

Concepts of Microdosimetry*

II. Probability Distributions of the Microdosimetric Variables

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Summary. This is the second part of an investigation of microdosimetric concepts relevant to numerical calculations. Two different types of distributions of the microdosimetric quantities are discussed. The sampling procedures are considered, which lead from the initial pattern of energy transfers, the so-called inchoate distribution, to the distribution of specific energy and their mean values. The dependence of the distributions of specific energy on absorbed dose is related to the sampling procedures.

Introduction

A preceding article [14] has dealt with the definition and interpretation of microdosimetric quantities. In the following the probability distributions of these quantities will be considered. As in the earlier article the purpose is not to give a survey of theoretical relations or of numerical data and their biological implications; such surveys exist [22, 23, 12]. Instead certain concepts will be reviewed which are essential to numerical computations in microdosimetry. All definitions will be given in terms of the specific energy, z . It will be evident how the definitions are generalized to the other random variables, namely energy imparted, ϵ , lineal energy, y , and number of ions, n .

In an ideal microdosimetric experiment one would register all the spatial coordinates of electronic interactions, *i.e.* of transfer points [14], in charged particle tracks. However, such an experiment is not feasible with present-day techniques. Experiments with cloud chambers and evaluation of photographic emulsions have led to useful information, but these methods do not as yet permit the spatial resolution which is necessary to establish precise microdosimetric distributions. The theoretician can, however, derive simulated charged particle tracks from interaction cross sections which are either measured or interpolated from experimental data.

The computational approach has been used extensively by Berger [1, 2] who has also derived microdosimetric data from simulated particle tracks for electrons of various energies in microscopic tissue regions of cellular or subcellular size. Paretzke [18, 19], Patau *et al.* [20], and Terrissol *et al.* [26] have developed similar

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methods to generate particle tracks with high spatial resolution of the individual ionizations and excitations in the track. Caswell and Coyne [4, 5] have obtained a considerable amount of microdosimetric data for neutrons; in the cases which they have treated the tracks of the recoil particles can be approximated by straight line segments without regard to statistical fluctuations.

The following considerations will not be concerned with the derivation of simulated charged particle tracks. They will deal with the relation between such particle tracks, *i.e.* the inchoate distributions [14], and the microdosimetric distributions. The resulting concepts are germane to the numerical derivation of the probability distributions; however, the numerical techniques themselves are not the topic of the present study.

Sampling Procedures Leading to the Different Probability Distributions

General Remarks

There are, as pointed out earlier [14], two distinct ways to look at the microdosimetric variables and their probability distributions. The first possibility is to consider a single spherical site and the succession of a large number of events occurring in this site. Each event corresponds to energy deposition due to an ionizing particle appearing in the vicinity of the site or the site itself. This is the usual situation in microdosimetric experiments, where a tissue-equivalent spherical proportional counter is exposed to a radiation field, *i.e.* is submitted to a succession of events, and where the probability distribution of increments produced by the individual events is then determined (see *e.g.* [3, 6—9, 16, 17, 21, 24, 25, 27]). An analogous approach can be used in calculations, *i.e.* one may specify a microscopic site in an extended medium and randomly generate charged particles in and around this site. Such a procedure may, however, be wasteful if only a small part of each particle track is contained in the site. The reason is that all the information regarding the structure of the track outside the site remains unutilized.

For the computational procedure it will therefore in general be more efficient to consider one or several random tracks, *i.e.* an inchoate energy distribution, in an extended medium, and then to sample the values of the microdosimetric variables throughout the medium. In this second approach one thus uses a large number of spheres but only one or a few random tracks. Accordingly the information contained in the simulated tracks is fully used. This approach which reflects the fact that the problems of microdosimetry are in essence problems of pattern analysis will be adopted in the following. It will be found useful not only in computations but also in theoretical considerations. However, it will require careful attention to the details of the sampling procedure.

Assume that the inchoate distribution of energy deposition is given in an extended medium. As pointed out [14] this inchoate distribution can be specified by the coordinates of the transfer points, T_i , and the corresponding energy transfers, ϵ_i . A transfer point has been defined as a point where an ionizing particle loses energy. The definition of the energy transfer, ϵ_i , can be formalized in analogy to the definition of the energy imparted which has been cited in the preceding article [14]:

$$\epsilon_i = \epsilon_{in} - \sum \epsilon_{ex} + \sum Q, \quad (1)$$

where

ϵ_{in} = the energy (excluding rest energy) of the ionizing particle before it undergoes an interaction at the transfer point, T_i ,
 $\sum \epsilon_{ex}$ = the sum of the energies (excluding rest energies) of all ionizing particles (including the primary particle) resulting from the interaction,
 $\sum Q$ = the sum of all the energies released, minus the sum of all the energies expended, in any transformation of nuclei or elementary particles occurring in the interaction.

The total volume which is being considered will in the following be called the *sampling region*. If one wants to determine the probability distribution or the expectation value of a microdosimetric quantity, such as specific energy, z , one must determine its value at various points in the sampling region. These points will be called *sampling points*. The specific energy, z , at a sampling point refers to the sphere of radius r centered at this point.

In the following, sampling procedures will be discussed which lead to two important distributions. These distributions are familiar in microdosimetry; however it is useful to reconsider them in the present context. It will be understood that the remarks apply equally to the two different interpretations of the microdosimetric quantities which have been suggested in the preceding article [14].

Two Basic Distributions

The most obvious sampling procedure is the random selection of points with constant probability throughout the sampling region. If one performs such *unweighted* sampling for a sufficiently large number of points in a sufficiently large sampling region one approximates a probability distribution of z which is often called the *frequency distribution* of specific energy. The sum distribution is commonly designated as $F(z)$. The value $F(z)$ is the probability to find a specific energy in excess of z ; in other words $F(z)$ is the fraction of the total volume with values of specific energy exceeding z .

The corresponding differential distribution is $f(z)$. The probability to find a value of specific energy between z and $z + dz$ is equal to $f(z)dz$; accordingly, $f(z)dz$ is the fraction of the total volume with values of the specific energy between z and $z + dz$.

The formal relations between the sum distribution and the differential distribution are:

$$F(z) = \int_z^{\infty} f(z') dz' \quad (2)$$

and:

$$f(z) = - \frac{d F(z)}{dz}^* \quad (3)$$

The frequency distribution of specific energy determines the relative probability with which certain amounts of energy are imparted to spherical sites within

* In contrast to normal usage in probability theory the sum distribution is here taken to be a decreasing function of the random variable, *i.e.* the integration is performed over the part of the distribution which belongs to high values of z . This has the advantage that this part which is particularly relevant to the biological effects of different ionizing radiations can be depicted more clearly. A similar convention will be adopted for the other microdosimetric distributions.

the irradiated medium; it follows that the mean value of this distribution is the absorbed dose.

Although sampling with constant probability throughout the irradiated medium may appear to be the obvious procedure, it is not the only procedure of interest. The more general situation is outlined in the Appendix; in the present context it is sufficient to deal with one special case. This special case results if one uses a weight factor for the sampling points which is proportional to the value z at these points. In this way one obtains a distribution which is often called the *dose distribution* of specific energy; *i.e.* one obtains a distribution of absorbed dose in z instead of a distribution of the volume in z . The sum distribution is designated as $D(z)$ and the corresponding differential distribution is $d(z)$. The value $D(z)$ is equal to the probability to find a specific energy larger than z if one samples with a selection probability proportional to z . Accordingly $d(z)dz$ is the probability to find a value of specific energy between z and $z + dz$ if this sampling procedure is applied. One can also say that $D(z)$ is the fraction of absorbed dose appearing in sites with specific energy exceeding z .

The relations between the sum distribution and the differential distribution are:

$$D(z) = \int_z^{\infty} d(z') dz' \quad (4)$$

and:

$$d(z) = - \frac{d D(z)}{d z} \quad (5)$$

The distributions $f(z)$ and $d(z)$ have here been introduced independently as distributions resulting from two different sampling procedures. This is justified because the two distributions are of different nature; the one being the distribution of volume in z , the other being the distribution of dose in z . On the other hand, the separate treatment of $f(z)$ and $d(z)$ may appear confusing, because $d(z)$ is closely linked to $f(z)$ and is in fact commonly defined in terms of $f(z)$:

$$d(z) = z f(z)/D. \quad (6)$$

However, as will be seen in the next section, this relation follows readily from the definitions which have been given here.

Details of the Sampling Procedures

After these general remarks it is useful to consider the sampling procedures in detail.

The sampling with constant selection probability throughout the medium is simple. One can use a Monte Carlo technique to generate N points randomly in the volume of interest and determine the corresponding values z_i , $i = 1, \dots, N$. The sum distribution $F(z)$ is then approximated by:

$$F(z) = N_z/N, \quad (7)$$

where N_z is the number of sampling points with values z_i exceeding z .

The relation for the differential distribution, $f(z)$, is:

$$f(z) \Delta z = \Delta N_z/N, \quad (8)$$

where ΔN_z is the number of sampling points with values z_i between z and $z + \Delta z$.

The expectation value of a function, $g(z)$, of the specific energy is obtained from:

$$\overline{g(z)_F} = \sum_i g(z_i)/N \quad (9)$$

and for the special case of the mean value of z one has:

$$\bar{z}_F = \sum_i z_i/N. \quad (10)$$

As stated before, \bar{z}_F is equal to the absorbed dose, D .

The question of the statistical convergence of the expressions will not be considered in the present context; it will simply be assumed that the number, N , of sampling points is sufficiently large.

An alternative which avoids Monte Carlo calculations is to determine the values of the specific energy throughout the region of interest, *i.e.* to establish a three-dimensional grid of points throughout the medium with sufficient resolution and to determine the value of the specific energy on all these points. This latter procedure may often be inapplicable because it may require excessive computing times. Nevertheless it is of conceptual interest, since it implies that Eqs. (7 to 10) can also be written as volume integrals. Thus one obtains for the mean value of a function, $g(z)$:

$$\overline{g(z)_F} = \int_V g(z) dV / \int_V dV, \quad (11)$$

where the integrals extend over the whole sampling region, V , and z is a function of the spatial coordinates.

In particular one has:

$$\bar{z}_F = \int_V z dV / \int_V dV = D. \quad (12)$$

One can now consider the second somewhat more complicated situation, where the sampling is performed with a selection probability proportional to z . One possibility is to apply one of the methods mentioned above, *i.e.* to use a constant selection probability, but to apply the value z as a compensation factor, in order to arrive at the proper weight factor. It may appear unnecessary in the present context to introduce the three separate notions of weight factor, selection probability and compensation factor. The situation can, however, be complicated in actual computations where it may be advantageous to select certain sub-spaces in the sampling region, such as straight lines parallel to particle tracks, and to determine the distribution of the specific energy in these sub-spaces. It is then not always trivial to determine appropriate selection probabilities and compensation factors. A precise definition of the concepts is therefore essential, and it will be helpful to use the rule that the weight factor is equal to the product of the selection probability and the compensation factor.

If z_i , $i = 1, \dots, N$, are the values of the specific energy at the N sampling points chosen with constant selection probability, then the sum distribution, $D(z)$, is obtained as:

$$D(z) = \sum_{z_i > z} z_i / \sum_i z_i, \quad (13)$$

where the summation in the numerator extends over all sampling points with z_i larger than z , and the summation in the denominator extends over all N points. The corresponding relation for the differential distribution is:

$$d(z) \Delta z = z \Delta N_z / \sum_i z_i, \quad (14)$$

where ΔN_z is again the number of points with values of the specific energy in the interval which extends from z to $z + \Delta z$.

The expectation value of a function $g(z)$ of z is obtained as:

$$\overline{g(z)_D} = \sum_i g(z_i) z_i / \sum_i z_i \quad (15)$$

and, in particular, the relation for the expectation value of z is:

$$\overline{z}_D = \sum_i z_i^2 / \sum_i z_i. \quad (16)$$

As in the case of the frequency distribution one can formulate these relations in terms of volume integrals. Thus one obtains the following formulae for the mean values:

$$\overline{g(z)_D} = \int_V g(z) z \, dV / \int_V z \, dV \quad (17)$$

and:

$$\overline{z}_D = \int_V z^2 \, dV / \int_V z \, dV = \overline{z_F^2} / \overline{z_F}. \quad (18)$$

From Eqs. (8) and (14) one obtains Eq. (6) between the dose distribution and the frequency distribution.

Sampling over Individual Transfers

Use of a constant selection probability of sampling points and subsequent application of the compensation factor, z , may be disadvantageous insofar as one may obtain many sampling points with $z = 0$. These points are not relevant to the distribution $d(z)$. It will therefore, in general, be more effective to sample only the associated volume, *i.e.* only that part of the sampling region where the specific energy is larger than 0. The following method can be used to make the selection probability of sampling points proportional to z .

Assume that one deals with M transfer points T_i , with $i = 1, \dots, M$. Let ε_i be the corresponding energy transfers. As a first step one selects randomly a transfer point; this is done with a selection probability proportional to ε_i . As a second step one selects a sampling point, P , randomly in the sphere of radius r around the transfer point. If the selection of sampling points, P , is performed in this manner no compensation factors are necessary because the probability to arrive at a point P is then proportional to the value z at this point. That this is so follows from the fact that each point, P , can be reached from all those transfer points, T_i , which contribute to the specific energy at P . The selection probability of P is proportional to the sum of the selection probabilities of the points T_i . This sum, however, is proportional to the sum of the transfers ε_i and therefore to the specific energy at P .

In practice one can avoid the random choice of transfer points and instead consider all transfer points consecutively. The value ε_i must then be used as a compensation factor.

This method of obtaining the distribution $d(z)$ is not only suitable for numerical calculations, it will also prove an important tool in theoretical arguments concerning the mean values \bar{z}_D and \bar{y}_D . The method will be referred to as *sampling over individual transfers*.

According to the procedure one has the following expression for \bar{z}_D :

$$\bar{z}_D = \sum \frac{\varepsilon_i (\int z dV / \int dV)}{S_i} / \sum \varepsilon_i, \quad (19)$$

where the summations extend over all transfer points, T_i , and the integrals extend over the sphere, S_i , of radius r around each transfer point. The expression in the bracket is the average of z without weight factor over the sphere around a transfer point; one can also say that it is the average of z in all spheres of radius r containing the transfer point, T_i . According to the equation, \bar{z}_D is the mean of this average over all transfer points*. One could state this in the following form. If a transfer point is selected randomly in the exposed medium (with a selection probability proportional to its energy transfer), then \bar{z}_D is equal to the expected specific energy in a sphere of radius r which contains the transfer point at a random position in its interior.

Eq. (19) will be used in the next section to derive the dependence of \bar{z}_D on absorbed dose.

Dependence of the Distributions and Their Mean Values on Absorbed Dose

The microdosimetric distributions depend on absorbed dose; one may indicate this by writing them in the form $f(z; D)$ and $d(z; D)$ instead of $f(z)$ and $d(z)$. However, the dose-dependent distributions can be calculated from the distributions which apply to isolated, *i.e.* non-overlapping, charged particle tracks. These latter distributions are called *single event distributions*, and are designated by $f_1(z)$ and $d_1(z)$. They are independent of absorbed dose. The relations between the dose-dependent distributions and the single event distributions have been set out in earlier works (22—24). It will, however, be useful to list the essential points in the present context.

Report 19 of the ICRU [11] defines an *energy deposition event* as energy deposition in a region due to an ionizing particle and/or its secondaries. This definition implies that energy imparted in the same event is due to statistically correlated particles. In this context it is useful to introduce the notion of a *track* as the entirety of transfer points T_i and energy transfers ε_i in an exposed medium due to one ionizing particle and its secondaries.

With these conventions the single event distributions can be defined as the distributions which result if exactly one event has occurred in the region of reference. Alternatively one can state that the single event distributions result from sampling the associated volumes of individual, *i.e.* non-overlapping, tracks.

* If one deals not with a spherical site with sharp boundary, but with a diffuse site (see [14]) the integrals are slightly altered. They must then contain the additional factor $h(x)$, where x is the distance from the transfer point. As pointed out in the earlier article, the function $h(x)$ is a step function if one deals with a site with sharp boundaries while it is a continuously decreasing function, for example a Gaussian distribution, in the case of a diffuse boundary.

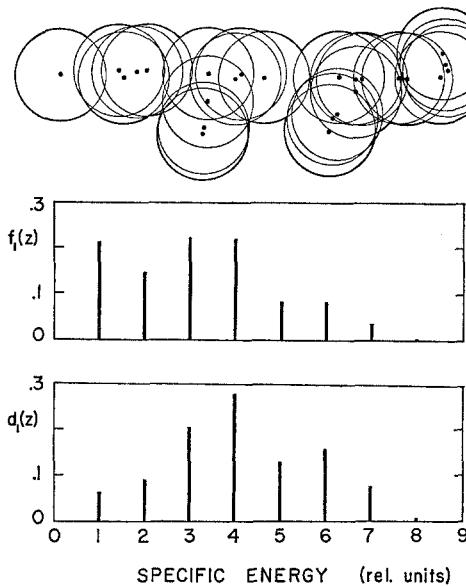


Fig. 1. Schematic diagram of a particle track with its associated volume and the frequency distribution, $f_1(z)$, and dose distribution, $d_1(z)$, corresponding to the pattern

It is assumed that each energy transfer produces a unit increment of z . The resulting mean values are $z_F = 3.2$ and $z_D = 4.1$

The distribution $d_1(z)$ is the limit of $d(z; D)$ as the dose goes towards zero:

$$\lim_{D \rightarrow 0} d(z; D) = d_1(z). \quad (20)$$

The same relation does not hold for $f_1(z)$. In the dose-dependent distribution $f(z; D)$ there is always a finite probability for $z = 0$, while no such component is included in $f_1(z)$. At small doses $f(z; D)$ can be approximated by:

$$f(z; D) = (1 - n) \delta(z) + n f_1(z), \quad (21)$$

where $\delta(z)$ is the delta-function at $z = 0$ and n is the mean event frequency at absorbed dose D :

$$n = D/\bar{z}_{F1}. \quad (22)$$

\bar{z}_{F1} is the mean specific energy produced in one event, and consequently $1/\bar{z}_{F1}$ is the event frequency per unit dose.

From Eqs. (6), (20), and (21) one obtains the relation between the single event distributions:

$$d_1(z) = z f_1(z)/\bar{z}_{F1}. \quad (23)$$

These distributions are given in Fig. 1 for the same two-dimensional example of a particle track which has been used in the preceding article. For simplicity it is assumed that all transfers, ε_i , represented by dots, are equal. In the example the absolute units are meaningless because one deals with a two-dimensional case; therefore the contribution of each transfer to z is arbitrarily set equal to 1.

The dose-dependent distributions $f(z; D)$ can be represented as a superposition of multi-event spectra, $f_\nu(z)$, according to the Poissonian probabilities for the occurrence of ν events, when the mean number of events is $n = D/\bar{z}_{F1}$:

$$f(z; D) = \sum_{\nu=0}^{\infty} e^{-n} \frac{n^\nu}{\nu!} f_\nu(z). \quad (24)$$

The spectra $f_\nu(z)$ which belong to exactly ν events can be obtained as convolutions of $f_1(z)$. There are computational procedures [12] involving Fourier transforms which permit an even more direct derivation of $f(z; D)$ from $f_1(z)$.

The mean value of $f(z; D)$ is, as pointed out, equal to absorbed dose, in fact this can be considered as the definition of absorbed dose:

$$\bar{z}_F = D. \quad (25)$$

The mean value of $d_1(z)$ will be designated by \bar{z}_{D_1} . According to Eq. (23) this quantity is equal to the ratio of the second to the first moment of $f_1(z)$:

$$\bar{z}_{D_1} = \bar{z}_{F_1}^2 / \bar{z}_{F_1}. \quad (26)$$

Consequently \bar{z}_{D_1} is always larger than \bar{z}_{F_1} .

The mean, \bar{z}_D , of $d(z)$ can be expressed in terms of the mean of $d_1(z)$:

$$\bar{z}_D = \bar{z}_{D_1} + D. \quad (27)$$

This relation has been derived earlier [10, 12], it follows from Eqs. (18) and (24). However, since the relation is of considerable importance in radiobiology [15], it is desirable to demonstrate its validity in a more direct and more easily comprehensible way. To this purpose one may reconsider the procedure which has been termed sampling over individual transfers. As stated, such sampling is achieved by randomly selecting first a transfer point, T_i , and then a point in the surrounding sphere of radius r . The mean value of z at the resulting points is equal to \bar{z}_D . At each point the specific energy is the sum of two independent components. The first component is the contribution from the track to which T_i belongs, its mean value is \bar{z}_{D_1} . The second component is the contribution from other tracks. These other tracks are not statistically correlated to the sampling point; their mean contribution is therefore equal to D . This proves Eq. (27)*. Analogous relations result for the variables ϵ and n .

A more formal statement of this argument can be based on Eq. (19). In this equation the variable z under the integral is the specific energy in the vicinity around a transfer point, T_i . One can separate z into two components. z_1 is the part of z which is due to the energy transfer at T_i and at other transfer points belonging to the same track. z_2 is the contribution of independent tracks. Since there is no spatial correlation of the region of integration to the other tracks the expectation value of z_2 is equal to D . Therefore:

$$\begin{aligned} \bar{z}_D &= \sum_i \frac{\epsilon_i (\int (z_1 + z_2) dV / \int dV)}{\sum_i \epsilon_i} \\ &= \sum_i \frac{\epsilon_i (\int z_1 dV / \int dV)}{\sum_i \epsilon_i} + D. \end{aligned} \quad (28)$$

Since the first term is equal to the limit, \bar{z}_{D_1} , of \bar{z}_D as D goes towards zero, one obtains Eq. (27).

The quantity \bar{z}_{D_1} is of considerable importance in radiobiology [15]. Formulae for this quantity will be derived in the subsequent, last part of this study.

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* The relation holds regardless of the form of the function $h(x)$, i.e. it applies not only to a sharp boundary but also to a blurred boundary (see [14]).

Appendix

The microscopic distribution of energy deposition determines the spatial pattern of the concentration of radiochemical products, such as free radicals, or of cellular sublesions, such as the single-strand breaks in DNA. The effectiveness of an irradiation may depend in various ways on the resulting local concentrations. Accordingly, one may consider different microdosimetric distributions. The following remarks will deal with one case of particular importance, namely a second order reaction of radiation products.

Assume that at the transfer points (ionizations or excitations) of charged particle tracks two different species, U and R , of free radicals are formed with yields proportional to the energy transfers ϵ_i and that these species diffuse over spheres with the radii u and r around their points of formation. The resulting concentration of the two species at any point in the medium is then proportional to the variable $z_u z_r$, where z_u and z_r are the values of the specific energy belonging to the radii u and r .

If the cellular effect is proportional to the interaction product of the two types of free radicals then it is proportional to the spatial average, $\bar{z}_u z_r$, of the variable $z_u z_r$.

It may neither be easy nor of great practical interest to evaluate this expression in the general case of two different radii u and r . Nevertheless, it may be of interest to consider the quantity from a theoretical point of view and to investigate two aspects of the problem. The first is the dose dependence of the expression, the second is the fact that the frequency average, \bar{z}_F , and the dose average, \bar{z}_D , of the specific energy are special cases of the general expression.

It will be convenient to consider the expression $\bar{z}_u z_r / \bar{z}_u$ instead of $\bar{z}_u z_r$. For brevity this expression will be designated as \bar{z}_{ur} :

$$\bar{z}_{ur} = \frac{\bar{z}_u z_r}{\bar{z}_u} = \frac{\int z_u z_r dV}{\int z_u dV} \cdot \quad (A.1)$$

The quantity \bar{z}_{ur} is the expectation value of z_r which results from sampling with the weight factor z_u . Eq. (A.1) corresponds to Eq. (18). Going through the arguments which lead to Eqs. (19) and (28) one obtains an expression which corresponds to Eq. (28), and merely differs from this equation insofar as the regions of integration are spheres of radius u while the specific energy under the integral refers to spheres of radius r . As in the earlier case one therefore concludes that the mean value \bar{z}_{ur} is equal to the absorbed dose plus a term which is independent of absorbed dose and depends merely on the energy concentration in individual tracks:

$$\bar{z}_{ur} = \bar{z}_{ur,1} + D. \quad (A.2)$$

Since according to Eq. (A.1) $\bar{z}_u z_r$ is equal to $D \bar{z}_{ur}$ one obtains the linear-quadratic equation:

$$\bar{z}_u z_r = \bar{z}_{ur,1} D + D^2. \quad (A.3)$$

This equation applies to the case of two interacting free radicals which has been discussed above.

In the special case where the diffusion distances of the two radicals are the same the quantity $\bar{z}_{ur,1}$ reduces to \bar{z}_{D1} .

As stated, \bar{z}_{ur} is the mean value of z_r which results from sampling with a weight factor z_u . One may go further and consider not only the mean value but also the corresponding probability distribution which may be designated $f_{ur}(z)$. This function is of interest because it contains the commonly used probability distributions as special cases.

The first case results in the limit of a large radius u . The weight factor z_u is then equal to absorbed dose, *i.e.* it is constant. Therefore $f_{ur}(z)$ reduces to the frequency distribution $f(z)$.

The second special case is that of two equal radii, $u = r$. In this case the function reduces to the dose distribution, $d(z)$.

A third case of interest leads to a distribution which has not been dealt with in this article but which is useful in certain applications. This distribution results when u goes toward 0, *i.e.* when the inchoate density is used as weight factor. Under this condition one samples the values of the specific energy only for those spheres of radius r which are centered at the transfer points. The selection probability for each transfer point is proportional to ϵ_i . The resulting probability distribution may be designated by $c(z)$; the letter c is chosen because the distribution deter-

mines the relative frequencies of different values of specific energy in spheres centered at the transfer points, *i.e.* at ionization and excitations. Accordingly one may call this distribution the *centered* distribution of specific energy. $C(z)$ is the probability to find a value of specific energy exceeding z in a sphere of radius r around a transfer point. $c(z) dz$ is the probability to find a value between z and $z + dz$.

One can apply the centered distribution to situations where sublesions, *e.g.* single-strand breaks in DNA, are produced at the transfer points, and where the probability that two such sublesions interact, *e.g.* for the formation of double-strand breaks, is a function of their distance. Although the distribution $c(z)$ may in many cases be similar to the distribution $d(z)$ there appears to be no general mathematical relation between $c(z)$ and $d(z)$.

The mean value, \bar{z}_c , of the distribution $c(z)$ is a useful concept. It is the average specific energy in spherical sites around ionizations and excitations. According to the general relation expressed in Eq. (A.2) \bar{z}_c consists of a term which is independent of absorbed dose, and a term which is equal to absorbed dose. The first term is the contribution from the same track, the second term is the contribution from other tracks:

$$\bar{z}_c = \bar{z}_{c_1} + D \quad (A.4)$$

Whenever the first term is larger than the second term, it follows that the intratrack interaction of sublesions which leads to a linear component in absorbed dose is larger than the intertrack interaction which leads to a term which is quadratic in absorbed dose. The numerical evaluation of z_{c_1} shows that even with sparsely ionizing radiations the linear component dominates in the dose range of a few hundred rad except when the interaction distance, r , is larger than fractions of a micrometer [13].

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