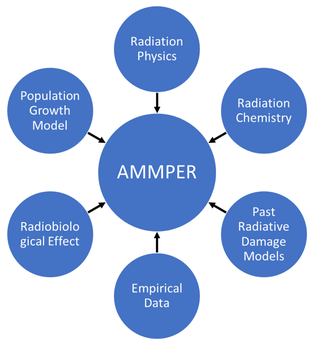
AMMPER: Agent-based Model for Microbial Populations Exposed to Radiation

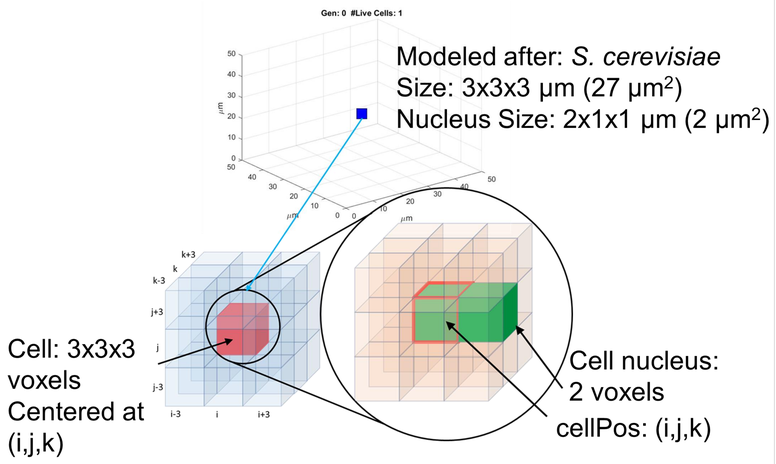
Amrita Singh[1,2,3], Matthew Lera[1], Sergio Santa Maria[1] , Jessica Audrey Lee[1]
[1]NASA Ames Research Center, Moffett Field, CA 94035, [2]University of Southern California , [3]Universities Space Research Association

ABSTRACT

Exposure of microbial populations to galactic cosmic radiation (GCR) in the deep-space radiation environment may lead to intracellular damage that compromises the ability of cells to repair and replicate. While simulation programs of deep-space radiation do exist, they focus primarily on single-cell damage, rather than population-wide effects. In this work, a new application and graphical user interface, Agent-Based Model for Microbial Populations Exposed to Radiation (AMMPER) is presented, which simulates the effects of proton-based GCR on *Saccharomyces cerevisiae* population growth. AMMPER consists of a 50x50x50 μm simulation space, analogous to an aqueous culture medium with non-limiting nutrient and pH buffering, in a microwell plate or microfluidic culture card. This model utilizes Relativistic Ion Tracks (RITRACKS) to create detailed track structures of the radiation traversals. AMMPER then calculates the radiation dose present at each cell, and subsequently determines the damage (chromosomal aberrations, oxidative stress, etc.) and resulting loss of cell viability from both primary and secondary radiation-induced effects. Through implementing cell replication, repair, damage, and death, the effect of radiation exposure on the population growth can be determined. AMMPER can be used to predict effects of long-duration exposure to the deep-space environment on entire populations, making it a powerful tool to assess the feasibility of sustaining life in space.



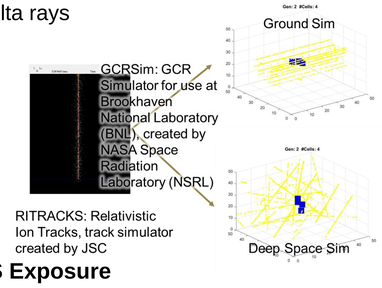
CELL DEFINITION



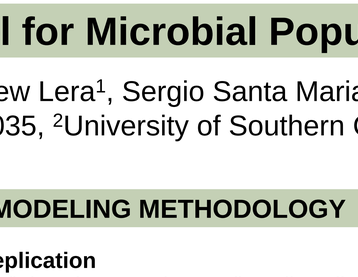
MODELING METHODOLOGY

Model 1: Cell Replication
IF cell is "Healthy" (no damage detected), cell replicates into random empty space bordering it. Exponential growth model is maintained through allowing the cells to move through a Brownian Motion random-walk algorithm.

Model 2: Core/Penumbra Radiation
Energy deposition data from RITRACKS is used with GCRSims' report of the fluence of particle tracks to create the radiation environment from protons and delta rays



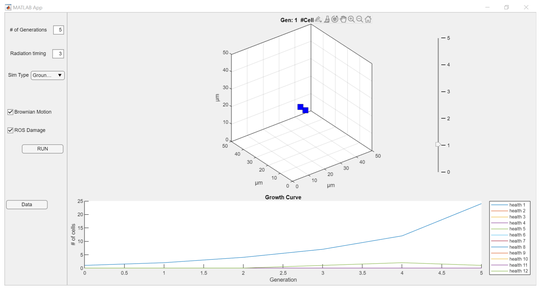
Model 3: ROS Exposure
The energy deposition in water is used to calculate the radiolytic yield of H_2O_2 and OH^-. The probability of cell apoptotic death due to H_2O_2 exposure was applied, as was the probability of damage due to OH^-. ROS species were set to disappear after 1 generation, due to the short lifespan and high reactivity.



Model 4: DNA Repair
Cell damage is grouped into two categories: non-DSBs and DSBs. Non-DSB damage is repaired using a fast-repair model, which allows the cell to repair the non-DSB quickly and accurately (30 minutes, 100% success). DSBs use a complex repair model which implements a longer repair time and a lower probability of success (90 minutes, 50% success). When all damage in the cell has been healed, the cell is recorded as being "Healthy."

USER INTERFACE

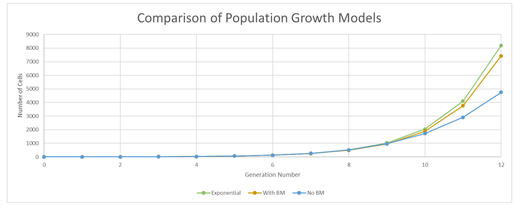
AMMPER has an associated GUI in order to increase usability and maximize simulation flexibility. The user may choose the number of generations to run the simulation, the generation at which a radiation event occurs, the radiation type (deep-space GCR or ground-testing GCR), and toggle on and off the calculations for secondary radiation-induced effects and cell movement.



VERIFICATION & VALIDATION

The V&V process for AMMPER is ongoing, split into separate V&V processes for each of the models.

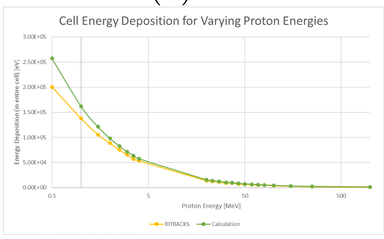
Model 1: Cell Replication
Currently, the Brownian Motion algorithm is found to be inconsistently effective in increasing the growth rate closer to the ideal exponential growth rate. This ability of the algorithm is highly dependent on both chance as well as the placement of the cells (cells that are in a cluster grow faster when the Brownian Motion algorithm is not activated).

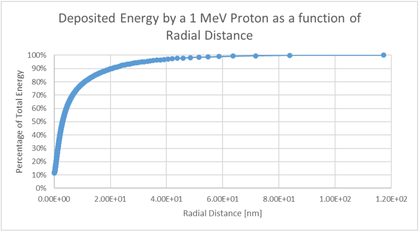


Model 2: Core/Penumbra Radiation
The energy deposition of the direct proton energy has been validated using microdosimetry, and the energy deposition of the penumbra has also been validated by a plot of electron-based radiation dose as a function of distance from the particle track core.

$$\Delta E = \left(\frac{2}{d^2}\right)\int_0^{\min(R,d)} dl\, l^2 [S(l) - S_{rad}(l)] \qquad \text{(Stewart et al., 2011)}$$

$$\Delta E = \frac{2}{d^2}\left(\frac{L^3}{3}\right) LET$$





Model 3: ROS Exposure
Through a use of alternative simulations, the radiolytic yield constants that are used to determine the generation of ROS species will be determined. A comparison of empirical data on irradiation of hydrated *S. cerevisiae* repair mutant cultures to the simulation will be used to quantify the accuracy of the modeled effect of ROS exposure.

Model 4: DNA Repair
Through a comparison to empirical data on the growth rates and metabolic activity of irradiated populations of *S. cerevisiae*, the radiobiological effect on and the ability of the simulated cells to repair will be evaluated.

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BNL | NSRL User Guide. from https://www.bnl.gov/nsrl/userguide/SimGCRSim.php; Cucinotta, et al. (1996). Radial dose distributions in the delta-ray theory of track structure. https://doi.org/10.1063/1.50083; Madeo, et al. (1999). Oxygen Stress: A Regulator of Apoptosis in Yeast. https://doi.org/10.1083/jcb.145.4.757; Plante, I. (2021). A review of simulation codes and approaches for radiation chemistry. https://doi.org/10.1088/1361-6560/abbd19; Plante, et al. (2013). Calculation of the energy deposition in nanovolumes by protons and HZE particles: Geometric patterns of initial distributions of DNA repair foci. https://doi.org/10.1088/0031-9155/58/18/6393; Plante, I., & Wu, H. (2014). *RITRACKS: A Software for Simulation of Stochastic Radiation Track Structure, Micro and Nanodosimetry, Radiation Chemistry and DNA Damage for Heavy Ions*. https://ntrs.nasa.gov/citations/20140012609; Santa Maria, et al. (2020). BioSentinel: Long-Term *Saccharomyces cerevisiae* Preservation for a Deep Space Biosensor Mission. https://doi.org/10.1089/ast.2019.2073; Simonsen, et al. (2020). NASA's first ground-based Galactic Cosmic Ray Simulator: Enabling a new era in space radiobiology research. https://doi.org/10.1371/journal.pbio.3000669; Stewart, et al. (2011). Effects of Radiation Quality and Oxygen on Clustered DNA Lesions and Cell Death. https://doi.org/10.1667/RR2663.1; Wingate, C. L., & Baum, J. W. (1976). Measured radial distributions of dose and LET for alpha and proton beams in hydrogen and tissue-equivalent gas. *Radiation Research*, *65*(1), 1–19.

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