	ANT-DNA	**ANT•DNA**	**IMI•DNA**	**IMI•DNA(c)**	**DNA**	**ANT**	**IMI**
$box\,(\text{Å}^3)$	$58 \times 72 \times 58$	$60 \times 62 \times 66$	$64 \times 59 \times 66$	$66 \times 67 \times 78$	$56 \times 55 \times 56$	$45 \times 36 \times 35$	$47 \times 47 \times 46$
$n^\circ\, waters$	6000	7700	8000	8900	5500	1900	2900
$n^\circ\, c.ions$	22	22	22	26	22	0	0
$time\,(ns)$	$21\,ns$	$19\,ns$	$19\,ns$	$20\,ns$	$21\,ns$	$6\,ns$	$10\,ns$

Tab S. 1: Box dimensions, number of waters, number of counterions, and simulated time for the various system.

		drug-guanine in **ANT-DNA**	**ANT**	**IMI**
BONDS	c-na	440.21 1.380	399.325 1.400	454.964 1.360
	hn-nc	523.07 0.969	520.644 0.970	
	N2-c3	470.33 1.350		
ANGLES	H-N2-c3	49.235 117.570		454.964 1.360
	N2-c3-h1	55.896 99.790		
	N2-c3-nc	72.447 115.340		
	N2-c3-c3	66.234 122.030		
	CA-N2-c3	64.986 127.530		
	oh-c3-nc		71.805 107.000	
	c3-nc-hn	46.639 114.750	47.838 107.020	
	c3-nc-ca	62.383 128.500	59.542 139.090	
	nc-c3-c3	66.692 107.840	67.561 104.750	
	hn-nc-ca	50.129 116.730	50.609 113.890	
	ca- c-na	66.730 119.510	61.391 124.550	67.230 118.420
	na-c2-cd	71.957 111.540	73.222 110.910	72.382 112.600
	c2-cd-c2	67.754 122.670	68.080 121.260	65.474 124.820
	cd-c2-hc	49.903 116.750	49.187 115.980	47.352 116.820
	c2- c- n	69.249 120.260	70.544 122.430	69.315 120.030
	c3-cc-h4			45.339 117.520
	cc-c3-na			66.982 109.850
	cc-nc-ca			66.940 124.340
DIHEDRAL	X-c3-nc-X	0.000	0.000	2.000
	X-N2-c3-X	0.000	0.000	3.000
	X-cc-c2-X	4.000	180.000	2.000
	na-c2-cd-c3	26.600	180.000	2.000
	na-c2-cd-c2	26.600	180.000	2.000
	ha-c2-cd-c3	26.600	180.000	2.000
	ha-c2-cd-c2	26.600	180.000	2.000
	c2-cd-c2-hc	16.000	180.000	2.000
	c2-cd-c2-c2	16.000	180.000	2.000

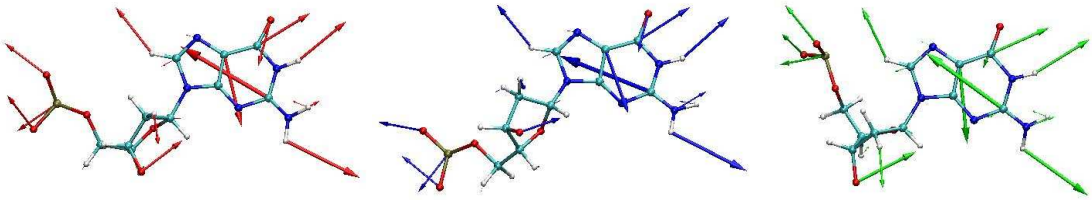
TabS. 2: Force field parameters calculated with the *parmcal* module of AMBER. Force constants, equilibrium distances and angles, together with the V_n, γ and n values for dihedrals are reported.

	atom\system	**IMI•DNA**	**ANT•DNA**	**ANT-DNA**
	H9(PHE)	0.449	0.474	0.441
	O9(PHE)	-0.619	-0.666	-0.638
DIAZEPINE	H16	-	0.297	0.261
DIAZEPINE	N10	-0.443	-0.314	-0.269
DIAZEPINE	C11	0.122	0.213	0.156
DIAZEPINE	H11	0.352	0.054	-0.005
DIAZEPINE	O2	-	-0.591	-
DIAZEPINE	H1	-	0.403	-
	H7(PYR)	0.059	0.072	0.203
TAIL	H10	0.126	0.109	0.122
TAIL	H14	0.407	0.404	0.421
TAIL	N15	-0.880	-0.872	-0.972
TAIL	H15	0.407	0.404	0.421
BASE G10	H22	0.423	0.423	-
BASE G10	H21	0.423	0.423	0.244
BASE G10	N2	-0.923	-0.923	-0.196
BASE G10	C2	0.743	0.743	0.338
BASE G10	N3	-0.664	-0.664	0.426

TabS. 3: RESP charges extracted from the minimization of the electronic structure of the subsystem $G10 - drug$.

$H-bond \backslash system$	IMI•DNA 1	IMI•DNA 2	ANT•DNA	ANT-DNA	DNA	IMI	ANT
$\mathbf{NH_{G11}...O9_{Ant}}$	2.2 ± 0.3Å 58%	–	1.9 ± 0.3Å 73%	2.2 ± 0.3Å 59%	–	–	–
$\mathbf{NH_{G10}...O9_{Ant}}$	–	2.2 ± 0.3Å 60%	–	–	–	–	–
$\mathbf{N_{G11}...HO9_{Ant}}$	2.4 ± 0.4Å 50%	–	–	–	–	–	–
$\mathbf{O_{C15}...HO9_{Ant}}$	–	–	–	1.9 ± 0.2Å 81%	–	–	–
$\mathbf{N_{A16}...HO9_{Ant}}$	–	2.3 ± 0.3Å 39%	–	–	–	–	–
$\mathbf{N_{G11}...HN10_{Ant}}$	–	–	2.7 ± 0.2Å 16%	–	–	–	–
$\mathbf{O_{C15}...HN10_{Ant}}$	–	–	–	2.1 ± 0.2Å 65%	–	–	–
$\mathbf{NH_{G10}...N10_{Ant}}$	2.4 ± 0.3Å 69%	–	–	–	–	–	–
$\mathbf{O4'_{G11}...HO11_{Ant}}$	–	–	3.3 ± 0.9Å 14%	–	–	–	–
$\mathbf{N_{A17}...HN15_{Ant}}$	–	–	–	1.9 ± 0.3Å 61%	–	–	–
$\mathbf{HO9_{Ant}...wat}$	s : 75%	s : 17%	s : 79% d : 11%	s : 50%	–	s : 36% d : 42% t : 14%	s : 22% d : 61% t : 12%
$\mathbf{HO11_{Ant}...wat}$	–	–	s : 90% d : 17%	–	–	–	s : 17% d : 62% t : 19%
$\mathbf{HN10_{Ant}...wat}$	–	–	–	–	–	–	s : 37%
$\mathbf{N10_{Ant}...wat}$	–	–	-	–	–	s : 10%	–
$\mathbf{HN15_{Ant}...wat}$	s : 96%	s : 99%	s : 84% d : 6%	s : 33%	–	s : 68% d : 21%	s : 66% d : 21%
$\mathbf{HN_{G11}...wat}$	–	s : 74%	s : 17%	–	s : 71%	–	–
$\mathbf{N3_{G11}...wat}$	-	s : 69%	s : 14%	–	s : 74%		
$\mathbf{O4'_{G11}...wat}$	-	-	s : 27%	-	s : 39%	–	–
$\mathbf{O2_{C14}...wat}$	s : 84%	s : 86%	s : 87%	s : 83%	s : 85%	–	–
$\mathbf{HN_{G10}...wat}$	-	-	s : 17%	–	s : 71%	–	–
$\mathbf{N3_{G10}...wat}$	–	-	s : 63%	–	s : 76%	–	–
$\mathbf{O2_{C15}...wat}$	s : 77%	s : 78%	s : 8%	–	s : 83%	–	–
$\mathbf{O2_{T9}...wat}$	s : 95%	–	s : 91% d : 14%	s : 91%	s : 70% d : 14%	–	–
$\mathbf{N3_{A16}...wat}$	–	–	–	–	s : 85%	–	–
$\mathbf{O2_{T8}...wat}$	s : 91%	s : 95%	s : 85%	s : 70% d : 13%	s : 85% d : 6%	–	–
$\mathbf{N3_{A17}...wat}$	s : 73%	–	s : 82%	s : 19%	s : 81%	–	–
$\mathbf{HN_{G7}...wat}$	s : 71%	s : 68%	s : 72%	s : 67%	s : 70%	–	–
$\mathbf{N3_{G7}...wat}$	s : 55%	s : 65%	s : 59%	s : 65%	s : 64%	–	–
$\mathbf{O2_{C18}...wat}$	s : 90% d : 11%	s : 98%	s : 85% d : 10%	s : 91%	s : 85% d : 7%	–	–

TabS. 4: H-bonds among the drug, the oligonucleotide and the solvent. The table shows only bonds formed at the drug-DNA interface. We report hydrogen-acceptor distances (only for the drug-DNA network) and life times, expressed as percentage over the simulation time. The symbols *s, d* and *t* indicate the formation of 1, 2 and 3 bonds respectively, and the labeling of the atoms refers to Fig. 7.

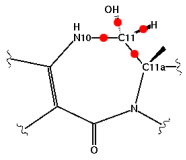


FigS. 1: Electrostatic forces acting on guanines along the first strand of **DNA**. From left to right: $G7$, $G10$, $G11$.

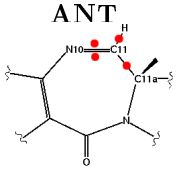
step\system	**IMI•DNA**	**IMI•DNAc**
C12-C15	6.8 ± 0.7	6.1 ± 0.6
G11-C16	4.9 ± 0.4	5.1 ± 0.4
G10-A17	4.4 ± 0.4	4.4 ± 0.4
T9-C18	4.4 ± 0.7	4.0 ± 0.6

TabS. 5: Average values (in Å) of minor groove widths calculated between C4' atoms at d[TG*GC]$_2$. As can be seen the differences are absolutely not dramatic.

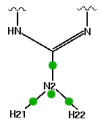
		bioframe	**no bioframe**	**no solvent**	**vacuo**
IMI•DNA	**C11 – H11**	0.66 ± 0.01	0.68 ± 0.04	0.66 ± 0.01	0.68
	C11 – N10	0.57 ± 0.01	0.54 ± 0.01	0.58 ± 0.01	0.55
	C11 – N10	0.58 ± 0.01	0.55 ± 0.01	0.59 ± 0.01	0.56
	C11 – C11a	0.51 ± 0.01	0.51 ± 0.01	0.50 ± 0.01	0.51
	N2 – H21	0.57 ± 0.01	0.59 ± 0.01	0.57 ± 0.01	0.59
	N2 – H22	0.59 ± 0.01	0.58 ± 0.01	0.57 ± 0.01	0.58
	N2 – C2	0.36 ± 0.04	0.37 ± 0.04	0.38 ± 0.06	0.33
	N2 lone pair	0.21 ± 0.05	0.19 ± 0.05	0.21 ± 0.07	0.24
ANT•DNA	**C11 – H1**	0.66 ± 0.01	0.68 ± 0.04	0.66 ± 0.01	0.67
	C11 – N10	0.57 ± 0.01	0.57 ± 0.01	0.58 ± 0.01	0.57
	C11 – C11a	0.50 ± 0.01	0.50 ± 0.01	0.50 ± 0.01	0.51
	C11 – O11	0.63 ± 0.01	0.62 ± 0.01	0.62 ± 0.01	0.62
	N2 – H21	0.57 ± 0.01	0.59 ± 0.01	0.57 ± 0.01	0.59
	N2 – H22	0.58 ± 0.01	0.58 ± 0.01	0.59 ± 0.01	0.58
	N2 – C2	0.37 ± 0.04	0.38 ± 0.04	0.38 ± 0.04	0.33
	N2 lone pair	0.20 ± 0.05	0.15 ± 0.06	0.15 ± 0.06	0.24



ANT

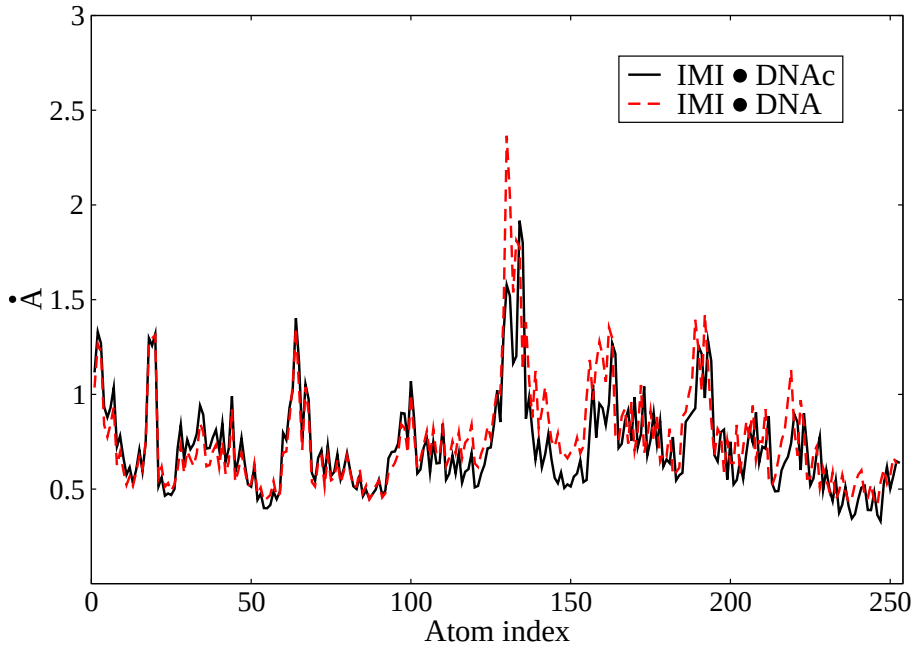


IMI

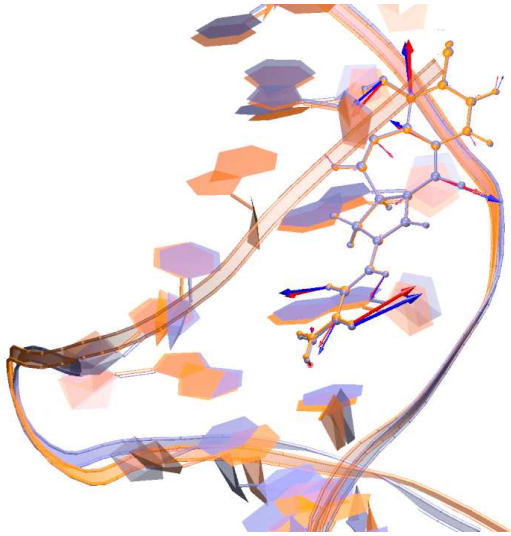


GUA

Tab S. 6: Bond ionicity of X-$N2_{G10}$ and X-$C11_{drug}$ bonds. Last column refers to calculations *in vacuo* on the drug or the guanosine. Two rows with the same label indicate a double bond, while the last row in each system represents the BI associated to the lone pair of the guanine nitrogen. The figures on the right side depict the BO's considered for the BI calculations (see Methods).



FigS. 2: Comparison between RMSFs around the average structure at d[TG*GC]$_2$ in **IMI•DNA** and **IMI•DNAc** . The flexibility at the end of the oligonucleotide is very similar.



FigS. 3: Average electrostatic forces acting on the drug in **IMI•DNA** (cyan) and **IMI•DNAc** (orange). Again, no dramatic effects are seen.