Electronic Supplementary Information

DPT tautomerisation of the wobble guanine·thymine DNA base mispair is not mutagenic: QM and QTAIM arguments¹

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¹ Dedicated to Dr. Viktor I. Danilov (1936-2014), our colleague and collaborator, founder of the quantum biophysics in Ukraine.

Table S1 Electron-topological, structural, vibrational and energetical characteristics of the intermolecular H-bonds revealed in the wG·T, wG*.T* and TS_{wG·T↔wG*.T*} and polar characteristics of the latters obtained at the B3LYP/6-311++G(d,p) level of theory in vacuum

Complex	AH···B H-bond	ρ^a	$\Delta\rho^b$	$100\cdot\epsilon^c$	$d_{A\cdots B}^d$	$d_{H\cdots B}^e$	Δd_{AH}^f	$\angle AH\cdots B^g$	$\Delta\nu^h$	E_{HB}^i	μ^j
wG·T	N3H···O6	0.032	0.107	3.13	2.866	1.837	0.024	171.8	389.6	6.17	7.99
	N1H···O2	0.035	0.118	4.43	2.833	1.806	0.016	176.8	291.9	5.24	
wG*.T*	O6H···N3	0.052	0.098	5.11	2.722	1.710	0.044	179.7	838.1	9.32	7.71
	O2H···N1	0.084	0.072	4.73	2.580	1.526	0.090	173.0	1645.6	13.22	
TS_{wG·T↔wG*.T*}	O6H···N3	0.064	0.092	4.86	2.659	1.628	-	178.9	-	10.87*	7.86
	N2H···O2	0.008	0.038	458.00	3.140	2.421	-	127.7	-	1.91**	

^aThe electron density at the (3,-1) BCP of the H-bond, a.u.

^bThe Laplacian of the electron density at the (3,-1) BCP of the H-bond, a.u.

^cThe ellipticity at the (3,-1) BCP of the H-bond

^dThe distance between the A (H-bond donor) and B (H-bond acceptor) atoms of the AH···B H-bond, Å

^eThe distance between the H and B atoms of the AH···B H-bond, Å

^fThe elongation of the H-bond donating group AH upon the AH···B H-bonding, Å

^gThe H-bond angle, degree

^hThe redshift of the stretching vibrational mode $\nu(AH)$ of the AH H-bonded group, cm^{-1}

ⁱEnergy of the H-bonds, calculated by Iogansen's [1], Nikolaenko-Bulavin-Hovorun (marked with an asterisk) [2] or Espinose-Molins-Lecomte (marked with a double asterisk) [3,4] formulas, $\text{kcal}\cdot\text{mol}^{-1}$

^jThe dipole moment of the complex, D

Table S2 Electron-topological and structural characteristics of the intermolecular H-bonds revealed in the 9 key points and polar characteristics of the latters obtained at the B3LYP/6-311++G(d,p) level of theory in vacuum along the IRC of the $wG\cdot T \leftrightarrow wG^*\cdot T^*$ tautomerisation *via* the DPT

Complex	AH...B H-bond/A-H-B covalent bond	ρ	$\Delta\rho$	$100\cdot\epsilon$	$d_{A\cdots B}$	$d_{H\cdots B}$	$\angle AH\cdots B$	μ
Key point 1 (-8.63 Bohr): wG·T	N3H...O6	0.032	0.107	3.13	2.866	1.837	171.8	7.99
	N1H...O2	0.035	0.118	4.43	2.833	1.806	176.8	
Key point 2 (-1.41 Bohr): $\Delta\rho_{O6\cdots H}=0$	N3H...O6	0.123	0.000	1.93	2.583	1.325	179.3	7.95
	N1H...O2	0.079	0.169	3.67	2.552	1.497	172.9	
	N2H...O2	0.009	0.038	68.69	3.142	2.395	130.2	
Key point 3 (-1.29 Bohr): $\rho_{O6-H}=\rho_{H-N3}$	N3-H-O6	0.145	-0.212	3.68	2.585	1.320	179.3	8.02
	N1H...O2	0.081	0.166	3.65	2.550	1.490	172.9	
	N2H...O2	0.009	0.038	68.77	3.141	2.394	130.2	
Key point 4 (-0.98 Bohr): $\Delta\rho_{H\cdots N3}=0$	O6H...N3	0.100	0.000	4.21	2.602	1.464	179.3	8.40
	N1H...O2	0.087	0.155	3.57	2.541	1.464	172.7	
	N2H...O2	0.009	0.038	70.59	3.140	2.396	129.9	
Key point 5 (-0.31 Bohr): $\Delta\rho_{H\cdots O2}=0$	O6H...N3	0.070	0.078	4.79	2.651	1.601	178.5	8.21
	N1H...O2	0.135	0.000	2.73	2.491	1.297	173.1	
	N2H...O2	0.009	0.038	154.66	3.140	2.417	127.9	
Key point 6 (-0.17 Bohr): $\rho_{N1-H}=\rho_{H-O2}$	O6H...N3	0.067	0.085	4.83	2.654	1.614	178.7	8.00
	N1-H-O2	0.164	-0.273	3.59	2.490	1.269	173.1	
	N2H...O2	0.009	0.038	241.66	3.139	2.418	127.8	
Key point 7 (0.00 Bohr): TS_{wG·T↔wG*·T*}	O6H...N3	0.064	0.092	4.86	2.659	1.628	178.9	7.86
	N2H...O2	0.008	0.038	457.99	3.140	2.421	127.7	
Key point 8 (0.18 Bohr): $\Delta\rho_{N1\cdots H}=0$	O6H...N3	0.062	0.095	4.91	2.668	1.644	179.0	7.80
	O2H...N1	0.115	0.000	4.19	2.508	1.404	172.9	
Key point 9 (1.17 Bohr): wG*·T*	O6H...N3	0.052	0.098	5.11	2.722	1.710	179.7	7.71
	O2H...N1	0.084	0.072	4.73	2.580	1.526	173.0	

Notes: for footnote definitions see Table 1.

Table S3 Energetical and kinetic characteristics of the $wG \cdot T \leftrightarrow wG^* \cdot T^*$ tautomerisation *via* the DPT obtained at the different levels of QM theory for the geometry calculated at the B3LYP/6-311++G(d,p) level of QM theory *in vacuo*

Level of QM theory	ΔG^a	ΔE^b	$\Delta \Delta G_{TS}^c$	$\Delta \Delta E_{TS}^d$	$\Delta \Delta G^e$	$\Delta \Delta E^f$		τ^g
						kcal·mol ⁻¹	cm ⁻¹	
MP2/6-311++G(2df,pd)	10.87	11.89	9.66	12.23	-1.20	0.34	118.6	$1.77 \cdot 10^{-14}$
MP2/6-311++G(3df,2pd)	11.46	12.48	10.34	12.90	-1.12	0.42	148.3	$2.04 \cdot 10^{-14}$
MP2/cc-pVTZ	10.83	11.85	9.74	12.30	-1.09	0.45	158.2	$2.14 \cdot 10^{-14}$
MP2/cc-pVQZ	11.28	12.30	10.20	12.76	-1.09	0.46	159.8	$2.15 \cdot 10^{-14}$

^aThe relative Gibbs free energy of the $wG^* \cdot T^*$ base pair ($\Delta G_{wG \cdot T} = 0.00$; T=298.15 K), kcal·mol⁻¹

^bThe relative electronic energy of the $wG^* \cdot T^*$ base pair ($\Delta E_{wG \cdot T} = 0.00$), kcal·mol⁻¹

^cThe Gibbs free energy of activation for the forward reaction of the $wG \cdot T \rightarrow wG^* \cdot T^*$ tautomerisation *via* the DPT, kcal·mol⁻¹

^dThe activation electronic energy for the forward reaction of the $wG \cdot T \rightarrow wG^* \cdot T^*$ tautomerisation, kcal·mol⁻¹

^eThe Gibbs free energy of activation for the reverse reaction of the $wG \cdot T \rightarrow wG^* \cdot T^*$ tautomerisation, kcal·mol⁻¹

^fThe activation electronic energy for the reverse reaction of the $wG \cdot T \rightarrow wG^* \cdot T^*$ tautomerisation

^gThe lifetime of the $wG^* \cdot T^*$ base mispair, s

The frequency of the vibrational mode in the $wG^* \cdot T^*$ base pair, which becomes imaginary in the $TS_{wG \cdot T \leftrightarrow wG^* \cdot T^*}$ of the $wG \cdot T \leftrightarrow wG^* \cdot T^*$ DPT tautomerisation, is equal to 2050.8 cm⁻¹ and the zero-point vibrational energy associated with this normal mode is equal to 2.93 kcal·mol⁻¹ or 1025.4 cm⁻¹ (B3LYP/6-311++G(d,p) level of QM theory).

The periods T ($2.03 \cdot 10^{-12}$, $1.30 \cdot 10^{-12}$, $5.53 \cdot 10^{-13}$, $4.77 \cdot 10^{-13}$, $3.48 \cdot 10^{-13}$ and $3.16 \cdot 10^{-13}$ s, respectively) of all 6 low-frequency intermolecular vibrations in the $wG^* \cdot T^*$ DNA base mispair (16.5, 25.6, 60.3, 69.9, 96.0 and 105.6 cm⁻¹) are significantly less than the lifetime of the $wG^* \cdot T^*$ base mispair.

Table S4 Interbase interaction energies (in kcal/mol) for the studied base pairs in vacuum obtained at the MP2/6-311++G(2df,pd)//B3LYP/6-311++G(d,p) level of theory

Complex	$-\Delta E_{\text{int}}^{\text{a}}$	$\Sigma E_{\text{HB}}^{\text{b}}$	$\Sigma E_{\text{HB}}/ \Delta E_{\text{int}} , \%$	$-\Delta G_{\text{int}}^{\text{c}}$
wG·T	16.71	11.41	68.3	4.74
wG*·T*	28.11	22.55	80.2	16.85

^aThe counterpoise-corrected electronic interaction energy

^bThe total energy of the intermolecular H-bonds

^cThe counterpoise-corrected Gibbs free energy of interaction (T=298.15 K)

Fig. S1 Geometric structures of the 9 key points describing the evolution of the wG·T $\leftrightarrow$ wG*·T* tautomerisation *via* the DPT along the IRC obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*. Coordinates of the 9 key points are presented for each structure. The dotted lines indicate AH $\cdots$ B H-bonds, while continuous lines show covalent bonds (their lengths are presented in angstroms). Carbon atoms are in light-blue, nitrogen in dark-blue, hydrogen in grey and oxygen in red.

Fig. S2 Profiles of: **(a)** the electronic energy E and **(b)** the first derivative of the electronic energy with respect to the IRC - $dE/dIRC$ along the IRC of the $wG \cdot T \leftrightarrow wG^* \cdot T^*$ tautomerisation *via* the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

Fig. S3 Profile of the dipole moment μ along the IRC of the $wG \cdot T \leftrightarrow wG^* \cdot T^*$ tautomerisation *via* the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

Fig. S4 Profiles of: (a) the electron density ρ ; (b) the Laplacian of the electron density $\Delta\rho$; (c) the ellipticity ϵ and (d) the energy of the H-bond E_{HB} , estimated by the EML formula [3,4], at the (3,-1) BCPs of the intermolecular covalent and hydrogen bonds along the IRC of the wG·T ↔ wG*·T* tautomerisation via the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

Fig. S5 Profiles of: **(a)** the distance $d_{A \cdots B}$ between the electronegative A and B atoms; **(b)** the distance $d_{AH/HB}$ between the hydrogen and electronegative A or B atoms and **(c)** the angle $\angle AH \cdots B$ of the intermolecular covalent and hydrogen bonds along the IRC of the $wG \cdot T \leftrightarrow wG^* \cdot T^*$ tautomerisation *via* the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

Fig. S6 Profiles of: **(a)** the electron density ρ ; **(b)** the Laplacian of the electron density $\Delta\rho$; **(c)** the ellipticity ϵ and **(d)** the energy E_{HB} , estimated by the EML formula [3,4], at the (3,-1) BCP of the third $N2H\cdots O2$ H-bond along the IRC of the $wG\cdot T \leftrightarrow wG^*\cdot T^*$ tautomerisation *via* the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

Fig. S7 Profiles of: (a) the distance $d_{N2 \cdots O2}$ between the N2 and O2 atoms of the $N2H \cdots O2$ H-bond; (b) the distances d_{N2H} and $d_{H \cdots O2}$ of the $N2H \cdots O2$ H-bond and (c) the angle $\angle N2H \cdots O2$ of the $N2H \cdots O2$ H-bond along the IRC of the $wG \cdot T \leftrightarrow wG^* \cdot T^*$ tautomerisation *via* the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

Fig. S8 Profiles of the NBO charges of the hydrogen atoms involved in the $\text{N3H}_\text{I}\cdots\text{O6}/\text{O6H}_\text{I}\cdots\text{N3}$, $\text{N1H}_\text{II}\cdots\text{O2}/\text{O2H}_\text{II}\cdots\text{N1}$ and $\text{N2H}_\text{III}\cdots\text{O2}$ H-bonds along the IRC of the $\text{wG}\cdot\text{T} \leftrightarrow \text{wG}^*\cdot\text{T}^*$ tautomerisation *via* the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

Fig. S9 Profiles of: (a) the distance $R(\text{H-H})$ between the glycosidic hydrogens and (b) the α_1 ($\angle\text{N1H(T)H(G)}$) and α_2 ($\angle\text{N9H(G)H(T)}$) glycosidic angles along the IRC of the $\text{wG}\cdot\text{T} \leftrightarrow \text{wG}^*\cdot\text{T}^*$ tautomerisation *via* the DPT obtained at the B3LYP/6-311++G(d,p) level of theory *in vacuo*.

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