Title: **Sustaining Human Life beyond Earth**

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Summary:

- Exploration of space and celestial bodies has outpaced our understanding of how living in space alters organisms and how sustaining human life beyond Earth can be feasible
- Designing the framework to successfully and ethically sustain human life beyond Earth requires scientific integration across at least thirteen domains of biology
- Solutions must provide resilient human-designed ecosystems that thrive in unknown environments
- Solutions would also provide a new experimental platform to elucidate "Rules of Life" guiding biology on Earth

Introduction & Background

Engineering dominates the training of our first astronauts. Yet the growing feasibility of human colonization outside Earth demands an additional set of expertise to design and lead missions to space stations, the Moon, Mars and beyond. Researchers from every subdomain of biology are needed as space pioneers in order to sustainably, ethically plan for human life in space (Table 1). **Broader Impacts:** The potential impact of identifying ways to sustain human life in space and on other planets would enable new perspectives on key biological questions on Earth. Among the many questions that would be addressed include: How do organisms adapt to new environments? Do principles of evolution and selection hold in all environmental contexts? How can sustainability be ingrained in a new society? What are the bare minimal biological, agricultural and ecological requirements for sustaining human life across generations?

An open discussion of reintegrating biology to identify ways to sustain human life beyond Earth is prescient now. Our biological understanding of space and space travel lags behind our ability to explore. The advent of new engineering technologies is rapidly changing the space ecosystem: (1) commercial technologies to explore space are becoming accessible to laypeople; (2) exploration by robotic systems, advances in chemical sensors, and transmission across space by high-powered antennas have enabled near real-time knowledge about the soil and chemical make-up of nearby moons and planets, and rare ecosystems on Earth (Belilla et al., Nature Ecology & Evolution, 2019); and (3) the first attempts at growing plants on the Moon have already been reported (NASA, 2015, *"LPX First flight of Lunar plant growth experiment;"* Wong, New Scientist, 2019, *"First moon plants sprout in China's Chang'e 4 biosphere experiment").* At the same time, biological research on the development of new ecosystems and societies from scratch has a long history, riddled with varying degrees of failure and minimal success (e.g., the Biosphere in Arizona, BIOS-3)

Reproducing a model system to study developing space ecosystems brings a myriad of challenges. While we have successfully sent astronauts to live in space for many months, and living organisms across taxa are being studied in the space, we have yet to identify native life outside Earth. Understanding how stressors in space impact living organisms including humans has provided more insight including characterizing the effects of radiation, zero gravity and hypoxia on molecular expression, cell phenotypes and physiology (Beheshti et al., Int J Mol Sci. 2019; Song et al., Nature Ecology & Evolution, 2019; Hanawalt and Sweasy, Environ Mol Mutagen, 2019; Seyednasrollah et al., Sci Data. 2019; Park et al., Sci Rep. 2019). Rapid technical advances in sensing technology are also enabling quantitative studies of how microorganisms evolve “in the wild” in space and how the ecosystem of other planets change over time and planetary distance from the Earth and our Sun. However, numerous challenges remain that span fields of biology (Table 1). **How to Start? Implementation** Two potential starting points make the biological challenge trackable: (1) terrestrial landscapes of abiotic biomorphs (e.g., Belilla et al., Nature Ecology & Evolution, 2019), and (2) highly controlled experimental platforms applied to study organisms (including humans) in space. Furthermore, introducing and sustaining life beyond Earth becomes more feasible by our ability to leverage biological paradigms and tools on Earth. Among these are:

- Paradigms:
  - Systematic, evolutionary and sustainability studies of increasingly complex biological organisms can provide a framework to guide how new societies are designed (e.g., Dinerstein E, et al., Sci Adv. 2019; Schrodt et al., PNAS, 2019; Song et al., Nature Ecology & Evolution, 2019).
  - Research on morphological (Lewis et al., Nature Ecology & Evolution, 2019) and ecosystem responses to novelty (Lugo et al., Encyclopedia of the Anthropocene, 2018)
- Technology & Tools:
  - New quantitative and sensing methodologies that enable real-time studies of adaptation to space
  - Machine-learning / AI-enabled exploration: predictions of adaptation of the human body across scales and the ability to anticipate and/or generate unknown new life via genetic manipulation
  - Advances in mechanosignaling and the ability to study the detailed effects of microgravity on cell transcription and protein turnover across organisms

The goal of this short vision outline/paper is to catalyze discussions as to how to integrate domains of biology and build from existing paradigms and tools to address ways to ethically, sustainably enable human life beyond Earth. A follow-up manuscript is in preparation by the above authors, and we welcome researchers across domains to join us.

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Table 1. Domains of biology that need to be integrated to support a framework for sustaining human life on another celestial body and/or in space.

Domain of Biology	Challenge to Sustain Human Life beyond Earth	Tools or Paradigms to Leverage
Anthropology	Understand how to optimize the development of new human societies and cultures	deep time & historical records
Bioethics	Advise on the ramifications of introducing and sustaining life beyond Earth	ethics frameworks
Biophysics	Decipher how physical forces and electromagnetic fields in space alter biology	mechanosensors, mechano-genomics
Cell Biology	Characterize the constraints on cell biology in space	cell atlases, cell & tissue engineering
Developmental Biology	Determine how space alters development in all taxa	model systems of development
Ecology & Evolution	Identify ways to predict and control the developing extraterrestrial ecosystem	evolutionary theories and models
Genetics	Predict and/or optimize the genetic and epigenetics of organisms living outside Earth	gene editing, epigenetic sequencing
Mechanobiology	Predict how zero gravity alters organisms	mechanosensors, mechano-imaging
Neurobiology	Understand how brains develop and respond to the extraterrestrial environment	measurements of cognition & brain dev.
Paleontology	Guide the design of new ecosystems that are resilient and sustainable	fossil records
Plant Biology	Guide the planning for initial flora ecosystems beyond Earth	molecular tools
Psychology	Optimize the human space pioneers' interactions across generations	paradigms and tests
Systems Biology	Integrate the knowledge of extraterrestrial effects on living systems across scales of biology and time	biosensing, machine learning, AI, multiscale modeling

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