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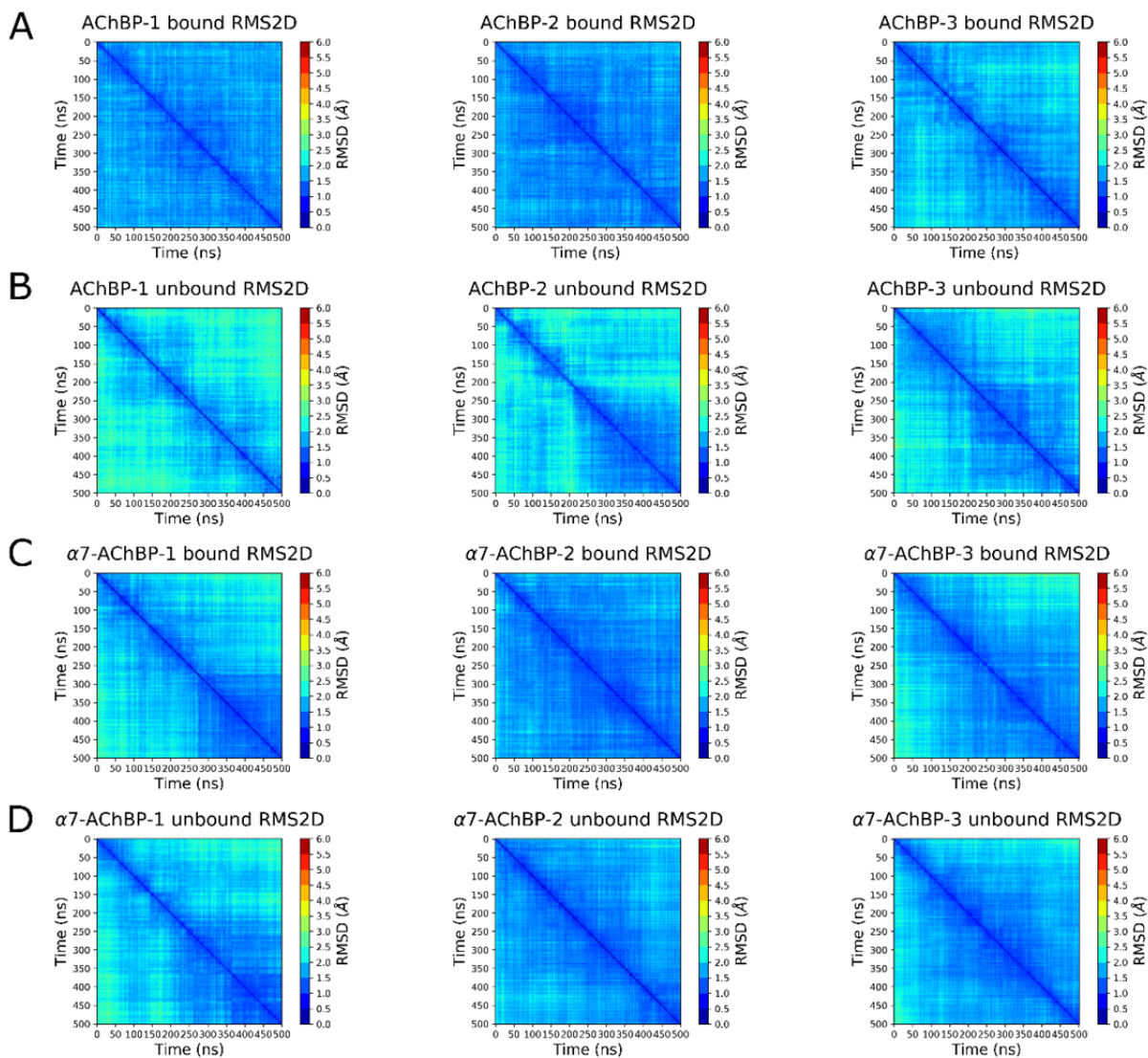
**Supplemental Information**

**A Computational Analysis of the Factors Governing the Dynamics of  $\alpha 7$   
nAChR and Its Homologs**

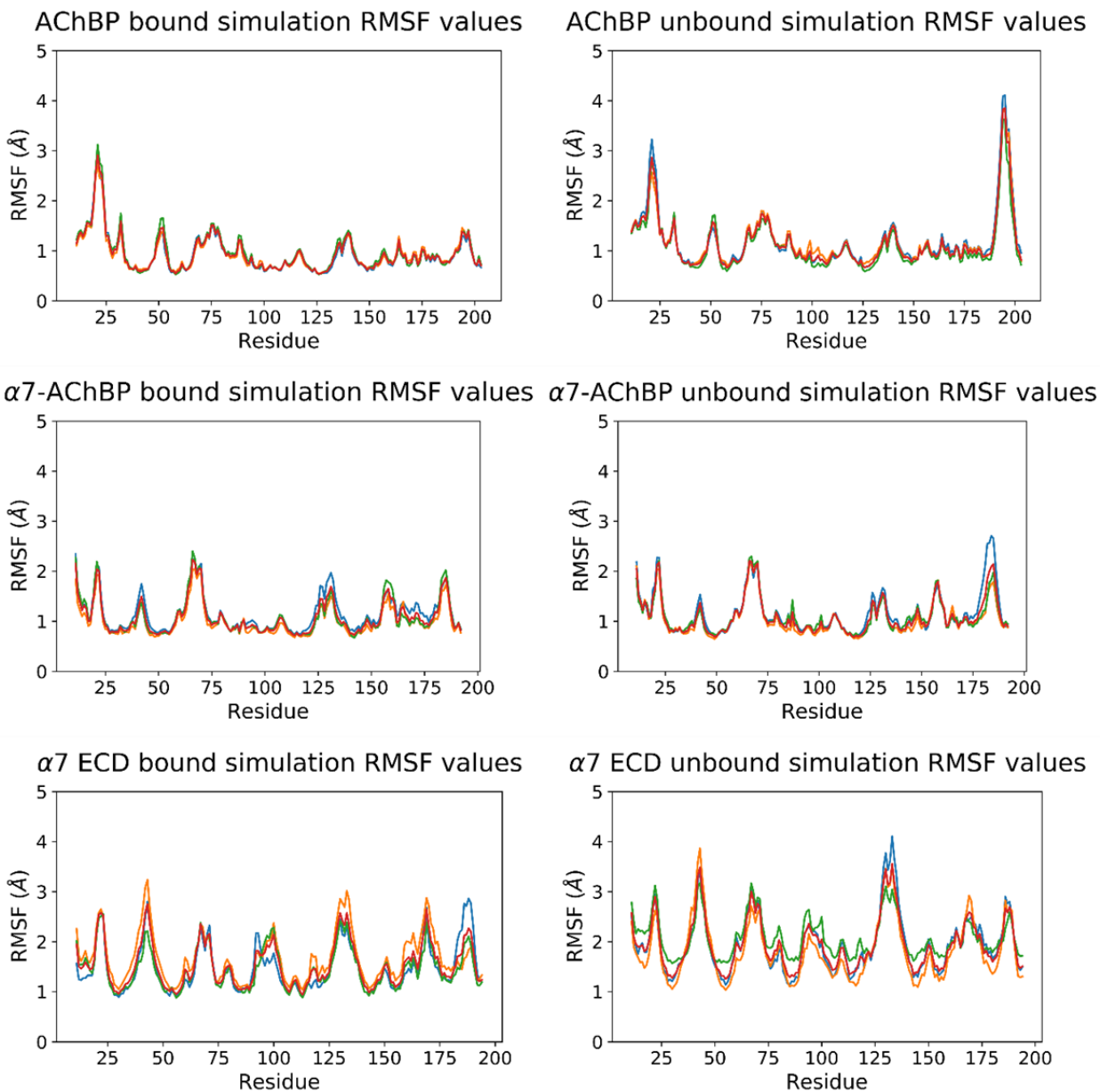
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# Supporting Information

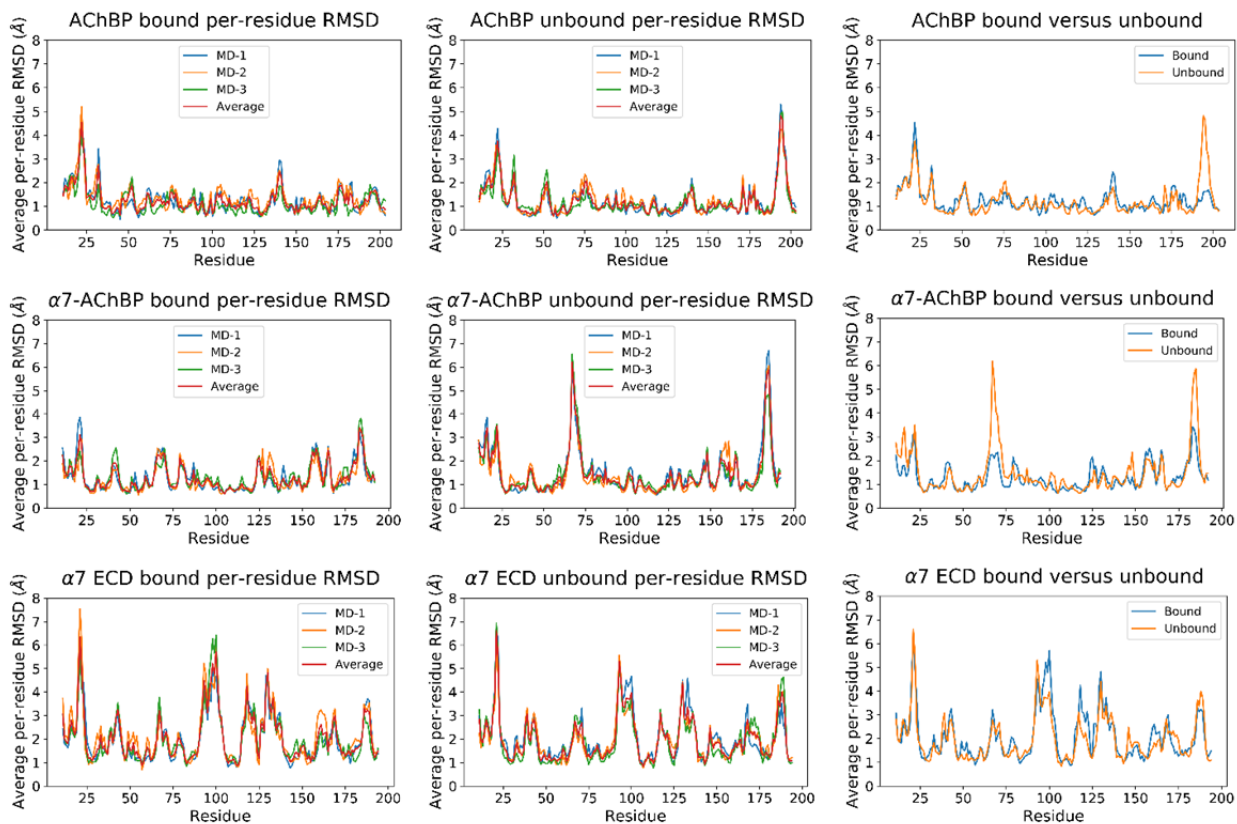
## Supporting Figures



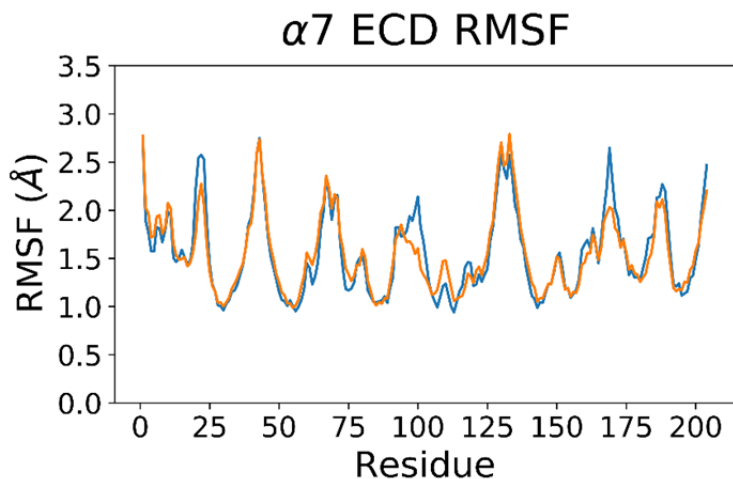
Supporting Figure 1: 2D RMSD plots calculated for the epibatidine-bound and unbound AChBP and  $\alpha$ 7-AChBP simulations.



**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)  $\alpha 7$ -AChBP, bottom row: epibatidine-bound (left) and unbound (right)  $\alpha 7$  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.**

AChBP	DDDKLHSQANLMRLKSDLFNRSMPYGPPTKDDPLTVTLGFTLQDIVKADSSTNEVDLVVY	60	SRN 60
$\alpha$ 7-AChBP	-----QRKLYKELVKNY-NPDVIPTQ-RDRPVTYFSLSLQIMDVDEKNQVVDVFW	51	
$\alpha$ 7 ECD	-----QRKLYKELVKNY-NPLERPVANDSQPLTVYFSLSLQIMDVDEKNQVLTNIW	52	
AChBP	EQQRWKLNSLMWDPNEYGNITDFRTSAADIWTPDITAYSST-RPVQVLSQIAVVTHDGS	119	SRN 120
$\alpha$ 7-AChBP	LQMSWTDHYLQWNVSEYPGVKQVSVPISSLWVPDLAAYNAISKPE-VLTPQLALVNSSGH	110	
$\alpha$ 7 ECD	LQMSWTDHYLQWNVSEYPGVKTVRFPDGGQIWKPDILLYNSADERFDATFHTNVLVNSSGH	112	
AChBP	VMFIPAQRSLFMCDPTGV-DSEEGATCAVKFGSWVYSGFEIDLKTDTDQVDLSSYYASSK	178	SRN 180
$\alpha$ 7-AChBP	VQYLPsirQRFSCDVSGV-DTESGATCKLKFGSWTHHSRELDLQM--QEADISGYIPYSR	167	
$\alpha$ 7 ECD	CQYLPpGIFKSSCYIDVRWFPFDVQhCKLKFGSWSYGGWSLDLQM--QEADISGYIPNGE	170	
AChBP	YEILSATQTRVQVQHYSCCPEPYIDVNLVVKFRERR	213	SRN 215
$\alpha$ 7-AChBP	FELVGVTQKRSErFYECCKEPYPDVTFTVTFRKKG	202	
$\alpha$ 7 ECD	WDLVGIPGKRSErFYECCKEPYPDVTFTVTMRRR-	204	

**Supporting Figure 5: Alignment of the AChBP,  $\alpha$ 7-AChBP, and  $\alpha$ 7 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),  $\alpha$ 7-AChBP (middle row), and  $\alpha$ 7 ECD simulations (bottom row).**

<b>AChBP bound</b>					<b>AChBP unbound</b>			
<b>Simulation</b>	<b>1</b>	<b>2</b>	<b>3</b>		<b>Simulation</b>	<b>1</b>	<b>2</b>	<b>3</b>
<b>1</b>	<b>0.00</b>	<b>0.05</b>	<b>0.44</b>		<b>1</b>	<b>0.00</b>	<b>0.51</b>	<b>0.54</b>
<b>2</b>	<b>0.05</b>	<b>0.00</b>	<b>0.38</b>		<b>2</b>	<b>0.51</b>	<b>0.00</b>	<b>0.61</b>
<b>3</b>	<b>0.44</b>	<b>0.38</b>	<b>0.00</b>		<b>3</b>	<b>0.54</b>	<b>0.61</b>	<b>0.00</b>
<b><math>\alpha</math>7-AChBP bound</b>					<b><math>\alpha</math>7-AChBP unbound</b>			
<b>Simulation</b>	<b>1</b>	<b>2</b>	<b>3</b>		<b>Simulation</b>	<b>1</b>	<b>2</b>	<b>3</b>
<b>1</b>	<b>0.00</b>	<b>0.56</b>	<b>0.64</b>		<b>1</b>	<b>0.00</b>	<b>0.59</b>	<b>0.53</b>
<b>2</b>	<b>0.56</b>	<b>0.00</b>	<b>0.65</b>		<b>2</b>	<b>0.59</b>	<b>0.00</b>	<b>0.50</b>
<b>3</b>	<b>0.64</b>	<b>0.65</b>	<b>0.00</b>		<b>3</b>	<b>0.53</b>	<b>0.50</b>	<b>0.00</b>

$\alpha 7$ bound	ECD				$\alpha 7$ unbound	ECD		
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,  $\alpha 7$ -AChBP, and  $\alpha 7$  ECD simulations. Each distance was calculated as the  $\alpha$ -carbon distances between the positive and negative face residues C195 and I123 for AChBP, C184 and L114 for  $\alpha 7$ -AChBP, and C190 and L119 for  $\alpha 7$  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	$\alpha 7$ -AChBP-1 bound	$\alpha 7$ -AChBP-2 bound	$\alpha 7$ -AChBP-3 bound	$\alpha 7$ -AChBP-1 unbound	$\alpha 7$ -AChBP-2 unbound	$\alpha 7$ -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	$\alpha 7$ ECD-1 bound	$\alpha 7$ ECD-2 bound	$\alpha 7$ ECD-3 bound	$\alpha 7$ ECD-1 unbound	$\alpha 7$ ECD-2 unbound	$\alpha 7$ ECD-3 unbound
<b>AB</b>	20.2	8.2	15.7	10.5	7.4	8.9
<b>BC</b>	12.4	10.6	10.8	8.4	8.4	8.8
<b>CD</b>	9.5	11.3	10.1	16.7	8.0	11.8
<b>DE</b>	8.5	8.4	13.1	13.4	8.5	8.4
<b>EA</b>	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  $\alpha 7$  ECD and the other two proteins. Green color indicates identical residues, orange color indicates similar residues, and red color indicates gaps and different residues.**

$\alpha 7$ -AChBP 38-46	D	V	D	E	K	N	Q	V	V
$\alpha 7$ 42-50	D	V	D	E	K	N	Q	V	L
$\alpha 7$ -AChBP 164-169	P	Y	S	R	F	E			
$\alpha 7$ 170-175	P	N	G	E	W	D			
$\alpha 7$ -AChBP 91-99	A	I	S	K	P	E	-	V	L
$\alpha 7$ 95-104	S	A	D	E	R	F	D	A	T
$\alpha 7$ -AChBP 127-130	G	V	-	D	T				
$\alpha 7$ 132-136	V	R	W	F	P				
AChBP 74-80	P	N	E	Y	G	N	I		
$\alpha 7$ -AChBP 65-71	V	S	E	Y	P	G	V		