Type of file: figure
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Fig S1. Docking results for outward-facing SERT model: 1) 4D docking into 47 binding pocket conformations; 2) 4D docking into 5 binding pocket conformations; 3) 4D docking into 3 binding pocket conformations. Colour coding: green-favourable score, red-unfavourable score, black-ligand not in the binding pocket. Score in kcal/mol. NO_2 out mean 6-nitroquinolone moiety directed towards the extracellular regions of SERT and NO_2 in means 6-nitroquinolone moiety directed towards the intracellular regions of SERT.

1)

47 RECEPTOR CONFORMATIONS								
Compounds	Parallel 1		Parallel 2		Parallel 3		Parallel 4	
	NO_2 out	NO_2 in	NO_2 out	NO_2 in	NO_2 out	NO_2 in	NO_2 out	NO_2 in
1	-3.91		-3.41		-0.78		-1.32	
2	-2.80		-1.55		-1.67		3.90	
3		0.51				39.74		
4					13.34		15.29	
5	23.79							
6	3.19				0.71		20.79	
7				29.74				4.69
8							12.52	
9	11.37		16.80				9.94	
10		-6.15			7.14			
11	16.96				8.02			
12							22.05	
13		-1.34	8.04		2.19		7.53	
14		4.28		7.53	7.34			
15	6.91						9.77	
16		1.57	-6.39			-1.52	6.06	
17	7.49					1.58	-8.23	
18		-1.28				6.55		
19		-8.98		2.97		10.99		23.69

2)

5 SERT CONFORMATIONS								
Compounds	Parallel 1		Parallel 2		Parallel 3		Parallel 4	
	NO_2 out	NO_2 in	NO_2 out	NO_2 in	NO_2 out	NO_2 in	NO_2 out	NO_2 in
1	0.98		-1.02		-2.81		-1.00	
2	-5.85		-3.09		-2.79		-2.45	
3		26.07				33.32		
4	12.60		13.94		12.87		10.10	
5	23.60				23.44		26.19	
6		55.07	21.01			60.74	21.95	
7		34.89	19.61				19.65	
8	15.06		13.39		14.31			26.51
9					16.67			
10		16.67	10.05		10.17			-1.00
11								
12	4.89				10.86		8.83	
13		-4.10	0.83				6.81	
14	6.81			8.87		-1.78		7.80
15	7.11		7.21			8.61		8.86
16	13.33			3.47		42.19	14.35	
17	13.17			-9.91	15.24			
18	3.21		0.28			7.97	2.82	
19		7.35	1.97		2.07		4.33	

3)

3 SERT CONFORMATIONS								
Compounds	**Parallel 1**		**Parallel 2**		**Parallel 3**		**Parallel 4**	
	NO_2 out	**NO_2 in**	**NO_2 out**	**NO_2 in**	**NO_2 out**	**NO_2 in**	**NO_2 out**	**NO_2 in**
1	-1.73		-2.72		-1.27		-2.58	
2	-2.49		-2.38		-2.47		-2.38	
3	16.16			59.98	18.28		-5.70	
4	10.81			13.71	11.28		13.82	
5	26.15		24.65		26.37		27.07	
6			23.54		21.00			
7	18.80				21.71		18.02	
8		24.17	20.02		14.44		13.69	
9				19.43		19.52		-1.81
10		24.35	10.93		9.73			18.15
11								
12	3.99		22.62			13.82		16.62
13			-2.06		3.19		-1.92	
14		-1.80	14.52		14.35		7.07	
15	2.97			9.041	6.93		4.97	
16		-3.76	11.84		12.75			-0.59
17	10.35		6.85		8.67		11.52	
18		0.83	12.86			17.39		-0.89
19	4.46		3.20		4.30			9.82

Type of file: figure
Label: Figure S2
Filename: FigS2.doc

Fig S2. Docking results for occluded SERT model: 1) 4D docking into 5 substrate binding pocket conformations; 2) 4D docking into 5 vestibular binding pocket conformations. Colour coding: green-favourable score, red-unfavourable score, black-ligand not in the binding pocket. Score in kcal/mol. NO_2 out mean 6-nitroquinolone moiety directed towards the extracellular regions of SERT and NO_2 in means 6-nitroquinolone moiety directed towards the intracellular regions of SERT.

1)

Compounds	SUBSTRATE BINDING POCKET
1	-0.14
2	-10.09
3	116.30
4	168.80
5	117.50
6	119.40
7	109.20
8	131.80
9	100.60
10	115.50
11	133.30
12	119.7
13	82.02
14	46.00
15	77.39
16	101.50
17	7.87
18	120.60
19	155.10

2)

Compounds	VESTIBULAR BINDING POCKET
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	

Type of file: figure
Label: Figure S3
Filename: FigS3.doc

Fig S3. SERT docking results: 1) Regular docking into binding pocket refined using ligand **9** and 2) Regular docking into binding pocket refined using ligand **13**. Colour coding: green-favourable score, red-unfavourable score, black-ligand not in the binding pocket. Score in kcal/mol. NO_2 out mean 6-nitroquinolone moiety directed towards the extracellular regions of SERT and NO_2 in means 6-nitroquinolone moiety directed towards the intracellular regions of SERT.

1)

REFINED STRUCTURE (9)								
Compounds	**Parallel 1**		**Parallel 2**		**Parallel 3**		**Parallel 4**	
	NO_2 out	**NO_2 in**	**NO_2 out**	**NO_2 in**	**NO_2 out**	**NO_2 in**	**NO_2 out**	**NO_2 in**
1	-20.27		-22.09		-20.15		-18.66	
2	-8.10		-6.49		-7.22		-8.03	
3	-5.55		-5.85		-5.52		-5.72	
4		0.45	-13.3			-1.51	-13.46	
5		30.77		30.91	3.98			31.24
6	4.08		4.16		4.17		4.24	
7	-8.20		-10.76			6.77	-8.92	
8	-7.62			6.39	-7.03		-8.64	
9	-12.72		-8.53		-4.94			-9.98
10	-14.99		-16.71		-16.07		-18.61	
11	0.93		8.55		4.61		7.51	
12	-13.01		-13.48		-10.95		-11.57	
13	-10.59		-16.02		-15.97			-1.17
14	-15.92		-12.86		-18.72		-9.96	
15	-10.10		-12.15		-12.22			-7.28
16	-11.55		-5.08		-11.13			42.84
17		9.18	-4.88		-6.09			15.53
18	-10.33		-10.11		-11.42		-13.72	
19	-9.82		-11.66			4.84	-9.92	

2)

REFINED STRUCTURE (13)								
Compounds	**Parallel 1**		**Parallel 2**		**Parallel 3**		**Parallel 4**	
	NO_2 out	**NO_2 in**	**NO_2 out**	**NO_2 in**	**NO_2 out**	**NO_2 in**	**NO_2 out**	**NO_2 in**
1	-20.27		-22.09		-20.15		-18.66	
2	-8.10		-6.49		-7.22		-8.03	
3	-6.56		-6.56		-3.04		-6.14	
4	-9.71		-2.58		-2.84		-2.98	
5				3.47				30.01
6	4.47		-1.77		-4.04		3.01	
7	-6.57		-10.78		-6.44		-10.39	
8	-6.33		-5.10			10.64	-6.74	
9	-3.42		-1.87		-4.73		-7.88	
10		6.82	-10.35		-10.09		-3.43	
11	16.20		7.46					17.91
12	-10.78			-6.08	-11.30		-11.86	
13	-16.16		-16.14		-16.61		-15.91	
14	-18.41		-18.10			-8.01	-18.44	
15	-10.69		-10.80		-6.77		-12.72	
16		10.86	-2.33		3.68		1.52	
17	-3.20		-2.26		-2.81		-2.86	
18	-3.52		-3.69		-8.09		-5.09	
19	-9.77		-10.85		-11.27		-5.91	