Study of biological effects of long-term exposure to low dose-rate radiation with Whack-A-Mole model

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1. Introduction

Biological effects of radiation

Radiation exposure → Effects

1. Genetic effects
2. Cancer
3. Non-cancerous disease
4. ……..

Drosophila experiment by Muller

Total dose↑⇒Mutation frequency↑
= LNT（Linear non-threshold）

Mega-mouse experiment by Russell

Dose-rate↑⇒Mutation frequency↑

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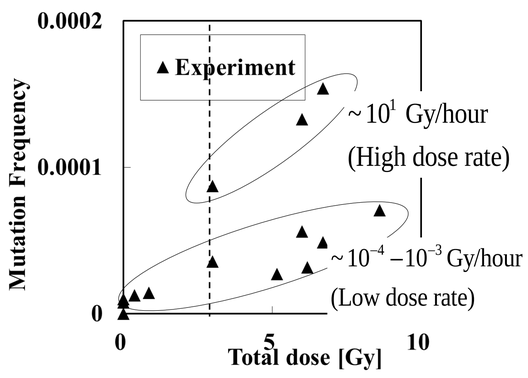


- Repair mechanism of DNA
- Cell deaths
  - Necrosis
  - Apoptosis

Long-term exposure to low dose-rate radiation

Inclusion of dose rate effects
Transition between normal and mutated cells

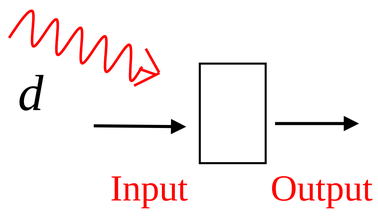
$$\frac{dN_n}{dt} = T_{nn}N_n + T_{nm}N_m$$
$$\frac{dN_m}{dt} = T_{nm}N_n + T_{mm}N_m$$

We determine four parameters by χ^2 fit

2. WAM model

Whack-A-Mole (WAM) Model

1.Important variable is dose-rate
2.Proliferation, cell death, recovery effect



$$\frac{d}{dt}F(t) = (a_0 + a_1 d) - (b_0 + b_1 d)F(t)$$

4 parameters

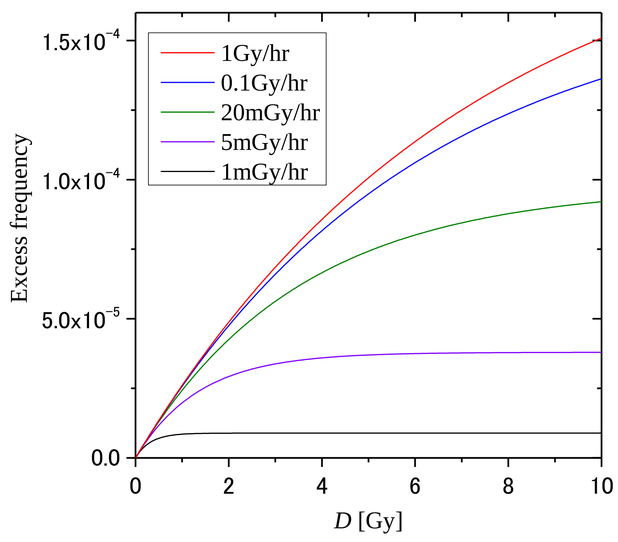
a_0, a_1, b_0, b_1

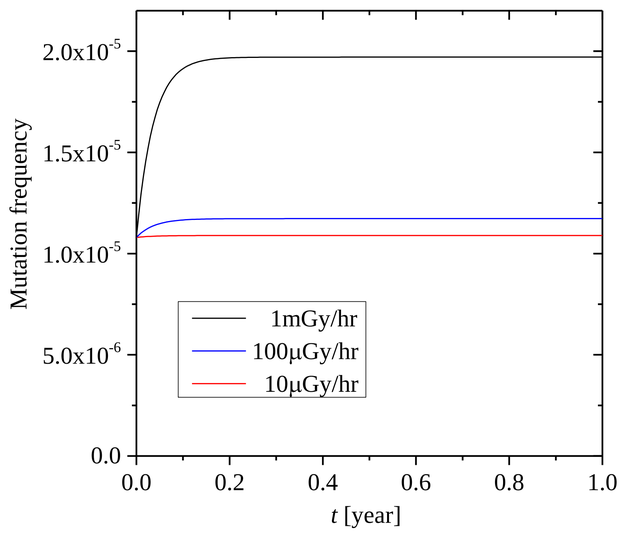
F: mutation frequency
d: dose rate [Gy/hour]
D: total dose [Gy]

$$F(t) = \frac{A}{B}\left(1 - e^{-Bt}\right) + F(0)e^{-Bt}$$
$$A = a_0 + a_1 d,\ B = b_0 + b_1 d$$

Saturation behavior

$$F(t) \to F(\infty) = \frac{A}{B} \quad (t \to \infty)$$





$$F(t) \approx F(0) + \left(\frac{A}{B} - F(0)\right)Bt = \frac{a_0}{b_0} + \left(a_1 - \frac{a_0 b_1}{b_0}\right)D \quad (t < t_c)$$

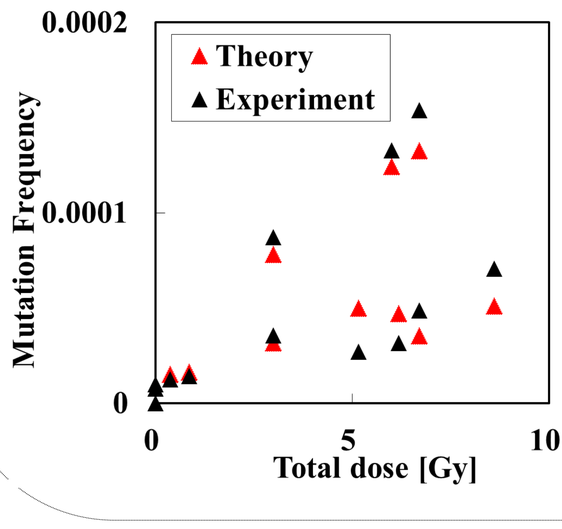
3. Results

Mega-mouse

a_0	[1/hr]	3.24 x 10^{-8}
a_1	[1/Gy]	2.94 x 10^{-5}
b_0	[1/hr]	3.00 x 10^{-3}
b_1	[1/Gy]	1.36 x 10^{-1}

$$d_{\text{eff}} = \frac{a_0}{a_1} = \frac{3.24\cdot10^{-8}}{2.94\cdot10^{-5}} = 1.10\,[\text{mGy/hr}]$$

$$F_s = \frac{a_0}{b_0} = \frac{3.24\cdot10^{-8}}{3.00\cdot10^{-3}} = 1.08\cdot10^{-5}$$



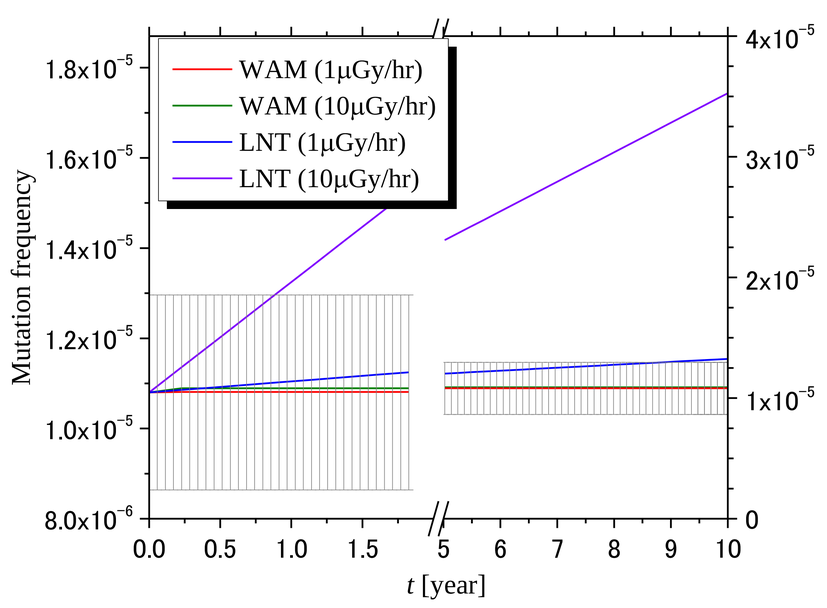
$$t_c \approx \left(1 - \frac{a_0 b_1}{b_0 a_1}\frac{d}{d_{\text{eff}}}\right)\frac{1}{b_0} = \left(1 - 0.051\frac{d}{d_{\text{eff}}}\right)\cdot 3.33\cdot10^2\,[\text{hr}]$$

$$F(\infty) \approx \left(1 + \left(1 - \frac{a_0 b_1}{b_0 a_1}\right)\frac{d}{d_{\text{eff}}}\right)\frac{a_0}{b_0} = \left(1 + 0.95\frac{d}{d_{\text{eff}}}\right)\cdot F_s$$

We estimate effects to human using parameters for mouse

$$\text{"DDREF"} = \frac{1 - e^{-\frac{B_{\text{ref}} D}{d_{\text{ref}}}}}{B_{\text{ref}}/d_{\text{ref}}} \frac{B/d}{1 - e^{-\frac{BD}{d}}} \to \frac{B/d}{1 - e^{-\frac{BD}{d}}}$$

"DDREF"	Total dose D			
Dose rate d	20 mGy	50 mGy	0.2 Gy	1 Gy
0.1 Gy/hr	1.00	1.00	1.00	1.01
20 mGy/hr	1.00	1.00	1.01	1.07
5 mGy/hr	1.01	1.01	1.06	1.32
1 mGy/hr	1.03	1.08	1.33	3.06
0.1 mGy/hr	1.33	1.93	5.96	28.1
10 μGy/hr	6.01	15.0	59.2	280
1 μGy/hr	59.9	149	592	2800



4. Summary

1. WAM model has been applied to estimate the biological effects of long-term exposure to low dose rate radiation.
2. Dose and dose rate effects factor is not constant but changes with dose and dose rate.
3. The effects do not accumulate linearly with time but show saturating behavior when the low dose exposure lasts for many years.