

DNA damage by UV light, OH/H radicals and low energy electrons: A theoretical insight from CASSCF/CASPT2 computations

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UV light, OH radicals, and low-energy (0-3 eV) electrons are frequent sources of damage to the DNA/RNA strands or its monomeric constituents.¹ Even though the isolated nucleobases are known experimentally and theoretically to be characterized by ultrafast decay channels, which make them photo-stable against the UV radiation,² new photochemical paths arise in the DNA/RNA environment producing lesions. Thus, adjacent pyrimidine dimers may react via a [2+2] photo-cycloaddition giving rise to the cyclobutane pyrimidine dimers (CPDs). On the other hand, excited-state double proton transfer may also take place in the Watson-Crick base pairs producing tautomeric forms of the nucleobases. Meanwhile, one common lesion caused by reactive oxygen species (ROS) is the addition of the OH radical, and also $\cdot\text{H}$, to the ethylene bond of pyrimidines. Finally, low-energy ballistic electrons originated during the irradiation of the biological material produce dissociative electron-attachment processes in the nucleobases and might end in strand breaks.

During the last years, we have performed accurate photochemical reaction-path computations using multi-reference multiconfigurational methods to determine the mechanisms of the aforementioned DNA/RNA lesions. On the basis of the results obtained, we could rationalize the different quantum yields of formation of CPDs³ and describe the thermal and photochemical inter-conversion between the canonical and tautomeric nucleobases.⁴ In addition, we determined the absorption properties of the transient radicals formed by the addition of the $\cdot\text{OH}/\cdot\text{H}$ to the pyrimidines and we explored the photochemistry of these adducts.⁵ In this context, we found photochemical paths which regenerate the canonical nucleobase. These channels might be accessible by irradiation of visible light and therefore might imply a photo-protection mechanism. For the DEA phenomena in nucleobases, we described the role of dipole- and valence bound anionic states of the bases and the distinct behavior of guanine as compared to adenine and the pyrimidines.⁶ In this contribution, we will briefly summarize the findings obtained and comment on their relevance in the field of DNA/RNA damage.

References

- [1] (a) Cadet, J.; Vigny, P. In *Bioorganic Photochemistry*; Morrison, H., Ed.; John Wiley & Sons: New York, 1990; Vol. 1, pp 1-272. (b) von Sonntag, C. *Free-Radical-Induced DNA Damage and Its Repair: A Chemical Perspective*; Springer-Verlag: Berlin, 2006. (c) Baccarelli, I.; Bald, I.; Gianturco, F. A.; Illenberger, E.; Kopyra, J. *Phys. Rep.* **2011**, *508*, 1-44.
- [2] Barbatti, M.; Borin, A.C.; Ullrich, S. Eds. *Photoinduced Phenomena in Nucleic Acids I - Nucleobases in the Gas Phase and in Solvents*, *Top. Curr. Chem.* Springer International Publishing: Switzerland, 2015, Vol. 355.
- [3] (a) Roca-Sanjuán, D.; Olaso-González, G.; González-Ramírez, I.; Serrano-Andrés, L.; Merchán, M. *J. Am. Chem. Soc.* **2008**, *130*, 10768–10779. (b) González-Ramírez, I.; Roca-Sanjuán, D.; Climent, T.; Serrano-Pérez, J. J.; Merchán, M.; Serrano-Andrés, L. *Theor. Chem. Acc.* **2011**, *128*, 705–711.
- [4] (a) Gobbo, J.P.; Sauri, V.; Roca-Sanjuán, D.; Serrano-Andrés, L.; Merchán, M.; Borin, A.C. *J. Phys. Chem. B* **2012**, *116*, 4089–4097. (b) Sauri, V.; Gobbo, J.P.; Serrano-Pérez, J.J.; Lundberg, M.; Coto, P.B.; Serrano-Andrés, L.; Borin, A.C.; Lindh, R.; Merchán, M. Roca-Sanjuán, D. *J. Chem. Theor. Comput.* **2013**, *9*, 481–496.
- [5] (a) Francés-Monerris, A.; Merchán, M.; Roca-Sanjuán, D. *J. Chem. Phys.* **2013**, *139*, 071101. (b) Francés-Monerris, A.; Merchán, M.; Roca-Sanjuán, D. *J. Phys. Chem. B* **2014**, *118*, 2932-2939.
- [6] González-Ramírez, I.; Segarra-Martí, J.; Serrano-Andrés, L.; Merchán, M.; Rubio, M.; Roca-Sanjuán, D. *J. Chem. Theor. Comput.* **2012**, *8*, 2769–2776.