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Article

A complete assessment of dopamine receptor-ligand interactions through computational methods

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SUPPLEMENTARY INFORMATION

FIGURES

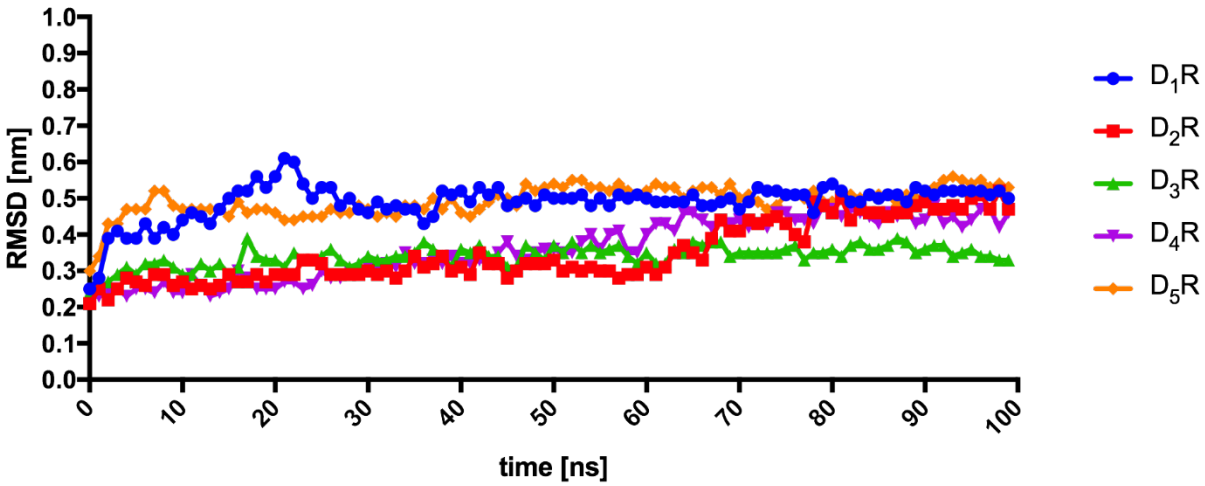


Figure S1 – RMSD throughout the 100 ns of simulation for all DR models.

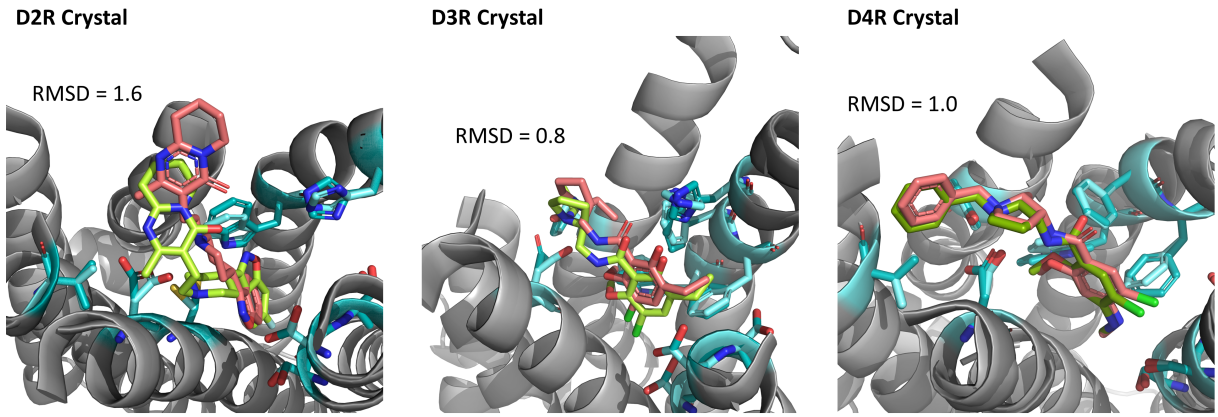


Figure S2 – Redocking of ligands with their respective DR and bound ligand (D_2R, D_3R and D_4R PDB-ids are respectively: 6CM4 [1], 3PBL [2], 5WIU [3])**.** RMSD values between ligand pose in crystal (pink) and docking output (green) are displayed. Interacintg residues were chosen according to Figure 2.

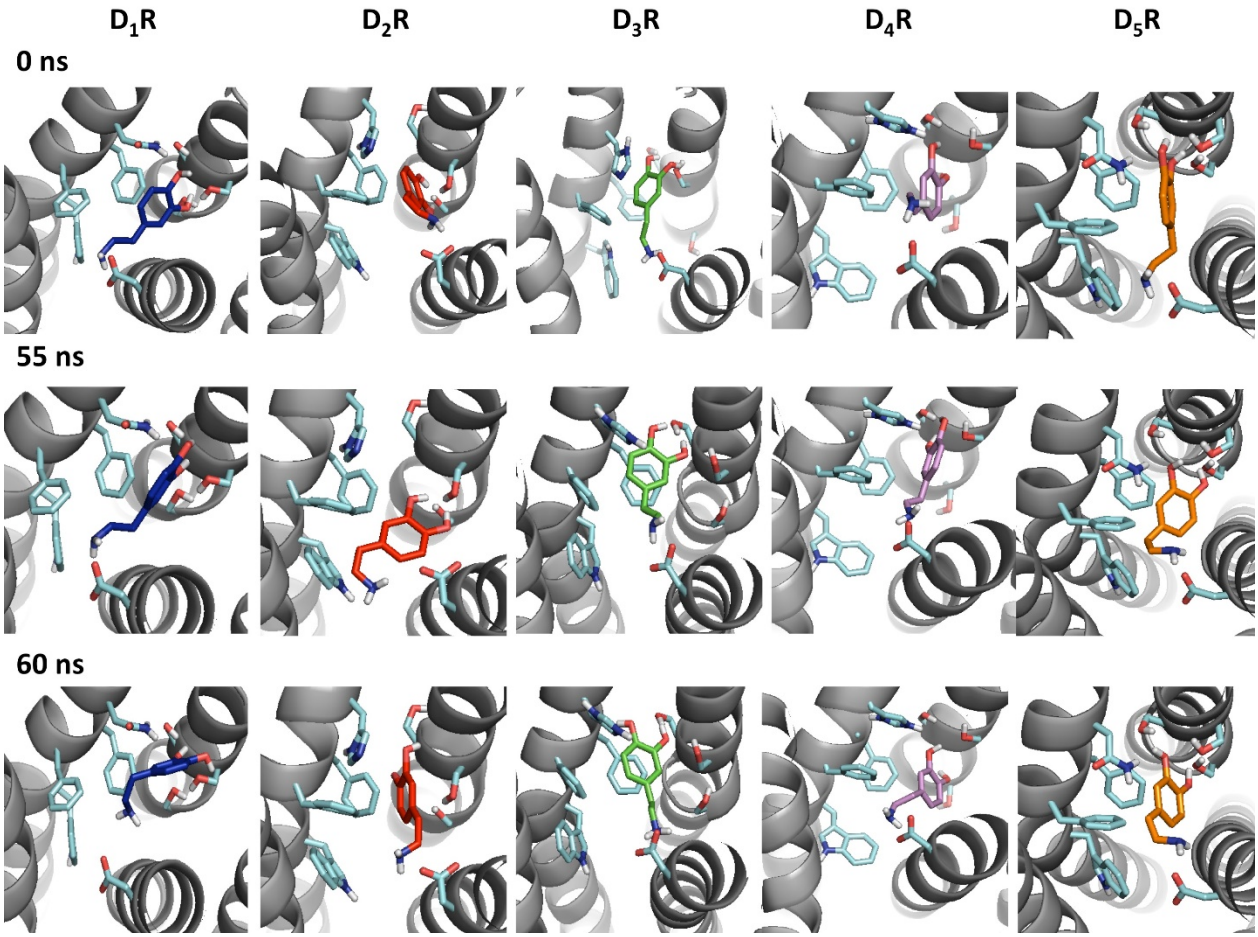


Figure S3 - Molecular docking of Dopamine at the $D_{1\text{-}5}R$ during 0 – 60 ns. The images correspond to the cluster with the lowest binding energy [kcal/mol] and highest number of conformations. D_1R, D_2R, D_3R, D_4R and D_5R were colored blue, red, green, violet and orange, respectively. Interacting residues are colored cyan.

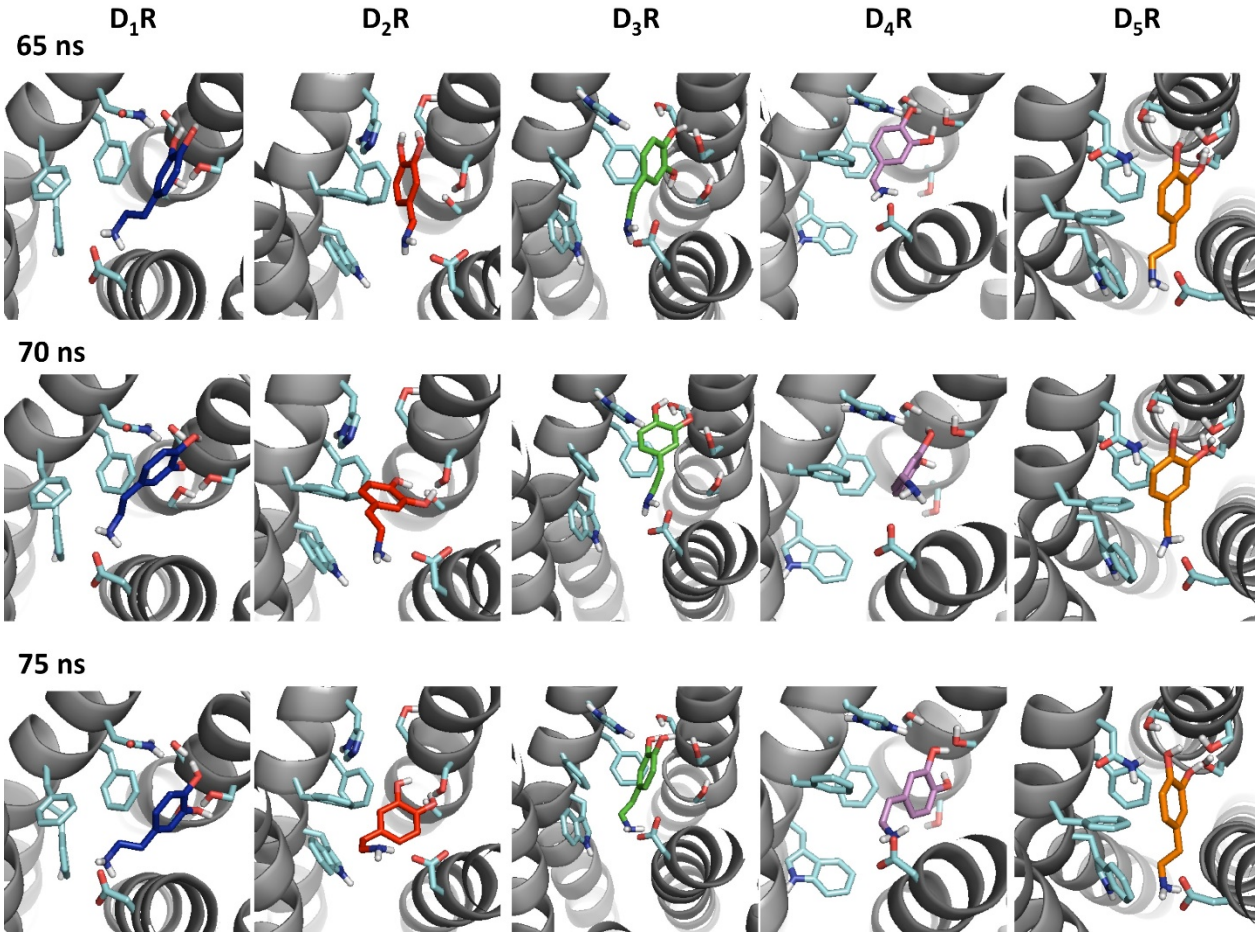


Figure S4 - Molecular docking of Dopamine at the $D_{1-5}R$ during 65 – 75 ns. The images correspond to the cluster with the lowest binding energy [kcal/mol] and highest number of conformations. D_1R, D_2R, D_3R, D_4R and D_5R were colored blue, red, green, violet and orange, respectively. Interacting residues are colored cyan.

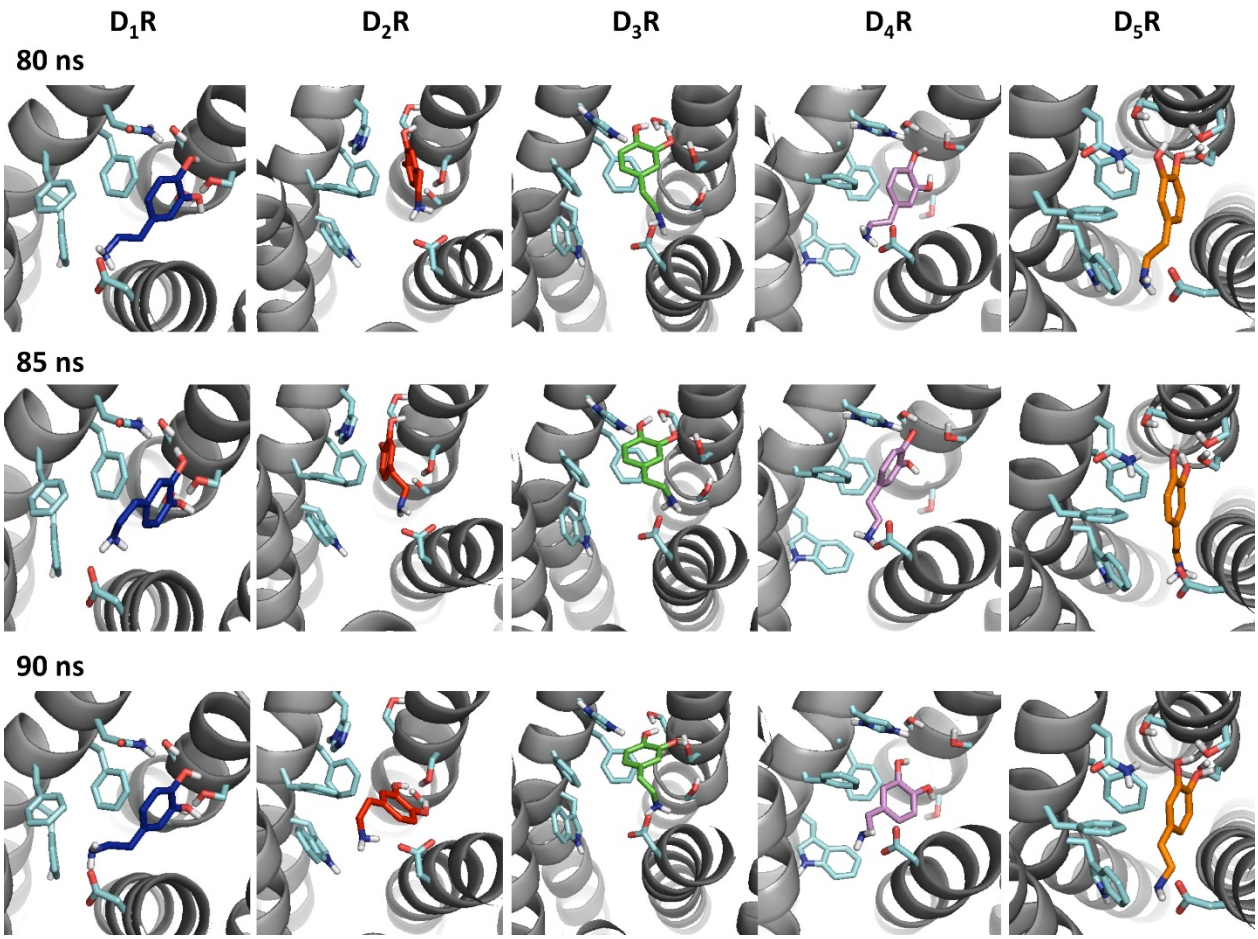


Figure S5 - Molecular docking of Dopamine at the $D_{1\text{-}5}R$ during 80 –90 ns. The images correspond to the cluster with the lowest binding energy [kcal/mol] and highest number of conformations. D_1R, D_2R, D_3R, D_4R and D_5R were colored blue, red, green, violet and orange, respectively. Interacting residues are colored cyan.

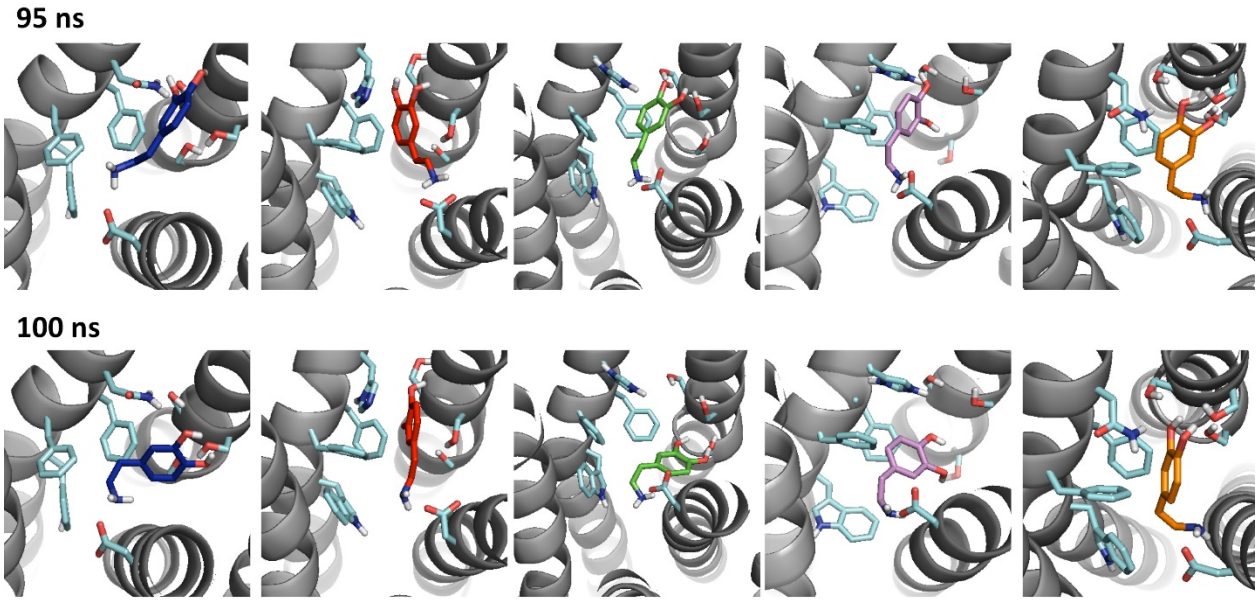


Figure S6 - Molecular docking of Dopamine at the $D_{1\text{-}5}R$ during 95 and 100 ns. The images correspond to the cluster with the lowest binding energy [kcal/mol] and highest number of conformations. D_1R, D_2R, D_3R, D_4R and D_5R were colored blue, red, green, violet and orange, respectively. Interacting residues are colored cyan.

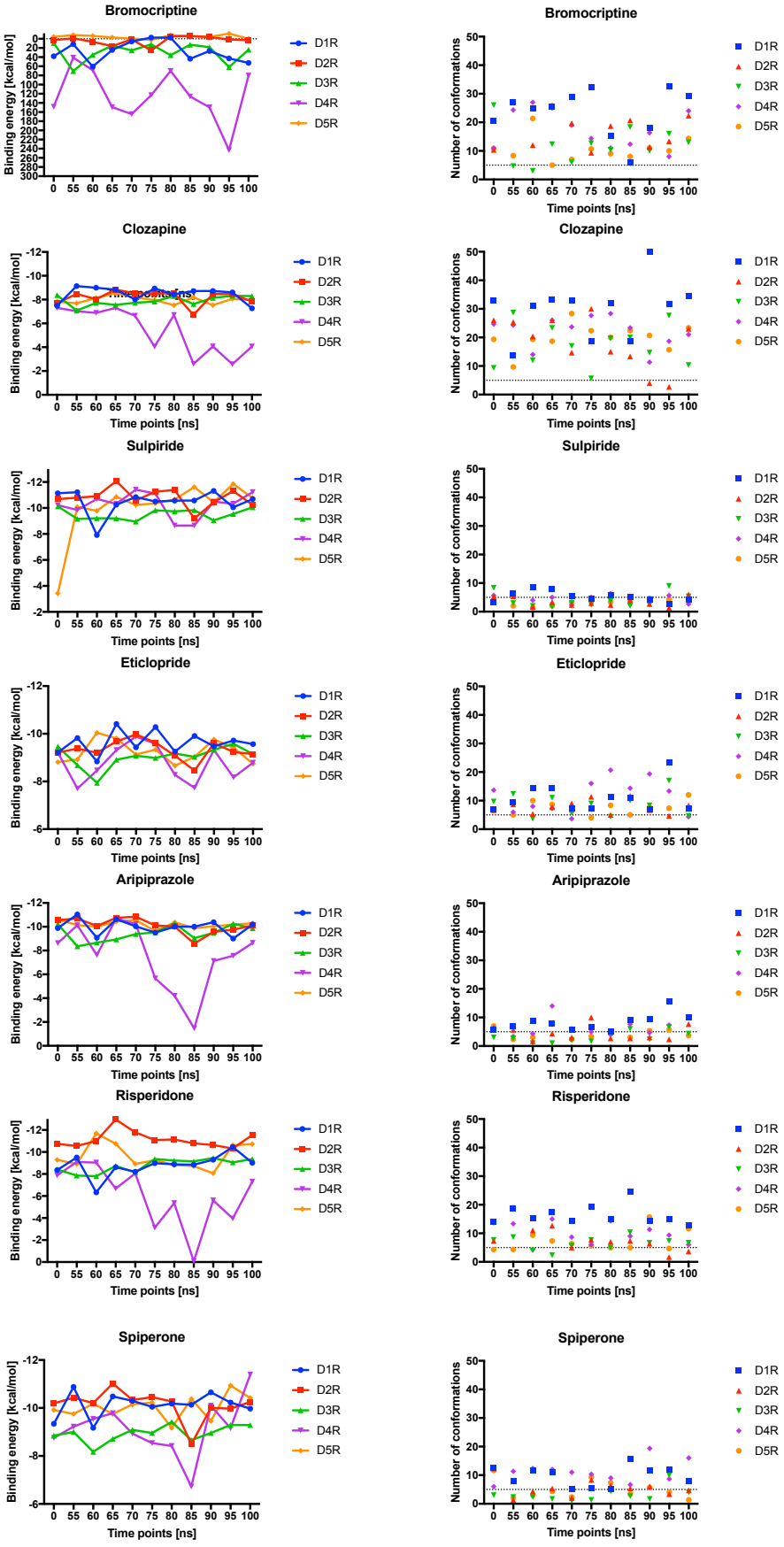

Bromocriptine
Binding energy [kcal/mol]
Number of conformations
Time points [ns]
D1R
D2R
D3R
D4R
D5R
Clozapine
Sulpiride
Eticlopride
Aripiprazole
Risperidone
Spiperone

Figure S7 - Results of the molecular docking of bromocriptine, clozapine, sulpiride, eticlopride, aripiprazole, risperidone and spiperone for all DR subtypes at different receptor conformations in various time points [ns]. The average of the 3 lowest binding energies of dopamine were calculated in the left plots. The number of conformations of the three clusters with the lowest binding energies were plotted for each time point and receptor (right plot).

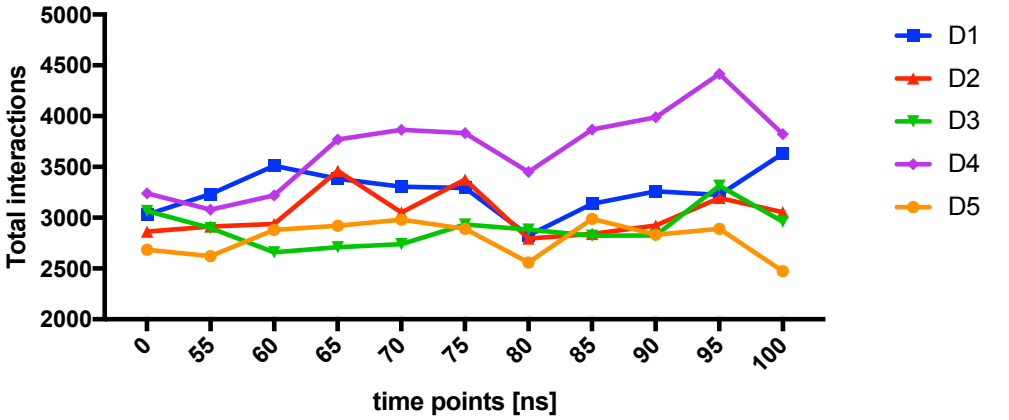


Figure S8 - Total interactions counted for each DR over time points [ns]. The interactions were summarized for all ligands and interaction types. The DR-subtypes are color-coded.

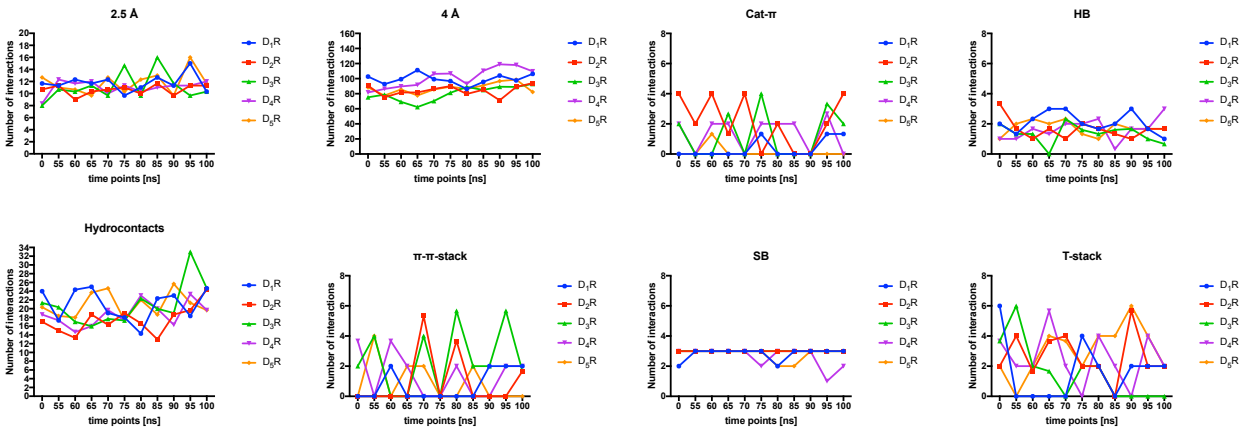


Figure S9 – Pairwise interactions results for dopamine. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cation-π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

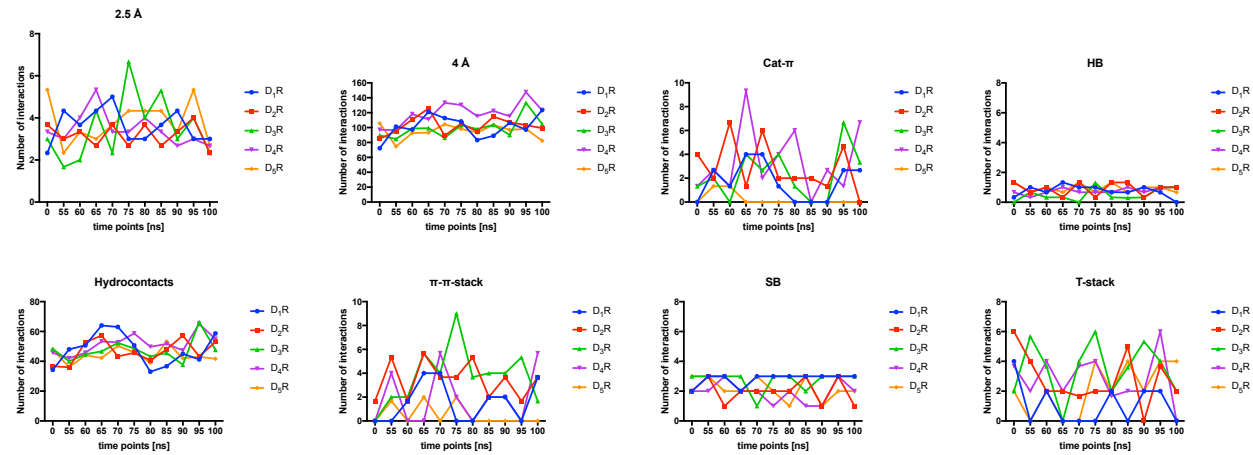


Figure S10 - Pairwise interactions results for 7-OH-DPAT. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

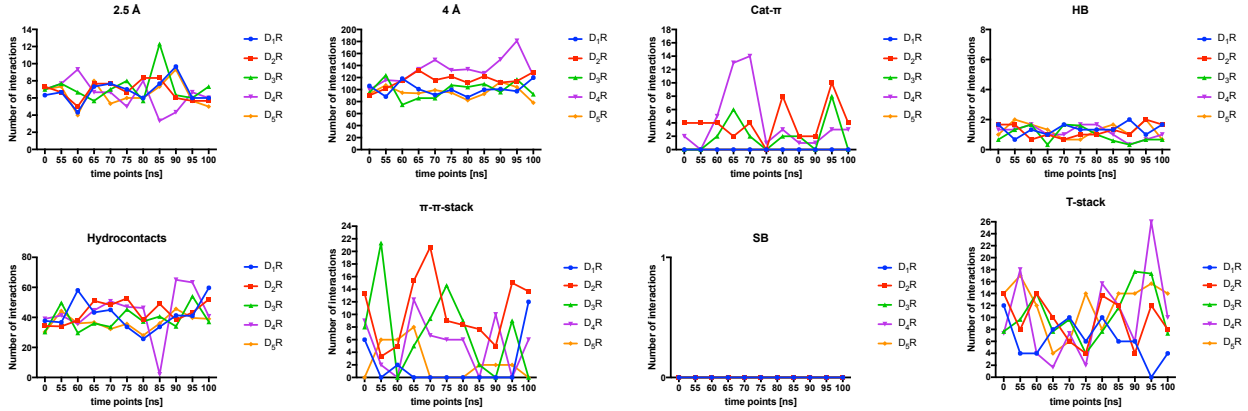


Figure S11 - Pairwise interactions results for apomorphine. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

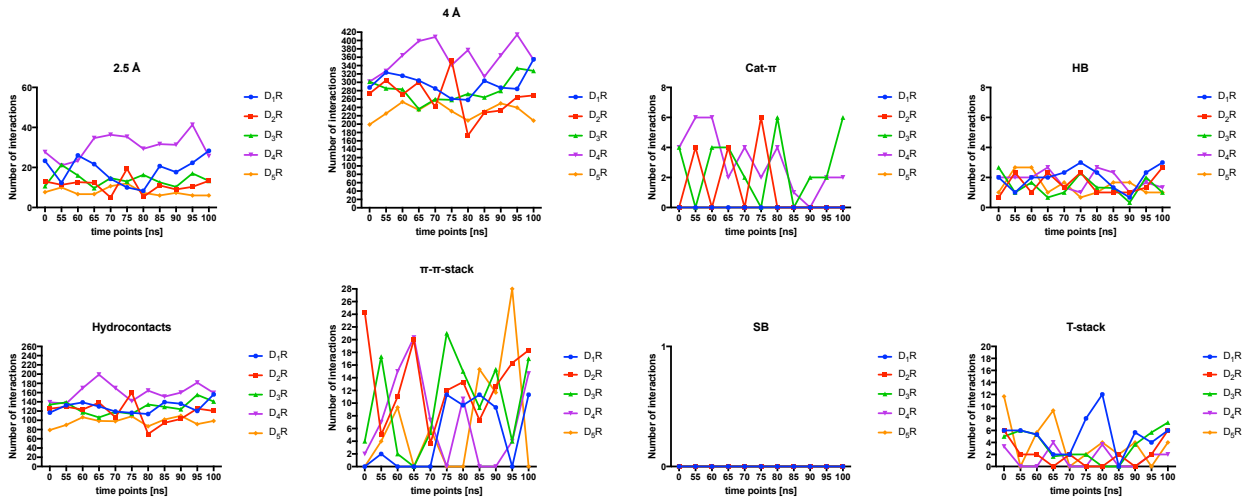


Figure S12 - Pairwise interactions results for bromocriptine. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

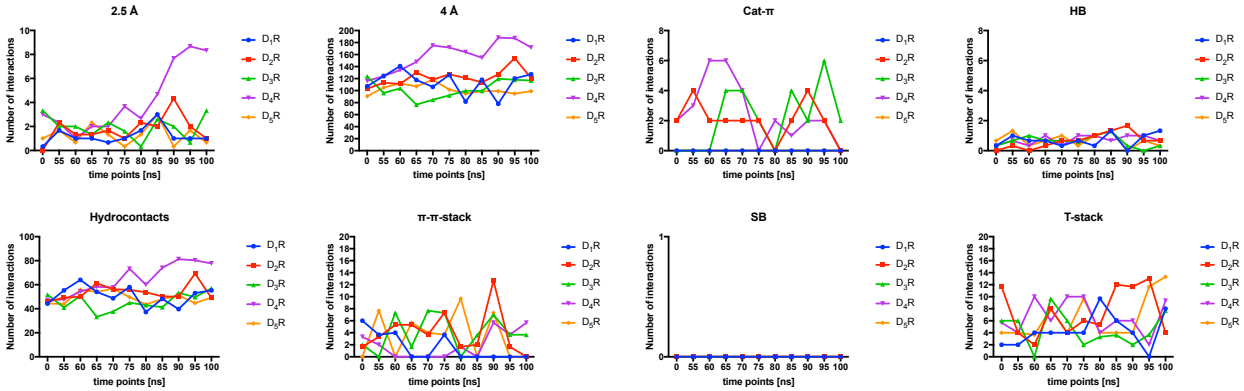


Figure S13 - Pairwise interactions results for clozapine. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

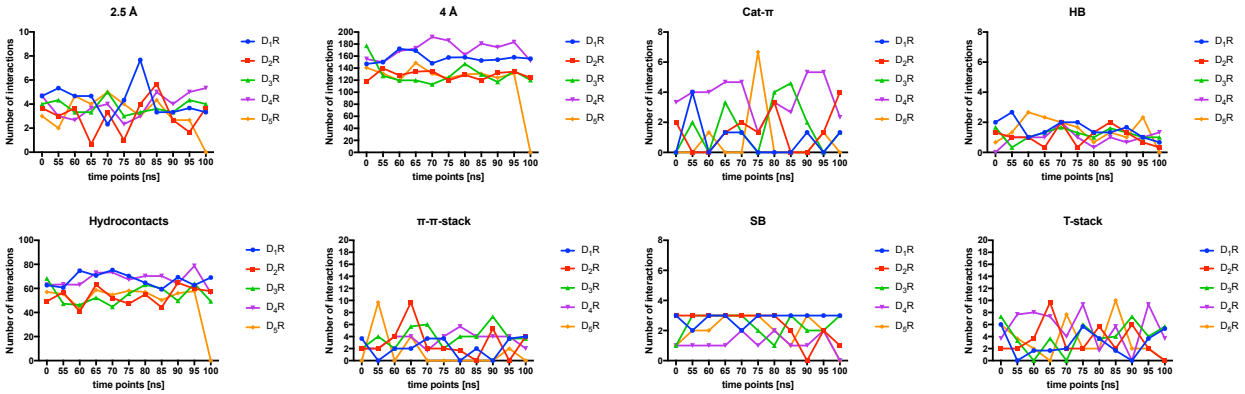


Figure S14 - Pairwise interactions results for nemonapride. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

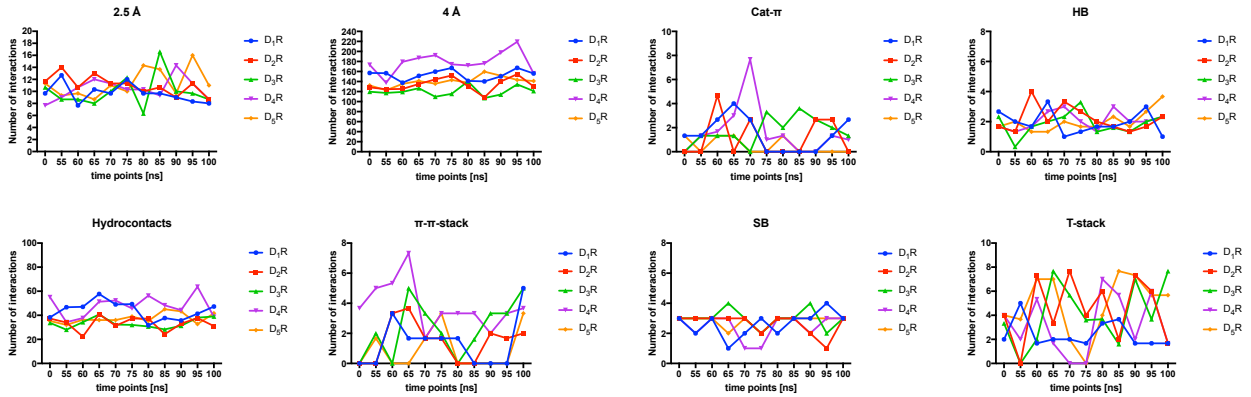


Figure S15 - Pairwise interactions results for sulpiride. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

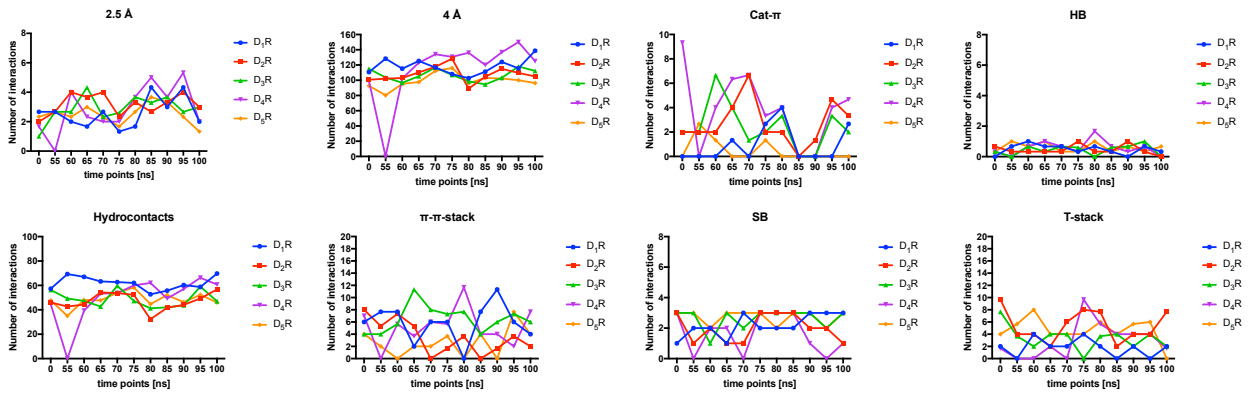


Figure S16 - Pairwise interactions results for SCH23390. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

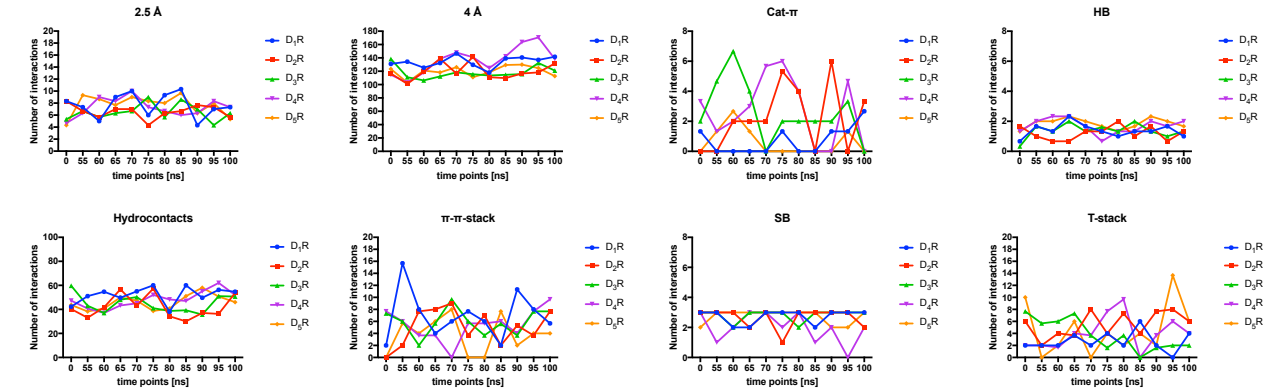


Figure S17 - Pairwise interactions results for SKF38393. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

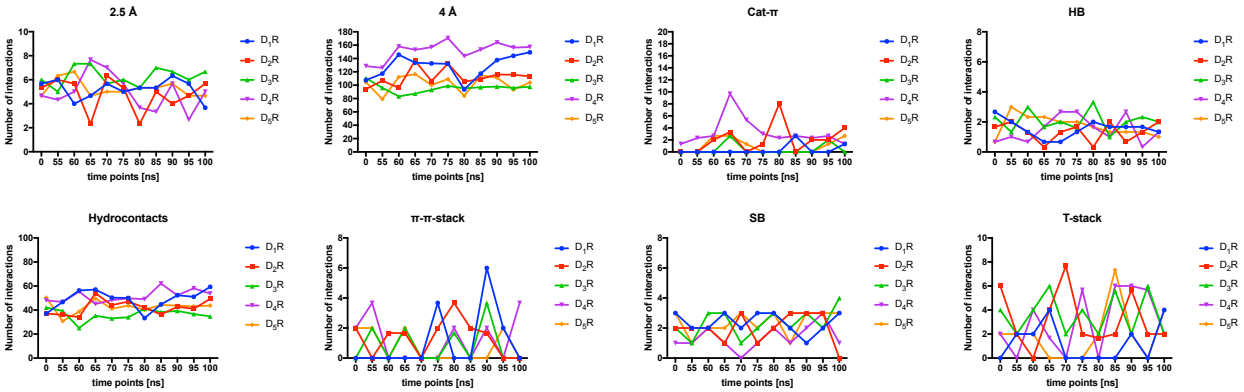


Figure S18 - Pairwise interactions results for eticlopride. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

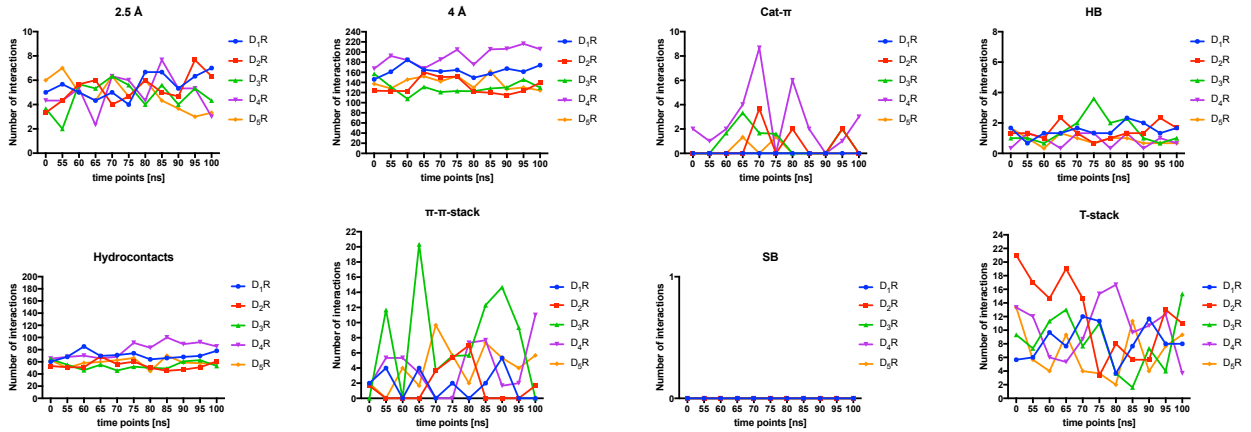


Figure S19 - Pairwise interactions results for risperidone. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

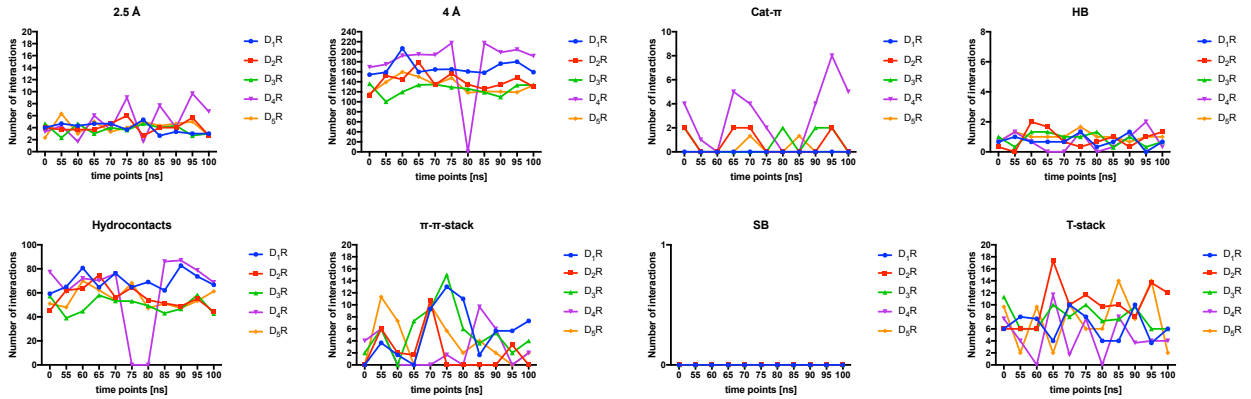


Figure S20 - Pairwise interactions results for aripiprazole. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

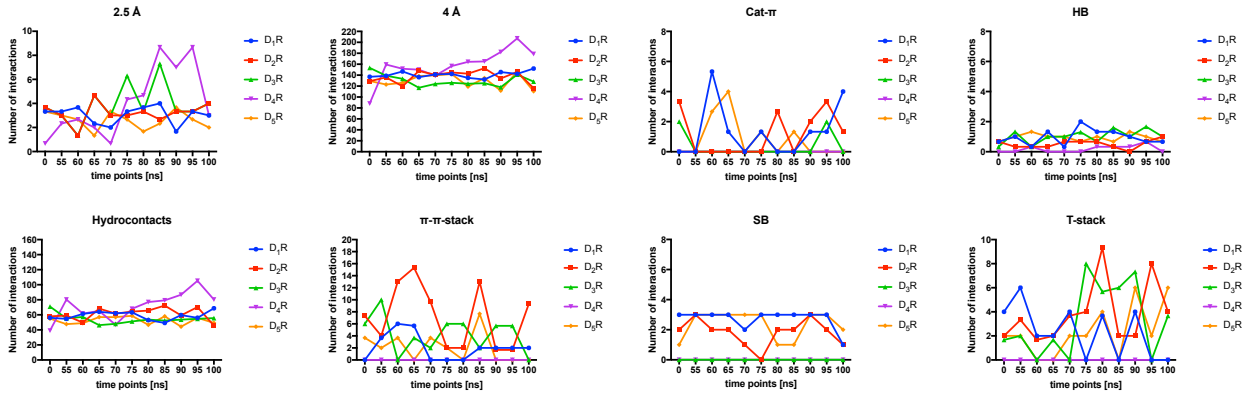


Figure S21 - Pairwise interactions results for haloperidole. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

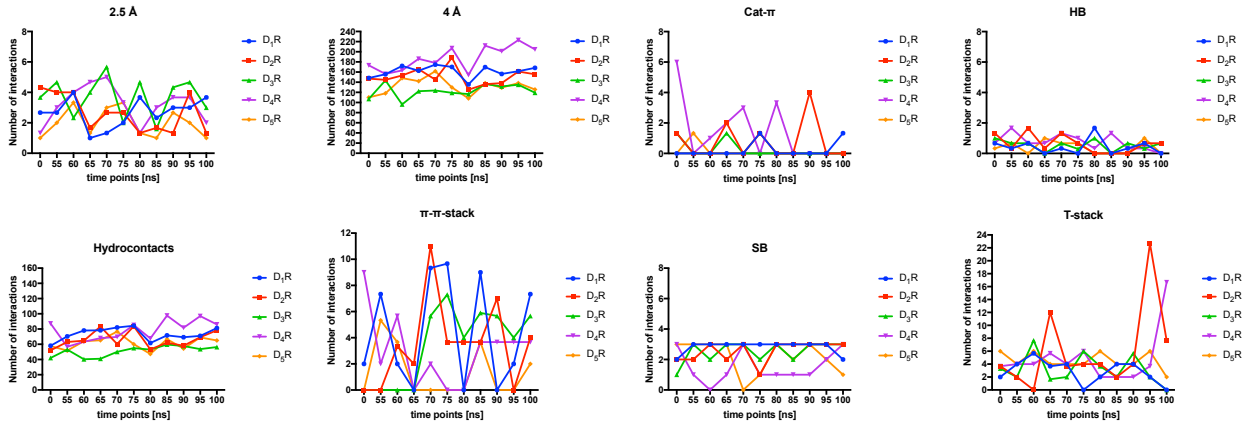


Figure S22 - Pairwise interactions results for spiperone. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

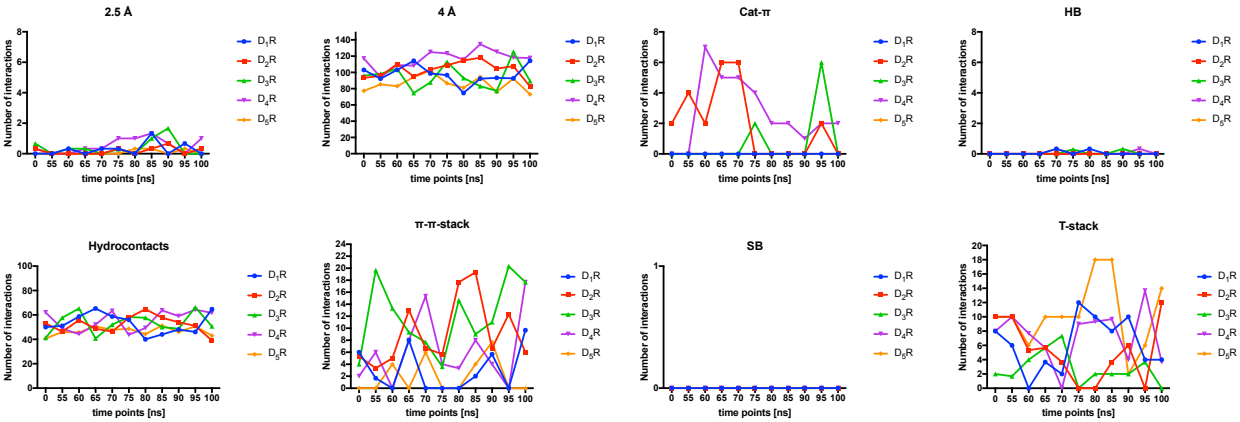


Figure S23 - Pairwise interactions results for chlorpromazine. Each type of interaction is displayed over all time points for each DR. The DR-subtypes are color-coded. Abbreviations: 2.5 Å – interactions within 2.5 Å; 4 Å – interactions within 4 Å; cat-π – cationic π-interactions; HB – hydrogen bonds; π-π-stack – interactions involving π-π-stacking; SB – salt-bridge; T-stack – aromatic superposition (edge-face-interactions).

TABLES

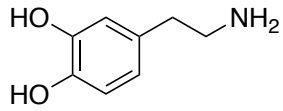
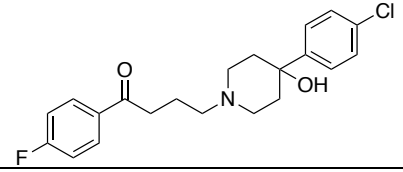
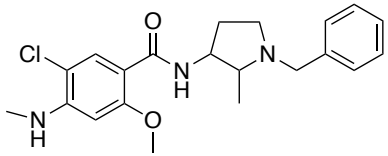
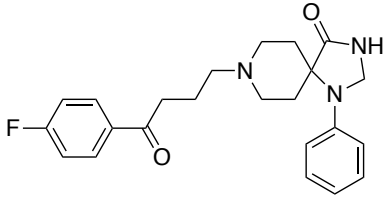
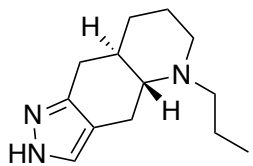
Table S1 - Comparison between the total and transmembrane specific identity [%] of the DR model with their crystal structure templates calculated with Clustal Omega.

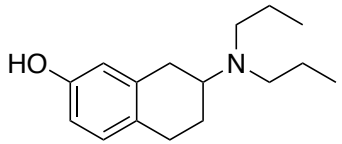
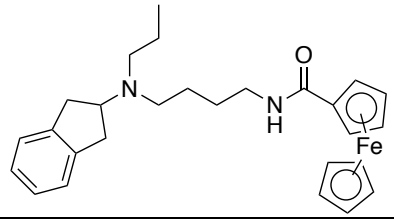
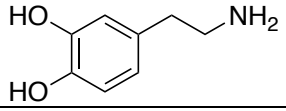
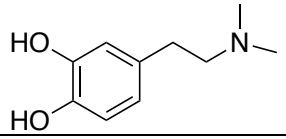
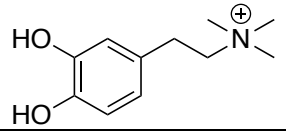
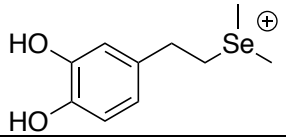
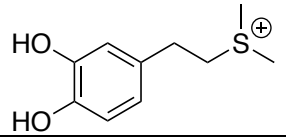
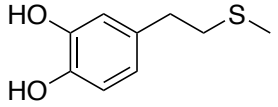
	D_1R	**D_2R**	**D_3R**	**D_4R**	**D_5R**
Total similarity with the template [%]	39.5	100.0	99.3	100.0	39.1
TM1	44.0	100.0	100.0	100.0	21.4
TM2	60.0	100.0	100.0	100.0	54.8
TM3	51.5	96.7	96.7	100.0	52.9
TM4	23.1	100.0	100.0	100.0	26.1
TM5	36.1	92.3	100.0	97.6	29.7
TM6	34.5	94.6	100.0	100.0	29.7
TM7	37.5	100.0	100.0	100.0	40.0

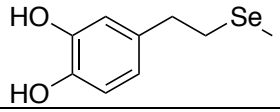
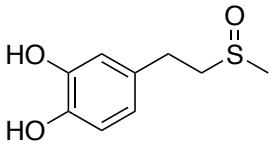
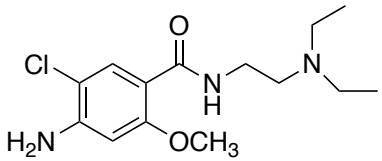
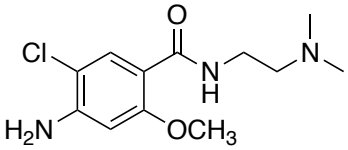
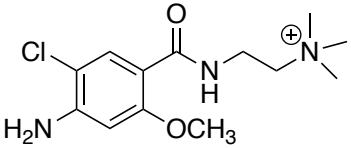
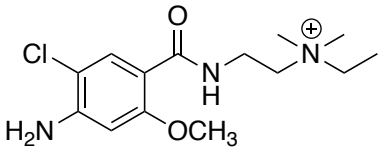
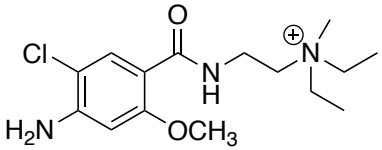
Table S2 – Averages RMSD values for Cα atoms of TM throughout the simulations. Structure was fitted to the TM domains in study.

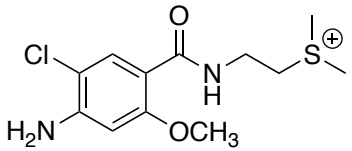
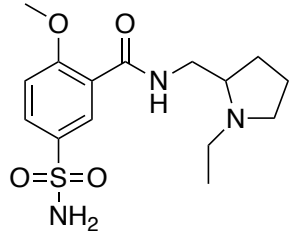
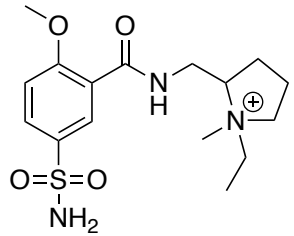
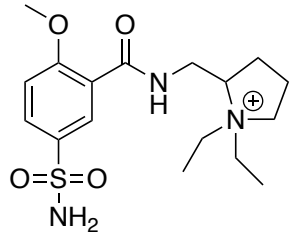
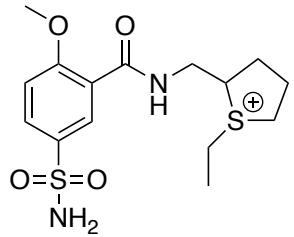
	TM1	**TM2**	**TM3**	**TM4**	**TM5**	**TM6**	**TM7**
D_1R	0.08 ± 0.01	0.09 ± 0.01	0.11 ± 0.01	0.07 ± 0.01	0.07 ± 0.01	0.07 ± 0.01	0.08 ± 0.01
D_2R	0.11 ± 0.02	0.10 ± 0.01	0.10 ± 0.01	0.10 ± 0.01	0.11 ± 0.01	0.14 ± 0.02	0.12 ± 0.01
D_3R	0.06 ± 0.01	0.05 ± 0.01	0.07 ± 0.01	0.08 ± 0.01	0.08 ± 0.01	0.08 ± 0.02	0.07 ± 0.01
D_4R	0.09 ± 0.02	0.07 ± 0.01	0.05 ± 0.01	0.07 ± 0.02	0.06 ± 0.01	0.05 ± 0.01	0.08 ± 0.02
D_5R	0.05 ± 0.01	0.07 ± 0.01	0.09 ± 0.01	0.10 ± 0.02	0.13 ± 0.02	0.10 ± 0.02	0.13 ± 0.03

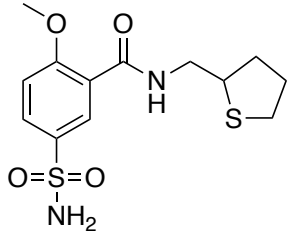
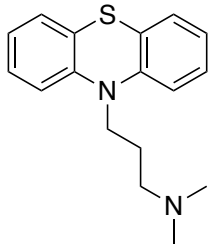
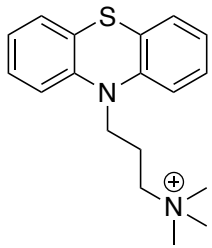
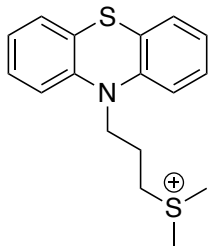
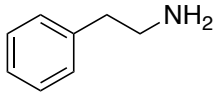
Table S3 - Summary of the structures used in literature for defining the binding pocket for the D_2R and source (experimental and computational) [2,39,44,47,49,51,99].

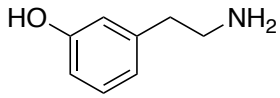
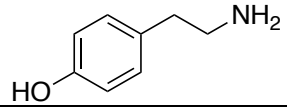
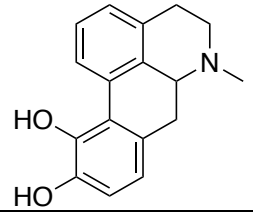
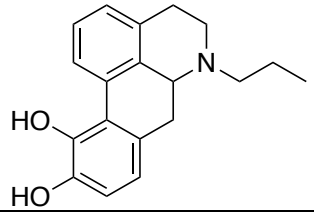
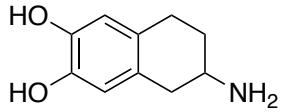
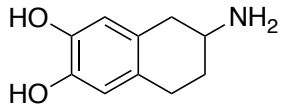
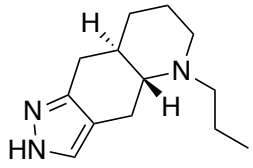
Reference	Ligands		Binding pocket (Experimental data)	Flexible residues (Computational data)
Tschammer *et al.*	Dopamine		Asp86, Val87, Ser165, Ser169, Trp236, Phe239, Phe 240, His243	
	Haloperidole			
	Nemonapride			
	Spiperone			
	Quinpirole			

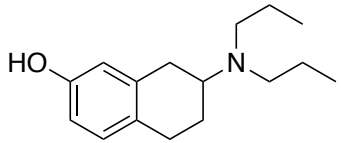
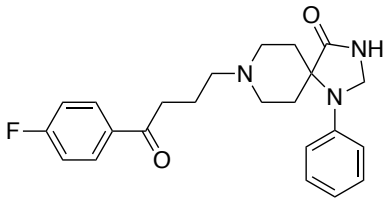
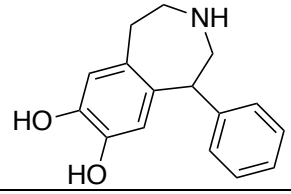
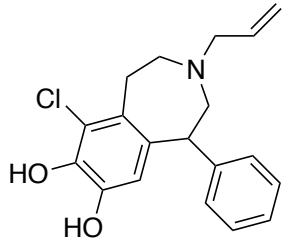
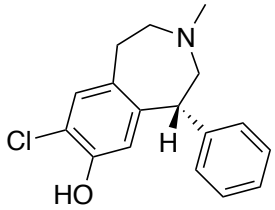
	7-Hydroxy-*N*,*N*-dipropyl-2-aminotetralin (7-OH-DPAT)		
	FAUC185		
Floresca *et al.*	Dopamine		Ser165, Ser166, Ser169, Trp236, Phe239, Phe240, His243
	N-Dimethyldopamine		
	N-Trimethyldopamine		
	N-Dimethylselenodopamine		
	N-Dimethylsulfodopamine		
	Monomethylsulfoniumdopamine		

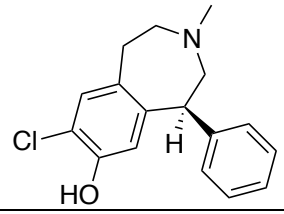
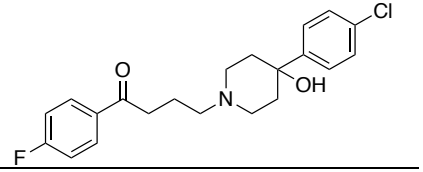
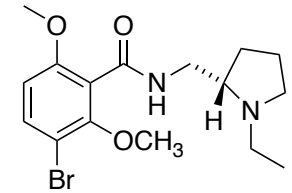
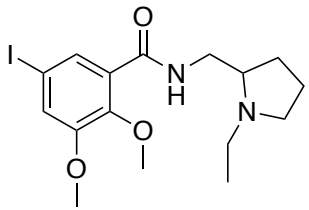
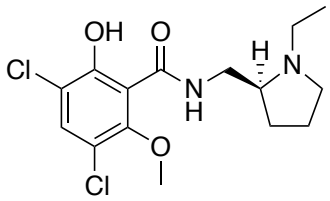
Monomethylselemoniumdopamine	
Monomethylsulfoxidedopamine	
Metoclopramine (met-N(et)$_2$)	
Met-N(me)$_2$	
Met-N+(me)$_3$	
Met-N+(me)$_2$(et)	
Met-N+(me)(et)$_2$	

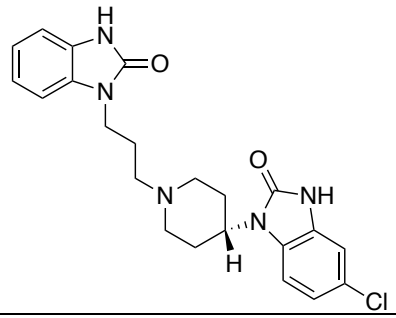
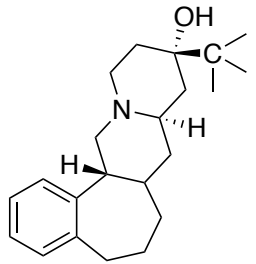
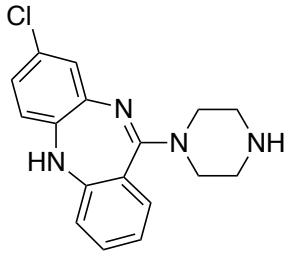
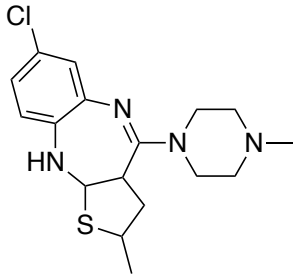
Met-S+(me)$_2$	
Sulpiride N-et	
Sulpiride N+(et)(me)	
Sulpiride N+(et)$_2$	
Sulpiride S+(et)	

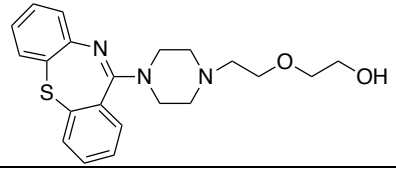
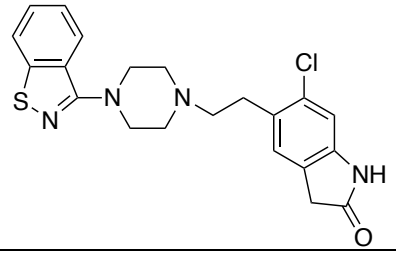
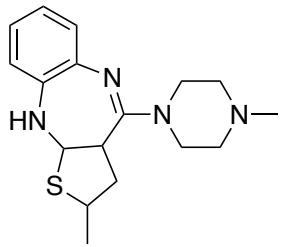
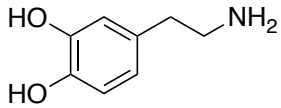
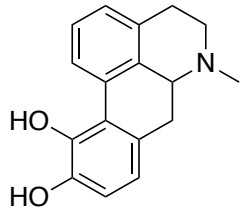
Sulpiride S	
Chlorpromazine (CPZ-N(Me)$_2$)	
CPZ-N+(Me)$_3$	
CPZ-S+(Me)$_2$	
Beta-Phenylethylamine (PEA)	

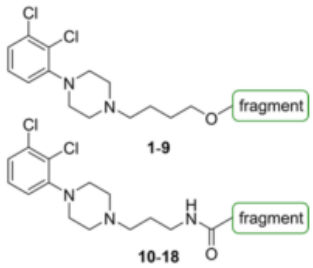
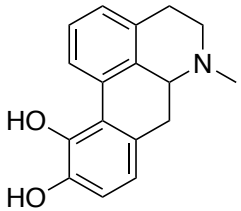
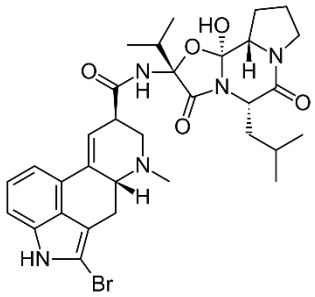
Meta-Tyramine	
Para-Tyramine	
Apomorphine	
Norpropylapomorphine/ N-Proplapomorphine	
6,7-ADTN	
5,6-ADTN	
Quinpirole	

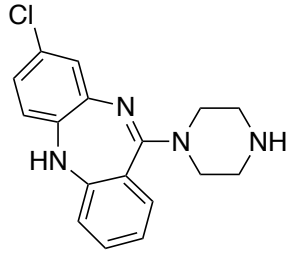
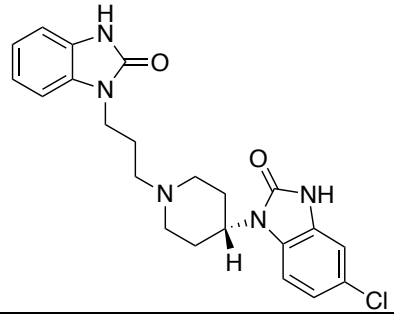
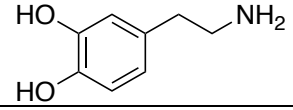
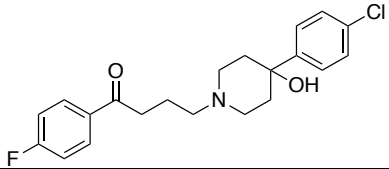
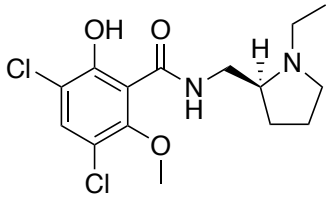
7-OH-DPAT	
Spiperidone	
SKF38393	
SKF82958	
SCH23390	

SCH23388	
Haloperidole	
Remoxipride	
Epidipride	
Raclopride	

Domperidone	
(+)-Butaclamol	
Clozapine	
Olanzapine	

	Quetiapine			
	Ziprasidone			
	Risperidone			
Durdagi *et al.*	Dopamine		Asp86, Phe239, Phe240, Ser165, Ser166, Ser169, His243, Ile156, Trp236, Tyr258, Tyr266	<u>Glide/IFD:</u> Asp86, Trp236, Phe240, Tyr266 <u>GOLD:</u> Asp86, Cys90, Ser165, Ser166, Ser169, Phe170, His243, Tyr258, Thr262, Tyr266
	Apomorphine			

Männel *et al.*	1,4 DAPs for compounds representing the "fragment"		- Asp86 forming a salt-bridge - Secondary binding pocket: Glu67, Ser259, Tyr258, Thr262, Tyr266
Kalani *et al.*	Apomorphine		Asp86, Ser165, Ser169, Phe82, Met89, Cys90, Phe144, Phe170, Val172, Trp236, Phe240, His243
	Bromocriptine		

Clozapine	
Domperidone	
Dopamine	
Haloperidole	
Raclopride	

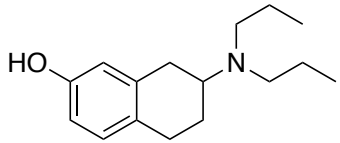
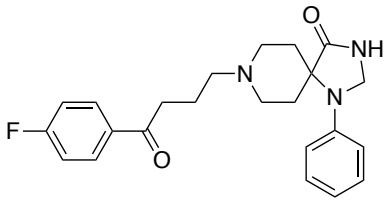
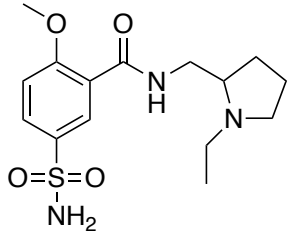
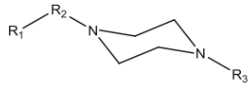
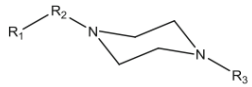
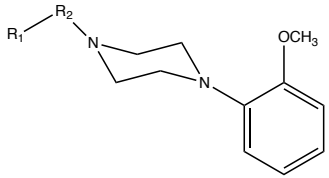
	7-OH-DPAT			
	Spiperone			
	Sulpiride			
Sukalovic *et al.*	Arylpiperazines for compounds representing the residues R_1, R_2 and R_3	1) To construct the model  2) To test the model  3) To probe the ECL2 area of the model 	Asp86, Ser165, Ser169, Phe82, Met89, Cys90, Phe144, Phe170, Val172, Trp236, Phe240, His243	<u>Glide:</u> Asp86, Ser139, Ser165, Ser169, Phe232, Trp236, Tyr266

Table S4 - Docking results for the D_1R. The lowest binding energy ΔG_{bind} [kcal/mol] of every run was measured using AutoDock4.2. Calculated conformations were clustered and ranked by energy level. A populated cluster indicates, that the position docked into the receptor is more likely to depict the conformational binding position of the ligand. The three best clusters were chosen and analyzed. NA – Not Available, cases were the number of clusters was lower than 3.

Receptor state of the MD simulation [ns]	**Top**	**0**	**55**	**60**	**65**	**70**	**75**	**80**	**85**	**90**	**95**	**100**
Dopamine		Lowest binding energy [kcal/mol]										
	1	-10.71	-10.19	-9.29	-10.65	-9.92	-11.50	-10.67	-10.31	-10.96	-10.73	-9.35
	2	-9.56	-9.63	-8.64	-9.45	-9.42	-10.67	-9.81	-8.93	-10.80	-9.91	-9.21
	3	-8.61	-9.16	-7.48	-8.70	-8.18	-9.00	-7.82	-8.85	-10.04	-9.56	-7.97
		Number of conformations in cluster										
	1	64	13	12	18	49	45	68	74	61	19	15
	2	14	17	8	32	29	31	21	7	19	11	27
	3	1	4	5	11	4	5	1	4	2	43	1
7-OH-DPAT		Lowest binding energy [kcal/mol]										
	1	-9.33	-10.16	-8.39	-10.09	-9.08	-9.85	-9.27	-9.62	-9.98	-9.04	-9.78
	2	-8.19	-9.68	-8.33	-9.18	-8.38	-9.23	-9.00	-7.82	-9.46	-8.73	-9.07
	3	-8.09	-8.66	-7.97	-8.77	-7.79	-8.45	-7.59	-7.65	-8.91	-8.57	-8.25
		Number of conformations in cluster										
	1	46	13	10	2	13	24	37	55	44	13	10
	2	9	12	14	12	13	14	29	2	10	7	9
	3	18	5	18	2	3	8	5	6	3	9	2
Apomorphine		Lowest binding energy [kcal/mol]										
	1	-10.39	-10.47	-9.93	-10.79	-10.11	-11.39	-10.79	-10.09	-10.77	-10.44	-9.93
	2	-9.33	-8.87	-9.58	-10.08	-9.41	-11.17	-10.53	-9.99	-9.97	-9.88	-8.80
	3	-8.96	-8.82	-8.86	-9.00	-9.24	-9.60	-9.21	-8.64	-9.34	-8.95	-8.49
		Number of conformations in cluster										
	1	64	25	40	33	12	27	29	36	22	44	31
	2	12	11	26	21	37	32	34	20	16	14	6
	3	17	15	6	7	7	5	15	25	6	5	3
Bromocriptine		Lowest binding energy [kcal/mol]										

	1	+7.85	+2.32	+35.03	+15.82	+2.66	-5.33	-5.78	+26.43	+15.05	+35.22	+31.70
	2	+47.13	+10.47	+72.18	+16.34	+5.87	-4.82	-1.29	+49.89	+29.78	+40.32	+53.05
	3	+59.56	+22.09	+74.60	+40.56	+9.03	+1.52	-0.56	+54.28	+35.11	+52.86	+73.04
		Number of conformations in cluster										
	1	7	51	37	49	33	25	27	10	5	58	25
	2	21	28	22	22	35	28	12	5	46	37	35
	3	34	2	16	5	19	44	7	3	3	3	28
Clozapine		Lowest binding energy [kcal/mol]										
	1	-8.09	-9.32	-9.47	-9.43	-8.49	-9.52	-8.89	-9.14	-9.05	-8.76	-8.33
	2	-7.23	-9.14	-8.87	-8.84	-8.33	-9.00	-8.41	-8.91	-8.39	-8.56	-7.18
	3	-7.12	-8.94	-8.63	-8.24	-7.22	-8.28	-7.99	-8.09	NA	-8.48	-6.28
		Number of conformations in cluster										
	1	43	36	31	39	80	45	74	14	88	38	84
	2	54	1	50	52	18	2	9	38	12	17	14
	3	2	4	12	9	1	9	13	4	NA	40	1
Nemonapride		Lowest binding energy [kcal/mol]										
	1	-10.01	-10.84	-9.81	-11.15	-10.76	-11.02	-10.80	-10.73	-11.82	-11.08	-11.52
	2	-9.91	-10.24	-9.54	-10.90	-9.83	-10.77	-10.39	-10.26	-11.37	-10.79	-9,81
	3	-9.90	-10.00	-9.23	-10.79	-9.25	-10.70	-10.24	-10.00	-11.30	-10.66	-9.51
		Number of conformations in cluster										
	1	15	2	24	5	20	7	6	24	16	13	4
	2	22	15	11	4	16	1	6	13	17	20	2
	3	12	4	13	3	3	3	25	13	17	2	15
Sulpiride		Lowest binding energy [kcal/mol]										
	1	-11.43	-11.73	-8.76	-10.55	-12.51	-11.38	-10.88	-10.87	-11.64	-10.43	-10.95
	2	-11.24	-11.25	-7.61	-10.22	-11.16	-11.07	-10.68	-10.70	-10.30	-10.43	-10.76
	3	-10.73	-10.67	-7.36	-9.98	-8.85	-9.06	-10.13	-10.15	-10.01	-9.29	-10.35
		Number of conformations in cluster										
	1	4	14	5	8	11	8	12	10	6	3	7
	2	3	3	16	14	2	1	4	3	2	3	2
	3	3	2	5	2	3	5	1	2	5	2	4

SCH23390	Lowest binding energy [kcal/mol]										
	1	-9.31	-9.86	-9.33	-9.49	-9.78	-10.01	-9.05	-9.94	-10.01	-10.59	-9.45
	2	-8.44	-9.62	-9.21	-9.27	-9.51	-9.86	-9.03	-9.72	-9.71	-9.62	-8.73
	3	-8.16	-9.15	-9.02	-9.23	-8.71	-9.84	-8.54	-9.09	-9.69	-9.17	-8.68
	Number of conformations in cluster											
	1	13	2	30	41	39	16	15	4	11	18	5
	2	3	6	29	5	6	5	17	4	5	6	3
	3	1	11	5	6	2	1	3	1	6	3	4
SKF38393	Lowest binding energy [kcal/mol]											
	1	-12.23	-11.73	-8.91	-10.11	-11.44	-13.06	-11.87	-12.18	-12.50	-12.00	-11.88
	2	-11.00	-9.15	-8.58	-9.45	-9.25	-11.90	-11.32	-10.37	-11.35	-11.09	-9.41
	3	-9.40	-9.13	-8.36	-9.05	-9.05	-8.74	-9.55	-8.97	-9.45	-10.99	-9.26
	Number of conformations in cluster											
	1	38	3	8	6	36	56	32	29	50	16	26
	2	22	6	7	6	1	8	19	17	3	30	4
	3	4	3	9	12	5	3	1	1	9	2	20
Eticlopride	Lowest binding energy [kcal/mol]											
	1	-9.65	-10.53	-9.39	-10.99	-9.85	-10.47	-10.06	-10.61	-9.67	-10.15	-9.75
	2	-9.57	-9.56	-8.69	-10.52	-9.26	-10.34	-8.88	-9.61	-9.61	-9.82	-9.66
	3	-8.43	-9.37	-8.44	-9.73	-9.19	-10.04	-8.82	-9.51	-9.14	-9.18	-9.29
	Number of conformations in cluster											
	1	12	13	10	7	12	2	6	16	16	25	4
	2	2	7	14	29	9	6	3	14	3	23	4
	3	7	8	19	7	1	14	25	3	2	12	14
Risperidone	Lowest binding energy [kcal/mol]											
	1	-9.17	-10.19	-7.51	-9.12	-8.50	-9.96	-9.60	-10.35	-9.72	-11.60	-9.66
	2	-8.29	-9.42	-6.36	-8.82	-8.16	-8.98	-8.62	-9.11	-9.40	-10.48	-8.71
	3	-7.62	-8.90	-5.11	-7.91	-7.95	-8.02	-8.40	-7.08	-8.78	-9.31	-8.70
	Number of conformations in cluster											
	1	9	31	6	30	32	32	40	42	31	10	8
	2	27	20	25	19	4	18	3	29	8	28	24

	3	6	5	15	3	7	8	4	3	4	7	6
Aripiprazole	Lowest binding energy [kcal/mol]											
	1	-10.26	-11.59	-10.11	-11.79	-10.73	-9.99	-10.51	-10.29	-11.12	-9.85	-10.68
	2	-9.74	-11.24	-8.93	-10.64	-10.02	-9.31	-9.86	-10.06	-10.08	-8.72	-9.95
	3	-9.64	-10.28	-8.17	-9.43	-9.37	-9.20	-9.63	-9.67	-9.96	-8.43	-9.94
	Number of conformations in cluster											
	1	8	7	10	5	14	12	6	19	16	29	5
	2	1	3	5	18	1	6	8	1	9	14	9
	3	8	11	11	1	2	2	1	7	3	4	16
Haloperidole	Lowest binding energy [kcal/mol]											
	1	-9.84	-11.35	-10.73	-11.68	-10.58	-10.65	-10.55	-9.87	-11.19	-10,93	-10.47
	2	-9.81	-10.99	-9.68	-10.87	-10.21	-10.50	-10.49	-9.52	-10.08	-10.58	-10.15
	3	-9.33	-10.91	-9.64	-10.61	-10.10	-10.50	-9.73	-9.51	-9.90	-10.51	-9.60
	Number of conformations in cluster											
	1	28	20	42	4	37	4	9	27	32	4	7
	2	6	22	7	31	2	9	5	4	13	5	5
	3	1	9	10	4	8	16	7	3	9	9	7
Spiperone	Lowest binding energy [kcal/mol]											
	1	-9.70	-11.12	-9.30	-10.93	-11.09	-10.37	-10.76	-10.56	-10.76	-10.81	-10.35
	2	-9.31	-10.95	-9.23	-10.46	-9.99	-10.03	-9.97	-10.33	-10.71	-10.10	-9.93
	3	-9.02	-10.56	-8.99	-10.05	-9.81	-9.75	-9.81	-9.50	-10.48	-9.77	-9.63
	Number of conformations in cluster											
	1	29	9	8	13	2	1	4	2	11	26	7
	2	14	11	10	7	4	3	8	35	8	4	7
	3	5	4	17	13	9	12	3	10	16	6	10
Chlorpromazine	Lowest binding energy [kcal/mol]											
	1	-8.10	-8.70	-9.19	-9.04	-8.92	-8.93	-8.02	-8.06	-8.68	-8.91	-8.82
	2	-7.98	-8.55	-9.00	-8.87	-8.39	-8.70	-7.94	-8.01	-8.67	-8.75	-8.51
	3	-7.92	-8.52	-8.95	-8.79	-8.35	-8.59	-7.92	-8.00	-8.63	-8.72	-8.43
	Number of conformations in cluster											
	1	16	24	14	17	25	24	12	13	5	23	1

	2	9	30	22	2	13	24	22	17	4	26	17
	3	21	4	12	2	4	9	17	8	35	9	19

Table S5 - Docking results for the D_2R. The lowest binding energy ΔG_{bind} [kcal/mol] of every run was measured using AutoDock4.2. Calculated conformations were clustered and ranked by energy level. A populated cluster indicates, that the position docked into the receptor is more likely to depict the conformational binding position of the ligand. The three best clusters were chosen and analyzed.

Receptor state of the MD simulation [ns]	**Top**	**0**	**55**	**60**	**65**	**70**	**75**	**80**	**85**	**90**	**95**	**100**
Dopamine		Lowest binding energy [kcal/mol]										
	1	-9.72	-9.76	-9.69	-9.29	-9.11	-9.57	-9.37	-8.93	-9.15	-10.31	-9.78
	2	-9.71	-9.15	-9.27	-9.02	-9.02	-9.05	-8.98	-8.82	-8.89	-9.91	-9.04
	3	-8.61	-8.64	-8.30	-8.44	-8.98	-8.91	-8.73	-8.71	-8.76	-8.91	-8.60
		Number of conformations in cluster										
	1	32	24	19	16	24	23	33	3	15	6	12
	2	29	17	19	32	4	18	20	31	8	26	19
	3	6	20	15	11	8	4	10	10	22	29	13
7-OH-DPAT		Lowest binding energy [kcal/mol]										
	1	-9.26	-8.16	-8.30	-9.02	-8.46	-9.26	-8.59	-8.08	-8.92	-8.37	-9.30
	2	-8.28	-7.99	-7.85	-8.72	-8.34	-8.34	-8.31	-7.33	-7.76	-8.25	-8.31
	3	-8.06	-7.98	-7.73	-8.59	-8.25	-7.93	-7.89	-7.06	-7.50	-7.86	-8.21
		Number of conformations in cluster										
	1	26	8	11	2	17	43	20	8	19	20	21
	2	17	17	10	14	15	6	5	41	13	4	2
	3	14	28	1	6	6	9	5	4	15	16	2
Apomorphine		Lowest binding energy [kcal/mol]										
	1	-10.05	-10.21	-10.28	-11.38	-11.09	-11.10	-10.03	-10.31	-10.61	-10.82	-10.44
	2	-9.62	-10.04	-9.88	-11.31	-10.03	-10.22	-9.97	-9.71	-10.35	-9.69	-10.10
	3	-9.60	-9.76	-9.41	-10.72	-9.68	-9.78	-9.36	-9.15	-9.51	-9.51	-9.82

	1	34	16	36	2	5	45	31	14	19	14	12
	2	22	11	10	13	21	15	21	3	4	16	25
	3	25	21	4	7	17	1	7	23	3	23	3
Bromocriptine	Lowest binding energy [kcal/mol]											
	1	-3.47	-7.61	+2.18	+14.69	-2.36	+20.66	-5.43	-6.76	-6.36	-0.24	-3.38
	2	+5.75	-1.33	+4.49	+15.35	+2.84	+23.11	-5.26	-5.82	-5.19	+1.49	+6.48
	3	+6.87	+5.01	+13.20	+17.48	+3.32	+32.17	-4.99	-4.88	+0.45	+2.79	+6.62
	Number of conformations in cluster											
	1	13	79	9	14	21	24	7	42	24	25	36
	2	12	2	19	22	16	3	24	7	7	12	2
	3	6	1	8	42	22	1	25	13	3	3	29
Clozapine	Lowest binding energy [kcal/mol]											
	1	-8.10	-9.20	-8.50	-9.39	-8.66	-8.54	-8.71	-7.44	-8.88	-8.75	-8.19
	2	-7.59	-8.12	-8.14	-8.81	-8.56	-8.54	-8.68	-6.70	-8.28	-8.45	-7.96
	3	-7.42	-8.09	-7.47	-8.34	-8.34	-8.44	-8.24	-6.00	-8.25	-8.16	-7.37
	Number of conformations in cluster											
	1	21	66	18	19	26	41	14	27	3	2	1
	2	2	9	40	56	7	4	13	7	2	1	55
	3	55	1	3	3	11	45	18	6	7	5	13
Nemonapride	Lowest binding energy [kcal/mol]											
	1	-10.10	-10.56	-11.39	-10.08	-10.58	-10.32	-11.11	-10.72	-10.23	-10.45	-11.86
	2	-9.43	-9.92	-10.04	-9.79	-10.30	-9.88	-10.64	-10.60	-10.00	-10.35	-11.17
	3	-9.34	-9.60	-9.79	-9.73	-10.30	-9.80	-9.98	-10.43	-9.97	-10.08	-10.62
	Number of conformations in cluster											
	1	9	3	5	7	6	9	7	5	2	17	5
	2	7	5	2	18	3	8	15	28	3	5	1
	3	7	19	16	7	20	3	2	3	6	1	4
Sulpiride	Lowest binding energy [kcal/mol]											
	1	-11.39	-11.20	-11.35	-12.39	-11.39	-11.63	-11.90	-9.41	-10.98	-11.51	-10.44
	2	-10.43	-10.74	-10.95	-12.10	-10.25	-11.22	-11.20	-9.09	-10.18	-11.48	-10.16
	3	-10.23	-10.44	-10.41	-11.72	-10.11	-10.90	-11.07	-9.06	-10.14	-10.94	-10.11

	Number of conformations in cluster											
	1	7	1	2	4	1	5	3	4	3	1	9
	2	7	5	2	2	1	1	2	1	3	2	1
	3	2	10	1	4	5	3	2	7	2	1	8
SCH23390	Lowest binding energy [kcal/mol]											
	1	-9.60	-9.06	-10.05	-9.93	-9.91	-9.49	-8.83	-8.50	-9.98	-9.87	-10.17
	2	-9.36	-8.89	-9.31	-9.81	-9.89	-9.39	-8.75	-8.34	-8.89	-9.74	-9.86
	3	-8.81	-8.50	-8.80	-9.07	-9.76	-9.28	-8.58	-8.17	-8.77	-9.39	-9.73
	Number of conformations in cluster											
	1	10	10	1	24	1	10	16	53	4	4	8
	2	4	4	17	3	12	12	11	5	5	2	18
	3	4	2	3	6	31	2	19	1	10	6	1
SKF38393	Lowest binding energy [kcal/mol]											
	1	-11.35	-11.98	-10.73	-12.33	-12.41	-10.38	-10.35	-9.36	-11.13	-11.02	-10.81
	2	-10.04	-10.48	-10.07	-11.26	-10.12	-9.74	-10.18	-8.89	-9.99	-10.34	-10.79
	3	-9.85	-10.29	-10.06	-9.92	-9.90	-9.62	-9.75	-8.63	-9.96	-10.04	-10.00
	Number of conformations in cluster											
	1	15	14	16	5	55	45	25	29	23	19	8
	2	25	24	14	6	1	4	6	2	11	6	2
	3	1	17	6	4	7	1	27	42	9	4	2
Eticlopride	Lowest binding energy [kcal/mol]											
	1	-9.33	-9.52	-9.37	-9.87	-10.44	-10.08	-9.19	-8.67	-10.61	-9.88	-9.36
	2	-9.22	-9.31	-9.22	-9.62	-9.95	-9.93	-9.04	-8.66	-9.61	-9.01	-9.20
	3	-9.10	-9.30	-9.02	-9.54	-9.53	-8.89	-9.00	-8.04	-8.59	-8.82	-8.88
	Number of conformations in cluster											
	1	12	15	10	18	6	1	6	2	12	4	1
	2	6	9	5	1	10	22	3	10	5	4	9
	3	2	2	1	4	11	11	6	23	3	6	15
Risperidone	Lowest binding energy [kcal/mol]											
	1	-10.94	-11.24	-11.72	-14.83	-11.91	-11.78	-11.83	-10.98	-11.10	-10.54	-12.61
	2	-10.66	-10.59	-10.69	-12.46	-11.74	-10.83	-11.07	-10.73	-10.65	-10.39	-11.20

	3	-10.63	-9.80	-10.59	-11.56	-11.71	-10.66	-10.52	-10.63	-10.16	-10.03	-10.86
	Number of conformations in cluster											
	1	9	9	18	8	6	14	11	14	10	1	3
	2	2	38	4	17	1	7	2	6	7	2	6
	3	11	10	11	13	8	2	8	2	2	2	2
Aripiprazole	Lowest binding energy [kcal/mol]											
	1	-10.77	-11.08	-10.87	-10.87	-11.17	-10.54	-10.27	-9.34	-9.96	-10.95	-10.74
	2	-10.60	-10.51	-9.85	-10.76	-10.70	-10.10	-10.13	-8.29	-9.50	-9.31	-10.05
	3	-10.30	-10.50	-9.48	-10.59	-10.66	-9.68	-9.65	-8.12	-9.25	-9.01	-9.52
	Number of conformations in cluster											
	1	12	7	1	5	4	24	2	1	5	3	3
	2	3	8	3	2	2	3	3	6	3	2	18
	3	3	2	1	6	3	3	3	1	1	2	2
Haloperidole	Lowest binding energy [kcal/mol]											
	1	-10.66	-10.84	-10.84	-12.69	-11.13	-12.52	-12.06	-10.62	-10.23	-11.73	-12.02
	2	-10.41	-10.03	-10.06	-12.09	-11.10	-11.23	-11.21	-10.19	-10.23	-11.45	-11.69
	3	-10.39	-9.98	-9.95	-11.82	-10.53	-10.75	-11.08	-10.12	-10.18	-11.32	-10.52
	Number of conformations in cluster											
	1	6	20	7	5	7	14	7	8	7	8	11
	2	3	1	7	6	3	6	1	3	1	4	6
	3	8	1	2	11	6	3	4	2	2	2	2
Spiperone	Lowest binding energy [kcal/mol]											
	1	-10.39	-11.13	-10.43	-11.75	-10.41	-10.56	-10.61	-8.66	-10.86	-10.09	-10.86
	2	-10.17	-10.30	-10.17	-10.95	-10.37	-10.54	-10.41	-8.45	-9.61	-10.01	-10.06
	3	-10.02	-9.85	-10.00	-10.37	-10.22	-10.25	-9.80	-8.35	-9.55	-9.81	-9.83
	Number of conformations in cluster											
	1	23	1	3	4	4	2	11	1	4	3	8
	2	7	2	5	6	1	22	4	9	12	4	5
	3	7	1	5	6	1	1	4	6	2	3	1
Chlorpromazine	Lowest binding energy [kcal/mol]											
	1	-8.01	-8.13	-8.28	-8.91	-8.93	-9.00	-9.34	-8.91	-8.28	-8.44	-8.39

	2	-7.91	-7.96	-8.03	-8.88	-8.40	-8.97	-8.42	-8.14	-8.19	-8.35	-8.38
	3	-7.76	-7.93	-7.97	-8.77	-8.39	-8.87	-8.01	-7.86	-8.08	-8.17	-8.32
						Number of conformations in cluster						
	1	2	16	9	6	13	20	2	1	1	1	8
	2	24	16	2	7	2	25	1	3	14	1	8
	3	3	1	11	24	8	2	2	1	2	2	9

Table S6 - Docking results for the D_3R. The lowest binding energy ΔG_{bind} [kcal/mol] of every run was measured using AutoDock4.2. Calculated conformations were clustered and ranked by energy level. A populated cluster indicates, that the position docked into the receptor is more likely to depict the conformational binding position of the ligand. The three best clusters were chosen and analyzed.

Receptor state of the MD simulation [ns]	**Top**	**0**	**55**	**60**	**65**	**70**	**75**	**80**	**85**	**90**	**95**	**100**
Dopamine						Lowest binding energy [kcal/mol]						
	1	-9.76	-9.63	-8.92	-9.34	-8.97	-8.75	-9.88	-9.87	-9.77	-9.51	-8.86
	2	-9.55	-9.48	-8.67	-8.79	-8.95	-8.72	-9.59	-8.81	-9.00	-8.79	-8.72
	3	-8.64	-8.64	-8.49	-8.34	-8.27	-8.18	-8.82	-8.26	-8.18	-7.96	-8.07
						Number of conformations in cluster						
	1	17	42	14	34	23	35	69	56	40	43	8
	2	47	17	22	11	27	12	5	6	7	11	29
	3	18	16	2	15	10	11	12	6	12	6	12
7-OH-DPAT						Lowest binding energy [kcal/mol]						
	1	-9.11	-8.35	-8.43	-9.43	-8.37	-9.47	-9.75	-8.20	-8.36	-9.38	-8.57
	2	-8.89	-7.99	-7.56	-7.67	-7.70	-8.53	-8.93	-8.02	-8.07	-8.91	-8.21
	3	-8.52	-7.60	-7.53	-7.61	-7.54	-8.29	-7.92	-7.55	-7.87	-7.83	-7.85
						Number of conformations in cluster						
	1	5	46	35	29	39	20	28	35	41	13	8
	2	51	4	34	3	12	7	20	12	5	3	9
	3	1	12	1	5	4	5	3	1	3	4	8
Apomorphine						Lowest binding energy [kcal/mol]						
	1	-9.89	-10.19	-9.40	-10.18	-9.28	-9.51	-10.52	-9.91	-10.11	-9.40	-9.87

	2	-9.81	-9.46	-9.02	-9.34	-8.93	-9.33	-9.64	-9.46	-9.68	-9.17	-9.28
	3	-9.81	-8.51	-8.45	-8.75	-8.75	-8.97	-9.42	-9.26	-9.18	-9.12	-9.13
		Number of conformations in cluster										
	1	36	2	28	22	18	1	3	9	27	10	23
	2	22	38	25	33	22	11	31	22	13	31	19
	3	14	21	10	2	2	15	16	3	23	24	2
Bromocriptine		Lowest binding energy [kcal/mol]										
	1	-2.28	+29.67	+33.62	+10.12	+23.21	+10.12	+19.76	+1.48	+11.26	+42.39	+4.31
	2	+13.56	+81.44	+34.66	+11.36	+24.67	+10.32	+34.46	+10.88	+20.50	+61.90	+23.94
	3	+16.35	+100.91	+36.66	+22.89	+28.29	+15.51	+52.78	+26.06	+23.50	+80.64	+43.10
		Number of conformations in cluster										
	1	73	5	3	18	2	13	2	27	17	19	34
	2	4	8	4	12	5	22	2	27	6	9	2
	3	1	1	2	7	11	3	27	1	7	20	3
Clozapine		Lowest binding energy [kcal/mol]										
	1	-8.48	-7.16	-8.72	-8.12	-8.36	-8.16	-9.15	-8.33	-8.49	-8.37	-8.51
	2	-8.43	-7.12	-7.23	-7.27	-7.47	-7.69	-7.90	-7.29	-8.08	-8.37	-8.46
	3	-8.20	-6.95	-7.22	-7.26	-7.38	-7.65	-7.85	-7.24	-7.85	-8.19	-7.90
		Number of conformations in cluster										
	1	13	6	17	14	25	9	40	25	2	49	21
	2	7	38	11	24	14	1	12	31	6	17	7
	3	8	49	8	32	12	7	7	4	36	17	3
Nemonapride		Lowest binding energy [kcal/mol]										
	1	-10.97	-10.63	-9.12	-10.00	-9.91	-9.85	-10.17	-9.89	-9.94	-10.09	-10.01
	2	-10.86	-10.23	-8.92	-9.85	-9.48	-9.53	-9.82	-9.66	-9.59	-10.00	-9.71
	3	-10.26	-9.96	-8.68	-9.40	-9.12	-9.45	-9.71	-9.59	-9.32	-9.90	-9.55
		Number of conformations in cluster										
	1	2	4	1	1	12	1	2	8	5	1	5
	2	3	1	4	3	3	5	2	6	2	19	2
	3	1	2	2	2	1	2	2	1	4	3	6
Sulpiride		Lowest binding energy [kcal/mol]										

	1	-10.55	-9.69	-9.77	-8.93	-9.30	-9.94	-10.24	-10.01	-9.73	-9.99	-10.55
	2	-10.25	-8.90	-9.41	-8.91	-8.86	-9.84	-9.63	-9.78	-8.85	-9.46	-9.81
	3	-9.59	-8.89	-8.44	-8.85	-8.70	-9.68	-9.34	-9.71	-8.55	-9.17	-9.79
	Number of conformations in cluster											
	1	12	1	1	2	3	2	4	2	4	1	3
	2	6	7	1	1	3	2	4	2	2	19	1
	3	7	1	4	2	3	3	3	2	1	7	12
SCH23390	Lowest binding energy [kcal/mol]											
	1	-10.59	-9.38	-8.64	-9.96	-10.13	-9.76	-10.34	-9.59	-10.39	-10.71	-9.72
	2	-9.69	-9.07	-8.33	-9.65	-9.72	-9.19	-9.64	-9.16	-9.81	-10.00	-9.68
	3	-9.56	-8.70	-8.21	-8.98	-9.47	-9.03	-9.44	-8.64	-8.71	-9.71	-9.41
	Number of conformations in cluster											
	1	11	30	10	3	31	1	11	5	9	28	2
	2	2	12	1	9	5	8	30	20	30	9	23
	3	6	10	28	30	2	5	19	39	36	2	2
SKF38393	Lowest binding energy [kcal/mol]											
	1	-11.68	-10.68	-9.36	-11.04	-11.53	-10.47	-11.15	-10.41	-10.85	-10.69	-10.08
	2	-11.34	-10.28	-9.33	-10.88	-10.24	-10.30	-10.69	-10.35	-10.69	-10.24	-9.74
	3	-11.08	-10.23	-9.25	-10.83	-10.15	-9.66	-9.95	-9.87	-10.07	-9.78	-9.63
	Number of conformations in cluster											
	1	1	20	30	21	12	23	16	58	31	9	26
	2	36	9	6	5	8	22	56	5	20	1	2
	3	2	32	4	23	8	1	2	2	8	7	2
Eticlopride	Lowest binding energy [kcal/mol]											
	1	-9.98	-8.71	-7.99	-9.04	-9.45	-9.36	-9.58	-9.19	-9.41	-9.85	-9.23
	2	-9.34	-8.69	-7.95	-8.90	-9.02	-8.81	-9.10	-8.99	-9.37	-9.47	-9.17
	3	-9.07	-8.64	-7.88	-8.80	-8.76	-8.79	-8.83	-8.92	-9.20	-9.43	-9.03
	Number of conformations in cluster											
	1	14	31	7	9	7	5	1	9	2	7	6
	2	2	5	2	12	8	5	10	12	15	27	5
	3	13	2	2	12	2	17	2	9	8	17	3

Risperidone	Lowest binding energy [kcal/mol]										
	1	-8.87	-8.09	-7.91	-8.88	-8.67	-9.59	-9.44	-9.46	-9.51	-9.11	-9.72
	2	-8.23	-7.76	-7.77	-8.71	-7.89	-9.43	-9.14	-9.06	-9.48	-9.05	-9.47
	3	-8.17	-7.73	-7.73	-8.61	-7.87	-9.07	-9.09	-8.93	-9.37	-9.03	-8.86
	Number of conformations in cluster											
	1	16	1	6	2	12	7	2	15	12	7	5
	2	5	23	3	1	4	12	4	1	1	5	4
	3	2	2	3	4	1	4	9	15	7	10	11
Aripiprazole	Lowest binding energy [kcal/mol]											
	1	-10.40	-8.59	-8.89	-8.97	-9.79	-10.13	-10.37	-9.24	-9.74	-10.34	-10.44
	2	-10.27	-8.24	-8.66	-8.96	-9.25	-9.33	-10.30	-8.95	-9.45	-10.22	-9.61
	3	-9.99	-8.23	-8.45	-8.86	-8.97	-9.10	-10.19	-8.94	-9.27	-10.16	-9.59
	Number of conformations in cluster											
	1	3	3	1	1	3	2	5	12	5	4	8
	2	4	3	1	1	1	1	3	3	1	12	2
	3	2	2	1	1	2	2	5	3	1	4	3
Haloperidole	Lowest binding energy [kcal/mol]											
	1	-11.07	-11.00	-10.36	-10.89	-9.68	-10.26	-11.88	-10.84	-10.31	-10.67	-10.43
	2	-10.63	-10.79	-9.44	-9.45	-9.50	-10.21	-11.20	-10.35	-10.28	-10.50	-10.30
	3	-10.24	-10.01	-9.21	-9.42	-9.30	-10.18	-10.57	-10.34	-10.23	-10.38	-10.12
	Number of conformations in cluster											
	1	3	1	1	1	1	2	1	1	3	2	18
	2	2	1	1	3	5	3	5	5	3	6	1
	3	2	1	3	2	5	3	1	1	1	5	5
Spiperone	Lowest binding energy [kcal/mol]											
	1	-9.29	-9.25	-8.75	-8.88	-9.38	-9.50	-9.50	-8.75	-9.12	-9.38	-9.50
	2	-8.67	-9.00	-7.88	-8.75	-9.00	-8.75	-9.38	-8.62	-9.00	-9.38	-9.25
	3	-8.58	-8.75	-7.88	-8.50	-8.88	-8.62	-9.38	-8.62	-8.75	-9.12	-9.12
	Number of conformations in cluster											
	1	4	2	3	3	1	1	5	2	1	15	2
	2	3	3	1	1	1	2	1	2	3	1	9

	3	2	2	3	1	1	1	7	4	1	14	1
Chlorpromazine	Lowest binding energy [kcal/mol]											
	1	-8.29	-7.88	-8.03	-7.79	-7.89	-8.91	-8.63	-7.61	-8.06	-8.56	-8.74
	2	-8.28	-7.81	-7.69	-7.71	-7.64	-8.33	-8.38	-7.30	-7.60	-8.17	-7.95
	3	-8.27	-7.81	-7.51	-7.63	-7.49	-8.06	-7.98	-7.13	-7.56	-8.16	-7.81
	Number of conformations in cluster											
	1	26	2	1	5	1	1	5	5	7	23	2
	2	10	11	14	30	7	2	18	5	7	9	5
	3	14	1	1	24	2	21	4	3	18	3	10

Table S7 - Docking results for the D_4R. The lowest binding energy ΔG_{bind} [kcal/mol] of every run was measured using AutoDock4.2. Calculated conformations were clustered and ranked by energy level. A populated cluster indicates, that the position docked into the receptor is more likely to depict the conformational binding position of the ligand. The three best clusters were chosen and analyzed. NA – Not Available, cases were the number of clusters was lower than 3.

Receptor state of the MD simulation [ns]	**Top**	**0**	**55**	**60**	**65**	**70**	**75**	**80**	**85**	**90**	**95**	**100**
Dopamine	Lowest binding energy [kcal/mol]											
	1	-10.04	-9.84	-9.60	-9.99	-10.09	-9.78	-9.41	-8.53	-7.52	-9.87	-9.29
	2	-9.54	-8,68	-8.96	-9.60	-9.45	-8.16	-9.23	-7.81	-7.45	-7.41	-9.11
	3	-9.40	-7.75	-8.68	-8.36	-8.80	-7.71	-9.06	-6.95	-7.16	-6.99	-7.79
	Number of conformations in cluster											
	1	69	62	60	39	62	68	41	39	30	86	13
	2	15	28	19	21	10	6	17	13	30	5	55
	3	8	1	3	8	9	4	7	2	8	2	8
7-OH-DPAT	Lowest binding energy [kcal/mol]											
	1	-9.52	-7.75	-8.28	-8.32	-8.74	-9.25	-8.98	-7.46	-7.56	-9.62	-8.83
	2	-8.44	-7.68	-7.97	-7.82	-8.25	-8.70	-8.45	-7.05	-7.60	-9.41	-8.17
	3	-7.8	-7.52	-7.71	-7.71	-8.17	-8.46	-7.54	-6.53	-7.50	-7.38	-8.04
	Number of conformations in cluster											
	1	30	11	13	5	13	14	6	42	11	15	23

	2	19	20	3	1	10	10	13	9	48	3	1
	3	17	20	1	27	1	7	26	4	16	55	2
Apomorphine	Lowest binding energy [kcal/mol]											
	1	-9.24	-10.33	-9.48	-10.11	-10.19	-9.92	-10.08	-8.41	-9.26	-9.91	-10.10
	2	-9.05	-9.69	-9.09	-9.59	-9.50	-9.83	-9.72	-8.09	-8.98	-9.86	-10.01
	3	-8.94	-9.51	-8.25	-9.27	-9.32	-8.77	-9.56	7-82	-8.72	-7.77	-9.30
	Number of conformations in cluster											
	1	34	44	13	27	28	2	2	12	7	8	10
	2	16	19	39	7	40	51	5	1	21	7	19
	3	9	31	1	42	10	35	13	41	4	51	2
Bromocriptine	Lowest binding energy [kcal/mol]											
	1	+103.73	+34.39	+43.40	+138.76	+154.29	+65.12	+35.85	+87.57	+133.51	+238.63	+57.61
	2	+142.07	+39.22	+73.40	+139.02	+162.10	+127.27	+79.19	+129.02	+156.83	+240.75	+69.87
	3	+198.99	+49.74	+88.72	+169.12	+176.68	+141.46	+95.36	+161.26	+158.24	+250.54	+113.81
	Number of conformations in cluster											
	1	12	38	45	57	4	36	22	26	23	5	58
	2	18	32	15	10	51	1	2	1	18	11	10
	3	3	3	21	8	2	6	9	54	8	8	4
Clozapine	Lowest binding energy [kcal/mol]											
	1	-7.73	-7.05	-7.12	-7.95	-7.64	-6.04	-8.96	-4.70	-5.20	-1.03	-6.09
	2	-7.44	-7.05	-7.06	-7.17	-6.25	-4.27	-6.58	-2.40	-3.52	-0.72	-3.17
	3	-6.75	-6.96	-6.47	-6.76	-6.04	-1.84	-4.58	-0.68	-3.46	+1.59	-2.93
	Number of conformations in cluster											
	1	59	50	8	11	38	49	65	27	15	8	58
	2	2	6	13	22	2	27	13	40	14	44	1
	3	13	17	21	45	31	7	7	3	5	4	4
Nemonapride	Lowest binding energy [kcal/mol]											
	1	-10.46	-9.12	-10.45	-10.09	-10.68	-10.89	-9.92	-9.84	-10.48	-9.59	-10.62
	2	-9.85	-9.07	-9.31	-9.98	-9.50	-10.41	-9.12	-8.77	-10.15	-9.53	-10.26
	3	-9.50	-9.07	-9.08	-9.55	-9.45	-10.29	-8,.93	-7.71	-9.53	-8.34	-9.86
	Number of conformations in cluster											

	1	10	15	1	1	5	20	23	12	25	19	7
	2	3	14	7	1	1	17	15	16	25	16	8
	3	15	12	3	3	4	1	7	6	18	12	1
Sulpiride	Lowest binding energy [kcal/mol]											
	1	-10.62	-10.20	-11.12	-10.65	-12.10	-11.36	-9.20	-8.98	-10.71	-10.53	-12.14
	2	-10.43	-9.83	-10.71	-10.23	-11.06	-11.08	-8.39	-8.63	-10.49	-10.48	-11.29
	3	-9.59	-9.52	-10.25	-10.08	-11.06	-10.91	-8.35	-8.33	-10.28	-9.97	-10.26
	Number of conformations in cluster											
	1	14	4	6	6	1	7	2	2	2	6	1
	2	1	5	5	8	4	4	7	5	2	6	4
	3	2	7	1	1	2	4	10	1	6	5	3
SCH23390	Lowest binding energy [kcal/mol]											
	1	-9.69	-7.15	-9.50	-9.45	-9.71	-10.84	-8.93	-9.93	-8.92	-8.52	-9.60
	2	-9.38	-6.89	-9.37	-9.43	-8.85	-9.47	-8.50	-8.98	-8.75	-8.25	-8.81
	3	-9.22	-6.74	-9.04	-9.02	-8.42	-9.20	-8.50	-8.41	-8.50	-8.23	-8.64
	Number of conformations in cluster											
	1	45	20	11	11	27	28	6	27	71	33	7
	2	17	4	4	6	46	2	9	10	2	22	2
	3	26	5	14	18	8	3	12	5	22	11	18
SKF38393	Lowest binding energy [kcal/mol]											
	1	-10.94	-9.93	-11.02	-10.82	-11.87	-10.18	-10.17	-9.16	-10.16	-9.62	-10.67
	2	-10.19	-9.70	-9.87	-10.72	-9.90	-9.63	-10.10	-8.99	-9.66	-9.01	-10.58
	3	-9.48	-9.60	-9.76	-10.36	-9.17	-9.38	-9.35	-8.60	-8.94	-8.68	-10.28
	Number of conformations in cluster											
	1	14	29	4	42	19	13	5	45	1	31	3
	2	9	14	21	3	17	17	3	16	30	30	12
	3	3	1	7	9	2	3	7	8	3	4	2
Eticlopride	Lowest binding energy [kcal/mol]											
	1	-9.60	-7.73	-8.55	-9.53	-10.50	-9.78	-9.57	-9.10	-9.58	-8.34	-9.02
	2	-9.38	-7.70	-8.48	-9.23	-9.73	-9.53	-7.77	-7.24	-9.48	-8.09	-8.71
	3	-8.64	-7.68	-8.36	-9.20	-9.42	-9.44	-7.49	-6.86	-8.90	-8.08	-8.63

	Number of conformations in cluster										
	1	20	9	11	2	3	32	46	24	6	10	7
	2	8	8	9	11	1	6	5	13	23	2	2
	3	13	1	4	9	7	10	4	6	29	28	4
Risperidone	Lowest binding energy [kcal/mol]										
	1	-8.30	-9.60	-9.16	-7.80	-8.25	-4.64	-6.17	-1.21	-5.83	-4.65	-7.74
	2	-8.27	-9.45	-9.04	-6.79	-8.04	-2.42	-6.13	+0.50	-5.57	-4.63	-7.20
	3	-7.08	-8.23	-8.93	-5.45	-7.86	-2.31	-3.76	+0.51	-5.42	-2.60	-6.97
	Number of conformations in cluster										
	1	12	37	1	28	10	14	9	12	20	14	2
	2	18	1	6	14	14	3	17	5	12	6	6
	3	11	2	6	3	2	1	17	10	2	8	10
Aripiprazole	Lowest binding energy [kcal/mol]										
	1	-8.92	-11.08	-8.05	-11.43	-12.23	-7.46	-4.70	-1.97	-7.60	-8.30	-9.26
	2	-8.86	-9.85	-7.53	-10.35	-9.26	-4.85	-4.05	-1.45	-7.05	-7.83	-8.92
	3	-8.10	-9.44	-7.28	-10.34	-9.08	-4.65	-3.83	-0.97	-6.73	-6.55	-7.75
	Number of conformations in cluster										
	1	2	6	2	6	12	10	7	14	9	6	2
	2	11	1	9	33	2	2	2	4	3	5	20
	3	6	3	2	3	4	3	4	5	2	11	8
Haloperidole	Lowest binding energy [kcal/mol]										
	1	-9.41	-0.40	-10.32	-9.16	-10.42	-6.29	-1.94	+5.37	-0.35	-4.67	-9.18
	2	-8.26	+0.88	-9.66	-8.32	-9.36	-6.08	-1.34	+5.41	+0.12	-1.78	-8.73
	3	NA	+2.57	-9.36	-8.08	-8.98	-5.94	-0.80	+6.89	+0.56	-1.14	-8.55
	Number of conformations in cluster										
	1	33	69	2	58	58	6	30	29	9	35	21
	2	67	13	7	16	13	18	25	1	20	20	7
	3	NA	6	60	15	21	13	2	6	6	2	28
Spiperone	Lowest binding energy [kcal/mol]										

	1	-9.02	-9.64	-10.16	-10.23	-9.16	-9.99	-8.91	-7.42	-10.27	-9.93	-11.67
	2	-8.79	-9.02	-9.36	-9.72	-9.05	-8.42	-8.29	-6.50	-10.17	-9.05	-11.37
	3	-8.45	-9.01	-9.11	-9.40	-8.59	-7.20	-8.05	-6.26	-9,85	-8.49	-11.14
		Number of conformations in cluster										
	1	1	9	24	17	5	4	6	5	19	14	10
	2	16	10	1	16	2	16	12	9	35	3	20
	3	1	15	12	3	26	11	9	6	4	9	18
Chlorpromazine		Lowest binding energy [kcal/mol]										
	1	-8.55	-7.88	-8.24	-8.60	-9.09	-8.91	-8.08	-8.20	-8.44	-8.24	-9.16
	2	-8.42	-7.82	-8.09	-8.40	-9.00	-8.66	-8.00	-7.78	-8.35	-7.80	-8.64
	3	-7.80	-7.75	-8.02	-8.36	-8.84	-8.42	-7.53	-7.56	-8.35	-7.26	-8.30
		Number of conformations in cluster										
	1	5	24	8	11	10	6	3	1	3	30	1
	2	12	14	22	36	12	8	35	25	11	6	5
	3	16	3	22	7	10	7	14	11	5	9	6

Table S8 - Docking results for the D_5R. The lowest binding energy ΔG_{bind} [kcal/mol] of every run was measured using AutoDock4.2. Calculated conformations were clustered and ranked by energy level. A populated cluster indicates, that the position docked into the receptor is more likely to depict the conformational binding position of the ligand. The three best clusters were chosen and analyzed.

Receptor state of the MD simulation [ns]	**Top**	**0**	**55**	**60**	**65**	**70**	**75**	**80**	**85**	**90**	**95**	**100**
		Lowest binding energy [kcal/mol]										
	1	-10.86	-10.36	-9.72	-9.53	-10.86	-10.45	-10.38	-10.59	-10.55	-10.14	-10.16
	2	-9.67	-9.59	-9.20	-9.29	-10.28	-9.14	-8.68	-9.47	-8.54	-10.09	-9.77
	3	-8.26	-8.02	-8.42	-7.86	-9.66	-7.22	-7.93	-8.27	-8.21	-9.84	-7.83
Dopamine		Number of conformations in cluster										
	1	29	37	30	32	45	30	45	58	38	23	32
	2	37	12	30	10	14	17	9	10	10	29	24
	3	7	9	9	7	20	15	2	6	8	12	1

7-OH-DPAT	Lowest binding energy [kcal/mol]										
	1	-8.85	-8.33	-9.32	-9.10	-9.34	-9.77	-9.44	-10.09	-9.46	-9.93	-8.79
	2	-8.66	-7.83	-8.68	-8.84	-9.05	-8.80	-7.89	-8.46	-7.88	-8.14	-8.42
	3	-8.50	-7.55	-8.57	-8.35	-8.21	-8.30	-6.98	-8.26	-7.63	-8.12	-6.77
	Number of conformations in cluster											
	1	28	36	27	25	14	18	26	24	38	36	2
	2	4	19	2	18	32	6	15	14	9	9	3
	3	1	4	12	15	8	18	10	1	4	4	1
Apomorphine	Lowest binding energy [kcal/mol]											
	1	-10.92	-10.35	-10.11	-10.99	-10.30	-10.61	-10.39	-11.41	-10.73	-10.41	-10.06
	2	-10.37	-10.31	-9.26	-10.52	-9.12	-9.14	-8.73	-10.27	-10.69	-9.53	-9.01
	3	-9.14	-8.32	-8.78	-10,15	-9.02	-10.48	-8.69	-8.89	-9.07	-8.96	-8.91
	Number of conformations in cluster											
	1	47	31	50	24	65	34	38	45	34	39	49
	2	18	9	17	4	2	8	3	11	19	7	3
	3	14	2	3	7	12	20	24	17	9	40	37
Bromocriptine	Lowest binding energy [kcal/mol]											
	1	-5.09	-9.65	-7.33	-9.33	-7.25	-2.14	-8.74	-9.59	-9.15	-12.23	-5.89
	2	-4.79	-7.87	-7.05	-1.84	+0.25	+2.71	-7.79	-4.62	-5.91	-10.85	-0.24
	3	-3.19	-7.20	-5.01	+2.31	+4.64	+5.97	-6.76	-3.99	+2.43	-10.62	+5.64
	Number of conformations in cluster											
	1	22	16	33	11	9	3	2	15	17	17	24
	2	7	1	25	1	1	23	5	4	6	12	8
	3	3	8	6	3	11	6	20	5	10	1	11
Clozapine	Lowest binding energy [kcal/mol]											
	1	-8.11	-7.80	-8.78	-8.88	-8.52	-8.33	-7.68	-8.73	-8.02	-8.53	-8.24
	2	-7.79	-7.68	-7.93	-8.45	-8.06	-8.07	-7.53	-7.94	-7.46	-8.19	-8.09
	3	-7.58	-7.57	-7.70	-8.31	-7.95	-7.49	-7.36	-7.88	-7.11	-7.47	-7.53
	Number of conformations in cluster											
	1	30	2	45	8	53	62	51	58	45	15	25

	2	15	15	4	16	15	3	8	8	11	15	40
	3	13	12	9	32	17	2	1	2	6	17	5
Nemonapride	Lowest binding energy [kcal/mol]											
	1	-9.84	-10.45	-10.98	-11.11	-10.78	-10.68	-10.86	-10.97	-10.09	-10.58	-4.42
	2	-9.70	-10.41	-10.39	-10.71	-10.74	-10.48	-10.58	-10.06	-9.79	-10.06	-4.08
	3	-9.66	-8.93	-10.28	-10.43	-9.87	-9.92	-9.61	-10.03	-9.70	-9.52	-4.07
	Number of conformations in cluster											
	1	15	5	13	12	11	5	5	17	15	11	1
	2	9	2	6	9	10	5	20	7	14	2	1
	3	2	1	7	4	5	7	6	14	13	8	1
Sulpiride	Lowest binding energy [kcal/mol]											
	1	-10.25	-11.82	-10.13	-11.08	-10.68	-10.42	-19.97	-11.73	-11.40	-12.53	-11.56
	2	-10.10	-9.31	-9.74	-10.99	-10.03	-10.33	-10.53	-11.62	-10.39	-11.56	-10.62
	3	-10.08	-9.10	-9.48	-10.51	-10.01	-10.32	-10.47	-11.47	-9.56	-11.46	-10.11
	Number of conformations in cluster											
	1	5	3	1	2	2	6	4	5	7	2	6
	2	3	2	2	2	5	3	3	4	6	6	4
	3	2	1	1	2	3	3	3	3	1	5	3
SCH23390	Lowest binding energy [kcal/mol]											
	1	-10.05	-9.95	-9.75	-10.53	-10.62	-9.97	-9.32	-9.02	-8.11	-9.88	-10.16
	2	-10.00	-9.44	-9.70	-9.13	-9.25	-9.68	-8.31	-8.94	-8.08	-9.67	-10.00
	3	-9.31	-9.12	-9.53	-8.96	-8.89	-9.53	-8.04	-8.55	-8.01	-9.16	-8.79
	Number of conformations in cluster											
	1	3	32	13	16	9	4	9	2	1	4	3
	2	8	9	6	2	2	5	1	3	4	22	9
	3	2	4	7	10	2	2	3	12	13	5	16
SKF38393	Lowest binding energy [kcal/mol]											
	1	-11.18	-12.56	-11.58	-12.16	-12.88	-11.10	-11.81	-13.61	-10.12	-12.19	–.01
	2	-9.80	-10.78	-10.70	-11.53	-11.25	-10.74	-9.98	-11.02	-9.04	-10.29	-10.55
	3	-9.75	-10.48	-10.54	-11.30	-10.90	-9.00	-9.51	-9.89	-9.03	-10.11	-9.68
	Number of conformations in cluster											

	1	5	30	9	10	6	27	11	14	2	24	6
	2	18	13	12	14	14	13	5	6	3	3	20
	3	9	3	9	14	26	1	2	6	12	1	2
Eticlopride	Lowest binding energy [kcal/mol]											
	1	-8.86	-10.12	-10.59	-10.00	-9.34	-9.39	-8.89	-9.87	-10.29	-9.86	-8.89
	2	-8.80	-8.55	-9.99	-9.78	-9.17	-9.34	-8.62	-8.70	-9.79	-9.82	-8.82
	3	-8.77	-8.10	-9.71	-9.64	-8.89	-9.27	-8.48	-8.53	-9.20	-8.56	-8.51
	Number of conformations in cluster											
	1	6	2	5	5	6	3	2	9	4	5	28
	2	2	10	7	4	3	7	9	2	9	5	2
	3	12	3	18	17	10	2	14	4	10	12	6
Risperidone	Lowest binding energy [kcal/mol]											
	1	-9.98	-9.76	-12.22	-11.40	-9.02	-9.77	-8.85	-10.46	-8.50	-10.74	-10.96
	2	-8.97	-8.63	-11.92	-10.55	-8.94	-9.49	-8.84	-9.72	-8.15	-10.71	-10.70
	3	-8.91	-8.34	-10.94	-10.29	-8.79	-8.52	-8.80	-8.59	-7.54	-10.39	-10.50
	Number of conformations in cluster											
	1	2	5	7	2	4	3	4	5	2	5	17
	2	9	6	11	13	14	1	8	1	30	3	8
	3	2	2	10	17	1	13	3	9	15	6	10
Aripiprazole	Lowest binding energy [kcal/mol]											
	1	-10.87	-10.91	-10.59	-11.52	-12.00	-10.81	-11.04	-10.15	-10.95	-11.08	-10.55
	2	-10.78	-9.84	-9.74	-10.08	-9.97	-9.14	-10.08	-10.07	-9.73	-9.84	-10.39
	3	-10.20	-9.64	-9.67	-9.71	-9.68	-8.93	-9.97	-9.45	-9.44	-9.64	-9.90
	Number of conformations in cluster											
	1	9	2	2	7	2	3	4	3	10	5	1
	2	2	2	6	11	3	2	1	3	3	6	3
	3	10	3	1	5	2	5	8	3	3	6	7
Haloperidole	Lowest binding energy [kcal/mol]											
	1	-9.88	-10.35	-10.36	-10.26	-9.98	-10.38	-9.94	-10.92	-10.28	-10.36	-10.13
	2	-9.54	-9.40	-9.94	-10.23	-9.96	-10.04	-9.67	-10.71	-9.57	-9.92	-10.12
	3	-9.54	-9.31	-9.91	-9.83	-9.80	-9.90	-9.62	-10.32	-9.53	-9.87	-10.05

	Number of conformations in cluster											
	1	8	2	1	9	1	17	2	3	14	3	11
	2	4	4	3	7	5	1	8	9	15	9	16
	3	10	2	2	15	1	5	5	1	3	3	3
Spiperone	Lowest binding energy [kcal/mol]											
	1	-10.57	-10.14	-10.45	-10.17	-10.29	-10.45	-9.39	-10.60	-9.53	-11.51	-10.54
	2	-9.80	-9.87	-10.20	-9.55	-10.21	-10.12	-10.53	-10.38	-9.42	-10.73	-10.51
	3	-9.38	-9.25	-9.88	-9.53	-9.94	-10.11	-10.47	-10.14	-9.42	-10.58	-10.20
	Number of conformations in cluster											
	1	21	1	4	5	2	3	4	1	13	2	1
	2	9	4	2	4	2	20	9	7	2	1	2
	3	5	1	3	4	3	5	9	2	2	9	1
Chlorpromazine	Lowest binding energy [kcal/mol]											
	1	-8.06	-7.69	-8.22	-8.77	-7.98	-8.60	-7.46	-8.16	-7.60	-8.02	-8.11
	2	-7.78	-7.65	-7.96	-8.60	-7.90	-8.51	-7.12	-8.08	-7.28	-7.74	-7.89
	3	-7.56	-7.45	7.94	-7.87	-7.64	-7.99	-7.10	-7.99	-7.28	-7.69	-7.88
	Number of conformations in cluster											
	1	20	25	7	15	8	12	7	13	6	13	17
	2	22	23	8	17	16	23	13	13	2	10	4
	3	3	10	8	3	14	6	14	4	20	15	14

Table S9 - Docking results for the crystal structure templates of D_2R (PDBid: 6CM4), D_3R (PDBid: 3PBL) and D_4R (PDBid: 5WIU) docked with their co-crystalized ligands. The lowest binding energy ΔG_{bind} [kcal/mol] of every run was measured using AutoDock4.2. Calculated conformations were clustered and ranked by energy level. A populated cluster indicates, that the position docked into the receptor is more likely to depict the conformational binding position of the ligand. The three best clusters were chosen and analyzed. As proof of concept the outcome was compared to the corresponding DR-models docked to risperidone, eticlopride and nemonapride at time point 0 ns using the ligand-coordinates used for all dockings.

Crystal structure template		**D_2R (6CM4)**		**D_3R (3PBL)**		**D_4R (5WIU)**	
Co-crystalized ligand		**Risperidone**		**Eticlopride**		**Nemonapride**	
		Lowest binding energy [kcal/mol]	Number of conformations in cluster	Lowest binding energy [kcal/mol]	Number of conformations in cluster	Lowest binding energy [kcal/mol]	Number of conformations in cluster
Structure from PDB file	1	-13.31	36	-9.31	37	-10.99	5
	2	-13.01	19	-8.97	15	-10.45	1
	3	-12.98	1	-8.94	1	-10.18	32
Corresponding DR models	1	-10.94	9	-9.98	14	-10.46	10
	2	-10.66	2	-9.34	3	-9.85	3
	3	-10.63	11	-9.07	14	-9.50	15

Table S10 - D_1R residues with Ballesteros & Weinstein-numbering [4] **participating in different interaction types sorted by ligands.** Data was summarized for all time points. Abbreviations: Hydrocontacts – hydrophobic contacts; SB – salt-bridges; 2.5 Å – 2.5 Å-interactions; HB – hydrogen bonds; cat-π – cat-π-interactions, T-stack – T-stacking-interactions; π-π-stack – π-π-stacking-interactions. Duplicate residues per interaction type are colored red, while unique residues per interaction type are colored green.

Interaction type	Hydrocontacts	SB	2.5 Å	HB	Cat-π	T-stack	π-π-stack
Dopamine	156Asp	3.32Asp	157Gly	74Pro	6.42Gly	6.43Val	
	160Thr	74Pro	160Thr	6.46Cys			
	169Cys		161Ser	3.32Asp			
	172Ser		169Cys	172Ser			
	274Cys		172Leu	172Leu			
	3.29Val		172Ser	169Cys			
	3.32Asp		3.32Asp	157Gly			
	3.33Ile		3.36Ser				
	3.36Ser		5.37Thr				
	5.37Thr		6.46Cys				
	6.30Glu		74Pro				
	6.31Thr						
	6.34Leu						
	6.39Val						
	6.42Gly						
	6.43Val						
	6.46Cys						
	71Gly						
	74Pro						
	75Phe						
7-OH-DPAT	164Glu	3.32Asp	160Thr	156Asp	6.42Gly	6.43Val	
	169Cys		169Cys	169Cys	6.31Thr		
	172Ser		172Leu	172Leu	6.30Glu		
	173Leu		172Ser	172Ser	231Phe		
	2.53Val		3.37Thr	3.37Thr			
	2.57Val		5.37Thr	6.34Leu			
	231Phe		6.34Leu	6.46Cys			
	264Phe		6.46Cys				
	265Cys						
	266Gly						
	271Gln						
	274Cys						
	275Ile						
	3.23Phe						

	3.28Trp 3.29Val 3.32Asp 3.33Ile 3.36Ser 5.37THR 6.30Glu 6.31Thr 6.34Leu 6.39Val 6.42Gly 6.43Val 6.46Cys 7.33Asn 71Gly 74Pro 75Phe						
Apomorphine	156Asp 169Cys 172Ser 173Leu 2.57Val 274Cys 275Ile 3.24Phe 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.36Ser 5.37THR 6.34Leu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.48Trp 6.58Leu 6.59Pro 7.33Asn 7.34Thr		160Thr 169Cys 172Ser 173Leu 6.34Leu 6.46Cys	169Cys 172Leu 6.34Leu		6.42Gly 6.43Val 6.58Leu 274Cys	274Cys

	71Gly 74Pro 75Phe						
Bromocriptine	1.31Val 1.45Ser 1.55Ala 1.59Arg 132Leu 157Gly 160thr 161ser 168Asn 169Cys 172Ser 1Arg 2.37val 2.41phe 2.45ser 2.50asp 2.53val 2.57val 2.58met 231Phe 264Phe 266Gly 267Ser 269Glu 270Thr 274Cys 274Ile 3.24phe 3.29val 3.32asp 3.33Ile 3.35Cys 3.37Thr 3.39Ser 3.40Ile 336Ser 34Phe 36His		1.31Val 1.59Arg 132Leu 157Gly 169Cys 172Ser 2.37val 2.50asp 2.53val 231Phe 266Gly 269Glu 270Thr 274Cys 274Ile 3.24phe 3.28Trp 3.32asp 3.33Ile 3.37Thr 3.39Ser 3.40Ile 336Ser 36His 37leu 5.37Thr 6.29Arg 6.31Thr 6.39Val 6.42Gly 6.43Val 6.46Cys 6.59Pro 7.33Asn 7.36Asp 7.37Val 75phe	157Gly 169Cys 172Ser 2.50Asp 3.28Trp 3.32Asp 3.36Ser 3.42Phe 6.39Val 6.46Cys 7.33Asn 7.36Asp		274Cys 6.42Gly 6.43Val 6.58Leu 7.34Thr	6.39Val

	37leu 5.37Ser 5.38Tyr 6.29Arg 6.30Glu 6.31Thr 6.34Leu 6.35Lys 6.38Ser 6.39Val 6.42Gly 6.43Val 6.46Cys 6.58Leu 6.59Pro 7.33Asn 7.34Thr 7.36Asp 7.37Val 74pro 75phe						
Clozapine	172Ser 2.41Phe 2.53Val 2.57Val 231Phe 266Gly 267Ser 269Glu 271Gln 274Cys 274Ile 3.23Ser 3.27Ile 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.42Phe		3.28Trp 3.32Asp 3.36Ser 3.42Phe 6.39Val 6.46Cys	3.28Trp 3.32Asp 3.36Ser 3.42Phe 6.39Val		274Cys 6.39Val 6.42Gly 6.43Val 7.34Thr	6.39Val 274Cys

	5.37Thr 6.30Glu 6.34Leu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.59Pro 7.33Asn 7.34Thr 7.36Asp 7.37Val 71Gly 74Pro 75Phe						
Nemonapride	169Cys 172Leu 172Ser 2.41Phe 2.45Ser 2.46Leu 2.49Ser 2.53Val 2.57Val 2.61Lys 2.67Ala 231Phe 264Phe 265Cys 266Gly 267Ser 269Glu 270Thr 271Gln 274Cys 274Ile 3.23Ser 3.28Trp 3.29Val 3.32Asp 3.33Ile	3.32Asp 74Pro	172Ser 2.45Ser 2.50Asp 2.67Ala 266Gly 3.28Trp 3.32Asp 3.36Ser 6.39Val 7.33Asn 7.34Thr 74Pro	172Leu 172Ser 2.45Ser 2.61Lys 2.67Ala 3.28Trp 3.32Asp 6.46Cys 7.33Asn 74Pro	6.30Glu 6.39Val 6.42Gly 7.34Thr	3.28Trp 6.42Gly 6.43Val 7.34Thr	7.34Thr 227Phe

	3.35Cys 3.36Ser 3.39Ser 3.40Ile 3.42Phe 5.37Thr 6.30Glu 6.35Lys 6.39Val 6.42Gly 6.43Val 6.46Cys 6.59Pro 7.32Ser 7.33Asn 7.34Thr 7.36Asp 74Pro						
Sulpiride	1.36Ala 1.43Ile 1.46Thr 1.47Leu 1.51Thr 2.41Phe 2.45Ser 2.53Val 2.57Val 231Phe 264Phe 266Gly 267Ser 274Cys 274Ile 3.23Ser 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 6.29Arg	3.32Asp 74Pro	156Asp 160Thr 169Cys 172Leu 172Ser 3.28Trp 3.32Asp 3.36Ser 3.42Phe 5.37Thr 6.29Arg 6.34Leu 6.39Val 6.46Cys 7.33Asn	156Asp 169Cys 172Leu 3.32Asp 3.36Ser 6.34Leu 6.46Cys	6.42Gly 274Cys	3.28Trp 6.39Val 6.42Gly 7.34Thr	

	6.30Glu 6.34Leu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.58Leu 6.59Pro 7.33Asn 7.34Thr 71Gly 74Pro 75Phe						
SCH23390	169Cys 172Leu 2.41Phe 2.45Ser 2.53Val 231Phe 264Phe 265Cys 266Gly 274Cys 274Ile 3.23Ser 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.40Ile 3.42Phe 6.30Glu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.58Leu 6.59Pro 7.32Ser 7.33Asn	3.32Asp	169Cys 172Leu 172Ser 266Gly 3.32Asp 3.36Ser 5.37Thr 6.39Val 6.46Cys 74Pro	172Ser 3.32Asp 6.39Val 6.46Cys 74Pro	6.30Glu 6.39Val 6.42Gly	6.39Val 6.42Gly	6.39Val 6.42Gly 6.43Val

	7.34Thr 74Pro						
SKF38393	160Thr 172Leu 172Ser 231Phe 274Cys 3.29Val 3.32Asp 3.33Ile 3.36Ser 3.42Phe 6.30Glu 6.31Thr 6.34Leu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.58Leu 7.33Asn 71Gly 74Pro 75Phe	3.32Asp 74Pro	157Gly 160Thr 161Ser 169Cys 172Leu 172Ser 3.32Asp 5.37Thr 6.34Leu 6.39Val 6.46Cys 71Gly	161Ser 169Cys 172Leu 172Ser 3.32Asp 6.34Leu 6.46Cys		6.43Val	274Cys 6.30Glu 6.39Val 6.42Gly 6.43Val
Eticlopride	169Cys 172Leu 172Ser 2.41Phe 2.45Ser 2.46Leu 2.53Val 2.57Val 2.67Ala 231Phe 264Phe 266Gly 267Ser 271Gln 274Cys 274Ile 3.28Trp	3.32Asp 74Pro	267Ser 3.28Trp 3.32Asp 3.36Ser 6.39Val 6.46Cys 7.33Asn 74Pro	3.32Asp 3.36Ser 6.39Val 6.46Cys 7.33Asn 74Pro	6.42Gly	274Cys 6.42Gly	6.39Val 6.42Gly

	3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.42Phe 5.37Thr 6.30Glu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.48Trp 6.59Pro 7.32Ser 7.33Asn 7.34Thr 74Pro						
Risperidone	160Thr 168Asn 169Cys 172Leu 172Ser 2.45Ser 2.49Ser 2.50Asp 2.53Val 2.57Val 2.58Met 231Phe 264Phe 265Cys 266Gly 267Ser 274Cys 274Ile 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys		266Gly 274Cys 3.28Trp 3.32Asp 5.37Thr 6.34Leu 6.39Val 6.46Cys 6.58Leu 7.36Asp	266Gly 3.28Trp 3.32Asp 6.46Cys 7.36Asp		6.58Leu 6.43Val 6.42Gly 274Cys 231Phe	264Phe 6.30Glu

	3.36Ser 3.39Ser 3.40Ile 3.42Phe 5.37Thr 6.30Glu 6.31Thr 6.34Leu 6.35Lys 6.39Val 6.42Gly 6.43Val 6.46Cys 6.58Leu 6.59Pro 7.32Ser 7.33Asn 7.34Thr 7.36Asp 74Pro 75Phe						
Aripiprazole	157Gly 168Asn 169Cys 172Ser 2.53Val 2.57Val 264PHE 266Gly 274Cys 275Ile 3.24Phe 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.39Ser 3.40Ile 5.37THR		157Gly 160Thr 161Ser 169Cys 172Leu 172Ser 2.50Asp 3.28Trp 3.36Ser 3.39Ser 5.37Thr 6.34Leu 6.46Cys 7.33Asn 7.34Thr 7.36Asp	157Gly 169Cys 172Leu 3.39Ser 6.46Cys 7.36Asp		274Cys 6.42GLY 6.43VAL 6.58Leu 7.34Thr	7.34Thr

	6.30Glu 6.34Leu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.58LEU 6.59PRO 7.33Asn 7.34Thr 7.36Asp 71Gly 74Pro 75Phe						
Haloperidole	172Leu 172Ser 2.45Ser 2.53Val 2.57Val 2.61Lys 231Phe 264Phe 265Cys 266Gly 267Ser 271Gln 274Cys 274Ile 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.42Phe 5.37Thr 6.30Glu 6.39Val 6.42Gly 6.43Val 6.46Cys	3.32Asp 74Pro	3.28Trp 3.32Asp 6.39Val 6.46Cys 7.33Asn 74Pro	3.28Trp 3.32Asp 7.33Asn 74Pro	274Cys 6.42Gly	6.42Gly 6.43Val	231Phe 6.31Thr 6.43Val

	6.58Leu 6.59Pro 7.33Asn 7.34Thr 7.36Asp 71Gly 74Pro						
Spiperone	168Asn 169Cys 172Ser 2.45Ser 2.53Val 2.57Val 2.61Lys 2.67Ala 231Phe 264Phe 266Gly 267Ser 271Gln 274Cys 274Ile 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.40Ile 5.37Thr 6.30Glu 6.31Thr 6.34Leu 6.35Lys 6.39Val 6.42Gly 6.43Val 6.46Cys 6.48Trp 6.55Asn 6.58Leu	3.32Asp 74Pro	172Leu 172Ser 2.61Lys 2.67Ala 274Cys 274Ile 3.28Trp 3.37Thr 5.37Thr 6.34Leu 6.39Val 6.46Cys 7.33Asn 7.34Thr	2.61Lys 3.28Trp 6.46Cys		274Cys 6.42Gly 6.43Val	3.28Trp 6.39Val 6.42Gly 7.34Thr

	6.59Pro 7.32Ser 7.33Asn 7.34Thr 7.36Asp 71Gly 74Pro 75Phe						
Chlorpromazine	2.41Phe 2.45Ser 2.53Val 2.57Val 231Phe 264Phe 266Gly 267Ser 271Gln 274Cys 274Ile 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.42Phe 5.37Thr 6.30Glu 6.31Thr 6.34Leu 6.39Val 6.42Gly 6.43Val 6.46Cys 6.58Leu 6.59Pro 7.32Ser 7.33Asn 7.34Thr 74Pro 75Phe		6.39Val 7.33Asn	3.28Trp		274Cys 6.30Glu 6.39Val 6.42Gly	264Phe 274Cys 3.28Trp 6.39Val 6.42Gly

Table S11 - D_2R residues with Ballesteros & Weinstein-numbering [4] **participating in different interaction types sorted by ligands.** Data was summarized for all time points. Abbreviations: Hydrocontacts – hydrophobic contacts; SB – salt-bridges; 2.5 Å – 2.5 Å-interactions; HB – hydrogen bonds; cat-π – cat-π-interactions, T-stack – T-stacking-interactions; π-π-stack – π-π-stacking-interactions. Duplicate residues per interaction type are colored red, while unique residues per interaction type are colored green.

Interaction type	Hydrocontacts	SB	2.5 Å	HB	Cat-π	T-stack	π-π-stack
Dopamine	156Ile	3.32Asp	3.32Asp	3.32Asp	6.55His	6.51Phe	6.48Trp
	3.32Asp		5.39Val	5.39Val			6.55His
	3.33Val		5.42Ser	5.42Ser			
	3.36Cys		5.43Ser	5.43Ser			
	5.38Phe		5.46Ser	5.46Ser			
	5.39Val		6.48Trp	7.43Tyr			
	5.42Ser		6.55His				
	5.43Ser		7.35Tyr				
	5.46Ser		7.43Tyr				
	5.47Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.39Thr						
	7.43Tyr						
7-OH-DPAT	156Ile	3.32Asp	5.39Val	5.39Val	6.48Trp	6.51Phe	5.47Phe
	3.28Phe		5.42Ser	5.43Ser	6.55His	6.55His	6.48Trp
	3.29Val		5.43Ser	6.55His			6.52Phe
	3.32Asp		6.45Ile				6.55His
	3.33Val		6.55His				
	3.36Cys						
	3.37Thr						
	5.38Phe						
	5.39Val						
	5.42Ser						
	5.43Ser						
	5.45Val						
	5.46Ser						
	5.47Phe						
	5.48Tyr						
	6.44Phe						
	6.45Ile						
	6.48Trp						

	6.51Phe 6.52Phe 6.55His 7.35Tyr 7.39Thr 7.42Gly 7.43Tyr 72Trp						
Apomorphine	156Ile 3.32Asp 3.33Val 3.36Cys 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 7.39Thr 7.42Gly 7.43Tyr 72Trp		3.32Asp 3.36Cys 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.55His	3.32Asp 5.39Val 5.42Ser 5.46Ser 6.55His	6.55His	6.48Trp 6.51Phe 7.35Tyr	5.38Phe 6.48Trp 6.51Phe 6.55His
Bromocriptine	156Ile 2.53Val 2.57Val 3.28Phe 3.29Val 3.32Asp 3.36Cys 3.39Ser 3.40Ile 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe		156Ile 2.53Val 3.29Val 3.32Asp 3.36Cys 3.40Ile 5.38Phe 5.39Val 5.43Ser 5.46Ser 5.47Phe 5.48Tyr 6.44Phe 6.48Trp 6.52Phe	3.32Asp 3.36Cys 5.38Phe 5.42Ser 5.46Ser 5.48Tyr 6.45Ile 6.48Trp 7.35Tyr 7.43Tyr	6.55His		6.48Trp 6.51Phe 6.55His

	5.48Tyr 6.44Phe 6.45Ile 6.48Trp 6.49Leu 6.51Phe 6.52Phe 6.55His 6.58Asn 7.35Tyr 7.39Thr 7.43Tyr 72Trp		6.55His 6.58Asn 7.35Tyr 7.43Tyr				
Clozapine	156Ile 2.53Val 2.57Val 3.28Phe 3.29Val 3.32Asp 3.33Val 3.36Cys 3.39Ser 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.45Val 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.54Thr 6.55His 6.58Asn 7.35Tyr 7.39Thr 7.42Gly 7.43Tyr 7.45Asn		3.32Asp 3.36Cys 5.42Ser 5.46Ser 6.55His 6.58Asn	3.32Asp 5.46Ser 6.55His 6.58Asn	6.55His	5.38Phe 6.48Trp 6.51Phe 6.55His 7.35Tyr 7.43Tyr	3.28Phe 6.48Trp 6.55His

	72Trp						
Nemonapride	1.44Ala	1.53Val	1.44Ala	3.32Asp	3.28Phe	3.28Phe	3.28Phe
	1.45Val	3.32Asp	3.32Asp	3.36Cys	6.55His	6.48Trp	5.38Phe
	1.48Phe		5.43Ser	5.43Ser		6.52Phe	
	1.49Gly		5.46Ser	5.46Ser		72Trp	
	1.50Asn		6.48Trp	6.48Trp			
	1.53Val		6.52Phe	7.43Tyr			
	1.54Cys		6.55His				
	155Ile		7.35Tyr				
	156Ile		7.43Tyr				
	2.57Val						
	2.61Val						
	2.64Leu						
	3.28Phe						
	3.29Val						
	3.32Asp						
	3.33Val						
	3.36Cys						
Sulpiride	3.43Leu						
	3.48Ile						
	3.52Thr						
	3Arg						
	4Pro						
	5.38Phe						
	5.39Val						
	5.42Ser						
	5.43Ser						
	5.46Ser						
	5.47Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.35Tyr						
	7.36Ser						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
	72Trp						
SCH23390	156Ile	3.32Asp	3.32Asp	3.32Asp	6.55His	3.28Phe	6.51Phe
	2.53Val		5.39Val	5.39Val	only at	5.38Phe	6.55His

					timetpoint 70 ns		
	2.61Val 2.64Leu 3.28Phe 3.29Val 3.32Asp 3.33Val 3.36Cys 5.38Phe 5.39Val 5.42Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 7.35Tyr 7.36Ser 7.39Thr 7.40Trp 7.42Gly 7.43Tyr 72Trp		5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.55His 7.35Tyr 7.39Thr 7.40Trp 7.43Tyr	5.42Ser 5.43Ser 5.46Ser 6.48Trp 7.35Tyr 7.43Tyr		6.48Trp 6.51Phe	
SKF38393	156Ile 3.29Val 3.32Asp 3.33Val 3.36Cys 3.39Ser 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His	3.32Asp	5.39Val 5.42Ser 5.43Ser 5.46Ser 6.55His 7.35Tyr 7.43Tyr	5.39Val 5.42Ser 5.43Ser 6.55His	6.48Trp 6.51Phe 6.55His	5.38Phe 6.48Trp 6.51Phe 6.55His	5.47Phe 6.48Trp 6.51Phe 6.55His

	7.35Tyr 7.39Thr 7.42Gly 7.43Tyr						
Eticlopride	156Ile 3.32Asp 3.33Val 3.36Cys 5.38Phe 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 7.35Tyr 7.39Thr 7.42Gly 7.43Tyr	3.32Asp	3.32Asp 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.55His 7.43Tyr	3.32Asp 3.33Val 5.39Val 5.42Ser 5.46Ser 6.55His 7.43Tyr	6.55His	6.48Trp 6.51Phe	6.48Trp 6.51Phe 6.52Phe 6.55His
Risperidone	156Ile 2.57Val 2.61Val 2.64Leu 3.28Phe 3.29Val 3.32Asp 3.33Val 3.36Cys 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 7.35Tyr		3.32Asp 3.36Cys 5.42Ser 5.46Ser 6.48Trp 7.35Tyr 7.40Trp 7.43Tyr	3.32Asp 5.46Ser 6.48Trp 7.35Tyr 7.43Tyr	6.55His	5.38Phe 6.48Trp 6.51Phe 6.55His 72Trp	6.48Trp 6.52Phe

	7.36Ser 7.39Thr 7.40Trp 7.42Gly 7.43Tyr 72Trp						
Aripiprazole	156Ile 2.57Val 2.61Val 2.64Leu 3.28Phe 3.29Val 3.32Asp 3.33Val 3.36Cys 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.54Thr 6.55His 7.35Tyr 7.36Ser 7.39Thr 7.40Trp 7.42Gly 7.43Tyr 7.45Asn 72Trp		3.32Asp 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.55His 7.35Tyr 7.43Tyr	5.39Val 5.42Ser 5.43Ser 5.46Ser 6.51Phe 7.35Tyr	6.55His	3.28Phe 5.38Phe 6.48Trp 6.51Phe 6.55His 72Trp	6.48Trp 6.51Phe 6.55His 7.43Tyr
Haloperidole	156Ile 2.53Val 2.57Val 3.28Phe 3.29Val 3.32Asp	3.32Asp	3.32Asp 3.36Cys 3.40Ile 5.42Ser 5.46Ser 6.48Trp	3.32Asp 5.42Ser 5.46Ser 6.48Trp	6.48Trp 6.55His	6.52Phe 6.55His 7.43Tyr	3.28Phe 5.47Phe 6.48Trp 6.52Phe 6.55His

	3.33Val 3.36Cys 3.39Ser 3.40Ile 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 7.35Tyr 7.39Thr 7.42Gly 7.43Tyr 72Trp		7.43Tyr				
Spiperone	156Ile 2.53Val 3.28Phe 3.29Val 3.32Asp 3.33Val 3.35Met 3.36Cys 3.39Ser 3.40Ile 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His	3.32Asp	156Ile 3.32Asp 3.33Val 3.36Cys 6.48Trp 6.55His 7.35Tyr 7.39Thr 7.42Gly 7.43Tyr 7.46Ser	6.48Trp 6.55His 7.35Tyr 7.43Tyr	6.48Trp 6.55His	3.28Phe 6.48Trp 6.51Phe 6.55His 7.43Tyr	6.48Trp 6.51Phe 6.55His

	7.35Tyr 7.38Phe 7.39Thr 7.42Gly 7.43Tyr 72Trp						
Chlorpromazine	156Ile 2.53Val 2.57Val 3.29Val 3.32Asp 3.33Val 3.36Cys 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 7.39Thr 7.42Gly 7.43Tyr		6.55His only at timepoint 85		6.55His	5.38Phe 6.48Trp 6.51Phe	6.48Trp 6.51Phe 6.55His

Table S12 - D_3R residues with Ballesteros & Weinstein-numbering [4] **participating in different interaction types sorted by ligands.** Data was summarized for all time points. Abbreviations: Hydrocontacts – hydrophobic contacts; SB – salt-bridges; 2.5 Å – 2.5 Å-interactions; HB – hydrogen bonds; cat-π – cat-π-interactions, T-stack – T-stacking-interactions; π-π-stack – π-π-stacking-interactions. Duplicate residues per interaction type are colored red, while unique residues per interaction type are colored green.

Interaction type	Hydrocontacts	SB	2.5 Å	HB	Cat-π	T-stack	π-π-stack
Dopamine	159Ile	3.32Asp	3.32Asp	3.32Asp	2.48Val	6.51Phe	2.48Val
	2.42Leu		3.33Val	5.39Val	6.55His	6.52Phe	35Ala
	2.44Val		5.38Phe	5.42Ser		6.55His	38Thr
	2.45Ser		5.39Val	5.43Ser			6.52Phe
	2.46Leu		5.42Ser	6.51Phe			
	2.47Ala		5.43Ser				
	2.48Val		5.46Ser				
	3.32Asp		6.52Phe				
	3.33Val		74Phe				
	3.36Cys						
	34Arg						
	35Ala						
	38Thr						
	5.38Phe						
	5.39Val						
	5.42Ser						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
7-OH-DPAT	1.58Leu	3.32Asp	1.58Leu	5.39Val	2.14Tyr	2.46Leu	2.48Val
	159Ile		3.36Cys	5.43Ser	2.42Leu	2.47Ala	2.49Ala
	2.41Tyr		5.39Val		2.48Val	2.50Asp	35Ala
	2.42Leu		5.42Ser		2.49Ala	5.38Phe	6.52Phe
	2.43Val		5.43Ser		34Arg	6.52Phe	6.55His
	2.44Val		5.46Ser		6.48Trp	6.55His	
	2.45Ser				6.55His		
	2.46Leu						
	2.47Ala						
	2.48Val						
	2.49Ala						
	2.50Asp						
	3.29Val						
	3.32Asp						

	3.33Val 3.36Cys 34Arg 35Ala 38Thr 5.38Phe 5.39Val 5.42Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 69Gly 7.39Thr 7.42Gly 7.43Tyr 70Gly 73Asn						
Apomorphine	159Ile 2.41Tyr 2.42Leu 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.50Asp 2.57Val 3.29Val 3.32Asp 3.33Val 3.35Met 3.36Cys 34Arg 35Ala 38Thr 39Thr 5.38Phe 5.39Val 5.42Ser		2.14Tyr 2.47Ala 3.32Asp 3.36Cys 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.52Phe 6.55His	3.32Asp 5.39Val 5.42Ser 5.43Ser 5.46Ser	2.48Val 38Thr 6.55His	2.41Tyr 2.42Leu 2.43Val 2.45Ser 2.46Leu 38Thr 6.48Trp 6.51Phe 6.52Phe 6.55His	2.44Val 2.48Val 34Arg 38Thr 6.48Trp 6.52Phe 6.55His

	5.46Ser						
	6.44Phe						
	6.47Cys						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.35Tyr						
	7.38Thr						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
	70Gly						
	74Phe						
Bromocriptine	1.54Cys		1.58Leu	159Ile	38Thr	2.42Leu	2.42Leu
	1.57Val		157Cys	2.48Val	6.55His	2.43Val	2.43Val
	1.58Leu		159Ile	2.60Trp		2.45Ser	2.45Ser
	157Cys		2.39Thr	3.29Val		2.46Leu	2.46Leu
	158Ser		2.41Tyr	3.32Asp		34Arg	34Arg
	159Ile		2.43Val	3.35Met		38Thr	38Thr
	2.39Thr		2.44Val	3.36Cys		6.48Trp	6.48Trp
	2.41Tyr		2.48Val	5.39Val		6.51Phe	6.51Phe
	2.42Leu		2.60Trp	5.46Ser			
	2.43Val		2.61Val	6.55His			
	2.44Val		2.64Leu	7.35Tyr			
	2.45Ser		3.29Val	7.38Thr			
	2.46Leu		3.32Asp				
	2.48Val		3.33Val				
	2.53Val		3.36Cys				
	2.57Val		3.40Ile				
	2.60Trp		34Arg				
	2.61Val		38Thr				
	2.64Leu		39Thr				
	2.65Glu		5.38Phe				
	2.66Val		5.39Val				
	3.28Phe		5.42Ser				
	3.29Val		5.46Ser				
	3.32Asp		5.47Phe				
	3.33Val		6.44Phe				
	3.35Met		6.48Trp				
	3.36Cys		6.51Phe				

	3.40Ile		6.52Phe				
	34Arg		6.55His				
	35Ala		69Gly				
	38Thr		7.35Tyr				
	39Thr		7.38Thr				
	5.38Phe		7.39Thr				
	5.39Val		7.42Gly				
	5.42Ser		7.43Tyr				
	5.43Ser		74Phe				
	5.46Ser						
	5.47Phe						
	6.44Phe						
	6.47Cys						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	69Gly						
	7.35Tyr						
	7.38Thr						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
	70Gly						
	71Val						
	73Asn						
	74Phe						
	75Ser						
Clozapine	1.58Leu		2.46Leu	3.32Asp	2.48Val	2.45Ser	1.58Leu
	157Cys		3.32Asp	38Thr	38Thr	2.46Leu	2.43Val
	158Ser		3.36Cys	6.48Trp	6.55His	34Arg	2.49Ala
	159Ile		35Ala	6.55His		6.51Phe	3.28Phe
	2.41Tyr		38Thr				6.48Trp
	2.42Leu		6.48Trp				
	2.43Val		6.52Phe				
	2.44Val		6.55His				
	2.45Ser		71Val				
	2.46Leu						
	2.48Val						
	2.49Ala						
	2.53Val						

	2.57Val 3.28Phe 3.29Val 3.32Asp 3.33Val 3.36Cys 34Arg 35Ala 38Thr 39Thr 5.38Phe 5.39Val 5.42Ser 5.43Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 6.56Val 7.39Thr 7.42Gly 7.43Tyr 71Val 74Phe 75Ser						
Nemonapride	1.58Leu 159Ile 2.41Tyr 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.50Asp 2.53Val 2.57Val 2.61Val 2.64Leu 3.28Phe	3.32Asp	2.53Val 2.61Val 3.32Asp 3.36Cys 5.42Ser 5.46Ser 6.48Trp 6.55His 7.42Gly 7.43Tyr 75Ser	2.61Val 3.32Asp 3.36Cys 5.42Ser 6.48Trp 7.43Tyr 75Ser	2.42Leu 38Thr 6.55His	2.41Tyr 2.43Val 6.48Trp 6.51Phe 7.43Tyr 74Phe	1.58Leu 2.42Leu 2.50Asp 6.48Trp

	3.29Val						
	3.32Asp						
	3.33Val						
	3.35Met						
	3.36Cys						
	3.39Ser						
	34Arg						
	35Ala						
	38Thr						
	5.38Phe						
	5.39Val						
	5.42Ser						
	5.46Ser						
	6.44Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.38Thr						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
	70Gly						
	73Asn						
	75Ser						
Sulpiride	1.58Leu	3.32Asp	1.58Leu	2.45Ser	1.39Tyr	2.45Ser	2.43Val
	158Ser		2.45Ser	2.49Ala	2.48Val	2.50Asp	2.44Val
	159Ile		2.48Val	3.32Asp	38Thr	3.28Phe	2.48Val
	2.41Tyr		2.49Ala	38Thr	5.38Phe	38Thr	38Thr
	2.42Leu		3.32Asp	5.39Val	6.48Trp	6.48Trp	5.38Phe
	2.44Val		3.36Cys	5.42Ser	6.55His	6.51Phe	6.51Phe
	2.45Ser		38Thr	5.46Ser		6.55His	6.52Phe
	2.46Leu		5.39Val	6.48Trp			
	2.47Ala		5.42Ser	7.43Tyr			
	2.48Val		5.43Ser	74Phe			
	2.49Ala		5.46Ser				
	2.50Asp		6.48Trp				
	2.53Val		6.55His				
	2.57Val		7.39Thr				
	2.61Val		7.43Tyr				
	3.28Phe						

	3.29Val 3.32Asp 3.33Val 3.35Met 3.36Cys 34Arg 35Ala 38Thr 5.38Phe 5.39Val 5.42Ser 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 69Gly 7.35Tyr 7.36Ser 7.39Thr 7.43Tyr 70Gly 73Asn 74Phe						
SCH23390	1.58Leu 159Ile 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.53Val 2.57Val 3.29Val 3.32Asp 3.33Val 3.35Met 3.36Cys 34Arg	3.32Asp	1.58Leu 2.42Leu 2.48Val 3.36Cys 5.39Val 5.42Ser 5.43Ser 6.48Trp 7.39Thr 7.43Tyr	2.48Val 5.38Phe 5.43Ser	2.48Val 34Arg 6.55His	2.44Val 34Arg 5.38Phe 6.51Phe 6.55His	2.42Leu 2.45Ser 2.47Ala 2.48Val 34Arg 35Ala 38Thr 6.48Trp 6.51Phe 6.52Phe 6.55His

	35Ala 38Thr 5.38Phe 5.39Val 5.42Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 7.35Tyr 7.39Thr 7.43Tyr 70Gly 74Phe						
SKF38393	1.58Leu 159Ile 2.41Tyr 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.49Ala 2.50Asp 2.57Val 3.32Asp 3.33Val 3.36Cys 34Arg 35Ala 5.38Phe 5.39Val 5.42Ser 5.46Ser 5.47Phe 6.48Trp 6.51Phe 6.52Phe 6.55His	3.32Asp	159Ile 2.49Ala 2.50Asp 3.32Asp 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.51Phe 6.55His	2.49Ala 3.32Asp 3.33Val 5.39Val 5.42Ser 5.43Ser 6.51Phe	2.48Val 6.51Phe 6.55His	2.44Val 35Ala 38Thr 5.38Phe 6.48Trp 6.51Phe 6.52Phe 6.55His	1.58Leu 2.45Ser 2.48Val 6.52Phe

	70Gly						
Eticlopride	1.54Cys 1.58Leu 157Cys 158Ser 159Ile 2.41Tyr 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.50Asp 2.53Val 2.57Val 2.61Val 2.65Glu 3.28Phe 3.29Val 3.32Asp 3.33Val 3.35Met 3.36Cys 34Arg 35Ala 38Thr 5.39Val 5.42Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 69Gly 7.39Thr 7.43Tyr 70Gly 73Asn 74Phe	3.32Asp	1.58Leu 2.42Leu 2.43Val 3.32Asp 3.36Cys 38Thr 6.48Trp 6.55His 7.43Tyr 74Phe	1.58Leu 3.32Asp 38Thr 6.55His 7.43Tyr 74Phe	2.48Val 6.52Phe 6.55His	2.45Ser 6.51Phe 6.52Phe	38Thr 7.35Tyr

	75Ser						
Risperidone	1.58Leu 158Ser 159Ile 2.41Tyr 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.48Val 2.50Asp 2.53Val 2.57Val 2.61Val 2.64Leu 2.65Glu 3.28Phe 3.29Val 3.32Asp 3.33Val 3.35Met 3.36Cys 34Arg 35Ala 38Thr 39Thr 5.38Phe 5.39Val 5.42Ser 5.46Ser 5.47Phe 6.44Phe 6.47Cys 6.48Trp 6.51Phe 6.52Phe 6.55His 69Gly 7.35Tyr 7.38Thr		159Ile 2.43Val 2.48Val 2.50Asp 2.61Val 3.32Asp 3.36Cys 38Thr 6.48Trp 6.51Phe 6.55His 7.39Thr 7.43Tyr 74Phe	159Ile 2.43Val 3.32Asp 38Thr 6.48Trp 6.55His 7.43Tyr 74Phe	2.48Val 6.55His	2.42Leu 2.45Ser 2.46Leu 34Arg 6.44Phe 6.48Trp 6.51Phe 6.55His 7.43Tyr	1.58Leu 35Ala 6.48Trp

	7.39Thr 7.42Gly 7.43Tyr 71Val 75Ser						
Aripiprazole	1.39Tyr 1.58Leu 158Ser 159Ile 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.49Ala 2.53Val 2.57Val 2.61Val 2.64Leu 2.65Glu 2.66Val 3.28Phe 3.29Val 3.32Asp 3.33Val 3.35Met 3.36Cys 34Arg 35Ala 5.38Phe 5.39Val 5.42Ser 5.46Ser 6.47Cys 6.48Trp 6.51Phe 6.52Phe 6.55His 7.32Pro		159Ile 2.48Val 2.49Ala 2.61Val 3.32Asp 3.37Thr 38Thr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.47Cys 6.55His 7.43Tyr 75Ser	159Ile 2.61Val 38Thr 5.39Val 5.42Ser 5.46Ser 7.43Tyr 75Ser	2.48Val 2.50Asp 38Thr	2.46Leu 2.50Asp 2.61Val 34Arg 6.51Phe 6.52Phe 7.43Tyr 74Phe	2.41Tyr 3.28Phe 6.48Trp 6.51Phe 7.35Tyr 7.43Tyr

	7.35Tyr 7.36Ser 7.38Thr 7.39Thr 7.42Gly 7.43Tyr 70Gly 71Val 74Phe 75Ser						
Haloperidole	1.58Leu 159Ile 2.41Tyr 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.50Asp 2.53Val 2.61Val 2.65Glu 2.66Val 3.28Phe 3.29Val 3.32Asp 3.33Val 3.36Cys 34Arg 35Ala 38Thr 5.38Phe 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.48Trp 6.51Phe		1.58Leu 159Ile 2.41Tyr 3.29Val 3.32Asp 3.33Val 3.36Cys 35Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.55His 7.43Tyr 71Val	159Ile 3.32Asp 5.42Ser 5.46Ser 7.43Tyr 71Val	2.48Val	2.50Asp 6.48Trp 6.51Phe 6.55His	2.48Val 35Ala 5.47Phe 6.52Phe 6.55His

	6.52Phe 6.55His 7.35Tyr 7.39Thr 7.43Tyr 71Val 73Asn						
Spiperone	1.39Tyr 1.44Leu 1.58Leu 110Met 152Gly 155Thr 156Val 157Cys 159Ile 1Gln 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.50Asp 2.53Val 2.57Val 2.61Val 2.64Leu 2.65Glu 2Ala 3.23Ile 3.24Cys 3.27Val 3.28Phe 3.31Leu 3.32Asp 3.33Val 3.36Cys 3.52Thr 34Arg	1.44Leu 75Ser	1.43Ile 2.48Val 2.50Asp 3.24Cys 3.27Val 3.33Val 3.36Cys 3.52Thr 38Thr 3Arg 5.57Val 6.48Trp 6.55His 70Gly 72Trp	3.52Thr 38Thr 5.57Val 7.43Tyr 72Trp	152Gly	1.35Tyr 159Ile 2.61Val 6.51Phe	2.42Leu 2.64Leu 35Ala 6.48Trp 75Ser

	35Ala 38Thr 3Arg 5.38Phe 5.42Ser 5.53Val 5.56Leu 5.57Val 6.48Trp 6.51Phe 6.52Phe 7.38Thr 7.39Thr 7.42Gly 7.43Tyr 70Gly 71Val 72Trp 73Asn 74Phe 75Ser						
Chlorpromazine	1.54Cys 1.58Leu 158Ser 159Ile 2.39Thr 2.41Tyr 2.42Leu 2.43Val 2.44Val 2.45Ser 2.46Leu 2.47Ala 2.48Val 2.53Val 2.56Leu 2.57Val 2.61Val 3.28Phe 3.29Val 3.32Asp		6.48Trp 7.43Tyr 75Ser		2.48Val	2.14Tyr 34Arg 6.51Phe	1.58Leu 2.42Leu 2.43Val 2.44Val 2.45Ser 2.48Val 6.48Trp 6.51Phe

	3.33Val 3.35Met 3.36Cys 3.40Ile 34Arg 35Ala 38Thr 5.38Phe 5.39Val 5.42Ser 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 7.38Thr 7.39Thr 7.42Gly 7.43Tyr 71Val 73Asn 74Phe 75Ser						

Table S13 - D4R residues with Ballesteros & Weinstein-numbering [4] **participating in different interaction types sorted by ligands.** Data was summarized for all time points. Abbreviations: Hydrocontacts – hydrophobic contacts; SB – salt-bridges; 2.5 Å – 2.5 Å-interactions; HB – hydrogen bonds; cat-π – cat-π-interactions, T-stack – T-stacking-interactions; π-π-stack – π-π-stacking-interactions. Duplicate residues per interaction type are colored red, while unique residues per interaction type are colored green.

Interaction type	Hydrocontacts	SB	2.5 Å	HB	Cat-π	T-stack	π-π-stack
Dopamine	156Arg 157Leu 3.32Asp	3.32Asp	156Arg 3.32Asp 5.39Val	3.32Asp 5.42Ser 5.43Ser	6.55His only at timepoint 65 ns	6.52Phe 6.55His	6.52Phe only at timepoint 65 ns

	3.33Val 3.36Cys 3.37Thr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55His		5.42Ser 5.43Ser 5.46Ser 6.55His 7.43Tyr	6.55His 7.43Tyr		only at timepoints 0 and 95 ns	
7-OH-DPAT	156Arg 157Leu 2.53Leu 3.29Met 3.32Asp 3.33Val 3.36Cys 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 7.39Thr 7.42Gly 7.43Tyr	3.32Asp	156Arg 3.36Cys 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.55His	156Arg 5.38Tyr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.55His	6.51Phe 6.48Trp 6.55His	6.52Phe 6.55His	5.38Tyr 6.51Phe 6.52Phe 6.55His
Apomorphine	156Arg 157Leu 3.29Met 3.32Asp 3.33Val 3.36Cys 3.37Thr 3.40Ile 4.56Val		156Arg 3.36Cys 3.37Thr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.55His	156Arg 5.42Ser 5.43Ser 5.46Ser 6.55His	156Arg 6.55His	6.48Trp 6.51Phe 6.52Phe 6.55His	6.52Phe 6.55His

	5.39Val						
	5.42Ser						
	5.43Ser						
	5.46Ser						
	6.44Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.35Val						
	7.38Val						
	7.39Thr						
	7.43Tyr						
Bromocriptine	156Arg		156Arg	156Arg	156Arg	6.48Trp	6.48Trp
	157Leu		157Leu	157Leu	6.55His		6.51Phe
	2.53Leu		2.53Leu	3.32Asp			6.52Phe
	3.29Met		3.29Met	3.36Cys			6.55His
	3.32Asp		3.32Asp	4.56Val			
	3.33Val		3.33Val	5.36Arg			
	3.36Cys		3.36Cys	5.43Ser			
	3.37Thr		3.37Thr	6.48Trp			
	3.39Ser		3.40Ile	6.55His			
	3.40Ile		3.41Phe	7.38Val			
	3.41Phe		4.52Leu	7.39Thr			
	4.52Leu		4.56Val	7.43Tyr			
	4.53Ser		5.36Arg				
	4.56Val		5.38Tyr				
	5.36Arg		5.39Val				
	5.38Tyr		5.42Ser				
	5.39Val		5.43Ser				
	5.40Val		5.45Cys				
	5.41Tyr		5.46Ser				
	5.42Ser		5.47Phe				
	5.43Ser		6.44Phe				
	5.45Cys		6.48Trp				
	5.46Ser		6.51Phe				
	5.47Phe		6.52Phe				
	5.48Phe		6.55His				
	6.44Phe		6.56Ile				
	6.48Trp		7.35Val				
	6.51Phe		7.38Val				

	6.52Phe		7.39Thr				
	6.54Val		7.42Gly				
	6.55His		7.43Tyr				
	6.56Ile						
	7.35Val						
	7.36Ser						
	7.38Val						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
Clozapine	155Cys		156Arg	156Arg	156Arg	6.48Trp	6.48Trp
	156Arg		157Leu	3.33Val	6.55His	6.51Phe	6.51Phe
	157Leu		3.32Asp	5.42Ser		6.52Phe	6.55His
	2.53Leu		3.33Val	5.46Ser		7.43Tyr	
	3.29Met		3.36Cys	6.55His			
	3.32Asp		5.39Val	7.43Tyr			
	3.33Val		5.42Ser				
	3.36Cys		5.46Ser				
	3.37Thr		6.48Trp				
	3.40Ile		6.51Phe				
	4.56Val		6.52Phe				
	5.38Tyr		6.55His				
	5.39Val		7.43Tyr				
	5.42Ser						
	5.43Ser						
	5.46Ser						
	6.44Phe						
	6.47Cys						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.35Val						
	7.38Val						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
Nemonapride	154Val	3.32Asp	156Arg	156Arg	6.51Phe	6.48Trp	6.48Trp
	155Cys		3.32Asp	3.32Asp	6.55His	6.51Phe	6.51Phe
	156Arg		3.36Cys	5.42Ser	7.43Tyr	6.52Phe	7.43Tyr
	157Leu		5.42Ser	5.46Ser		6.55His	

	2.53Leu		5.46Ser	6.48Trp		7.43Tyr	
	2.57Val		6.48Trp	7.42Gly			
	2.58Leu		6.55His	7.43Tyr			
	2.61Phe		7.42Gly				
	3.28Leu		7.43Tyr				
	3.29Met		7.46Ser				
	3.32Asp						
	3.33Val						
	3.35Leu						
	3.36Cys						
	3.37Thr						
	3.39Ser						
	4.56Val						
	5.38Tyr						
	5.39Val						
	5.42Ser						
	5.43Ser						
	5.46Ser						
	5.47Phe						
	6.44Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
	7.45Asn						
	7.46Ser						
Sulpiride	154Val	3.32Asp	156Arg	156Arg	6.52Phe	6.48Trp	154Val
	155Cys		3.29Met	3.32Asp	6.55His	6.51Phe	155Cys
	156Arg		3.32Asp	5.42Ser		6.52Phe	156Arg
	157Leu		3.33Val	5.43Ser			157Leu
	2.53Leu		3.36Cys	5.46Ser			2.53Leu
	2.57Val		4.56Val	6.48Trp			2.57Val
	3.29Met		5.39Val	6.55His			3.29Met
	3.32Asp		5.42Ser	7.43Tyr			3.32Asp
	3.33Val		5.43Ser				3.33Val
	3.35Leu		5.46Ser				3.35Leu
	3.36Cys		6.48Trp				3.36Cys
	3.39Ser		6.51Phe				3.39Ser

	4.56Val		6.52Phe				4.56Val
	5.38Tyr		6.55His				5.38Tyr
	5.39Val		7.43Tyr				5.39Val
	5.42Ser						5.42Ser
	5.46Ser						5.46Ser
	6.48Trp						6.48Trp
	6.51Phe						6.51Phe
	6.52Phe						6.52Phe
	6.55His						6.55His
	6.58Gln						6.58Gln
	7.35Val						7.35Val
	7.38Val						7.38Val
	7.39Thr						7.39Thr
	7.42Gly						7.42Gly
	7.43Tyr						7.43Tyr
SCH23390	155Cys	3.32Asp	156Arg	156Arg	156Arg	6.51Phe	6.51Phe
	156Arg		157Leu	3.32Asp	6.51Phe	6.52Phe	6.52Phe
	157Leu		3.32Asp	5.42Ser	6.52Phe	6.55His	6.55His
	3.29Met		3.37Thr	6.55His	6.55His		
	3.32Asp		5.39Val				
	3.33Val		5.42Ser				
	3.36Cys		5.43Ser				
	5.38Tyr		5.46Ser				
	5.39Val		6.48Trp				
	5.42Ser		6.55His				
	5.43Ser		7.43Tyr				
	5.46Ser						
	5.47Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.39Thr						
	7.43Tyr						
SKF38393	155Cys	3.32Asp	156Arg	3.32Asp	156Arg	5.47Phe	6.44Phe
	156Arg		3.32Asp	5.39Val	6.52Phe	6.51Phe	6.48Trp
	157Leu		3.36Cys	5.42Ser	6.55His	6.52Phe	6.51Phe
	2.53Leu		5.39Val	5.43Ser		6.55His	6.52Phe
	3.29Met		5.42Ser	5.46Ser		7.43Tyr	
	3.32Asp		5.43Ser	7.42Gly			
	3.33Val		5.46Ser	7.43Tyr			

	3.36Cys 5.38Tyr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 7.38Val 7.39Thr 7.42Gly 7.43Tyr		6.55His 7.38Val 7.42Gly 7.43Tyr				
Eticlopride	154Val 155Cys 156Arg 157Leu 2.53Leu 2.61Phe 3.28Leu 3.29Met 3.32Asp 3.33Val 3.35Leu 3.36Cys 3.37Thr 3.39Ser 5.38Tyr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55His 7.39Thr 7.42Gly 7.43Tyr 7.46Ser	2.50Asp 3.32Asp	156Arg 157Leu 3.32Asp 3.33Val 3.36Cys 5.42Ser 6.55His 7.43Tyr	156Arg 3.32Asp 3.33Val 6.55His 7.43Tyr	156Arg 6.51Phe 6.55His	6.48Trp 6.51Phe 6.52Phe 6.55His	

Risperidone	154Val		156Arg	156Arg	156Arg	6.51Phe	5.38Tyr
	155Cys		157Leu	157Leu	6.55His	6.52Phe	6.48Trp
	156Arg		2.64Ser	3.32Asp		6.55His	6.55His
	157Leu		3.32Asp	6.48Trp		7.43Tyr	
	2.53Leu		3.36Cys	6.55His			
	2.61Phe		3.37Thr	7.43Tyr			
	2.64Ser		5.39Val				
	2.65Glu		5.42Ser				
	3.28Leu		5.43Ser				
	3.29Met		6.48Trp				
	3.32Asp		6.51Phe				
	3.33Val		6.52Phe				
	3.35Leu		6.55His				
	3.36Cys		7.43Tyr				
	3.37Thr						
	3.39Ser						
	4.56Val						
	5.38Tyr						
	5.39Val						
	5.42Ser						
	5.43Ser						
	5.46Ser						
	6.44Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.54Val						
	6.55His						
	69Gly						
	7.35Val						
	7.36Ser						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
	7.45Asn						
	71Trp						
Aripiprazole	154Val		156Arg	156Arg	156Arg	6.48Trp	6.48Trp
	156Arg		1Ala	5.36Arg		6.51Phe	7.43Tyr
	157Leu		3.31Met	5.42Ser		6.52Phe	
	2.53Leu		3.32Asp	5.43Ser		7.43Tyr	
	2.57Val		3.36Cys	5.46Ser			

	2.61Phe		3.37Thr	6.48Trp			
	2.64Ser		5.36Arg				
	3.28Leu		5.39Val				
	3.29Met		5.42Ser				
	3.32Asp		5.43Ser				
	3.33Val		5.46Ser				
	3.36Cys		6.48Trp				
	3.37Thr		6.55His				
	4.56Val		7.43Tyr				
	5.39Val		70Ala				
	5.42Ser						
	5.43Ser						
	5.46Ser						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55His						
	7.38Val						
	7.39Thr						
	7.42Gly						
	7.43Tyr						
	7.46Ser						
	154Val		156Arg	156Arg			
	156Arg		157Leu				
	157Leu		2.64Ser				
	2.53Leu		3.32Asp				
	2.57Val		3.36Cys				
	2.60Leu		5.36Arg				
	2.61Phe		5.42Ser				
	2.64Ser		6.48Trp				
	3.28Leu		6.55His				
Haloperidole	3.29Met		7.42Gly				
	3.32Asp		7.43Tyr				
	3.33Val		7.46Ser				
	3.36Cys						
	3.37Thr						
	3.40Ile						
	4.56Val						
	5.38Tyr						
	5.39Val						
	5.41Tyr						

	5.42Ser 5.43Ser 5.45Cys 5.46Ser 5.47Phe 6.44Phe 6.48Trp 6.51Phe 6.52Phe 6.55His 7.36Ser 7.39Thr 7.42Gly 7.43Tyr 7.45Asn 7.46Ser						
Spiperone	154Val 155Cys 156Arg 157Leu 2.53Leu 2.61Phe 3.28Leu 3.29Met 3.32Asp 3.33Val 3.35Leu 3.36Cys 3.37Thr 3.39Ser 3.40Ile 4.56Val 5.38Tyr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.44Phe	3.32Asp	156Arg 2.53Leu 3.36Cys 5.38Tyr 5.39Val 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.55His 7.43Tyr	156Arg 5.39Val 6.48Trp 6.55His 7.43Tyr	156Arg only at timepoint 60 and 70 ns	6.48Trp 6.51Phe 6.52Phe 6.55His 7.43Tyr	6.48Trp 6.51Phe 6.55His

	6.48Trp 6.51Phe 6.52Phe 6.54Val 6.55His 7.35Val 7.36Ser 7.38Val 7.39Thr 7.42Gly 7.43Tyr 7.45Asn						
Chlorpromazine	156Arg 157Leu 2.53Leu 3.29Met 3.32Asp 3.33Val 3.36Cys 3.37Thr 3.39Ser 3.40Ile 5.39Val 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.47Cys 6.48Trp 6.51Phe 6.52Phe 6.55His 7.35Val 7.38Val 7.39Thr 7.42Gly 7.43Tyr		156Arg	6.48Trp	156Arg 6.55His	6.48Trp 6.51Phe 6.52Phe 6.55His 7.43Tyr	6.48Trp 6.51Phe 6.52Phe

Table S14 - D_5R residues with Ballesteros & Weinstein-numbering [4] **participating in different interaction types sorted by ligands.** Data was summarized for all time points. Abbreviations: Hydrocontacts – hydrophobic contacts; SB – salt-bridges; 2.5 Å – 2.5 Å-interactions; HB – hydrogen bonds; cat-π – cat-π-interactions, T-stack – T-stacking-interactions; π-π-stack – π-π-stacking-interactions. Duplicate residues per interaction type are colored red, while unique residues per interaction type are colored green.

Interaction type	Hydrocontacts	SB	2.5 Å	HB	Cat-π	T-stack	π-π-stack
Dopamine	3.32Asp 3.33Ile 3.36Ser 5.42Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn	3.32Asp	3.32Asp 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.55Asn	3.32Asp 5.38Tyr 5.42Ser 5.43Ser 6.55Asn		6.48Trp 6.51Phe 6.52Phe	6.52Phe 5.38Tyr
7-OH-DPAT	3.28Trp 3.29Val 3.32Asp 3.33Ile 3.36Ser 5.35Asn 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.39Val 7.42Gly	3.32Asp	5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.55Asn	5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.55Asn only with No 11		6.52Phe	6.52Phe
Apomorphine	164Leu 3.28Trp 3.29Val 3.32Asp 3.33Ile		5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.55Asn	5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.55Asn		6.48Trp 6.51Phe 6.52Phe 7.35Phe	5.38Tyr 7.35Phe only at timepoints 85, 90 ns

	3.36Ser 5.35Asn 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe						
Bromocriptine	164Leu 2.53Val 2.57Val 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.40Ile 5.35Asn 5.38Tyr 5.39Ala 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.47Cys 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.38Phe 7.39Val 7.42Gly 7.45Asn		164Leu 2.57Val 3.28Trp 3.32Asp 3.33Ile 3.36Ser 3.39Ser 5.35Asn 5.39Ala 5.42Ser 5.46Ser 6.48Trp 6.52Phe 6.55Asn 7.35Phe 7.39Val 7.45Asn 7.49Asn	3.32Asp 3.39Ser 5.42Ser 5.43Ser 6.55Asn 7.45Asn		6.48Trp 7.35Phe	6.48Trp 6.52Phe
Clozapine	164Leu 2.53Val		3.32Asp 5.35Asn	3.32Asp 5.42Ser		6.51Phe 6.52Phe	5.38Tyr 6.48Trp

	2.57Val 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.39Ser 5.38Tyr 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.44Phe 6.47Cys 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.39Val 7.42Gly 7.45Asn		5.39Ala 5.42Ser 6.55Asn 7.45Asn	6.55Asn 7.45Asn		7.35Phe	6.52Phe
Nemonapride	2.53Val 2.57Val 2.58Met 2.61Lys 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.36Ser 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.38Phe	3.32Asp	3.32Asp 3.36Ser 5.42Ser 5.46Ser 6.48Trp 6.55Asn	3.32Asp 5.42Ser 5.46Ser 6.48Trp 6.55Asn	3.28Trp	6.48Trp 6.51Phe 6.52Phe	6.48Trp 6.51Phe 6.52Phe

	7.39Val 7.42Gly 7.43Trp 7.46Ser						
Sulpiride	2.53Val 2.57Val 2.58Met 2.61Lys 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.36Ser 5.39Ala 5.42Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.38Phe 7.39Val 7.42Gly 7.43Trp	3.32Asp	2.61Lys 3.29Val 3.32Asp 3.36Ser 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.52Phe 6.55Asn	3.29Val 3.32Asp 3.36Ser 5.39Ala 5.42Ser 5.43Ser 6.48Trp 6.55Asn	6.51Phe	6.48Trp 6.51Phe 6.52Phe	3.28Trp 6.48Trp
SCH23390	2.53Val 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.36Ser 5.39Ala 5.42Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.39Val 7.42Gly	3.32Asp	5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.55Asn	5.39Ala		6.48Trp 6.51Phe 6.52Phe	6.48Trp 6.51Phe
SKF38393	3.28Trp	3.32Asp	3.32Asp	3.32Asp		6.51Phe	5.38Tyr

	3.29Val		5.39Ala	5.39Ala		6.52Phe	6.48Trp
	3.32Asp		5.42Ser	5.42Ser		7.35Phe	6.51Phe
	3.33Ile		5.43Ser	5.43Ser			6.52Phe
	3.36Ser		5.46Ser	5.46Ser			
	5.39Ala		6.48Trp	6.48Trp			
	5.42Ser		6.52Phe	6.55Asn			
	5.43Ser		6.55Asn				
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55Asn						
	7.35Phe						
	7.38Phe						
	7.39Val						
Eticlopride	2.53Val		3.32Asp	6.48Trp	6.48Trp	6.48Trp	3.32Asp
	2.57Val		3.36Ser	6.51Phe	6.51Phe	6.51Phe	6.51Phe
	2.58Met		5.39Ala	6.52Phe	6.52Phe		
	2.61Lys		5.43Ser				
	3.28Trp		6.48Trp				
	3.29Val		6.55Asn				
	3.32Asp						
	3.33Ile						
	3.35Cys						
	3.36Ser						
	5.39Ala						
	5.42Ser						
	5.43Ser						
	5.46Ser						
	5.47Phe						
	6.48Trp						
	6.51Phe						
	6.52Phe						
	6.55Asn						
	7.35Phe						
	7.39Val						
	7.42Gly						
	7.43Trp						
Risperidone	164Leu		2.57Val	2.57Val		6.48Trp	5.38Tyr
	2.53Val		3.28Trp	3.32Asp		6.51Phe	6.48Trp
	2.57Val		3.32Asp	6.48Trp		6.52Phe	6.51Phe
	2.58Met		3.35Cys	6.55Asn			7.35Phe

	2.61Lys 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.36Ser 5.35Asn 5.38Tyr 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.39Val 7.42Gly 7.43Trp 7.46Ser		5.35Asn 5.42Ser 5.46Ser 6.48Trp 6.55Asn				
Aripiprazole	164Leu 2.53Val 2.57Val 2.58Met 2.61Lys 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 5.35Asn 5.38Tyr 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe		164Leu 2.61Lys 3.28Trp 3.32Asp 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.55Asn	164Leu 2.61Lys 3.32Asp 5.35Asn 5.42Ser 5.46Ser 6.48Trp 6.55Asn	2.61Lys	6.48Trp 6.51Phe 6.52Phe	5.38Tyr 6.48Trp 6.51Phe

	6.55Asn 7.35Phe 7.39Val 7.42Gly 7.43Trp 7.46Ser						
Haloperidole	2.53Val 2.57Val 2.58Met 2.61Lys 3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 3.39Ser 5.39Ala 5.42Ser 5.43Ser 5.46Ser 5.47Phe 6.44Phe 6.47Cys 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.38Phe 7.39Val 7.41Phe 7.42Gly 7.43Trp 7.46Ser	3.32Asp	3.32Asp 3.35Cys 3.36Ser 5.46Ser 6.48Trp 6.55Asn 7.49Asn	3.32Asp	6.48Trp 6.51Phe	6.51Phe 6.52Phe	6.48Trp 6.51Phe 6.52Phe
Spiperone	2.53Val 2.57Val 2.58Met 2.61Lys 3.28Trp 3.29Val 3.32Asp	3.32Asp	3.28Trp 5.46Ser 6.48Trp 6.55Asn	3.28Trp 5.46Ser 6.48Trp	6.48Trp		6.48Trp

	3.33Ile 3.35Cys 3.36Ser 5.38Tyr 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.47Cys 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.39Val 7.42Gly 7.43Trp 7.46Ser						
Chlorpromazine	3.28Trp 3.29Val 3.32Asp 3.33Ile 3.35Cys 3.36Ser 5.38Tyr 5.39Ala 5.42Ser 5.43Ser 5.46Ser 6.48Trp 6.51Phe 6.52Phe 6.55Asn 7.35Phe 7.39Val 7.42Gly					6.51Phe 6.52Phe	5.38Tyr

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