AMMPER
Agent-based Model for Microbial Populations Exposed to Radiation

A user-friendly agent-based model that recapitulates simple metabolic responses of yeast to deep-space radiation

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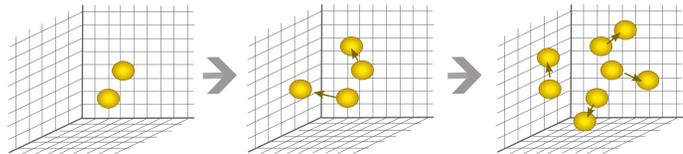
Contact: jessica.a.lee@nasa.gov
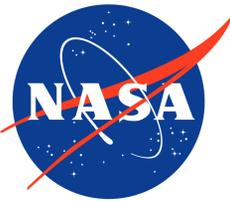
Yeast cell replication

AMMPER models yeast cells as individual agents. They can:
- move via Brownian motion
- reproduce once per timestep
- be damaged, and repair damage.

Metabolism is not explicitly simulated in AMMPER.

Radiation and ROS generation

AMMPER includes energy deposition data for protons, generated by RITRACKS [5]. Users can choose from 3 radiation environments:
- *150 MeV proton*: parallel tracks, 2.5 - 30 Gy
- *GCRSim*: parallel tracks, 20-1000 MeV protons, 1.19 Gy
- *Deep Space*: omnidirectional tracks, 42-120 MeV protons, 4.49 mGy

RITRACKS

Proton tracks
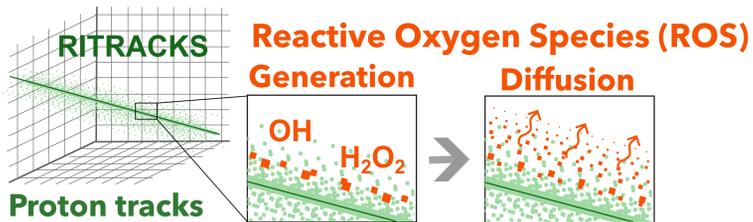
Gamma (v 2.0)

AMMPER v2.0 includes an option for gamma radiation, simulated as a random distribution of cell damage and ROS across space.

Reactive Oxygen Species (ROS)
Generation

OH H_2O_2

Diffusion

ROS (reactive oxygen species) are generated at a rate of 2.5 •OH / 100 eV or 0.7 H_2O_2 / 100 eV. AMMPER v 2.0 includes the option to simulate ROS diffusion through space.

Experimental data

Empirical data from BioSentinel ground experiments [1-3] are used to:
- estimate basal growth rate
- fit alamarBlue reaction parameters
- test model outcomes

Graphical user interface (v 2.0)

AMMPER v 2.0 includes a graphical user interface. Learn more at Madeline Marous's poster on Saturday! (UH45)

Overview

AMMPER is an agent-based model designed to predict the dynamics of yeast growth and alamarBlue reduction upon radiation exposure, to facilitate design and interpretation of NASA flight experiments such as BioSentinel [1-3] and LEIA [4].
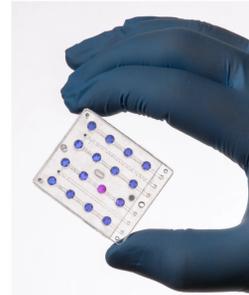
Simulation space:
64 x 64 x 64 um or
300 x 300 x 300 um

Cell damage and repair

H healthy

DSBs SSBs

D damaged

healthy

P(repair)

damaged

nonviable
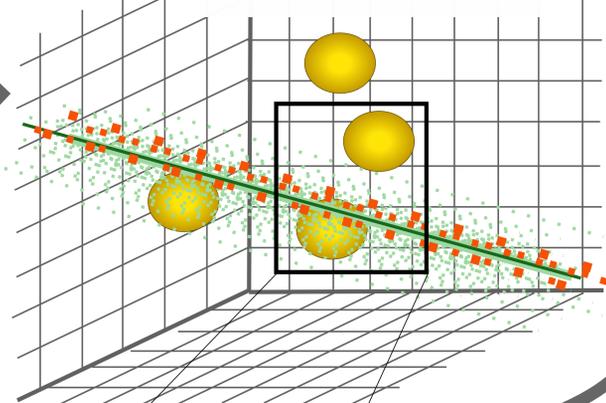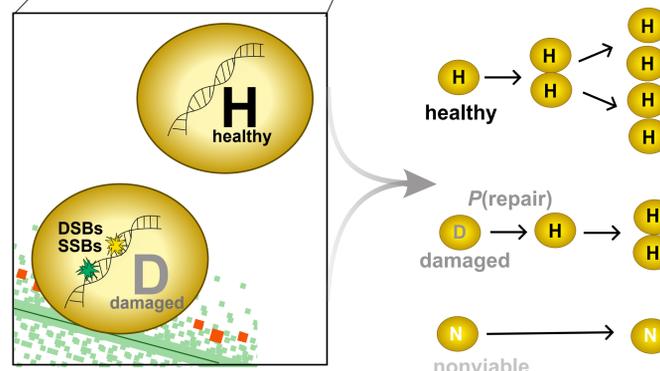
DSB=Double-Strand Break; SSB=Single-Strand Break

Each cell accumulates DNA damage
- from radiation: 35 DSBs / cell / Gy
- from ROS: 1 SSB / •OH molecule
- H_2O_2 determines apoptosis (death) probability

DNA repair is probabilistic
- SSB: 3 per timestep, 100% chance of success
- DSB: 1 per timestep, 80% chance of success

Damage determines cell health state and activity
- (H) Healthy: no damage. Reproduces once per timestep. Full alamarBlue reduction rate.
- (D) Damaged: some SSBs or DSBs. No reproduction. alamarBlue reduction rate is reduced by a constant scaling parameter.
- (N) Nonviable / dead: no activity, no chance of repair

Population growth

AMMPER tracks the number of healthy and damaged cells over time, generating growth curves for comparison with experimental data.
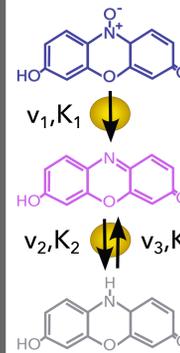
Simulation
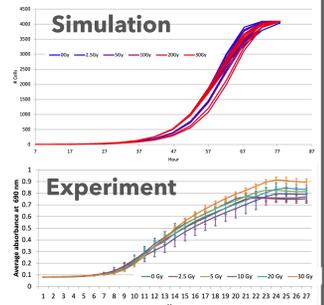
Experiment

— AMMPER simulation   ••• Experimental data

Cells / **Generations**
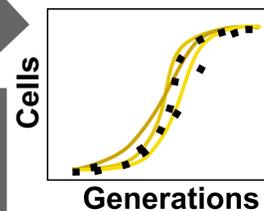
As a stochastic model, it generates variability among replicate runs similar to variability among real biological replicates.
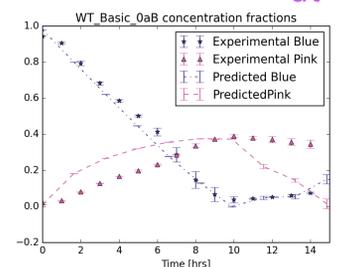
alamarBlue dynamics (v 2.0)

AMMPER v 2.0 simulates dynamics of alamarBlue metabolic dye. After a model run, the number of healthy and damaged cells at each timestep is used to calculate the rate of blue-> pink and pink->uncolored reactions, using Michaelis-Menten kinetics.

v_1, K_1

v_2, K_2 v_3, K_3

blue-> pink per cell: $\dfrac{d[\text{pink}]}{dt} = v_1 \dfrac{[\text{blue}]}{[\text{blue}] + K_1}$

per timestep: $V_{\text{pink}} = ([\text{healthy}] + k[\text{damaged}]) \dfrac{d[\text{pink}]}{dt}$

The pink-> uncolored reaction uses similar equations. Parameters v_1, v_2, v_3, K_1, K_2, K_3 are estimated by fitting to experimental data using Bayesian optimization.

WT_Basic_0aB concentration fractions

Preprint and code

Read more about AMMPER v 1.0 in Singh et al. (2023) on bioRxiv! Open-source software available at **github.com/nasa/AMMPER**

bioRχiv

AMMPER GITHUB

Next steps

Stay tuned for the official release of AMMPER v 2.0, including gamma radiation, alamarBlue reduction, and the GUI. Future work includes single-cell experiments for better parameterization.

Acknowledgments

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References

[1] Santa Maria et al. (2020) doi: 10.1089/ast.2019.2073
[2] Padgen et al. (2021) doi: 10.1089/ast.2020.2305
[3] Liddell et al. (2023) doi: 10.1089/ast.2022.0124
[4] https://www.nasa.gov/technology/science-instruments/what-is-the-lunar-explorer-instrument-for-space-biology-applications/
[5] Plante & Wu (2014) NASA software MSC-25937-1