RADIATION INDUCED AND OXIDATIVE DNA DAMAGES: FROM PHOTOCHEMISTRY TO EPIGENETIC MODULATION

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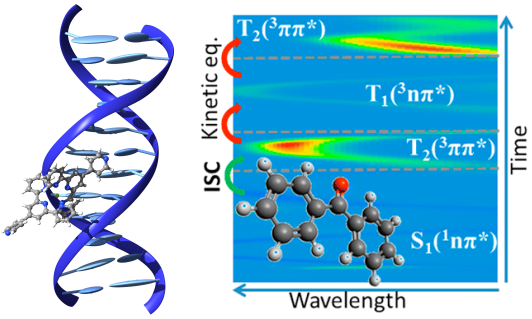
DNA is constantly exposed to organic and organometallic compounds that may give raise to stable aggregates; hence inducing mutations or influencing replications and ultimately cell viability. Furthermore, the interaction of DNA with drugs may induce photoactivated or oxidative lesions, for instance via the activation of singlet oxygen and reactive species. On the other hand the same processes can be exploited in the design of novel anticancer drugs showing enhanced specificity and less side effects.

In this talk we will illustrate the use of multiscale computational methods (molecular dynamics and QM/MM) to model and simulate the interaction of drugs with DNA, also via the precise determination of binding free energies. We will illustrate, also using non-adiabatic dynamics, the pathways leading to benzophenone DNA photosensitization via triplet energy transfer.
Subsequently, we will clarify the production of and the oxidative reactions induced by $^1O_2$ rationalizing its selectivity toward guanine as well as the different products obtained in different molecular environments (B-DNA or solvated nucleotide).
The sensitization of non-canonical DNA structures, such as G-quadruplexes, that are selected targets in modern anticancer therapies, will be illustrated, together with the modeling of electronic circular dichroism as a tool to bridge the gap between simulation and experimental structural determination. This will also open the way to the possible use of DNA sensitizers as tools to induce epigenetic modulations in cancer therapies.



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