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ABSTRACT

Most of the energy absorbed in the cell nucleus from a radiation field goes into the aqueous medium that surrounds macromolecules, like DNA, which are critical to the normal function of cells. This part of the energy deposition produces numerous reactive species that can diffuse to DNA sequences and induce chemical changes. The average diffusion distance of the free radicals that mediate this indirect mode of DNA damage is only a few nanometers because the cellular medium contains a high concentration of molecules that rapidly scavenge the radiation-induced species. Under these conditions, direct interaction of the radiation field with DNA can not be neglected as a potential mode of damage induction. Two aspects of the direct effect will be discussed in this paper: (1) screening of the interaction between DNA and charged particles by the dielectric response of the aqueous medium and (2) the impact-parameter dependence of these interactions.

INTRODUCTION

Technical advances in molecular biology have made it possible to construct chemically well-defined DNA targets (oligonucleotides, plasmids, mini-chromosomes, etc.) for radiation studies. Use of these targets in traditional radiolysis experiments, (dilute aqueous solutions exposed to low LET radiation) has the potential to reveal many interesting aspects of the interaction of macromolecules with homogeneously distributed free radicals that escape from the tracks of charged particles slowing down

developed by Bohr[4], one expects that components that are close to the particle trajectory and that have low-energy excitation modes with high oscillator strength will have the greatest probability of receiving energy from a fast charged projectile.

In this paper we will describe calculations of cross sections differential in the energy of secondary electrons for direct ionization of DNA in solution and the semiclassical representation of these cross sections as an integral over impact parameters. Calculations of this type, tested whenever possible by experimental data, should provide the input data needed for track-structure simulations of DNA damage by direct interaction with charged particles in a radiation field.

METHODS

The first Born approximation for the differential cross section to eject electrons from absorption band i of a homogeneous condensed medium by energy transfer $\hbar\omega$ from a fast particle with nuclear charge Z and kinetic energy E is[5]

$$\pi a_o n_i E \frac{d\sigma_i}{d(\hbar\omega)} = \int_{k_{min}}^{k_{max}} Im\ [\epsilon_i\ (k,\omega)\,]\ \frac{Z^2}{|\epsilon|^2}\ \frac{dk}{k} \qquad (1)$$

where a_o is the Bohr radius (0.0529 nm) and n_i is the density of electrons involved in the transition that gives rise to the ith absorption band. The integral is over the range of momentum transfer allowed by the conservation of energy and momentum in the collision. $Im[\epsilon_i(k,\omega)]$ is the contribution from the ith band to the imaginary part of the complex dielectric response function ϵ and is analogous to the generalized oscillator strength of an electronic subshell of an atom or molecule in the gas phase.

The extension of this theory to a heterogenous medium is trivial when the macromolecular solute is present in such low concentration that its effect on the bulk dielectric response function is negligible. In this case, i denotes an impurity band in the medium, $Im[\epsilon_i]$ is proportional to the generalized oscillator strength of the band, and $|\epsilon|^2$ is the square modulus of the complex dielectric response function of the medium in the absence of the impurity. At this level of approximation, the impurity is treated as a gas-phase molecule with a solvation structure.

The effects of collective modes of excitation in the medium, if they are present, are contained in $|\epsilon|^2$. The primary role of the bulk medium in the collision process can be interpreted as an effect on the electromagnetic field of the projectile. Localized electronic polarization of the medium by the projectile may give rise to the condition $|\epsilon|^2 > 1$; then screening of the impurity site from the projectile occurs in a manner that is somewhat analogous to the effect of bound electrons on a projectile in the gas phase. Collective modes of excitation of the bulk medium by the projectile may be characterizes roughly by the condition $|\epsilon|^2 < 1$. This anti-screening effect can be interpreted as an electronic polarization wave excited in the bulk medium that may excite an electron of the impurity site[6].

The general approach to obtaining an impact-parameter representation of collision cross sections involves the application of Fourier-transform analysis to

spectrum, then a sum of terms like Eq.(4) is fitted to the experimental photoabsorption data. After the parameters of the OPWD model have been determined from the optical limit, the full dependence of Im[ϵ] on momentum and energy transfer can be calculated from a somewhat more complicated analytic function[11]. The real part of the dielectric response function is evaluated numerically using the Kramers-Kronig[12] relationship. It should be noted that the OPWD model is constrained to satisfy the Bethe sum rule.

RESULTS

Fig.(1) shows the result of fitting the liquid-water photoabsorption data[9] by a sum of four terms like Eq.(4). Theoretical methods based on sum rules were
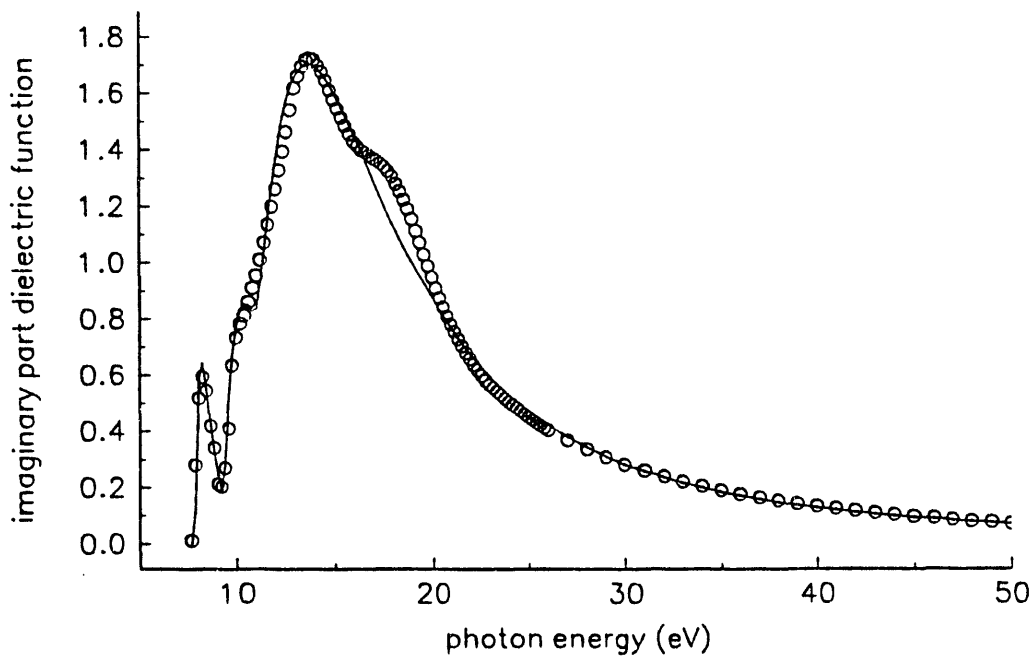

Figure 1. Fit of the OPWD model (solid curve) to liquid-water photoabsorption data (open circles) from ref.(9).

applied by Painter and coworkers[13] to extend the experimental data from 25.5 eV to 100 eV. The optimum parameter values are given in Table I. The parameters of the model are strongly coupled and the optimum values given in Table I are not unique. Hence, little, if any, physical interpretation should be given to their value. A similar approach to obtaining the dielectric response function of liquid water has been carried out by others[14]. An alternative scheme for representing $\epsilon(k,\omega)$ for water based on the same optical data[9] was incorporated early on into the Oak Ridge Monte Carlo code OREC[15].

Table 1. Parameters for the OPWD model of liquid water.

Peak #	Threshold (eV)	Alpha (au)	Eta (au)
1	7.76	0.285	0.00047
2	9.25	0.531	0.0030
3	10.88	0.880	0.024
4	16.33	1.764	0.013

Photoabsorption data of DNA[10] were multiplied by the ionization efficiency[16] to obtain the experimental photoionization data for DNA that are shown by the open circles in Fig.(2). The solid curve in this figure is a fit to these data by Eq.(4) with
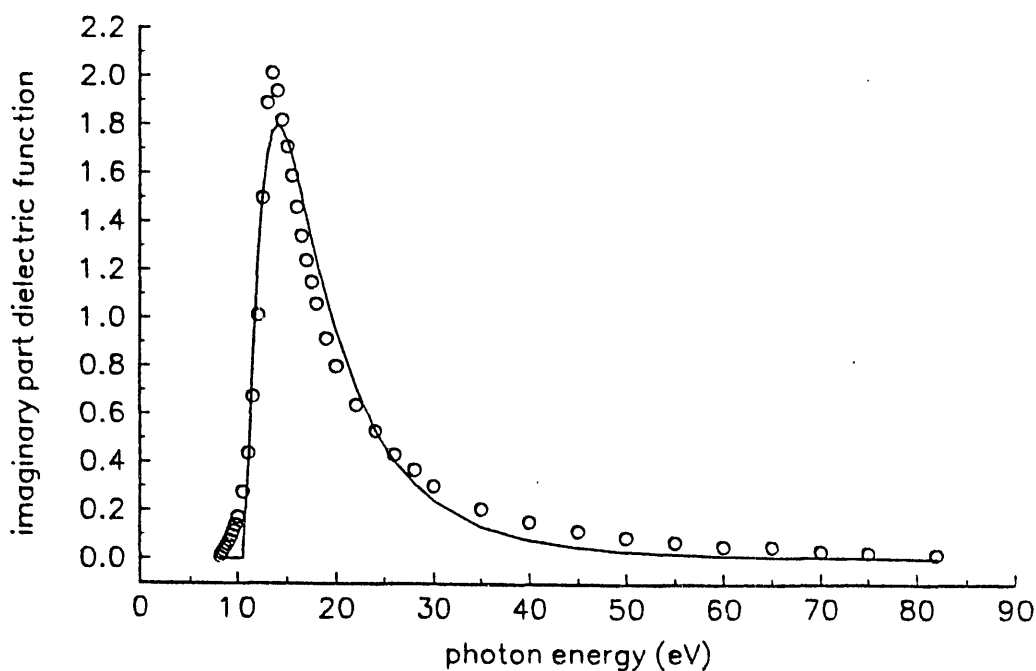

Figure 2. Fit of OPWD model (solid curve) to DNA photoionization data (open circles) from refs.(10) and (16).

an ionization threshold of 10.6 eV, α = 0.875 au, and η = 0.0289 au. Using these parameters to evaluate $\mathrm{Im}[\epsilon_i(k,\omega)]$ in Eq.(1) and the parameters in Table 1 to evaluate $|\epsilon|^2$, we obtain the differential ionization cross sections shown by the filled circles in Fig.(3) for a primary electron with a velocity of 3 au (122.5 eV). To illustrate the effects of the solvent, the open circles show the result obtained for the same primary- and secondary-electron energies but with $|\epsilon|^2$ = 1. Clearly, the screening effect of the solvent dramatically reduces the cross section for ejection of low-energy secondary electrons and shifts the peak in the spectrum to a higher energy[17]. The small anti-screening effect for energy transfers between about 25 and

50 eV is consistent with the general finding that collective modes of excitation in liquid water have a broad energy spectrum and short lifetime[18].
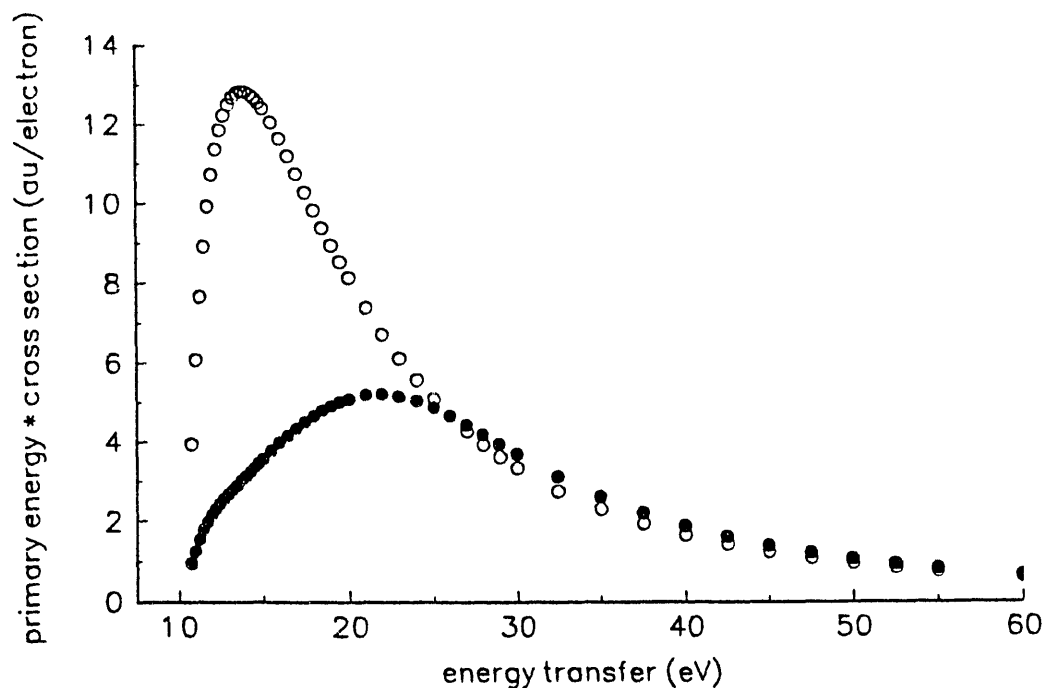

Figure 3. Differential cross sections for ionization of DNA with (solid) and without (open) screening by a water medium. The primary-electron energy is 122.5 eV.

Impact-parameter probability densities calculated from Eq.(2) with the normalization $dP/db = (d^2\sigma_i/d\omega db)/(d\sigma_i/d\omega)$ are shown in Fig.(4) for ionization of DNA by 122.5 eV primary electrons. The following levels of energy transfer are illustrated: (1) 11 eV which is slightly above the threshold for ionization, (2) 22 eV which is near the maximum in the differential energy-transfer cross section (see Fig.(3)), and (3) 54 eV which is close to the energy transfer needed to produce the maximum secondary-electron energy in the usual convention of track simulation that the more energetic electron after an electron-impact ionization is the primary. The probability distributions calculated in the second and third cases conform to the expectation that as Bohr's maximum effective impact parameter, v/ω, decreases, larger impact parameters become less efficient in collisional energy transfer. However, collisions with energy transfers near the ionization threshold appear to be an exception to this rule. Even though the maximum effective impact parameter is twice as large, the distribution of impact parameters in collisions where a 122.5 eV primary electron transfers 11 eV to the target is slightly more concentrated at small values than for collisions where 22 eV of energy is transferred. This effect is probably a consequence of the energy- and momentum-transfer dependence of the dielectric functions used in Eq.(2).
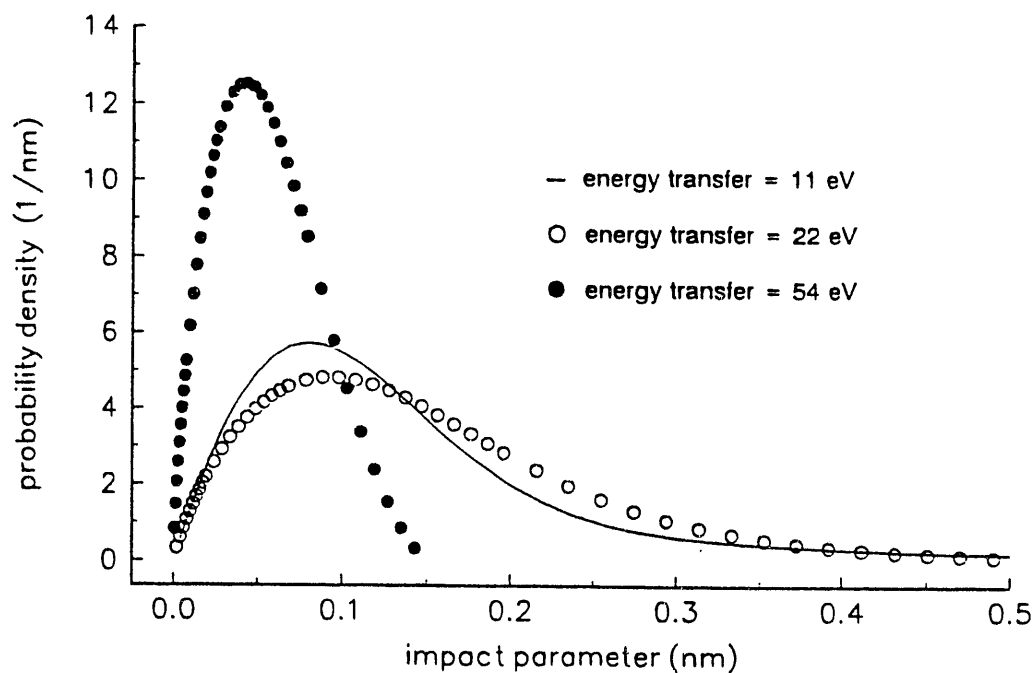
Figure 4. Impact-parameter distributions for three levels of energy transfer in ionizing collisions of DNA in water with 122.5 eV primary electrons.

DISCUSSION

Our calculations show that Bohr's maximum effective impact parameter, $b_c = v/\omega$, determines the scale of the impact-parameter distribution in most cases. The probability to select an impact parameter much larger than b_c in a Monte Carlo simulation of inelastic collisions will be very small. Hence, it is useful to compare b_c with the characteristic size of the target of interest, the DNA double helix. This comparison is shown in Fig.(5) as a function of primary-electron energy for two levels of energy transfer. The filled circles show the ratio of the maximum effective impact parameter to the DNA radius (1.23 nm) for transfer of energy that is just sufficient to ionize the target (10.6 eV in our model of the DNA photoionization spectrum). The open circles show the ratio b_c / 1.23 nm for the average energy transfer in an ionizing collision by a primary electron at the specified energy. Our results discussed above for 122.5 eV primary electrons suggest that the closed circles in Fig.(5) over estimate of the scale of the impact-parameter distribution in collisions that produce very low-energy secondary electrons. In general, Fig.(5) suggests that the scale of the impact parameter distribution is comparable to or smaller than the DNA radius for many of the electron energies that are encountered in radiation fields of radiological interest.
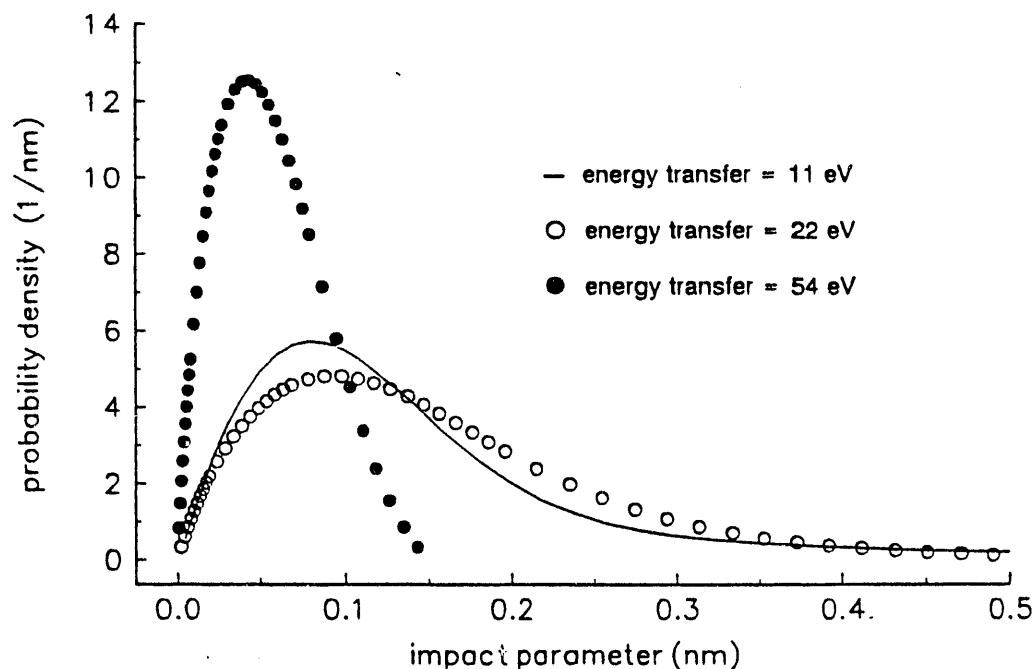
Figure 5. Ratio of the maximum effective impact parameter to the DNA radius for ionizing collisions with primary electrons of different energy.

A cylinder with a 1.23 nm radius centered on the helical axis contains not only the atoms of DNA in the standard B conformation but also most of the water in the first two hydration shells, about 80 water molecules per nucleotide pair[19]. The consequences of ionizing an atom in this volume are probably unaffected by the presence of radical scavengers in the medium; hence, the results presented in this paper that ignore the finite size and internal structure of the target may be useful in estimating the non-scavengeable component of DNA damage for comparison with experiments[20]. However, the atoms within this volume are not equivalent with respect to the probability that ionization leads to a specific product. For example, ionization of a sugar moiety is more likely to result in strand scission than ionization of a base. Furthermore, the recent data obtained by Wheeler and coworkers[3] with DNA at various levels of hydration suggest that ionization of water in the first hydration shell frequently leads to charge transfer to DNA bases while ionization of water in the second hydration shell appears to induce free radicals similar to those that result from ionization of bulk water.

Fig.(6) illustrates the next level of theoretical development that we feel is needed to address questions concerning observable products that result from direct interaction between DNA and charged particles in a radiation field. This extension of the present model would include the internal structure of DNA by identifying the functional groups that make up the polymer (phosphate, sugar, and the DNA bases adenine, guanine, cytosine and thymine). We propose to develop an impact
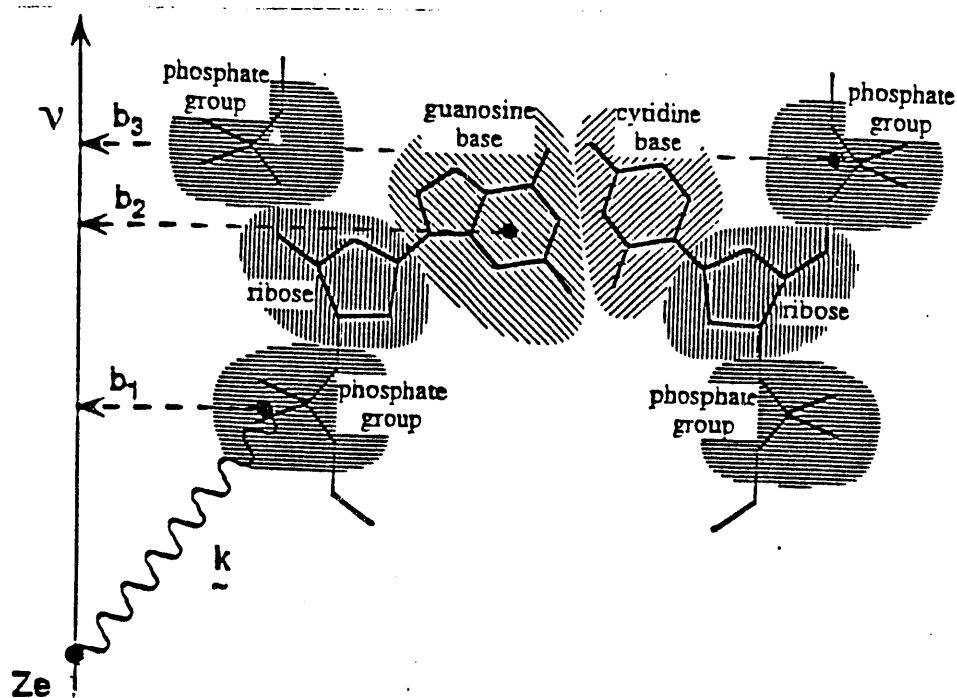
Figure 6. Spatial relationship between functional groups of DNA and a particle trajectory that passes close to the double helix.

parameter distribution for each group by methods similar to those discussed above making use of optical data on the groups in isolation but with the constraint that the model remain consistent with DNA photoabsorption data[10]. This approach will allow us to include the internal structure of DNA in determining the impact parameter to a given functional group, which we argue on the basis of Fig.(5) will have a major effect on the probability to transfer energy to the group in many of the cases of current interest. Furthermore, this extension of the current theory will permit the different ionization thresholds of the components of DNA[16] to be included in the model.

SUMMARY AND CONCLUSIONS

A semiempirical model has been presented from which differential inverse mean free paths can be calculated for electron- and ion-impact ionization of DNA in solution. The model includes the screening effect that results from the dielectric response of the aqueous medium, which strongly influences the cross section for ejection of low-energy electrons. An impact-parameter representation of the differential inverse mean free path has been developed that will allow simulation of energy transfer to DNA when the trajectory of the charged particle slowing down does

not penetrate the electron cloud of the target DNA molecule. Since the scale of the impact-parameter probability distribution is roughly equal to Bohr's maximum effective impact parameter, v/ω, this long-range mode of energy transfer is most important for ejection of low-energy secondary electrons by fast projectiles. In future applications of track-structure simulation to model direct induction of DNA lesions under cellular conditions, an extension of the current theory that allows for the internal structure of DNA will be required. An outline for future development of our model to meet this need has been presented.

ACKNOWLEDGEMENTS

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