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Francis A. Cucinotta

Rockwell International Space Systems Division, Houston, Texas

William Atwell

Rockwell International Space Systems Division, Houston, Texas

Alva C. Hardy

Johnson Space Center, Houston, Texas

Michael J. Golightly

Johnson Space Center, Houston, Texas

John W. Wilson

Langley Research Center, Hampton, Virginia

See next page for additional authors

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Authors Francis A. Cucinotta Townsend, Judy Shi	a, William Atwell, Alva C. Hardy, Michael J. Golightly, John W. Wilson, Lawrence W. nn, John E. Nealy, and Robert Katz	

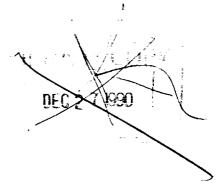
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# Predictions of Cell Damage Rates for Lifesat Missions

Francis A. Cucinotta and William Atwell Rockwell International Space Systems Division Houston, Texas

Alva C. Hardy and Michael J. Golightly Johnson Space Center Houston, Texas

John W. Wilson, Lawrence W. Townsend, Judy Shinn, and John E. Nealy Langley Research Center Hampton, Virginnia

Robert Katz University of Nebraska Lincoln, Nebraska

National Aeronautics and Space Administration Lyndon B. Johnson Space Center Houston, Texas

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#### Introduction

Radiological experiments with cell cultures are expected to be performed on Lifesat to study possible gravitational dependence on cellular response. Predictions of cell damage rates for well-studied systems are expected to help guide in the selection of orbits and the design of experiments. In this report we estimate the fractions of cell death and neoplastic transformation of C3H10T1/2 cells (cultured mouse cells) for the proposed Lifesat orbits. The parametric cellular track model of Katz et al. (refs. 1 and 2) is employed using cellular response parameters derived from the experiments of Yang et al. (refs. 3 and 4). The contributions to the biological endpoints from the trapped protons and electrons, and GCR particles are considered for typical levels of spacecraft shielding. For the proton and GCR contributions the effects of nuclear reactions are taken into account. Expected counting rates for other possible cell culture experiments on Lifesat are discussed.

#### Cellular Response Model

Biological damage from heavy ions is caused by delta-ray production. In the Katz model (ref. 1), cellular damage proceeds through two modes of response. In the ion kill mode, damage occurs through the action of single ions, while in the gamma-kill mode, cells not damaged in the ion-kill mode can be sublethally damaged from a passing ion and then inactivated by cumulative addition of sublethal damage due to delta-rays from other passing ions. The response of the cell is described by four cellular response parameters, two of which (m, the number of targets per cell, and  $D_o$ , the characteristic x-ray dose) are extracted from the response of the system to x- or  $\gamma$ -ray irradiation. The other two  $(\sigma_o)$ , interpreted as the cross-sectional area of the cell nucleus, within which the damage sites are located, and  $\kappa$ , a measure of the size of the damage site) are found from survival measurements with track segment irradiations by energetic charged particles.

The surviving fraction of a cellular population  $N_o$ , after irradiation by a fluence of particles F is written (see ref. 1)

$$\frac{N}{N_o} = \pi_i \times \pi_\gamma \tag{1}$$

where the ion-kill survivability is

$$\pi_i = e^{-\sigma F} \tag{2}$$

and the gamma-kill survivability is

$$\pi_{\gamma} = 1 - (1 - e^{-D_{\gamma}/D_o})^m \tag{3}$$

The gamma-kill dose fraction is defined

$$D_{\gamma} = (1 - P)D \tag{4}$$

where D is the absorbed dose and P is the fraction of cells damaged in the ion-kill mode, given by

$$P = \sigma/\sigma_0 \tag{5}$$

where  $\sigma$  is the single-particle inactivation cross section.

For the mixed radiation fields seen in space the ion-kill term is written (ref. 5)

$$\sigma F = \sum_{j} \int dE_{j} \Phi_{j}(x, E_{j}) \sigma_{j}(E_{j})$$

$$+ \sum_{j} \sum_{\alpha} \int dE_{j} dE_{\alpha} \Phi_{\alpha}(x, E_{\alpha}; E_{j}) \sigma_{\alpha}(E_{\alpha})$$
(6)

the subscript j and  $\alpha$  label the projectile fragment and target fragment type, respectively;  $\Phi$  is the number of particles of a particular type with energy E at x per cm<sup>2</sup>, and  $\sigma_j$  is

$$\sigma_j(E_j) = \sigma_o \left( 1 - e^{-z_j^{*2}/\kappa \beta_j^2} \right)^m \tag{7}$$

where  $\beta$  is the particle velocity and z\* the effective charge number. The first term on the right-hand side of equation (6) then corresponds to the contributions from the incident space radiation, including projectile fragments, and the second term from target fragments produced from shielding materials. Similarly, the gamma-kill dose fraction becomes for the space radiation case (ref. 5)

$$D_{\gamma} = \sum_{i} \int dE_{j} \Phi_{j}(x, E_{j}) (1 - P_{j}(E_{j})) S_{j}(E_{j})$$

$$+ \sum_{i} \sum_{\alpha} \int dE_{j} dE_{\alpha} \Phi_{\alpha}(x, E_{\alpha}; E_{j}) (1 - P_{\alpha}(E_{o})) S_{\alpha}(E_{\alpha})$$
(8)

where S is the stopping power and where the first and second terms in equation (8) correspond to the projectile and target ion contributions, respectively. The target terms will be most important for low LET ions, where the direct ionization leads only to a small inactivation cross section. Predictions of damage rates for the ion fields seen in space are made after transport methods are employed to determine the differential flux of particles at the biological endpoint (refs. 6 and 7). For damage from the trapped electrons, only the gamma-kill mode operates and the electron dose determines the damage as given by equation (3) with

$$D_{\gamma} = D. \tag{9}$$

#### Radiation Environment for Lifesat Orbits

The trapped protons and electrons, and GCR particles contribute to the radiation exposures seen in earth orbit. Schimmerling (ref. 8) has suggested the following orbits for possible Lifesat missions:

- (1) A polar orbit of 400 km perigee and 36,000 km apogee.
- (2) An equatorial orbit of 400 km perigee and 36,000 km apogee.
- (3) A circular polar orbit of 900 km.
- (4) A circular polar orbit of 200 km.

We consider the evaluation of the exposures seen in these orbits for solar minimum, assuming quiet geomagnetic conditions and Earth shadow shielding. The 200 km orbit may not be stable against decay and is chosen to illustrate a minimum trapped proton environment. The trapped particle spectra for these orbits are taken from the AP8 and AE8 models (ref. 9). The GCR solar min environment is taken from the NRL CREME model (ref. 10) with the corresponding transmission functions (calculated assuming quiet-time conditions and including earth shadowing) for the orbits under consideration shown in Fig. 1. The absorbed doses for the individual contributions is shown in Fig. 2 as calculated using BRYNTRN (ref. 6) for the trapped protons, EDOSE (ref. 11) for the trapped electrons (including bremsstrahlung), and HZETRN (ref. 7) for GCR transport. The trapped electrons contribution to the circular orbits is small and their absorbed dose is not shown. Similarly, the trapped protons were found to give only a small contribution to the 200 km circular polar orbit and the polar elliptic orbit. The transmission factor for the polar elliptic orbit allows for almost exact correspondence to the GCR free-space exposure.

#### Results for Lifesat Orbits

We consider the production of cell death and neoplastic transformations for C3H10T1/2 cells behind aluminum shielding, with tissue present locally, for Lifesat orbits of 60 days. Waligorski et al. (ref. 2) have found cellular response parameters for these two endpoints for both immediate plating and delayed plating experiments. Here we use the delayed plating values which are listed in Table 1, along with cellular response parameters for some other biological endpoints. The delayed plating model was used to account for the repair expected for protracted exposure. Results are shown in Figs. 3 and 4 for cell death and transformation, for the Lifesat orbits. Fluence levels for the GCR particles are such that only the ion-kill mode contributes. The trapped protons show an important contribution from both the ion kill and gamma kill modes. A pure GCR exposure could be obtained for the polar elliptic orbit for shields of >4g/cm<sup>2</sup>. To study the possible changes in repair mechanisms from gravity, the elliptic equatorial or the 900 km circular polar orbit would be sufficient for the

C3H10T1/2 system. Dose protraction effects (ref. 4) may become important for the highly exposed proton orbits.

Production rates will have an exponential or shouldered response with mission duration, corresponding to a changing dose for the GCR or trapped particles, respectively. The GCR fluences are such that a linear production rate with mission duration may be assumed. In Table 1, we also show cellular response parameters for cell killing and mutation of V79 Chinese hamster cells and HF19 Human Diploid Fiberblast cells. In comparing with the C3H10T1/2 parameters we should expect that cell death experiments would occur with approximately the same frequency for these two systems, while the mutation endpoints would have production rates much smaller than that for C3H10T1/2 transformations.

#### Conclusions

Preliminary predictions of cell damage rates on proposed Lifesat orbits have been made using the parametric cellular track model. The accuracy of the results depends heavily on the radiation environmental models, the particle transport codes and assumption that delayed plating effects are a good approximation to cell repair during low exposure rates. Cellular parameters are available for a wide variety of cell systems, and the methods employed herein could thus have a variety of application in planning and analyzing Lifesat experiments. The methods of this work could be used for *in vivo* systems, if results from ground-based experiments would be presented in a favorable fashion for obtaining cellular response parameters. In regard to the low probability of cell transformation we must remember that there are about 10<sup>9</sup> cells/cm<sup>3</sup> and that cancer induction may depend on the number of transformed cells rather than the fraction of transformed cells. Information on the minimum number of cells needed for tumor induction would also be highly regarded by the present formalism.

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Table 1. Cellular Response Parameters

Endpoint	m	D, cGy	$\sigma_o,\mathrm{cm}^2$	κ
Cell Death for C3H10T1/2	3	280	5.0E-7	750
Transformation for C3H10T1/2	2	26000	1.15E-10	750
Cell Death V79 Chinese Hamster	2.5	159	6.9E-7	1400
Mutation V79 Chinese Hamster	3.5	5.94E6	5. <b>75</b> E-11	1000
Cell Death HF19 Human Diploid Fiberblast	3	112	9.9E-7	900
Mutation HF19 Human Diploid Fiberblast	3.5	2.7E6	9.9E-11	1000

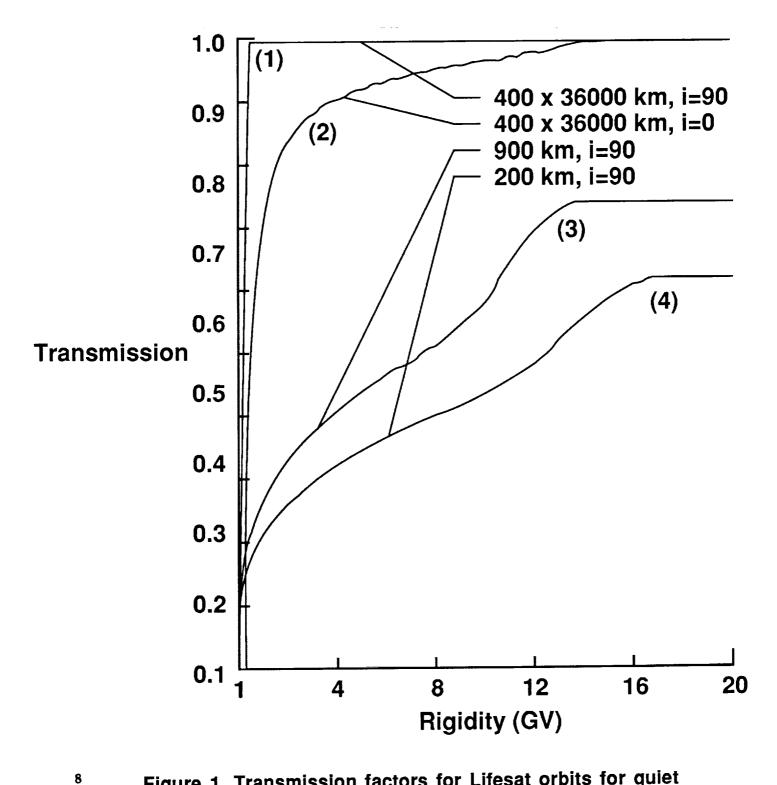


Figure 1. Transmission factors for Lifesat orbits for quiet magnetic field conditions.

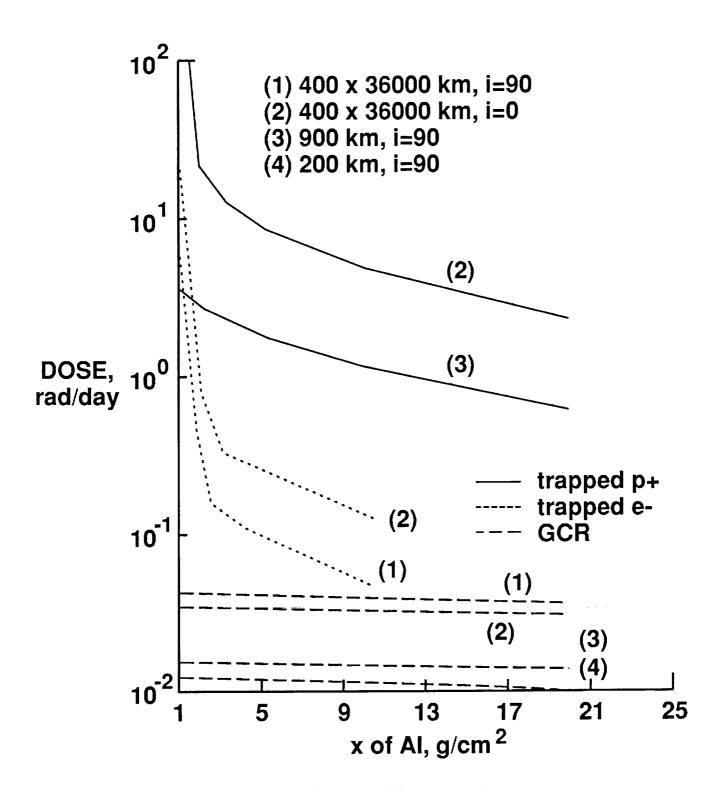


Figure 2. Absorbed doses for Lifesat orbits.

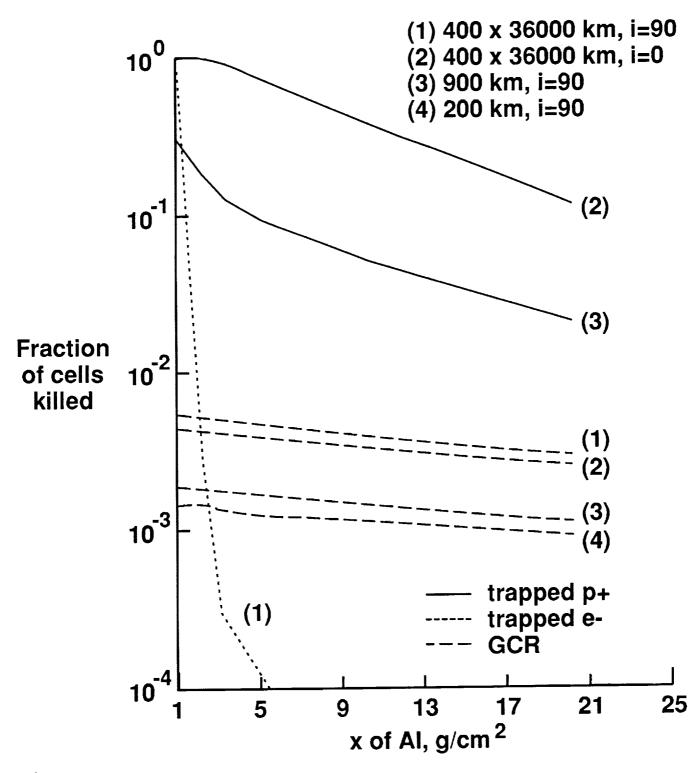


Figure 3. Damage to C3H10T1/2 cells in 60 days.

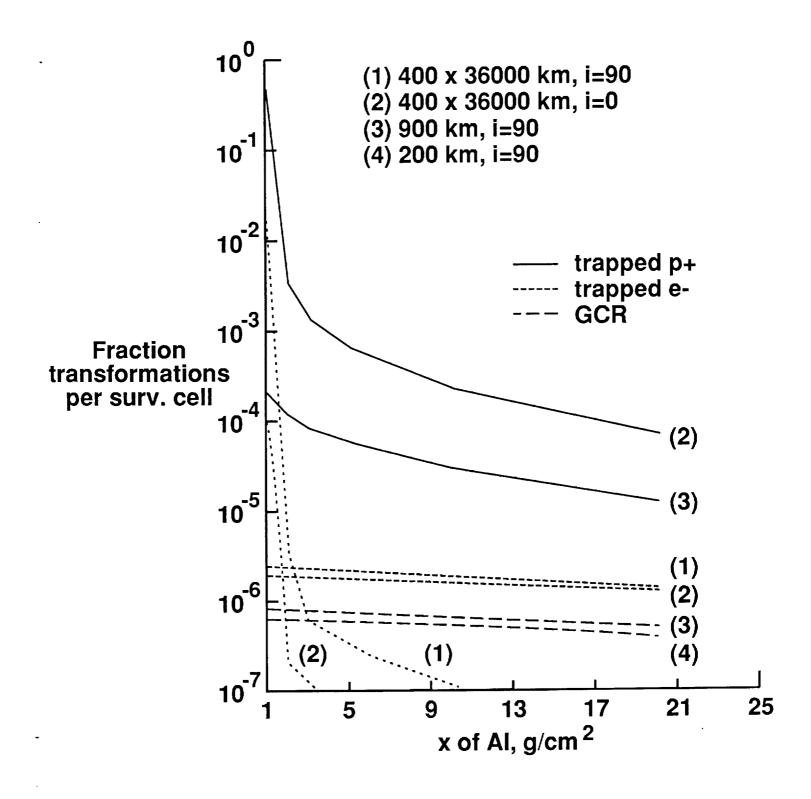


Figure 4. Damage to C3H10T1/2 cells in 60 days.

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