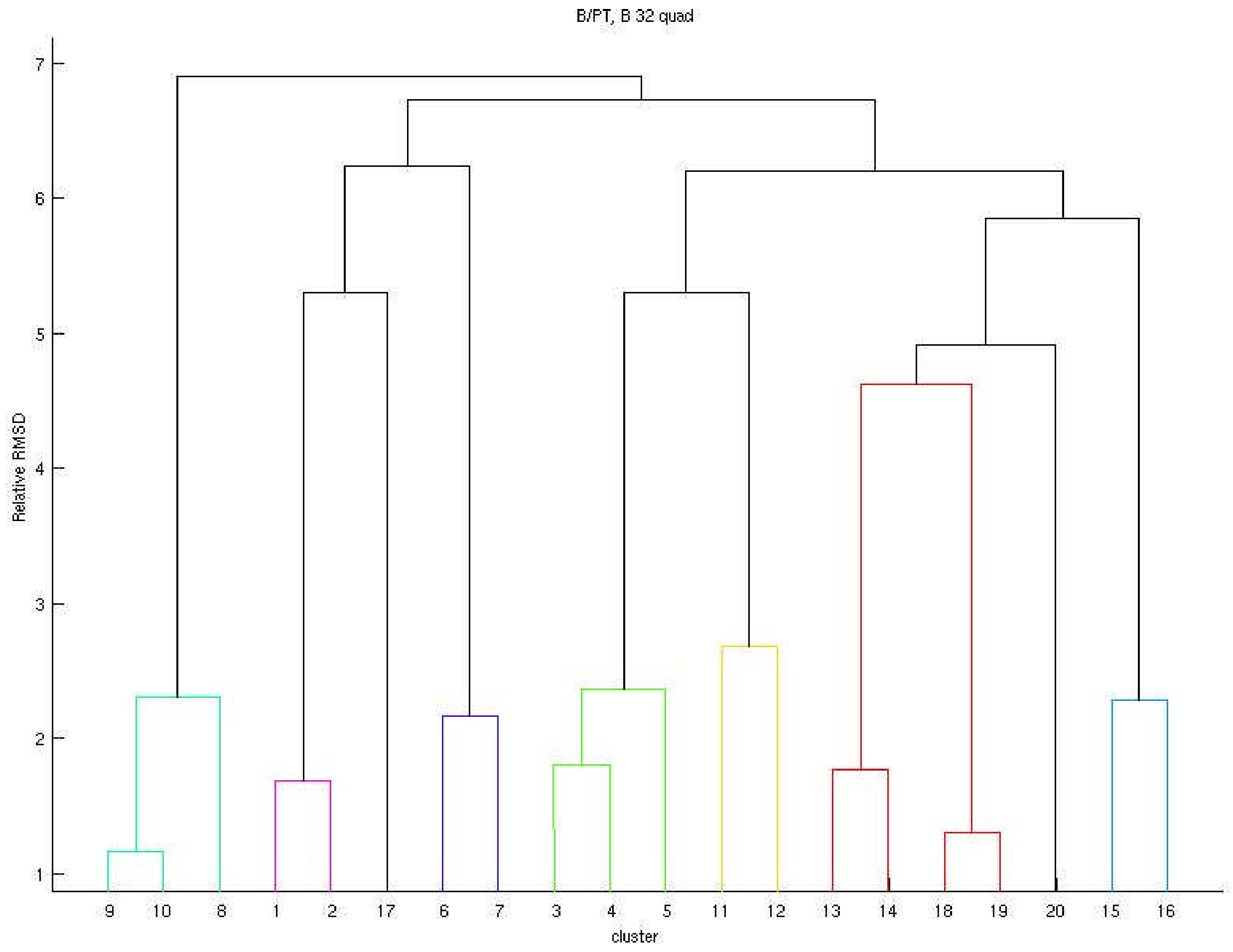
Supplementary Material

Clustering Analysis



conf(obj)	60(1)	33(2)	126(3)	83(4)	115(5)	142(6)	160(7)	194(8)	201(9)	232(10)	272(11)	283(12)
weight	6.69	10.79	2.89	13.58	6.47	9.21	7.17	13.89	3.10	5.35	12.58	8.29

conf(obj)	15(13)	47(14)	79(15)	102(16)	148(17)	180(18)	192(19)	218(20)
weight	14.66	12.38	12.16	4.32	23.37	8.06	7.56	17.47

Figure S1. Clustering Analysis: Dendrogram. Platinum cross-linked system (B/PT) is represented by objects from 1 to 12, corresponding in the order to the conformations 60, 33, 126, 83, 115, 142, 160, 194, 201, 232, 272, and 283. Mismatched system (B_32_quad) is represented by objects from 13 to 20, corresponding in order to the frames 15, 47, 79, 102, 148, 180, 192, and 218. “weight” represents the weight of the representative conformations in the overall trajectory. The two systems are clustered independently, with one exception, object 17, which weights for 23.37 % of the mismatched conformations. At the second level of hierarchy the exception is associated with conformations 33 and 60, the only two conformations from the platinated system indicated as “repair conformations”. Considering the binding affinity, their structural similarities seem to be beyond the binding mode.

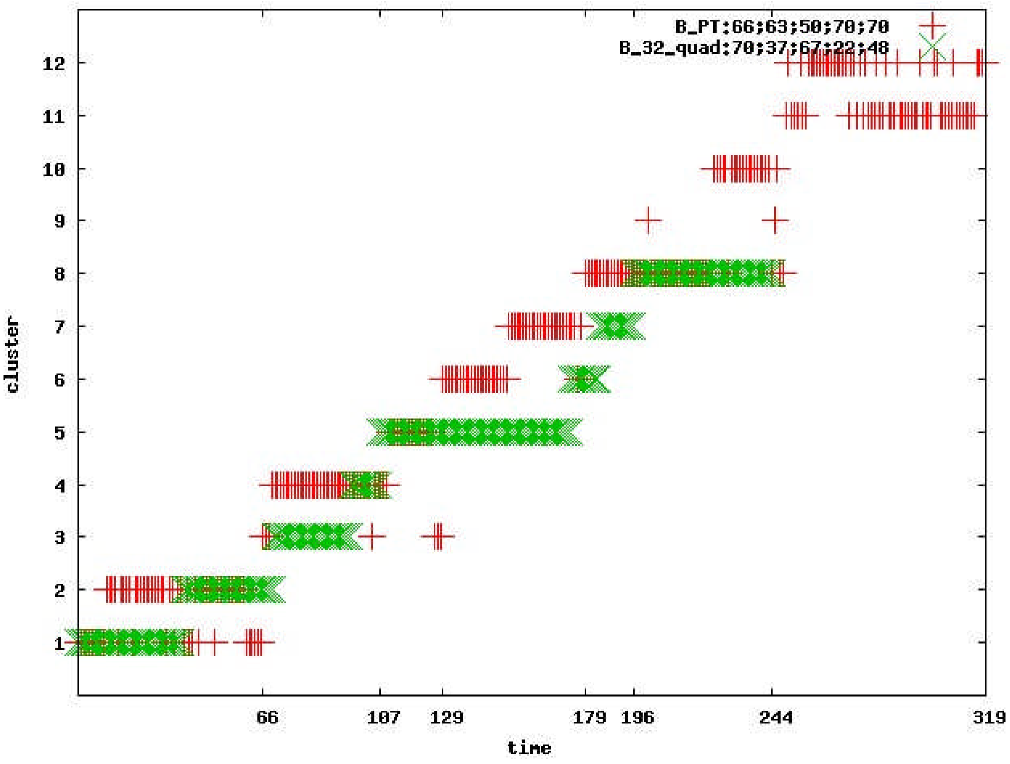


Figure S2. Clustering Analysis: Representative Conformations. Representative conformations for platinum cross-linked MutSα-DNA complex, B_PT, 66, 63, 50, 70 and 70 corresponding to the five independent trials are clustered in 12 clusters, while the representative conformations from the mismatched complex, B_32_quad, 70, 37, 67, 22 and 48, are clustered in eight clusters.

Mapping the DNA Binding Sites

Table S1. The binding mode for the platinum cross-linked MutSα-DNA complex

Frame 142. Interactions with MSH6

	DNA	**type**	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	THR46	CYT11	2.920
2		O-H...O	THR46	CYT11	2.515
3		O-H...O	THR46	CYT11	1.931
4		N-H...O	GLY48	CYT11	1.898
5		C-H...O	GLY48	CYT11	2.651
6		N-H...O	MET 49	CYT11	1.957
7		C-H...O	LYS 70	CYT7	2.519

8		C-H...O	LYS 70	CYT7	2.333
9		C-H...O	LYS 92	CYT7	2.654
10		C-H...O	LYS 92	CYT6	2.558
11		N-H...O	LYS 92	CYT7	1.732
12		C-H...O	TYR 108	CYT10	2.875
13		C-H...O	CYT11	THR46	2.640
14		C-H...S	CYT7	MET91	2.755
	GUA				
1		C-H...O	GLY69	GUA8	2.876
2		C-H...O	GLY69	GUA8	2.917
3		N-H...O	LYS70	GUA8	2.534
4		N-H...N	LYS70	GUA8	2.915
5		C-H...O	LYS70	GUA8	2.490
6		C-H...N	PHE71	GUA8	2.463
7		C-H...N	PHE71	GUA9	2.893
8		C-H...O	LEU88	GUA9	2.881
9		C-H...O	PRO101	GUA9	2.528
10		C-H...N	PRO101	GUA 9	2.843
11		C-H...O	VAL147	GUA 10	2.591
12		C-H...O	VAL147	GUA10	2.621
13		C-H...O	VAL147	GUA10	2.846
14		N-H...O	VAL148	GUA10	1.984
15		O-H...O	TYR484	GUA 9	1.821
16		C-H...O	ARG613	GUA8	2.965
17		C-H...O	ARG 613	GUA8	2.475
18		N-H...O	GUA8	VAL68	2.018
19		C-H...N	GUA8	ARG613	2.842
20		C-H...N	GUA8	ARG613	2.457
21		C-H...N	GUA10	ARG150	2.675
22		N-H...O	GUA10	GLU73	2.941
23		N-H...O	GUA10	GLU73	1.784
24		C-H...O	GUA9	GLY99	2.792
	THY				
1		C-H...O	MET91	THY8	2.919
2		C-H...O	MET91	THY8	2.679
3		C-H...O	TRP609	THY13	2.435
4		C-H...N	THY3	ARG146	2.948
5		C-H...N	THY3	ARG146	2.885
6		C-H...O	THY8	VAL89	2.955
7		N-H...O	THY8	GLU73	2.126
8		C-H...O	THY 8	GLY99	2.995
9		C-H…pi	THY8	PHE71	4.012

Frame 33

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CTY				

1		C-H...O	THR46	CYT 11	2.264
2		C-H...O	PRO47	CYT 11	2.630
3		C-H...O	LYS639	CYT15	2.803
4		N-H...O	LYS639	CYT15	1.656
	GUA				
1		C-H...N	PHE71	GUA9	2.694
2		C-H...N	PHE71	GUA9	2.689
3		C-H...O	PRO101	GUA9	2.587
4		C-H...O	PRO101	GUA9	2.894
5		C-H...O	VAL147	GUA10	2.514
6		N-H...O	VAL148	GUA10	2.326
7		C-H...O	TYR484	GUA9	2.520
8		O-H...O	TYR484	GUA 9	1.773
9		C-H...O	ARG 613	GUA 8	2.722
10		C-H…N	GUA10	ARG146	2.796
	THY				
1		C-H…O	MET91	THY8	2.928
2		C-H…pi	THY8	PHE71	3.956

Frame 33

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS512	ADE4	2.895
	CYT				
1		N-H...O	LYS546	CYT2	1.694
	GUA				
1		N-H…O	LYS512	GUA5	1.686
2		C-H…O	GLN545	GUA6	2.624

Frame 115

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	PRO47	CYT 11	2.715
2		C-H...O	PRO47	CYT11	2.595
3		C-H...O	PRO47	CYT11	2.977
4		C-H...O	LYS70	CYT7	2.569

5		C-H...O	MET91	CYT7	2.885
6		C-H...O	MET91	CYT7	2.453
7		N-H...O	LYS92	CYT7	2.451
8		C-H...O	LYS92	CYT 7	2.969
9		C-H...O	PRO101	CYT 10	2.849
10		C-H...O	CYT7	LYS92	2.567
11		C-H...N	CYT7	LYS92	2.849
12		C-H...O	CYT 7	LYS92	2.295
	GUA				
1		C-H...N	GLY69	GUA8	2.883
2		N-H...O	LYS70	GUA8	2.991
3		C-H...O	LYS70	GUA8	2.504
4		C-H...N	MET91	GUA10	2.985
5		C-H...O	PRO101	GUA9	2.448
6		C-H...N	PRO101	GUA9	2.889
7		C-H...N	PRO101	GUA9	2.766
8		O-H...O	TYR108	GUA9	2.360
9		C-H...O	TYR108	GUA9	2.991
10		C-H...O	PRO128	GUA9	2.822
11		C-H...O	PRO128	GUA9	2.366
12		C-H...O	VAL147	GUA10	2.607
13		N-H...O	VAL148	GUA10	1.795
14		C-H...O	VAL148	GUA10	2.908
15		O-H...O	TYR484	GUA8	2.721
16		O-H...O	TYR484	GUA9	1.751
17		C-H...O	ILE611	GUA12	2.734
18		C-H...O	ILE611	GUA12	2.601
19		N-H...O	GUA8	VAL68	1.827
20		C-H...N	GUA9	GLY69	2.945
21		C-H...O	GUA9	GLN124	2.951
22		C-H...O	GUA9	TYR108	2.751
	THY				
1		C-H...O	MET91	THY8	2.959
2		C-H...O	LYS92	THY8	2.891
3		C-H...O	LYS92	THY8	2.765
4		N-H...O	LYS92	THY8	2.669
5		N-H...O	LYS92	THY8	2.295
6		C-H...O	ILE611	THY13	2.727
7		C-H...O	THY8	PHE90	2.787
8		N-H...O	THY8	GLU73	1.696

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS512	ADE4	2.617
2		C-H...O	THR526	ADE4	2.777

3		O-H...O	THR526	ADE4	2.470
4		C-H...O	LYS528	ADE4	2.468
	CYT				
1		N-H...O	LYS550	CYT5	1.092
	GUA				
1		N-H...O	LYS6	GUA11	1.584
2		N-H...O	LYS512	GUA5	1.582
3		C-H...O	ARG524	GUA5	2.986
4		C-H...O	GLN545	GUA6	2.533
5		N-H...O	LYS546	GUA6	1.971
6		C-H...O	LYS546	GUA6	2.852
7		N-H...O	ASN547	GUA6	1.779
8		C-H...O	ASN547	GUA6	2.847
9		C-H...O	ASN547	GUA6	2.801
	THY				
1		N-H...O	LYS509	THY3	2.373
2		N-H...O	LYS528	THY3	1.594

Frame 126

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	PRO47	CYT11	2.688
2		C-H...O	PRO47	CYT11	2.709
3		C-H...O	PRO47	CYT11	2.968
4		C-H...O	LYS70	CYT7	2.709
5		N-H...O	LYS70	CYT7	2.412
6		N-H...O	LYS92	CYT7	2.692
7		O-H...O	TYR108	CYT10	2.111
8		C-H...O	LYS639	CYT15	2.741
9		C-H...N	CYT7	LYS92	2.849
	GUA				
1		N-H...O	LYS70	GUA8	2.747
2		N-H...N	LYS70	GUA8	2.887
3		C-H...O	LYS70	GUA8	2.701
4		N-H...O	LYS70	GUA8	1.779
5		C-H...N	PHE71	GUA8	2.951
6		C-H...N	PHE71	GUA8	2.685
7		C-H...O	LEU88	GUA9	2.659
8		N-H...O	VAL89	GUA9	2.907

9		C-H...O	PRO101	GUA9	2.501
10		C-H...N	PRO101	GUA9	2.884
11		O-H...O	TYR108	GUA9	2.105
12		C-H...O	TYR108	GUA9	2.914
13		C-H...O	PRO128	GUA9	2.918
14		C-H...O	PRO128	GUA9	2.969
15		N-H...O	VAL148	GUA10	1.991
16		C-H...O	TYR484	GUA9	2.992
17		O-H...O	TYR484	GUA8	2.703
18		O-H...O	TYR484	GUA9	1.818
19		N-H...O	GUA8	VAL68	1.853
20		N-H...O	GUA10	GLU73	2.884
21		N-H...O	GUA10	GLU73	2.131
22		N-H...O	GUA10	GLU73	2.597
23		C-H...O	GUA9	GLY99	2.553
24		C-H...O	GUA9	TYR 108	2.904
	THY				
1		C-H...O	MET91	THY8	2.761
2		C-H...O	MET91	THY8	2.849
3		C-H...O	MET91	THY8	2.892
4		C-H...O	SER98	THY8	2.512
5		C-H...O	LYS143	THY12	2.888
6		N-H...O	LYS143	THY12	1.700
7		N-H...O	TRP609	THY14	2.749
8		N-H...O	LYS643	THY14	1.989
9		C-H...O	THY8	PHE90	2.897
10		C-H...O	THY8	VAL89	2.478
11		N-H...O	THY8	GLU73	1.694
12		C-H...N	THY8	GLY99	2.985
13		C-H...O	THY 8	GLY99	2.723

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS512	ADE4	2.650
2		C-H...O	LYS528	ADE4	2.708
	CYT				
1		C-H...O	GLN545	CYT5	2.615
		C-H...N	CYT 5	GLN545	2.851
	GUA				
1		N-H...O	LYS509	GUA14	2.945
2		N-H...N	LYS509	GUA14	2.003
3		N-H...N	LYS509	GUA14	2.997
4		N-H...O	LYS512	GUA5	1.707
		C-H...O	ARG524	GUA5	2.796

5		C-H...O	LYS546	GUA6	2.459
6		N-H...O	ASN547	GUA6	2.187
7		C-H...O	ASN547	GUA6	2.982
	THY				
		None			

Frame 201

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	PRO47	CYT11	2.970
2		C-H...O	PRO47	CYT11	2.824
3		C-H...O	PRO47	CYT11	2.908
4		N-H...O	GLY48	CYT11	2.967
5		C-H...O	LYS70	CYT7	2.577
6		N-H...O	LYS70	CYT7	2.065
7		C-H...O	MET91	CYT7	2.385
8		N-H...O	LYS92	CYT7	2.648
9		N-H...N	LYS92	CYT7	2.001
10		C-H...N	LYS92	CYT7	2.723
11		N-H...O	ARG136	CYT2	2.193
12		N-H...O	ILE141	CYT1	2.472
13		C-H...O	ARG146	CYT2	2.500
14		N-H...O	LYS636	CYT5	2.589
15		C-H...O	LYS639	CYT15	2.626
16		N-H...O	LYS639	CYT15	1.622
17		C-H...O	CYT1	CYS135	2.890
18		C-H...N	CYT1	HIS140	2.558
	GUA				
1		C-H...N	VAL68	GUA10	2.921
2		C-H...O	GLY69	GUA8	2.856
3		C-H...N	PHE71	GUA9	2.809
4		C-H...N	PHE71	GUA9	2.747
5		C-H...N	PHE71	GUA8	2.820
6		C-H...O	PRO101	GUA9	2.772
7		C-H...O	PRO101	GUA9	2.907
8		C-H...O	PRO128	GUA9	2.951
9		C-H...O	VAL147	GUA10	2.610
10		N-H...O	VAL148	GUA10	2.572
11		C-H...O	LYS636	GUA6	2.501

12		N-H...O	LYS636	GUA6	2.053
13		C-H...N	GUA8	LYS70	2.918
14		N-H...O	GUA10	GLU73	2.180
15		N-H...O	GUA10	GLU73	2.910
16		C-H...O	GUA9	GLY99	2.566
	THY				
1		C-H...O	SER98	THY8	2.345
2		N-H...O	GLY99	THY8	2.754
3		N-H...O	TRP609	THY13	1.732
4		C-H...O	ILE611	THY13	2.495
5		C-H...N	THY3	ARG146	2.950
6		C-H...S	THY8	MET91	2.968
7		N-H...O	THY8	GLU73	1.952
8		C-H...O	THY8	GLY99	2.566

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS512	ADE4	2.874
2		O-H...O	THR526	ADE4	1.823
3		C-H...O	LYS528	ADE4	2.995
4		C-H...O	LYS528	ADE4	2.550
5		C-H...O	LYS528	ADE4	2.538
	CYT				
1		C-H...O	LYS546	CYT7	2.959
2		N-H...O	LYS546	CYT7	1.704
3		C-H...N	CYT5	GLN545	2.858
	GUA				
1		C-H…O	LYS6	GUA11	2.733
2		N-H…O	LYS6	GUA11	1.747
3		C-H...O	LYS512	GUA5	2.918
4		N-H...O	LYS512	GUA5	1.595
5		C-H...O	ARG524	GUA5	2.914
6		C-H...O	GLN545	GUA6	2.781
7		C-H...O	GLN545	GUA6	2.739
8		N-H...O	LYS546	GUA6	1.636
9		C-H...O	LYS546	GUA6	2.603
10		C-H...O	LYS546	GUA6	2.824
11		C-H...O	LYS546	GUA6	2.883
12		N-H...O	LYS546	GUA6	2.976
	THY				
1		N-H...O	LYS509	THY3	2.573
2		N-H...O	LYS509	THY3	2.328
3		N-H...O	LYS528	THY3	1.597

Frame 232

A. Interactions with MSH6

		type	donor	acceptor	distance, Ä
	ADE				
		None			
	CYT				
1		C-H...O	PRO47	CYT11	2.456
2		C-H...O	LYS70	CYT7	2.569
3		C-H...O	LYS70	CYT7	2.652
4		C-H...O	MET91	CYT7	2.500
5		C-H...O	MET91	CYT7	2.733
6		C-H...N	MET91	CYT7	2.860
7		N-H...O	LYS92	CYT7	2.100
8		N-H...N	LYS92	CYT7	2.358
9		C-H...N	LYS92	CYT7	2.887
10		C-H...O	LYS92	CYT7	2.603
11		C-H...O	LYS92	CYT7	2.962
12		N-H...O	LYS92	CYT7	2.416
13		N-H...O	LYS92	CYT7	2.582
14		N-H...O	LYS92	CYT7	1.713
15		N-H...O	LYS92	CYT7	2.505
16		C-H...O	PRO101	CYT10	2.863
17		C-H...O	TYR108	CYT10	2.682
18		C-H...O	CYS135	CYT2	2.645
19		N-H...O	ARG136	CYT2	1.714
20		C-H...O	HIS140	CYT1	2.560
21		N-H...O	ILE141	CYT1	2.462
22		C-H...O	ILE141	CYT1	2.641
23		C-H...O	ARG146	CYT2	2.821
24		N-H...O	LYS636	CYT5	2.646
25		N-H...O	LYS636	CYT5	2.962
26		C-H...O	LYS639	CYT15	2.935
27		C-H...O	LYS639	CYT15	2.912
28		C-H...O	LYS639	CYT15	2.190
29		C-H...O	CYT1	ALA139	2.622
30		C-H...N	CYT2	ARG146	2.904
31		N-H...O	CYT7	LYS92	2.302
	GUA				
1		C-H...O	GLY69	GUA8	2.534
2		C-H...O	GLY69	GUA9	2.725
3		C-H...O	LYS70	GUA8	2.995
4		C-H...N	PHE71	GUA9	2.601
5		C-H...O	LEU88	GUA9	2.553
6		C-H...O	PRO101	GUA9	2.797
7		C-H...O	VAL147	GUA10	2.714

8		N-H...O	VAL148	GUA10	2.100
9		C-H...O	LYS636	GUA6	2.823
10		N-H...O	LYS636	GUA6	1.680
11		C-H...N	GUA9	GLY69	2.690
12		C-H...N	GUA10	ARG150	2.874
13		N-H...O	GUA10	GLU73	2.239
14		N-H...O	GUA10	GLU73	2.509
15		C-H...O	GUA9	GLY99	2.568
	THY				
1		C-H...O	MET91	THY8	2.790
2		C-H...O	SER98	THY8	2.784
3		N-H...O	TRP609	THY13	2.381
4		C-H...S	THY8	MET91	2.769
5		N-H...O	THY8	GLU73	1.922
6		C-H...O	THY8	GLY99	2.552

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		C-H...O	LYS509	ADE4	2.865
2		N-H...N	LYS509	ADE4	2.297
3		N-H...O	LYS509	ADE4	2.137
4		N-H...N	LYS509	ADE4	2.962
5		N-H...N	LYS509	ADE4	2.594
6		O-H...O	THR526	ADE4	1.851
7		C-H...O	LYS528	ADE4	2.307
8		C-H...O	LYS528	AD1E4	2.729
9		C-H...N	ADE4	LYS509	2.902
	CYT				
1		C-H...O	LYS546	CYT7	2.500
2		N-H...O	LYS546	CYT7	1.612
3		C-H...N	CYT5	GLN545	2.827
4		C-H...N	CYT7	LYS546	2.996
	GUA				
1		C-H...O	LYS6	GUA11	2.787
2		N-H...O	LYS6	GUA11	1.635
3		C-H...O	LYS512	GUA5	2.858
4		C-H...O	ARG524	GUA5	2.887
5		C-H...O	ARG524	GUA5	2.633
6		C-H...O	GLN545	GUA6	2.911
7		C-H...O	GLN545	GUA6	2.760
8		N-H...O	LYS546	GUA6	2.001
9		C-H...O	LYS546	GUA6	2.905
10		N-H...O	LYS546	GUA6	2.892
	THY				
1		N-H...O	LYS528	THY3	1.726

2		N-H...O	LYS528	THY3	2.962
3		C-H...N	THY3	LYS528	2.977

Frame 272

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		none			
	CYT				
1		C-H...O	THR46	CYT11	2.860
2		C-H...O	THR46	CYT11	2.798
3		O-H...O	THR46	CYT11	1.542
4		C-H...O	PRO47	CYT11	2.583
5		N-H...O	GLY48	CYT11	2.788
6		N-H...O	GLY48	CYT11	1.914
7		N-H...O	MET49	CYT11	2.004
8		C-H...N	PHE71	CYT7	2.669
9		C-H...N	PHE71	CYT7	2.935
10		C-H...O	MET91	CYT7	2.797
11		C-H...O	MET91	CYT7	2.714
12		C-H...O	TYR108	CYT10	2.804
13		C-H...O	CYT7	LYS92	2.874
	GUA				
1		C-H...O	GLY48	GUA10	2.864
2		C-H...O	GLY69	GUA8	2.541
3		N-H...N	LYS70	GUA8	2.771
4		C-H...O	LYS70	GUA8	2.475
5		C-H...N	PHE71	GUA9	2.632
6		C-H...N	PHE71	GUA8	2.800
7		C-H...O	LEU88	GUA9	2.280
8		N-H...O	VAL89	GUA9	2.514
9		C-H...O	PRO101	GUA9	2.674
10		N-H...O	GUA8	GLU73	2.859
11		N-H...O	GUA8	GLU73	2.637
12		N-H...O	GUA10	GLU73	2.094
13		N-H...O	GUA10	GLU73	2.445
	THY				
1		C-H...O	GLU73	THY8	2.686
2		N-H...O	VAL89	THY8	2.870
3		C-H...O	MET91	THY8	2.956
4		C-H...O	MET91	THY8	2.561
5		C-H...O	GLY99	THY8	2.997
6		N-H...O	TRP609	THY13	2.182
7		N-H...O	LYS643	THY14	2.410
8		C-H...O	THY8	VAL89	2.298

9		N-H...O	THY8	GLU73	2.213

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS512	ADE4	2.368
2		O-H...O	THR526	ADE4	1.764
3		C-H...O	LYS528	ADE4	2.998
	CYT				
1		C-H...O	LYS546	CYT7	2.672
2		N-H...O	LYS546	CYT7	2.895
3		N-H...O	LYS546	CYT7	1.813
4		C-H...N	CYT5	GLN545	2.969
	GUA				
1		N-H...O	LYS6	GUA11	1.695
2		C-H...O	LYS509	GUA15	2.548
3		C-H...O	LYS512	GUA5	2.478
4		N-H...O	LYS512	GUA5	1.649
5		C-H...O	GLN545	GUA6	2.409
6		N-H...O	LYS546	GUA6	1.753
7		N-H...O	LYS546	GUA6	2.973
8		C-H...O	LYS546	GUA6	2.588
	THY				
1		C-H...O	LYS528	THY3	2.566
2		C-H...O	LYS528	THY3	2.709
3		N-H...O	LYS528	THY3	1.716

Frame 160

A. MSH6 interactions

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	THR46	CYT11	2.850
2		O-H...O	THR46	CYT11	1.646
3		C-H...O	PRO47	CYT11	2.723
4		C-H...O	PRO47	CYT11	2.816
5		N-H...O	GLY48	CYT11	2.842
6		N-H...O	GLY48	CYT11	1.940
7		C-H...O	GLY48	CYT11	2.725
8		N-H...O	MET49	CYT11	2.381
9		C-H...O	MET49	CYT11	2.934

10		C-H...O	LYS70	CYT7	2.369
11		O-H...O	TYR108	CYT10	2.135
12		C-H...O	TYR108	CYT10	2.861
13		C-H...O	ARG604	CYT15	2.600
14		C-H...O	LYS639	CYT15	2.643
	GUA				
1		C-H...O	GLY48	GUA10	2.576
2		C-H...O	GLY69	GUA8	2.614
3		N-H...O	LYS70	GUA8	2.931
4		N-H...N	LYS70	GUA8	2.440
5		C-H...O	LYS70	GUA8	2.717
6		C-H...N	LYS70	GUA8	2.770
7		N-H...N	PHE71	GUA8	2.977
8		C-H...N	PHE71	GUA8	2.537
9		C-H...N	PHE71	GUA9	2.888
10		C-H...N	PHE71	GUA9	2.860
11		C-H...N	PHE71	GUA9	2.771
12		C-H...O	LEU88	GUA9	2.997
13		N-H...O	VAL89	GUA9	2.888
14		C-H...O	PRO101	GUA9	2.645
15		C-H...N	PRO101	GUA9	2.585
16		O-H...O	TYR108	GUA9	2.706
17		C-H...O	VAL147	GUA10	2.721
18		C-H...O	VAL147	GUA10	2.834
19		C-H...O	VAL147	GUA10	2.889
20		N-H...O	VAL148	GUA10	2.034
21		O-H...O	TYR484	GUA9	1.686
22		C-H...O	ARG613	GUA8	2.903
23		N-H...O	GUA8	VAL68	1.901
24		C-H...N	GUA8	ARG613	2.689
25		C-H...N	GUA8	ARG613	2.899
26		C-H...N	GUA9	GLY69	2.926
27		C-H...O	GUA9	GLN124	2.651
28		C-H...N	GUA10	ARG150	2.762
29		C-H...N	GUA10	ARG150	2.836
30		N-H...O	GUA10	GLU73	1.982
	THY				
1		C-H...N	THY3	ARG146	2.999
2		N-H...O	THY8	GLU73	1.725
3		C-H...O	THY8	GLY99	2.866

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS110	ADE2	2.536

2		N-H...O	LYS110	ADE2	2.340
3		C-H...O	ASN547	ADE4	2.939
4		C-H...O	ASN547	ADE4	2.599
	CYT				
1		C-H...O	LYS6	CYT10	2.609
2		N-H...O	LYS546	CYT7	1.900
	GUA				
1		C-H...O	LYS6	GUA11	2.842
2		N-H...O	LYS6	GUA11	1.726
3		C-H...O	LYS509	GUA15	2.921
4		C-H...O	ASN547	GUA5	2.295
	THY				
		None			

Frame 283

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	THR46	CYT11	2.692
2		O-H...O	THR46	CYT11	1.595
3		C-H...O	PRO47	CYT11	2.839
4		N-H...O	GLY48	CYT11	1.738
5		C-H...O	GLY48	CYT11	2.470
6		C-H...O	LYS70	CYT7	2.802
7		C-H...O	MET91	CYT7	2.837
8		C-H...O	GLY93	CYT6	2.914
9		C-H...N	ASN94	CYT6	2.891
10		O-H...O	TYR108	CYT10	2.711
11		C-H...O	TYR108	CYT10	2.899
12		C-H...N	CYT11	ASN94	2.646
13		C-H...pi	CYT11	TR6 95	4.304
14		C-H...pi	CYT11	TR6 95	4.634
	GUA				
1		C-H...O	VAL68	GUA10	2.572
2		C-H...N	PHE71	GUA9	2.588
3		C-H...N	PHE71	GUA9	2.734
4		C-H...O	LEU88	GUA9	2.965
5		C-H...O	PRO101	GUA9	2.577
6		C-H...N	PRO101	GUA9	2.961
7		C-H...N	PRO101	GUA9	2.889
8		C-H...O	ILE103	GUA11	2.837

9		O-H...O	TYR108	GUA9	2.221
10		C-H...O	GUA8	GLY69	2.583
11		N-H...S	GUA10	MET91	2.952
12		N-H...O	GUA10	GLU73	1.931
	THY				
1		C-H...O	GLU73	THY 8	2.946
2		C-H...O	MET91	THY 8	2.505
3		C-H...O	MET91	THY8	2.772
4		C-H...O	MET91	THY8	2.483
5		C-H...O	TRP609	THY13	2.889
6		N-H...O	THY8	GLU73	1.793

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		O-H...O	THR526	ADE4	1.749
2		C-H...O	LYS528	ADE4	2.912
3		C-H...O	LYS528	ADE4	2.449
	CYT				
1		C-H...O	LYS6	CYT10	2.937
2		N-H...O	LYS546	CYT7	1.628
	GUA				
1		C-H...O	LYS6	GUA11	2.802
2		N-H...O	LYS6	GUA11	1.671
3		C-H...O	LYS512	GUA5	2.821
4		N-H...O	LYS512	GUA5	2.896
	THY				
1		C-H...O	LYS528	THY3	2.841
2		N-H...O	LYS528	THY3	1.859

Frame 60

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	THR46	CYT11	2.636
2		C-H...O	PRO47	CYT11	2.370
3		C-H...O	PHE71	CYT7	2.832
4		C-H...O	LYS92	CYT7	2.752

5		C-H...O	LYS92	CYT6	2.778
6		C-H...O	LYS92	CYT7	2.540
7		N-H...O	LYS 92	CYT6	2.603
8		N-H...O	LYS92	CYT6	2.968
9		C-H...O	LYS636	CYT5	2.641
10		N-H...O	LYS639	CYT15	2.448
11		N-H...O	LYS639	CYT15	2.814
12		C-H...N	CYT6	LYS 92	2.963
	GUA				
1		C-H...O	GLY69	GUA9	2.465
2		N-H...O	LYS70	GUA8	2.943
3		C-H...N	PHE71	GUA9	2.742
4		C-H...N	PHE71	GUA9	2.794
5		C-H...O	PHE71	GUA8	2.519
6		C-H...O	LEU88	GUA9	2.659
7		C-H...O	PRO101	GUA9	2.468
8		C-H...N	PRO101	GUA9	2.674
9		C-H...O	VAL147	GUA10	2.662
10		N-H...O	VAL148	GUA10	2.195
11		O-H...O	TYR484	GUA9	1.759
12		C-H...pi	GUA8	PHE71	4.968
	THY				
1		C-H...O	MET91	THY8	2.846
2		C-H...O	GLY99	THY8	2.516
3		C-H...O	LYS639	THY14	2.732
4		N-H...O	LYS639	THY14	1.865
5		C-H...O	THY8	GLY99	2.813

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS528	ADE4	1.770
	CYT				
1		C-H...O	LYS6	CYT10	2.632
2		N-H...O	LYS6	CYT10	1.886
3		C-H...O	GLN545	CYT5	2.823
4		C-H...O	LYS546	CYT7	2.698
5		C-H...O	LYS546	CYT7	2.777
6		C-H...O	LYS546	CYT7	2.718
7		C-H...N	CYT5	GLN545	2.475
	GUA				
1		C-H...O	GLN545	GUA6	2.681
2		C-H...O	GLN545	GUA6	2.571
3		N-H...O	LYS546	GUA6	1.784
4		C-H...N	GUA5	ASN547	2.797
	THY				

		None			

Frame 83

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	PRO47	CYT11	2.822
2		C-H...O	PRO47	CYT11	2.717
3		C-H...O	PRO47	CYT11	2.875
4		C-H...O	PRO101	CYT10	2.687
5		O-H...O	TYR108	CYT10	2.440
6		C-H...O	TYR108	CYT10	2.402
7		C-H...O	LYS639	CYT15	2.335
8		N-H...O	LYS639	CYT15	1.673
	GUA				
1		C-H...N	GLY69	GUA8	2.929
2		C-H...O	GLY69	GUA8	2.940
3		N-H...O	LYS70	GUA8	2.619
4		N-H...N	LYS70	GUA8	2.465
5		C-H...N	PHE71	GUA8	2.728
6		C-H...N	PHE71	GUA8	2.776
7		C-H...O	LEU88	GUA9	2.633
8		N-H...O	VAL89	GUA9	2.226
9		C-H...O	PRO101	GUA9	2.618
10		C-H...N	PRO101	GUA9	2.741
11		O-H...O	TYR108	GUA9	2.145
12		C-H...O	TYR108	GUA9	2.821
13		C-H...O	PRO128	GUA9	2.727
14		C-H...O	PRO128	GUA9	2.942
15		C-H...O	VAL147	GUA10	2.609
16		C-H...O	VAL147	GUA10	2.804
17		N-H...O	VAL148	GUA10	1.943
18		O-H...O	TYR484	GUA8	2.823
19		O-H...O	TYR484	GUA9	1.972
20		N-H...O	GUA8	VAL68	1.841
21		C-H...O	GUA9	GLN124	2.683
22		N-H...O	GUA10	GLU73	2.974
23		C-H...pi	GUA8	TYR484	4.120
	THY				
1		C-H...O	PHE71	THY8	2.978
2		C-H...N	PHE71	THY8	2.917
3		N-H...O	VAL89	THY8	2.708

4		C-H...O	MET91	THY8	2.362
5		C-H...O	MET91	THY8	2.998
6		C-H...O	SER98	THY8	2.838
7		N-H...O	TRP609	THY13	2.551
8		N-H...O	LYS643	THY14	1.635
9		C-H...O	THY8	PHE90	2.987
10		C-H...O	THY8	VAL89	2.361
11		C-H...pi	THY8	PHE71	4.459

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS512	ADE4	2.485
	CYT				
1		C-H...O	LYS6	CYT10	2.579
	GUA				
1		N-H...N	LYS509	GUA14	2.098
2		N-H...N	LYS509	GUA14	2.997
3		N-H...O	LYS512	GUA5	1.785
4		C-H...O	ARG524	GUA5	2.525
5		C-H...O	GLN545	GUA6	2.538
6		N-H...O	LYS546	GUA6	1.795
7		C-H...O	LYS546	GUA6	2.823
8		N-H...O	ASN547	GUA6	2.019
9		C-H...O	ASN547	GUA6	2.534
10		C-H...N	GUA14	LYS509	2.772
11		C-H...N	GUA5	LYS512	2.756
	THY				
1		N-H...O	LYS528	THY3	1.739

Frame 194

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				

1		C-H...O	THR46	CYT11	2.749
2		C-H...O	PRO47	CYT11	2.866
3		C-H...O	PRO47	CYT11	2.821
4		C-H...O	PRO47	CYT11	2.433
5		C-H...O	MET91	CYT7	2.908
6		C-H...N	MET91	CYT7	2.714
7		N-H...O	LYS92	CYT7	1.852
8		C-H...O	LYS92	CYT7	2.795
9		C-H...O	LYS92	CYT7	2.939
10		N-H...O	LYS92	CYT7	2.490
11		N-H...O	LYS92	CYT7	1.781
12		N-H...O	LYS92	CYT7	1.793
13		N-H...O	LYS92	CYT7	2.422
14		C-H...O	PRO101	CYT10	2.924
15		O-H...O	TYR108	CYT10	1.783
16		C-H...O	TYR108	CYT10	2.525
17		C-H...O	CYS135	CYT2	2.473
18		C-H...O	ARG136	CYT2	2.983
19		C-H...O	ARG136	CYT2	2.959
20		N-H...O	ARG136	CYT2	1.584
21		C-H...O	HIS140	CYT 1	2.332
22		N-H...O	ILE141	CYT1	2.015
23		C-H...O	ILE141	CYT2	2.677
24		C-H...O	ARG146	CYT2	2.813
25		C-H...O	ARG146	CYT 2	2.547
26		N-H...O	LYS636	CYT5	2.794
27		N-H...O	LYS639	CYT15	1.759
28		C-H...O	CYT1	ALA139	2.533
29		C-H...N	CYT2	ARG136	2.805
	GUA				
1		C-H...O	GLY69	GUA8	2.949
2		C-H...O	PHE71	GUA9	2.866
3		C-H...O	PHE71	GUA9	2.873
4		C-H...N	PHE71	GUA9	2.865
5		C-H...N	PHE71	GUA9	2.566
6		C-H...O	LEU88	GUA9	2.468
7		N-H...O	VAL89	GUA9	2.188
8		C-H...O	PRO101	GUA9	2.725
9		O-H...O	TYR108	GUA9	2.384
10		C-H...O	VAL147	GUA10	2.941
11		N-H...O	VAL148	GUA10	2.308
12		N-H...O	LYS636	GUA6	1.655
13		C-H...O	GUA9	GLY99	2.743
	THY				
1		C-H...N	GLU73	THY8	2.833
2		N-H...O	LYS143	THY12	1.711
3		N-H...O	THY8	GLU73	1.776

B. Interactions with MSH2

		type	donor	acceptor	distance, Ä
	ADE				
1		N-H...O	LYS528	ADE4	1.535
	CYT				
1		C-H...O	GLN518	CYT4	2.844
2		N-H...O	LYS546	CYT7	1.984
3		N-H...O	LYS550	CYT5	2.175
	GUA				
1		C-H...O	LYS6	GUA11	2.916
2		N-H...O	LYS6	GUA11	1.688
3		C-H...O	GLN545	GUA6	2.579
4		C-H...O	GLN545	GUA6	2.296
5		N-H...O	LYS546	GUA6	1.958
	THY				
		None			

Mismatched DNA complex

Table S2. The binding mode for the mismatched MutSα-DNA complex

Frame 148

A. Interactions with MSH6

		type	donor	acceptor	distance, Ä
	ADE				
		None			
	CTY				
1		C-H...O	PRO47	CYT11	2.879
2		C-H...O	LYS70	CYT7	2.973
3		C-H...O	LYS70	CYT7	2.626
4		C-H...O	TRP95	CYT11	2.944
5		O-H...O	TYR108	CYT10	2.777
6		C-H...O	TYR108	CYT10	2.892
7		C-H...O	PRO128	CYT9	2.973
8		C-H...O	PRO128	CYT9	2.970
9		C-H...O	PRO128	CYT9	2.849
10		C-H...O	ARG136	CYT2	2.922
11		C-H...O	ARG136	CYT2	2.918
12		O-H...O	TYR484	CYT9	1.824
13		C-H...N	CYT7	ARG613	2.736
14		C-H...O	CYT9	GLN124	2.990
15		C-H...O	CYT9	VAL68	2.983
16		C-H...N	CYT2	ARG146	2.493

	GUA				
1		N-H...N	LYS70	GUA8	2.700
2		C-H...O	LYS70	GUA8	2.632
3		N-H...O	LYS70	GUA8	1.871
4		C-H...N	PHE71	GUA9	2.785
5		C-H...N	PHE71	GUA8	2.442
6		C-H...O	LEU88	GUA9	2.819
7		N-H...O	VAL89	GUA9	2.305
8		C-H...O	PRO101	GUA9	2.689
9		C-H...N	PRO101	GUA9	2.924
10		C-H...O	PRO101	GUA9	2.986
11		C-H...N	PRO101	GUA9	2.947
12		C-H...N	PRO101	GUA9	2.601
13		O-H...O	TYR108	GUA9	2.236
14		C-H...O	VAL147	GUA10	2.769
15		N-H...O	VAL148	GUA10	1.917
16		O-H...O	TYR484	GUA8	2.898
17		N-H...O	GUA8	VAL68	1.936
	THY				
1		C-H...N	MET91	THY8	2.922
2		N-H...O	TRP609	THY14	1.986
3		C-H...O	ILE611	THY13	2.341
4		N-H...O	GLY612	THY13	2.101

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		C-H...O	LYS528	ADE4	2.226
2		N-H...O	LYS528	ADE4	1.781
	CYT				
1		N-H...O	LYS546	CYT7	1.551
	GUA				
1		C-H...O	GLN545	GUA6	2.978
2		C-H...O	GLN545	GUA6	2.332
3		N-H...O	LYS546	GUA6	2.156
4		C-H...O	LYS546	GUA6	2.783
	THY				
1		C-H…N	THY3	LYS528	2.980

Frame 15

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	PRO47	CYT11	2.769
2		C-H...O	PRO47	CYT11	2.830
3		N-H...O	GLY48	CYT11	2.782
4		C-H...O	LYS70	CYT7	2.943
5		C-H...O	CYS135	CYT1	2.665
6		C-H...O	ILE141	CYT1	2.649
7		C-H...O	ARG146	CYT1	2.585
8		O-H...O	TYR484	CYT9	1.683
9		O-H...O	TYR484	CYT9	2.953
10		N-H...O	LYS636	CYT5	2.712
11		N-H...O	LYS636	CYT5	2.976
12		C-H...N	CYT4	LYS639	2.753
13		C-H...N	CYT9	ARG150	2.955
14		C-H...N	CYT9	GLY69	2.861
	GUA				
1		C-H...N	GLY69	GUA8	2.879
2		C-H...O	GLY69	GUA8	2.927
3		N-H...O	LYS70	GUA8	2.995
4		N-H...N	LYS70	GUA8	2.957
5		N-H...N	LYS70	GUA8	1.952
6		C-H...O	LYS70	GUA8	2.949
7		C-H...N	LYS70	GUA8	2.705
8		C-H...N	LYS70	GUA8	2.918
9		C-H...N	LYS70	GUA9	2.997
10		N-H...O	LYS70	GUA8	1.658
11		C-H...O	PHE71	GUA9	2.939
12		C-H...N	PHE71	GUA9	2.615
13		C-H...O	LYS92	GUA7	2.839
14		C-H...O	LYS92	GUA7	2.728
15		C-H...O	PRO101	GUA9	2.713
16		C-H...N	PRO101	GUA9	2.973
17		C-H...O	VAL147	GUA10	2.652
18		N-H...O	VAL148	GUA10	1.969
19		C-H...O	TYR484	GUA8	2.569
20		C-H...O	LYS636	GUA6	2.818
21		N-H...O	LYS636	GUA6	1.603
22		C-H...N	GUA6	LYS636	2.931
23		N-H...O	GUA8	VAL68	1.992
24		C-H...pi	GUA8	TYR484	3.916

25		C-H...pi	GUA8	TYR484	4.291
	THY				
1		C-H...O	MET91	THY8	2.937
2		N-H...O	TRP609	THY13	2.576
3		C-H...O	LYS639	THY14	2.673
4		C-H...O	LYS639	THY14	2.354
5		C-H...pi	THY8	PHE71	4.465

B. Interactions with MSH2.

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		C-H...O	LYS509	ADE4	2.697
2		N-H...N	LYS509	ADE4	2.804
3		O-H...O	THR526	ADE4	1.758
4		C-H...O	LYS528	ADE4	2.438
5		C-H...O	LYS528	ADE4	2.746
	CYT				
1		C-H...O	LYS6	CYT10	2.928
2		C-H...O	ALA517	CYT4	2.818
3		C-H...O	GLN518	CYT4	2.913
4		C-H...O	LYS546	CYT7	2.834
5		C-H...O	LYS546	CYT7	2.525
	GUA				
1		C-H...O	LYS6	GUA11	2.809
2		N-H...O	LYS6	GUA11	1.602
3		N-H...O	LYS509	GUA5	2.123
4		N-H...O	LYS512	GUA5	1.663
5		C-H...O	GLN545	GUA6	2.771
6		C-H...O	GLN545	GUA6	2.616
7		C-H...O	GLN545	GUA6	2.774
8		N-H...O	LYS546	GUA6	1.921
	THY				
1		C-H...O	LYS528	THY3	2.840
2		N-H...O	LYS528	THY3	1.500

Frame 79

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				

1		C-H...O	THR46	CYT11	2.648
2		O-H...O	THR46	CYT11	2.420
3		C-H...O	PRO47	CYT11	2.890
4		C-H...O	PRO47	CYT11	2.561
5		N-H...O	GLY48	CYT11	2.286
6		C-H...O	LYS70	CYT7	2.481
7		C-H...O	TYR108	CYT10	2.572
8		O-H...O	TYR108	CYT10	1.819
9		C-H...O	PRO128	CYT9	2.913
10		C-H...O	HIS140	CYT1	2.643
11		N-H...O	ILE141	CYT1	1.920
12		O-H...O	TYR484	CYT9	1.816
13		N-H...O	LYS636	CYT5	2.298
	GUA				
1		N-H...N	LYS70	GUA8	2.197
2		C-H...O	LYS70	GUA8	2.729
3		C-H...N	LYS70	GUA8	2.943
4		N-H...N	PHE71	GUA8	2.759
5		C-H...N	PHE71	GUA8	2.746
6		C-H...O	PHE71	GUA9	2.892
7		C-H...N	PHE71	GUA9	2.490
8		C-H...N	PHE71	GUA8	2.681
9		N-H...O	VAL89	GUA9	2.742
10		C-H...O	MET91	GUA7	2.964
11		C-H...N	PRO101	GUA9	2.876
12		O-H...O	TYR108	GUA9	2.717
13		C-H...O	VAL147	GUA10	2.874
14		N-H...O	VAL148	GUA10	2.075
15		O-H...O	TYR484	GUA8	2.523
16		C-H...O	ILE611	GUA12	2.924
17		C-H...O	ARG613	GUA8	2.641
18		C-H...O	LYS636	GUA6	2.552
19		N-H...O	LYS636	GUA6	1.711
20		C-H...N	GUA8	LYS70	2.998
21		N-H...O	GUA8	VAL68	2.004
22		C-H...O	GUA7	MET91	2.675
23		C-H...O	GUA9	GLY99	2.834
	THY				
1		C-H...O	MET91	THY8	2.871
2		C-H...O	MET91	THY8	2.756
3		C-H...O	MET91	THY8	2.413
4		C-H...O	GLY99	THY8	2.899
5		C-H...O	TRP609	THY14	2.600
6		N-H...O	TRP609	THY13	2.528
7		C-H...O	THY8	GLY99	2.880

B. Interactions with MSH2

		type	donor	acceptor	distance, Ä
	ADE				
1 2 3 4		C-H...O O-H...O C-H...O C-H...O	GLN510 THR526 LYS528 LYS528	ADE4 ADE4 ADE4 ADE4	2.487 1.803 2.789 2.906
	CYT				
1		N-H...O	LYS546	CYT7	1.644
	GUA				
1		N-H...O	LYS6	GUA11	1.669
	THY				
1		N-H...O	LYS528	THY3	1.584

Frame 47

A. Interactions with MSH6

		type	donor	acceptor	distance, Ä
	ADE				
1		C-H...N	LYS639	ADE3	2.865
	CYT				
1 2 3 4 5 6 7 8 9 10 11		C-H...O C-H...O C-H...O C-H...O N-H...O O-H...O C-H...O O-H...O N-H...O N-H...O N-H...O	PRO47 PRO47 PRO47 LYS70 LYS70 TYR108 TYR484 TYR484 LYS639 LYS639 LYS639	CYT11 CYT11 CYT11 CYT7 CYT7 CYT10 CYT9 CYT9 CYT4 CYT4 CYT4	2.476 2.903 2.871 2.559 2.789 1.878 2.569 1.761 2.404 2.383 2.926
	GUA				
1 2 3 4 5 6 7		N-H...N N-H...N C-H...N C-H...N C-H...N N-H...O N-H...N	LYS70 LYS70 LYS70 LYS70 LYS70 LYS70 PHE71	GUA8 GUA8 GUA8 GUA8 GUA8 GUA8 GUA8	2.812 2.018 2.793 2.975 2.930 1.841 2.540

8		C-H...N	PHE71	GUA8	2.912
9		C-H...N	PHE71	GUA9	2.512
10		C-H...N	PHE71	GUA8	2.679
11		C-H...N	PHE71	GUA8	2.892
12		C-H...O	PRO101	GUA9	2.915
13		C-H...N	PRO101	GUA9	2.749
14		O-H...O	TYR108	GUA9	2.450
15		C-H...O	VAL147	GUA10	2.894
16		C-H...O	VAL147	GUA10	2.369
17		N-H...O	VAL148	GUA10	2.119
18		N-H...O	LYS636	GUA6	1.737
19		N-H...O	GUA8	VAL68	1.650
20		N-H...N	GUA8	LYS70	2.955
21		C-H...pi	GUA8	TYR484	4.013
22		C-H...pi	GUA8	TYR484	3.958
	THY				
1		C-H...O	MET91	THY8	2.763
2		C-H...O	MET91	THY8	2.905
3		C-H...O	TRP609	THY14	2.726
4		N-H...O	TRP609	THY13	2.123
5		C-H...O	LYS639	THY14	2.713
6		C-H...O	LYS639	THY14	2.877
7		C-H...O	LYS639	THY14	2.985
8		C-H...N	THY13	TRP609	2.711

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		C-H...O	THR526	ADE4	2.921
2		O-H...O	THR526	ADE4	1.680
3		C-H...N	ADE4	GLN510	2.801
	CYT				
1		C-H...O	LYS6	CYT10	2.772
2		N-H...O	LYS546	CYT7	1.751
	GUA				
1		N-H...O	LYS6	GUA11	2.556
2		N-H...O	LYS6	GUA11	2.307
3		N-H...O	LYS509	GUA14	2.032
4		C-H...O	LYS512	GUA5	2.810
5		N-H...O	LYS512	GUA5	1.818
6		C-H...O	GLN545	GUA6	2.409
7		N-H...O	LYS546	GUA6	1.996
8		N-H...O	LYS546	GUA6	2.964
9		C-H...O	LYS546	GUA6	2.655
10		C-H...O	LYS546	GUA6	2.857

	THY				
1		C-H...O	LYS528	THY3	2.914

Frame 192

A. Interactions with MSH6

		type	donor	acceptor	distance, Ä
	ADE				
		None			
	CYT				
1		C-H...O	THR46	CYT11	2.712
2		C-H...O	PRO47	CYT11	2.808
3		C-H...O	PRO47	CYT11	2.592
4		C-H...O	PRO47	CYT11	2.577
5		N-H...O	GLY48	CYT11	2.628
6		O-H...O	TYR108	CYT10	2.165
7		C-H...O	TYR108	CYT10	2.881
8		C-H...O	PRO128	CYT9	2.728
9		O-H...O	TYR484	CYT9	1.694
10		C-H...O	ARG604	CYT15	2.757
11		C-H...O	LYS636	CYT5	2.780
12		C-H...O	LYS639	CYT15	2.919
	GUA				
1		N-H...O	LYS70	GUA8	2.704
2		N-H...N	LYS70	GUA8	2.630
3		C-H...O	LYS70	GUA8	2.428
4		C-H...N	PHE71	GUA8	2.657
5		C-H...N	PHE71	GUA9	2.663
6		C-H...N	PHE71	GUA9	2.869
7		C-H...N	PHE71	GUA8	2.817
8		C-H...O	LEU88	GUA9	2.582
9		N-H...O	VAL89	GUA9	1.811
10		C-H...O	PRO101	GUA9	2.816
11		C-H...N	PRO101	GUA9	2.644
12		O-H...O	TYR108	GUA9	2.646
13		C-H...O	TYR108	GUA9	2.783
14		C-H...O	VAL147	GUA10	2.752
15		C-H...O	VAL147	GUA10	2.691
16		N-H...O	VAL148	GUA10	2.117
17		O-H...O	TYR484	GUA8	2.768
18		N-H...O	GUA8	GLU73	2.942
19		N-H...O	GUA8	VAL68	1.805
	THY				
1		C-H...O	GLU73	THY8	2.801
2		C-H...O	MET91	THY8	2.903

3		C-H...O	MET91	THY8	2.763
4		C-H...O	GLY99	THY8	2.652
5		N-H...O	TRP609	THY13	1.847
6		C-H...O	LYS639	THY14	2.898
7		C-H...O	LYS639	THY 14	2.755
8		C-H...O	THY8	VAL89	2.942
9		N-H...O	THY8	GLU73	2.291
10		C-H...O	THY8	GLY99	2.605

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		C-H...O	LYS110	ADE2	2.732
2		N-H...O	LYS110	ADE2	1.787
	CYT				
1		C-H...O	GLN545	CYT5	2.964
2		C-H...O	LYS546	CYT7	2.671
3		N-H...O	LYS546	CYT7	1.727
4		C-H...N	CYT5	GLN545	2.431
	GUA				
1		C-H...O	LYS6	GUA11	2.560
2		N-H...O	LYS6	GUA11	1.732
3		C-H...O	GLN545	GUA6	2.528
4		C-H...O	GLN545	GUA6	2.395
5		C-H...O	GLN545	GUA6	2.540
6		N-H...O	LYS546	GUA6	1.770
7		C-H...O	ASN547	GUA5	2.880
8		C-H...O	ASN547	GUA5	2.740
	THY				
		None			

Frame 102

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	THR46	CYT11	2.913
2		O-H...O	THR46	CYT11	2.482
3		C-H...O	PRO47	CYT11	2.769

4		C-H...O	PRO47	CYT11	2.526
5		N-H...O	GLY48	CYT11	1.926
6		C-H...O	GLY48	CYT11	2.889
7		C-H...O	GLY69	CYT9	2.610
8		C-H...O	LYS70	CYT7	2.824
9		C-H...O	PRO101	CYT10	2.970
10		C-H...O	TYR108	CYT10	2.748
11		O-H...O	TYR108	CYT10	2.545
12		C-H...O	PRO128	CYT9	2.863
13		C-H...O	PRO128	CYT9	2.971
14		C-H...O	PRO128	CYT9	2.728
15		C-H...O	HIS140	CYT1	2.901
16		N-H...O	HIS140	CYT1	2.014
17		N-H...O	ILE141	CYT1	1.966
18		O-H...O	TYR484	CYT9	2.381
19		N-H...O	LYS640	CYT15	1.873
20		C-H...O	CYT9	GLN124	2.633
21		C-H...N	CYT9	GLN124	2.994
22		C-H...N	CYT9	GLY69	2.659
23		C-H...O	CYT9	VAL68	2.611
	GUA				
1		N-H...O	LYS70	GUA8	2.969
2		N-H...N	LYS70	GUA8	2.032
3		C-H...O	LYS70	GUA8	2.447
4		C-H...N	LYS70	GUA8	2.682
5		N-H...N	PHE71	GUA8	2.591
6		C-H...N	PHE71	GUA8	2.862
7		C-H...O	PHE71	GUA9	2.691
8		C-H...N	PHE71	GUA8	2.664
9		C-H...N	PHE71	GUA8	2.863
10		C-H...O	PRO101	GUA9	2.692
11		C-H...O	ILE103	GUA11	2.508
12		C-H...O	TYR108	GUA9	2.922
13		O-H...O	TYR108	GUA9	2.056
14		C-H...O	VAL147	GUA10	2.880
15		N-H...O	VAL148	GUA10	2.002
16		C-H...O	ILE611	GUA12	2.907
17		N-H...O	ARG613	GUA8	2.199
18		C-H...O	LYS636	GUA6	2.379
19		C-H...N	GUA8	LYS70	2.995
20		N-H...O	GUA8	VAL68	1.714
21		C-H...O	GUA7	MET91	2.933
22		C-H...pi	GUA8	TYR484	4.222
	THY				
1		C-H...O	MET91	THY8	2.541
2		N-H...O	TRP609	THY13	1.881
3		O-H...O	THR638	THY14	1.874
4		C-H...O	LYS639	THY14	2.749

B. Interactions with MSH2

		type	donor	acceptor	distance, Ä
	ADE				
1		O-H...O	THR526	ADE4	1.855
2		N-H...O	LYS528	ADE4	1.898
	CYT				
1		N-H...O	LYS546	CYT7	1.693
	GUA				
1		N-H...O	LYS 6	GUA11	1.610
2		C-H...O	LYS509	GUA14	2.879
3		C-H...O	LYS512	GUA5	2.551
4		N-H...O	LYS512	GUA5	1.895
5		N-H...O	LYS512	GUA5	2.410
	THY				
		None			

Frame 180

A. Interactions with MSH6

		type	donor	acceptor	distance, Ä
	ADE				
		None			
	CYT				
1		C-H...O	THR46	CYT11	2.833
2		C-H...O	PRO47	CYT11	2.641
3		N-H...O	GLY48	CYT11	2.464
4		C-H...O	TRP95	CYT11	2.707
5		O-H...O	TYR108	CYT10	1.873
6		C-H...O	TYR108	CYT10	2.766
7		C-H...O	HIS140	CYT1	2.872
8		N-H...O	ILE141	CYT1	1.853
9		C-H...O	ILE141	CYT1	2.906
10		C-H...O	ILE141	CYT2	2.764
11		O-H...O	TYR484	CYT9	1.990
12		C-H...O	ARG604	CYT15	2.972
13		N-H...O	ARG604	CYT15	1.764
14		C-H...N	THR605	CYT15	2.817
15		C-H...O	THR605	CYT15	2.519
16		C-H...O	LYS636	CYT5	2.511
17		C-H...N	CYT7	ARG613	2.926
18		C-H...O	CYT9	TYR484	2.940
19		C-H...N	CYT9	GLY69	2.725
20		O-H...N	CYT1	HIS140	2.637
21		O-H...N	CYT1	HIS140	2.870

	GUA				
1		C-H...N	GLY69	GUA8	2.903
2		N-H...N	LYS70	GUA8	2.376
3		C-H...O	LYS70	GUA8	2.943
4		C-H...O	LYS70	GUA8	2.412
5		C-H...N	PHE71	GUA8	2.812
6		C-H...N	PHE71	GUA9	2.690
7		C-H...N	PHE71	GUA9	2.847
8		C-H...N	PHE71	GUA8	2.790
9		C-H...O	LEU88	GUA9	2.759
10		N-H...O	VAL89	GUA9	2.507
11		N-H...O	LYS92	GUA7	1.547
12		C-H...O	PRO101	GUA9	2.862
13		O-H...O	TYR108	GUA9	2.316
14		C-H...O	VAL147	GUA10	2.926
15		C-H...O	VAL147	GUA10	2.599
16		N-H...O	VAL148	GUA10	2.494
17		O-H...O	TYR484	GUA8	2.570
18		C-H...O	ARG613	GUA8	2.955
19		N-H...O	ARG613	GUA8	1.680
20		N-H...O	GUA8	VAL68	1.875
21		C-H...S	GUA7	MET91	2.800
22		C-H...pi	GUA8	TYR484	4.123
	THY				
1		C-H...O	GLU73	THY8	2.669
2		C-H...O	TRP609	THY14	2.751
3		N-H...O	TRP609	THY13	2.308
4		C-H...O	LYS639	THY14	2.667
5		C-H...O	LYS639	THY14	2.797
6		N-H...O	LYS639	THY14	2.207
7		N-H...O	LYS643	THY14	1.785
8		C-H...N	THY13	TRP609	2.781
9		C-H...pi	THY8	PHE71	4.206
10		C-H...pi	THY13	PR5 609	4.684

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		N-H...O	LYS110	ADE2	1.626
	CYT				
1		C-H...O	LYS6	CYT10	2.598
2		C-H...O	LYS546	CYT7	2.847
3		N-H...O	LYS546	CYT7	1.645
4		C-H...N	CYT5	GLN545	2.562

	GUA				
1		C-H...O	LYS6	GUA11	2.926
2		N-H...O	LYS512	GUA5	1.741
3		C-H...O	GLN545	GUA6	2.558
4		C-H...O	GLN545	GUA6	2.740
5		N-H...O	LYS546	GUA6	1.729
6		C-H...O	LYS546	GUA6	2.545
	THY				
		None			

Frame 218

A. Interactions with MSH6

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
		None			
	CYT				
1		C-H...O	PRO47	CYT11	2.732
2		N-H...O	LYS92	CYT11	2.915
3		N-H...O	LYS92	CYT11	2.752
4		C-H...O	ILE103	CYT10	2.896
5		O-H...O	TYR484	CYT9	2.285
6		N-H...O	GLY612	CYT7	2.654
7		N-H...O	ARG613	CYT7	1.823
8		C-H...O	ARG613	CYT7	2.470
9		C-H...O	ARG613	CYT7	2.653
10		C-H...O	ARG613	CYT7	2.848
11		N-H...O	ASN614	CYT7	2.960
12		N-H...O	LYS636	CYT5	2.091
13		N-H...O	LYS639	CYT15	2.852
14		C-H...O	LYS639	CYT15	2.353
15		C-H...O	LYS639	CYT15	2.418
16		C-H...O	LYS639	CYT15	2.958
17		N-H...O	LYS639	CYT15	1.986
18		C-H...O	CYT9	TYR484	2.736
	GUA				
1		C-H...N	GLY69	GUA8	2.777
2		N-H...N	LYS70	GUA8	2.736
3		C-H...O	LYS70	GUA8	2.789
4		C-H...O	LYS70	GUA8	2.548
5		N-H...O	LYS70	GUA8	1.781
6		C-H...N	PHE71	GUA8	2.855
7		C-H...O	PHE71	GUA9	2.575
8		C-H...N	PHE71	GUA9	2.878
9		C-H...N	PHE71	GUA8	2.710

10		C-H...O	PRO101	GUA9	2.749
11		C-H...O	PRO101	GUA9	2.914
12		C-H...O	VAL147	GUA10	2.762
13		C-H...O	VAL147	GUA10	2.237
14		N-H...O	VAL148	GUA10	1.967
15		O-H...O	TYR484	GUA8	2.561
16		C-H...O	ILE611	GUA6	2.998
17		C-H...O	ILE611	GUA6	2.790
18		N-H...O	ARG613	GUA8	1.817
19		C-H...O	LYS636	GUA6	2.991
20		C-H...O	LYS636	GUA6	2.665
21		N-H...O	LYS636	GUA6	2.911
22		N-H...O	GUA8	VAL68	1.934
23		C-H...O	GUA7	MET91	2.806
	THY				
1		C-H...O	PHE71	THY8	2.799
2		C-H...O	MET91	THY8	2.514
3		C-H...O	MET91	THY8	2.992
4		C-H...O	GLY99	THY8	2.418
5		C-H...O	TRP609	THY13	2.864
6		C-H...O	THY8	PHE90	2.879
7		C-H...O	THY8	GLY99	2.563

B. Interactions with MSH2

		type	**donor**	**acceptor**	**distance, Ä**
	ADE				
1		C-H...O	ASN109	ADE2	2.714
2		C-H...O	LYS509	ADE4	2.547
3		N-H...O	LYS509	ADE4	2.847
4		O-H...O	THR526	ADE4	1.753
5		C-H...O	LYS528	ADE4	2.732
6		C-H...O	LYS528	ADE4	2.754
7		N-H...O	LYS528	ADE4	1.890
8		C-H...O	ADE4	LYS509	2.413
	CYT				
1		C-H...O	LYS6	CYT10	2.718
2		C-H...O	LYS546	CYT7	2.756
3		N-H...O	LYS546	CYT7	1.701
	GUA				
1		C-H...O	LYS6	GUA11	2.682
2		C-H...O	LYS6	GUA11	2.874
3		N-H...O	LYS6	GUA11	1.508
4		C-H...O	LYS110	GUA1	2.811
5		C-H...O	LYS512	GUA5	2.542
6		N-H...O	LYS512	GUA5	1.724
7		C-H...O	GLN545	GUA6	2.746

8		C-H...O	GLN545	GUA6	2.889
9		C-H...O	GLN545	GUA6	2.700
10		N-H...O	LYS546	GUA6	2.063
	THY				
1		N-H...O	LYS509	THY3	1.821
2		C-H...O	LYS528	THY3	2.686

Table S3. Protein-DNA hydrogen bonds in the solved MutSα-DNA complex , 208B (MSH2/MSH6 bound to ADP and a G-T mismatch)

		donor	**acceptor**	**type**	**distance, Ä**
1	**MSH2**	LSY6	CYT10	C-H…O	2.738
		LYS6	GUA11	C-H…O	2.831
		LYS6	CYT10	C-H…O	2.706
		LYS6	CYT10	C-H…O	2.807
		LYS6	CYT10	C-H…O	2.496
		LYS6	GUA11	N-H…O	2.315
2		LYS512	GUA5	N-H…O	2.411
		GUA5	LYS512	O-H…N	2.529
3		CYT4	GLN518	C-H…O	2.375
4		CYT5	GLN545	C-H…N	2.870
		GLN545	GUA6	C-H…O	2.951
5		LYS546	GUA6	N-H…O	2.302
		LYS546	GUA6	C-H…O	2.683
		LYS546	CYT7	C-H…O	2.822
6	**MSH6**	THR46	CYT11	C-H…O	2.725
		THR46	CYT11	O-H…O	2.830
7		CYT11	PRO47	O-H…N	2.653
8		GLY48	CYT11	N-H…O	2.365
		GLY48	CYT11	N-H…O	1.552
		GLY48	GUA10	C-H…O	2.671
		GLY48	CYT11	C-H…O	2.660
		GLY48	CYT11	C-H…O	2.877
9		MET49	CYT11	N-H…O	2.102
10		GUA9	VAL68	N-H…O	1.877
11		GLY69	GUA8	C-H…N	2.665
		GLY69	GUA8	C-H…O	2.539
		GLY69	CYT9	C-H…O	2.826
		CYT9	GLY69	C-H…N	2.818
12		LYS70	GUA8	N-H…O	2.787
		LYS70	GUA8	N-H…N	2.988
		LYS70	GUA8	C-H…O	2.828
		LYS70	GUA9	C-H…N	2.920
		LYS70	CYT7	N-H…O	2.005
		CYT7	LYS70	C-H…N	2.949

13		PHE71	GUA9	C-H…N	2.962
		PHE71	CYT7	C-H…N	2.908
		PHE71	GUA9	C-H…N	2.542
		PHE71	GUA8	C-H…N	2.774
14		GLU73	THY8	C-H…O	2.559
15		LEU88	GUA9	C-H…O	2.354
16		VAL89	GUA9	N-H…O	1.821
		GUA9	VAL89	O-H…N	1.939
17		MET91	THY8	C-H…O	2.799
		MET91	GUA7	C-H…O	2.573
		MET91	THY8	C-H…O	2.848
		MET91	THY8	C-H…O	2.511
		MET91	GUA7	C-H…O	2.915
		MET91	GUA7	C-H…O	2.697
18		LYS92	THY8	N-H…O	2.764
		LYS92	GUA7	C-H…O	2.641
		THY8	LYS92	O-H…N	2.808
19		GLY99	THY8	C-H…O	2.282
		THY8	GLY99	C-H…O	2.766
20		PRO101	GUA9	C-H…O	2.638
		PRO101	GUA9	C-H…N	2.673
		PRO101	GUA9	C-H…O	2.903
		PRO101	GUA9	C-H…N	2.534
		PRO101	CYT10	C-H…O	2.611
21		CYT10	ARG107	O-H…N	1.811
22		TYR108	GUA9	O-H…O	2.032
		TYR108	GUA9	C-H…O	2.847
		GUA9	TYR108	C-H…O	2.977
23		CYT9	GLN124	C-H…O	2.643
24		PRO128	CYT9	C-H…O	2.677
		PRO128	CYT9	C-H…O	2.853
		PRO128	CYT9	C-H…O	2.994
		PRO128	CYT9	C-H…O	2.470
		PRO128	CYT9	C-H…O	2.687
		PRO128	CYT9	C-H…O	2.541
25		VAL147	GUA10	C-H…O	2.697
		VAL147	GUA10	C-H…O	2.359
26		VAL148	GUA10	N-H…O	1.909
27		GUA10	ARG150	C-H…N	2.538
28		TYR484	CYT9	C-H…O	2.883
29		TRP609	THY13	C-H…O	2.310
30		ARG613	GUA8	N-H…O	2.706
		ARG613	GUA8	N-H…O	2.598
31		THR638	THY14	C-H…O	2.410
32		LYS639	CYT15	N-H…O	2.040
		LYS639	CYT15	N-H…O	2.995

		LYS639	CYT15	C-H…O	2.344
33		LYS643	THY14	N-H…O	1.894
		LYS643	THY14	N-H…O	1.922

Conclusion:

In the experimental mismatched MSH2/MSH6 complex there are 33 residues involved in hydrogen bonds with the DNA fragment. Simulations for the same complex predicted 54 such residues, with 13 from MSH2. All but MET49 and ARG107, which is 93.93% of those present in the crystal structure are predicted by simulations, and they are present at least 14.66% of the simulation time.

In addition, all residues predicted to be involved in hydrogen bonding with the DNA fragment during in the entire simulation time are among the experimental.

Table S4. Different binding modes for mismatched (mis) and cross-linked (plat) DNA fragments by MutSα.

Residue		**Interactions Type**	**% conf**	**Residue**		**Interactions Type**	**% conf**
Thr46	mis	O-H..O, C-H…O; Cyt11	32.11	Val147	mis	C-H…O; Gua10;	**100**
	plat	O-H…O, C-H…O; Cyt11;	68.61		plat	C-H…O; Gua10;	76.25
Pro47	mis	C-H…O; Cyt11;	**100**	Val148	mis	N-H…O; Gua10;	**100**
	plat	C-H…O; Cyt11;	90.79		plat	N-H…O; Gua10;	79.14
Gly48	mis	N-H…O; Cyt11;	32.10	Arg150	mis	C-H…N; Cyt9;	14.66
	plat	N-H…O; Cyt11; C-H…O; Gua10, Cyt11;	40.34		plat	C-H…N; Gua10;	21.73
Val68	mis	N-H…O; Gua8; C-H…O; Cyt9;	**100**	Tyr484	mis	O-H…O, C-H…O; Gua8, Cyt9;	**100**
	plat	N-H…O; Gua8; C-H…O; Gua10;	63.28		plat	O-H…O; Gua8, Gua9;	56.80
Gly69	mis	C-H…N, C-H…O; Cyt9; Gua8;	44.52	Arg604	mis	N-H…O, C-H…O; Cyt15;	15.63
	plat	C-H…N, C-H…O; Gua8, Gua9;	74.23		plat	C-H…O; Cyt15;	7.17
Lys70	mis	N-H…O; Cyt7, Gua8; N-H…N; Gua8; C-H…O; Cyt7, Gua8; C-H…N; Gua8, Gua9;	**100**	Thr605	mis	C-H…O, C-H…N; Cyt15;	8.06
	plat	N-H…O; Cyt7, Gua8; N-H…N; Gua8; C-H…O; Cyt7, Gua8; C-H…N; Gua8;	75.32		plat	-	0
Phe71	mis	N-H…N; Gua8; C-H…O ; Gua9 ; C-H…N ; Gua8, Gua9 ;	**100**	Trp609	mis	N-H…O, C-H…O; Thy13, Thy14; C-H…N; Thy13;	100
	plat	C-H…O, C-H…N; Gua8, Gua9;	93.53		plat	N-H…O; Thy13, Thy14; C-H…O; Gua10, Thy13;	42.42
Glu73	mis	N-H…O ; Gua8 ; Thy8 ; C-H…O ; Thy8 ;	15.63	Ile611	mis	C-H…O; Gua6, Gua12, Thy13;	57.33
	plat	N-H…O; Gua8, Thy8, Gua10; C-H…O, C-H…N; Thy8;	82.52		plat	C-H…O; Gua12, Thy13;	9.57

Leu88	mis	C-H…O ; Gua9 ;	39.00	Gly612	mis	N-H…O ; Cyt7 , Thy13 ;	40.85
	plat	C-H…O; Gua9;	75.57		plat	-	0
Val89	mis	N-H…O ; Gua9	51.15	Arg613	mis	N-H…O ; Cyt7, Gua8 ; C-H…O; Cyt7; Gua8; C-H…N; Cyt7;	65.39
	plat	N-H…O; Thy8, Gua9; C-H…O; Thy8;	59.31		plat	C-H…O, C-H…N; Gua8;	27.17
Phe90	mis	C-H…O ; Thy8 ;	17.47	Asn614	mis	N-H…O; Cyt7;	17.47
	plat	C-H…O; Thy8;	22.94		plat	-	0
Met91	mis	C-H…O ; Gua7 ; Thy8 ;	100	Lys636	mis	N-H…O, C-H…O ;Cyt5, Gua6; C-H…N ; Gua6 ;	76.63
	plat	C-H….O; Cyt7, Thy8 ; C-H…N ; Cyt7; C-H…S; Thy8;	92.83		plat	N-H…O, C-H…O; Cyt5, Gua6;	29.03
Lys92	mis	N-H…O ; Gua7 ; Cyt11 ; C-H…O ; Gua7 ;	40.19	Thr638	mis	O-H…O ; Thy14 ;	4.32
	plat	N-H…O, C-H…O; Cyt6, Cyt7, Thy8; N-H…N; Cyt7; C-H…N; Cyt6, Cyt7;	67.34		plat	-	0
Gly93	mis	-	0	Lys639	mis	N-H...O ; Cyt4, Thy14 ; C-H…O ; Thy14, Cyt15 ; C-H…N, Ade3, Cyt4 ;	64.47
	plat	C-H…O; Cyt6;	8.29		plat	N-H…O, C-H…O; Cyt15, Thy14;	63.46
Asn94	mis	-	0	Lys640	miss	N-H…O ; Cyt15 ;	4.32
	plat	C-H…N ; Cyt11 ;	8.29		plat	-	0
Trp95	mis	C-H…O ; Cyt11 ;	31.43	Lys643	mis	N-H…O ; Thy14 ;	8.06
	plat	-	0		plat	N-H…O ; Thy14 ;	29.06
Ser98	mis	-	0	Lys6	mis	N-H…O ; Gua11 ; C-H…O ; Cyt10, Gua11 ;	76.63
	plat	C-H…O; Thy8;	24.93		plat	N-H…O, C-H…O; Cyt10, Gua11;	77.11
Gly99	mis	C-H…O ; Thy8 ;	37.20	Asn109	mis	C-H…O ; Ade2 ;	17.47
	plat	C-H…O; Thy8, Gua9; C-H…N, N-H…O; Thy8;	54.18		plat	-	0
Pro101	mis	C-H…O, C-H…N; Gua9;	100	Lys110	mis	N-H…O; Ade2; C-H…O; Gua1, Ade2 ;	33.10
	plat	C-H…O, C-H…O; Gua9;	100		plat	N-H…O; Ade2;	7.17
Ile103	mis	C-H…O ; Cyt10 ; Gua11 ;	21.80	Lys509	mis	N-H…O, C-H…O; Ade4; Gua14;	48.84
	plat	C-H…O; Gua11;	8.29		plat	N-H…O; Thy3, Ade4, Gua14; N-H…N; Ade4, Gua14; C-H…O; Ade4, Gua15; C-H…N; Ade4, Gua14;	43.97
Tyr108	mis	O-H…O ; C-H…O ;Gua9 ; Cyt10 ;	67.86	Gln510	mis	C-H…O, C-H…N; Ade4;	24.55
	plat	O-H…O, C-H…O; Gua9, Cyt10;	79.42		plat	-	0
Gln124	mis	C-H…O ; C-H…N ; Cyt9 ;	27.69	Lys512	mis	N-H…O, C-H…O ; Gua5 ;	56.90
	plat	C-H…O ; Gua9 ;	27.22		plat	N-H…O ; Ade4, Gua5 ; C-H…O, C-H…N ; Gua5 ;	63.04
Pro128	mis	C-H…O ; Cyt9 ;	47.42	Ala517	mis	C-H…O ; Cyt4 ;	14.66
	plat	C-H…O ; Gua9 ;	26.04		plat	-	0
Cys135	mis	C-H…O ; Cyt1 ;	14.66	Gln518	mis	C-H…O ; Cyt4 ;	14.66
	plat	C-H…O ; Cyt1, Cyt2 ;	22.34		plat	C-H…O ; Cyt4 ;	13.89
Arg136	mis	C-H…O ; Cyt2 ;	23.37	Arg524	mis	-	0
	plat	N-H…O, C-H…O, C-H…N ; Cyt2	22.34		plat	C-H…O ; Gua5 ;	31.39
Ala139	mis	-	0	Thr526	mis	O-H…O; Ade4;	61.00
	plat	C-H…O; Cyt1;	19.24		plat	O-H…O; Ade4;	35.78

His140	mis	O-H…H , C-H…O ; Cyt1 ;	24.55	Lys528	mis	N-H…O, C-H…O ; Th3, Ade4 ;	84.37
	plat	C-H…O, C-H…N ; Cyt1 ;	22.34		plat	N-H…O, C-H…O, C-H…N ; Thy3, Ade4 ;	75.35
Ile141	mis	N-H…O ; Cyt1 ; C-H…O ; Cyt1 ; Cyt2 ;	39.20	Gln545	mis	C-H…N ; Cyt5 ; C-H…O ; Cyt5, Gua6 ;	83.52
	plat	N-H…O, C-H…O ; Cyt1 ; C-H…O ; Cyt2 ;	22.34		plat	C-H…O ; Cyt5, Gua6 ; C-H…N ; Cyt5 ;	68.64
Lys143	mis	-	0	Lys546	mis	N-H…O, C-H…O ; Gua6, Cyt7 ;	100
	plat	N-H…O, C-H…O ; Thy12 ;	16.78		plat	N-H…O ; Gua6, Cyt7 ; C-H…O ; Gua6 ; C-H…N ; Cyt7 ;	90.79
Arg146	mis	C-H…O ; Cyt1 ; C-H…N; Cyt2;	38.03	Asn547	mis	C-H…O ; Gua5 ;	7.56
	plat	C-H…O ; Cyt2 ; C-H…N ; Cyt2, Thy3, Gua10 ;	49.51		plat	N-H…O ; Gua6 ; C-H…O ; Ade4, Gua5, Gua6 ; C-H…N ; Gua5 ;	36.80
				Lys550	mis	-	0
					plat	N-H…O ; Cyt5 ;	20.35

DNA hydrogen bonds analysis: MutS versus MSH2/MSH6

In *Nucleic Acids Research*, 2006, Vol.34, No. 8, there are reported 23 residues of MutS involved in hydrogen bonds with DNA, maintained for more than 90% of the simulation time. When compared with the mismatched MSH2/MSH6, 43.48% of the corresponding MutS homologues are not involved in hydrogen bonds with the DNA fragment.

	MutS	**MutSα***	
	Segment A	MSH6	%
1	MET 31	GLY 48	32.11
2	GLU 38	GLU 73	15.63
3	THR 56	MET 91	100
4	ARG 58	GLY 93	0
5	SER 61	ALA 96	0
6	GLY 70	GLY 99	37.21
7	TYR 79	TYR 108	67.86
8	VAL 106	VAL 148	100
9	ARG 108	ARG 150	14.66
10	GLN 476	GLN 617	0
11	LYS 496	LYS 640	4.32
12	ARG 500	ARG 644	0
	Segment B	MSH2	%
1	ARG 32	ASP 38	0
2	MET 33	ARG 39	0
3	GLY 97	-	
4	LYS 464	LYS 512	56.9
5	ASN 468	SER 516	0
6	ALA 469	ALA 517	14.66
7	SER 468	THR 526	61
8	GLN 493	ASP 543	0

9	LYS 496	LYS 546	100
10	ASN 497	ASN 547	7.57
11	ARG 500	LYS 550	0

Note: * the mismatched system

If considered the MutSα residues involved in hydrogen bonds with the DNA fragment less than 20% of the simulation time, it corresponds to 21.74% of the similar homologues of MutS residues. Similarly, for those involved in hydrogen bonds present less than 40%, 60%, 80% and 100% of the simulation time, the corresponding MutS residues are representing 30.43%, 34.78%, 39.13% and 43.48%, respectively.

Dimer Interactions

Table S5. Interactions at the heterodimer interface in the platinum cross-linked MutSα-DNA complex

	MSH2 donor	**MSH6 acceptor**	frame #(cluster#)	% conf	**MSH6 donor**	**MSH2 acceptor**	frame#(cluster#)	% conf
1	ALA2	LEU86	160(7), 194(8), 283(12), 33(2), 60(1), 83(4)	60.41	ARG107	GLN4	126(3), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2), 83(4)	70.47
2	LYS6	ARG107	115(5), 142(6), 160(7), 194(8), 201(9), 232(10), 83(4), 33(2)	69.56	ARG107	PRO5	160(7), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2)	61.17
3	ARG55	GLU399	115(5), 126(3), 272(11), 283(12), 83(4)	43.81	SER111	ALA2	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
4	MET83	GLY87	11595), 126(3), 142(6), 201(9), 33(2), 60(1)	39.15	GLY388	GLN718	115(5), 126(3), 142(6), 160(7), 232(10), 60(1)	37.78
5	ASN311	MET823	142(6), 160(7), 194(8), 232(10), 272(11), 33(2)	59.99	GLY388	LEU719	115, 126, 142, 194, 201, 232, 272, 283, 33, 60, 83	92.73
6	ILE544	SER637	115(5), 126(3), 142(6), 160(7), 194(8), 201(9), 232(10), 33(2), 83(4)	72.54	THR389	LYS720	115, 126, 142, 160, 194, 201, 232, 272, 283, 60, 83	89.21
7	ASN671	GLY857	115(5), 126(3), 160(7), 272(11), 283(12), 33(2), 60(1), 83(4)	68.46	ASN390	GLY721	115(5), 126(3), 160(7), 201(9), 232(10), 272(11), 283(12), 60(1), 83(4)	66.12
8	GLN718	GLY388	115(5), 126(3), 142(6), 160(7), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2), 60(1)	86.42	ASN390	LYS720	115(5), 126(3), 160((7) 194(8), 201(9), 232(10), 33(2), 60(1), 83(4)	79.13

9	LEU719	ASN390	115(5), 126(3), 142(6), 160(7), 272(11), 283(12), 83(4)	60.19	LYS636	ILE544	126, 142, 160, 194, 201, 232, 283, 33, 60, 83	80.95
10	LYS720	GLY391	115(5), 126(3), 142(6), 160(7), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2), 83(4)	93.31	SER637	ILE544	126(3), 142(6), 160(7), 194(8), 201(9), 232(10), 33(2), 83(4)	65.98
11	LYS720	GLY395	115(5),126(3), 201(9), 232(10), 272(11), 83(4)	43.97	ARG821	ASP716	115(5), 142(6), 160(7), 194(8), 201(9), 232(10), 33(2), 60(1)	67.32
12	LYS720	THR393	126(3), 194(8), 201(9), 232(10), 272(11), 60(1)	44.50	ARG821	GLY715	142(6), 194(8), 201(9), 232(10),272(11),283(12)	52.42
13	ALA733	ASN946	194(8), 232(10), 272(11), 33(2), 60(1)	49.30	MET823	ASN311	115(5), 142(6), 160(7), 194(8), 60(1), 83(4)	57.01
14	SER755	HIS887	115(5), 126(3), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2), 60(1), 83(5)	83.62	SER827	ASN671	115, 126, 142, 160, 194, 232, 283, 33, 60, 83	84.32
15	GLY761	GLY955	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	THR828	ASN671	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
16	LYS773	GLU950	126(3), 160(7), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2), 60(1)	70.75	PHE829	ASN671	115, 126, 142, 160, 201, 232, 272, 283, 33, 60, 83	86.11
17	HIS785	THR860	115(5), 142(6), 160(7), 272(11), 283(12), 33(2), 60(1)	61.20	ALA859	HIS783	126(3), 160(7), 272(11), 283(12), 33(2), 60(1)	48.41
18	SER825	ASP862	126(3), 142(6), 160(7), 272(11), 283(12), 33(2)	57.76	ALA865	ALA844	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
19	GLY827	ASP852	115(5), 126(3), 142(6), 160(7), 194(8), 272(11), 283(12), 60(1), 83(4)	80.77	ALA869	ALA844	142(6), 160(7), 194(8), 283(12), 33(2)	52.45
20	ILE828	ASP862	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	ALA869	VAL840	142(6), 160(7), 201(9), 232(10), 272(11), 283(12), 33(2), 60(1)	63.18
21	PHE836	LEU833	126(3), 160(7), 272(11), 283(12), 33(2), 83(4)	55.30	HIS887	GLY753	142(6), 83(4), 115(5), 194(8), 201(9), 232(10), 33(2), 60(1)	69.08

22	ALA844	ALA865	126(3), 160(7), 194(8), 201(9), 283(12), 33(2)	46.13	HIS887	THR754	115(5), 126(3), 142(6), 160(7), 194(8), 83(4)	53.21
23	LYS847	ASN868	115(5), 126(3), 142(6), 160(7), 201(9), 232(10), 272(11), 33(2), 60(1)	64.24	LYS935	ASP758	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
24	LYS847	ASP894	142(6), 160(7), 194(8), 201(9), 232(10), 272(11), 33(2), 60(1)	68.78	PHE939	ASP758	115(5), 142(6), 194(8), 201(9), 232(10), 283(12), 33(2), 60(1), 83(4)	77.37
25					ALA945	MET729	126(3), 194(8), 272(11), 283(12), 33(2), 83(4)	62.02
26					LYS954	GLU768	115(5), 126(3), 142(6), 194(8), 201(9), 272(11), 283(12), 33(2), 83(4)	80.80
27					GLY955	GLY761	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
28					ALA959	TYR757	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
29					ARG973	GLN850	115(5), 126(3), 142(6), 160(7), 272(11), 283(12)	46.61

Dimer Interactions

Table S6. Interactions at the heterodimer interface in the mismatched MutSα-DNA complex

	MSH2 donor	**MSH6 acceptor**	frame #(cluster#)	% conf	**MSH6 donor**	**MSH2 acceptor**	frame#(cluster#)	% conf
1	MET1	SER111	15(1), 180(6), 218(8), 47(2), 79(3)	64.73	ARG107	GLN4	102, 148, 15, 180, 192, 218, 47, 79	**100**
2	LYS6	ARG107	148(5), 15(1), 180(6), 218(8), 47(2), 79(3)	88.12	ARG107	PRO5	102(4), 148(5), 15(1), 218(8), 47(2)	72.20
3	GLN61	SER171	15(1), 180(6), 192(7), 47(2), 79(3)	54.82	SER111	ALA2	148(5), 15(1), 180(6), 192(7), 218(8), 47(2)	87.84
4	ILE544	SER637	102, 148, 15, 180, 192, 218, 47, 79	**100**	SER171	THR60	102(4), 15(1), 180(6), 192(7), 47(2), 79(3)	82.53

5	ASN671	GLY857	148(5), 15(1), 180(6), 192(7), 218(8), 47(2)	83.50	GLY388	GLY721	102(4), 15(1), 192(7), 47(2), 79(3)	51.08
6	SER717	THR389	102(4), 15(1), 192(7), 218(8), 79(3)	64.25	GLY388	LYS720	148(5), 15(1), 192(7), 218(8), 79(3)	75.22
7	GLN718	THR389	102, 15, 180, 192, 218, 47, 79	76.63	THR389	GLY721	102(4), 15(1), 180(6), 192(7), 47(2), 79(3)	59.16
8	LEU719	THR389	102(4), 15(1), 218(8), 47(2), 79(3)	60.99	THR389	SER723	102, 148, 15, 180, 192, 218, 47	87.84
9	LYS720	ASN387	102(4), 1591), 180(6), 192(7), 47(2), 79(3)	56.21	ASN390	GLY721	102, 148, 15, 180, 192, 47, 79	82.53
10	LYS720	GLU394	102(4), 15(1), 180(6), 192(7), 47(2), 79(3)	76.63	GLY391	LEU719	102(4), 15(1), 180(6), 192(7), 79(3)	46.76
11	LYS720	SER392	102(4), 148(5), 180(6), 218(8), 79(3)	72.96	LYS636	ILE544	102(4), 15(1), 180(6), 192(7), 218(8), 79(3)	87.62
12	GLY721	ASN390	148(5), 180(6), 192(7), 218(8), 47(2)	68.84	SER637	ILE544	102, 15, 180, 192, 218, 47, 79	76.63
13	MET729	ALA942	15(1), 180(6), 192(7), 47(2), 79(3)	54.82	PRO774	GLY753	102(4), 148(5), 180(6), 47(2), 79(3)	60.29
14	GLY753	ASN775	148(5), 15(1), 180(6), 192(7), 79(3)	65.81	ASN775	GLY753	102, 148, 15, 180, 192, 47, 79	82.53
15	TYR757	ASN966	102(4), 148(5), 180(6), 192(7), 218(8)	60.78	MET776	MET726	148 (5), 180(6), 192(7), 218(8)	56.46
16	TYR757	GLU893	148(5), 15(1), 192(7), 218(8), 47(2), 79(3)	87.60	ASP820	SER717	148(5), 180(6), 192(7), 218(8)	56.46
17	GLY761	GLY955	102(4), 148(5), 15(1), 180(6), 218(8), 79(3)	80.06	SER827	ASN671	148(5), 15(1), 180(6), 192(7), 218(8), 47(2)	83.52
18	ALA765	VAL951	102(4), 15(1), 180(6), 47(2), 79(3)	51.58	THR828	ASN671	180(6), 192(7), 47(2), 79(3)	40.16
19	TYR769	GLU950	102(4), 148(5), 15(1), 218(8), 79(3)	71.98	PHE829	ASN671	148(5), 180(6), 192(7), 218(8), 79(3)	68.62
20	GLY827	ASP826	148(5), 15(1), 180(6), 218(8), 47(2), 79(3)	88.10	ALA837	ASN835	102(4), 148(5), 192(7), 218(8), 79(3)	64.88
21	ILE828	ASP862	148(5), 15(1), 180(6), 192(7), 218(8), 79(3)	83.30	ALA859	SER825	102(4), 148(5), 15(1), 192(7), 47(2)	62.29
22	PHE836	LEU833	102(4), 15(1), 180(6), 192(7), 47(2), 79(3)	59.14	THR860	HIS783	148(5), 180(6), 218(8), 47(2)	61.28

23					PHE861	GLN855	102(4), 180(6), 47(2), 79(3)	36.92
24					ALA865	ALA844	102, 148, 15, 180, 192, 218, 47, 79	**100**
25					ALA869	ALA844	102(4), 148(5), 192(7), 218(8), 47(2), 79(3)	77.26
26					ALA869	VAL840	102, 148, 15, 180, 192, 218, 47, 79	**100**
27					HIS887	THR754	148(5), 15(1), 192(7), 218(8), 47(2)	75.44
28					TYR888	THR756	148(5), 180(6), 192(7), 218(8), 79(3)	68.62
29					HIS889	SER755	148(5), 180(6), 192(7), 218(8), 79(3)	68.62
30					HIS889	THR756	148(5), 15(1), 180(6), 192(7), 47(2), 79(3)	78.19
31					SER890	TYR757	148(5), 15(1), 180(6), 192(7), 218(8), 47(2)	83.50
32					LYS935	ASP758	148, 15, 180, 192, 218, 47, 79	95.68
33					PHE939	ASP758	102, 148, 15, 180, 192, 47, 79	82.53
34					LYS954	GLU768	102, 148, 15, 180, 192, 218, 47, 79	**100**
35					GLY955	GLY761	102, 148, 15, 180, 192, 218, 47, 79	**100**
36					ALA959	TYR757	102(4), 148(5), 15(1), 192(7), 218(8), 79(3)	79.54
37					ARG973	GLU850	15(1), 180(6), 192(7), 218(8), 47(2)	60.13

Nucleotide binding sites

Table S7. Hydrogen bonding for ADP molecules at the ATPase binding site in the platinum cross-linked MutSα-DNA complex.

	MSH2	frame #(cluster#)	%	**MSH6**	frame#(cluster#)	%

			conf			conf
1	ILE648	201(9), 33(2), 60(1)	20.58	THR739	60(1)	6.69
2	ALA649	126(3), 210(9), 232(10), 272(11), 283(12), 33(2), 60(1)	49.69	LYS740	115, 142, 160, 194, 201, 232, 272, 283, 60, 83	86.32
3	PHE650	126(3), 160(7), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2), 60(1)	70.75	THR741	33(2), 60(1)	17.48
4	ILE651	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	PHE742	160(7), 201(9), 232(10), 33(2), 60(1)	33.10
5	ASN653	142(6), 194(8)	23.10	PHE743	160(7)	7.17
6	ASN671	126(3), 142(6), 33(2), 60(1)	29.58	ASP746	115(5), 272(11), 33(2)	29.84
7	MET672	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	PHE747	115, 126, 142, 160, 194, 272, 283, 33, 60, 83	91.55
8	GLY673	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	ILE748	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
9	GLY674	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	ASN750	194(8), 201(9), 232(10), 60(1)	29.03
10	LYS675	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	ASN775	115, 126, 142, 160, 194, 272, 60, 83	72.47
11	SER676	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	MET776	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
12	THR677	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**	GLY777	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
13	TYR815	115(5), 126(3), 160(7), 194(8), 201(9), 232(10), 272(11), 283(12), 60(1), 83(4)	80.00	GLY778	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
14	VAL722	115(5), 126(3)	9.36	LYS779	115, 126, 142, 160, 201, 232, 272, 283, 33, 60, 83	86.11

15				SER780	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
16				THR781	115, 126, 142, 160, 194, 201, 232, 272, 283, 33, 60, 83	**100**
17				ARG784	283(12)	8.29
18				TYR926	160(7), 194(8), 201(9), 232(10), 272(11), 283(12), 33(2), 60(1)	67.86
				SER824	115, 126, 194, 201, 232, 272, 283, 33, 60, 83	83.62
				GLY825	194(8), 201(9), 232(10), 33(2), 60(1)	39.82
				SER827	115(5), 126(3), 83(4)	22.94

Note: in red are the hydrogen bonds made by either MSH2 or MSH6 with the neighboring ADP.

Table S8. Hydrogen bonding for ADP molecules at the ATPase binding site in the mismatched MutSα-DNA complex.

	MSH2	frame #(cluster#)	% conf	**MSH6**	frame#(cluster#)	% conf
1	ILE648	218(8)	17.42	ILE738	15(1), 47(2)	27.04
2	ALA649	102(4), 148(5), 15(1), 218(8), 79(3)	71.93	LYS740	148(5), 180(6), 192(7), 218(8), 47(2), 79(3)	81.02
3	PHE650	102, 148, 15, 192, 218, 47, 79	91.94	ASN746	102(4), 148(5), 15(1), 180(6), 192(7), 47(2)	70.35
4	ILE651	102, 148, 15, 180, 192, 218, 47, 79	**100**	PHE747	102((4), 180(6), 192(7), 218(8), 47(2), 79(3)	61.97
5	ASN653	102(4)	4.32	ILE748	102, 148, 15, 180, 192, 218, 47, 79	**100**
6	ASN671	102, 148, 15, 192, 218, 47, 79	91.94	ASN775	148(5)	23.37
7	MET672	102, 148, 15, 180, 192, 218, 47, 79	**100**	MET776	102(4), 148(5), 15(1), 218(8), 47(2), 79(3)	84.38
8	GLY673	102(4), 148(5), 15(1), 180(6), 192(7), 47(2), 79(3)	82.58	GLY777	102(4), 148(5), 15(1), 218(8), 47(2), 79(3)	84.38

9	GLY674	102, 148, 15, 180, 192, 218, 47, 79	**100**	GLY778	102, 148, 15, 180, 192, 218, 47, 79	**100**
10	LYS675	102, 148, 15, 180, 192, 218, 47, 79	**100**	LYS779	102, 148, 15, 192, 218, 47, 79	91.94
11	SER676	102, 148, 15, 180, 192, 218, 47, 79	**100**	SER780	102, 148, 15, 180, 192, 218, 47, 79	**100**
12	THR677	102, 148, 15, 180, 192, 218, 47, 79	**100**	THR781	102, 148, 15, 180, 192, 218, 47, 79	**100**
13	MET813	79(3)	12.16	TYR926	102(4), 15(1), 180(6), 192(7), 47(2), 79(3)	59.21
14	TYR815	102(4), 15(1), 180(6), 192(7), 47(2)	46.98	LYS927	180(6)	8.06
15	SER723	47(2), 79(3), 102(4), 148(5), 180(6), 192(7)	67.92	MET823	47(2), 192(7)	19.94
16	SER724	180(6), 192(7)	15.62	SER824	15(1), 79(3), 102(4), 148(5), 192(7)	62.07
				GLY825	79(3), 148(5), 192(7)	43.09
				SER827	79(3)	12.16

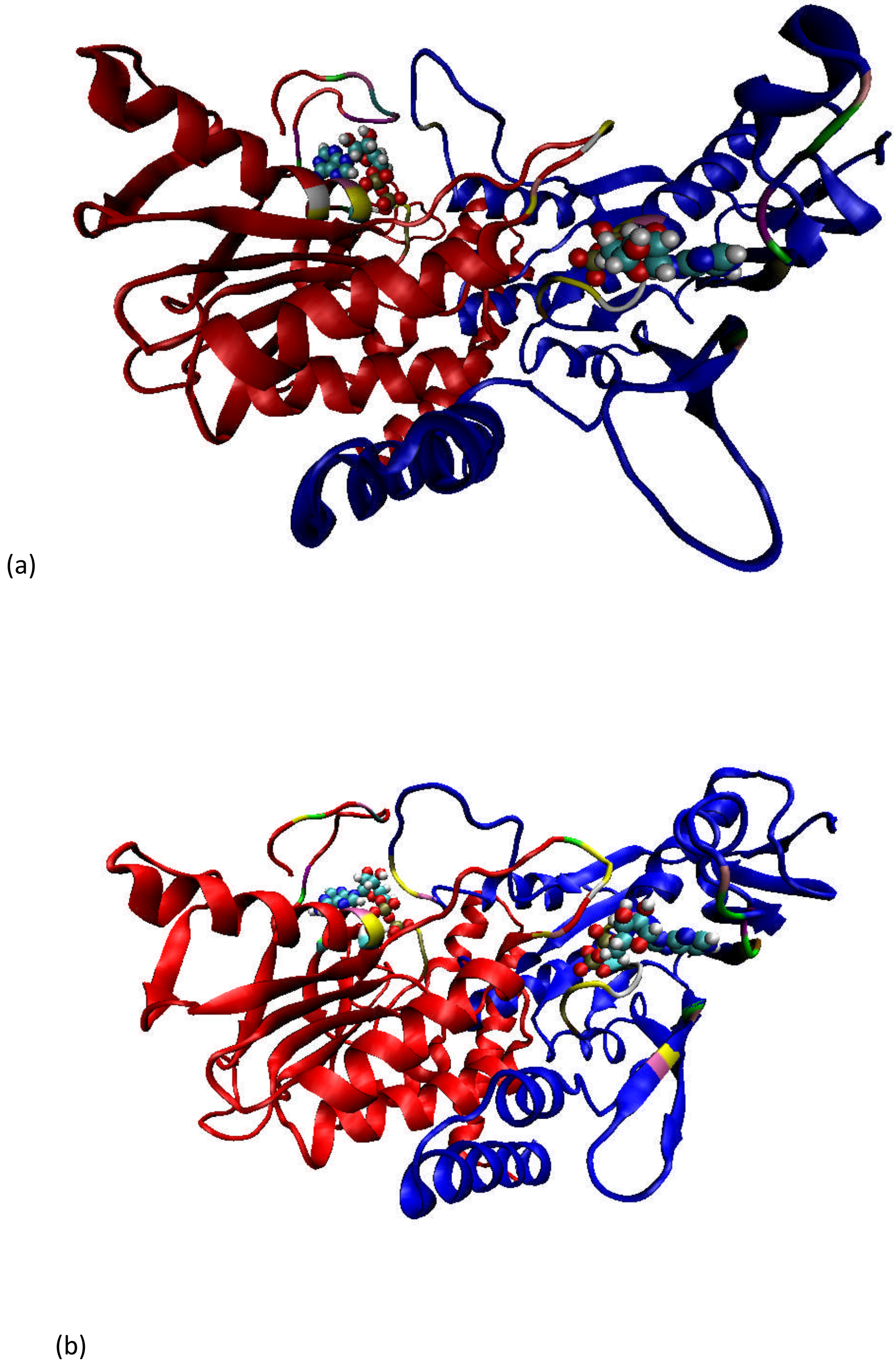


Figure S3. Nucleotide binding sites in platinum cross-linked (a) and mismatched (b) MutSα-DNA complexes. Since the ATPase domains in the protein are almost superinposible, the binding modes for ADP molecules are almost identical.. Notice the possibility of disorganized loop in either mer to stabilize the alternative ADP molecule.

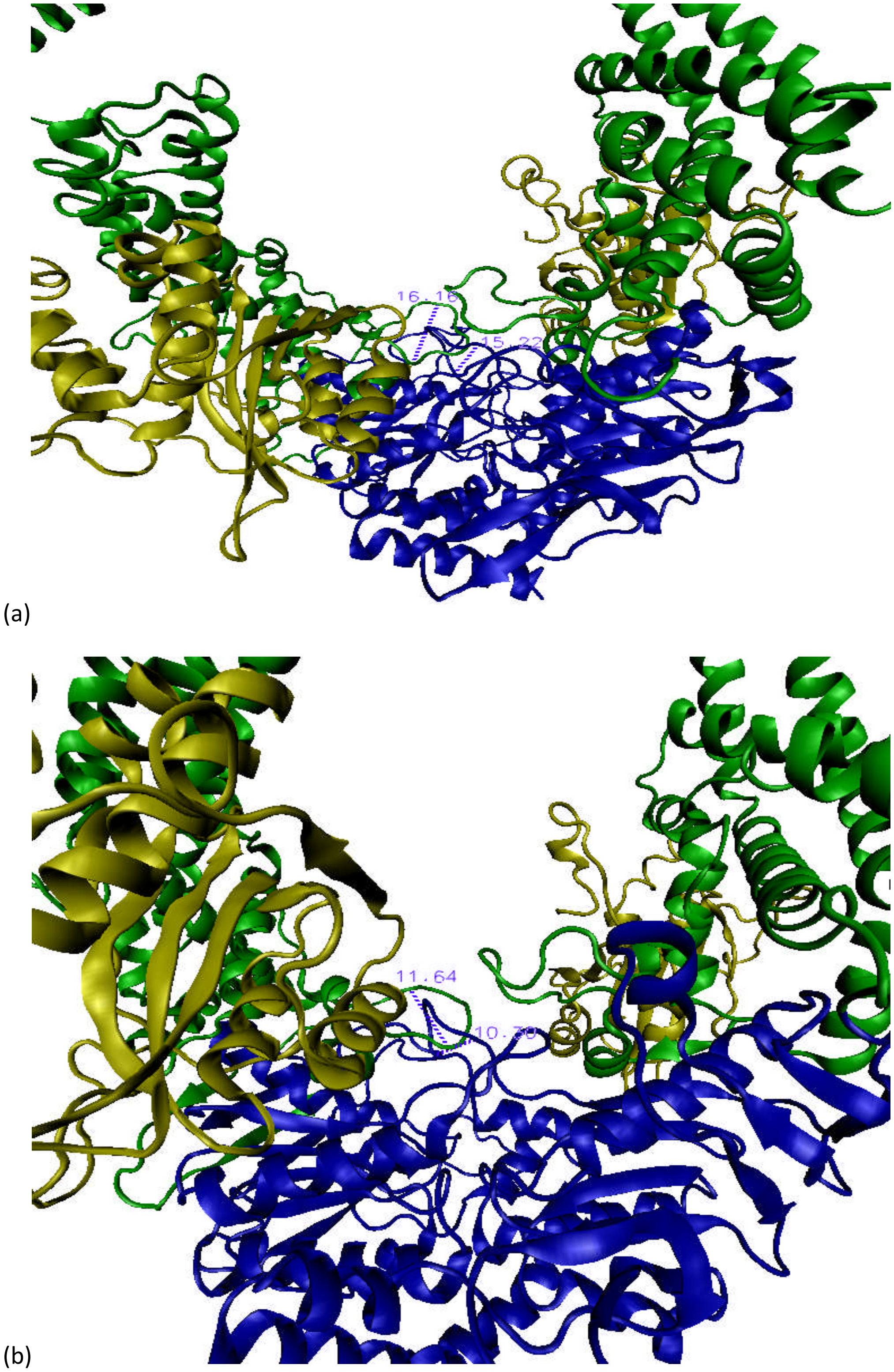
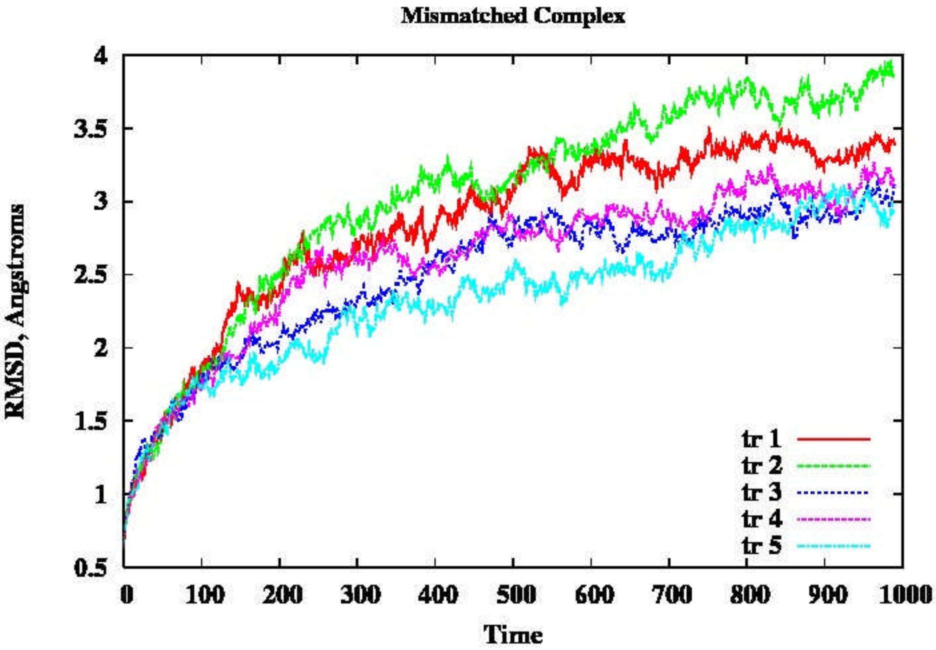


Figure S4. Allosteric communications between lever and ATPase domains at the heterodimer interface. In response to the distinctive conformational changes associate with the different binding modes for DNA fragments by MutSα, the wide and contracted interconnected loops in the mismatch complex, panel **(a)**, are narrow and elongated in the platinum cross-linked complex, panel **(b)**. The changes at the lever-ATPase interface are shown in the general context of the multi-domain protein, with the connector domain in yellow, the lever domain in green and the ATPase domain in blue.



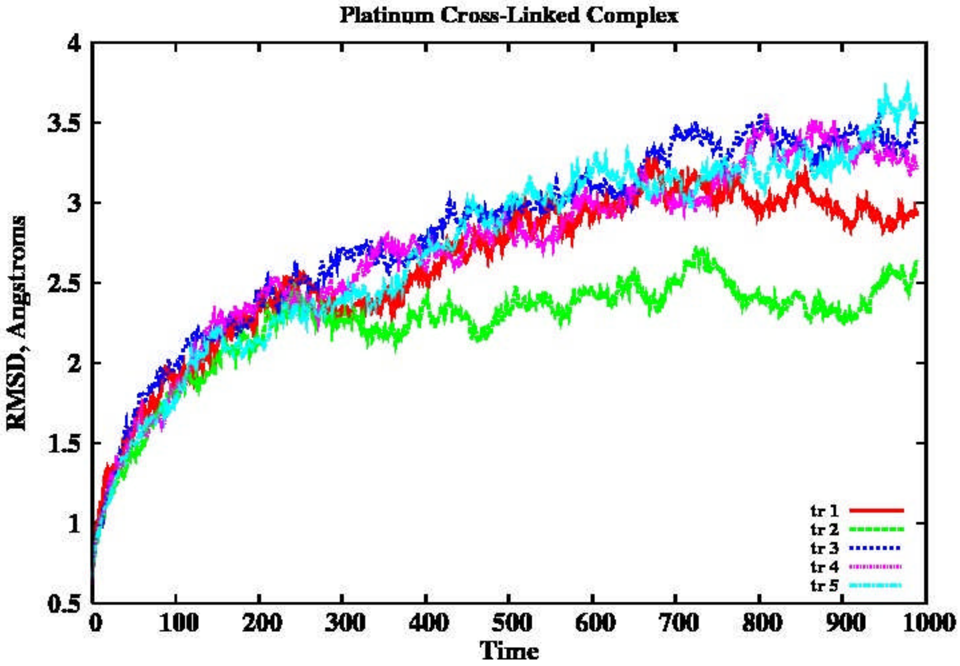


Figure S5. C-α root mean square deviations calculated from the initial structure for every 50th snapshot, plotted as a function of time. There are five simulations for each of the mismatched and platinum cross-linked MutSα-DNA complexes. They show that the simulations are equilibrated, with RMSD approximately levering off at about 5 ns.

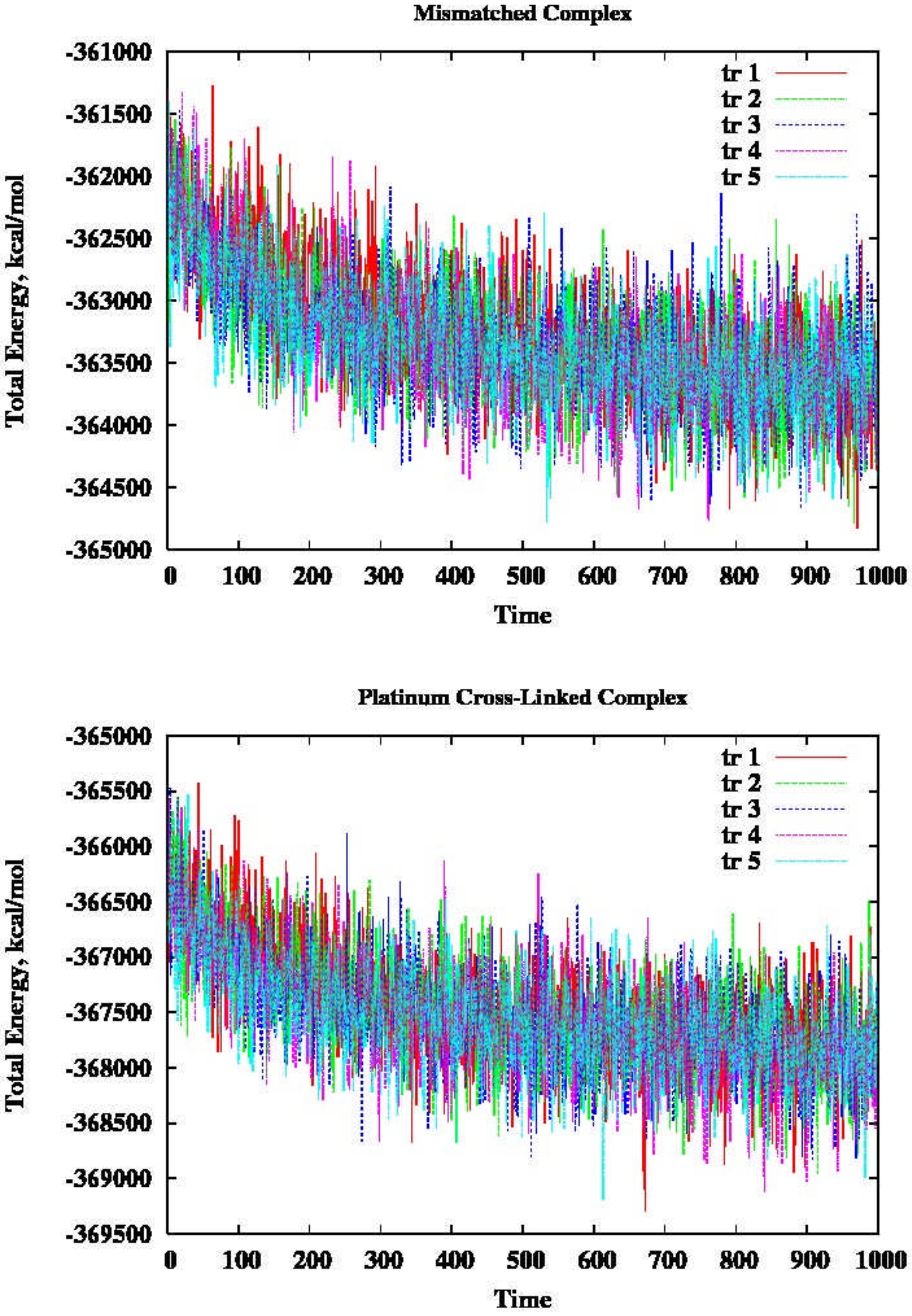


Figure S6. Total energies, presented for every 50th snapshot, for the five simulations of the mismatched and platinum cross-linked MutSα-DNA complexes also show that the systems equilibrate at about 5ns.

1 M
2 A
3 V
4 Q
5 P
6 K
7 E
8 T
9 L
10 Q
11 L
12 E
13 S
14 A
15 A
16 E
17 V
18 G
19 F
20 V
21 R
22 F
23 F
24 Q
25 G
26 M
27 P
28 E
29 K
30 P
31 T
32 T
33 T
34 V
35 R
36 L
37 F
38 D
39 R
40 G
41 D
42 F
43 Y
44 T
45 A
46 H
47 G
48 E
49 D
50 A
51 L
52 L
53 A
54 A
55 R
56 E
57 V
58 F
59 K
60 T
61 Q
62 G
63 V
64 I
65 K
66 Y
67 M
68 G
69 P
70 A
71 G
72 A
73 K

78 V
79 V
80 L
81 S
82 K
83 M
84 N
85 F
86 E
87 S
88 F
89 V
90 K
91 D
92 L
93 L
94 L
95 V
96 R
97 Q
98 Y
99 R
100 V
101 E
102 V
103 Y
104 K
105 N
106 R
107 A
108 G
109 N
110 K
111 A
112 S
113 K
114 E
115 N
116 D
117 W
118 Y
119 L
120 A
121 Y
122 K
123 A
124 S
125 P
126 G
127 N
128 L
129 S
130 Q
131 F
132 E
133 D
134 I
135 L
136 F
137 G
138 N
139 N
140 D
141 M
142 S
143 A
144 S
145 I
146 G
147 V
148 V
149 G
150 V

151 K
152 M
153 S
154 A
155 V
156 D
157 G
158 Q
159 R
160 Q
161 V
162 G
163 V
164 G
165 Y
166 V
167 D
168 S
169 I
170 Q
171 R
172 K
173 L
174 G
175 L
176 C
177 E
178 F
179 P
180 D
181 N
182 D
183 Q
185 S
186 N
187 L
188 E
189 A
190 L
191 L
192 I
193 Q
194 I
195 G
196 P
197 K
198 E
199 C
200 V
201 L
202 P
203 G
204 G
205 E
206 T
207 A
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723 S
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729 M
730 L
731 E
732 T
733 A
734 S
735 I

736 L
737 R
738 S
739 A
740 T
741 K
742 D
743 S
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748 D
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811 L
812 T
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814 L
815 Y
816 Q
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818 K
819 K
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853 E
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Figure S7. Residues sequence and numbering for MSH2 subunit: mismatched binding domain, 1 - 124; connector domain,125-297; leveler domain, 300-456 and 554-619; clamp domain, 457-553; ATP-ase domain, 620-855.

1 P
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3 V
4 W
5 Y
6 H
7 E
8 T
9 L
10 E
11 W
12 L
13 K
14 E
15 E
16 K
17 R
18 R
19 D
20 E
21 H
22 R
23 R
24 R
25 P
26 D
27 H
28 P
29 D
30 F
31 D
32 A
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34 T
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36 Y
37 V
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39 E
40 D
41 F
42 L
43 N
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46 T
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124 Q
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Figure S8. Residues sequence and numbering for MSH6 subunit: mismatch binding domain, 1-157; connector domain, 158-356; lever domain: 357-573 and 648-714; clamp domain, 574-647; ATPase domain, 715-974.