The First Stage of Radiolysis of Solvated DNA by High Energy Transfer Particles

Insights from First Principles Simulations

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SUPPLEMENTARY INFORMATION

Computational details

General computational parameters.

Model (GR-CR)_{wat} have been prepared in was prepared by running classical molecular dynamics simulations with the AMBER package¹. We constructed a guanine-cytosine ribonucleosides dimer solvated by 50 water molecules. This systems was equilibrated and optimized at the QM/MM level with the deMon2k program. The final structure was used for subsequent electron dynamics simulations. Models G, GR, GR-C have been generated from this (GR-CR)_{wat} structure by removing unnecessary atoms.

Model (DNA)_{wat} was prepared by running classical molecular dynamics simulations with the AMBER package. The DNA model was solvated in a 12x12x12 Å cubic box and 12 sodium counter-ions were included to ensure electric neutrality. Subsequently, water molecules and the full system were optimized in a total of 4,000 optimization steps. MD simulation was launched from this optimized structure. We used a time step of 2fs to propagate the Newton equations of motion. Non-bonded interactions were evaluated with the Particle Mesh Ewald method using a grid spacing of 1 Å and a cutoff of 10 Å for calculating the direct space summation of electrostatic interactions. Thermal equilibration was achieved by first running a 200 ps NVT simulation and 200 ps NPT simulation with strong harmonic restraints (50 kcal/mol/Å²) on DNA atoms positions. This was followed by five successive 100 ps MD trajectories in the NPT ensemble during which the harmonic restraints were gradually decreased: 20, 10, 5 and finally 1 kcal/mol/Å². The system was finally relaxed for 11 ns without any constraint. The final structure was taken as starting structure for QM/MM simulations.

QM/M simulations have been carried out with the in-deMon2k² implementation³. The molecular system extracted from MD simulations has been converted to deMon2k format. The QM region was defined including all DNA atoms and all water molecules having at least one atom situated with less than 2.1 Å from DNA.

Real-Time TDDFT simulations

All the electron dynamics simulations have been carried out with a developer version of the deMon2k program (version 4.2.5)⁴. Time propagation was operated by the second order Magnus propagator coupled⁵⁻⁶ to a predictor/corrector algorithm⁷ with a time step of 0.5 or of 1 as. We relied either on Chebyshev or on Taylor expansions to estimate the exponential of the Hamiltonian matrix⁵. The Scalapack library⁸ was used to carry out Taylor expansions (including 40 to 45 terms depending on the systems

simulated). XC energies and potentials have been calculated by numerical integration over adaptive Levedev grids providing an accuracy on the diagonal elements of the XC matrix of 10^{-7} or 10^{-8} Ha⁹. Population analyses have been carried out on-the-fly every 5 as following a Hirshfeld¹⁰ partitioning scheme. The kinetic energy density was also integrated over atoms. The expression of KED (K) reads¹¹:

$$K(r) = L(r) + G(r)$$
, where $L(r) \equiv -0.25\nabla^2 \rho(r)$ and $G(r) \equiv \frac{1}{8} \sum_{i=1,3} \nabla \rho_i(r) \cdot \nabla \rho_i(r) / \rho_i(r)$

Integration of K over the entire space leads to the total electron kinetic energies while L, which can locally takes positive or negative values globally integrates to zero. When the Laplacian contribution is integrated over atoms (defined here by the Hirshfeld scheme) we found that the integrated values are already close to zero (typically 10^{-2} Ha). The gradient component of the kinetic energy is systematically much larger than Laplacian contribution at the level of atoms.

Mathematical expression of Complex Absorbing Potentials

The CAP can be seen as a virtual detection screen. The shape of the CAP is inspired by the work of Reference ¹². The total CAP function is written as a superposition of atom centered spherical CPA:

$$CAP(R) = \min_{a} CAP_{a}(R)$$

$$CAP_{a}(R) = \begin{cases} 0 & \text{for } R < R^{\circ} \\ V^{max} \sin^{2} \left(\frac{\pi}{2W} (R - R^{\circ}) \right) \text{for } & R^{\circ} + W < R < R^{\circ} \\ V^{max} & R > R^{\circ} + W \end{cases}$$

where V^{max} is the maximum value of the absorbing potential, W is the width of increase of the atomic IAP and R° is the distance threshold at which starts the atomic IAP. In extensive preliminary tests we defined adequate values for these parameters. These parameters ensure that in absence of IoR the total energy of the molecule is conserved within 10⁻⁸ Ha during RT-TDDFT simulations launched from stationary electron densities. The number of electron is also preserved up to 10⁻⁵ e-. Therefore CAP doesn't affect the ground state density. On the other hand IAP must be placed in region where basis functions permit to describe emitted electrons. The KS matrix elements for CAP were calculated by numerical integration on a grid of points. We have used fixed grids built on 200 radial shells and 1202 angular Lebedev grid points per shell. Ideally CAP would remove only unbound electrons and not loosely bound electrons. In fact some Rydberg states can be extremely diffuse and the electrons reaching these states might be absorbed by the CAP. This is a possible limitation of the methodology used in this work that the reader should be aware of.

		Deposited energy (Ha)			
	kinetic energy (MeV)	G	GR	GR-C	(GR-CR) _{wat}
Trajectory 1	1	2.909880	2.530002	2.619163	3.295091
	0.5	3.869884	3.263801	3.388662	4.307208
	0.1	4.109813	3.506874	3.623262	4.467893
	0.01	3.184676	2.869052	2.931518	3.678523
Trajectory 2	1	3.062625	3.243912	3.367992	6.555885
	0.5	3.997376	4.310461	4.354313	8.927183
	0.1	3.925396	4.220624	4.208716	7.996797
	0.01	3.036949	3.268571	3.203728	4.693960
Trajectory 3	1	2.423658	3.164707	3.234728	3.487375
	0.5	3.073826	4.091788	4.270945	4.374233
	0.1	3.124636	4.140236	4.185914	4.323178
	0.01	2.512564	3.042405	3.214836	2.980710
Average energy	1	76.16	81.08	83.64	120.98
deposition (eV)	0.5	99.24	105.81	108.97	159.71
	0.1	101.22	107.64	109.01	152.27
	0.01	79.22	83.26	84.81	102.98

Table S1: Energy deposited on guanine models for four projectile kinetic energy (He²⁺). Note that the averages are given in eV.



Figure S1: energy profiles for collision of models G (orange), GR (red), GR-C (green) and (GR-CR)_{wat} (blue) with 0.1 MeV He²⁺ for trajectories sets 2 (left) and 3 (right, see Scheme 1 of the main text).



Figure S2: collision of the circled water molecule by the projectile in the three propagation trajectories. Note that none of the water molecules apart from the circled one, are struck by the projectiles.



Figure S3: fragment charges along collision dynamics by a 1 MeV He²⁺ projectile. The collision takes place at 267 as. Color code for fragment charge: guanine base in black, ribose (guanine) in red, cytosine base in green, ribose (cytosine) in blue and water molecules in yellow. The total charge is shown is the dashed violet line. Plain, dashed and dashed-dotted lines correspond respectively to the propagation trajectories 1, 2 and 3 shown in Scheme 1 (main article). From top to bottom: models A, B C and D (not showing water charges for clarity).



Figure S4: fragment charges along collision dynamics by a 0.5 MeV He²⁺ projectile. The collision takes place at 377 as. Color code for fragment charge: guanine base in black, ribose (guanine) in red, cytosine base in green, ribose (cytosine) in blue and water molecules in yellow. The total charge is shown is the dashed violet line. Plain, dashed and dashed-dotted lines correspond respectively to the propagation trajectories 1, 2 and 3 shown in Scheme 1 (main article). From top to bottom: models A, B C and D (not showing water charges for clarity).



Figure S5: fragment charges along collision dynamics by a 0.1 MeV He²⁺ projectile. The collision takes place at 846 as. Color code for fragment charge: guanine base in black, ribose (guanine) in red, cytosine base in green, ribose (cytosine) in blue and water molecules in yellow. The total charge is shown is the dashed violet line. Plain, dashed and dashed-dotted lines correspond respectively to the propagation trajectories 1, 2 and 3 shown in Scheme 1 (main article). From top to bottom: models A, B C and D (not showing water charges for clarity).



Figure S6: fragment charges along collision dynamics by a 0.01 MeV He²⁺ projectile. The collision takes place at 2,200 as. Color code for fragment charge: guanine base in black, ribose (guanine) in red, cytosine base in green, ribose (cytosine) in blue and water molecules in yellow. The total charge is shown is the dashed violet line. Plain, dashed and dashed-dotted lines correspond respectively to the propagation trajectories 1, 2 and 3 shown in Scheme 1 (main article). From top to bottom: models A, B C and D (not showing water charges for clarity).



Figure S7: Ionization time length as a function of the speed of the projectile for the five molecular fragment collided in model E. violet crosses: first fragment (H₂O); orange crosses: second fragment (cytosine); blue crosses: third fragment (thymine); blue and green points: fourth and fifth collided fragments.



Figure S8: charge fluctuations of the molecular fragments composing the QM region upon collision with 0.01 MeV proton and helium nuclei (left and right respectively). Color code: DNA bases in red, ribose groups in green, phosphate backbone groups in violet and water molecules in blue.

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