BIOLOGY 4U03/6U03

DAY CLASS — A.J. Rainbow

DURATION OF EXAMINATION: 3 hours

McMaster University Final Examination — December 2008

THIS EXAMINATION PAPER INCLUDES 7 PAGES AND 10 QUESTIONS. YOU ARE RESPONSIBLE FOR ENSURING THAT YOUR COPY OF THE PAPER IS COMPLETE. BRING ANY DISCREPANCY TO THE ATTENTION OF YOUR INVIGILATOR.

SPECIAL INSTRUCTIONS:

- All students are to answer **all** questions in Section A, **two (2)** questions only from Section B and **two (2)** questions only from Section C.
- Please write clearly and neatly in correct grammatical English, and use diagrams whenever appropriate. State any assumptions you make and show all your working.
- Use of any calculator is allowed.

SECTION A – (Answer all questions)

MARKS

(1.5) 1. (a) Describe ***briefly*** how (i) terminal deletions of chromosomes and (ii) dicentric chromosomes arise following exposure of human lymphocytes to ionizing radiation.

(2) (b) With the aid of graphs, show the relationship between aberration frequency and dose for both types of aberration for both x-rays and α-particles at both high and low dose rates.

(1.5) (c) Describe ***briefly*** an experiment to detect chromosome aberrations in circulating human lymphocytes and discuss ***briefly*** the limitations in the use of chromosome aberrations in circulating human lymphocytes as a method of biological dosimetry.

(2) 2. (a) Describe what is meant by the Law of Bergonié and Tribondeau, and put the following tissues in order of increasing sensitivity to ionizing radiation (most resistant first): hemopoietic (bone marrow) tissue, nerve tissue, thyroid epithelium, fine vasculature.

(1) (b) Which human tissue type is most sensitive to radiation induced cancer and which human tissue is most resistant to radiation induced cancer.

(2) (c) Describe briefly what you understand by the bystander effect as applied to radiation biology.

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MARKS

(2) 3. (a) Using the Poison distribution, derive a relationship between surviving fraction and dose for an organism or molecule obeying single-hit, single-target theory. Define clearly any symbols you use. Under what conditions would you expect survival curves of this shape to arise following exposure of mammalian cells to ionizing radiation and why?

A mammalian cell line, A, has a greater DNA content compared to that of mammalian cell line B. Both show morphologically similar colonies and following exposure to alpha particles, both cell types exhibit exponential survival according to single-hit, single-target theory. A mixture of cell type A and type B is irradiated with alpha-particles and assayed for colony survival, with the following result:

Absorbed dose to cell mixture in Gray	0	1	2	3	4	6	8	12	16	20	24	28
Percent colony formation	100	52	34	20	13.5	5.4	3.6	1.85	1.35	0.95	0.7	0.5

Draw the survival curve for colony formation of the composite cells mixture on the semi logarithmic graph paper provided and determine:

(1) (b) The Do value for the inactivation of colony formation for cell type B;

(1) (c) How much greater is the DNA content of cell type A compared to that of cell type B;

(1) (d) What is the ratio of the number of type B cells compared to that of type A cells in the original mixture?

(2) 4. (a) Using the radiation weighting factors and the tissue weightings factors (given in Tables 1 and 2 on page 3), calculate the effective dose for a male radiation worker who has received the following exposures over the past 12 months:

- 20 mGy of 3 Mev alpha-particles to the skin,
- 2 mGy of 50 Kev neutrons, whole body,
- 5 mGy of gamma rays to the stomach and liver,
- 500 mGy of beta particles to the thyroid.

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Table 1. Radiation weighting factors[1]

Type and energy range[2]	Radiation weighting factor, w_R
Photons, all energies	1
Electrons and muons, all energies[3]	1
Neutrons, energy < 10 keV	5
10 keV to 100 keV	10
> 100 keV to 2 MeV	20
> 2 MeV to 20 MeV	10
> 20 MeV	5
(See also Figure 1)	
Protons, other than recoil protons, energy > 2 MeV	5
Alpha particles, fission fragments, heavy nuclei	20

Table 2. Tissue weighting factors[1]

Tissue or organ	Tissue weighting factor, w_T
Gonads	0.20
Bone marrow (red)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Oesophagus	0.05
Thyroid	0.05
Skin	0.01
Bone surface	0.01
Remainder	0.05[2,3]

<u>**MARKS**</u>

(1.5) 4. (c) What are the current International Commission on Radiological Protection (ICRP) recommended dose limits for occupational exposure to ionizing radiation, which are designed to provide protection against both the stochastic and the non-stochastic (deterministic) effects of radiation? Is the individual in part (a) within the recommended dose limits?

(1.5) (d) Give an estimate for the effective dose equivalent and the risk of fatal cancer due to radiation exposure from (i) one chest radiograph taken in a good hospital and (ii) a computerized tomography examination of the abdomen.

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SECTION B – (Answer only two (2) questions)

MARKS

(5) 5. (a) Give an account of the chemical and biological factors that can influence the survival of mammalian cells following exposure to ionizing radiation. Indicate clearly how the survival is affected by each of the factors you describe and give the underlying mechanism(s) for the change in each case.

A human tumor cell line is irradiated in air and nitrogen with 14-Mev neutrons and in nitrogen with 250 kVp x-rays. Survival of cells following radiation is determined using an *in vitro* colony assay with the results shown in Table 3, below:

	Percent clonogenic survival		
Dose (cGy)	Neutron/air	Neutron/nitrogen	X-ray/nitrogen
0	100	100	100
60	68	80	ND
100	40	62	ND
200	11	25	95
300	3	10	ND
400	0.8	4.3	80
500	ND*	1.7	67
600	ND	ND	51
800	ND	ND	17
1200	ND	ND	10

* Not determined

(1) (b) Plot the three (3) survival curves on the semi-logarithmic graph paper provided and label the curves.

(2) (c) Assuming an oxygen enhancement ratio (OER) of 2.4 for exposure of this tumor cell line to 250 kVp x-rays, **draw** on the semi-logarithmic paper provided [next to the curves plotted in 6 (b)], the expected survival curve for exposure of cells to 250 kVp x-rays in the presence of oxygen. **Determine** the parameters Dq, Do, D_{37} and extrapolation number, n, for this survival curve.

(1) (d) Calculate the OER for 14-Mev neutrons and the Relative Biological Efficiency (RBE) of 14-Mev neutrons under anoxic conditions, stating clearly any assumptions you make.

(1) (e) A human tumor contains 10^9 well oxygenated cells only. Use the parameters of the appropriate human tumor cell survival curve above in order to calculate the dose of x-rays required to result in a 90% probability that the tumor is cured.

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MARKS

(6) 6. (a) Give a detailed account of the clinical symptoms, cellular abnormalities and the specific nature of the DNA repair deficiencies at the molecular level in cells from patients with Cockayne syndrome, xeroderma pigmentosum and xeroderma pigmentosum variants.

Human adenovirus is a double stranded DNA virus with a length of 35 kbp (kilobase pairs) that forms plaques on human fibroblasts. UV irradiation of the virus results in 6×10^{-3} thymine dimers/J/m^2/kbp and following infection of human fibroblasts with UV irradiated adenovirus, one "unrepaired" thymine dimer is sufficient to inactivate the plaque forming ability of the virus. UV irradiated adenovirus is assayed for plaque forming ability on several different human fibroblast strains.

(2) (b) Calculate the Do for plaque forming ability of the virus following infection of a strain of xeroderma pigmentosum fibroblasts which are unable to repair thymine dimers.

(2) (c) Adenovirus is UV-irradiated with a fluence of 190 J/m^2 and used to infect human fibroblasts which are capable of repairing 90% of the UV-induced thymine dimers. Calculate the surviving fraction of plaques after this UV exposure and also the fraction of adenovirus genomes that contain exactly 2 "unrepaired" thymine dimers.

Assume that viral inactivation follows a single-hit, 1 single target survival curve and that thymine dimers are induced, as well as repaired, at random in the viral DNA. Assume also that the average number of thymine dimers induced in the viral genome increases linearly with UV dose and that the "unrepaired" thymine dimers are the only cause of UV-induced viral inactivation.

(5) 7. (a) With reference to the different stages of embryogenesis in mammals, discuss the effects of radiation on the developing embryo and fetus. Indicate how the possible effects of radiation are influenced by the stage of embryogenesis at which radiation takes place. Discuss the implications for women radiation workers of reproductive capacity and for the use of ionizing radiation in medical diagnosis.

(5) (b) Describe the method used by the Russell's in their Mega Mouse project to detect radiation-induced recessive mutations in the mouse in the first generation following exposure to radiation. With reference to gametogenesis (germ line production) in mammals, give an account of the effects of ionizing radiation on germ cell production and gene mutation in the male and female. Indicate how the effects of radiation are influenced by the stage of gametogeneis at which radiation takes place, as well as the dose and dose-rated employed. Discuss the implications for men and women receiving exposure from diagnostic x-rays or other ionizing radiation sources.

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SECTION C – (Answer only two (2) questions)

MARKS

(5) 8. (a) Define or describe briefly what is meant by exposure, absorbed dose, equivalent dose (or dose equivalent) and effective dose (or effective dose equivalent) for ionizing radiation. Give the units in which each is measured and the relationships between these four (4) ways by which the amount of ionizing radiation is measured. Which method of measurement most closely relates to the risk of cancer from the radiation exposure?

(3) (b) ***List*** the four major components of "natural" background radiation in Canada and give the value for the total average annual effective dose equivalent for natural background radiation to the Canadian population. What source of "natural" radiation and what source of "man-made" radiation give the greatest contribution to the effective dose equivalent to the Canadian population?

(2) (c) Compare the effective dose received from natural background radiation to that received by: (i) radiation workers and (ii) individuals undergoing various medical procedures involving ionizing radiation such as diagnostic radiology and nuclear medicine.

(1) 9. (a) Define $LD_{50/60}$ and give its value in humans following whole body exposure to ionizing radiation.

(3) (b) Discuss the factors affecting the $LD_{50/30}$ in mammals following whole body exposure to ionizing radiation, indicating how the $LD_{50/30}$ is affected by each factor you discuss.

(6) (c) Describe the three radiation syndromes for humans following acute whole body exposure to ionizing radiation. Indicate for each syndrome, the signs and symptoms, the disturbance in cellular kinetics that leads to death, the mean survival time, the doses of radiation involved and the possible methods of treatment.

(3) 10. (a) With reference to named examples describe how the concept of oncogenes and tumor suppressor genes provides a model for the mechanisms of cancer induction by radiation.

(4) (b) Give an account of the carcinogenic effects of ionizing radiations. Discuss the data from exposed human populations as well as that from animal and tissue culture experiments giving the magnitude of the radiation doses for the data you describe.

(3) (c) Discuss the evidence that the linear non-threshold model for radiation induced cancer might (i) overestimate and (ii) underestimate the carcinogenic risk of ionizing radiation to the human population at low doses.

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TABLE OF CONSTANTS		
Avogardo's number (# molecules in the gram molecular weight) = 6.023×10^{23}		
A solution at a concentration of 1 M = the gram molecular weight in 1 liter		
1 ev	=	1.6×10^{-12} ergs
1 erg	=	6.24×10^{11} ev
1 Joule	=	10^7 ergs
$e^{-0.1}$	=	0.9
e^{-1}	=	0.367
$e^{-1.6}$	=	0.2
e^{-2}	=	0.135
e^{-3}	=	0.05
$\log_e 1.4$	=	0.3333
$\log_e 2$	=	0.693
$\log_e 2.72$	=	1
$\log_e 10$	=	2.3

The End

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10 MM/CM

10 MM/CM