Name: ___________________________________ Date: ____________________

In this exam sheet, there are 17 questions.
Each answer yields up to 2 points according to its correctness and completeness.

1. What is the radiolysis of water?

2. Using the table below, find **a.** how many of H_3O^+ ions are produced, on average, when 10^6 electrons – each with 1 keV kinetic energy – stop in water, and **b.** how many OH^- ions are produced by in the same process.

Table 13.3 *G* Values (Number per 100 eV) for Various Species in Water at 0.28 μs for Electrons at Several Energies

	Electron Energy (eV)							
Species	**100**	**200**	**500**	**750**	**1000**	**5000**	**10,000**	**20,000**
OH	1.17	0.72	0.46	0.39	0.39	0.74	1.05	1.10
H_3O^+	4.97	5.01	4.88	4.97	4.86	5.03	5.19	5.13
e^-_{aq}	1.87	1.44	0.82	0.71	0.62	0.89	1.18	1.13
H	2.52	2.12	1.96	1.91	1.96	1.93	1.90	1.99
H_2	0.74	0.86	0.99	0.95	0.93	0.84	0.81	0.80
H_2O_2	1.84	2.04	2.04	2.00	1.97	1.86	1.81	1.80
Fe^{3+}	17.9	15.5	12.7	12.3	12.6	12.9	13.9	14.1

3. A 10 cm^3 sample of water is given a dose of 1 Gy with 1 keV electrons. Use the table in the previous exercise to find how many e_{aq}^- ions are produced in the sample.

4. What is the LD_{50} dose for a human being? And what is the LD_{50} dose for an extremophile like the D. radiodurans?

5. What is a stem cell? (explain)

6. What is a ribosome? (explain)

7. What are the introns? And what are the exons?

8. What are the codons and how many different codons exist?

9. What is oxidative stress? How do cells counter oxidative stress? (explain)

10. Explain how the degree of hypoxia of the tumor microenvironment can affect radiotherapy.

11. What is the difference between the Poisson model and the multitarget model in radiobiology? What is the expression of the survival probability in the Poisson model?

12. Describe the weaknesses of the Poisson model and of the multitarget model in radiobiology.

13. The following image – taken from Barendsen, Proc. Conf. "Microdosimetry", Ispra 1967 – illustrates an important feature of the survival curve. Explain the meaning of the plots

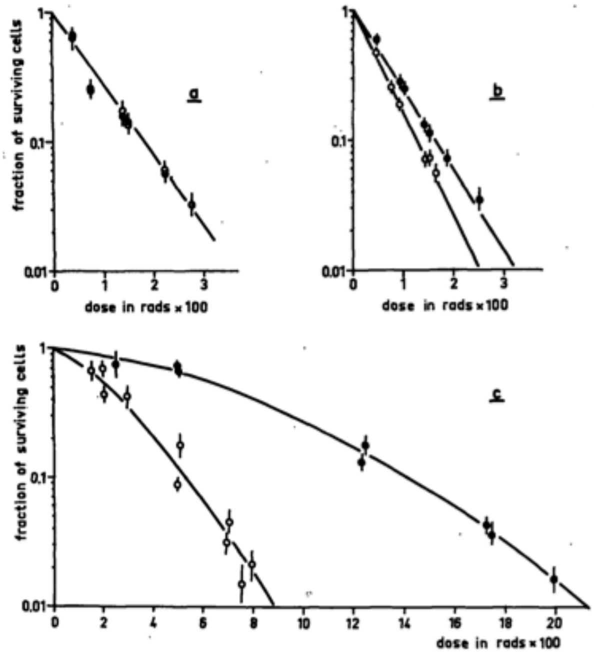

Figure 2. Dose-survival curves for cultured cells of human origin in equilibrium with air and nitrogen respectively: open symbols, air; filled symbols, nitrogen. (a) 2.5 MeV α-particles, LET_∞ = 166 keV/μ, OER = 1.0 + 0.1. (b) 4.0 MeV α-particles, LET_∞ = 110 keV/μ, OER = 1.3 ± 0.1. (c) 14.9 MeV deuterons, LET_∞ = 5.6 keV/μ, OER = 2.6 ± 0.3.

14. What is the mathematical expression of the TCP in the context of the multitarget model?

16. The U-251MG cell line (one of the cell lines of the brain tumor *glioblastoma multiforme*) has the following LQ parameters: $\alpha = 0.36$ Gy^{-1} and $\beta = 0.06$ Gy^{-2}. When we irradiate these cells in a fractionated treatment with a series of 2.5 Gy doses, what is the effective D_0?
(Hint: the effective D_0 is defined in the Poisson model description of the surviving fraction: $S(D) = e^{-D/D_0}$)

17. Explain the concept of Equivalent Uniform Dose.

18. What is a dose-volume histogram? Explain how it is read.

Answers

1. The radiolysis of water is the process by which water molecules are broken into ions by the action of ionizing particles. The resulting ions can combine with neighboring water molecules or other ions to form several types of radiochemical species.

2. $4.86 \cdot 10^7$ H_3O^+ ions; $3.9 \cdot 10^6$ OH^- ions.

3. 10 cm^3 of water have a mass of 0.01 kg, and therefore 1 Gy correspond to a deposited energy of 0.01 J. Since 1 eV ≈ 1.6 10^{-19} J, the deposited energy in eV is ≈ 6.25 10^{16} eV. This means that about 6.25 10^{13} electrons have been absorbed in the sample, and using the table in exercise 2, we find on average a production of 6.2 e_{aq}^- ions per electron. Finally, this means that about 3.88 10^{14} e_{aq}^- ions are produced by the electrons in the water mass.

4. The LD_{50} dose for a human is about 5 Gy. The LD_{50} dose for D. radiodurans is about 5000 Gy.

5. Stem cells are undifferentiated cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells, and adult stem cells, which are found in various tissues.

6. The ribosomes are large protein-RNA complexes that convert the genetic instructions carried by mRNA into polypeptide chains (or, roughly speaking, proteins) by binding together aminoacids transported by tRNA.

7. The introns are the noncoding sections of DNA. The exons are the coding sections of DNA.

8. A codon is a triplet of nucleotides that encodes an aminoacid or an instruction that corresponds to the start or stop of the genetic sequence that encodes a whole gene. Since there are 4 types of nucleotides, there are $4^3 = 64$ different codons.

9. Oxidative stress is caused by the Reactive Oxygen Species, and it can be both endogenous and exogenous. Radiation is a powerful exogenous source of ROS. Cells counter oxidative stress with an array of different enzymes, like catalase and superoxide dismutase.

10. Radiation kills cells more effectively when oxygen is copious: this is the Oxygen Effect. A hypoxic tumor microenvironment means that radiation is less effective in killing tumor cells.

11. In the Poisson model, a cell dies if a single sensitive target is hit; in this model, the probability of NOT being hit is $S(D) = e^{-D/D_0}$, and this is also the expression of the

survival probability in the Poisson model. In the multitarget model we assume that a cell dies only when multiple targets are all hit.

12. The Poisson model fails describe the behavior of the survival fraction for low doses. The multitarget model fails to describe the same behavior in many practical cases. Both models describe the high-dose survival fraction.

13. The figure shows the OER for different particles and different values of LET. The oxygen effect is quite apparent for low LET (panel c). At higher LET (panel b) the effect is much less apparent, and at higher still LET (panel a) it disappears completely.

14. The TCP is the probability of killing all the cells in a tumor. If the tumor has N cells then the average number of surviving cells is $NS(D)$, and the probability that no cell survives is $e^{-NS(D)}$. When we use the multitarget model, we find

$$TCP = e^{-NS(D)} = e^{-N(1-(1-e^{-D/D_0})^n)}$$

16. The surviving fraction in the LQ model is described by the expression

$$S(D) = e^{-(\alpha D + \beta D^2)}$$

In the present case $\alpha D = 0.9$; $\beta D^2 = 0.375$, and therefore $\ln S(2.5\text{ Gy}) = -1.275 = -\frac{2.5\text{ Gy}}{D_0}$. Thus, $D_0 \approx 1.96$ Gy.

17. For any dose distribution, the corresponding Equivalent Uniform Dose (EUD) is the dose in Gy, which, when distributed uniformly across the target volume, causes the survival of the same number of clonogens. Therefore, two different nonuniform target dose distributions are equivalent, i.e., they have the same EUD, if the corresponding expected number of surviving clonogens are equal.

18. Dose Volume Histograms (DVH) are empirical cumulative distributions of dose that are often used in radiotherapy. The horizontal scale represents dose, and the vertical scale represents a fraction of a population of cells. DVH's are read off so that for a given dose, the corresponding number on the vertical scale represents the fraction of cells that receives *at least* that dose.