Supplementary Information for All-Atom MD Predicts Magnesium-Induced Hairpin in Chemically Perturbed RNA Analog of F10 Therapeutic

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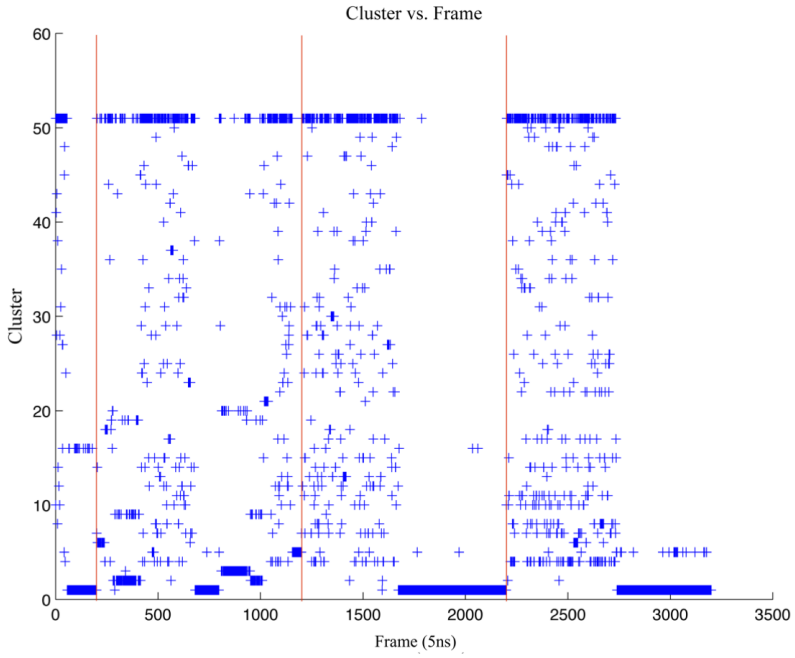

Figure S1: Clumps of points signify a single structure persisting over some length of time, with the exception of cluster 51 which is a catchall for unique states. Between frames 1700-2200 and again between 2700-3200, FUMP10 has found a preferred state. The time interval between any two frames is 5 nanoseconds. For this analysis, 3 5-nanosecond simulations were concatenated along with one 1-microsecond simulation. Vertical lines demarcate simulations.

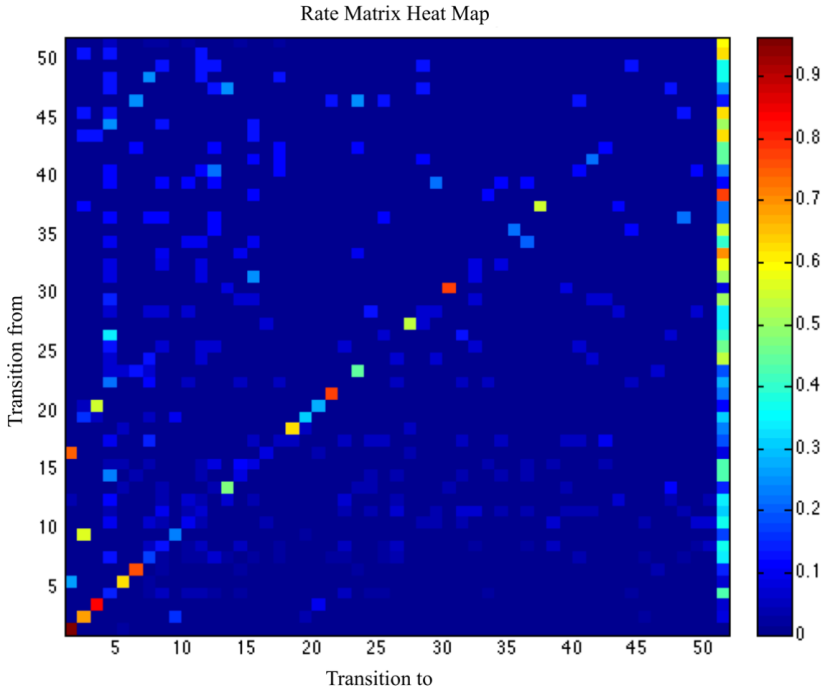

Figure S2: A heat map of a Markov rate matrix shows kinetic traps in clusters 1, 2, 3, 6, 21 and 30. Microstates in cluster 1 here are members of the folded macrostate discussed in the paper proper; cluster 2 microstates belong to the unfolded macrostate; and clusters 3-51 belong to the partially folded macrostate.

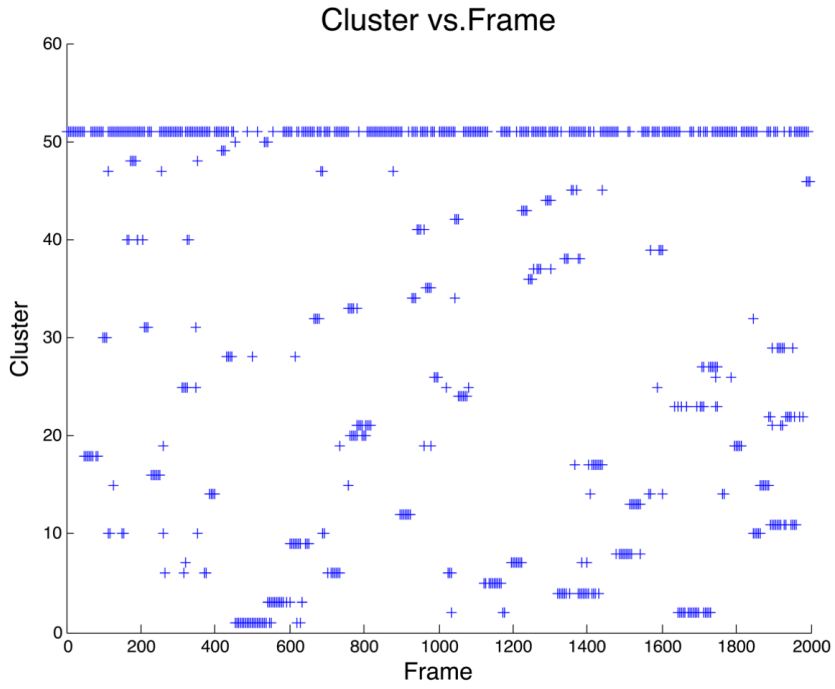

Figure S3: The longest-lived state in polydT simulations is 80ns, seen as cluster 1 between frames 400 and 600.

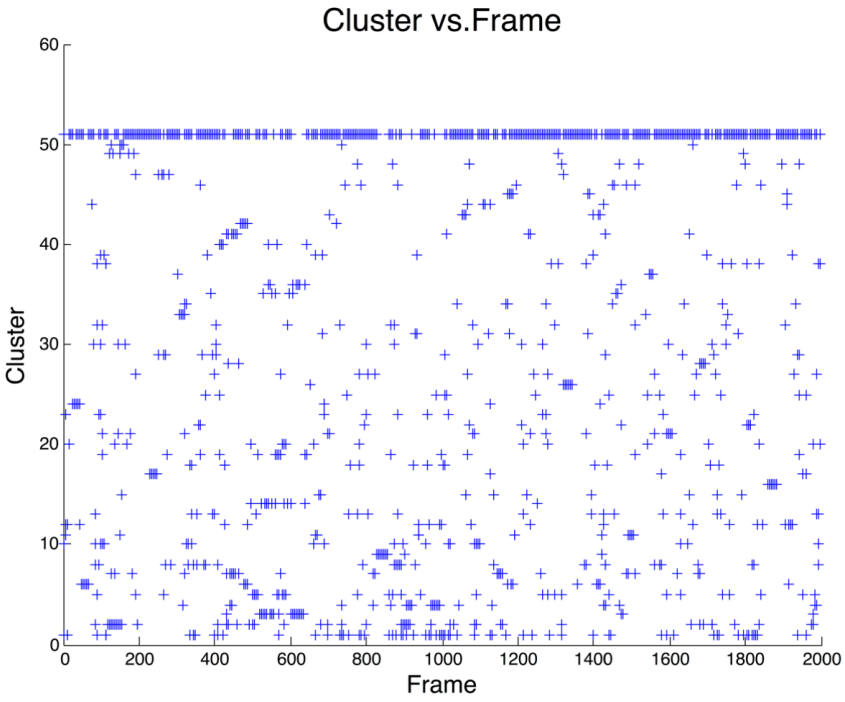

Figure S4: PolyU's structures have lifetimes on the order of 10ns

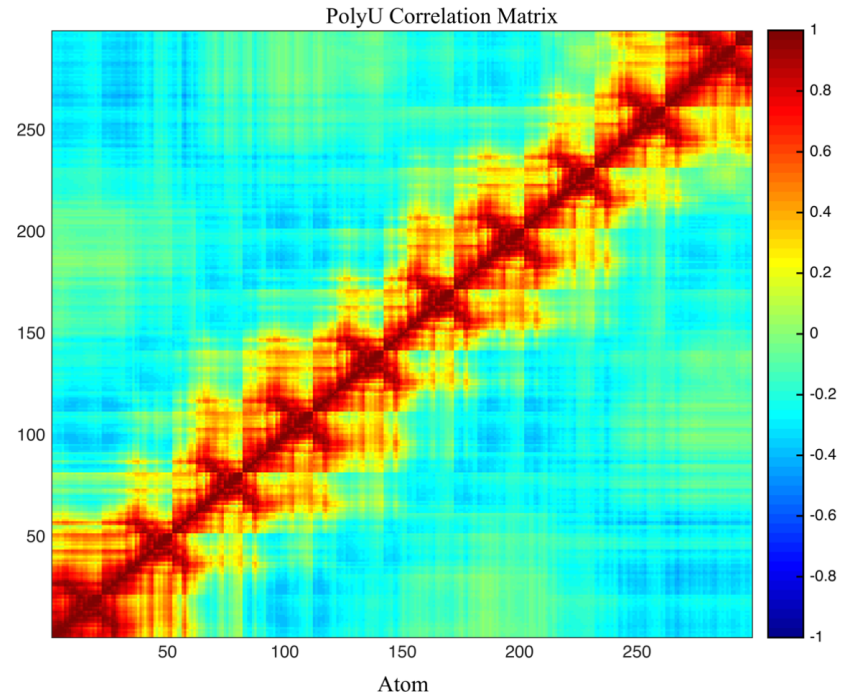

Figure S5: The correlation matrix for polyU closely resembles that of FUMP10's extended state, indicating little to no correlation in atomic motions.

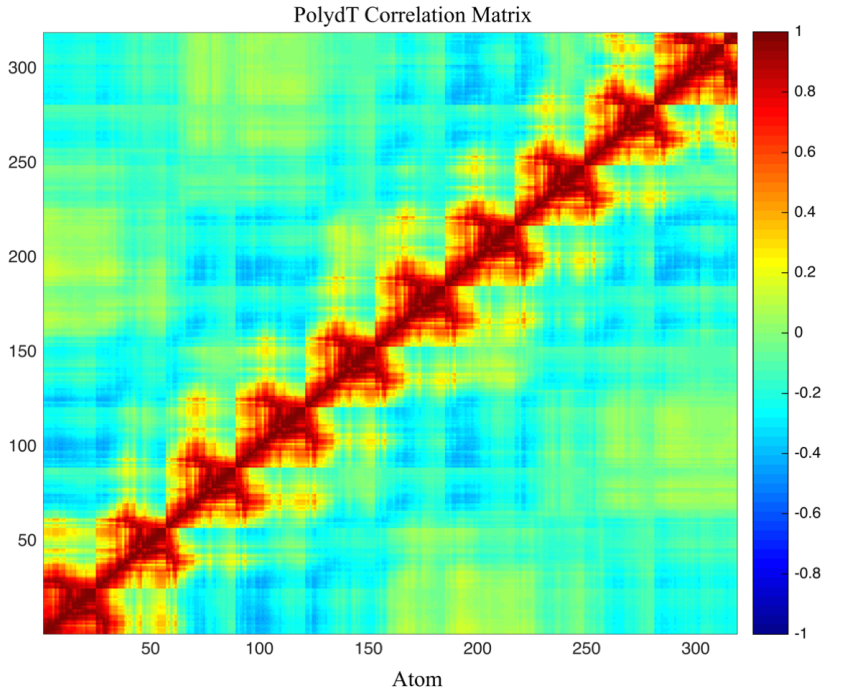

Figure S6: The correlation matrix for polydT closely resembles that of FUMP10's partially folded state, indicating some medium-range correlation in atomic motions.

Structure	Occupancy (%)	Survival (%)
1	37.78	96.36
2	4.00	67.97
3	3.47	82.88
4	3.16	13.86
5	2.56	62.20
6	1.53	75.51
7	1.50	16.67
8	1.25	12.50
9	1.09	22.86
10	1.03	9.09
11	1.00	6.25
12	0.84	0.00
13	0.84	48.15
14	0.81	7.69
15	0.81	7.69
16	0.72	8.70
17	0.66	4.76
18	0.66	61.90
19	0.59	31.58
20	0.56	27.78
21	0.56	77.78
22	0.56	0.00
23	0.50	43.75
24	0.47	0.00
25	0.47	0.00
26	0.47	0.00
27	0.47	53.33
28	0.47	6.67
29	0.44	0.00
30	0.41	76.92
31	0.38	0.00
32	0.38	8.33
33	0.31	0.00
34	0.31	0.00
35	0.28	22.22
36	0.28	0.00
37	0.28	55.56
38	0.28	0.00
39	0.28	0.00
40	0.28	11.11
41	0.28	22.22
42	0.28	11.11
43	0.25	0.00
44	0.25	0.00
45	0.25	0.00
46	0.25	0.00
47	0.25	12.50
48	0.25	0.00
49	0.25	0.00
50	0.25	0.00
51	24.69	59.62

Table S1: These occupancy and survival probabilities correspond to clusters in Supplementary Figures 1 and 2. Note: Cluster 51 is a catchall for unique states – i.e., 1-member macrostates.

Donor	Acceptor	Occupancy
U5-Side-O2'	U6-Side-OP1	70.99%
U8-Side-N3	U4-Side-OP2	55.29%
U9-Side-N3	U3-Side-OP2	54.04%
U6-Side-O2'	U7-Side-OP1	48.69%
U7-Side-N3	U5-Side-OP2	43.12%
U9-Side-N3	U4-Side-OP2	39.25%
U10-Side-N3	U3-Side-OP2	38.45%
U10-Side-N3	U2-Side-OP2	37.54%
U8-Side-N3	U5-Side-OP2	37.32%
U1-Side-O2'	U2-Side-OP1	13.42%
U6-Side-N3	U5-Side-OP2	13.20%
U7-Side-O2'	U8-Side-OP1	11.26%
U9-Side-O2'	U10-Side-OP1	10.58%
U7-Side-O2'	U8-Side-OP2	9.67%
U6-Side-O2'	U7-Side-OP2	8.42%
U1-Side-O5'	U3-Side-OP2	6.26%
U1-Side-O5'	U2-Side-OP2	5.80%
U5-Side-O2'	U6-Side-OP2	4.44%
U4-Side-N3	U9-Side-OP2	4.21%
U5-Side-N3	U8-Side-OP1	4.21%
U3-Side-N3	U10-Side-OP2	4.10%
U1-Side-O2'	U2-Side-OP2	3.98%
U10-Side-O3'	U9-Side-OP2	3.30%
U9-Side-O2'	U10-Side-OP2	2.96%
U1-Side-O5'	U3-Side-OP1	2.39%
U10-Side-O2'	U9-Side-OP2	2.39%
U4-Side-O2'	U5-Side-OP2	2.16%
U3-Side-O2'	U4-Side-OP2	2.05%
U10-Side-O3'	U9-Side-OP1	1.37%
U8-Side-O2'	U9-Side-OP2	1.37%
U2-Side-O2'	U3-Side-OP2	1.25%
U2-Side-O2'	U3-Side-OP1	1.14%
U10-Side-O2'	U9-Side-OP1	0.91%
U2-Side-N3	U10-Side-OP1	0.80%
U1-Side-N3	U3-Side-OP1	0.57%
U5-Side-O2'	U7-Side-OP2	0.57%
U3-Side-N3	U2-Side-OP2	0.34%
U1-Side-N3	U3-Side-OP2	0.34%
U8-Side-N3	U5-Side-OP1	0.34%
U1-Side-O5'	U2-Side-OP1	0.34%
U9-Side-N3	U2-Side-OP2	0.23%
U9-Side-N3	U4-Side-OP1	0.23%
U3-Side-O2'	U4-Side-OP1	0.23%
U2-Side-N3	U10-Side-OP	0.11%
U1-Side-N3	U4-Side-OP2	0.11%
U6-Side-N3	U4-Side-OP1	0.11%
U8-Side-N3	U4-Side-OP1	0.11%
U4-Side-N3	U8-Side-OP1	0.11%
U4-Side-N3	U8-Side-OP2	0.11%
U10-Side-O3'	U3-Side-OP2	0.11%
U7-Side-O2'	U9-Side-OP2	0.11%
U6-Side-N3	U8-Side-OP1	0.11%
U6-Side-O2'	U8-Side-OP2	0.11%
U10-Side-N3	U2-Side-OP1	0.11%
U1-Side-N3	U10-Side-OP	0.11%

Table S2: For phosphate interactions in the folded macrostate, shown here are the hydrogen bond donors, acceptors and occupancy.