Ionization of RNA-uracil by highly charged carbon ions

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Abstract. We present a theoretical description of highly charged carbon ion-induced ionization of isolated RNA-uracil molecules. A comparison between recent experimental and theoretical total cross sections is provided.

1. Introduction
Besides their great importance in fundamental physics, atomic and molecular ionization processes are of prime interest in diverse areas of science ranging from astrophysics - where the effects of space radiation on astronauts is an important concern of missions for the human exploration of the solar system - to radiobiology, in particular for predicting the radio-induced damage at the sub-cellular scale [1]. Indeed, it is nowadays recognized that lethal events for living cells are - in their majority - attributed to complex clustered damages coupling DNA base lesions with single- and double-strand breaks [2]. Thus, the ionization process being known to be one of the main elicitors of these double strand breaks (DSBs), it is worth noting that a detailed knowledge of the underlying physics of the ionizing radiation remains of prime importance for radiobiologists. In this context, accurate cross sections for describing the ionization of biomolecules like the DNA/RNA components represent useful data, in particular for Monte Carlo type numerical simulations devoted to the modeling of radio-induced cellular damage [3-4]. Additionally, knowledge of the energy deposition patterns in the biological medium is of crucial importance in medicine and more particularly in cancer therapy where focused ion beams are used to deliver highly localized doses within tumors while sparing the surrounding normal tissue. This particular ballistic property may only be achieved by highly charged particles which offer the possibility to concentrate the radiation dose in a well defined depth called Bragg peak (BP). Besides, it has been shown that the ratio of BP versus dose in the entrance region is larger for heavy ions than for protons. Indeed, due to their larger mass, angular and energy straggling becomes negligible for heavy ions as compared to protons. Therefore, heavy ions offer an improved dose conformation as compared to photon and proton radiation therapy, with a better sparing of normal tissue structures close to the target. Consequently, if the irradiated volume of normal tissue can be minimized by conformal radiation therapy, a higher dose can be delivered to the tumor and thus a
better outcome can be achieved without increasing the risk of side effects. This property is the basis of most developments in the field of radiation therapy in the last decades, the highest degree of dose conformation being currently achieved with protons and carbon ions. Moreover, in addition to the dose conformation, heavy ions exhibit a strong increase of the Linear Energy Transfer (LET) in the BP as compared to the entrance region, leading to a radiobiological advantage of high LET radiation versus neutron therapy.

However, investigations concerning proton- and heavy ion-induced ionization of DNA/RNA constituents remain limited. On the experimental side, Tabet et al. [5-6] have measured proton-impact total ionization cross sections of nucleobases such as adenine and uracil by means of a time-of-flight fragment ion measurements at proton energies below 150 keV. Previously, Moretto-Capelle and Le Padellec [7] have published energy distributions of secondary electrons emitted from uracil by protons with energies below 100 keV. Very recently, Iriki et al. have reported two extensive studies where a large set of absolute doubly and singly differential cross sections was provided for 500 keV, 1 MeV and 2 MeV protons impacting with adenine [8-9]. Finally, Agnihotri et al. have - in a recent work [10] - reported absolute total ionization cross sections for uracil molecules impacted by helium-like carbon and oxygen ions over a wide energy range (100 keV-60 MeV) which approximately covers the BP region. Detailed angular distributions in terms of doubly differential cross sections for MeV bare carbon ions on uracil were also studied by the same authors [11].

With regard to the theoretical work, let us first mention that still today they are relatively scarce. In this context, we have recently proposed a classical model combining a classical trajectory Monte Carlo (CTMC) approach with a classical over-the-barrier (COB) criterion. Herewith we described total cross sections for single and multiple ionizing processes induced by impact of fast H\(^{+}\), He\(^{2+}\) and C\(^{6+}\) ions on RNA uracil and DNA bases [12-13]. Simultaneously, we have developed two quantum mechanical models, within the first-order Born approximation and the continuum distorted wave-eikonal initial state (CDW-EIS) framework, where ionization induced by protons on the four DNA bases was investigated [14-15]. These two models are referred to as CDW-EIS and CB1-CWB models, respectively. A detailed comparison between the CTMC-COB, CB1-CWB and CDW-EIS predictions was also reported in [10-11] where a good qualitative agreement was observed in terms of total and differential ionization cross sections for all the investigated cases.

In the current work, we present an extension of our previous work [14-15] to the case of C\(^{q+}\) ions (with \(q\) ranging from 4 to 6). The theoretical CB1-CWB and CDW-EIS predictions are compared with measured total ionization cross sections for isolated uracil (C\(_4\)H\(_4\)N\(_2\)O\(_2\)) molecules impacted by keV-MeV C\(^{q+}\) ions, i.e. for incident energies which largely cover the maximum of the Bragg Peak region.

In the following we briefly describe the experimental set-up built to measure total cross sections (TCS) for electron emission from uracil. In section 3 we briefly present the different theoretical models developed for describing the ionization process while section 4 contains a detailed comparison of theoretical and experimental TCS.

Note that in the following sections atomic units (a.u.) are used throughout unless indicated otherwise.

2. Experimental set-up

In this section we briefly report the experimental set-up used to measure the ionization cross sections; for more details we refer to our previous work [10-11,16].

The experiments were carried out by using two different accelerator facilities both based at the Tata Institute of Fundamental Research (Mumbai, India). Whereas low energy C-ion beams (60 keV-1 MeV) were delivered from a newly installed Electron Cyclotron Resonance ion-source, a 14 MV tandem Pelletron accelerator was used to produce high-energy carbon beams. A Wiley McLaren type recoil-ion time-of-flight spectrometer was used along with channel electron multipliers (CEM) to detect electrons and ions. A narrow slit was placed in front of the electron-CEM to reduce the excessive count rate.
The well-collimated ion beams were crossed with a gaseous uracil target in the interaction region between the pusher and puller plates, the molecules effusing through a nozzle of 1 mm diameter. The gaseous target of uracil was produced by heating the (99% pure, Sigma-Aldrich) powder in an oven at 160°C. The evaporation rate was monitored by means of a quartz crystal thickness monitor suitably mounted to monitor the flow of molecules throughout the experiments. Variation of the deposition rate, if at all, was very smooth and was found to vary by about 5-10% over a long period i.e. in about ten hours. The absolute error (~20%) includes this variation. Chamber pressure was better than 4x10^{-7} Torr. For absolute normalization of the TCS we have used another experimental technique based on electron spectroscopy, detailed in [11]. Total cross sections were then obtained by adding all the counts under the single ionization and fragmentation peaks (see Agnihotri et al. [10]).

3. Theory

The different models used in the present study for predicting total cross sections of carbon-induced ionization of uracil have been presented in previous publications, so hereafter only a brief outline is presented; for more details we refer to our previous work [13-15].

3.1. The classical description of the ionization process

The model here employed is based on the classical over-the-barrier (COB) approximation - initially developed by Bárány et al. [17] and Niehaus [18] - combined to statistical features of the CTMC model introduced by Abrines and Percival [19].

In this approach, the collision process is described within the impact parameter approximation - with a projectile trajectory considered as a straight line (see figure 1) - and where all the particles are described by classical Newtonian laws. Under these conditions, the target position is considered as fixed in the laboratory frame whereas the active target electrons, namely, those which will be extracted from the target are, in a first step, considered as virtual particles and really taken into account only if they are created, i.e. if ionization and/or capture processes occur (see the criteria given below). In addition, the initial positions of the target as well as that of the ejected electron are fixed at the origin of the laboratory frame and then, step by step, modified via the Newtonian laws and according to the above mentioned criteria.

Figure 1. Geometry of a collision between a projectile $P$ and a target $T$. $Z_P$ and $Z_T$ represent the charge of the projectile and the target, respectively, after the electron ejection. $b$ and $\vec{v}$ represent the impact parameter and the impact velocity, respectively, whereas $\vec{x}$ is the position vector of the created electron and $\vec{R}$ is the internuclear vector.

At the beginning of each simulation, the system is only constituted by two particles, namely, the projectile nucleus $P$ and the residual target $T$. Then, for each step $\Delta t$ we evaluate the possibility for extracting one electron from the target by two simultaneous conditions: i) the maximum of the interaction potential seen by a target electron which has to be lower than the binding energy $\varepsilon_\alpha$ of the impacted orbital ($\varepsilon_\alpha < 0$) and ii) the ratio $\Delta t/t_e$, where $t_e$ denotes the classical orbital period of the target electron given by $t_e = 2\pi Z_T / \sqrt{2|\varepsilon_\alpha|}$ with $\Delta t \ll t_e$, which has to be greater than a random
number \( \delta \) (chosen in the \([0,1]\) interval). In fact, this last condition is essentially introduced to compensate the lack of target electron spatial density representation in the current model. Thus, if conditions \( i) \) and \( ii) \) are simultaneously satisfied, an electron is created and ejected from the target. The system becomes thus a three-free particle problem (the projectile, the residual target and the created electron).

At the end of the collision, the population of the different reacting channels is determined via energetic criteria. So, at the end of each simulation, \( i.e. \) at large values of \( R (\approx 200 \text{ a.u.}) \), the electron-projectile energy \( H_P \) and the electron-target energy \( H_T \) are intra-compared. Thus, if we have simultaneously \( H_P > 0 \) and \( H_T > 0 \) a single ionization (SI) process is considered while a single capture (SC) is considered if \( H_P \leq 0 \) or \( H_T \leq 0 \), respectively. The corresponding total cross section \( \sigma_{SI,SC} \) is then simply determined by

\[
\sigma_{SI,SC} = \int_{i}^{\max} 2\pi \int_0^{b_{\max}} b, db P_{SI,SC}^i (b) (1)
\]

where the upper limit \( b_{\max} \) of the integral has been found to be of the order of 15 a.u. for the system here studied (see [12]), whereas the mono-electronic probability \( P_{SI,SC}^i (b) \) is simply defined by the ratio \( P_{SI,SC}^i (b) = N_{SI,SC}^i / N_{\text{tot}} \) where \( N_{SI,SC}^i \) corresponds to the number of SI or SC processes occurring among \( N_{\text{tot}} (\approx 500) \) simulations - for a given molecular orbital labelled \( i \). Similar procedures are finally repeated for a large number (\( \geq 100 \)) of impact parameters.

Besides, \( I \) denotes the number of molecular subshells considered in the RNA-uracil description (\( I = 21 \)). At this stage, it is important to note that in the current CTMC approximation, the biomolecule is simply described via its molecular orbital (MO) energies \( \epsilon_{a} \equiv \alpha^{0} \) in contrast to the hereafter developed quantum mechanical approaches which need an accurate description of the target in terms of molecular wave functions.

3.2. The CDW-EIS and CB1-CWB descriptions of the ionization process

Two different models are used to investigate the ionization reaction: the first-order Born approximation (denoted as CB1-CWB) and the continuum distorted wave-eikonal initial state one (CDW-EIS). The main difference between both models resides in the fact that in the CB1-CWB model, one-center wave functions (target and continuum states in the only presence of the residual target) are chosen, whereas in CDW-EIS, two-center wave functions (target and continuum states in the simultaneous presence of the projectile and residual target fields) are selected (for more details we refer the reader to [20]). For simplicity we describe here a mono-electronic target, being now \( Z_P \) and \( Z_T \) the projectile and nuclear charges, respectively.

Thus, in the CB1-CWB approach the initial and final wave functions are respectively given by the expressions

\[
\chi_{\alpha}^- = \varphi_{\alpha} (\vec{x}) \exp(-i\epsilon_{\alpha}t) \exp \left[-iZ_p \frac{v}{v} \ln(vR - \vec{v} \cdot \vec{R}) \right] (2)
\]

and

\[
\chi_{\beta}^+ = (2\pi)^{-3/2} \exp(i\vec{k} \cdot \vec{x} - i\frac{k^2}{2}t) N' (\xi) F_i (-i\xi; 1; -ikx - i\vec{k} \cdot \vec{x}) \exp \left[iZ_p \frac{v}{v} \ln(vR + \vec{v} \cdot \vec{R}) \right] (3)
\]
where $\bar{v}$ is the collision velocity. The eikonal phases associated with the internuclear potential are neglected considering that they do not affect the calculation of cross sections integrated over the projectile scattering angle.

In equation (2) $\varphi_a(x)$ represents a target bound state with corresponding orbital energy $\epsilon_a$, whereas $\tilde{k}$ (see equation (3)) denotes the linear momentum of the emitted electron as measured from the target nucleus and $\zeta = \frac{Z_p}{k}$.

In equation (2) $\alpha$ represents a target bound state with corresponding orbital energy $\alpha \epsilon$, whereas $k_r$ (see equation (3)) denotes the linear momentum of the emitted electron as measured from the target nucleus and $T_{Z_p} = \frac{\alpha}{\alpha} \frac{\pi}{\Delta x}$ refers to the normalization constant of the continuum factor $i F_i(-i \zeta; \frac{1}{2}; -ikx - i k \tilde{x})$.

Similarly, in the CDW-EIS framework, initial and final distorted wave functions are chosen as

$$\chi^+ = \varphi_a(x) \exp \left(-i \frac{Z_p}{\bar{v}} \ln \left(\sqrt{v^2 + \bar{v} \cdot s}\right)\right)$$

and

$$\chi^{-} = (2 \pi)^{-3/2} \exp \left(i k \bar{x} \cdot \frac{k^2}{2} \right) N(\zeta) F_i(-i \zeta; \frac{1}{2}; -ikx - i k \tilde{x}) \exp \left(-i \frac{Z_p}{\bar{v}} \ln \left(\sqrt{v^2 + \bar{v} \cdot s}\right)\right)$$

with $\zeta = \frac{Z_p}{p}$ with $\tilde{p} = |k - \bar{v}|$ being the linear momentum of the ejected electron as seen from the projectile and where $\bar{s}$ denotes the position of the ejected electron with respect to the projectile nucleus.

Under these conditions, the doubly differential cross section of a given MO labeled $j$, namely, differential with respect to the ejected electron direction $\Omega$ and the emitted electron energy $E$, is given by

$$\sigma^{(2)}(\Omega, E) = \mu k \int \left| T_{\beta\alpha} \right|^2 \frac{d^2\sigma}{d\Omega dE}(\mu, k) \, d\Omega, \quad (6)$$

where $\mu$ and $k_s$ refer to the projectile mass and the momentum of the scattered particle, respectively. The scattering amplitude $T_{\beta\alpha}$ reported in equation (6) is given by

$$T_{\beta\alpha} = \frac{-Z_p}{2\pi} \left< \chi^{(+)}_{\beta}\right| V \left| \chi^{(+)}_{\alpha}\right>$$

where $V$ is the interaction between the incoming ion and the target.

Finally, for the multi-electronic target an independent active electron approximation is employed for describing the ionization process as it has been done in our previous work [14-15]. The passive target electrons (those non-ionized) are then considered frozen in their initial orbitals during the collision process. This assumption is generally made to overcome the difficulty of taking into account the dynamical correlation between active and passive electrons, in particular, for large molecules such as those investigated here (see also recent work of Monti et al. [21] where the influence of electron correlation on ionization of atomic targets has been analyzed in detail).

3.3. The target description and the cross section calculations

The input parameters used for describing the occupied molecular orbitals (MOs) of uracil were obtained by using ab initio methods (for more details we refer to our previous work [14-15]). Total-energy calculations were performed in the gas phase with the Gaussian 09 software at the RHF/3-21G level of theory [22]. The equilibrium geometries of the nucleobase were obtained without symmetry constraints applied while the computed ionization energies of the occupied molecular orbitals were scaled in a way that the calculated Koopmans ionization energy, i.e. the ionization

$^1$ Note that the present equation (5) replaces the equation (2) of reference [15] where a typo has been recently detected in the argument of the second $i F_i$ function.
energy of the highest occupied molecular orbital (HOMO), coincides with the experimental value of the ionization potential measured by Hush and Cheung [23].

Thus, for each MO labeled \( j \), the effective number of electrons \( \xi_j \), relative to the atomic component \( i \) of the MO was derived from a standard Mulliken population analysis and their sum for each occupied MO is very close to 2, since only atomic shells with very small population have been discarded.

In the laboratory frame, the doubly differential cross sections can be written as

\[
\sigma^{(2)}(\Omega, E) = \sum_{j=1}^{N} \sigma^{(2)}_j(\Omega, E),
\]

(8)

where \( \sigma^{(2)}_j \) refers to the doubly differential cross section of the \( j \)th-orbital, the latter being obtained as a weighted sum of atomic doubly differential cross sections corresponding to the different atomic components involved in the CNDO (complete neglected differential overlap) description, namely,

\[
\sigma^{(2)}_j(\Omega, E) = \sum_i \xi_{j,i} \sigma^{(2)}_{ai}(\Omega, E).
\]

(9)

Then, singly differential cross sections \( \sigma^{(1)}(E) \) and total cross sections are obtained by successive numerical integrations over the ejected electron direction \( \Omega \) and the emitted electron energy \( E \). Note that in the present quantum mechanical calculations, an effective target charge \( Z_{\text{T}}^* \) is considered in the continuum factor describing the electron-residual target interaction, being \( Z_{\text{T}}^* = Z_{\text{T}} \sqrt{1 - 2n_{\alpha}^2 e_{\alpha}} \) where \( n_{\alpha} \) refers to the principal quantum number of each atomic orbital component used in each MO expansion.

4. Results and discussions

In figure 2, we report absolute total ionization cross sections provided by the CB1-CWB and CDW-EIS descriptions, as a function of energy of the C-ions for two different charge states, namely, C\(^{4+}\) and C\(^{6+}\) [10]. We note that both sets of theories (solid and dashed lines) overestimate the experimental data even if the energy dependence is well reproduced. Besides, we also report in figure 2 the TCS provided by our previously published COB-CTMC model (dotted line). We note a better agreement than that reported by the quantum mechanical models in particular for bare C\(^{6+}\) projectiles. Indeed, the CTMC-COB model overestimates the experimental data only by a factor of 1.2-1.4. Even for He-like C-ion this model gives a result closest to the experimental data, i.e. within a factor of ~1.5. The CDW-EIS and the CB1-CWB results differ from the experimental data by a factor of about 2 and 3, respectively. It is interesting to analyze the possible origin of this overestimation of the experimental data. In the case of proton beams impacting on uracil, CB1-CWB and CDW-EIS were shown to be in close agreement with measured total cross sections [15]. In principle, the effect could be attributed to the stronger projectile field created by a multi-charged ion in comparison with a proton beam. In CDW-EIS it is taken into account through the multiplicative factor distorting the initial bound orbitals, whereas in CB1-CWB this interaction is included only at asymptotic internuclear separations. For example, recently it has been shown for impact of multiply charged ions on He targets [24], that an excellent description of experimental data in the binary encounter region of double differential cross sections is obtained, if the eikonal phase of CDW-EIS is replaced by a corresponding continuum factor as in the CDW approximation. It is obvious that the models need to be fine-tuned in order to give a better agreement with the experiments.
5. Conclusions

Single ionization of DNA-Uracil impacted by highly charged carbon ions has been studied by employing three different theoretical models, based on a CDW-EIS, CB1-CWB and CTMC-type approach, respectively.

A brief description of the experimental apparatus as well as the different theories has been reported while focusing our study on the differences between both quantum mechanical models.

An interesting experiment/theory confrontation has then clearly pointed out a theoretical overestimation of the experiment in particular when the CB1-CWB and the CDW-EIS models were used. Concurrently, the classical results have shown a better agreement with the experimental total ionization cross sections in particular when bare $C^{6+}$ ions were studied.

This disagreement between theoretical predictions and measurements is a matter of our present interest and still remains an open question.

Acknowledgments

This work has been developed as part of the activities planned in the Programme de Coopération ECOS-Sud A09E04, the Project Simulation Monte Carlo Haute Performance pour l’Hadronthérapie partially funded by the Conseil Régional de Lorraine and the French Agence Nationale de la Recherche Contract No. ANR-09-BLAN-0135-01. Furthermore, some of the authors (MEG, OF and RDR) acknowledge partial support from the Agencia Nacional de Promoción Científica y Tecnológica (Project PICT 2006 No. 1912) and the Consejo Nacional de Investigaciones Científicas y Técnicas (PIP-CONICET No. 1026/10 and No. 0033/10), both institutions from the República Argentina.

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