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A Hypothesis on Biological Protection from Space Radiation Through the use of therapeutic gases

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Purpose & Content

Propose a method of biologically protecting from space radiation that would enable safe human presence in space for long durations.

1. IDENTIFY THE CHALLENGE OF SPACE RADIATION
2. RADIATION CHEMISTRY OF WATER & RADIATION BIOLOGY
   a. radiolysis process
      - *illustrate radiation's role in generating reactive species (radicals)*

   b. similarities between radiolysis & radiation biology
      - *show the role of radicals in causing damage*
      - *show the process for radiation induced damage*
3. HYPOTHESIS
      - *identify methods for protection*
      - *purpose desirable biochemical attributes for applying methods*
      - *examine implementation/application for space exploration*
4. SUMMARY

Radiation & The Space Environment Summary

- COMPOSITION: highly charged, high energy (HZE) nuclei
- NATURE: HZE creates the following character traits:
  - highly ionizing
  - penetrating
  - generates secondary radiation from interactions
  - typically low intensity
- IMPLICATIONS: nature & character causes:
  - difficulty shielding
  - biological damage harder to repair
  - uncertainty of biological risk from low intensities & unpredictability of true exposure
- CONCLUSION: need to understand & reduce risk

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Radiation Chemistry & Biology Overview

- RADIOLYSIS: dissociation of water by radiation
  - appears to have a fundamental role in how radiation causes biological damage
  - process outcome depends on net result of competing reactions & can be altered
- RADIATION DAMAGE: results from a chain of events
  - initiated by ionization
  - propagated by chemical reactions
  - cause molecular & biological transformations
  - ultimately manifest into medical diseases
- HYPOTHESIS: applying medical gases may increase natural resistance to radiation
  - possess chemical properties for effective radical scavenging & bond repair
  - capacity to induce biological processes which enhance & support natural resistance & repair mechanisms

Radiolysis: Dissociation of Water by Radiant Energy

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Energy Deposition

MECHANISMS

- ionization
- excitation

YIELDS

- ions (H_2O^+, sub-excitation electrons (e^-)
- excited molecules (H_2O^*)

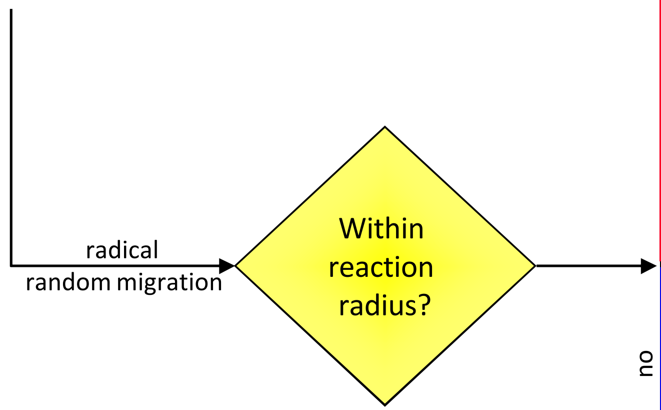
IF DECOMPOSITION CAUSES CORROSION IN MECHANICAL SYSTEMS, DOES IT ALSO CAUSE DAMAGE IN BIOLOGICAL SYSTEMS?

$\leq 10^{-15}$ sec

Free Radical Formation

MECHANISMS

1. ionization — $H_2O^+ + H_2O \rightarrow H_3O^+ + OH$
   charge neutralization — $H_3O^+ + e^- \rightarrow 2H + OH$
2. decomposition — $H_2O^* \rightarrow H + OH$ (10^{-14} sec)
   ionization — $H_2O^* \rightarrow H_2O^+ + e^-$
3. thermalization — $e^- \rightarrow e^-_{aq}$ (10^{-12} sec)

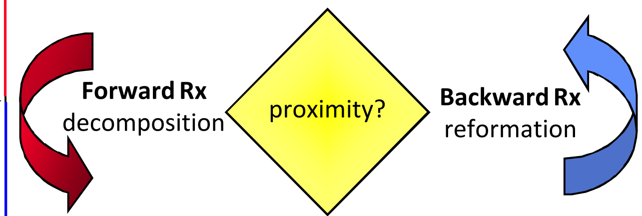


10^{-15} - 10^{-12} sec

Chemical Reactions

radical-radical rx.

- like—like: water decomposition
  - "forward reaction"
  - transformation into different molecular decomposition products (H_2O_2, O_2, H_2, etc.)
  - removes chemically active radicals
  - alters electrochemical nature of water
  - potential for (1) corrosion (2) pressure rise



- radical—molecular decomposition product
  - "backward reaction"
  - water reformation
  - reduces potential (1) corrosion (2) pressure rise.

Radicals diffuse into bulk of water

10^{-6} sec

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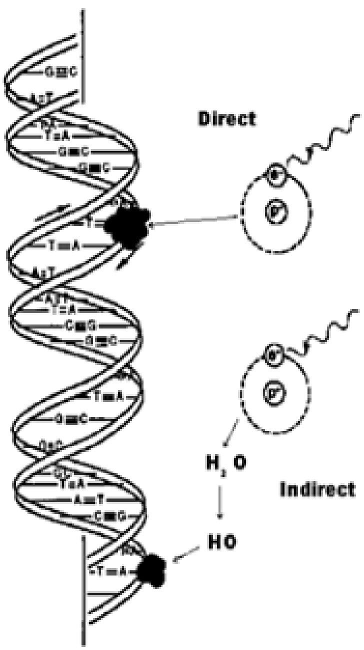
Is Radiolysis Related to Radiation Induced Damage?

Cellular Composition

- **80%—water**
- 5%—DNA
- 10-20%—RNA
- remainder—protein

Elkind, M.M., "*Introduction to The Biology of The Mammalian Cell*"", in Physical Mechanisms in Radiation Biology, USAEC conference 721001 Oct. 11-14 1972.

DNA Damage By Radiation



Effect of Radiolysis Products on DNA

IONS: little or no effect

- *"ions will probably have little effect as the DNA contains numerous ionizable positions at the phosphate group."*

EXCITED MOLECULES: may caused localized breaks

- *"Excited hydrolysis products may transfer the excitation energy to the DNA, leading to a localized break in the sugar-phosphate chain."*

MOLECULAR DECOMPOSITION PRODUCTS: highly reactive

- *"Free radicals like OH and oxidizing products like H_2O_2 are highly reactive and can add to unsaturated bonds which upsets the sensitive hydrogen-π-bonding and may break the bonding between two helices."*

THE ROLE OF RADIOLYSIS: dominating effect for large doses & dose rates

- *"The matrix effect considers the particle-water interaction in which ions, radicals and excited atoms are produced. This is the dominating effect at large radiation does and dose rates…Free radicals and oxidizing products interact directly with cell DNA, causing the DNA-strands to break.* ***One can state that at such high does the cell is simply poisoned by decomposition products and the whole organ may be destroyed."***

Chopping, G., Liljenzin, J., Rydberg, J., "*Radiochemistry and Nuclear Chemistry*", Butterworth-Heinemann, 3rd. ed., 2002.

Effect of Linear Energy Transfer (LET) on Radiolysis

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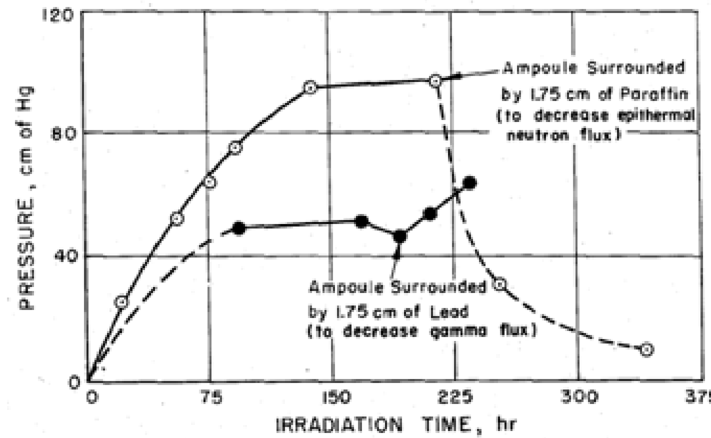
e⁻
E=40 keV
LET = 0.08 ev/Å

Dueteron
E=18 MeV
LET = 0.5 ev/Å

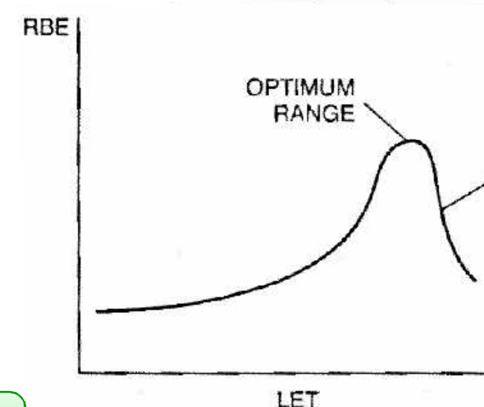
α particle (He ion)
E = 5.5 MeV
LET = 9 ev/Å

Allen, Augustine, O., *The Radiation Chemistry of Water and Aqueous Solutions*, D. Van Nostrand Company, Inc., Princeton, New Jersey, 1961. pp. 10-11.

Monson, H.O., "Water Decomposition," *The Reactor Handbook*, vol. 2, U.S. Atomic Energy Commission, U.S. Government Printing Office, Washington D.C., 1955, pp. 180.



Biological Analogue: Relative Biological Effectiveness (RBE)



$$RBE = \frac{D_x}{D}$$

(+) LET

- (+) localized energy deposition
  - (+) local radical production
    - (+) radical packing density within the tracks & spurs
      - (+) probability of radical-radical rx

(+) LET → water decomposition

Higher LET Radiation Could Have A More Biological Effect Because It Produces More Water Decomposition Products

Effect of Dose Rate on Radiolysis

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100 Gy
in 100 sec

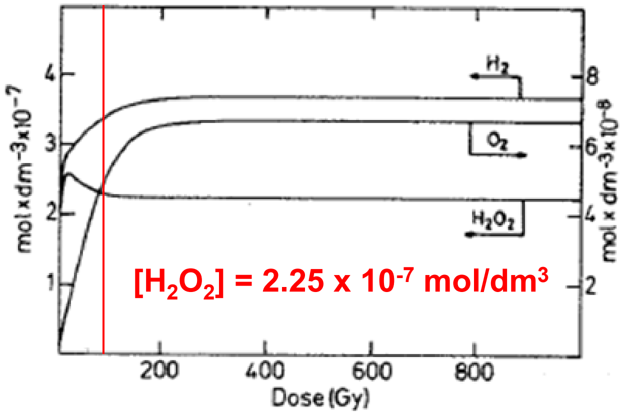


Fig. 1. Radiolytic products in air-free pure water. Dose rate: 1 Gy per second. Doses up to 1000 Gy.

100 Gy
in 1μs

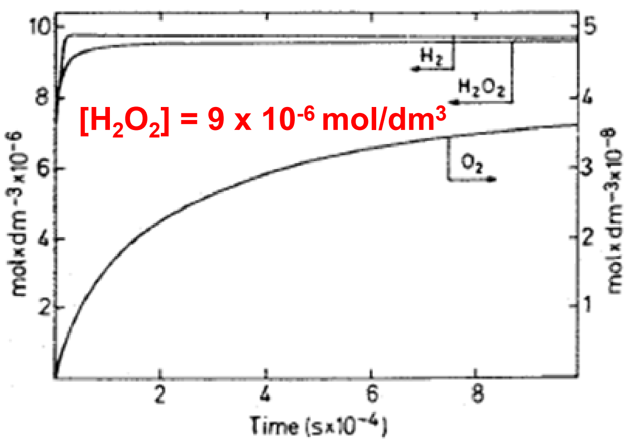


Fig. 2. Formation of radiolytic products in air-free pure wa following a 100 Gy electron pulse delivered in 1×10^{-6} secon

Bjergbakke, E., Draganic, Z. D., Sehested, K., and Draganic, I.G., "Radiolytic Products in Waters Part I: Computer Simulation of Some Radiolytic Processes in the Laboratory," in *Radiochimica Acta*, vol. 48, Munchen, 1989, pp. 66.

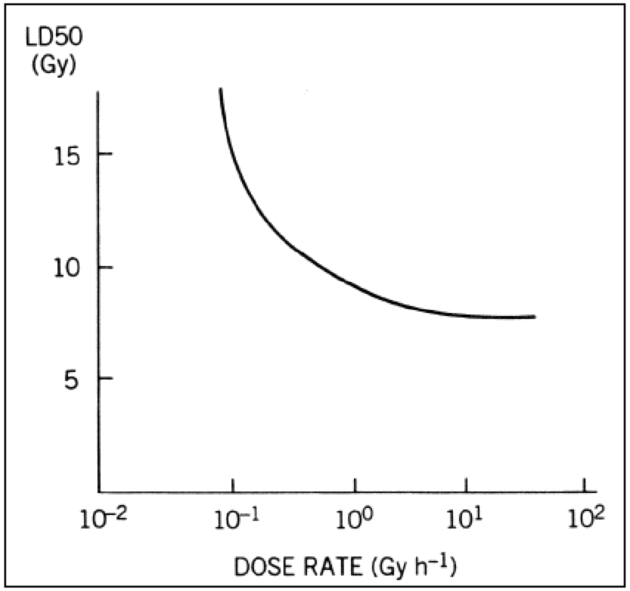
(+) dose rate

- (+) frequency of energy deposition
  - (+) number of particle tracks
    - (+) over lapping of particle tracks
      - (+) probability of radical-radical rx

(+) dose rate → water decomposition

Higher Dose Rates Could Be More Lethal Because Higher Dose Rates Produce More Water Decomposition Products

Biological Analogue of Dose Rate Effect



Turner, James E., *Atoms, Radiation, and Radiation Protection*. John Wiley & Sons, Inc., 2nd ed., 1995. pp. 421-422.

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Effect of Impurities on Radiolysis

- SUSPENDED PARTICLES: little or no effect
  - *"…in general, the presence of suspended or colloidal impurities does not result in increased decomposition rates or equilibrium concentrations of decomposition products."*

    Monson, H.O., "Water Decomposition," *The Reactor Handbook*, vol. 2, U.S. Atomic Energy Commission, U.S. Government Printing Office, Washington D.C., 1955, pp. 184.

- DISSOLVED IONIC IMPURITIES: promotes water reformation or decomposition depending on type
  - *"…in general, the presence of ionic impurities results in increased decomposition rates and equilibrium concentrations of decomposition products, some impurities producing slight increase and other producing very large increases."*

    Monson, H.O., "Water Decomposition," *The Reactor Handbook*, vol. 2, U.S. Atomic Energy Commission, U.S. Government Printing Office, Washington D.C., 1955, pp. 182.

  - *"At low temperatures, some ionic impurities such as KBr, KI, and CuSO4 may produce partial pressures of 1,500 psi under radiation conditions that produce only a partial pressure of less than 10 psi for relatively pure water. At high temperature, i.e., above 400°F, exploratory work has shown that certain impurities strongly catalyze the backward reaction. Such impurities are copper, rhodium, palladium, platinum, silver, and iodine; and tin, iron, and titanium to a lesser extent."*

    Calkins, Vincent P., "Radiation Damage To Liquids and Organic Materials," *Nuclear Engineering Handbook*, edited by Etherington, Harold, McGraw-Hill Book Company, Inc., New York, 1958, pp.10-132.

- BIOLOGICAL ANALOG: chemical modifiers
  - *"A number of radiosensitizing chemicals and drugs are known. Some sensitize hypoxic cells, but have little or no effect on normally aerated cells. Other agents known as radioprotectors reduce biological effectiveness….which* ***scavenge free radicals****."*

    Turner, James E., *Atoms, Radiation, and Radiation Protection*. John Wiley & Sons, Inc., 2nd ed., 1995. pp. 421-422.

INTERFERING WITH CHEMICAL REACTIONS AFFECTS THE BALANCE OF WATER DECOMPOSITION VS. REFORMATION

Effect of Dissolved Gas Impurities on Radiolysis

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Dissolved Gases Can Alter The Chemical Reaction Scheme To Affect the Balance Between Water Decomposition vs. Reformation

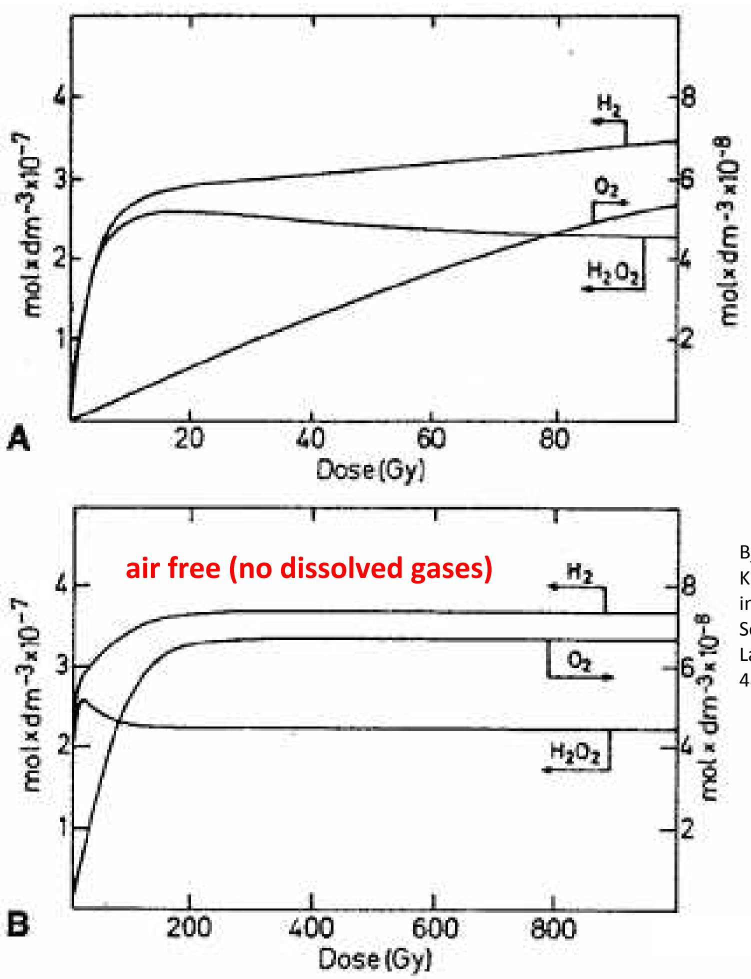

Fig. 1. Radiolytic products in air-free pure water. Dose rate: 1 Gy per second. Part A: Doses up to 100 Gy. Part B: Doses up to 1000 Gy.

Bjergbakke, E., Draganic, Z. D., Sehested, K., and Draganic, I.G., "Radiolytic Products in Waters Part I: Computer Simulation of Some Radiolytic Processes in the Laboratory," in *Radiochimica Acta*, vol. 48, Munchen, 1989, pp. 66.

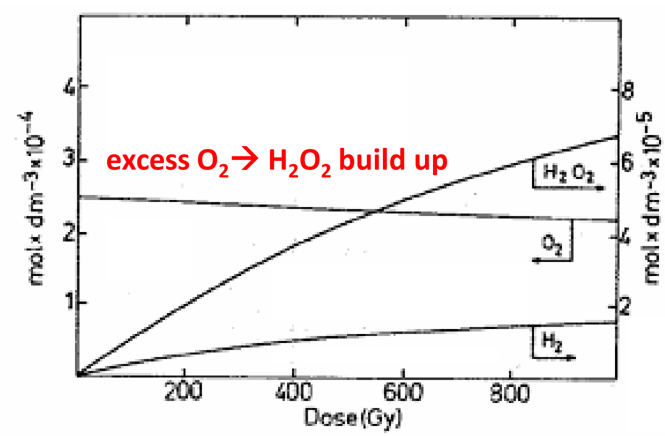

Fig. 4. Oxygen depletion and build-up of hydrogen and hydrogen peroxide in air-saturated water. Dose rate: 1 Gy per second.

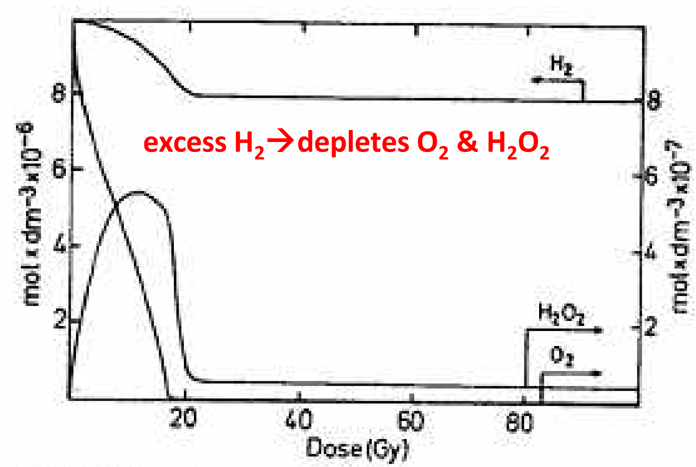

Fig. 5. Depletion of oxygen by irradiation in the presence of surplus hydrogen. Dose rate: 1 Gy per second.

Biological Analogue for the Effect of Dissolved Gases

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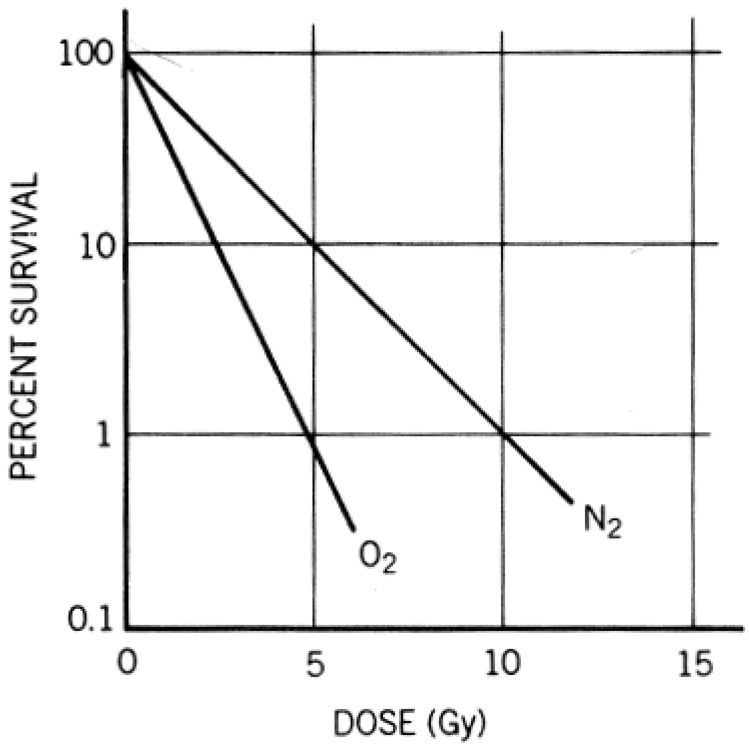
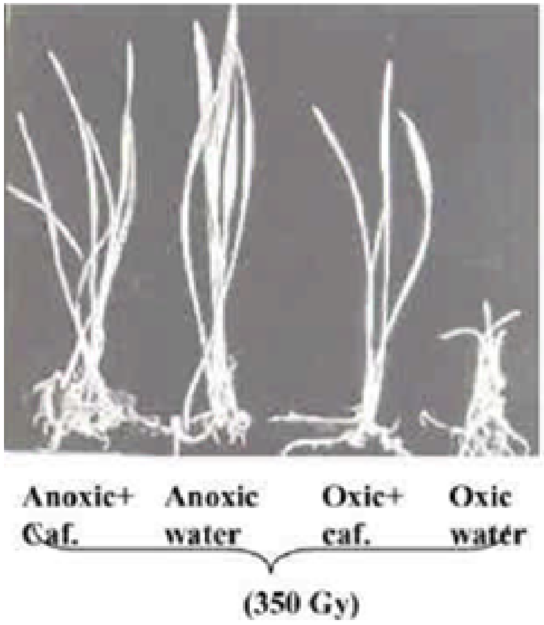
O_2 Radiosensitizing Effect Could Be A Result of Water Decomposition
N_2 Desensitizing Effect Could Be From Hypoxia Which Reduces O_2 Concentrations & Thus Water Decomposition

Radiosensitivity Effect of O_2



Turner, James E., *Atoms, Radiation, and Radiation Protection*. John Wiley & Sons, Inc., 2nd ed., 1995. pp. 421-422.

Effect of Dissolved Oxygen



Kesavan, P.C., "Oxygen effect in radiation biology: Caffeine and serendipity" Current Science, Vo. 89, No.2 25 July 2005. pp. 318-328.

What Would the Biological Effect of H_2 Be?

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Radical Scavenging in Nuclear Reactors

Ionic Impurities

$OH + Br^- \rightarrow Br + OH^-$

$H + Br \rightarrow Br^- + H^+$

$OH + Cu^+ \rightarrow Cu^{++} + OH^-$

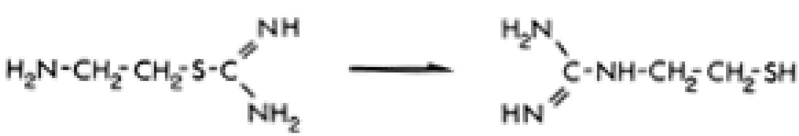
$H + Cu^{++} \rightarrow Cu^+ + H^+$

Ionic Radical Scavengers Neutralized But Are Consumed & Produce Ionic Byproducts

Biological Analog: Radioprotectors

Cysteine

Cysteamine (MEA)



S, 2-Aminoethylisothiuronium-Br-HBr (AET)

2-Mercaptoethylguanidine-HBr (MEG)

Could H_2 Be a Highly Effective Radioprotector With Less Poisonous Byproducts Permitting Administration of Higher Dosage?

Hydrogen Water Chemistry (HWC)

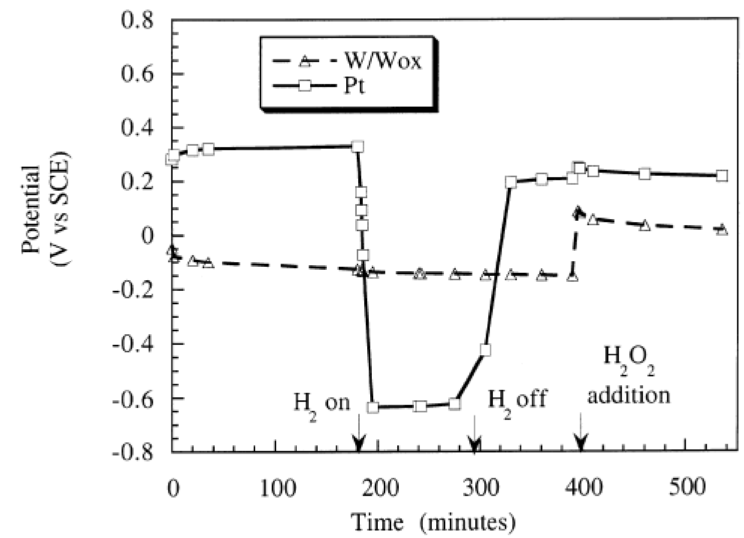
$2H_2 + OH \rightarrow H_2O + H$

$H + H_2O_2 \rightarrow H_2O + OH$

$2H_2 + O_2 \rightarrow 2H_2O$

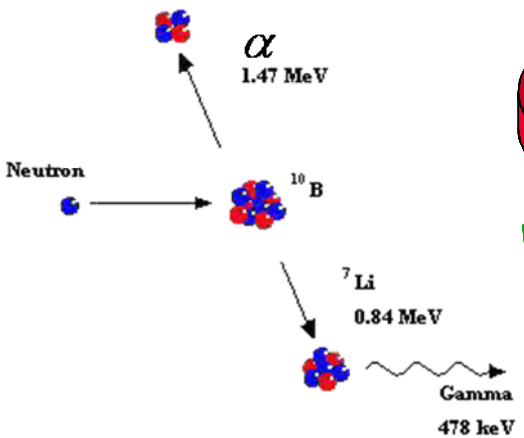
H_2 Scavengers Neutralize But No Scavenger Loss & Produce Water Byproducts

Reduction of Corrosion Potential in a Mechanical System

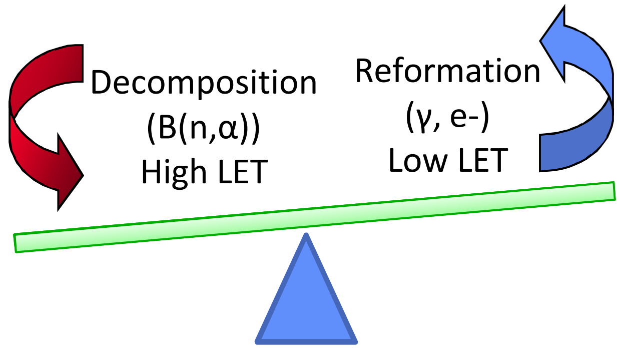


Lillard, R.S., Pile, D.L., Butt, D.P., "The Corrosion of Materials in Water Irradiated by 800 MeV Protons," *Journal of Nuclear Materials*, **278**, 200, pp. 277-289.

Competing Processes in Nuclear Systems



Hart, E.J., McDonell, W.R., and Gordon, S., "The Decomposition of Light and Heavy Water Boric Acid Solutions by Nuclear Reactor Radiations," in proceedings of *International Conference on the Peaceful Uses of Atomic Energy*, Geneva 1955, P/839, Vol. 7, United Nations, New York, 1956, pp. 594.



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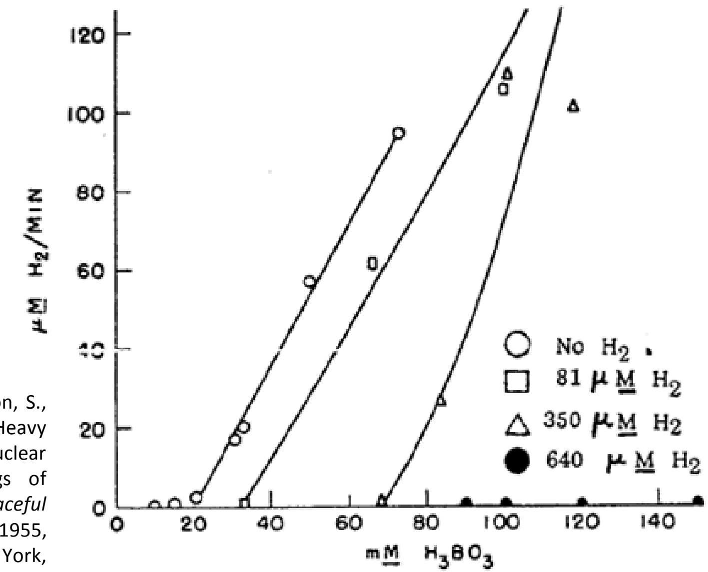
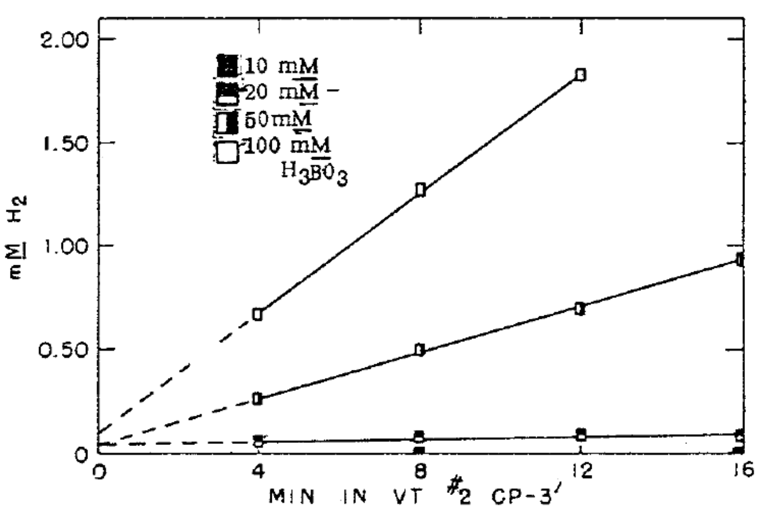
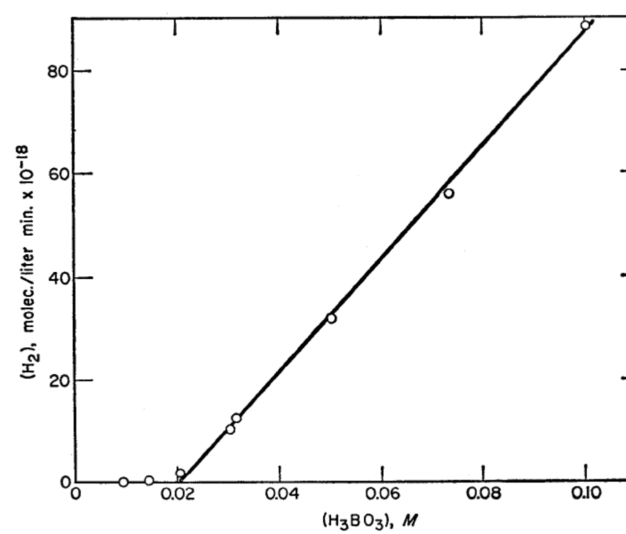




RADICAL SCAVENGERS CAN ENHANCE THE SCAVENGING CAPACITY OF THE SYSTEM CHANGING THE CRITICAL POINT WHERE THE DECOMPOSITION PROCESS DOMINATES

Allen, Augustine, O., *The Radiation Chemistry of Water and Aqueous Solutions*, D. Van Nostrand Company, Inc., Princeton, New Jersey, 1961. pp. 95.



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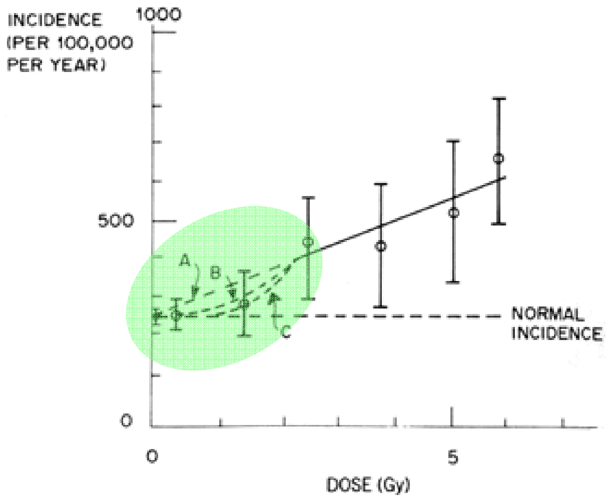
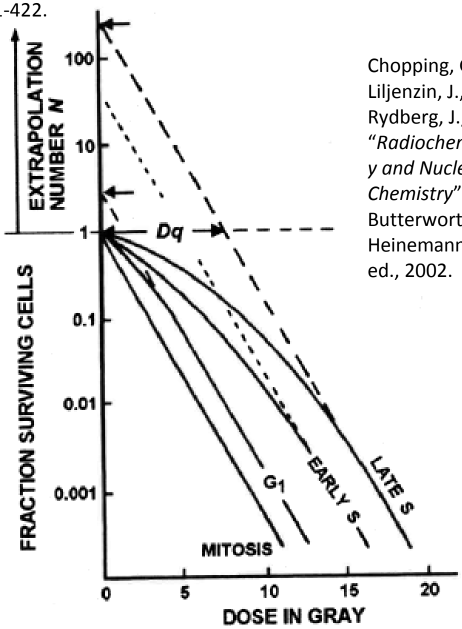
Biological Analogue of Competing Processes

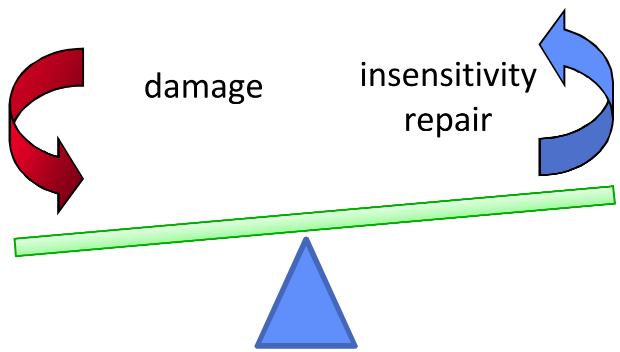


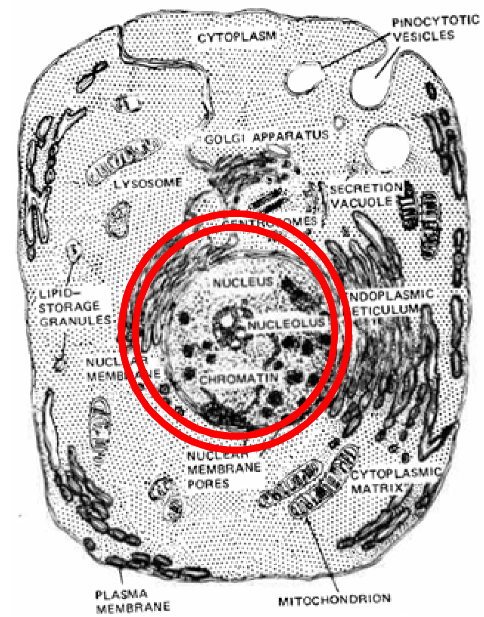
Turner, James E., *Atoms, Radiation, and Radiation Protection*. John Wiley & Sons, Inc., 2nd ed., 1995. pp. 421-422.



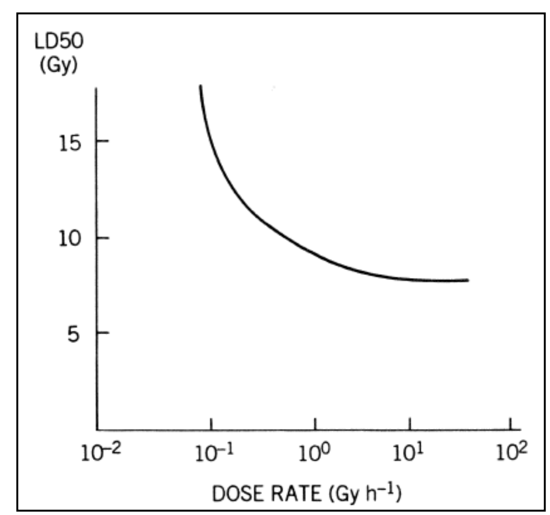
Chopping, G., Liljenzin, J., Rydberg, J., "*Radiochemistry and Nuclear Chemistry*", Butterworth-Heinemann, 3rd. ed., 2002.

IT APPEARS THAT THERE ARE BIOLOGICALLY THERE ARE ALSO COMPETING PROCESS BETWEEN REPAIR VS. DAMAGE





Elkind, M.M., "*Introduction to The Biology of The Mammalian Cell*"", in Physical Mechanisms in Radiation Biology, USAEC conference 721001 Oct. 11-14 1972.



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How Does Biological Repair Work & Can It be Supported or Enhanced?

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- Multiple mechanisms but the details are unknown
  - *"The cell is protected by different DNA repair mechanism which try to restore the damage. We don't know the details, except when the repair goes wrong (e.g. a replacement of a lost nucleotide by a 'wrong" base pair, etc.)…"*

    Chopping, G., Liljenzin, J., Rydberg, J., "*Radiochemistry and Nuclear Chemistry*", Butterworth-Heinemann, 3rd. ed., 2002.

- More effective in vivo
  - *"The repair system is believed to be more effective in a living organism, where the cells are in continuous exchange with the surrounding cells and body fluids, than in the tissue samples often studied in the laboratory…"*

    Chopping, G., Liljenzin, J., Rydberg, J., "*Radiochemistry and Nuclear Chemistry*", Butterworth-Heinemann, 3rd. ed., 2002.

- Related to scavenging so can be supported/enhanced similar to the "competing reactions" scenario
  - ***"The cell contains natural radical scavengers. As long as they are in excess of the radiolysis products, the DNA may be protected. When the products exceed the amount of scavengers, radiation damage and cancer induction may occur. In principle, there could thus be a threshold dose for radiation damage, at which the free radicals formed exceed the capacity of scavenging.*** *The scavenging capacity may differ from individual to individual depending on his/her physical condition."*

    Chopping, G., Liljenzin, J., Rydberg, J., "*Radiochemistry and Nuclear Chemistry*", Butterworth-Heinemann, 3rd. ed., 2002.

  - *"Also,* ***chemical protectors can be introduced into the system which will compete successfully for the OH and H radicals formed. This will reduce the indirect effect***"

    Casarett, A.P., "*Radiation Biology*", Prentice-hall, Inc., New Jersey, 1968.

Protection Through Enhancement of Scavenging Capacity

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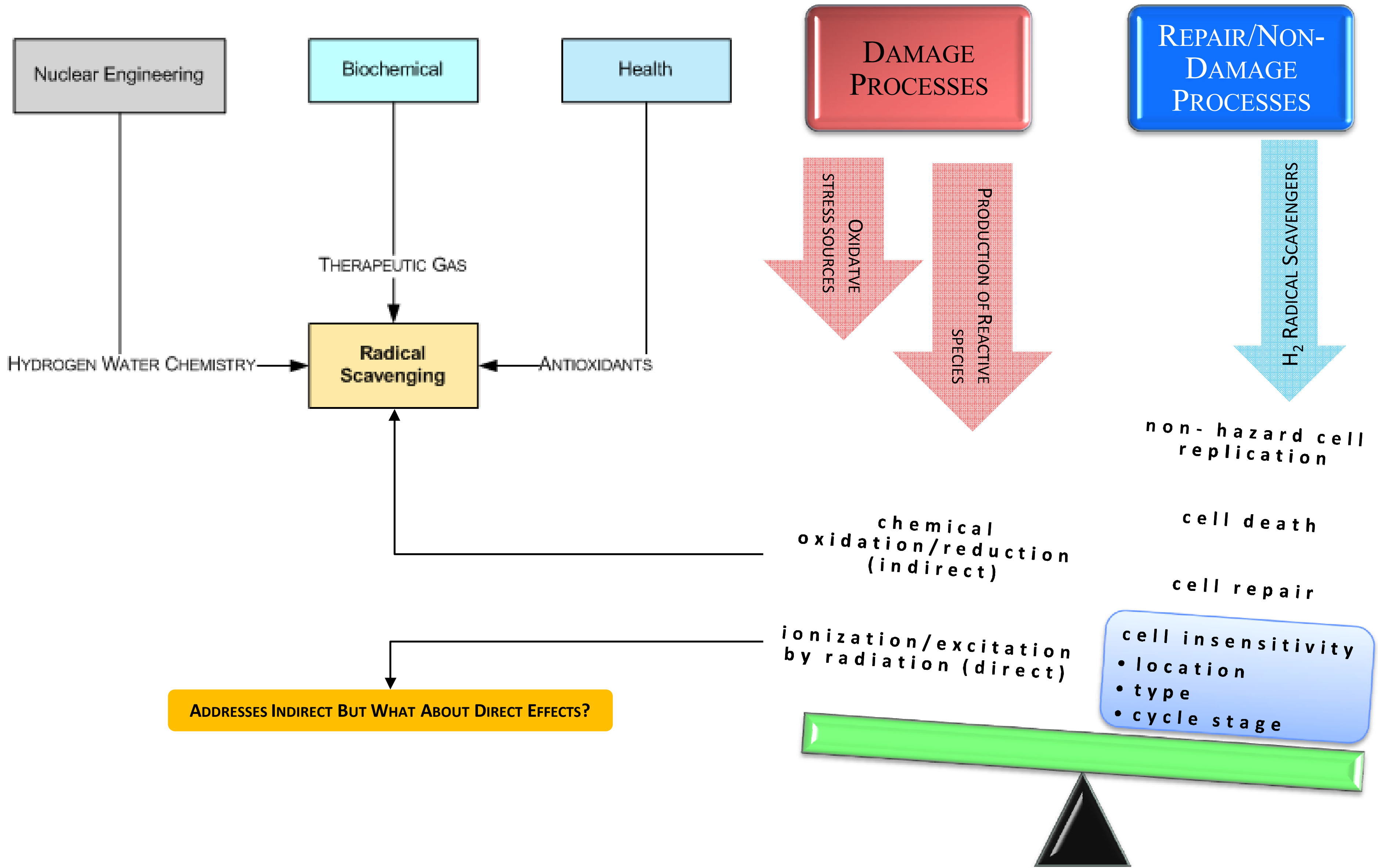

Relative Contribution of Direct & Indirect Damage Mechanisms

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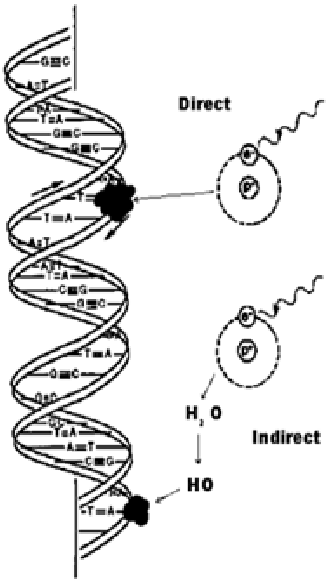

1. indirect ionization may dominate for DNA damage
   - *"… an excess of water in dilute solutions of DNA, however, the indirect effect predominates and double chain breaks are produced…."*

2. direct ionization has negligible contribution for dilute solutions with small molecules
   - *"Normally, in dilute solutions of small molecules, the radiation dose that will cause a considerable proportion of the solute to react with free radicals will only suffice to ionize directly a negligible proportion of the solute molecules. Thus, the direct action of the radiation on the solute molecules is small."*

3. direct ionization contribution increases when mobility is inhibited (e.g solid, frozen solution, etc.) or large molecules in solution
   - *"However, the fraction of the total reactions which are related to the direct effect can be increased in several ways. If material is irradiated dry, the water molecules have been removed so that there will be only direct interactions with the molecules of the material. If a solution is frozen, the mobility of the radicals which are produced in the water molecules is decreased. This will decrease the possibility of indirect action and result in a greater proportion of the interactions being of the direct type."*
   - *"The dose required to produce a chemical change in a given proportion of the molecules of a substance, by **direct action, is inversely proportional to the molecular weight of the substance** assuming that the ionic yield is constant. (the larger molecules are more likely to be in the path of the radiation) ….*
   - ***The direct effect is not very important in consideration of simple chemical systems, but is of importance in macromolecular and biological systems because of the presence of many large molecules**."*

Casarett, A.P., "*Radiation Biology*", Prentice-hall, Inc., New Jersey, 1968.

CAN SCAVENGERS AID IN REPAIRING DAMAGE FROM THE DIRECT EFFECT?

What is Radiation Damage?

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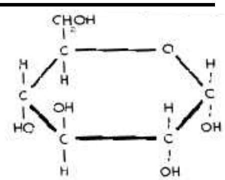
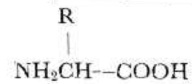
Biologically Important Molecules

- Proteins
- Enzymes
- Nucleic Acids
- Lipids
- Carbohydrates

LIPIDS

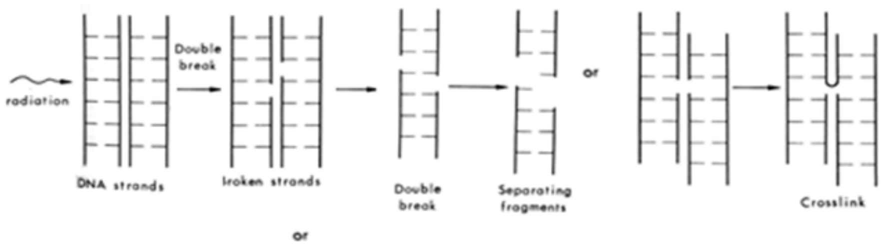


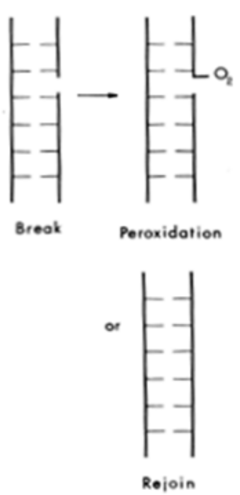
CARBOHYDRATES

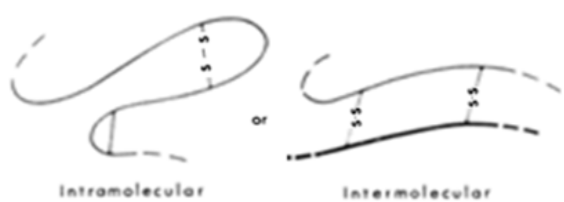


PROTEINS

DNA Changes from Radiation







"Cross linking process is thought to be primarily a direct effect of the radiation, while double-chain breaks are largely indirect."

Casarett, A.P., "*Radiation Biology*", Prentice-hall, Inc., New Jersey, 1968.

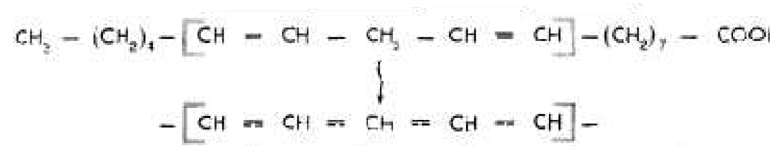
Chemical Changes from Radiation

Appears to predominately involve loss of H atom

- *"when aqueous organic solution is irradiated, the usual "indirect" reaction on the organic molecule is the **removal of either a H atom** or an entire radical group (such as the –CH_3 "methyl" group) from the molecule"*
- *"saturated hydrocarbons probably undergo **a hydrogen extraction** & are converted into alcohols in a two step process"*
- *"acetic acid most **frequently loses a hydrogen atom…**"*
- *"energy which is absorbed any place in the molecule can be transmitted down the molecular chain to the weakest bond…. **They hydrogen bonds are among the weakest in the molecule and thus, are the first to be broken by radiation.**"*

Casarett, A.P., "*Radiation Biology*", Prentice-hall, Inc., New Jersey, 1968.

1. Loss of H atom in Lipid leading to resonant structure
2. Enables formation of organic peroxide in presence of oxygen



Perhaps H Atom Donation Could Prevent DNA Mutation & Facilitate Repair From Direct Ionization

Progression of Radiation Induced Damage

Chemical Changes

- ionization breaks bonds
- loss of H atom or radical group (--CH_3)
- creates chemically reactive organic radicals

Molecular Transformation

- reactions enable cross linking, peroxidation, etc.
- alter molecular structure

Macro Molecular Changes

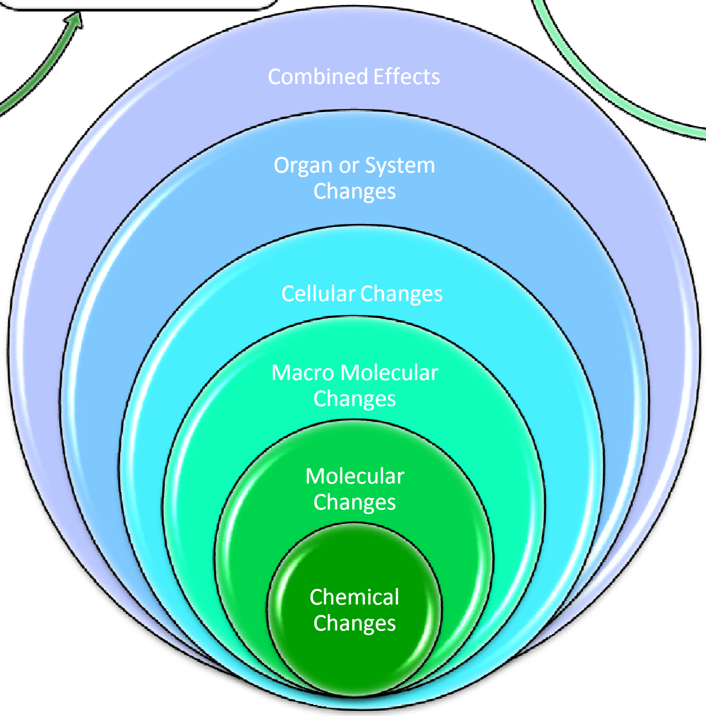
- new properties as a result of structural changes
- biochemical functionality altered

Cellular Changes

- increased membrane permeability
- chromosome aberrations
- chemical change in DNA molecule

Tissue & Organ System Changes

- decreased concentration of all cellular elements
- ulcers & erosion potentiating infection
- necrosis
- hemorrhaging
- etc.



1. **Biological Damage Results From A Chain of Events That Begins with Chemical Changes Leading to Biological Changes.**
2. **Protection Might Be Provided By Interrupting the Damage Process Early In The Chain of Events**

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Biochemical Enhancement & Protection

"A number of radiosensitizing chemicals and drugs are known. Some sensitize hypoxic cells, but have little or no effect on normally aerated cells. Other agents known as radioprotectors reduce biological effectiveness….which scavenge free radicals. Still other chemicals modifiers have little effect on cell killing but substantially enhance some multistep processes, such as oncogenic cell transformation. For carcinogensis or transformation, such biological promoters can dwarf the effects of physical factors such as LET and dose rate, on dose-response relationships"

Turner, James E., *Atoms, Radiation, and Radiation Protection*. John Wiley & Sons, Inc., 2nd ed., 1995. pp. 421-422.

CHEMICAL PROTECTION

1. Increase Radical Scavenging Capacity
2. Inhibit Radical Production (e.g. reduce oxygen concentrations via tissue hypoxia)
   - ➢ decrease blood flow through vasoconstrictor
   - ➢ lower blood pressure through vasodilator
   - ➢ impair oxygen transport (e.g. CO)
3. Repair Biological Radicals
   - ➢ H atom donation

BIOLOGICAL PROTECTION

1. Increase Time for Natural Repair Mechanism
   - ➢ delay cell in radiation resistant phase of cell cycle through interference with mitosis
   - ➢ anti-apoptosis (prior to mitosis of mutation)
2. Management of Biological Response to Insult
   - ➢ anti-inflammatory
   - ➢ alter metabolic rates
   - ➢ destroy mutation (trigger apoptosis)

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Evolution of Radiation Damage & Purposed Protection Strategies

Inhibition of Direct Ionization

natural cell insensitivity (target type, cell type, cell cycle stage)

natural repair mechanism

increase time for natural repair mechanism

Inhibition of Indirect Ionization

natural radical scavenging

antioxidant radical scavenging

decrease radical generation

Correction of Mutations

natural DNA repair mechanisms

apoptosis (cell death) / non-harmful replication

recombinant DNA technology

triggering of apoptosis of mutated cells

H donation from H_2 scavenger

Management of Biological Response

Anti-inflammatory

Immune System Stimulation / Regulation

Treatment of Manifestations

radiotherapy

surgery

medical treatments

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energy deposition
$\leq 10^{-15}$ sec

free radical formation
$10^{-15} - 10^{-12}$ sec

chemical reactions
$10^{-12} - 10^{-6}$ sec

radical reactions w/ biological molecules complete
$\leq 10^{-3}$ sec

biochemical changes
≤ 1 sec

cell division affected
minutes

gastrointestinal & central nervous systems changes
days

lung fibrosis
weeks

cataracts, cancer, & genetic effects in offspring
years

RADIOLYSIS

RADIATION CHEMISTRY

RADIATION INTERACTIONS

RADIATION BIOLOGY

MOLECULAR BIOLOGY & BIOCHEMISTRY

CHEMISTRY

BIOLOGY

MEDICINE

Therapeutic Gases (H_2, CO, H_2S, & NO) Possess Many of These Biochemical Properties

Administration & Application In Space

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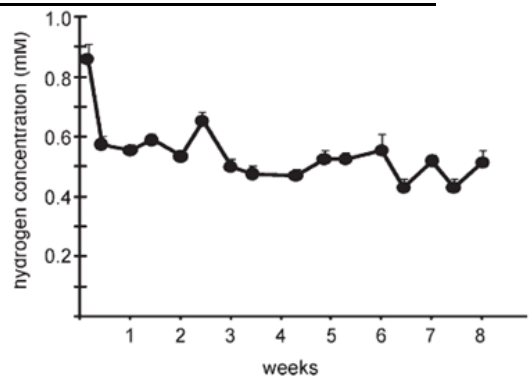
Drinking, Injection, or Inhalation

Generation By Chemical Reaction

Magnesium Stick Insert

$Mg + 2H_2O \rightarrow Mg(OH)_2 + H_2$



Nakao, A., Toyoda, Y., Sharma, P., Evans, M. and Guthrie, N., "Effectiveness of Hydrogen Rich Water on Antioxidant Status on Subjects with Potential Metabolic Syndrome—An Open Label Pilot Study," *J. Clin. Biochem. Nutr.*, **46**, March 2010, pp. 140-149.

Dissolution In Solution

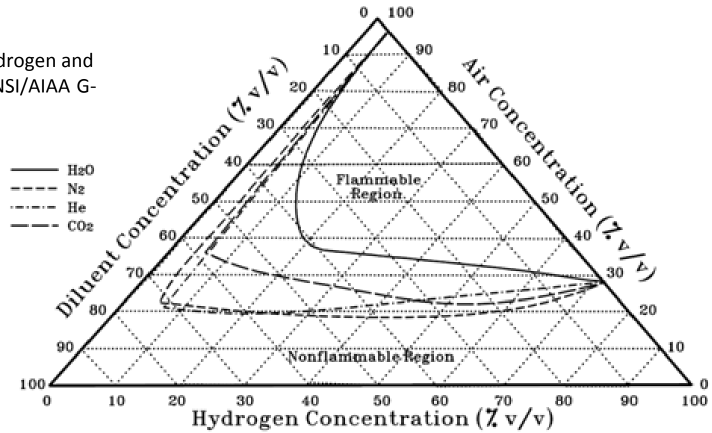
Drinking Water

Qian, L. et al., "Radioprotective effect of Hydrogen in Cultured Cells and Mice," *Free Radical Research*, **44(3)**, March 2010, pp. 275-282.

Saline Injection

H_2, H_2S, CO & NO Additions to Atmosphere (Spacecraft/Station/Suit)

Guide to Safety of Hydrogen and Hydrogen Systems, ANSI/AIAA G-095-2004.



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Summary

1. High charge & energy (HZE) nature of space radiation makes it difficult to shield and particularly damaging to DNA.

2. Biological damage develops from a series of events that start with chemical modifications initiated by ionization (direct & indirect) and which lead to molecular transformations that manifest into biological diseases.

3. Hypothesized a biochemical approach to interrupt the damage process by interfering with chemical reactions and managing biological responses.

4. Hypothesized that medical gases can support & enhance natural repair & protection as: radical scavengers, tissue pre-conditioners, and signaling molecules to manage biological response.

5. Administration of a medical gas therapy in space applications appears feasible & reasonable.

6. Qualification & optimization of a medical gas therapy for human application remains to be addressed.

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QUESTIONS?

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Radiation Chemistry & Biology Summary

- RADIATION CHEMISTRY OF WATER: radiolysis has a fundamental role in radiation induced damage
  - radiation generates deleterious radicals similar to biochemically damaging reactive oxygen species (ROS)
  - factors leading to higher radical production also lead to more biological lethality
  - radical production is the net result of competing chemical processes in which the outcome can be altered

- BIOLOGY OF RADIATION DAMAGE: loss of atom/molecule by bond breakage from ionization
  - chain of chemical events initiated by direct & indirect ionization
  - natural biological resistance from radical scavengers (damage avoided when in excess of radicals)
  - natural repair occurs from uncertain mechanism (more effective in-vivo)
  - biological factors relate to chemical aspects that affect radical production (e.g. tissue hypoxia, metabolic rate, circulation & transport, etc.)

- HYPOTHESIS: biochemically enhance & support natural resistance & repair mechanisms
  - chemical protection by reducing radical generation (e.g. biological induction of tissue hypoxia)
  - chemical protection by increasing scavenger capacity & efficacy using H_2 gas as an antioxidant
  - potentially enhance natural repair by H atom donation
  - enhance natural repair by providing more time for repair mechanism action
  - biologically manage response to damage (e.g. anti-inflammatory, etc.)

Application/Implementation Considerations

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<u>GENERAL CONSIDERATIONS FOR SPACE EXPLORATION SYSTEMS</u>: minimize weight, size, & power consumption

<u>ADMINSTRATION BY DRINKING WATER</u>:

- loss of medical gas from solution?
- loss of medical gas from host?
- if gas generated by reaction, consumption of byproducts?

<u>ADMINSTRATION BY INHALATION</u>:

- gas mixture flammability limits?
- gas interactions?
- O_2 concentrations / partial pressure (asphyxiation)?

<u>ADMINSTRATION BY INJECTION</u>:

- loss of gas from solution?

<u>QUALIFICATION OF MEDICAL GAS THERAPY</u>:

- optimum therapy or custom therapy development (mixture for preconditioning & post exposure treatment)?
- understanding mechanics? (penetration, distribution, detoxification)
- effectiveness? (dose reduction factor, DRF = LD50:LD30)