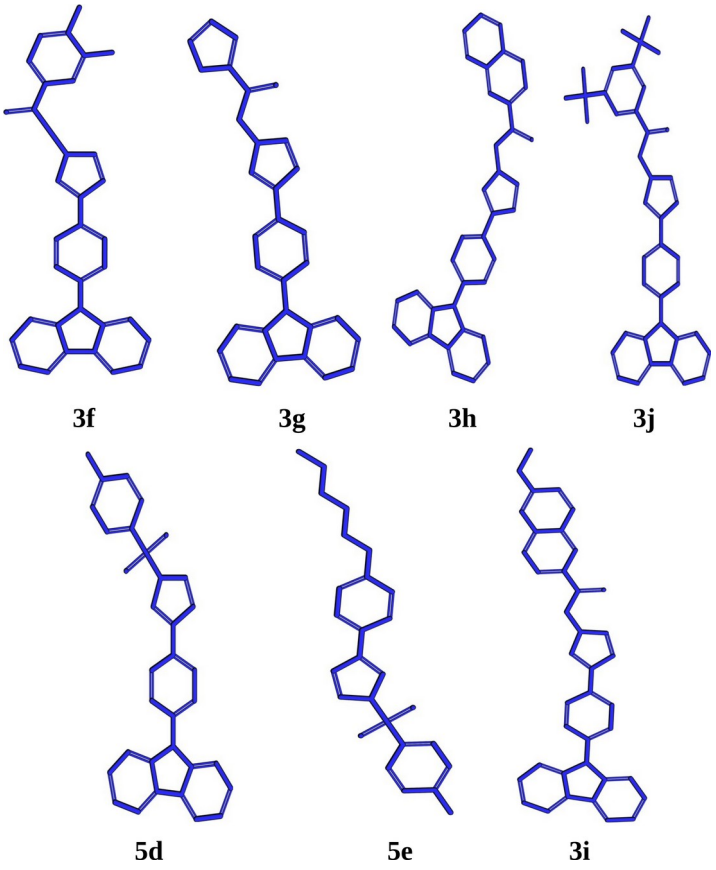


Fig. S1: 2D representaion for 1,2,3 triazole molecules.

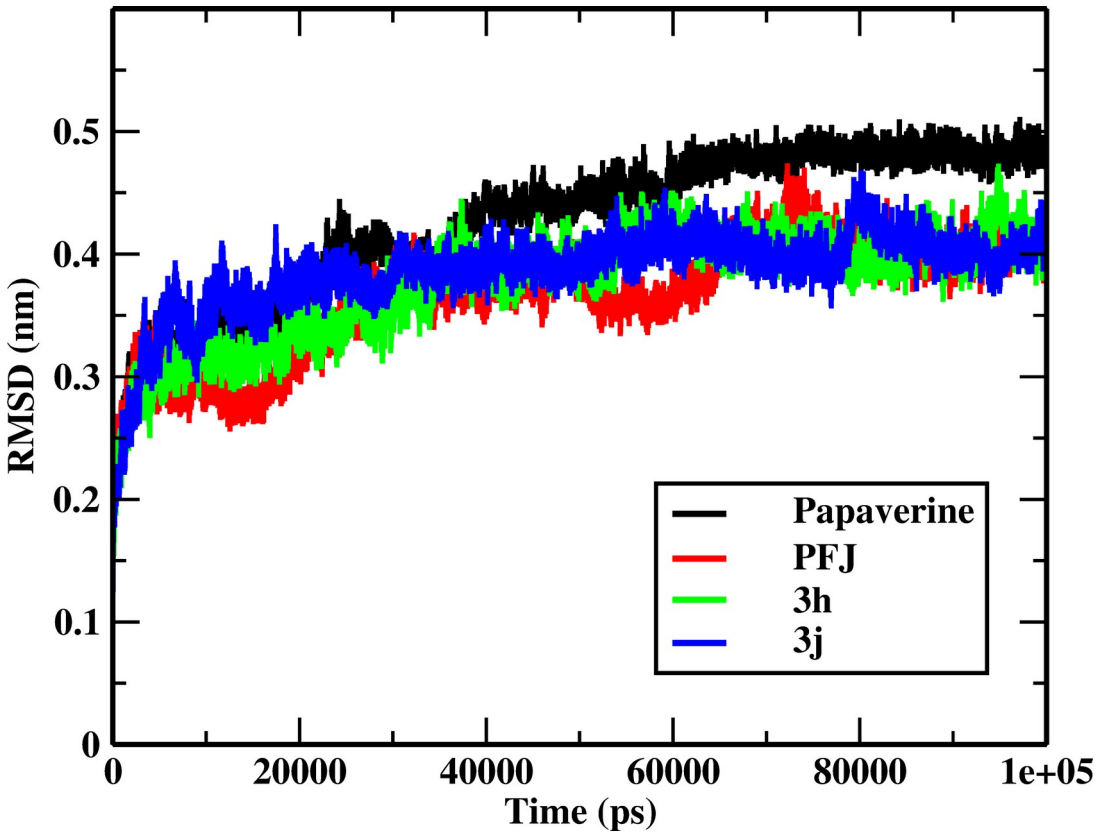


Fig. S2: Time dependent RMSD of PDE10A complexed with cocrystallized (Papaverine & PFJ) and molecules 3h and 3j.

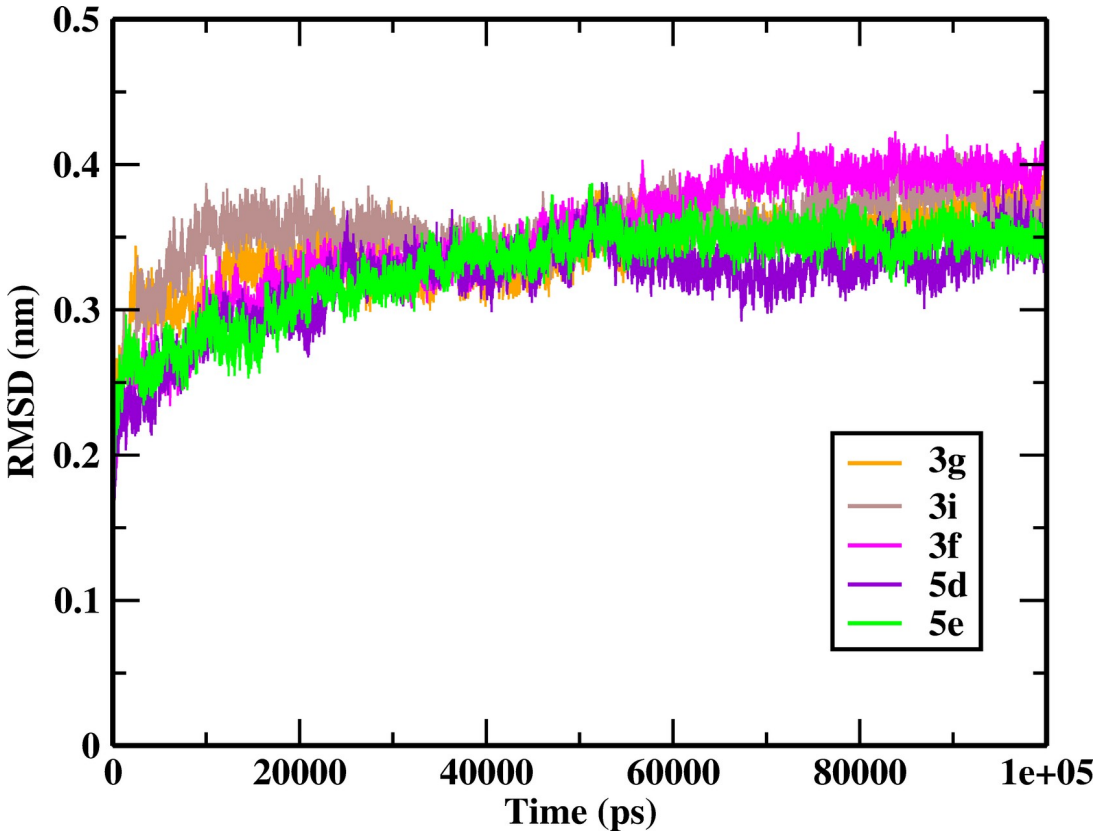


Fig. S3: Time dependent RMSD of PDE10A complexed with molecules 3f, 3g, 5d, 5e and 3i.

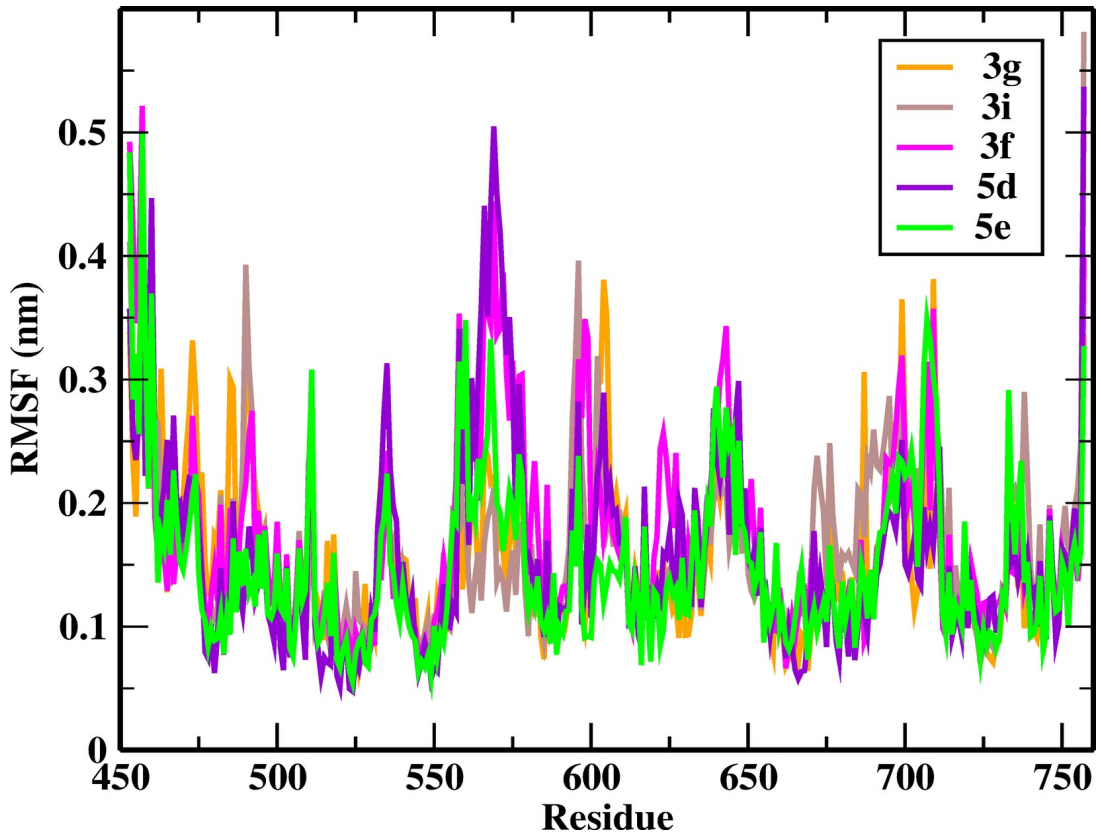


Fig. S4: Time dependent RMSF plot for c-α atoms of amino acid residues of PDE10A complexed with molecules 3f, 3g, 5d, 5e and 3i.

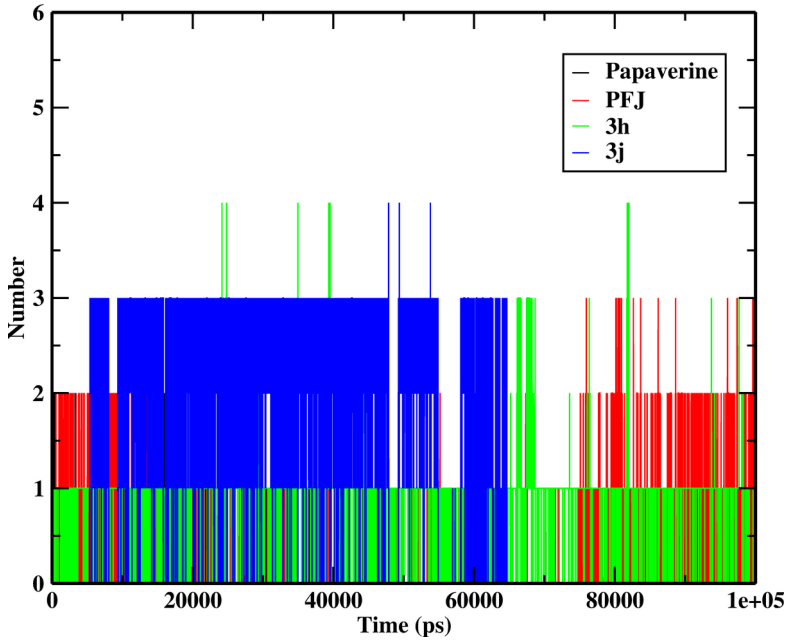


Fig. S5: Hydrogen bonding pattern of PDE10A with cocrystallized ligand (papaverine and PFJ) and molecules 3h and 3j

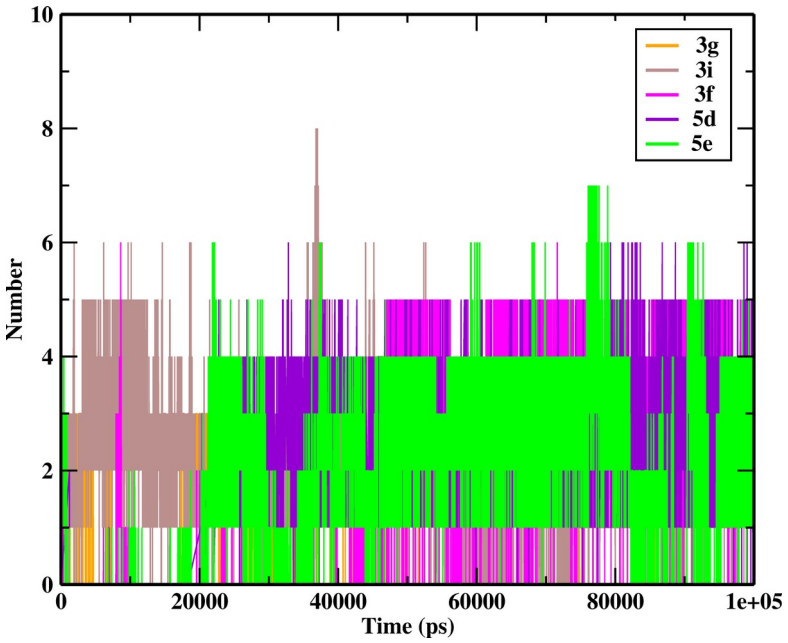


Fig. S6: Hydrogen bonding pattern of PDE10A with molecules 3f, 3g, 5d, 5e and 3i

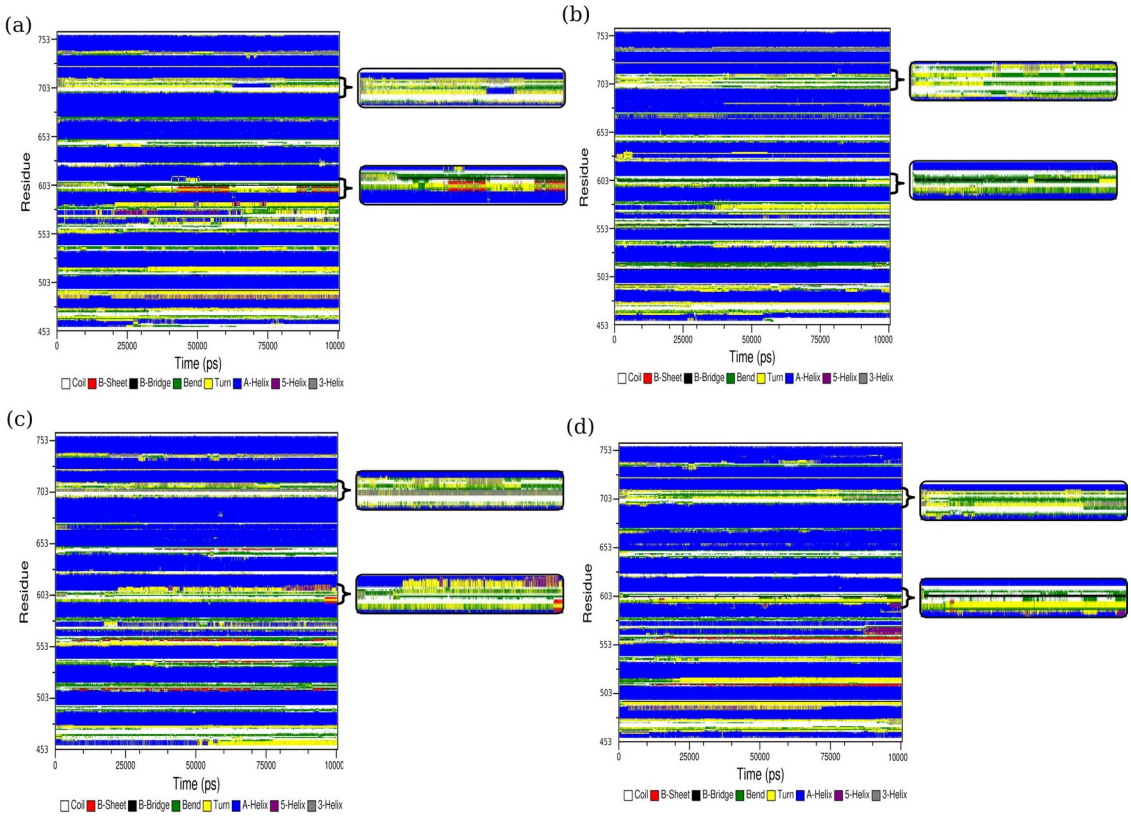
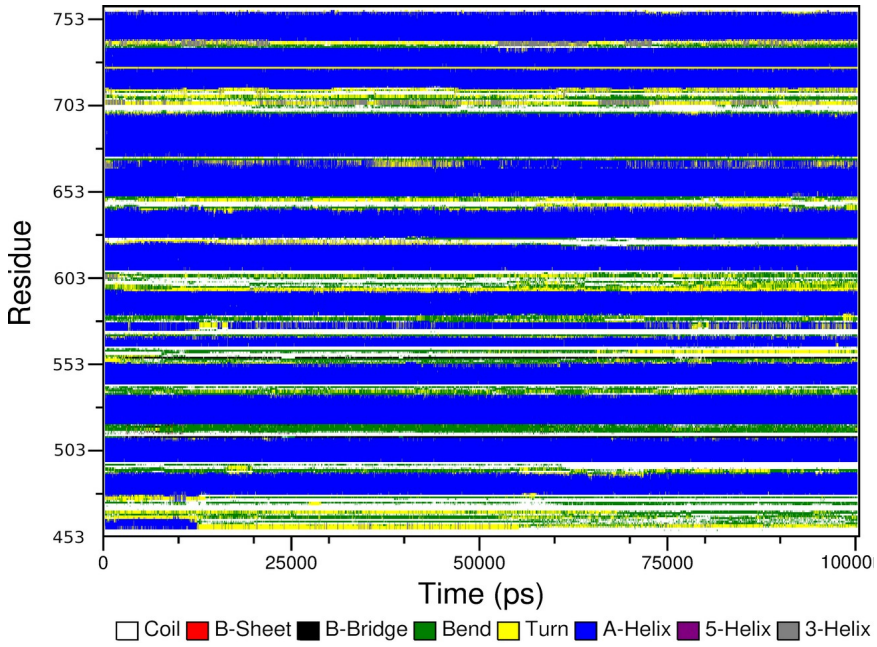
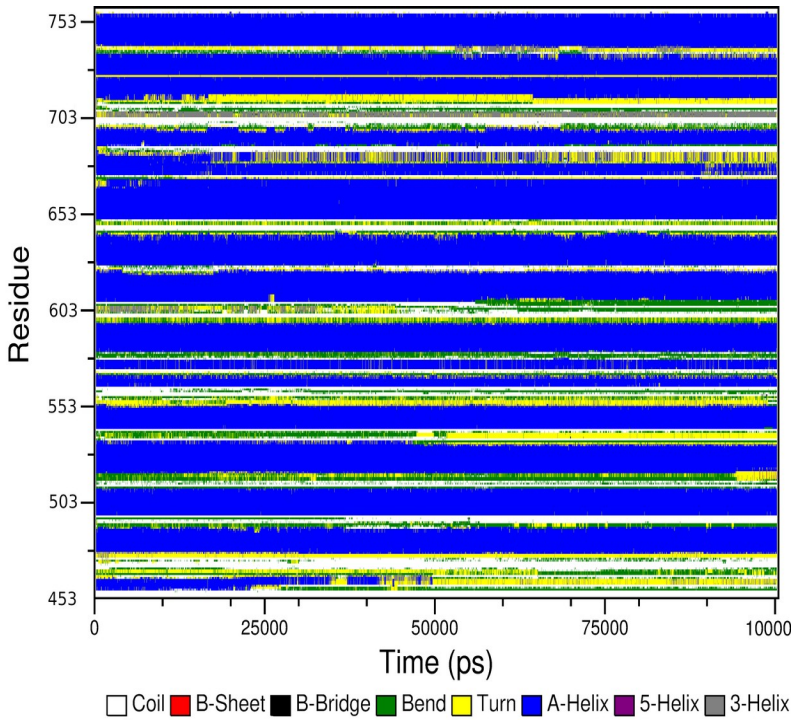


Fig. S7: Secondry structure analysis of PDE10A complexed with (a)PFJ, (b) Papaverine, (c) 3h and (d) 3j

(a)


753
703
653
603
553
503
453
Residue
0
25000
50000
75000
10000
Time (ps)
Coil
B-Sheet
B-Bridge
Bend
Turn
A-Helix
5-Helix
3-Helix

(b)


753
703
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503
453
Residue
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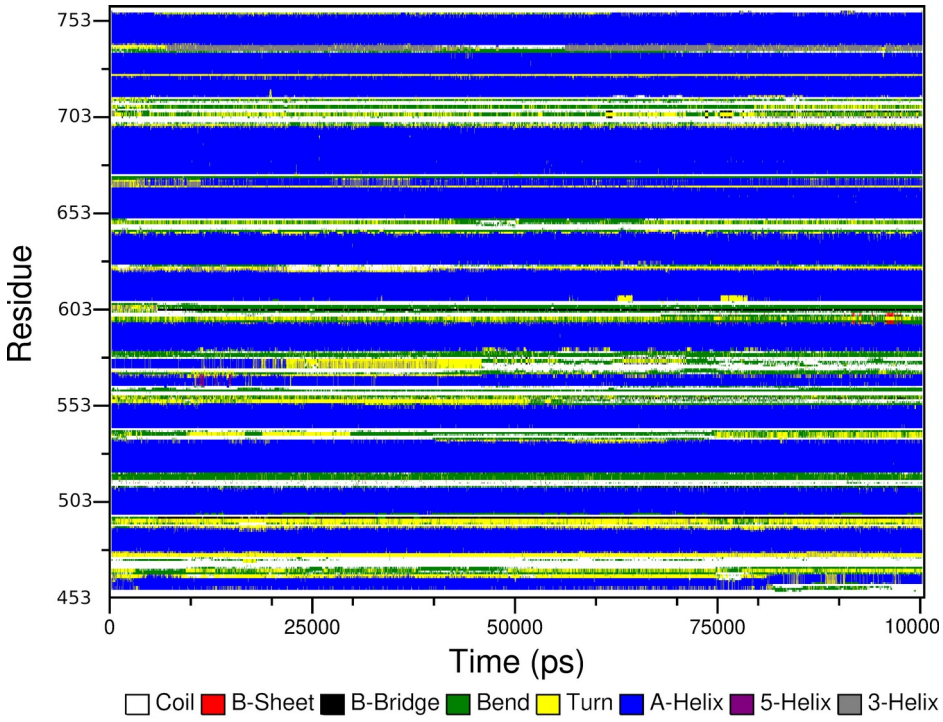
25000
50000
75000
10000
Time (ps)
Coil
B-Sheet
B-Bridge
Bend
Turn
A-Helix
5-Helix
3-Helix

(c)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Residue
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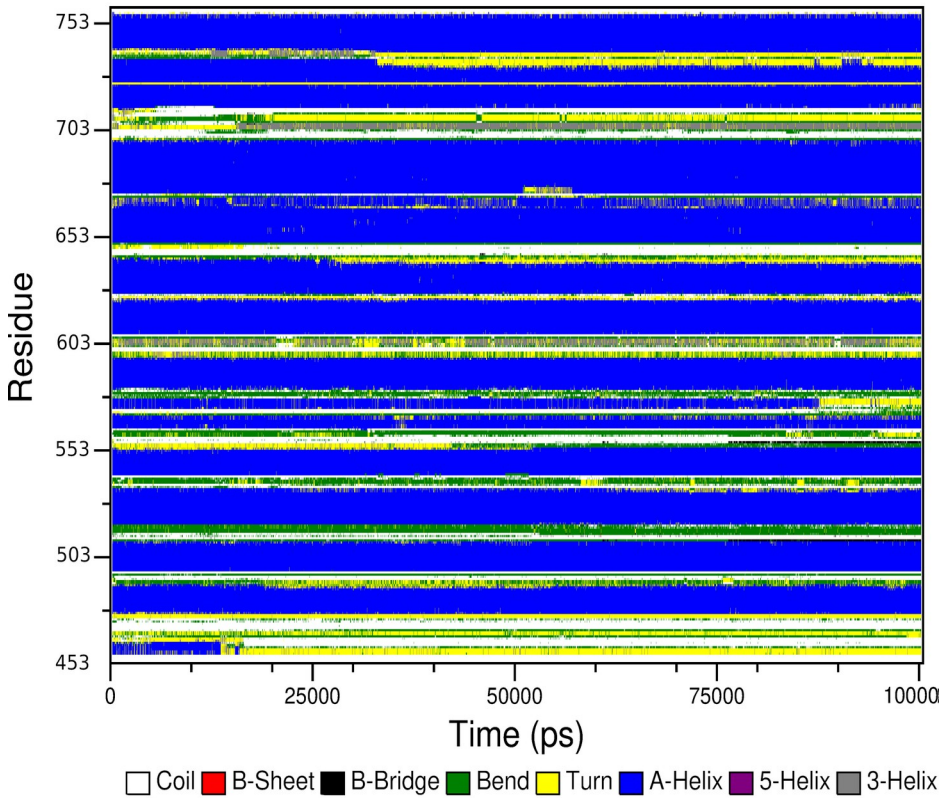
Time (ps)
Coil
B-Sheet
B-Bridge
Bend
Turn
A-Helix
5-Helix
3-Helix

(d)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Time (ps)
Coil
B-Sheet
B-Bridge
Bend
Turn
A-Helix
5-Helix
3-Helix

(e)

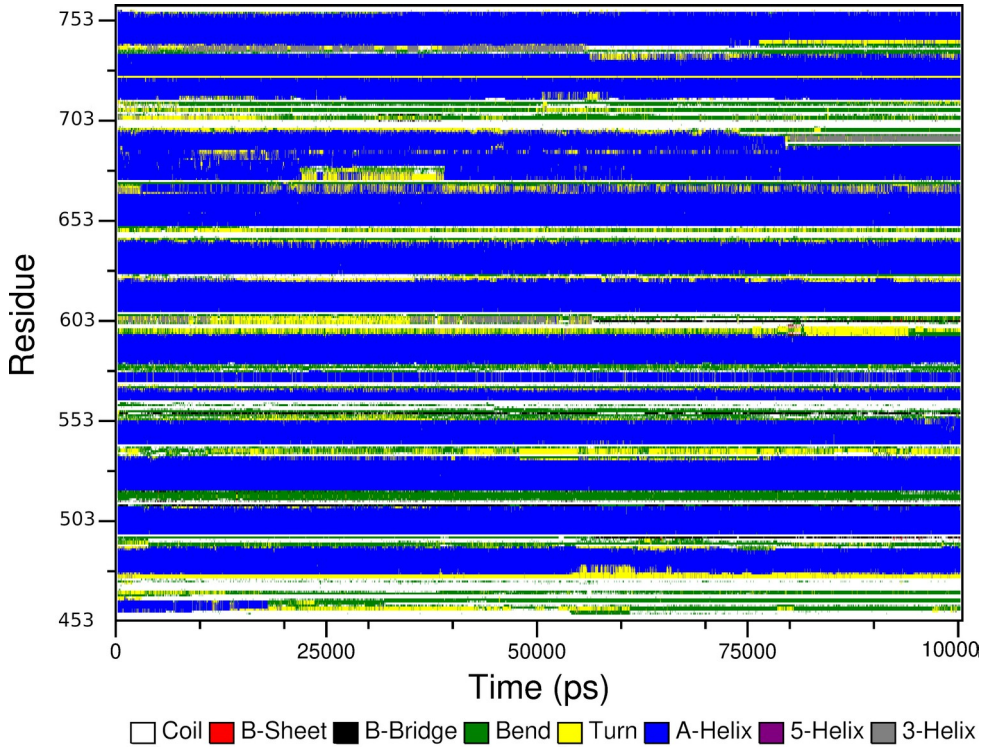

Fig. S8: Secondry structure analysis of PDE10A complexed molecules (a) 3f, (b) 3g, (c) 5d, (d) 5e and (e) 3i

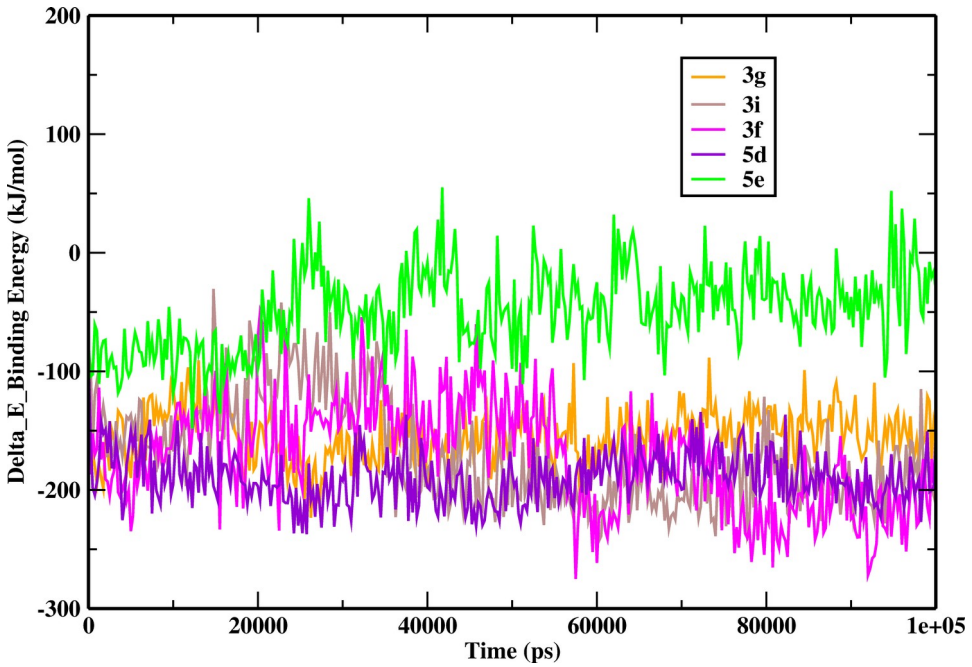

Fig. S9: MM-PBSA analysis of PDE10A with 3f, 3g, 5d, 5e and 3i.

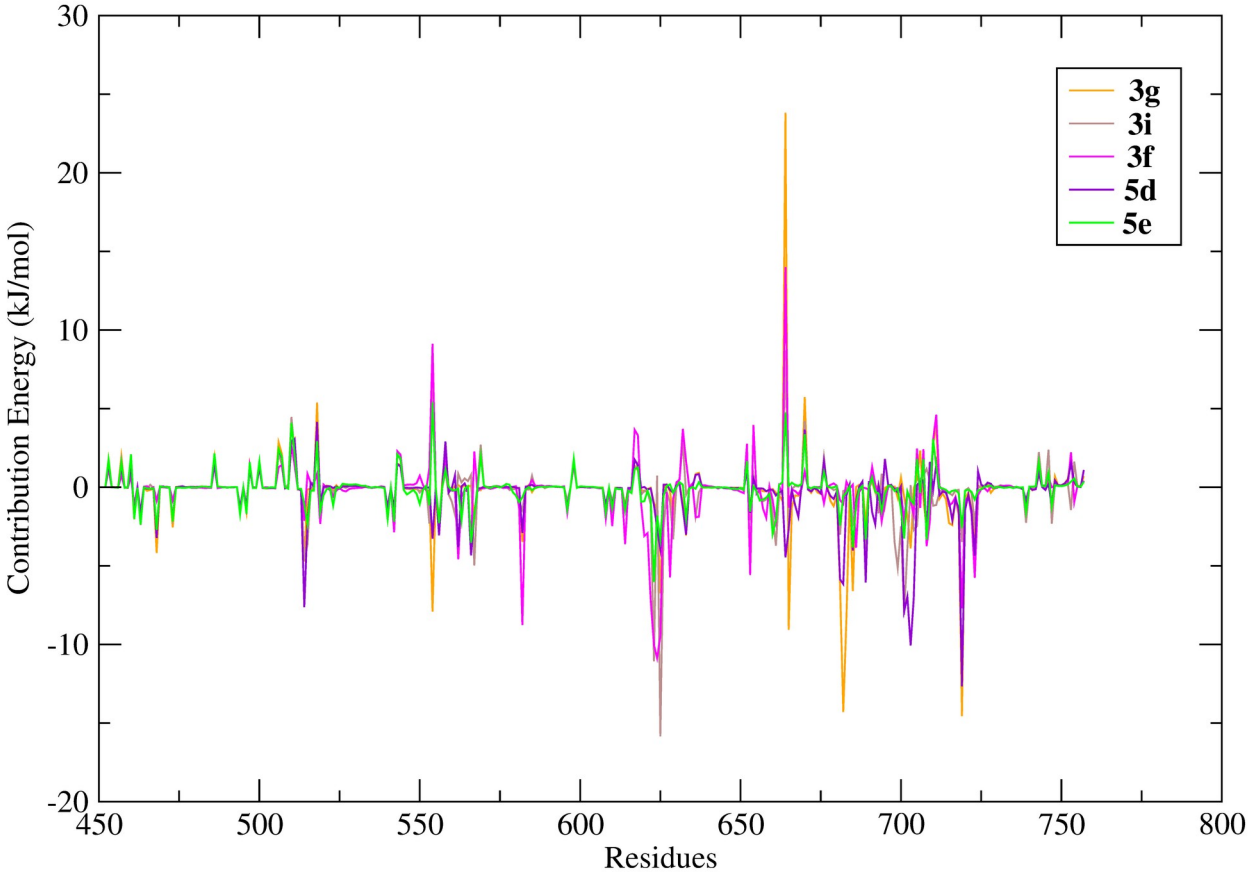

Fig. S10: Contribution energy of different amino acid residues of PDE10A bound with 3f, 3g, 5d, 5e and 3i.

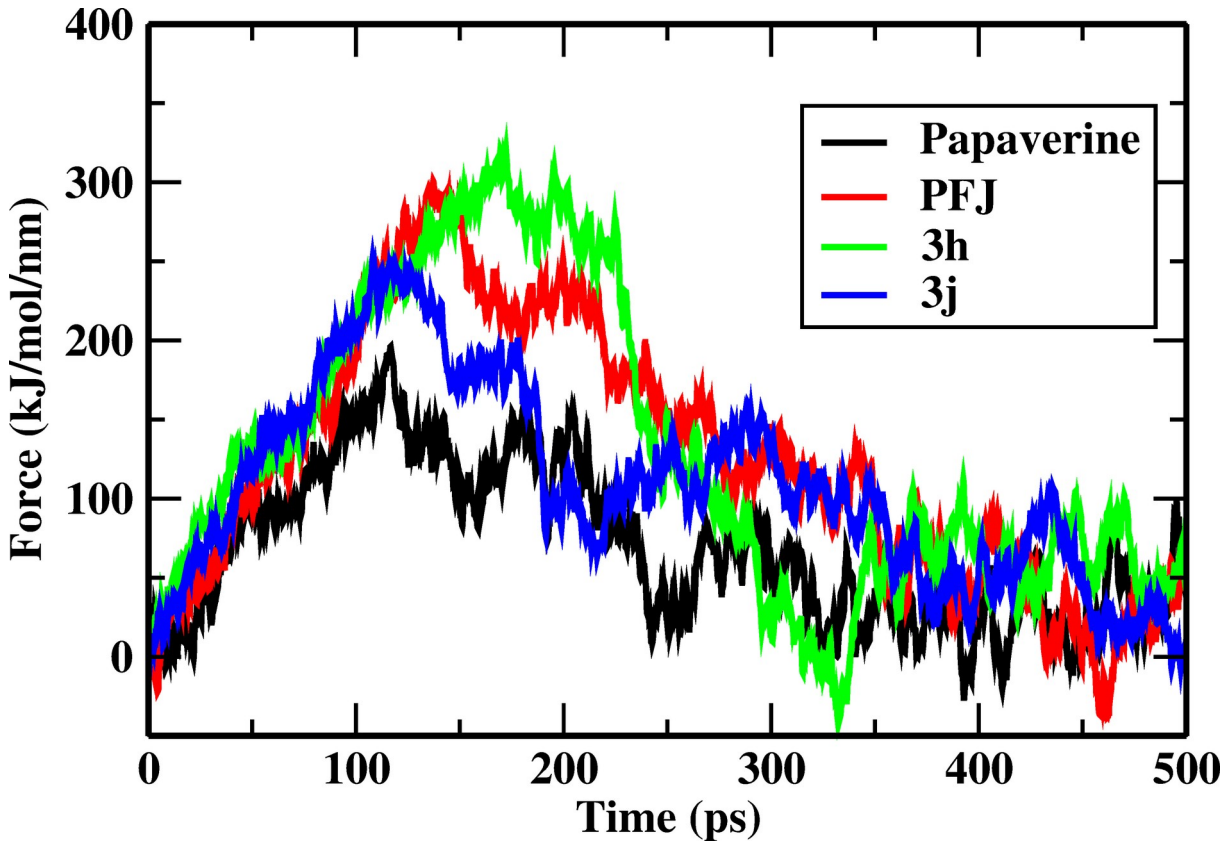

Fig. S11: Influence of pull force on PDE10A complexed with papaverine, PFJ, 3h and 3j during SMD simulations

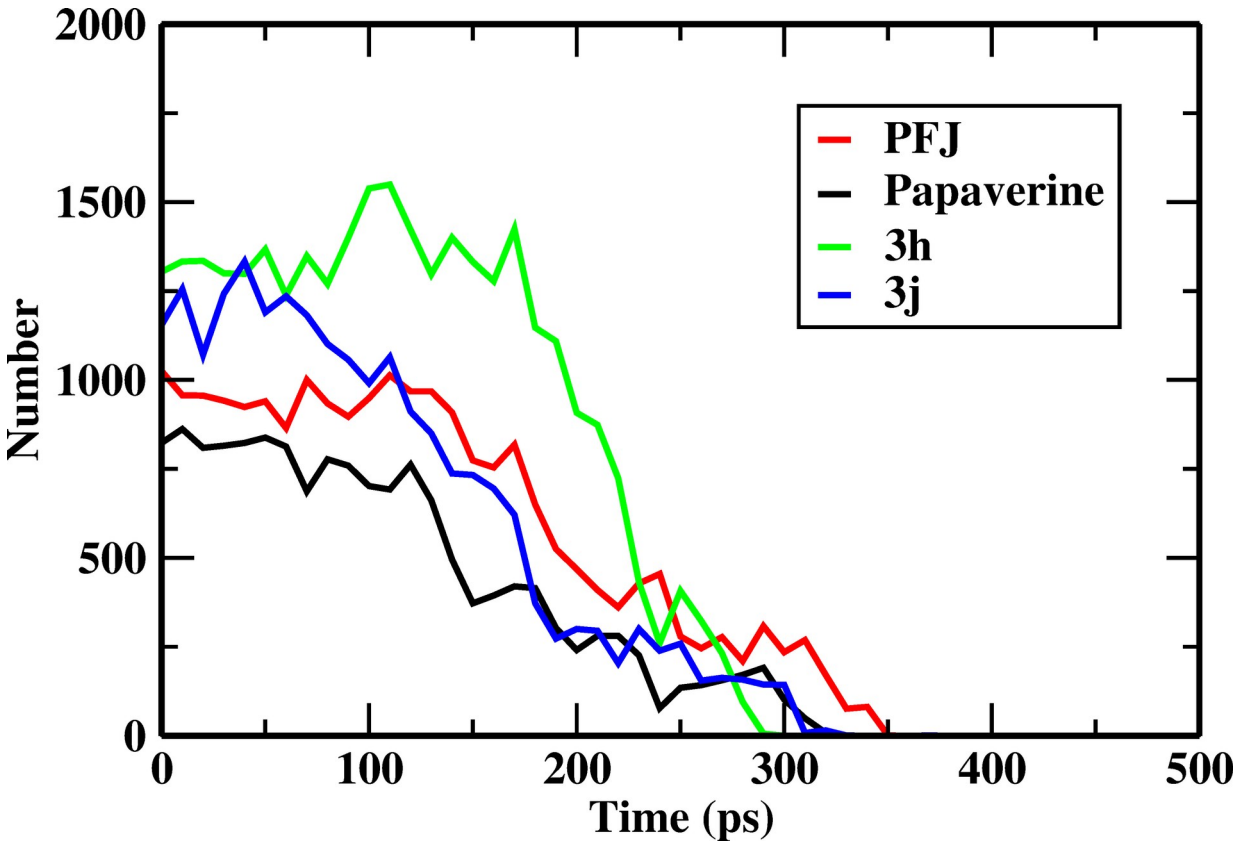

Fig. S12: Number of contacts formed by molecules with PDE10A during pulling simulations.

Table S1: Entropy of PDE10A complexes using Quasiharmonic (QH) method

Complex	**Entropy (kJ/mol)**
Papaverine	35756.7
PFJ	36341.5
3f	36027.3
3g	35470.0
3h	36161.1
3j	36245.8
5d	35421.5
5e	35407.9
3i	36277.1

Table S2: Physicochemical and drug-likeness properties of selected molecules.

Molecules	MW (g/mol)	Skin Sensitization	HBD	HBA	Intestinal absorption (human)	BBB (log BB)	CYP2D6/ CYP3A4 Inhibitor	AMES	hERG I inhibitor
3f	464.475	No	0	5	98.696	0.331	No	No	No
3g	434.524	No	0	6	99.108	0.61	No	No	No
3h	478.555	No	0	5	99.971	0.699	No	No	No
3j	564.489	No	0	5	93.856	0.635	No	No	No
5d	464.55	No	0	6	99.835	-0.963	No	No	No
5e	385.489	No	0	6	95.775	-0.985	No	No	No
3i	508.581	No	0	6	95.987	0.303	No	No	No
Papaverine	339.391	No	0	5	99.428	0.439	Yes	No	No
PFJ	405.458	No	1	8	92.861	-0.908	No	No	No

MW: Molecular weight = 50-500, HBA: Number of H-Bond acceptors = 0-10, HBD: Number of H-bond Donors = 0-5, BBB= logBB>0.3 (Cross BBB); logBB<-1 (poorly distributed); Intestinal absorption= >30% (Highly absorbed)