Supplementary Information

Numerical datasets supporting the theoretical figures

Occupancy-Driven Attenuation in Radiation-Sensitive Chromatin Domains: A Statistical-Mechanical Model of the Overkill Effect and RBE Maximum

Ladan Rezaee

Overview

The Supplemental Data included here presents the numeric data and formulas needed to reproduce all the theoretical figures in the main article.

For the purpose of completeness, the formulas and values used in the preparation of each figure are presented below. Numeric data corresponding to each figure is computed directly from the formulas using the parameter values mentioned in the manuscript. These data are made available to assist with visualization, reproducibility of the graphs, and future comparisons.

In addition, for Figure 5, the supplementary information is made available along with the experimental results of RBE based on the radiobiological data published in the cited studies for qualitative comparison with the theoretical data obtained using the current model.

The full set of numerical data is further made available in an Excel file.

Reproduction of the figures

In order to provide the opportunity for independent reproduction of theoretical calculations described in the main article, the information for each theoretical figure is arranged in the same format. For each theoretical figure, the following information is presented:

1. **Short description**: A short description of the physical quantity under consideration.

2. **Analytical equations**: Analytical equations that are used to calculate the plot curves.

3. **Model parameters**: Numerical values of all parameters needed for the calculations.

4. **Complete numerical dataset**: Information about full numerical dataset calculated using Microsoft Excel and provided separately from the article (in separate file).

5. **Representative numerical dataset**: Selected subset of calculated numerical values (about 10–15 rows), which demonstrate the behavior of the function.

The information is structured in such a way to increase transparency, allow for independent verification of the calculations, and future comparison with other theoretical approaches or experiments.

Supplementary Table S1

Data used for Figure 1

1. Short description

Figure 1 shows the dependence on LET of the chromatin domain occupancy function, $\Theta(\mathrm{LET})$, and its complement attenuation function, $\psi(\mathrm{LET})$. The attenuation function is the fractional number of sensitive chromatin domains that can still take part in additional biological independent lethal events.

2. Analytical equations

Figure 1: $\psi(\mathrm{LET})$ and $\Theta(\mathrm{LET})$ vs. LET

$$\psi(\mathrm{LET}) = \frac{1}{1+z_1 \exp\left[z_2(\mathrm{LET}-\mathrm{LET}_0)\right]} \tag{S1.1}$$

$$\Theta(\mathrm{LET}) = 1 - \psi(\mathrm{LET}) \tag{S1.2}$$

3. Model parameters

Table S1.1. Model parameter values used to generate the theoretical curves. The values correspond to carbon-ion irradiation of V79 cells and were taken from Ref. [1].

Parameter	Value	Unit
z_1	0.1	—
z_2	0.01	μm keV^{-1}
LET_0	150	keV $\mu\mathrm{m}^{-1}$

4. Complete numerical dataset

The complete numerical dataset used to generate Figure 1 is provided in the accompanying Excel file:

Supplementary_Data.xlsx

Sheet: **Figure1**

5. Representative numerical values

Table S1.2. Numerical values used to generate Figure 1.

LET (keV μm^{-1})	Equilibrium occupancy, ψ	Attenuation function, Θ
5	0.976982	0.023018
25	0.972143	0.027857
50	0.964515	0.035485
75	0.954951	0.045049
100	0.943349	0.056651
125	0.929645	0.070355
150	0.909091	0.090909
175	0.887481	0.112519
200	0.864061	0.135939
225	0.839038	0.160962
250	0.812691	0.187309
275	0.785393	0.214607
300	0.690522	0.309478

Supplementary Table S2

Data used for Figure 2

1. Short description

The occupancy fluctuation function $\Lambda(\mathrm{LET})$ represents the ratio between the occupied and unoccupied radiation-sensitive chromatin domains in the proposed statistical mechanics model. It is found as the product of the occupancy fraction $\Theta(\mathrm{LET})$ and the fraction of unoccupied domains $\psi(\mathrm{LET})$. This function has a maximum value that defines the LET interval when the change in occupancy is greatest and the occupancy effects are expected to be noticeable. The numerical data below refer to the fluctuation function shown in Fig. 2 in the main text and was obtained using Equation (S2.1) with the following parameters given in Table S1.1. The sample set of numerical data is shown below, and the full set can be found in the Excel file attached to this document.

2. Analytical equations

Figure 2: $\Lambda(\mathrm{LET})$ vs. LET

$$\Lambda(\mathrm{LET}) = \Theta(\mathrm{LET})\psi(\mathrm{LET}) \tag{S2.1}$$

$\psi(\mathrm{LET})$ and $\Theta(\mathrm{LET})$ are calculated using equations (S1.1) and (S1.2), respectively. Then,

$$\Lambda(\mathrm{LET}) = \frac{z_1 \exp\left[z_2(\mathrm{LET}-\mathrm{LET}_0)\right]}{(1+z_1 \exp\left[z_2(\mathrm{LET}-\mathrm{LET}_0)\right])^2} \tag{S2.2}$$

3. Model parameters

These parameter values correspond to carbon-ion irradiation of V79 cells and were adopted from Ref. [1]. The values used in the present calculations are summarized in Table S1.1.

4. Complete numerical dataset

The complete numerical dataset used to generate Figure 2 is provided in the accompanying Excel file:

Supplementary_Data.xlsx

Sheet: **Figure2**

5. Representative numerical values

Table S2.1. Numerical values used to generate Figure 2.

LET (keV μm^{-1})	**Occupancy variance Λ(LET)**
5	0.022394
25	0.027077
50	0.034224
75	0.043071
100	0.053915
125	0.067033
150	0.082645
175	0.100843
200	0.121504
225	0.144189
250	0.16805
275	0.191788
300	0.213699
325	0.231846
350	0.244364
380 (peak)	**0.25**
400	0.24758
425	0.237895
450	0.221905
475	0.201338
500	0.178141

Supplementary Table S3

Data used for Figure 3

1. Short description

The effective lethal-lesion production function $L_{\text{eff}}(\text{LET})$ consists of the damage-producing function $\phi(\text{LET})$ based on LET and the occupancy-based attenuation function $\psi(\text{LET})$. As discussed in this paper, $L_{\text{eff}}(\text{LET})$ is obtained through a statistical mechanical treatment. $L_{\text{eff}}(\text{LET})$ is scaled to its maximum value for presentation purposes. The values below refer to the normalized curve depicted in Fig. 3 of the main paper.

2. Analytical equations

Figure 3: $\frac{L_{\text{eff}}(\text{LET})}{Max\ (L_{\text{eff}})}$ vs. LET

$$L_{\text{eff}}(\text{LET}) = \phi(\text{LET})\psi(\text{LET}) \tag{S3.1}$$

$$\phi(\text{LET}) = a_1 + a_2(\text{LET} - a_3)^m \tag{S3.2}$$

$\psi(\text{LET})$ is calculated using equation (S1.1).

3. Model parameters

Table S3.1. Parameter values used in the present calculations. These values correspond to carbon-ion irradiation of V79 cells and were taken from Ref. [1].

Parameter	Value	Unit
a_1	0	DSB cell^{-1} Gy^{-1}
a_2	38.19 ± 3.13	DSB cell^{-1} Gy^{-1}(keV µm^{-1})$^{\text{m}}$
a_3	14.59 ± 2.90	(keV µm^{-1})^m
m	0.23 ± 0.01	-

4. Complete numerical dataset

The complete numerical dataset used to generate Figure 3 is provided in the accompanying Excel file:

Supplementary_Data.xlsx

Sheet: **Figure3**

5. Representative numerical values

Table S3.2. Numerical values used to generate Figure 3.

LET (keV μm^{-1})	**Normalized lethal lesion function, $\frac{L_{\mathrm{eff}}(\mathrm{LET})}{Max\,(L_{\mathrm{eff}})}$**
25	0.583448
50	0.767124
75	0.85875
100	0.918185
125	0.958469
150	0.984336
175	0.99769
192 (peak)	**1**
225	0.988933
250	0.966825
275	0.932899
300	0.887555
325	0.831753
350	0.767119
375	0.695918
400	0.620881
425	0.544922
450	0.47081
475	0.40088
500	0.336844

Supplementary Table S4

Data used for Figure 4

1. Short description

Figure 4 shows the predicted survival response that was derived using the occupancy-based attenuation model. This was done by calculating the product of the normalized effective lethal-lesion production function with the exponential survival model presented below. Survival curves were produced for typical values of LET covering the low-, intermediate-, and high-LET regimes to show the change in the predicted biological response.

The theoretical survival curves were calculated from the normalized survival function

$$S(D, \mathrm{LET}) = \exp\left[-\frac{D}{D_{ref}} \frac{\phi(\mathrm{LET})\psi(\mathrm{LET})}{\max\left[\phi(\mathrm{LET})\psi(\mathrm{LET})\right]}\right] \quad \text{(S4.1)}$$

where D is the absorbed dose, $D_{ref} = 1$ Gy, and $\max[\phi(\mathrm{LET})\psi(\mathrm{LET})] = 190$, corresponding to the maximum effective lethal-lesion production obtained in Figure 3 at $\mathrm{LET}_{\mathrm{peak}} = 192$ keV $\mu\mathrm{m}^{-1}$. The curves were evaluated for five representative LET values (50, 150, 192, 300, and 380 keV/μm). The numerical values reported below correspond to the survival curves presented in Figure 4 of the main article.

2. Analytical equations

Figure 4: Survival $S(D, \mathrm{LET})$ vs. dose D

$\psi(\mathrm{LET})$ and $\phi(\mathrm{LET})$ are calculated using equations (S1.1) and (S3.1), respectively.

3. Model parameters

The calculations were performed using the parameter values listed in Tables S1-1 and S3-1.

4. Complete numerical dataset

The complete numerical dataset used to generate Figure 4 is provided in the accompanying Excel file:

Supplementary_Data.xlsx

Sheet: **Figure4**

5. Representative numerical values

Table S4.1. Numerical values used to generate Figure 4.

Dose (Gy)	**Survival Fraction**				
	LET $= 50$ keV μm^{-1}	LET $= 150$ keV μm^{-1}	LET $= 192$ keV μm^{-1}	LET $= 300$ keV μm^{-1}	LET $= 380$ keV μm^{-1}
0	1	1	1	1	1
2	0.215415	0.139474	0.135195	0.169243	0.255902
4	0.046414	0.019491	0.01829	0.028611	0.065541
6	0.010002	0.002724	0.002474	0.004836	0.016784
8	0.002155	0.00038	0.000335	0.000818	0.0043
10	0.000464	0.000053	0.000045	0.000139	0.001097

Supplementary Table S5

Data used for Figure 5

1. Short description

Figure 5 shows a comparison between the LET dependence of the RBE calculated by the proposed occupancy-based model and experimental data on RBE of carbon ion radiation of V79 cells. Figure 5 depicts the RBE of the reference model (solid line), the upper and lower boundaries of the theoretical RBE (shaded area), and the experimental data of RBE from the literature.

2. Analytical equations

Figure 5: RBE_{10} vs. dose LET

The RBE values were calculated at the 10% survival level using the normalized effective lethal-lesion production function introduced in the main text.

For a survival level of S=0.1, the survival model gives

$$0.1 = \exp\left(\frac{D_{10}}{D_{ref}} . \frac{\phi(LET)\psi(LET)}{\max[\phi(LET)\psi(LET)]}\right) \tag{S5.1}$$

The RBE at the 10% survival level is defined as

$$\mathrm{RBE}_{10}(LET) = \frac{D_{10,\gamma}}{D_{10}(LET)} \tag{S5.2}$$

where the reference photon dose was taken as

$$D_{10,\gamma} = 7.07\ Gy \tag{S5.3}$$

according to Furusawa *et al.* [3].

Substituting the survival expression yields

$$RBE_{10}(LET) = \frac{7.07}{\ln(10)} . \frac{\phi(LET)\psi(LET)}{\max[\phi(LET)\psi(LET)]} \tag{S5.4}$$

with

$$\max[\phi(LET)\psi(LET)] = 109\ \mathrm{DSB\ cell^{-1}\ Gy^{-1}} \tag{S5.6}$$

corresponding to the maximum effective lethal-lesion production obtained in Figure 3.

$\psi(\mathrm{LET})$ and $\phi(\mathrm{LET})$ are taken from equation (S1.1) and (S3.1), respectively.

3. Model parameters

The parameter values used in the calculations are listed in Tables S1.1 and S3.1.

4. Complete numerical dataset

The complete numerical datasets used to generate the reference curve, the upper and lower theoretical bounds, and the compiled experimental RBE values are provided in the accompanying Microsoft Excel file.

Supplementary_Data.xlsx

Sheet: **Figure5**

5. Representative numerical values

Table S5.1. Numerical values used to generate Figure 5.

LET (keV μm^{-1})	RBE	Lower bound RBE	Upper bound RBE
15	0.854051	0.768646	1.152969
25	1.792275	1.613048	2.419572
50	2.356502	2.120852	3.181278
75	2.637965	2.374169	3.561253
100	2.820542	2.538488	3.807731
125	2.944288	2.64986	3.974789
150	3.02375	2.721375	4.082062
175	3.064771	2.758294	4.137441
192 (peak)	3.071867	2.76468	4.14702
225	3.037869	2.734082	4.101123
250	2.969957	2.672961	4.009442
275	2.865742	2.579168	3.868752
300	2.72645	2.453805	3.680708
325	2.555034	2.29953	3.449295
350	2.356489	2.12084	3.18126
375	2.137769	1.923992	2.885988
400	1.907264	1.716537	2.574806
425	1.673927	1.506534	2.259801
450	1.446265	1.301638	1.952457
475	1.231449	1.108304	1.662456
500	1.034739	0.931265	1.396898

Experimental data

The experimental RBE values shown in Figure 5 were calculated from the published radiobiological parameters reported for carbon-ion irradiation of V79 cells in the following studies:

- Weyrather *et al* [2]
- Furusawa *et al* [3]
- Aoki *et al* [4]
- Belli *et al* [5]

The numerical values used in the comparison are provided in the accompanying Microsoft Excel file.

Table S5.2. Experimental values used to generate Figure 5.

LET (keV μm^{-1})	RBE (Furusawa *et al* [3])	LET (keV μm^{-1})	RBE (Weyrather *et al* [2])	LET (keV μm^{-1})	RBE (Belli *et al* [5])	LET (keV μm^{-1})	RBE (Aoki *et al* [4])
30	1.47292	32.4	1.5	40	1.87	60	2.58
31	1.7371	153.5	3.8	50	2	110	3.15
40.1	2.34884	275	3	75	2.6	152	3.15
40.6	2.15549	339.1	2.6	94	3.98	237	2.09
50.3	2.76172	482	2	222	3.19		
57.6	2.36455			303	2.25		
60	2.66792						
78.5	3.28837						
80.6	3.12832						
88	3.35071						
102	3.62564						
117	4.18343						
127	3.44878						
142	4.44654						
206	4.06322						
232	3.27315						
255	3.28837						
276	3.62564						
360	3.28837						
432	2.58974						
493	2.57091						
502	2.38851						

References

1. Rezaee, L. A mechanistic and time-resolved analytical model of oxygen-mediated DSB fixation: bridging LET physics and hypoxic biology for predictive heavy ion radiotherapy. *Phys. Med. Biol*. **71**, 055002 (2026).
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3. Furusawa, Y. *et al*. Inactivation of aerobic and hypoxic cells from three different cell lines by accelerated 3He-, 12C- and 20Ne-ion beams. *Radiat. Res*. **154**, 485–496 (2000).
4. Aoki, M., Furusawa, Y. & Yamada, T. LET dependency of heavy-ion induced apoptosis in V79 cells. *J. Radiat. Res*. **41**, 163–175 (2000).
5. Belli, M. *et al*. Effectiveness of monoenergetic and spread-out Bragg peak carbon ions for inactivation of various normal and tumour human cell lines. *J. Radiat. Res*. **49**, 597–607 (2008).