SUPPLEMENTAL MATERIAL

Table S1: Thermodynamic Parameters for seven Linearly Independent Sequences with Internal I·C Mismatches in 1 M NaCl.

Propagation Sequence	ΔG_{37} (kcal/mol)	ΔH (kcal/mol)	ΔS (cal/K*mol)
AIA/TCT	-1.55 ± 0.09	-13.8 ± 2.1	-39.4 ± 2.1
AIC/TCG	-2.03 ± 0.10	-13.9 ± 2.2	-38.1 ± 2.2
AIG/TCC	-1.84 ± 0.11	-17.2 ± 2.2	-49.3 ± 2.2
AIT/TCA	-1.85 ± 0.08	-17.7 ± 2.0	-50.9 ± 2.0
CIA/GCT	-1.73 ± 0.11	-10.3 ± 2.3	-27.6 ± 2.3
GIA/CCT	-1.45 ± 0.11	-11.7 ± 2.3	-33.0 ± 2.3
TIA/ACT	-1.05 ± 0.09	-10.8 ± 2.2	-31.3 ± 2.2

Table S2: Thermodynamics of Duplex Formation of Oligonucleotides with Internal Inosine Mismatches.

DNA Duplex	1/Tm Method				Curve fit Method		
I/C	$-\Delta G°_{37}$ (kcal/mol)	$-\Delta H°$ (kcal/mol)	$-\Delta S°$ (cal/K*mol)	T_M (°C)	$-\Delta G°_{37}$ (kcal/mol)	$-\Delta H°$ (kcal/mol)	$-\Delta S°$ (cal/K*mol)
CGCIGAACIGGC	14.31 ± 0.48	94.2 ± 6.2	257.6 ± 18.4	64.9	14.33 ± 0.26	94.4 ± 2.7	258.1 ± 8.0
CCGICTGTIGCG	14.00 ± 0.08	90.6 ± 1.0	247.1 ± 3.0	64.7	14.31 ± 0.14	94.9 ± 2.4	259.7 ± 7.2
CGAITCCAITCC	12.27 ± 0.11	85.7 ± 1.9	236.8 ± 5.6	59.2	12.92 ± 0.07	96.7 ± 1.8	270.1 ± 5.6
CGAITCCTIACC	11.79 ± 0.18	87.7 ± 3.3	244.9 ± 10.0	56.8	11.83 ± 0.13	88.2 ± 2.0	246.3 ± 5.9
CAAACAAAG[4]	6.08 ± 0.12	58.0 ± 2.9	167.4 ± 10.0	34.6	Data not reported		
CAAAIAAAG[4]	6.51 ± 0.13	66.0 ± 3.3	191.8 ± 11.5	36.9	Data not reported		
CGCIAATTCGCG[24]	12.60 ± 0.25	77.2 ± 3.9	208.3 ± 12.5	63.4	Data not reported		
GTGICTTCIGTC	11.06 ± 0.12	73.9 ± 2.3	202.5 ± 7.0	57.2	12.15 ± 0.17	94.4 ± 3.3	265.2 ± 10.6
GCATIATCG	8.51 ± 0.03	67.7 ± 1.1	190.9 ± 3.5	46.3	8.57 ± 0.08	70.2 ± 1.5	198.8 ± 4.7
CGGITCAGITGC	13.94 ± 0.16	97.6 ± 2.4	269.8 ± 7.2	62.5	13.79 ± 0.35	95.3 ± 5.4	262.9 ± 16.3
GAAICCTAICCG	12.26 ± 0.08	87.2 ± 1.3	241.7 ± 4.1	58.8	12.13 ± 0.07	85.1 ± 1.3	235.2 ± 3.9
GAAGIACGIAGG	10.83 ± 0.05	79.2 ± 1.1	220.3 ± 3.3	54.8	10.71 ± 0.04	76.4 ± 1.3	211.8 ± 4.2
CCAIGTGAICCG	13.67 ± 0.08	93.2 ± 1.2	256.3 ± 3.8	62.7	13.80 ± 0.07	95.1 ± 1.1	262.2 ± 3.2
CCTIGTGTICCG	12.56 ± 0.11	85.3 ± 1.9	234.5 ± 5.7	60.6	12.65 ± 0.11	86.6 ± 1.3	238.5 ± 3.8
CGTICCATIGGG	12.25 ± 0.16	87.7 ± 2.9	243.4 ± 8.7	58.6	11.60 ± 0.11	75.4 ± 2.7	205.6 ± 8.6
CCAICTGTICCG	12.81 ± 0.07	81.8 ± 1.0	222.6 ± 2.9	62.8	13.00 ± 0.18	84.5 ± 2.3	230.5 ± 6.7
CCAIGTGTIGCG	13.09 ± 0.06	89.0 ± 0.9	244.6 ± 2.6	61.7	12.96 ± 0.12	86.8 ± 2.2	238.0 ± 6.7
CGCITCACITGG	14.00 ± 0.08	92.5 ± 1.2	253.0 ± 3.6	64.2	13.95 ± 0.08	91.8 ± 1.5	251.1 ± 4.7

Non-Two State Behavior or Outliers in Nearest Neighbor Determination

Sequence							
CCGICAAGICCG	10.65 ± 0.04	59.3 ± 0.6	156.8 ± 1.8	60.2	10.99 ± 0.11	64.3 ± 1.1	172.0 ± 3.2
CGTIACCTIACC	Non-Two State: Data could not be fit.						
CCAITTGCIACG	Non-Two State: Data could not be fit.						
CGGICTTTIAGG	Non-Two State: Data could not be fit.						
CCAITGGCIGCG	12.24 ± 0.50	74.3 ± 6.8	200.0 ± 20.5	62.8	12.23 ± 0.72	73.8 ± 10.3	198.6 ± 30.8
GCACIGTCG	11.86 ± 0.72	79.5 ± 10.2	218.2 ± 30.6	59.3	11.84 ± 0.17	79.1 ± 2.0	217.0 ± 6.1
CGAICCAAIGGG	11.30 ± 0.12	69.6 ± 2.1	188.0 ± 6.3	59.8	11.49 ± 0.26	72.2 ± 4.0	195.9 ± 12.1
I/A							
CGCIGAACIGGC	12.45 ± 0.26	75.7 ± 3.8	203.9 ± 11.4	63.3	13.05 ± 1.01	83.2 ± 14.9	226.1 ± 44.8
CCGICAAGICCG	15.35 ± 0.22	95.1 ± 2.5	257.2 ± 7.3	68.7	15.26 ± 0.05	94.2 ± 0.6	254.5 ± 1.9
CCGICTGTIGCG	14.46 ± 0.17	94.6 ± 2.3	258.4 ± 6.7	65.4	14.71 ± 0.42	98.2 ± 5.8	269.3 ± 17.3
CGTIACCTIACC	8.85 ± 0.09	67.0 ± 3.1	187.5 ± 0.8	48.1	8.87 ± 0.07	68.2 ± 2.4	191.4 ± 7.6
CGAITCCAITCC	10.05 ± 0.05	76.4 ± 1.4	214.0 ± 4.3	52.0	10.34 ± 0.08	84.5 ± 2.4	239.0 ± 7.6
CGAITCCTIACC	9.47 ± 0.04	76.8 ± 1.5	217.1 ± 4.7	49.3	9.51 ± 0.10	79.4 ± 4.5	225.4 ± 14.2
CAAAAAAAG[4]	4.61 ± 0.09	48.0 ± 2.4	139.9 ± 8.4	25.1	Data not reported		
CAAAIAAAG[4]	5.28 ± 0.11	63.0 ± 3.2	186.1 ± 11.2	31.0	Data not reported		
CGCIAATTAGCG[24]	9.45 ± 0.19	54.7 ± 2.7	145.9 ± 8.8	54.5	Data not reported		
GCATIATCG	7.00 ± 0.00	56.8 ± 0.6	160.4 ± 2.0	39.6	7.01 ± 0.07	62.2 ± 1.5	178.0 ± 4.8
GCACIGTCG	9.21 ± 0.04	61.7 ± 1.2	169.2 ± 3.7	51.1	9.29 ± 0.14	63.8 ± 4.0	175.7 ± 12.6
GCAGIGTCG	9.72 ± 0.05	63.8 ± 1.1	174.3 ± 3.4	53.3	9.84 ± 0.13	66.2 ± 2.1	181.7 ± 6.5
GCAAICTCG	9.12 ± 0.05	63.4 ± 1.5	175.1 ± 4.6	50.2	9.32 ± 0.19	68.7 ± 3.4	191.3 ± 10.3
CCAIGTGAICCG	12.60 ± 0.08	88.7 ± 1.3	245.4 ± 4.1	59.8	12.63 ± 0.09	89.4 ± 1.8	247.4 ± 5.7
CCTIGTGTICCG	11.37 ± 0.08	84.0 ± 1.7	234.0 ± 5.1	56.0	11.18 ± 0.02	80.3 ± 0.4	223.0 ± 1.2
CCAICTGTICCG	12.47 ± 0.04	86.2 ± 0.6	237.7 ± 1.9	59.9	12.47 ± 0.05	86.3 ± 0.8	237.9 ± 2.4
CCAIGTGTIGCG	11.80 ± 0.13	82.1 ± 2.4	226.6 ± 7.4	58.3	11.88 ± 0.10	83.5 ± 1.2	231.0 ± 3.7
CGCITCACITGG	9.73 ± 0.09	56.7 ± 1.9	151.3 ± 6.0	55.6	9.91 ± 0.26	59.7 ± 4.8	160.4 ± 14.7
GAAGIACGIAGG	10.38 ± 0.05	75.8 ± 1.1	210.8 ± 3.3	53.6	10.25 ± 0.08	72.2 ± 2.2	199.7 ± 6.8
Non-Two State Behavior or Outliers in Nearest Neighbor Determination							
CCAITTGCIACG	Non-Two State: Data could not be fit.						
GTGICTTCIGTC	Non-Two State: Data could not be fit.						
CGGICTTTIAGG	Non-Two State: Data could not be fit.						
CCAITGGCIGCG	Non-Two State: Data could not be fit.						
CGAICCAAIGGG	10.91 ± 0.07	72.1 ± 1.3	197.4 ± 4.1	57.0	11.08 ± 0.12	75.2 ± 1.8	206.7 ± 5.5
CGTICCATIGGG	10.11 ± 0.11	71.0 ± 2.6	196.4 ± 7.9	53.5	10.00 ± 0.05	68.1 ± 1.8	187.5 ± 5.6
I/T							
CGCIGAACIGGC	10.11 ± 0.14	68.0 ± 3.3	186.7 ± 10.1	54.2	10.68 ± 0.42	80.7 ± 7.9	225.8 ± 24.4
CCGICAAGICCG	11.86 ± 0.67	95.1 ± 12.1	268.3 ± 37.0	55.4	11.05 ± 0.17	79.4 ± 4.0	220.3 ± 12.3
CGTIACCTIACC	7.43 ± 0.01	76.9 ± 1.9	223.9 ± 6.0	40.7	7.42 ± 0.15	70.8 ± 17.4	204.4 ± 56.4
CGAITCCAITCC	7.55 ± 0.02	71.4 ± 2.0	205.9 ± 6.3	41.5	7.51 ± 0.09	63.1 ± 1.8	179.4 ± 6.0
CGAITCCTIACC	7.26 ± 0.02	72.7 ± 2.4	210.9 ± 7.8	40.2	7.26 ± 0.08	67.8 ± 1.0	195.1 ± 3.2

CCAITTGCIACG	8.12 ± 0.02	71.7 ± 1.3	205.1 ± 4.1	44.0	8.02 ± 0.08	63.7 ± 1.8	179.6 ± 5.9
CAAATAAAG[4]	4.04 ± 0.08	50.0 ± 2.5	148.2 ± 8.9	22.3	Data not reported		
CAAAIAAAG[4]	3.82 ± 0.08	58.0 ± 2.9	174.7 ± 10.5	23.1	Data not reported		
CGCIAATTTGCG[24]	8.66 ± 0.17	58.9 ± 2.9	162.0 ± 9.7	48.6	Data not reported		
GTGICTTCIGTC	7.96 ± 0.01	60.6 ± 0.8	169.9 ± 2.6	44.5	7.85 ± 0.09	52.4 ± 0.6	143.7 ± 1.9
CCAITGGCIGCG	10.01 ± 0.08	76.5 ± 2.0	214.3 ± 6.2	51.7	9.72 ± 0.04	68.6 ± 2.6	189.8 ± 8.1
GCATIATCG	7.00 ± 0.00	56.8 ± 0.6	160.4 ± 8.0	39.6	7.00 ± 0.07	62.2 ± 1.5	178.0 ± 4.8
GCACIGTCG	7.56 ± 0.07	46.3 ± 2.7	124.9 ± 8.5	44.0	7.71 ± 0.15	53.0 ± 4.7	145.9 ± 14.6
GCAGIGTCG	7.84 ± 0.04	54.6 ± 1.9	150.7 ± 5.9	44.6	8.09 ± 0.10	66.0 ± 0.8	186.6 ± 2.7
GAAGIACGIAGG	7.53 ± 0.03	62.6 ± 2.5	177.5 ± 7.9	42.0	7.55 ± 0.08	65.0 ± 2.4	185.2 ± 7.6
CCTIGTGTICCG	8.99 ± 0.15	79.5 ± 5.6	227.2 ± 17.7	46.9	8.87 ± 0.16	74.1 ± 2.4	210.2 ± 7.4
CGTICCATIGGG	7.44 ± 0.05	75.2 ± 4.1	218.3 ± 13.3	40.8	7.50 ± 0.15	70.0 ± 13.4	201.5 ± 43.4
CCAICTGTICCG	9.88 ± 0.03	82.1 ± 1.0	232.7 ± 3.2	50.2	9.91 ± 0.04	83.1 ± 1.1	235.8 ± 3.4
CCAIGTGTIGCG	8.61 ± 0.03	70.6 ± 1.9	199.9 ± 5.9	46.4	8.64 ± 0.08	72.3 ± 2.4	205.2 ± 7.7
CGCITCACITGG	10.44 ± 0.08	86.0 ± 2.3	243.5 ± 7.3	51.8	10.36 ± 0.11	83.7 ± 2.3	236.4 ± 7.0
Non-Two State Behavior or Outliers in Nearest Neighbor Determination							
CCGICTGTIGCG	8.30 ± 0.02	49.1 ± 0.7	131.4 ± 2.3	48.6	8.45 ± 0.13	54.2 ± 2.1	147.5 ± 6.5
CGGITCCGITCC	Non-Two State: Data could not be fit.						
CGGICTTTIAGG	Non-Two State: Data could not be fit.						
CGTIGCCTIGCC	7.74 ± 0.17	45.8 ± 4.5	122.7 ± 14.2	45.4	7.82 ± 0.18	50.6 ± 3.6	137.9 ± 11.6
CCAIGTGAICCG	9.12 ± 0.06	96.6 ± 3.8	282.1 ± 12.0	45.5	8.73 ± 0.38	72.1 ± 8.2	204.3 ± 25.2
I/G							
CCGICAAGICCG	11.80 ± 0.10	79.4 ± 1.7	218.1 ± 5.1	59.0	11.54 ± 0.14	74.5 ± 3.2	203.1 ± 9.8
CCGICTGTIGCG	10.50 ± 0.10	80.0 ± 2.0	224.2 ± 6.1	53.2	10.41 ± 0.06	78.0 ± 1.4	218.0 ± 4.3
CGTIACCTIACC	6.17 ± 0.27	59.0 ± 7.7	170.3 ± 25.0	35.1	6.17 ± 0.19	61.0 ± 2.8	176.8 ± 9.0
CGAITCCAITCC	8.04 ± 0.04	68.4 ± 2.4	194.7 ± 7.5	44.0	8.11 ± 0.08	72.6 ± 1.1	207.9 ± 3.4
CGAITCCTIACC	6.94 ± 0.04	68.0 ± 3.3	196.8 ± 10.7	38.9	6.96 ± 0.10	63.0 ± 2.7	180.7 ± 8.8
GTGICTTCIGTC	7.77 ± 0.03	54.2 ± 2.3	149.7 ± 7.5	44.2	7.79 ± 0.09	51.0 ± 2.7	139.4 ± 8.8
CAAAGAAAG[4]	3.83 ± 0.08	52.0 ± 2.6	155.3 ± 9.3	21.7	Data not reported		
CAAAIAAAG[4]	4.27 ± 0.09	57.0 ± 2.9	170.0 ± 10.2	25.2	Data not reported		
CGCIAATTGGCG[24]	6.47 ± 0.13	40.8 ± 2.0	110.7 ± 6.6	36.5	Data not reported		
GCATIATCG	5.67 ± 0.07	52.2 ± 2.4	150.0 ± 8.0	32.0	5.56 ± 0.04	57.7 ± 2.4	168.0 ± 7.7
GCACIGTCG	7.25 ± 0.02	48.3 ± 1.8	132.4 ± 5.7	41.7	7.33 ± 0.10	53.5 ± 4.0	148.8 ± 12.6
CGGITCCGITCC	8.33 ± 0.05	59.7 ± 1.9	165.6 ± 6.0	46.6	8.28 ± 0.04	56.9 ± 2.0	156.8 ± 6.4
GAAGIACGIAGG	7.43 ± 0.05	60.3 ± 3.1	170.3 ± 9.9	41.7	7.43 ± 0.06	58.3 ± 2.3	164.0 ± 7.1
CCAIGTGAICCG	9.46 ± 0.03	75.5 ± 1.1	212.8 ± 3.3	49.5	9.24 ± 0.09	68.2 ± 0.6	190.1 ± 1.6
CCTIGTGTICCG	7.86 ± 0.01	62.0 ± 1.2	174.6 ± 3.8	43.8	7.87 ± 0.04	61.6 ± 1.6	173.1 ± 5.0
CCAICTGTICCG	9.94 ± 0.02	79.9 ± 0.7	225.4 ± 2.2	50.8	9.97 ± 0.03	81.0 ± 1.7	228.9 ± 5.4
CCAIGTGTIGCG	7.96 ± 0.03	48.6 ± 1.7	130.6 ± 5.5	47.1	8.09 ± 0.15	55.7 ± 5.5	153.4 ± 17.3
Non-Two State Behavior or Outliers in Nearest Neighbor Determination							

Sequence							
CGCIGAACIGGC	?	?	?	?	?	?	?
CGTIGCCTIGCC	6.64 ± 0.03	30.5 ± 1.2	76.8 ± 4.0	38.1	6.66 ± 0.07	33.4 ± 3.5	86.1 ± 11.2
CCAITTGCIACG		Non-Two State: Data could not be fit.					
CGGICTTTIAGG		Non-Two State: Data could not be fit.					
CCAITGGCIGCG		Non-Two State: Data could not be fit.					
CGAICCAIGGG	7.33 ± 0.00	42.3 ± 0.5	112.7 ± 1.8	42.9	7.38 ± 0.06	45.1 ± 3.3	121.7 ± 10.6
CGTICCATIGGG	6.40 ± 0.06	36.8 ± 1.6	98.0 ± 5.4	35.9	6.29 ± 0.11	41.6 ± 3.2	114.0 ± 10.1
CGCITCACITGG		Non-Two State: Data could not be fit.					
I/I							
CGCIGAACIGGC	8.72 ± 0.27	60.0 ± 6.5	165.4 ± 20.3	48.7	8.88 ± 0.24	62.7 ± 8.1	173.4 ± 25.5
CCGICAAGICCG	10.37 ± 0.08	66.6 ± 1.9	181.2 ± 5.8	56.0	10.70 ± 0.37	73.2 ± 8.7	201.5 ± 27.1
CGAITCCAITCC	7.53 ± 0.05	77.7 ± 4.0	226.3 ± 12.8	41.0	7.51 ± 0.09	73.8 ± 1.5	213.6 ± 4.7
CGAITCCTIACC	6.37 ± 0.03	65.4 ± 1.8	190.3 ± 5.9	36.2	6.38 ± 0.11	64.3 ± 3.5	186.6 ± 11.5
GTGICTTCIGTG	7.19 ± 0.07	61.9 ± 4.1	176.5 ± 13.2	40.4	7.19 ± 0.12	55.1± 2.0	154.3 ± 6.3
CGGICTTTIAGG	6.35 ± 0.05	48.5 ± 2.9	136.0 ± 9.6	35.8	6.31 ± 0.04	53.6 ± 2.8	152.3 ± 9.0
CAAAIAAAG[4]	4.04 ± 0.08	47.0 ± 2.4	138.5 ± 8.3	21.4	-	-	-
GCATIATCG	5.51 ± 0.02	56.9 ± 0.7	165.6 ± 2.3	31.6	5.32 ± 0.34	61.9 ± 6.4	182.3 ± 21.6
GCACIGTCG	7.13 ± 0.02	47.6 ± 1.5	130.4 ± 4.8	40.9	7.19 ± 0.07	52.1 ± 4.9	144.9 ± 15.6
GAAGIACGIAGG	6.95 ± 0.00	59.1 ± 0.7	168.3 ± 2.2	39.2	6.95 ± 0.05	64.0 ± 2.5	183.9 ± 7.9
Non-Two State Behavior or Outliers in Nearest Neighbor Determination							
CCGICTGTIGCG	13.57 ± 0.07	86.4 ± 1.0	234.7 ± 2.9	64.5	13.88 ± 0.24	90.3 ± 2.8	246.5 ± 8.1
CGTIACCTIACC		Non-Two State: Data could not be fit.					
CCAITTGCIACG		Non-Two State: Data could not be fit.					
CCAITGGCIGCG		Non-Two State: Data could not be fit.					

Table S3: Thermodynamics of Duplex Formation of Oligonucleotides with Internal Tandem I-I Mismatches.

DNA Duplex	1/Tm Method				Curve fit Method		
	$-\Delta G°_{37}$ (kcal/mol)	$-\Delta H°$ (kcal/mol)	$-\Delta S°$ (cal/K*mol)	T_M (°C)	$-\Delta G°_{37}$ (kcal/mol)	$-\Delta H°$ (kcal/mol)	$-\Delta S°$ (cal/K*mol)
GGTA<u>I</u> <u>I</u>GTGTCG							
I I / C C	12.18 ± 0.06	93.8 ± 1.2	263.3 ± 3.8	56.9	12.20 ± 0.11	94.5 ± 2.3	265.2 ± 7.1
I I / A C	10.78 ± 0.04	86.3 ± 1.1	243.3 ± 3.3	53.1	10.83 ± 0.03	87.4 ± 0.4	246.8 ± 1.4
GGTT<u>I</u> <u>I</u>GAGTCG							
I I / C A	10.44 ± 0.13	84.0 ± 3.3	237.1 ± 10.1	52.1	10.75 ± 0.12	92.7 ± 2.9	264.3 ± 9.2
I I / A A	11.29 ± 0.12	83.4 ± 2.3	232.6 ± 7.1	55.8	11.67 ± 0.24	91.5 ± 5.4	257.3 ± 16.6
I I / T A	9.37 ± 0.06	77.3 ± 2.2	218.9 ± 6.8	48.8	9.60 ± 0.21	85.0 ± 4.9	243.2 ± 15.1
I I / G A	9.53 ± 0.04	81.2 ± 1.2	231.2 ± 3.8	48.9	9.50 ± 0.04	80.0 ± 0.9	227.4 ± 2.7
GGTGC<u>I</u> <u>I</u>GGTCG							
I I / C T	12.07 ± 0.08	87.8 ± 1.4	244.2 ± 4.3	57.9	12.18 ± 0.03	89.8 ± 0.6	250.4 ± 2.0
I I / A T	11.34 ± 0.04	85.0 ± 0.9	237.5 ± 2.7	55.6	11.33 ± 0.06	84.6 ± 1.1	236.3 ± 3.5
I I / T T	9.96 ± 0.02	78.5 ± 0.7	220.8 ± 2.1	51.2	9.88 ± 0.02	75.9 ± 1.0	213.0 ± 3.1
I I / G T	10.82 ± 0.05	84.3 ± 1.2	236.8 ± 3.6	53.6	10.65 ± 0.06	80.5 ± 0.9	225.0 ± 2.7
GGTT<u>I</u> <u>I</u>AGTTCG							
I I / T G	6.39 ± 0.13	57.0 ± 4.7	163.3 ± 15.3	36.3	6.45 ± 0.14	57.8 ± 8.0	165.5 ± 26.1
I I / G G	6.34 ± 0.07	66.0 ± 4.1	192.5 ± 13.4	36.1	6.36 ± 0.06	62.4 ± 5.1	180.6 ± 16.6
Non-Two State Behavior							
GGTA<u>I</u> <u>I</u>GTGTCG							
I I / I I	9.21 ± 0.15	68.8 ± 3.7	192.2 ± 11.4	49.6	9.80 ± 0.09	83.8 ± 0.6	238.4 ± 1.8
GGTT<u>I</u> <u>I</u>AGTTCG							
I I / I I	6.13 ± 0.04	83.1 ± 3.8	248.0 ± 12.3	35.5	6.25 ± 0.09	67.3 ± 3.3	197.0 ± 10.7
GGTA<u>I</u> <u>I</u>GTGTCG							
I I / T C			Non-Two State: Data could not be fit.				
I I / G C			Non-Two State: Data could not be fit.				
GGTT<u>I</u> <u>I</u>AGTTCG							
I I / C G			Non-Two State: Data could not be fit.				
I I / A G			Non-Two State: Data could not be fit.				

Table S4: Thermodynamics of duplex formation of oligonucleotides with internal tandem self-complementary inosine mismatch pairs.

DNA Duplex	1/Tm Method				Curve fit Method		
	-ΔG°$_{37}$ (kcal/mol)	-ΔH° (kcal/mol)	-ΔS° (cal/K*mol)	T$_M$ (°C)	-ΔG°$_{37}$ (kcal/mol)	-ΔH° (kcal/mol)	-ΔS° (cal/K*mol)
GGT AIC GTG TCG CCA TCI CAC AGC	12.40 ± 0.10	87.2 ± 1.72	241.2 ± 5.1	59.4	12.88 ± 0.10	95.1 ±0.72	265.0 ± 2.1
GGT ACI GTG TCG CCA TIC CAC AGC	11.37 ± 0.06	85.4 ± 1.3	238.7 ± 3.9	55.6	11.55 ± 0.12	89.03 ± 2.1	249.8 ± 6.3
GGT TIA GAG TCG CCA AAI CTC AGC	11.28± 0.09	80.98 ± 1.8	224.8 ± 5.5	56.3	11.64 ± 0.23	87.85 ± 4.3	245.7 ± 13.2
GGT TAI GAG TCG CCA AIA CTC AGC	11.01 ± 0.21	85.0 ±4.8	238.5 ± 14.6	54.3	11.02 ± 0.12	85.1 ± 1.0	238.8 ± 2.9
GGT TIG AGT TCG CCA AGI TCA AGC	6.81 ± 0.02	67.0±1.9	194.0 ± 6.2	38.3	6.76 ± 0.09	71.7 ± 4.9	209.5 ± 16.1
GGT TGI AGT TCG CCA AIG TCA AGC	6.99 ± 0.01	69.0 ± 1.6	200.1 ± 5.2	39.1	6.99 ± 0.04	69.5 ± 2.6	201.6 ± 8.5
GGT GCI TGG TCG CCA CGT ICC AGC	10.21 ± 0.06	77.4 ± 1.6	216.7 ± 5.1	52.5	10.36 ± 0.10	81.7 ± 1.8	230.1 ± 5.7
GGT GCT IGG TCG CCA CGI TCC AGC	10.24 ± 0.41	81.6 ± 8.9	230.0 ± 27.6	51.8	10.35 ± 0.21	84.5 ± 3.2	239.1 ± 10.0
GGT AIA GTG TCG CCA TCI CAC AGC	11.52 ± 0.12	84.2 ± 2.5	234.3 ± 7.6	56.5	11.77 ± 0.19	89.4 ± 3.0	250.3 ± 9.1
GGT AIC GTG TCG CCA TAI CAC AGC	11.12 ± 0.05	82.2 ± 1.0	229.2 ± 3.2	55.3	11.41 ± 0.12	88.2 ± 1.5	247.5 ± 4.6
GGT TIG AGT TCG CCA ATI TCA AGC	7.25 ± 0.01	72.1 ± 1.8	208.9 ± 5.7	40.1	7.27 ± 0.04	75.1 ± 0.70	218.6 ± 2.2
GGT TIT AGT TCG CCA AGI TCA AGC	7.24 ± 0.06	65.3 ± 3.8	187.3 ± 12.4	40.4	7.27 ± 0.12	73.0 ± 2.8	212.0 ± 8.9

Table S5: Experimental thermodynamics parameters for internal tandem self-complementary inosine mismatch pairs.

DNA Duplex	-ΔG°$_{37}$ (kcal/mol)	-ΔH° (kcal/mol)	-ΔS° (cal/K*mol)	T$_M$ (°C)
GGT A<u>IC</u> GTG TCG CCA T<u>CI</u> CAC AGC	12.65 ± 0.07	93.9 ± 0.7	261.6 ± 1.9	58.9
GGT A<u>CI</u> GTG TCG CCA T<u>IC</u> CAC AGC	11.41 ± 0.05	86.4 ± 1.1	241.7 ± 3.3	55.6
GGT T<u>IA</u> GAG TCG CCA A<u>AI</u> CTC AGC	11.33 ± 0.08	82.0 ± 1.7	227.85 ± 5.1	56.3
GGT T<u>AI</u> GAG TCG CCA A<u>IA</u> CTC AGC	11.02 ± 0.11	85.1 ± 1.0	238.8 ± 2.9	54.3
GGT T<u>IG</u> AGT TCG CCA A<u>GI</u> TCA AGC	6.81 ± 0.02	67.6 ± 1.8	196.0 ± 5.8	38.3
GGT T<u>GI</u> AGT TCG CCA A<u>IG</u> TCA AGC	6.99 ± 0.01	69.2 ± 1.4	200.5 ± 4.5	39.1
GGT GC<u>I</u> TGG TCG CCA CG<u>T</u> ICC AGC	10.25 ± 0.05	79.3 ± 1.2	222.6 ± 3.8	52.5
GGT GC<u>T</u> IGG TCG CCA CG<u>I</u> TCC AGC	10.33 ± 0.18	84.2 ± 3.0	238.1 ± 9.4	51.7
GGT A<u>IA</u> GTG TCG CCA T<u>CI</u> CAC AGC	11.60 ± 0.10	86.3 ± 1.9	240.8 ± 5.8	56.4
GGT A<u>IA</u> GTG TCG CCA T<u>CI</u> CAC AGC	11.16 ± 0.05	84.1 ± 0.9	235.4 ± 2.6	54.9
GGT T<u>IG</u> AGT TCG CCA A<u>TI</u> TCA AGC	7.25 ± 0.01	74.7 ± 0.6	217.4 ± 2.0	40.0
GGT T<u>IT</u> AGT TCG CCA A<u>GI</u> TCA AGC	7.25 ± 0.05	70.3 ± 2.3	203.6 ± 7.2	39.8

I-C Free Energy Correlation

$y = 1.0069x + 0.0715$
$R^2 = 0.9812$
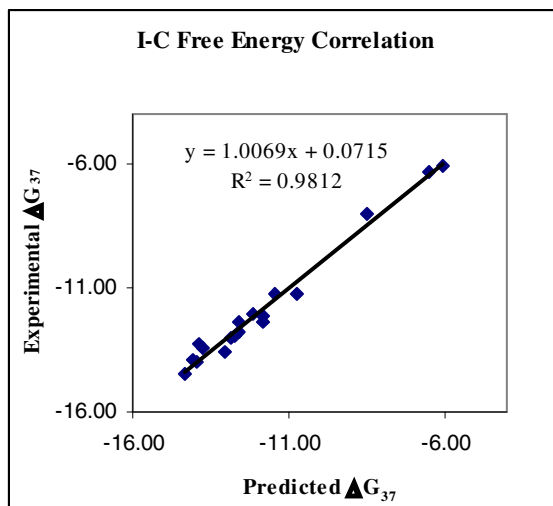
Experimental ΔG_{37}

Predicted ΔG_{37}

Figure S1a: Comparison of the experimental versus the predicted free energies of 18 I-C measurements. The average deviation is 0.26 kcal/mol.

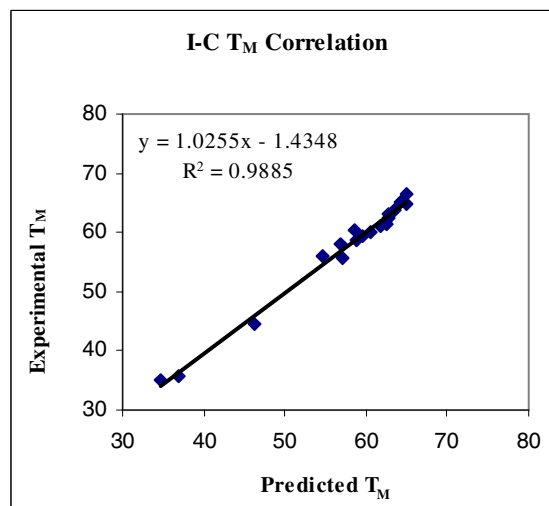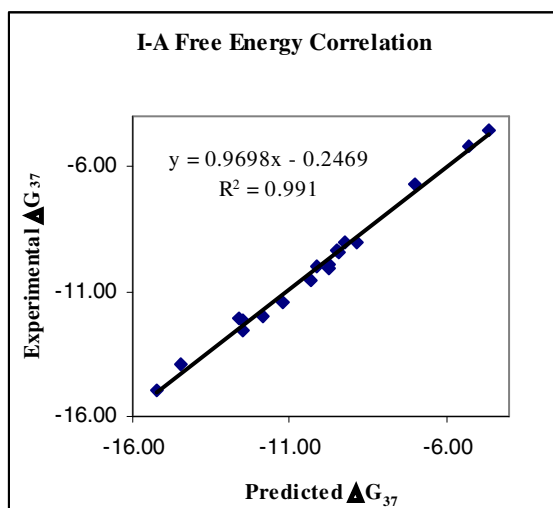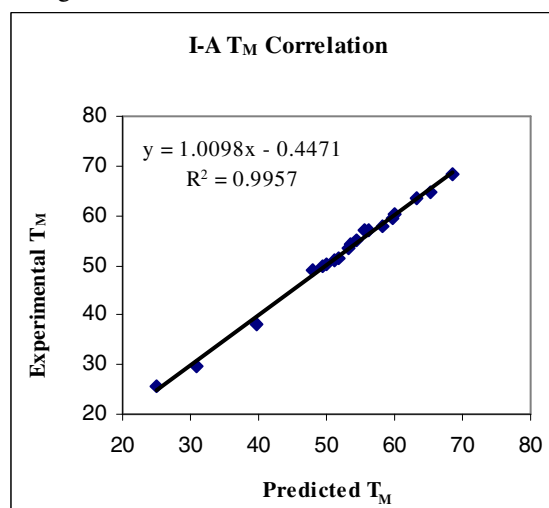**I-C T_M Correlation**

$y = 1.0255x - 1.4348$
$R^2 = 0.9885$

Experimental T_M

Predicted T_M

Figure S1b: Comparison of the experimental versus the predicted Tm's of 18 I-C measurements. The average deviation is 0.8 ° C.

I-A Free Energy Correlation

$y = 0.9698x - 0.2469$
$R^2 = 0.991$
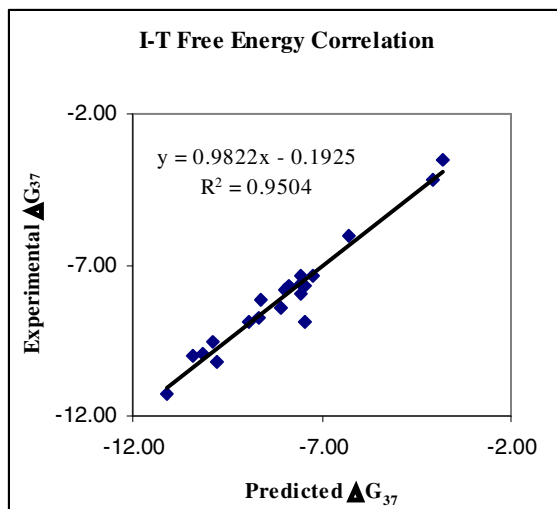
Experimental ΔG_{37}

Predicted ΔG_{37}

Figure S2a: Comparison of the experimental versus the predicted free energies of 19 I-A measurements. The average deviation is 0.20 kcal/mol.

I-A T_M Correlation

$y = 1.0098x - 0.4471$
$R^2 = 0.9957$

Experimental T_M

Predicted T_M

Figure S2b: Comparison of the experimental versus the predicted Tm's of 19 I-A measurements. The average deviation is 0.6 ° C.

I-T Free Energy Correlation

$$y = 0.9822x - 0.1925$$
$$R^2 = 0.9504$$

Experimental ΔG_{37}

Predicted ΔG_{37}

Figure S3a: Comparison of the experimental versus the predicted free energies of 20 I-T measurements. The average deviation is 0.30 kcal/mol.

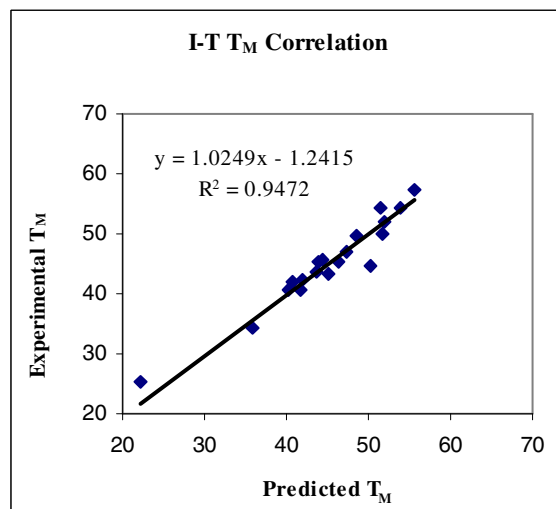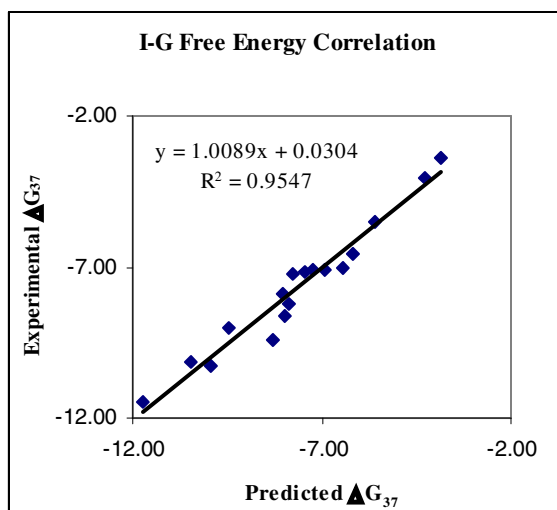**I-T T_M Correlation**

$$y = 1.0249x - 1.2415$$
$$R^2 = 0.9472$$

Experimental T_M

Predicted T_M

Figure S3b: Comparison of the experimental versus the predicted Tm's of 20 I-T measurements. The average deviation is 1.6 ° C.

I-G Free Energy Correlation

$$y = 1.0089x + 0.0304$$
$$R^2 = 0.9547$$

Experimental ΔG_{37}

Predicted ΔG_{37}

FigureS4a: Comparison of the experimental versus the predicted free energies of 17 I-G measurements. The average deviation is 0.34 kcal/mol.
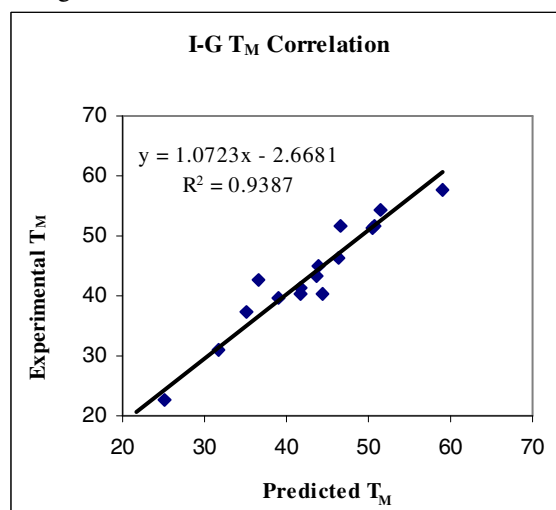
I-G T_M Correlation

$$y = 1.0723x - 2.6681$$
$$R^2 = 0.9387$$

Experimental T_M

Predicted T_M

Figure S4b: Comparison of the experimental versus the predicted Tm's of 17 I-G measurements. The average deviation is 2.0 ° C.

I-I Free Energy Correlation

$y = 1.006x + 0.0358$
$R^2 = 0.9556$

Experimental ΔG_{37}

Predicted ΔG_{37}

I-I T_M Correlation

$y = 1.0319x - 1.0006$
$R^2 = 0.9623$

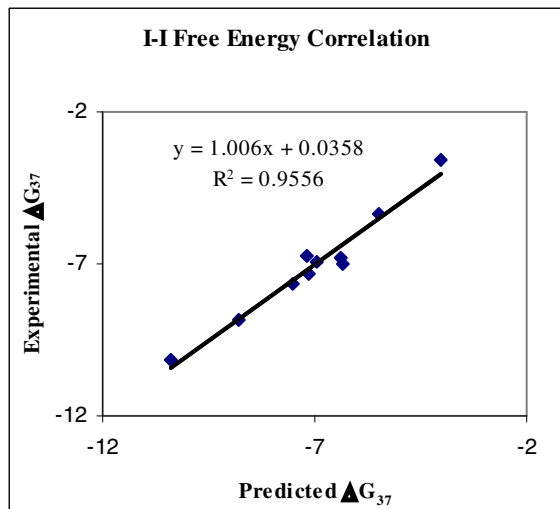Experimental T_M

Predicted T_M

Figure S5a: Comparison of the experimental versus the predicted free energies of 10 I-I measurements. The average deviation is 0.29 kcal/mol.

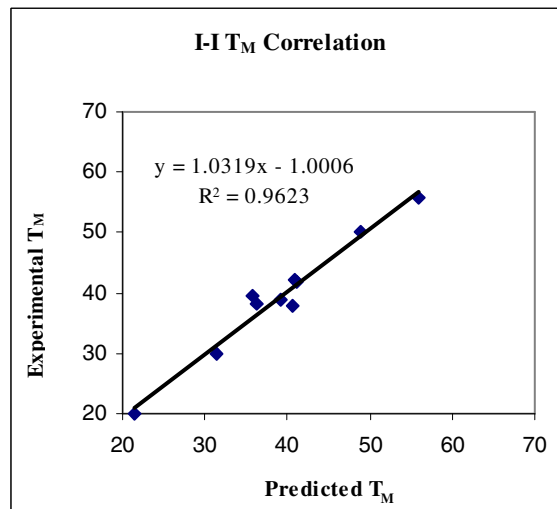**Figure S5b:** Comparison of the experimental versus the predicted Tm's of 10 I-I measurements. The average deviation is 1.5 ° C.
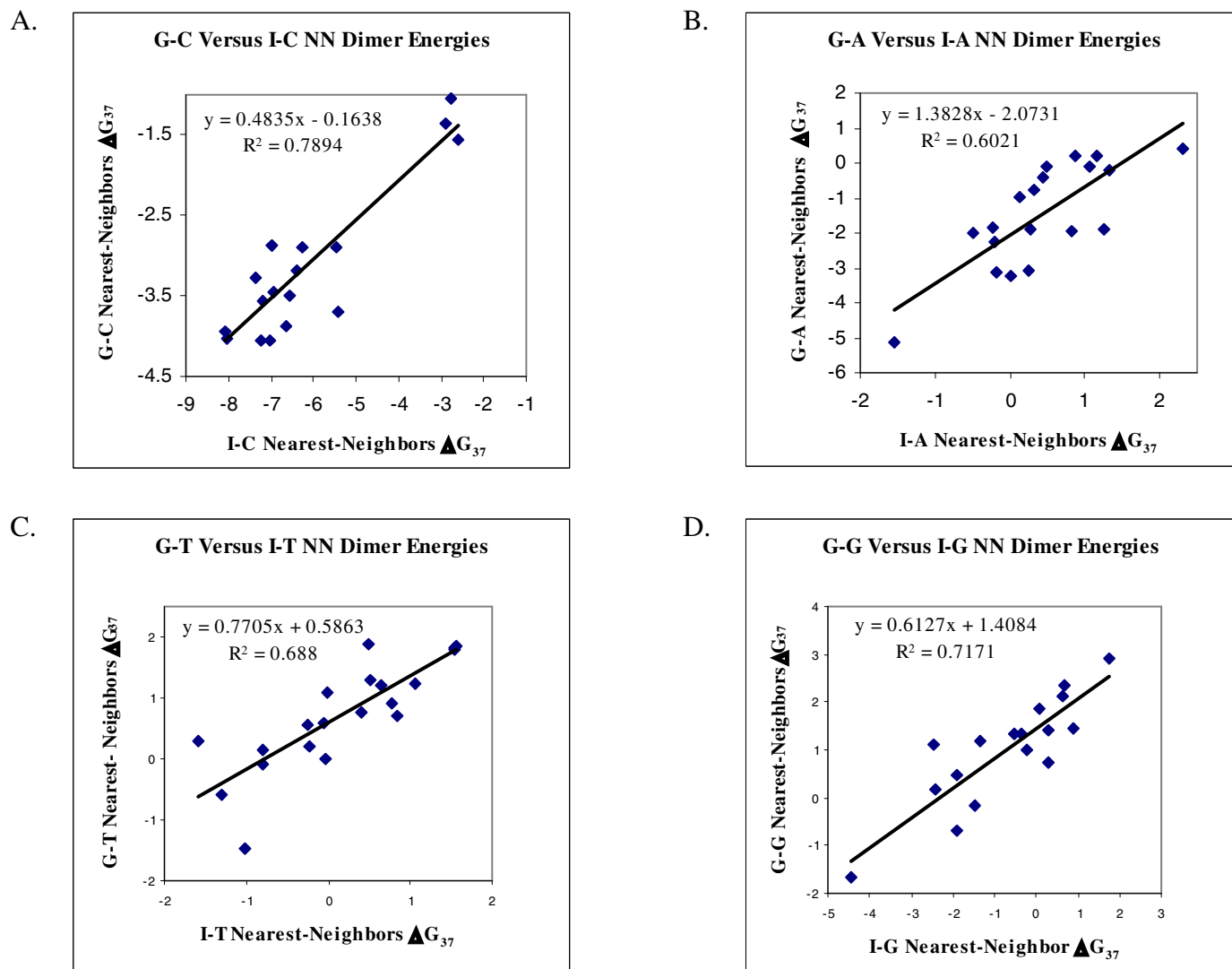
Figure S6: Comparison of G•X with I•X dimer nearest-neighbor $\Delta G°_{37}$ parameters.