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Supplemental Information

A Computational Analysis of the Factors Governing the Dynamics of α7 nAChR and Its Homologs

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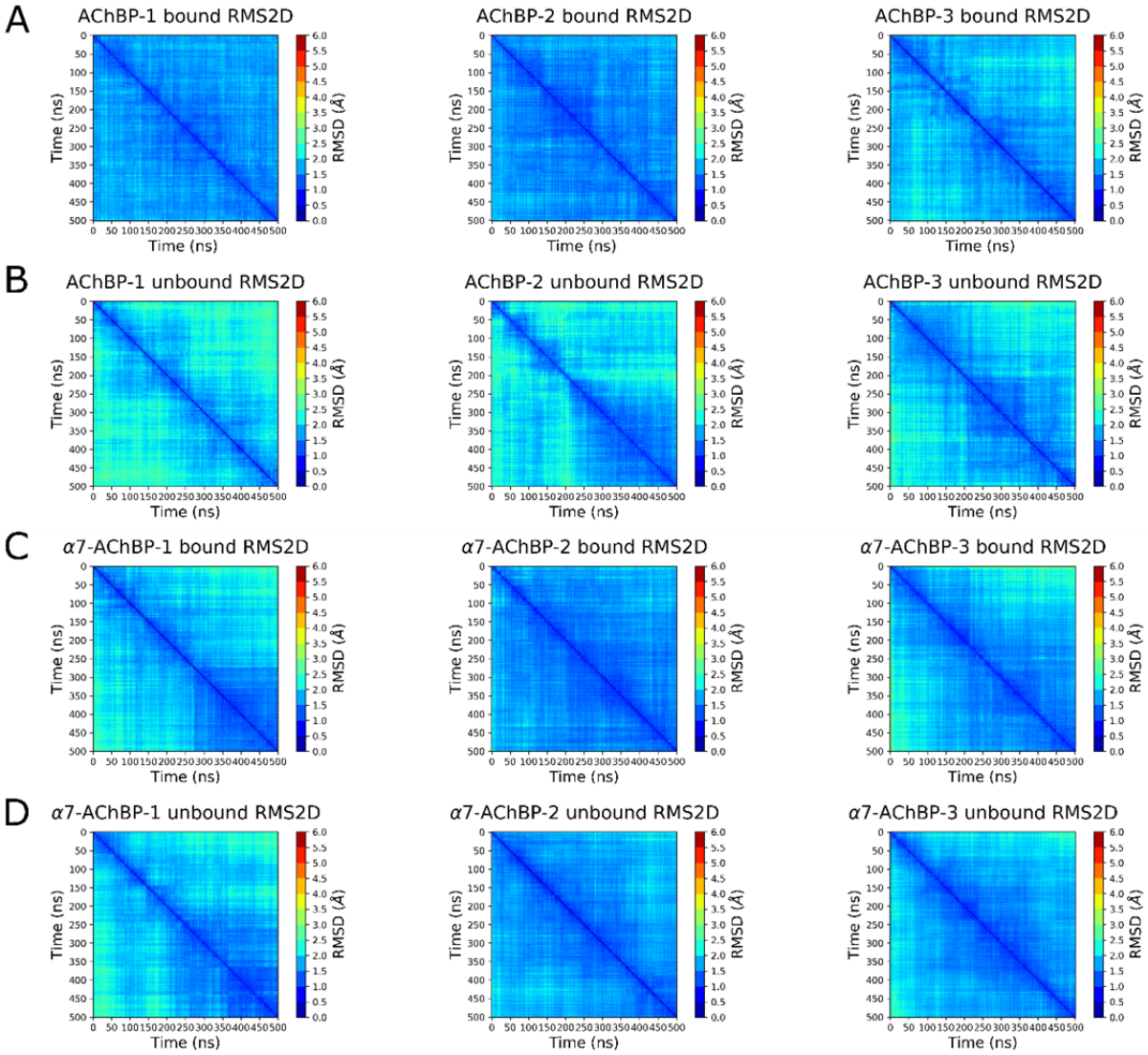
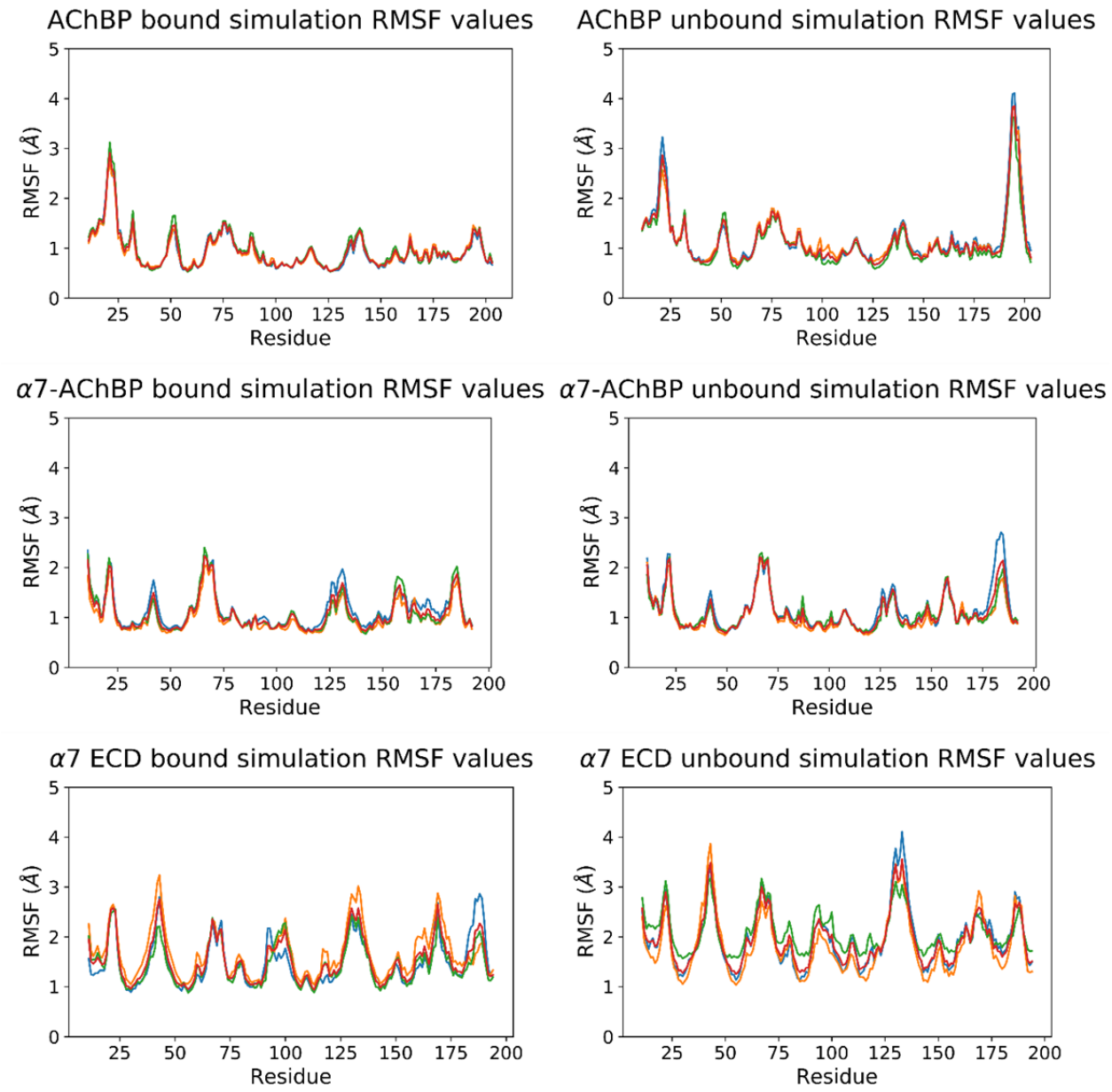
Supporting Information

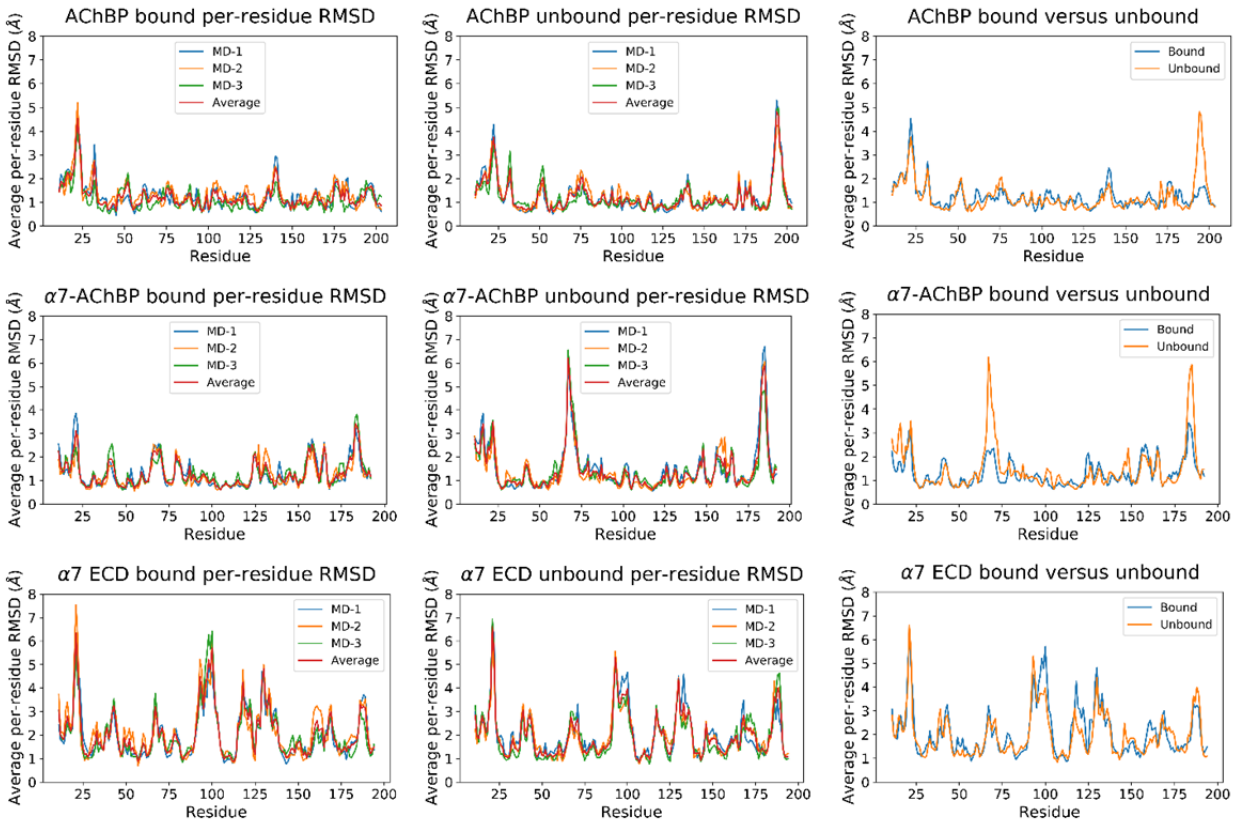
Supporting Figures



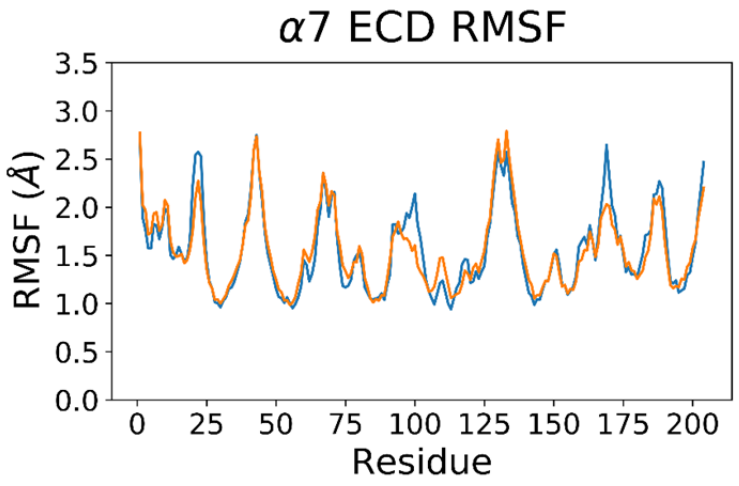
Supporting Figure 1: 2D RMSD plots calculated for the epibatidine-bound and unbound AChBP and α7-AChBP simulations.



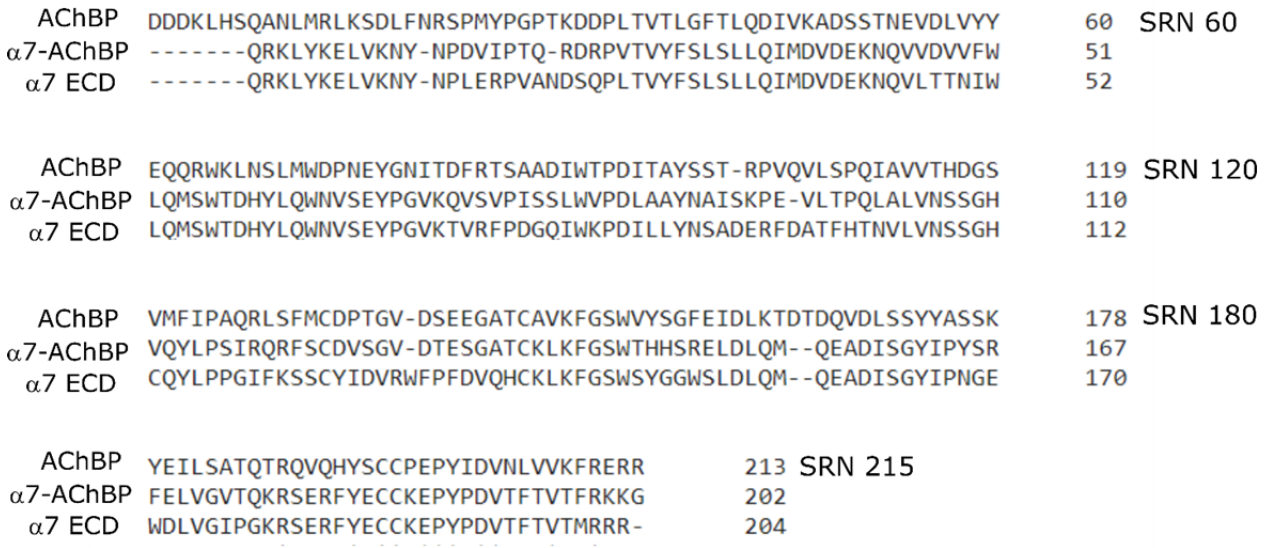
Supporting Figure 2: The RMSF values calculated for each individual simulation and the average RMSF calculated from the individual values. Blue, orange, and green stand for the independent replica simulations, and red stands for the average RMSF calculated for the replica simulations. Top row: Epibatidine-bound (left) and unbound (right) AChBP, middle row: epibatidine-bound (left) and unbound (right) α7-AChBP, bottom row: epibatidine-bound (left) and unbound (right) α7 ECD.



Supporting Figure 3: Average per-residue RMSD values calculated for the replica simulations.



Supporting Figure 4: Normalized α7 ECD epibatidine-bound (blue) and unbound (orange) RMSF values.



Supporting Figure 5: Alignment of the AChBP, α7-AChBP, and α7 ECD sequences and the corresponding standard residue numbering (SRN).

Supporting Tables

Supporting Table 1: Jensen-Shannon divergences calculated for the epibatidine-bound and unbound simulations of AChBP (top row), α7-AChBP (middle row), and α7 ECD simulations (bottom row).

AChBP bound					**AChBP unbound**			
Simulation	**1**	**2**	**3**		**Simulation**	**1**	**2**	**3**
1	**0.00**	**0.05**	**0.44**		**1**	**0.00**	**0.51**	**0.54**
2	**0.05**	**0.00**	**0.38**		**2**	**0.51**	**0.00**	**0.61**
3	**0.44**	**0.38**	**0.00**		**3**	**0.54**	**0.61**	**0.00**
α7-AChBP bound					**α7-AChBP unbound**			
Simulation	**1**	**2**	**3**		**Simulation**	**1**	**2**	**3**
1	**0.00**	**0.56**	**0.64**		**1**	**0.00**	**0.59**	**0.53**
2	**0.56**	**0.00**	**0.65**		**2**	**0.59**	**0.00**	**0.50**
3	**0.64**	**0.65**	**0.00**		**3**	**0.53**	**0.50**	**0.00**

α7 ECD bound					α7 ECD unbound			
Simulation	**1**	**2**	**3**		**Simulation**	**1**	**2**	**3**
1	**0.00**	**0.64**	**0.65**		**1**	**0.00**	**0.59**	**0.63**
2	**0.64**	**0.00**	**0.61**		**2**	**0.59**	**0.00**	**0.57**
3	**0.65**	**0.61**	**0.00**		**3**	**0.63**	**0.57**	**0.00**

Supporting Table 2: The C-loop opening distances calculated for the epibatidine-bound and unbound AChBP, α7-AChBP, and α7 ECD simulations. Each distance was calculated as the α-carbon distances between the positive and negative face residues C195 and I123 for AChBP, C184 and L114 for α7-AChBP, and C190 and L119 for α7 ECD. All units are in Angstroms.

Interface	AChBP-1 bound	AChBP-2 bound	AChBP-3 bound	AChBP-1 unbound	AChBP-2 unbound	AChBP-3 unbound
AB	9.1	9.2	9.7	16.2	17.4	9.6
BC	9.1	9.3	8.9	16.6	9.2	18.4
CD	9.3	9.0	9.8	16.6	13.7	8.2
DE	9.0	9.2	9.1	14.3	7.7	11.7
EA	10.5	10.5	9.2	8.1	15.3	8.5
Interface	**α7-AChBP-1 bound**	**α7-AChBP-2 bound**	**α7-AChBP-3 bound**	**α7-AChBP-1 unbound**	**α7-AChBP-2 unbound**	**α7-AChBP-3 unbound**
AB	12.8	14.1	18.1	10.9	9.9	11.6
BC	9.7	8.0	11.9	13.0	13.5	7.5
CD	10.7	12.5	7.2	10.8	13.8	11.3
DE	13.9	11.3	9.3	12.2	10.1	13.0
EA	10.7	9.8	11.7	19.8	11.3	9.9

Interface	α7 ECD-1 bound	α7 ECD-2 bound	α7 ECD-3 bound	α7 ECD-1 unbound	α7 ECD-2 unbound	α7 ECD-3 unbound
AB	20.2	8.2	15.7	10.5	7.4	8.9
BC	12.4	10.6	10.8	8.4	8.4	8.8
CD	9.5	11.3	10.1	16.7	8.0	11.8
DE	8.5	8.4	13.1	13.4	8.5	8.4
EA	12.6	11.8	11.4	8.4	8.8	5.8

Supporting Table 3: Sequences of the regions that showed a large RMSF difference between α7 ECD and the other two proteins. Green color indicates identical residues, orange color indicates similar residues, and red color indicates gaps and different residues.

α7-AChBP 38-46	D	V	D	E	K	N	Q	V	V
α7 42-50	D	V	D	E	K	N	Q	V	L
α7-AChBP 164-169	P	Y	S	R	F	E			
α7 170-175	P	N	G	E	W	D			
α7-AChBP 91-99	A	I	S	K	P	E	-	V	L
α7 95-104	S	A	D	E	R	F	D	A	T
α7-AChBP 127-130	G	V	-	D	T				
α7 132-136	V	R	W	F	P				
AChBP 74-80	P	N	E	Y	G	N	I		
α7-AChBP 65-71	V	S	E	Y	P	G	V		