Supplementary Information

Figure A: RMSD of MAO-A

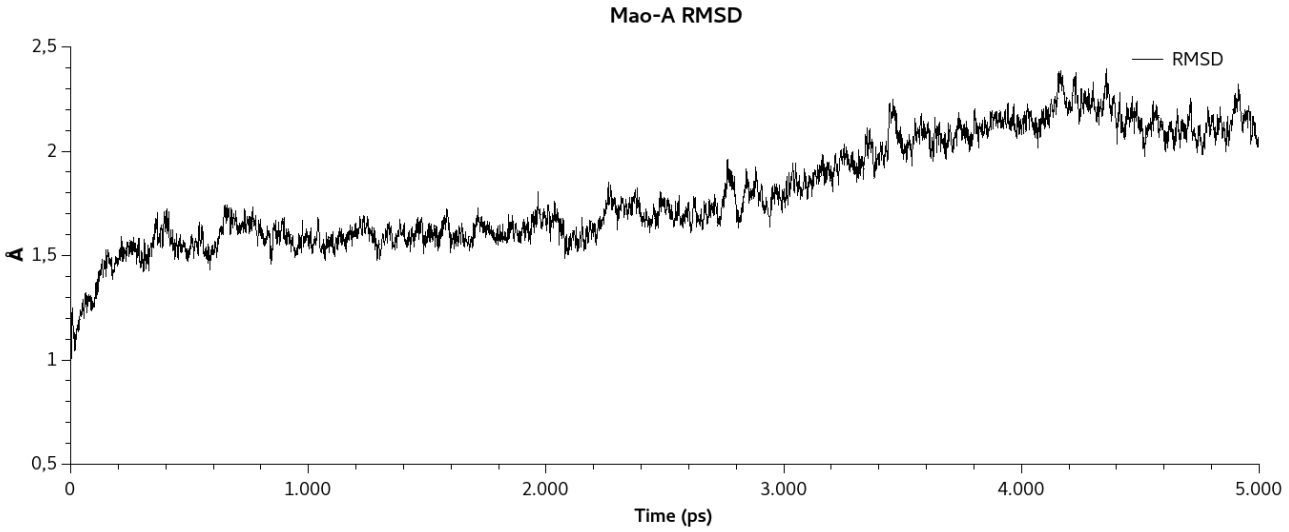


Figure A shows the RMSD of MAO-A in a simulation of 5 ns

Figure B: RMSD of MAO-B

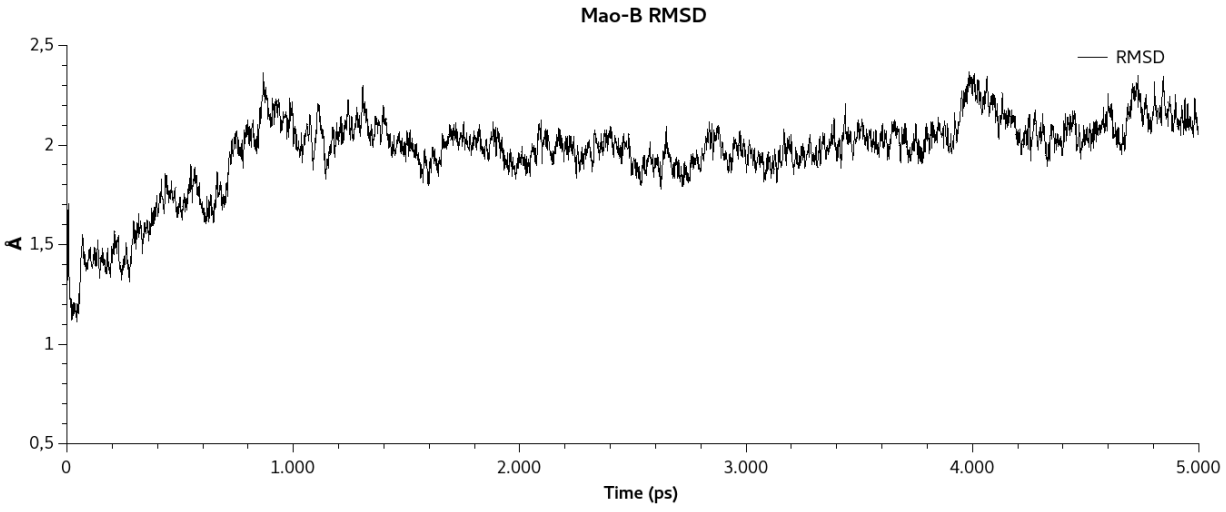


Figure B shows the RMSD of MAO-B in a simulation of 5 ns

Figure C: RMSD of SERT

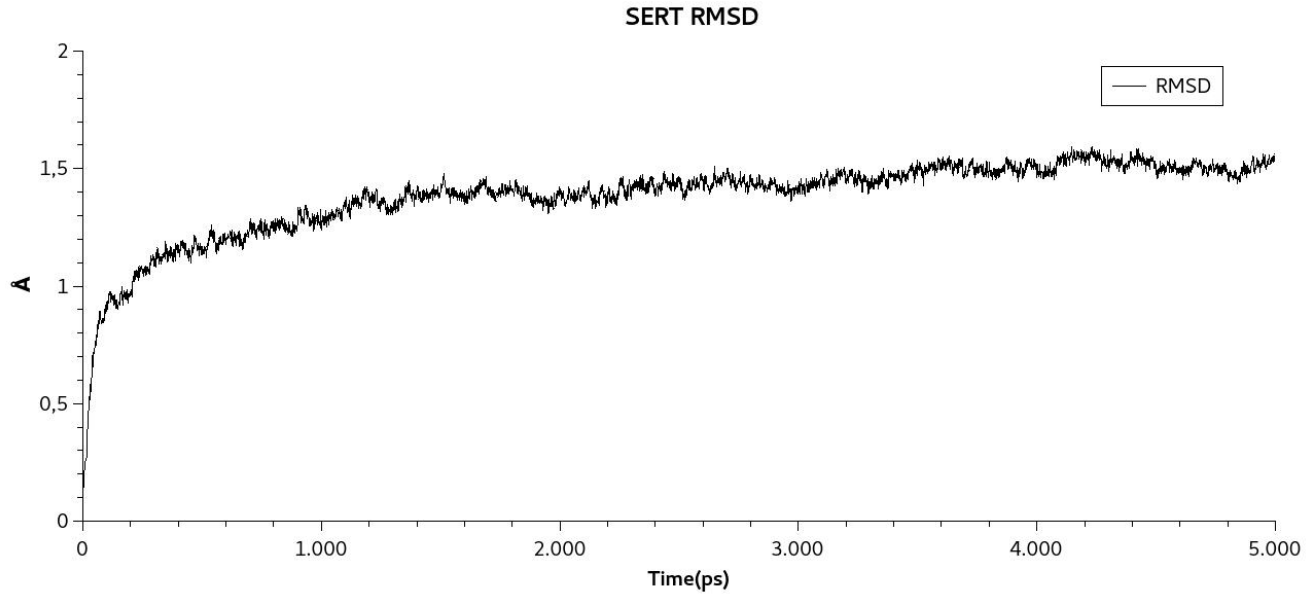


Figure C shows the RMSD of SERT in a simulation of 5 ns

Figure D: RMSD of DAT

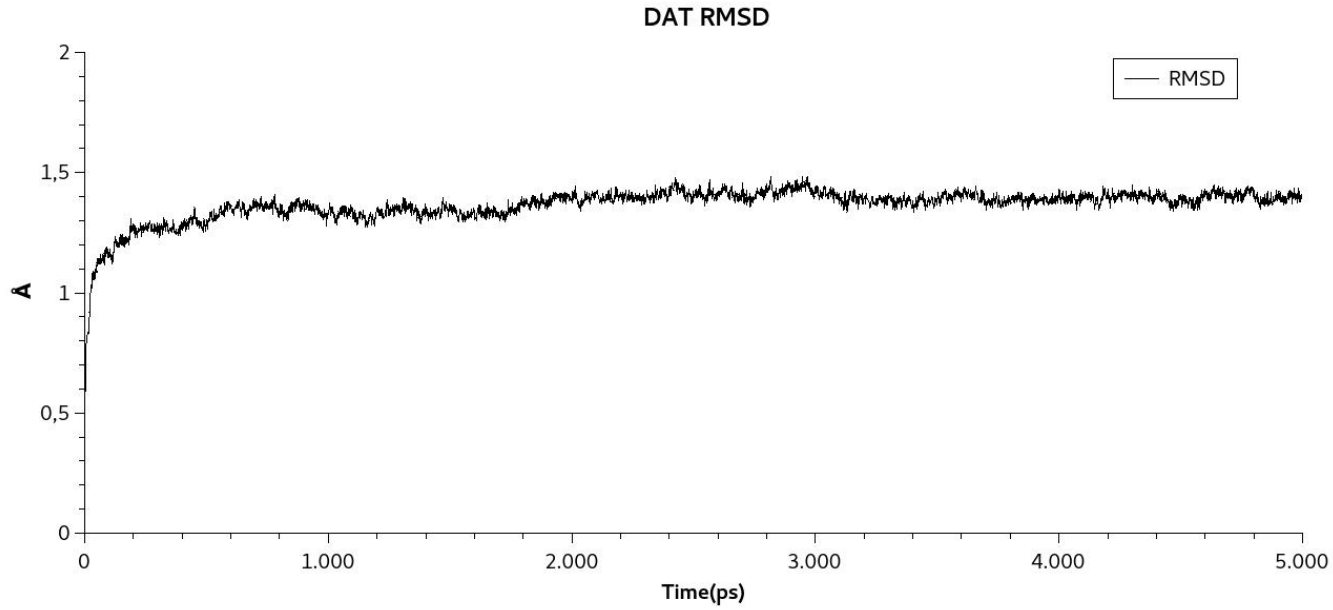


Figure D shows the RMSD of DAT in a simulation of 5 ns

Figure E: ProsaII evaluation of DAT

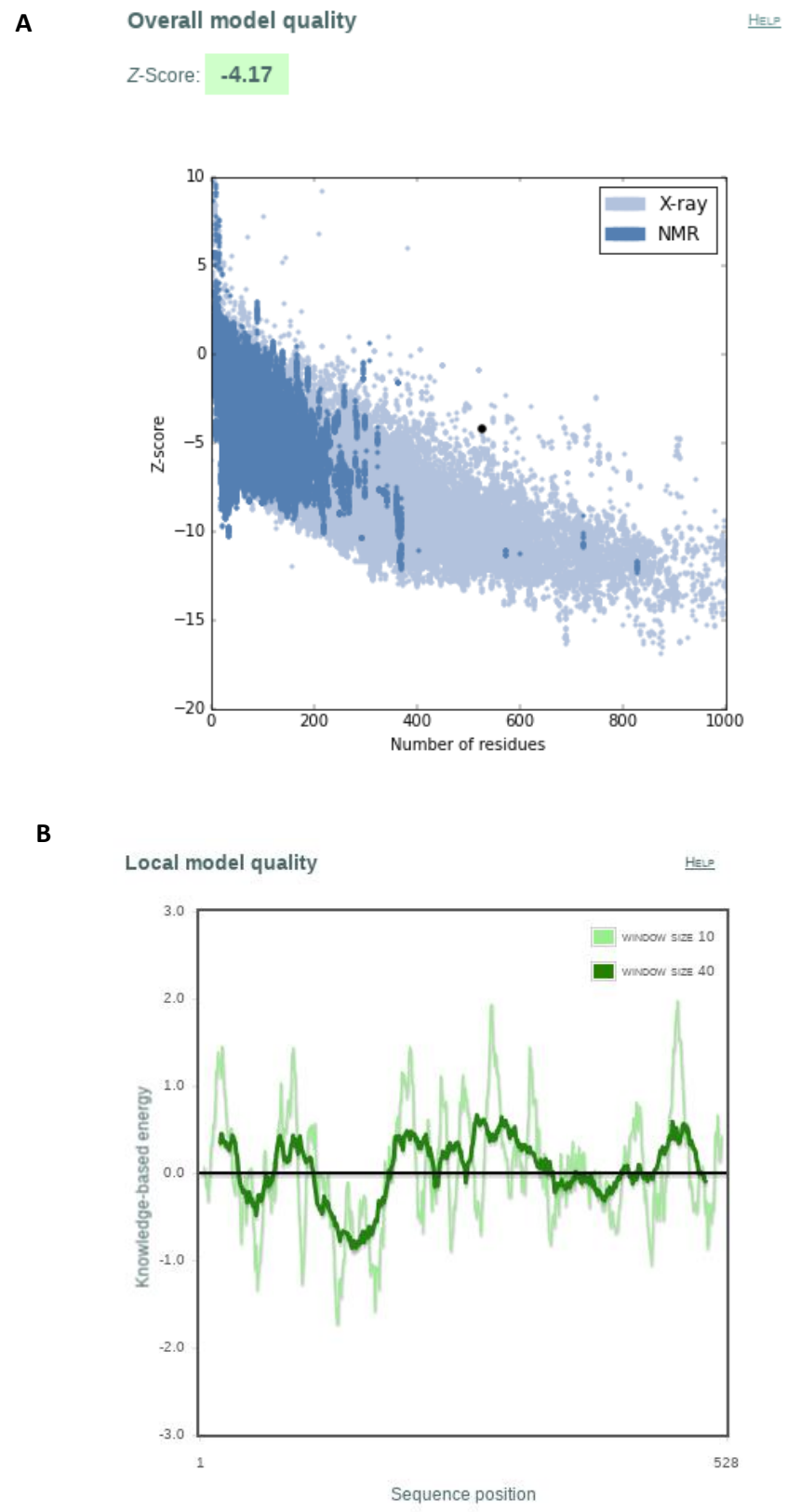
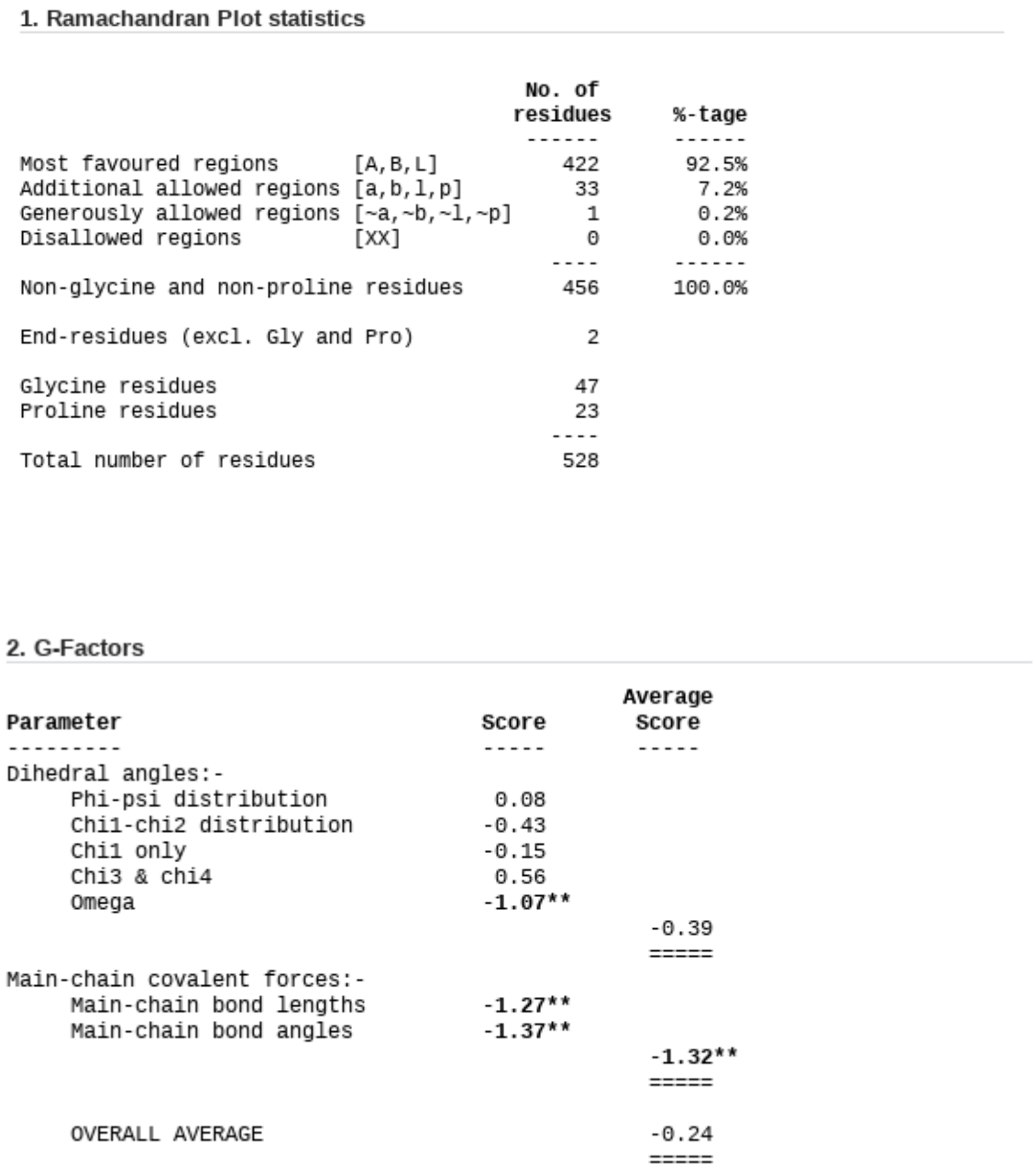


Figure E shows the evaluation of the homology model of the human DAT

Figure F: Procheck evaluation of DAT



1. Ramachandran Plot statistics

		No. of residues	%-tage
Most favoured regions	[A,B,L]	422	92.5%
Additional allowed regions	[a,b,l,p]	33	7.2%
Generously allowed regions	[~a,~b,~l,~p]	1	0.2%
Disallowed regions	[XX]	0	0.0%
Non-glycine and non-proline residues		456	100.0%
End-residues (excl. Gly and Pro)		2	
Glycine residues		47	
Proline residues		23	
Total number of residues		528	

2. G-Factors

Parameter	Score	Average Score
Dihedral angles:-		
Phi-psi distribution	0.08	
Chi1-chi2 distribution	-0.43	
Chi1 only	-0.15	
Chi3 & chi4	0.56	
Omega	**-1.07****	
		-0.39
Main-chain covalent forces:-		
Main-chain bond lengths	**-1.27****	
Main-chain bond angles	**-1.37****	
		-1.32**
OVERALL AVERAGE		-0.24

Figure F shows the evaluation of the homology model of the human DAT

Figure G: RMSD between SERT and DAT

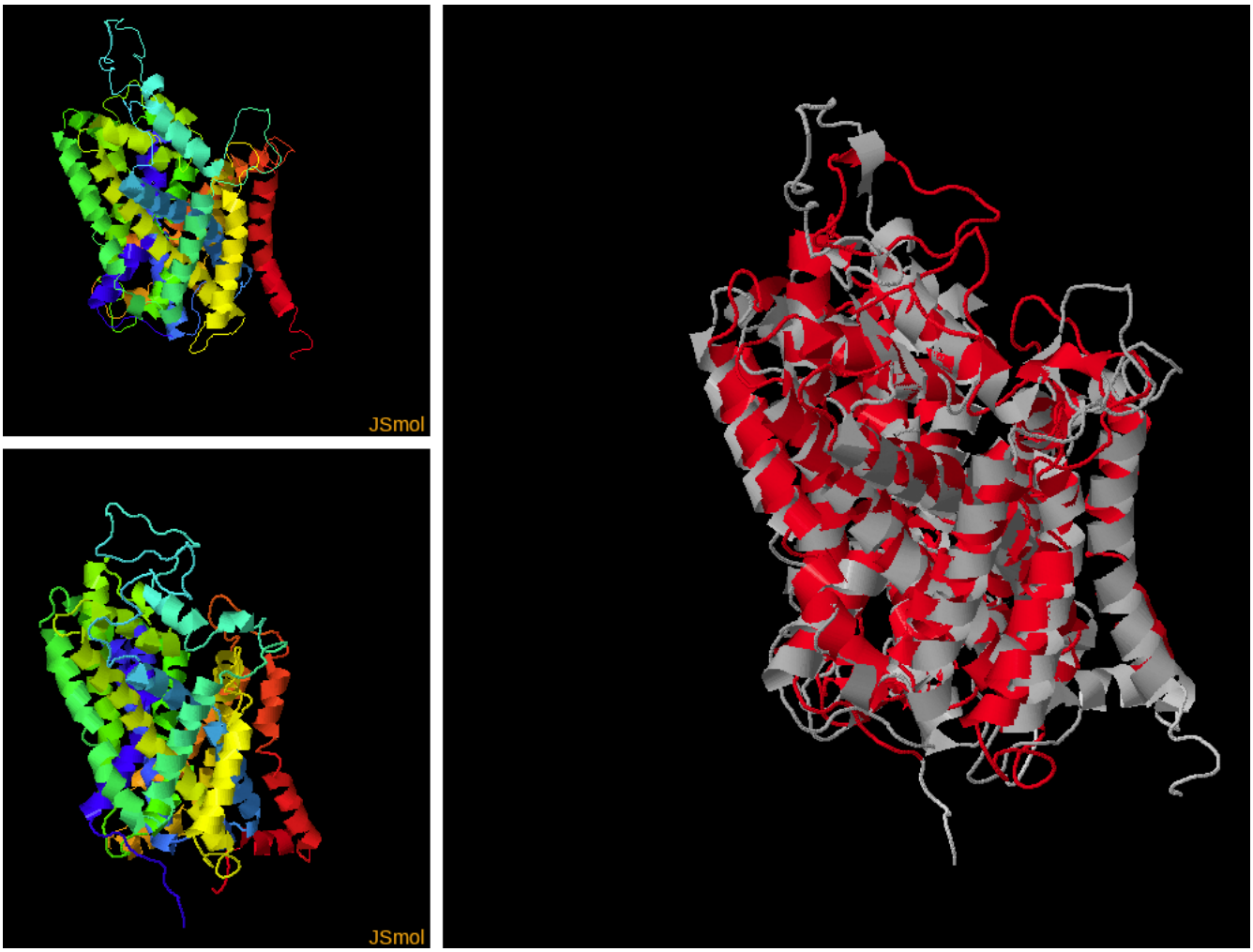


Figure G shows the structure alignment of SERT and DAT, which contains 466 equivalent positions with an RMSD of 3.0 Å (left top: DAT, left bottom: SERT). The structure alignment and the RMSD value were obtained using FatCat server (http://fatcat.burnham.org)

Figure H: Average of Similarity between all dummy atoms in DAT and MAO-B

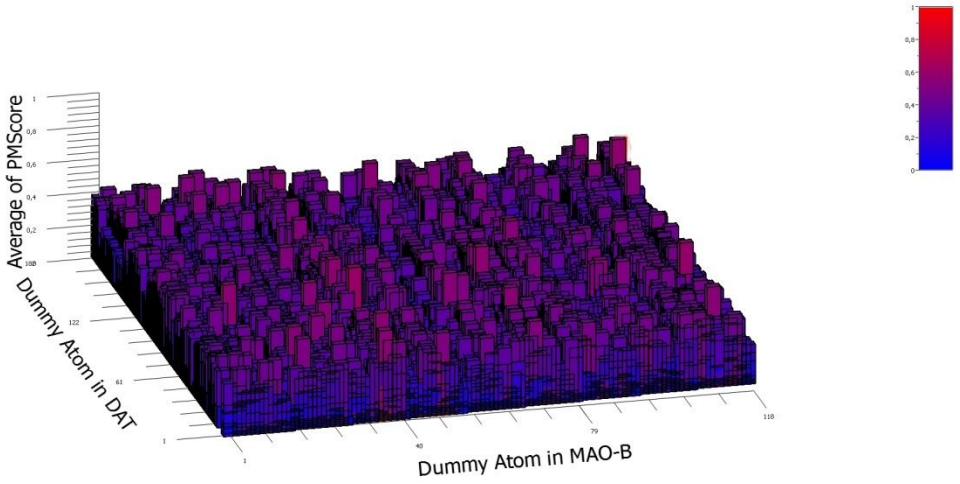


Figure H shows the average of similarity between all patterns around each dummy atom in DAT versus all patterns around each dummy atom in MAO-B (red). The dummy atoms inserted in DAT are represented on the Y axis, sorted by the Z coordinate. The dummy atoms inserted in MAO-B are represented on the X axis, sorted by the Z coordinate. The average of the PMScore is represented on the Z axis. Each colored block represents the mean of the PMScores obtained after comparing all patterns (3-10 Å). Red represents high similarity scores (PMScore > 0.5). Blue represents low similarity scores (PMScore < 0.5).

Figure I: Average of Similarity between all dummy atoms in SERT and MAO-A.

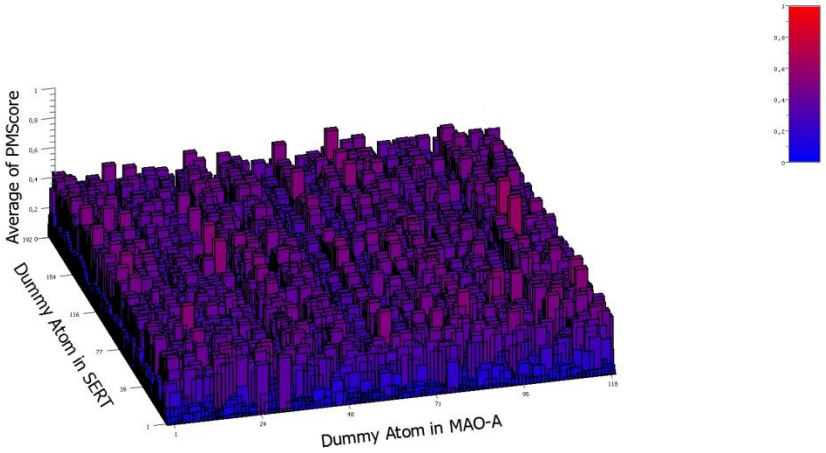


Figure I shows the average of similarity between all patterns around each dummy atom in SERT versus all patterns around each dummy atom in MAO-A (red). The dummy atoms inserted in SERT are represented on the Y axis, sorted by the Z coordinate. The dummy atoms inserted in MAO-A are represented on the X axis, sorted by the Z coordinate. The average of the PMScore is represented on the Z axis. Each colored block represents the mean of the PMScores obtained after comparing all patterns (3-10 Å). Red represents high similarity scores (PMScore > 0.5). Blue represents low similarity scores (PMScore < 0.5).

Table A: Binding sites similarities between MAOA/SERT, MAOA/DAT, MAOB/SERT and MAOB/DAT

Protein A	Protein B	PMScore
Mao-A	SERT	78,05 %
Mao-B	SERT	68,94 %
Mao-A	DAT	92,61 %
Mao-B	DAT	95,92 %

Table A shows the PMScore using MTA as ligand between the active site of MAOs and the S2 binding site of the transporters.

Figure J: Representation of a sequence-based alignment between SERT and MAO-A.

A

Range 1: 277 to 308 Graphics ▼ Next Match ▲ Previous Match

Score	Expect	Method	Identities	Positives	Gaps
16.9 bits(32)	2.4	Compositional matrix adjust.	9/32(28%)	15/32(46%)	3/32(9%)

```
Query  447  ITAVLDEFPHVWAKRRE---RFVLAVVITCFF  475
            +TA +   P + A+R +   R  +  VI C
Sbjct  277  LTAKIHFRPELPAERNQLIQRLPMGAVIKCMM  308
```

Range 2: 25 to 42 Graphics ▼ Next Match ▲ Previous Match ▲ First Match

Score	Expect	Method	Identities	Positives	Gaps
15.4 bits(28)	7.8	Compositional matrix adjust.	8/18(44%)	8/18(44%)	0/18(0%)

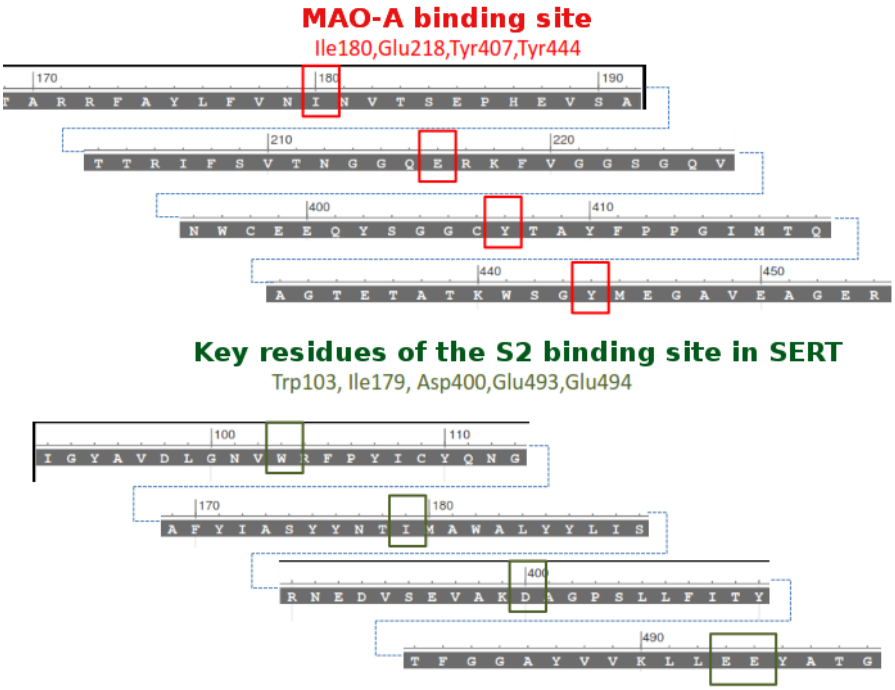
```
Query  485  GAYVVKLLEEYATGPAVL  502
            G   KLL EY    VL
Sbjct  25   GLSAAKLLTEYGVSVLVL  42
```

Range 3: 349 to 386 Graphics ▲ Previous Match ▲ First Match

Score	Expect	Method	Identities	Positives	Gaps
15.4 bits(28)	7.9	Compositional matrix adjust.	5/38(13%)	20/38(52%)	0/38(0%)

```
Query  382  VLGYMAEMRNEDVSEVAKDAGPSLLFITYAEAIANMPA  419
            ++G++   + + ++++ K+     +   YA+ + +  A
Sbjct  349  IMGFILARKADRLAKLHKEIRKKKICELYAKVLGSQEA  386
```

B



A) Blastp alignment between human SERT and MAO-A. B) Some key residues of the binding sites of MAO-A and SERT are remarked in boxes.