Illinois Institute of Technology

Physics 561

Radiation Biophysics

Andrew Howard

Illinois Institute of Technology

Physics 561

Radiation Biophysics:

Modifiers of the Radiation Response

Andrew Howard

BCPS Department

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Class Plan

- Review Midterm
- Biological Modifiers of Radiation Response
- Break
- Chemical/Physical Modifiers of Radiation Response

Midterm, Problem 1

Half-life of ^{32}P = 14.29 days

τ = Mean life = $T_{1/2}$/ 0.693 = 14.29 / 0.693 days = 20.62 days

Decay constant = 0.693 /$T_{1/2}$ = 0.0485 day^{1}

= 0.0485 day^{1} / 86400 sec/day = 5.613*10^{7} sec^{1}

after 10 days: $A = A_0 \exp(-\lambda t)$

A = 3.000 mCi * exp(-0.0485 day^{1} * 10 day) = 3.000 * exp(-0.485) = 1.847 mCi = 1.847*3.700*10^{7} Bcq = 6.834*10^{7} Bcq.

Midterm, Problem 2

Eqn. 4.20a and $\nu = c/\lambda$ means that

$hc/\lambda' = [hc/\lambda]/(1 + \alpha(1 - \cos\theta))$

so $\lambda'/\lambda = 1 + \alpha(1 - \cos\theta)$

Thus $(\lambda'/\lambda - 1)/\alpha = 1 - \cos\theta$

$\cos\theta = 1 - (\lambda'/\lambda - 1)/\alpha$

But $\lambda' > \lambda$: the photon has to lose energy.

$\lambda' = \lambda * 1.0001$; $\lambda'/\lambda = 1.0001$, $\lambda'/\lambda - 1 = 10^{-4}$

now $\alpha = h\nu/m_0c^2 = hc/(\lambda m_0c^2)$.

For λ in nm, E in eV, $E = hc/\lambda = 1239.84 / \lambda$.

$hc/\lambda = 1239.84 / 0.15$ eV = 8265.6 eV =

= $8.2656 * 10^{-3}$ MeV

$\alpha = hc/(\lambda m_0c^2) = 8.2656*10^{-3}/0.511 = 0.01618$

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Midterm problem 2, concluded

$\cos\theta = 1 - (\lambda'/\lambda - 1)/\alpha = 1 - 10^{-4}/0.01618$

so $\cos\theta = 1 - 0.006180 = 0.99382$

We can compute $\theta = \arccos(0.99382) = 6.373°$.

We can also compute it by an expansion:

To first order $\cos(x) = 1 - x^2/2$ so

$1 - \theta^2/2 = 0.99382$,

i.e. $\theta^2/2 = 0.006180$, $\theta^2 = 0.0123609$,

$\theta = 0.11118$ rad = 6.37°.

KE_{max} = the missing energy = $hc/\lambda' - hc/\lambda$ =

$(hc/\lambda)(10\text{-}4)$ = 8265.6 eV * 10-4 = 0.82656 eV.

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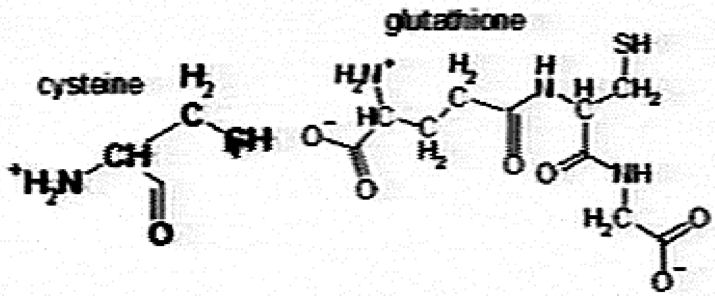
Midterm I, problem 3.



Eqn. 6-14, p.117

DNA• + R-SH → R-S• + DNA-H

•OH + RSH → R-S• + H_2O

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Midterm 1, problem 3, concluded

Cysteine and glutathione contain thiol (-SH) groups, which are good free-radical scavengers. *They are likely to reduce the effects of radiation* on cells by reacting with free radicals and producing relatively innocuous products--specifically, disulfide compounds, in which two molecules of a sulfur-containing free radical react with one another to pair up. This would then reduce the chemical damage in biological tissue that otherwise would arise from the reactions of water with the free radicals.

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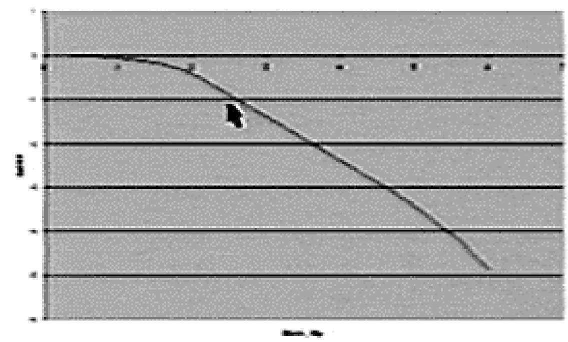
Midterm problem 4

Does this curve display MTSH survival characteristics? *Yes, since it's more or less linear at intermediate doses and flattens out at low dose.*



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Midterm problem 4, continued

- Estimate n, D_0, D_q:
  n is the intercept on the S axis. If we extrapolate up from the linear portion we find that it hits the y axis at about $\ln(S) = 1.6$. This corresponds to $n = e^{1.6} = 4.95$.
- D_q is the dose in Grays at which the linear portion of the curve hits S=1, i.e. $\ln S = 0$. On the graph that appears to happen at about D = 1.7, so $D_q = 1.7$
- Two ways to calculate D_0:
  - $D_0 = -1/\text{slope} = 1/[(-2.45-1.45)/(4-3)] = -1$ Gy.
  - $D_0 = D_q/\ln n = 1.7/1.6 \sim 1$ Gy.

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Midterm, Problems 5-7

- 5. *Recombination*:
  Recently produced free-radical pair joins up again to reform the original molecule

  A—B + hv →A˙ + ˙B →A—B   fast (≈10-11 s)
- 6. 1 Gy is a unit of absorbed dose:
  1 Gy unit of energy transferred per unit mass.
  1 Gy = 1 Joule of transferred energy per kilogram of mass
- 7. Hydroxyl radical
  •OH or O-H•
  (or draw out the dots for all valence electrons)

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Midterm, Problem 8

- High - LET Radiation

  LET = *Linear energy transfer so high - LET* radiation is radiation that transfers large amounts of energy per unit linear travel or energy per thickness in a medium.

  Neutrons and alpha particles *are examples of* high - LET radiation

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Midterm Problem 9: Extra Credit

- *Would recombinational repair be as effective in dealing with lesions in the Y chromosome as it is in dealing with lesions in chromosome 4?*
- *No.* Recombinational repair requires the presence of homologous duplex DNA. There are two copies of chromosomes 1-22 in every human cell that has a nucleus, so the homologous duplex DNA is present in the "other" copy of the chromosome. The Y chromosome is present in only *one* copy in the male (and absent altogether in the female), so there is no homologous duplex DNA from which to make a correction.

Effectors of Radiation Sensitivity

- Biological
  - Cells go through life cycles & are much more sensitive to radiation damage at some stages than at others
- Chemical
- Physical

Cellular Life Cycles

Phases

- Mitotic — M — (short)
  - Sensitive
- Presynthetic — G_1 — (variable)
  - Radiation causes 1/2 h delay here
- Synthetic — S — (4 - 8 h)
  - DNA synthesis
  - Least sensitive
- Postsynthetic — G_2 — (usually short 1 - 2h)
  - Radiation causes 3 - 4 h delay here
  - End of G_2 sensitive

14 h

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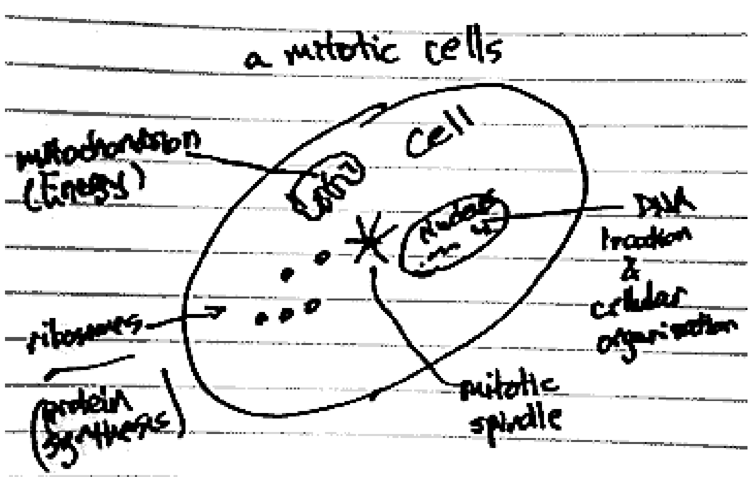

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Physical & Chemical Effectors

- Water

$h\nu + H_2O \rightarrow$ free radicals
- •OH, •H
- $•O_2$, etc

$h\nu + H_2O \rightarrow$ ionized species

Pure water

$$\frac{1\text{kg}}{1\text{L}} \qquad MW(H_2O) = 18$$

water 18g/mole

$$1\,\text{kg}\ H_2O = \frac{1000\text{g}}{18\text{g}/\text{mole}} = 55.5\,\text{moles}$$

$$\rho = \frac{1\text{kg}}{\text{L}} = 55.5\frac{\text{moles}}{\text{L}} = 55.5\,\text{M}$$

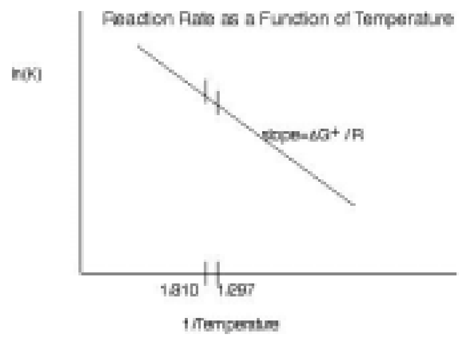
Assignment for 9 March

1. Problem 1, ch.9, Alpen

2. A human has a fever such that her body temperature is 39°C. This fever is accompanied by an increase in white-blood cells. How will these conditions affect her sensitivity to radiation?

Radiation & Temperature

Kinetics



$37^oC = 310K$
$27^oC = 300K$

p199
- T < 100K
- 100 < T < 170 K
- 170 < T < 420 K

$R-H \xrightarrow{h\nu} R-H^{\bullet +} + e^- \rightarrow R^{\bullet} + H^+ + e^-$ (direct)

$R-H + {}^{\bullet}OH \rightarrow R^{\bullet} + H_2O$ (indirect)

Radiation and Temperature

- Effects in various temperature ranges:
  - T_{min} T_{max} Effects
  - 0K 100K temp-insensitive; no charge migration, target must be hit
  - 100K 170K excitation localized at site; exciton migration crucial
  - 170K 420K disruption of disulfides, ionization
- Does this matter much with biological systems, where T ~ 310K almost all the time? Probably not, other than for understanding mechanisms.

Oxygen and Radiation

- FACT: O_2 is a radiation-sensitive molecule
- H_2O free-radical chemistry in the presence of O_2 is different from H_2O free radical chemistry in the absence of O_2.
- $P(O_2)$ in tissue varies widely
  - Hemoglobin transports O_2
  - Myoglobin stores O_2

Damage Fixation by Oxygen

$R\bullet + O_2 \rightarrow RO_2^{\bullet}$

semi stable

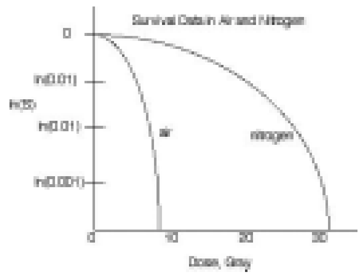
10^{-7} - 10^{-3} sec?

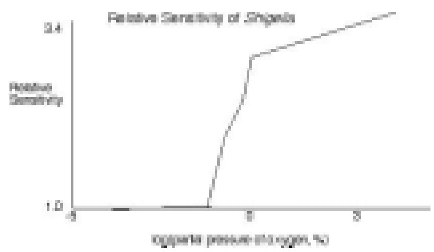
Mitigators of $\left\{ \begin{array}{l} O_2 \text{ fixation} \\ \text{radical presence} \end{array} \right.$

$R\bullet + R'SH \rightarrow R\text{-}H + R'S$

$R'\text{-}S\bullet + R'\text{-}S\bullet \rightarrow R'\text{-}S\text{-}S\text{-}R'$ (dimerization)

Experiments on Oxygen Sensitivity





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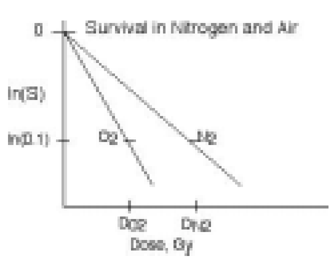
Oxygen Enhancement Ratio

$$\text{OER} \equiv \frac{\text{dose in } N_2 \text{ for surviving fraction } S/S_o}{\text{dose in } O_2 \text{ for surviving fraction } S/S_o}$$

if $S = S_o/10$



$$\text{OER} = \frac{D_N}{D_o}$$

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Quantitative Oxygen Sensitivity

$$\frac{S}{S_N} = \frac{m[O_2]+k}{[O_2]+k}$$

k is in concentration units

m is unitless

$[O_2]$ if $[O_2] >> k$, $S/S_N = m$

Organism	m	K,μM
Shigella	2.9	4.0
E.coli	3.1	4.7
S.cerevisiae	2.4	5.8

Thiol Mitigators

1. [macro]-R• + R´SH → [macro]-R-H + R´S•
   2R´S• → R´-S-S-R´

2. [small]• + R´SH → [small]-H + R´S•
   2R´S• → R´-S-S-R´

$e^- + O_2$ + radiation $\rightarrow$ $O_2^{-\cdot}$ superoxide

$H_2O + O_2^{-\cdot} \xrightarrow{SOD} OH^- + H_2O_2$

$O_2^{-\cdot} + \frac{3}{2}H_2O \rightarrow O_2 + H_2O_2 + OH^-$

$O_2^{-\cdot} + \frac{3}{2}H_2O \rightarrow O_2 + H_2O_2 + OH^-$

$(O_2^{-\cdot} \xrightarrow{SOD} O_2 + H_2O_2)$ somehow

'in presence of SOD, oxygen produces less damage than in absence of SOD

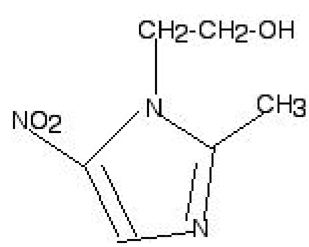
Maybe!

Sensitization by Nitroaromatics

How do we make the cells in the rapidly growing tumor as rad-sensitive as they would be if P_{O_2} were higher?

Nitroaromatics react with radicals to "fix" (stabilize) the damage

metronidazole



$\frac{S_x}{S_N}$ = 2.05 at 0.355%

translate that to molarity:

mass fraction = 0.355% = $3.55 \cdot 10^{-3}$

$\frac{\text{mass } O_2}{\text{total mass}} = 3.55 \cdot 10^{-3}$

mole fraction = $\frac{\frac{3.55 \cdot 10^{-3}\ g/mol}{32\ g/mole}}{\frac{1\ g}{18\ g/mole}} = 3.55 \cdot 10^{-3} \ldots = 3.1 \cdot 10^{-3}$

mole frac = $3.1 \cdot 10^{-3}$.

but at STP 1 mole of gas → 22.4 l

0°C, 1 atm

$\frac{\text{mole fraction}}{22.4\ l} = \frac{3.1 \cdot 10^{-3}}{22.4}$ M

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mole frac = $3.1 \cdot 10^{-3}$.

but at STP 1 mole of gas → 22.4 l

0°C, 1 atm

$\frac{\text{mole fraction}}{22.4\ l} = \frac{3.1 \cdot 10^{-3}}{22.4}$ M

$= 0.138 \cdot 10^{-3}$ M = 138 μM

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$0.355\% = 3.55 \cdot 10^{-3}$ g/g H_2O

1 g occupies 1 mL $= 10^{-3}$ L

$\Rightarrow \dfrac{3.55 \cdot 10^{-3} \text{ g}}{(10^{-3} \text{ L})([illegible] \text{ g/mole})}$

— [illegible] —