THINDOWN IN RADIOBIOLOGY: *E. COLI B/r*, *Bs*-1, *B. SUBTILUS* SPORES, AND V-79 CHINESE HAMSTER CELLS*

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ABSTRACT

Track theory rested on the foundation of the radial distribution of dose from δ rays as the central contribution of atomic physics to heavy ion radiobiology. Here, a new calculation of the radial distribution of dose is applied, in which the classical angular distribution of dose of delta rays and a logarithmic polynomial representation of the electron range-energy relation are used, to form the basis of the present thindown calculation. Calculations of inactivation cross sections for heavy ions in the track width regime displaying thindown for *E. Coli B/r* and *Bs*-1, and for *Bacillus Subtilus* are straightforward for these are 1-hit detectors, Calculations for V-79 hamster cells are more complex. They follow the original development of this model for eucaryotic cells, and make use of the cross sections calculated for hypothetical internal targets which are then asserted to be proportional to the measured cellular inactivation cross sections. The results are in reasonable agreement with experimental data.

Keywords *E. Coli B/r* and *Bs*-1, *Bacillus Subtilus* spores, V-79 Chinese hamster cells, Thindown effect, Track theory, Heavy ions, Inactivation cross sections

1 INTRODUCTION

In the study of particle tracks in emulsion it is observed that tracks of heavy ions first increase in width as the speed of the ion decreases from relativistic values, and then takes on the appearance of a sharpened pencil as the ion approaches the end of its range[1]. This effect, call 'thindown", results from the kinematic limit on the speed of secondary electrons to twice the speed of the ion which collides with electrons at rest. This then limits the width of the track. Similar effects are observed for many detectors. In heavy ion radiobiology the effect is seen as a decrease in interaction cross section from a maximum value with an increase in the LET (linear energy transfer) of bombarding ions, and results in a hook shaped appearance of the plot of cross section vs LET, for the cross section, first increases and then decreases with an increase in LET.

Track theory (also called Katz theory, or the theory of RBE) connects the response of a detector to γ rays with action cross sections for heavy ion bombardment through the radial distribution of dose from delta rays[2]. The kinematic limitation in the speed of delta rays leads quite naturally in this model to the inference of thindown. The dose in

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coaxial cylindrical shells about the ion's path, taken to represent the average from many ions, is converted to the probability for target inactivation through the dose response relation for γ rays, taken to represent the probability for target inactivation as a function of the dose of secondary electrons. The radial integral of the inactivation probability is the inactivation cross section[3]. The dose diminishes quadratically with radial distance to a limit determined by the maximal delta ray energy. Because of the gradient in radial dose the average energy deposited in a target must be calculated to estimate the inactivation probability as a function of distance from the ion's path, called an "extended target" calculation. This is particularly the case at distances below about three target radii. At larger distances the difference in dose across the target may be neglected, in a "point target" calculation, where the dose at the center of the target is taken to represent the average dose. For simple target structures, as in "1-hit" detectors, the cross section calculation is straightforward. For complex target structures, as for eucaryotic cells, a more involved approximation is required.

Inactivation cross sections, for very heavy ion bombardment of *E. Coli B/r* and *Bs-1*[4], and *Bacullus Subtilus* spores[5], are calculated as 1-hit detectors, following the theory of Butts and Katz and the new radial dose distribution around the path of a heavy ion was calculated by numerical integration accounting for the ejection angles of secondary electrons on the basis of classical collision dynamics and the range-energy relationship of a logarithmic polynomial proposed by Zhang *et al*[6]. The distribution of radial dose around a path of a heavy particle in water is given by

$$D(t)=\frac{Cz^2\omega_{\mathrm{m}}^{1/2}}{2\pi\beta^2 t}\cdot\int_t^T\frac{1}{(\omega_{\mathrm{m}}-g^{-1}(r))^{1/2}}\cdot g'^{-1}\left[r-\left(\frac{\omega_{\mathrm{m}}}{\omega_{\mathrm{m}}-g^{-1}(r)}\right)^{1/2}\cdot t\right]\cdot\frac{g^{-1}(r)}{(g^{-1}(r)+I)^2}\cdot\mathrm{d}r \quad (1)$$

where ω is the energy of electron ejected at angle θ to the ion path from an atom with mean ionization potential I, ω_{m} the maximum energy delivered to a secondary electron of mass m by an ion moving at relative speed $\beta = v/c$(c is the speed of light). If r is the range of secondary electron with the initial energy ω, the range-energy relationship of the secondary electron is expressed by

$$r = g(\omega) \quad (2)$$

$$\omega = g^{-1}(r) \quad (3)$$

A logarithmic polynomial instead of two segments of power-law function is used to express the experimental data of range-energy for electrons between 20 eV and 20 MeV in aluminum obtained, that is

$$r=\exp\left(\sum_{i=0}^{3}A_i(\ln\omega)^i\right) \quad (4)$$

where $A_0 = -4.787$, $A_1 = 1.432$, $A_2 = 0.063$ and $A_3 = 0.0065$, r is in units mg/cm^2 and ω in keV. The maximum range of secondary electron with energy ω_{m} is $T = g(\omega_{\mathrm{m}})$.

Inactivation cross sections for very heavy ion bombardment of mammalian cells in the thindown region calculated from the track theory of biological cells and the new radial dose distribution agree with measured inactivation cross sections for V-79 Chinese hamster cells [7].

These results confirm the validity of an earlier conclusion that the disagreement between measured cross sections and those calculated from a radial dose formula based on normal ejection of delta rays was due to an incorrect evaluation of the dose in the outer limits of the "penumbra region"[8]. The differences in the radial dose calculations are twofold. In the old calculation delta rays were taken to be normally ejected and to obey a power law range-energy relationship. In the present calculation we make a more precise fit to electron range energy relations and take the delta rays to be ejected with an angular distribution in accordance with classical kinematics. The current improved agreement between measured cross sections and those calculated from the model confirms our earlier suggestion that the disagreement encountered earlierly was due to an incorrect evaluation of the maximal radial deposition of dose from delta rays. In the earlier work in order to gain an agreement with measured data we arbitrarily reduced the maximal radial penetration of delta rays by factor 5, reasonably consistent with the present work, where the maximal radial penetration of delta rays is 3 to 5 times smaller than in the earlier work, depending on the ion energy.

2 CALCULATION

2.1 *E. Coli B/r* and *Bs*-1

In earlier work of Katz and Zachariah[9] these *E. Coli* varieties were treated as 1-hit detectors with the target "radius" $a_0 = 0.5\,\mu$m, and D-37 (or D_0) of 36.5 Gy for *B/r* and 12.6 Gy for *Bs*-1, based on experimental work of Takahashi *et al*[10]. These values differ from those reported by Schäfer *et al*[4], namely 47.6 and 15.4 Gy, respectively. In the present work in which we calculate cross sections for comparison with the measurements of Schafer we retain the earlier target "radius" parameter, and have based our calculations on D-37 values adjusted from those of Schäfer. For good visual agreement with the reported cross sections we use adjusted value of 44.6 and 13.8 Gy, respectively, about 8% less than the measured values. Both measured and calculated cross sections for the two *E. Coli* varieties are reported in Figs.1 and 2, where σ is plotted against LET to display thindown in a customary setting. There the notation D_0, the dose at which there is an average of 1 hit per target, is used, equal to D-37 for 1-hit detectors. While there are a number of discrepancies between experimental values, plotted as points and theoretical calculations plotted as curves, it seems reasonable to claim that the theoretical calculation of inactivation cross sections, agrees with experiment for these 1-hit detectors, into the thindown region.

2.2 *Bacillus Subtilus* Spores

Calculations for the inactivation cross sections of *B. Subtilus* spores are in reasonable agreement with most measured values for Ar, Kr, Xe, Pb and U ions but disagree with

values for Ne ions. We have based our calculations on a fitted values of the D-37 dose of 400 Gy for these spores as 1-hit detectors, and on an estimated target "Radius" of 0.3 μm[11]. Both measured and calculated values are reported in Fig.3 where σ is plotted against z^2/β^2 of the bombarding ion, where z is the effective charge of the ion given by

$$z = Z[1 - \exp(-125\beta/Z^{2/3})] \tag{5}$$

where Z is the atomic number and β the speed of the ion divided by the speed of light. There are a number of discrepancies between experimental values (points) and theoretical calculations (curves) which appear above 12 MeV/u for all ions, of order 20%, and for all Ne bombardments. For these we have no explanation.

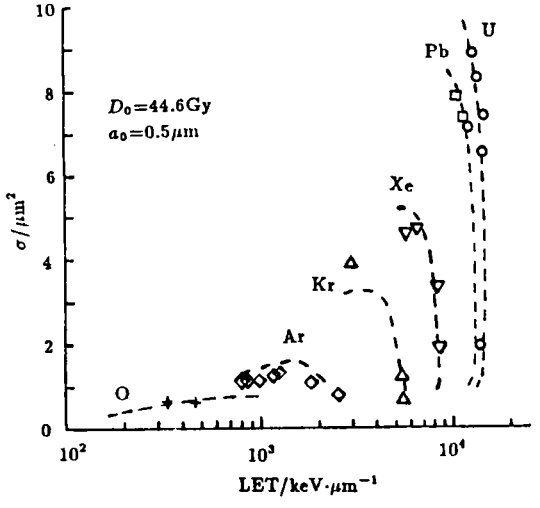

Fig.1 Inactivation cross section vs LET for *E. Coli B/r.*

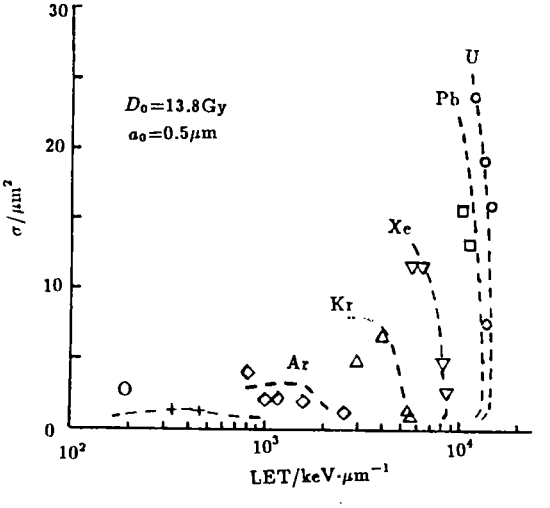

Fig.2 Inactivation cross section vs LET for *E. Coli Bs*-1

Experimental data are plotted as points while theoretical calculations are plotted as curves

2.3 V-79 hamster cells

In earlier work a set of parameters was fitted to data for the survival of V-79 Chinese hamster cells after irradiation with energetic heavy ions, at energies such that the irradiations were in the grain count regime. These parameters are $D_0 = 1.82$Gy, $m = 3$, $k = 1100$, and $\sigma_0 = 4.28 \times 10^{-7}$ cm^2. From these values a hypothetical target radius of $a_0 = 0.7\,\mu$m was extracted, from our equation $k = D_0 a_0^2 \times 10^{11}/K$, where D_0 is in Gy, a_0 is in cm, and K is a constant derived from the average dose deposited in an extended target by an ion passing through it, here taken to equal 1, reduced from an value of 2 which was based on the radial dose distribution of Butts and Katz. This change in K reflects the fact that is the average dose in the radial distribution of dose, and additionally on the assumed shape of the target. Thus we do not infer that a_0 is an accurate representation of target size for mammalian cells.

Inactivation cross sections are calculated for a hypothetical target of "radius" a_0, target number m and characteristic dose D_0 having the above numerical values from the expression

$$\sigma = \int_0^\infty 2\pi t dt (1 - \exp(-\overline{D}(t)/D_0))^m \tag{6}$$

where $\overline{D}(t)$ is the average dose experienced by the target of "radius" a_0 whose center is at radial distance t from the ion's path.

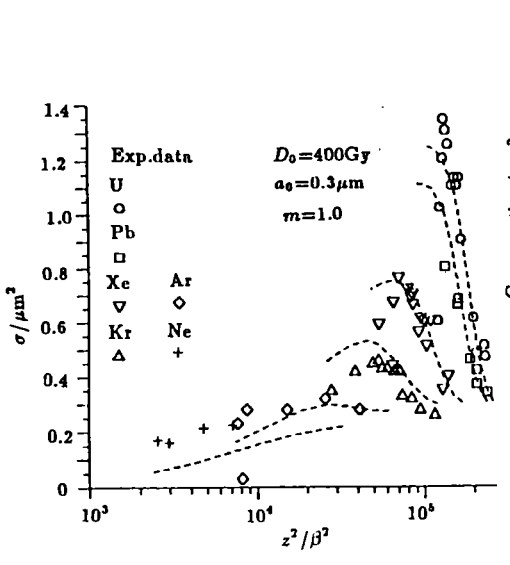

Fig.3 Inactivation cross section vs z^2/β^2 for *B. Subtilus* spores

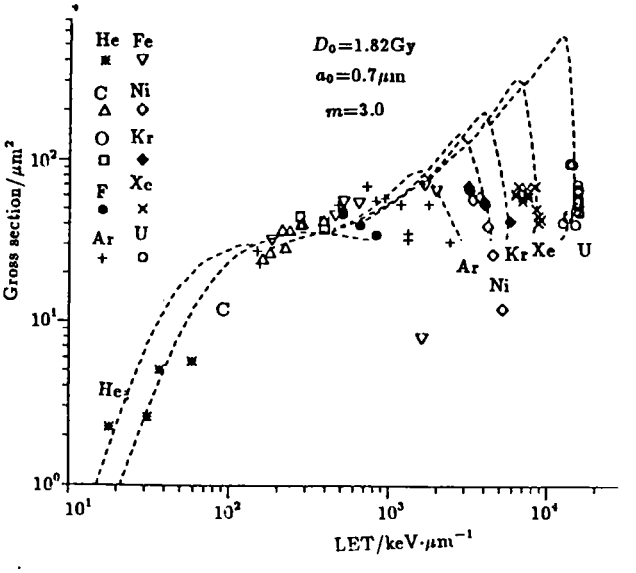

Fig.4 Calculated cross sections vs LET for V-79 Chinese hamster cells

The cross sections for cellular inactivation are then asserted to be proportional to those calculated for such a target, roughly in proportion to the ratio of the measured plateau value of the cellular cross section to the geometric cross sectional area of the target, but no mechanistic interpretation is implied in terms of the number of targets in a nucleus. One must recall that we do not know the identity, size, or spatial distribution of targets, which we call "bean bag". The calculated cross sections for the hypothetical internal target of radius 0.7 μm, having the parameters D_0 and m for V-79 hamster cells, are multiplied by factor 20, as displayed in Fig.4, so that the calculated curves for target cross sections lie near the top of the measured plateau values of the cellular cross sections for C and O bombardments. In the present calculation the location of the hooks along the LET axis is in agreement with experiment without further adjustment, unlike our earlier calculation of thindown for these cells.

3 DISCUSSION

The perspectives of track theory are now widely accepted as the best presently available model of high LET radiation effects, though questions remain about quantitative

details. Here we show that an improved calculation of the radial dose distribution leads to improved agreement between calculated and measured cross sections for V-79 cells in the thindown region where "hooks" are observed in plots of cross section vs LET or z^2/β^2.

This is the first time such calculations have been made for *E. Coil* varieties and for *B. Subtilus* spores.

We know of no other calculations for thindown in these cells. Our track model has been applied to similar calculations for tracks in nuclear emulsions, and for the response of scintillators and thermoluminescent dosimeters to energetic heavy ions, where thindown is also displayed.

We emphasize once again that thindown in eucaryotic cells is caused by the reduced inactivation cross section of internal targets within the cell caused by the kinematic limitation in delta ray energy, rather than from the entire cell or the entire nucleus as target. This is because delta rays from a heavy ion of these energies passing through a nucleus frequently do not extend beyond it. If the entire cell or the entire nucleus were the target, the delta rays could not generate the "track width regime" required for thindown. The observed changes of cellular inactivation cross sections with LET or are parallel to the changes in target cross sections presumably because there are many targets within the nucleus of a cell of which m or more (in this model) must be (in)activate the cell.

REFERENCES

1 Katz R, Kobetich E J. Phys Rev, 1969; 186:344
2 Butts J J, Katz R. Radiat Res, 1967; 30:855
3 Katz R. Appl Radiat and Isotopes, 1990; 41:563
4 Schäfer M, Facius R, Bücker H. In: Grundinger U, ed. GSI Scientific Report 1986, GSI 87–1
5 Schäfer M, Facius R, Bücker H. In: Grundingeer U, ed. GSI Scientific Report 1984, GSI 85–1
6 Zhang C X, Liu X W, Li M F *et al.* Radiat Prot Dosim, 1994, 52:93
7 Wulf H, Kraft-Weyrather W, Miilenburger H G *et al.* Radiat Res, 1985, 104(Suppl):S122
8 Katz R, Dunn D E, Sinclair G L. Radiat Prot Dosim, 1985, 13:281
9 Katz R, Zachariah R. Radiat Res, 1993; 134:261
10 Takahashi T, Ytaga F, Konno S. Adv Space Res, 1986; 6:117
11 Takahashi T, Ytaga F, Kitayama S. Adv Space Res, 1983; 3:95

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