Proton track structure code in biological matter

M A Quinto$^1$, J M Monti$^2$, M E Galassi$^2$, P F Weck$^3$, O A Fojón$^2$, J Hanssen$^2$, R D Rivarola$^2$ and C Champion$^1$

$^1$Université Bordeaux, CNRS/IN2P3, Centre d’Etudes Nucléaires de Bordeaux Gradignan, CENBG, Gradignan, France
$^2$Instituto de Física Rosario, CONICET, Universidad Nacional de Rosario, Rosario, Argentina
$^3$Sandia National Laboratories, Albuquerque, NM, USA

E-mail: quinto@cenbg.in2p3.fr

Abstract. Several numerical codes for proton and electron transport in water - a commonly used surrogate of the living matter - have been reported in the literature. In the current work, we report on a home-made step-by-step Monte Carlo code, called TILDA-V, based on a complete set of multiple-differential and total cross sections for describing all the inelastic processes occurring throughout the slowing-down of protons in water and DNA.

1. Introduction
Understanding the radiation-induced effects at the cellular level is of prime importance in predicting the fate of irradiated biological organisms. Thus, whether it is in radiobiology to identify the DNA critical lesions or in medicine to adapt the radio-therapeutic protocols, an accurate knowledge of the numerous interactions induced by charged particles in living matter is required. To do that, Monte-Carlo track-structure codes represent the most suitable and powerful tools, in particular for modeling the full slowing-down of the ionizing particles in biological matter. It is worth noting that those numerical codes are reliable only if the input database used for modeling the charged particle induced interactions is precise and complete enough. In this context, several numerical codes for proton and electron transport in water - a commonly used surrogate of the living matter - have been reported in the literature. Some of these existing codes use theoretical models for describing the physical processes but the majority of them remains nevertheless based on semi-empirical fits to experimental cross sections (for a review, see [1-2] and references therein). In this context, the current work aims at going beyond this artifice with the development of a Monte Carlo code, called TILDA-V, based on a complete set of quantum-mechanically calculated multiple differential and total cross sections for describing all the inelastic processes occurring throughout the slowing-down of protons in water and DNA. TILDA-V (a French acronym for Transport d’Ions Lourds Dans l’Aqua & le Vivo) refers to an extension of the TILDA Monte Carlo code previously developed by Champion for modeling heavy ion and secondary electron histories in liquid and gaseous water for impact energies ranging from 10 keV/amu to 100 MeV/amu [1].
2. **TILDA-V: a full-differential quantum-mechanically based Monte Carlo code**

*TILDA-V* represents an event-by-event charged particle transport simulation, which includes a variety of theoretical models independently developed within the quantum mechanical framework for describing the single ionizing processes induced by proton and electron impact in water and DNA (see [3-5] and [6-7], respectively). Besides, due to the lack of theoretical support in its present form, *TILDA-V* also includes semi-empirical models for describing the excitation processes both induced by \( \text{H}^+ \) and \( \text{H}_0^+ \) impact as well as the electron loss and the electron capture processes induced by \( \text{H}_0^+ \) impact. Some of them are currently under study within the quantum mechanical approach (see Figure 1).

![Figure 1](image1.png)

*Figure 1.* (Color online) Total cross sections for proton/hydrogen induced interactions in water. Theoretical and semi-empirical predictions (solid lines): ionization [3-4], capture [5] and excitation [8] induced by proton impact; ionization [9], capture [8], excitation [8] and stripping [10] induced by hydrogen impact. Experimental data: ionization and capture induced by proton impact (red squares, stars and circles [11-13], and magenta triangles, squares and circles [14-16], respectively) and hydrogen-induced ionization (blue circles [17]).

2.1. **Biological matter modeling: from water to DNA**

Whether it is to describe the biological matter by water or by including some DNA components, the biological medium has been modeled by means of molecular wave functions, all based on quantum mechanical calculations. In the first case, we followed the SCF-LCAO (*self-consistent field - linear combination of atomic orbitals*) approach reported by Moccia [18] who described the water molecule by means of single-center wave functions, all centered at a common origin (the oxygen atom). The latter refer to the equilibrium configurations calculated in the self-consistent field method and agree very well with the experimental geometrical and energetic properties of the water molecule. On the other hand, due the complexity of their multi-center nature, the DNA components were described by using the Gaussian 09 software based on the restricted Hartree-Fock method with geometry optimization a the RHF/3-21G level of theory. Their equilibrium geometries in the gas phase were obtained without symmetry constraints applied and the simulated molecular wave functions were described as linear combinations of atomic orbitals (for more details we refer the reader to our previous work [4]).

2.2. **Particle tracking in TILDA-V: proton, neutral hydrogen and electron transport**

From a general point of view, the charged particle transport simulation comprises series of sampling steps, which determine the distance between two successive interactions as well as the type of interaction occurring at the selected point. In all cases, the interaction type is randomly selected according to the relative magnitude of the individual total cross sections of all the processes (ionization, capture, excitation induced by proton and ionization, capture, excitation and electron loss induced by hydrogen atom) while the complete kinematics of the interaction is defined thanks to the multiple differential cross sections of the corresponding process.
Thus, if the selected process is ionization or stripping, singly and doubly differential cross sections are successively used to determine the kinetic energy as well as the ejection direction of the secondary electron. Then, the incident particle energy is reduced by the total energy (kinetic + potential) transferred during the collision. Besides, let us note that the charge state of the primary proton particle may also change according to the selected collision. Thus, the electron capture will decrease the initial proton charge (from +1 to 0) whereas the electron loss process (stripping) will increase the hydrogen charge (from 0 to +1). Note that the formation of $H^-$ may also occur, in particular when the hydrogen atom captures an electron. However, due to its short lifetime, the negative ion $H^-$ will rapidly eject its “additional” electron leading then to a final state characterized by a free electron and a hydrogen atom. The secondary electrons also liberated are then followed by means of a complete set of cross sections including triply, doubly and singly differential cross sections needed to characterize the complete kinematics of the electron-induced collisions. All these steps are repeated for all primary and secondary particles until their kinetic energy falls below a predetermined cut-off value. For the primary particles, namely, proton and hydrogen, the cut-off energy is here fixed at 10 keV while for the secondary electrons the latter is fixed at 7.4 eV i.e. the excitation threshold of the water molecule. Secondary electrons with kinetic energies lower than this threshold are not followed and assumed as locally absorbed by the medium.

3. Simulation of proton transport in water

TILDA-V is able to provide the coordinates of all the interactions as well as the type of collision together with the energy loss, including the deposited as well as the kinetic energy of the resultant particle(s) potentially created. An accurate dosimetry of any proton-beam irradiation may then be achieved from the macroscopic (cellular) to the microscopic (subcellular) scale. To illustrate this feature, we report in Figures 2 and 3 a comparison between our simulations and available data in terms of CSDA (Continuous Slowing-Down Approximation) range and electronic stopping power for proton energies ranging from 10 keV to 100 MeV. In both cases, a very good agreement is observed.

![Figure 2](image1.png)  
**Figure 2.** (Color online) Proton range in water: computed prediction (red line) compared with published data (diamonds [19], circles [20] and stars [21]).

![Figure 3](image2.png)  
**Figure 3.** (Color online) Electronic stopping power for $H^+/H_0$ in water: computed prediction (red line) compared with experimental data (green, blue, orange and magenta circles [22-25]).
4. Conclusions
In the current work, we have briefly reported on the development of a home-made Monte Carlo code called TILDA-V able to describe the full proton track structure in water and DNA within the energy range 10 keV-100 MeV. The current version is based on a complete set of quantum-mechanical and semi-empirical multiple differential and total cross sections for modeling all the electron- and proton/hydrogen-induced interactions in water and biological targets (DNA nucleobases and sugar-phosphate backbone). Preliminary comparisons with available data in terms of proton range and stopping power in water have clearly pointed out the performance of our code. Further results will be reported in a forthcoming study focused on proton tracking in a realistic biological medium.

Acknowledgments
This work has been developed as part of the activities planned in the Programme PICS 5921 (THEOS) as well as in the INSERM project PhysiCancer called ‘‘MICRONAUTE’’. Sandia National Laboratories is a multi-program laboratory managed and operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy’s National Nuclear Security Administration under contract DE-AC04-94AL85000.

References
[1] Champion C, L'Hoir A, Politis M F, Fainstein P D, Rivarola R D and Chetioui A 2005 Radiat. Res. 163 222
[2] Champion C 2003 Phys. Med. Biol. 48 2147
[3] Champion C, Lekadir H, Galassi M E, Fojón O, Rivarola R D and Hanssen J 2010 Phys. Med. Biol. 55 6053
[4] Galassi M E, Champion C, Weck P F, Rivarola R D, Fojón O and Hanssen J 2012 Phys. Med. Biol. 57 2081
[5] Champion C, Weck P F, Lekadir H, Galassi M E, Fojón O, Abufager P, Rivarola R D and Hanssen J 2012 Phys. Med. Biol. 57 3039
[6] Champion C 2010 Phys. Med. Biol. 55 11
[7] Champion C 2013 J. Chem. Phys. 138 184306
[8] Green A E S and McNeal R J 1971 J. Geophys. Res. 76 133
[9] Champion C, Monti J M, Quinto M A, Weck P F, Rivarola R D, Fojón O A and Hanssen J, private communication
[10] Dingfelder M, Inokuti M and Paretzke H G 2000 Radiat. Phys. Chem. 59 255
[11] Rudd M E, Goffe T V, DuBois R D and Toburen L H 1985 Phys. Rev. A 31 492
[12] Bolorizadeh M A and Rudd M E 1986 Phys. Rev. A 33 888
[13] Luna H, Barros A L F, Sigaud G M, Santos A C F, Senthil V, Shah M B, Latimer C J and Montenegro E C 2007 Phys. Rev. A 75 042711
[14] Dagnat R, Blanc D and Molina D 1970 J. Phys. B 3 1239
[15] Toburen L H 1998 Radiat. Environ. Biophys. 37 221
[16] Gobet F, Farizon B, Farizon M and Gaillard M J 2001 Phys. Rev. Lett. 86 3751
[17] Gobet F, Eden S, Coupier B, Tabet J, Farizon B, Farizon M, Gaillard M J, Ouaskit S, Carre M and Märk T D 2006 Chem. Phys. Lett. 421 68
[18] Moccia R 1964 J. Chem. Phys. 40 2186
[19] Janni J F 1982 Atomic Data Nuclear tables 27 149
[20] Uehera S, Toburen L H and Nikjoo H 2010 Int. J. Radiat. Biol. 77 139
[21] International Commission on Radiation Units and Measurements 1993 ICRU Report 49 ICRU, Washington DC
[22] Mitterschiffthaler C and Bauer P 1990 Nucl. Instrum. Methods Phys. Res. B 48 58
[23] Phillips J A 1953 Phys Rev 90 532
[24] Baek W Y, Grosswendt B and Willems G 2006 Radiat. Prot. Dosimetry 122 32
[25] Reynolds H K, Dunbar D N F, Wenzel W A and Whaling W 1953 Phys. Rev. 92 742