Received: 13 July 2023 | Revised: 29 January 2024 | Accepted: 30 January 2024

DOI: 10.1002/ajhb.24048

SPECIAL ISSUE ARTICLE

American Journal of Human Biology WILEY

The human biology of spaceflight

Mallika S. Sarma | **Mark Shelhamer**

Human Spaceflight Lab, Johns Hopkins School of Medicine, Baltimore, Maryland, USA

Correspondence
Mallika S. Sarma, 1501 E. Jefferson St., Human Spaceflight Lab, Johns Hopkins Medicine, Baltimore, MD, USA.
Email: msarma1@jhu.edu

Funding information
Translational Research Institute for Space Health; National Institutes of Health

Abstract

To expand the human exploration footprint and reach Mars in the 2030s, we must explore how humans survive and thrive in demanding, unusual, and novel ecologies (i.e., extreme environments). In the extreme conditions encountered during human spaceflight, there is a need to understand human functioning and response in a more rigorous theoretically informed way. Current models of human performance in space-relevant environments and human space science are often operationally focused, with emphasis on acute physiological or behavioral outcomes. However, integrating current perspectives in human biology allows for a more holistic and complete understanding of how humans function over a range of time in an extreme environment. Here, we show how the use of evolution-informed frameworks (i.e., models of life history theory to organize the adaptive pressures of spaceflight and biocultural perspectives) coupled with the use of mixed-methodological toolkits can shape models that better encompass the scope of biobehavioral human adjustment to long-duration space travel and extra-terrestrial habitation. Further, we discuss how we can marry human biology perspectives with the rigorous programmatic structures developed for spaceflight to model other unknown and nascent extremes.

1 | INTRODUCTION

By the next century, we aim to be an interplanetary species. With the launch of Artemis I on November 16, 2022, the first of several Artemis missions to return human presence to the moon and build out the gateway for upcoming Mars missions, a future as a spacefaring and interplanetary species moves beyond science fiction to a tangible potential reality. With the rapid development of spaceflight access and capability, we are on the precipice of an unprecedented expansion of human habitation. However, the biggest challenge to interplanetary habitation is the *human* problem. Our species has taken thousands of years to adapt to the myriad environments on Earth (Wells & Stock, 2007), but trying to keep humans alive and well outside the safe confines of our home planet is a complex challenge. A multidisciplinary perspective has thus been necessary through the development of space research and practice with opportunities for contributions and collaborations from a variety of disciplinary experts, including human biologists.

Human biologists are an interdisciplinary group with backgrounds in anthropology, anatomy, public health, endocrinology, genetics, nutrition, and other fields that study human biological variation in evolutionary, social, historical, and environmental contexts worldwide (humbio.org). As highlighted in this special issue, human biologists have long-developed expertise in the acclimatization and adaptation processes of humans in extreme settings. The cost, distance, and inevitable "unknowns" of the spaceflight environment(s) make it a distinctly extreme setting. Human biologists are particularly well suited to further develop research in human spaceflight given the discipline's foundations in evolutionary perspectives, biocultural interactions, and mixed methodological toolkits (Niclou et al., 2023). Here, we argue that current perspectives in human biology can critically contribute to the emerging human-spaceflight research infrastructure. Further, we show that the unique conditions of human-spaceflight research can bolster our understanding of human biology at the extremes. Thus, using spaceflight as a case study, we can use similar frameworks to assess human biology at other novel and unknown extremes.

Long-term habitation of humans in multiple spaceflight environments (e.g., spacecraft, moons, and planets) is predicated on the capacities of human acclimatization and adaptation, demonstrated to startling effect in terrestrial extremes. On Earth, humans have lived for extended periods (including over generations) in a range of extreme environments with varying success: from high-altitude environments to desert environments to extreme cold to environments that are resource-abundant but with high parasitic and pathogenic burdens (Beall, 2014; Frisancho, 2013; Moran, 2008; Niclou et al., 2023; Siddle & Quintana-Murci, 2014). Space, including but not limited to environments of weightlessness in a spacecraft, and celestial bodies like the moon or Mars, is the newest of these extremes. Current perspectives in human biology can contribute to the spaceflight-research ecosystem in two interrelated ways: (1) building out theoretical frameworks, and (2) research practice through field/lab-based research collection. Human biologists use theoretical frameworks that rely on evolutionary perspectives to explain variation through space and time and biocultural perspectives to explain the effects that human culture has had on our biology (Stinson et al., 2012). This lays the foundation for frameworks such as Life History Theory, which focuses on how evolutionary forces shape the timing of life events such as growth, maturation, reproduction, and death based on the ecology of energy production and mortality hazards (Hill & Kaplan, 1999), and can critically help organize acclimatizing and adaptive pressures from the ecological-social spaceflight environment. The second key contribution is to spaceflight research and practice given the foundational core of human biology work as field-based mixed-methodological research. This proficiency in field-based studies with human subjects provides the basis for robust in situ data collection in humans while in austere environments through coordinated mixed methods. Further, in recent years, human biologists in the field have embraced a dialectic engagement with resident communities who experience environmental pressures firsthand. As the population participating in spaceflight grows, this dialectic engagement will be crucial for continued research and general management of population health.

Integrating human biology perspectives with the unique history and conditions of human spaceflight presents an opportunity to further develop models of unknown extremes. Since its inception, research in human spaceflight has been extensive, comprehensive, and exceedingly well-documented. While limited given the reticence to reporting personal medical data, there is a record from the very first time a human experienced the spaceflight environment, which is unlike humans in any other extreme. By understanding the integration of human biology perspectives with the robust and detailed data of what we know about humans in space, we can better understand terrestrial extremes. Additionally, given the operational priorities in human spaceflight work and robust programmatic structures, there are opportunities for human biologists to develop similar structures for engaged work in other extremes, particularly those that are also novel and unknown.

1.1 | Brief review of human biological responses during spaceflight

Following World War II, the "Space Race" began between the United States and the Soviet Union in the pursuit of sociopolitical, economic, and cultural dominance. This initial impetus determined the first fliers into space, with an emphasis on elite, über-healthy, military-trained men. The first human to journey to outer space was Soviet cosmonaut Yuri Gagarin in April 1961. This was swiftly followed by American and Soviet orbital missions, an eventual lunar program, and culminated in the first lunar landing mission by Americans Neil Armstrong, Buzz Aldrin, and Michael Collins less than 10 years later. Since 1969, there have been numerous flights of the American Space Shuttle and Russian Soyuz spacecraft, and the development of the International Space Station, enabling a continuous human presence and international collaboration in space for the past two decades. Most spaceflight has been in low-earth orbit (LEO)—relatively close to Earth and protected in many ways by this proximity. Lunar flights of the Apollo program succeeded in taking a small number of astronauts into cislunar space, where the radiation environment is more harsh and urgent return to Earth more problematic. Future flights beyond Earth's moon will be even more challenging. While the landscape is rapidly changing, the origins of Cold War nationalism shaped the priorities of flight and influenced spaceflight personnel (Neufeld, 2018). Both spaceflight researchers and research subjects (including astronauts) were once primarily white men of European descent, which determined everything from prevailing perspectives on the "ideal" human body, to who should be allowed to and/or is preferred to fly, to what variation is normal and what is aberrant or pathological (Neufeld, 2018; Smith et al., 2020).

We describe a brief and selective overview of human biological and behavioral changes in response to human spaceflight, both seen and conjectured. Importantly, limited sample sizes in this area of research mean that the incidence rates of responses are not necessarily representative of what would be likely in a much larger (and much more diverse) population. However, functional significance and risk are evaluated using reasonable determinations from what has been observed (Antonsen, 2020). NASA defines five main hazards of spaceflight: (1) altered gravity, (2) isolation and confinement, (3) hostile/closed environment, (4) radiation, and (5) distance from Earth (Childress et al., 2023). All hazards have significant downstream effects on human physiology and behavior, but these distinct hazards guide how spaceflight is tackled operationally, with specific health and performance risks assigned to the consequences of each hazard.

1.1.1 | Altered gravity

Gravity levels different from that of Earth's surface fail to provide the appropriate chronic load that helps maintain the integrity of many body systems. In a spaceflight setting, these environments include the weightlessness experienced in a spacecraft or a spacesuit during an extravehicular activity, as well as differing gravity levels on the Earth's moon (1/6th of Earth's gravity) or Mars (1/3rd of Earth's gravity). This hazard is also related to transitions between different gravitational fields. There are intense acceleration/deceleration forces experienced during launch and landing transitions through various atmospheres, which can be many times the force of Earth's gravity (up to 3–6 g) (Demontis et al., 2017). These different gravitational fields and transition forces subject biological systems to stress, inducing cellular and molecular adaptations and changes in the genome, epigenome, as well as proteome. (Afshinnekoo et al., 2020; Demontis et al., 2017). These changes create risks for a range of pathologies and impact spatial orientation, hand-eye coordination, bone and muscle loading, and subsequent remodeling, balance, and locomotion. Weightlessness can lead to substantial cephalad fluid shifts that impact cardiovascular function and brain structures (Afshinnekoo et al., 2020; Hughson et al., 2018). Further, the synergistic effects of prolonged weightlessness, and other gravitational field shifts, may exacerbate complex health problems (Jillings et al., 2020).

1.1.2 | Isolation and confinement

Deep-space travel and extended habitation beyond Earth will require astronauts to be isolated from everyday communities and confined with their crewmates for prolonged periods, likely in limited-size habitats. This is expected to contribute to increasing psychological, behavioral, and physiological health risks (Pagel & Choukèr, 2016). Studies indicate that isolation and confinement lead to declines in mood, cognition, morale, and interpersonal interaction as well as circadian rhythm dysfunction, nutritional deficiency, and immune dysregulation (Crucian et al., 2015; Desai et al., 2022; Pagel & Choukèr, 2016; Palinkas & Suedfeld, 2021). They further suggest that isolation and confinement can specifically impact neurological function, including impaired hippocampal function and increased anxiety (Leser & Wagner, 2015; Wallace et al., 2009). Animal models have further demonstrated that the confluence of social isolation with other spaceflight hazards like weightlessness likely worsens these effects, exacerbating negative psychological, behavioral, and physiological outcomes (Tahimic et al., 2019).

1.1.3 | Hostile/closed environments

Human spaceflight environments (spacecraft, habitat systems, etc.) are in tightly regulated ecosystems (spacecraft, habitat systems, etc.,). Current ecosystems like the International Space Station can be maintained with resources from Earth and can jettison waste products to burn up in the atmosphere; however, as spaceflight endeavors proceed to farther destinations over longer periods, ecosystems will be required to approximate a true closed loop system as much possible. If not properly designed, maintained, and operated, this closed loop system can produce a biologically hostile environment with adverse impacts on astronaut health. Additionally, the various spaceflight ecosystems require design choices and tradeoffs on temperature, atmospheric composition and pressure, lighting, and noise that will apply to all crewmembers, regardless of individual variation and preferences. The system then must be continuously monitored for temperature, air quality, microbial contaminants, pressure, lighting, and noise. Because of engineering limitations and the limited efficacy of air recycling systems, elevated CO_2 is common in spacecraft and can lead to hypoxic/hypercapnic responses and significant physiological, behavioral, and mood deficits (Beheshti et al., 2018; Kelly, 2017). Constant noise, high carbon dioxide levels, and limited microorganism ecosystems can impair cardiovascular function, sleep, immune function, and cognitive function (Afshinnekoo et al., 2020; Crucian et al., 2015; Münzel et al., 2020). Further, prolonged confinement in these artificially maintained and highly regulated ecosystems likely reduces the variability of the environmental and internal microbiome; the magnitude of the impact of the microbiome is still not fully known, but this declining diversity will likely adversely affect astronaut immune function and metabolism (Siddiqui et al., 2021; Voorhies et al., 2019; Voorhies & Lorenzi, 2016).

1.1.4 | Radiation

When leaving the protection of Earth's atmosphere and magnetic field, astronauts encounter a more severe space-radiation environment. This contains energetic solar particles, electrons and positrons, protons, helium nuclei, and heavier ions (high-energy and high-charge particles or HZE particles) that originate from solar flares, coronal mass ejections, and galactic cosmic rays. These can cause substantial damage to biological systems at different rates (Durante & Cucinotta, 2008). Engineering to protect biological systems is thus crucial. Solar particle events are sporadic and can be shielded by spacecraft (Nelson, 2016), but the health effects of chronic exposure to galactic cosmic rays, especially high-energy particles, are of particular concern due to their ionizing nature, high penetrability, and high-energy deposition (Afshinnekoo et al., 2020; Niemantsverdriet et al., 2012). Without protection from Earth's atmosphere, organisms experience substantially greater radiation doses than on Earth's surface (Barthel & Sarigul-Klijn, 2019; Chancellor et al., 2018). In animal models and terrestrial-based observations of humans experiencing significant and prolonged radiation (e.g., Chernobyl and atomic bomb fallout), radiation is related to a damaged central nervous system, altered cognitive function, reduced motor function, and behavioral changes (Barratt & Pool, 2008; Chancellor et al., 2018; Clément et al., 2020). Radiation contributes to mitochondrial dysregulation as well as oxidative stress, leading to spaceflight-related dysregulation of cardiovascular, immune, neurological, and metabolic systems (Afshinnekoo et al., 2020). Our understanding of the impacts of radiation on the human body, however, is limited, particularly given ethical considerations of intentionally exposing humans to radiation. Much more research is needed to fully understand the impacts of radiation as experienced during spaceflight, including the cumulative effects of different kinds of radiation over time.

1.1.5 | Distance from earth

Future spaceflights will entail greater distances from Earth, which can produce intense and distressing logistical and psychological problems. Radio communication in spaceflight missions is subject to significant delay due to the finite speed of light: on the International Space Station orbiting the Earth, at its closest approach, there is a near zero-second time delay; at the moon a 1.3-second time delay; and at Mars a delay of up to 20 min each way (Parisi et al., 2023). For missions beyond LEO, there are challenges in returning to Earth in an emergency, but the distance and cost mean that there are also limited opportunities to provide the crew with additional supplies once their mission has started (Antonsen, Myers, et al., 2022). The combination of communication delays and hamstrung resupply creates a unique clinical decision system that must account for the constraints in medical treatment options and equipment capabilities without the option of rapid evacuation or immediate rescue for any mission beyond low-earth orbit (Russell et al., 2023). With limited-to-no resupply, pharmaceutical shelf life and safety of consumption also become a primary issue (Blue et al., 2019; Reichard et al., 2023). Further, the psychological distress of being distant from Earth and all that it represents (e.g., access to help, friends and family, and flora/fauna) can be substantial and may have an impact on crew dynamics, both increasing dependencies and feelings of closeness among the crew and exacerbating interpersonal issues (Stuster, 2021; Stuster et al., 2019). Research is currently underway to address some of the more pressing issues: autonomous health support for flight medical officers (including surgical interventions; (Panesar & Ashkan, 2018)), health-monitoring and wearable sensors (Bellisle et al., 2020), AI-assisted medical diagnostics, as well as onboard genetics and sequencing capacity (Castro-Wallace et al., 2017; McIntyre et al., 2019) and health-risk prediction models (Chancellor et al., 2018; Scott et al., 2020).

1.1.6 | Convergence of hazards

While the above hazards are typically treated as distinct and separate issues, it is observed that these hazards—and their consequences—are deeply interconnected. These hazards jointly create unique cellular responses to spaceflight, which include oxidative stress, DNA damage, mitochondrial dysregulation, epigenetic and gene regulation changes, telomere-length dynamics, and microbiome shifts (Afshinnekoo et al., 2020). Further, these hazards together contribute to critical health risks, such as cardiovascular dysregulation, CNS impairments, increased cancer risk, muscle degeneration, bone loss, immune dysfunction, increased liver disease and lipid dysregulation, circadian rhythm dysregulation, and space-associated neuro-ocular syndrome (Afshinnekoo et al., 2020). Importantly, the robust decade-spanning research on humans in space has demonstrated that the most difficult to anticipate dangers to human function and performance in these spaces often lies in the confluence of multiple hazards. For example, on the International Space Station, circadian rhythm dysfunction from isolation and confinement, subsequent stress response, and further susceptibility to immune dysfunction are exacerbated by the 90 min light–dark cycles as the station orbits the Earth, sleep disruption from changing gravity fields, and noise and CO_2 levels derivative of habitat system function. The simultaneous impact of multiple stressors and hazards of spaceflight leads to additive, compounding, and even compensatory effects across systems across individual lifetimes. Adverse effects of the spaceflight environment begin at launch, continue throughout the mission, and in many cases can continue across the lifetime of crewmembers (Afshinnekoo et al., 2020; Barratt & Pool, 2008; Garrett-Bakelman et al., 2019). These spaceflight changes and risks are multifold, primarily because the spaceflight context itself is dynamic. The spaceflight experience can last from short days-long or even minutes-long orbital and suborbital flights to longer durations in a vessel orbiting the Earth like the International Space Station, or longer still when journeying to other celestial bodies like the moon or Mars—all of which contribute to increasingly troublesome biological and behavioral responses.

To fully understand humans in spaceflight settings, there is a need to account for complex interactions, including understanding change over multiple timescales (i.e., acclimatization vs. developmental trajectories vs. adaptation and evolutionary drivers), impacts of biological and cultural factors, and the best methodologies to capture this data in situ in humans. For over a decade, NASA has tracked and managed approximately 30 specific risks to astronaut health and performance that occur before, during, and after spaceflight. Historically, research, development, and operations relevant to a single risk have been conducted in isolation from other risks, for operational considerations and to allow for initial characterization of each specific risk. However, in spaceflight, the impact on any given individual is cumulative, and not independent of other risks (Antonsen, Myers, et al., 2022; Reynolds et al., 2022). Though recent work at NASA and work by other spaceflight researchers have begun to explore an integrative systems approach, the various intersecting feedback loops that connect these risks are vastly understudied (Antonsen, Myers, et al., 2022; Reynolds et al., 2022; Shelhamer, 2015; Shelhamer & Gersh, 2023). Additionally, *human* function and performance are further complicated by our complex behavioral, cultural, and sociopolitical contexts (Le Roy et al., 2023). Perspectives and methodologies from many disciplines ranging from biology to physics to the social sciences are required. Models of these complex contexts and interactions (i.e., directed acyclic graphs, the Contributing Factor Map, etc.) allude to this broad-reaching expertise (see Antonsen, Reynolds, et al., 2022; Mindock & Klaus, 2014; Reynolds et al., 2022), however there is still a need for a theoretical framework and empirical approach to address the factors affecting spaceflight risks.

2 | CONTRIBUTIONS TO SPACEFLIGHT RESEARCH AND PRACTICE

2.1 | Evolutionary perspectives in human spaceflight

While extreme spaces are highly variable, they share distinct characteristics in their outsized impacts on human function. A way to characterize extreme spaces, like spaceflight settings, is to use theoretical models that can frame our understanding of environmental risks and their interface with human biology. One such model is the framework of life history theory (LHT). LHT is an evolutionary theory of variation in an organism's allocation strategies between systems of growth, maintenance, and reproduction; it is assumed that resources are limited, and functions are mutually exclusive, with resources invested in one no longer available for use in another (Hill & Hurtado, 1996; McDade, 2003; Sear, 2020). While aspects of LHT continue to be debated (Frankenhuis & Nettle, 2020), it provides two important theoretical contributions: (1) there are tradeoffs between the demands of growth, maintenance, and reproduction, and (2) features of the environment shape life history tradeoffs. As such, in a spaceflight setting, one can expect that in addition to the classic mass/power/volume thresholds, the built environment must accommodate an organism's balance of tradeoffs related to its growth, maintenance, and reproduction. In addition, this balance varies between individuals given the developmental effects on later life tradeoffs. As such, factors including (but not limited to) nutrition, oxygen saturation levels, or viral exposure on craft require closer consideration.

Emerging from LHT, it is proposed that a fundamental environmental influence on life history variation across species is extrinsic mortality risk (Promislow & Harvey, 1990). There is interest in applying this principle to intra species variation in life history pace and strategy based on two environmental conditions that shape the dynamics of extrinsic mortality risk: harshness (externally caused morbidity-mortality) and unpredictability (spatiotemporal variability in harshness) (Ellis et al., 2009). These conditions shape behavioral and physiological outcomes across the life course, such as reproductive decisions, risk-taking behaviors, physiological resource allocation, immune function, and others. Critically, this distinction between "harshness" and "unpredictability" can describe changing contexts and energetic constraints, which may help explain how the same life history and behavioral traits do not always cluster together in the same ways (though the actual *adaptive* capacity of this clustering remains debated) (Coall & Chisholm, 2003; Kuzawa & Bragg, 2012; Promislow & Harvey, 1990; Sear, 2020; Walker et al., 2006). Early uses of these terms are specific to determining fast or slow life given early developmental environments (Belsky et al., 2012; Frankenhuis & Nettle, 2020; Sear, 2020). However, "harshness" and "unpredictability" can be repurposed; if placed on a matrix they can be a useful heuristic to describe and characterize the extreme setting (i.e., what makes it extreme and in what ways). The environment can be evaluated for indicators of harshness and unpredictability; in a spaceflight setting harshness indicators could be things like oxygen availability, radiation exposure, crew competence, or access to key resources like medical supplies or support personnel, whereas indicators of unpredictability could be factors such as carbon dioxide scrubber functionality, reliability of radiation shielding, crew dynamics, and availability of key resource access. For spaceflight environments, this heuristic is particularly valuable to extrapolate and characterize dimensions that are yet unknown and have undefined impacts on the human body.

In this matrix, we assume that ecological and social shifts indicating varying degrees of harshness and unpredictability would shape everyday outcomes and functions in humans, depending on the conditions of a given environment. This matrix operates across timescales and allows for conceptualizing change and subsequent organismal variation at the acute (i.e., acclimatization response) and chronic (i.e., phenotypic changes or developmental trajectories) levels. Moreover, indicators of harshness and unpredictability are derived from both biological and cultural factors (i.e., biocultural inheritance) (Worthman, 2003). The biocultural lens represents a more complete effect of the environment but also implies that environments can be extreme due to environmental and/or social factors (though most likely both). Integrating biocultural perspectives into the framework of harshness and unpredictability allows the integration of environmental hazards with the more amorphous sociopolitical–economic contexts that equally shape human function and performance that are often overlooked (or at least, not systematically evaluated), in current spaceflight research. This would allow for hazards such as radiation from a solar flare to be considered alongside crew fatigue or even the United States–Russia tensions and subsequent impacts on crew performance or mission resources.

By examining individual tradeoffs between growth, reproduction, and maintenance over a life course on the axes of harshness and unpredictability, LHT may create a more robust scaffold to understand spaceflight missions, particularly as missions move toward long-term habitation and away from highly controlled operational needs. In this case, the many simultaneous and often confounding changes in spaceflight may be better mapped as responding to harshness and unpredictability rather than only to specific hazards. Harshness and unpredictability likely affect specific, individual phenotypic traits (including behavioral and physical trajectories) that impact human health and performance in space. Examples may include immune response or vestibular function. These traits are plastic, where individuals respond to the cues of the specific spaceflight environment to shift allocations so that the same genotype produces different phenotypes or observable characteristics (Sear, 2020; West-Eberhard, 2003). Further with these frameworks in place, we may then be able to better tease apart and predict potential adaptive outcomes in the evolutionary sense, where there are heritable adaptive traits across generations. Given the operational priorities, current perspectives in spaceflight are siloed and necessarily concerned with short-term acclimatization and impacts on immediate crew health and performance (insofar as it impacts the success or failure of the immediate mission) (Antonsen, 2020). However, as we expand to longer-term missions, we will need to consider frameworks like life history tradeoffs to provide a more rigorous explanation for why certain physiological and behavioral systems respond in particular ways. Framing the human response to spaceflight in this way can help better illuminate what we know and do not know in the many spaceflight contexts. In spaceflight, where human environments need to be built from the ground up, this more rigorous and theoretically grounded understanding of human-environment interaction can be a matter of life and death, and at a larger scale may determine the success of long-term habitation beyond our home planet. Additionally, by placing human spaceflight into this matrix of unpredictability and harshness (see Figure 1), we can also compare it to other intensively studied environmental extremes, like high altitude, cold, or traumatic spaces.

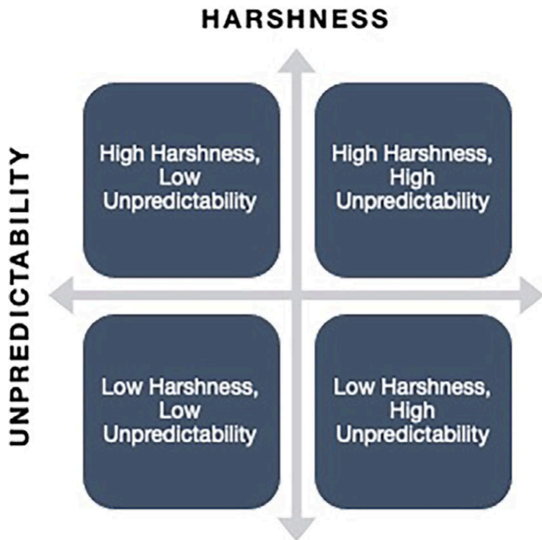

FIGURE 1 Determining Extremes via Environmental Risk: Harshness-Unpredictability Matrix.

Our current understanding of evolution is predicated on human variability and plasticity, allowing for phenotypic and genotypic diversity within species (Laland et al., 2015). Previous work by biological anthropologists at extremes has demonstrated the wide range of human function and performance and the possibility for plasticity even within an individual (Frisancho, 2013; Mascie-Taylor & Bogin, 1995; Niclou et al., 2023; Sarma et al., 2022; Wells & Stock, 2007). This understanding of human variability and diversity fundamentally changes how we should approach humans in space, complementing sociopolitical shifts as spaceflight grows increasingly more global and accessible. Primarily, there is a shift from finding "ideal" body types within the narrow scope of individuals deemed "fit to fly" to instead understanding how human diversity, variability, and plasticity can allow for the flourishing of the entire species in space. As humans become a regularly spacefaring species, there is a necessary perspective shift that should incorporate these evolution-informed principles—humans in spaceflight environments will be diverse and varied rather than highly trained ultra-healthy individuals. This perspective shift also includes reevaluating the structures that allow for access and opportunities that will inevitably shape behavior and biology, and what these structures require to ensure health and safety.

2.2 | Field-based perspectives for human spaceflight work

Given practical constraints in funding, energy, time, and privacy for doing human-centered spaceflight research, current work depends heavily on animal models, simulation experiments (e.g., head-down-tilt bedrest or sleep disruption studies), or analog settings (e.g., the Hawai'i Space Exploration Analog and Simulation, Human Exploration Research Analog, Nazemnyy Eksperimental'-nyy Kompleks) with limited data collected on humans during spaceflight. However, the capacity of human-spaceflight research is increasing with crews planned for long-duration missions to the moon and Mars as well as options for civilians to fly commercially. A robust understanding of in situ field-based outcomes will thus be essential while research likely becomes increasingly constrained due to operational challenges. Missions to the moon and Mars will likely be too demanding, dangerous, and expensive for high-volume research, and thus maximizing low-earth orbit and terrestrial analogs will be essential. Analogous research frameworks to maximize data collection under constrained circumstances in extreme terrestrial settings are already used by human biologists (Leonard, this issue; Niclou et al., 2023; Ocobock, 2023). As this research in extreme settings has developed over decades, human biology work as we see it today has acquired an agile methodological toolkit developed for use in intensive field-based research, biocultural perspectives, and a research infrastructure that relies on dialectic engagement and communication between researchers and resident communities.

Much of human biology work in extreme environments has been done successfully in "the field"—working in an environment of interest with human populations engaged in everyday living in energy-intensive and resource-limited settings. Here, human biologists have developed protocols to allow for in situ field measurements that minimize deviation from standard everyday activity (Gurven et al., 2017; Pontzer et al., 2015; Sarma et al., 2020). Methodologies have been developed using robust minimally-to-non-invasive biomarkers such as the use of wearable monitors or neuroendocrine and DNA extraction from biomaterials like hair, saliva, bloodspots, and fingernails (See *American Journal of Human Biology* special issues "Minimally Invasive Biomarkers in Human Population Biology Part I and Part II"). Additionally, there is an active integration of a mixed-methods approach to maximize data collection, collecting time-synced data streams that can "speak" to each other in post-processing. This is key to successful research in these settings since in most cases the environment or circumstance of data collection is where participant time, access, energy, and attention may be limited. Collecting any data at all in these settings can be prohibitively expensive, and oftentimes specific circumstances are nonrepeatable (particularly compared with controlled settings in laboratory work), and thus the data must be highly contextualized for analysis and outcomes of value. A theoretical and practical emphasis on biocultural perspectives critically contextualizes the data, where the different kinds of factors impacting human function and performance, whether biological or cultural, are accounted for.

The research infrastructure itself relies on dialectic engagement and communication between the researcher and resident communities, which shapes appropriate and high-fidelity research protocols, and questions being asked, and establishes reciprocity with subject communities. This symbiotic relationship goes further—many researchers today have integrated point-of-care into their work, which in many circumstances, given the austere settings with limited medical care, ethically must accompany research (Madimenos et al., 2022). This dialectical engagement can and should be the foundation for future best practices in spaceflight research.

Through the application of these field practices, there is an opportunity to functionally engage a "systems" framework, where mixed-method data collection and dialectic engagement can create the robust, interconnected, multisystem perspective of human spaceflight that is a goal in a small but growing group of human-spaceflight researchers (Mindock & Klaus, 2014; Reynolds et al., 2022; Shelhamer, 2017). Many of the field ready mixed-methods that human biologists use (e.g., wearable monitors, minimally invasive biomarkers, quantitative surveys, interviews, etc.) can very easily be translated to human spaceflight research and, in some cases, are already used. However, situating this data within rigorous theoretical frameworks, as done in human biology work, satisfies this systems perspective. For example, the qualitative information about the health, behavior, and performance of astronauts collected by personnel on the ground and even among the astronauts themselves could benefit from a systematic evaluation as it connects to quantitative outcomes. The combination of both qualitative and quantitative evidence on human-spaceflight risk is commonly addressed in focused deliberations among scientists, engineers, and physicians in discussions among themselves and in forums to inform decision-makers, particularly given its ability to capture data that is observed but not satisfactorily categorized. Pragmatic integration of qualitative and quantitative data through time-synced mixed methods and continued communication to curate and adjust data collection fills an important gap in current spaceflight work. It also increases the rigor in the concurrent use of qualitative and quantitative data (as well as the reciprocal influence between them).

3 | SPACEFLIGHT AS A MODEL FOR NOVEL EXTREMES

> Prediction is very difficult, especially if it is about the future—Niels Bohr

What happens next in human spaceflight? There has been a repeated call in spaceflight research for a birds-eye view or "systems" perspective, which accounts for how complex systems including individual physiology and behavior, team dynamics, the built habitat, training, and other factors interact with each other to create even more complicated system (Antonsen, Myers, et al., 2022; Mindock & Klaus, 2014; Shelhamer, 2015; Shelhamer & Gersh, 2023). Thus, all parts of the spaceflight ecosystem, including humans in spacecraft or new lunar or planetary ecologies, are inherently part of a system of interacting subsystems. This perspective mirrors how many human biologists view terrestrial extremes, where subsystems may be environmental or biocultural influences. Since the spaceflight environment is a built environment and must be tightly regulated, there is a need to identify and characterize the subsystems and their complex interactions to manage known risks. After all, the biggest concern in future spaceflight missions, from extended time in space to lunar/Martian habitation, is the unknown unknowns. While researchers can anticipate to the best of their ability, the key will be to understand the connections and interactions between systems. Theoretically, grounded modeling through evolutionary frameworks that connect impacted subsystems together as well as strategic mixed methods could address some of the programmatic silos and fragmentation in spaceflight research. Building on existing evolutionary frameworks, we can project what might happen to human acclimatization and adaptation as we become a multiplanetary species. Placing spaceflight on the existing spectrum of extremes and within the harshness-unpredictability matrix while using an established convergent and parallel mixed-methods toolkit is a way to address this. Further, utilizing evolutionary perspectives that are rooted in human variability and diversity will be vital. The broad-ranging work done in human biology has demonstrated how an understanding of human function based on a limited sample size limits our understanding of human adaptation (Graves Jr., 2021; Wiley, 2021).

Conversely, the extensive and deeply comprehensive study of human spaceflight provides a unique opportunity for modeling other novel extreme environments. For over four decades, astronauts have been monitored almost continuously by scientists, engineers, physicians, and various support personnel during missions ranging from a few days to many months (and occasionally up to a year) all while confined to an exceedingly well-designed and largely controllable habitat. The human-spaceflight research community has developed a detailed structure of hazards and associated risks to human health and performance in spaceflight environments. Through entities such as NASA, this has germinated a programmatically principled approach to multidisciplinary research on human vulnerability and response to spaceflight settings in the United States. However, this operationally driven approach is actively in contrast to an open-science framework and de-prioritizes topics that fail to have urgent and clear risk, thus potentially missing salient, but less obvious, interactions. Terrestrial environments have very rarely been explored to such specifications, but following the spaceflight model, analogous programs of research could be developed for extreme terrestrial environments on Earth. However, it is the integration of human biology perspectives with the robust extensive data collection and operational frameworks of human spaceflight that may provide a pathway to approach other untapped exciting extremes. These theoretical and programmatic collaborations and learnings can transcend our approach to spaceflight to other unexpected spaces, such as climate-change-ravaged environments and extremes yet to be.

ACKNOWLEDGMENTS

A special thanks to the L.T. Gettler, A. Niclou, B.P. Croom, and the reviewers for invaluable feedback and help in the development of this manuscript. Mallika S. Sarma conceptualized the paper. Mallika S. Sarma and Mark Shelhamer contributed to writing the paper. Mallika S. Sarma is supported by the Translational Institute for Space Health through the National Aeronautics and Space Administration Cooperative Agreement NNX16AO69A and the National Institute on Deafness and Other Communication Disorders of the National Institute of Health under Award Number 5T32DC000023-33. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the National Aeronautics and Space Administration.

CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Mallika S. Sarma https://orcid.org/0000-0002-6693-9382

REFERENCES

Afshinnekoo, E., Scott, R. T., MacKay, M. J., Pariset, E., Cekanaviciute, E., Barker, R., Gilroy, S., Hassane, D., Smith, S. M., Zwart, S. R., Nelman-Gonzalez, M., Crucian, B. E., Ponomarev, S. A., Orlov, O. I., Shiba, D., Muratani, M., Yamamoto, M., Richards, S. E., Vaishampayan, P. A., … Beheshti, A. (2020). Fundamental biological features of spaceflight: Advancing the field to enable deep-space exploration. *Cell*, *183*(5), 1162–1184. https://doi.org/10.1016/j.cell.2020.10.050

Antonsen, E. L. (2020). *Human System Risk Management Plan* (Other - JSC Numbered Document JSC 66705). https://ntrs.nasa.gov/citations/20205008887

Antonsen, E. L., Myers, J. G., Boley, L., Arellano, J., Kerstman, E., Kadwa, B., Buckland, D. M., & Van Baalen, M. (2022). Estimating medical risk in human spaceflight. *NPJ Microgravity*, *8*(1), 8. https://doi.org/10.1038/s41526-022-00193-9

Antonsen, E. L., Reynolds, R. J., Monti, A., Charvat, J. M., Petersen, D., Connell, E. S., Shelhamer, M. J., Van Baalen, M., Abukmail, A., Marotta, K., Buckland, D. M., Anton, W., & Brown, C. (2022). Directed Acyclic Graph Guidance Documentation.

Barratt, M. R., & Pool, S. L. (2008). *Principles of clinical medicine for spaceflight*. Springer Science & Business Media. https://doi.org/10.1007/978-0-387-68164-1_27%5Cnpapers3://publication/doi/10.1007/978-0-387-68164-1_27

Barthel, J., & Sarigul-Klijn, N. (2019). A review of radiation shielding needs and concepts for space voyages beyond Earth's magnetic influence. *Progress in Aerospace Sciences*, *110*, 100553. https://doi.org/10.1016/j.paerosci.2019.100553

Beall, C. M. (2014). Adaptation to high altitude: Phenotypes and genotypes. *Annual Review of Anthropology*, *43*, 251–272. https://doi.org/10.1146/annurev-anthro-102313-030000

Beheshti, A., Cekanaviciute, E., Smith, D. J., & Costes, S. V. (2018). Global transcriptomic analysis suggests carbon dioxide as an environmental stressor in spaceflight: A systems biology GeneLab case study. *Scientific Reports*, *8*(1), 4191. https://doi.org/10.1038/s41598-018-22613-1

Bellisle, R., Bjune, C., & Newman, D. (2020). Considerations for Wearable Sensors to Monitor Physical Performance During Spaceflight Intravehicular Activities. 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), Montreal, Quebec, Canada, 4160–4164. https://doi.org/10.1109/EMBC44109.2020.9175674

Belsky, J., Schlomer, G., & Ellis, B. (2012). Beyond cumulative risk: Distinguishing harshness and unpredictability as determinants of parenting and early life history strategy. *Developmental Psychology*, *48*(3), 662–673. https://doi.org/10.1037/a0025837

Blue, R. S., Bayuse, T. M., Daniels, V. R., Wotring, V. E., Suresh, R., Mulcahy, R. A., & Antonsen, E. L. (2019). Supplying a pharmacy for NASA exploration spaceflight: Challenges and current understanding. *Npj Microgravity*, *5*(1), 14. https://doi.org/10.1038/s41526-019-0075-2

Castro-Wallace, S. L., Chiu, C. Y., John, K. K., Stahl, S. E., Rubins, K. H., McIntyre, A. B. R., Dworkin, J. P., Lupisella, M. L., Smith, D. J., Botkin, D. J., Stephenson, T. A., Juul, S., Turner, D. J., Izquierdo, F., Federman, S., Stryke, D., Somasekar, S., Alexander, N., Yu, G., … Burton, A. S. (2017). Nanopore DNA sequencing and genome assembly on the international Space Station. *Scientific Reports*, *7*(1), 18022. https://doi.org/10.1038/s41598-017-18364-0

Chancellor, J. C., Blue, R. S., Cengel, K. A., Auñón-Chancellor, S. M., Rubins, K. H., Katzgraber, H. G., & Kennedy, A. R. (2018). Limitations in predicting the space radiation health risk for exploration astronauts. *NPJ Microgravity*, *4*(1), 1–11. https://doi.org/10.1038/s41526-018-0043-2

Childress, S. D., Williams, T. C., & Francisco, D. R. (2023). NASA space flight human-system standard: Enabling human spaceflight missions by supporting astronaut health, safety, and performance. *NPJ Microgravity*, *9*(1), 31. https://doi.org/10.1038/s41526-023-00275-2

Clément, G. R., Boyle, R. D., George, K. A., Nelson, G. A., Reschke, M. F., Williams, T. J., & Paloski, W. H. (2020). Challenges to the central nervous system during human spaceflight missions to Mars. *Journal of Neurophysiology*, *123*(5), 2037–2063. https://doi.org/10.1152/JN.00476.2019

Coall, D. A., & Chisholm, J. S. (2003). Evolutionary perspectives on pregnancy: Maternal age at menarche and infant birth weight. *Social Science & Medicine*, *57*(10), 1771–1781. https://doi.org/10.1016/S0277-9536(03)00022-4

Crucian, B., Stowe, R. P., Mehta, S., Quiriarte, H., Pierson, D., & Sams, C. (2015). Alterations in adaptive immunity persist during long-duration spaceflight. *NPJ Microgravity*, *1*, 1–10. https://doi.org/10.1038/npjmgrav.2015.13

Demontis, G. C., Germani, M. M., Caiani, E. G., Barravecchia, I., Passino, C., & Angeloni, D. (2017). Human pathophysiological adaptations to the space environment. *Frontiers in Physiology*, *8*, 547. https://www.frontiersin.org/articles/10.3389/fphys.2017.00547

Desai, R. I., Limoli, C. L., Stark, C. E. L., & Stark, S. M. (2022). Impact of spaceflight stressors on behavior and cognition: A molecular, neurochemical, and neurobiological perspective. *Neuroscience and Biobehavioral Reviews*, *138*, 104676. https://doi.org/10.1016/j.neubiorev.2022.104676

Durante, M., & Cucinotta, F. A. (2008). Heavy ion carcinogenesis and human space exploration. *Nature Reviews. Cancer*, *8*(6), 465–472. https://doi.org/10.1038/nrc2391

Ellis, B. J., Figueredo, A. J., Brumbach, B. H., & Schlomer, G. L. (2009). Fundamental dimensions of environmental risk: The impact of harsh versus unpredictable environments on the evolution and development of life history strategies. *Human Nature*, *20*(2), 204–268. https://doi.org/10.1007/s12110-009-9063-7

Frankenhuis, W. E., & Nettle, D. (2020). Current debates in human life history research. *Evolution and Human Behavior*, *41*(6), 469–473. https://doi.org/10.1016/j.evolhumbehav.2020.09.005

Frisancho, A. R. (2013). Developmental functional adaptation to high altitude: Review. *American Journal of Human Biology*, *25*(2), 151–168. https://doi.org/10.1002/ajhb.22367

Garrett-Bakelman, F., Darshi, M., Green, S., Gur, R., Lin, L., Macias, B., McKenna, M., Meydan, C., Mishra, T., Nasrini, J., Piening, B., Rizzardi, L., Sharma, K., Siamwala, J., Taylor, L., Viaterna, M., Afkarian, M., Afshinnekoo, E., Ahadi, S., … Turek, F. (2019). The NASA twins study: A multidimensional analysis of a year-long human spaceflight. *Science*, *144*, 1–20. https://doi.org/10.1126/science.aau8650

Graves, J. L., Jr. (2021). Human biological variation and the "normal". *American Journal of Human Biology*, *33*(5), e23658. https://doi.org/10.1002/ajhb.23658

Gurven, M., Stieglitz, J., Trumble, B., Blackwell, A. D., Beheim, B., Davis, H., Hooper, P., & Kaplan, H. (2017). The Tsimane health and life history project: Integrating anthropology and biomedicine. *Evolutionary Anthropology*, *26*, 54–73. https://doi.org/10.1002/evan.21515

Hill, K., & Hurtado, A. (1996). *Ache life history*. Aldine de Gruyter.

Hill, K., & Kaplan, H. (1999). Life history traits in humans: Theory and empirical studies. *Annual Review of Anthropology*, *28*(1), 397–430. https://doi.org/10.1146/annurev.anthro.28.1.397

Hughson, R. L., Helm, A., & Durante, M. (2018). Heart in space: Effect of the extraterrestrial environment on the cardiovascular system. *Nature Reviews Cardiology*, *15*(3), 167–180. https://doi.org/10.1038/nrcardio.2017.157

Jillings, S., Van Ombergen, A., Tomilovskaya, E., Rumshiskaya, A., Litvinova, L., Nosikova, I., Pechenkova, E., Rukavishnikov, I., Kozlovskaya, I. B., Manko, O., Danilichev, S., Sunaert, S., Parizel, P. M., Sinitsyn, V., Petrovichev, V., Laureys, S., Eulenburg, P., Sijbers, J., Wuyts, F. L., & Jeurissen, B. (2020). Macro- and microstructural changes in cosmonauts' brains after long-duration spaceflight. *Science. Advances*, *6*(36), eaaz9488. https://doi.org/10.1126/sciadv.aaz9488

Kelly, S. (2017). *Endurance: A year in space, A Lifetime of Discovery*. Knopf.

Kuzawa, C. W., & Bragg, J. M. (2012). Plasticity in human life history strategy. *Current Anthropology*, *53*, S369–S382. https://doi.org/10.1086/667410

Laland, K. N., Uller, T., Feldman, M. W., Sterelny, K., Muller, G. B., Moczek, A., Jablonka, E., & Odling-Smee, J. (2015). *The extended evolutionary synthesis: Its structure, assumptions and predictions*. Proceedings of the Royal Society B.

Le Roy, B., Martin-Krumm, C., Pinol, N., Dutheil, F., & Trousselard, M. (2023). Human challenges to adaptation to extreme professional environments: A systematic review. *Neuroscience & Biobehavioral Reviews*, *146*(2022), 105054. https://doi.org/10.1016/j.neubiorev.2023.105054

Leser, N., & Wagner, S. (2015). The effects of acute social isolation on long-term social recognition memory. *Neurobiology of Learning and Memory*, *124*, 97–103. https://doi.org/10.1016/j.nlm.2015.07.002

Madimenos, F. C., Gildner, T. E., Eick, G. N., Sugiyama, L. S., & Snodgrass, J. J. (2022). Bringing the lab bench to the field: Point-of-care testing for enhancing health research and stakeholder engagement in rural/remote, indigenous, and resource-limited contexts. *American Journal of Human Biology*, *34*(11), e23808. https://doi.org/10.1002/ajhb.23808

Mascie-Taylor, C. G. N., & Bogin, B. (Eds.). (1995). *Human variability and plasticity*. Cambridge University Press.

McDade, T. W. (2003). Life history theory and the immune system: Steps toward a human ecological immunology. *American Journal of Physical Anthropology*, *122*(S37), 100–125. https://doi.org/10.1002/ajpa.10398

McIntyre, A. B. R., Alexander, N., Grigorev, K., Bezdan, D., Sichtig, H., Chiu, C. Y., & Mason, C. E. (2019). Single-molecule sequencing detection of N6-methyladenine in microbial reference materials. *Nature Communications*, *10*(1), 579. https://doi.org/10.1038/s41467-019-08289-9

Mindock, J. A., & Klaus, D. M. (2014). Contributing factor map: A taxonomy of influences on human performance and health in space. *IEEE Transactions on Human-Machine Systems*, *44*(5), 591–602. https://doi.org/10.1109/THMS.2014.2328971

Moran, E. F. (2008). *Human adaptability: An introduction to ecological anthropology*. Westview Press.

Münzel, T., Kröller-Schön, S., Oelze, M., Gori, T., Schmidt, F. P., Steven, S., Hahad, O., Röösli, M., Wunderli, J.-M., Daiber, A., & Sørensen, M. (2020). Adverse cardiovascular effects of traffic noise with a focus on nighttime noise and the new WHO noise guidelines. *Annual Review of Public Health*, *41*(1), 309–328. https://doi.org/10.1146/annurev-publhealth-081519-062400

Nelson, G. A. (2016). Space Radiation and Human Exposures, A Primer. Radiation Research, 185(4), 349–358.

Neufeld, M. J. (2018). *Spaceflight: A concise history*. MIT Press.

Niclou, A., Sarma, M., Levy, S., & Ocobock, C. (2023). To the extreme! How biological anthropology can inform exercise physiology in extreme environments. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology*, *284*, 111476. https://doi.org/10.1016/j.cbpa.2023.111476

Niemantsverdriet, M., Van Goethem, M.-J., Bron, R., Hogewerf, W., Brandenburg, S., Langendijk, J. A., Van Luijk, P., & Coppes, R. P. (2012). High and low LET radiation differentially induce Normal tissue damage signals. *International Journal of Radiation Oncology, Biology, Physics*, *83*(4), 1291–1297. https://doi.org/10.1016/j.ijrobp.2011.09.057

Ocobock, C. (2023). Human bodies in extreme environments. *Annual Review of Anthropology*, *52*(1), 257–277. https://doi.org/10.1146/annurev-anthro-052721-085858

Pagel, J. I., & Choukèr, A. (2016). Effects of isolation and confinement on humans-implications for manned space explorations. *Journal of Applied Physiology*, *120*(12), 1449–1457. https://doi.org/10.1152/japplphysiol.00928.2015

Palinkas, L. A., & Suedfeld, P. (2021). Psychosocial issues in isolated and confined extreme environments. *Neuroscience and Biobehavioral Reviews*, *126*, 413–429. https://doi.org/10.1016/j.neubiorev.2021.03.032

Panesar, S. S., & Ashkan, K. (2018). Surgery in space. *British Journal of Surgery*, *105*(10), 1234–1243. https://doi.org/10.1002/bjs.10908

Parisi, M., Panontin, T., Wu, S.-C., Mctigue, K., & Vera, A. (2023). Effects of Communication Delay on Human Spaceflight Missions. 14th International Conference on Applied Human Factors and Ergonomics (AHFE 2023), San Francisco, CA. https://doi.org/10.54941/ahfe1003920

Pontzer, H., Raichlen, D. A., Wood, B. M., Emery Thompson, M., Racette, S. B., Mabulla, A. Z. P., & Marlowe, F. W. (2015). Energy expenditure and activity among Hadza hunter-gatherers. *American Journal of Human Biology*, *27*(5), 628–637. https://doi.org/10.1002/ajhb.22711

Promislow, D. E. L., & Harvey, P. H. (1990). Living fast and dying young: A comparative analysis of life-history variation among mammals. *Journal of Zoology*, *220*(3), 417–437. https://doi.org/10.1111/j.1469-7998.1990.tb04316.x

Reichard, J. F., Phelps, S. E., Lehnhardt, K. R., Young, M., & Easter, B. D. (2023). The effect of long-term spaceflight on drug potency and the risk of medication failure. *NPJ Microgravity*, *9*(1), 35. https://doi.org/10.1038/s41526-023-00271-6

Reynolds, R. J., Scott, R. T., Turner, R. T., Iwaniec, U. T., Bouxsein, M. L., Sanders, L. M., & Antonsen, E. L. (2022). Validating causal diagrams of human health risks for spaceflight: An example using bone data from rodents. *Biomedicine*, *10*(9), 2187. https://doi.org/10.3390/biomedicines10092187

Russell, B. K., Burian, B. K., Hilmers, D. C., Beard, B. L., Martin, K., Pletcher, D. L., Easter, B., Lehnhardt, K., & Levin, D. (2023). The value of a spaceflight clinical decision support system for earth-independent medical operations. *NPJ Microgravity*, *9*(1), 46. https://doi.org/10.1038/s41526-023-00284-1

Sarma, M. S., Boyette, A. H., Lew-Levy, S., Miegakanda, V., Samson, D., Kilius, E., & Gettler, L. T. (2020). Sex differences in daily activity intensity and energy expenditure and their relationship to cortisol among BaYaka foragers from The Congo Basin. *American Journal of Physical Anthropology*, *172*, 423–437.

Sarma, M. S., Ocobock, C. J., Martin, S., Rochelle, S., Croom, B. P., & Gettler, L. T. (2022). Sex differences and shifts in body composition, physical activity, and total energy expenditure across a 3-month expedition. *American Journal of Human Biology*, *34*, 1–17. https://doi.org/10.1002/ajhb.23634

Scott, R. T., Grigorev, K., Mackintosh, G., Gebre, S. G., Mason, C. E., Del Alto, M. E., & Costes, S. V. (2020). Advancing the integration of biosciences data sharing to further enable space exploration. *Cell Reports*, *33*(10), 108441. https://doi.org/10.1016/j.celrep.2020.108441

Sear, R. (2020). Do human 'life history strategies' exist? *Evolution and Human Behavior*, *41*(6), 513–526. https://doi.org/10.1016/j.evolhumbehav.2020.09.004

Shelhamer, M. (2015). A call for research to assess and promote functional resilience in astronaut crews. *Journal of Applied Physiology*, *120*(7), 471–472. https://doi.org/10.1152/japplphysiol.00717.2015

Shelhamer, M. (2017). Why send humans into space? Science and non-science motivations for human space flight. *Space Policy*, *42*, 37–40. https://doi.org/10.1016/j.spacepol.2017.10.001

Shelhamer, M., & Gersh, J. R. (2023 IEEE Aerospace Conference, 1–8.). A mission architecture to integrate human and spacecraft functional performance. https://doi.org/10.1109/AERO55745.2023.10115715

Siddiqui, R., Akbar, N., & Khan, N. A. (2021). Gut microbiome and human health under the space environment. *Journal of Applied Microbiology*, *130*(1), 14–24. https://doi.org/10.1111/jam.14789

Siddle, K. J., & Quintana-Murci, L. (2014). The red Queen's long race: Human adaptation to pathogen pressure. *Current Opinion in Genetics & Development*, *29*, 31–38. https://doi.org/10.1016/j.gde.2014.07.004

Smith, M. G., Kelley, M., & Basner, M. (2020). A brief history of spaceflight from 1961 to 2020: An analysis of missions and astronaut demographics. *Acta Astronautica*, *175*, 290–299. https://doi.org/10.1016/j.actaastro.2020.06.004

Stinson, S., Bogin, B., & O'Rourke, D. (Eds.). (2012). *Human biology: An evolutionary and biocultural perspective*. John Wiley & Sons, Ltd. https://doi.org/10.1002/9781118108062.fmatter

Stuster, J., Adolf, J., Byrne, V., & Greene, M. (2019). *Generalizable skills and knowledge for exploration missions* (pp. 1–188). NASA STI Program Office https://ntrs.nasa.gov/search.jsp?R=20190023004

Stuster, J. W. (2021). Behavioral challenges of space exploration. In L. R. Young & J. P. Sutton (Eds.), *Handbook of bioastronautics* (pp. 385–397). Springer International Publishing. https://doi.org/10.1007/978-3-319-12191-8_34

Tahimic, C. G. T., Paul, A. M., Schreurs, A.-S., Torres, S. M., Rubinstein, L., Steczina, S., Lowe, M., Bhattacharya, S., Alwood, J. S., Ronca, A. E., & Globus, R. K. (2019). Influence of social isolation during prolonged simulated weightlessness by Hindlimb unloading. *Frontiers in Physiology*, *10*, 1147. https://doi.org/10.3389/fphys.2019.01147

Voorhies, A. A., & Lorenzi, H. A. (2016). The challenge of maintaining a healthy microbiome during long-duration space missions. *Frontiers in Astronomy and Space Sciences*, *3*, 1–7. https://www.frontiersin.org/articles/10.3389/fspas.2016.00023

Voorhies, A. A., Mark Ott, C., Mehta, S., Pierson, D. L., Crucian, B. E., Feiveson, A., Oubre, C. M., Torralba, M., Moncera, K., Zhang, Y., Zurek, E., & Lorenzi, H. A. (2019). Study of the impact of long-duration space missions at the international Space Station on the astronaut microbiome. *Scientific Reports*, *9*(1), 9911. https://doi.org/10.1038/s41598-019-46303-8

Walker, R., Gurven, M., Hill, K., Migliano, A., Chagnon, N., De Souza, R., Djurovic, G., Hames, R., Hurtado, A. M., Kaplan, H., Kramer, K., Oliver, W. J., Valeggia, C., & Yamauchi, T. (2006). Growth rates and life histories in twenty-two small-scale societies. *American Journal of Human Biology*, *18*(3), 295–311. https://doi.org/10.1002/ajhb.20510

Wallace, D. L., Han, M.-H., Graham, D. L., Green, T. A., Vialou, V., Iñiguez, S. D., Cao, J.-L., Kirk, A., Chakravarty, S., Kumar, A., Krishnan, V., Neve, R. L., Cooper, D. C., Bolaños, C. A., Barrot, M., McClung, C. A., & Nestler, E. J. (2009). CREB regulation of nucleus accumbens excitability mediates social isolation–induced behavioral deficits. *Nature Neuroscience*, *12*(2), 200–209. https://doi.org/10.1038/nn.2257

Wells, J. C., & Stock, J. T. (2007). The biology of the colonizing ape. *Yearbook of Physical Anthropology*, *50*, 191–222. https://doi.org/10.1002/ajpa

West-Eberhard, M. (2003). *Developmental plasticity and evolution*. Oxford University Press.

Wiley, A. S. (2021). Pearl lecture: Biological normalcy: A new framework for biocultural analysis of human population variation. *American Journal of Human Biology*, *33*(5), e23563. https://doi.org/10.1002/ajhb.23563

Worthman, C. M. (2003). Energetics, sociality, and human reproduction: Life history theory in real life. In *offspring: Human fertility behavior in biodemographic perspective*. National Academies Press. https://www.ncbi.nlm.nih.gov/books/NBK97289/

How to cite this article: Sarma, M. S., & Shelhamer, M. (2024). The human biology of spaceflight. *American Journal of Human Biology*, *36*(3), e24048. https://doi.org/10.1002/ajhb.24048