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1 Electron transport in DNA bases: An extension of the Geant4-DNA  
2 Monte Carlo toolkit

3

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## Abstract

34 The Geant4-DNA Monte Carlo toolkit is extended to include electron interactions with the four  
35 DNA bases using cross sections implemented in Geant-DNA CPA100 models. Electron cross  
36 sections for elastic scattering, ionisation, and excitation are calculated in the four DNA bases  
37 (adenine, thymine, guanine and cytosine) with relativistic energy range. These are implemented  
38 within the “option6” physics constructor to extend its capability of tracking electrons in DNA  
39 material in addition to liquid water. Differential and integrated cross sections calculations are in  
40 good agreement with the literature for all DNA bases. Stopping power, range and inelastic mean  
41 free path calculations in the four bases agree well with other studies, especially for high energy  
42 electrons with some deviations at low energies. Differences from water simulations emphasize  
43 the need to include DNA bases cross sections in track structure codes for better estimation of  
44 radiation effects on biological material.

45

46 **Keywords:** Geant4-DNA, DNA bases, Monte Carlo, Electron cross sections, Stopping power,  
47 Range, Inelastic mean free path.

48

### 49 **Highlights:**

- 50 • Electron interactions in DNA bases
- 51 • Geant4-DNA electron transport in DNA
- 52 • Electron stopping power in DNA
- 53 • Electron range in DNA
- 54 • Inelastic mean free path in DNA

55

## 56 **1. Introduction**

57 Track structure Monte Carlo codes are computational tools used to simulate accurately ionizing  
58 radiation interactions within biological material, mainly approximated as liquid water [1]. They  
59 have many applications in radiobiology, medical physics and radioprotection [2]. Some of these  
60 codes, such as CPA100 [3] and KURBUC [4], not only simulate the physical stage but also the  
61 chemical stage of radiological electron-water interactions. An additional characteristic of  
62 CPA100 is the possibility to track electrons in DNA material [5]. PARTRAC code provides further  
63 options since it is able to simulate the different radiation interaction stages in water targets  
64 including DNA damage and repair [6]. The general purpose Monte Carlo code PENELOPE [7, 8]  
65 also provides detailed track structures for electrons down to 50 eV. Among them, the open  
66 source toolkit Geant4-DNA [9-12] simulates particle interactions step by step as a low energy  
67 physics extension of Geant4 [13-15] in liquid water. The physico-chemical and chemical  
68 radiation stages can also be simulated to estimate the yields of molecular species created from  
69 water radiolysis [16].

70 Since deoxyribonucleic acid (DNA) is considered the most radiation sensitive target within cells,  
71 accurate damage assessment is important. Previous studies approximate DNA damage through  
72 geometrical distribution of possible strand breaks within a homogeneous water medium [6, 17,  
73 18]. DNA is a double stranded helical macromolecule forming the genetic code of living cells. It is  
74 composed of a sugar phosphate backbone and a long ladder-like sequence formed by four  
75 different nitrogenous bases: adenine, thymine, guanine and cytosine [19]. The integrity of this  
76 sequence is essential to the cell's health and replication and any damage or error in the sequence

77 may result in carcinogenesis and cell death. A recent study by Francis *et al.* calculated the proton  
78 interaction cross sections within the four DNA bases using the semi-empirical Rudd model [20].  
79 Total electron ionisation cross sections were also calculated with the BEB model. These cross  
80 sections were tested in Geant4-DNA where proton and electron stopping powers within the  
81 nucleobases were calculated in addition to lineal and specific energies of protons. Moreover, the  
82 current public version of Geant4-DNA provides interaction cross sections of electrons in DNA  
83 precursors tetrahydrofuran and trimethylphosphate ranging between 10 eV - 1 keV [21].  
84 However, the electron interaction cross sections within DNA nucleobases are not yet available.  
85 Therefore, it is beneficial to perform direct determination of electron cross sections in DNA  
86 nucleobases and not derive them from DNA precursors.

87 Since 2017 Geant4-DNA has provided an alternative set of discrete physics models for the  
88 simulation of electron interactions in liquid water over the energies ranging between 11 eV and  
89 256 keV under the “option6” physics constructor [12, 22]. These models implement the  
90 ionisation, electronic excitation and elastic scattering interactions of electrons obtained from the  
91 CPA100 track structure code developed by Terrissol *et al.* [3, 22]. In addition to physical  
92 interactions in liquid water, the original CPA100, coded in Fortran, also provides the water  
93 radiolysis simulation and radiation transport in different biological targets such as DNA bases  
94 [5]. For a better determination of radiation damage, it is important to consider a more realistic  
95 biological medium instead of using liquid water as the irradiated medium. The aim of this work  
96 is thus a continuation of our recently published work [22] in order to extend the  
97 “G4EmDNAPhysics\_option6” constructor (which will be referred to as “option6” throughout the  
98 text and which contains CPA100 models for liquid water only) to include electron interactions in  
99 DNA material in addition to liquid water. Therefore, new sets of electron cross sections in the  
100 four DNA nucleobases, adenine ( $C_5N_5H_5$ , 1.35 g/cm<sup>3</sup>), thymine ( $C_5N_2O_2H_6$ , 1.48 g/cm<sup>3</sup>), cytosine  
101 ( $C_4N_3OH_5$ , 1.3 g/cm<sup>3</sup>) and guanine ( $C_5N_5OH_5$ , 1.58 g/cm<sup>3</sup>), were calculated specifically for this  
102 purpose. The new cross sections are extended to 1 MeV taking into account relativistic  
103 corrections of electron transport in the nucleobases, which are not DNA-bound as previously  
104 presented in the works of Edel [23] and Peudon [24].

105 In the following sections, the physics models for elastic scattering, electronic excitation and  
106 ionisation for electrons of energy range 11 eV – 1 MeV within the four nucleobases are  
107 presented. The interaction cross sections are calculated and compared to values from the  
108 literature. The physics models are implemented within Geant4-DNA according to the calculated  
109 cross sections. The collision stopping power, continuous-slowing-down approximation (CSDA)  
110 range and inelastic mean free path (IMFP) are calculated within the four nucleobases to verify  
111 the implementation and comparison with experimental and theoretical data are presented.

## 112 2. Materials and Methods

### 113 2.1 Physics models of electron interactions

114 In Geant4-DNA the new models for the physics processes of electrons in the four DNA  
115 bases (adenine, thymine, cytosine and guanine) are implemented on the basis of elastic  
116 scattering, electronic excitation and ionisation cross sections. The incident electron energy  
117 ranges from 11 eV to 1 MeV. The 11 eV lower limit is restricted by the elastic scattering, and  
118 the upper 1 MeV limit is chosen in accordance with the highest electron energy provided by the  
119 current Geant4-DNA version. The three different interactions cross sections governing the  
120 electron transport in the four DNA bases are calculated as described in the following sections.

#### 121 2.1.1 Elastic scattering

122 The elastic cross section in the four bases is calculated according to the well-known  
123 independent atom model (IAM) [25] similar to elastic cross section in water in the CPA100  
124 code [22, 23]. In this approximation, the electron-molecule interaction is reduced to a collision

125 with individual atoms constituting the molecule. This approach gives good results for many  
 126 polyatomic molecules at high and intermediate incident energy corresponding to wavelengths  
 127 shorter than the internuclear distances [25]. Therefore, the calculation of the elastic scattering  
 128 differential cross section of a molecule requires the differential cross section of each atom  $\frac{d\sigma_A}{d\Omega}$ ,  
 129 the complex scattering amplitudes of the atoms  $i$  ( $f_i(\theta, k)$ ) and  $j$  ( $f_j^*(\theta, k)$ ), and the  
 130 internuclear distance between the atoms  $i$  and  $j$  ( $r_{ij}$ ).

$$\frac{d\sigma}{d\Omega} = \sum_{i=1}^N \frac{d\sigma_{A,i}}{d\Omega} + \sum_{i \neq j=1}^N f_i(\theta, k) f_j^*(\theta, k) \frac{\sin(sr_{ij})}{sr_{ij}} \quad \text{Eq 1}$$

131 where  $k$  is the incident electron wave number,  $s$  ( $s = 2k \sin \frac{\theta}{2}$ ) is the magnitude of the  
 132 momentum transfer during the collision,  $\theta$  is the scattering angle and  $N$  is the total number of  
 133 atoms in the target.

134 The geometry of the DNA bases was imported from the Chemical Structures Project, an  
 135 open source software that provides 3D molecular structures for various molecules [26].

136 The scattering amplitudes are given by the ELastic Scattering of Electrons and Positrons  
 137 by neutral Atoms (ELSEPA) code [27]. The elastic differential cross section per unit solid angle  
 138  $d\Omega$  for atoms (H, C, N and O) are calculated using the corresponding scattering amplitudes  
 139 derived from the partial wave expansion.

140 ELSEPA is a Fortran code developed by Salvat *et al.* [27]. This code allows not only to  
 141 calculate electron elastic scattering differential and integrated cross sections but also to  
 142 perform phase shift calculations for atoms with energies ranging from a few eV up to 1 GeV.  
 143 Relativistic corrections are included in the Dirac partial wave approach within the static-  
 144 exchange approximation. The interaction potential is the sum of different potentials  
 145 (electrostatic, exchange, and correlation-polarization) and the Dirac partial wave analysis is  
 146 performed. This code provides more recent and precise data compared to those that are used  
 147 in CPA100, which is limited to low energy (<256 keV). Moreover, new elastic models in Geant4-  
 148 DNA for gold [28] and water [29] targets were previously computed with ELSEPA.

### 149 2.1.2 Ionisation

150 The Binary Encounter Bethe (BEB) model for electron ionisation was initially developed  
 151 by Kim and Rudd [30]. Since it has further developments and has been successfully used to  
 152 calculate total cross sections and energy differential ones for a large number of atmospheric  
 153 molecules [31], it was later used for industrial applications [32]. The agreement with  
 154 experimental data is excellent for small size molecules at low energy. It has already been applied  
 155 for water in CPA100 code [23] and "option6" within Geant4-DNA code [22].

156 The relativistic Binary Encounter Bethe Vriens model (RBEBV), developed by Guerra *et al.*  
 157 [33], is used to calculate the ionisation cross section from the ionisation energy threshold to  
 158 1 MeV for each molecular orbital (MO) as a function of the incident kinetic energy  $T$ . This model  
 159 also allows to calculate the energy of the ejected electron  $W$  using the energy differential cross  
 160 section.

161 The analytical form of the cross section only depends on 3 parameters representative of  
 162 the molecular orbital. This form is also convenient because it allows obtaining the energy loss by  
 163 directly sampling this expression without using interpolation in large cross section tables [22].

164 The Monte Carlo track structure simulation codes require the precise knowledge of the  
 165 energy of primary and ejected electrons after ionisation, which is given by the energy differential  
 166 cross section (EDCS). The energy differential cross section for each molecular orbital  $\frac{d\sigma_{ion,MO}}{dw}$   
 167 written in the reduced form is in the RBEBV model:

$$\frac{d\sigma_{ion,MO}}{dw} = \frac{4\pi a_0^2 \alpha^4 N}{(\beta_t^2 + \beta_u^2 + \beta_b^2)2b'} \cdot \left[ -\frac{\phi}{t+1} \cdot \left( \frac{1}{w+1} + \frac{1}{t-w} \right) \cdot \frac{1+2t'}{(1+t'/2)^2} + \frac{1}{(w+1)^2} + \frac{1}{(t-w)^2} + \frac{b'^2}{(1+t'/2)^2} + \left( \text{Ln} \left( \frac{\beta_t^2}{1-\beta_t^2} \right) - \beta_t^2 - \text{Ln}(2b') \right) \cdot \left( \frac{1}{(w+1)^3} + \frac{1}{(t-w)^3} \right) \right] \quad \text{Eq 2}$$

169

$$\text{with } w = \frac{W}{B}$$

170

$$\beta_t^2 = 1 - \frac{1}{(1+t')^2} \quad \text{and} \quad t' = \frac{T}{mc^2} \quad \text{and} \quad t = \frac{T}{B}$$

$$\beta_u^2 = 1 - \frac{1}{(1+u')^2} \quad \text{and} \quad u' = \frac{U}{mc^2} \quad \text{and} \quad u = \frac{U}{B}$$

$$\beta_b^2 = 1 - \frac{1}{(1+b')^2} \quad \text{and} \quad b' = \frac{B}{mc^2}$$

171 where  $\alpha$ ,  $m$ ,  $a_0$  and  $c$  are the fine structure constant, the electron mass, the Bohr's radius and the  
172 speed of light in vacuum, respectively.

173  $B$  is the electron binding energy,  $U$  the bound electron kinetic energy and  $N$  the occupation  
174 number of the subshell to be ionized.

175 The relativistic form of the Vriens function  $\phi$  is written as

$$\phi = \cos \left[ \sqrt{\frac{\alpha^2}{(\beta_t^2 + \beta_b^2)}} \text{Ln} \left( \frac{\beta_t^2}{\beta_b^2} \right) \right] \quad \text{Eq 3}$$

176 In the BEB formalism of Kim *et al.* [34], the Vriens function is equal to its asymptotic  
177 form (=1).

178 The total cross section per shell  $\sigma_{ion,MO}$  can be obtained from the single differential cross  
179 section (Eq 2) integrated from  $w=0$  to  $w=(t-1)/2$ . The theoretical expression of this cross section  
180 per molecular orbital as a function of the incident energy is

$$\sigma_{ion,MO} = \frac{4\pi a_0^2 \alpha^4 N}{(\beta_t^2 + \beta_u^2 + \beta_b^2)2b'} \left[ \left( 1 - \frac{1}{t} + \frac{t-1}{2} \frac{b'^2}{(1+t'/2)^2} \right) - \phi \frac{\text{Ln}(t)}{t+1} \frac{1+2t'}{(1+t'/2)^2} + \frac{1}{2} \left( \text{Ln} \left( \frac{\beta_t^2}{1-\beta_t^2} \right) - \beta_t^2 - \text{Ln}(2b') \right) \left( 1 - \frac{1}{t^2} \right) \right] \quad \text{Eq 4}$$

181 The total ionisation cross section of the molecule is the sum of the cross sections (Eq 4)  
182 for all molecular orbitals:

$$\sigma_{ion}(T) = \sum_1^{nMO} \sigma_{ion,MO}(T) \quad \text{Eq 5}$$

183 The required data ( $B$ ,  $U$ , and  $N$ ) to calculate the cross sections for each MO of Eq2 and Eq4  
184 are obtained from molecular electronic structure calculations since experimental data are not  
185 available. There are 35 MOs for adenine, 39 for guanine, 29 for cytosine and 33 for thymine. The  
186 number of inner shells is 10, 11, 8 and 9 for adenine, guanine, cytosine and thymine,  
187 respectively.

188 The molecular orbitals for the four DNA bases were obtained through calculations at  
189 restricted Hartree-Fock (RHF) level with basis-set cc-pVTZ on geometries previously optimized  
190 at the same level of theory. It is worth noting that basis-set cc-pVTZ is a correlation-consistent

191 triple-zeta basis-set with polarization functions and, particularly, with Gaussian-type functions up  
 192 to the f shell. The corresponding data (B, U and N) were calculated as follows: B corresponds to  
 193 the orbital energy of each MO resulting from the self-consistent resolution of the Hartree-Fock  
 194 equations, U is the one-electron kinetic energy expectation value associated with the considered  
 195 molecular orbital, and N is the molecular orbital occupation number, which, for an RHF  
 196 computation on a 2n-electron closed-shell system, it is always equal to two for the first  
 197 (occupied) n MOs and equal to zero for the remaining M-n (virtual) orbitals (with M as the  
 198 number of basis functions used in the calculation). All the above-mentioned RHF computations  
 199 were performed exploiting the quantum chemistry packages Gaussian09[35] and GAMESS-UK  
 200 [36].

201

### 202 2.1.3 Excitation

203 Due to the lack of data for this process in DNA bases, the hypothesis to derive the  
 204 electronic excitation cross section is based on the inelastic cross sections in water calculated by  
 205 Dingfelder *et al.* [37]. In brief, the total excitation cross section is extracted from the total  
 206 ionisation cross section of the base and the water models for excitation and ionisation (Eq 6), as  
 207 proposed in the original version of the CPA100 code [23]. The assumption is that the ratio of the  
 208 total ionisation cross section over total excitation cross section is the same in water and DNA  
 209 components for each incident energy. For energies higher than 400 eV, this ratio in water tends  
 210 to a constant.

$$\sigma_{exc,base} = \sigma_{ion,base} \left[ \frac{\sigma_{exc}}{\sigma_{ion}} \right]_{water} \quad \text{Eq 6}$$

211 Only the electronic levels with a threshold lower than 20 eV can be excited in analogy with  
 212 water [23]. With this assumption, there are 14, 12, 15 and 14 levels for adenine, cytosine,  
 213 guanine and thymine, respectively, that can be excited.

214 The final hypothesis concerns how to select the levels. Without information, the  
 215 probability is chosen to be the same for each level.

216

217

## 218 2.2 Implementation in Geant4-DNA

219 The electron interaction processes, elastic scattering, ionisation, and electronic excitation,  
 220 were implemented as classes of Geant4-DNA physics models inherited from the G4VEmModel  
 221 class [9] with Geant4.10.05.p01 version. Total and differential cross section data tables were  
 222 calculated for each process as described in the previous sections. Each electron is tracked step  
 223 by step and according to its energy prior to collision with the target material. A random process  
 224 and a random target energy level are sampled according to the total cross section tables. For  
 225 elastic process, the angle is randomly sampled according to the angular differential cross section  
 226 tables and, for ionisation, the transferred energy is randomly sampled according to the energy  
 227 differential cross section tables. Interpolation between consecutive energy points in the cross  
 228 sections data tables was applied. Electrons are tracked down to 11 eV below which the track is  
 229 killed and the energy is deposited locally. Therefore, the classes allow to simulate the stochastic  
 230 nature of the electronic interactions.

231 The implementation of the new Geant4-DNA models for the four DNA bases was validated  
 232 by performing three different calculations over the incident electron energies ranging from 11  
 233 eV to 1 MeV. Collision stopping power, CSDA range and inelastic mean free path of electrons  
 234 were calculated using Geant4-DNA examples (called “spower”, “range” and “mfp”, respectively)  
 235 developed for calculations in homogeneous targets of liquid water [12]. The targets in the three  
 236 examples were replaced by uniform targets of adenine (A), thymine (T), guanine (G) and  
 237 cytosine (C), respectively, and the physics models of water were replaced by new DNA bases

238 models. Table 1 summarizes the model classes created for this study compared to liquid water  
 239 models.

240 *Table 1 : Electron interaction processes, the physics models and the model classes used in the*  
 241 *G4EmDNAPhysics\_option6 constructor. The liquid water models are already available in the*  
 242 *current public version of Geant4-DNA [22] and the four DNA bases models are presented in this*  
 243 *work. Incident electron energy ranges are presented for each model.*

G4EmDNAPhysics_option6			
Process	Geant4-DNA model class	Liquid water models [22]	Four DNA bases models
Elastic Scattering	G4DNACPA100ElasticModel	Independent Atom Method model (11 eV – 256 keV)	Independent Atom Method model (11 eV – 1 MeV)
Ionisation	G4DNACPA100IonisationModel	Binary Encounter Bethe model (11 eV – 256 keV)	Relativistic Binary Encounter Bethe Vriens model (11 eV – 1 MeV)
Excitation	G4DNACPA100ExcitationModel	Dielectric model (11 eV – 256 keV)	Derived from water and ionisation cross sections (Eq 6) (11 eV- 1MeV)

244

### 245 3. Results

246 To the best of our knowledge, we tried to collect all existing published data whether calculated  
 247 or from experiments concerning DNA bases. In the following sections, the results of the  
 248 quantities calculated in this study are shown in comparison with those published in the  
 249 literature.

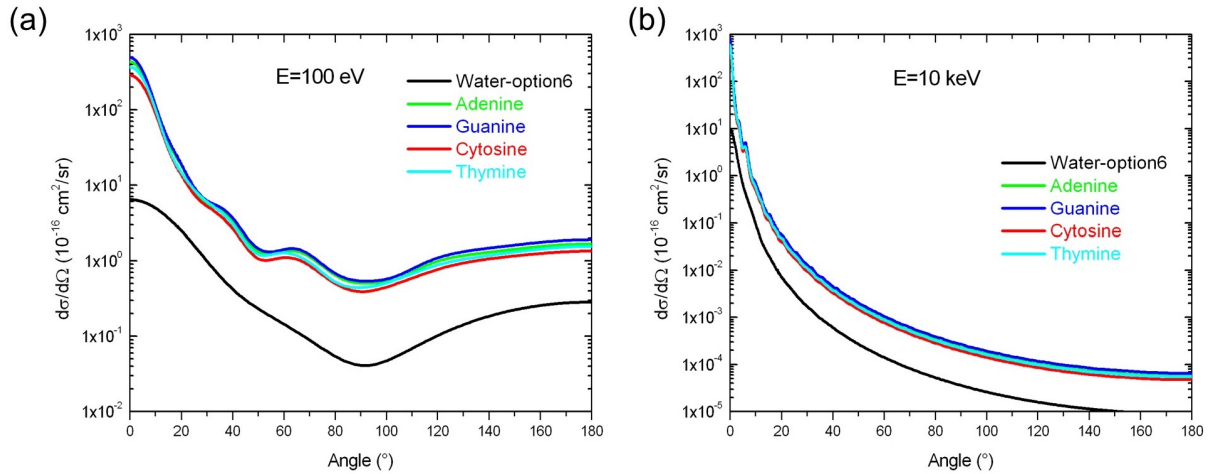
#### 250 3.1 Electron interaction physics models: comparison with liquid water and available data

##### 251 3.1.1 Elastic scattering

252 Figure 1 presents two electron incident energies (100 eV and 10 keV) variation of the  
 253 differential cross sections as a function of the scattering angle for the four DNA bases molecules.  
 254 The results are compared with differential elastic cross section in water (water-option6,  
 255 implemented in Geant4-DNA [22]), obtained from CPA100 code. For all incident energies and  
 256 scattering angles, the elastic cross section in water is always lower than in DNA bases by about  
 257 one order of magnitude as shown in Figure 1. The angular dependence of the cross sections  
 258 values for the four bases is very similar. The lowest values of the differential cross sections are  
 259 obtained for the smallest molecule (i.e. cytosine) and the highest for the largest (i.e. guanine)  
 260 since the mass of the molecule, and the number of electrons are in the following decreasing  
 261 order  $G > A > T > C$ . The observed minimum at 100 eV for all the molecules disappears at higher  
 262 energies, showing a monotonical decrease as a function of the increasing scattering angle. The  
 263 four bases exhibit the same minimum differential cross section value at  $90^\circ$  scattering angle.

264





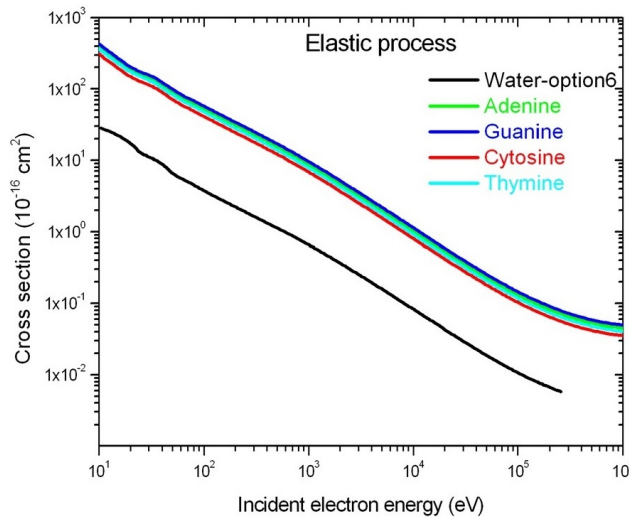
265  
 266 *Figure 1 : Elastic differential cross section for 100 eV (a) and 10 keV (b) electron collisions with*  
 267 *adenine, guanine, cytosine, thymine and water respectively*

268

269 The integrated elastic cross sections of all four DNA bases and the liquid water option6 of  
 270 Geant4-DNA are shown in Figure 2. The integrated elastic cross sections monotonically decrease  
 271 with increasing incident energy (Figure 2). The integrated cross section curves of the DNA bases  
 272 follow the same trend as the differential cross section curves where the molecular size  
 273 dependence is observed ( $\sigma_C < \sigma_T < \sigma_A < \sigma_G$ ,  $\sigma$  stands for integrated cross section). As for differential  
 274 cross section, the integrated elastic cross section in water is one order of magnitude lower than  
 275 in the DNA bases.

276

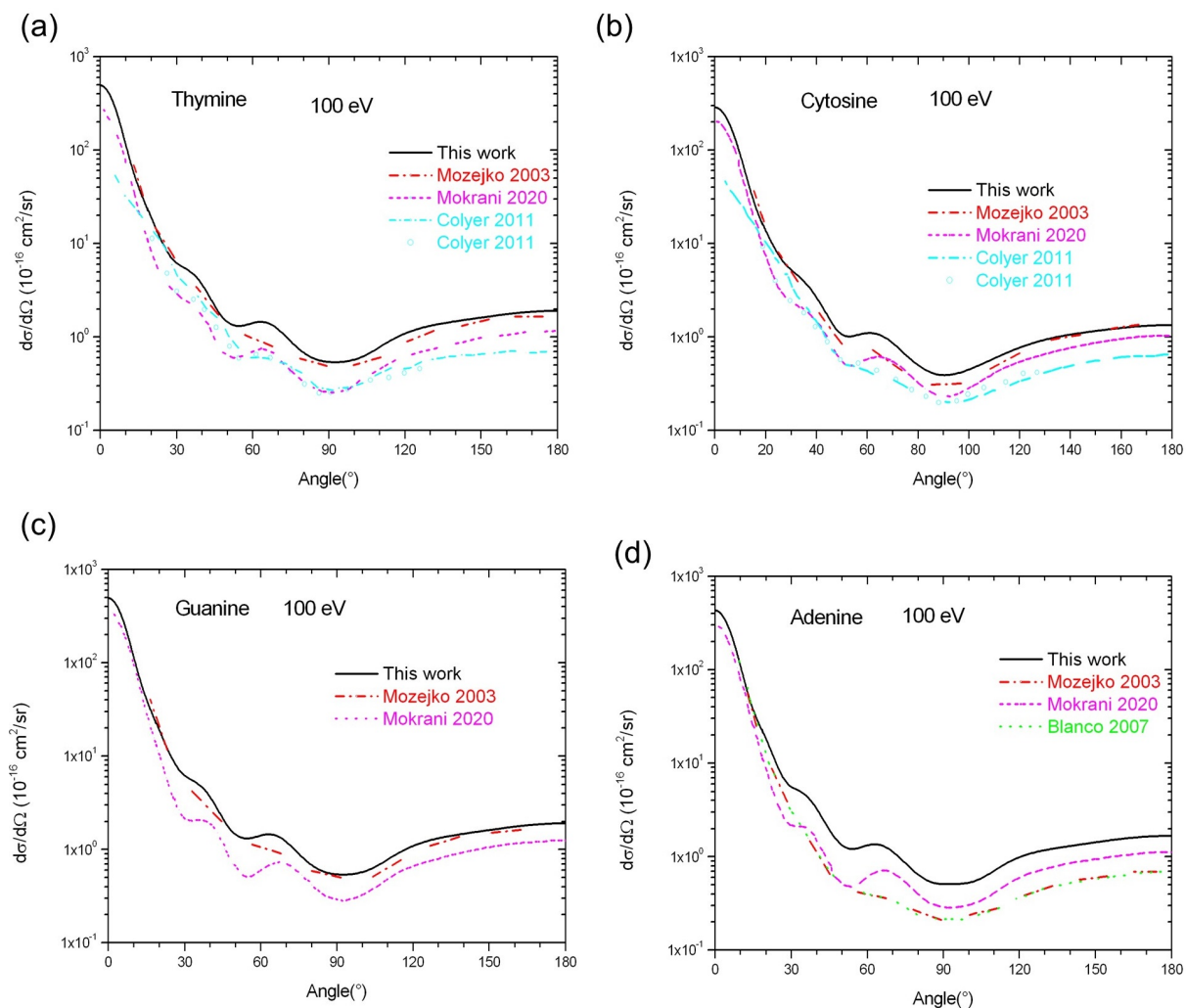
277



278  
 279 *Figure 2 : Integrated elastic cross section for adenine, guanine, cytosine and thymine and water*  
 280 *collisions with electrons.*

281

282 Figure 3 shows as an example the elastic differential cross sections of 100 eV electrons  
 283 for all four DNA bases in comparison with published calculations [38-41] of differential cross  
 284 section curves.



285  
 286 *Figure 3 : Elastic differential cross section for 100 eV incident electron energy from thymine (a),*  
 287 *cytosine (b), guanine (c) and adenine (d), compared with published data (symbols are*  
 288 *measurements [38] and lines are calculations [38-41]).*  
 289

290 Figure 4 presents a comparison of the integral elastic cross sections with available  
 291 calculated data [39-44] obtained with approximation procedures for each base over a large  
 292 incident energy range. The *ab initio* calculations limited to the low energy regime (between 0  
 293 and 20 eV for cytosine and thymine [45]) are not included.

294

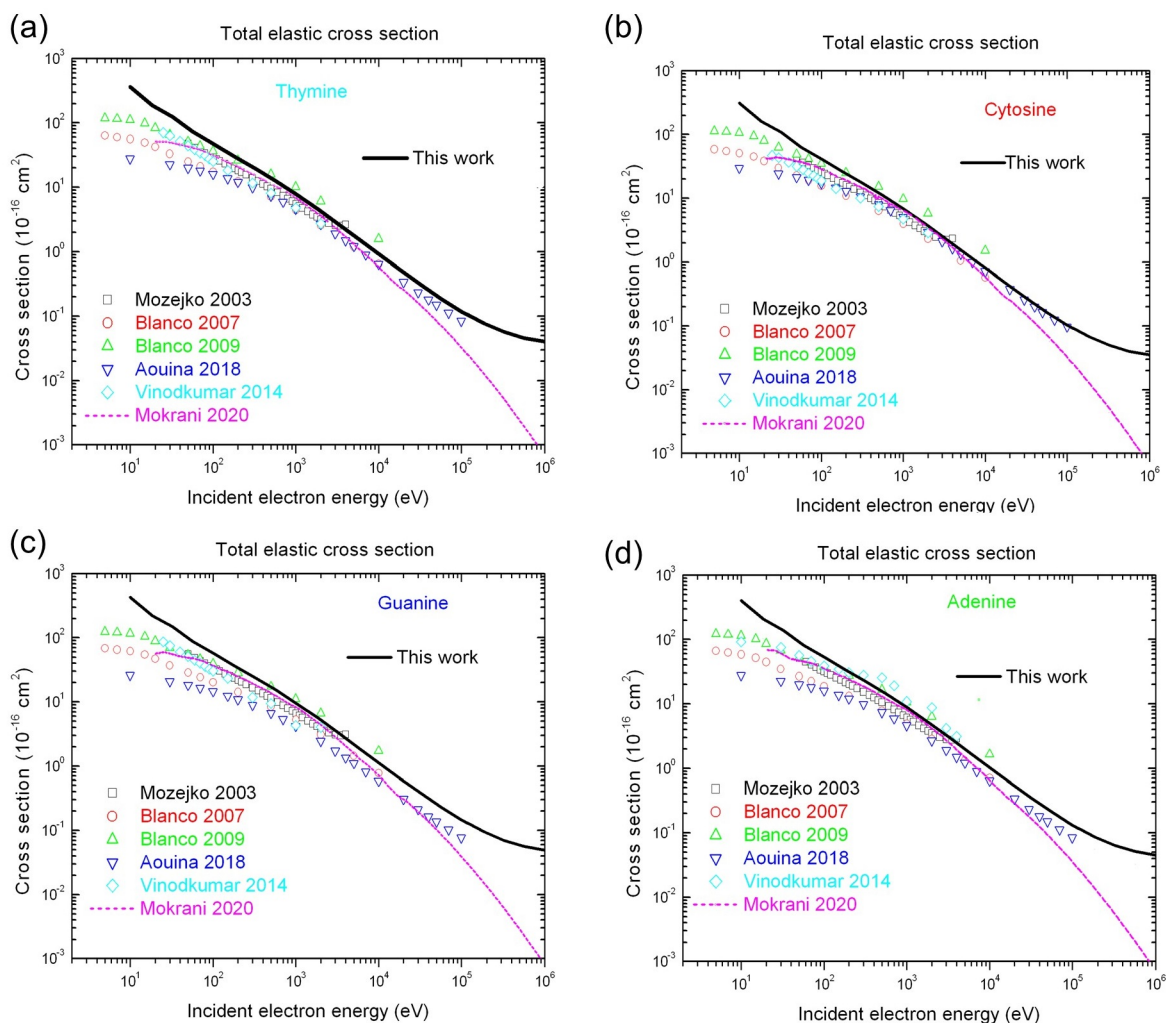


Figure 4 : Elastic integrated cross section of electron collisions with thymine (a), cytosine (b), guanine (c) and adenine (d), compared with published calculations [39-44]

295

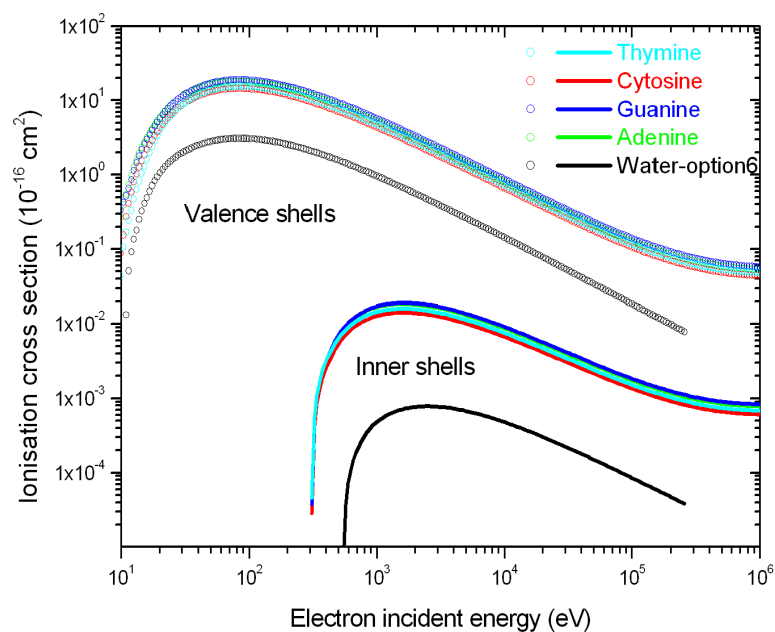
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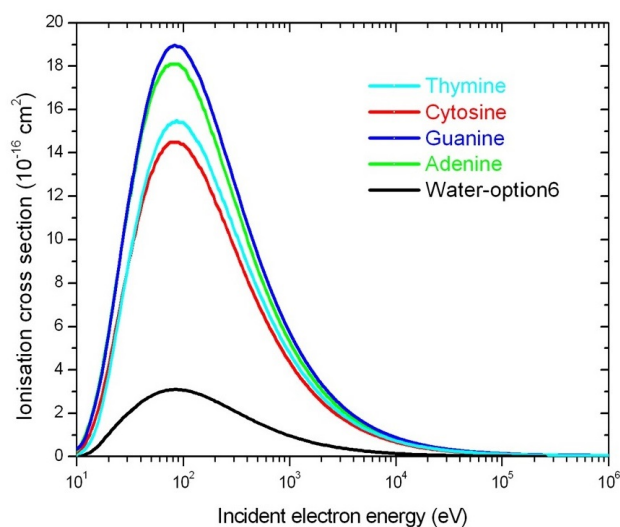
### 299 3.1.2 Ionisation

300 The total ionisation cross section is obtained by summing the contribution of each orbital  
 301 of the molecule calculated with eq 4. For each DNA base, Figure 5 gives the cross section for the  
 302 sum of the valence shells (25 for adenine, 28 for guanine, 21 for cytosine and 24 for thymine)  
 303 and the sum of the inner shells as a function of the incident energy between the threshold and 1  
 304 MeV. As we have observed, BEB calculations are more sensitive to binding energy than to mean  
 305 kinetic energy.



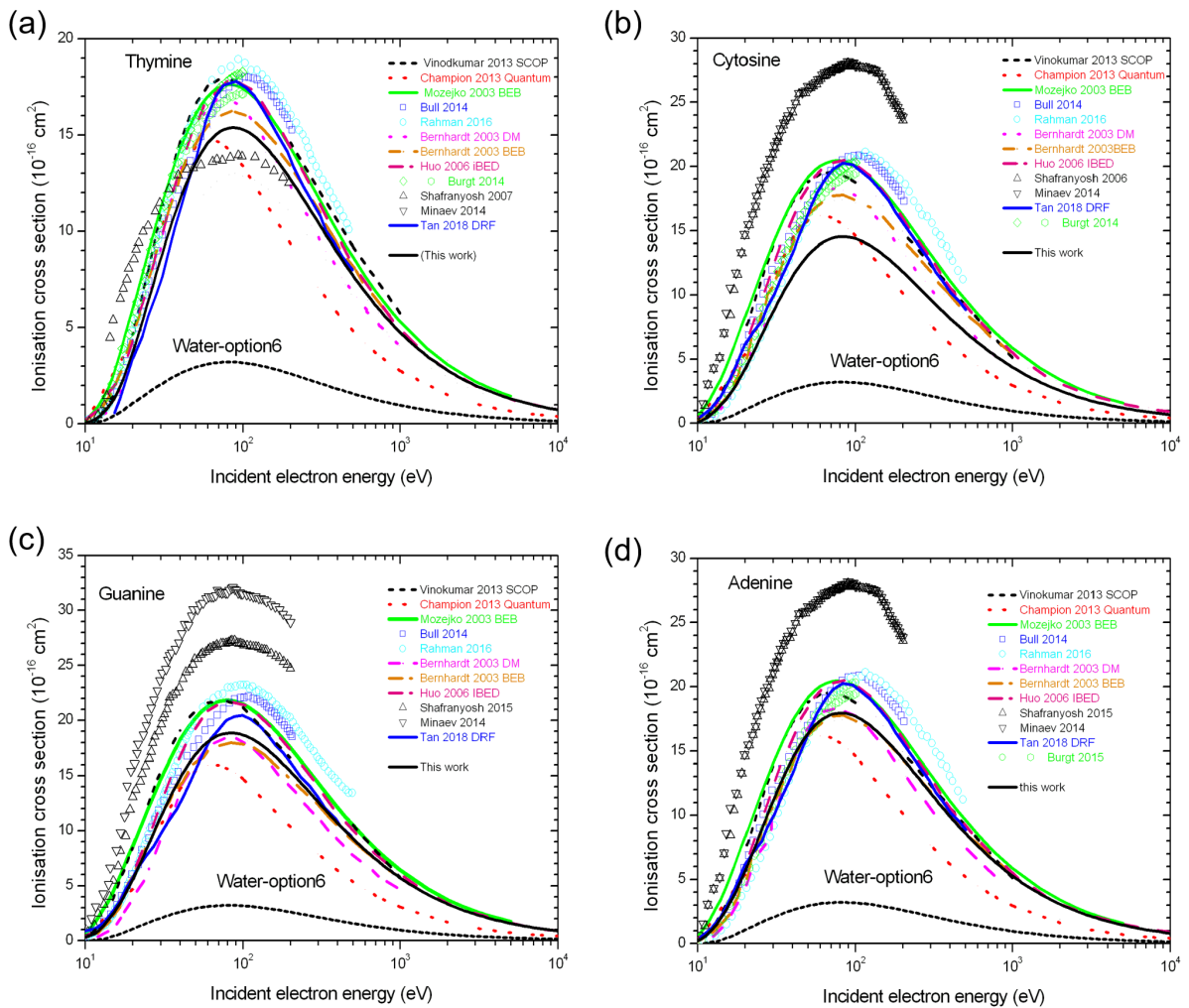
306  
 307 *Figure 5: The sum of valence shell ionisation cross sections (in lines), and the sum of internal shells*  
 308 *ionisation cross sections (in symbols) for adenine, cytosine, guanine, thymine and water.*

309 In Figure 6 the total ionisation cross sections for the DNA bases and water option6 are  
 310 shown.



311  
 312 *Figure 6 : Total ionisation cross sections for the DNA bases and water.*

313 Figure 7 presents a comparison of experimental data [46-55], and theoretical  
 314 calculations of the total ionisation cross section [39, 56-60] for the four bases. The theoretical  
 315 method used is indicated in the legend of the figures.

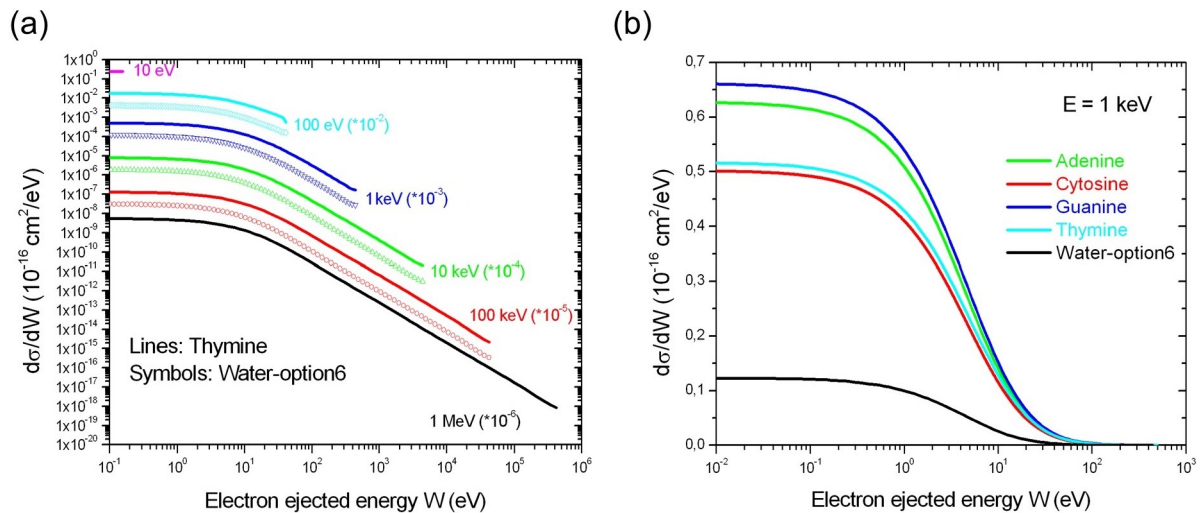


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Figure 7 : Total ionisation cross sections by electrons for the DNA bases, thymine (a), cytosine (b), guanine (c) and adenine (d), compared with available data (lines: calculations and the used method [39, 56-60], symbols and symbols: measurements [46-55] ). For comparison, the cross section in water is added.

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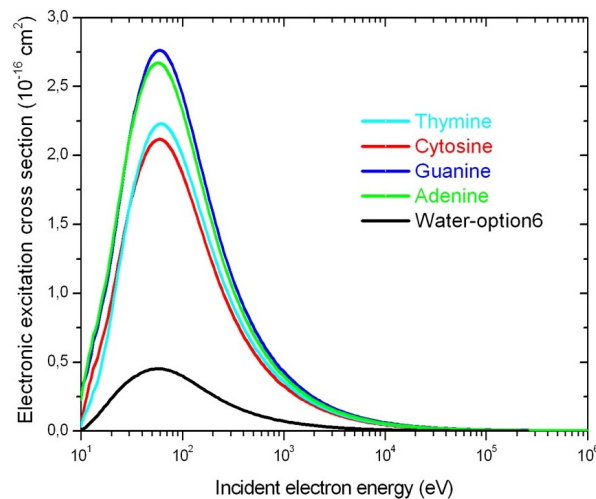
The energy differential cross sections (EDCS) were calculated using Eq. 2. Figure 8.a represents the variation of the EDCS for thymine at different incident energies as a function of the electron ejected energy. The results are compared to CPA100 data for water previously calculated in Geant4-DNA water-option6 [22]. The differential cross section in water is always lower than in thymine for any incident energy. The same trend is observed for other DNA bases (not plotted). If we compare the variation of the EDCS for one incident electron energy for the four DNA bases and water, the trend is similar to what was obtained for the elastic and total ionisation cross sections: the impact of the size of the molecule has the same effect on the variations of the EDCS (Figure 8.b at 1 keV). Analogous results are obtained with other incident energies (same curve shape, not shown here). There are no experimental data with which to compare these calculations.



333  
 334 *Figure 8 : Differential cross sections by electrons as a function of the electron ejected energy in*  
 335 *thymine and in water at different incident electron energies (scaling factors in parenthesis were*  
 336 *introduced for clarity) (a), and in the four bases and water at 1keV incident electron energy (b).*  
 337

### 338 3.1.3 Electronic excitation

339 Figure 9 presents the calculated total electronic excitation cross section for the four DNA  
 340 bases obtained using eq 6. Except at low energy (<~30 eV), the variations are directly related to  
 341 the molecular size, as observed for the total ionisation cross sections. Being an inelastic process,  
 342 the maximum appears for energy lower than 100 eV, at approximately the same value regardless  
 343 of the DNA base. Like other processes, the cross section for electronic excitation in water is  
 344 lower than in the DNA bases.



345  
 346 *Figure 9 : Electronic excitation collision cross section in the DNA compounds.*  
 347

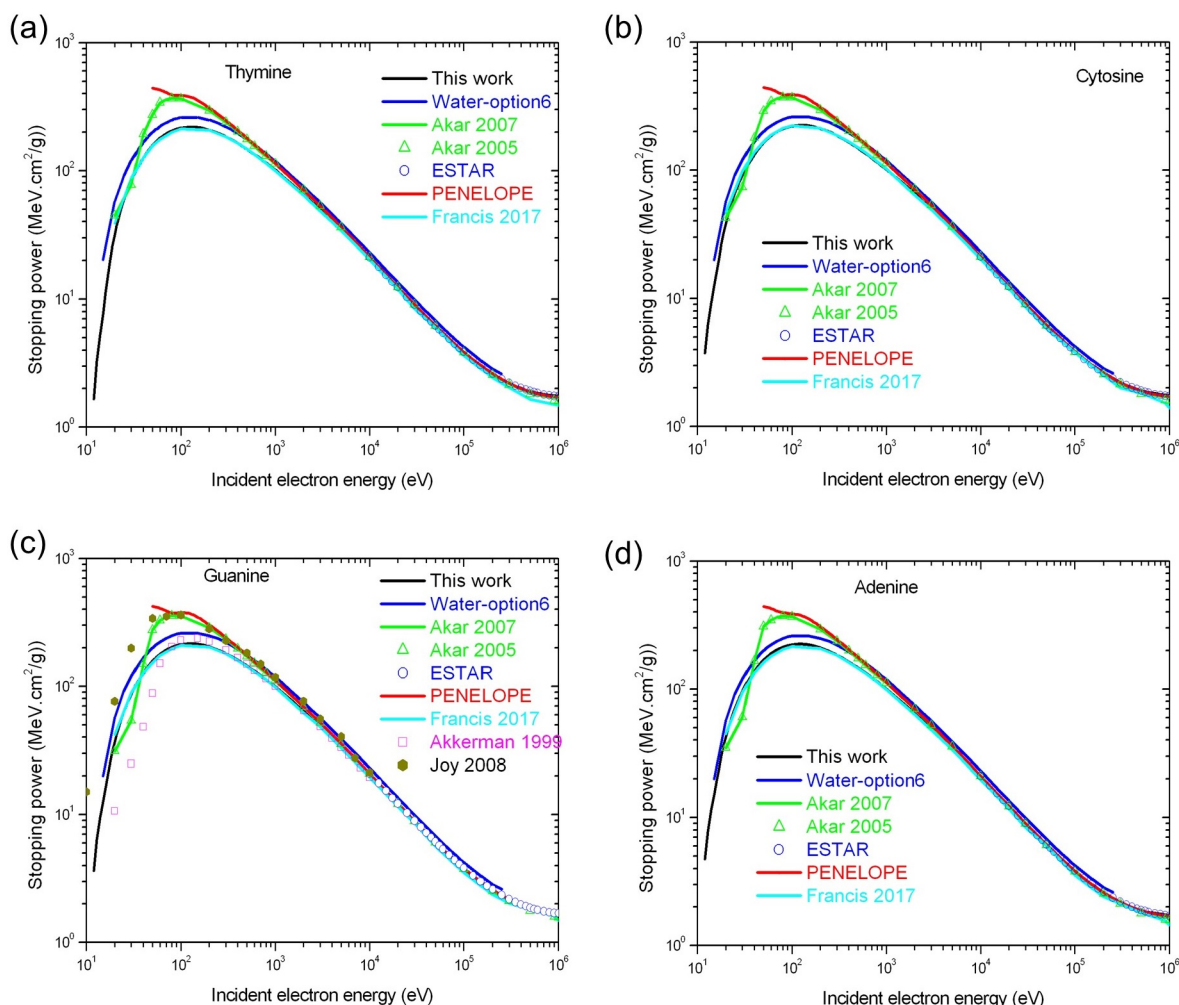
## 348 3.2 Verification of physics models in Geant4-DNA

### 349 3.2.1 Collision stopping power

350 Collision stopping power was calculated for the four DNA bases and compared with  
 351 theoretical calculations [61-65], previous Geant4-DNA Monte Carlo [20] simulations and data  
 352 derived from the input material data file of PENELOPE code, as shown in figure 10 and were also  
 353 compared with calculations in water-option6. The values were compared with calculations of

354 Akar *et al.* [63, 64] and ESTAR [61] database. Calculations by Akkerman *et al.* [65] and Joy [62]  
 355 are only available for guanine.

356



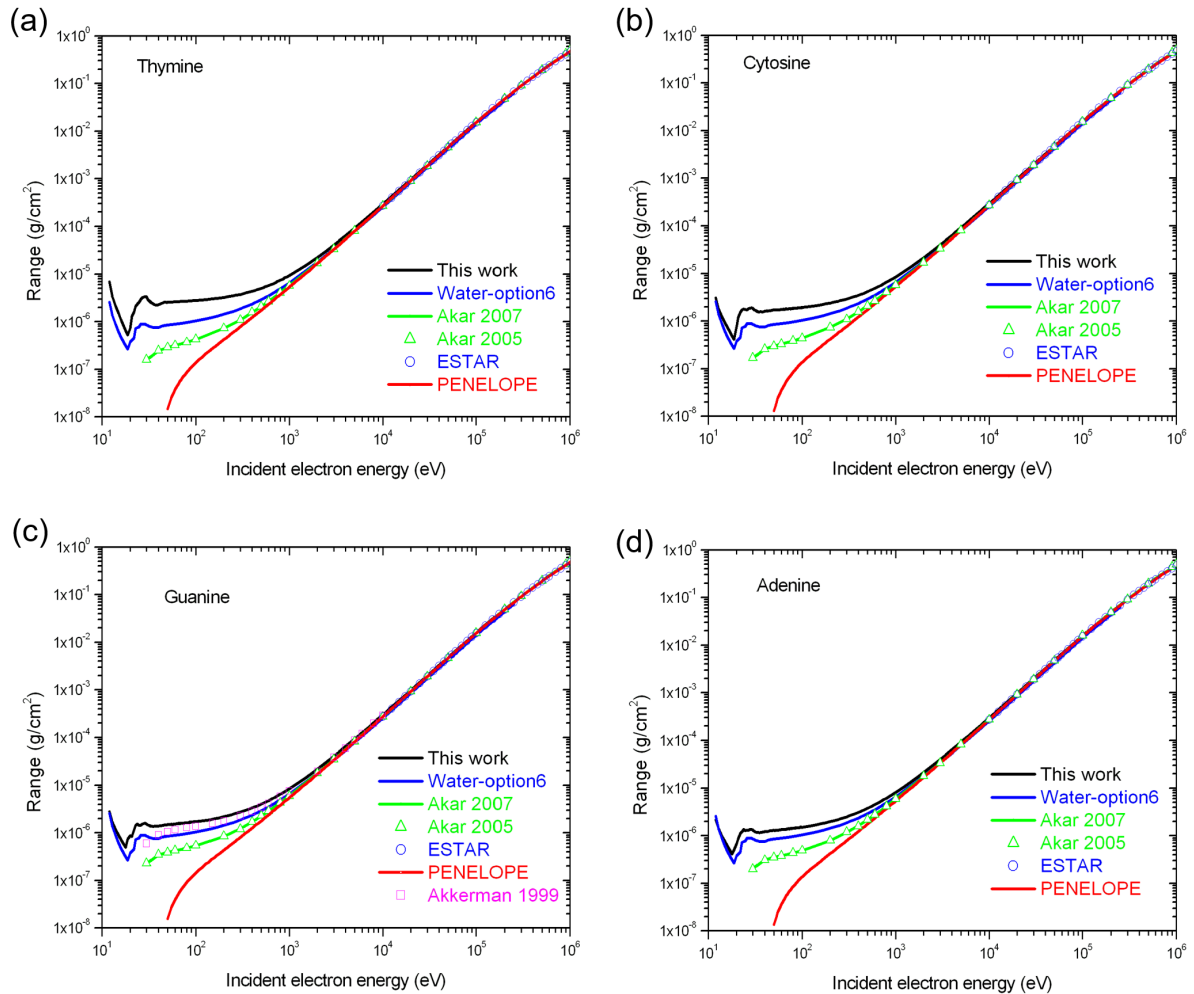
357  
 358 *Figure 10: Stopping power of the four nucleobases for electrons ranging from 11 eV - 1 MeV as*  
 359 *calculated in this work in comparison with Geant4-DNA water-option6 simulation and other*  
 360 *results from the literature [20, 61-65]. Stopping power in the four nucleobases was derived from*  
 361 *the input material data file of PENELOPE code.*

362

363

### 364 3.2.2 CSDA Range

365 The CSDA range is calculated for all four bases and compared with results from the  
 366 literature and water-option6 Geant4-DNA simulation as Figure 11 shows. Calculations by Akar *et*  
 367 *al.* [63, 64], Akkerman *et al.* [65] (guanine only) and ESTAR [61] are shown. Values derived from  
 368 PENELOPE code are also plotted for comparison.



369  
 370 *Figure 11: CSDA Range of electrons ranging from 11 eV - 1 MeV in the four nucleobases as*  
 371 *calculated in this work in comparison with Geant4-DNA water-option6 simulation and other*  
 372 *results from the literature [61, 63-65]. Range in the four nucleobases was derived from the input*  
 373 *material data file of PENELOPE code.*

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### 377 3.2.3 Inelastic mean free path

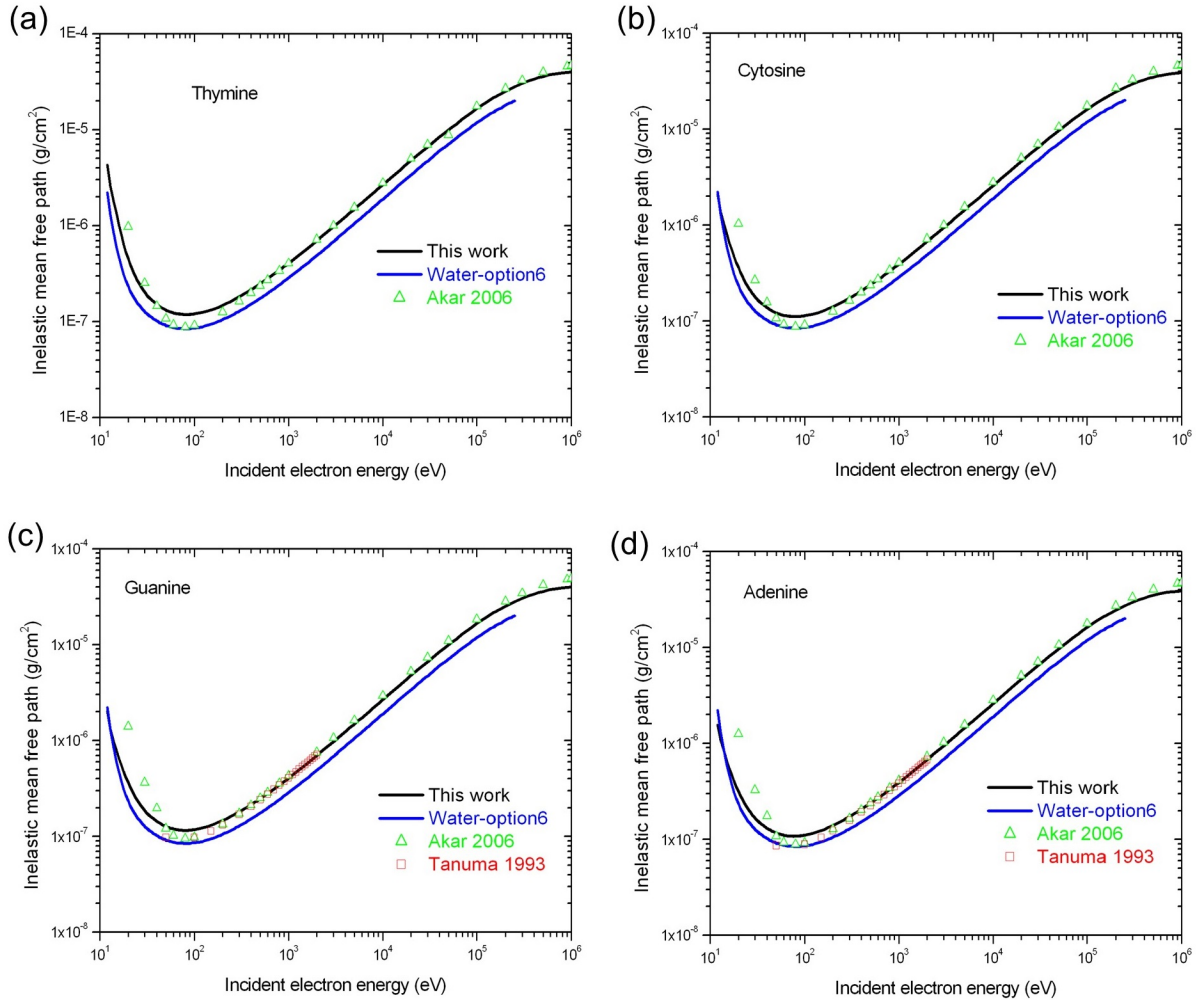
378

379 In Figure 12, the IMFP of electrons in the four DNA bases and water are shown.  
 380 Comparison with calculations of Akar *et al.* [66] and Tanuma *et al.* [67] (for adenine and  
 381 guanine) are also shown.

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Figure 12: Inelastic mean free path of electrons ranging from 11 eV - 1 MeV in the four nucleobases as calculated in this work in comparison with Geant4-DNA water-option6 simulation and other results from the literature [66, 67]. IMFPs from Tanuma *et al.* [67] were normalized to the nucleobase densities as reported by Tan *et al.* [68]

389

#### 390 4. Discussion

391

392 There is a direct target size dependence of the calculated electron cross sections.  
393 Obviously larger molecules induce higher interaction probability that reflects into the elastic and  
394 inelastic total and differential cross sections. This clear distinction between the different DNA  
395 bases and the water targets emphasises the importance of tracking electrons in the actual  
396 biomolecules. Since the cross sections of biomolecules are larger than those of water, the  
397 simulation with water alone will underestimate the damage.

398 There are few studies that calculated elastic differential cross sections for DNA bases and  
399 no experimental data is available apart from the single study by Colyer *et al.* [38] where only  
400 thymine and cytosine differential cross sections were measured for six discrete incident electron  
401 energies between 60 eV and 500 eV and scattering angles between 15° and 130°. Other studies  
402 calculated theoretical differential cross sections for the four bases [38-41] using different  
403 approximations. Colyer *et al.* [38] provided theoretical values for cytosine and thymine, and

404 Blanco *et al.*[41] provided theoretical values for adenine only. Apart from the study of Mokrani  
405 et al., which calculated cross sections in the 10 eV – 5 MeV[40], these studies are limited to low  
406 energy ranges (50 – 4000 eV[39] and 5 – 10000 eV[41]). The differential cross sections  
407 calculated in this work are in good agreement with data from the literature regarding shape and  
408 magnitude, as shown in Figure 3. Oscillations (Figure 3 for 100 eV incident energy) are clearly  
409 observed in the recent calculations of Mokrani *et al.* [40], although the values are lower than  
410 around a factor of 2. The observed discrepancies can be attributed to the different potentials  
411 used in the calculations.

412 All integral elastic cross section results of Figure 4 are in a relatively good agreement at  
413 the intermediate energy range (200 eV-10 keV). At low energy (< 100 eV), our results are  
414 systematically higher. All the available integral elastic cross sections data take into account  
415 different potentials and partial wave expansions in their calculations. The values obtained by  
416 Blanco and Garcia [42] are based on a simplified procedure of the method used in their previous  
417 paper [41]. The differences observed at high energy with the results obtained by Mokrani *et al.*  
418 [40] are due to the fact that they do not introduce correction terms linked with relativistic  
419 effects. Aouina and Chaoui [43] used the same screen-corrected additivity rule as Blanco and  
420 Garcia [41], but with a different decomposition based on the relativistic Dirac partial wave  
421 expansion instead of the Schrödinger one. The method proposed by Vinodkumar *et al.* [44] is  
422 based on the Schrödinger equation with spherical potential for molecules including exchange  
423 and polarization.

424 For all molecules, a peak is observed around 80 eV in the total ionisation cross section  
425 (Figure 6a). Since the ionisation potentials are approximately the same, the peaks are very close  
426 to each other. Similarly to elastic scattering and except at very low energy (< 25 eV) where the  
427 influence of the ionisation potential is important, the amplitude of total ionisation cross section  
428 is linked to the size of the molecule: the highest cross section is for guanine, which is the largest  
429 molecular system investigated in this work. The total ionisation cross section in water is around  
430 one order of magnitude lower than in the DNA bases. If we compare the ionisation cross section  
431 per valence electron (which is the sum of the cross section for all the levels divided by the  
432 number of valence electron of the base), the differences between water and DNA bases vanish  
433 because both molecules are built with low-Z atoms which are covalently bonded.

434 The total ionisation cross sections (Figure 7) exhibit the same typical shape with a  
435 maximum – whose amplitude varies according to the model used – and a gradual decrease  
436 towards high impact energies. The results are scarce and the height and the corresponding  
437 energy of the peak differ. However, the same quantitative behaviour of curves is observed and  
438 differences mainly appear in the magnitude mostly expressed at the peaks.

439 The limited number of experimental results [46-55] is mainly due to the preparation  
440 requirements of these pure target-biomolecules in the gas phase. The experiments carried out  
441 between 2006 and 2015, are limited to low energy (<500 eV). Experimental data [50, 52-55] are  
442 generally far from the theoretical results.

443 The theoretical studies devoted to ionisation impact in DNA bases are mainly based on  
444 semi-classical formalisms. An evident shift regarding the position of the maximum predicted by  
445 different models may be noted. Some calculations are based on BEB formalism or derived from it  
446 [39, 56, 58]. The oldest ones [39, 56] used low-order Hartree-Fock method and smaller basis set  
447 in the geometry optimization and the differences in the results are due to the target description  
448 and more particularly the vertical ionisation potential. In the work of Huo *et al.* [58], the  
449 correlation-consistent polarized valence double-zeta (cc-pVDZ) basis set of Gaussian functions  
450 was used. The results are comparable to the cross sections of Mozejko and Sanche [39], but are

451 larger than those of Bernhardt and Paretzke [56]. Even with the same formalism, there are  
452 variations in the results linked to the parameters used. For example, the choice of the binding  
453 energy of the first ionisation potential differs depending on whether it is obtained from  
454 experiments or calculations and induces differences in the cross section especially at low energy.  
455 That is why main discrepancies with BEB results appear at low binding energy.

456 Bernhardt and Paretzke [56] calculated the total ionisation cross sections using two  
457 formalisms: BEB and Deutsch-Märk (DM). Both formalisms show quite a similar trend; however,  
458 DM calculations reach higher peaks at slightly higher energy than BEB and the decrease in the  
459 DM curve is steeper compared to the BEB one.

460 Other types of calculation [57, 59, 60] cover a larger energy range, although limited to 10  
461 keV. Vinodkumar *et al.* [60] used the spherical complex optical potential formalism to calculate  
462 the inelastic cross section, and the group additivity rule. For their results, the best agreement is  
463 found with the DM results of Bernhardt and Paretzke [56] in adenine and cytosine. In guanine,  
464 the best agreement is observed with the results obtained by Huo *et al.* [58] and with the DM  
465 results beyond the peak. For thymine, the best agreement is obtained with Mozejko and Sanche  
466 [39] and Huo *et al.* [58]. Recently, in 2013, Champion [57] developed a theoretical quantum  
467 mechanical model to calculate the differential and the total ionisation cross sections of the  
468 different DNA components up to 10 keV. In this case, the curve rises more rapidly than the other  
469 results. Tan *et al.* [59] used a simple semi-empirical method based on dielectric formalism for  
470 proton interaction extended by adding the exchange interaction of electrons and by taking into  
471 account a mean binding energy to correctly reproduce the low energy part of the cross section.

472 Our results are comparable to the other available results in amplitude and location of the  
473 peak. More precisely, the position of the peak in our calculations is in better agreement with the  
474 position of the calculations of dielectric response function (DRF) [59], DM [56], improved Binary  
475 Encounter Dipole (iBED) [58], although the amplitude is lower. The difference from the  
476 ionisation total cross section in water is important.

477 ESTAR [61] stopping powers, calculated from the theory of Bethe are only available for  
478 high incident electron energies (>10 keV) and our results are in good agreement with less than  
479 4% average difference at 10 keV, decreasing to 1% at 1 MeV for all four DNA bases (Figure 11). A  
480 general agreement in the shape of the stopping power curves is observed for the different  
481 calculations. The peak stopping power was at 80 eV in the calculations of Akar *et al.* [63, 64], and  
482 at 100 eV in the Monte Carlo simulations of Francis *et al.* [20] similar to our results, whereas the  
483 calculations performed by Akkerman *et al.* [65] reached the peak stopping power at 120 eV. At  
484 low incident energies < 1keV, theoretical calculations of Akar *et al.* [63, 64] using Bethe theory  
485 with Generalized Oscillator Strength method score higher stopping power somewhat similar to  
486 the results of Joy [62]. The inelastic stopping power [63] and total stopping power including  
487 Bremsstrahlung effects [64] calculated by the two studies of Akar *et al.* are almost identical for  
488 low energy electrons. For energies higher than 300 keV, Bremsstrahlung effects are observed  
489 with 1% difference between both stopping powers increasing to about 6.4% for 1 MeV electrons.

490 The best agreement for our results is with those obtained by Francis *et al.* [20] for all four  
491 DNA bases, which used the Rudd model cross sections implementation in Geant4-DNA. When  
492 compared with water-option6 calculations, the stopping power of all four DNA bases is  
493 consistently lower over the whole incident energy range.

494 Good agreement is observed with range results by ESTAR [61] for all four bases, with a  
495 10% difference at 10 keV incident electron energy decreasing to 1% at 1MeV (Figure 12). Our  
496 results are in good agreement with calculations of Akar *et al.* [63, 64] and Akkerman *et al.* [65]

497 (guanine only) as well as PENELOPE data for energies higher than 1 keV. However, for lower  
498 energies a deviation is observed between all types of calculations since each of them follows a  
499 different physical model. Electrons have smaller range in water compared to DNA bases and this  
500 reflects the higher stopping power of water, as shown in Figure 10. Similar to water, fluctuations  
501 in range are observed at very low energies for all bases due to the rapid decrease of inelastic  
502 cross sections [12, 69].

503 There are not plenty of results in the literature for IMFP. Therefore, in Figure 12 we  
504 show a comparison with calculations done by Akar *et al.* [66] for the four DNA bases and with  
505 those carried out by Tanuma *et al.* [67] for adenine and guanine only over a short incident  
506 electron energy range (50-2000 eV). IMFPs from Tanuma *et al.* [67] were normalized to the  
507 nucleobase densities as reported by Tan *et al.* [68] The IMFP plots (Figure 12) show a  
508 reasonably good agreement with the results of Akar *et al.* and of Tanuma *et al.* with small  
509 deviations at low energies (< 100 eV). As expected, an inverse relation with stopping power is  
510 shown and electrons in water score consistently lower values than in the DNA bases.

511 In this study, the various electron cross sections with the four DNA bases were calculated  
512 using distinct physics models. To guarantee the correct implementation of these cross sections  
513 in Geant4-DNA, it was important to verify our simulation results with published data for  
514 available energy ranges, even though the physical models used in the literature may differ from  
515 ours. The good agreement of our calculations with published data shows the reliability of the  
516 physical models and the simulations. The stopping power, range and IMFP calculations show  
517 obvious difference between the DNA bases and the water targets as well. The obvious distinction  
518 between water results and biomolecules therefore requires transport codes capable of tracking  
519 particles in various biomolecules, which is introduced in this work.

520

## 521 **5. Conclusion**

522 There is a growing need for the availability of track structure Monte Carlo simulations in  
523 DNA material to model the detailed particle-biological matter interactions. This study  
524 introduced a new set of electron interaction cross sections in the four DNA nucleobases over a  
525 large incident electron energy range. The cross sections were successfully implemented in the  
526 open source Geant4-DNA simulation toolkit. Good agreement with experiments and calculations  
527 from the literature in terms of cross sections, stopping power, range and inelastic mean free  
528 path was shown. The results of this study will enable the extension of Geant4-DNA classes to be  
529 used in various biological molecules in addition to liquid water targets. The obvious differences  
530 of interaction cross sections and physical parameters between DNA bases and water will induce  
531 differences in energy deposition and their localization, which will affect the radiation damage  
532 estimation and, therefore, the importance of accurate simulation of these data.

533

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537 Geant4-DNA.

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