Trifluoperazine Regulation of Calmodulin Binding to Fas: A Computational Study

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Running Title: Role of TFP in CaM-Fas binding

Supporting Information

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Trifluoperazine (TFP) structure and force field charge parameters

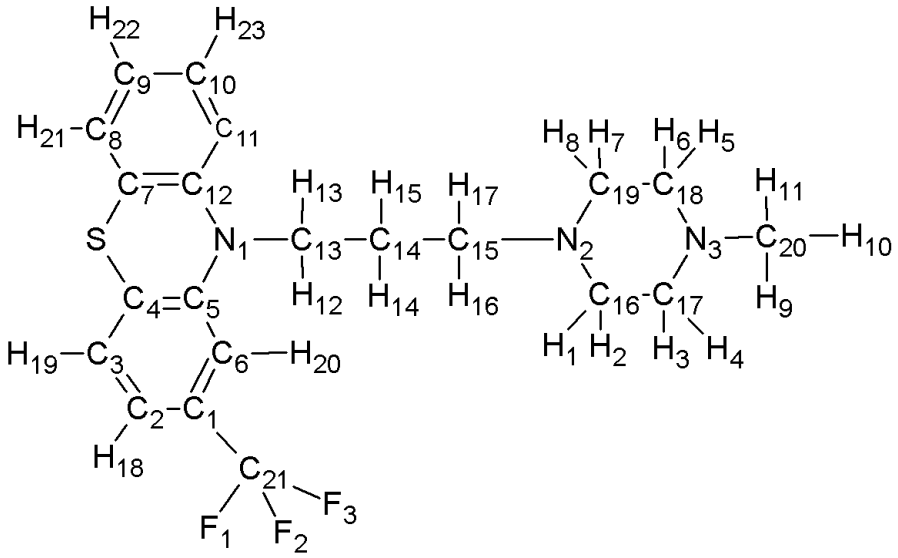


Figure 1S. Trifluoperazine (TFP), including the atom naming scheme used elsewhere in this paper.

Table 1S. TFP force field charge parameters (in electron units); see Figure 1S for atom naming scheme.

Atom	C1	C2	C3	C4	C5	C6	C7	C8
Charge(e)	-0.0674	-0.2458	-0.0264	-0.0595	0.2753	-0.2516	-0.0818	-0.0335
Atom	C9	C10	C11	C12	C13	C14	C15	C16
Charge(e)	-0.2525	-0.1140	-0.2605	0.3496	0.0019	0.2154	-0.1486	-0.1330
Atom	C17	C18	C19	C20	C21	N1	N2	N3
Charge(e)	-0.1501	-0.1501	-0.1330	-0.2580	0.7292	-0.3961	-0.2651	-0.2216
Atom	F1	F2	F3	S	H1	H2	H3	H4
Charge(e)	-0.2368	-0.2368	-0.2368	-0.1432	0.1116	0.1116	0.1160	0.1160
Atom	H5	H6	H7	H8	H9	H10	H11	H12
Charge(e)	0.1160	0.1160	0.1116	0.1116	0.1060	0.1060	0.1060	0.0505
Atom	H13	H14	H15	H16	H17	H18	H19	H20
Charge(e)	0.0505	-0.0118	-0.0118	0.0661	0.0661	0.1758	0.1376	0.1760
Atom	H21	H22	H23	H24				
Charge(e)	0.1390	0.1630	0.1524	0.1493				

Table.2S Binding energy of the top three complexes of Fas with CaM bound to different number of TFP calculated from RDOCK program (unit: kcal/mol)

	CaM_1TFP_Fas			
	ΔE_{elec}	ΔE_{Vdw}	ΔG_{ACE}	$\Delta G_{binding}$
Rank:1st	-33.74	-39.20	13.50	-16.87
Rank:2nd	-33.18	-36.03	15.82	-14.04
Rank:3rd	-30.30	-48.07	13.78	-13.49

	CaM_2TFP_Fas			
	ΔE_{elec}	ΔE_{Vdw}	ΔG_{ACE}	$\Delta G_{binding}$
Rank:1st	-28.55	-31.38	10.07	-15.625
Rank:2nd	-27.71	-40.86	9.37	-15.569
Rank:3rd	-30.33	-33.80	13.72	-13.577

	CaM_4TFP_Fas			
	ΔE_{elec}	ΔE_{Vdw}	ΔG_{ACE}	$\Delta G_{binding}$
Rank:1st	-46.67	-69.15	21.02	-20.983
Rank:2nd	-35.67	-53.71	14.19	-17.913
Rank:3rd	-27.01	-23.94	7.12	-17.189

All values in this table were expressed in terms of kcal/mol. ΔE_{Vdw} is the van der Waals energy, ΔE_{elec} is the electrostatic energy, ΔG_{ACE} is the atomic contact energy.

The energy information for top3 structure in CaM-Fas complex with different number of TFP are listed above. The $\Delta G_{binding}$ information indicate the complex is energy favorable, and also the value of $\Delta G_{binding}$ energy is within the reasonable range of binding energy.

Table.3S Size of the periodic box for the six systems simulated in this study

System	TFP - CaM complex	CaM - Fas complex	Size of the periodic box (unit: nm)
1	1TFP – CaM		7.2 × 7.3 × 7.1
2	2TFP – CaM		7.7 × 7.3 × 8.0
3	4TFP – CaM		7.6 × 8.1 × 6.9
4		1TFP bound CaM – Fas	7.5 × 12.2 × 8.4
5		2TFP bound CaM – Fas	8.8 × 10.8 × 8.2
6		4TFP bound CaM – Fas	9.5 × 10.9 × 9.1

Equilibration of the TFP-CaM complexes

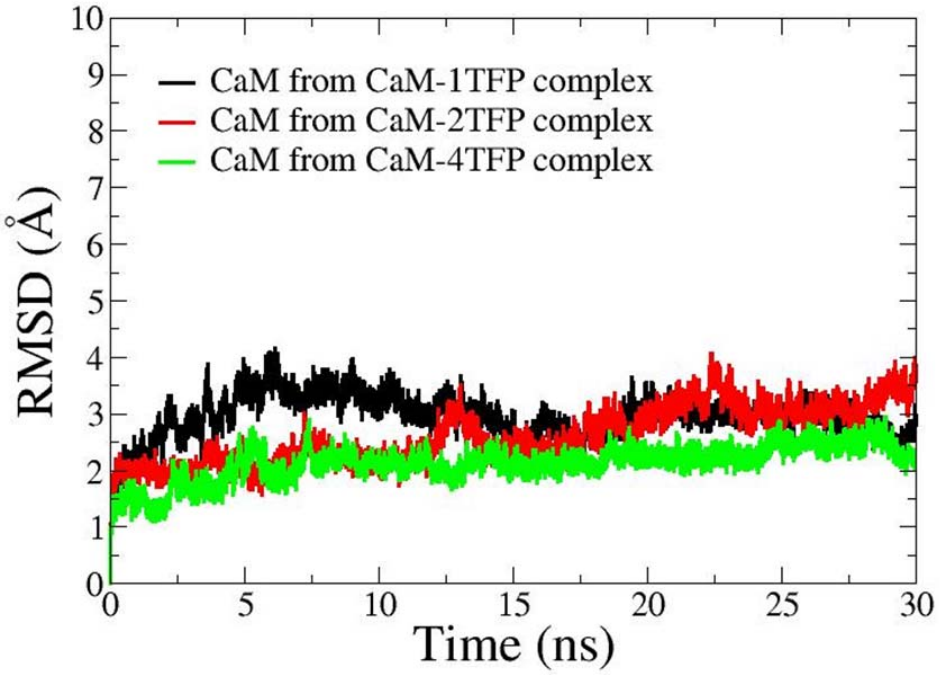


Figure 2S. Root mean squared deviation (RMSD) for CaM in the TFP-CaM complexes over the 30ns MD simulation for different simulation cases.

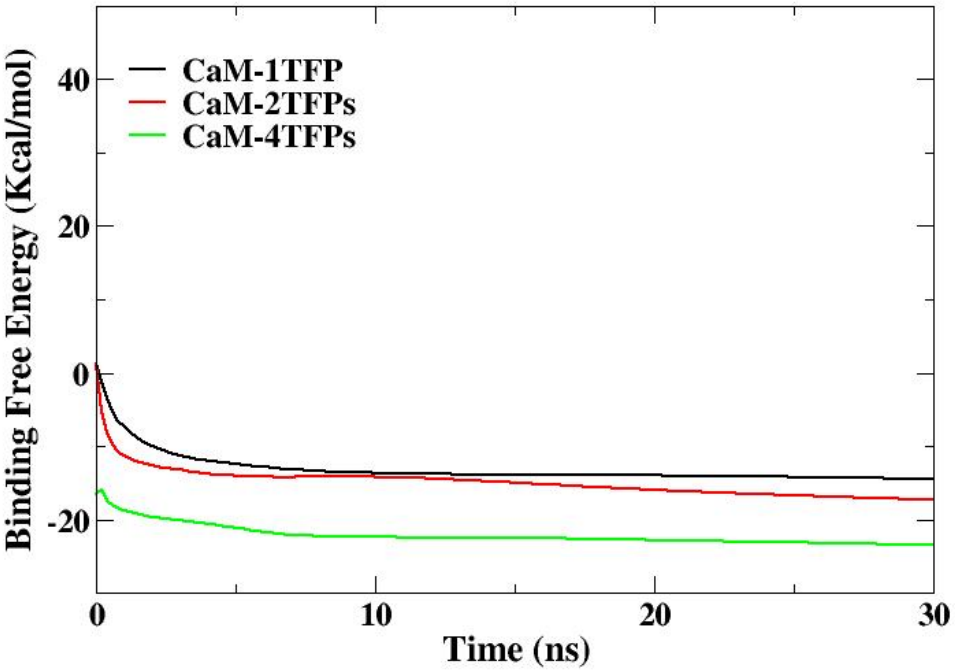


Figure 3S. Binding free energy between CaM with TFP molecule(s) in the TFP-CaM complexes as a function of cumulative time over the 30ns MD simulation for different simulation cases.

Equilibration of the TFP-bound CaM/Fas complexes

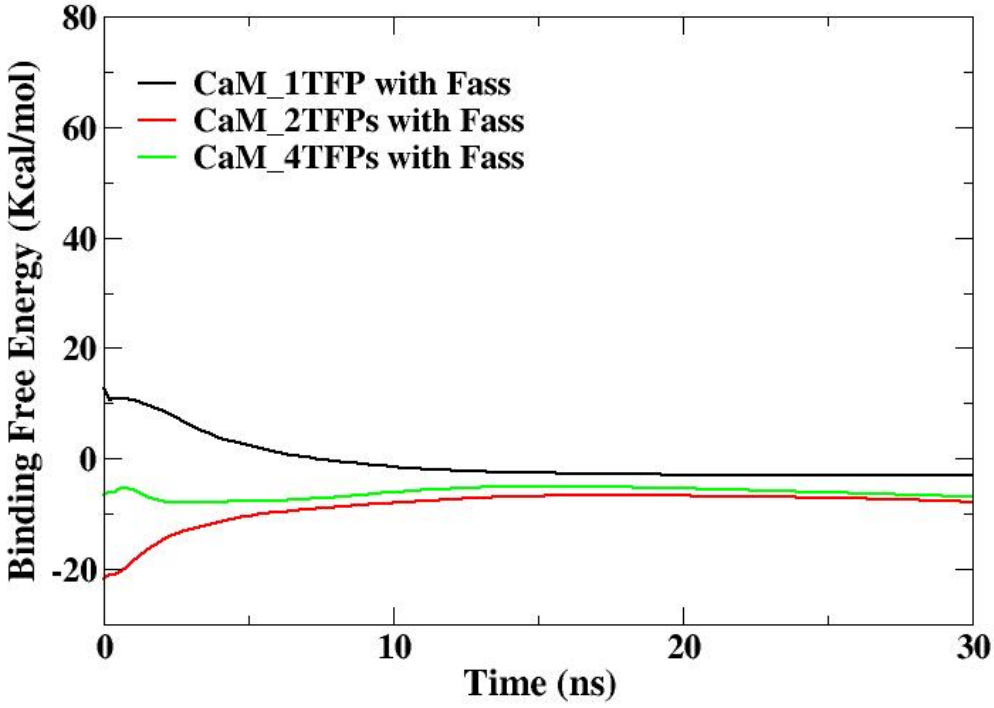


Figure 4S. Binding free energy of Fas-CaM complexes as a function of cumulative time over the 30ns MD simulation for different simulation cases.

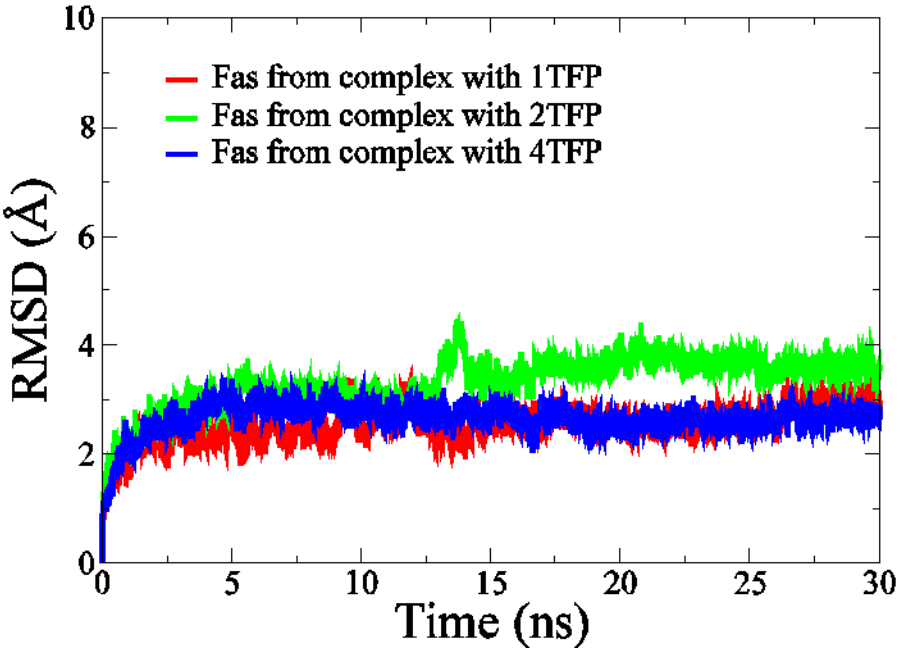


Figure 5S. RMSD for the Fas Death Domain protein core (res 225-318) in the CaM-Fas complexes over the 30ns MD simulation for different simulation cases.

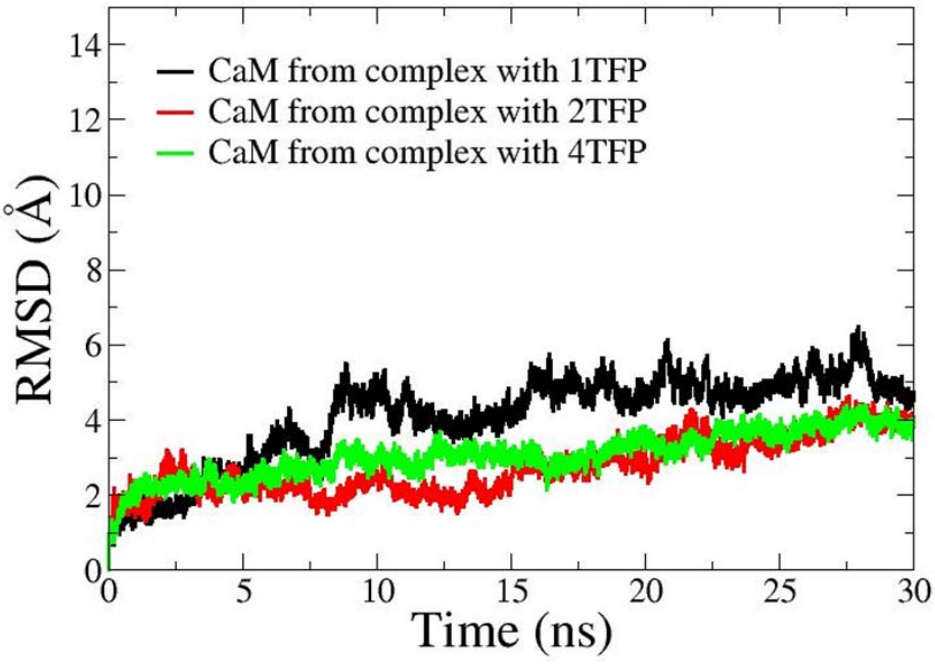


Figure 6S. RMSD for CaM in the CaM-Fas complexes over the 30ns MD simulation for different simulation cases.

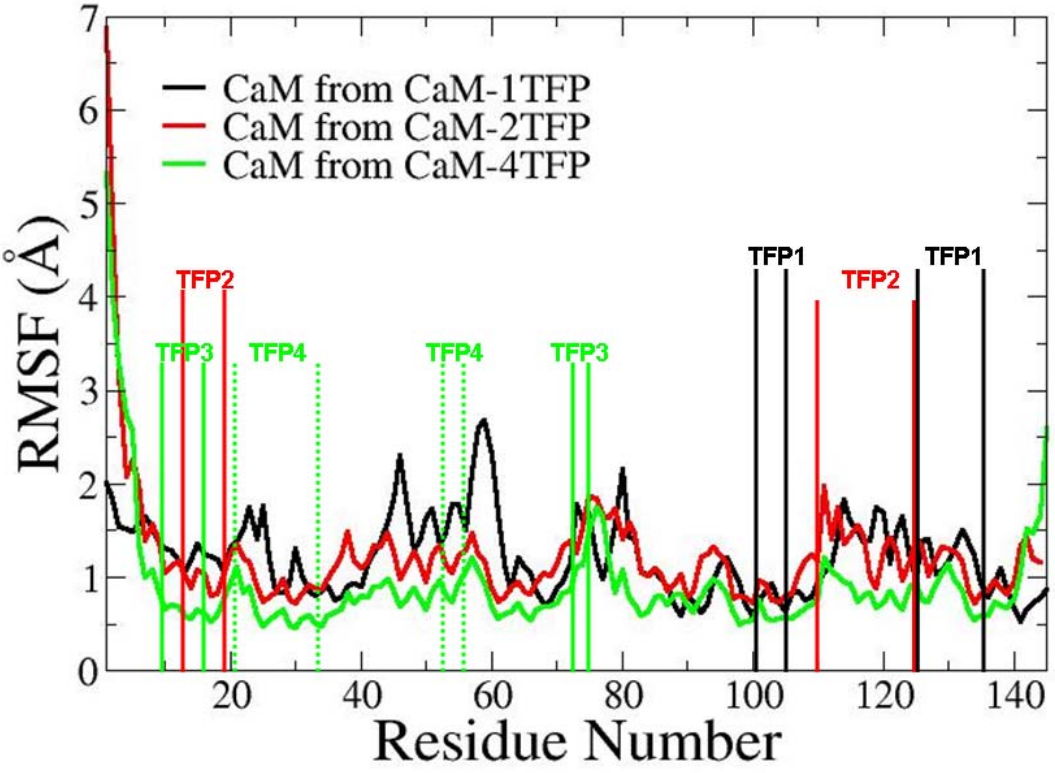


Figure 7S. Root mean squared fluctuation (RMSF) comparison of CaM in different TFP-CaM complexes

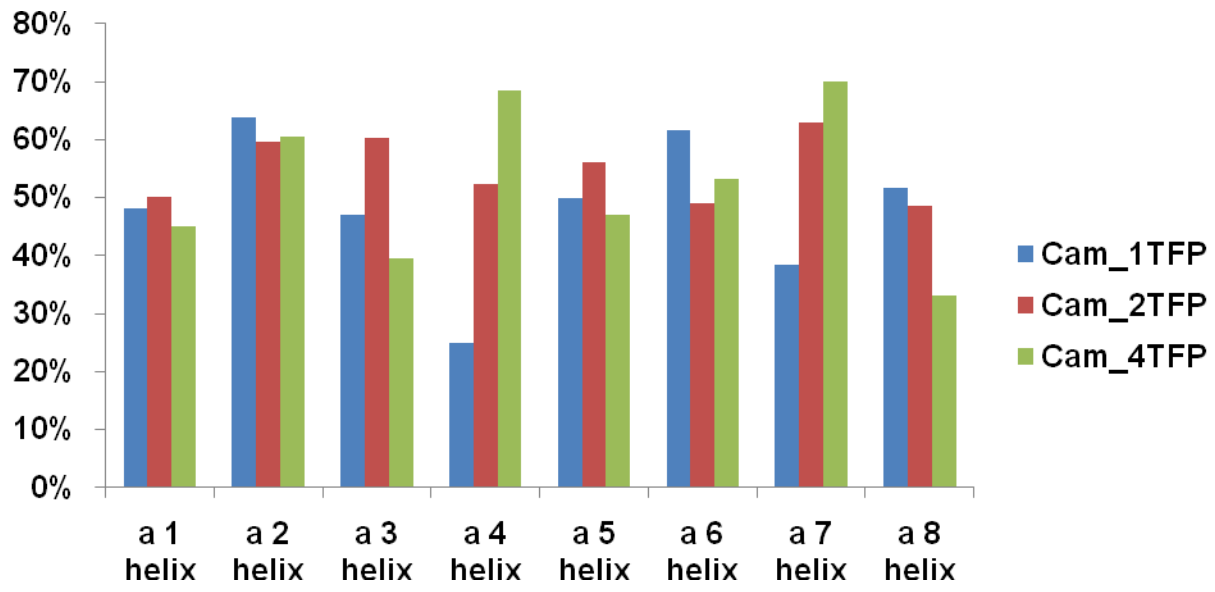


Figure 8S. Hydrogen bond occupancy of each α helix of CaM in TFP-CaM complexes.

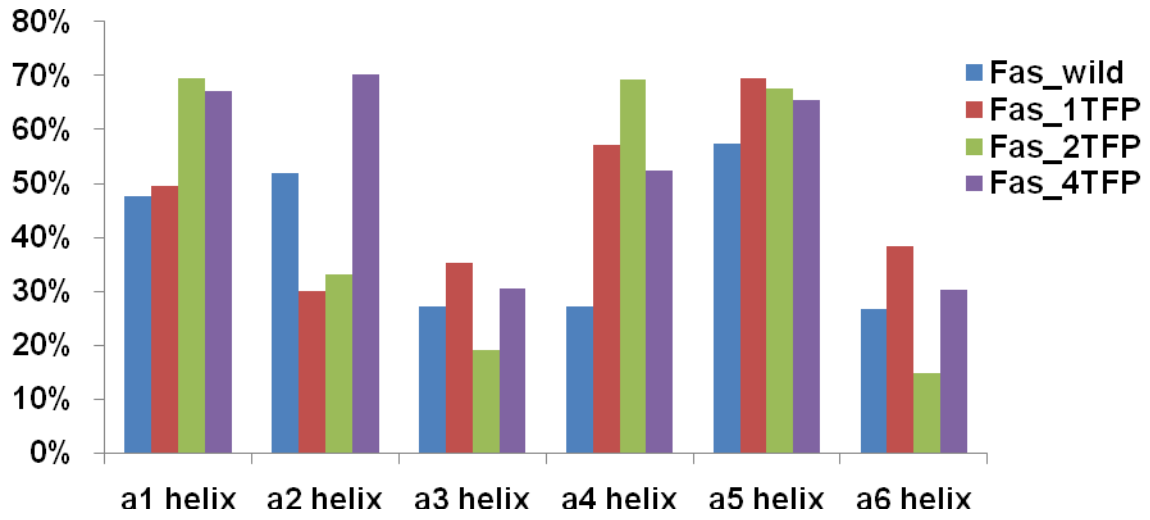
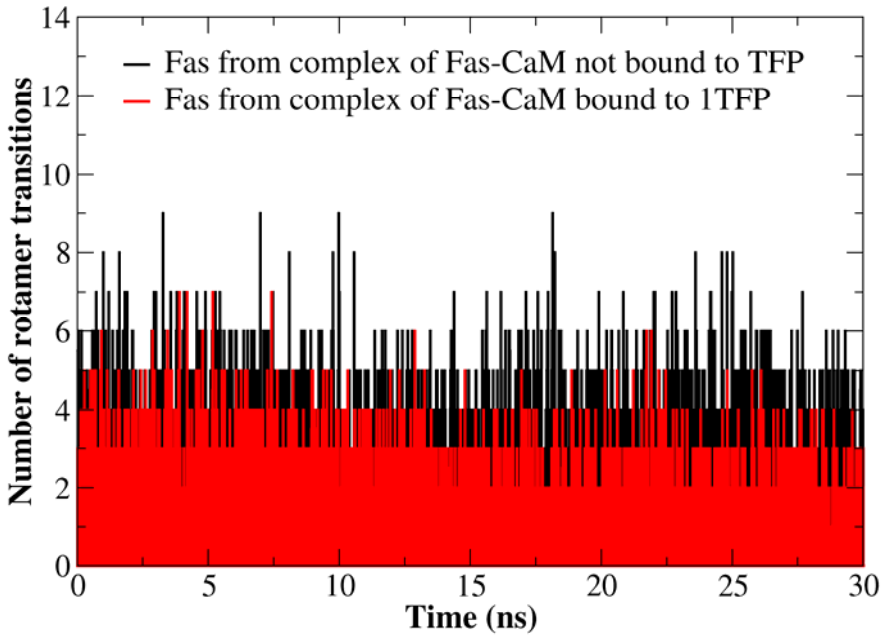
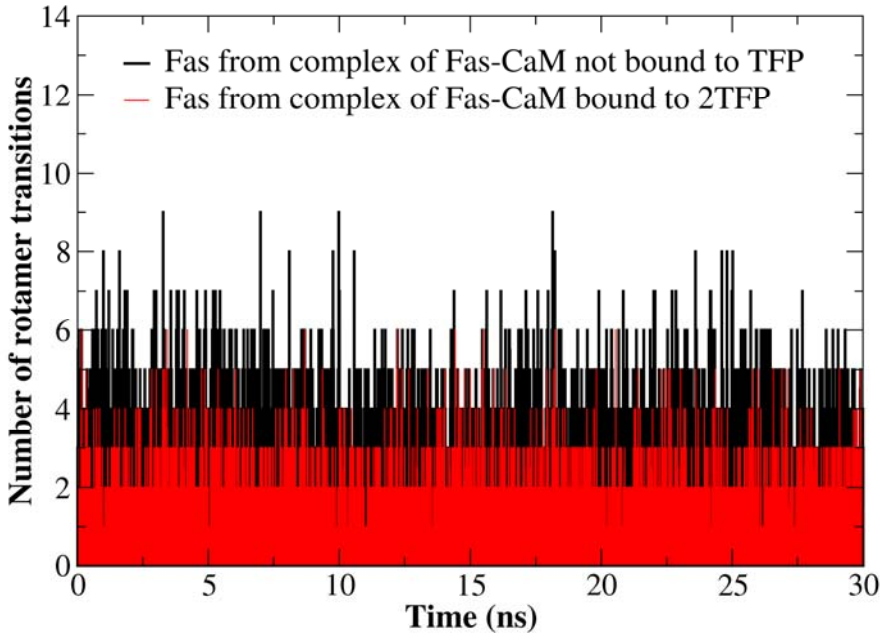


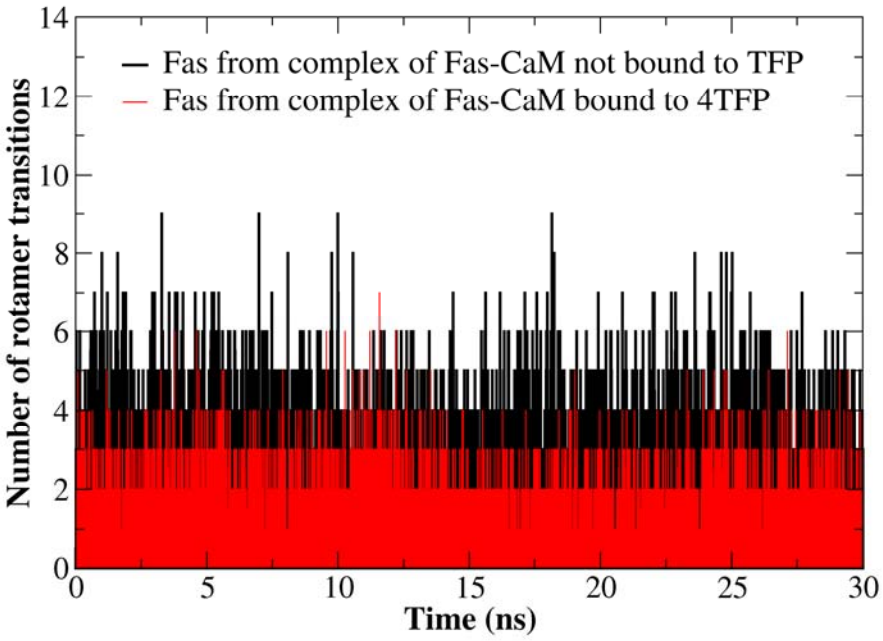
Figure 9S. Hydrogen bond occupancy of each α helix of Fas in CaM-Fas complexes.


Fas from complex of Fas-CaM not bound to TFP
Fas from complex of Fas-CaM bound to 1TFP
Number of rotamer transitions
Time (ns)
0
2
4
6
8
10
12
14
0
5
10
15
20
25
30

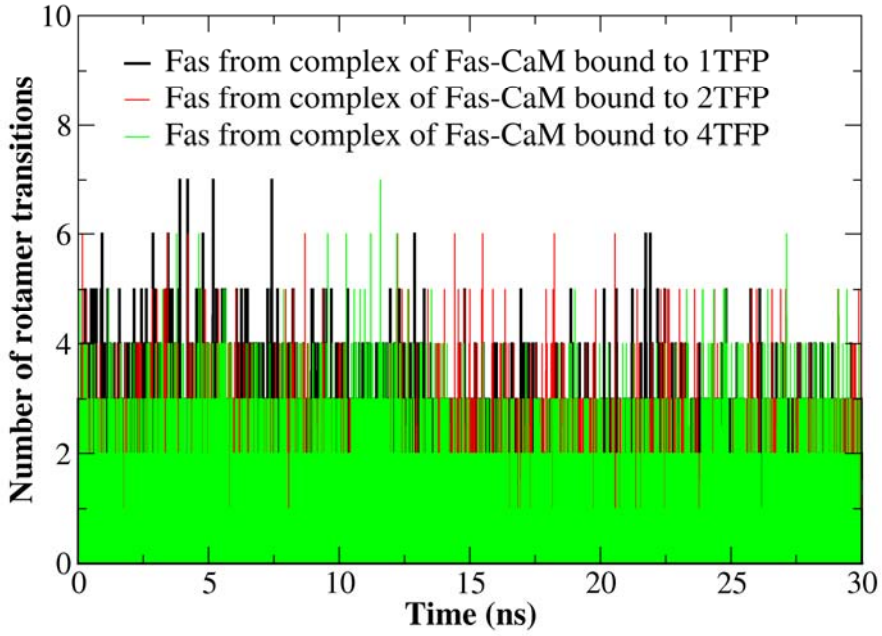
(A)


Fas from complex of Fas-CaM not bound to TFP
Fas from complex of Fas-CaM bound to 2TFP
Number of rotamer transitions
Time (ns)
0
2
4
6
8
10
12
14
0
5
10
15
20
25
30

(B)



(C)



(D)

Figure 10S. The number of dihedral angle transition for all residues of Fas from CaM-Fas complexes over time. (A) Fas DD from wildtype CaM-Fas complex [ref 6] compared to the Fas DD from CaM-1TFP-Fas complex. (B) Fas DD from wildtype CaM-Fas complex [ref 6] compared to the Fas DD from CaM-2TFPs-Fas complex. (C) Fas DD from wildtype CaM-Fas complex [ref 6] compared to the Fas DD from CaM-4TFPs-Fas complex. (D) The comparison of

Fas DD from CaM-1TFP-Fas complex, CaM-2TFPs-Fas complex and CaM-4TFPs-Fas complex.