Microbe_IT

Kick–off meeting

WP2 - linking MD to RB

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Generalized stochastic microdosimetric model: The main formulation

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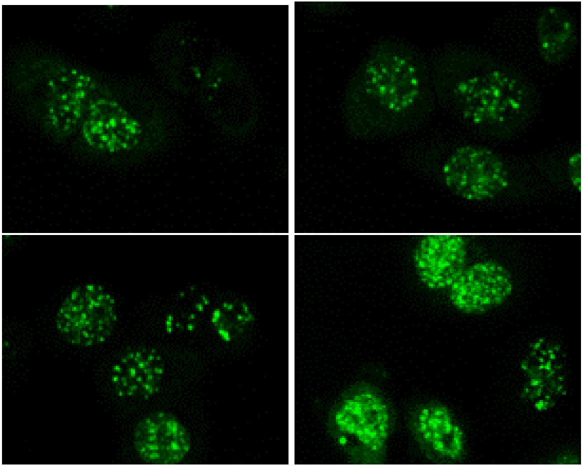
The main motivation

Clear stochastic fluctuations in the number of DNA damages among cells.



The model

Microdosimetric Kinetic Model (MKM)

$$\frac{d}{dt}\bar{y}(t) = a\bar{x} + b\bar{x}^2$$

Average number of lethal lesions

$$\frac{d}{dt}\bar{x}(t) = -(a+r)\bar{x} - 2b\bar{x}^2$$

Average number of sublethal lesions

Generalized Stochastic Microdosimetric Model (GSM^2)

$$\partial_t p(t,y,x) = \mathcal{E}^{-1,2}\left[x(x-1)bp(t,y,x)\right] + \mathcal{E}^{-1,1}\left[xap(t,y,x)\right] + \mathcal{E}^{0,1}\left[xrp(t,y,x)\right]$$

Probability distribution of lethal and sublethal lesions

The model

Microdosimetric Kinetic Model (MKM)

$$\frac{d}{dt}\bar{y}(t) = \underbrace{\boxed{a\bar{x}}}_{\text{death}} + b\bar{x}^2\,, \quad \frac{d}{dt}\bar{x}(t) = -\underbrace{\boxed{(a+r)\bar{x}}}_{\text{death}} - 2b\bar{x}^2$$

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The model

Microdosimetric Kinetic Model (MKM)

$$\frac{d}{dt}\bar{y}(t) = a\bar{x} + \underbrace{\boxed{b\bar{x}^2}}_{\text{double death}} \quad , \quad \frac{d}{dt}\bar{x}(t) = -(a+r)\bar{x} - \underbrace{\boxed{2b\bar{x}^2}}_{\text{double death}}$$

Generalized Stochastic Microdosimetric Model (GSM^2)

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repair

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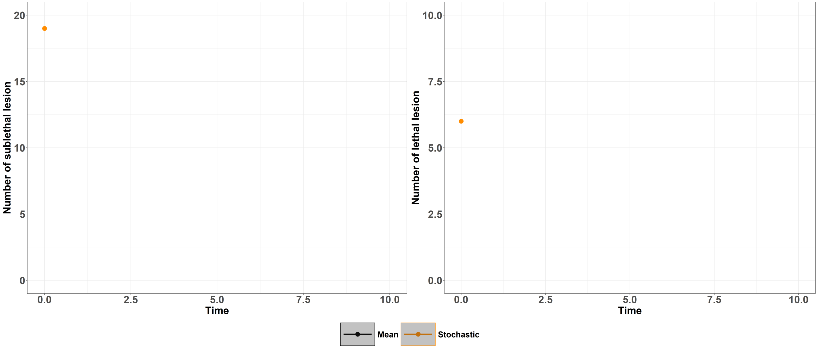
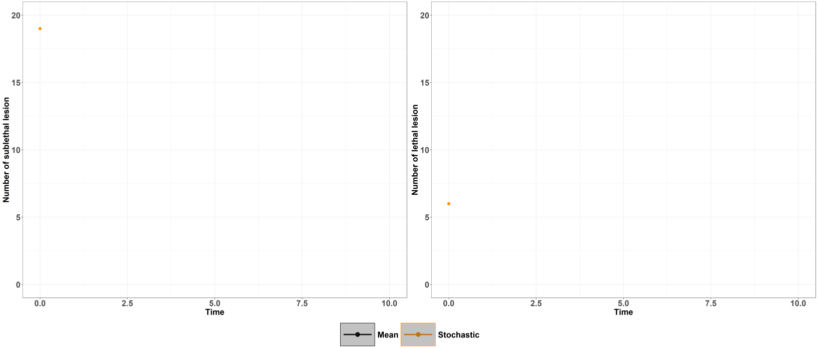
repair

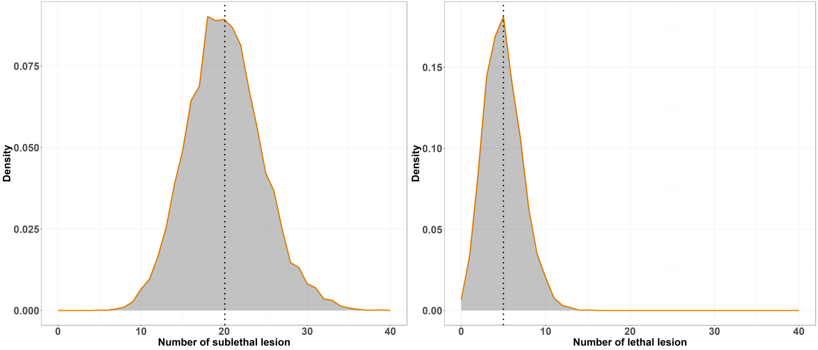
DNA damage time evolution



DNA damage time evolution



DNA damage time evolution



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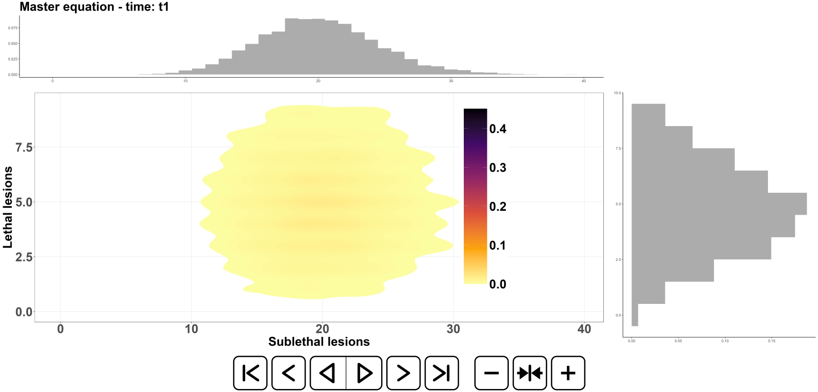

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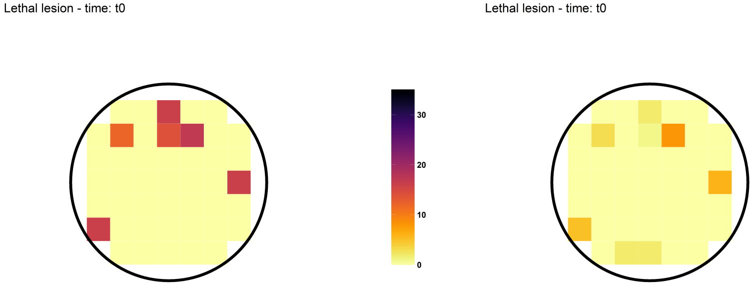

Main improvements

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- less sensitive to domains;

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$$+ \boxed{\sum_{i,j=1}^{N} {}^{X}\mathcal{E}_{i,j}^{-1,1}\left[x_i \kappa_{i;j}^{X} p(t,y,x)\right] + \sum_{i,j=1}^{N} {}^{Y}\mathcal{E}_{i,j}^{Y;-1,1}\left[y_i \kappa_{i;j}^{Y} p(t,y,x)\right]}$$

domain interconnection

Main improvements

- no assumption on Poisson distribution;
- less sensitive to domains;
- general irradiation conditions;

$$\partial_t p(t,y,x) = \mathcal{E}^{-1,2}\left[x(x-1)bp(t,y,x)\right] + \mathcal{E}^{-1,1}\left[xap(t,y,x)\right] + \mathcal{E}^{0,1}\left[xrp(t,y,x)\right] +$$

$$+ \boxed{\mathcal{E}_{\dot{d}}^{-y,-x}\left[\dot{d}p(t,y,x)\right]}$$

protracted dose

Main improvements

- no assumption on Poisson distribution;
- less sensitive to domains;
- general irradiation conditions;
- encompass the linear–quadratic survival setting;

$$S(z_n) = \exp\left[-N_d \frac{z_n}{z_F} \int_0^\infty \left(2 - e^{-\kappa z} - e^{-\lambda z}\right) f_{1;d}(z) dz\right] \left(1 + \sum_{k=1}^\infty z_n^k G_k(M)\right)^{N_d}$$

M: moment generating function it considers the whole microdosimetric distribution not only firsts moments.

The survival function

$$S(z_n) = \exp\left[-N_d \frac{z_n}{z_F} \int_0^{\infty} \left(2 - e^{-\kappa z} - e^{-\lambda z}\right) f_{1;d}(z) dz\right] \left(1 + \sum_{k=1}^{\infty} z_n^k G_k(M)\right)^{N_d}$$

Low dose: Linear–quadratic

$$\log S(z_n) \sim_0 -\alpha_0(M) z_n - \beta_0(M) z_n^2$$

High dose: Linear

$$\log S(z_n) \sim_\infty -\alpha_\infty(M) z_n$$

M: moment generating function it considers the whole microdosimetric distribution not only firsts moments.

Thank you for your attention!