Inner shell ionization effects on molecules of biological interest in an aqueous medium

The radiation chemistry of aqueous solutions has been studied for over a hundred years, both with regards to the degradation of biological material and for radiobiology, but also for its numerous implications in the nuclear industry.

In photochemistry, simple excitation events in the Ultra-Violet, corresponding to an energy deposition of a few eV per molecule, are fairly well described. To a certain extent, the effects of valence ionization by high energy particles are also known (deposition of a few tens of eV, leading in particular to the breaking of OH and CH bonds) particularly, by radiolysis studies. In contrast, the effects of the most energetic events that can be envisaged in chemistry – inner shell ionizations bringing energy deposition of several hundreds of eV at the scale of an atom - are still poorly understood in the condensed phase. While they remain rare events, when an environment is exposed to high energy particles, their effects on biomolecules, proteins and DNA could be very significant (1) and be the limiting factor for structural studies, in particular, with X-ray microscopes or high energy free electron (XFEL) lasers (2,3).

The aim of this thesis is to better understand these rare events, generated in the hundreds of picoseconds after irradiation, by using "soft" X-ray radiation (100 -10 keV) to trigger them selectively around the different ionization thresholds of the biological material constituents (such as carbon, oxygen, nitrogen or various metals also present in some proteins). This thesis is co-funded by the SOLEIL Synchrotron and the National Research Agency, in the framework of the project ANR-17-CE30-0017-HighEnech (internet link).

At the CEA, the PhD student will first implement spectroscopic analysis methods (4) to distinguish the products of the inner shell ionization from the radiolytic background. These studies will be developed on small molecules of biological interest (peptides, sugars, models of DNA bases). These approaches will be validated by using, as a model source, an electron beam of a few keV. These methods will then be applied to irradiations either in an ultrathin window cell (150 nm silicon nitride), which was successfully tested on the SOLEIL METROLOGY beamline, or in a newly developed microfluidic cell, when anoxic condition is required. These measurements will give access to degradation products over long times (up to the microsecond).

In a second step, the PhD student will work at the PLEIADES beamline of the SOLEIL Synchrotron, to perform electron spectroscopy of these same small organic molecules in liquid phase, using the technique of vacuum liquid jet (system that has just been developed and successfully tested at SOLEIL). The electron spectroscopy will help to understand the energy transfer between the organic molecule and the solvent involved, in ultra-short time (from several tens of femtoseconds to the picosecond), after inner shell excitation or ionization. In addition, the structural changes of the biomolecules after different irradiation doses can be followed. The PhD student may be involved, if he wishes, in a future technical development at the PLEIADES beamline (time resolved fluorescence coupled with the liquid micro-jet technique), aimed at accessing the intermediate steps of the mechanisms.

Finally, in a third step, the PhD student will use the collected data to simulate, thanks to ab-initio molecular dynamics codes, the reaction mechanisms involved during the irradiation. He/She will use for the sub-femto second stages the methodologies developed by Marie Anne Hervé of Penhoat at the Pierre et Marie Curie University (5) and for the longer times the methods set up at the CEA (6).

These complementary approaches will allow us to have a precise idea of the different physicochemical processes that may occur in the first moments following an inner shell excitation or ionization by implementing competences, unique in the world, in irradiation with low penetrating radiation.

In addition, the doctoral student may be involved, in the context of collaborations already established, in experiments using free-electron lasers (LCLS (USA), SACLA (Japan)).

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Desired formations
Physicochemistry, liquid physics, biophysics, medical physics ...

Summary:
The aim of this thesis is to better understand the physicochemical impact of inner shell ionizations on molecules of biological interest in solution. These extreme events, injecting hundreds of electron volts at the atomic scales, could indeed play a major role in radiobiology.
This thesis will be conducted in the framework of a collaboration between CEA Saclay and the SOLEIL synchrotron and Pierre and Marie Curie University. On the one hand, it will deal with spectroscopic developments to monitor the creation of radical species and the structural changes in ionized biomolecules, and on the other hand to run irradiation experiments, with soft X-rays, on the METROLOGIES and PLEIADES beamlines. An *ab-initio* molecular dynamics simulation component will also be developed in collaboration with Pierre et Marie Curie University. This thesis is co-financed by the Synchrotron SOLEIL and the National Research Agency, within the framework of the project ANR-17-CE30-0017-HighEneCh.