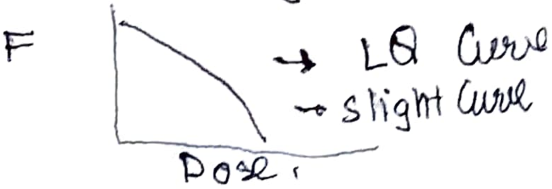
Hand-Written Primary Analysis

MSA - Multi-Scale Approach For IBT

Earlier → $\boxed{\text{LQ Model}}$
- ↳ Empirical & Semi-Empirical Modes
- ↳ Theoretical predictions x possible
- ↳ Failed to realize the Full Potential of IBT.

Now → $\boxed{\text{MSA}}$



→ Prediction across different conditions, spaces, times based on Physical, chemical effects of dose

MSA → Helps to Theoretically analyze IBT
↳ Will Play a mayor Role in the Forth coming advancements of IBT.

LQ :- $F_{survial}$ → $-\ln F = ad + \beta d^2$

α, β → Empirical   d - dose of Particle.

Lethality :-

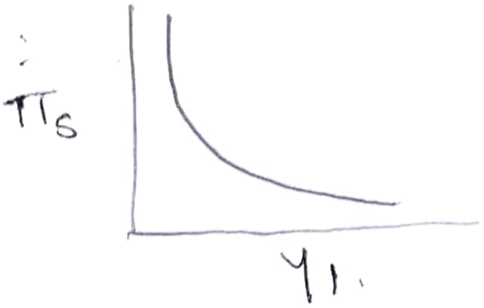
Minimum :- 2SSB
+ 1DSB
in 2 Twists of DNA can be lethal for Tumor cell

Yield → Y_1 → The yield of Clustered Damage in a DNA.

Different Experiments show

$$\Pi_S \propto e^{-Y_1}$$

Exponential Rel^n.



$\Pi_S \downarrow$ as $Y_1 \uparrow$

$$\boxed{Y_1 \propto \text{Dose}}$$

∵ IBT → Gives Excellent Dose Localizati

∴ Empirical Determenistics ∵ Yield of clustered damage ↑ as Dose of Particle ↑

$$\therefore \boxed{\Pi_S = e^{-Y_1}}$$

$$\therefore \boxed{\Pi_d = 1-e^{Y_1}}$$ → Our Inference (Additional).

Cell Repair

MSA Analysis for IBT

IBT

- Under Hypoxia (Nitrogen only)
- Aerobic Condition (Oxygen Present)

Oxygen changes the Dynamics of chemical Interactions Molecular Repair & Damage Fixation

OER → Oxygen Enhancement Ratio.

↳ Dose delivered under hypoxic to that under aerob

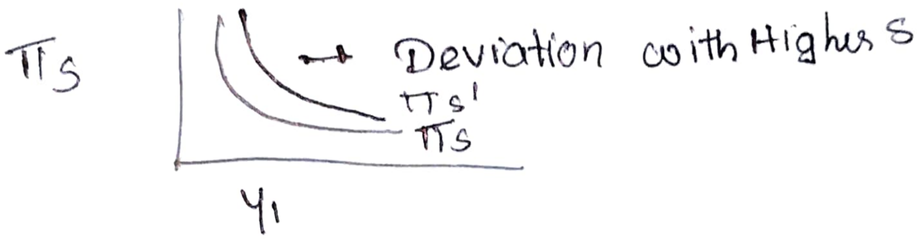
↳ $\frac{3}{1} = \frac{\text{Dose aerobi}}{\text{Dose Hypoxic}}$

∴ New π_s Eqⁿ Taking into account survival

$$\pi_s' = e^{-y_1} + \sum_{\mu=1}^{\infty} x^{\mu} \frac{y_1^{\mu} e^{-y_1}}{\mu!}$$

$$= e^{-1(1-x)y_1}.$$

x → Function of Probability of Repair



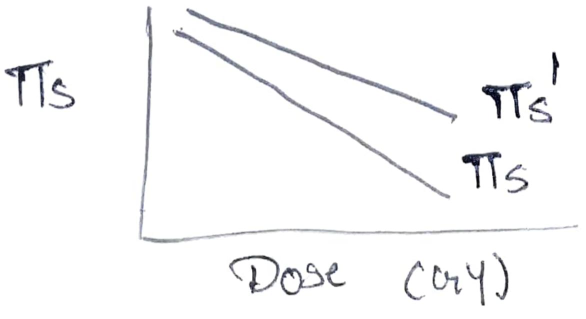
X → Functional dependence on x_1 & x_0

They are out of scope of Paper

Directly used in the Paper

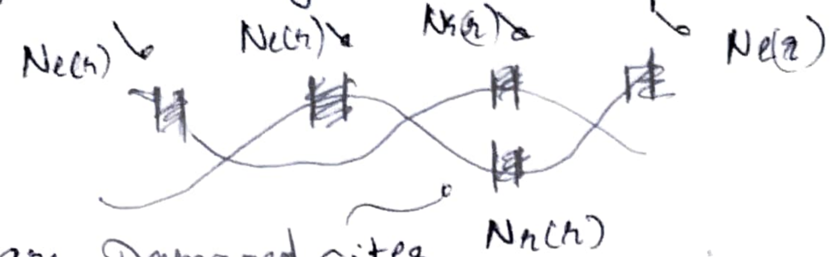
$$\therefore \pi_s' = \exp\left[-1(1-x_0)y_1 - x_1 y_1^2\right]$$

This the Basic overview when Plotted on Log Scale. the graph Turns out to be



Detailed Analysis of Physical & chemical Effects

★ They Helps us in Deriving the above Eq^n.



All are Damaged sites

Multiple Damage sites.

↳ Bought By several Independent agents

$N(r) = N_e(r) \quad N_r(r)$

LC:- Lethality Criterion

Poisson PMF

To Estimate Damage from Incoming species

$$P_l(r) = \lambda \sum_{v=3}^{\infty} \frac{(N(r))^v}{v!} e^{-N_r}$$

$\nu = 3$

∴ 3 SSB Required

as 2 1 + SSB

↳ Converts to DSB with $P_r = \lambda$

This meets criterion of lethal Damage

★ Number of lethal lesions Per Ions Path:

$$\frac{dN_l}{dx} : n_s \int_0^\infty P_l \; 2\pi r \, dr$$

$$= n_s \, \sigma$$

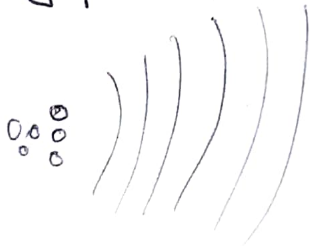
Number of lethal lesions ┘

↳ Effective cross Section of Damaged site

$$n_s = \frac{N_{base-pairs}}{20 \ Volume} = \frac{\pi}{16} \frac{N_g}{ANZ}$$

Diffusion & Travel

Effect of Reactive species formed near ion paths strongly depends on their transport.



→ shock waves for Longer Propogation.

Bragg's Peaks  Estimated 900 KeV LET

Also each Ion's Path is Independent from one another

$$N_R(r) = \begin{cases} N_R & r \le R_R \\ 0 & r > R_R \end{cases}$$

Uniformly Distributed

Value 5 to 10mm as radius

N_R Hypoxic = 0.04 N_R Environ (Aerobic) = 0.08.

& Average lethal lesions:

$$Y_1 = \frac{dN_1}{dx} \sum_{i=1}^{\infty} z_i \, i \, P_i(d)$$

$$P_i(d) = \frac{N_{ion}^{i} e^{N_{ion}}}{i!}$$

i → Number of ions traverse the cell Nucleus on average.

∴ There is also dependence on Dose & LET

$$\therefore \boxed{Y_1 = \frac{dN_1}{dx} \Sigma N_{ion} = \frac{\pi}{16} 6 N_g \frac{1}{Se} d}$$

∴ For an R.V. of dose we get yield for each value of Dose

$Y_1 \propto d$ & Survival ∝ dose (LQ)

** ∴ This gives a Possibility that LQ & MSA can be connected

Replacing the values.

$$-\ln \Pi_{survival} = (1-x_0) \frac{\pi}{16} 6 \, N_g \frac{d}{Se} + x_1 \left(\frac{\pi}{16} 6 N_g\right)^2 \frac{d^2}{Se^2}$$

$$\therefore \boxed{\alpha = (1-x_0) \frac{\pi}{16} \frac{6 N_g}{Se} \qquad \beta = x_1 \left(\frac{\pi}{16} N_a\right)^2 \frac{1}{Se^2}}$$

For $Y_1 > x_0 > x_1$ & C.V. surpassed

$$-\ln \Pi_{survival} = \frac{\pi}{16} 6 N_g \frac{d}{Se}.$$

$$\therefore \boxed{\alpha = \frac{\pi}{16} 6 N_g \frac{1}{Se}}$$

Also tells us about Deviation from semi-logarithmic