P35462	3pbl	2ycw	37.9	Galaxy	78.6	3.57	3.57	3.57	9.22	8.83	9.74	0.26	0.25	0.32
P41145	4djh	4s0v	27.7	Galaxy	75.0	1.25	2.50	-2.50	28.42	5.55	17.79	0.12	0.12	0.17
P41146	4ea3	4dkl	58.9	Galaxy	85.9	1.56	1.56	0.00	15.34	-6.02	6.14	0.18	0.07	0.16
P41146	5dhg	4dkl	58.9	Galaxy	87.5	1.79	1.79	0.00	19.48	-0.26	7.14	0.28	0.13	0.29
P41146	5dhh	4dkl	58.9	Galaxy	82.8	1.57	0.00	3.13	21.25	5.69	15.12	0.61	0.14	0.51
P41594	4oo9	4daj	9.2	Galaxy	32.5	3.75	5.00	3.75	3.63	3.31	7.27	10.82	10.95	11.51
P41594	5cgd	4daj	9.2	Galaxy	38.2	5.26	5.26	3.95	3.89	-0.65	7.40	1.47	1.37	2.14
P41595	4ib4	4iaq	31.1	Galaxy	77.0	1.00	2.00	0.00	15.02	5.38	14.47	0.04	0.02	0.13
P42866	5c1m	4ea3	59.2	Galaxy	72.5	5.00	0.00	2.50	7.27	-7.27	-0.73	0.36	0.05	0.47
P51681	4mbs	4rwd	25.8	Galaxy	64.5	2.64	1.32	5.27	0.91	-3.23	7.68	0.03	0.04	-0.10
P61073	3odu	4mbs	32.4	Galaxy	86.4	2.28	2.28	2.28	15.04	9.42	18.52	0.24	0.10	0.29
Q13255	4or2	4daj	9.4	Galaxy	32.1	4.77	2.39	3.58	-0.19	1.34	0.09	1.83	1.28	1.45
Q99835	4jkv	2hpy	11.5	Galaxy	30.3	1.32	0.00	2.63	-1.82	-5.93	-3.35	0.08	0.08	-0.24
Q99835	4qim	2hpy	11.5	Galaxy	42.2	0.00	0.00	0.00	7.05	2.16	7.50	0.20	1.19	1.90
Q99835	4o9r	2hpy	11.5	Galaxy	32.7	0.00	0.00	1.92	-0.42	-0.28	3.08	0.05	0.11	-0.10
Q99835	4qin	2hpy	11.5	Galaxy	33.9	0.00	0.00	1.79	4.61	2.79	10.49	0.10	-0.04	0.25
Q99835	4n4w	2hpy	11.5	Galaxy	39.3	2.38	3.57	4.76	2.94	-3.38	0.52	-0.07	0.01	0.05
Q9H244	4pxz	4n6h	22.2	Galaxy	45.7	2.17	1.08	1.08	5.06	4.27	4.83	0.41	0.77	5.99
Q9H244	4ntj	4n6h	22.2	Galaxy	53.1	4.69	3.13	6.26	9.09	7.39	4.44	0.73	0.47	2.11
O43614	4s0v	4buo	22.5	Modeller	72.4	3.94	3.94	10.52	14.95	4.65	20.91	0.25	0.13	0.33
P07550	2rh1	4iaq	35.5	Modeller	77.9	2.94	1.47	4.42	3.10	-3.74	6.31	0.36	0.32	0.24
P07550	3ny8	4iaq	35.5	Modeller	76.9	1.93	-1.92	1.93	1.26	-12.03	4.06	0.18	-0.08	0.06
P07550	3sn6	4iaq	35.5	Modeller	79.4	0.00	0.00	7.36	12.21	5.59	10.52	0.04	0.11	0.34
P07550	4lde	4iaq	35.5	Modeller	79.2	-0.01	-0.01	5.55	8.98	-1.18	7.06	0.07	-0.04	0.28
P07550	3d4s	4iaq	35.5	Modeller	80.9	1.47	-1.47	0.00	1.28	-9.42	-2.04	0.05	-0.01	0.19
P07700	3zpr	4gbr	59.9	Modeller	100.0	0.00	-1.67	-3.33	7.14	-8.70	-0.26	0.02	-0.04	-0.12
P07700	4amj	4gbr	59.9	Modeller	98.3	1.67	0.00	-3.33	-3.40	-17.94	-10.79	0.01	-0.06	-0.13
P07700	4bvn	4gbr	59.9	Modeller	95.3	1.57	0.00	-1.56	7.27	-11.88	-3.51	0.04	0.04	-0.03
P07700	3zpq	4gbr	59.9	Modeller	97.2	2.78	2.78	-2.78	8.49	-6.46	2.23	0.08	-0.01	-0.15
P07700	5a8e	4gbr	59.9	Modeller	95.6	0.00	-1.47	-1.47	6.48	-14.31	-2.84	0.11	0.06	-0.02
P07700	2y00	4gbr	59.9	Modeller	91.2	4.41	0.00	0.00	10.05	-9.20	-0.43	0.10	0.00	-0.04
P08172	4mqs	4ldl	28.0	Modeller	83.9	7.14	7.14	10.71	20.28	-2.38	29.93	0.10	0.09	0.37
P08172	3uon	4ldl	28.0	Modeller	72.1	1.47	1.47	5.88	15.64	-0.36	17.70	0.07	0.06	0.18
P08483	4u15	3pds	34.0	Modeller	79.7	1.56	-1.57	1.56	10.13	4.80	17.40	0.14	0.24	0.45
P21453	3v2w	3rfm	26.6	Modeller	67.2	1.56	1.56	-1.57	-2.96	-3.07	4.09	0.10	0.10	0.64
P25116	3vw7	4phu	21.1	Modeller	35.7	1.19	1.19	7.14	3.54	7.88	1.72	0.05	0.10	0.34
P28222	4iaq	2rh1	36.2	Modeller	70.0	2.50	3.75	5.00	7.95	9.67	3.64	0.21	0.22	0.56
P28222	4iar	2rh1	36.2	Modeller	71.4	1.19	2.38	3.57	15.00	13.27	7.00	-0.07	-0.08	0.23
P29274	2ydo	3zev	19.5	Modeller	57.7	1.93	1.93	7.70	16.36	17.62	17.48	-0.98	-1.22	0.10
P29274	2ydv	3zev	19.5	Modeller	60.0	0.00	0.00	5.00	8.61	12.13	7.76	-2.17	-1.14	-1.01
P29274	4ug2	3zev	19.5	Modeller	50.0	1.32	1.31	5.27	8.79	11.01	12.42	0.47	0.23	1.27
P29274	3qak	3zev	19.5	Modeller	51.1	2.17	3.26	5.43	9.57	9.65	11.46	0.17	0.11	0.46

P29274	3eml	3zev	19.5	Modeller	58.3	2.08	2.08	4.17	11.82	11.97	15.46	-0.29	-0.04	0.64
P32300	4n6h	4ea3	59.2	Modeller	82.7	5.77	3.85	1.93	8.94	-6.52	5.60	0.03	0.02	-1.10
P34998	4k5y	4l6r	33.5	Modeller	77.1	2.08	0.00	0.00	5.79	2.48	5.46	0.04	0.03	0.44
P35367	3rze	4iaq	36.7	Modeller	78.6	1.79	-1.79	3.57	2.34	-11.95	5.97	0.57	0.43	0.94
P35462	3pbl	2ycw	37.9	Modeller	82.1	0.00	0.00	-1.78	5.06	-10.52	1.03	0.11	0.09	0.03
P41145	4djh	4s0v	27.7	Modeller	76.3	1.25	1.25	0.00	9.67	-7.37	1.44	0.09	0.06	0.21
P41146	4ea3	4dkl	58.9	Modeller	87.5	1.56	0.00	1.56	6.37	-9.32	2.84	0.22	0.19	0.07
P41146	5dhg	4dkl	58.9	Modeller	89.3	0.00	0.00	-1.79	4.55	-10.91	2.73	0.15	0.23	0.25
P41146	5dhh	4dkl	58.9	Modeller	84.4	3.12	1.56	3.12	0.34	-7.16	7.05	0.52	0.48	0.42
P41594	4oo9	4daj	9.2	Modeller	32.5	3.75	3.75	8.75	5.13	3.21	2.99	0.53	0.59	1.99
P41594	5cgd	4daj	9.2	Modeller	39.5	2.64	2.64	5.27	4.55	5.85	2.21	1.08	1.22	3.02
P41595	4ib4	4iaq	31.1	Modeller	75.0	3.00	3.00	1.00	11.31	-1.18	7.27	0.04	0.07	0.32
P42866	5c1m	4ea3	59.2	Modeller	75.0	2.50	0.00	0.00	14.36	7.63	6.00	0.28	-0.04	0.47
P51681	4mbs	4rwd	25.8	Modeller	63.2	2.63	1.31	6.58	10.20	9.90	16.16	-0.04	0.08	-0.61
P61073	3odu	4mbs	32.4	Modeller	88.6	2.27	2.27	2.27	20.66	-1.49	20.50	0.14	0.16	0.29
Q13255	4or2	4daj	9.4	Modeller	35.7	1.19	0.00	1.19	2.88	1.35	1.73	1.01	1.36	2.39
Q99835	4jkv	2hpy	11.5	Modeller	31.6	1.31	1.31	2.63	-1.15	-0.86	-1.63	-0.04	-0.06	12.25
Q99835	4qim	2hpy	11.5	Modeller	35.9	1.56	3.12	3.12	2.39	1.26	0.34	0.54	0.53	0.15
Q99835	4o9r	2hpy	11.5	Modeller	25.0	3.85	3.84	7.70	0.70	1.95	3.77	-0.42	0.14	0.27
Q99835	4qin	2hpy	11.5	Modeller	32.1	0.00	0.00	0.00	0.14	1.95	-0.14	1.37	1.46	1.74
Q99835	4n4w	2hpy	11.5	Modeller	41.7	2.38	3.57	2.38	1.21	-3.47	0.60	-0.13	3.64	4.92
Q9H244	4pxz	4n6h	22.2	Modeller	47.8	0.00	-1.09	-1.09	5.69	4.98	9.48	5.00	0.32	6.13
Q9H244	4ntj	4n6h	22.2	Modeller	54.7	1.56	1.56	0.00	7.16	2.73	5.11	1.02	0.57	1.57
O43614	4s0v	4buo	-	I-TSSR	80.3	2.62	3.94	2.63	10.00	11.82	5.15	0.36	0.38	0.36
P07550	2rh1	4iaq	-	I-TSSR	100.0	0.00	-1.47	-2.94	3.21	-15.61	0.11	-0.07	-0.13	-0.24
P07550	3ny8	4iaq	-	I-TSSR	96.2	0.00	-3.85	-5.77	3.78	-20.70	-4.33	0.00	-0.10	-0.23
P07550	3sn6	4iaq	-	I-TSSR	85.3	1.47	1.47	-0.01	11.17	1.95	2.21	0.09	0.09	-0.01
P07550	4lde	4iaq	-	I-TSSR	84.7	2.78	1.39	0.00	8.99	-3.21	6.63	0.04	0.13	0.07
P07550	3d4s	4iaq	-	I-TSSR	98.5	0.00	0.00	-4.41	4.71	-17.65	-0.32	0.03	-0.03	-0.21
P08172	4mqs	4ldl	-	I-TSSR	78.6	1.79	1.79	-3.57	-2.24	-8.53	-9.79	0.08	0.17	-0.54
P08172	3uon	4ldl	-	I-TSSR	100.0	0.00	0.00	-8.82	11.87	-2.43	4.72	-0.07	-0.11	-0.56
P21453	3v2w	3rfm	-	I-TSSR	100.0	-1.39	0.00	-8.33	11.31	1.31	0.20	-0.10	-0.07	-0.41
P25116	3vw7	4phu	-	I-TSSR	100.0	-2.38	-1.19	-15.48	24.34	23.94	21.31	-0.11	-0.10	-0.51
P28222	4iaq	2rh1	-	I-TSSR	100.0	0.00	-1.25	-11.25	-1.15	-11.58	-12.05	-0.06	-0.10	-0.54
P28222	4iar	2rh1	-	I-TSSR	98.8	0.00	-1.19	-13.09	4.36	-11.00	-7.09	-0.06	-0.11	-0.62
P29274	2ydo	3zev	-	I-TSSR	84.6	0.00	0.00	0.00	5.04	6.30	11.89	0.01	-0.04	0.16
P29274	2ydv	3zev	-	I-TSSR	88.3	0.00	-1.67	0.00	0.24	2.06	6.30	-0.03	-0.11	0.19
P29274	4ug2	3zev	-	I-TSSR	82.9	1.32	1.32	-1.31	1.41	5.15	13.54	0.11	0.03	0.20
P29274	3qak	3zev	-	I-TSSR	76.1	0.00	1.08	2.17	10.12	6.40	11.30	0.08	0.04	0.23
P29274	3eml	3zev	-	I-TSSR	97.9	0.00	-2.09	-4.17	22.42	8.48	10.76	0.02	0.02	-0.18
P35367	3rze	4iaq	-	I-TSSR	100.0	0.00	0.00	-1.78	19.74	0.52	25.97	-0.07	-0.18	-0.22
P35462	3pbl	2ycw	-	I-TSSR	91.1	-1.79	-1.79	-5.35	10.26	-11.17	2.86	-0.13	-0.21	-0.39
P41145	4djh	4s0v	-	I-TSSR	97.4	0.00	-2.63	-2.63	16.16	-3.23	16.67	-0.02	-0.04	-0.08
P41146	4ea3	4dkl	-	I-TSSR	98.4	-3.13	-3.13	-6.25	8.18	1.82	8.86	-0.09	-0.07	-0.16
P41146	5dhg	4dkl	-	I-TSSR	100.0	-1.78	-1.78	-7.14	10.65	6.75	17.79	-0.08	-0.07	-0.16
P41146	5dhh	4dkl	-	I-TSSR	96.9	0.00	0.00	-4.69	17.95	8.29	16.59	-0.04	-0.04	-0.14
P41595	4ib4	4iaq	-	I-TSSR	97.0	2.00	0.00	-3.00	6.56	-1.35	3.24	0.01	-0.03	-0.12
P51681	4mbs	4rwd	-	I-TSSR	97.4	0.00	-1.32	-13.16	-1.01	-1.82	-7.27	-0.13	-0.14	-0.79
P61073	3odu	4mbs	-	I-TSSR	100.0	-2.08	-4.17	-12.50	14.39	-0.61	2.88	-0.12	-0.19	-0.82
Q99835	4jkv	2hpy	-	I-TSSR	95.8	1.39	1.39	-2.77	-23.63	-30.81	-20.00	0.00	-0.02	-0.15
Q99835	4qim	2hpy	-	I-TSSR	93.3	0.00	0.00	0.00	-18.18	-23.76	-23.64	0.01	0.01	-0.05
Q99835	4o9r	2hpy	-	I-TSSR	82.7	7.69	9.62	5.77	-28.12	-26.72	-18.33	0.15	0.16	0.01
Q99835	4qin	2hpy	-	I-TSSR	96.4	0.00	0.00	0.00	-9.79	-14.13	-4.89	0.04	0.02	0.01
Q99835	4n4w	2hpy	-	I-TSSR	98.8	0.00	0.00	0.00	-12.28	-14.00	-15.37	0.01	0.02	-0.03
Q9H244	4pxz	4n6h	-	I-TSSR	100.0	-2.17	-3.26	-8.69	12.41	11.31	11.23	-0.08	-0.06	-0.21
Q9H244	4ntj	4n6h	-	I-TSSR	84.4	0.00	0.00	0.00	10.34	8.75	11.02	0.02	0.00	0.14
Mean	-	-	33.0	-	74.6	1.76	1.18	0.68	7.71	-0.16	5.94	0.24	0.23	0.51
Median	-	-	31.8	-	78.6	1.56	1.31	1.47	8.49	1.31	5.94	0.06	0.04	0.16

[a] PDB ID of the template GPCR used for model building with GalaxyTBM and MODELLER

[b] Sequence identity of the input GPCR and the selected template

[c] Model building method used for each input structure; 'Galaxy' for GalaxyTBM (1), 'Modeller' for MODELLER (2), and 'I-TSSR' for GPCR-I-TASSER (3)

[d] GDT-HA of the input GPCR structure

[e-g] The results were evaluated by applying LGA method as used in CASP (5,6)

[h] Results of applying GalaxyRefine (7,8). The number of conformations generated was 120 for each target and the 10 lowest refinement energy structures were selected for evaluation.

[i] Results of applying MPrelax (9). The number of conformations generated was 120 for each target and the 10 lowest score structures were selected for evaluation. In addition to the given Rosetta protocol to run MPrelax, atom-pair constraints with weight 1.0 were applied to prevent drift-away from the input structure.

Figure S1. Ligand RMSD of the complex structures predicted by Galaxy7TM versus the sequence identity of the query to the template GPCR. Blue dots marked as A–G represent the specific targets explained in detail in Figure S2. Only the targets with input structure generated using GalaxyTBM or MODELLER are shown.

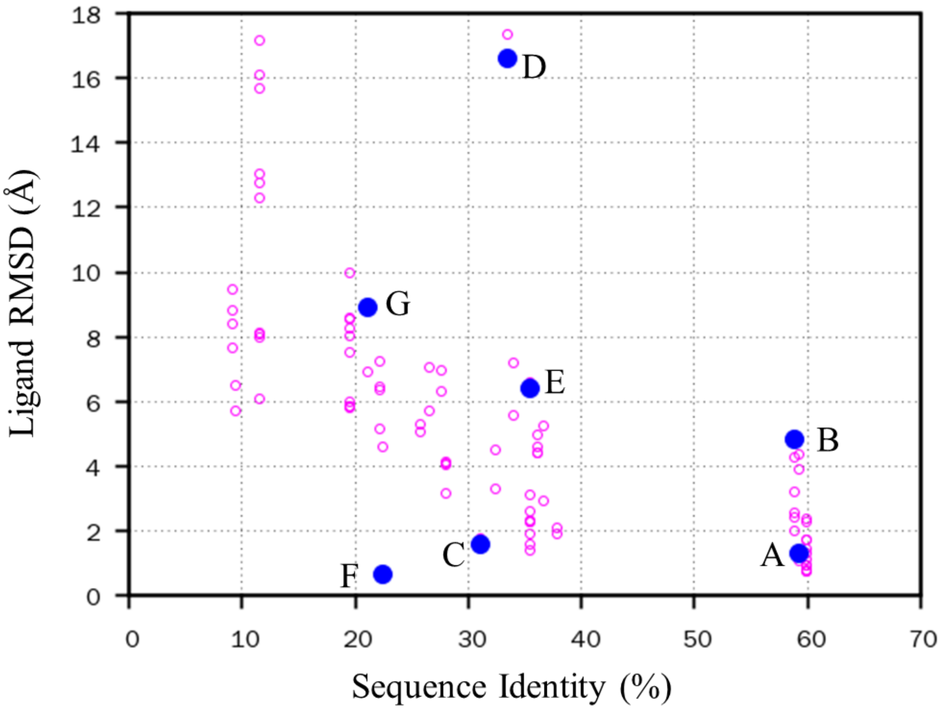
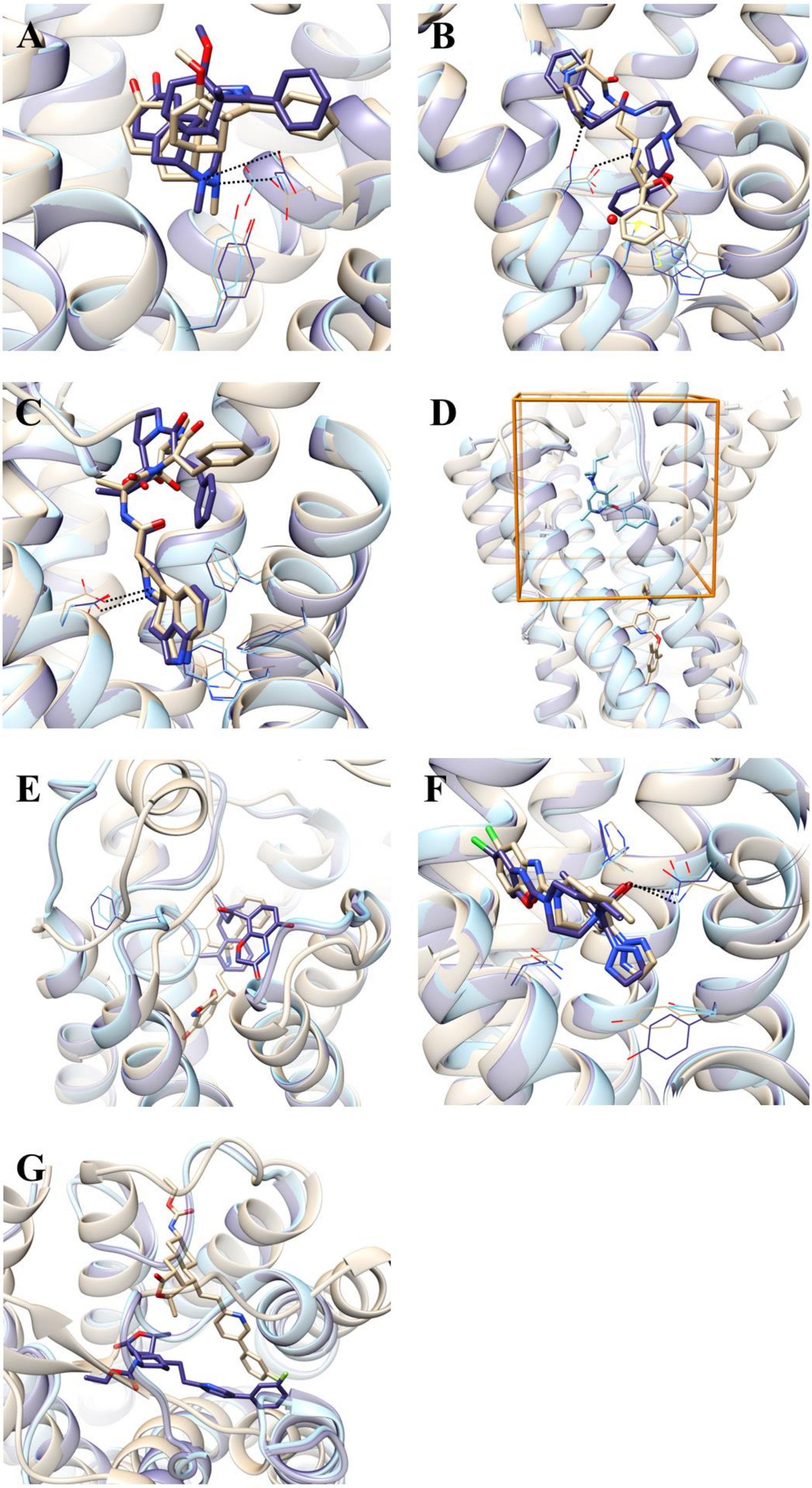


Figure S2. Seven examples of Galaxy7TM predictions are shown in detail. Input GPCR structure is shown in sky blue, Galaxy7TM result in purple, and the crystal structure in brown. (A) μ-opioid receptor (P42866) bound to the agonist BU72 (PDB ID: 5c1m). Sequence identity (59.2%) and GDT-HA of input structure (46.9) are high. A very accurate prediction with ligand RMSD = 1.31 Å and contact ratio = 30.3% was achieved. Charge interaction between the positive N atom of the ligand and a negative O atom of Asp147 could be captured. (B) Nociceptin receptor (P41146) bound to a peptide-mimetic antagonist compound-24 (PDB ID: 4ea3). Although sequence identity (58.9%) and GDT-HA of input structure (74.2) are high, a low-accuracy prediction with ligand RMSD = 4.82 Å and contact ratio = 16.1% was obtained. A wrong interaction between a positive N atom of ligand and a negative O atom of Asp130 was made. Sidechain structure of an important binding pocket residue Met134 was inaccurately predicted. In addition, the docked ligand took place of a water molecule observed in the crystal structure, which could not be explicitly considered in the current method. (C) 5-Hydroxytryptamine receptor 2B (P41595) bound to ergotamine (PDB ID: 4ib4). Sequence identity (31.1%) and GDT-HA of input structure (52.2) are intermediate, and a high-accuracy prediction with ligand RMSD = 1.60 Å and contact ratio = 44.7% was achieved. Hydrophobic interaction between binding site residues (Trp337, Phe340, and Phe341) and hydrophobic moiety of ligand was predicted accurately. Charge interaction between a positive N atom of the ligand and a negative O atom of Asp135 could be captured. (D) Corticotropin-releasing factor receptor (P34998) bound to CP-376395 (PDB ID: 4k5y). Sequence identity (33.5%) and GDT-HA of input structure (46.0) are intermediate, and a very low-accuracy prediction with ligand RMSD = 16.6 Å and contact ratio = 3.3% was obtained. This failure is mainly due to the wrong assignment of the docking grid box position. If binding residues are known in advance and provided as optional input, this problem can be avoided. (E) β-2 adrenergic receptor (P07550) bound to the agonist BI167107 (PDB ID: 4lde). Sequence identity (35.5%) and GDT-HA of input structure (56.9) are intermediate, and a low-accuracy prediction with ligand RMSD = 6.39 Å and contact ratio = 11.1% was obtained. Due to the wrong sequence alignment near the extracellular loop region, the loop structure blocked the native ligand-binding position in the input structure. Currently, Galaxy7TM does not perform loop modeling for structure refinement but is considered to be implemented in the future. Using models with different sequence alignments for loop anchor regions can alleviate the problem for now. (F) Orexin receptor type 2 (O43614) bound to suvorexant (PDB ID: 4s0v). Sequence identity (22.5%) and GDT-HA of input structure (60.9) are relatively low, but a high-accuracy prediction with ligand RMSD = 0.68 Å and contact ratio = 40.7% was obtained. The input structure quality is relatively high considering the sequence identity. Local interactions such as that between a ligand O atom and a N atom of Asn324 could be captured. (G) Proteinase-activated receptor 1 (P25116) bound to vorapaxar (PDB ID: 3vw7). Sequence identity (21.1%) and GDT-HA of input structure (45.8) are low, and a low-accuracy prediction with ligand RMSD = 8.90 Å and contact ratio = 8.6% was obtained. The transmembrane helix orientations of the input structure are incorrect, resulting in a binding pocket with inaccurate shape. Galaxy7TM has limitations for input structures generated by using templates with sequence identity lower than 20%.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