Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information of

Characterization of the Binding Mode of the PET Tracer [^{18}F]ASEM with a Chimera Structure of the α7 Nicotinic Acetylcholine Receptor

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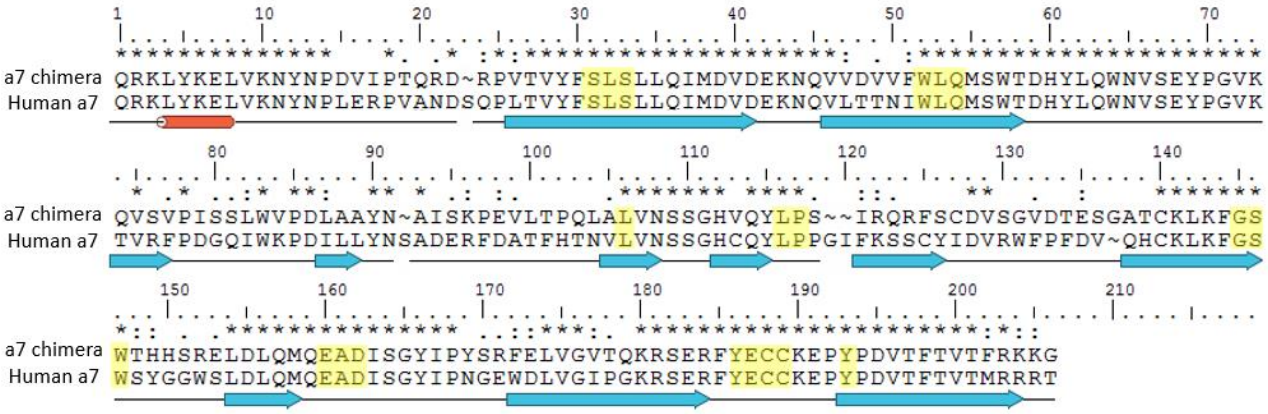
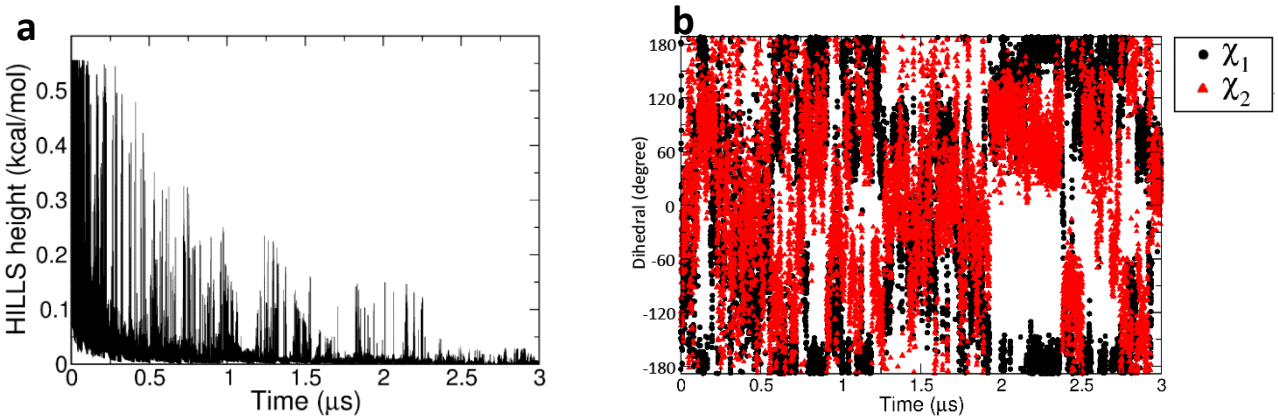
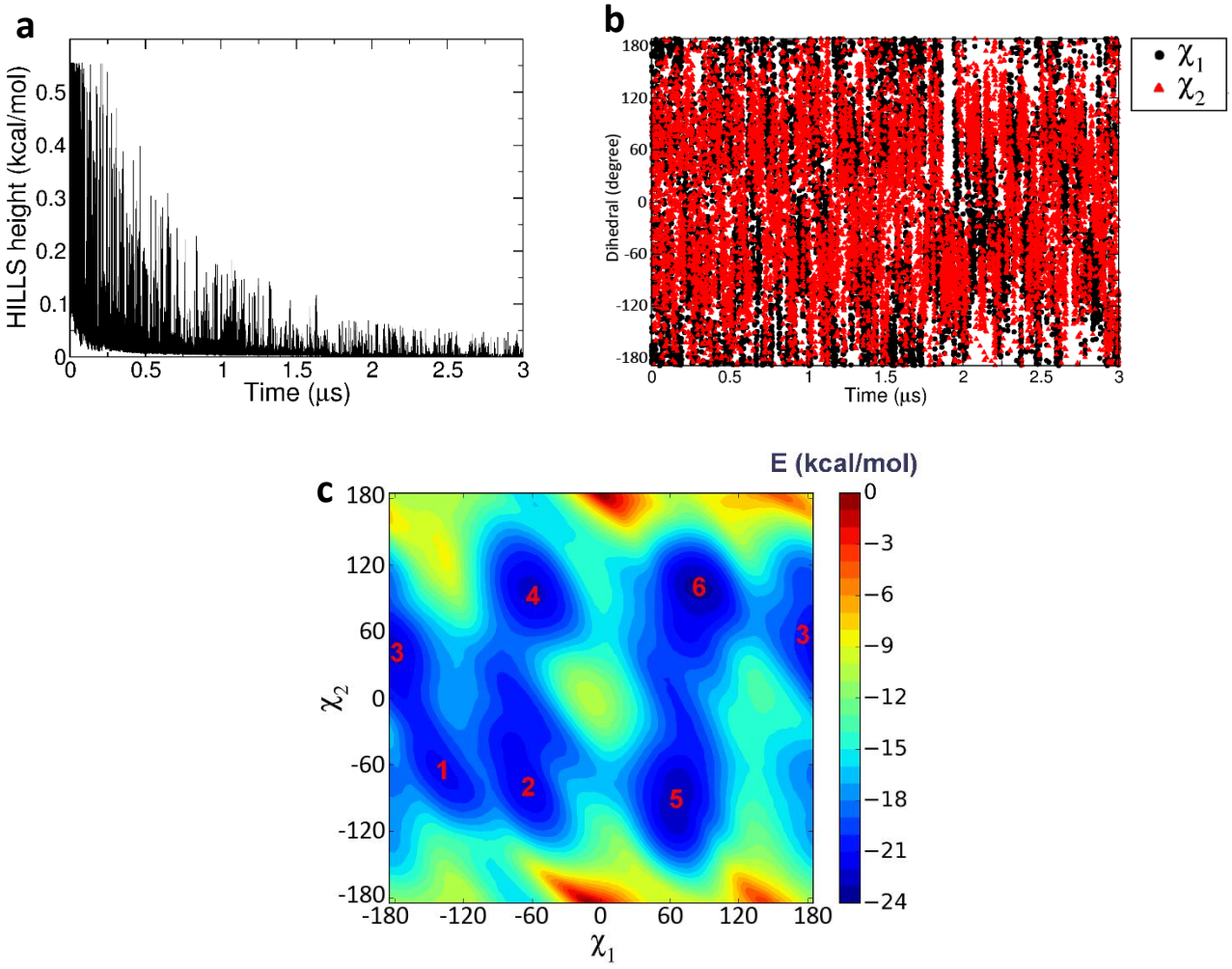


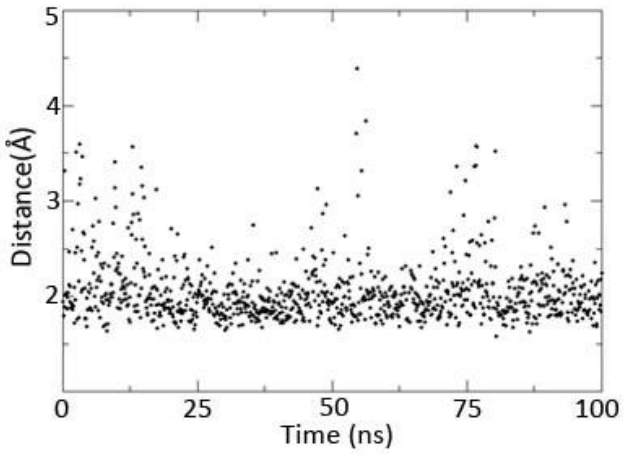
Supplementary Fig. S1. Sequence alignment between α7-AChBP with α7-nAChR. Yellow indicates binding site residues. Secondary structures are shown schematically below the sequence.



Supplementary Fig. S2. (**a**) Evolution of the HILLS height of the Gaussian potentials added in the metadynamics simulation for the holo-system. (**b**) Evolution of two collective variables (the side chain dihedral angles χ_1 and χ_2 of Trp53) in the metadynamics simulation for the holo-system.

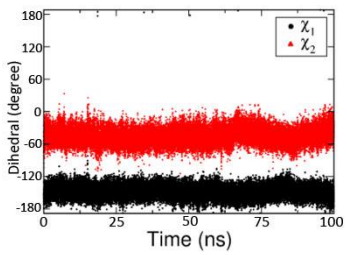
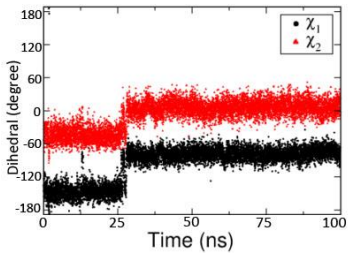
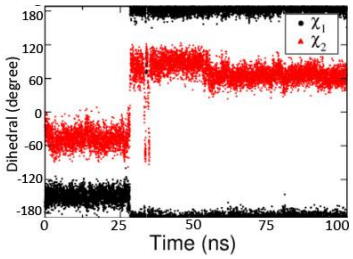
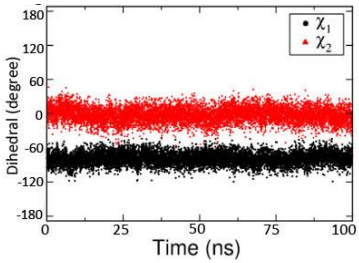
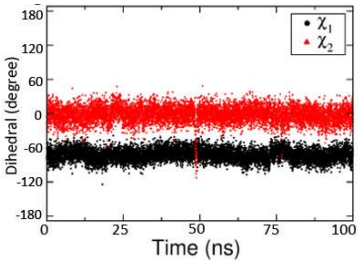
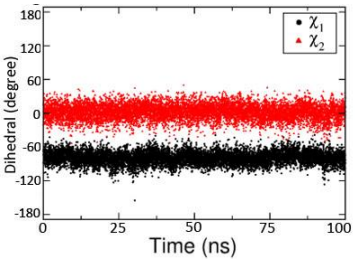
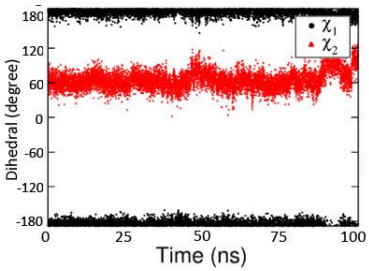
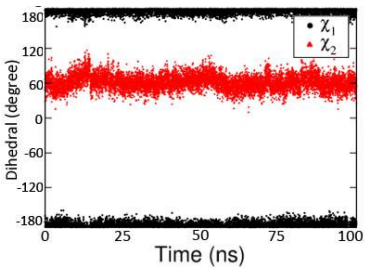
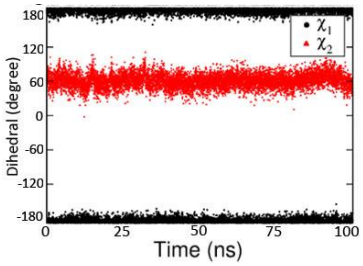
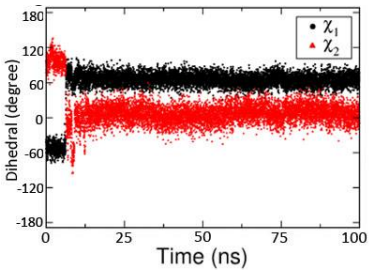
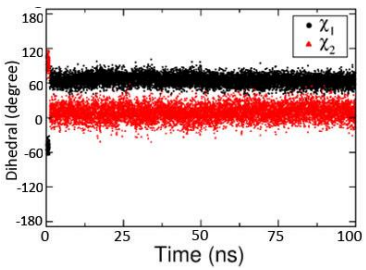
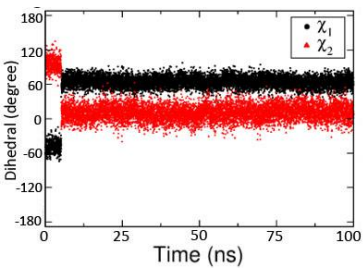
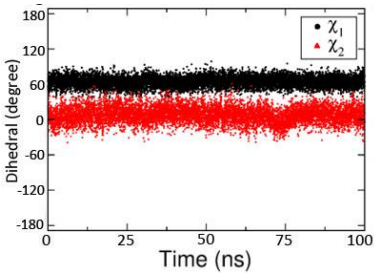
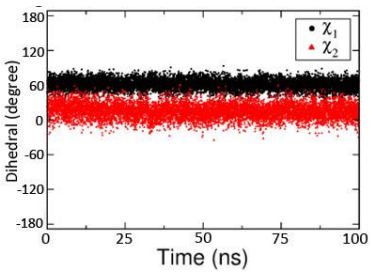
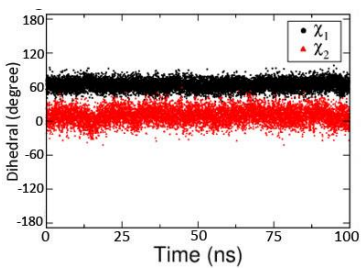
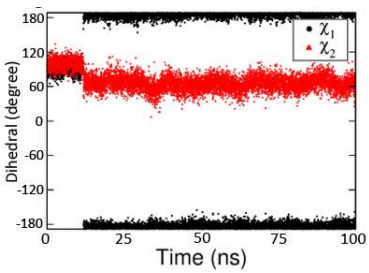
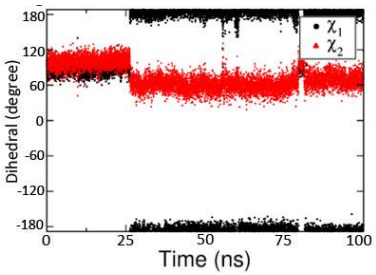
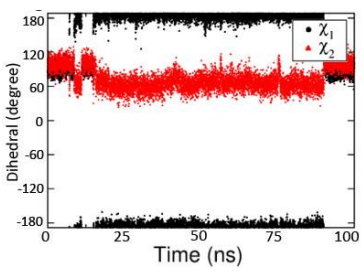


Supplementary Fig. S3. (**a**) Evolution of the HILLS height of the Gaussian potentials added in the metadynamics simulation for the apo-system. (**b**) Evolution of two collective variables (the side chain dihedral angles χ_1 and χ_2 of Trp53) in the metadynamics simulation for the apo-system. (**c**) Free energy surface (FES) with respect to the two collective variables obtained from metadynamics simulation for the apo-system.



Supplementary Fig. S4. Evolution of the distance between the polar hydrogen on the diazobicyclic head group of ASEM and the backbone oxygen of Trp145 for state 5.

Supplementary Table S1. Evolution of χ_1 and χ_2 of Trp53 of the α7-AChBP/ASEM complex. For each state, three independent MD simulations were carried out.

	Simulation 1	Simulation 2	Simulation 3
State 1			
State 2			
State 3			
State 4			
State 5			
State 6			

Supplementary Table S2. Decomposition of docking score for binding site residues of state 5.

	[a]E_{vdw} (kcal/mol)	[b]E_{coul} (kcal/mol)
Leu33	-0.951	0.668
Ser34	-0.841	-0.392
Trp53	-9.445	0.056
Leu54	-2.105	-1.495
Gln55	-4.862	0.405
Tyr91	-1.931	-2.805
Leu116	-4.601	-0.730
Ser144	-1.172	-9.331
Trp145	-4.957	-4.484
Tyr184	-6.300	-2.325
Cys186	-2.839	-0.615
Cys187	-1.267	-1.085
Tyr191	-3.074	0.942

[a] Van der Waals energy decomposition from Glide docking;

[b] Electrostatic energy decomposition from Glide docking.

Supplementary Table S3. Hydrogen bond analysis for ASEM and Trp145 in state 5.

#Acceptor	DonorH	Donor	Frames	Frac	AvgDist	AvgAng
Trp145@O	**ASEM@H20**	**ASEM@N1**	**638**	**0.638**	**2.81**	**148.8°**

Supplementary Table S4. MM/GBSA decomposition for binding site residues of state 5.

Residue	[*](+)Tyr91	(+)Trp145	(+)Tyr184	(+)Glu185	(+)Cys186	(+)Tyr191	(-)Ser34	(-)Trp53	(-)Gln55	(-)Leu116
ΔG (kcal/mol)	-1.50±1.20	-1.92±0.88	-3.60±0.66	-1.92±0.43	-3.09±0.57	-2.43±0.56	-1.36±0.32	-3.35±0.47	-0.88±0.42	-0.94±0.31

[*] (+) represents the principal face and (-) the complementary face.