Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Supplementary Information

Sequence Dependence in Base Flipping: Experimental and Computational Studies

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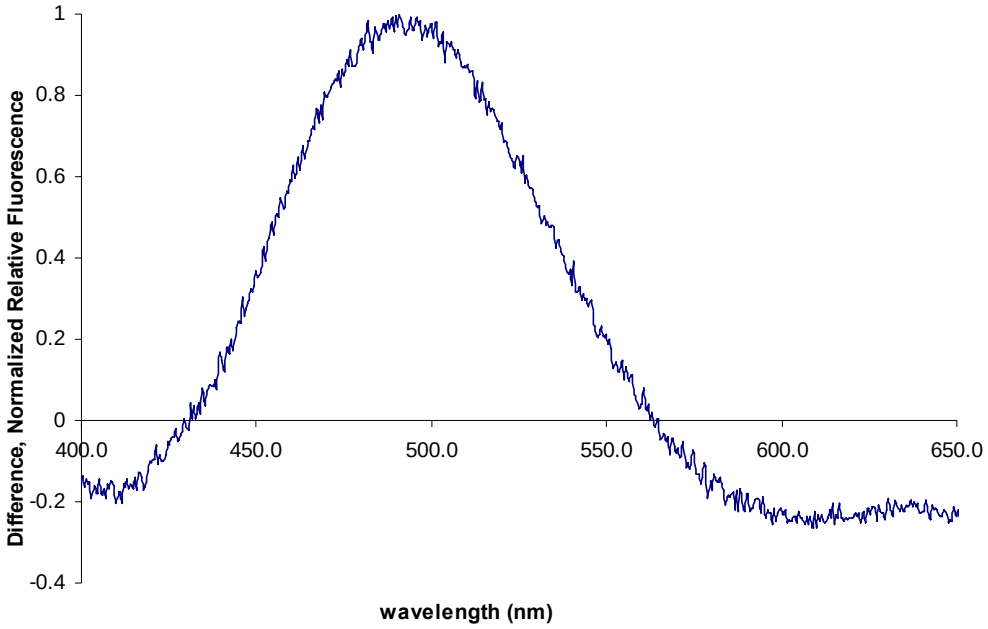


Figure S1. Difference of the fluorescence of 1 µM dansyl-cyclen in the presence of 10 µM thymine and 1 µM dansyl-cyclen in buffer.

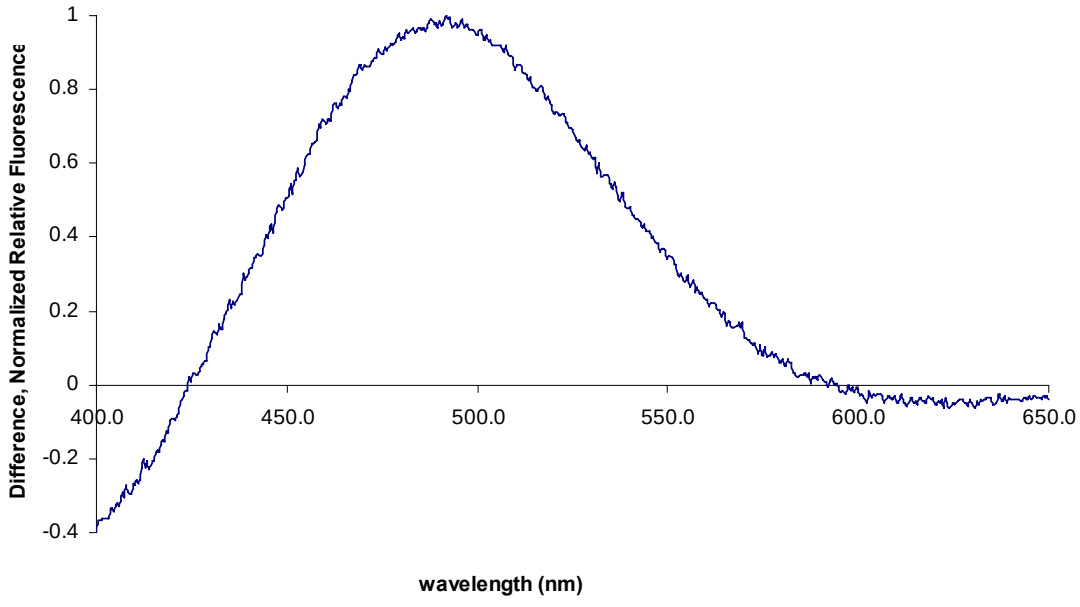


Figure S2. Difference of the fluorescence of 1 µM dansyl-cyclen in the presence of 11 µM 5'-GGTGG-3' and 1 µM dansyl-cyclen in buffer. Fluorescence was corrected for the fluorescence of DNA strand by subtracting the fluorescence of a buffer solution containing 11 µM 5'-GGTGG-3'.

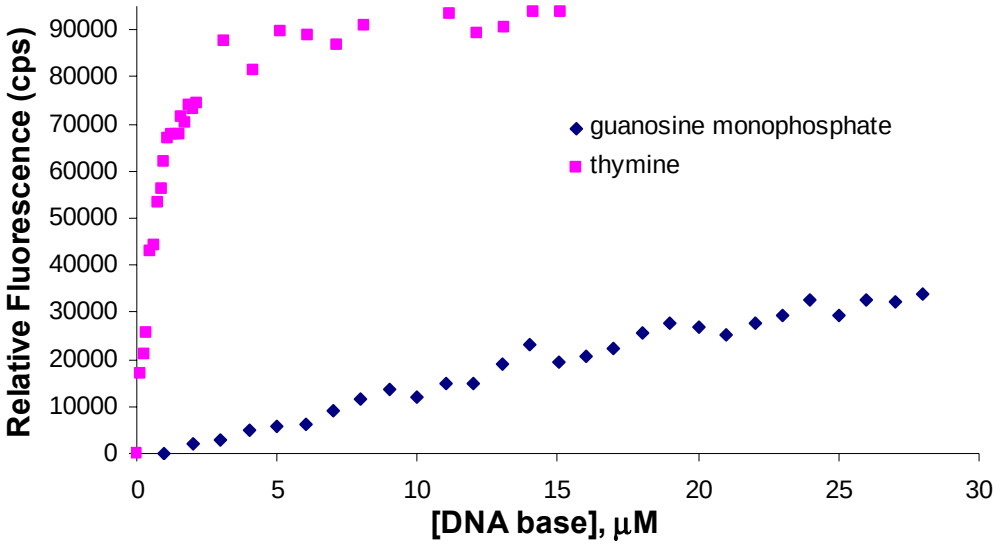


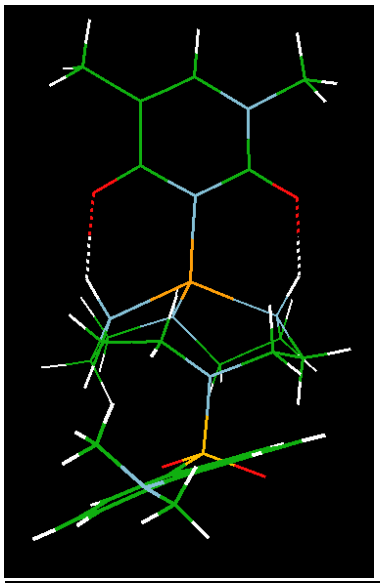
Figure S3. Relative fluorescence of dansyl-cyclen in the presence of thymine and guanosine monophosphate. Fluorescence has not been normalized in order to show the difference in signal between the two titrations.

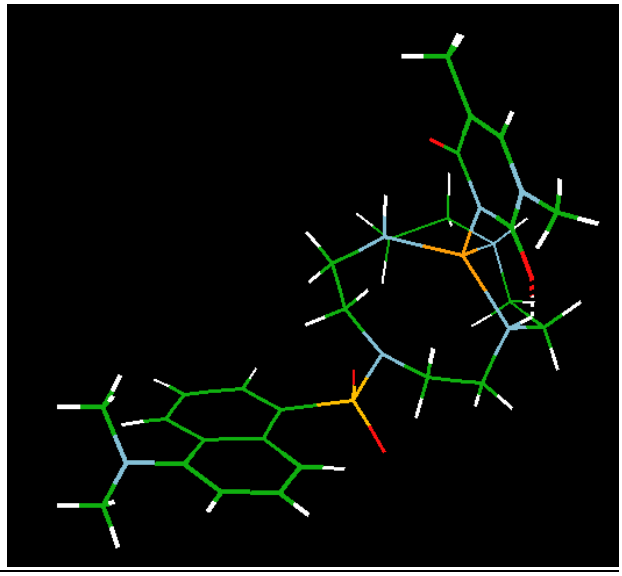
Table S1. R^2 and F_{max} values of data fit using one-site binding model.

$$y = \frac{Fx}{K + x}$$

	R^2			F_{max}		
System	**Trial 1**	**Trial 2**	**Trial 3**	**Trial 1**	**Trial 2**	**Trial 3**
Thymine	0.98363	0.97348	0.97458	1.05±0.01	0.99±0.02	1.06±0.02
Thymidine monophosphate	0.96251	0.92456	0.95749	1.00±0.02	1.07±0.04	1.081±0.02
Guanosine monophosphate	0.97626			135±61		
5'-AATAA-3'	0.97744	0.92067	0.92045	1.01±0.02	1.10±0.05	1.03±0.04
5'-GGTGG-3'	0.96771	0.89706	0.91119	1.00±0.02	0.91±0.02	0.91±0.03
5'-CCTCC-3'	0.97658	0.95983	0.94509	1.06±0.03	1.20±0.06	1.14±0.06
5'-GCACGAATAACGACG-3' 3'-CGTGCTTXTTGCTGC-5' *a*	0.9687	0.9664	0.9361	1.00±0.01	0.99±0.02	0.99±0.02
5'-GCACGGGTGGCGACG-3' 3'-CGTGCCCXCCGCTGC-5'	0.95835	0.9124	0.95781	1.06±0.04	1.09±0.05	1.01±0.02
5'-GCACGCCTCCCGACG-3' 3'-CGTGCGGXGGGCTGC-5'	0.96342	0.93164	0.95988	1.15±0.05	1.02±0.04	0.97±0.02
5'-GCACGTTTTTCGACG-3' 3'-CGTGCAAXAAGCTGC-5'	0.97787	0.96633	0.95501	1.00±0.02	1.10±0.02	0.99±0.03

a As previously reported in ref. 5.





Figures S4 (left) and S5 (right). Optimized geometry of anionic thymine bound to dansyl-cyclen.

Cartesian coordinates of optimized geometry of anionic thymine-cyclen complex

N	4.45705500	2.95374600	0.99781800
C	4.90470200	3.41067200	-0.22292400
H	5.44676900	4.35013600	-0.18887100
C	4.69532600	2.74837100	-1.38741600
C	5.18329200	3.23571800	-2.72175500
H	5.85189400	2.50168000	-3.18516500
H	4.34802500	3.37969900	-3.41627200
H	5.72183500	4.18322800	-2.62639700
C	3.95571900	1.49648200	-1.31716800
O	3.70885200	0.79850200	-2.32140600
N	3.51684600	1.07620700	-0.06927100
C	3.75538300	1.75899400	1.09517600
O	3.37306700	1.35276500	2.20646300
C	4.72073400	3.68696300	2.24009700
H	3.78032200	3.93601100	2.73664300
H	5.31879500	3.07578300	2.92027500
H	5.26170900	4.60244500	1.99708600
Zn	2.53561300	-0.61320400	-0.05818700
H	2.58788600	-3.16758800	2.79384300
C	2.96314100	-2.56590000	1.95926300
H	4.02775800	-2.38162800	2.14624800
C	2.79168500	-3.32522100	0.63644700
H	3.27578300	-4.30826500	0.68202300

H	1.72655200	-3.48098400	0.43576400
N	2.26572100	-1.25265200	1.88478800
H	2.82955900	-0.50878800	2.31784200
N	3.35155100	-2.49072900	-0.46051500
H	4.36929900	-2.52467100	-0.41021800
C	0.93165400	-1.22547500	2.54602900
H	1.05724000	-0.98116300	3.60798400
H	0.48326800	-2.21816200	2.49073000
C	2.93648300	-2.83059700	-1.84915000
H	3.67782900	-2.37533900	-2.51296700
H	2.95031500	-3.91454700	-2.01839900
C	1.53997400	-2.28163600	-2.16706100
H	0.76541300	-2.82996700	-1.62790300
H	1.35253100	-2.40590100	-3.24123300
C	-0.01770500	-0.20782700	1.90798300
H	-0.85834200	-0.04279900	2.58792200
H	0.49700300	0.75164300	1.79348900
N	-0.46673400	-0.63051000	0.56577700
N	1.43033200	-0.85068300	-1.76988800
H	2.06696500	-0.29123500	-2.35356300
C	0.05392200	-0.29000900	-1.87609000
H	-0.62758400	-1.07298000	-2.21323900
H	0.04376900	0.49819500	-2.63673400
C	-0.44831700	0.31847600	-0.56011800
H	-1.43646500	0.76472200	-0.73555500
H	0.21592700	1.13830500	-0.26753000
S	-1.62843700	-1.90227900	0.51807700
O	-1.85862100	-2.28355400	1.91568200
O	-1.09241100	-2.90709200	-0.41588300
C	-3.12098600	-1.22919400	-0.22971200
C	-3.92091700	-0.23001100	0.42066500
C	-3.45728700	-1.75254000	-1.46509000
C	-3.70758400	0.23443100	1.74488900
C	-5.03468600	0.29244900	-0.32729100
C	-4.61409000	-1.30127200	-2.12824900
H	-2.84340000	-2.53241300	-1.90030000
C	-4.54511300	1.18500300	2.28438900
H	-2.93921900	-0.21577500	2.35808000
C	-5.83676100	1.35371300	0.23199800
C	-5.37329800	-0.29518600	-1.57290200
H	-4.90531400	-1.75698000	-3.06927200
C	-5.59003100	1.75951200	1.53397800
H	-4.39101500	1.51386000	3.30843300
H	-6.27830000	0.04186100	-2.06506500
H	-6.19481400	2.53818600	1.98470300
N	-6.87466600	1.90176100	-0.55442200

C	-7.99376800	2.50672000	0.16036600
H	-7.75458300	3.49112900	0.59869000
H	-8.81934700	2.64905700	-0.54418900
H	-8.33204800	1.83879700	0.95645800
C	-6.44918400	2.73157800	-1.68890400
H	-7.28095700	2.83774200	-2.39310800
H	-6.13938000	3.73970900	-1.36504000
H	-5.61065800	2.26933300	-2.21236400

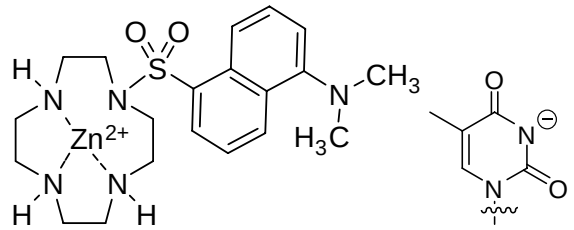


Table S2. Atom types and charges for anionic thymine/dansyl-cyclen complex as used in Amber 8.0. Thymine atom types are first, starting with glycosidic nitrogen and continuing clockwise. Cyclen atom types start with Zinc, move into the cyclen ring with the sulfonamide nitrogen and move counter-clockwise. Dansyl atom types start with the sulfur, move into the naphthalene ring and begin by moving away from ring junction, continuing around entire ring and ending with tertiary amine.

Table Entry	Atom Type	RESP Charge
1	N*	-0.0048
2	CM	-0.2066
3	H4	0.2012
4	CM	0.0168
5	CT	-0.3957
6	HC	0.1289
7	HC	0.1289
8	HC	0.1289
9	C	0.6096
10	O	-0.5279
11	N	-0.7929
12	C	0.6662
13	O	-0.5997
14	Zn	0.7475
15	n	-0.2358
16	c3	0.0103
17	h1	0.0507
18	h1	0.0507
19	c3	-0.0201
20	h1	0.0610
21	h1	0.0610
22	n3	-0.1318
23	hn	0.2452
24	c3	-0.1831
25	h1	0.1050
26	h1	0.1050
27	c3	0.0864
28	h1	0.0770
29	h1	0.0770
30	n3	-0.5801

31	hn	0.3378
32	c3	0.0864
33	h1	0.0770
34	h1	0.0770
35	c3	-0.1831
36	h1	0.1050
37	h1	0.1050
38	n3	-0.1318
39	hn	0.2452
40	c3	-0.0201
41	h1	0.0610
42	h1	0.0610
43	c3	0.0103
44	h1	0.0507
45	h1	0.0507
46	s4	0.7323
47	o	-0.4411
48	o	-0.4411
49	ca	-0.0561
50	ca	-0.0735
51	ha	0.1351
52	ca	-0.1657
53	ha	0.1430
54	ca	-0.0622
55	ha	0.1106
56	ca	-0.0400
57	ca	0.2087
58	ca	-0.1407
59	ha	0.1246
60	ca	-0.0961
61	ha	0.1357
62	ca	-0.3262
63	ha	0.2040
64	ca	0.1709
65	na	-0.2159
66	c3	-0.2221
67	h1	0.1058
68	h1	0.1058
69	h1	0.1058
70	c3	-0.2221
71	h1	0.1058
72	h1	0.1058
73	h1	0.1058

Bond Parameters

N-CT	337.0	1.449
Zn-n3	250.0	2.053
N-Zn	250.0	2.150

Angle Parameters

Zn-N-C	20.0	115.9
c3-n3-Zn	20.0	115.9
hn-n3-Zn	20.0	106.8
N-Zn-n3	20.0	101.4
n3-Zn-n3	20.0	97.0
CM-C-N	50.0	117.7
N*-C-N	70.0	117.2
n-s4-ca	64.3	117.6
c3-n-s4	60.0	117.6

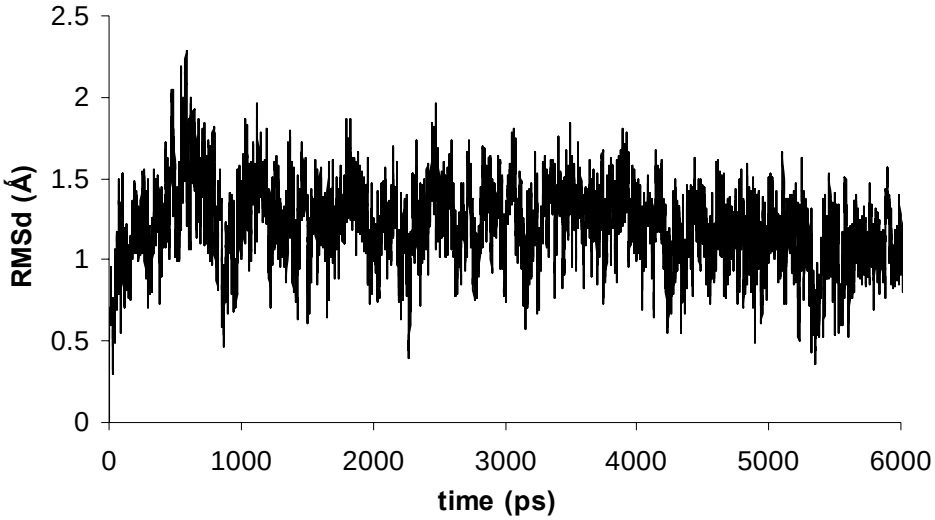


Figure S6. RMSd vs. time for dansyl-cyclen bound to 5'-GGTGG-3'. RMSd calculated from minimized, equilibrated structure over 6 ns of trajectory (data saved every 1 ps). "All atom" RMSd include all heavy atoms of DNA (C, N, O, P) but not hydrogens.

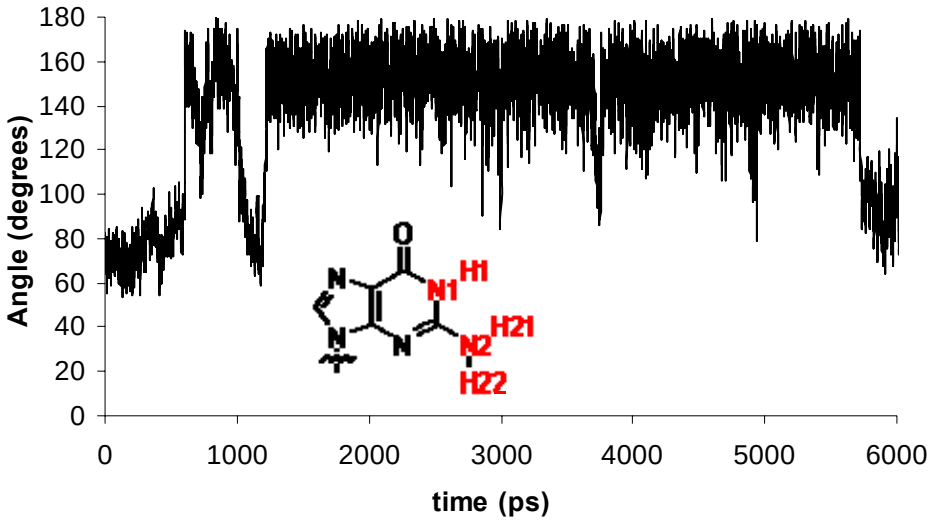


Figure S7. Plot of N1-H1-O3 (sulfonamide oxygen) angle over time for 5'-GGTGG-3' MD simulation calculated from data saved every 1 ps over 6 ns trajectory.

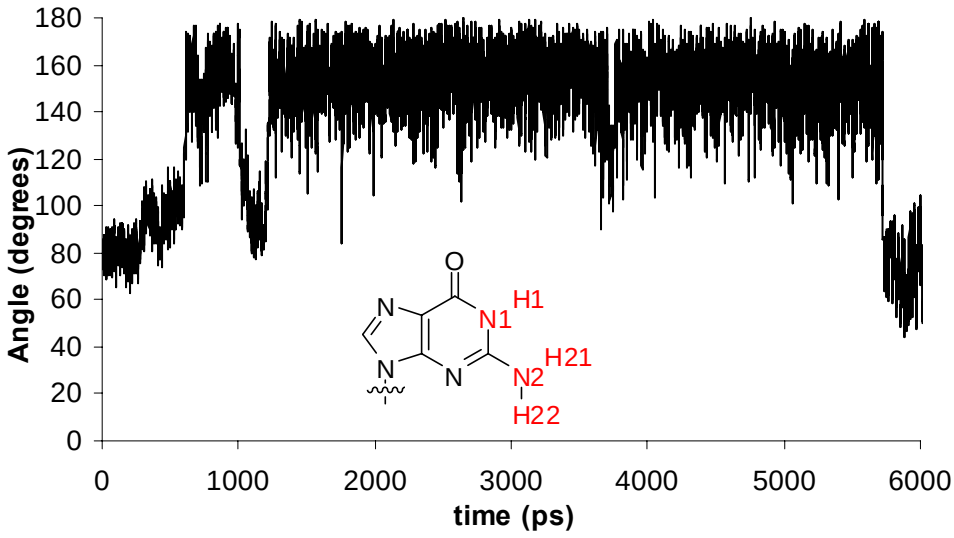


Figure S8. Plot of N2-H21-O4 (sulfonamide oxygen) angle over time for 5'-GGTGG-3' MD simulation calculated from data saved every 1 ps over 6 ns trajectory.

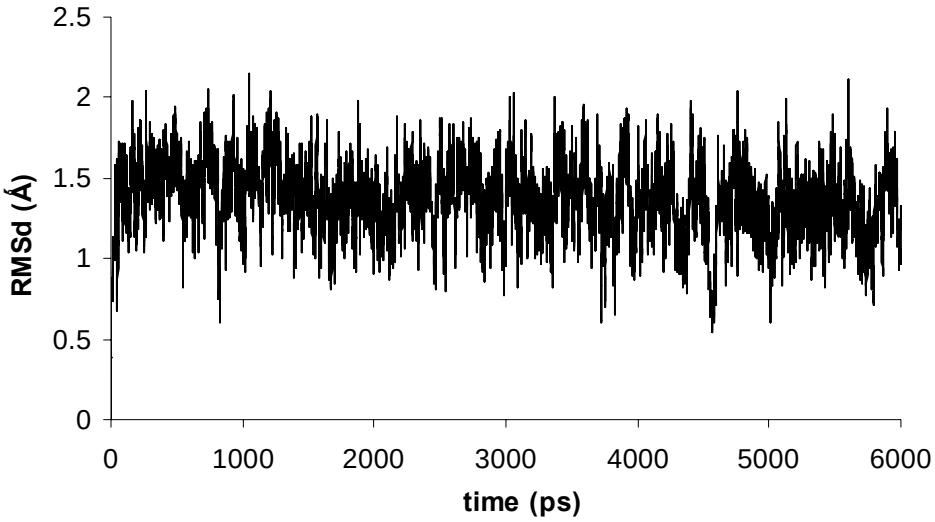


Figure S9. RMSd vs. time for dansyl-cyclen bound to 5'-CCTCC-3'. RMSd calculated from minimized, equilibrated structure over 6 ns of trajectory (data saved every 1 ps). "All atom" RMSd include all heavy atoms of DNA (C, N, O, P) but not hydrogens.

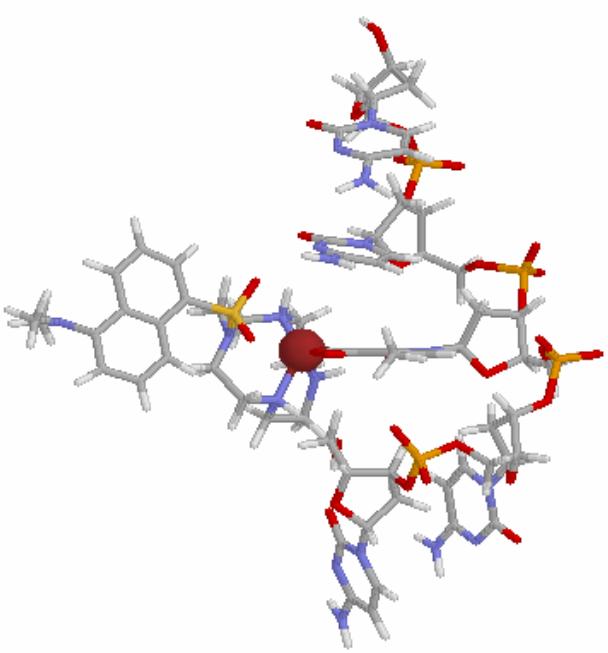


Figure S10. Snapshot at 3000 ps of dansyl-cyclen bound to 5'-CCTCC-3'.

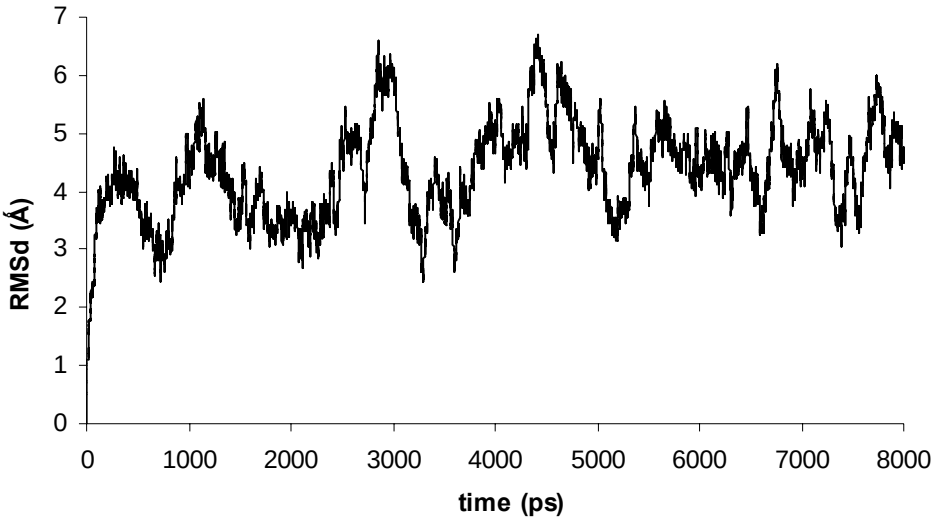


Figure S11. RMSd vs. time for dansyl-cyclen bound to 5'-CGACGAATAAGCACG-3'/3'-GCTGCTTATTCGTGC-3'. RMSd calculated from minimized, equilibrated structure over 8 ns of trajectory (data saved every 1 ps). "All atom" RMSd include all heavy atoms of DNA (C, N, O, P) but not hydrogens.