# 22.01 Fall 2015, Problem Set 9 Solutions (Normal Version)

Due: December 2, 11:59PM on Stellar

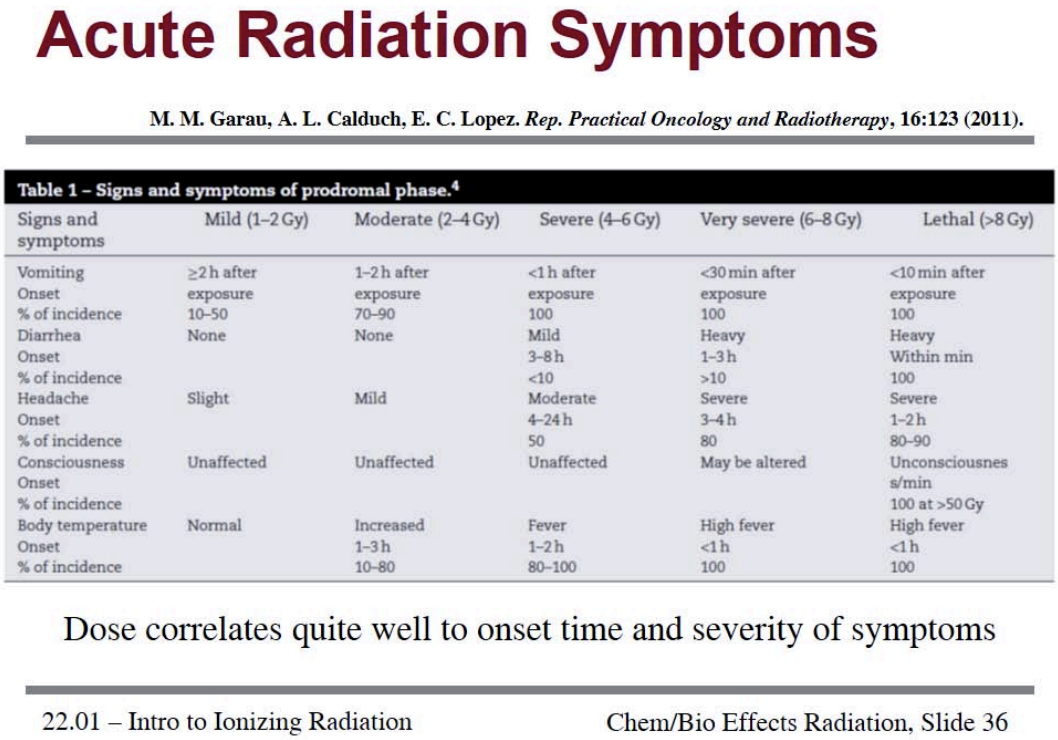
December 14, 2015

Complete all the assigned problems, and do make sure to show your intermediate work. Please upload your full problem set in PDF form on the Stellar site. Make sure to upload your work at least 15 minutes early, to account for computer/network issues.

---

## 1 Conceptual Questions

1. **Define** the major short-term biological **effects** due to intense gamma radiation exposure, and explain their origins.
   **During an intense gamma ray exposure, the following major things will happen: (1) Very sensitive cells (like stem cells) will die, leaking their fluids into the intercellular spaces, (2) the cascade of radiolysis products will be produced, causing much oxidative damage to the tissue. The follow-on effects take four phases, as described below:**



Acute Radiation Symptoms

M. M. Garau, A. L. Calduch, E. C. Lopez. *Rep. Practical Oncology and Radiotherapy*, 16:123 (2011).

**Table 1 – Signs and symptoms of prodromal phase.[4]**

| Signs and symptoms | Mild (1–2 Gy) | Moderate (2–4 Gy) | Severe (4–6 Gy) | Very severe (6–8 Gy) | Lethal (>8 Gy) |
|---|---|---|---|---|---|
| Vomiting | | | | | |
| Onset | ≥2 h after exposure | 1–2 h after exposure | <1 h after exposure | <30 min after exposure | <10 min after exposure |
| % of incidence | 10–50 | 70–90 | 100 | 100 | 100 |
| Diarrhea | None | None | Mild | Heavy | Heavy |
| Onset | | | 3–8 h | 1–3 h | Within min |
| % of incidence | | | <10 | >10 | 100 |
| Headache | Slight | Mild | Moderate | Severe | Severe |
| Onset | | | 4–24 h | 3–4 h | 1–2 h |
| % of incidence | | | 50 | 80 | 80–90 |
| Consciousness | Unaffected | Unaffected | Unaffected | May be altered | Unconsciousnes s/min |
| Onset | | | | | |
| % of incidence | | | | | 100 at >50 Gy |
| Body temperature | Normal | Increased | Fever | High fever | High fever |
| Onset | | 1–3 h | 1–2 h | <1 h | <1 h |
| % of incidence | | 10–80 | 80–100 | 100 | 100 |

Dose correlates quite well to onset time and severity of symptoms

22.01 – Intro to Ionizing Radiation Chem/Bio Effects Radiation, Slide 36

# Acute Radiation Symptoms

M. M. Garau, A. L. Calduch, E. C. Lopez. *Rep. Practical Oncology and Radiotherapy*, 16:123 (2011).

**Table 2 – Signs and symptoms of latent phase.[4]**

| Signs and symptoms | Mild (1–2 Gy) | Moderate (2–4 Gy) | Severe (4–6 Gy) | Very severe (6–8 Gy) | Lethal (>8 Gy) |
|---|---|---|---|---|---|
| Latency period | 21–35 days | 18–28 days | 8–18 days | ≤7 days | None |
| Lymphocytes G/L (days 3–6) | 0.8–1.5 | 0.5–0.8 | 0.3–0.5 | 0.1–0.3 | 0.0–0.1 |
| Granulocytes G/L | >2.0 | 1.5–2.0 | 1.0–1.5 | ≤0.5 | ≤0.1 |
| Diarrhea | None | None | Rare | Appears on days 6–9 | Appears on days 4–5 |
| Depilation | None | Moderate, beginning on day 15 or later | Moderate, beginning on day 11–21 | Complete earlier than day 11 | Complete earlier than day 10 |

**Table 3 – Signs and symptoms of critical phase.[4]**

| Signs and symptoms | Mild (1–2 Gy) | Moderate (2–4 Gy) | Severe (4–6 Gy) | Very severe (6–8 Gy) | Lethal (>8 Gy) |
|---|---|---|---|---|---|
| Onset of symptoms | >30 days | 18–28 days | 8–18 days | <7 days | <3 days |
| Clinical manifestations | Fatigue, weakness | Fever, infections, weakness, depilation | High fever, infections, bleeding, depilation | High fever, diarrhea, vomiting, dizziness, desorientation, hypotension | High fever, diarrhea, unconsciousness |
| Lymphocytes G/L (days 3–6) | 0.8–1.5 | 0.5–0.8 | 0.3–0.5 | 0.1–0.3 | 0.0–0.1 |
| Platelets G/L | 60–100 | 30–60 | 25–35 | 15–25 | <20 |
| % of incidence | 10–25 | 25–40 | 40–80 | 60–80 | 80–100 |
| Lethality | 0% | 0–50% | 20–70% | 50–100% | 100% |
| Onset time | | 6–8 week | 4–8 week | 1–2 week | 1–2 week |

22.01 – Intro to Ionizing Radiation Chem/Bio Effects Radiation, Slide 37



# Acute Radiation Symptoms

M. M. Garau, A. L. Calduch, E. C. Lopez. *Rep. Practical Oncology and Radiotherapy*, 16:123 (2011).

**Table 4 – The time course and severity of clinical signs and symptoms.**

| Absorbed dose level | Prodromal phase | Latent phase | Manifest illness | Final phase |
|---|---|---|---|---|
| 0.5–1.5 Gy | Absence of symptoms or nausea and vomiting for 1 day | 1 day–several weeks | No symptoms or weakness, nausea and vomiting, temporary hair loss | Recovery |
| 1.5–4 Gy | Nausea, vomiting, fatigue, weakness, diarrhea for up to two days | 1–3 weeks | Hematopoietic syndrome (HS): leucopenia and trombocitopenia, hair loss | Recovery possible with supportive care |
| 4–6 Gy | Nausea, vomiting, weakness, diarrhea for up to two days | <1–3 weeks | HS: bleeding, immunosuppression and sepsis, permanent hair loss | Death without supportive care |
| 6–15 Gy | Severe nausea and vomiting, diarrhea in shorter period of time | Several days | HS + gastrointestinal syndrome: diarrhea, bleeding, fluid loss and electrolyte imbalance | Variable with supportive care |
| >15 Gy | Immediate severe nausea and vomiting | Non-existent | Neurovascular syndrome | Death within 48 h |

Modified from Ref. 5.

**Leucopenia – reduced white blood cell count**
**Thrombocitopenia – reduced platelet count**
**Depilation – hair loss**
**Hypotension – abnormally low blood pressure**

22.01 – Intro to Ionizing Radiation Chem/Bio Effects Radiation, Slide 38



**The loss of hair stems directly from killing the hair follicles, the gastrointestinal syndrome (diarrhea, lack of nutritional uptake) follows from the killing of stem cells in the villi of the intestine, the general infections and sepsis comes from killing the bone marrow which produces white blood cells, ditto for hemophilia and platelets, and the jury is still out on**

**the vomiting (though it may have to do with chemical signals sent out during intestinal cell death).**

2. Starting from the entry of a quantum of ionizing radiation into the body, explain, step by step, the most likely mechanism to induce mutations in a cell.
   **It is much more likely that indirect DNA damage will cause cell mutation, as there is much more water surrounding the DNA than actual DNA itself. First, the physical ionization of a water molecule would take place, followed by the chain of radiolysis products being produced. The G-Values tell how many of each oxidative species will remain after about a microsecond, which is the timescale between when the species are created, and they diffuse far enough away that they cease to inter-react. Then the oxidative species may encounter (diffuse to) DNA, where they can cause an ionization and a kink in the chain, changing a gene to either cause lack of cell reproduction or triggering cancer.**

3. List some of the other, non-radioactive sources of the free radicals responsible for DNA damage and eventual cell mutations. Where do they come from?
   **Many of the same free radicals produced from radiation are present from the foods we eat, as well as oxidative metabolic by-products of the cell's own metabolism. So far, research shows that they are not unique to any particular source, including radiation.**

4. You are given four cookies containing dangerous levels of a high-activity isotope. Each has the same half life, the same concentration, therefore the same activity. One emits alpha particles, one emits beta particles, one emits gamma rays, and one emits neutrons, all at the same energies. You may put one in your pocket, hold one in your hand, eat one, and give one to a "friend." What do you do, and why? Use your knowledge of stopping power, range, and relative biological effectiveness (RBE) to answer the question.
   **First of all, eat the gamma cookie, as its RBE is very low, and its range is extremely high, so most gammas will travel right through you. Give the neutron cookie to the "friend," as its range is decently high (~cm) in water-based lifeforms, though it causes tons of damage. Put the alpha cookie in your pocket, as your pocket will block all the alpha particles, and hold the beta cookie out at arms length, to minimize the dose through the dead layer of skin.**

5. Explain why cancerous tumors are relatively resistant to radiation compared to normal cells, making radiation therapy more difficult.
   **There are two supposed reasons for this: (1) In the center of a tumor the cells are not dividing much and the environment is quite hypoxic, meaning that the cells aren't as susceptible to oxidative mutation, and that radiation is less effective in a reducing environment (the same is true in reactors!). (2) You only have to mutate one normal cell to induce a tumor, but you have to mutate/destroy *all* cancerous cells to stop it.**

## 2 Analytical Questions

For these questions, read the following article on The Demon Core accident, and this article detailing the resulting radiation effects suffered by the two workers exposed.

1. Explain, step by step, what caused the high exposure to radiation.
   **First, it should be noted that Daghlian's lack of adherence to basic safety protocols is what caused this to happen! Physically speaking, the plutonium sphere was a sub-critical mass on its own, but completely surrounded by WC (tungsten carbide), it could become supercritical. That is exactly what happened, Daghlian's slipping of the brick caused the neutron non-leakage terms in the six-factor formula to increase, raising the criticality of the sphere. Most of the neutrons from fission were reflected, and any alphas or betas didn't make it out of the sphere, so the dose incurred by Daghlian was mostly from gammas produced by fission and x-rays from ionization of the Pu and WC, and**

**subsequent relaxation of excited electron states. Daghlian's quick thinking in moving the brick away demonstrated knowledge of ways to make the core more sub-critical.**
**The next incident occurred when a similar experiment was being tried, but this time by using a screwdriver to tweak the amount of neutron leakage of the core by increasing or decreasing the physical space from which neutrons could escape without being reflected back in. When the screwdriver holding up the beryllium half-sphere held by Slotin slipped, the assembly went critical, and Slotin's removal of the top hemisphere stopped the reaction from continuing. The flash of blue light observed in Slotin's eyes would have been Cherenkov radiation, from a multitude of particles traveling faster than the speed of light in water.**

2. Calculate or find the total energy, dose, and equivalent dose absorbed by Daghlian and Hemmerly in the following units:

   (a) Roentgen
   **(Source: second article): Daghlian: 590 Roentgens, Hemmerly: 14.45 Roentgens**

   (b) Rad
   **(Source: first article): Daghlian: 330 Rad, Hemmerly: 8.1 Rad**

   (c) Rem
   **(Source: first article): Assume that gammas have a quality factor of 1, while the neutrons from fission were fast (1MeV) with a quality factor of 20. This gives effective doses of Daghlian: 4,110 Rem, Hemmerly: 160,1 Rem**

   (d) Sieverts
   **(Source: first article): Assume that gammas have a quality factor of 1, while the neutrons from fission were fast (1MeV) with a quality factor of 20. This gives effective doses of Daghlian: 41.1 Sv, Hemmerly: 1.601 Sv**

   (e) Gray
   **(Source: first article): Daghlian: 3.3 Gy, Hemmerly: 0.081 Gy**

3. If the men's equivalent doses had been due to fast neutrons instead of gamma and x-rays, what would the energy absorbed in Roentgens been for each person?
   **If the full doses had been in neutrons, rather than a mix of neutrons and gammas, things would have been even worse for Daghlian in terms of equivalent dose. However, the energy in Roentgens would have been the same, as the dose in Roentgens is just a measure of the charge created (ionizations) per kg of weight, it does not take into account the relative effectiveness of each type of radiation. Were this question to be asked in terms of Sieverts, Daghlian would have have 66 Sv of fast neutron radiation, while Hemmerly would have had 1.62 Gy, a negligible increase.**

# 3 Radiation Resistance, G-Values, and Fevers

For these questions, you will calculate a few parameters related to radiation resistance and sensitivity by changing someone's body temperature. We will focus on two free radicals produced by radiation: hydrogen peroxide ($H_2O_2$) and the uncharged hydroxide group (OH). The first liberates free oxygen in water, while the other tears electrons from other molecules to form the more stable $OH^-$ hydroxide ion.

1. Standard diffusion of species in liquids and solids follows the well known Arrhenius law:

$$D(T) = D_0 e^{\frac{-E_A}{kT}} \tag{1}$$

   where $D(T)$ is the diffusion coefficient in $\left[\frac{m^2}{sec}\right]$, $D_0$ is the diffusion prefactor, $E_A$ is the activation energy in $eV$ for the species to move, $k$ is Boltzmann s constant, and $T$ is the temperature in Kelvin. Using the data for hydrogen peroxide from this article (see p. 558) and this article for hydroxide ion

data (see Table 1), find the values of $D_0$ and $E_A$ for each molecule's diffusion.
**The following data were used for this calculation:**

| | **D at 25C** $\left(\frac{m^2}{s}\right)$ | **D at 37C** $\left(\frac{m^2}{s}\right)$ | **D at 40C** $\left(\frac{m^2}{s}\right)$ |
|---|---|---|---|
| (OH) | $4.56 \cdot 10^{-9}$ | | $5.54 \cdot 10^{-9}$ |
| ($H_2O_2$) | $1.43 \cdot 10^{-9}$ | $1.83 \cdot 10^{-9}$ | |

**These can be solved using a set of simultaneous equations:**

$$D\left(T_1\right) = D_0 e^{\frac{-E_A}{kT_1}}; \qquad D\left(T_2\right) = D_0 e^{\frac{-E_A}{kT_2}} \tag{2}$$

**Divide the two equations by each other to get:**

$$\frac{D\left(T_1\right) = \cancel{D_0} e^{\frac{-E_A}{kT_1}}}{D\left(T_2\right) = \cancel{D_0} e^{\frac{-E_A}{kT_2}}} \tag{3}$$

**Take the natural log of both sides:**

$$ln\left(\frac{D\left(T_1\right)}{D\left(T_2\right)}\right) = E_A\left(\frac{1}{kT_2} - \frac{1}{kT_1}\right); \quad \frac{ln\left(\frac{D(T_1)}{D(T_2)}\right)}{\left(\frac{1}{kT_2} - \frac{1}{kT_1}\right)} = E_A \tag{4}$$

**Using this equation, we can find the values of $E_A$, and plug into either equation to get values of $D_0$. The following data were obtained:**

| | **D at 25C** $\left(\frac{m^2}{s}\right)$ | **D at 37C** $\left(\frac{m^2}{s}\right)$ | **D at 40C** $\left(\frac{m^2}{s}\right)$ | $D_0$ $\left(\frac{m^2}{s}\right)$ | $E_A$ $(eV)$ |
|---|---|---|---|---|---|
| (OH) | $4.56 \cdot 10^{-9}$ | | $5.54 \cdot 10^{-9}$ | $2.62 \cdot 10^{-7}$ | **0.104** |
| ($H_2O_2$) | $1.43 \cdot 10^{-9}$ | $1.83 \cdot 10^{-9}$ | | $5.12 \cdot 10^{-8}$ | **0.089** |

2. Calculate the distance that one of each molecule will travel in $10^{-6}$ seconds at body temperature ($37C$), or about the time that intracascade reactions stop.
**For OH-, we need to calculate the diffusion coefficient at 37C using this Arrhenius relation, which we find to be $5.34 \cdot 10^{-9} \frac{\mathrm{m}^2}{\mathrm{sec}}$. The value for ($H_2O_2$) was found in the paper. Using the following equation from the notes:**

$$\frac{\lambda^2}{6\tau} = D \tag{5}$$

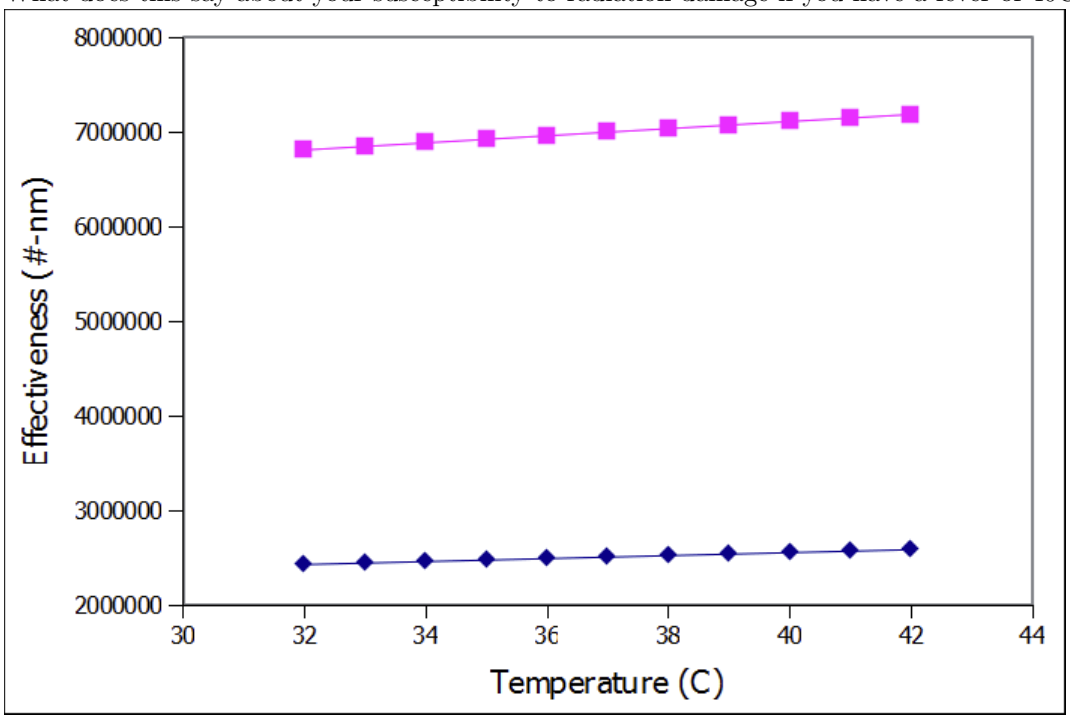
**which relates the average distance traveled by a particle in a time $\tau$ to its diffusion coefficient, we find the following data:**

| | **D, 25C** $\left(\frac{m^2}{s}\right)$ | **D, 37C** $\left(\frac{m^2}{s}\right)$ | **D, 40C** $\left(\frac{m^2}{s}\right)$ | $D_0$ $\left(\frac{m^2}{s}\right)$ | $E_A$ $(eV)$ | $\lambda$, $\tau = 10^{-6}s$, $37C$ |
|---|---|---|---|---|---|---|
| (OH) | $4.56 \cdot 10^{-9}$ | $5.34 \cdot 10^{-9}$ | $5.54 \cdot 10^{-9}$ | $2.62 \cdot 10^{-7}$ | **0.104** | **179 nm** |
| ($H_2O_2$) | $1.43 \cdot 10^{-9}$ | $1.83 \cdot 10^{-9}$ | | $5.12 \cdot 10^{-8}$ | **0.089** | **105 nm** |

3. Suppose that someone has ingested an alpha emitter, perhaps by smoking, which releases 4MeV alpha particles. Which of the two molecules do you expect to do more damage to DNA? You should consider both the amount of each produced, as well as how far they can travel. Develop an expression for the "damage effectiveness" of each of these ions, based on your calculations.
**Looking up the G-values for alpha particles from the notes, we get values of 0.35 ($OH$) per 100eV of energy for 4 MeV $\alpha$, while the value for ($H_2O_2$) is 1.64. We can define a simple measure of damage effectiveness, or just the G-value, times the particle energy in units of 100 eV, times the distance each particle will travel as a measure of the average "reach" of each particle. By doing so, we get the following table:**

| | **D, 25C** $\left(\frac{m^2}{s}\right)$ | **D, 37C** | **D, 40C** | $D_0$ | $E_A$ $(eV)$ | $\lambda$ | **G** | **#-nm** |
|---|---|---|---|---|---|---|---|---|
| (OH) | $4.56 \cdot 10^{-9}$ | $5.34 \cdot 10^{-9}$ | $5.54 \cdot 10^{-9}$ | $2.62 \cdot 10^{-7}$ | **0.104** | **179 nm** | **0.35** | **2,506,000** |
| ($H_2O_2$) | $1.43 \cdot 10^{-9}$ | $1.83 \cdot 10^{-9}$ | | $5.12 \cdot 10^{-8}$ | **0.089** | **105 nm** | **1.64** | **6,888,000** |

4. Graph this "damage effectiveness" as a function of temperature from 32-42C (the range of body temperatures that won't ensure death). Does your answer to (3.3) change with changing temperature? What does this say about your susceptibility to radiation damage if you have a fever of 40C?




**Yes, the answer does indeed change with temperature, suggesting that increasing one's body temperature may make one more susceptible to radiation damage of DNA by free radical diffusion.**

5. Suppose now that cryogenic freezing actually works, and that people can be stored at liquid nitrogen temperatures for thousands of years (see Figure 1). Compare the expected amount of DNA damage to a given cell in this person during 1,000 years of freezing, compared to 100 years of life.
**Let's start with a couple of assumptions:**
**-Each cell is 10 microns in diameter**
**-Cells are made of just water, plus a nugget of DNA in the center nucleus**
**-Free radicals spread isotropically once created, with a number and spread given by their effectiveness as defined above.**
**For the 100 years of life calculation, let's calculate the probability of any DNA damage at all, from both direct and indirect sources. From direct sources, we take an incoming gamma flux of $\Phi$ incident on each cell. The total reaction rate with DNA will therefore be approximately:**

$$R_{DNA,Direct} = \bar{\sigma}_{DNA} N_{DNA} \Phi \tag{6}$$

**Now we must calculate the total number density of DNA in a single cell. Each cell has about 3 billion base pairs, or 6 billion nucleotides, while each base pair contains about 35 atoms. Let's also assume that DNA is equal amounts of H, C, O, N, and P. That puts the number density of each type of atom in a 10 micron diameter cell as $4.2 \cdot 10^{10}$ $\frac{\text{each atom}}{\text{cell}}$, or $8.0 \cdot 10^{25}$ $\frac{\text{each atom}}{\text{m}^3}$. Using this number, we can look up the cross sections (in mass attenuation coefficients times density) for each element for 1 MeV gamma rays, which we'll take as our single energy, and we use this paper[1] to find the total cross section for all processes (tot-h, including Klein-Nishina plus pair production plus photoelectric):**

[1] **http://www.ge.infn.it/geant4/temp/saracco/cor/Storm_israel_photon_pub_1970.pdf**

| Element | $\sigma_{tot}$ at 1 MeV (b) |
|---|---|
| **H** | **0.0929** |
| **C** | **0.557** |
| **N** | **0.650** |
| **O** | **0.743** |
| **P** | **1.39** |

**Assuming all the elements contribute equally to number density, this yields an average direct damage reaction rate of:**

$$R_{DNA,Direct} = \left(\frac{0.0929 + 0.557 + 0.65 + 0.743 + 1.39}{5}\right) * 10^{-28} \frac{m^2}{barn} * 5N_{each\ atom}\Phi = 0.0275\Phi \quad (7)$$

**Now we estimate the direct DNA damage. We start with the probability that a damage cascade made at any point inside the cell will overlap the center point, which is just a ratio of two sphere volumes:**

$$P_{overlap} = \frac{\frac{4}{3}\pi r^3_{cascade}}{\frac{4}{3}\pi r^3_{cell}} \quad (8)$$

**Reusing our table fro the last problem, we can get the distance traveled by each type of ion (OH or $H_2O_2$):**

$$P_{overlap,OH} = \frac{\frac{4}{3}\pi r^3_{cascade}}{\frac{4}{3}\pi r^3_{cell}} = 5.7 \cdot 10^{-6} \quad (9)$$

$$P_{overlap,H_2O_2} = \frac{\frac{4}{3}\pi r^3_{cascade}}{\frac{4}{3}\pi r^3_{cell}} = 1.2 \cdot 10^{-6} \quad (10)$$

**Then we multiply by the G-values for each species for 1 MeV gammas (see the class notes on chem/bio effects, p. 15):**

$$Effectiveness_{OH} = 5.7 \cdot 10^{-6} * 2.8 * 10,000 = 1.6 \cdot 10^{-5} \quad (11)$$

$$Effectiveness_{H_2O_2} = 1.2 \cdot 10^{-6} * 0.7 * 10,000 = 8.4 \cdot 10^{-7} \quad (12)$$

**Let us now assume that the probability of indirect DNA damage is directly proportional to the number of oxidative molecules present. We can now calculate the reaction rate of 1 MeV gammas with the water in the cell, multiplied by the probability and effectiveness of each of the two molecules considered at causing indirect DNA damage, assuming a number density for water of $3.34 \cdot 10^{28}\ \frac{\text{atoms}}{\text{m}^3}$:**

$$R_{DNA,Direct} = \left(\frac{2\,(0.0929) + 0.743}{3}\right) * 10^{-28} \frac{m^2}{barn} * N_{H_2O\ in\ cell} * (Eff_{OH} + Eff_{H_2O_2})\,\Phi = 1.7\Phi \quad (13)$$

**Because the indirect damage to DNA is more than 10x stronger than the direct damage to DNA, then cryogenic freezing a person (stopping indirect DNA damage) will indeed cause them to incur less DNA damage and mutation.**

22.01 Introduction to Nuclear Engineering and Ionizing Radiation
Fall 2015