# Calculation of response and thindown of V-79 cell

# for ion irradiation

CHEN Li-Xin1, LIU Xiao-Wei2

(<sup>1</sup> Department of Radiation Therapy, Cancer Center of Zhongshan University, Guangzhou 510060;
 <sup>2</sup> Department of Physics, Zhongshan University, Guangzhou 510060)

**Abstract** A cellular survival model and the cross section calculation with low and high LET for ion irradiation were presented. Based on our formula of surviving fraction calculation, the survival data of Chinese hamster cell (V-79) for ion irradiation including He, Li, B, C, O, Ne and Ar were calculated; the cross sections for ion irradiation including He, Ni, C, Ar, Kr, Xe and U were shown. The calculated results show that the presented model is a good description of radiation effects of V-79 cell for different ion irradiation. In this model splitting energy between ion-kill mode and gamma-kill model is avoided, the calculated results of cross section needn't be multiplied by a factor to fit the experimental data.

Keywords Irradiation, Survival fraction, Cross section CLC number QR144.1

# 1 Introduction

The radiation effects of ions are dependent on the distribution of physical and chemical events, such as ionization, excitation and the formation of free radicals around the ion's path. A full description of all interactions that occur in the medium is very complicated, and at present it is virtually impractical for completely interpreting the radiation effects. In the Katz's track structure theory of delta rays,<sup>[1,2]</sup> the energy deposition by delta rays ejected from the medium by a passing ion is considered as characteristic quantity to describe radiation effects of the ions. Radiation effects produced by an ion can be determined by the distribution of energy deposition by delta electrons while the difference of energy spectra of delta rays is neglected, and radiation response of a detector is the sum of radiation effects produced by the distribution of energy deposition. Since gamma rays always interact with a medium through secondary electrons, a detector exposed to gamma rays can be calibrated, whereby the target in the detector is bathed in a uniform field of secondary electrons. According to the theory, for single target/single-hit detector, such as dry enzymes and viruses, the inactivation cross sections of ions can be calculated by using the numerical integration methods<sup>[1]</sup> or a simplified analytical formula.<sup>[3]</sup> The results show that the theory is a good description of the experimental results.

The biological cell is more complex than the single-hit detector. Cells may be inactivated by a burst of delta rays accompanying the passage of a single energetic ion, or first damaged by the passage of an ion and then inactivated by the passage of other ions. The first case is a single particle effect which is suitably described by an inactivation cross section, and the second case is a multi-particle effect. These two kinds of inactivation are called as ion-kill mode and gamma-kill mode in the Katz's theory.<sup>[1,2]</sup> Based on the track structure theory of delta rays, Katz gave a four-parameter model to describe the response of cells for ion irradiation considering biological cells as multi-targets/single-hit detector<sup>[2,4]</sup> and splitting the energy deposition by delta electron between ion-kill mode and gamma-kill mode. The four parameters are the size of a cell  $\sigma_0$ , the number of target in a cell *m*, the

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characteristic dose to gamma ray  $D_0$  and K, related radiation sensitivity of cells to ions. The response of cells to ions can be calculated successfully using the model. In Katz's model the number of target *m* is not an integer that means averaged characteristics of cell inactivation. If cells are of simple structure, i.e. in each of them there is only one sensitive element, it would be expected that the cross section for one sensitive element is equal to the cross section for a cell, so parameter  $\sigma_0$  could be determined by parameters  $D_0$ and K, because the radius  $a_0$  of a sensitive element is related with K and  $D_0$  as  $K=D_0a_0^2/(2\times 10^{-7})$  erg cm<sup>-1</sup> according to Katz's model. The calculated results show that there is an order of magnitude difference between the value of calculated results and the fitting parameter  $\sigma_0$ . It implies that a cell is a complex structure in which more than one sensitive element are contained.

Based on the track structure theory of delta rays the interaction cross section of an ion with one sensitive element is calculated in the present work. Assuming that one biological cell contains multi- sensitive elements, a model of cell inactivation for ion irradiation is proposed and the response in low LET and the extrapolated cross section in high LET of V-79 cell are calculated.

## 2 Materials and methods

### 2.1 Cell inactivation model assumption

The cell model including multi-sensitive elements is assumed as follows: 1) biological cell contains multi-sensitive elements, in each of which there are two targets, every target is a hit detector; 2) when two targets in one element were hit one or two times, the sensitive element is completely damaged; the cell will be inactivated while every sensitive element was completely damaged; when only one target was hit the element is partly damaged; the cell containing partly damaged elements is partly inactivated.

A sensitive element was completely damaged including two sides: 1) two targets in a sensitive element are hit by delta electrons produced by an ion, this is called "one particle effect", which cross section is represented as  $\sigma_{si}$ ; 2) one of two targets in a sensitive element is hit by delta electrons produced by an ion and the other is hit by delta electrons produced by other ions, this is called "multi-particle effect", which cross section is represented as  $\sigma_{s1}$  and  $\sigma_{s1+1}$ , respectively.

Assuming that in a cell the number of sensitive elements is *n*, then in a partly inactivated cell the number of partly damaged sensitive elements may possibly be 1, 2, or..., *n*, and so on. Respectively we called the cells as "1-time, 2-times, ..., *n*-times damaged cell". For "*i*-times damaged cell " to be inactivated it can be classified as two categories: 1) two targets in one element were not hit completely before hit by the delta electrons produced by an ion, the cross section of which is represented as  $(n-i)\sigma_{si}$  because the "*i*-times damaged cell" contains (n-i) completely not hit elements; 2) one target was hit before, now the-not-hit-target is hit by delta electrons produced by other ions, the cross section of which is represented as  $i\sigma_{s1+1}$ .

Suppose the initial number of cell in a thin specimen is  $N_{I0}$ , when the ion beam with flux *F* radiates the specimen, the number of "*i*-times damaged" cell will be *n*-*i*. We have

$$\frac{\mathrm{d}N_0}{\mathrm{d}F} = -n\sigma_{si}N_0 - n\sigma_{s1}N_0 \tag{1}$$

$$\frac{\mathrm{d}N_1}{\mathrm{d}F} = n\sigma_{s1}N_0 - (n-1)\sigma_{s1}N_1 - \sigma_{s1+1}N_1 - (n-1)\sigma_{s1}N_1$$
(2)

$$\frac{\mathrm{d}N_i}{\mathrm{d}F} = (n-i+1)\sigma_{s1}N_{i-1} - (n-i)\sigma_{si}N_i - i\sigma_{s1+1}N_i - (n-i)\sigma_{s1}N_i$$
(3)

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$$\frac{\mathrm{d}N_n}{\mathrm{d}F} = \sigma_{s1}N_{n-1} - n\sigma_{s1+1}N_n \tag{4}$$

On the right-hand side of the Eq.(3), the first term represents the portion from  $N_{i-1}$  to  $N_i$ ; the second term and the third one correspond to the first kind and the second kind of the "*i*-times damaged cell" process as described above; and the last term represents the portion from  $N_i$  to  $N_{i+1}$ .

The solutions of the above equations are:

$$N_{i} = N_{Ri} \sum_{j=0}^{i} a_{j} e^{-[(n-j)\sigma_{s} + j\sigma_{s+1}]F}$$
(5)

where

$$N_{Ri} = \frac{n(n-1)...(n-i+1)\sigma_{s1}^{i}}{i!(\sigma_{s} - \sigma_{s1+1})^{i}} N_{I0},$$
  
$$a_{j} = (-1)^{i-j} \frac{i!}{(i-j)!j!} \text{ and } \sigma_{s} = \sigma_{si} + \sigma_{s1}.$$

The number of surviving cells in the specimen after irradiation by the ion beam is  $N = \sum_{i=0}^{n} N_i$ . Using Eq.(5) we can get the surviving fraction SF:

$$SF = \frac{N}{N_{10}}$$
$$= e^{-n\sigma_s F} \left\{ 1 + \frac{\sigma_{s1}}{\sigma_s - \sigma_{s1+1}} \times \left[ e^{(\sigma_s - \sigma_{s1+1})F} - 1 \right] \right\}^n$$
(6)

For the thin specimen there is a relation between the absorbed dose D and the flux F of ion beam:  $D=F\times$ LET, the surviving fraction related to the absorbed dose can be obtained with Eq.(6).

#### 2.2 Calculation of cross section

The cross section of an ion interacting with a sensitive element can be obtained by calculating the hitting probability of targets contained in the sensitive elements. According to the target theory, the average number of hit per target  $\overline{m}$  is proportional to the absorbed dose D:  $\overline{m} = D/D_0$ , where  $D_0$  represents the characteristic dose. According to the Poisson statistics the probability of the hitting target and no hitting target is  $1 - \exp(-\overline{m})$  and  $\exp(-\overline{m})$  respectively. Since the energy deposition of delta rays produced by ions is not uniform, the cross sections can be represented as:

$$\sigma_{si} = \int_{0}^{\infty} 2\pi t \left\{ 1 - \exp\left[-\bar{D}(t)/D_0\right] \right\}^2 dt \qquad (7)$$

$$\sigma_{s1} = 2R \int_{0}^{\infty} 2\pi t \left\{ 1 - \exp\left[-\overline{D}(t) / D_{0}\right] \right\} \cdot \exp\left[-\overline{D}(t) / D_{0}\right] dt$$

$$\exp\left[-\overline{D}(t) / D_{0}\right] dt$$
(8)

$$\sigma_{s1+1} = \int_{0}^{\infty} 2\pi t \left\{ 1 - \exp\left[-\overline{D}(t)/D_0\right] \right\}$$

(9)

where D(t) is the mean dose deposited in a sensitive element whose center is at radial distance t from the path of an ion. Considering that a partly damaged sensitive element may be repaired, and the probability of a sensitive element partly damaged is smaller than the probability of one of two targets in the sensitive element being hit, we introduce a fitting parameter R in Eq.(8) to represent the effect.

When the sensitive element is represented by a cylinder which radius is  $a_0$  (the axis of the cylinder is parallel to the ion's path), the mean energy deposition can be expressed by

$$\overline{D}(t) = \frac{1}{\pi a_0^2} \int_0^{a_0} \int_0^{2\pi} D\left[ (t^2 + r^2 + 2rt\cos\theta)^{1/2} \right] r \mathrm{d}\theta \mathrm{d}r \ (10)$$

where D(t) is the distribution dose of all points in the radius of the ion's path.

Based on different assumptions there are different models to deal with the radial distribution of dose about the ion's path.<sup>[5-7]</sup> These models agree at the same point: when the distance *t* is not very near  $T_{\text{max}}$ , D(t) is proportional to  $1/t^2$ , where *t* is called penumbra radius. When *t* is very near  $T_{\text{max}}$ , D(t) decrease rapidly. For practical purposes it may be assumed that there is a sudden cut-off at the point of  $T_{\text{max}}$ , the radial distribution of dose around the path of an ion can be ex-

pressed as:<sup>[5]</sup> 
$$\overline{D}(t) = C \frac{Z_{eff}^2}{\beta^2} \times t^{-2}$$
 (for  $t \leq T_{max}$ ).

When  $t > T_{\text{max}}$ ,  $\overline{D}(t) = 0$ . In this equation C is a co-

efficient only depending on the absorbing medium, and when the medium is water,  $C=1.25\times10^{-8}\text{erg}\cdot\text{cm}^{-1}$ ;  $\beta$  is the ion's velocity relative to that of light in vacuum;  $Z_{\text{eff}}$  is the effective ion's charge number. Considering the ejecting angle of secondary electrons, the maximum distance of delta electron in the ion's path is  $T_{\text{max}}=6.16\times10^{-2} (E/M_i)^{1.7}$ , where the unit of  $T_{\text{max}}$  is  $\mu$ m, E is MeV, and  $M_i$  is the mass of an ion in atomic mass unit.<sup>[5]</sup>

The mean dose deposition in an element can be

calculated using above equations. To avoid the divergence in the calculation, we replace  $1/t^2$  with  $1/(t^2+\varepsilon^2)$ ,

and assume that  $\varepsilon^2$  is  $3.5 \times 10^{-5} \ \mu\text{m}$ , then the equation becomes:<sup>[8]</sup>

$$\overline{D}(t) = C \frac{Z_{eff}^2}{\beta^2 a_0^2} \ln \frac{a_0^2 - t^2 + \varepsilon^2 + \sqrt{a_0^4 - 2a_0^2(t^2 - \varepsilon^2) + (t^2 + \varepsilon^2)^2}}{2\varepsilon^2}$$
(11)

When  $t \leq T_{\max} + a_0$ , the secondary electrons can interact with the sensitive elements whose center is in the distance  $t \leq T_{\max} + a_0$ . When  $t > T_{\max} + a_0$ ,  $\overline{D}(t) = 0$ . When  $t \gg a_0$ ,  $\overline{D}(t)$  varies with  $1/t^2$ .

## 2.3 Results and discussion

Fig.1 shows the variation of  $\overline{D}(t)$  with t based on Eq.(11). When  $t < a_0$ , there is a plateau with  $\overline{D}(t)$ varying with  $Z_{eff}^2 \beta^{-2} a_0^{-2}$ . When  $t > a_0$ ,  $\overline{D}(t)$  declines rapidly with the increment of t and then varies with t as  $1/t^2$ . When t is 1.1  $a_0$ ,  $\overline{D}(t)$  is smaller than 4 times  $\overline{D}(a_0)$ .

The survival curves of V-79 cells irradiated by ions He, Li, B, C, O, Ne and Ar were calculated with the above model and compared with the experimental results.<sup>[9]</sup> In Fig.2, the points represent experimental data<sup>[10]</sup> and the lines represent calculated results. The fitting parameters are:  $a_0=7.3\times10^{-5}$ cm,  $D_0=4.9\times10^4$ erg · cm<sup>-3</sup>, n=20, R=0.15. The survival curves are horizontally displaced by a factor *s* to avoid overlap. It can be seen that theoretical results are in good agreement with experimental data. The four parameters for V-79 cell in the Katz's model are: m=2.5,  $D_0=1.95 \times 10^4 \text{ erg} \cdot \text{cm}^{-3}$ ,  $K=1.4 \times 10^{-3}$ ,  $\sigma_0=5 \times 10^7 \text{ cm}^2$ .



**Fig.1** The mean dose D(t) deposited by secondary electrons in a cylinder sensitive element of radius  $a_0$ , whose center is at radial distance t from the path of an ion of effective charge number  $Z_{\text{eff}}$  moving at relative speed  $\beta$ .



**Fig.2** Survival data of Chinese hamster cells(solid square)<sup>[8]</sup> are superimposed on fitted survival curves using the multi- sensitivity element model, where  $\beta$  is the velocity of an ion relative to that of light in vacuum. The curves are nested using horizontal displacement parameters. The charge number Z of ions is 2,3,5,6,8,10 and 18 for He, Li, B, C, O, Ne and Ar respectively. The lines represent the calculated results.

Evaluating the logarithmic derivative of the surviving fraction with respect to the beam flux F in the high flux (extrapolated) region, which is identified as negative extrapolated cross section  $\sigma_{\text{ext}}$ , we can find

from Eq.(6) that:

 $\sigma_{\text{ext}} = n(\sigma_{\text{s1}} + \sigma_{\text{si}}) \quad \text{for} \quad \sigma_{\text{s1}} + \sigma_{\text{si}} < \sigma_{\text{s1}+1},$  $\sigma_{\text{ext}} = n\sigma_{\text{s1}+1} \quad \text{for} \quad \sigma_{\text{s1}} + \sigma_{\text{si}} < \sigma_{\text{s1}+1},$ 

which include single-particle and multi-particle effects. From Eqs.(7), (8) and (9) it can be verified that

# $\sigma_{s1}+\sigma_{si}<\sigma_{s1+1}$ when R<1/2.

We also have calculated the extrapolated cross section  $\sigma_{\text{ext}}$  and compared it with experimental data for V-79 cell irradiated by ions as the same as above. The result was shown in Fig.3, where the lines represent calculated results and the points represent experimental data.<sup>[8]</sup> It is also shown that we needn't multiply by a factor to fit the experimental data of cross sections. In Fig.3 we have seen the decrease of the cross section from a maximum value with an increase in LET of ions, which is called the thindown effect.<sup>[8,11]</sup>

In Katz's cellular survival model, the extrapolated cross section  $\sigma_{\text{ext}}$  is equal to the inactivation cross section which represents single-particle effect in the thindown region. Fig.4 shows the calculated result of inactivation cross sections of cells  $\sigma_{\text{ci}}=n\sigma_{\text{si}}$  compared with experimental cross sections.<sup>[8]</sup>



**Fig.3** Calculated results of inactivation cross section  $\sigma_{\text{ext}}$  vs. LET for V-79 Chinese hamster cells. The points represent the experimental data, and the lines represent the calculated results.



**Fig.4** Calculated results of inactivation cross section of cells  $\sigma_{ci}=n\sigma_{si}$  vs. LET for V-79 Chinese hamster cells. The points represent the experiment data, and the lines represent the calculated results.

## 3 Conclusions

In the study of heavy ion irradiation biology, the Katz's cellular track model has been widely used in describing experiments with heavy ion exposure to mammalian cell cultures. In this paper, based on the Katz's track structure theory, a formulation of inactivation of cells for ion irradiation is given when considering that a biological cell is a structure containing multi-sensitive elements and there are two targets in each sensitive element. Using the interaction cross sections of an ion with a cell the response and the extrapolated cross sections are calculated. In this calculation, the splitting energy between ion- kill mode and gamma-kill mode in Katz's cellular model is avoided, and the cross section needn't be multiplied by a factor (while the Katz's model needs) to fit the experimental data. The calculated results show that the model gives a good description of the response and the thindown effect of V-79 cell to different LET ions.

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