The Role of High-Energy Ion-Atom/Molecule Collisions in Radiotherapy

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Abstract. The need for ions in radiotherapy stems from the most favorable localization of the largest energy deposition, precisely at the tumor site with small energy losses away from the target. Such a dose conformity to the target is due to heavy masses of ions that scatter predominantly in the forward direction and lose maximal energy mainly near the end of their path in the vicinity of the Bragg peak. The heavy masses of nuclei preclude noticeable multiple scattering of the primary ion beam. This occurrence is responsible for only about 30% of ion efficiency in killing tumor cells. However, ionization of targets by fast ions yields electrons that might be of sufficient energy to produce further radiation damage. These $\delta$-electrons, alongside radicals produced by ion-water collisions, can accomplish the remaining 70% of tumor cell eradication. Electrons achieve this chiefly through multiple scattering due to their small mass. Therefore, energy depositions by both heavy (nuclei) and light (electrons) particles as well as highly reactive radicals need to be simultaneously transported in Monte Carlo simulations. This threefold transport of particles is yet to be developed for the existing Monte Carlo codes. Critical to accomplishing this key goal is the availability of accurate cross section databases. To this end, the leading continuum distorted wave methodologies are poised to play a pivotal role in predicting energy losses of ions in tissue as discussed in this work.

1. Introduction
There could be no adequate particle transport theory without relying upon the most accurate collisional cross sections. As to electromagnetic interactions, the existing \textit{ab initio} quantum-mechanical theories of fast ion-atom collisions \cite{1-5} can abundantly provide cross section databases that are indispensable for proper Monte Carlo simulations of energy losses in matter. The use of these theories derived from first principles of physics would obviate the need for customary resorting to empirical formulae for cross sections. One such fitting formula is due to Rudd \cite{6} who suggested a phenomenological expression by adjusting the involved free parameters to approximately reproduce the available experimental data for ionization in proton-water collisions. For other ions of nuclear charge $Z_P > 1$, this formula relies upon the $Z_P^3$-scaling rule borrowed from the first Born approximation. Such a scaling is not justified because it neglects the effect of electron capture to continuum, which scales like $Z_P^3$ \cite{7,8}. Another \textit{ad hoc} formula proposed by Hansen, Kocbach and Stolterfoht (HKS) \cite{6} empirically modifies the semi-classical version of the binary encounter approximation. The reason for which none of the existing empirical formulae is warranted is that they all lack the predictive power without which theoretical modeling is void of substance.
Energy losses of ions are needed for dose-planning systems in hadron therapy of deep-seated tumors. Ions possess certain special features of a particular relevance to hadron therapy because of their Bragg-tailored dose distributions [9–11] showing that most energy is deposited at the treated target due to a negligible role of multiple scattering effects. Hence conformity of ion dose distributions to the tumor topology. In their passage through the tissue from the entrance and within the plateau region, impact energies of ions are high and ionization dominates. However, at their range, i.e. in the close vicinity of the Bragg peak, the initially fast ions abruptly slow down such that electron capture and electron loss processes become the dominant channel for energy losses. Therefore, especially near the Bragg peak, reliable particle transport theories must account for electron transfer and electron loss from dressed ions. In the latter process, above 150 keV, the largest contribution comes from double ionization via simultaneous emission of one electron from the target and the other from the dressed projectile, as seen in Fig. 1. Within the last few millimeters around the Bragg peak, thousands of electron capture and electron loss processes take place. The Bragg peak on the plot of stopping power versus the traversed path is reminiscent of the Massey peak of the cross section as a function of the incident energy. Thus, collisions near the Bragg peak in ion transport phenomena in tissue are associated with the Massey maximum as a resonant effect, which is manifested whenever the incident velocity matches the classical orbiting velocity of the active electron from the target. It is these and several other related circumstances that promote the role of quantum-mechanical theories from atomic and molecular collisions in providing the necessary non-phenomenological databases of cross sections for track structure computations and detailed Monte-Carlo simulations of ion transport in tissue.

2. Energy deposition by fast ions
Over the years, the subject of hadron therapy has been inspired by the seminal work of Wilson [16] who in the 1940s was the first to suggest that protons, alpha particles or carbon nuclei and some other light ions, with their dose distributions ending with the Bragg peak, should provide optimal target conformity and tumor control. The significance of Wilson’s proposal was in having been conveyed in such a convincing manner that physicians were quick to accept it. Moreover, physicians wasted no time in beginning patient treatments by light ions already in the 1950s in Berkeley [17] and Uppsala [18].

High-energy light ion beams from protons to carbon nuclei, as a powerful part of hadron therapy of deep-seated tumors, are increasingly in demand worldwide, and this motivates construction of hospital-based accelerators. Positron-emitting secondary ions generated from collisions of primary projectiles with the treated tissue provide the possibility for special tomographic verifications of dose depositions at the targeted sites. Such information is of utmost importance, since any inaccuracy in dose delivery to the tumor relative to the prescribed dose planning system can be used to update the input data to the algorithmic codes for energy losses in order to provide the corrected doses in the subsequent fractionated treatments of the patient. This adaptive dose delivery and a proper inclusion of the relative biological effectiveness (RBE) are among the major constituents of biologically-optimized and, indeed, personalized radiotherapy which is suited to the specific needs of each patient.

The challenges for the theory are multifaceted, especially at intermediate impact energies where most of the otherwise powerful perturbation methods are of limited applicability. On the other hand, non-perturbative methods are expected to be more adequate for this particular energy region. The other level of challenges for theoreticians encompasses collisions with participation of two and more active electrons as these processes may become increasingly important near the Bragg peak. Such collisions are characterized by electron-electron correlation effects that are known to play an important role at low and high energies, but have been reported in the past literature to be of minor significance at intermediate energies. Yet another challenging
Figure 1. Total cross sections $Q$ as a function of the impact energy $E$ for electron loss process $H(1s) + H(1s) \rightarrow H^+ + e_1 + H(f)$. Theory (CB1-4B: the four-body boundary-corrected first Born approximation [3]): (i) Dotted curve: cross section $Q_1$ for target $H(1s)$ unaffected by collision with $f = 1s$ i.e. $H(1s) + H(1s) \rightarrow H^+ + e_1 + H(1s)$. (ii) Chained curve: cross sections $Q_{\sum_{n=1}^{6}}$ for all the target bound states symbolized as $H(\sum_{n=1}^{6})$ where the contributions from the principal quantum numbers $1 \leq n \leq 6$ are summed up i.e. $H(1s) + H(1s) \rightarrow H^+ + e_1 + H(\sum_{n=1}^{6})$ (also included here are the sums over all the pertinent degenerate levels of the angular and magnetic quantum numbers). (iii) Dashed curve: cross sections $Q_{c}$ for $H(c)$ with $f = c$ where $c$ stands for continuum of the target to denote ionization of the target electron via $H(1s) + H(1s) \rightarrow H^+ + e_1 + H(\sum_{n=1}^{6})$ (also included here are the sums over all the pertinent degenerate levels of the angular and magnetic quantum numbers). (iv) Full curve: cross sections $Q_{c+\sum_{n=1}^{6}}$ for all the target states $H(c+\sum_{n=1}^{6})$. No formation of the negative hydrogen ion $H^-$ by electron capture from the target $H(1s)$ by the projectile $H(1s)$ is taken into account in the computations. Experimental data (all the target states): △ [12], □ [13], ▽ [14] (without electron capture) and ◆ [15].
energetic ions at a given position located deeply in the treated body where the tumor resides. This is a very complex problem, which demands many-layered expertise from nuclear and atomic collision physics.

3. Plethora of cross sections for ion-atom/molecule collisions for hadron therapy

The atomic physics research field of high-energy collisions of ions with matter provides its versatile databases (cross sections, rate coefficients, ...) to other branches of physics (astrophysics, plasma physics, particle transport physics, ...) and applied disciplines (fusion research, radiation protection in manned space missions, hadron therapy). Such data describe various inelastic scattering events, including electron capture (or equivalently, electron transfer or charge exchange), excitation, electron loss (projectile ionization), ionization (target ionization) and their combinations (transfer excitation, transfer ionization, loss-excitation, loss-ionization) [1–3]. Probabilities for multiple electron transitions are enhanced for the increased nuclear charge of projectiles. Both sets of the mentioned data, those for single- and multiple-electron transitions, need to be very accurate in their role as the input data for subsequent stochastic simulations that employ deterministic cross sections for fast ion-atom collisions in various applications. These data from atomic collisions of ions with matter can be obtained from theories and measurements. A variety of such experimentally determined and theoretically predicted cross sections has extensively been accumulated in the literature particularly over the last three decades [1,2].

In exhaustive comparisons with measurements, past experience conclusively established that the most adequate quantum-mechanical theory for high-energy ion-atom collisions is the continuum distorted wave (CDW) method [19–21] which is valid in the region slightly above the Massey resonance peak [22]. The name of this method comes from correlating the projectile with the target through the allowance of electronic continuum intermediate states that act as a distortion in the total scattering wave function of the whole system. For example, in the entrance channel, the active electron is simultaneously bound to the target nucleus and free in the field of the projectile nucleus. Therefore, in the initial state of the system, the distortion associated with continuum intermediate states of the active electron stems from the Coulomb wave function centered on the impinging nuclear charge. Distorted waves are of especially critical importance to the exit channel for ionizing collisions, as they describe the two-center effects [20] that are completely missing from the first Born (B1) [23–27] and the Bethe-Bloch [28,29] approximations. The two-center effects include intermediate stages of collision and describe active electrons as simultaneously propagating in the two Coulomb fields, one of the projectile and the other of the target nuclei. In ionization of a target, the B1 approximation employs only one full Coulomb wave function centered on the target nucleus in the exit channel for the final scattering state \( \Psi_f \), whereas the electron motion in the projectile field is inadequately described by a plane wave [23–27]. By contrast, the CDW method describes the whole ionization collision in a more physically adequate manner by using three Coulomb wave functions. Two of these latter wave functions are for the electronic motions and they are centered on the projectile and target nuclei for \( \Psi_f \). The third Coulomb wave describes the relative motion of the two heavy nuclei. The physical significance of the additional electronic Coulomb wave function in the CDW method for ionization is in leading to a new source for production of emitted electrons due to the already mentioned effect of electron capture to continuum (ECC) of the projectile. Here, the electron is considered as being “captured” by the projectile albeit not in a bound, but rather in a continuum state. Through this mechanism, which has been experimentally detected in single ionization [30–33], the projectile and electron travel together in the same direction with nearly equal velocities vectors \( \vec{v} \) and \( \vec{v}_e \), respectively (\( \vec{v}_e \approx \vec{v} \)). This is recognized as a resonance effect (hence the resulting enhanced cross sections), which is manifested in an asymmetric cusp-shaped angular distribution for the forward emitted electrons. The description of the exit channel for ionization in the B1 approximation could be roughly satisfactory only for very
slow ejected electrons, that are near the target nucleus and simultaneously far away from the nucleus of the projectile. The cusp mechanism has also been observed experimentally in solid state targets and in this area the name “convoy electrons” is interchangeably used for ECC electrons [34]. This latter name stems from the circumstance that ECC electrons are aligned with and accompanied by scattered projectiles as reminiscent of a convoy-like moving away from the target rest. Emitted slow electrons provide the major contribution to the total cross sections. However, for thorough studies of collisional dynamics, it is imperative to look beyond total (integrated) cross sections to describe properly the differential cross sections that give the energy and angular distributions of electrons ionized from the target [20,35,36]. Both these distributions manifestly exhibit the two-center effect. The other two mechanisms for production of electrons are the emissions leading to the forward and binary peaks (both described by the CDW and B1 methods). The forward emission occurs at a zero-valued angle of the ejected electron, $\theta_e \approx 0$. The binary encounter (BE) peak corresponds to $\kappa \approx 2v\cos\theta_e$.

The most remarkable feature of an interplay between the BE and ECC mechanisms of ionization is manifested when passing from single to multiple ionization in the case of non-hydrogenlike targets. This has been evidenced in experimental measurements of doubly differential cross sections for single and multiple ionization of Ar by H$^+$ [37,38] as well as of He, Ne and Ar by F$^{8+,9+}$ and I$^{23+,26+}$ [39–41]. The ECC cusp effect involving two-electron continua was studied via simultaneous electron loss (projectile ionization) and target ionization in He–He collisions [32,33]. The striking observation reported in Refs. [37–41] is that the ECC cusp can even dominate the BE peak for ionization. Specifically, the coincidence experiment of Afrosimov et al. [38] (simultaneous measurements of double differential cross sections for near-forward-cone ejected electrons and charge state of the target rest) demonstrated that the BE electrons were produced almost entirely by single ionization of Ar by protons. Moreover, determination of the position of the BE peak in coincidence with detection of single-charged recoil ions showed that the emitted BE electrons stem from the valence M-shell of Ar. Among all the electron orbital velocities of Ar, the one which is associated with the M-shell of this atom matches most closely the condition $v_e \approx 2v$ for the forward emitted BE electrons ($\cos\theta_e \approx 1$). Furthermore, in the same experiments [37,38], the group of ECC electrons were found to be significant only when detected in coincidence with multiple charged Argon ions $\text{Ar}^{k+}$ ($k = 2, 3, 4, ...$), whereas totally negligible counts were recorded for $\text{Ar}^+$. In other words, the ECC electrons become a dominant mechanism for multiple ionization. To see from which target shell these electrons were emitted, it is sufficient to compare the binding electronic energies of various shells in Ar and find the level which matches best the ejected electron energy from the ECC peak at which the orbital electron velocity equalizes the projectile speed ($v_e \approx v, \cos\theta_e \approx 0$). This was found to be the L-shell energy of Ar [37,38]. Here, it is pertinent to emphasize certain remarkable similarities between the experimental data for ionization [38] and charge exchange [42]. Thus e.g. the charge-state distributions near the ECC peak was estimated to be 13%, 42%, 37% and 8% for the charge states 1+, 2+, 3+ and 4+, respectively [38]. This is very close to the corresponding charge-state distributions 13%, 50%, 30% and 7% for the same charge states 1+, 2+, 3+ and 4+ in the case of charge exchange [42]. The direct implication of the findings from the experiments reported in Refs. [37–41] is that theories for multiple ionization must include the two-center effect in order to account properly for emission of fast electrons that are predominantly from the ECC source. On the other hand, regarding various applications of such theories aimed at determination of energy losses of charged particles during their passage through matter, the main issue is the relative importance of slow versus fast electrons in single versus multiple ionization. Overall, these experiments with non-hydrogenlike atomic targets prove that the BE and ECC electrons play a remarkably complementary role as they appear to be generated by two completely different mechanisms (single and multiple ionization) and originate from the two well-separated target energy levels (outer and inner shells). Thus, while for single ionization...
the ECC mechanism is conspicuous, it became inconspicuous for multiple ionization. Single ionization is associated with slow electrons from the one-center BE mechanism which is a direct collision of the projectile and the target active electron, such that the target nucleus and the remaining electrons are considered as being passive as if they were mere spectators. On the other hand, multiple ionization is mediated by fast electrons due to the ECC mechanism which necessitates two centers thus activating both the projectile and target nucleus. As opposed to a single collision (projectile nucleus – target electron) in the BE effect, a double collision of the active electron on the projectile and target nucleus is required to produce the ECC cusp as reminiscent of the Thomas billiard-type two successive elastic encounters occurring in capture of an electron from the target by an energetic projectile. This type of correlation between electron capture and ionization permits obtaining the same angular distributions in a given theory for the Thomas peak in charge exchange by using the corresponding ionization transition amplitude in the vicinity of the ECC cusp [43].

In the CDW method [20], the distortions due to electronic continuum intermediate states are properly included in the entrance and exit channels. Nevertheless, the corresponding full Coulomb wave function within the initial scattering state was found in applications to lead to overestimation of experimentally measured total cross sections near and below the Massey peak. Typically, all total cross sections computed by the CDW method keep on rising as the impact energy $E$ decreases, whereas the corresponding experimental data generally decline in the same region exhibiting the Massey peak. This bending of the curve for the total cross sections can also be obtained within the CDW methodologies if the full Coulomb wave function for the distortion of the initial state in the entrance channel is approximated by its long range asymptotic eikonal form. The resulting simplification of the CDW method is acronymed as MCB (modified Coulomb Born) [44, 45], or alternatively, CDW-EIS [46], where EIS stands for the eikonal initial state. In this way, the Massey peak is systematically reproduced by the MCB or CDW-EIS method leading to quantitative agreement with measurements, as illustrated in Fig. 2 and reviewed in Refs. [4, 47, 48]. It is not necessary to start from the CDW method to introduce its simplified variant in the form of the CDW-EIS approximation as originally done by Crothers and McCann [46]. Rather, an alternative derivation [44, 45] yielding the same result is also possible without any reliance upon the CDW method. Irrespective of the way of deriving the transition amplitudes, the CDW and CDW-EIS methods share precisely the same description for the final total scattering state. They differ in the initial scattering state, where the CDW-EIS method uses the ansatz in the form of the logarithmic Coulomb phase factor for the electronic continuum intermediate states. With such an ansatz, the perturbation potential in the entrance channel is unequivocally defined by the application of the operator $H - E$ onto the initial state in the matrix element for the prior form of the transition amplitude $T_{ij}^-$. Here, $H$ and $E$ are the full Hamiltonian and the total energy of the whole system (projectile plus target). The CDW and CDW-EIS methods are computationally attractive since the fully analytical expressions are available for the transition amplitudes for inelastic collisions involving one active electron. The detailed illustrations of these methods for collisions of positively charged projectiles and either neutral targets or positively charged ions are abundantly available in the literature [1–5, 20, 43–52].

4. Adaptation of theories for ion-atom to ion-molecule collisions

Regarding electromagnetic interactions, the available state-of-the-art quantum-mechanical scattering theories from ion-atom collisions [1, 2] can be extended to a wider class of biomolecular targets of direct relevance to cancer therapy by energetic light ions. This can be accomplished by using molecular wave functions in terms of linear combinations of atomic orbitals (LCAO) in the form of the Slater-type orbitals (STOs). With such a convenient ansatz, especially with single center orbitals located on the heavy atomic constituent of a given molecule (e.g.
Figure 2. Total cross sections $Q$ as a function of the incident energy $E$ for electron detachment process $H^+ + H^- (1s^2) \rightarrow H^+ + H + e$. Theory (only the final ground state $H(1s)$ of the atomic hydrogen): (i) Dashed curves (Atomic Orbitals – AO method [53] with $N=29, 36$). (ii) Lower full curve $E \in [3, 20]$ keV (Molecular Orbitals – MO method [54] with $N=12$). (iii) Upper full curve $E \in [1.4, 2498]$ keV (MCB, or equivalently, CDW-EIS method [44, 45] with $N=61$). Integer $N$ associated with the acronyms is the number of variational parameters in the target Configuration Interaction (CI) wave function from Joachain and Terao [55] ($N=61$) as well as from atomic [53] ($N=29, 36$) and molecular [54] ($N=12$) orbitals. Experiment: ◦ [56] and □ [57].

Oxygen in the case of $H_2O$), these theories for ion-atom collisions can be directly adapted to ion-molecule scattering. This is possible because the matrix elements as the form factors for electron capture and ionization involving the STOs for bound states and hydrogenlike continuum with an effective charge in the Sommerfeld parameter for the Coulomb wave function [21] can be analytically calculated precisely in the same way for both atomic and molecular targets. The only difference is that in the case of a molecular target an additional triple integration is required over the three Euler angles for the orientation of the molecular axis. This is due to the fact that the variational parameters of the molecular orbitals are obtained for a particular orientation of the internuclear axis giving the minimum of the expectation value of the exact Hamiltonian of the given molecule. In general, experiments are performed with no reference to
any special orientation of the internuclear axis within the studied molecular target. Therefore, in order to compare such experimental data with theories, the latter must perform averaging over all the orientations of the internuclear axis of a molecular target. For the above-specified molecular orbitals used within e.g. the CDW and CDW-EIS approximations this averaging, which amounts to the said three integrals over Euler angles, can be calculated analytically by using the well-known properties of the Wigner rotation matrix. Thus, in this setting the usual codes for the CB1, CDW and CDW-EIS approximation from ion-atom collisions can readily be adapted for direct applications to ion-molecule scattering [58–66].

5. Major ion-tissue interactions in high-energy collisions

When ions enter the tissue, they are said to be transported through it up to a certain distance (called range \(R\)) which is determined primarily by the initial energy \(E\) of the projectile beam, its energy loss, range straggling and multiple scattering [6,67]. Ions lose their energy because they collide with electrons of the constituents of the traversed tissue. Due to their heavy mass, which is about 2000\(N\) times larger than the electron mass (\(N \geq 1\) being the number of protons and neutrons in a nucleus), ion trajectories deviate only slightly from their incident directions. In other words, they scatter mainly in the direction of a narrow forward cone (\(\theta_i \approx 0\)). Many small angle scatterings occur while the ions pass by the nuclei of atoms/molecules of the encountered tissue. Such a cumulative effect is called multiple scattering and this phenomenon is more enhanced in thicker than in thinner targets. A beam contains a large number of ions and this leads to certain statistical effects. One of them is range straggling, which represents fluctuations in the range \(R\) of individual ions. All the ions of the same energy do not attain the same range, since their collisions (by which they produce many secondary particles along their paths) are of a probabilistic i.e. statistical rather than deterministic nature. Thus, such ions are viewed as straggling to reach their range. Hence the term “range straggling”.

In particle transport physics, one of the most important observables that characterizes the penetration capability of particles is the stopping power \(S(z)\), which represents the loss of ion energy per unit of the traversed path length \(z\) along the particle track, as denoted by \(S(z) \equiv -dE/dz\). At high incident energies \(E \geq 350\) MeV/amu of interest for hadron therapy on deep seated tumors of the corresponding range of about \(\sim 25\) cm, the main scattering events that lead to energy loss of ions are nuclear collisions (mainly with neutron losses from projectile nuclei) and target ionizations. As mentioned, ions scatter mainly forward, meaning that their paths are practically straight lines along which they transfer their energy to the tissue which becomes ionized or excited (at high energies, the probability for ionization is about three times larger than that of excitation). Ions deposit several times more energy at their range \(R\) (i.e. in the vicinity of the Bragg peak) than elsewhere such that this inverse dose-depth distribution is in sharp contrast to electrons and photons [9–11]. The measurement of Bragg and Kleeman [11] was the first to report that \(\alpha\)–particles deposit nearly all their energy when they are about to stop i.e. very close to their range. Dose-depth distributions or profiles are the curves that display the stopping power \(S(z)\) as a function of depth \(z\). A dose-depth profile of an ion beam is mostly a plateau-like curve, which ends abruptly with a prominent maximum as the Bragg peak situated at the target position. By contrast, electrons and photons deposit maximum energy near the beginning of their track, so that afterwards their dose curves decrease with distance all the way up to the target which is tumor in radiotherapy [68]. The tumorous tissue needs to be destroyed to stop the uncontrollable production of clonogenic cells and ions can partially achieve this through nuclear and ionizing collisions with the tissue. However, as stated, only some 30\% of ionization of the tissue’s main target, the deoxy-ribonucleic acid (DNA) molecule, is accomplished by direct hits of ions counting all the primaries, secondaries and ions of higher-order generations. The remaining 70\% of ionization rate of DNA is achieved by radicals and the secondary \(\delta\)–electrons that are produced by the impact of ions on tissue. If the electrons emitted
from a target are sufficiently energetic to be able on their own to lead to further ionizations they are called $\delta$—electrons.

6. Discussion and conclusion

The Bragg curve $S(z)$ represents the stopping power as a function of the traversed length $z$. Given a beam which penetrates a fixed medium, the stopping power is the energy loss per unit of the traversed path length i.e. $-\frac{dE}{dz}$ so that $S(z) = -\frac{dE}{dz}$. Due to their heavy mass, energetic nuclei lose very small amount of their initial kinetic energy per each collision with electrons from the traversed medium. Therefore, the track of the primary particles is practically a straight line in the incident beam direction. Consequently, the stopping power varies slowly and gradually with $z$ until the range $R$ is reached at which point a sudden release of energy of the beam occurs resulting in the emergence of the Bragg peak. As such, qualitatively, the Bragg curve behaves like a hyperbola for all but the last couple of centimeters of $z$ prior to reaching the range $R$ at which point it sharply drops following a linear trend with the increased $z$. Such a behavior is reminiscent of a resonant cross section with a sharp maximum superimposed on a long background-type tail due to ‘potential scattering’ as encountered in resonant scattering theory. More concretely, the ‘inverse Bragg function’ (obtained via the replacement of the length $z$ on the abscissa by the corresponding energy $E$ extracted from the usual energy-range relationship) appears precisely as a curve typical for ionization or excitation total cross section as a function of impact energy. In this latter curve, the ‘inverse Bragg peak’ is recognized as the usual Massey peak from the field of ion-atom collision theory. On the other hand, the mechanism for the Massey peak is the well-known adiabatic hypothesis, which explains the resonance by a near matching of the incident velocity $v$ and the classical velocity $v_0$ of the electron in the orbit of the target atom from which ionization or excitation takes place. Hence, reference to the ‘inverse Bragg function’ is useful, since it determines that the underlying mechanism for the usual Bragg peak is resonance via the velocity-matching condition ($v \approx v_0$).

Specifically, in hadron therapy, clinical dose planning systems need very accurate predictions of the amount of the delivered radiation to tumorous tissues at a fixed depth. This would increase the tumor control by the clinician. The main task of radiotherapy is to maximally destroy the targeted tumor with clonogenic cells, and simultaneously spare the healthy surrounding tissue, which is under risk for collateral damage by the same beam of particles. Energetic heavy nuclei (protons, $\alpha$-particles and similar hadrons) are particularly well-suited for this task, since, by reference to the concept of the Bragg peak, they can, in principle, faithfully deliver the prescribed dose at any given location in the body of the treated patient. This assumes that the dose is computed by reliance upon accurate theoretical data for all the relevant energy losses suffered by the incident beam. Such losses are due to nucleus-nucleus and nucleus-electron collisions. At present, one of the most advanced Monte Carlo codes SHIELD-HIT for modeling of the passage of ions through tissue is excellent in nuclear stopping powers due to the availability of the best state-of-the-art data bases for nuclear reactions including transmutations\(^1\). However, the same code uses the electronic stopping powers of limited accuracy because of the exclusive reliance upon the high-energy Bethe-Bloch formula $\propto [(1/E) \ln (E) + \cdots]$, which is by way of two fitting parameters empirically sewn to the Lindhart-Scharf low-energy asymptote $\propto E^{1/2}$ to crudely cover the region down to $\sim 10 - 20$ keV/amu instead of having 1 MeV/amu as the usual cut-off energy of the projectile.

The Bethe-Bloch formula, as the high-energy asymptotic total cross section to the undistorted first Born approximation, includes energy losses of the primary particles using only single

\(^1\) The original Monte Carlo code SHIELD [69, 70] was designed for nuclear physics as well as for radiation protection purposes in manned space research programs with the main goal to assess the ways to improve shielding against intense radiations from galactic nuclei. More recently [71], this algorithm was adapted to applications within hadron therapy where it is called SHIELD-HIT with the acronym HIT standing for heavy ion transport.
ionization and excitation of targets. However, electron capture and electron loss channels are open with their enhanced probabilities when the penetrating beam of heavy particles is sufficiently slowed down to reach its range near the Bragg peak. For example, by directing a beam comprised of only \( \alpha \)–particles to traverse a given matter towards a target, charge-changing phenomena take place several thousand times, so that alongside the primaries (He\(^{2+} \)), the beam would also contain the secondaries (He\(^+ \) and He). Importantly, these changes of the initial charge of the primary particles occur almost entirely within the last few millimeters of the range within the Bragg peak which is clinically most relevant.

The field of the well-established theories on ion-atom collisions, such as the CDW and CDW-EIS methods, adapted to ion-molecule collisions by way of molecular orbitals in terms of linear combination of atomic orbitals, as discussed in this work, can come to the rescue for overcoming the incompleteness of the Bethe-Bloch descriptions of electromagnetic interactions. This can significantly improve the needed cross section databases for Monte Carlo simulations of energy losses of ions in molecular targets of the traversed tissue. Such \textit{ab initio} cross sections can readily be precomputed and stored as tables from which direct sampling can be made in stochastic simulations. In this way the predictions of Monte Carlo simulations would become much more accurate than any of the customary estimates using the Bethe-Bloch expression or employing some empirical formulae with fitting parameters. A direct clinical usefulness of this envisaged upgrade of particle transport theories and track structure predictions would be far more reliable dosimetric estimates of energy depositions in tissue traversed by ions. This, in turn, would improve dose planning system in conjunction with hadron therapy.

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