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Supplementary Materials

Self-Consistent Parameterization of DNA Residues for the Non-Polarizable AMBER Force Fields

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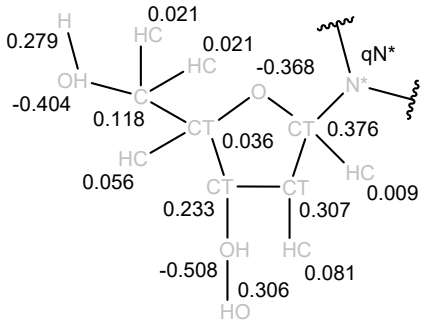
SUPPLEMENTAL METHODS

Restrained electrostatic potential (RESP) fitting. For the four canonical residues, ESPs were computed at HF/6-31G* with Gaussian 16 with the IOp keyword IOP(6/33=2). The outputs were processed by *espgen* to generate input files for RESP. Following the original workflow in ff94 [18], each nucleoside was combined with a dimethylphosphate (DMP) anion that had been HF/6-31G*-optimized to match the specified dihedrals of C1-O1-P-O2 = O1-P-O2-C2 = 73.1°. Two constraints were imposed: 1) the DMP moiety was assigned to carry all of the −1 charge, and 2) the methyl groups in DMP and terminal -OH groups of the nucleoside sum to zero. Across the nucleosides, the deoxyribose and backbone atoms were set to share charges, with exception to C1' and H1', which floated with each nucleobase. Hydrogen atoms in each methyl group were equivalenced. Fitting occurred in two stages. In the first, a hyperbolic restraint of 0.0005 A.U. was applied to all heavy atoms. In the second stage, a stronger restraint of 0.001 A.U. was used to refit methyl and methylene hydrogens only, while fixing all other atoms to their values from the first stage.

RESP charges for the non-canonical bases were globally fitted with the canonical bases. The charges of the canonical residues were constrained to their values in ff94 and imposed on the deoxyribose (except C1' and H1') and phosphate atoms across the entire set. The only floating charges were therefore the nucleobase atoms of the new bases. The same two-stage procedure was otherwise followed.

Parameterization of ff86 nucleosides. Following the fragment-based approach reported by Weiner et al [22], nucleosides were constructed by combining 1-aminodeoxyribose and a *N*9-methylpurine or *N*1-methylpyrimidine. For canonical residues, the atomic charges of the fragments were reported by Singh and Kollman [13]. Essentially, and unlike the procedure taken for amino acids, the excess atomic charges incurred from the removal of the amino and methyl substituents in the fragments were locally absorbed into the C1' and N1/N9 atoms. However, this was not done identically for each residue, but via the following rule, which was not explicitly described but inferred from Figure 2 in the Weiner et al paper [22]. For deoxycytidine only, the excess charges from both the amino and methyl groups (−0.237 + 0.055 = −0.182) were summed and assigned exclusively to C1' i.e., 0.558 – 0.182 = 0.376. The *N*1 atom in cytidine retained the charge in *N*1-methylcytosine (−0.187). The adjusted deoxyribose in deoxycytidine was then templated to the other nucleosides. Specifically, the glycosidic N atoms were adjusted by an amount equal to the

charge of the adjusted deoxyribose (0.055) plus the base of interest without the methyl group, with *no additional adjustment to the deoxyribose*:



$$qN^{*} = qN^{*}_{\mathrm{ESP}} - [0.055 + q(\text{base without } CH_3)]$$

Charge values in black are taken from Weiner et al [22]. These residual adjustments to the glycosidic N atoms in deoxythymidine, deoxyadenosine, and deoxyguanosine were −0.016, 0.010, and 0.020 respectively.

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Table S1. RESP-fitted atomic charges of QM- and MM-optimized canonical DNA nucleosides.

Reference values are atomic charges in ff94. The other charges are derived from QM- and MM-optimized models. Geometric specifications refer to the reference summary parameters in Table 1. Y/N refers to whether the optimization was constrained (QM) or restrained (MM). In all cases, H5' and H3' are constrained in the QM optimization and restrained in the MM minimization. Following geometry optimization, ESP fitting was performed at the HF/6-31G* level and the output passed onto the two-step RESP-fitting procedure for ff94 [18] described in *Supplemental Methods*. In particular, C1' and H1' from deoxyribose are not equivalenced and are reported with the bases. All parametric values are reported at the full precision available.

Nucleobase + non-equivalenced C1'/H1'

DAN		**Subject to (*q*, *W*, γ, χ) specifications**			
		N	Y	Y	N
Position	ff94	HF/6-31G *	HF/6-31G	MP2/6-31G*	MM(ff86)
C1'	0.0431	0.107555	0.070706	0.095582	0.032834
H1'	0.1838	0.157014	0.165702	0.165432	0.181715
N9	−0.0268	−0.062163	−0.050772	−0.047366	−0.027447
C8	0.1607	0.144636	0.174481	0.144843	0.168181
H8	0.1877	0.191428	0.185140	0.198879	0.183289
N7	−0.6175	−0.590904	−0.614204	−0.604670	−0.615574
C5	0.0725	0.019601	0.055616	0.057751	0.074189
C6	0.6897	0.696800	0.706390	0.705629	0.680556
N6	−0.9123	−0.914322	−0.937631	−0.942502	−0.906295
H61	0.4167	0.413237	0.419008	0.421292	0.414963
H62	0.4167	0.413237	0.419008	0.421292	0.414963
N1	−0.7624	−0.772924	−0.767573	−0.756753	−0.757845
C2	0.5716	0.606425	0.578445	0.544437	0.573199
H2	0.0598	0.048195	0.055215	0.069074	0.057312
N3	−0.7417	−0.775456	−0.752867	−0.734434	−0.734724
C4	0.3800	0.460465	0.421950	0.399293	0.370340
RMSD		0.034506	0.017795	0.020558	0.005530

DGN		**Subject to (*q*, *W*, γ, χ) specifications**			
		N	Y	Y	N
Position	ff94	HF/6-31G *	HF/6-31G	MP2/6-31G*	MM(ff86)
C1'	0.0358	0.114539	0.091560	0.133338	0.015220
H1'	0.1746	0.130511	0.134362	0.128628	0.173741
N9	0.0577	0.033421	0.023835	−0.001260	0.075520
C8	0.0736	0.068252	0.094789	0.086033	0.070204
H8	0.1997	0.202180	0.196165	0.204985	0.200477
N7	−0.5725	−0.552034	−0.574758	−0.568379	−0.572997
C5	0.1991	0.147480	0.200138	0.206863	0.201942
C6	0.4918	0.545239	0.501894	0.494264	0.489296
O6	−0.5699	−0.552780	−0.546155	−0.546107	−0.570949
N1	−0.5053	−0.567332	−0.521219	−0.533157	−0.496718
H1	0.3520	0.363692	0.354408	0.359601	0.350301
C2	0.7432	0.762123	0.709546	0.708897	0.739729
N2	−0.9230	−0.924639	−0.898491	−0.877218	−0.922955

H21	0.4235	0.401670	0.395934	0.383862	0.422815
H22	0.4235	0.401670	0.395934	0.383862	0.422815
N3	−0.6636	−0.635772	−0.622291	−0.609413	−0.657950
C4	0.1814	0.204604	0.192961	0.182979	0.169166
RMSD		0.035655	0.026965	0.039200	0.007824

DCN		**Subject to (*q*, *W*, γ, χ) specifications**			
		N	Y	Y	N
Position	ff94	HF/6-31G *	HF/6-31G	MP2/6-31G*	MM(ff86)
C1'	−0.0116	0.131453	0.040351	0.069357	−0.019945
H1'	0.1963	0.122635	0.173546	0.167499	0.200608
N1	−0.0339	−0.075401	−0.065204	−0.072971	−0.049423
C6	−0.0183	−0.034262	−0.015413	0.005525	−0.019243
H6	0.2293	0.213119	0.219090	0.218902	0.223781
C5	−0.5222	−0.474449	−0.500410	−0.495985	−0.509247
H5	0.1863	0.182040	0.188226	0.190456	0.184294
C4	0.8439	0.766984	0.786811	0.745479	0.844565
N4	−0.9773	−0.908439	−0.925120	−0.879898	−0.981574
H41	0.4314	0.398940	0.404086	0.384929	0.431705
H42	0.4314	0.398940	0.404086	0.384929	0.431705
N3	−0.7748	−0.760225	−0.764340	−0.731506	−0.781861
C2	0.7959	0.821355	0.832750	0.790352	0.813377
O2	−0.6548	−0.639867	−0.649846	−0.639288	−0.659086
RMSD		0.056237	0.031343	0.050659	0.008128

DTN		**Subject to (*q*, *W*, γ, χ) specifications**			
		N	Y	Y	N
Position	ff94	HF/6-31G *	HF/6-31G	MP2/6-31G*	MM(ff86)
C1'	0.068	0.110128	0.077476	0.092102	0.055576
H1'	0.1804	0.160001	0.172244	0.173644	0.182462
N1	−0.0239	−0.025585	−0.017366	−0.017414	−0.030756
C6	−0.2209	−0.280735	−0.267025	−0.253458	−0.207161
H6	0.2607	0.282872	0.272476	0.284520	0.254509
C5	0.0025	0.002703	0.001983	0.008076	−0.000128
C7	−0.2269	−0.241687	−0.250221	−0.268888	−0.258242
H71	0.077	0.080609	0.083468	0.087809	0.085186
H72	0.077	0.080609	0.083468	0.087809	0.085186
H73	0.077	0.080609	0.083468	0.087809	0.085186
C4	0.5194	0.598880	0.596151	0.557955	0.530958
O4	−0.5563	−0.562337	−0.561573	−0.557381	−0.560811
N3	−0.434	−0.488988	−0.489953	−0.460458	−0.438076
H3	0.342	0.340992	0.341802	0.336661	0.342964
C2	0.5677	0.598081	0.598190	0.565766	0.573119
O2	−0.5881	−0.593328	−0.595976	−0.586773	−0.590316
RMSD		0.032454	0.028696	0.020406	0.010691

Deoxyribose (except C1'/H1') and phosphate

		Subject to (q, W, γ, χ) specifications			
		N	Y	Y	N
Position	ff94	HF/6-31G *	HF/6-31G	MP2/6-31G*	MM(ff86)
H5T	0.4422	0.446230	0.445388	0.435760	0.439483
O5'	−0.6318	−0.636987	−0.633390	−0.623394	−0.625961
C5'	−0.0069	0.004901	−0.000928	−0.009135	−0.000599
H5'1	0.0754	0.072676	0.071630	0.076062	0.072956
H5'2	0.0754	0.072676	0.071630	0.076062	0.072956
C4'	0.1629	0.167846	0.204110	0.210710	0.161097
H4'	0.1176	0.106575	0.102110	0.107438	0.118168
O4'	−0.3691	−0.389816	−0.396500	−0.407692	−0.363252
C3'	0.0713	0.112604	0.072212	0.035804	0.076272
H3'	0.0985	0.079566	0.089587	0.099671	0.094382
C2'	−0.0854	−0.061643	−0.067813	−0.065441	−0.087246
H2'1	0.0718	0.053208	0.065339	0.069370	0.074064
H2'2	0.0718	0.053208	0.065339	0.069370	0.074064
O3'	−0.6549	−0.663996	−0.659344	−0.643722	−0.655119
H3T	0.4396	0.440127	0.442018	0.431357	0.439079
P	1.1659	1.222739	1.222542	1.222350	1.222350
OP1	−0.7761	−0.791043	−0.791334	−0.791383	−0.791383
OP2	−0.7761	−0.791043	−0.791334	−0.791383	−0.791383
O5'	−0.4954	−0.519575	−0.516493	−0.514824	−0.514824
O3'	−0.5232	−0.535703	−0.528709	−0.527277	−0.527277
RMSD		0.020729	0.019251	0.022258	0.014550

Goodness-of-fit metrics[a]

	Step 1				Step 2			
	ISS	RSS	SE	RRMS	ISS	RSS	SE	RRMS
HF/6-31G*, N	17.656	0.021	0.00528	0.03466	17.656	0.022	0.00535	0.03510
HF/6-31G*, Y	17.637	0.021	0.00525	0.03447	17.637	0.021	0.00530	0.03478
MP2/6-31G*, Y	17.715	0.021	0.00527	0.03458	17.715	0.022	0.00534	0.03505
MM (ff86)	18.011	0.021	0.00524	0.03404	18.011	0.022	0.00533	0.03465

[a] ISS, initial sum of squares; RSS, residual sum of squares; $SE=\sqrt{RSS/N}$, standard error of the estimates; $RRMS=\sqrt{RSS/ISS}$, relative RMS due to ESP.

Table S2. Reproducibility of legacy minimization results by contemporary versions of AMBER.

Energy minimization by steepest descent in uniform gas phase using AMBER5 yielded the closest agreement with the reported geometries in ff94 derivation over other settings. The results in AMBER16 were obtained by turning off the Generalized Born implicit solvent (*igb=0*). In all cases, H5' and H3' were restrained in *trans* with bonded heavy atoms. minimizations were converged to an RMS value of 10^{-4} kcal mol^{-1} $Å^{-1}$ for the energy gradient. All parametric values are reported at the full (single) precision reported by the software.

Nucleobase + non-equivalenced C1'/H1'

DAN	**parm94**	**AMBER5**	**AMBER16**
C1'	0.0431	0.033003	0.032834
H1'	0.1838	0.181649	0.181715
N9	−0.0268	−0.027489	−0.027447
C8	0.1607	0.168151	0.168181
H8	0.1877	0.183301	0.183289
N7	−0.6175	−0.615563	−0.615574
C5	0.0725	0.074204	0.074189
C6	0.6897	0.680531	0.680556
N6	−0.9123	−0.906281	−0.906295
H61	0.4167	0.414959	0.414963
H62	0.4167	0.414959	0.414963
N1	−0.7624	−0.757827	−0.757845
C2	0.5716	0.573170	0.573199
H2	0.0598	0.057316	0.057312
N3	−0.7417	−0.734703	−0.734724
C4	0.3800	0.370344	0.370340
RMSD		0.005515	0.005530

DGN	**parm94**	**AMBER5**	**AMBER16**
C1'	0.0358	0.015110	0.015220
H1'	0.1746	0.173741	0.173741
N9	0.0577	0.075474	0.075520
C8	0.0736	0.070274	0.070204
H8	0.1997	0.200652	0.200477
N7	−0.5725	−0.573131	−0.572997
C5	0.1991	0.201781	0.201942
C6	0.4918	0.489288	0.489296
O6	−0.5699	−0.570944	−0.570949
N1	−0.5053	−0.496754	−0.496718
H1	0.3520	0.350324	0.350301
C2	0.7432	0.740021	0.739729
N2	−0.9230	−0.923258	−0.922955
H21	0.4235	0.422893	0.422815
H22	0.4235	0.422893	0.422815
N3	−0.6636	−0.657994	−0.657950
C4	0.1814	0.169354	0.169166
RMSD		0.007803	0.007824

DCN	**parm94**	**AMBER5**	**AMBER16**

C1'	−0.0116	−0.020074	−0.019945
H1'	0.1963	0.200679	0.200608
N1	−0.0339	−0.049126	−0.049423
C6	−0.0183	−0.019435	−0.019243
H6	0.2293	0.223869	0.223781
C5	−0.5222	−0.509065	−0.509247
H5	0.1863	0.184290	0.184294
C4	0.8439	0.844480	0.844565
N4	−0.9773	−0.981543	−0.981574
H41	0.4314	0.431685	0.431705
H42	0.4314	0.431685	0.431705
N3	−0.7748	−0.781912	−0.781861
C2	0.7959	0.813423	0.813377
O2	−0.6548	−0.659234	−0.659086
RMSD		0.008133	0.008128

DTN	**parm94**	**AMBER5**	**AMBER16**
C1'	0.0680	0.055726	0.055576
H1'	0.1804	0.182407	0.182462
N1	−0.0239	−0.030772	−0.030756
C6	−0.2209	−0.207199	−0.207161
H6	0.2607	0.254528	0.254509
C5	0.0025	−0.000117	−0.000128
C7	−0.2269	−0.258219	−0.258242
H71	0.0770	0.085179	0.085186
H72	0.0770	0.085179	0.085186
H73	0.0770	0.085179	0.085186
C4	0.5194	0.530955	0.530958
O4	−0.5563	−0.560812	−0.560811
N3	−0.4340	−0.438061	−0.438076
H3	0.3420	0.342959	0.342964
C2	0.5677	0.573099	0.573119
O2	−0.5881	−0.590308	−0.590316
RMSD		0.010670	0.010691

Deoxyribose (except C1'/H1') and phosphate

	parm94	**AMBER5**	**AMBER16**
H5T	0.4422	0.439492	0.439484
O5'	−0.6318	−0.625980	−0.625961
C5'	−0.0069	−0.000596	−0.000600
H5'1	0.0754	0.072962	0.072956
H5'2	0.0754	0.072962	0.072956
C4'	0.1629	0.160995	0.161094
H4'	0.1176	0.118194	0.118169
O4'	−0.3691	−0.363238	−0.363251
C3'	0.0713	0.076323	0.076272
H3'	0.0985	0.094381	0.094382

C2'	−0.0854	−0.087307	−0.087246
H2'1	0.0718	0.074065	0.074064
H2'2	0.0718	0.074065	0.074064
O3'	−0.6549	−0.655127	−0.655119
H3T	0.4396	0.439085	0.439079
P	1.1659	1.222352	1.222350
OP1	−0.7761	−0.791383	−0.791383
OP2	−0.7761	−0.791383	−0.791383
O5'	−0.4954	−0.514836	−0.514824
O3'	−0.5232	−0.527279	−0.527277
RMSD		0.014553	0.014550

Table S3. Comparison of fits to charge models between experimental and optimized *ab initio* structures.

Properties for each substance were computed following ESP fits with the MK scheme at the indicated theory and basis set. Parametric values in the shaded boxes are as reported by Singh and Kollman [13], using experimentally derived structures as referenced in their paper. Unshaded values were computed in this work using *ab initio* structures (in Z-matrix format) that have been geometry-optimized at the mp2/aug-cc-pVTZ level. The precision in the values is exactly as reported by Singh and Kollman or Gaussian. RRMS is the relative fit of the atomic charges to the ESP. RMSD refers to the differences between the shaded and unshaded values over all the atoms in each structure.

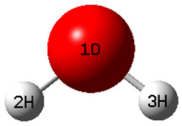
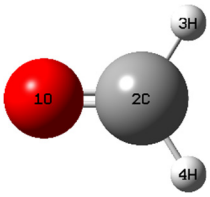
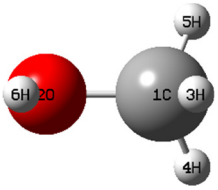
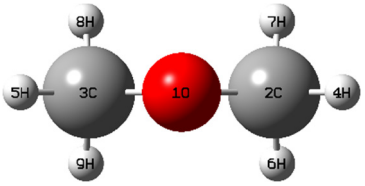
	Water HF/6-31G**		**Formaldehyde** HF/6-31G**		**Methanol** HF/6-31G**		**Dimethyl ether** HF/6-31G*	
								
Point group	C_{2v}		C_{2v}		C_s		C_{2v}	
Dipole, D	2.242	2.2365	2.79	2.7992	2.014	2.0173	1.7968	1.6395
Charge	1O −0.794	−0.793710	1O −0.463	−0.455295	1C 0.149	0.187178	1O −0.4038	−0.373840
	2H 0.397	0.396855	2C 0.421	0.402472	2O −0.656	−0.655165	2C 0.0095	−0.004309
	3H 0.397	0.396855	3H 0.021	0.026411	3H −0.001	−0.001455	3C 0.0095	−0.004309
			4H		4H 0.042	0.028724	4H 0.0799	0.077640
					5H 0.042	0.028724	5H 0.0799	0.077640
					6H 0.424	0.411994	6H 0.0562	0.057967
							7H 0.0562	0.055621
							8H 0.0562	0.055621
							9H 0.0562	0.057967
RRMS	0.105	0.10903	0.065	0.06466	0.134	0.13092	0.128	0.15227
RMSD	0.000		0.011		0.018		0.012	

Table S4. QM-optimized structures of nucleobase fragment analogs reproduce ff86 atomic charges.

Ab initio models of 9-methyl-R (R = adenine, guanine), 1-methyl-Y (Y = cytosine, thymine), and 1-aminodeoxyribose (ADR) were geometry-optimized at the HF/6-311++G(3df,2p), MP2/6-311++G(3df,2p) (purines and ADR) or MP2/aug-cc-pVTZ (pyrimidines) in Z-matrices. Constraints were imposed on the nucleobase structures to enforce symmetry in the C_s point group. Atom-centered charges were then computed by ESP fitting to the MK scheme at the HF/STO-3G level. Values reported by Singh and Kollman [13] (labeled REF) were used in deriving the atomic charges of nucleosides in the ff86 forcefield [22]. The atoms names and the precision in the reference charges follow the original literature.

9-methylpurines

9-CH_3-A				**9-CH_3-G**			
Atom	**REF**	**HF**	**MP2**	**Atom**	**REF**	HF	MP2
N1	−0.774	−0.744875	−0.728376	N1	−0.729	−0.756373	−0.729675
C2	0.661	0.608821	0.579707	C2	0.871	0.857102	0.843982
N3	−0.728	−0.701292	−0.678701	N3	−0.709	−0.716057	−0.697809
C4	0.546	0.534725	0.503614	C4	0.391	0.428305	0.400295
C5	−0.097	−0.008791	0.004678	C5	−0.060	−0.116132	−0.092204
C6	0.769	0.728420	0.710658	C6	0.690	0.743430	0.696486
N7	−0.543	−0.572461	−0.560941	N7	−0.543	−0.524076	−0.509725
C8	0.263	0.299245	0.269547	C8	0.266	0.232672	0.199470
N9	−0.063	−0.091396	−0.070974	N9	−0.022	0.024654	0.035340
N6	−0.768	−0.784211	−0.775230	O6	−0.458	−0.466985	−0.450154
H2	−0.032	−0.022335	−0.014404	N2	−0.778	−0.773501	−0.766500
H8	0.062	0.052360	0.059546	H1	0.336	0.345623	0.334649
C9M	−0.431	−0.473507	−0.475827	H8	0.046	0.049594	0.058134
HN6A	0.335	0.323998	0.322231	HN2A	0.339	0.328853	0.328171
HN68	0.324	0.338501	0.335330	HN2B	0.325	0.328276	0.325670
HC9A	0.158	0.167293	0.169263	C9M	−0.459	−0.477475	−0.461568
HC9B	0.159	0.172753	0.174939	HC9A	0.163	0.160717	0.158149
HC9C	0.159	0.172753	0.174939	HC9B	0.164	0.165686	0.163645
				HC9C	0.164	0.165686	0.163645
Σ	0.000	0.000001	−0.000001	Σ	−0.003	−0.000001	0.000001
RMSD		0.033232	0.041090	RMSD		0.025861	0.024423

1-methylpyrimidines

1-CH_3-C				**1-CH_3-T**			
Atom	**REF**	**HF**	**MP2**	**Atom**	**REF**	HF	MP2
N1	−0.187	−0.184349	−0.171619	N1	−0.233	−0.180511	−0.160248
C2	0.859	0.917796	0.885081	C1	0.849	0.849187	0.811385
N3	−0.86	−0.873709	−0.865841	N3	−0.851	−0.866361	−0.832776
C4	0.935	0.927792	0.933771	C4	0.809	0.834598	0.792023
C5	−0.576	−0.567869	−0.571429	C5	−0.176	−0.164261	−0.149743
C6	0.185	0.170583	0.172870	C6	0.034	0.005720	0.008643
O2	−0.508	−0.515315	−0.505440	O2	−0.488	−0.496127	−0.480788
N4	−0.834	−0.852182	−0.853372	O4	−0.464	−0.474602	−0.460371
C1M	−0.289	−0.354829	−0.369067	C5M	−0.382	−0.392113	−0.402636

HN4A	0.153	0.153567	0.152251	C1M	−0.251	−0.329030	−0.340033
HN4B	0.098	0.095509	0.098405	H3	0.355	0.356185	0.344152
H5	0.351	0.350757	0.350260	H6	0.134	0.125927	0.126969
H6	0.329	0.333776	0.333317	HC5A	0.119	0.116421	0.117727
HC1A	0.116	0.131746	0.136225	HC5B	0.111	0.116394	0.117658
HC1B	0.115	0.134980	0.138363	HC5C	0.111	0.116394	0.117658
HC1C	0.115	0.131746	0.136225	HC1A	0.118	0.131571	0.134371
				HC1B	0.103	0.125304	0.128004
				HC1C	0.103	0.125304	0.128004
Σ	0.002	−0.000001	0.000000	Σ	0.001	0.000000	−0.000001
RMSD		0.024562	0.024159	RMSD		0.026102	0.032364

1-aminodeoxyribose

Atom	REF	HF	MP2
O4	−0.368	−0.398285	−0.407510
C1'	0.558	0.645792	0.636814
C4'	0.036	0.033739	0.076483
C2'	−0.307	−0.319766	−0.299220
C3'	0.233	0.324864	0.270350
N	−0.869	−0.960932	−0.944870
O3'	−0.508	−0.551424	−0.522766
C5'	0.118	0.238037	0.200146
H1'	0.009	−0.017274	−0.015508
HHA	0.305	0.330877	0.326358
HHB	0.329	0.355927	0.349148
H2'	0.081	0.080602	0.077524
H2'	0.081	0.085355	0.082789
H3'	0.025	0.004437	0.015281
H4'	0.056	0.038744	0.034161
H03'	0.306	0.319956	0.304066
O5'	−0.404	−0.507202	−0.473610
H5'	0.003	−0.022468	−0.017577
H5'	0.039	0.007728	0.014764
H05'	0.279	0.311293	0.293177
Σ	0.002	0.000000	0.000000
RMSD		0.053999	0.039812

Table S5. Final RESP-fitted atomic charges and comparison with literature.

Charges given for the atoms that float (nucleobase and C1'/H1') in the RESP fit. The shared charges (remainder of the deoxyribose and phosphate) take on parm94 values such as those shown in Tables S1 and S2. Values are shown at the full precision computed or as reported in the literature. RMSD values relative to the charges reported in this work are reported at the precision of the literature values.

Deoxyuridylate (DU)

Atom	This work
C1'	0.070684
H1'	0.174261
N1	0.019695
C6	−0.125917
H6	0.246475
C5	−0.357841
H5	0.176562
C4	0.600792
O4	−0.575617
N3	−0.376442
H3	0.319106
C2	0.534284
O2	−0.584444

Abasic nucleotide (DABA)

Atom	This work
C1'	−0.147704
H1'1	0.134652
H1'2	0.134652

5-methyl-deoxycytidylate (D5MC)

Atom	This work	Lankas et al [34]	Carvalho et al [29]	Marco et al [32]	Schneider et al [31]
C1'	−0.008195	−0.011600	−0.0116	−0.0116	0.0706
H1'	0.205216	0.196300	0.1963	0.1963	0.1591
N1	−0.062430	−0.088800	−0.0389	−0.0339	−0.1389
C6	−0.160421	−0.082693	−0.1485	−0.0183	−0.1438
H6	0.261137	0.231353	0.2729	0.2293	0.2445
C5	−0.069175	−0.157695	−0.1927	−0.3185	−0.1052
C7	−0.244302	−0.310870	−0.2779	−0.3646	−0.2507
H71	0.075076	0.097824	0.0943	0.1157	0.0793
H72	0.075076	0.097824	0.0943	0.1157	0.0793
H73	0.075076	0.097824	0.0943	0.1157	0.0793
C4	0.617608	0.806980	0.7994	0.8439	0.7235
N4	−0.843162	−0.976814	−0.9571	−0.9773	−0.9037
H41	0.397341	0.428276	0.4163	0.4314	0.3978
H42	0.397341	0.428276	0.4163	0.4314	0.3978

N3	−0.723926	−0.794899	−0.7750	−0.7748	−0.7759
C2	0.785741	0.827845	0.7401	0.7959	0.8559
O2	−0.656402	−0.667531	−0.6009	−0.6548	−0.6507
RMSD		0.074840	0.0697	0.1089	0.0477

Deoxyinosinate (DI)

Atom	This work	Lankas et al [34]	Marco et al [32]
C1'	0.083144	0.043100	0.0431
H1'	0.157553	0.183800	0.1838
N9	−0.009820	−0.009401	−0.0138
C8	0.109175	0.077630	0.0783
H8	0.205646	0.211563	0.1773
N7	−0.577677	−0.538290	−0.5367
C5	0.209141	0.049936	0.1663
C6	0.522966	0.586826	0.5066
O6	−0.573726	−0.581501	−0.5472
N1	−0.437860	−0.497411	−0.4092
H1	0.336481	0.331128	0.3234
C2	0.290652	0.421687	0.2284
H2	0.149789	0.144911	0.1571
N3	−0.598230	−0.715215	−0.5392
C4	0.254365	0.429337	0.3033
RMSD		0.081416	0.0359

2-amino-deoxyribosylpurine nucleotide (D2AP)

Atom	This work	Case[a]	Remington et al [33]
C1'	0.056130	0.043100	–
H1'	0.160136	0.183800	–
N9	−0.012219	−0.116300	−0.047936
C8	0.181055	0.261000	0.150546
H8	0.182007	0.131000	0.165748
N7	−0.640042	−0.635000	−0.598370
C5	0.153173	0.090000	0.156676
C6	0.200186	0.234000	0.157719
H6	0.152956	0.137000	0.150049
N1	−0.751904	−0.748000	−0.674915
C2	1.012880	0.981000	0.879792
N2	−1.009343	−0.961000	−0.930086
H21	0.425372	0.400500	0.394869
H22	0.425372	0.400500	0.394869
N3	−0.758104	−0.758000	−0.682870
C4	0.343944	0.478000	0.378610
RMSD		0.055083	0.056490

[a] Unpublished data from Dr. David Case at http://amber.manchester.ac.uk/

2,6-diamino-ribosylpurine nucleotide (DDAP) = 2-amino-adenylate (D2AA)

Atom	This work	Lankas et al [34]
C1'	0.022913	0.0431
H1'	0.171954	0.1838
N9	0.079158	0.025808
C8	0.104267	0.118767
H8	0.190196	0.189502
N7	−0.613923	−0.648666
C5	0.160356	0.32085
C6	0.551922	0.399885
N6	−0.842037	−0.828851
H61	0.401201	0.408105
H62	0.401201	0.408105
N1	−0.759932	−0.662095
C2	0.901869	0.82052
N2	−0.930769	−0.898822
H21	0.404765	0.382157
H22	0.404765	0.382157
N3	−0.732276	−0.669702
C4	0.205970	0.14698
RMSD		0.0665

7-deaza-deoxyguanidylate (D7AG)

Atom	This work
C1'	−0.018878
H1'	0.185889
N9	0.140071
C8	−0.232052
H8	0.243381
C7	−0.424411
H7	0.236499
C5	−0.030296
C6	0.515155
O6	−0.588116
N1	−0.474387
H1	0.335679
C2	0.792251
N2	−0.980022
H21	0.434283
H22	0.434283
N3	−0.699623
C4	0.251894

Iso-deoxyguanidylate (iDG)

Atom	This work	Bachmann et al [30]
C1'	0.070203	0.035863
H1'	0.163308	0.174553
N9	0.023544	−0.588162
C8	0.142151	0.326728
H8	0.187259	0.148758
N7	−0.623484	−0.616939
C5	0.219531	0.070026
C6	0.340225	0.585878
N6	−0.820639	−0.868264
H61	0.420274	0.471138
H62	0.420274	0.452016
N1	−0.420543	−0.751656
H1	0.337469	0.455052
C2	0.770406	1.031195
O2	−0.660974	−0.647017
N3	−0.688186	−0.867736
C4	0.240781	0.712059
RMSD		0.235853

5-methyl-iso-deoxycytidylate (D5MiC)

Atom	This work
C1'	0.151775
H1'	0.106839
N1	−0.066254
C6	−0.271426
H6	0.264632
C5	−0.019659
C5M	−0.292265
H71	0.089458
H72	0.089458
H73	0.089458
C4	0.761736
O4	−0.621559
N3	−0.743440
C2	0.674113
N2	−0.920754
H21	0.414744
H22	0.414744

Table S6. Perturbation of global fitting on RESP-fitted charges.

RESP-fitted charges were computed for the following residues as a global fit with the four canonical bases as described in the text. In one case ("9+4"), all nine canonical bases were fitted simultaneously with the canonical base set. In the other case ("1+4"), only the shown residue was fitted with the canonical base set. All other settings were identical. Values are shown for the variable atoms (nucleobase and C1'/H1') at full single precision. The shared atoms are per parm94.

Deoxyinosinate (DI)

Atom	"9+4"	"1+4"
C1'	0.083144	0.083144
H1'	0.157553	0.157553
N9	−0.009820	−0.009820
C8	0.109175	0.109175
H8	0.205646	0.205646
N7	−0.577677	−0.577677
C5	0.209141	0.209141
C6	0.522966	0.522966
O6	−0.573726	−0.573726
N1	−0.437860	−0.437860
H1	0.336481	0.336481
C2	0.290652	0.290652
H2	0.149789	0.149789
N3	−0.598230	−0.598230
C4	0.254365	0.254365
RMSD		0.000000

2-amino-deoxyribosylpurine nucleotide (D2AP)

Atom	"9+4"	"1+4"
C1'	0.056130	0.056134
H1'	0.160136	0.160136
N9	−0.012219	−0.012222
C8	0.181055	0.181055
H8	0.182007	0.182006
N7	−0.640042	−0.640035
C5	0.153173	0.153155
C6	0.200186	0.200204
H6	0.152956	0.152952
N1	−0.751904	−0.751913
C2	1.012880	1.012888
N2	−1.009343	−1.009349
H21	0.425372	0.425374
H22	0.425372	0.425374
N3	−0.758104	−0.758110
C4	0.343944	0.343951
RMSD		0.000008

5-methyl-deoxycytidylate (D5MC)

Atom	"9+4"	"1+4"
C1'	−0.008195	−0.008193
H1'	0.205216	0.205216
N1	−0.062430	−0.062444
C6	−0.160421	−0.160403
H6	0.261137	0.261133
C5	−0.069175	−0.069181
C5M	−0.244302	−0.244313
H71	0.075076	0.075079
H72	0.075076	0.075079
H73	0.075076	0.075079
C4	0.617608	0.617612
N4	−0.843162	−0.843162
H41	0.397341	0.397341
H42	0.397341	0.397341
N3	−0.723926	−0.723930
C2	0.785741	0.785748
O2	−0.656402	−0.656403
RMSD		0.000007

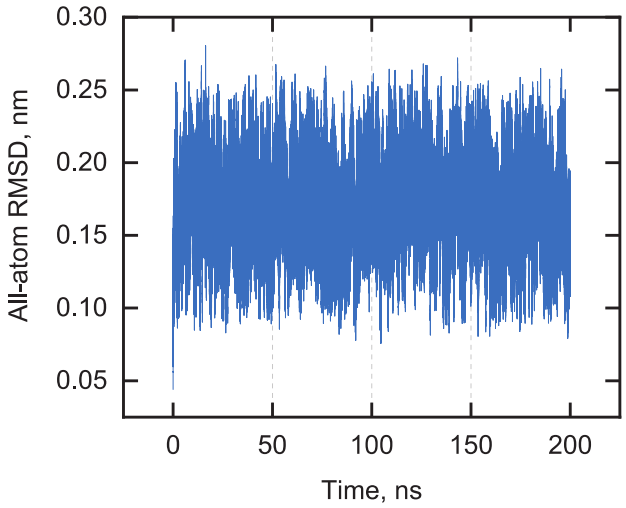


Figure S1. Equilibration of the DNA hairpin in unrestrained MD simulations. RMSD of all atomic positions in the hairpin following 200 ns of unrestrained simulation. The trajectory for the d(2AP):dT hairpin is shown; others are similar. Dashes delimit 50-ns blocks of trajectories for averaging of replicate structures starting at 50 ns.