Exploring the mechanisms of damage of biomolecules upon ionising irradiation with numerical simulations

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Biomolecules are highly radiosensitive, yet the mechanisms of the radiative damage they undergo remain poorly known. In the context of the latest innovations in the field of radiotherapy (FLASH), we developed a protocol to study the ionising irradiation of biomolecules with fast ions. On the basis of experimental data[1], we probe it on the simulation of the collision of collagen mimetic peptides (CMP) in the gas phase with a C^{4+} cation at the Bragg peak energy. After a preliminary work on the protonation of CMP, we describe the electronic dynamics of the collision with real-time time-dependent auxiliary density functional theory (RT- TD-ADFT)[2]. We developed a tool to generate a pool of ion beam trajectories that extensively samples the irradiation. A complex absorbing potential models the ionisation through the emission of secondary electrons[3]. Thereby, we compute the energy deposited by the colliding ion and what remains of it in the vibrational modes of the molecule after ionisation and electronic relaxation. The subsequent damage is to be studied thereafter with non adiabatic dynamics simulations (QM/MM Ehrenfest). The same simulation protocol will be applied for the ionising irradiation of the nucleosome, following the original interest for the biosystem that is the most relevant to radiotherapy. In either system, the limitation of the computational capacity calls for another approach. Therefore we work on machine learning code that may allow us to alleviate most of the RT-TD-ADFT calculations to compute energy depositions and electronic stopping powers. Finally, the damage structures are studied with classical molecular dynamics. Regarding the nucleosome, we have already started studying available structures bearing well-known radiative damage[4].

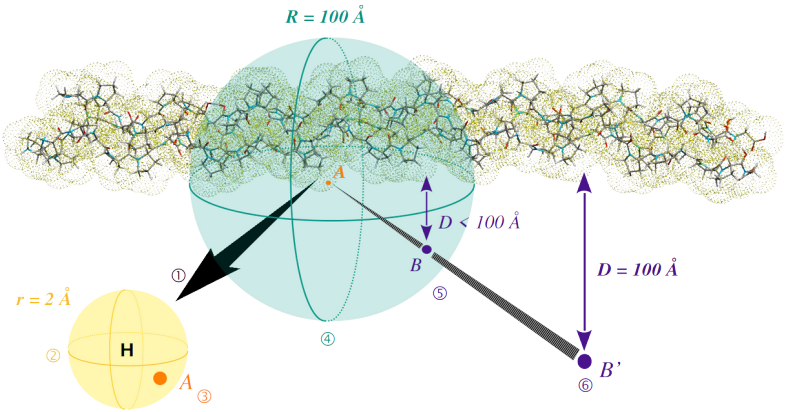

Figure 1: Sampling strategy to generate irradiation trajectories

1 M. Lalande et al. **Irradiation of isolated collagen mimetic peptides by x rays and carbon ions at the Bragg-peak energy** – Phys. Rev. A 98, 062701 – 2018

2 Omar, K.A. et al. **Current status of deMon2k for the investigation of the early stages of matter irradiation by time-dependent DFT approaches** – Eur. Phys. J. Spec. Top. 232, 2167–2193 (2023)

3 Damien Tolu, Dominique Guillaumont, and Aurélien de la Lande – The Journal of Physical Chemistry A 2023 127 (34), 7045-7057 DOI: 10.1021/acs.jpca.3c02117

4 Wen T. et al. **DNA–Histone Cross-Link Formation via Hole Trapping in Nucleosome Core Particles** – Journal of the American Chemical Society 2023 145 (43), 23702-23714