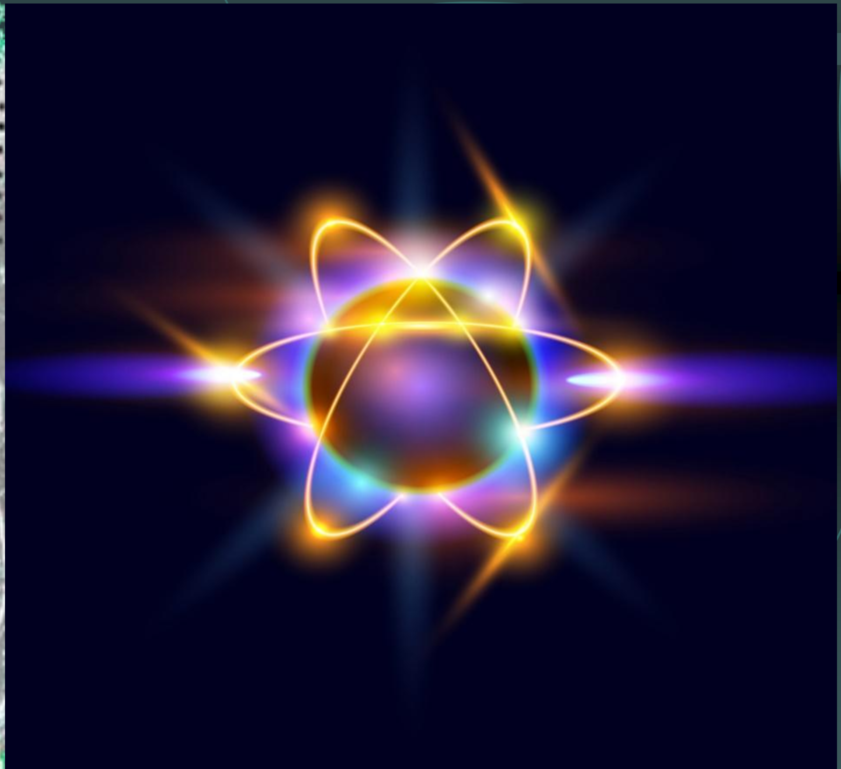
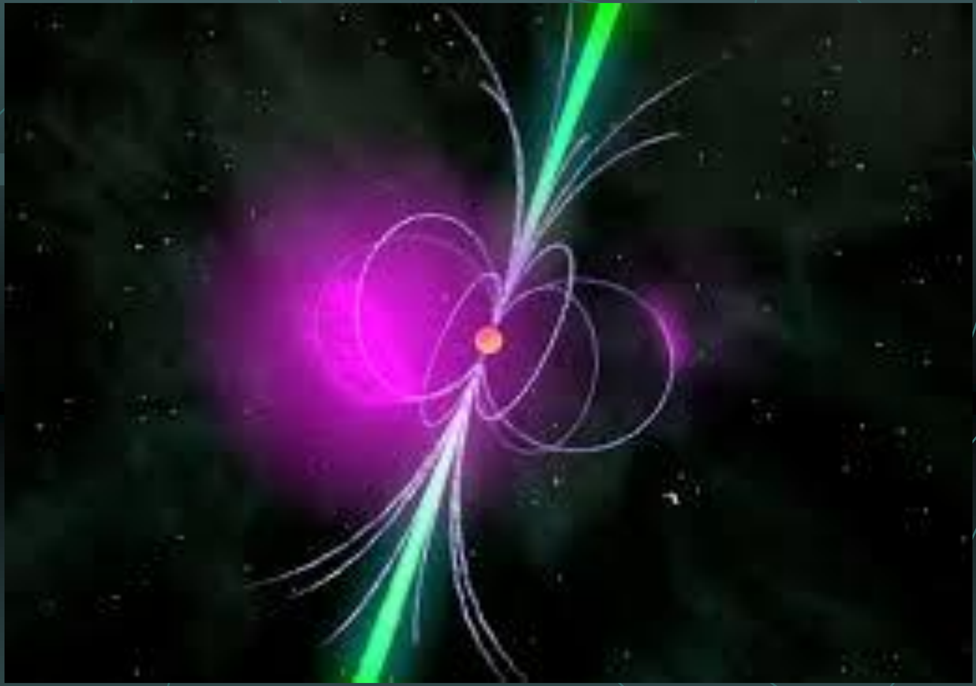
MEDICAL UNIVERSITY – PLEVEN

FACULTY OF PUBLIC HEALTH

CENTER FOR DISTANCE LEARNING

RADIOBIOLOGY AND RADIOLOGICAL PROTECTION

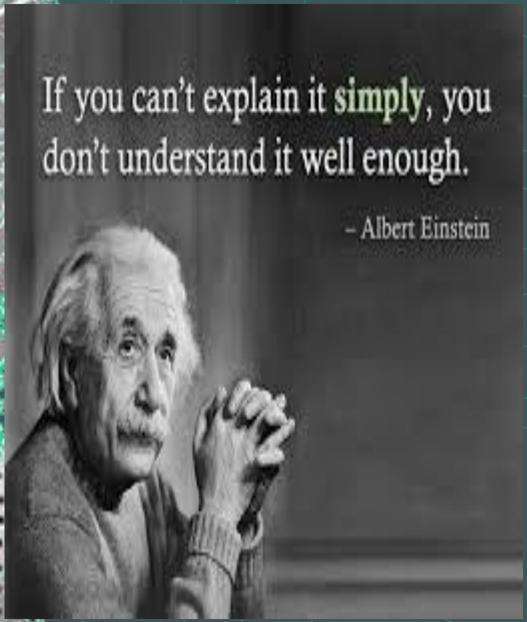


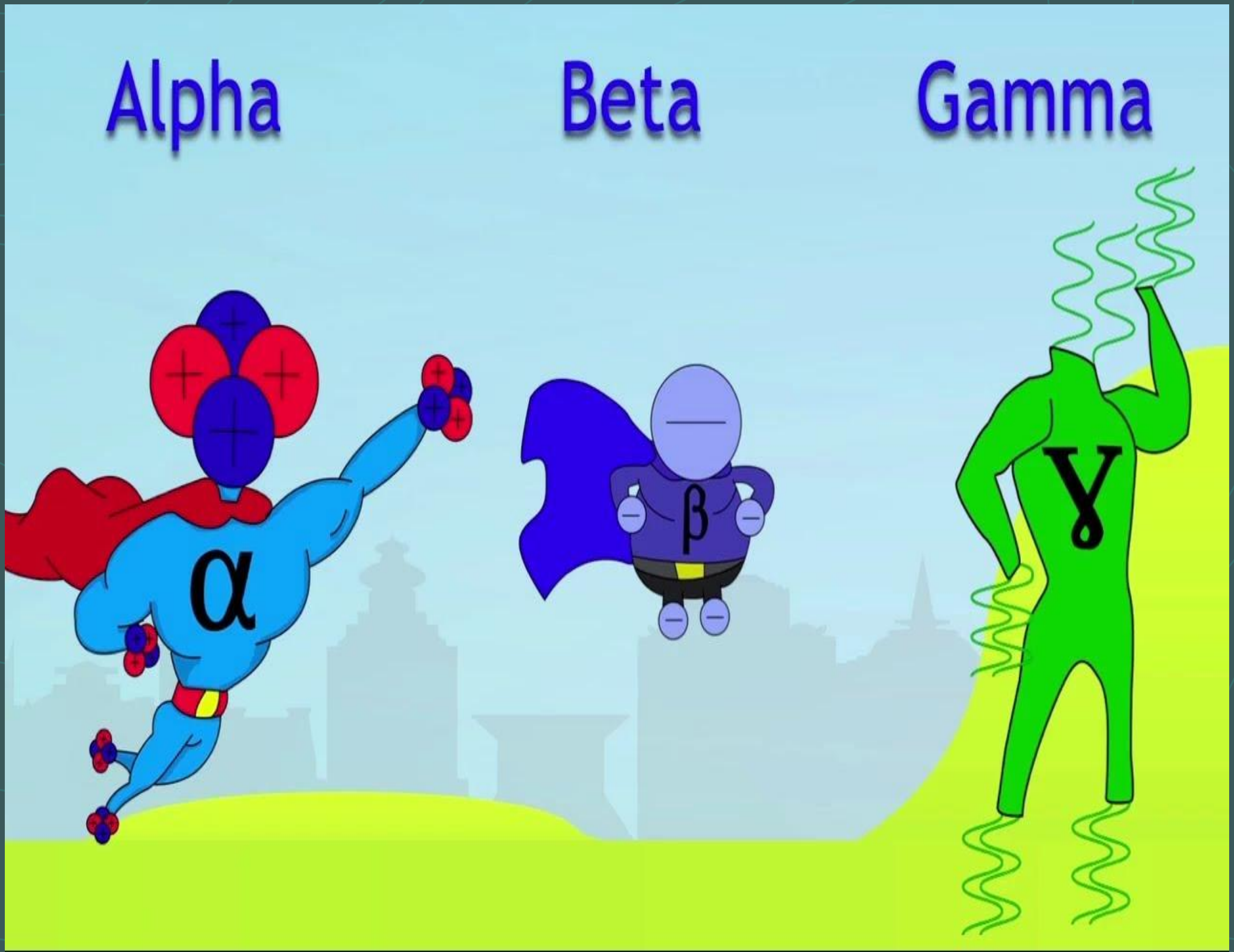


Лектор:

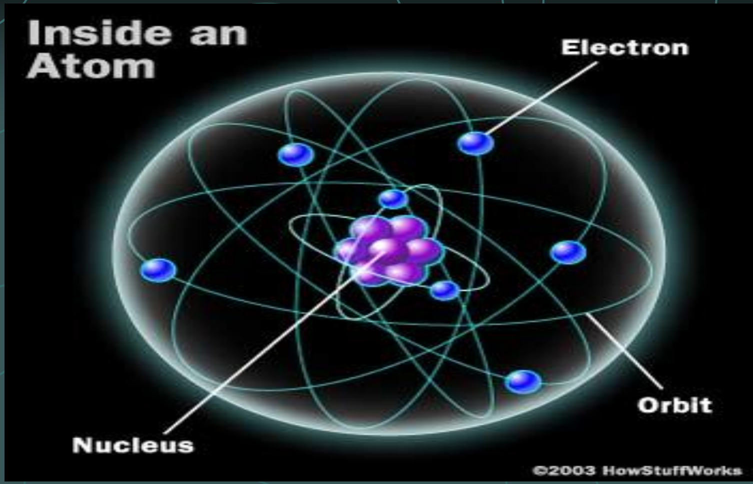
доц. д-р В. Данчева, дм

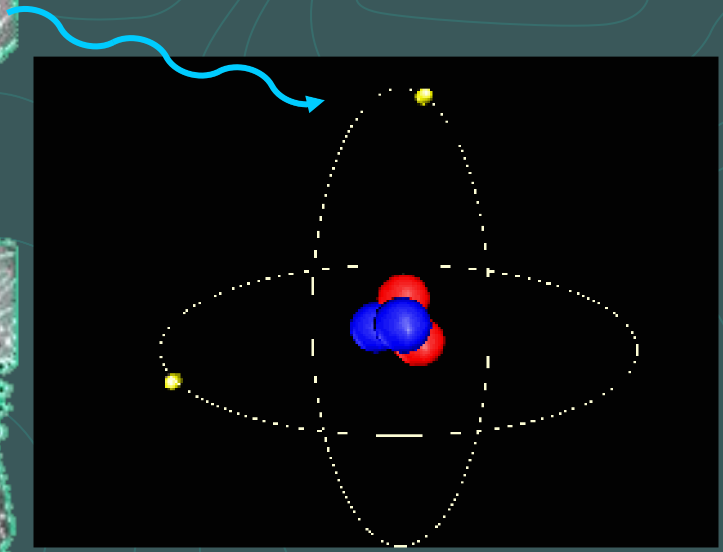
PHYSICS OF IONIZING RADIATION

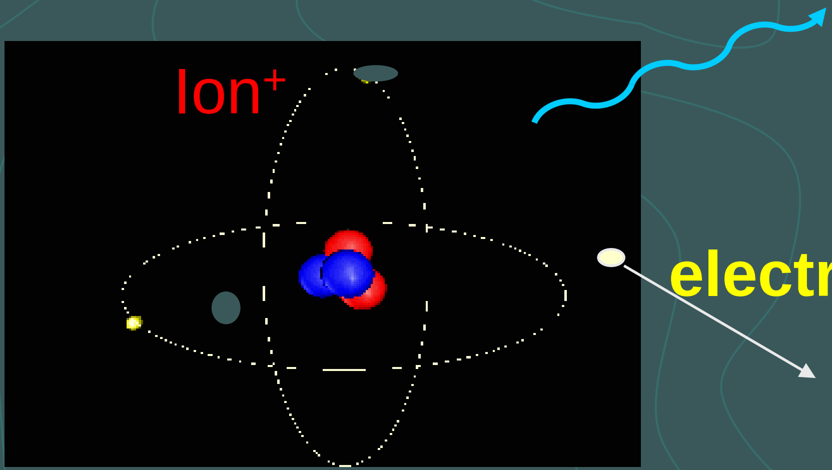




Ionizing radiation







Produces ions in matter during interaction with atoms

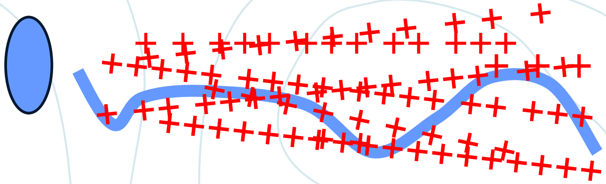
Creation ion$^+$ / e$^-$

- There are two classes of ionizing radiation:
  - particulate
  - electromagnetic

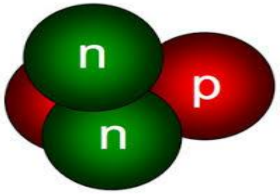
Particulate ionizing radiation are:

a) alpha radiation - high-energy helium nuclei ($_2He^4$)

- \- it consists of two neutrons and two protons and its mass is considerably large
- \- the kinetic energy of α - particles is several **MeV**
- \- the α - particle looses its energy through **ionization or excitation** of the molecules and atoms of the surrounding medium.

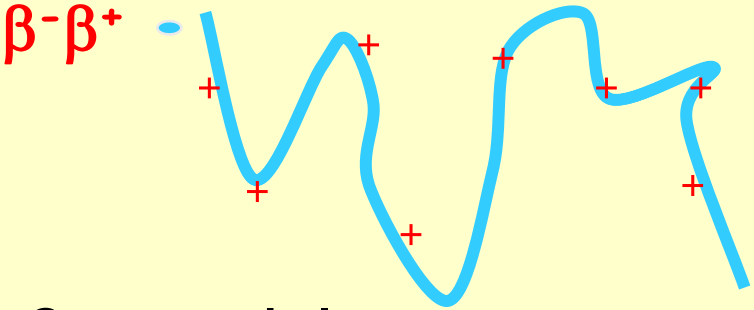


α particle



- The **ionizing power** of the α - particles, is characterized by the **linear ion density** (specific ionization), produced of **a particle path.** The ionizing power of α - particle is large.
- Alpha particles **do not penetrate in tissue** very well (0,02 - 0,06 mm) and their **tracks are short and thick**
- These particles induce chemical processes resulting in functional and morphological changes of the tissues.

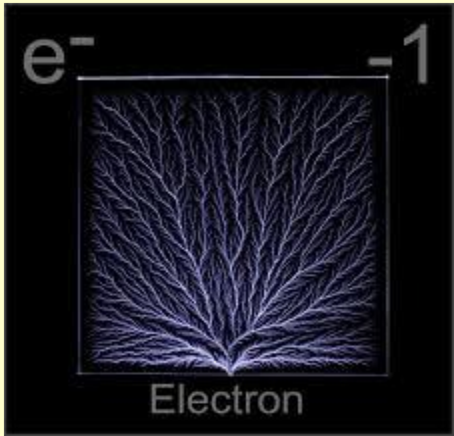
b) β-radiation



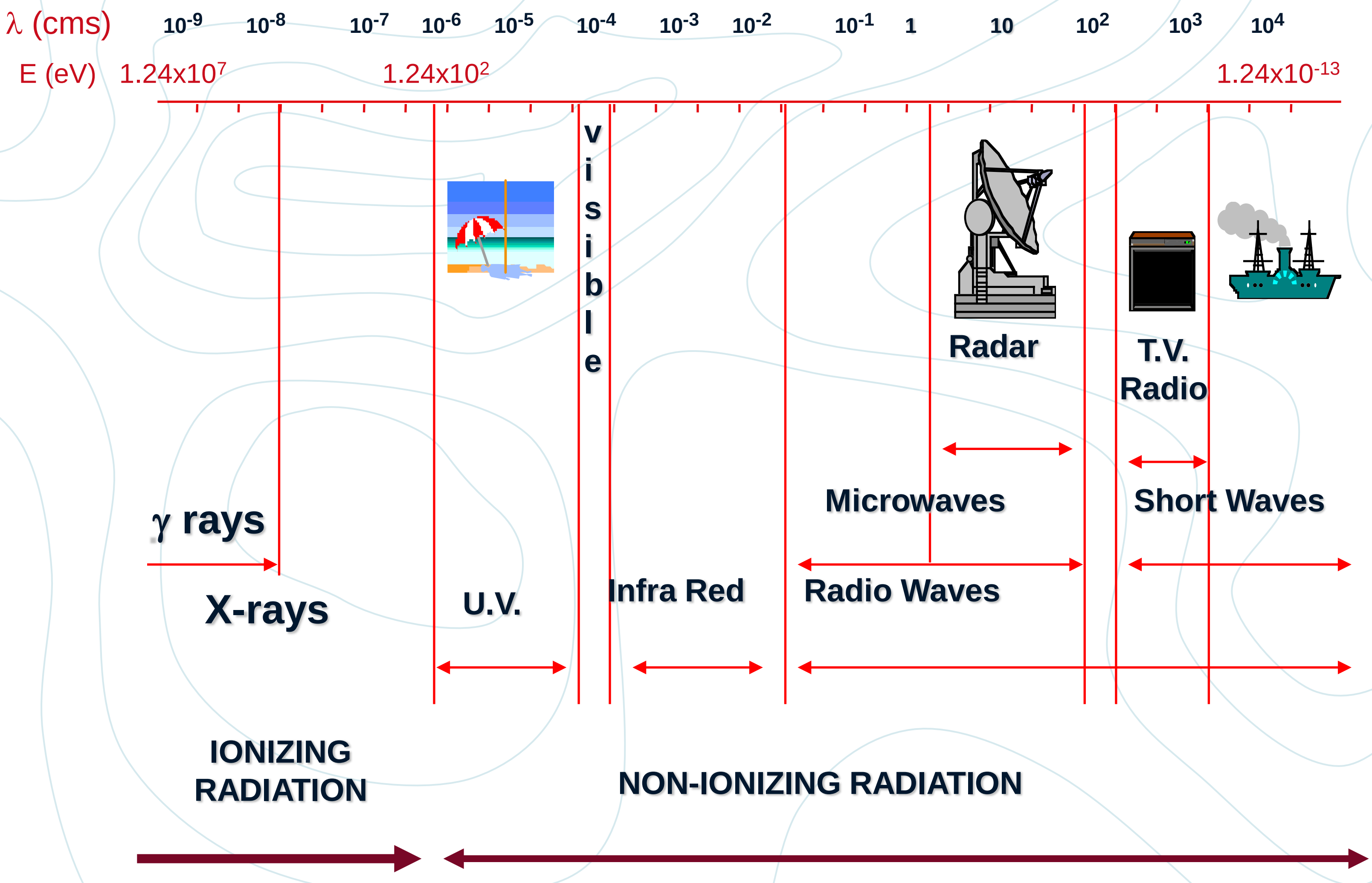
electrons β^-

positrons β^+

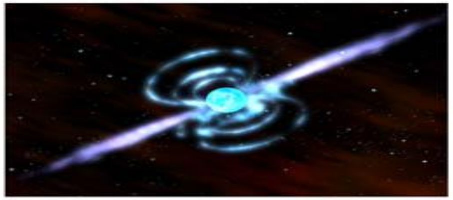
- The β - particles **penetrate from 10 cm to several m in air**, but in water and living tissues it is **only 1 - 2 cm**.
- The specific ionizing power of the β - particle is approximately 1 000 times smaller than that one of α - particle.
- **The track** of β - particle is **zigzagged**



ELECTROMAGNETIC RADIATIONS



Gamma radiation

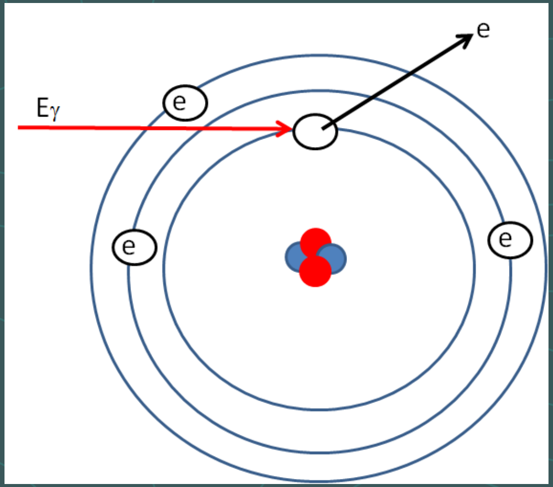


Gamma rays and x-rays

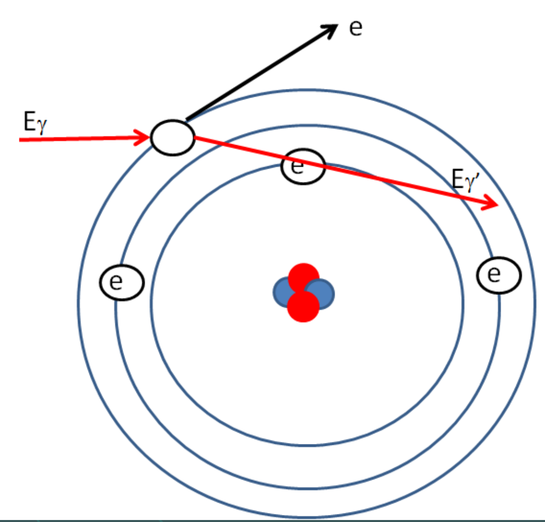
are **electromagnetic** radiation (waves)
The nature of these two types of radiation **is very similar** and their effects are essentially **the same**.

- **Gamma radiation results when the nucleus releases excess energy, usually after an alpha, beta or positron transformation**.
- **X-ray** occurs whenever an inner shell orbital electron is removed and **rearrangement of the atomic electron** results with the release of the element's characteristic x-ray energy.
- Gamma and x-rays penetrate several **hundred *m* in air** and **several *dm*** in living organism.
- Neither gamma rays nor x-rays carry a charge, and neither has mass. They create **moderate ionization** along their path.

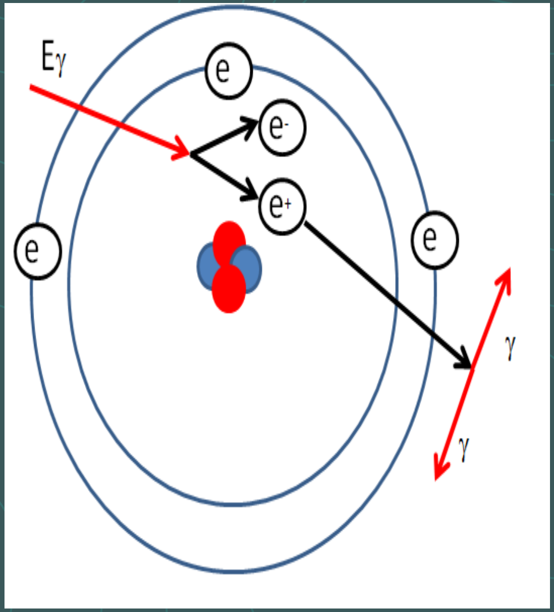
Interactions of ionizing radiation with matter



Photoelectric effect: incident photon is totally absorbed and ejects electron from atom. This effect dominates with low-energy photons interacting with heavier elements

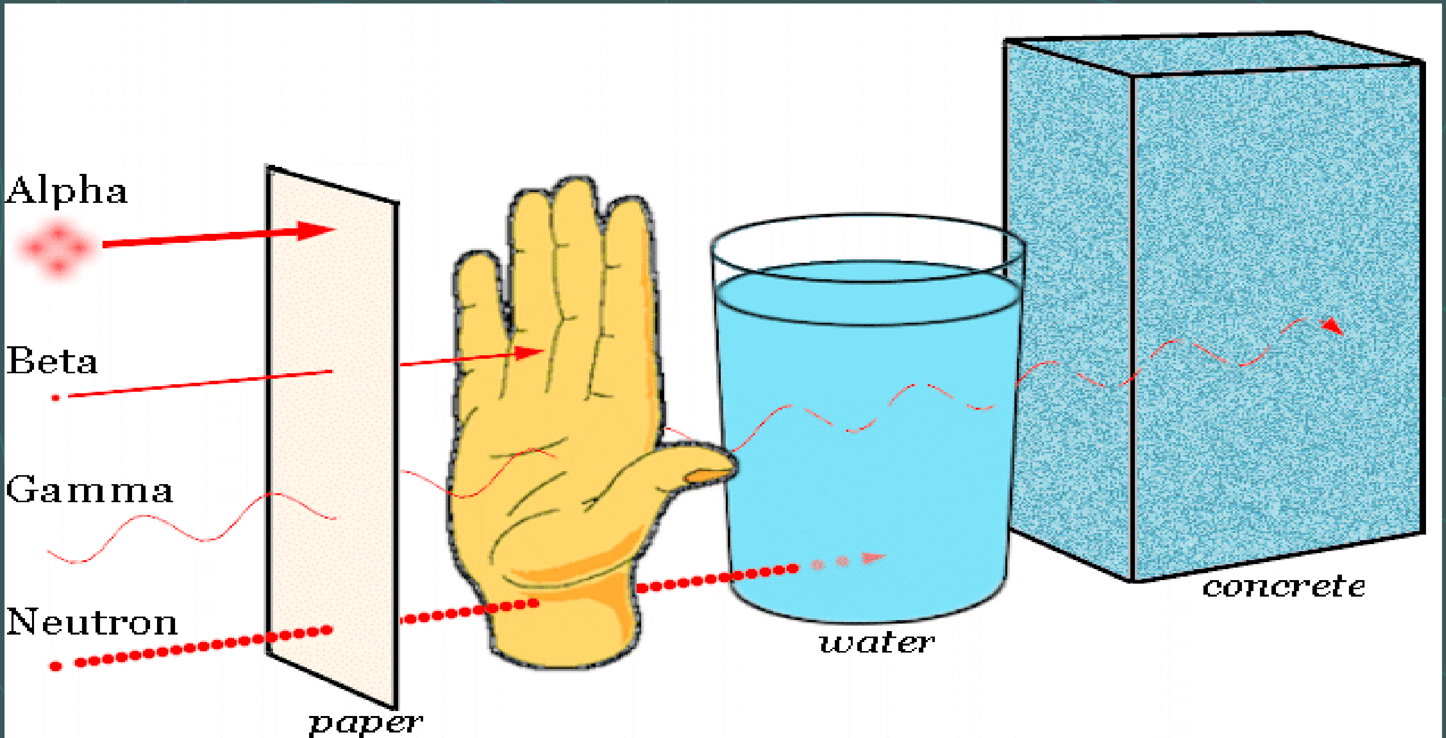


In **Compton scattering** electron is also ejected, but incident photon survives and is scattered by losing some of its energy. In water or biological tissues, this effect dominates at energies above 50 keV

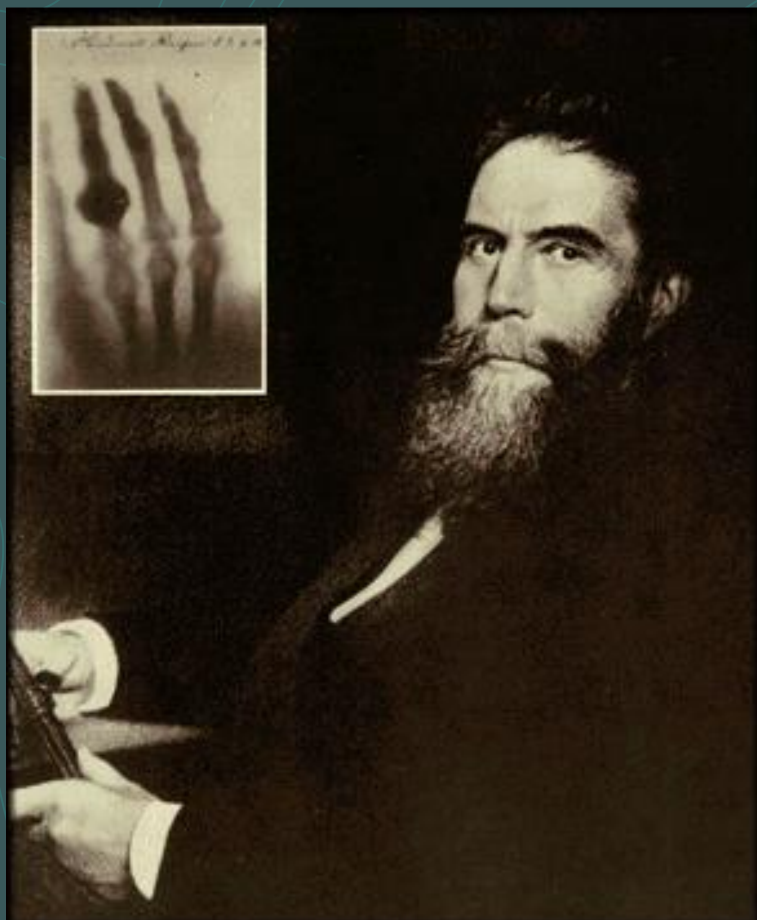


Pair production is process in which its energy is converted into electron-positron pair. This interaction starts occurring at energies higher than 1 MeV. Unlike electron, positron will eventually disappear annihilating one electron of surrounding material. Positron-electron pair is converted into two photons with energy of about 0.5 MeV

The penetrating powers of different rays



Roentgen with his wife's hand, 1895



- X-rays were rapidly adapted for use as a clinical treatment, initially for non-cancerous conditions, but soon for cancer, as well.

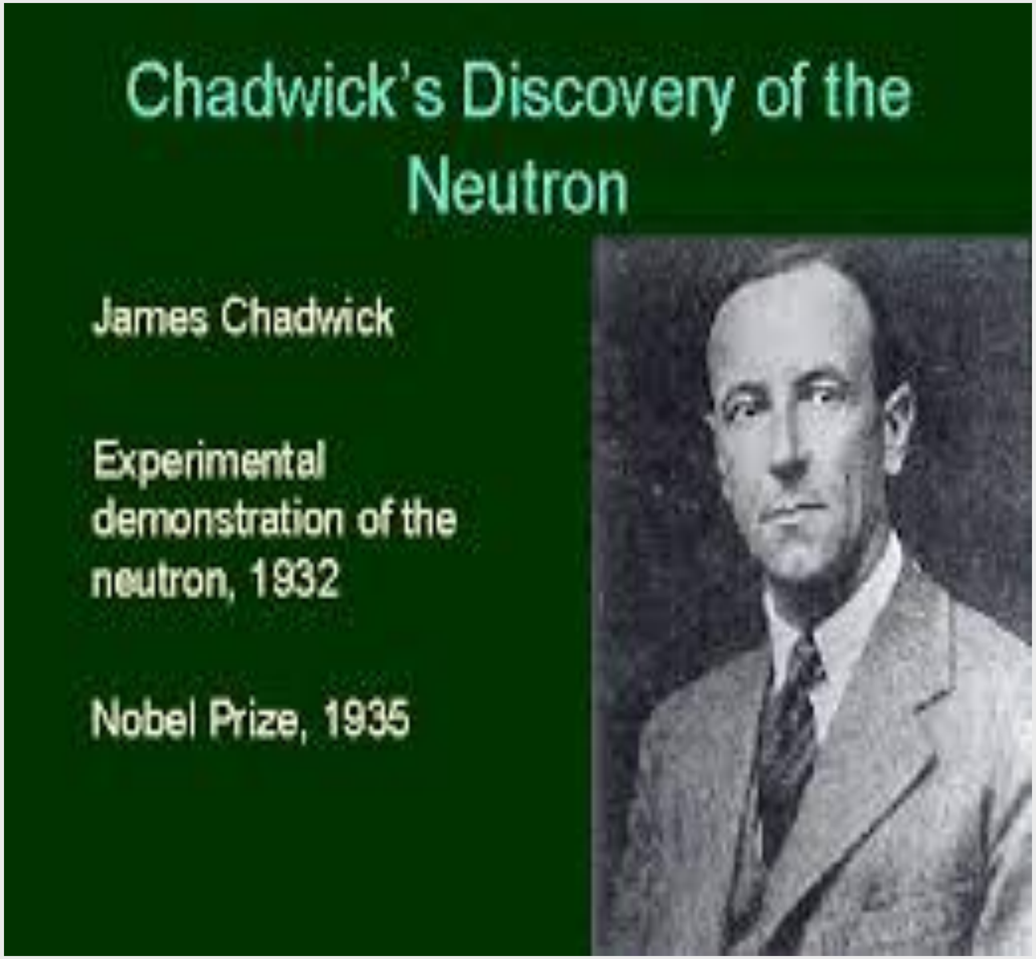
The Nobel Prize in Physiology or Medicine 1946
"for the discovery of the production of mutations by means of X-ray irradiation

Hermann J. Muller

However, its use for benign conditions has been limited in most countries for fear of radiation-induced cancer.

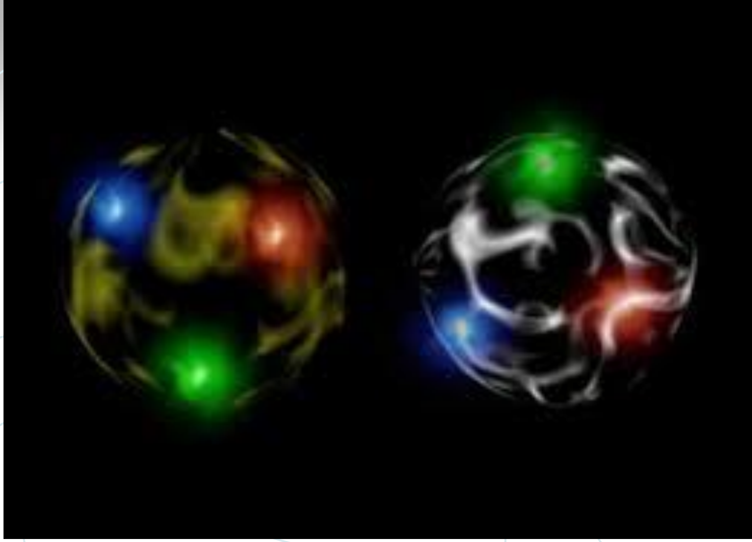
The carcinogenic effects of X-rays was discovered using fruit flies by Muller in 1946.

James Chadwick



c) Neutron radiation –

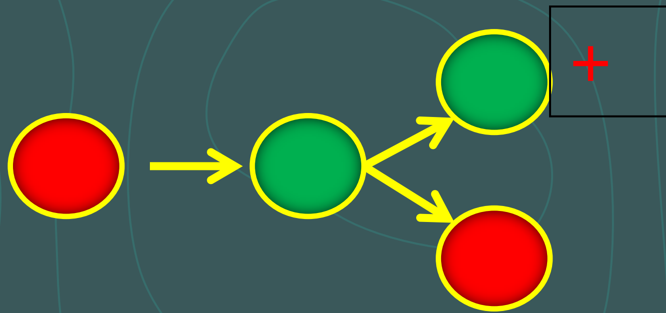
Produced by **bombardment of the nucleus** with particles (including photons). The resulting **highly excited nucleus emits a neutron.**



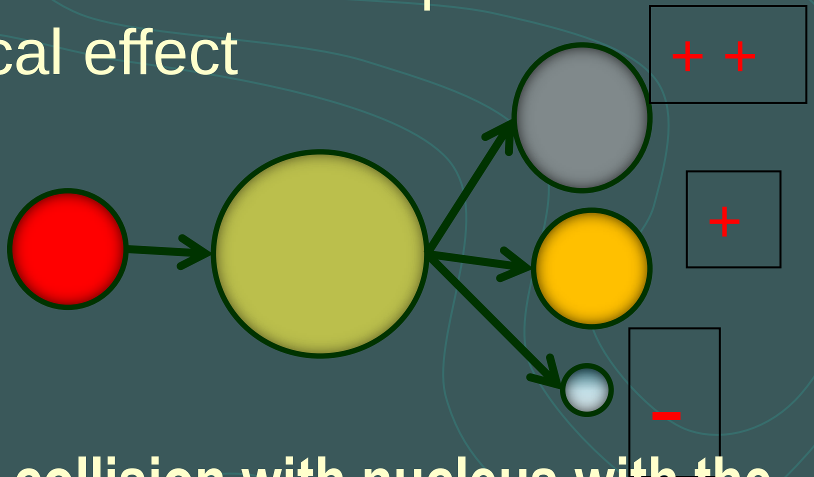
- The neutron has **no charge** and it does **not cause direct ionization.** On passing through some medium it interacts only **with the nuclei** and not with the electrons.
- Neutrons are generally ejected from site of their generation with **high energy (a few MeV)**
- They penetrate **several hundred *m* in air** and **several *dm* in living organisms**.

Neutrons

Neutrons interact with nuclei (elastic and inelastic diffusion, nuclear reactions, captures), and produce emission of secondary charged particles (like protons, alpha particles or nuclear fragments heavier than carbon, oxygen, nitrogen or hydrogen) which are responsible for tissue ionization and for biological effect



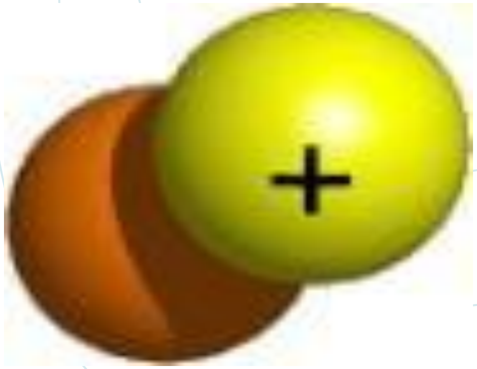
elastic diffusion with production of proton and another neutron



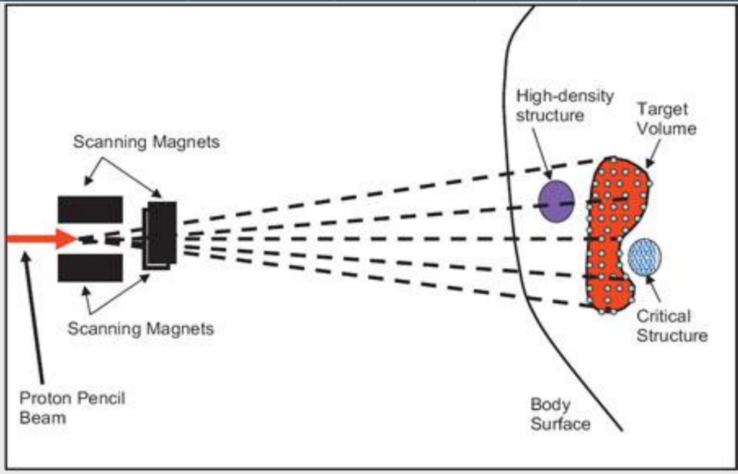
collision with nucleus with the production of various charged particles: protons, nuclear fragments, electrons

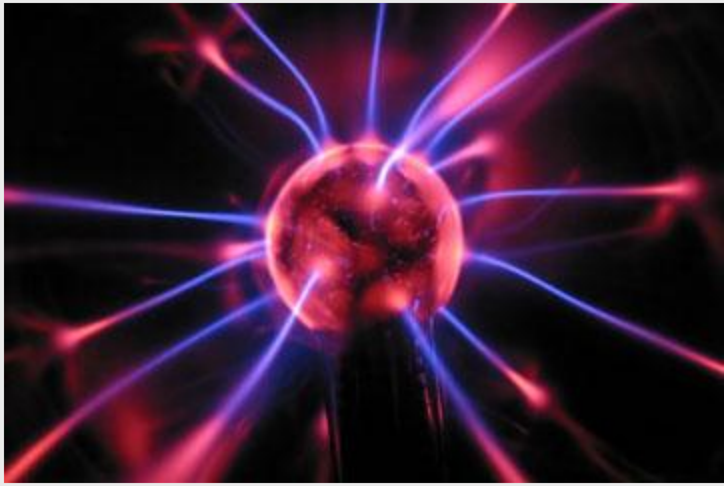
d) Proton radiation is produced either **by the acceleration of hydrogen ions** or **by bombardment of the nucleus** with some particles.

Like all other particles with an electric charge, the proton causes **ionization and excitation** of the medium. Proton therapy is ideal for tumors that are oddly shaped and/or situated in areas that can't handle much radiation exposure.



Proton beam radiation therapy (PBRT)



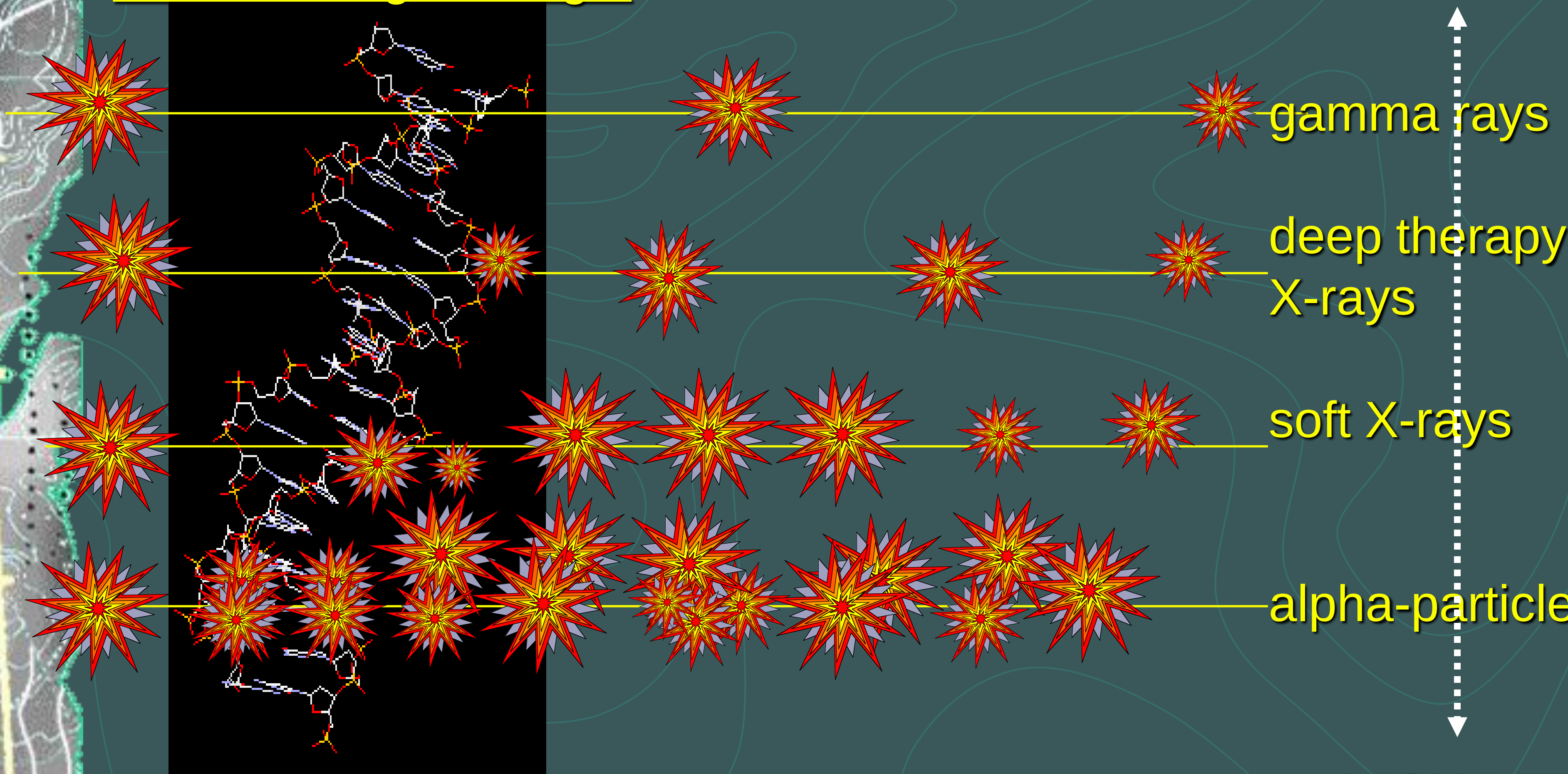


Advantages of proton therapy

During **conventional radiation**, a beam of photons transfers **the greatest dose** of radiation **to the front of the tumor**, after which the radiation penetrates the tumor and **healthy tissues of the patient behind the tumor**. **In contrast,** a **proton beam** transfers **a minimal dose** of radiation **to the front of the tumor** (depending on the depth of the tumor under the body surface), **a maximal dose to the tumor area itself** and **no dose behind the tumor**. The center of the tumor receives **70 – 80 %** of the beam's energy. The beam is rapidly delayed at that point and transfers its destructive effects directly to the tumor cells. The energetic value of the beam **decreases behind the tumor to zero**. Therefore, proton therapy **is safer for healthy tissue surrounding the tumor**. Proton beams can be used for the treatment of malignant tumors where therapeutic possibilities are restricted and conventional radiotherapy is associated with a high risk of adverse effects. This is particularly in the case of childhood tumors, eye tumors and for those in some areas of the brain. This is a unique property of proton therapy. With all other tumors proton therapy always shows a lower risk of adverse effects, making proton radiotherapy a clear treatment choice for the future.

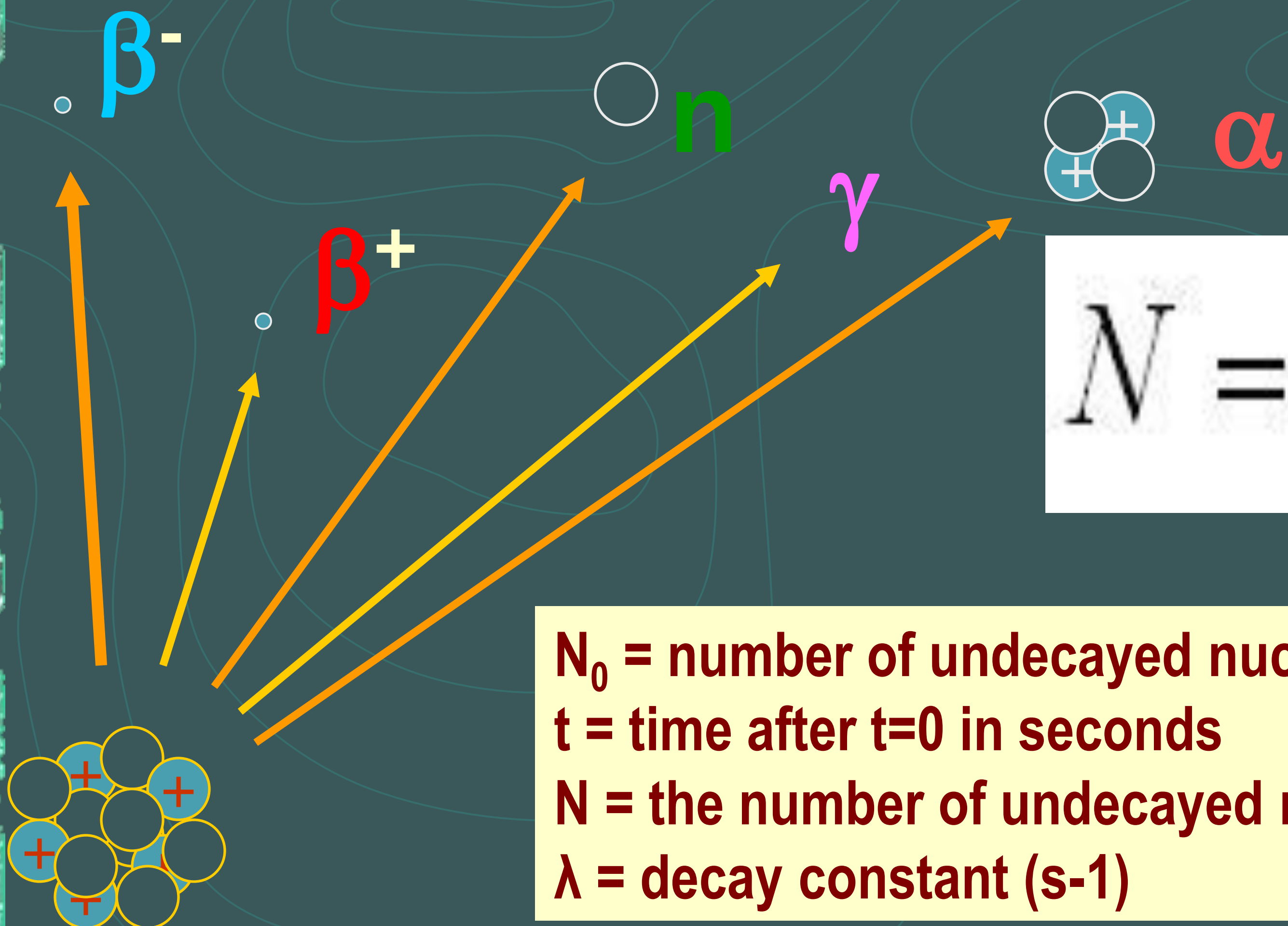
LINEAR ENERGY TRANSFER

Separation of ion clusters in relation to size of biological target



LET is average energy imparted by excitation and Ionization events caused by a charged particle travelling a set distance

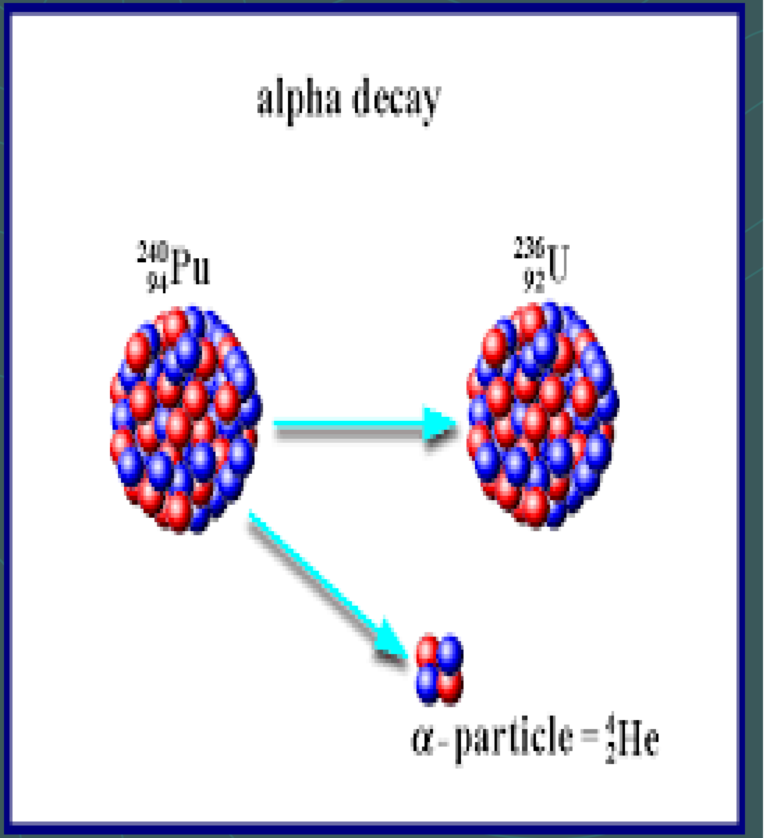
Decay Law



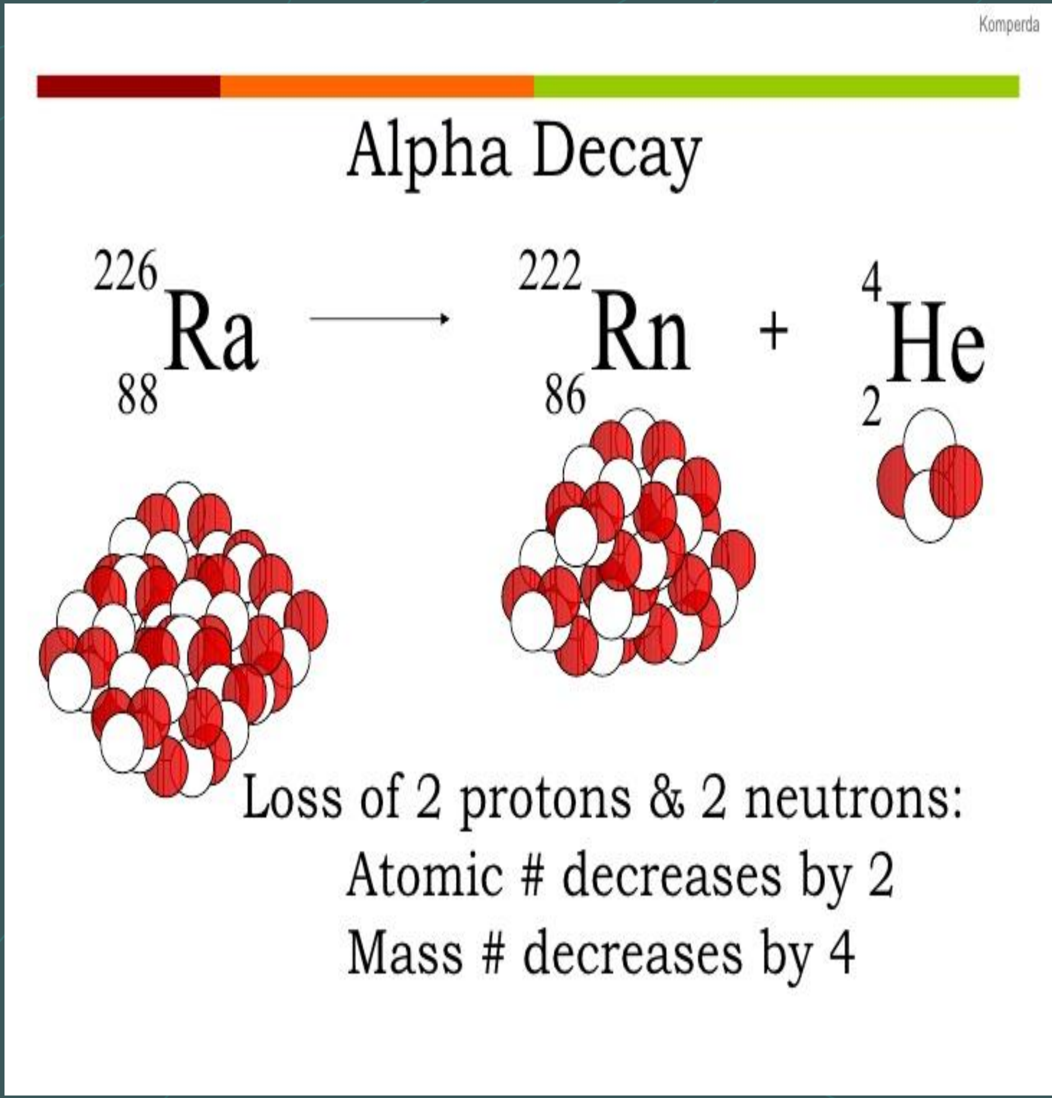
$$N = N_0 e^{-\lambda t}$$

N_0 = number of undecayed nuclei at t=0
t = time after t=0 in seconds
N = the number of undecayed nuclei at time t
λ = decay constant (s-1)

Alpha Decay



alpha decay
²⁴⁰₉₄Pu
²³⁶₉₂U
α - particle = ⁴₂He



Komperda
Alpha Decay
226 Ra 88
222 Rn 86
+
4 He 2
Loss of 2 protons & 2 neutrons:
Atomic # decreases by 2
Mass # decreases by 4

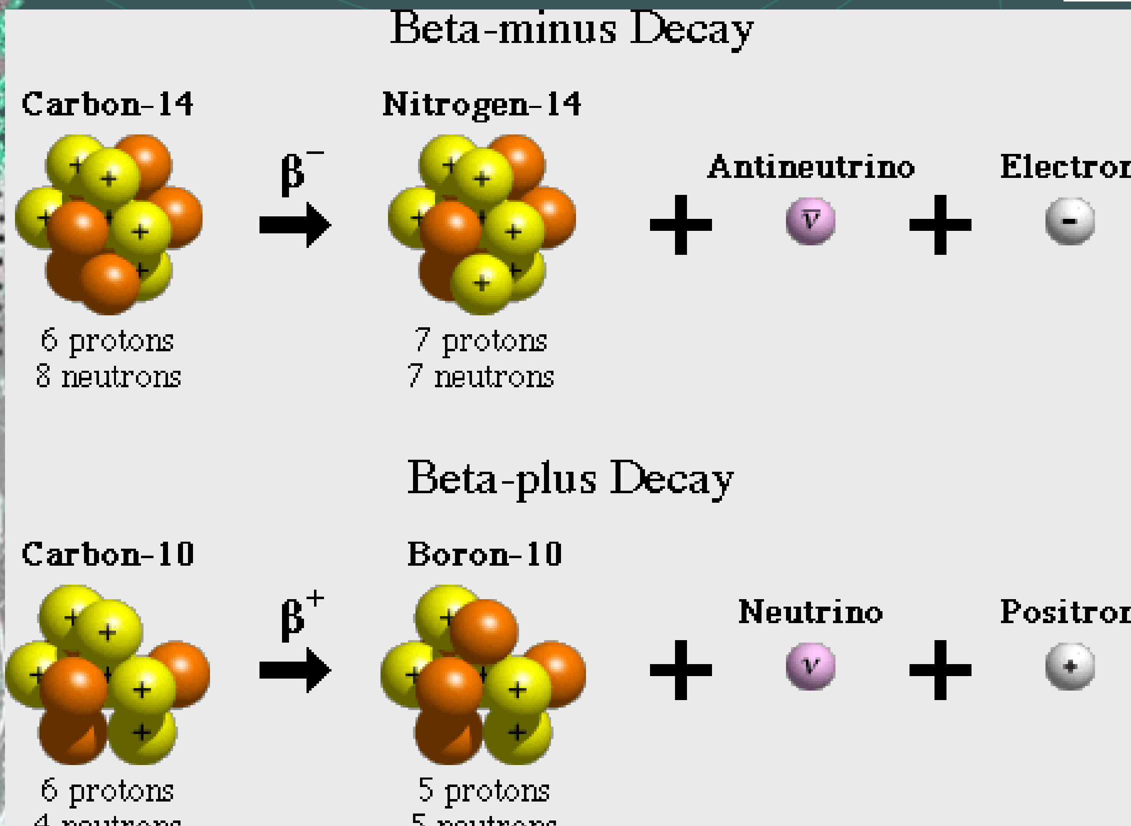
Beta decay

$$n^0 + \to p^+ + e^- + \bar{\nu}_e$$

$$\mathbf{p} \to \mathbf{n} + \mathbf{e}^+ + \nu$$

$$^{137}_{55}Cs \to {}^{137}_{56}Ba + {}^{0}_{1}\beta + \nu + \gamma - rays$$

$$^{A}_{X}\mathbf{X} \longrightarrow {}^{A}_{Z+1}\mathbf{Y} + {}^{0}_{-1}\mathbf{e} + {}^{0}_{0}\bar{\nu}_e + \mathbf{Q}$$

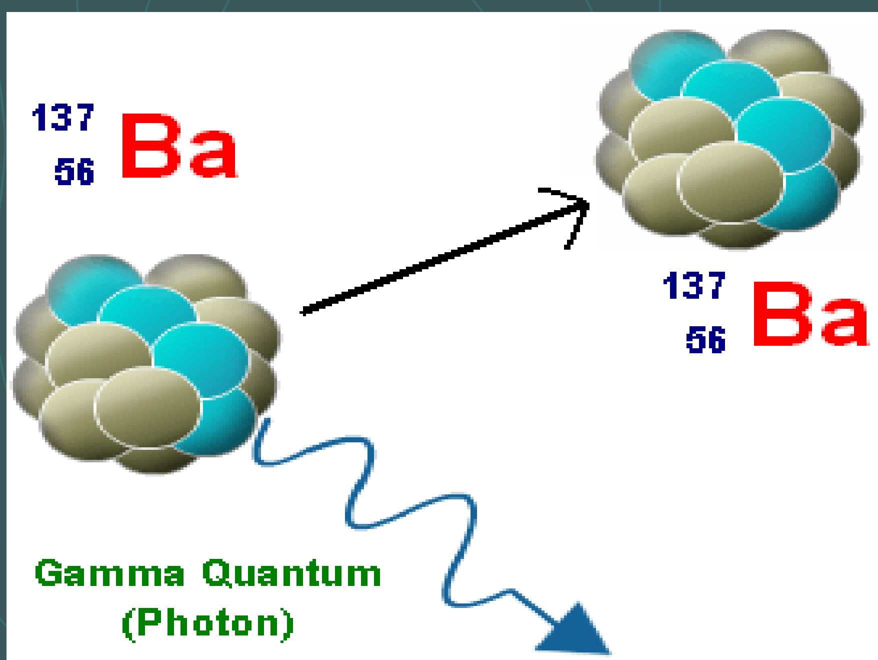


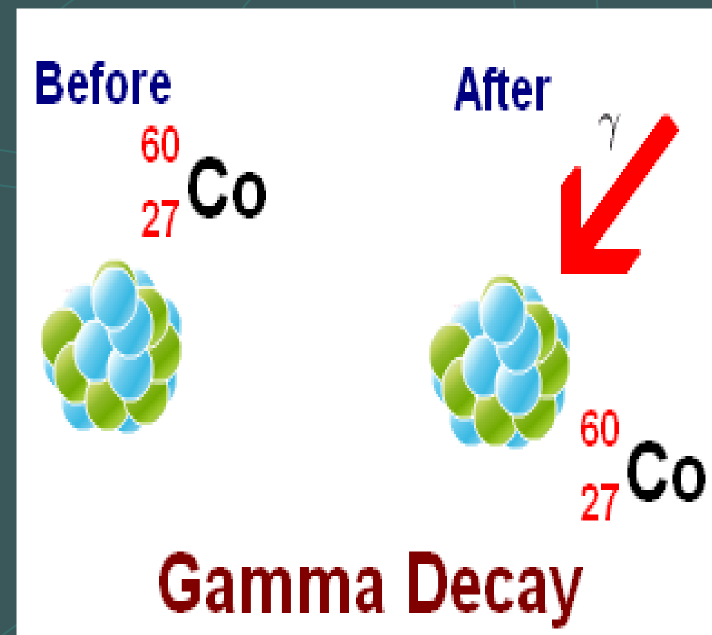
$$^{A}_{Z}X \to {}^{A}_{Z-1}Y + {}^{0}_{+1}e^+ + \nu_e$$

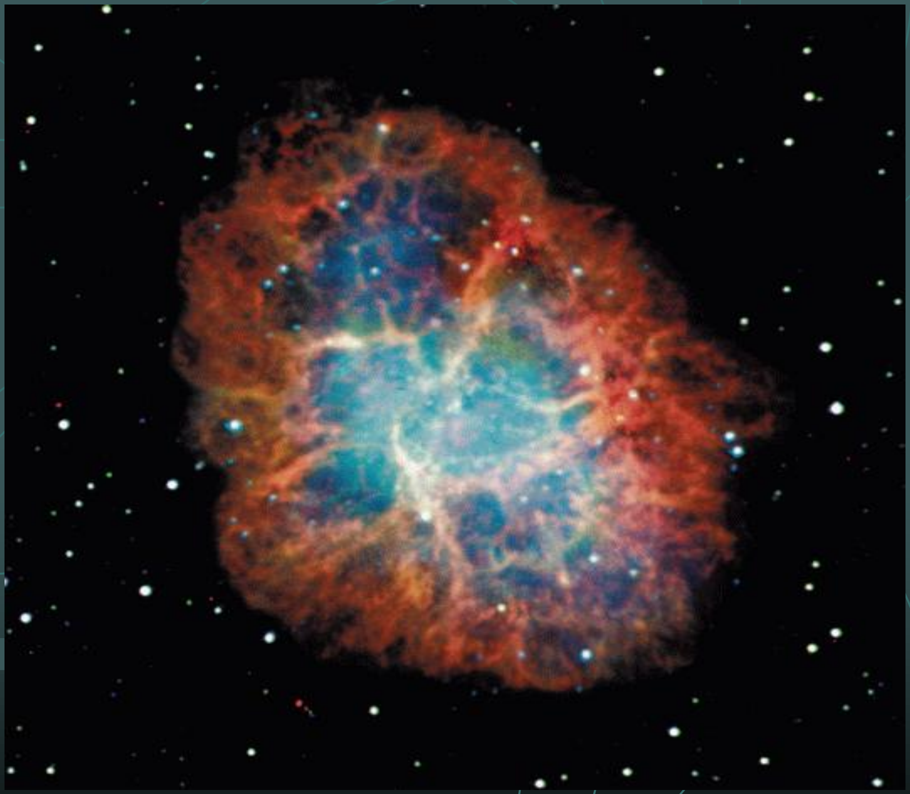
$$^{13}_{7}N \to {}^{13}_{6}C + {}^{0}_{+1}\beta + {}^{0}_{0}\nu$$

Gamma decay

$$^{A}_{Z}X \longrightarrow {}^{A}_{Z}X + {}^{0}_{0}\gamma$$







BACKGROUND RADIATION

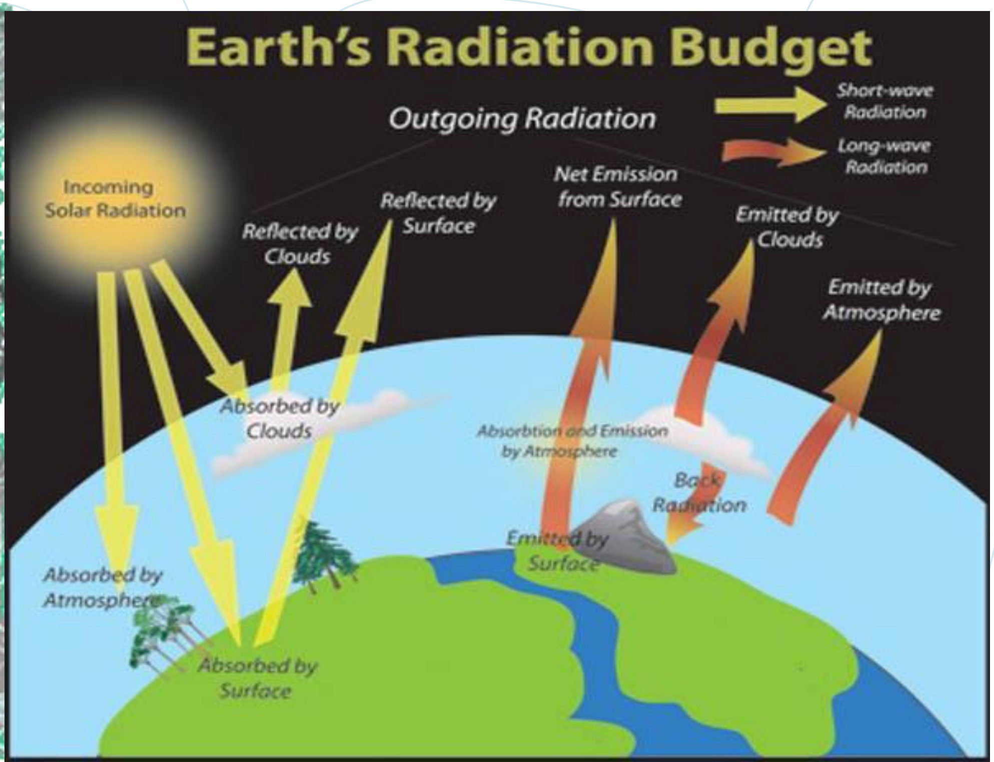
There are three major sources of background radiation:

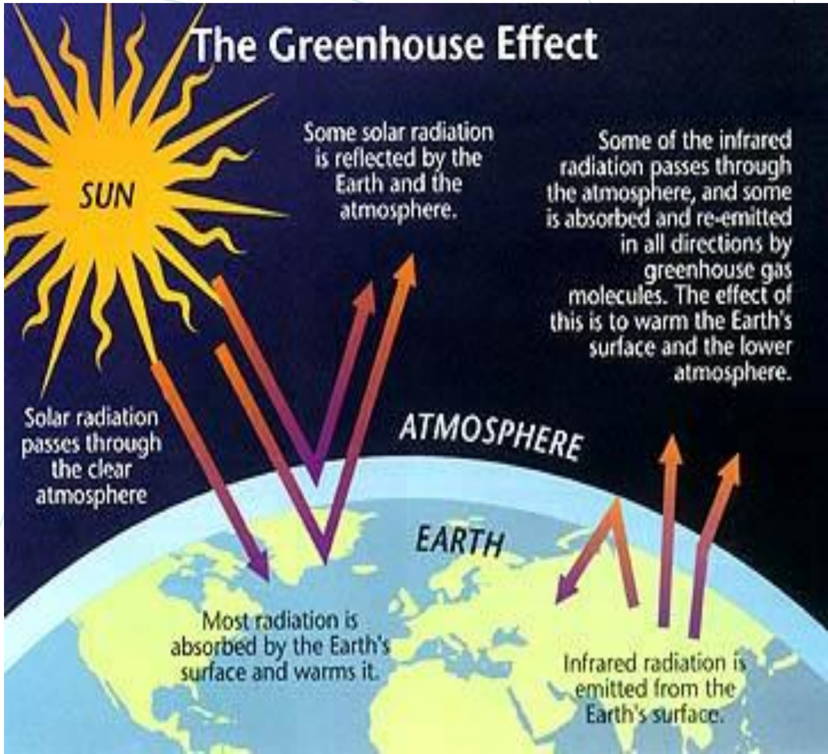
1. **Terrestrial radiation** due to the presence of naturally occurring radionuclides in **soil** and **earth**.
2. **Cosmic radiation** arising from **outer space**.
3. **Naturally** occurring radionuclides deposited **in the body**.

1. Terrestrial radiation

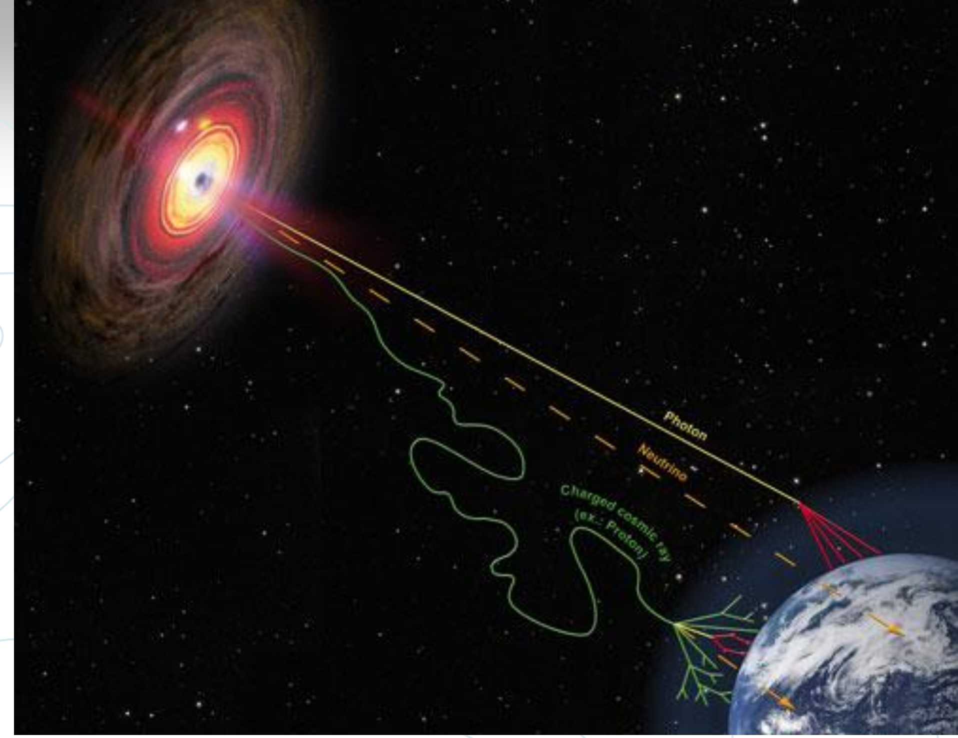
The rate at which a person is exposed to natural background radiation is a **function** of the **person's geographic location** and **living habits**

- There is evaluation that the average dose-equivalent rate from terrestrial sources is about **40 mrem/year**.





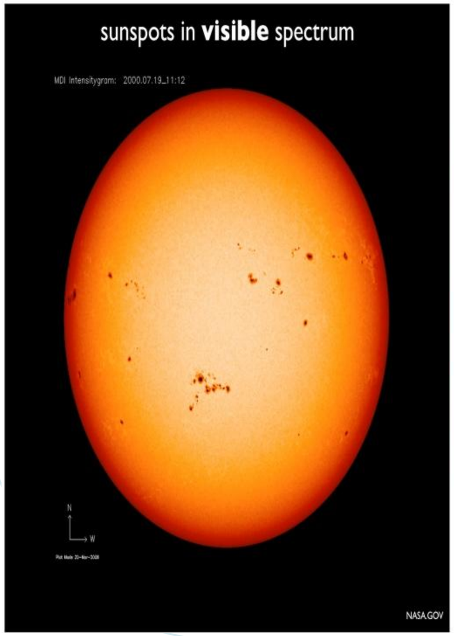
2. Cosmic radiation

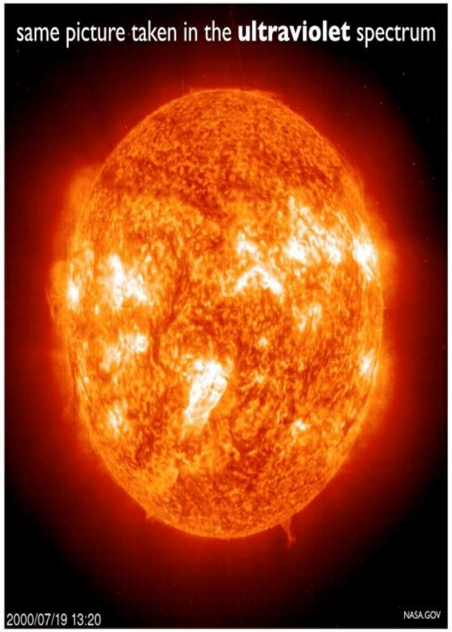


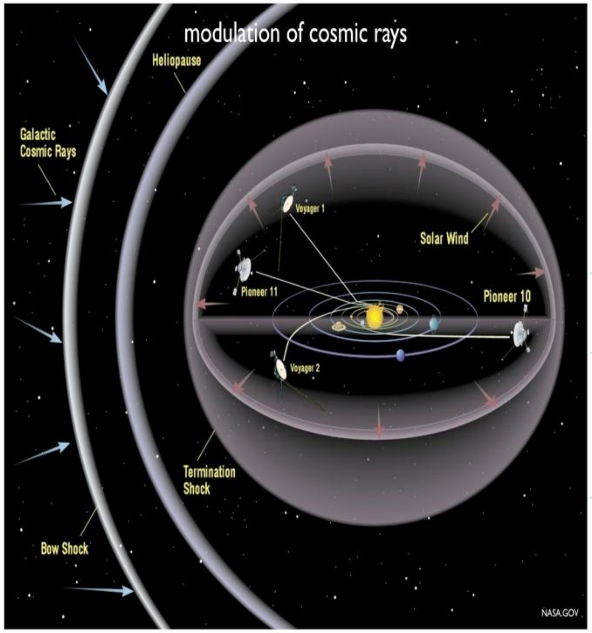
- **Cosmic radiation** includes **high-energy** primary particles arising from outer space that interact with **matter in the earth's atmosphere** and generate **less-energic secondary particles.**
- Thus, the atmosphere of the **earth** acts as a **shield** for high-energy radiation arising in outer space
- The **cosmic radiation** dose-equivalent rate increases with **altitude.**
- For example, the dose rate per year at 1800 m is about double that at sea levels

2. Cosmic radiation

- Cosmic radiation also interacts with the **earth's magnetic field**, which also **varies** from one region of the earth to another.
- The cosmic radiation dose rate varies due to **solar modulation**.







3. Naturally occurring radioisotopes deposited in the body

The primary sources of these radionuclides are the **atmosphere, food** or **water**.

- They include radioisotopes of **lead, polonium, radium, radon, potassium, carbon, hydrogen, uranium**, **thorium**, etc.
- The **averrage dose** rate depends upon the **organ** and varies from **24 mrem/year** to bone marrow to **60 mrem/year** to the bone surface.

Organ	mrem/year
Gonads	80
Bone marrow	80
GI tract	80
Lung	180 - 530

III. Basic Concepts of Dosimetry

- **1.Absorbed dose (D)** denotes the energy absorbed by some mass of the body.

$$D = \frac{d\overline{E}_{ab}}{dm}$$

- The unit for absorbed dose is **J/kg^{-1}** i.e. **the gray** (denoted by **Gy**).
- The former unit was the **rad**.

$$1\,Gy = 100\,rad$$

Louis Harold Gray

- 2. **Exposure** characterizes only **the ionizing power of radiation in the air** and it gives only indirect Information about radiation actually absorbed by the tissue.

$$X = Q/m$$

Exposure measures the electric charge (positive or negative) produced by electromagnetic radiation in a unit mass of air, at normal atmospheric conditions. Its unit is **C/kg (Coulomb)**. The earlier unit was the **Roentgen (R)**.

Charles-Augustin de Coulomb (1736-1806)

3.Dose equivalent (H) is used **in radiation protection**.
It is defined as the product of the absorbed dose (**D**) and **factors characteristic** of physical conditions influencing the biological effect.

$$H=DQN$$

where **Q** characterizes the **quality (type) of radiation** which is associated with the linear ion density.
All the other conditions (for example the dose rate) is included in the **N** factor.
The unit of **dose equivalent** is the **sievert** (denoted by **Sv**); Its value is 1, if the biological effect is the same as that produced by an absorbed x-ray dose of **1 Gy**.
The earlier unit was the **rem**. It was defined as the absorbed dose of ionizing radiation, which has the same biological effect as 1 rad x-ray.

1 Sv = 100 rem **1 rem=0,01 Sv**

- **The dose equivalent is used mainly if the organism is exposed to radiation of various effectivity and it is aimed to estimate the overall biological effect**. The expected effect can be measured as the sum of the dose equivalent (**He**).

Rolf Sievert in his laboratory, 1929.

Effective Dose (He)

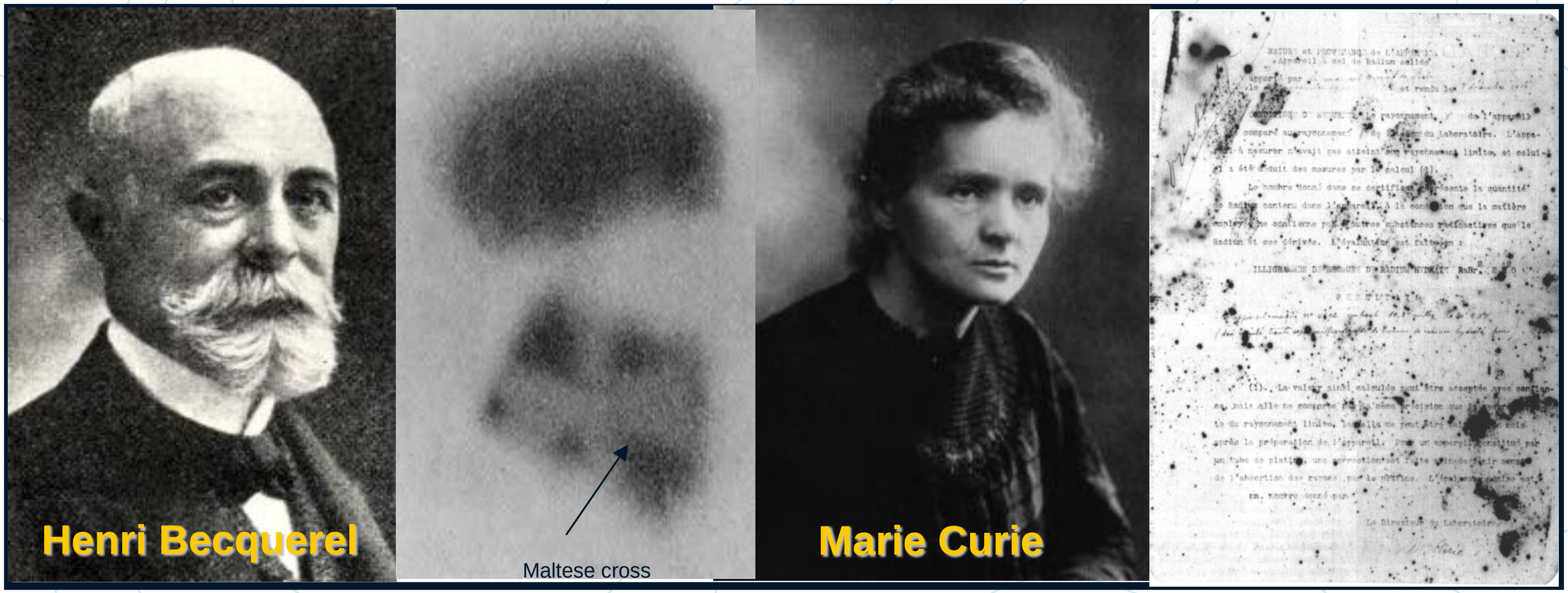
The stochastic effects of ionizing radiation on the whole body are measured with a unit called effective dose. When different organs and tissues are irradiated, the effect on whole body is calculated with the formula:

$$E\ (in\ Sv) = \sum_i H_i * W_{T,i}$$

Where **Hi** is the equivalent dose of organ or tissue “i” and **WTi** is the tissue weighting factor. The tissue weighting factor varies between 12% and 1% depending on the sensitivity of each organ to ionizing radiation. The effective dose is also measured in Sv.

Radioactivity $A = N/t$

Natural radioactivity was discovered by Becquerel, who was awarded the Nobel Prize in Physics in 1903 along with Marie and Pierre Curie "in recognition of the extraordinary services they have rendered by their joint researches on the radiation " phenomena"



The activity of a radioactive substance is characterized by the **decay rate**, which is the **decay number per second**. The **unit of activity** is the **Becquerel** (denoted by **Bq**). **1 Bq=1 decay/s**
Previously used unit of activity was **Curie** and is denoted by **Ci**.

Certain atoms are unstable and their nucleus disintegrates with emission of some radioactive atoms (**radioactive isotopes**). Numerous radioactive isotopes occur naturally, **mainly among the heavy atoms** of the end of the periodic table (i.g**. uranium, thorium, actinium**).Not only natural radioactive elements, but also more than a thousand **artificial radioactive isotopes** are known.

Z = A ≠

$^{1}_{1}H$ $^{2}_{1}H$ $^{3}_{1}H$

Hydrogen, deuterium, tritium

Z=1

^{12}C ^{14}C Z=6

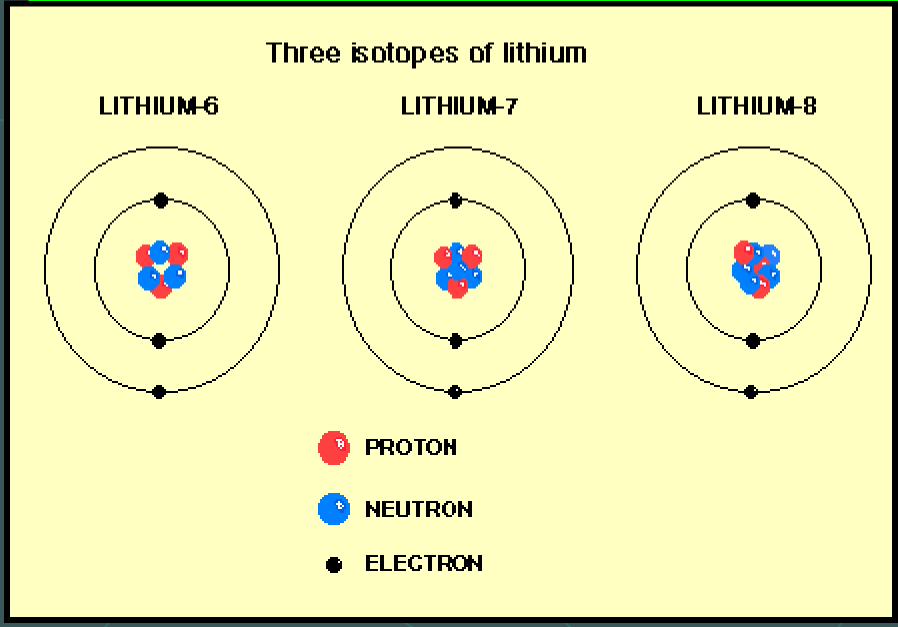
Uranium radioisotopes

^{234}U (99,275 %)

^{235}U (0,720 %)

^{238}U (0,005 %)

Z=92



Radioisotopes

BIOLOGICAL EFFECTS OF THE IONIZING RADIATION

- The **biological effect** of the radiation is mainly produced by the resulting **ionization** (and **excitation**) in the organism.

The **charged** particles cause ionization **directly**, while x**-rays (photons)** and **neutrons** do the same **indirectly**.

- There are **two main theories** (**direct and indirect**).

1. Target theory

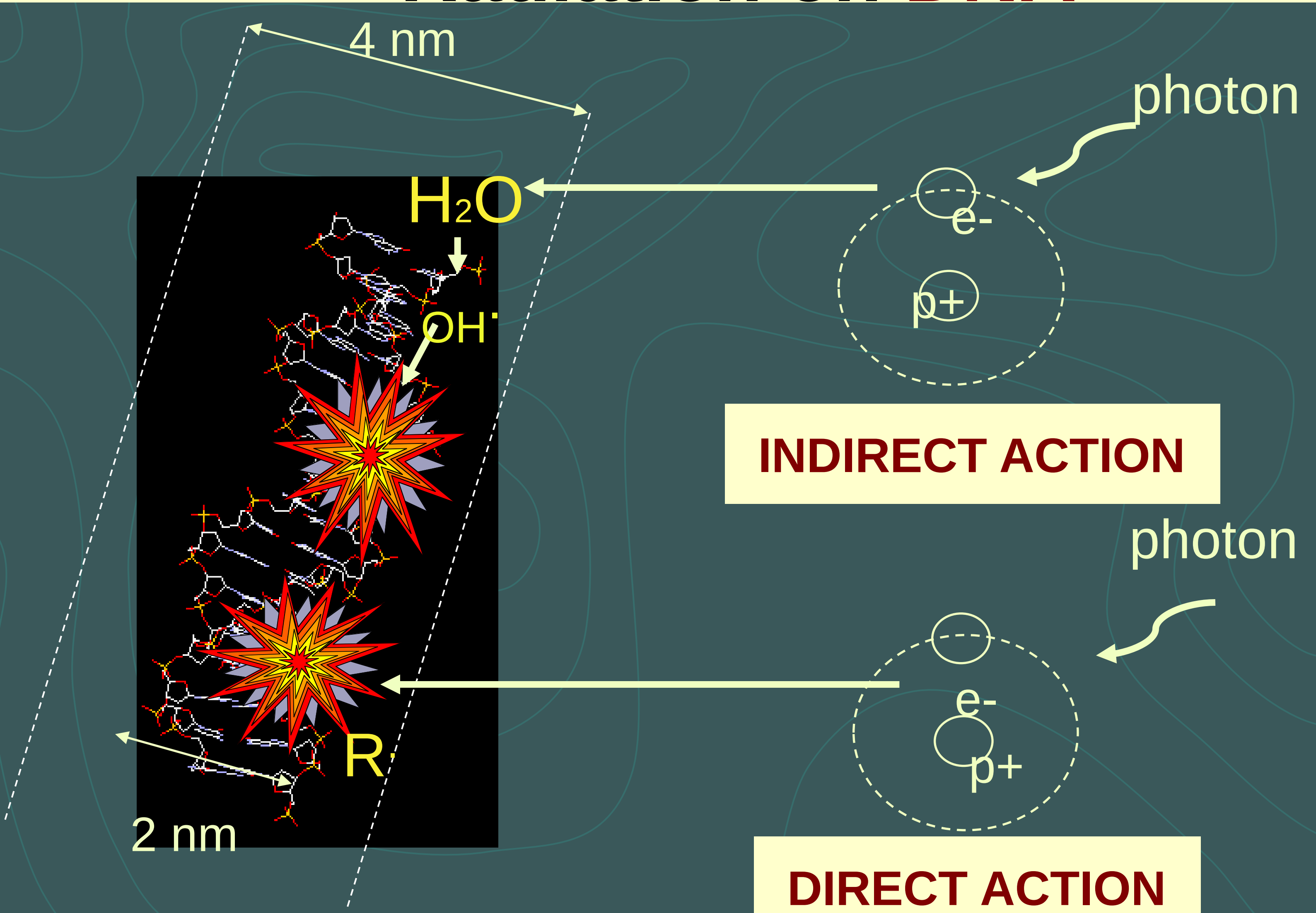
- According this concept, the effect of the ionizing radiation is a **result of ionizations and excitations in critical biologic macromolecules called targets** (**e.g. DNA**). So, this theory assumes that the inactivation of the molecules is caused by direct hit and therefore it is referred as "**direct action**" or "**direct effect**".
- Direct action is the dominant process whereby damage occurs **after high-LET** (linear energy transfer) **radiations**.

DNA is the primary target for biological damage!

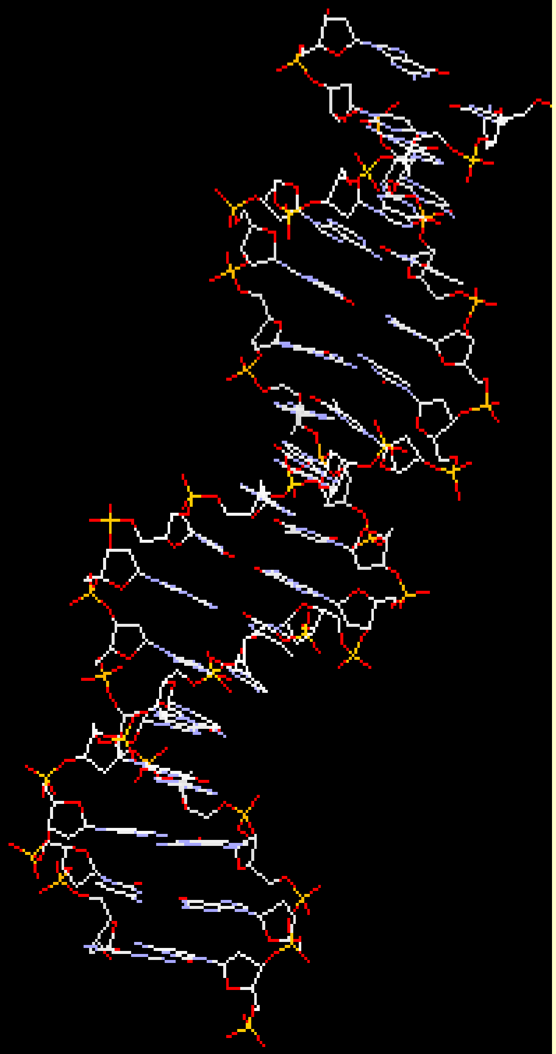
1. Target theory

- On the basis of target theory, **Sparrow** proposed a **new hypothesis** to explain the **radiosensitivity** of various species.
- According to this hypothesis, the radiosensitivity of a cell is **directly proportional** to its **interphase chromosomal** volume.
- This concept is consistent with his observations on several plant species.
- The validity of this hypothesis for mammalian species however remains to be established.

Direct and Indirect Action of Ionizing Radiation on DNA



DNA is the Primary, but not the only, Cellular Target for Radiation



- Microbeam irradiation of cell cytoplasm does not generally cause cell death, but irradiation of the nucleus does
- Radiation-induced chromosomal abnormalities correlate with cell death and carcinogenesis
- However, irradiation of the cytoplasm is not without biological consequences

2.Indirect theory (indirect effect)

- The target theory was found unable to explain cellular radiation injuries.
- Later it is developed the concept of **indirect effect** or **indirect radiation action** of the radiation.
- According this concept the critical site in the cell is damaged **by reactive oxygen species** (**ROS**) produced by ionizations.
- Since 80% of the cell consists of water indirect action primarily occurs **through ionization of water molecules.**
- **About 60% of DNA damage caused by x-rays is due to ROS.**
- **About 75% of the indirect action of radiation is due to hydroxyl radicals (OH•)**

3.Modern concepts of radiation injury

- When cells are irradiated primarily **ionization** and **free radicals produce damage**.

a) Free radicals

- Free radicals are neutral atoms or molecules having an unpaired electron.
- When x-ray interacts with water, **ion pair (HOH+, HOH-) is formed**. This occurs through the following reaction:

$$\mathbf{HOH} \xrightarrow{\text{Radiation}} \mathbf{HOH^{+} + e^{-}}$$

- The **free electron (e^-) is captured** by another water molecule, forming the **second ion**:

$$HOH + e^- \rightarrow HOH^-$$

- The two ions produced by the above reactions **are unstable** and rapidly **break down:**

$$HOH^+ \rightarrow H^+ + OH^\cdot$$

$$HOH^- \rightarrow OH^- + H^\cdot$$

- So, the **ultimate result** at the interaction of radiation with water is the formation of an **ion pair (H^+, OH^-)** and **free radicals ($H^\cdot$, $OH^\cdot$)**.
- **The consequences** of these products to the cell are **many and varied**. The ion pair and the radicals **may react as follow**:

The ions recombine and form a normal water molecule

$$H^{+} + OH^{-} = HOH$$

The effect in this case causes **no damage** to the cell.

The free radicals may also **recombine** as follow:

$$H^{\cdot} + H^{\cdot} \rightarrow H_2$$

$$OH^{\cdot} + OH^{\cdot} \rightarrow H_2O_2$$

When an organic molecule (**RH**) combines with free radical, an **organic free radical** (**R·**) is formed:

$RH + OH^{\cdot} \rightarrow R^{\cdot} + H_2O$ (**dehydrogenation by OH·**)

or similar reactions

$R_1H + H^{\cdot} \rightarrow R_1^{\cdot} + H_2$ (**dehydrogenation by H·**)

Two organic radicals may interact to formation of **new compound**:

$$R^{\cdot} + R^{\cdot}_{1} \rightarrow R : R_1 \text{ (new compound)}$$

- Because the free radicals contain unpaired electrons, they are very reactive and they can or **oxidize** or **reduce** the biological molecules within the cell.
- The free radicals **$OH^{\cdot}$** and **$HO_2^{\cdot}$** are **oxidizing agents**, whereas **$H^{\cdot}$** is a **reducing agent**.
- Free radicals can damage molecules such as **DNA**, **RNA**, and **proteins** as well as **membranes and** have been implicated in the **ethiology of cancer** as well as in **neurodegenerative** diseases.

b) Reactions in presence of an excess of oxygen

- **Oxygen is a powerful radiosensitizer**. If it is present during the irradiation it increases the biological effect of the radiation.
- Its main effect is probably connected with its **affinity for electrons**, **because the oxygen molecules contain two unpaired electrons**.
- A certain number of reactions with the radicals produced in the course of radiolysis of water occur **only in oxygenated solution**.

1. Capture of a radical $H^{\cdot}$ by a molecule of O_2

$$H^{\cdot} + O^{2} \rightarrow HO_2^{\cdot}$$

- The radical **$HO^{\cdot}_2$** is a less powerful oxidizing agent than **$OH^{\cdot}$**, but it has a larger lifespan and therefore it
- can diffuse further. The following reaction can take place:

$$HO_2^{\cdot} + HO_2^{\cdot} \rightarrow H_2O_2 + O_2$$

and

$$HO_2^{\cdot} + H^{\cdot} \rightarrow H_2O_2$$

2.Reaction of free (aqueous) electron with dissolved oxygen

$$O_2^- + H_2O \rightarrow HO_2^\cdot + OH^-$$

and

$$e^- + O^2 \rightarrow O_2^-$$

3.Chain reactions with dissolved organic radicals and formation of organic peroxides and hydroperoxides

Chain reactions:

$R^{\cdot} + O_2 \rightarrow ROO^{\cdot}$ (radical peroxide)

$ROO^{\cdot} + R_1H \rightarrow ROOH + R_1^{\cdot}$ (hydroperoxide)

$R_1 + O_2 \rightarrow R_1OO$ (etc)

$$ROO^{\cdot} + R_1^{\cdot} \rightarrow ROOR_1 \quad (peroxide)$$

Formation of peroxides:

- **Hydroperoxides and peroxides are toxic substances,** which accumulate in the course of the irradiation.
- In living mater an important action of oxygen is **peroxidation of unsaturated lipids (lipid peroxidation)**, which results in **structural and functional alteration of membranes**.

Free $OH^{\cdot}$ radicals generate organic radicals by:

- Addition $R + OH^{\cdot} \rightarrow {}^{\cdot}ROH$
- Hydrogen abstraction $RH + OH^{\cdot} \rightarrow R^{\cdot} + H_2O$
- Electron transfer $R + OH^{\cdot} \rightarrow R^{\cdot} + OH^{-}$

Where R is the organic moiety