Illinois Institute of Technology

PHYS 561

RADIATION BIOPHYSICS

Fourth Lecture:

Chemistry and Biology of Radiation

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Homework For 2/14

1. Alpen, Ch. 6, #3
2. Why is cancer more likely to occur in individuals deficient in DNA repair enzymes?
   (2 - 3 paragraphs)
3. Would you expect that the rate of restitution of an altered molecule to be temperature-dependent? Why?

Schedule Issues

- 1st two assignments will be graded by Monday 2/12.
- 3rd assignment by Friday 2/16
- Tonight we'll go back over parts of chapter 5 and then move on to chapter 6
- Next week we'll look over chapter 7 and do a brief discussion of various homework problems in preparation for the midterm on the 21st.

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Typos of the Week

- Page 79, first paragraph under "IMPORT□□□□□ANCE OF THE COMPTON PROCESS", 4th line:
  "with attention the the"
  "with attention to the"
- Page 87, 2nd paragraph, 1st line:
  "The four principle" -> "The four principal"

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Outline of Session

- Left over from chapter 5:
  - Interaction of photons with matter
    - Contributions of Compton, other processes
    - Attenuation coefficients: molecules + mixtures
  - Interaction of charged particles with matter
  - Size scales and biological cells
- Chapter 6:
  - Energy Deposition at different physical scales (ch.5)
  - Types of energy transfer from electrons (ch.6)
  - Free Radicals
  - Radiation Chemistry of water
  - Recombination, Restitution, Repair
  - Molecular Biology 101

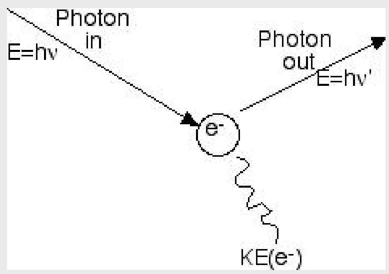
Photons interacting with matter

The interaction of a high-energy photon with a chunk of matter involves

- Photoelectric effect
- Coherent scatter
- Compton scatter
- Pair production

Compton Scattering

- The most important of these processes for hν > 100 KeV is Compton scatter, especially if the matter is water or tissue
- See fig. 5.2(B) in the text to see why: μ_{ab}/ρ (Compton) predominates above 100KeV



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Attenuation Coefficients for Molecules (and mixtures)

- Calculate mole fraction f_{mi} for each atom type i in a molecule or mixture, subject to $\Sigma_i f_{mi} = 1$
- Recognize that, in a molecule, f_{mi} is proportional to the product of the number of atoms of that type in the molecule, n_i, and to the atomic weight of that atom, m_i:
  $f_{mi} = Qn_i m_i$ (Q a constant to be determined)
- Thus $\Sigma_i f_{mi} = \Sigma_i Qn_i m_i = 1$ so $Q = (\Sigma_i n_i m_i)^{-1}$
- Then (σ/ρ) for the compound will be $(\sigma/\rho)_{Tot} = \Sigma_i f_{mi}(\sigma/\rho)_i$

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Calculating Mole Fractions and Attenuation Coefficients

- Example 1: Water (in book):
  - H_2: $n_1 = 2$, $m_1 = 1$; O: $n_2 = 1$, $m_2 = 16$
  - $Q = (\Sigma_i n_i m_i)^{-1} = (2*1 + 1 * 16)^{-1} = 1/18$
  - Thus $f_{H2} = 2/18$, $f_O = 16/18$,
  - $(\sigma/\rho)_{Tot} = \Sigma_i f_{mi}(\sigma/\rho)_I = (2/18)*(0.1129\text{cm}^2\text{g}^{-1}) + (16/18)(0.0570\ \text{cm}^2\text{g}^{-1}) = 0.0632$
- Benzene (C_6H_6):
  - C_6: $n_1 = 6$, $m_1 = 12$; H_6: $n_2 = 6$, $m_2 = 1$
  - Q = (6*12+6*1) = 1/78, $f_{C6} = 72/78$, $f_{H6} = 6/78$

Interaction of Charged Particles with Matter

- Recall diagram 5.3, p.84.
- The crucial equation is for $\Delta E(b)$, the energy imparted to the light particle:
  $\Delta E(b) = z^2 r_0^2 m_0 c^4 M/(b^2 E)$
  where E is the kinetic energy of the moving particle = $(1/2)Mv^2$.
- Thus it increases with decreasing impact parameter b
- Energy imparted is inversely proportional to the kinetic energy E of the incoming heavy particle!

Dose

$$\left[\frac{\textit{Energy deposited}}{\textit{Unit mass}}\right]$$

size scales ~1μm

$\rho \sim 1\ g/cm^3$ for water or soft tissue

mass of $(1\mu m)^3 \cdot \rho = (10^{-4}cm)^3 \cdot \rho$

$= 10^{-12}cm^3 \cdot 1g/cm^3$

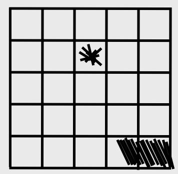
$= 10^{-12}g = 10^{-15}kg$

Energy Absorbed in a Cell

- Suppose *N* Joules of energy are deposited in a 70 kg human. Nominally the dose is *N*/70 Gy.
- How much energy is deposited in a single $(1\mu m)^3$ cell? $(N/70)Gy * 10^{-15}$ kg
  $= (N/70)*10^{-15}$ J $= (1.3*10^{-17})*N$ J
  $= [(1.3*10^{-17})*N]/1.609*10^{-19}$ J
  $= 85*N$ eV. So it's a lot of energy!
- Is the Bethe-Blocke continuous slowing-down approximation applicable here? No! Too much energy is being stopped per cell for it to be applicable. But we try to use it anyway.

Mozumder & Magee

[1 MeV "typical" electron]		Portion of energy deposited
◆ Spurs	6 - 100 eV	65%
◆ Blobs	100 - 500 eV	15%
◆ Tracks	500 - 5000 eV	20%



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Demonstration That Events Don't Interact Much

Spurs are 400 nm apart

1 nm = 10^{-9} m

400 nm = 0.4 μm

Hydrogen radical diffusion

$8 \times 10^{-5} cm^2 s^{-1}$ diffusion constant for H•

Typical lifetime ~ 10^{-6}s

→ Typical diffusion distance = 180 nm

This is smaller than the distance between spurs!

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Free Radicals - Definitions and Illustrations

A free radical is defined as molecular species containing an unpaired electron. It may be charged or uncharged.

Most biological free radicals are uncharged

Exception: superoxide ($O_2^{-}\bullet$)

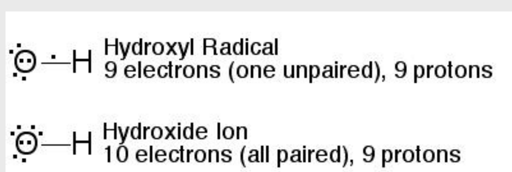
- OH^{-} Hydroxide ion -9 protons, 10 electrons
- $OH\bullet$ Hydroxyl Radical -9 protons, 9 electrons

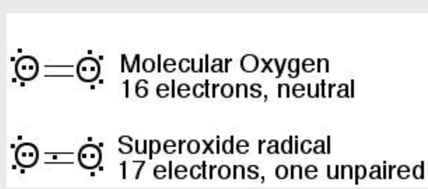
Free radicals are reactive because the unpaired electrons tend to seek out targets, either other unpaired electrons:

$H\bullet + H\bullet \rightarrow H_2$

. . . Or other acceptors of the unpaired electron

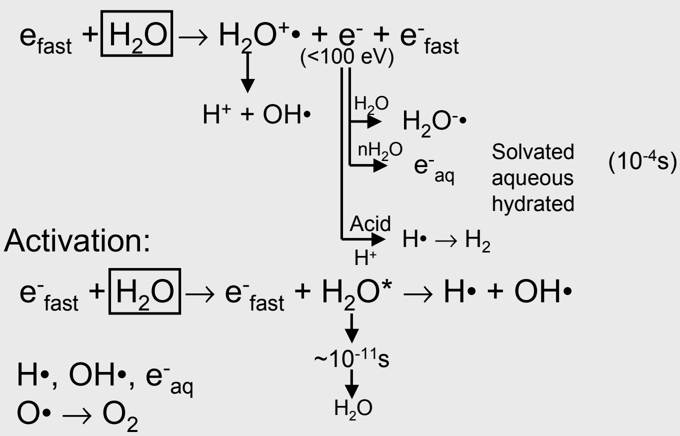
Cartoons of Electron Distributions: Ions and Radicals





10^{-16} - 10^{-12} s Scale Events and After

Ionization:



$H\bullet$, $OH\bullet$, e^{-}_{aq}
$O\bullet \rightarrow O_2$
$O_2^{-}\bullet$, H_2O_2

Radiation Chemistry of Water

- Since biological tissue is mostly water, we're very interested in the products produced when water absorbs ionizing radiation.
- The reactive species formed out of water are responsible for a large fraction of the biological activities of radiation.
- Ordinary ions (H^{+}, OH^{-}, H_3O^{+},) are among these species, as is hydrogen peroxide (H_2O_2);
- So are free radicals: $H\bullet$, $OH\bullet$, $O_2^{-}\bullet$, $HO_2\bullet$, $O_2^{-}\bullet$
- Often discuss "solvated electron", e_{aq}^{-}.

Fricke Dosimeter

- Bookkeeping tool for aqueous radical chemistry

  $Fe^{2+} \rightarrow Fe^{3+} + e^-$

  ferrous ferric

  $H\bullet + O_2 \rightarrow HO_2\bullet$ H-O=O

  $HO_2\bullet + Fe^{2+} \rightarrow HO_2^- + Fe^{3+}$

  $HO_2^- + H^+ \rightarrow H_2O_2$

  $OH\bullet + Fe^{2+} \rightarrow Fe^{3+} + OH^-$

  $H_2O_2 + Fe^{2+} \rightarrow Fe^{3+} + OH^- + OH\bullet$

  $H\bullet + H_2O \rightarrow OH\bullet + H_2$ (only in absence of O_2)

Fricke Dosimeter: bookkeeping

- Each hydrogen radical causes the oxidation of three molecules of errous ion
- H_2O_2 produced by radiolysis will oxidize two ferrous ions--one direct, one indirect.
- A radiolytically-produced OH• radical gives rise to one more oxidation.
- Therefore at acidic pH with oxygen: $G(Fe^{3+}) = 2G(H_2O_2) + 3G(H) + G(OH\bullet)$

Definition of Yield

G = Yield ≡ Number of events produced per 100 eV energy deposition

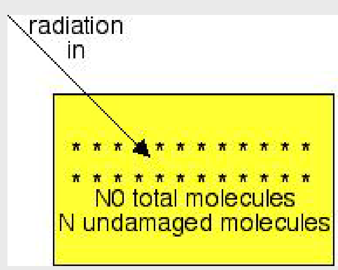
We're often interested in dG(E)/dE.

Yield is either unitless or has units of $(\text{energy})^{-1}$ depending on your perspective

Fricke dosimeter provides a way of measuring yield

Direct Action: the Model

Direct action of radiation on a species says that a single hit of radiation onto a molecule damages it. Then if *N* is the number of undamaged molecules after irradiation with dose *D*, we expect that the change in *N*, ΔN, with a small increase ΔD in dose is proportional to *N* and to ΔD.



Direct Action: the Integral

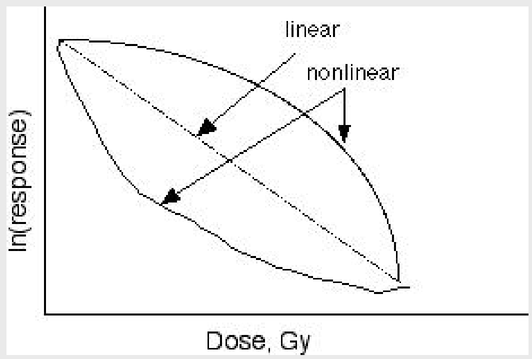
- in the limit of ΔD and ΔN small, $dN = -kNdD$, where k is the "inactivation constant".
- This gives us the usual differential equation $dN/N = -kdD$, which integrates to
  $\ln N = -kD + C$, or $N = e^{-kD} * e^{C} = N_0 e^{-kD}$
  where $N_0 = e^{C}$ has the physical meaning of the number of molecules in the system (number undamaged before the damage began)
- The inactivation constant has units of Gy^{-1} and is the reciprocal of the dose required to reduce the number of undamaged molecules by 1/e.

Indirect Action

- Indirect action arises when the initial absorption of radiative energy gives rise to secondary chemical events.
- In biological systems indirect action usually involves effects on water:
  Radiation + H_2O -> H_2O^*
  H_2O^* + biological macromolecule -> damaged biological macromolecules
- This species "H_2O^*" may be a free radical or an ion, but it's certainly an activated species derived from water

Dose-response for Indirect Action

Unlike the direct-action case, we can't write down a simple mathematical model for what's going to happen. Therefore the dose-response curve is not log-linear:



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Interactions of Energetic Electrons With Biological Tissue

- Direct

biol response

$e^-_{fast} + DNA \rightarrow DNA_{broken} + e^-_{fast}$

$e^-_{fast} + Protein \rightarrow Protein_{broken} + e^-_{fast}$

log - linear dose - response

$$\frac{dN}{N} = \text{constant} * D; N_{undamaged} = N_o e^{-kD}$$

- Indirect Action

$e^-_{fast} + H_2O \rightarrow H_2O^* + e^-_{fast}$

$e^-_{fast} + H_2O \rightarrow H_2O^{+\bullet} + e^-_{H_2O} + e^-_{fast}$

further radical chemistry

$$\begin{pmatrix} water \\ molecules \end{pmatrix} + biomolecules \rightarrow (biomolecules)^* + H_2O\ products$$

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Some Definitions

- *Catalyst*: a chemical species that increases the rate of a reaction in such a way that it is reconstituted at the end of the reaction.

C is a catalyst in this system:

$A \xrightarrow{\text{slow}} B$ (uncatalyzed)

$A + C \xrightarrow{\text{fast}} A \bullet\bullet\bullet C \xrightarrow{\text{fast}} B \bullet\bullet\bullet\bullet\bullet C \xrightarrow{\text{fast}} B + C$

- *Enzyme*: a biological molecule acting as a catalyst.

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Radical Fates/ Damaged Biomolecule Fates

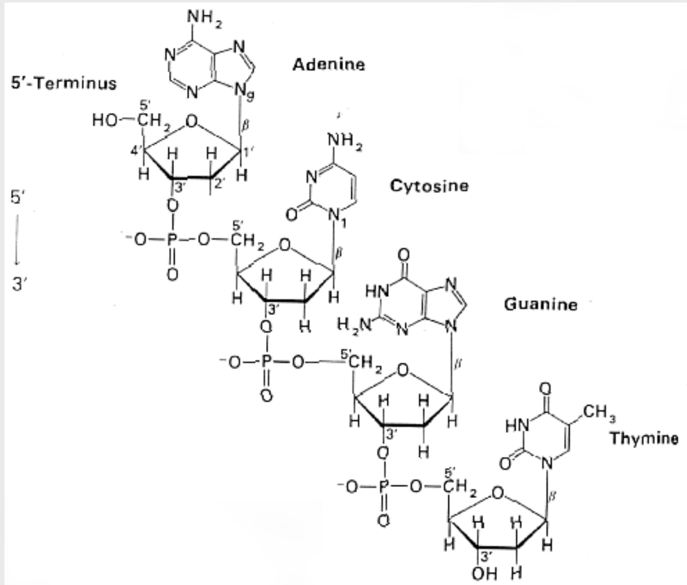
- Recombination $A\bullet + B\bullet \rightarrow A - B$ (timescale 10^{-11}s)

  Generally A = B i.e. $A\bullet + \bullet A \rightarrow A - A$
- Restitution: Non catalyzed regeneration of non-radical species

  $\underset{biological}{A\bullet} + \underset{diffusable}{X} \rightarrow \underset{biological}{A} + \underset{out}{X\bullet}$
- Repair: Catalyzed regeneration of undamaged species

  $A\bullet_{biol} + E + R \rightarrow A^{mod}_{biol} + E + R\bullet$ where E is enzyme

PHYS56104-28/20 biol biol



W. H. Brown & J. A. McClarin, Introduction to Organic and Biochemistry, 3rd Ed., 1981

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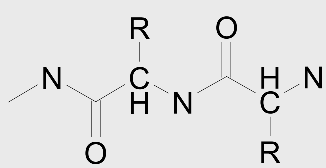
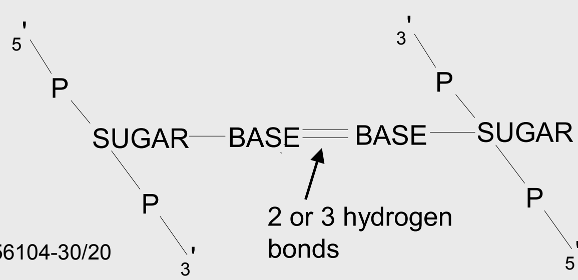
Protein Backbones and Nucleic Acid Backbones



R = 20 amino acid sidechains
(Alanine, Glycine,...)



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