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# From molecules to minds – an integrative framework for living in space

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As humanity transitions from episodic exploration to sustained habitation beyond low Earth orbit, the long-term viability of human life in space has become a critical scientific challenge. Survival in extraterrestrial environments requires more than engineering solutions; it demands an integrative approach that addresses molecular stability, physiological regulation, psychological adaptation, and ethical governance. This perspective proposes a unified framework that combines space medicine, multi-omics science, behavioral health, and agentic artificial intelligence to meet the complex demands of long-duration missions. Human heterogeneity, sex-specific physiology, epigenetic plasticity, and the operational boundaries of AI are examined alongside the distinction between adult astronaut adaptation and the unresolved biological risks of multi-generational colonization. By situating technological advancement within a human-centered, ethically governed paradigm, this framework offers a structured roadmap for a sustainable human presence beyond Earth.

KEYWORDS

space, astronautics, steam, living in space, technologies

## Introduction: living in space as a biological transition

Human physiology evolved under tightly regulated terrestrial conditions defined by gravity, magnetospheric protection, circadian rhythms, and environmental sensory feedback. Spaceflight disrupts these foundational parameters. Exposure to microgravity, ionizing radiation, prolonged isolation, sensory deprivation, altered sleep cycles, and communication latency places unprecedented strain on the human organism. These conditions challenge not only physical homeostasis but also cognitive stability and psychological regulation. Traditional spaceflight countermeasures have focused on discrete physiological systems; however, long-duration missions require an integrative model that recognizes the astronaut as a coupled biological, psychological, and technological system. A holistic framework is therefore essential for maintaining functional performance and health integrity in environments fundamentally incompatible with human biology.

## Molecular, genomic, and epigenetic adaptation in spaceflight

At the molecular level, microgravity and cosmic radiation induce widespread alterations in gene expression, mitochondrial function, oxidative stress pathways, immune regulation,

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and DNA repair processes. Findings from the NASA Twins Study demonstrated persistent transcriptional changes, telomere length variation, and epigenetic remodeling following extended spaceflight. These changes reflect environment-driven genomic plasticity rather than transient stress responses. Although epigenetic flexibility enables adaptive recalibration, it also introduces risks of immune dysregulation, cellular senescence, and potential oncogenic mutations. Multi-omics integration is therefore critical for characterizing individual susceptibility and guiding personalized countermeasures. Genetic data should be utilized to optimize health strategies rather than serve as a basis for exclusionary selection criteria. Beyond transcriptional and telomeric changes, spaceflight also induces shifts in DNA methylation patterns, histone modification dynamics, and chromatin accessibility, suggesting long-term reprogramming of gene regulatory networks. These modifications influence key systems including circadian regulation, oxidative defense pathways, inflammatory response mechanisms, and neuroendocrine signaling. Emerging evidence indicates that epigenetic alterations may persist across multiple cellular generations, raising implications for cumulative biological impact during repeated or extended missions. Of particular concern is the interaction between radiation exposure and epigenetic instability, which may elevate genomic mutation rates and compromise DNA repair fidelity. This has significant implications for carcinogenesis, immune dysfunction, and accelerated cellular senescence. Simultaneously, mitochondrial bioenergetics becomes increasingly compromised, leading to inefficient energy production and a heightened oxidative burden. These shifts are not uniformly distributed across individuals, reinforcing the necessity for personalized molecular health profiling. Integrative multi-omics platforms combining transcriptomics, metabolomics, proteomics, and epigenomics offer a pathway toward predictive health modeling and pre-emptive intervention. By correlating molecular changes with physiological and psychological performance parameters, space medicine can transition from reactive treatment to proactive health governance. This approach supports early identification of maladaptation patterns and enables targeted countermeasures such as adaptive nutritional modulation, pharmacogenomic adjustment, and timed circadian recalibration protocols.

## Human variability and ethical application of genetic insight

Human populations exhibit substantial variability in biological response to radiation exposure, metabolic stress, cognitive fatigue, and immune suppression. While genomic profiling can enhance predictive modeling of risk, ethical frameworks prohibit using such data to limit access to spaceflight opportunities. Instead, genetic insight must be applied toward individualized health optimization, including precision pharmacology, nutritional tailoring, and targeted physiological conditioning. This approach ensures that genetic data supports health preservation without compromising inclusivity, equity, or international ethical standards.

## Acute and chronic physiological recalibration

Physiological adaptation to space occurs along both immediate and long-term timelines. Acute responses include fluid redistribution, vestibular disturbance, cardiovascular deconditioning, muscle weakening, and circadian disruption. These changes impair coordination, concentration, and physical endurance. Chronic exposure leads to progressive musculoskeletal atrophy, bone demineralization, endocrine imbalance, immune suppression, and altered microbiome composition. These systemic shifts necessitate continuous monitoring via biosensors, adaptive exercise regimes, and responsive medical intervention systems capable of real-time data interpretation and preventive action.

## Sex-specific physiology and reproductive considerations

Female astronauts encounter additional physiological variables associated with hormonal cycling, menstrual suppression protocols, the menopausal transition, and increased sensitivity of reproductive tissues to radiation. These factors influence bone density, cardiovascular regulation, and endocrine stability. The biological feasibility of reproduction in extraterrestrial environments remains insufficiently understood. Developmental processes such as neural maturation, skeletal formation, and immune imprinting are gravity-dependent and cannot be ethically tested *in vivo*. Therefore, current mission planning must prioritize adult astronaut adaptability while deferring reproductive and generational concerns to long-term simulation and preclinical modeling frameworks.

## Psychological and behavioral adaptation is isolated environments

Psychological stability during long-duration missions requires adaptation to confined living conditions, communication delays, sensory deprivation, and prolonged separation from terrestrial environments. These stressors contribute to emotional dysregulation, cognitive fatigue, motivational decline, and altered temporal perception. Beyond operational performance, spaceflight impacts identity coherence and psychological continuity. Astronauts may experience altered self-perception, reduced emotional grounding, and shifts in existential orientation. Effective countermeasures include structured psychological support, guided reflection practices, behavioral health monitoring, and the cultivation of narrative continuity to reinforce resilience and maintain mission engagement. Psychological resilience in space is not defined solely by emotional stability but by the capacity to preserve coherent narrative identity in conditions of prolonged sensory deprivation, social restriction, and existential remoteness. Long-duration missions often induce phenomena such as derealization, depersonalization, and altered temporal consciousness, particularly when Earth becomes visually and psychologically distant. These states can undermine motivation, impair decision-making, and erode long-term mission engagement. Effective countermeasures must therefore address both clinical symptomology and the more profound psychological need for coherence, purpose, and continuity. Structured psychological interventions, such as cognitive reframing, emotion regulation training, and structured peer-support protocols, have shown potential for stabilizing intrapersonal and interpersonal dynamics. Additionally, purposeful environmental design incorporating simulated natural elements, cultural anchors, and aesthetic continuity supports emotional grounding and reduces cognitive fatigue. Notably, mental health monitoring should not be limited to crisis detection but should follow a longitudinal wellness model incorporating regular psychological check-ins, self-report tools, and adaptive therapeutic routines. Integration between human psychological specialists and AI-based mental state detection systems offers a balanced hybrid framework in which technology supports emotional wellbeing without replacing human empathic intervention.

## Artificial intelligence: functionality, boundaries, and ethical governance

Agentic AI systems provide significant value by supporting astronaut health through anomaly detection, predictive modelling, and decision support for medical intervention. Digital twin technologies enhance real-time pharmacokinetic modeling and physiological forecasting. However, AI systems lack moral reasoning, contextual awareness, and emotional intelligence. Excessive dependence on automated systems may undermine human autonomy, situational judgment, and decision-making capacity. For this reason, AI must function strictly as a decision-support tool rather than an autonomous authority in clinical or operational contexts. Ethical governance frameworks must incorporate transparency, explainability, human override protocols, and multidisciplinary oversight to ensure AI enhances rather than compromises cognitive sovereignty and mission safety. As AI becomes more deeply embedded into astronaut health ecosystems, the distinction between supportive intelligence and directive authority must remain explicitly defined. AI must not be permitted to override human clinical judgment in medical emergencies or psychological crises without human validation. Autonomous decision-making protocols, particularly those involving pharmacological intervention or behavioral modification, must operate within predefined ethical constraints and human oversight hierarchies. Furthermore, algorithmic bias, data misinterpretation, and system drift present significant risks in long-duration environments where adaptive learning systems may evolve unpredictably. AI governance models must therefore incorporate periodic system recalibration, external auditability, and contingency response protocols to address unexpected system behavior. This includes manual override, ethical fail-safes, and isolation mechanisms in the event of algorithmic malfunction. A system of distributed accountability involving mission medical officers, AI engineers, behavioral specialists, and ethics committees should guide the deployment and governance of intelligent support systems. This multidisciplinary oversight ensures that AI enhances mission safety while preserving human autonomy, dignity, and cognitive sovereignty.

## Adult adaptation versus multi-generational colonization

The biological adaptation of adult astronauts involves modifying pre-established physiological systems, whereas multi-generational colonization introduces unresolved risks to developmental biology, neurocognitive formation, and skeletal growth. The unknown effects of reduced gravity on embryonic development and childhood maturation present substantial ethical and scientific barriers. As such, current strategies should prioritize adult health preservation and mission sustainability while advancing research through analog environments and controlled simulation rather than direct implementation.

## Limitations and future directions

Despite substantial progress, data on multidecade habitation, reproductive sustainability, and intergenerational health outcomes remain limited. Future research must incorporate longer analog missions, integrative omics profiling, and interdisciplinary frameworks that unify biomedical science with ethical oversight and international governance.

## Conclusion

Sustainable human presence in space requires more than technological innovation; it necessitates an integrated framework that preserves biological function, psychological stability, and ethical responsibility. By aligning molecular science, physiological monitoring, behavioral resilience, and carefully governed AI systems, this perspective supports a model of space habitation that prioritizes safety, adaptability, and long-term physiological viability.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## Author contributions

SI-J: Conceptualization, Methodology, Writing – original draft, Writing – review and editing. RB: Writing – original draft. EJ: Writing – review and editing. SS: Writing – original draft. MS: Writing – original draft.

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## Generative AI statement

The author(s) declared that generative AI was used in the creation of this manuscript. We used AI for research and formatting the manuscript.

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