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Campaign:

A New NASA Flagship Facility: PRECISE – Proton Radiation Environmentally Controlled Investigations for Space Exploration

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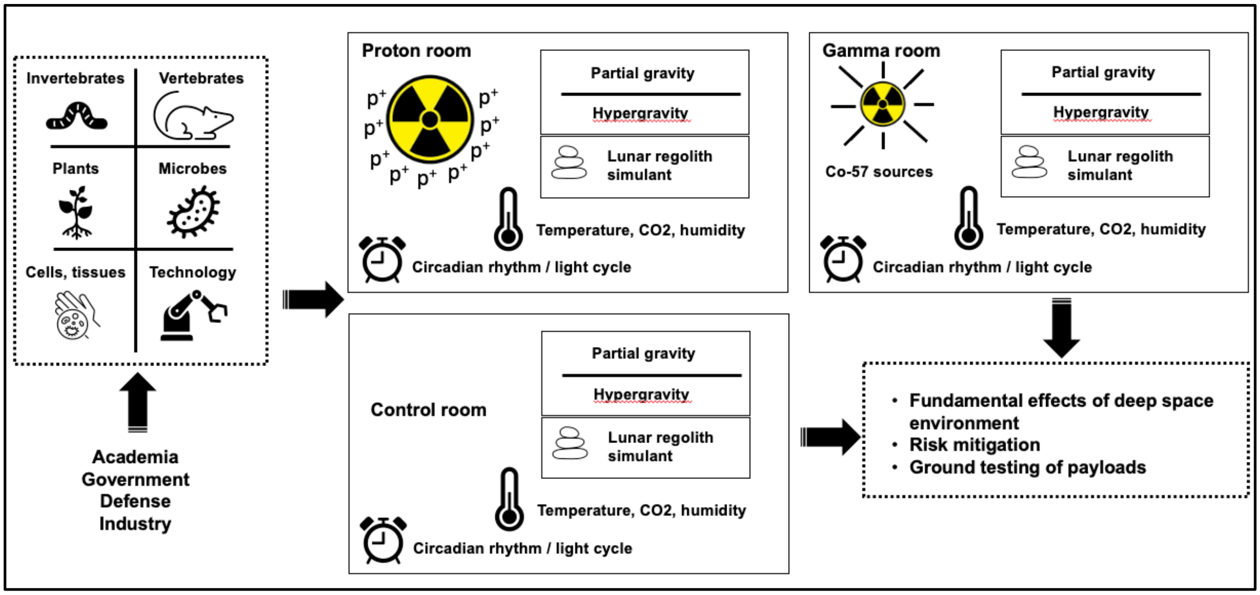

I. A brief introduction to space radiation encountered by astronauts.

This paper proposes a NASA-led investment in a flagship user facility at NASA Ames Research Center for simulating high energy protons and combined exposures to other spaceflight stressors for a wide variety of *in vivo, ex vivo,* and *in vitro* biological systems, as well as non-biological models of spacecraft and instruments.

One of the main risks in long-duration crewed missions is exposure to ionizing radiation. Ionizing radiation in space has two main sources: our sun and galactic cosmic radiation (GCR). Solar radiation consists primarily of protons, with a small percentage of helium and other light ions. GCR originates in supernovae in our galaxy and beyond and consist of 87% protons, 12$^{\%}$ ^{4}He particles and 1% heavier nuclei, often referred to as high energy-high charged (HZE) particles.

The relative contribution from each source depends on the mission profile. In low-Earth orbit (LEO), GCR and solar protons trapped by the Earth's magnetic field contribute approximately equally to the absorbed radiation dose, with protons comprising approximately 93.5% of the ionizing particles. Beyond low-Earth orbit (BLEO), *i.e.* beyond the trapped radiation belts, the proportion of protons in the total radiation field decreases from 93.5% to 87.5%.

Crews on extended missions beyond the Earth's magnetic field will also potentially be exposed to solar particle events (SPE), periodic emissions of very high numbers of high energy protons from the sun. SPE can last for tens of hours and produce acute doses, with dose rates as high as 0.5-1 Gy/hr. (A total body dose of 4 Gy is potentially lethal.) They are sporadic and difficult to predict. Designs for future exploration spacecraft and planetary habitats will likely include so-called "storm shelters", heavily shielded areas to which crews can retreat for the duration of the SPE.

Space radiation in the solar system is modulated by the 11-year solar cycle: when the sun is most active (solar maximum), the GCR is tempered by the solar wind, but the likelihood of SPEs is greater. At solar minimum, SPE are less likely but the GCR intensity is higher.

In addition to direct biological effects, protons and other charged particles interact with the surrounding material (*e.g.* spacecraft and habitat structures, and lunar or Martian soil, or "regolith") to generate secondary neutrons, which have high biological effectiveness, albeit with expected absorbed doses two orders of magnitude less than protons. Thus, when considering the biological effects of radiation, the radiation environment for space missions can be generally described as chronic low dose rate exposure to ionizing particles, primarily dominated by protons, with absorbed doses between 0.2 mGy/day and 0.7 mGy/day, depending on mission profile and point in the solar cycle.

II. An example to illustrate the need for improved ground facilities for space biology: radiation effects on plant biology.

The response of plants to ionizing radiation has been well-categorized in studies principally using *Arabidopsis thaliana* as a model organism.[1-3] For example, HZE radiation has previously been shown to induce transcriptional responses shared with plant reactions to a wide range of other environmental stressors such as high light and salt levels. Molecular genetic analysis has further characterized a cascade of events associated with to HZE-triggered DNA damage repair through classic signaling cascades such as the *ATR* and A*TM* kinases, which are also seen for mammalian systems.[4]

However, beyond *Arabidopsis thaliana*, there are few harvestable vegetable, fruit, or other edible plant studies on ionizing radiation impact, which would provide key insights that can be translated into crop improvements for deep space missions (Douglas *et al*., 2021 topical white paper; Haveman *et al*. 2021 topical white paper). The main constraints to progress in this area are: 1. the limited access to sources of ionizing radiation at low dose rates that would be comparable to spaceflight; and 2. large radiation rooms with low dose rates to allow growing reasonable number of larger harvestable plants. In addition, currently, there are no facilities to expose plants to multiple spaceflight stressors for extended periods of time. This is of concern for experimental work that has been conducted in the past as plants are highly environmentally sensitive and known to integrate multiple stimuli to drive appropriate physiology and development. It would therefore be critical to decipher how different space environmental stimuli interact. For example, creating a "lunar room", where plants are simultaneously exposed to protons while growing in regolith would be an ideal system to optimize growth for lunar missions.

Although this specific example concerns plant research, similar arguments apply to animal, microbial, and cell and tissue model research, which would strongly benefit from extended simulations under spaceflight conditions including low dose rate particle irradiation in combination with other spaceflight stressors.

III. Current state: lack of user facilities for simulating chronic space radiation.

In order to study the impacts of space radiation, NASA developed the NASA Space Radiation Laboratory (NSRL), a user facility at Brookhaven National Laboratory. The NSRL is capable of generating beams of protons and heavier ions at energies comparable to those in the GCR and SPE. However, this facility has inherent limitations, owing to its being part of a large accelerator complex operating principally for experimental high energy physics, making it difficult to conduct prolonged experiments or simulate the chronic low dose rate radiation environment. Space-relevant dose rates cannot be simulated, using instead daily fractionated exposures over several weeks, which provides a poor surrogate of space radiation environment.[5]

In an effort to simulate chronic low dose rates from space radiation, NASA has funded a user facility at Colorado State University for neutron irradiation of biological samples.[6] However, neutrons are secondary particles from the space radiation environment with particularly strong biological effects and do not accurately reflect the daily radiation dose and quality that astronauts face on the ISS or in deep space that is primarily composed of protons.

Although there are a number of proton irradiation facilities of sufficient energy in the United States, almost all of them are dedicated to cancer treatment, and researchers can only access the beam at night or on the weekends, when patients are not being treated. In addition, they offer only acute irradiation that can be used to simulate solar particle events, but are less relevant to GCR dose rates. As noted above, this lack of adequate resources has led the scientific community to simulate chronic radiation exposure by dose fractionation. Unfortunately, fractionation, which is a series of acute low dose irradiation doses at intervals of days or more, induces a biological response that is different from true chronic exposure. For example, it has been shown that tissue can be "primed" by radiation, leading to complicated processes such as adaptive response to reduce radiosensitivity.[7,8] Thus, there is no currently available method to reliably extrapolate from acute to chronic biological response-- dedicated chronic irradiation facilities are needed.

We thus conclude that NASA cannot effectively support human spaceflight research without a dedicated chronic space radiation simulator. The flagship user facility we are proposing here would be fully dedicated to chronic radiation studies, operating continuously and providing separate rooms dedicated to simulate various aspects of the space environment simultaneously: LEO room, lunar room, Mars room, space vehicle room (including hypergravity to simulate launch and landing), SPE room, etc. In contrast to traditional proton beams dedicated for radiotherapy, this facility would provide a large field of low fluence protons, allowing the exposure of various biological materials: plants, microorganisms (prokaryotes and eukaryotes), cell, tissue and organ models, invertebrate and vertebrate animals; to very low dose rates continuously for weeks to years. Lunar and Mars rooms could include regolith simulants that would also simulate exposure to secondary neutrons. Similarly, the vehicle room could be used to test biological effects behind different shielding materials and configurations.

A similar facility focused on acute neutron irradiation has been proposed in a Topical white paper by Weeks et al., which underlines the need for improved ground analogs for biological exposures to spaceflight stressors. It is possible that the recommendations from both papers could be combined to establish a single, comprehensive, multi-use facility, or alternatively, multiple smaller facilities could be established to allow easier access from different areas in the US and support collaborations among them as well as with the existing irradiation facilities at NSRL and Colorado State University.

IV. Challenges and opportunities in developing a new type of proton beam.

This project offers an exciting opportunity to develop a proton beam with capabilities that are not currently available, to meet a critical need for future human space exploration. By removing the need of a collimated beam for precise radiotherapy, this machine would not be as dependent on magnets to focus and shape the beam, leading to lower operating, maintenance and staff costs. Finally, the facility would remain in almost continuous operation, with only periodic interruptions for maintenance.

Multiple irradiation stations would be operating simultaneously with a technology to add and remove samples to achieve different doses. For even higher versatility, a non-uniform beam could be utilized where different dose rates are generated simultaneously in different locations across the beam cross section.

V. Recommendation: a new ground control facility for NASA.

Rationale. Ground controls for biological payloads are designed to accurately and precisely mimic the environment on the spacecraft, with the exception of gravitational changes and radiation exposure. For example, Space Biology Rodent Research (RR) mission ground control not only uses the same enclosure and food source, but also simulates the same light cycle, temperature, humidity, gas composition and other external variables based on telemetry data from the payload and the spacecraft (all simulated at Kennedy Space Center environmental chamber). This approach makes it possible to unfold the collective contribution of these environmental factors to the observed biological effects, for example, the impact of high CO_2 levels.[9] However, ground analogs simulate all the environmental factors *simultaneously,* making it difficult if not impossible to unfold their individual effects and the mechanisms controlling the biological responses. In addition, they include only limited spaceflight stressors: ground controls do not include arguably the two most significant ones (microgravity and ionizing radiation) as well as the stressors that are important for research beyond LEO, such as radiation originating from particle interactions with lunar regolith.[10]

Suggested Technology Developments. The proposed PRECISE (Proton Radiation Environmentally Controlled Investigations for Space Exploration) environmental simulation facility would address these limitations by including a chronic source of particle radiation and providing multiple rooms for individual or combined exposures to a panel of specific stressors selected based on needs of the space radiation biology community. Development cost is estimated at ~$30M over 4 years, with an annual maintenance cost of $5M (Fig. 1). One of the rooms would contain the proton beam setup for chronic low dose rate particle irradiation.
The panel of stressors will include the following:

- Radiation: chronic protons, chronic gamma rays and chronic UV rays; with acute protons, gamma rays and UV rays in a separate room to be used as a control.
- Gravitational changes: centrifuges (hypergravity during launch and landing), microgravity models: partial weight bearing and hindlimb unloading enclosures *in vivo*, rotating wall vessels and clinostats *in vitro.*
- Lunar and Mars regolith simulants.
- Proposed spacecraft materials and shielding configurations.
- Adjustable light system to simulate different day/night cycles and wavelength composition of natural vs. artificial light, due to the major effects of circadian rhythms on multiple biological systems.
- Adjustable temperature to reproduce low deep space temperature (3 to 4 K) and variation cycles. "Day and night" cycle caused by the rotation around the Earth has a period of 91 minutes resulting in fluctuation in temperature of 5 to 10°C. Moreover, the change in position of ISS orbital plane relative to the Sun can cause greater variations of temperature (up to 60°C) with a maximal reported temperature of about 50°C.[11]
- Adjustable pressure: The pressure varies from 10^{-1} Pa near Earth atmosphere to 10^{-14}Pa in deep space. Due to the degassing, pressure around the ISS is higher than in deep space ranging from 10^{-7}Pa in the Ram direction (e.g. front of the ISS relative to flight direction) to 10^{-4}Pa in the Wake direction (e.g. rear of the ISS relative to flight direction).[12]
- Adjustable gas composition to simulate the high CO_2, low humidity air on spacecraft.
- "Clean room" to simulate the microbiological environment of spacecraft.
- Adjustable noise and vibration levels using controlled platforms.

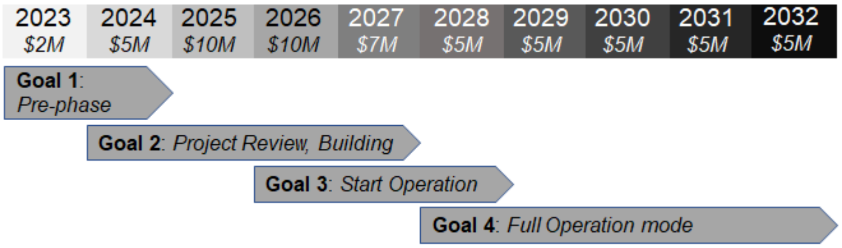

Fig. 1 – Cost and Timeline

Practical Considerations. The rooms will have to be of sufficient size to accommodate multiple experiments using different model systems: plants, microorganisms (both prokaryotes, such as bacteria, and eukaryotes, such as yeast), invertebrates (*D. melanogaster, C. elegans*) and vertebrates (mice and rats), as well as cell, tissue and organ models with the ability to operate under BSL2 precautions (for primary human cells). Other practical considerations include allocating sufficient space for large equipment, such as centrifuges for hypergravity simulations, as well as for animal colonies to ensure sufficient numbers for reproducible research, and cell culture, organ/tissue culture and microbial incubators (Ott et al., 2021 Topical White Paper), and plant and invertebrate environmental chambers. Finally, best practices to comply with the ALARA principle (keeping the radiation exposure as low as reasonably achievable) for the staff and researchers will determine the irradiation setup, possibly including automated retrieval of samples, movable shielding and designated instrument shutoff times for maintenance.

Collaborative Research Opportunities. In addition to its scientific value in understanding the fundamental biological effects of the space environment, this facility will provide a perfect testbed for new techniques and devices before launching them as payloads. It will be particularly advantageous for testing autonomous biological systems for launch readiness (described in more detail in Campaign White Paper *Telemetry-Based Biology for the Artemis Era and Beyond*, Principal Authors: Egle Cekanaviciute and Jared Broddrick), radiation hardening. Facility could be extended to collaborations with planetary science missions to test their instruments in the context of relevant space stressors, such as lunar regolith or simulate sterilization by ionizing radiation during transit to the science target for planetary protection.

Furthermore, it could be adapted for operational training of crew in preparation for their activities in lunar orbit and on lunar surface, possibly by creating the exact analog of the proposed lunar surface base for scientific research described in a companion Topical White Paper *Lab Facilities Required for Transformational Science* (Principal Author: Tara Ruttley).

We believe that the proposed research facility offers a unique opportunity to combine the best practices and fields of expertise among multiple NASA centers, including microgravity and plant research at KSC, animal and cell/tissue models at ARC, microbiology and "clean room" environments at JPL, human factors research at JSC and material science research at MSFC. Potential collaborators outside NASA include academic researchers as well as industry partners, such as proposed commercial space stations in LEO (e.g. Axiom Space, Sierra Space, Blue Origin) and commercial lunar payload systems (CLPS), as well as international partners.

Finally, the results generated by chronic proton irradiation may complement data generated using other simulators of space radiation both within the US (CSU neutron facility, NSRL) and internationally (GSI particle accelerator facility for ESA, RISE setup for ESA and BELSPO, Tsukuba space radiation simulator for JAXA). Sample and data sharing will be encouraged by making all research results open access and publicly available via NASA Open Science Initiative including GeneLab, Life Sciences Data Archive (LSDA) and NASA Biological Institutional Specimen Collection (NBISC).

In summary, we propose that the need for a dedicated **PRECISE** (Proton Radiation Environmentally Controlled Investigations for Space Exploration) ground facility to simulate the space environment, together with the benefits for scientific research and technological development provided by this facility, merit the institutional focus and funding at a Campaign level. Such a facility will significantly advance the understanding of the biological effects of the deep space environment and speed up the development of methods to mitigate the associated health risks, in addition to providing a testbed for new payload technologies. We envision that its use would extend beyond NASA to facilitate the collaboration among different public and private sectors and between different countries, with the common goal to advance human deep space exploration.

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