Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics

Molecular recognition between DNA and copper-based anticancer complexes

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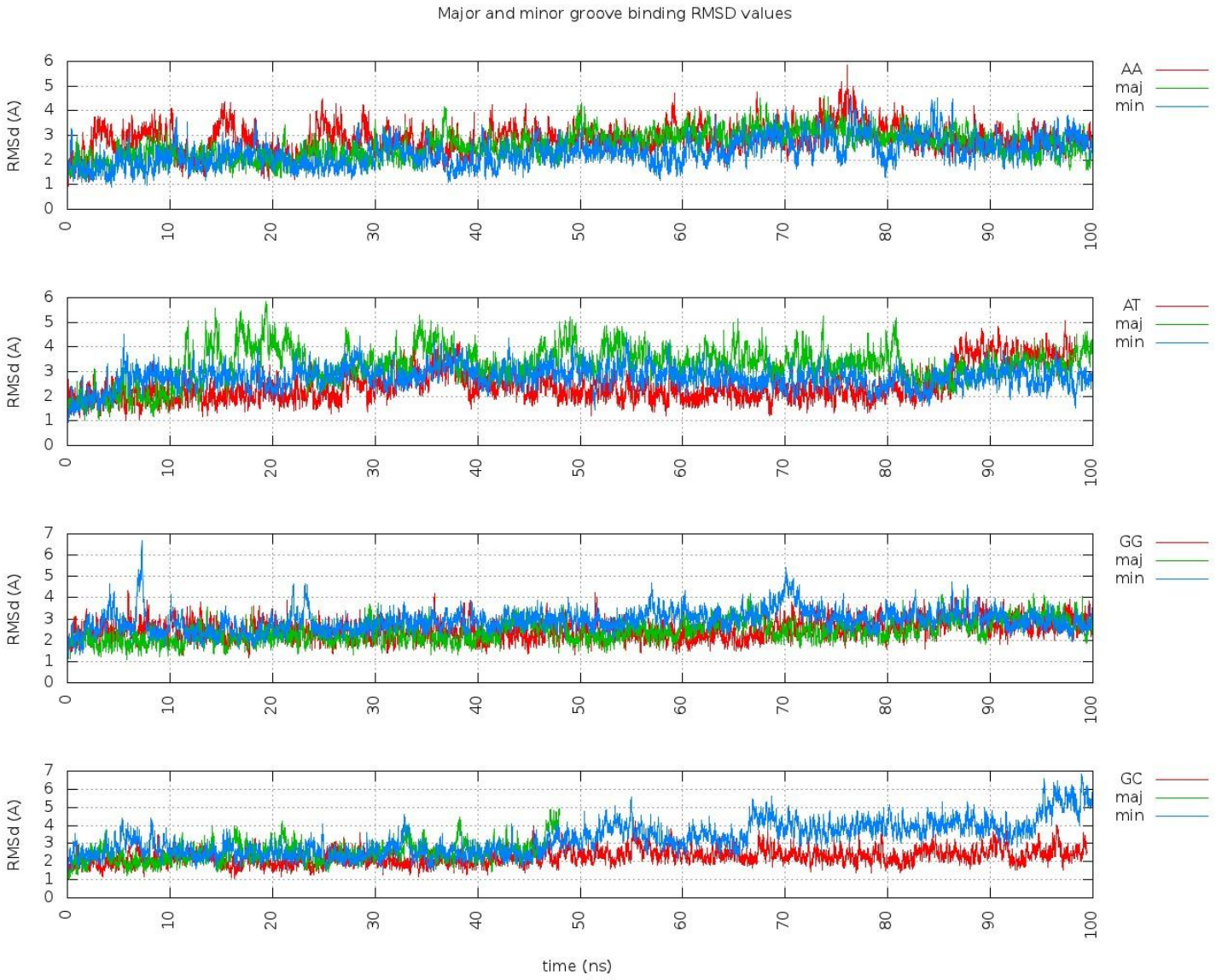
Supplementary Information

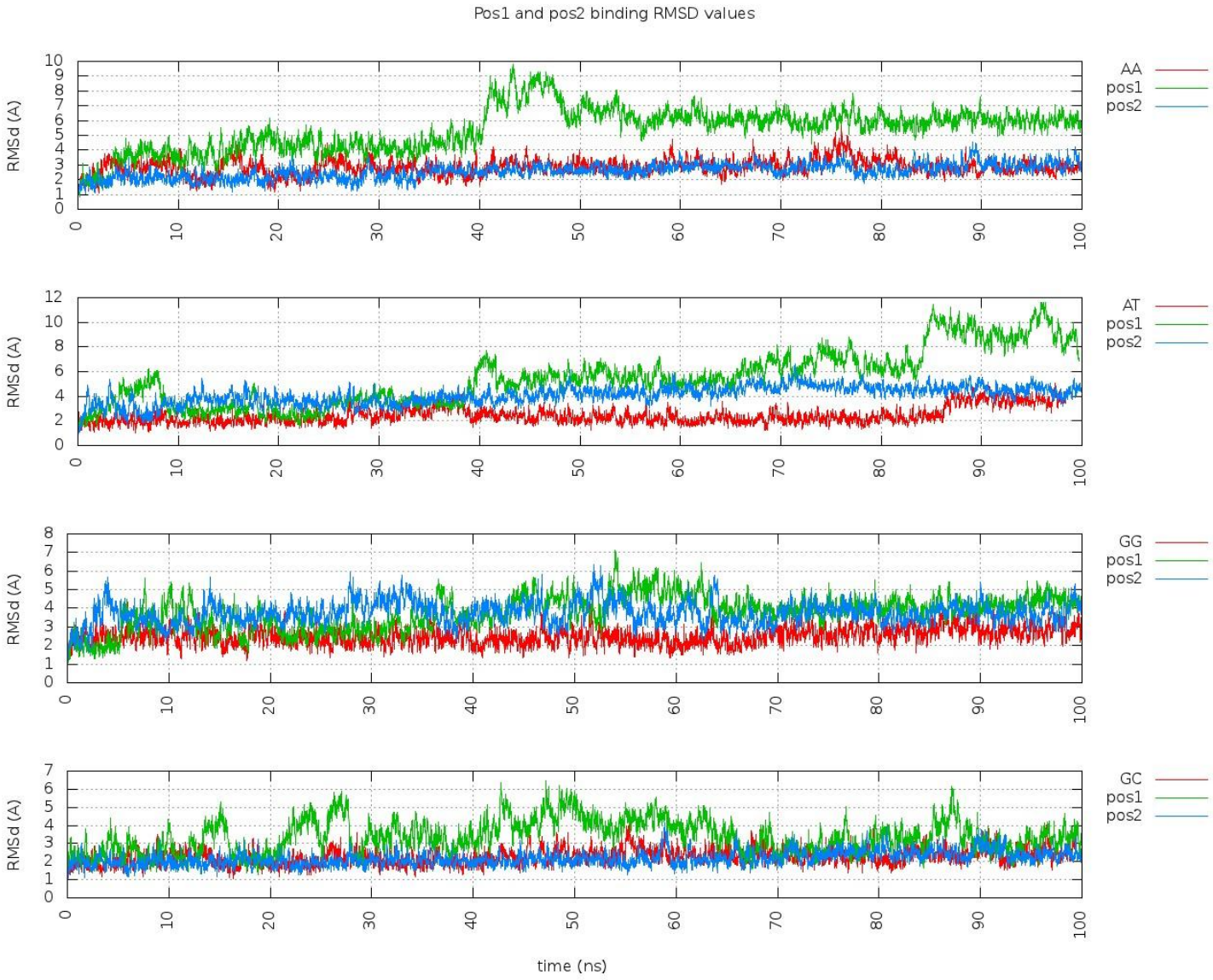
S1 – Structural comparison of *Cas*. Results from molecular dynamics simulations, quantum mechanics simulations and experiment values.

	[Cu(bipyridine)(acetylacetonate)]$^{2+}$		
	Cas (MD)[a]	Cas (DFT)[b]	Cas (exp)[c]
	Distances (A)		
Cu-N1	2.18	2.02	2.01
Cu-N2	2.18	2.02	2.02
Cu-O1	2.08	1.90	1.91
Cu-O2	2.09	1.90	1.93
	Angle (°)		
N1-Cu-N2	75.01	80.39	80.73
O1-Cu-O2	96.49	94.27	94.38

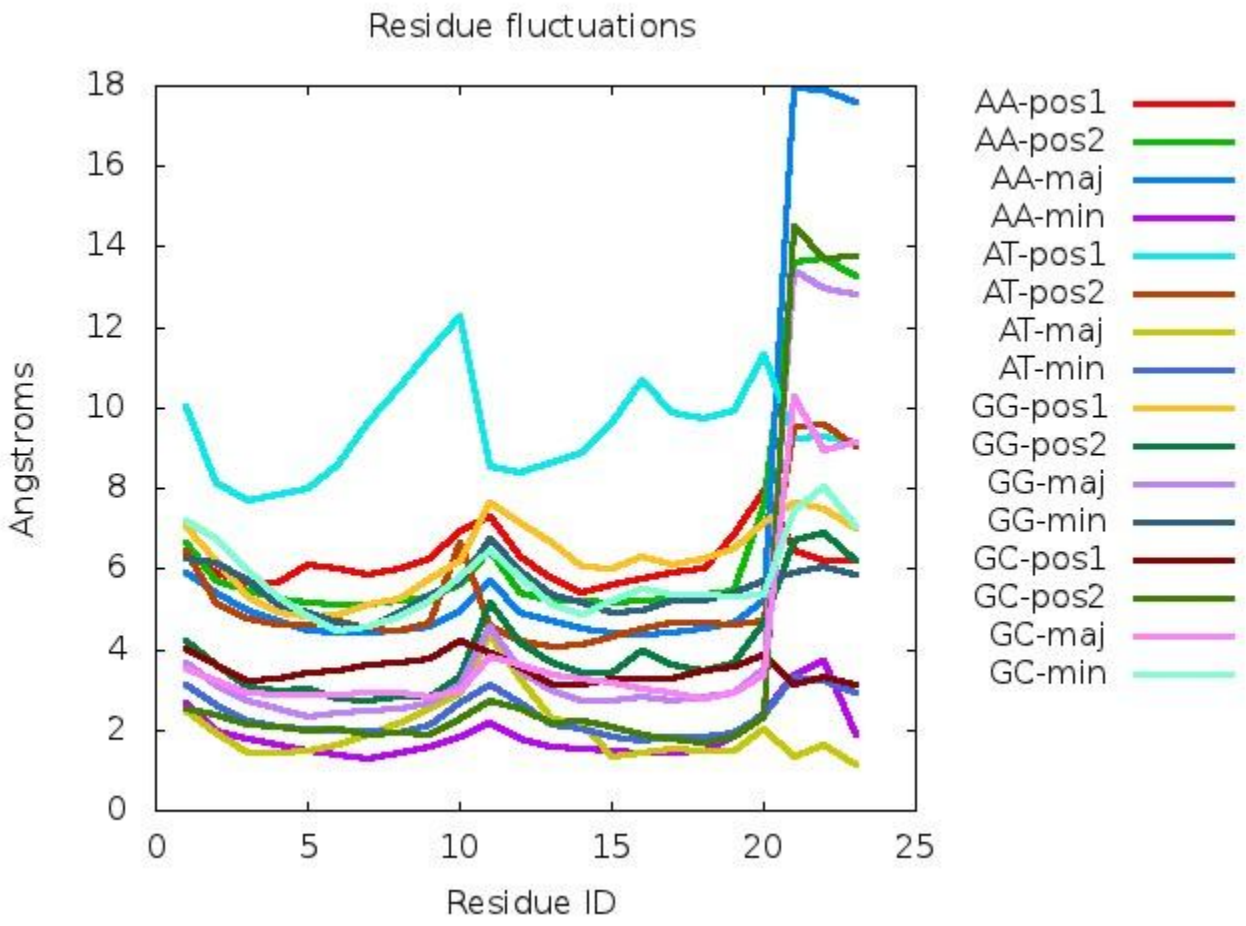
a. Average values obtained from a 5ns MD run
b. Geometry optimization using m05-2x/6-311++G(2d 2p)
c. From unpublished X-ray data



S2 – RMSD values over time. The red values correspond to the DNA decamer with no copper complex. Green values correspond to the decamer with the copper-complex starting position intercalating with the aromatic group to the DNA (**POS1**) and blue correspond to the copper-complex starting position intercalating with the non-aromatic group to the DNA (**POS2**).



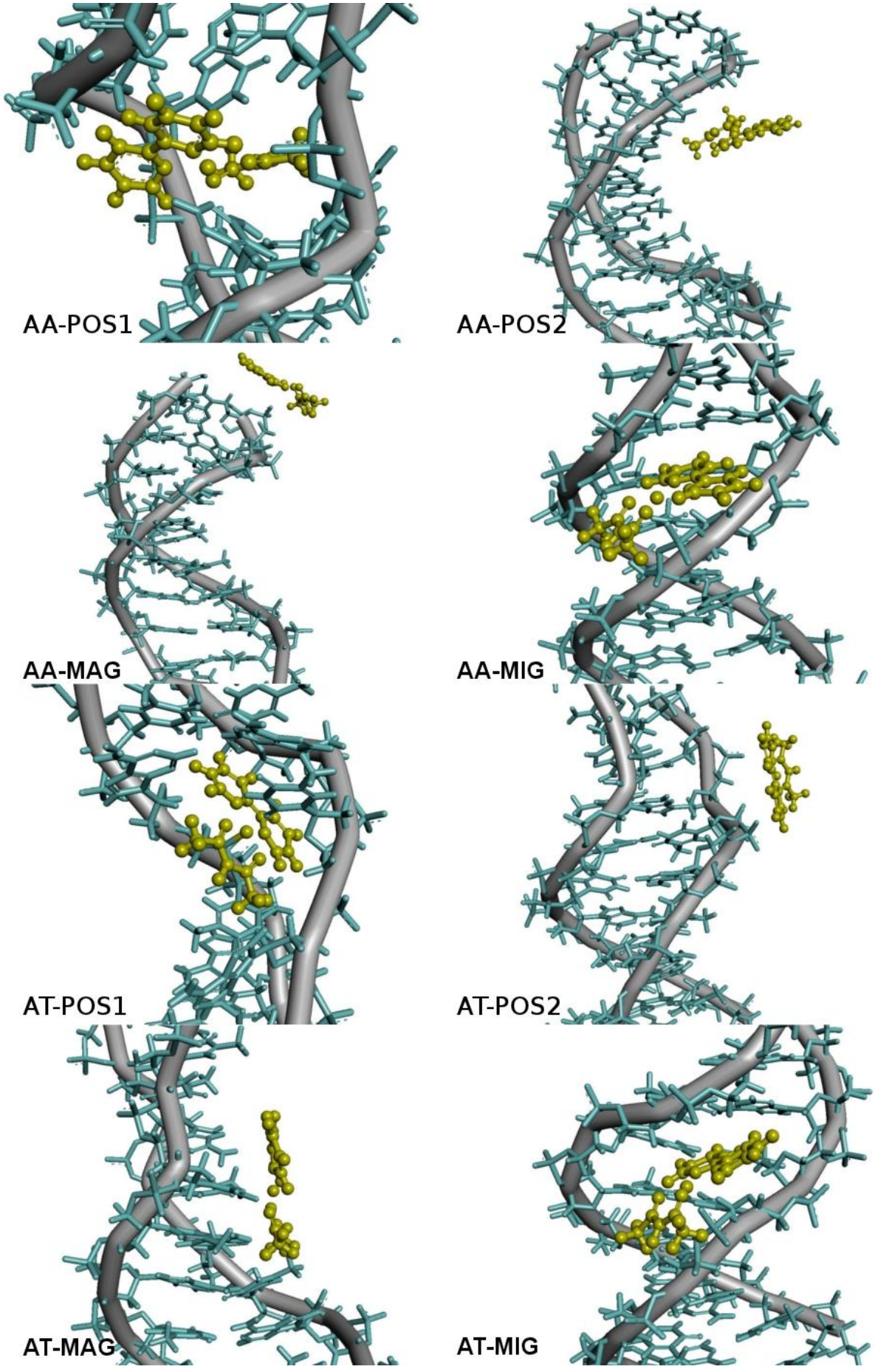
S2 – RMSD values over time. The red values correspond to the DNA decamer with no copper complex. Green values correspond to the decamer with the copper-complex starting at the major (**MAJ**) groove and blue correspond to the copper-complex starting in the minor (**MIN**) groove of the simulation.

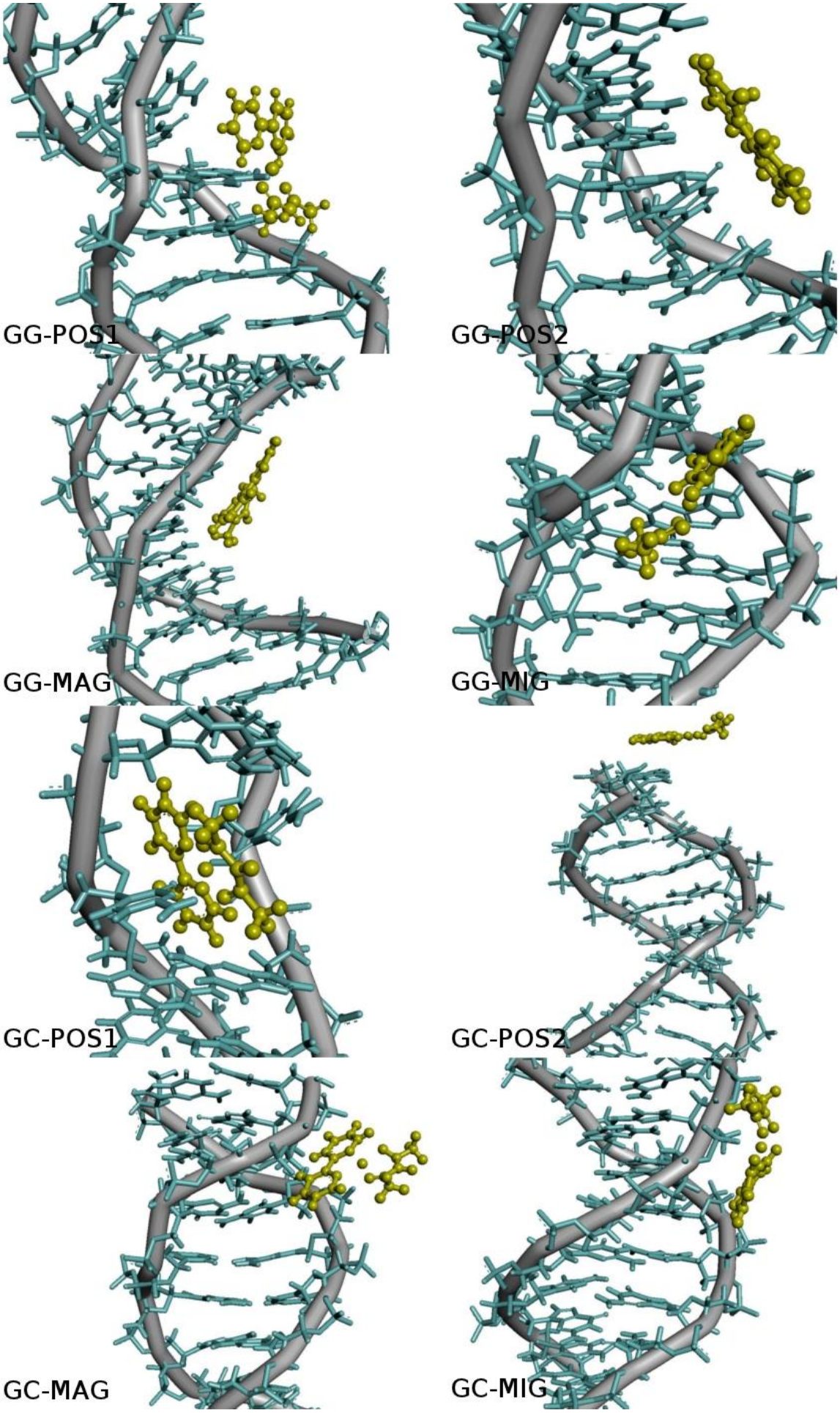


S3 – Residue fluctuation analysis.

Each line represents a single simulation and high values of fluctuations correspond to high mobility of each residue throughout the 100ns simulation. Residue ID 1 to 10 correspond to the 5'→3' DNA chain and residue ID 11 to 20 to the 3'→5'. ID's 21, 22 and 23 are the ligand constituents: acetylacetonate, bipyridine and the copper atom respectively. High values of fluctuations are observed for the residues at the initial positions of both DNA chains corresponding to ID's 1, 10, 11 and 20 due to lack of constrains. High elevated values of general fluctuations are observed in the simulations AT-pos1, AA-pos1, GG-pos2 and AA-min (refer to main text). Intercalation of the ligand causes the mayor fluctuation values of the bases residues around the ligand as is the case for the position-1 simulations. Minor groove simulations have the lowest value of overall fluctuations due to the interactions of the ligand with the phosphate group of the DNA backbone.

S4. Average structures using the final 10 ns of the MD simulations. Refer to the main text for a case by case description.





S5. Coordinates of cas01- deoxyribose-phosphate adduct

H -2.8343269984 -5.3303371421 -1.1264452519
C -2.2157829921 -4.7319853932 -1.7967532999
H -2.7824455863 -4.5230492186 -2.7068820003
H -1.3345197642 -5.3198141015 -2.0613566891
C -1.8208985917 -3.4359472494 -1.105636516
H -2.704642706 -2.8226509753 -0.9190065462
O -1.1927248833 -3.7181522584 0.1586019872
C 0.2147932249 -3.3598787187 0.1087848699
H 0.3490204747 -2.406680689 0.6215389339
C -0.7920956976 -2.612607249 -1.8791848978
H -0.9088656578 -2.6610644939 -2.9620583702
C 0.5174067965 -3.1969993749 -1.3711469115
H 0.6901871472 -4.1763387458 -1.8294116997
H 1.3850096458 -2.5690440744 -1.5515742776
O -0.9664007132 -1.2588929107 -1.4379643431
P 0.0319345013 -0.0904128853 -2.013688787
O -0.6973398871 1.2083978235 -1.7127555748
O 0.5379325107 -0.4236757693 -3.3740624402
O 1.2461906984 -0.2063870397 -0.9036649629
C 2.5782007546 0.0455429728 -1.3420013447
H 2.6073275344 0.9253821315 -1.994042008
H 2.9529021824 -0.8161130512 -1.8979248661
C 3.4265925814 0.3188663083 -0.112165368
H 3.0239611055 1.1973499387 0.3982326581
O 3.3866060531 -0.7493272471 0.8384496625
C 4.3657534156 -1.7215039564 0.4879273175
H 4.7874535036 -2.059542443 1.4416162235
C 4.9174731345 0.4683984709 -0.4424416591
H 5.0553300422 0.8885151429 -1.4421976361
C 5.4102116907 -0.9920804385 -0.3833189341
H 5.4231011079 -1.4438004925 -1.3765937947
H 6.4139125003 -1.0558460625 0.0410484258
O 0.5455956307 2.700047101 0.6463311215
C 0.845946003 3.7303400874 -0.0462988616
C -0.0498664877 4.5025512835 -0.794723428
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H -5.8373243701 -1.7554082599 0.367753325
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C -3.8664761728 0.8713981924 -0.421582055
H -3.7848209908 1.7676704313 -1.0228254633
N -2.8145989687 0.603794051 0.347548607
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C -0.1133256473 -1.8453007909 3.4221028409
H 0.0508167657 -2.6290508787 4.1515352714
C 0.9082881957 -0.966794709 3.0871907015
H 1.8979430947 -1.0461145803 3.513912322
C 0.6424579845 0.0305101551 2.1541874545
H 1.3912228411 0.7451584299 1.8478974402
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H -2.625646299 4.6465740803 -2.5684254279
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H -2.1966334843 3.4051591539 1.8648246617
H -0.8315054662 3.1195514184 2.4844110866
C 5.6198260633 1.3468633655 0.5929888292
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H 5.2412029482 2.3713726018 0.5629159758
H 5.447055686 0.9485641162 1.5963251598
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H 4.4328516966 -3.457432862 -0.5836444132
H 3.0439973475 -3.286956606 0.2853017018
N 1.0368216337 -4.3398861826 0.7625644637
H 0.785175337 -4.4096095249 1.740927647
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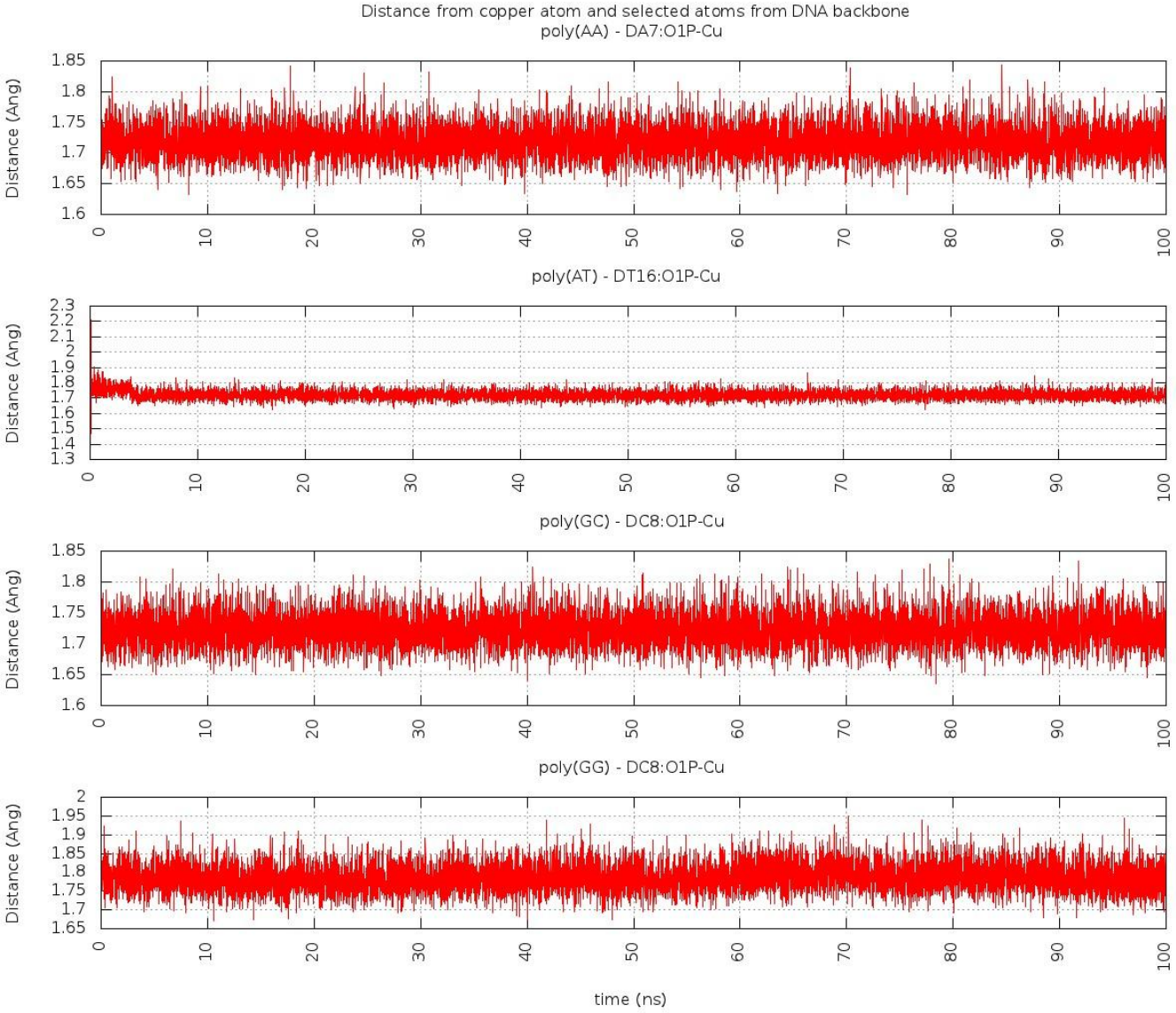
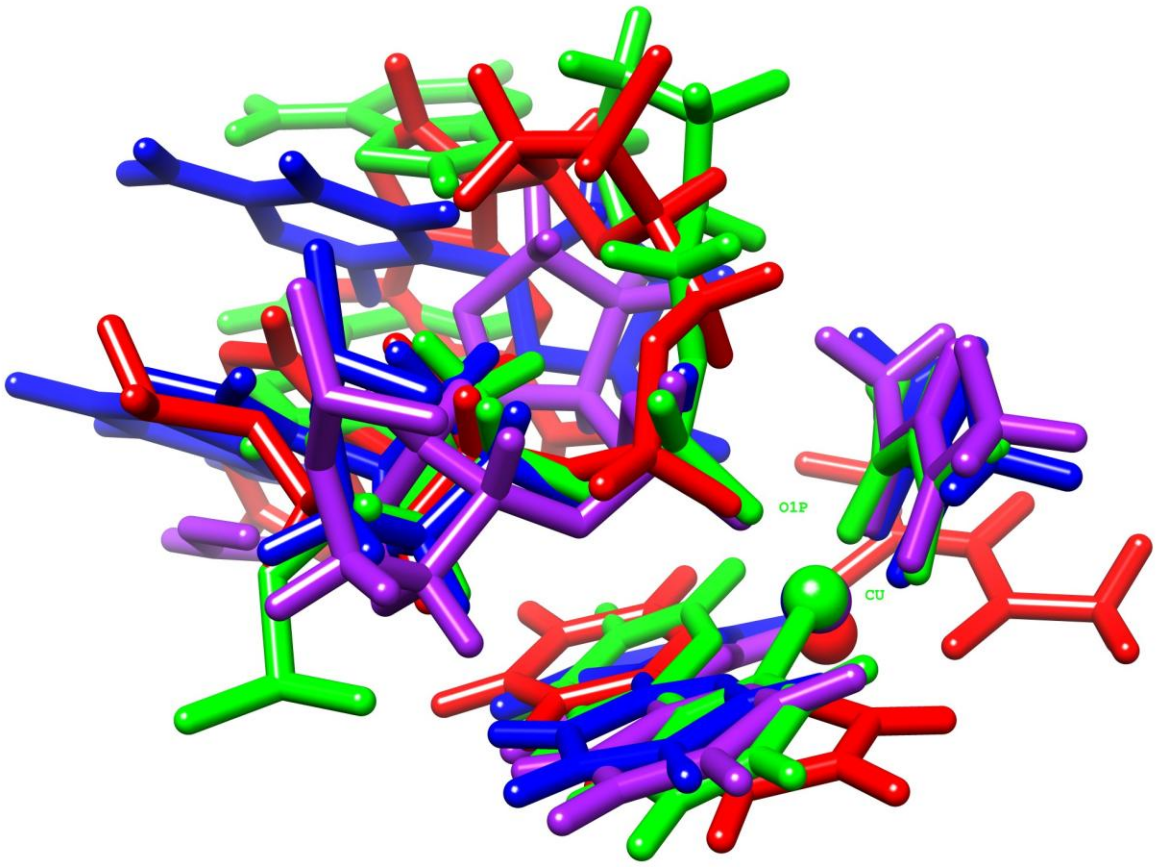


S6. Distance between oxygen atom from DNA backbone and copper atom of the Casiopeína molecule over 100ns MD simulation. Poly(AT) shows a short (< 0.5 ns) reorientation of the Cas ligand in the first 1ns or the production simulation, reorienting the copper atom to DT16:O1P.



S7. Superimposed structures of poly(AA)-Cas (green), poly(AT)-Cas (blue), poly(GG)-Cas (purple) and poly(GC)-Cas (red) simulations in the minor groove (**MIN**) showing a similar orientation with the copper atom interacting with the O1P atom of the phosphate group and the aromatic ligand pointing toward the sugar ring moiety of the DNA backbone.