Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Atomistic account of structural and dynamical changes induced by small binders in the double helix of a short DNA

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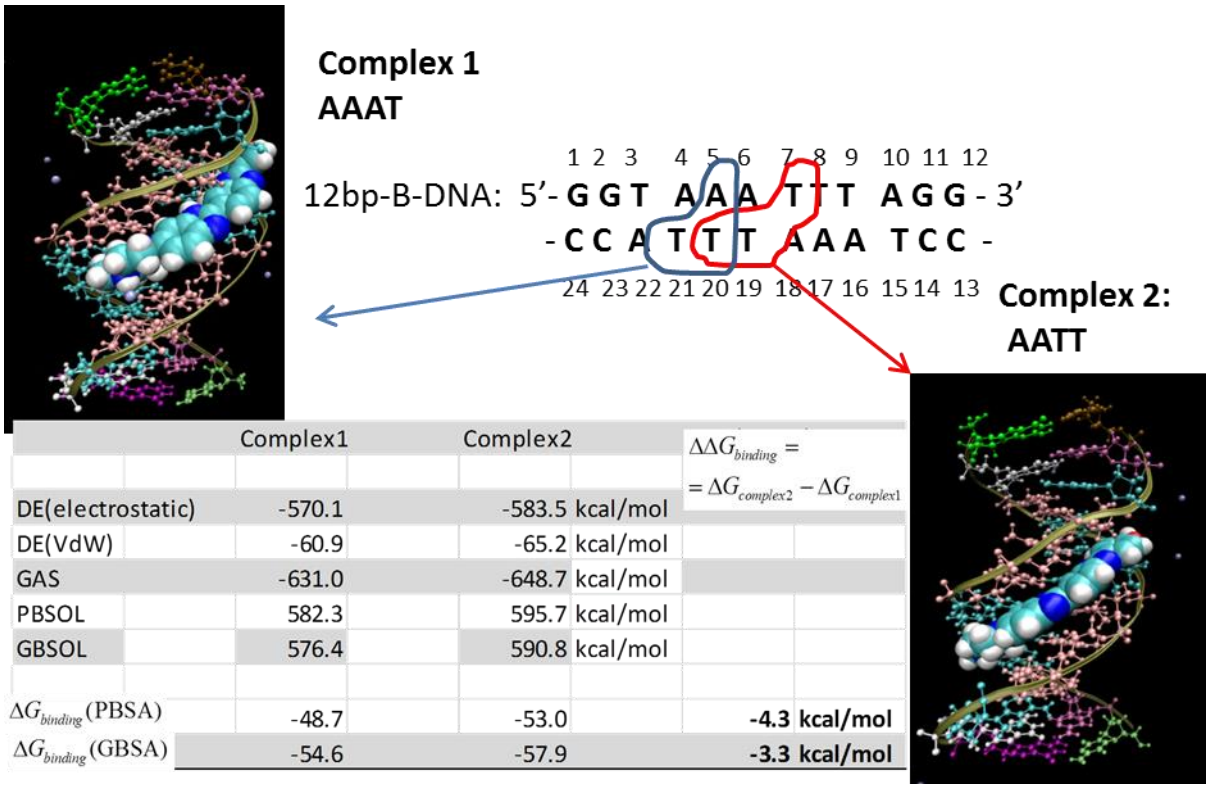
SUPPORTING INFORMATION



	Complex1	Complex2		$\Delta\Delta G_{binding} = \Delta G_{complex2} - \Delta G_{complex1}$
DE(electrostatic)	-570.1	-583.5	kcal/mol	
DE(VdW)	-60.9	-65.2	kcal/mol	
GAS	-631.0	-648.7	kcal/mol	
PBSOL	582.3	595.7	kcal/mol	
GBSOL	576.4	590.8	kcal/mol	
$\Delta G_{binding}$(PBSA)	-48.7	-53.0		**-4.3 kcal/mol**
$\Delta G_{binding}$(GBSA)	-54.6	-57.9		**-3.3 kcal/mol**

Figure SI-1: Two different binding sites investigated for the DNA-Hoechst complex and relative differences in the components of the MM-GBSA binding energy

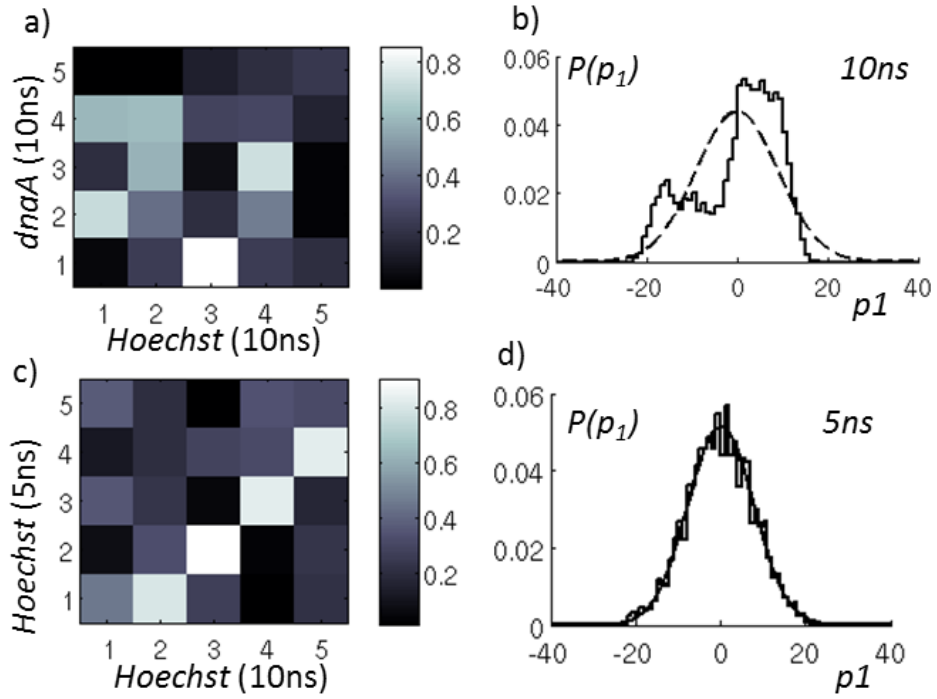


Figure SI-2: a) Matrix of the inner products between the principal components calculated on 10ns of the trajectories of the Hoechst complex and the free oligonucleotides. b) Probability distribution of the projection of the atomic positional fluctuations along the 1st principal component of the Hoechst complex. The bimodal distribution indicates a strongly anharmonic motion that is related to the opening of the terminal base pairs in the second halve of the trajectory. c) Matrix of the inner products between the principal components calculated on 10ns of the trajectories of the Hoechst complex and the principal components obtained from the first 5ns, prior to the opening of the terminal base pair. d) Probability distribution of the projection of the atomic positional fluctuations along the 1st principal component of the Hoechst complex calculated over 5ns. The anharmonic motion present when considering 10ns of trajectory is eliminated when considering the portion of the trajectory prior to the opening of the terminal base pair.

Table SI-1: number of principal components accounting for 90% of the variance, absolute value of the total variance during a portion of 5ns of trajectory, contributions of the first 2 eigenvectors resulting from the backbone (bb) and the all-atom (aa) PCA of the DNA dodecamer and the DNA complexes. $RMSIP_5$ is the overlap between the essential subspaces, spanned by the first 5 PCs, of the complex and the free oligonucleotide.

	N vectors (90%)		Total variance		% Explained the first/ second PCs		$RMSIP_5$
	bb	aa	bb	aa	bb	aa	aa
DNA 12-mer	17	33	410.7	1851.6	32.6%-14.5%	31.2%-13.7%	
DNA-Hoechst(1:1)	20	42	272.5	1286.9	22%-17.5%	21.7%-26.5%	0.85
DNA-Ethidium(1:1)	19	35	383.2	1752.1	27.9%-19.1%	26.7%-18.1%	0.82
DNA-Ethidium(1:2)	14	24	520.0	2378.2	46.1%-15.3%	44.2%-14.8%	0.79
DNA-Ethidium(1:3)	11	27	729.5	2191.3	55%-12%	37.6%-14.1%	0.77

Table SI-2 : MM-GBSA energy decompositions for the free DNA, the complexes, the ligands and the receptors of the ethidium complexes in the STP calculation.

DNA	Average	Std. Dev.	Std. Err. Mean	**DNA:Hoechst**	Average	Std. Dev.	Std. Err. Mean	**eth1mg**	Average	Std. Dev.	Std. Err. Mean
BOND	192.75	10.00	1.41	BOND	205.18	10.91	1.09	BOND	205.19	11.24	1.12
ANGLE	403.02	14.86	2.10	ANGLE	426.51	17.47	1.75	ANGLE	418.58	14.11	1.40
DIHED	531.76	10.28	1.45	DIHED	549.76	10.22	1.02	DIHED	558.53	10.72	1.07
VDWAALS	-410.25	7.73	1.09	VDWAALS	-478.29	7.92	0.79	VDWAALS	-430.62	8.64	0.86
EEL	2910.03	50.88	7.19	EEL	2421.21	42.64	4.26	EEL	2246.53	40.78	4.06
1-4 VDW	200.80	4.45	0.63	1-4 VDW	217.38	5.33	0.53	1-4 VDW	220.46	4.94	0.49
1-4 EEL	-1799.88	18.13	2.56	1-4 EEL	-2025.14	16.66	1.67	1-4 EEL	-1832.45	16.54	1.65
EGB	-6016.13	48.19	6.82	EGB	-5484.72	39.38	3.94	EGB	-5345.24	37.99	3.78
ESURF	35.08	0.27	0.04	ESURF	33.76	0.44	0.04	ESURF	36.11	0.36	0.04
G gas	2028.24	52.07	7.36	G gas	1316.61	44.21	4.42	G gas	1386.23	43.41	4.32
G solv	-5981.05	48.36	6.84	G solv	-5450.96	39.38	3.94	G solv	-5309.13	38.18	3.80
TOTAL	-3952.81	20.65	2.92	TOTAL	-4134.35	21.76	2.18	TOTAL	**-3922.91**	23.10	2.30
Ligand Hoechst				**Ligand ethidium (eth1mg)**				**Receptor (eth1mg)**			
BOND	12.72	2.97	0.59	BOND	10.54	2.35	0.23	BOND	194.65	11.23	1.12
ANGLE	21.49	3.06	0.61	ANGLE	15.57	2.59	0.26	ANGLE	403.01	14.05	1.40
DIHED	20.10	3.10	0.62	DIHED	20.90	2.67	0.27	DIHED	537.63	10.48	1.04
VDWAALS	-4.29	0.84	0.17	VDWAALS	-1.76	1.40	0.14	VDWAALS	-381.98	7.74	0.77
EEL	97.37	1.95	0.39	EEL	46.12	0.83	0.08	EEL	2726.52	47.41	4.72
1-4 VDW	15.54	1.15	0.23	1-4 VDW	19.23	1.01	0.10	1-4 VDW	201.23	4.84	0.48
1-4 EEL	-225.96	2.64	0.53	1-4 EEL	-26.74	0.87	0.09	1-4 EEL	-1805.71	16.53	1.64
EGB	-72.58	0.99	0.20	EGB	-40.46	0.26	0.03	EGB	-5841.33	45.38	4.52
ESURF	5.75	0.04	0.01	ESURF	4.47	0.03	0.00	ESURF	36.98	0.33	0.03
G gas	-63.03	6.02	1.20	G gas	83.86	4.03	0.40	G gas	1875.34	50.60	5.03
G solv	-66.83	0.97	0.19	G solv	-35.99	0.26	0.03	G solv	-5804.34	45.54	4.53
TOTAL	-129.86	5.79	1.16	TOTAL	47.88	4.05	0.40	TOTAL	-3929.00	22.41	2.23
eth1MG				**eth2**				**eth3**			
BOND	202.69	12.50	1.25	BOND	212.16	12.40	1.24	BOND	224.04	11.28	1.13
ANGLE	421.45	17.53	1.75	ANGLE	438.51	15.77	1.58	ANGLE	455.86	15.50	1.55
DIHED	551.72	10.65	1.07	DIHED	572.92	10.58	1.06	DIHED	596.65	11.22	1.12
VDWAALS	-424.92	8.06	0.81	VDWAALS	-445.90	8.42	0.84	VDWAALS	-465.55	8.35	0.84
EEL	2262.81	48.02	4.80	EEL	1756.49	47.28	4.73	EEL	1341.40	48.25	4.83
1-4 VDW	220.43	5.89	0.59	1-4 VDW	239.39	5.82	0.58	1-4 VDW	259.91	5.48	0.55
1-4 EEL	-1830.77	17.01	1.70	1-4 EEL	-1863.11	17.25	1.72	1-4 EEL	-1883.55	17.94	1.79
EGB	-5366.75	43.27	4.33	EGB	-4844.71	43.57	4.36	EGB	-4427.66	43.06	4.31
ESURF	33.32	0.22	0.02	ESURF	34.87	0.28	0.03	ESURF	39.18	0.41	0.04
G gas	1403.42	49.56	4.96	G gas	910.47	51.55	5.16	G gas	528.77	48.43	4.84
G solv	-5333.43	43.28	4.33	G solv	-4809.84	43.66	4.37	G solv	-4388.48	43.22	4.32
TOTAL	**-3930.01**	22.09	2.21	TOTAL	**-3899.37**	20.45	2.05	TOTAL	-3859.70	22.57	2.26
Receptor (eth1MG)				**Receptor (eth2)**				**Receptor (eth3)**			
BOND	192.07	12.10	1.21	BOND	201.83	12.30	1.23	BOND	213.58	11.41	1.14
ANGLE	406.19	16.98	1.70	ANGLE	423.45	15.50	1.55	ANGLE	440.30	15.36	1.54
DIHED	530.46	10.31	1.03	DIHED	551.72	10.18	1.02	DIHED	575.40	10.92	1.09
VDWAALS	-382.26	7.76	0.78	VDWAALS	-402.93	8.01	0.80	VDWAALS	-423.46	8.34	0.83
EEL	2726.75	53.13	5.31	EEL	2170.07	50.84	5.08	EEL	1694.27	50.85	5.09
1-4 VDW	201.06	5.69	0.57	1-4 VDW	220.01	5.81	0.58	1-4 VDW	240.55	5.46	0.55
1-4 EEL	-1804.07	17.05	1.70	1-4 EEL	-1836.35	17.15	1.71	1-4 EEL	-1856.77	17.93	1.79
EGB	-5846.19	48.54	4.85	EGB	-5274.73	46.95	4.69	EGB	-4797.09	45.49	4.55
ESURF	33.05	0.22	0.02	ESURF	34.59	0.28	0.03	ESURF	39.56	0.40	0.04
G gas	1870.20	53.75	5.37	G gas	1327.80	54.71	5.47	G gas	883.86	51.63	5.16
G solv	-5813.15	48.56	4.86	G solv	-5240.14	47.06	4.71	G solv	-4757.53	45.68	4.57
TOTAL	-3942.95	21.17	2.12	TOTAL	-3912.34	20.02	2.00	TOTAL	-3873.68	22.64	2.26
Ligand ethidium (eth1MG)				**Ligand ethidium (eth2)**				**Ligand ethidium (eth3)**			
BOND	10.62	2.88	0.29	BOND	10.33	2.50	0.25	BOND	10.47	2.68	0.27
ANGLE	15.27	3.01	0.30	ANGLE	15.06	2.91	0.29	ANGLE	15.56	3.35	0.33
DIHED	21.27	3.01	0.30	DIHED	21.20	2.89	0.29	DIHED	21.25	2.51	0.25
VDWAALS	-1.69	1.30	0.13	VDWAALS	-1.73	1.51	0.15	VDWAALS	-1.81	1.38	0.14
EEL	46.21	0.83	0.08	EEL	46.20	0.79	0.08	EEL	46.18	0.67	0.07
1-4 VDW	19.37	1.28	0.13	1-4 VDW	19.38	1.23	0.12	1-4 VDW	19.37	1.14	0.11
1-4 EEL	-26.70	0.83	0.08	1-4 EEL	-26.77	0.82	0.08	1-4 EEL	-26.77	0.71	0.07
EGB	-40.44	0.26	0.03	EGB	-40.45	0.27	0.03	EGB	-40.48	0.28	0.03
ESURF	3.00	0.02	0.00	ESURF	3.00	0.02	0.00	ESURF	4.45	0.03	0.00
G gas	84.35	4.66	0.47	G gas	83.68	4.40	0.44	G gas	84.25	4.50	0.45
G solv	-37.43	0.26	0.03	G solv	-37.45	0.27	0.03	G solv	-36.03	0.28	0.03
TOTAL	**46.92**	4.61	0.46	TOTAL	**46.23**	4.38	0.44	TOTAL	48.22	4.44	0.44

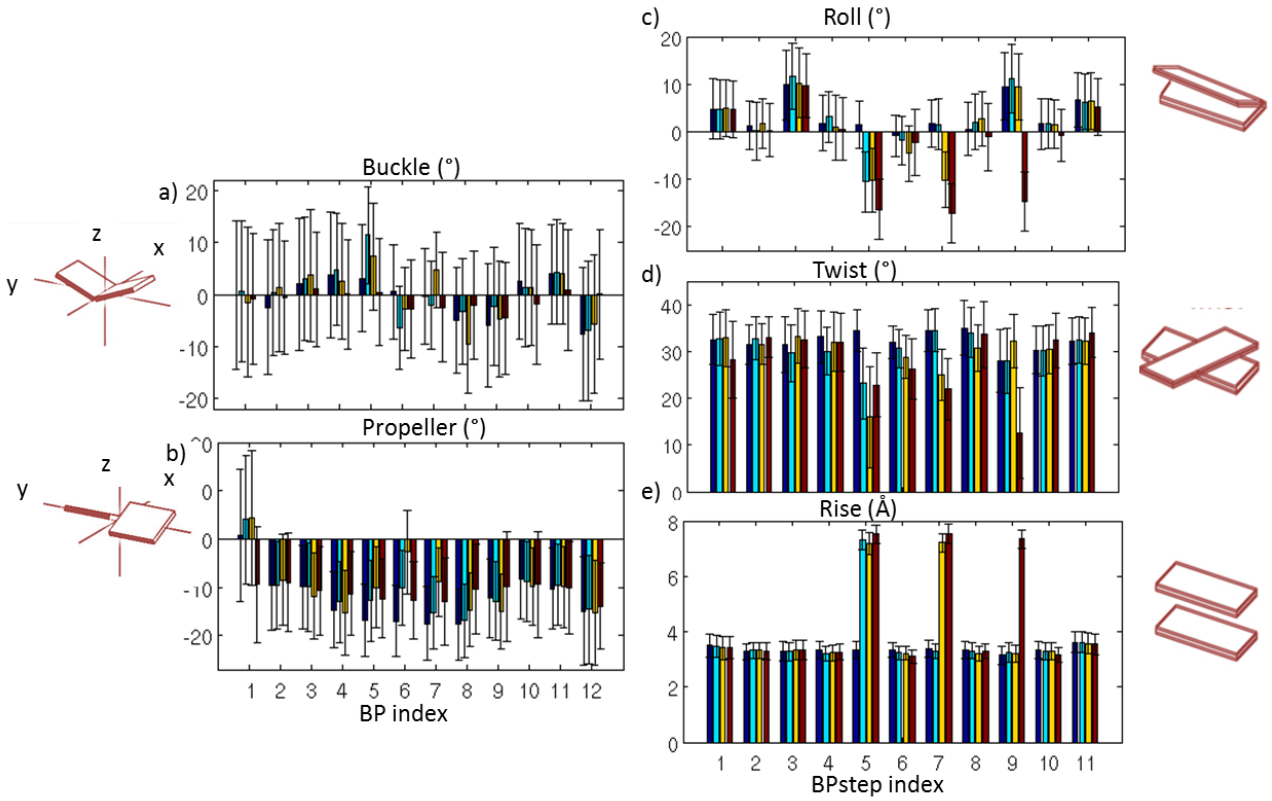


Figure SI-3: Selected parameters describing the conformation of the base pairs and of helix in the free oligonucleotide (blue), eth1MG (light blue), eth2 (yellow) and eth3 (brown). The height of the bars denotes the average value of the selected parameters while the error bars denote their variability quantified as standard deviation calculated along the trajectory.

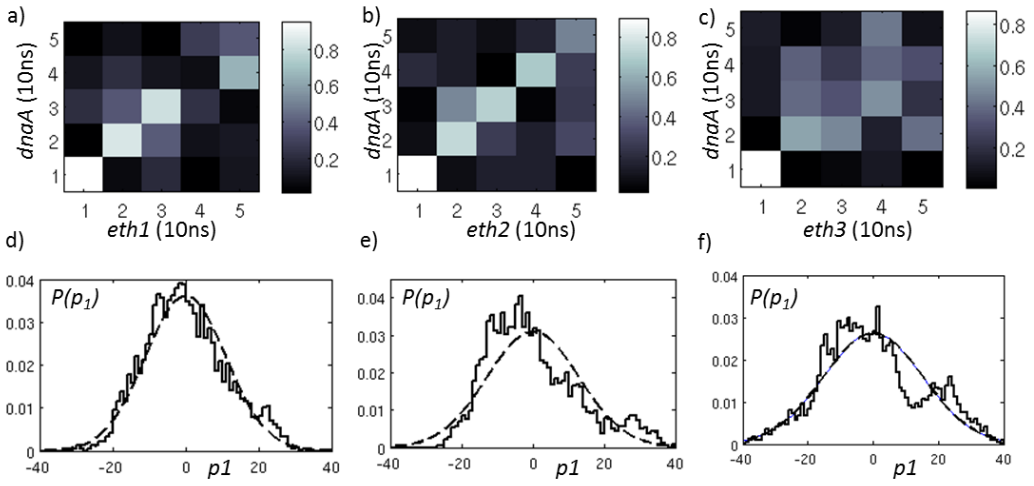


Figure SI-4: a-b-c) Matrices of the inner products between the principal components of the ethidium complexes and of the free oligonucleotides. d-e-f) Probability distribution of the projection of the atomic positional fluctuations along the 1st principal component of the three ethidium complexes: eth1, eth2 and eth3, respectively.