BioSentinel: NASA's first interplanetary biological mission

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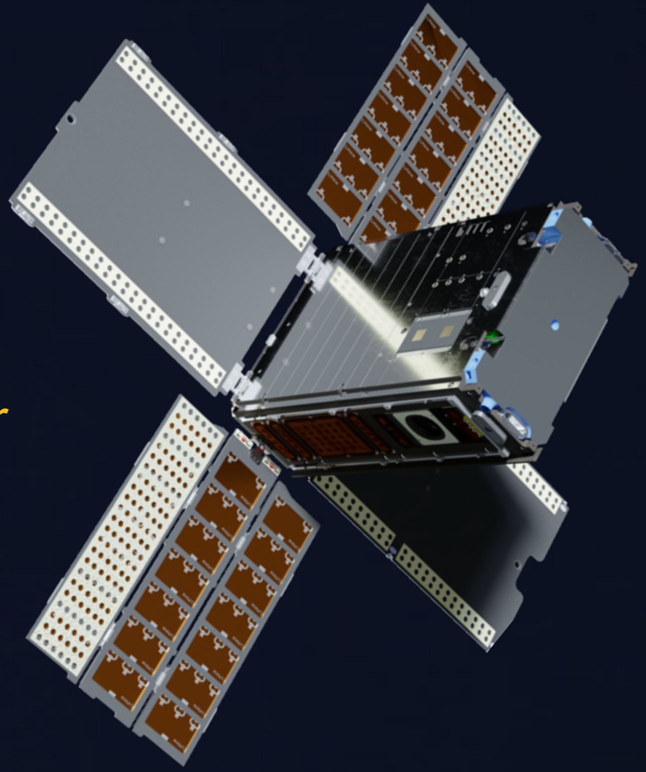

UBI VULT SPIRITUS SPIRAT

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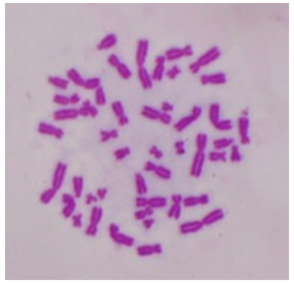

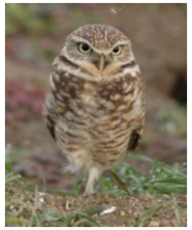

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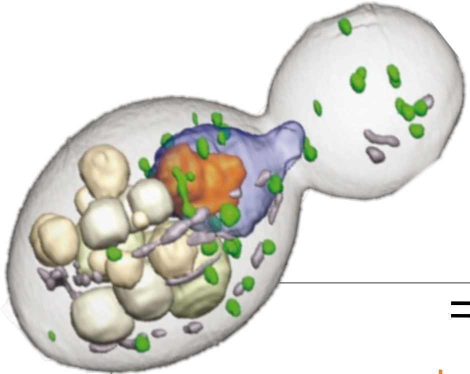

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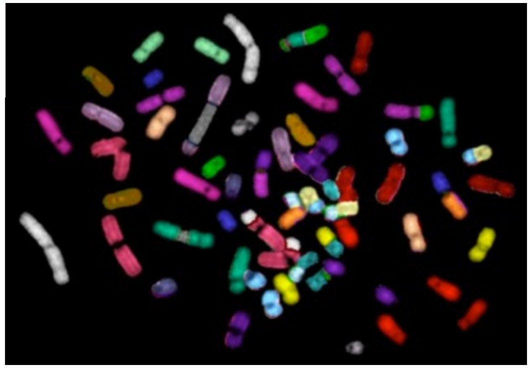

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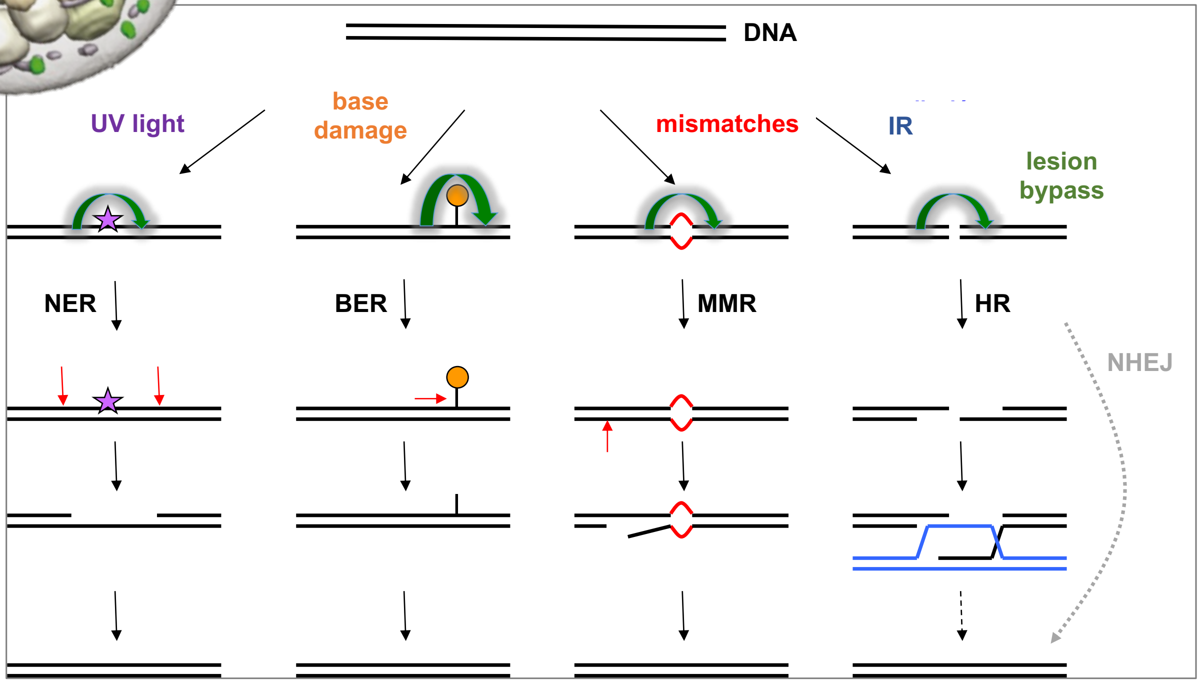

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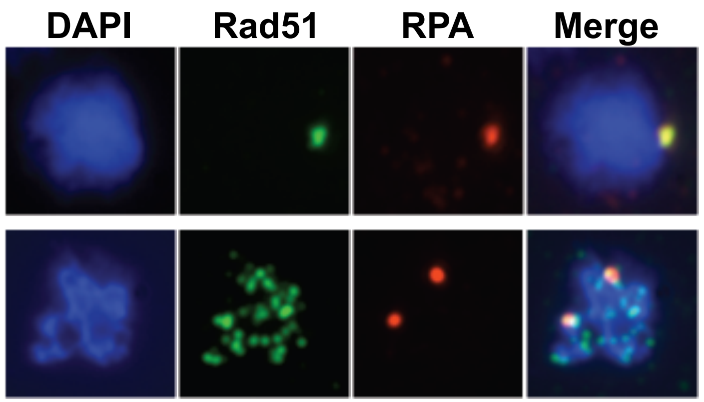

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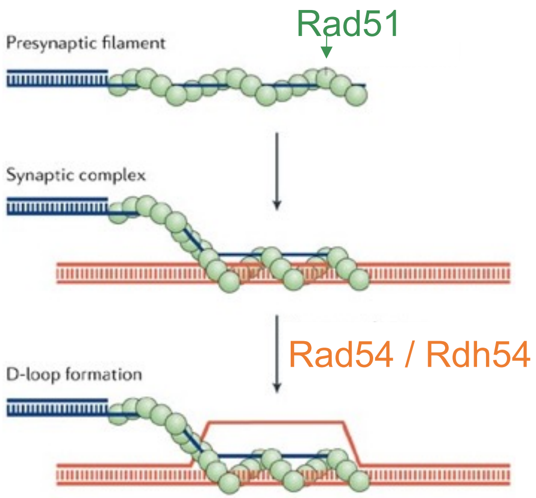
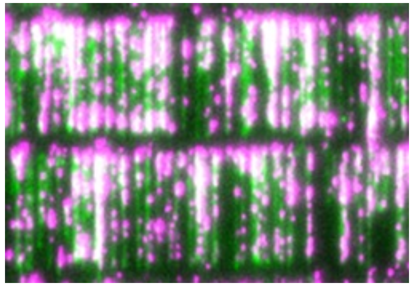
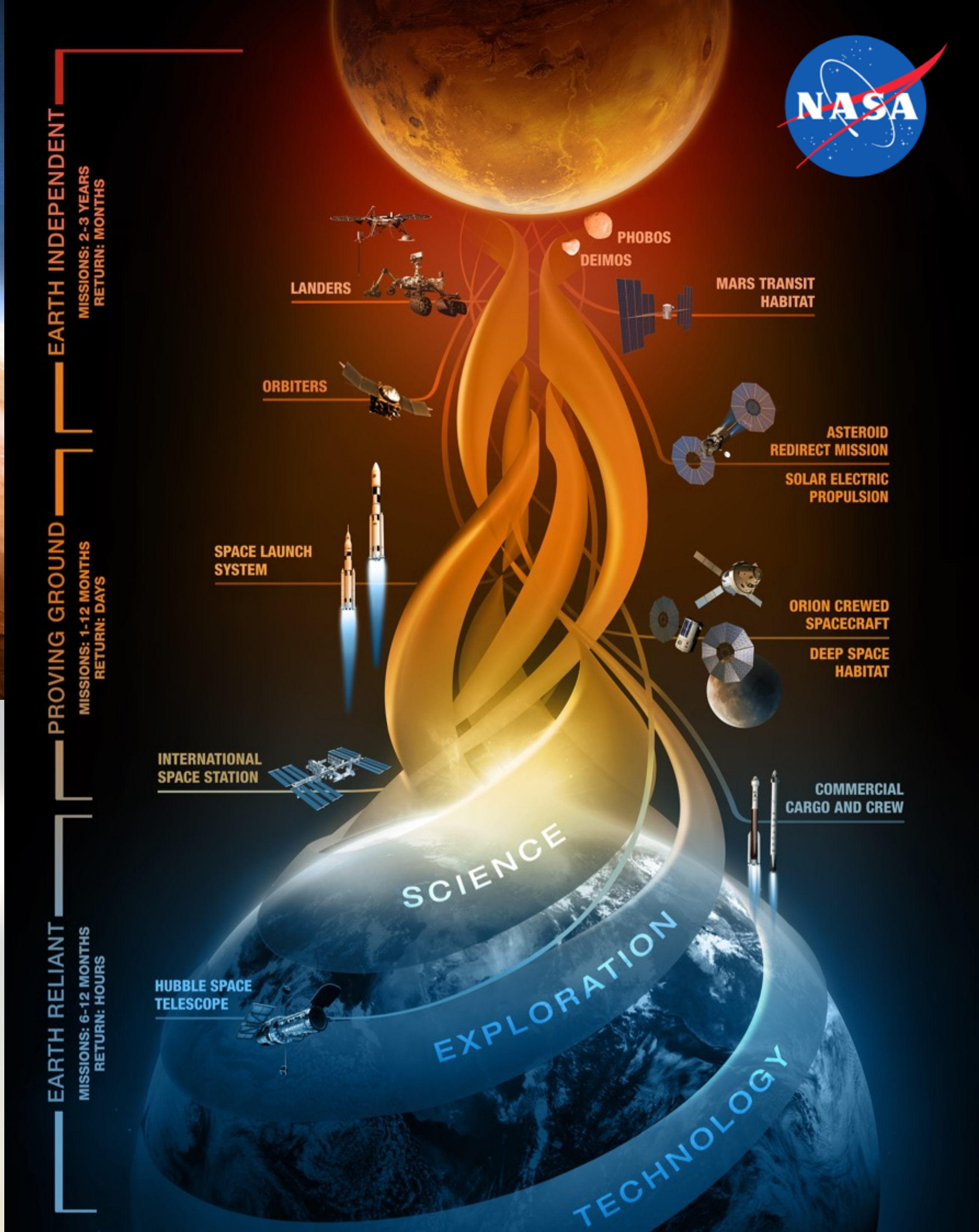


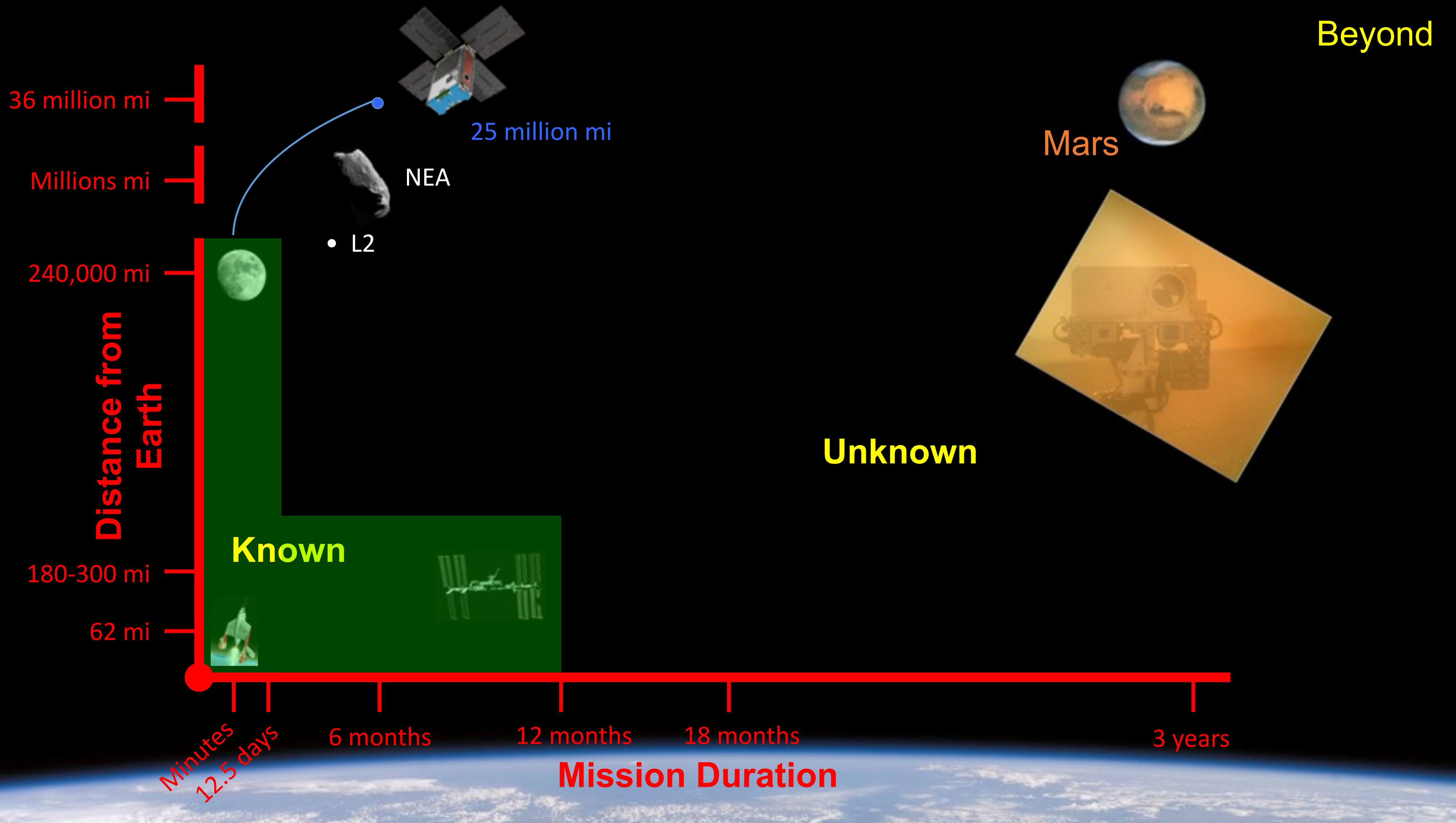


NASA

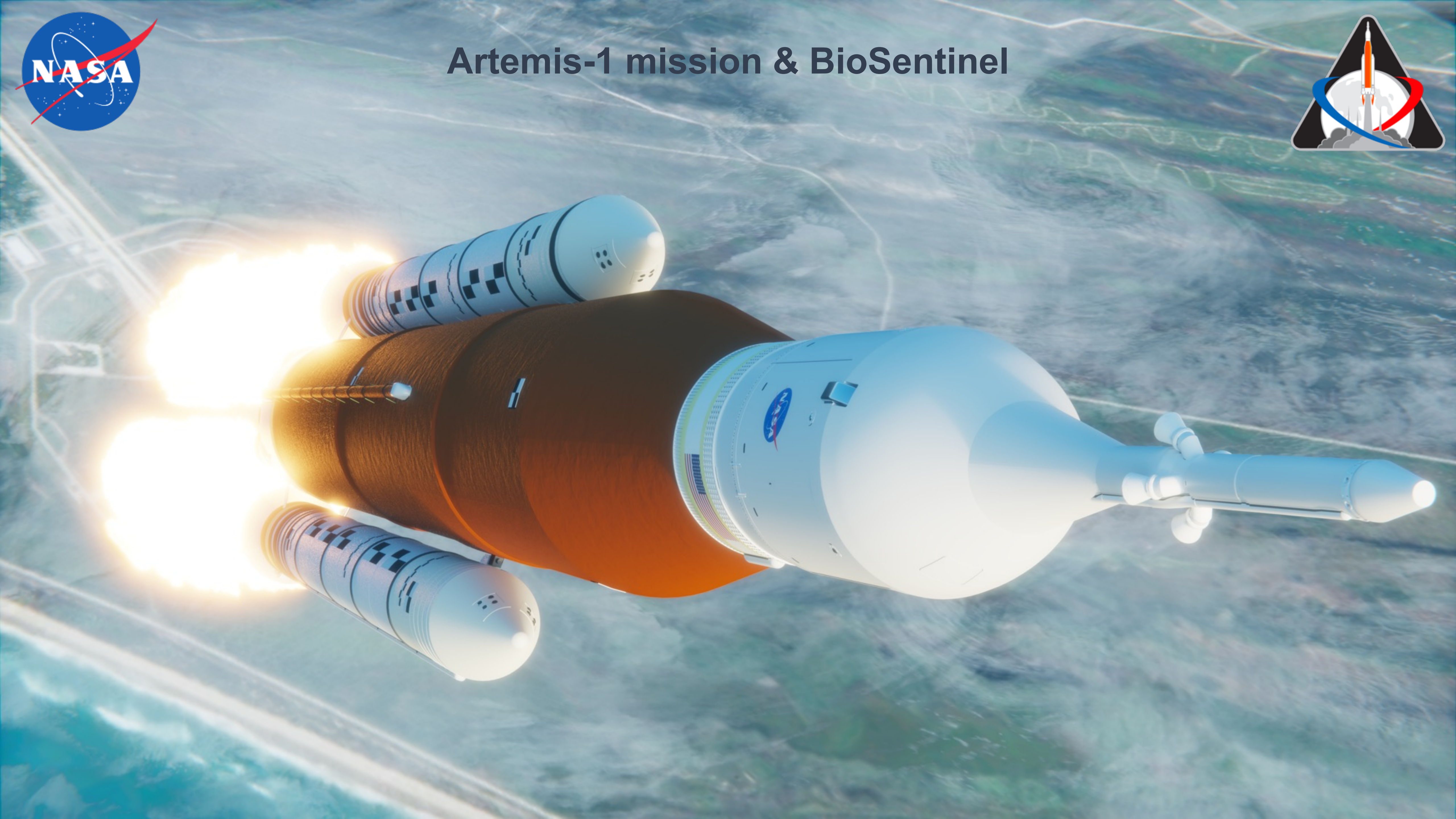

NASA'S JOURNEY TO
MARS


EARTH INDEPENDENT
MISSIONS: 2-3 YEARS
RETURN: MONTHS
PROVING GROUND
MISSIONS: 1-12 MONTHS
RETURN: DAYS
EARTH RELIANT
MISSIONS: 6-12 MONTHS
RETURN: HOURS
PHOBOS
DEIMOS
LANDERS
MARS TRANSIT HABITAT
ORBITERS
ASTEROID REDIRECT MISSION
SOLAR ELECTRIC PROPULSION
SPACE LAUNCH SYSTEM
ORION CREWED SPACECRAFT
DEEP SPACE HABITAT
INTERNATIONAL SPACE STATION
COMMERCIAL CARGO AND CREW
HUBBLE SPACE TELESCOPE
SCIENCE
EXPLORATION
TECHNOLOGY

The limits of life in space – as we know it – is 12.5 days on a lunar round trip or 1.2 years in LEO. As we send people further into space, we need to understand the biological risks and how they can be addressed

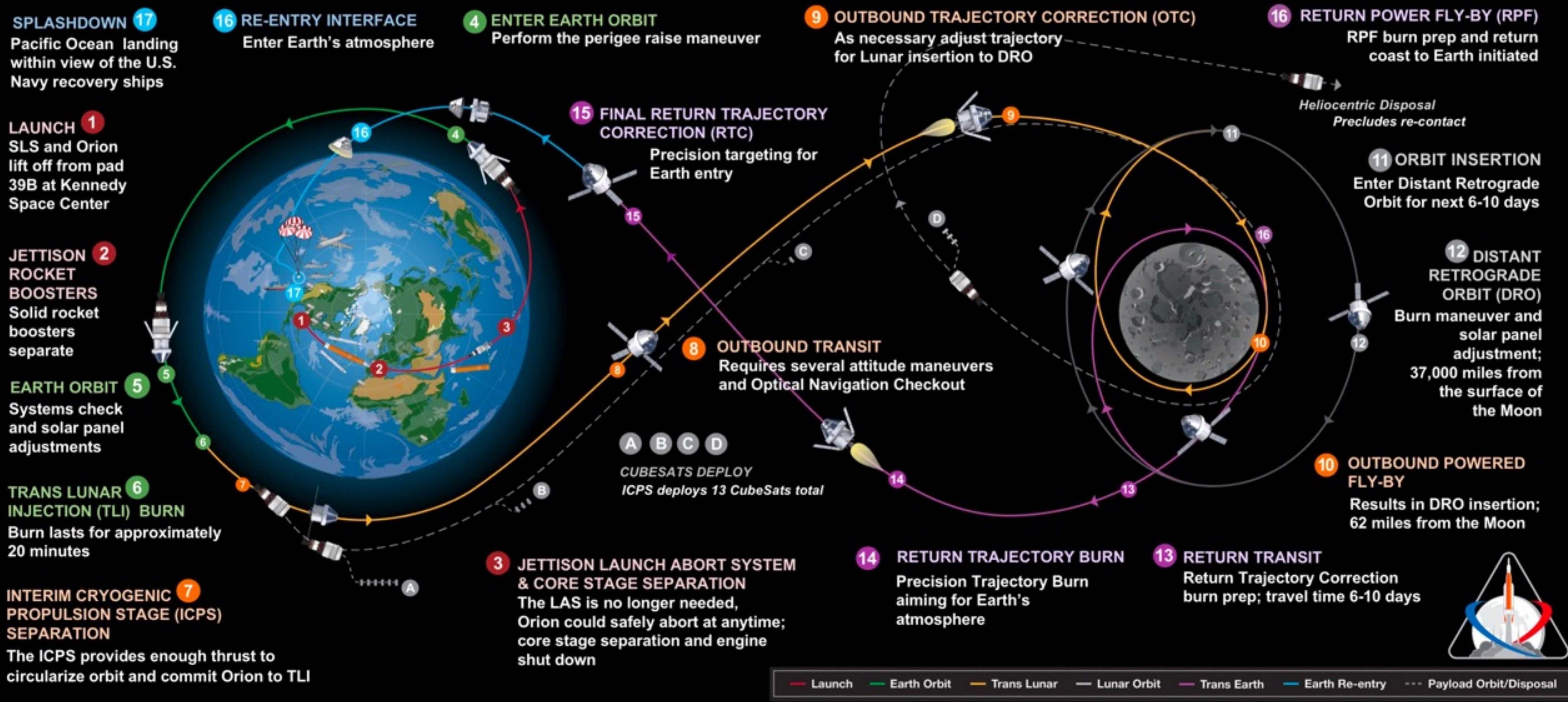


Artemis-1 mission & BioSentinel



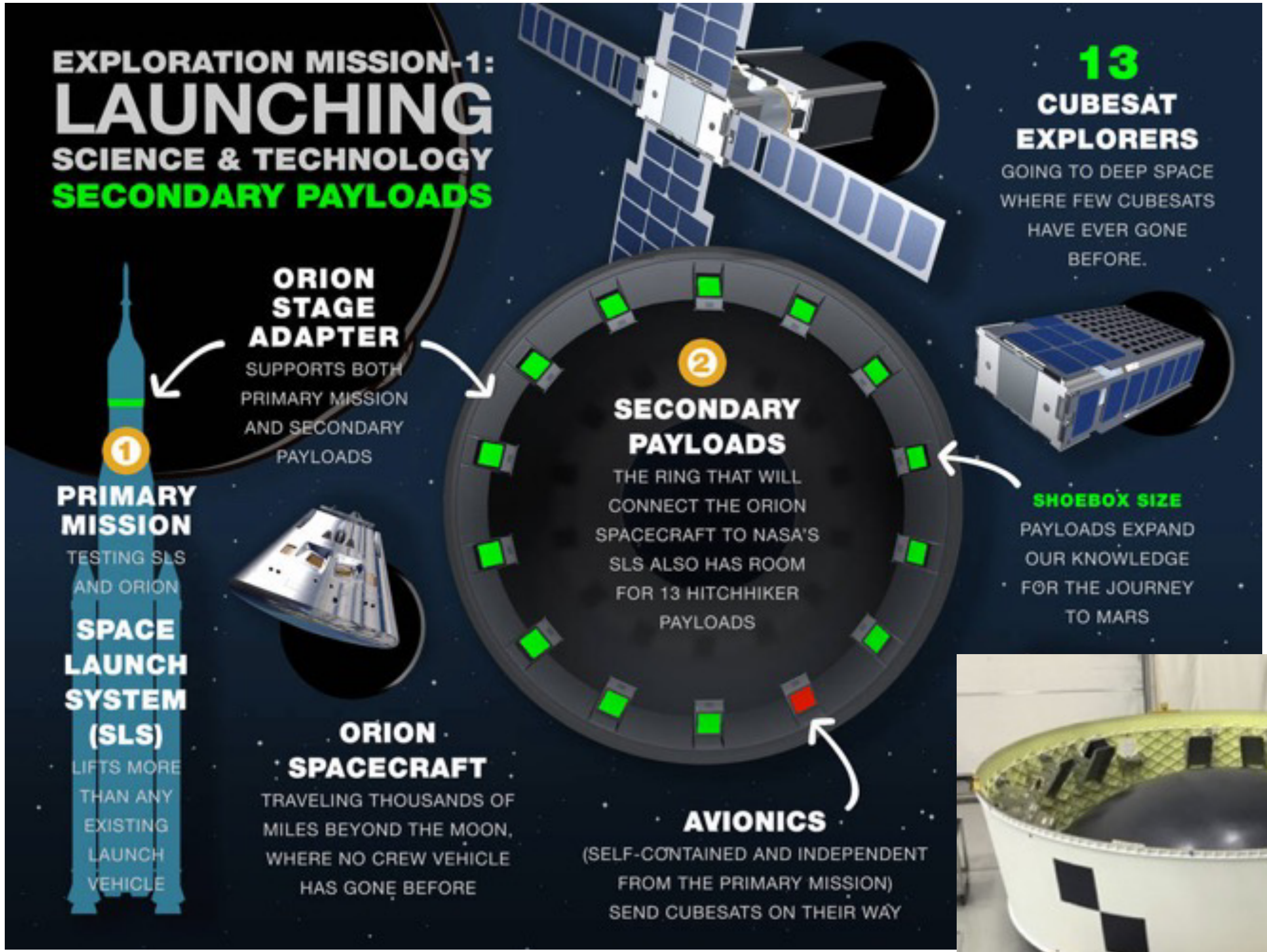
~~EXPLORATION MISSION-1~~ Artemis-1

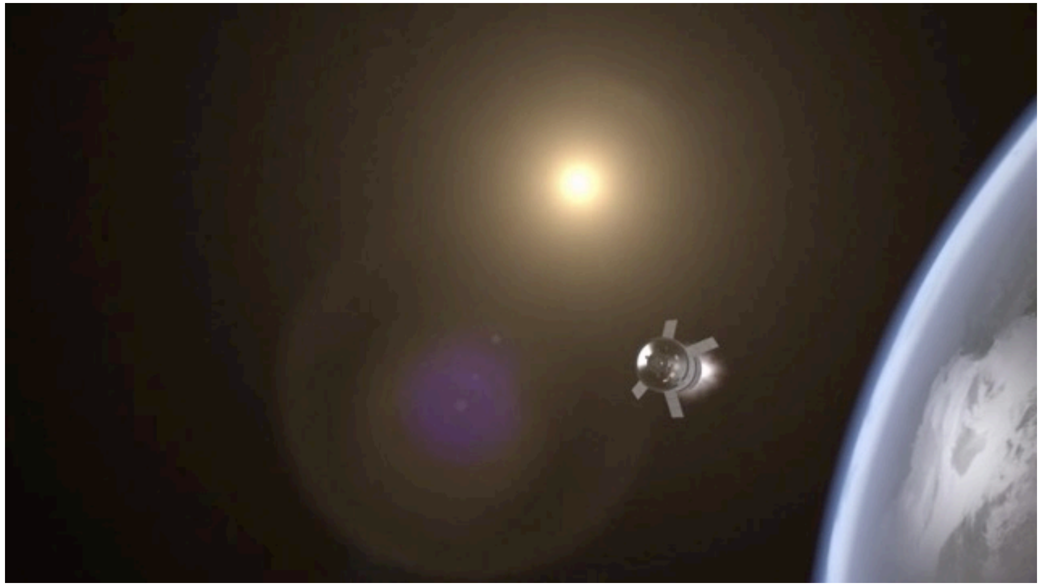
The first uncrewed, integrated flight test of NASA's Orion spacecraft and Space Launch System rocket, launching from a modernized Kennedy spaceport

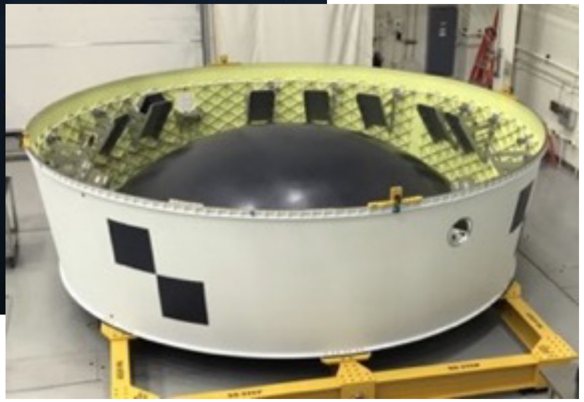


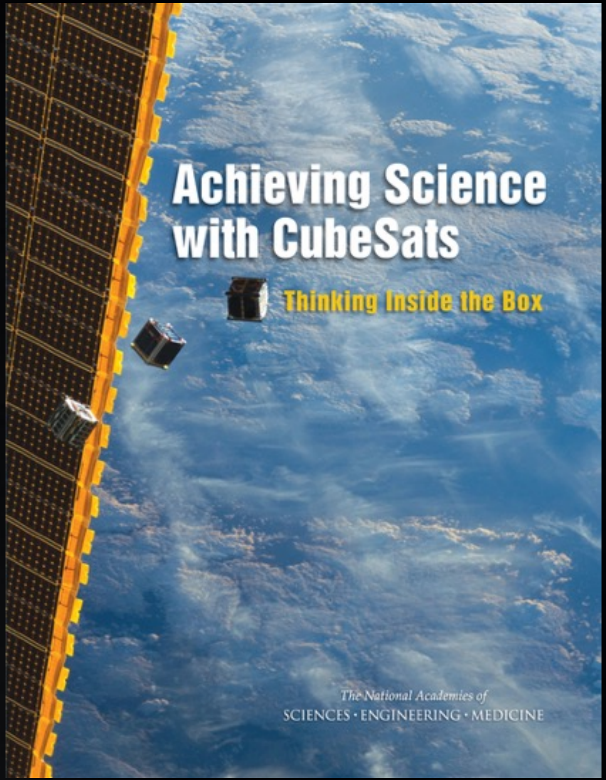
Total distance traveled: 1.3 million miles – Mission duration: 25.5 days – Re-entry speed: 24,500 mph (Mach 32) – 13 CubeSats deployed

Artemis-1: secondary payloads (6U CubeSats)



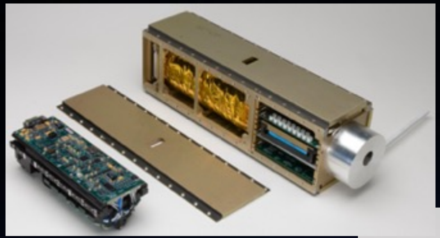


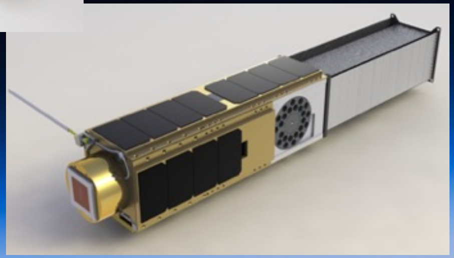


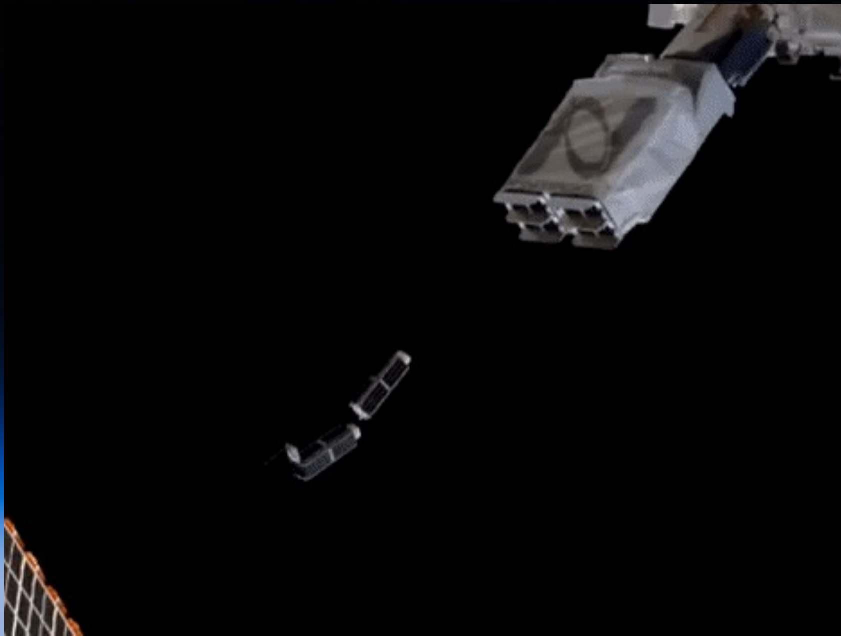


Why Cubesats?

- Small Sats are ever more capable: technology miniaturization
- Access to space: multiple low-cost launches possible (test, learn, iterate)
- Excellent education vehicle (worldwide)
- Autonomous operations
- Technology migration: ISS; landers/orbiters for moon, Mars, other planets

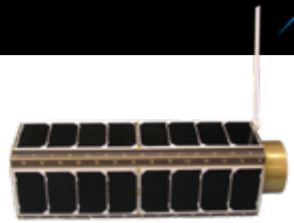


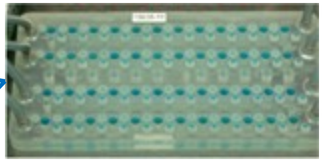


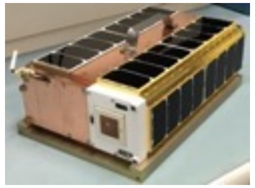


NASA Ames pioneering biological space missions

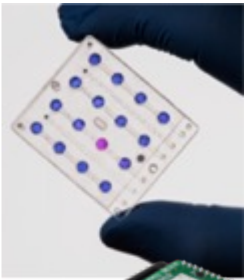
E. coli GeneSat-1 (2006 / 3U): ***gene expression***
EcAMSat (2017 / 6U): ***antibiotic resistance***

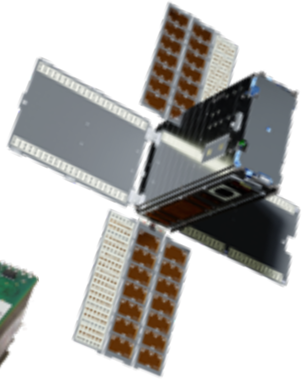






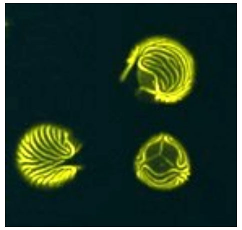
S. cerevisiae PharmaSat (2009 / 3U): ***drug dose response***
BioSentinel (2022 / 6U): ***DNA damage response***



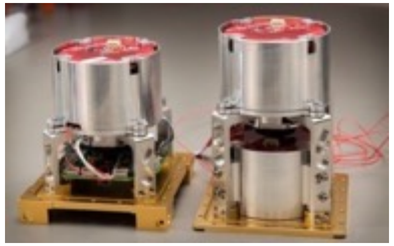


B. subtilis O/OREOS* (2010 / 3U): ***survival, metabolism***

**Organism/Organic Response to Orbital Stress*



C. richardii SporeSat-1 (2014 / 3U): ***ion channel sensors, microcentrifuges***



BioSentinel mission

<u>Objective</u>: develop a tool with autonomous life support technologies to study the biological effects of the space radiation environment at different orbits

- <u>NASA's first biological study in interplanetary deep space</u>
  - First CubeSat to combine bio studies with autonomous capability & physical dosimetry beyond LEO
  - Far beyond the protection of Earth's magnetosphere (~0.3 AU from Earth at 6 months)
  - BioSentinel will allow to compare different radiation & gravitational environments (free space, ISS, lunar surface)

SPACE

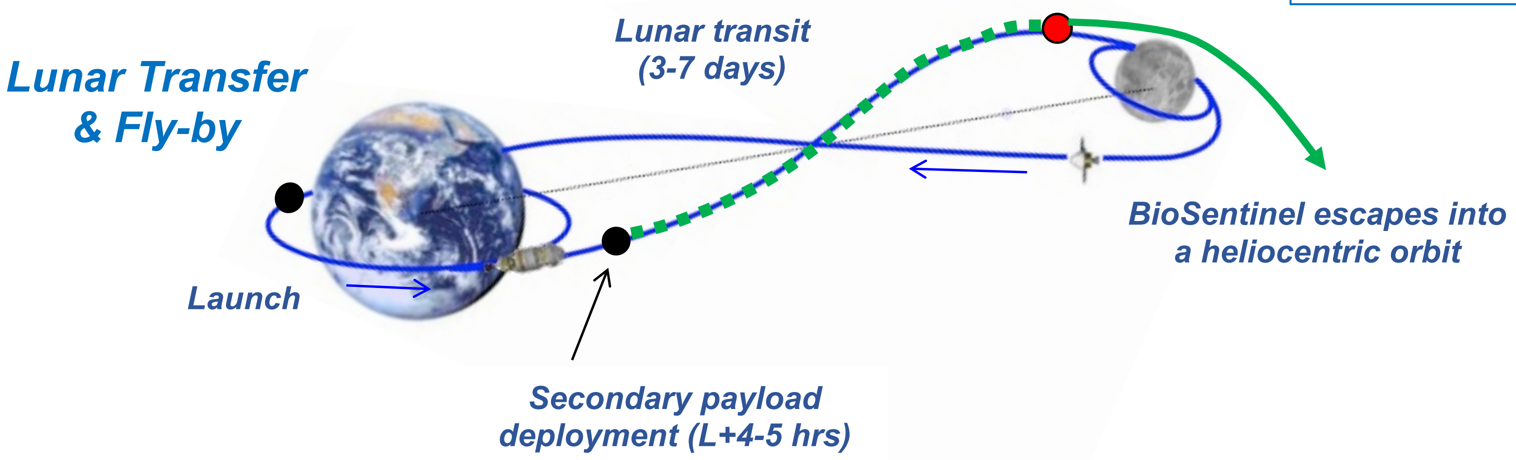
NASA IS SENDING SOME LUCKY YEAST INTO RADIATION-FILLED DEEP SPACE

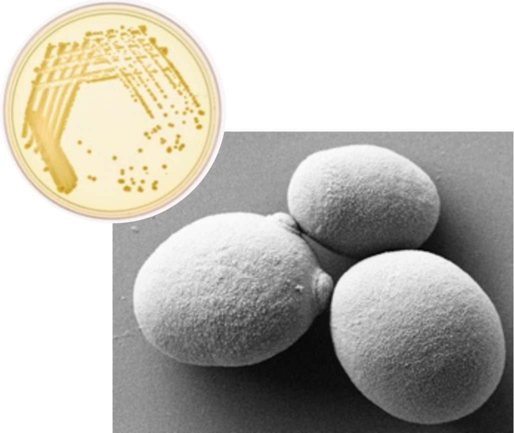
WHERE NO YEAST HAS GONE BEFORE

By Shannon Stirone May 15, 2015

POPULAR SCIENCE

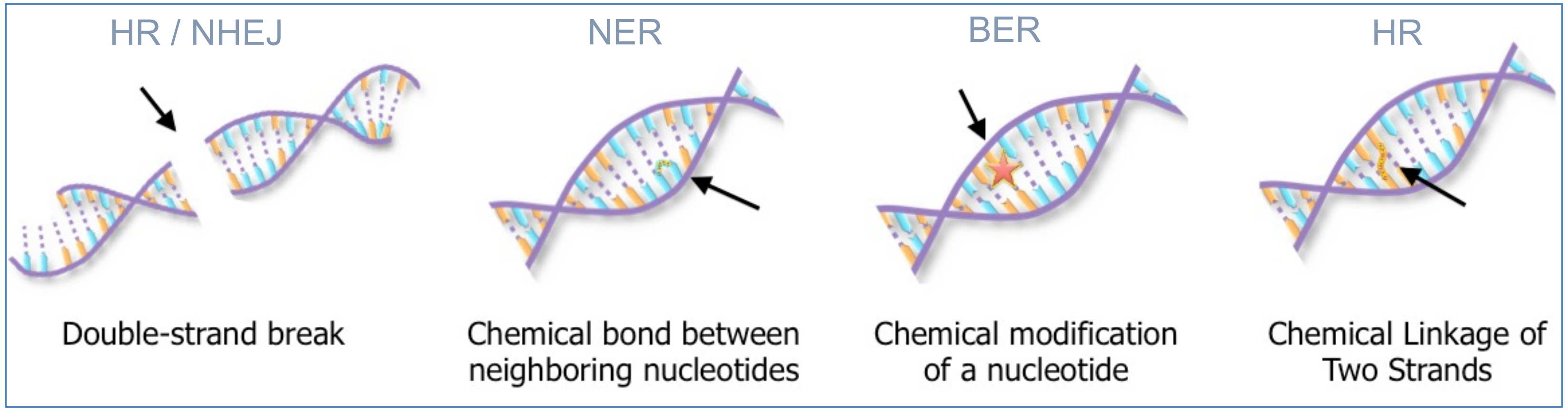
Distance to ISS:	~ 350 km
Distance to the Moon:	~385,000 km
Distance at 6 months:	~40'000,000 km

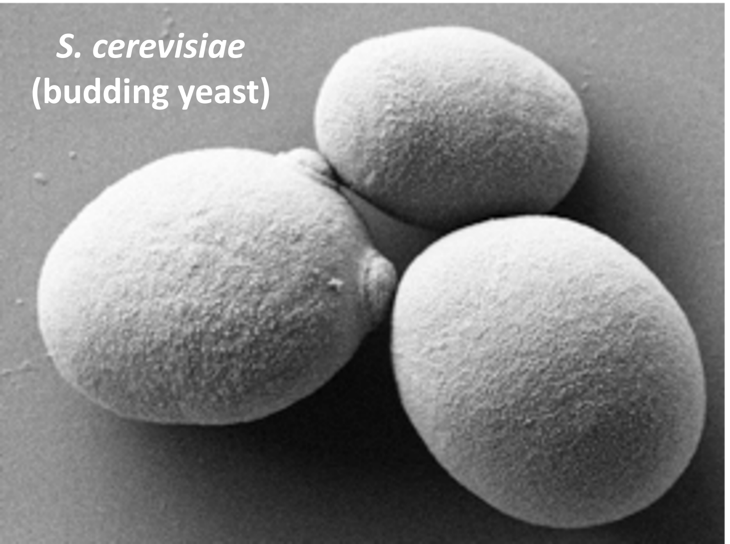


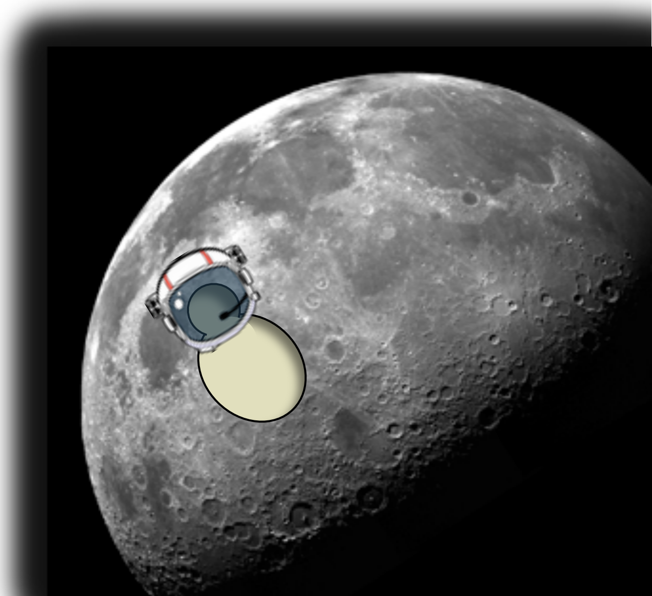


What is BioSentinel?

BioSentinel is a yeast radiation biosensor that will measure the DNA damage response caused by space radiation and will provide a tool to study the true biological effects of the space environment at different orbits.







What is BioSentinel?

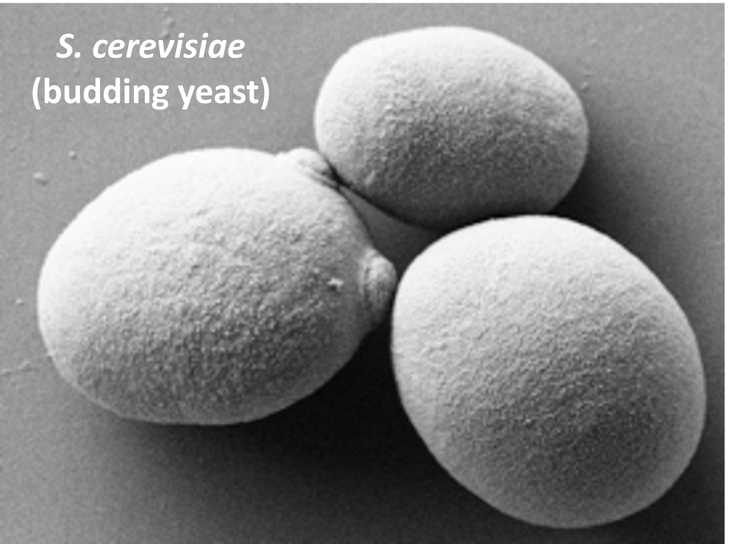
BioSentinel is a yeast radiation biosensor that will measure the DNA damage response caused by space radiation and will provide a tool to study the true biological effects of the space environment at different orbits.

Why?

Space radiation environment's unique spectrum cannot be duplicated on Earth. It includes high-energy particles, is omnidirectional, continuous, and of low flux.

How?

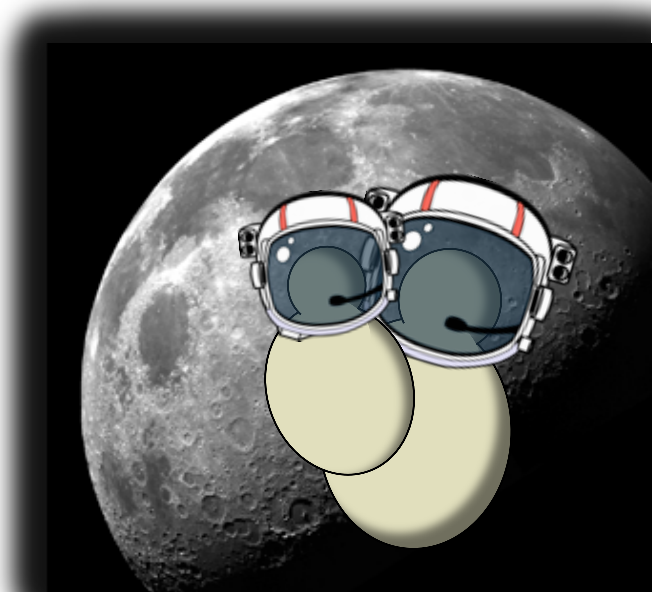
Lab-engineered *S. cerevisiae* cells will sense & repair direct (and indirect) damage to their DNA. Yeast cells will remain dormant until rehydrated and grown using a microfluidic and optical detection system.



Why budding yeast?

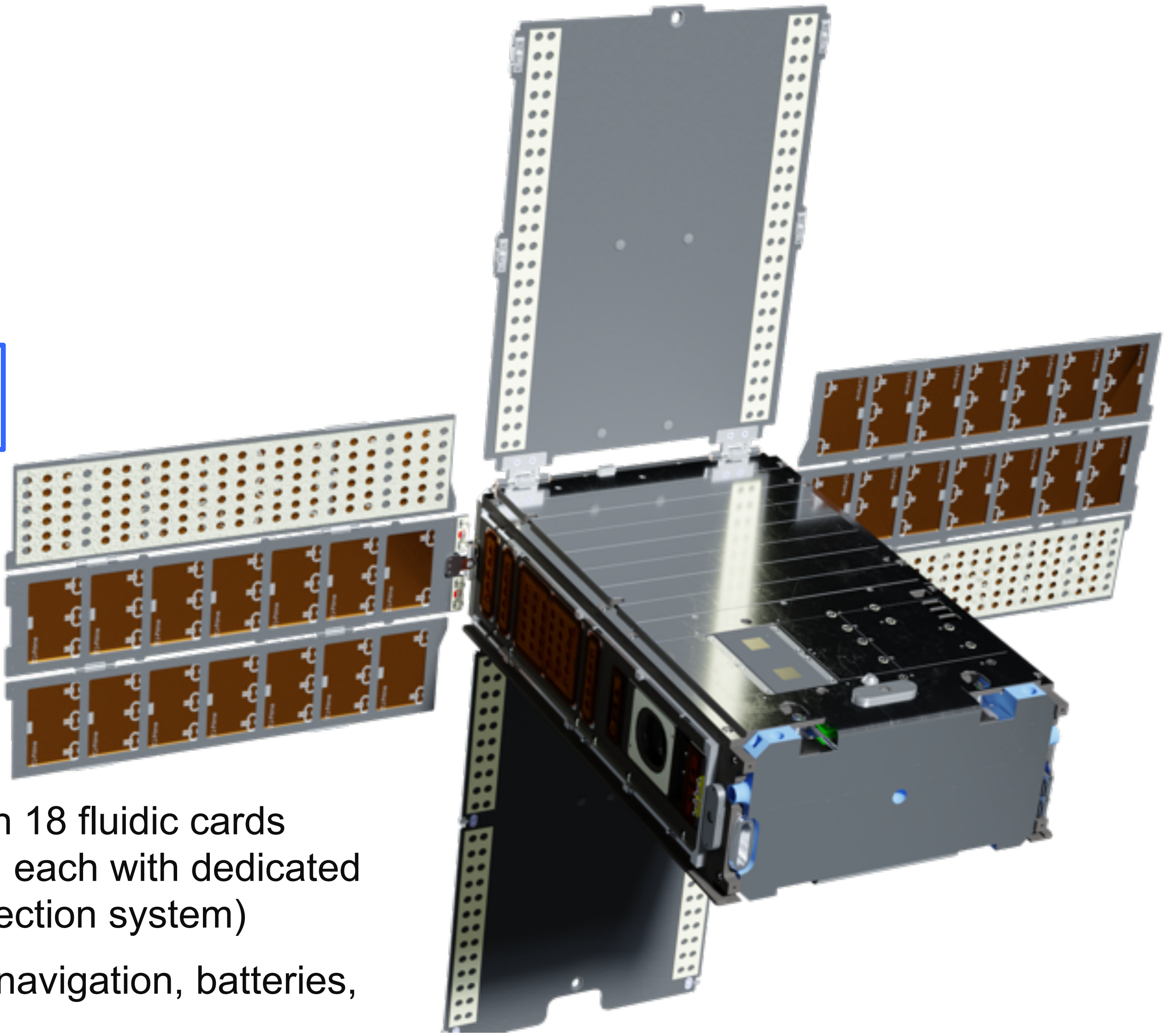
It is an eukaryote; easy genetic & physical manipulation; assay availability; flight heritage; ability to be stored in dormant state

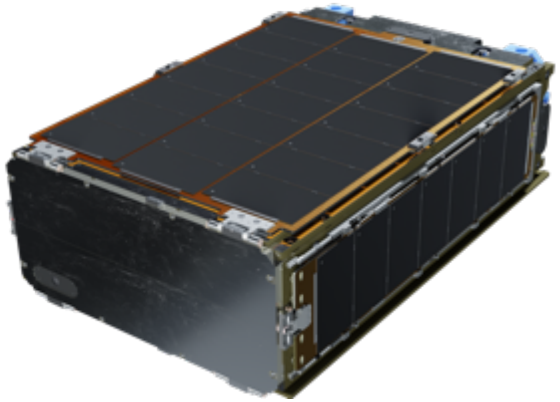
While it is a simple model organism, yeast cells are the best for the job given the limitations & constraints of spaceflight



BioSentinel: a bio CubeSat for deep space

6U Cubesat
37 x 24 x 12 cm ~ 10 L

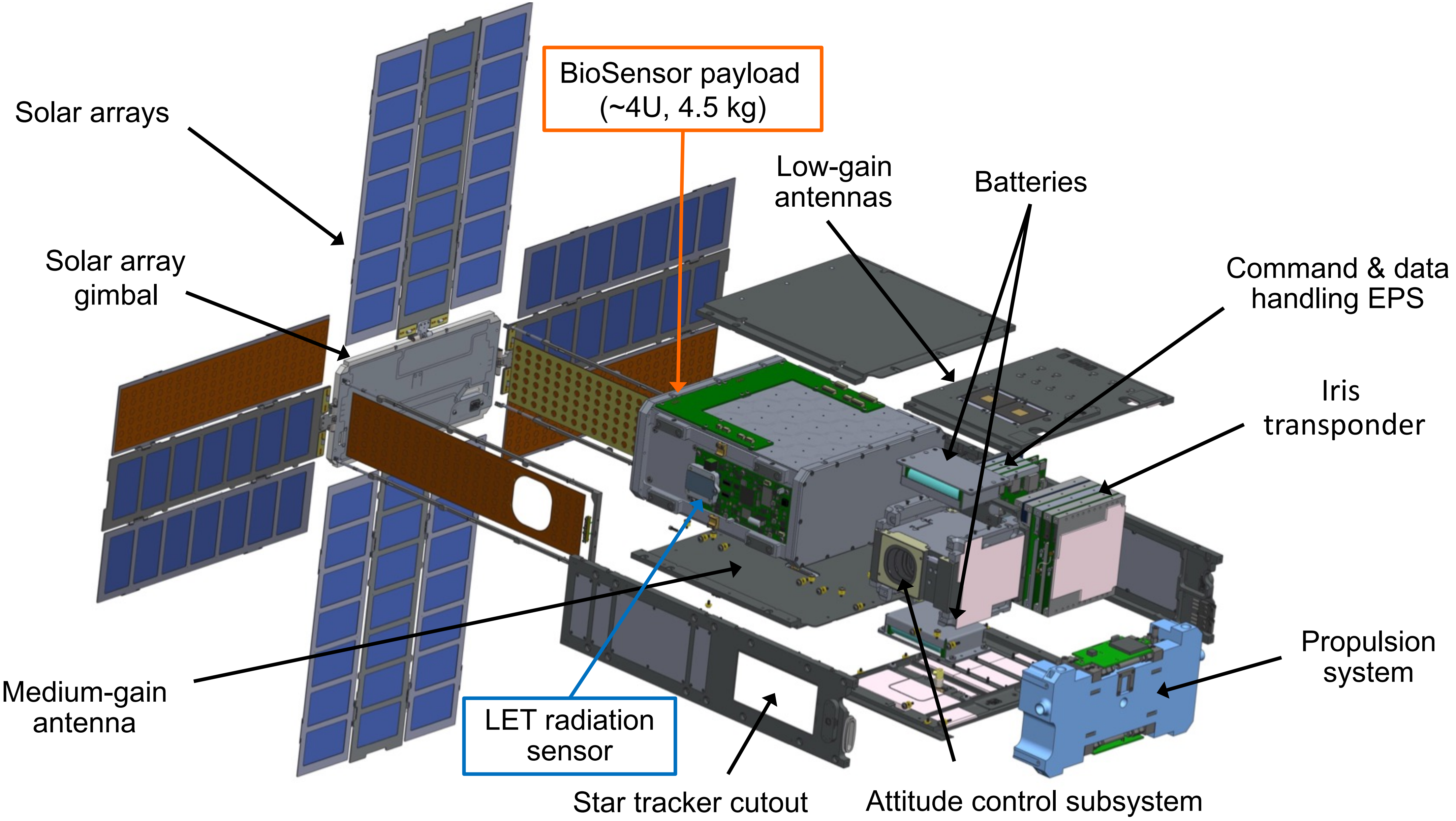




Spacecraft sections:

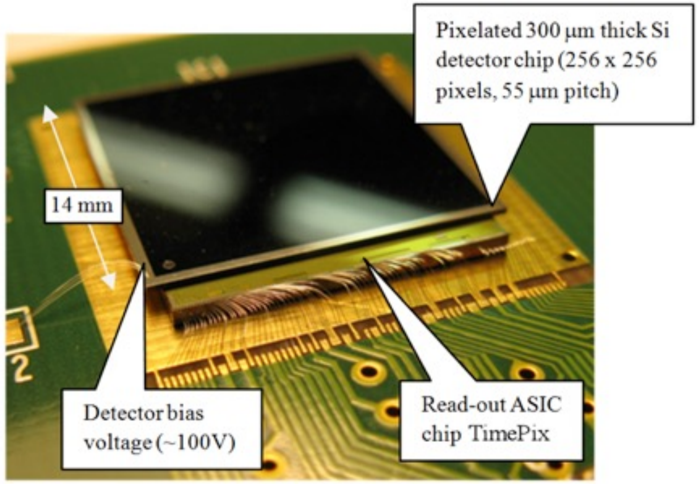
- BioSensor payload (~4U with 18 fluidic cards loaded with desiccated cells, each with dedicated thermal control & optical detection system)
- Spacecraft bus (propulsion, navigation, batteries, transponder, star tracker…)

BioSentinel: a bio CubeSat for deep space

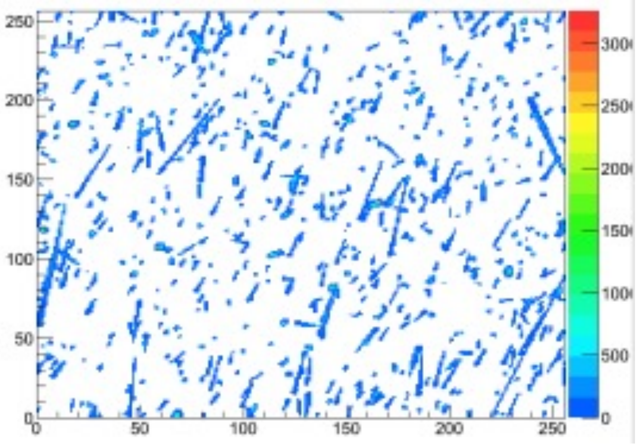


BioSentinel: LET spectrometer

- LET spectrometer device: Timepix solid-state device
  - Measures linear energy transfer (LET) spectra
  - Time-over-threshold (TOT) mode. Wilkinson-type ADC
    - *direct energy measurement per pixel*
  - LET 0.2 – 300 keV/µm into 256 bins, 3% width; store hourly bin totals
  - Download “local space weather” periodic snapshots
- SPE trigger (future missions): TID rate increase causes wetting of a fluidic card
  - LET shutter time and ground command as alternative / backup



TimePix Chip

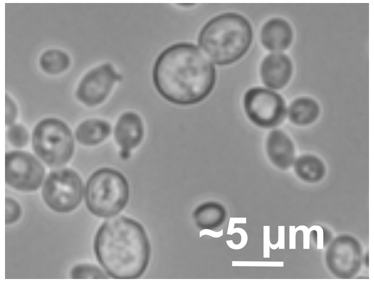


Typical TimePix frame
(256 x 256 x 14 bits)

LET spectrometer fit-check

BioSentinel: a bio CubeSat for deep space

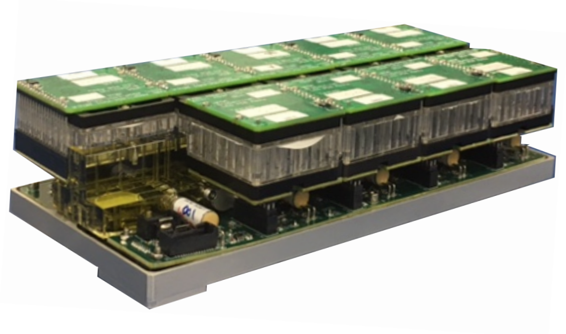
Budding yeast



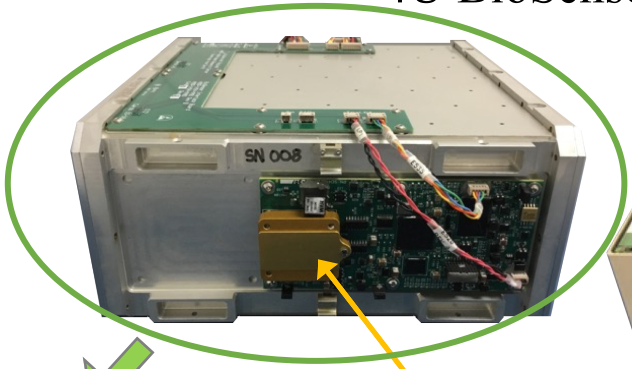
16-well fluidic card (x18)

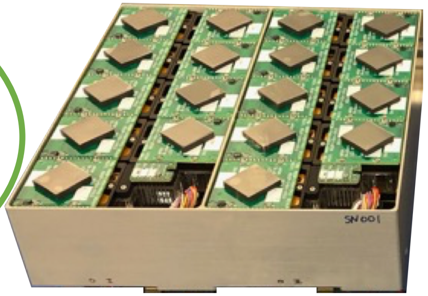
Card stack

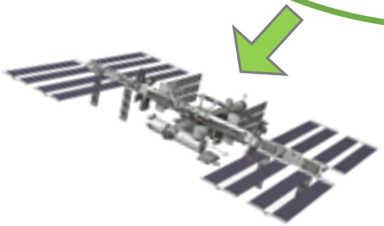
9-card fluidic manifold (x2)

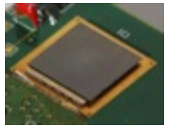


4U BioSensor payload



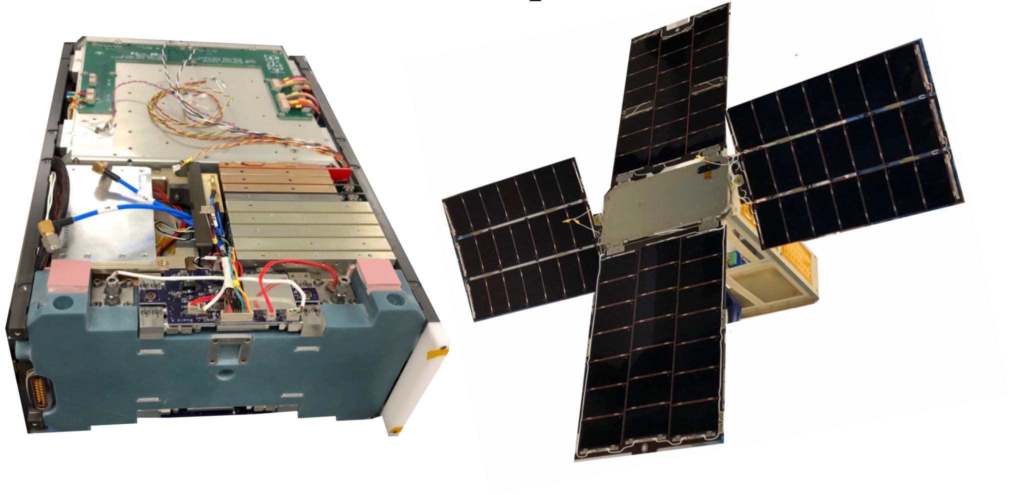




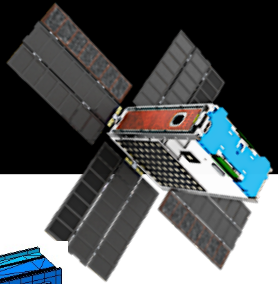


LET spectrometer

6U BioSentinel spacecraft

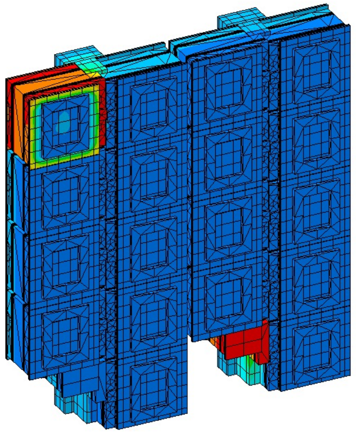


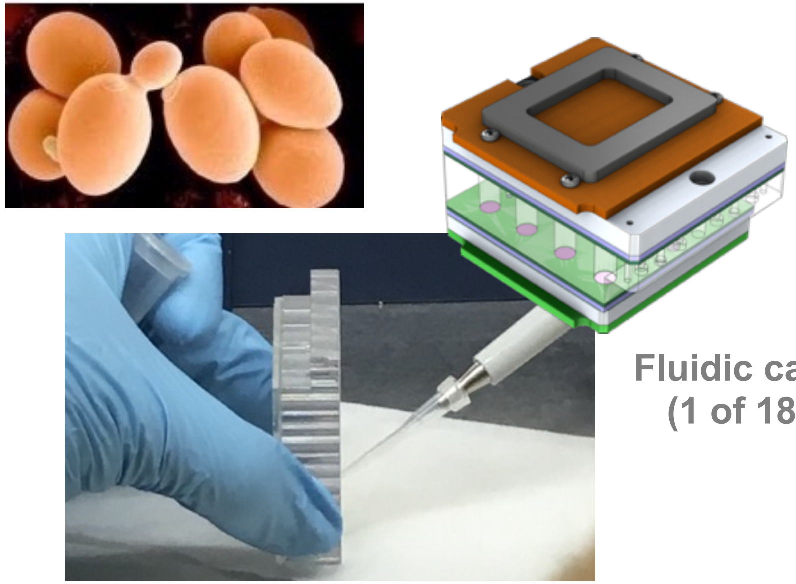
BioSentinel: experimental design



Initial parameters:

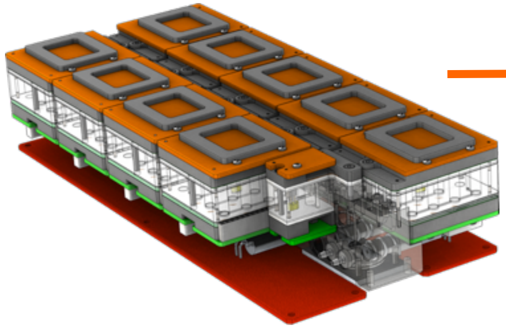
- 18 fluidic minicards (each card has 16 microwells) – yeast cells dried inside wells
- Yeast strains: wild type & HR-defective mutant strains
- Mission length: 6-9 months at KSC + 6-12 months in space (2 cards activated per time point)
- Dormant fluidic cards maintained at ~ 8-10°C to ensure longevity
- Active cards maintained at ~23°C for growth temperature
- One set of cards will be reserved in the event of an SPE

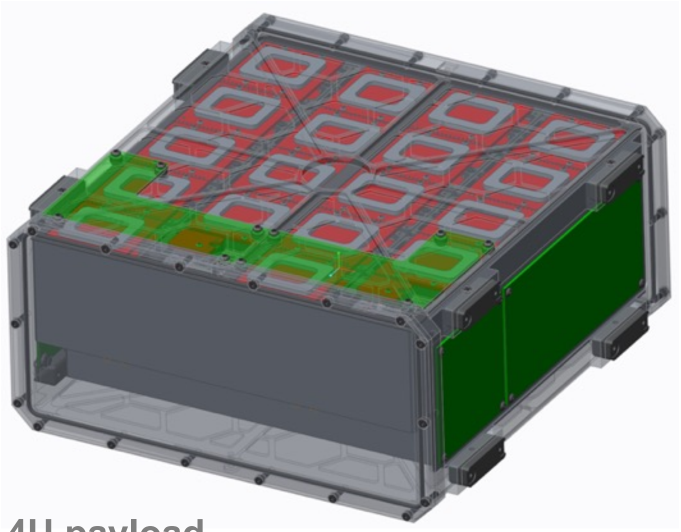




Fluidic card
(1 of 18)

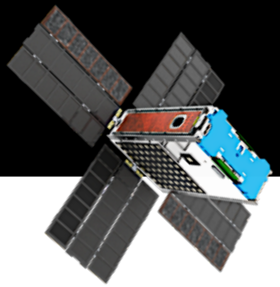
9-card manifold
(1 of 2)

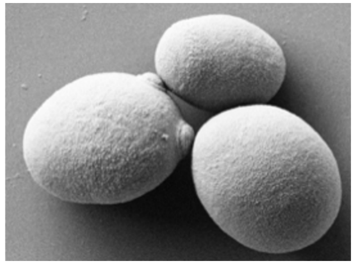


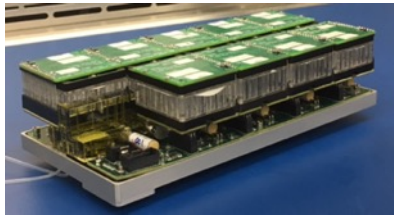


4U payload

Hardware and Testing Status





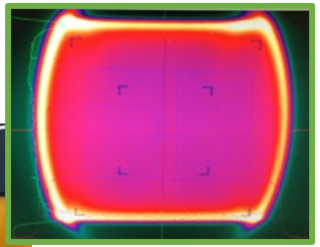


<u>Yeast strain selection</u>:

- Wild type strain (control for unrepairable DNA damage & yeast health)
- DNA repair defective mutants (radiation sensitive)

<u>Long-term biocompatibility & other tests:</u>

- Long-term medium & metabolic dye storage (<u>completed 2-year test</u>)
- Long-term yeast desiccation (<u>completed 2-year test</u>) & desiccation method selection (<u>completed</u>)
- Long-term biocompatibility in fluidic cards (<u>completed 2-year test</u>)
- Sterilization method selection (autoclaving *vs*. e-beam *vs*. EtO) (<u>completed</u>)
- Spacecraft EDU assembly, vibration & TVPM tests (<u>completed</u>)
- FlatSat optical calibration tests & EVT (<u>completed</u>)
- *Optical data processing & optimization*
- Integrated into Orion Stage Adapter on Sept 27, 2021 (aka <u>flight-ready</u>)

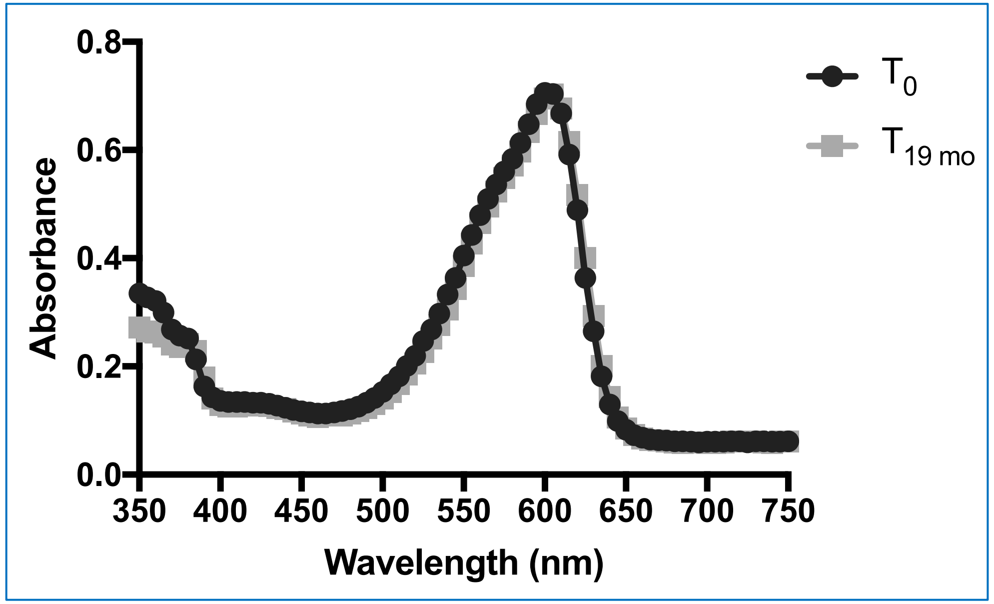


<u>Ongoing radiation experiments</u>:

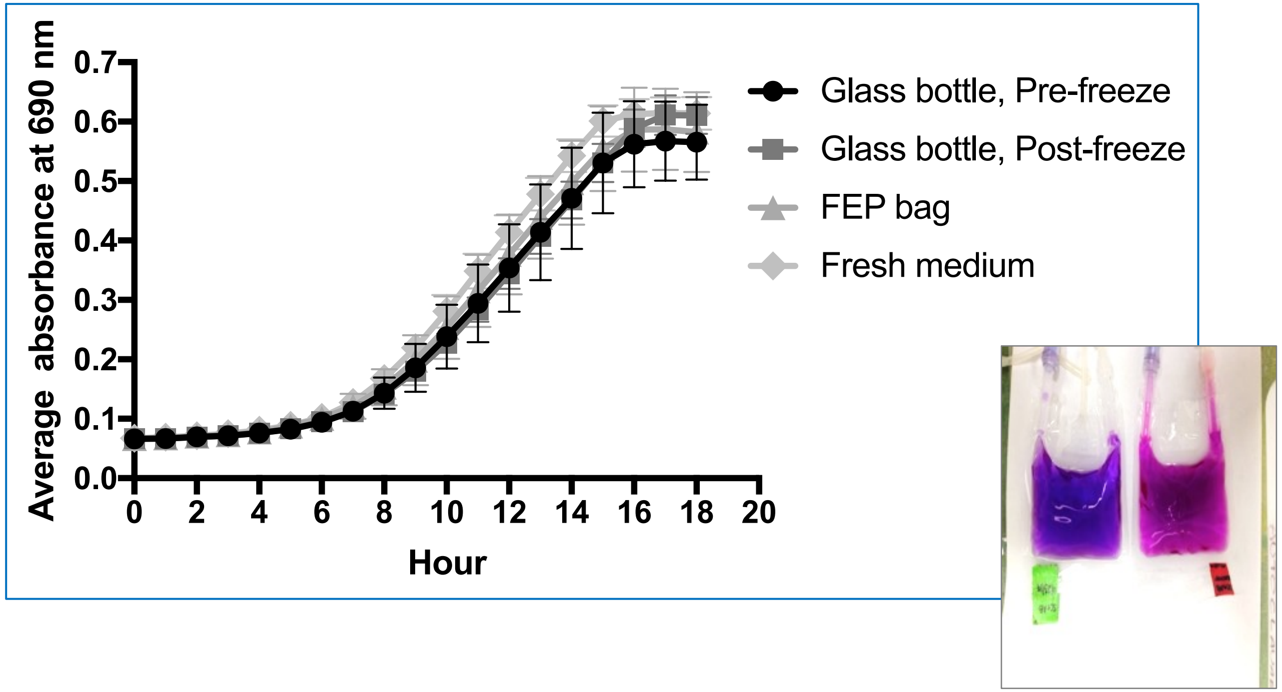
- Cells irradiated in suspension and in desiccated state (with & without shielding)
- Strain sensitivity via optical density readings in microplate readers or GSE optical units
- <u>Sources</u>: gamma (ARC); protons & SPE simulations (Loma Linda); HZE ions & GCR sims (NSRL)

BioSentinel: long-term reagent storage

alamarBlue full-spectrum analysis



Cell growth in aged and fresh SC medium

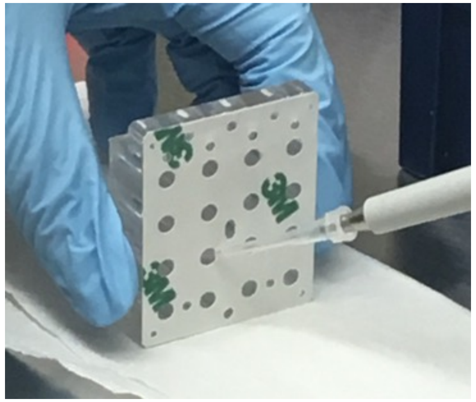


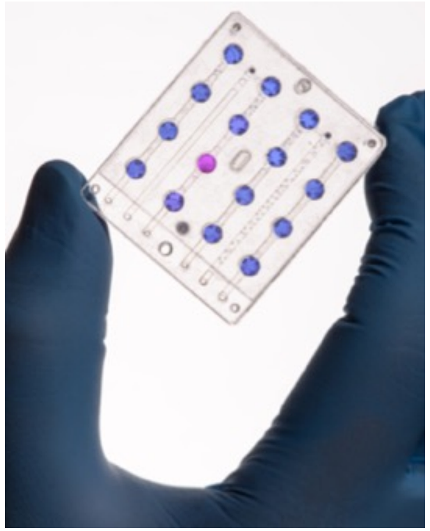
<u>Conclusions</u>:

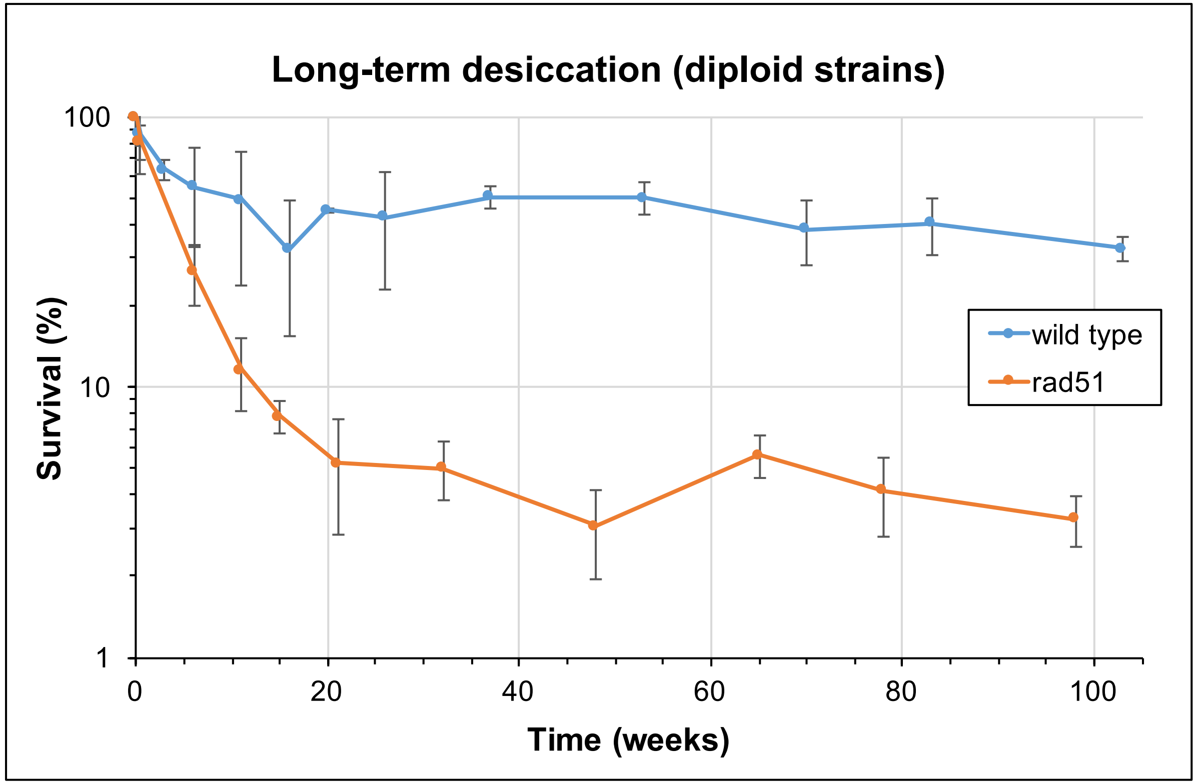
- Full-spectrum optical analysis (left): 19-month old alamarBlue dye shows no optical differences compared to fresh alamarBlue
- Wild type yeast cells grow similarly in freshly-made SC medium compared to SC stored in flight-like fluidic bags after 19 months (right)

BioSentinel: long-term yeast desiccation

Yeast cells are loaded into fluidic cards and air-dried prior to card sealing and payload integration. Cells will remain in desiccated / dormant state until activated in flight by addition of growth medium containing a metabolic dye



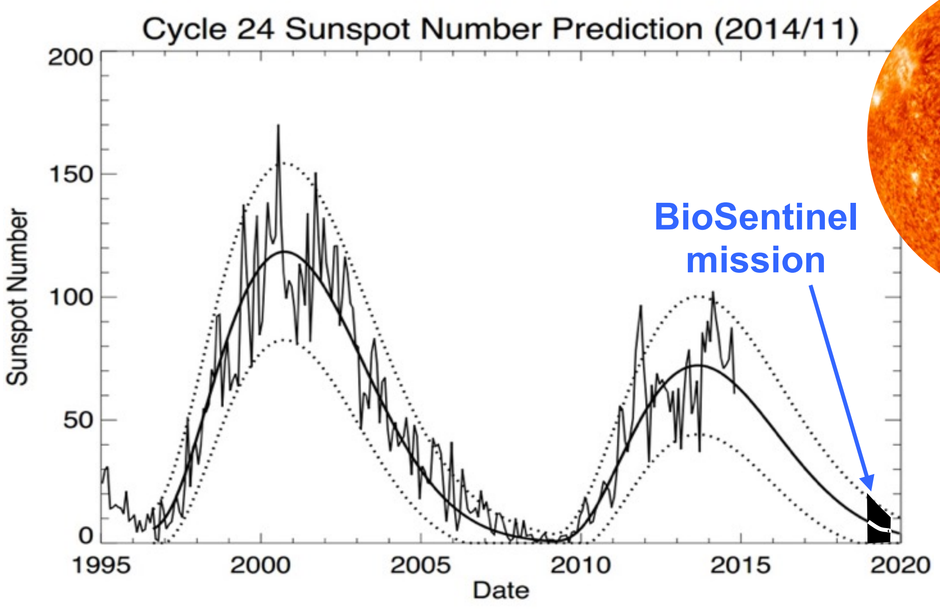


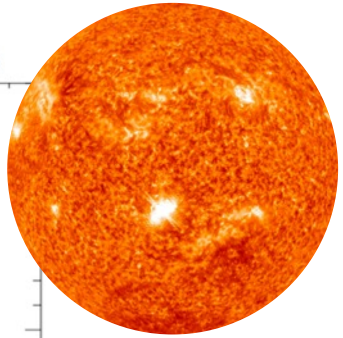


As expected, wild type cells show higher viability than DNA repair defective cells

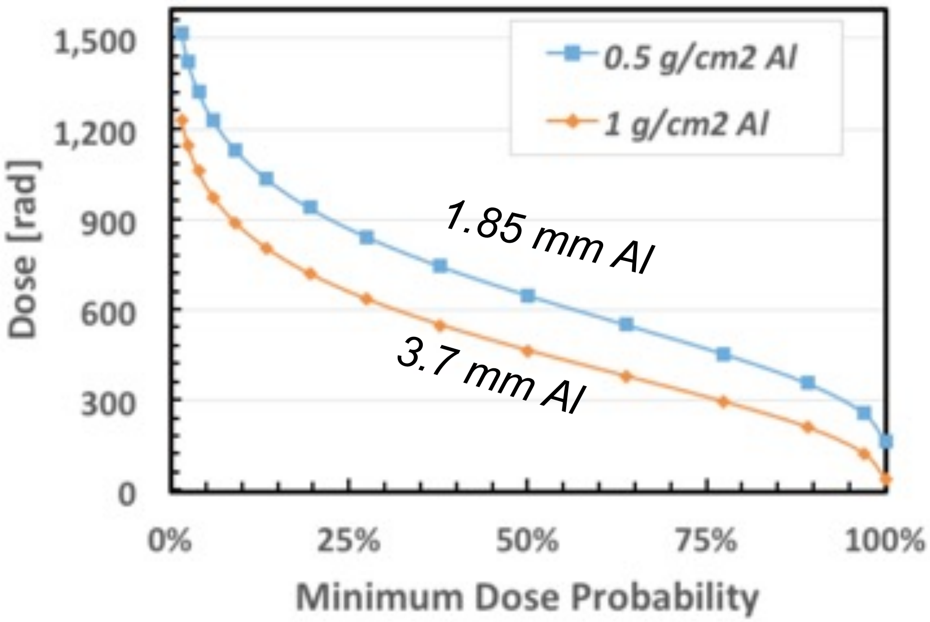
BioSentinel: interplanetary space radiation

What is BioSentinel going to encounter in deep space?





Total ionizing dose (Si) in 12 months: ambient flux + possible SPE(s)



Ben Klamm

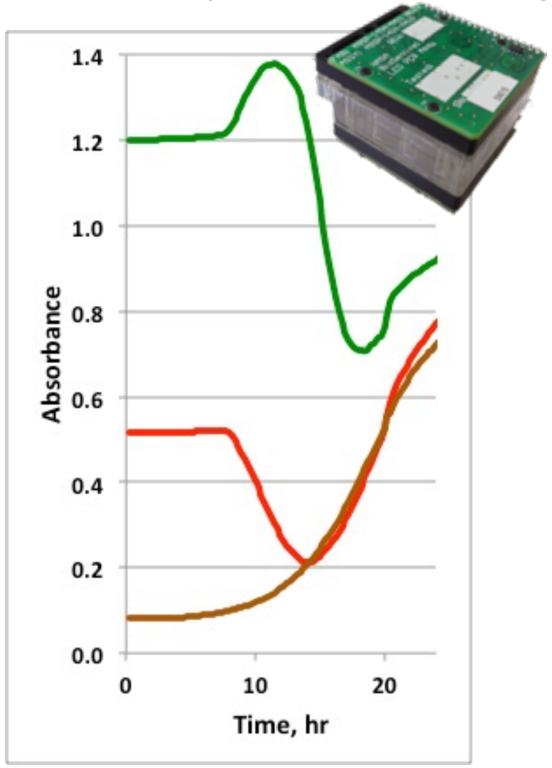
BioSentinel: optical detection system

Dedicated 3-color optical system at each well to track growth *via* optical density and cell metabolic activity *via* dye color changes

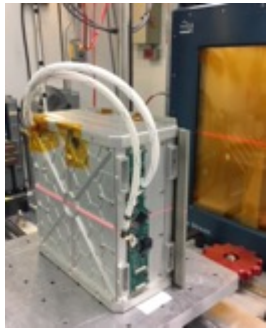
LEDs: 570 nm (green, measures pink)

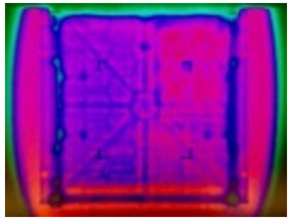
630 nm (red, measures blue)

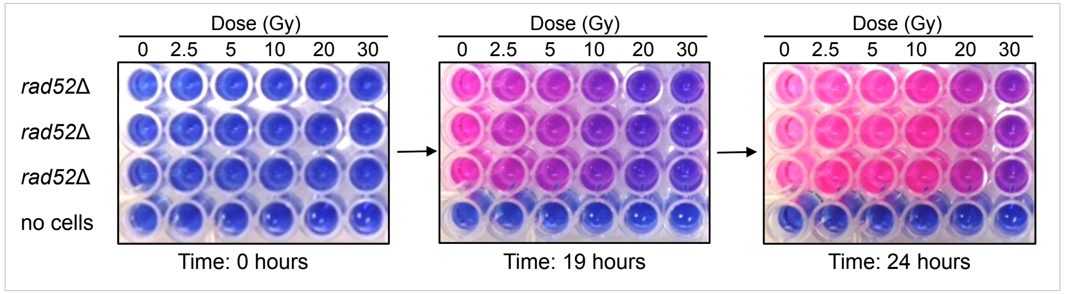
850 nm (infrared, measures growth)



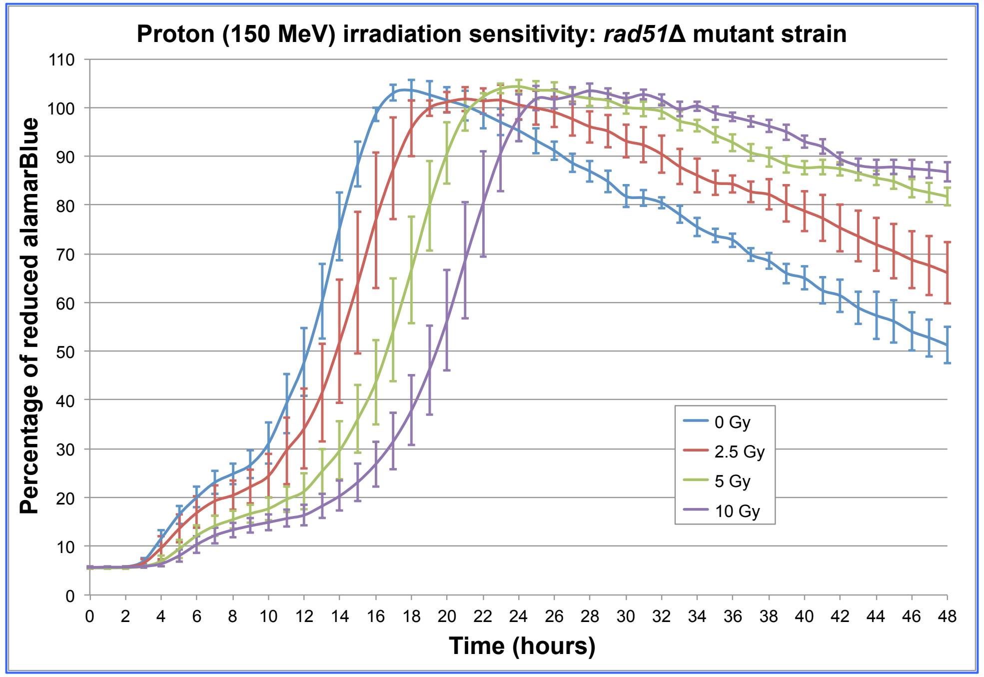
Yeast growth with flight-like optical unit





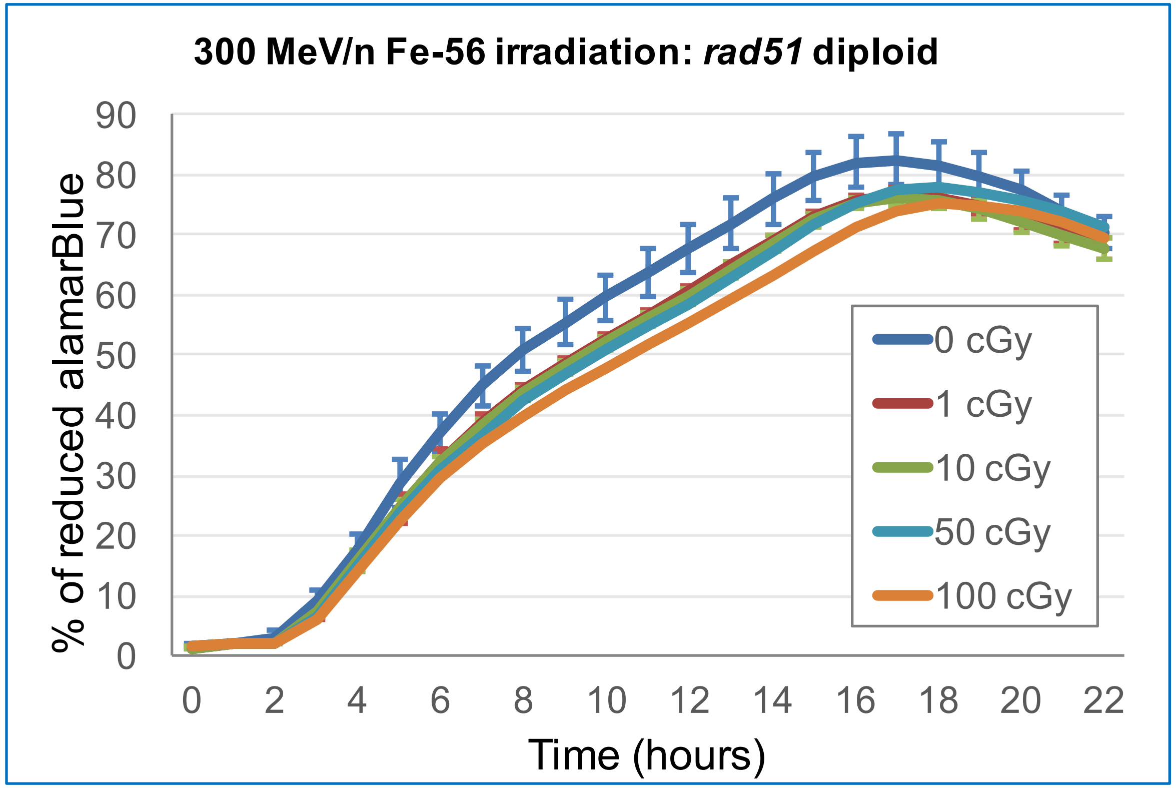


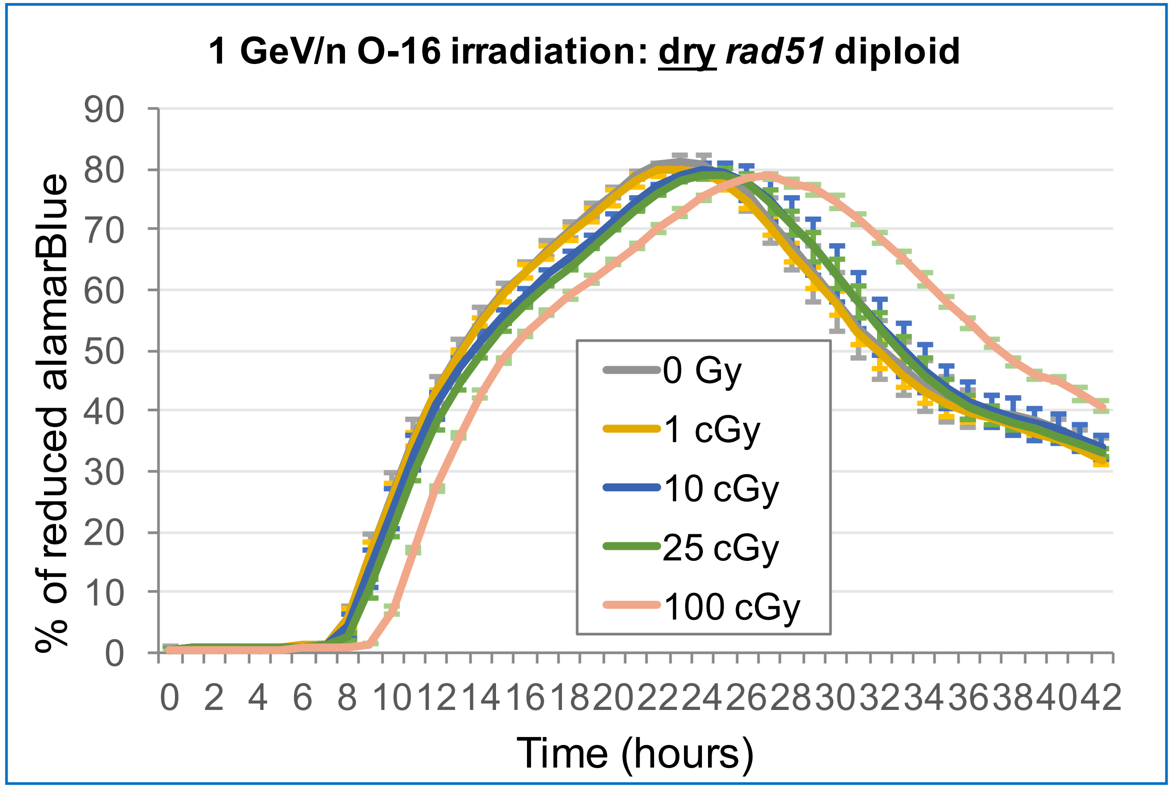
alamarBlue turns pink when cells are metabolically active



HR repair defective cells show sensitivity to ionizing radiation

BioSentinel: ground radiation studies



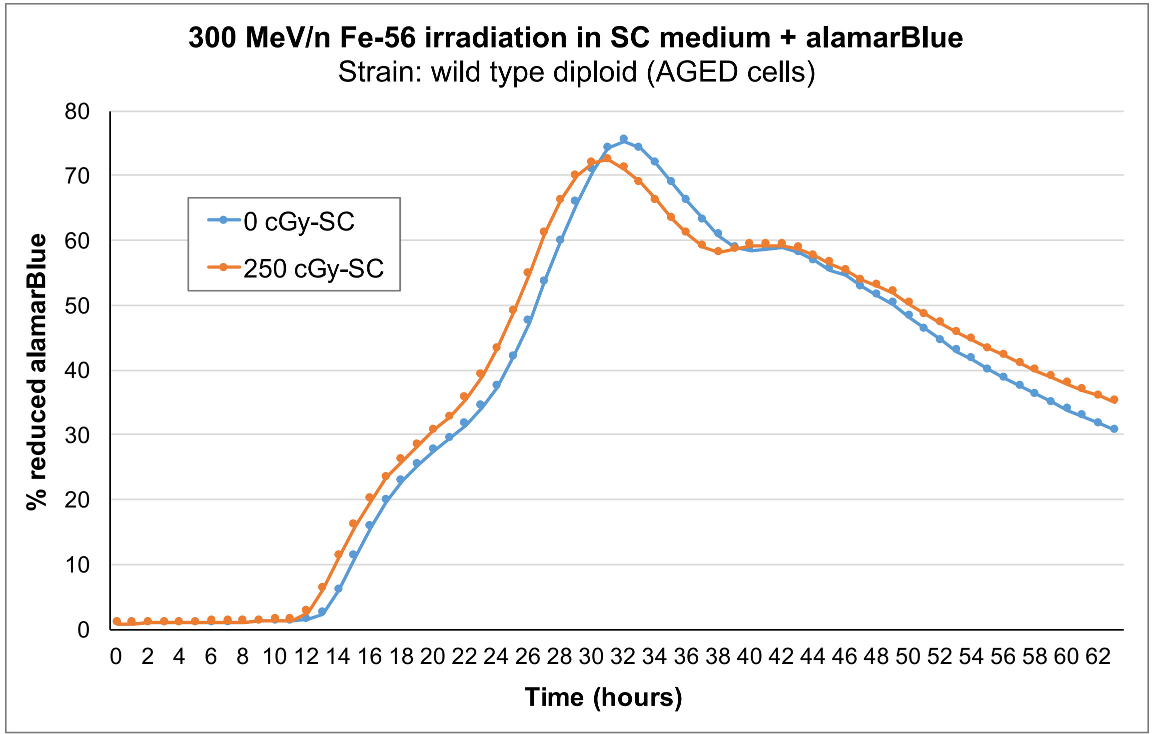


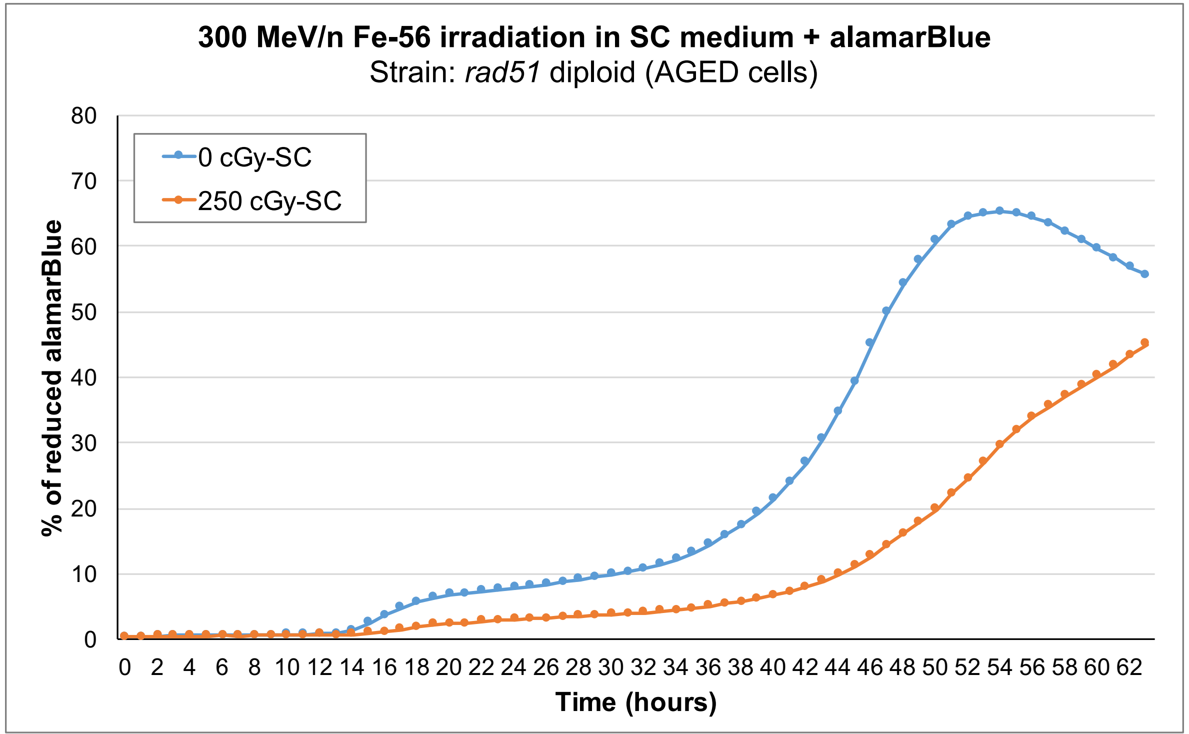
Strain	Dose (cGy)	Average of slope	*p*-value
rad51 diploid	0 cGy	5.48	
rad51 diploid	1 cGy	5.04	0.0369
rad51 diploid	10 cGy	4.90	0.00143
rad51 diploid	250 cGy	4.53	0.00445

Strain	Dose (cGy)	Average of slope	*p*-value
rad51 diploid	0 cGy	4.58	
rad51 diploid	10 cGy	3.89	0.000447
rad51 diploid	100 cGy	3.54	6.83E-05

HR-defective cells are sensitive to low doses of high-LET radiation

BioSentinel: ground radiation studies





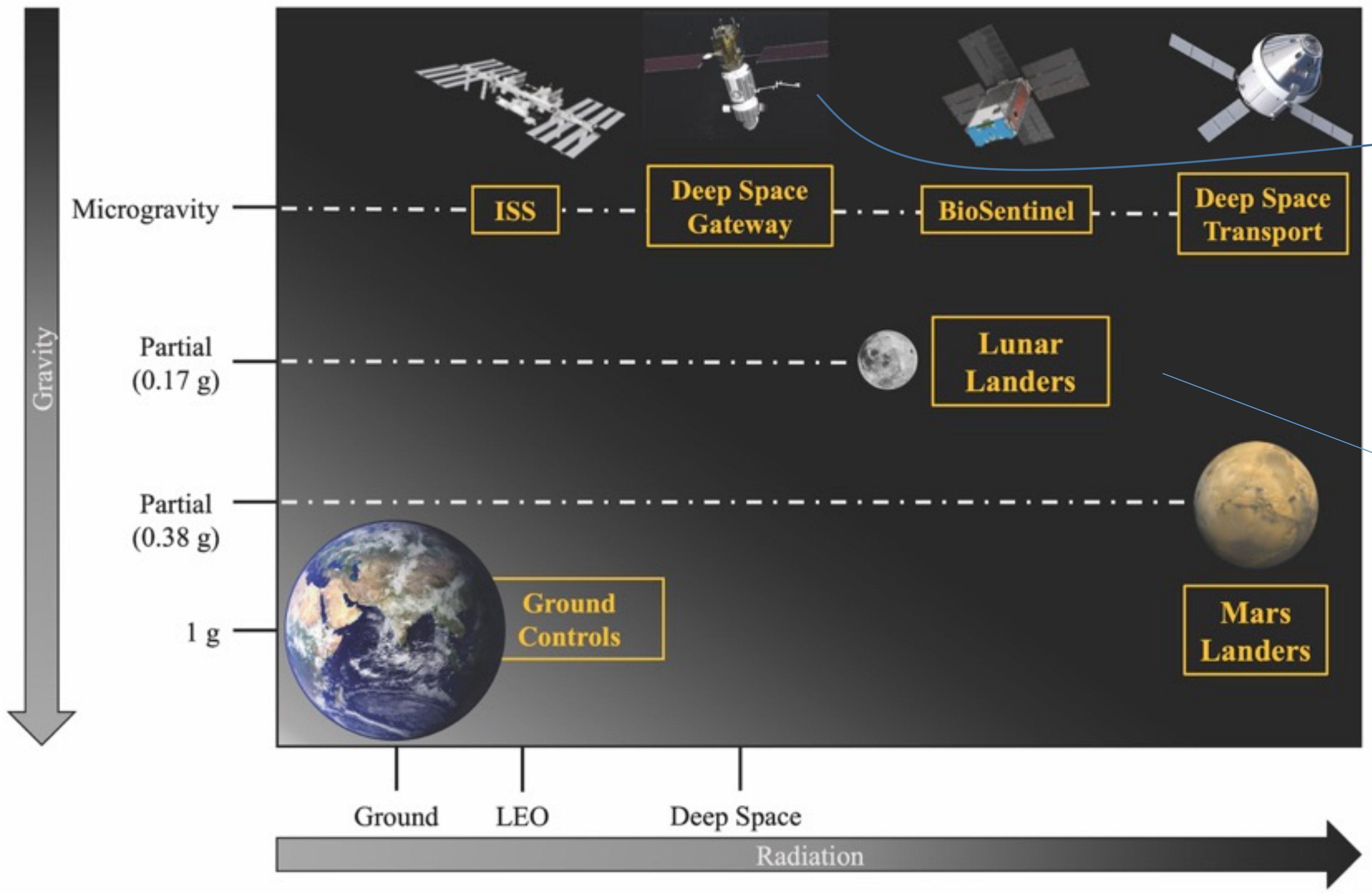
Strain	Dose (cGy)	Average of slope	p-value of Student's t-test
wt diploid	0 cGy	3.768446962	
wt diploid	250 cGy	3.797220975	0.389667098

Strain	Dose (cGy)	Average of slope	p-value of Student's t-test
rad51 diploid	0 cGy	1.669702202	
rad51 diploid	250 cGy	1.056909521	0.009304165

After 27 months in desiccated state, *rad51* mutant cells still show sensitivity to ionizing radiation

BioSentinel: future & ongoing objectives

A flexible design that can (and will be) used on different space platforms



Recent publications (2020 – 2021)

ASTROBIOLOGY
Volume 20, Number 8, 2020

DOI: 10.1089/ast.2019.2068

Introduction to BioSentinel

BioSentinel:
A Biological CubeSat for Deep Space Exploration

Sofia Massaro Tieze,[1,2] Lauren C. Liddell,[2,3] Sergio R. Santa Maria,[2,4] and Sharmila Bhattacharya[2]

ASTROBIOLOGY
Volume 20, Number 8, 2020
Mary Ann Liebert, Inc.
DOI: 10.1089/ast.2019.2073

Research Article

BioSentinel:
Long-Term *Saccharomyces cerevisiae* Preservation
for a Deep Space Biosensor Mission

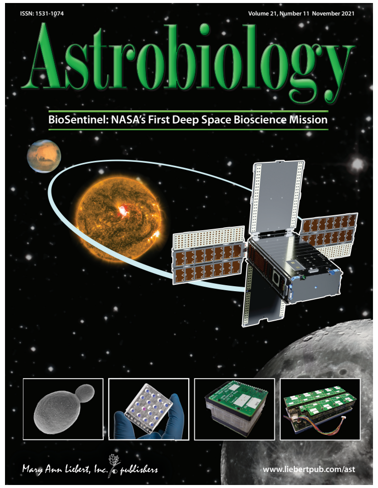
Sergio R. Santa Maria,[1,2] Diana B. Marina,[2,3] Sofia Massaro Tieze,[2,4]
Lauren C. Liddell,[2,5] and Sharmila Bhattacharya[2]

ASTROBIOLOGY
Volume 21, Number 5, 2021
Mary Ann Liebert, Inc.
DOI: 10.1089/ast.2020.2305

Research Article

BioSentinel:
A Biofluidic Nanosatellite Monitoring Microbial
Growth and Activity in Deep Space

Michael R. Padgen,[1] Lauren C. Liddell,[1,2] Shilpa R. Bhardwaj,[1,3] Diana Gentry,[1] Diana Marina,[1,4]
Macarena Parra,[1] Travis Boone,[1,5] Ming Tan,[1,6] Lance Ellingson,[1,5] Abraham Rademacher,[1,5]
Joshua Benton,[1,7] Aaron Schooley,[1,5] Aliyeh Mousavi,[8] Charles Friedericks,[1] Robert P. Hanel,[1]
Antonio J. Ricco,[1] Sharmila Bhattacharya,[1] and Sergio R. Santa Maria[1,9]



CubeSats for microbiology and astrobiology research **7**

Luis Zea[a], *Sergio R. Santa Maria*[b], *and Antonio J. Ricco*[b]
[a]BioServe Space Technologies, University of Colorado, Boulder, CO, United States,
[b]NASA Ames Research Center, Moffett Field, CA, United States

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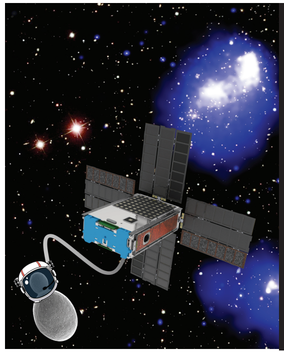
Proceedings

Developing Technologies for Biological Experiments in Deep Space †

Elizabeth M. Hawkins [1,2,3], Ada Kanapskyte [1,4] and Sergio R. Santa Maria [5,6,*]



Feature Article:

DOI. No. 10.1109/MAES.2019.2953760

BioSentinel: A 6U Nanosatellite for Deep-Space Biological Science

***Antonio J. Ricco, Sergio R. Santa Maria, Robert P. Hanel, Sharmila Bhattacharya, BioSentinel Team,* NASA Ames Research Center**
***Radworks Group,* Johnson Space Center**

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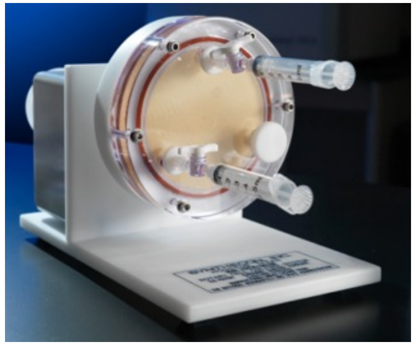
Perspective

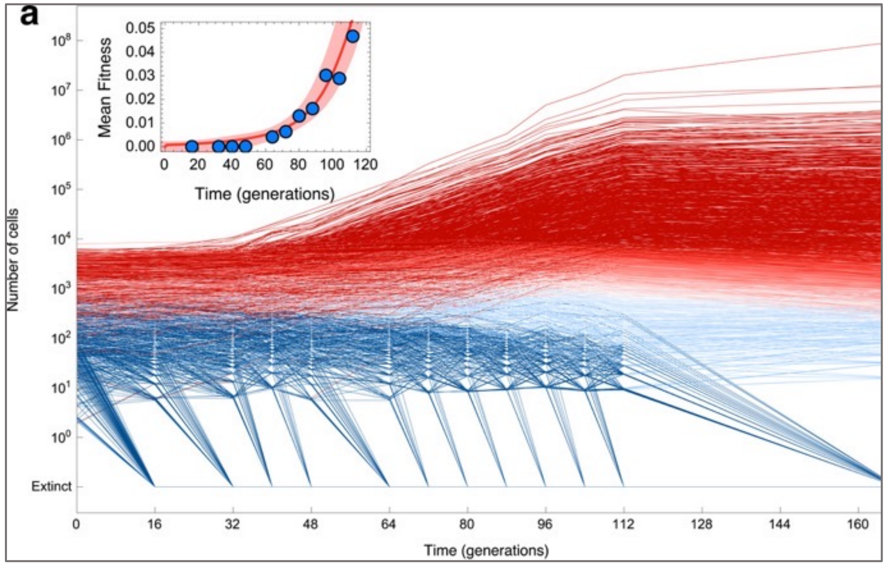
Space Biology Research and Biosensor Technologies: Past, Present, and Future †

Ada Kanapskyte [1,2], Elizabeth M. Hawkins [1,3,4], Lauren C. Liddell [5,6], Shilpa R. Bhardwaj [5,7], Diana Gentry [5] and Sergio R. Santa Maria [5,8,*]

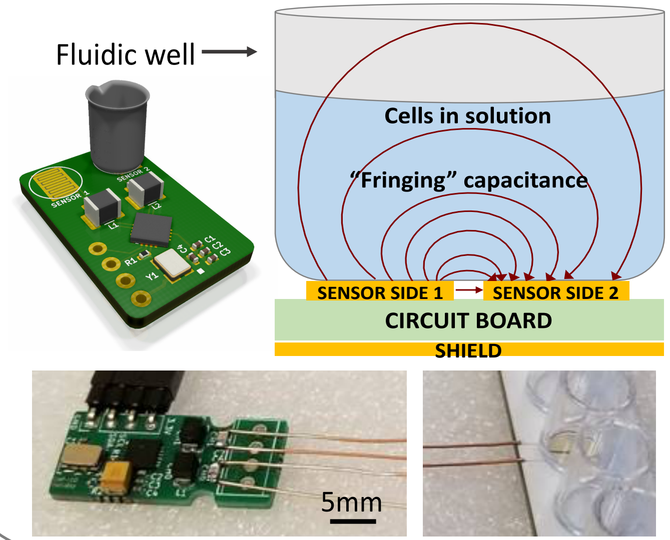
Other projects

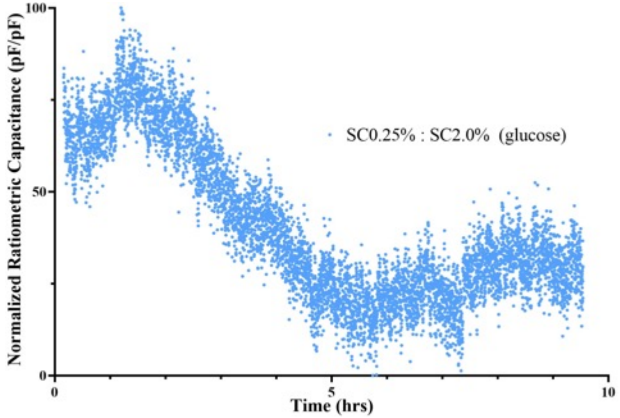
Adaptive evolution & acquisition of beneficial mutations under sim microgravity





Dielectric biosensors





LEIA ORGANA: biological response to lunar surface environment