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A molecular dynamics – based protocol to explore rearrangement and fragmentation mechanisms of ionized systems: application to a molecular model of protein – nucleic acid interactions

The absorption of high-energy radiation and following photo-ionization leads to an enhanced reactivity towards processes such as rearrangements and fragmentations. While experimental techniques such as photoelectron photo-ion coincidence (PEPICO) spectroscopy can suggest the species formed at defined binding energies, ab initio molecular dynamics simulations can explore, from a theoretical point of view, the cation potential energy surface. An integrated experimental – computational approach has been employed to characterize the reactive behavior of ionized systems. Benzyluracil (BU) has been chosen as model compound, since it can mimic the close interaction between uracil nucleobase and phenylalanine aminoacid in nucleic acid – protein complexes. UV light irradiation of BU leads to a photo-product with a covalent cross-link between the two moieties, but with reduced yield due to excited state deactivation.[1-3] Therefore, the reactivity of BU induced by ionization, rather than excitation, has been explored from both experimental and theoretical point of views. In particular, PEPICO spectroscopy allows to characterize the fragmentation channels induced by photo- ionized states at defined binding energies, revealing that BU isomers (5BU and 6BU) are resistant to fragmentation up to 12 eV, then dissociating, at higher energies, into a very complex pattern of fragments. On the other hand, ab initio molecular dynamics with excess kinetic energies have been performed to explore in depth 5BU and 6BU cation potential energy surfaces, allowing to identify the molecular identity of the detected fragments, as well as the pathways leading to them. The simulations and further energy refinements reveal that, at lower energies, ionized 5BU and 6BU can indeed rearrange, without fragmentation, giving cross-linked photoproducts, while higher energies are required instead to give fragmentation pathways, mainly involving the uracil moiety.[4] Such results allow a more detailed understanding of the interactions between proteins and nucleic acids induced by ionizing radiation, and suggest the optimal conditions to maximize the yield of the photo-product in cross-linking experiments, while avoiding the photo-damaging of the interacting nucleobase. [1] C.J. Fecko, K.M. Munson, A. Saunders, G. Sun, T.P. Begley, J.T. Lis, and W.W. Webb, Photochem. Photobiol., 2007, 83, 1394-1404 [2] G. Sun, C.J. Fecko, R.B. Nicewonger, W.W. Webb, and T.P. Begley, Org. Lett., 2006, 8, 681-683 [3] M. Valadan, E. Pomarico, B. Della Ventura, F. Gesuele, R. Velotta, A. Amoresano, G. Pinto, M. Chergui, R. Improta, and C. Altucci, Phys. Chem. Chem. Phys., 2019, 21, 26301-26310 [4] M. Valadan, F. Perrella, L. Carlini, G. Iuzzolino, J. Chiarinelli, F. Coppola, R. Richter, C. Schiano, A. Petrone, P. Bolognesi, L. Avaldi, C. Altucci, N. Rega, J. Chem. Phys., 2025, 163, 034305

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