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AXIOM-4 AS A NEW FRONTIER IN SPACE BIOTECHNOLOGY: ADVANCES IN HUMAN HEALTH, MICROBIAL SYSTEMS AND SUSTAINABLE EXPLORATION

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Abstract:

Space biotechnology is an emerging interdisciplinary field that applies microbiology, molecular biology, synthetic biology, and bioengineering to address the challenges of long-duration space exploration. It offers approaches for maintaining human health, producing food and pharmaceuticals, recycling waste, recovering resources, and reducing dependence on Earth-based supplies. Among spaceflight conditions, microgravity is a major biological factor that can alter cellular behaviour, tissue organization, microbial growth, and physiological processes, creating both challenges and opportunities for biotechnology. The Axiom-4 (Ax-4) mission, involving Indian astronaut Shubhanshu Shukla aboard the International Space Station (ISS), marked an important milestone in India's contribution to space-based biological research. Its investigations involving microalgae, cyanobacteria, muscle regeneration, plant growth, tardigrades, and seed physiology provided valuable opportunities to study biological responses under actual microgravity conditions. This review examines the emerging applications of space biotechnology, focusing on microgravity-induced biological responses, microbial and photosynthetic systems, bioregenerative life-support systems, in-space biomanufacturing, and synthetic biology. These biological systems can contribute to oxygen production, carbon fixation, food generation, nutrient recovery, waste recycling, and production of pharmaceuticals and biomaterials. Despite their potential, challenges including radiation, biological containment, system reliability, and long-term validation remain. Integrating biotechnology with space technologies could enable more efficient, resource-conscious, and autonomous systems for sustainable long-duration space exploration.

Keywords: *Space Biotechnology, Axiom-4, Microgravity, Space Microbiology, Microalgae, Bioregenerative Life-Support Systems, In-Space Biomanufacturing.*

1. Introduction

Space biotechnology is an emerging field that applies modern biological approaches to address the challenges associated with space exploration. It has considerable potential to support long-term human presence beyond Earth by contributing to human health, food production, resource recycling, and sustainable life-support systems. However, biological systems operating in space are exposed to environmental stresses that are distinct from, and in some cases more severe than, those encountered on Earth. These include microgravity, ionizing radiation, temperature fluctuations, reduced pressure, ultraviolet (UV) radiation, and limited nutrient availability. Understanding how living organisms respond and adapt to these conditions is therefore a major focus of space biology [1].

Space biotechnology can offer important advantages over conventional abiotic technologies, particularly by reducing the mass, power, and volume requirements of systems needed for long-duration crewed missions. Its applications extend beyond established areas such as food production and waste recycling to include in situ resource utilization (ISRU), in situ biomanufacturing (ISM), food and pharmaceutical synthesis, and life-support loop closure. Biological systems can be employed to generate essential feedstocks, such as biologically fixed carbon and nitrogen, produce fertilizers, manufacture materials and replacement components, synthesize food, nutrients, pharmaceuticals and therapeutic compounds, and recycle waste to regenerate essential resources required for life support.

These applications contribute to the emerging field of space bioprocess engineering, which integrates principles of biotechnology, synthetic biology, bioengineering, space science, and mission design to develop biological systems adapted to the constraints of space. By enhancing resource recovery, reducing dependence on Earth-based resupply, and improving the efficiency of biological production systems, these technologies could enable more sustainable and resource-efficient long-duration missions. In the future, such systems could support orbital biotechnology facilities, lunar habitats, interplanetary waystations, and biomanufacturing facilities on Mars [2].

Understanding how microorganisms adapt to the unique conditions of space is essential for developing strategies to minimize their potentially harmful effects while also exploiting their valuable biotechnological properties. Various microbial processes have been investigated through spaceflight experiments as well as laboratory-based platforms that simulate space conditions. However, current research has focused on a relatively limited number of microorganisms. Therefore, broader investigation of microorganisms with significant biotechnological potential is needed to develop biological systems capable of supporting the sustainability and resource independence of future long-duration space missions. [3]

2. Axiom-4: A new milestone in space biotechnology

The Axiom-4 (Ax-4) mission marked an important milestone in India's human spaceflight and space biotechnology research, with ISRO's Gaganyatri Shubhanshu Shukla participating aboard the International Space Station (ISS). The mission provided India with an opportunity to conduct biological research under actual microgravity conditions, generating knowledge relevant to future human space missions. The scientific research portfolio and experimental protocols were developed with the involvement of ISRO, along with student outreach activities that encouraged national participation. The knowledge gained from the mission is expected to contribute to the advancement of India's Human Space Programme and future space biotechnology research. [4]

Figure 1: Scientific Experiments by Shubhanshu Shukla During Axiom Mission 4 [5]

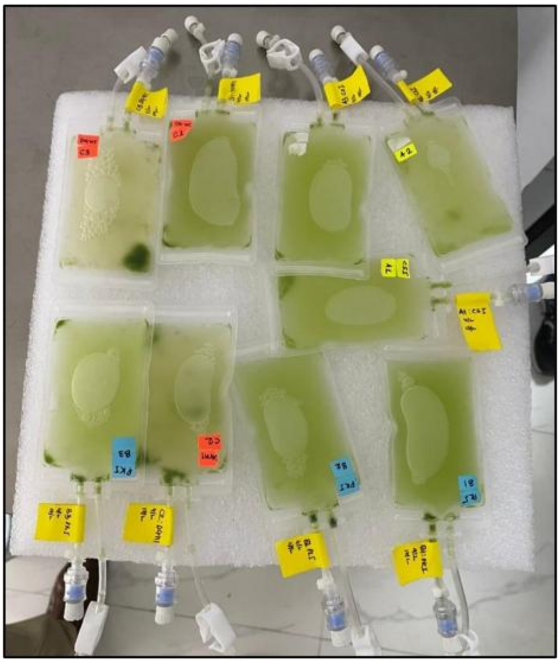

Figure 2: Axiom 4 Mission- Space Microalgae [27]

Under the coordination of the Human Space Flight Centre (HSFC), Indian research institutions conducted seven experiments covering key areas of space biotechnology and human spaceflight. These included Space Microalgae (ICGEB & BRIC-NIPGR, New Delhi) for studying the growth and radiation response of edible algae; Myogenesis (BRIC-InStem, Bengaluru) for investigating muscle regeneration; Sprouts (UAS & IIT Dharwad) for examining the growth of methi and moong; Tardigrade (IISc, Bengaluru) for studying resilience and ageing; Electronic Displays (IISc, Bengaluru) for cognitive testing; Cyanobacteria in Microgravity (ICGEB, New Delhi) for comparative growth and proteomic analysis; and Food Crop Seeds (IIST & KAU, Thiruvananthapuram) for assessing the effects of microgravity on seed physiology. All experiments were successfully completed, with samples returned to Earth for post-flight analysis. Shukla also contributed to ISS operations and joint scientific activities with the Axiom-4 and Expedition 73 crews, strengthening international collaboration in space-based research. [5]

Table 1: Biological and Biotechnology-Related Investigations Conducted During the Axiom-4 Mission

Experiment	Biological system studied	Main objective	Relevance to space biotechnology
Space Microalgae	Edible microalgae	To study growth and radiation responses under space conditions	Potential applications in food production and life-support systems
Myogenesis	Muscle cells/tissues	To investigate muscle regeneration under microgravity	Understanding and addressing muscle loss during spaceflight
Sprouts	Methi and moong	To examine plant growth under microgravity	Supports future space-based food production
Tardigrade	Tardigrades	To study resilience and ageing under space conditions	Provides insights into biological stress tolerance
Electronic Displays	Human participants	To assess cognitive performance during spaceflight	Supports understanding of human performance in space
Cyanobacteria in Microgravity	Cyanobacteria	To compare growth and proteomic responses under microgravity	Potential applications in oxygen production, carbon fixation, and life support
Food Crop Seeds	Crop seeds	To assess the effects of microgravity on seed physiology	Supports development of sustainable plant-based food systems

3. Microgravity as a biological environment

Microgravity refers to an environment in which the effects of gravity are greatly reduced, resulting in minimal gravitational forces. It occurs naturally during spaceflight and can also be reproduced using specialized ground-based systems designed to simulate space conditions. For cellular biology, microgravity provides a valuable setting to investigate how cells respond to substantial changes in gravitational forces, which normally influence several fundamental cellular processes on Earth. Under microgravity, the mechanical forces that regulate cell structure and function are altered, leading to changes in cytoskeletal organization, cell adhesion, and intracellular signaling. These alterations can subsequently influence essential cellular processes such as cell proliferation, differentiation, intercellular communication, and cell survival. [6]

3.1 Effects of microgravity on the musculoskeletal system

Microgravity significantly affects the musculoskeletal system by altering the mechanical forces that maintain bone and muscle structure. It disrupts the balance between osteoblast-mediated bone formation and osteoclast-mediated bone resorption, resulting in bone loss of approximately 1% per month, reduced bone mineral density, and increased fracture risk. Prolonged unloading also causes skeletal muscle atrophy, with astronauts potentially experiencing up to a 20% reduction in muscle mass and 30% reduction in muscle strength within one month. These changes can impair mission activities and increase injury risk after returning to higher-gravity environments, highlighting the need for effective countermeasures during long-duration space missions. [7]

3.2 Effects of microgravity on the immune system

The immune system is essential for pathogen defence, immune surveillance, and maintenance of physiological homeostasis, but it is significantly affected by spaceflight. Microgravity can impair antiviral immune responses by altering pathways such as RLR and TLR signalling and has been associated with increased susceptibility to infections and allergic responses during space missions. Studies have also reported changes in lymphoid organs, including reduced spleen and thymus mass. At the cellular level, microgravity can inhibit lymphocyte proliferation, activation, movement, and cytotoxic activity, while reducing monocyte levels, macrophage activation, and the phagocytic and oxidative functions of neutrophils. These changes can weaken immune defence and increase astronauts' susceptibility to disease, making a better understanding of microgravity-induced immune alterations essential for developing effective countermeasures and maintaining astronaut health during long-duration space missions. [8]

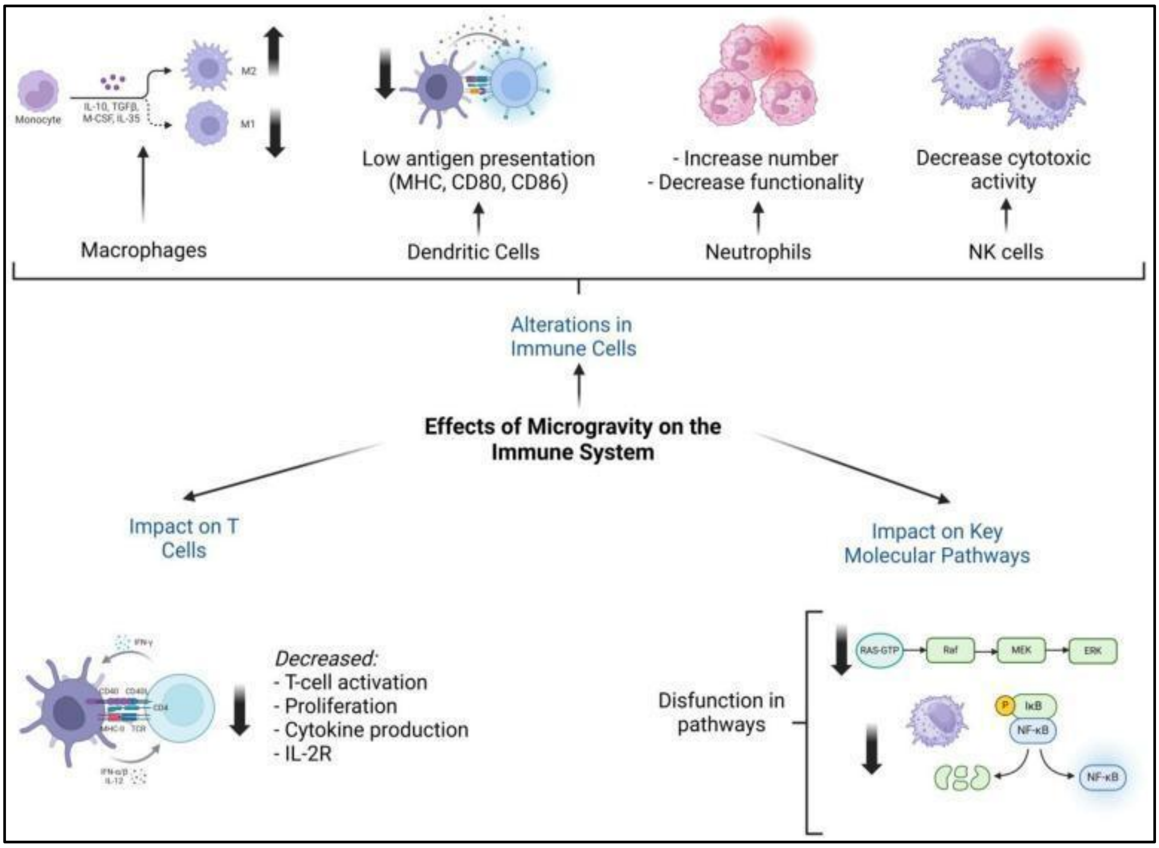

Figure 3: Effects of Microgravity on the Immune System [21]

3.3 Effects of microgravity on endothelial cells

Endothelial cells (ECs) play a key role in maintaining vascular integrity, blood flow, permeability, inflammation, and angiogenesis and are highly sensitive to changes in mechanical forces. Microgravity can cause morphological, functional, and biochemical alterations in ECs, including changes in cytoskeletal organization, cell membrane permeability, vasoactive and inflammatory mediators, and adhesion molecules. These changes can affect cell survival, proliferation, apoptosis, migration, and angiogenesis, contributing to cardiovascular alterations during spaceflight. Although responses may vary with cell type, exposure duration, and experimental conditions, spaceflight studies have demonstrated changes in endothelial morphology, membrane permeability, and cellular senescence. Understanding these effects is therefore important for developing strategies to protect vascular health during long-duration space missions. [9]

- Effects of Microgravity on Stem Cells: Microgravity actively influences stem cell behaviour, affecting proliferation, differentiation, mechanotransduction, secretory activity, and genomic stability. These effects vary depending on the stem cell type and surrounding cellular environment.
- Proliferation and Self-Renewal: Microgravity affects stem cell proliferation in a cell-type-dependent manner. Pluripotent stem cells (PSCs) may maintain self-renewal through factors such as Oct4 and Nanog, while mesenchymal stem cells (MSCs) and neural stem cells (NSCs) may show increased proliferation and spheroid formation. In contrast, hematopoietic stem cells (HSCs) can exhibit reduced colony formation or increased apoptosis. Microgravity can also alter cell-cycle progression and DNA damage responses.
- Cytoskeletal Remodeling and Mechanotransduction: Microgravity alters the cytoskeleton, including actin and microtubule organization, and affects mechanotransduction pathways. Changes in YAP/TAZ and FAK signalling can influence cell adhesion, survival, proliferation, and lineage commitment, thereby affecting stem cell fate.
- Secretome and Paracrine Signalling: Microgravity can modify the secretory profile of MSCs, increasing factors such as IL-10, TGF-β1, VEGF, and HGF. These changes may enhance their immunomodulatory, angiogenic, and regenerative properties and have generated interest in microgravity-conditioned secretomes and exosomes for cell-free therapeutic applications.
- Genomic Stability and DNA Damage: Microgravity, together with space radiation and oxidative stress, can affect genomic stability by increasing DNA damage, replication stress, and reactive oxygen species while altering DNA repair pathways and telomere-associated factors. These effects highlight the need to evaluate the long-term safety of stem cells exposed to space conditions.
- Epigenetic Alterations: Microgravity can induce epigenetic changes, including altered DNA methylation and histone modifications, which may affect gene expression, cellular memory, and differentiation potential. Such changes require careful evaluation for future space-based stem cell applications.
- Cancer Stem Cells: Microgravity can alter cancer stem cell behaviour, promoting three-dimensional spheroid and organoid formation and affecting cytoskeletal organization, proliferation, and therapeutic responses. These models provide useful platforms for tumour modelling and anticancer drug screening.
- Overall, microgravity influences stem cells through interconnected changes in proliferation, mechanotransduction, secretion, genomic stability, and epigenetic regulation. Understanding these responses is important for developing applications in tissue regeneration, disease modelling, and maintaining human health during long-duration space missions. [10]

3.4 Impact of microgravity on key molecular pathways

Microgravity alters key signalling pathways involved in cell growth, differentiation, survival, and immune regulation. Reduced RAS activity can impair cell proliferation, while changes in ERK signalling may affect the differentiation and activation of immune cells. Altered NF-κB activity can further disrupt inflammatory and immune responses. Microgravity also influences cancer-related pathways by promoting multicellular spheroid formation, cytoskeletal changes, and regulation of p53, NF-κB, and BAX. In breast, thyroid, and lung cancer cells, it can reduce cell adhesion and alter E-cadherin, VEGF, and vimentin expression, thereby influencing tumour proliferation, angiogenesis, migration, and dissemination. [11]

Table 2: Major Biological Effects of Microgravity and Their Implications [7-11]

Biological system	Major effects of microgravity	Underlying biological changes	Potential implications
Musculoskeletal system	Bone loss and muscle atrophy	Altered mechanical loading, increased bone resorption, and reduced muscle stimulation	Increased fracture risk, reduced muscle strength, and impaired physical performance
Immune system	Altered immune responses and reduced immune function	Changes in immune-cell proliferation, activation, signalling, and cytotoxic activity	Increased susceptibility to infections and impaired immune defence
Endothelial cells	Altered morphology, permeability, and angiogenic activity	Changes in cytoskeletal organization, cellular signalling, and membrane properties	Potential vascular and cardiovascular dysfunction
Stem cells	Altered proliferation, differentiation, and self-renewal	Changes in mechanotransduction, cytoskeletal organization, secretion, and gene regulation	Applications in tissue regeneration and disease modelling
Molecular pathways	Altered cell growth, survival, differentiation, and inflammatory responses	Changes in RAS, ERK, NF-κB, p53, BAX, and other signalling pathways	Effects on immune regulation, cellular function, and disease progression

4. Microbial biotechnology for sustainable space missions

4.1 Microalgae and cyanobacteria in space

Microalgae have considerable potential as biological resources for long-duration space missions because of their ability to tolerate radiation, vacuum, temperature fluctuations, and microgravity. Certain species can withstand these stresses through antioxidant defenses, DNA repair mechanisms, adjustments in photosynthetic metabolism, and protective structures. These adaptations allow microalgae to contribute to oxygen production, CO_2 fixation, waste recycling, nutrient recovery, food production, and water purification, making them valuable components of closed-loop life-support systems.

The performance of microalgae and cyanobacteria in space is highly species-dependent. Cyanobacteria such as Chroococcidiopsis show strong resistance to combined space stresses through biofilm formation, extracellular polymeric substance (EPS) production, efficient DNA repair, and dormancy. Similarly, Nostoc muscorum has maintained growth and photosynthetic activity in Mars regolith simulants, whereas Anabaena cylindrica showed metabolic decline and Chlorella vulgaris failed to grow. These contrasting responses demonstrate the varying resilience of photosynthetic microorganisms under extreme and resource-limited conditions.

Understanding these adaptive mechanisms can support the development of bioregenerative life-support systems (BLSS) and in situ resource utilization (ISRU) technologies. Future research should emphasize long-term space validation, strain improvement through synthetic biology, and the integration of biological and physicochemical processes to develop reliable and sustainable systems for human exploration beyond Earth [12]

Higher plants, algae, and other photosynthetic organisms are important components of life-support systems, particularly as primary food producers, while also depending on other supporting biological processes. Algae have demonstrated the ability to grow and photosynthesize in space and survive direct exposure to the space environment. However, the combined effects of microgravity and radiation on these organisms remain insufficiently understood. [13]

4.2 Microbial processing:

MELiSSA (Micro-Ecological Life Support System Alternative) is a bioregenerative life-support system developed by the European Space Agency (ESA) for recycling gaseous, liquid, and solid wastes during long-duration space exploration. It integrates microbial cultures, plants, and the human crew to support resource recovery and life-support functions. Inspired by Earth's ecological and geomicrobiological processes, MELiSSA aims to establish a closed-loop biological system for future crewed space missions. [14]

MELiSSA consists of interconnected biological compartments that progressively transform waste into useful resources. Compartment I uses anaerobic thermophilic fermentation to degrade crew waste and non-edible plant material, producing volatile fatty acids and CO_2. In Compartment II, these fatty acids are converted into microbial biomass by the anaerobic photosynthetic bacterium Rhodospirillum rubrum. Compartment III uses Nitrosomonas europaea and Nitrobacter winogradsky to convert ammonium into nitrate, making nitrogen more readily available for subsequent biological processes. Compartments IVa and IVb contain Spirulina platensis and higher plants, respectively, which use CO_2 and light to produce oxygen and edible biomass. Together, these compartments demonstrate how microbial processing can integrate waste degradation, nutrient recycling, gas regeneration, and food production within a closed-loop system. [15]

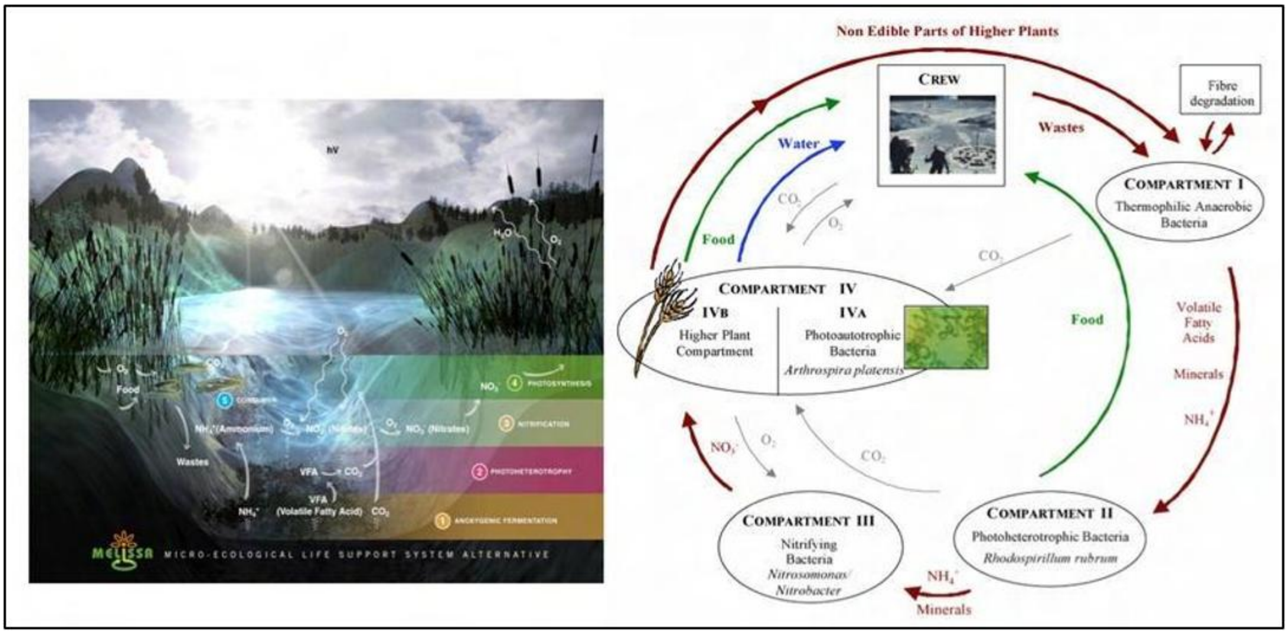

Figure 4: MELiSSA Closed-Loop Life Support System for Space Exploration [26]

4.3 Bioregenerative Life Support Systems (BLSS)

Long-duration space exploration requires reliable systems capable of providing food, water, and breathable air while efficiently recovering resources from waste. The current physicochemical-based Environmental Control and Life Support System (ECLSS) on the ISS has limited capabilities for in situ food production and complete recovery of water, oxygen, and nutrients, resulting in continued dependence on resupply missions from Earth. To address these limitations, bioregenerative life-support systems (BLSS) are being developed by integrating biological and physicochemical processes to enable the recovery and production of water, oxygen, food, and nutrients from waste streams, thereby reducing dependence on external supplies. [16]

The concept of Bioregenerative Life Support Systems (BLSS), also known as Closed or Controlled Ecological Life Support Systems (CELSS), has been explored since the early era of human space exploration. BLSSs are based on ecological networks in which waste generated by one component is used as a resource by another, enabling continuous cycling of biomass and nutrients. These systems generally include three interconnected components: biological producers, such as plants, microalgae, and photosynthetic bacteria; consumers, represented by the crew; and waste degraders and recyclers, including fermentative and nitrifying microorganisms. Together, these components support the recycling of waste, production of food and oxygen, and recovery of essential resources within a closed or semi-closed system.

Several ground-based facilities have been developed to evaluate BLSS technologies and their ability to support humans in isolated environments. Systems such as BIOS-1, BIOS-2 and BIOS-3, Biosphere 2, the Closed Ecology Experiment Facility (CEEF), and Lunar Palace 1 have tested different aspects of closed-loop life support. Antarctic facilities have also investigated individual functions, including wastewater recycling and food production. These studies have provided valuable information on biological waste treatment, controlled plant cultivation, food production, and air revitalization, while also examining the physiological and psychological effects of long-term confinement. Overall, these demonstrators have helped establish the feasibility of integrating biological processes into life-support systems for future long-duration space missions. [17]

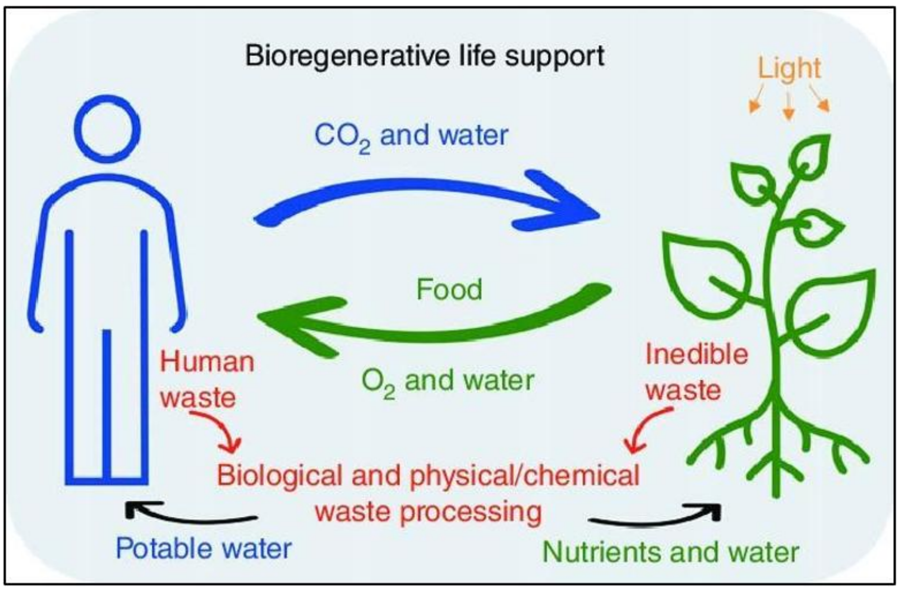

Figure 5: Foundations of Bioregenerative Life Support Systems [28]

4.4 Space biomanufacturing

In-space biomanufacturing involves producing biological materials, active pharmaceutical ingredients and their intermediates, biologics, and cellular therapeutic products in the space environment. It is an emerging approach with potential applications in both space exploration and biotechnology. The unique conditions of space, particularly microgravity, can alter the behaviour of cells, tissues, three-dimensional biological structures, and proteins compared with Earth-based conditions, creating new opportunities for biological production.

The concept developed from early spaceflight experiments that investigated how microgravity affects biological systems. Studies conducted during space shuttle and Mir missions in the 1980s and 1990s demonstrated that microgravity can influence cellular behaviour, suggesting that these changes could be harnessed for biomanufacturing. One of the early successes was the growth of protein crystals in space, demonstrating the potential of the space environment for producing biological materials with applications in biotechnology and medicine. In-space biomanufacturing has the potential to enable the on-site production of essential biological products, reducing dependence on resupply missions from Earth and supporting long-duration space exploration. Potential applications include 3D bioprinting of tissues and, in the longer term, organs, which could provide new approaches for managing injuries and medical conditions during extended missions. However, large-scale biomanufacturing in space is still at an early stage, with several technical and logistical challenges. These include developing reliable bioreactors capable of operating under microgravity, maintaining and transporting biological materials, and ensuring the safety, quality, and efficacy of space-manufactured products.

In-space organ bioprinting and implantation remains a long-term goal that will require substantial technological and clinical development before practical implementation. Nevertheless, advances in cryopreservation and thermal-management technologies, including cryogenic freezers aboard the ISS, have improved the long-term preservation of biological samples. As understanding of microgravity and biological processes advances, in-space biomanufacturing could play an important role in human health, medicine, biotechnology, and materials production, while reducing the logistical demands of future long-duration space missions. [18]

4.5 Synthetic biology for space exploration

Synthetic biology combines biological knowledge with engineering principles to modify existing biological systems or create new biological components, genetic circuits, and cellular systems for specific purposes. In space exploration, it offers the potential to develop organisms and biological systems that can function under the unique challenges of space while supporting applications such as resource production, environmental monitoring, and life support. [19]

- ***In-situ* protein production and nutrient recycling**

Among the nutritional challenges of long-duration space missions, protein availability is a major concern, as protein is essential for maintaining muscle mass, immune function, and metabolic balance. Microgravity and radiation can affect protein metabolism, creating a need for reliable and sustainable protein sources during extended missions. In situ protein production could reduce dependence on supplies from Earth and support self-sufficient space habitats.

Synthetic biology offers a promising approach by engineering microorganisms to produce nutrients, pharmaceuticals, and biomaterials from limited or unconventional resources. Microbial chassis such as *Deinococcus radiodurans*, *Yarrowia lipolytica*, and *Niallia tiangongensis* show potential for tolerating radiation, nutrient limitation, and other space-related stresses. Advances in CRISPR genome editing, metabolic engineering, adaptive evolution, portable DNA synthesis, and miniaturized bioreactors could further enable autonomous protein production and resource recycling, contributing to closed-loop life-support systems and sustainable habitats beyond Earth. [20]

- **Microorganisms as platforms for space applications**

Biological technologies offer diverse possibilities for space applications, with useful microorganisms found across all three domains of life: Bacteria, Archaea, and Eukaryota. These microbes are lightweight and versatile biological platforms that can serve as effective chassis for space-based applications, expanding the use of biotechnology beyond conventional approaches that have primarily focused on plants for food production. [21]

- **Bioregenerative life support and food production**

Long-duration missions beyond Low Earth Orbit (LEO) require reliable supplies of oxygen, potable water, and nutritious food. Bioregenerative Life Support Systems (BLSS) can reduce dependence on Earth by using plants, microalgae, photosynthetic bacteria, and microorganisms to regenerate resources, recycle waste, and produce food and oxygen. These systems function as engineered closed ecosystems, with microorganisms selected or engineered for specific resource-recovery processes.

- **Synthetic biology-based health monitoring**

Microgravity and radiation can cause several health problems during long-duration spaceflight, including immune dysfunction, sleep disturbances, visual impairment, anemia, and bone and muscle loss. Spaceflight can also alter the gut and skin microbiomes, potentially affecting immunity and increasing the risk of pathogen reactivation. Synthetic biology could help address these challenges through engineered bacteria that monitor microbiome changes and sense-and-respond systems that deliver nutrients or therapeutic molecules when required, offering potential strategies for maintaining astronaut health during extended missions.

Instead of human health give another subheading [22]

5. Technological and biological challenges in space exploration

i. **Challenges to human health:** During spaceflight, astronauts are exposed to several stressors, including microgravity, radiation, sleep deprivation, inadequate nutrition, isolation, and confinement. Extended exposure to these conditions may result in immune dysfunction, cognitive changes, anxiety, skin problems, cardiopulmonary and musculoskeletal deconditioning, gastrointestinal disturbances, and spaceflight-associated neuro-ocular syndrome (SANS). Maintaining a safe, life-supporting environment and protecting astronauts from the effects of microgravity and radiation are therefore major challenges for long-duration space missions. The level of health risk depends largely on the duration and distance of the mission. [23]

ii. **Safety, reliability and containment challenges:** Safety and system reliability in the space environment remain major concerns, particularly regarding the containment of engineered biological systems and the risk of unintended environmental contamination. [24]

iii. **Key challenges in space synthetic biology:**

- Resource Utilization: Ensuring engineered organisms remain functional under extreme space conditions while efficiently converting wastes, volatiles, and minerals into useful resources and manufacturing feedstocks.

- Manufacturing: Developing biological methods to produce construction materials such as biocement, biopolymers, and adhesives, as well as fuels for energy and propulsion.
- Life Support: Improving biological recycling of air, water, and waste while supporting nutrient recovery and the production of nutritious, acceptable food.
- Space Medicine and Human Health: Maintaining astronaut health by supporting the microbiome, producing therapeutic molecules, and developing biological approaches for protection against radiation and reduced gravity.
- Space Cybernetics: Developing biological sensors, actuators, and control systems that can operate independently or integrate with conventional electronic technologies.
- Terraforming: Developing multifunctional organisms capable of supporting essential biogeochemical cycles, particularly carbon and nitrogen cycling, to enable gradual environmental modification of planetary surfaces. [25]

6. Future perspectives

- Genetic Engineering for Space Agriculture: Genetically engineered plants could be developed to tolerate space conditions and support sustainable food production, reducing dependence on Earth. Genetic approaches may also help improve resistance to radiation and other space-related health risks.
- Microbiome Research: Monitoring the human microbiome during spaceflight could help maintain astronaut health. Studying microbial responses to microgravity may also support applications in life support, waste management, and medicine.
- Biomanufacturing in Space: Biological systems could produce pharmaceuticals, enzymes, and other essential products during missions, reducing resupply needs. Engineered microorganisms may also produce polymers, construction materials, and oxygen-supporting resources.
- Artificial Biospheres: Biotechnology could enable self-contained ecosystems for long-duration missions by integrating biological processes for oxygen production, food generation, water recycling, and waste management.
- Space Medicine: Biotechnology may increasingly support astronaut health through continuous health monitoring, disease diagnosis, and in-space treatment. Future systems could provide more autonomous medical care during deep-space missions, reducing dependence on Earth-based support. [21]

7. Conclusion

Space biotechnology is rapidly emerging as an important component of sustainable human space exploration, with microgravity serving as both a biological challenge and a unique experimental environment. The Axiom-4 mission represents an important step in advancing this field, particularly through India's participation in biological investigations involving microalgae, cyanobacteria, muscle regeneration, plants, tardigrades, and seed physiology. These studies demonstrate how spaceflight can provide valuable insights into biological adaptation while supporting the development of technologies for future missions.

The evidence reviewed highlights the broad potential of biological systems in addressing key requirements of space exploration. Microalgae, cyanobacteria, and other microorganisms can contribute to oxygen production, carbon fixation, food generation, nutrient recovery, waste recycling, and resource regeneration, while bioregenerative life-support systems can integrate these processes into more efficient closed or semi-closed biological cycles. Similarly, advances in in-space biomanufacturing and synthetic biology could enable the production of proteins, pharmaceuticals, biomaterials, and other essential resources directly during missions, reducing dependence on Earth-based resupply.

Despite this promise, significant challenges remain, including the effects of microgravity and radiation on biological systems, variability between microbial and cellular responses, biological containment, system reliability, scalability, and the need for long-term validation under actual spaceflight conditions. Addressing these limitations will require closer integration of space biology, biotechnology, synthetic biology, engineering, and systems-level approaches.

Overall, the transition toward more autonomous and resource-efficient space missions will increasingly depend on the ability to understand, engineer, and harness biological systems in space. Axiom-4 contributes to this growing body of knowledge and highlights the importance of continued space-based biological research. With further validation and technological development, space biotechnology has the potential to move beyond experimental applications and become an integral part of reliable, sustainable, and biologically enabled space exploration.

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