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Review Article

From ancient roots to contemporary innovations: The crucial role of microbes in the life sciences

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Abstract

Microorganisms have shaped Earth's biological and ecological landscape since the emergence of the first living cells. This review explores microbial evolution through major origin-of-life theories, including the Last Universal Common Ancestor (LUCA), the primordial soup hypothesis, and the hydrothermal vent theory. It highlights the diverse mechanisms of microbial communication—such as quorum sensing and interspecies electron transfer—and their roles in symbiosis, immunity, and ecosystem regulation. Key microbiome-mediated pathways, including the gut-brain, gut-skin, and soil-gut axes, are examined in the context of human health. The review also addresses the consequences of reduced microbial exposure due to modern lifestyles and urbanization. Applications in agriculture, medicine, and astrobiology are discussed, including microbial fuel cells, bio-mining, and planetary protection strategies. By synthesizing ancient origins with futuristic innovations, this review underscores the crucial role of microbes in shaping both Earth's biosphere and humanity's future in space.

Keywords: Microbes, Hygiene hypothesis, LUCA, Astrobiology, Microbial axis

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1. Introduction

Louis Pasteur, often called the father of microbiology, defined microorganisms as living entities too small to be seen by the naked eye, capable of fermentation and disease causation. It is exceedingly rare to find an environment completely devoid of microbial life. From the moment a human passes through the birth canal, our bodies begin to be colonized by microbes.

Interest in microorganisms has surged in recent years, contrasting sharply with the early 2000s, when excessive sanitization and a fear of “dirt” dominated public attitudes. This mindset, rooted in the belief that avoiding microbes would prevent disease, has since been challenged. Today, over-sanitization and antibiotic misuse are recognized as contributors to immune-related disorders such as allergies, obesity, and autoimmunity.

The understanding of microbial life took a pivotal turn with the discovery of the gut-brain axis and the role of microbes in space biology. The microbiome is now seen as essential to the balance of biological systems. From theories about microbial fuel cells (MFCs) generating energy in space to the Gaia hypothesis, which proposes that Earth acts as a self-regulating system due to microbial interactions with inorganic matter, microbes continue to inspire scientific curiosity.

This review delves into the fascinating world of microbes and their far-reaching significance.

2. The Beginning

The oldest known fossils on Earth, microbial mats and stromatolites, predate multicellular organisms by a billion years, clearly implying that life on Earth evolved from microorganisms.[1]

Charles Darwin, known as the father of evolution, illustrated in “*On the Origin of Species*” how evolution depicts the tree of life, where in the trunk of the tree is the

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earliest common ancestor to all life on earth, and as the branches, twigs, and leaves spread out, the diversity of species increases. This implies that if we trace back enough in time, all species on Earth share a universal common ancestor.

This last universal common ancestor, or LUCA, is not supposed to be the origin of life on Earth, but the emergence of life in its current form. LUCA is believed to be a primitive single-celled microorganisms that used DNA and RNA. Researchers have reconstructed LUCA's genome by studying genetic data across modern bacteria and archaea. The reconstructed genomes suggested that LUCA had a metabolism based on hydrogen gas and carbon dioxide and that it had a rudimentary defense against viruses and ultraviolet rays, hence making LUCA more complex than previously thought to be. By using paralogous genes, fossils, and geological data, LUCA is said to have existed 4.2 billion years ago, which indicates that life emerged quickly after the Earth's environment became habitable. The study of LUCA provides insight into both evolutionary biology and the potential development of life on other planets.[2-4]

How did life originate is a question scientists and philosophers have pondered for generations. Aristotle thought that life arises spontaneously from non-living matter based on the observations of small organisms like insects and maggots appearing on decaying matter. However, this theory was disproved by Louis Pasteur's swan neck experiment, where he showed that a sterile broth remained free of microbial growth when protected by a curved flask neck that trapped dust and microbes. Thus proving that microorganisms come from other microorganisms (biogenesis) rather than non-living matter.

Another popular theory is the primordial soup hypothesis, which proposes that the first life form on Earth had to be born from a pond or an ocean containing organic compounds, which eventually formed complex organic polymers and gave rise to life. However, this theory doesn't explain how organic molecules assemble to form a self-replicating system like RNA.

The Panspermia hypothesis states that life or its building blocks arrived on Earth from space via meteoroids or comets. This theory is backed by the discovery of organic molecules like amino acids and sugars on meteoroids. However, the survival of life through space is extremely rare and highly debated. This concept has again come into popularity in recent years since various extremophile microbes have been found to not only survive but thrive in space.[5] One more supposition on the origin of life that is widely studied today is the deep-sea hydrothermal vent theory. Life originated near underwater volcanic vents, where mineral-rich, heat-driven chemical reactions produce life's first molecule. LUCA is thought to have lived in such an environment. Modern thermophilic archaea resemble what early life might have looked like in such an environment.[6-7]

3. Microbial Symbiosis

The term symbiosis was first defined as the persistent association between dissimilar organisms. The Gaia principle suggests that Earth's living organisms interact with their inorganic surroundings to form a self-regulating complex system. Life, including microbial life, co-evolves with the environment, which ensures that Earth's systems stay favorable to life despite external challenges. The Gaia hypothesis underscores the vital influence of microbial life in sustaining Earth's habitability. These microbes are the driving force for essential biogeochemical cycles, playing a fundamental role in regulating planetary systems such as the atmosphere, hydrosphere, and lithosphere. Their metabolic processes help maintain environmental stability, influencing climate patterns, nutrient cycles, and atmospheric composition.[7-9] Current studies recognise symbiosis as a spectrum from mutualism (both partners benefit), to commensalism (one benefits without harming the other), to parasitism (one benefits at the host's expense).[10] Microbial symbiosis involves complex interactions between different microorganisms, including bacteria, fungi, archaea, and viruses. They communicate with each other using diverse signalling mechanisms. These molecular mechanisms regulate behaviours such as biofilm formation, virulence, and metabolic cooperation.[11]

One such mechanism is Quorum sensing (QS). QS enables bacteria to synchronise gene expression based on population density via signalling molecules called autoinducers. As the bacterial population grows, the concentration of autoinducers also increases, and upon the concentration reaching a certain threshold, certain bacteria detect it and result in biofilm formation or virulence.[12-13] Gram-negative bacteria use acyl-homoserine lactones (AHLs), while Gram- positive bacteria rely on peptide-based signals.[14-15] QS mechanisms can be therapeutically targeted using quorum sensing inhibitors (QSIs), such as halogenated furanones, to disrupt biofilm formation in pathogens like Pseudomonas aeruginosa.

P. aeruginosa is a pathogen known to kill people with cystic fibrosis and a compromised immune system, and it causes infections when you get a catheter, a stent, or a breathing tube. A QSI for these can be made by synthetic analogs (halogenated furanones) of AHLs that block QS receptors. QSI can be useful antibiotics and can be used to line medical instruments in order to prevent infections.[16]

A very crucial mechanism of signalling between microbes is interspecies electron transfer (IET). This is being widely studied to understand microbial existence in extreme environments. IET enables syntrophic microbes to exchange electrons directly via conductive nanowires or through mineral-based electron shuttling. This process enhances energy efficiency, supporting microbial life in extreme environments and influencing biogeochemical cycles.

Electric syntrophy reduces energy losses, enabling survival in nutrient-limited habitats.[17-18]

Microbes can also hijack host hormones to regulate their behaviours in cross-kingdom signalling. Pseudomonas aeruginosa produces estrogen-like molecules that modulate immune responses, while E. coli quorum sensing can be disrupted by human stress hormones. These interactions depict deep evolutionary connections between microbial and eukaryotic signaling systems.[19-20]

4. The Hygiene Hypothesis

The original hygiene hypothesis by Strachan suggested that reduced early childhood infections, especially from contact with siblings, contributed to the rise in allergies. However, further research shows that allergic disorders do not directly correlate with fewer infections or changes in domestic hygiene. Instead, a broader shift in lifestyle has reduced exposure to beneficial microbes (e.g., gut bacteria, helminths) crucial for immune regulation.[21-22] Experts have suggested renaming this hypothesis to “microbial exposure hypothesis” to emphasize the role of microbes in immune health while avoiding misconceptions that discourage good hygiene practices.[23] There is a stark difference between pre-industrial and industrial microbial exposure due to changes in agricultural practices, urbanization, sanitation, and food processing. In pre-industrial societies, frequent interaction with natural environments, including soil and natural fertilizers (including feces), facilitated exposure to a diverse range of microorganisms essential for immune system development. However, the widespread use of sanitation systems, hydroponic farming, processed foods, and limited outdoor activities has restricted human interaction with these microbial sources.[23-24] Thus causing a decrease in microbial diversity within the gut and immune system.[24] Consequently, the immune system is more prone to dysregulation, leading to an increased prevalence of allergic and autoimmune diseases.

This review proposes that this loss of natural microbial exposure may also underlie a global increase in vitamin B_{12} deficiency. Vitamin B_{12} (cyanocobalamin) is synthesized exclusively by certain bacteria, including *Pseudomonas denitrificans*, which are commonly found in soil. In the past, when people consumed minimally processed or unwashed produce, they may have indirectly ingested B_{12}-producing microbes, helping maintain adequate B_{12} levels without supplementation. As our diets became increasingly sanitized and detached from soil-based microbial sources, this incidental exposure may have been lost. This could explain the growing dependence on external supplementation, particularly in vegan and vegetarian populations.

In this context, the microbial exposure hypothesis extends beyond immune disorders to encompass nutrient acquisition, highlighting how shifts in microbial ecology may influence both metabolic and immunological health.

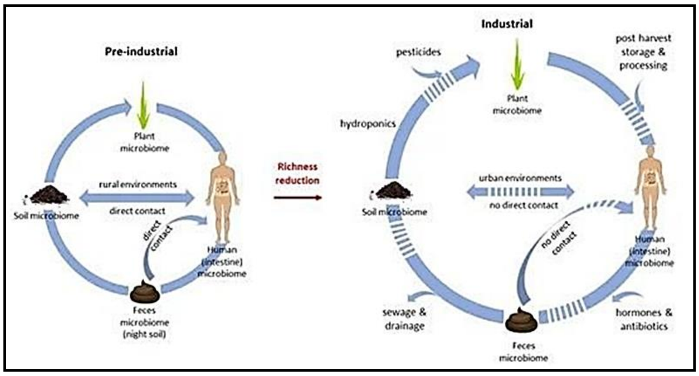

Figure 1: Decline in microbial diversity from rural to urban populations. Reproduced from Blum et al., Microorganisms, 2019 , under CC BY 4.0.25

Soil contains approximately the same number of active microorganisms as the human gut, yet gut microbial diversity is only 10% of soil's biodiversity. Urban populations exhibit 40% lower gut microbiome diversity compared to rural communities, with an increased prevalence of opportunistic pathogens.[25]

Figure 1 illustrates the reduction in microbial richness from rural to urban populations.

Table 1 summarizes the core differences in microbial diversity between rural and urban populations.

Table 1: Comparative gut microbiome diversity and composition: rural vs. urban populations

Metric	**Rural Population**	**Urban Population**	**Source**
Gut microbiome α-diversity (Shannon)	4.2 ± 0.3	2.5 ± 0.4	Vinogradova et al., [35]
Prevotella: Bacteroides ratio	~1.8	~0.6	Das et al., 2018 [36]
Core soil-derived Operations taxonomic units (OTUs) in the gut	~15%	~4%	Wicaksono et al., 2023 [33]

5. Soil Microbiome

By 2050, up to 90% of the planet’s soil may be degraded, but scientists and agribusinesses believe that harnessing microbial solutions could be crucial in preventing a global food crisis.[26] In Punjab, intensive tillage practices have significantly degraded soil health and the soil microbiome. The state’s rice-wheat cropping system, which relies heavily on conventional methods like puddled transplanted rice (PTR), has led to breakdown of soil structure, surface compaction, and poor water infiltration. Continuous deep tillage and excessive use of chemical fertilizers have also reduced soil organic matter, microbial biodiversity, and soil fertility. Over the years, Punjab’s soil has suffered from nutrient depletion, leading to increased reliance on synthetic fertilizers. For example, paddy yields have declined despite a 350% increase in fertilizer use, highlighting the diminishing returns of soil degradation. Additionally, intensive tillage has disrupted soil microbial communities, leading to a decline in beneficial bacteria, fungi, and earthworms, which are essential for soil regeneration and nutrient cycling. The soil organic carbon (SOC) levels in Punjab now range between 0.3-0.8%, far below the recommended 1%, indicating severe soil health degradation. Degraded soils lose the ability to hold and filter water, are more susceptible to erosion, and plant growth and productivity are suppressed.[27-28]

The soil bacteria are the most abundant microbial group in soil and play a crucial role in plant and soil health. They contribute to organic matter decomposition by secreting enzymes that convert complex compounds into plant-available nutrients. Bacillus species, for example, help break down organic matter, while Cellulomonas degrades cellulose, enriching soil organic carbon. Additionally, bacteria such as *Pseudomonas* and *Flavobacterium* aid in the degradation of environmental contaminants. These microbial processes increase soil organic carbon content, improving soil fertility and structure by enhancing microbial biomass and stabilizing soil aggregates.[29]

Bacteria also facilitate nutrient cycling by solubilizing phosphorus and mobilizing potassium, aiding plant uptake. Additionally, nitrogen-fixing bacteria such as *Rhizobium*, *Azobacter*, and *Frankia* convert atmospheric nitrogen (N2) into ammonia (NH3) through nitrogenase enzyme activity. This process, known as biological nitrogen fixation, occurs in symbiosis with plants or independently in the soil. In leguminous plants, Rhizobium forms nodules on roots, where it converts nitrogen into a usable form in exchange for carbon sources from the plant. This process enriches the soil with bioavailable nitrogen, reducing dependency on synthetic fertilizers.[29]

Beyond nutrient supply, certain bacteria protect plants from pathogens through antibiotic production and induced systemic resistance. Bacillus and Pseudomonas species, for example, are widely used in biocontrol. Some bacteria also produce plant hormones, such as indole acetic acid and gibberellins, which regulate growth and development. Furthermore, bacterial biofilms and polysaccharides improve soil aggregation, aeration, and water retention, enhancing soil structure.[30]

Environmental factors influence bacterial activity, and targeted applications can optimize their ecological benefits. Biofertilizers and biochar amendments, for example, promote beneficial bacteria that support plant growth, nutrient availability, and soil health. However, some interventions can unintentionally increase pathogenic bacteria, emphasizing the need for a thorough understanding of microbial interactions.[30-31]

6. Soil-Gut Axis

Beyond agriculture, the soil microbiome also maintains a crucial connection to human health via the soil-gut axis, highlighting how environmental microbes influence our internal ecosystems. The soil gut axis highlights the intricate relationship between soil microbiomes and the human gut microbiota. Historically, soil acted as a microbial reservoir for early humans, and co-evolution occurred. The co-evolution of gut and soil microbiomes played a critical role in shaping terrestrial ecosystems and human health.[25] Around 430 million years ago, as aquatic plants adapted to land, they formed symbiotic relationships with fungi, particularly mycorrhizal networks, facilitating nutrient acquisition from primitive soils. These early plant-microbe interactions set the foundation for terrestrial biodiversity, influencing the evolution of animal digestive systems, which similarly relied on microbial communities for nutrient extraction and immune function.[32] Fossil records and genomic analyses reveal significant functional similarities between soil and gut microbiomes, particularly in metabolic pathways related to cellulose degradation, vitamin synthesis, and xenobiotic detoxification. For example, Actinobacteria—abundant in soil—share metabolic functions with human gut-associated Bacteroidetes and Firmicutes, highlighting evolutionary pressures in nutrient-scarce environments.[81] Furthermore, the endosymbiotic theory suggests that mitochondria and chloroplasts originated from free-living soil bacteria, embedding microbial metabolic functions within eukaryotic cells.[25]

The connection between soil and gut microbiomes is also evident in food systems. A 2024 study demonstrated that organic produce introduces significantly higher microbial diversity to the human gut than conventionally grown crops, with soil-derived *Streptomyces* strains up-regulating butyrate-producing genes in the colon, thereby enhancing anti-inflammatory signaling. Differences in microbial composition between rural and urban populations further emphasize this link.[33] Rural gut microbiomes are enriched with *Prevotella* species, which specialize in fermenting dietary fiber, while urban gut microbiomes exhibit an increased abundance of *Bacteroides* and *Firmicutes* associated with fat metabolism. This shift correlates with dietary changes, as urban populations consume more processed foods and fats, whereas rural diets are traditionally higher in fiber-rich plant material.[34-36]

Microbial depletion in soil and gut ecosystems has profound immunological consequences. Soil microbes, such as *Mycobacterium vaccae*, play a role in immune system priming through molecular mimicry, triggering regulatory T-cell responses that reduce inflammation.[37-38] A 2024 clinical trial demonstrated that regular exposure to soil microbes through gardening led to increased fecal IgA levels, enhanced dendritic cell activity, and a 40% improved antibody response to pneumococcal vaccination.[39]

Additionally, disrupted soil microbiomes contribute to gut permeability issues through micronutrient depletion and toxin contamination. Selenium-deficient soils, which affect 40% of agricultural lands, impair gut antioxidant defenses by reducing glutathione peroxidase activity, making individuals more susceptible to oxidative stress.[43] Moreover, intensive tillage has been linked to increased *Fusarium* fungal proliferation, leading to higher concentrations of mycotoxins like deoxynivalenol (DON) in grains.[44] These mycotoxins compromise gut barrier integrity by disrupting tight junction proteins, thereby exacerbating intestinal permeability, or "leaky gut."[45,40,41,42]

7. Gut-Brain Axis (GBA)

The gut microbiome plays a critical role in regulating mental health, with growing evidence linking microbial composition to mood disorders such as anxiety and depression. The gut-brain axis, a bidirectional communication system between the gastrointestinal tract and the central nervous system, facilitates this interaction through metabolic, immune, and endocrine pathways. Dysbiosis, or an imbalance in gut microbial populations, has been consistently observed in individuals with mental health disorders, with specific changes in bacterial diversity correlating with symptom severity.[46-49]

Several studies have highlighted the relationship between the gut microbiota and depression. Patients with major depressive disorder (MDD) often exhibit a reduced abundance of beneficial bacteria such as *Faecalibacterium prausnitzii*, a known butyrate producer with anti-inflammatory properties, and an increase in pro-inflammatory species such as *Enterobacteriaceae*.50[50] A landmark fecal microbiota transplantation (FMT) study demonstrated that transferring gut microbiota from depressed individuals to germ-free mice induced depressive-like behaviors in the recipient animals, supporting a causal role for the microbiome in mental health.[51-52] Conversely, transplanting microbiota from healthy donors into depressed patients has shown promising effects in alleviating symptoms.[53-54]

Anxiety disorders have also been linked to gut microbial composition. Studies have identified decreased levels of *Lactobacillus* and *Bifidobacterium* in individuals with generalized anxiety disorder (GAD), while elevated levels of pro-inflammatory *Proteobacteria* have been reported.54-55 Experimental models further support this connection; for instance, supplementation with *Lactobacillus rhamnosus* has been shown to reduce anxiety-like behaviors in rodents by modulating GABAergic signaling.[50] Additionally, probiotic interventions in human trials have demonstrated reductions in stress and anxiety symptoms, with certain strains like *Bifidobacterium longum 1714* decreasing amygdala reactivity to negative emotional stimuli.[56] Mechanistically, the gut microbiome influences mental health through the production of neuroactive metabolites, immune regulation, and endocrine signaling. Short-chain fatty acids (SCFAs) such as butyrate and propionate exert neuroprotective effects by modulating inflammation and enhancing blood-brain barrier integrity. Gut bacteria also play a crucial role in the synthesis and regulation of neurotransmitters; for example, spore-forming Clostridia stimulate serotonin production in the gut, while Lactobacillus species contribute to GABA synthesis. Dysbiosis can lead to an overactivation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in elevated cortisol levels that contribute to stress-related disorders.[57]

Given these findings, microbiome-based interventions have emerged as potential therapeutic strategies for mental health disorders. Probiotics, particularly strains of *Lactobacillus* and *Bifidobacterium*, have shown efficacy in reducing depressive and anxiety symptoms by restoring microbial balance and modulating neurochemical pathways. Diet also plays a significant role in shaping the gut microbiota, with fiber-rich diets promoting SCFA production and reducing inflammation. Moreover, FMT and psychobiotic formulations are being explored as novel treatments, with clinical trials indicating potential benefits for mood stabilization and cognitive function.[58-59,46,60]

Despite promising advances, challenges remain in establishing causality and developing targeted microbiome-based therapies. Individual variations in gut microbiota composition necessitate personalized approaches to treatment. Future research should focus on elucidating specific microbial signatures associated with different psychiatric disorders and optimizing therapeutic interventions tailored to an individual’s microbiome profile. As our understanding of the gut-brain axis deepens, microbiome modulation may become a cornerstone in the management of mental health conditions, offering a novel paradigm for treating anxiety, depression, and related disorders.

7.1. Skin microbial ecosystems

A bidirectional relationship between gut and skin microorganisms exists, mediated by immune regulation mechanisms, microbial metabolites, and neural communication pathways. Either of these communities in disarray leads to skin diseases that become inflammatory, autoimmune, and infectious.

The gut microbiome, dominated by *Firmicutes* and *Bacteroidetes*, produces short-chain fatty acids (SCFAs), bile acids, and neurotransmitters, regulating skin barrier integrity, immune responses, and microbial balance. The skin barrier strengthens when exposed to short-chain fatty acids, while indole derivatives control immune functions via aryl hydrocarbon receptor (AhR) signaling.

Bile acids influence lipid metabolism and the production of antimicrobial peptides, while gut-derived neurotransmitters link stress to skin inflammation. Dysbiosis impairs mucosal immunity, allowing microbial translocation, while lipopolysaccharide (LPS) triggers inflammation via NF-κB activation.[61]

Gut-skin axis dysfunction contributes to dermatologic conditions:

1. **Atopic dermatitis (AD):** Characterized by reduced Bifidobacterium levels, decreased SCFA production, and *Staphylococcus aureus* overgrowth.[62]
2. **Psoriasis:** Driven by gut-mediated IL-23/TH17 axis activation, often exacerbated by high-fat diets and LPS-induced inflammation.[63]
3. **Acne:** Gut dysbiosis alters insulin-like growth factor 1 (IGF-1) and androgen levels, promoting *Cutibacterium acnes* proliferation.[64]
4. **Rosacea:** Small intestinal bacterial overgrowth (SIBO) and *Helicobacter pylori* infection contribute to neurovascular inflammation; SCFAs help regulate substance P release.[61]

Therapeutic strategies focus on restoring microbial homeostasis:

1. **Probiotics:** Lactobacillus rhamnosus GG enhances ceramide synthesis in AD, while Bifidobacterium longum 1714 reduces stress-related inflammation.[65]
2. **Prebiotics:** Galacto-oligosaccharides (GOS) nourish SCFA producers.[65]
3. **Dietary interventions:** Low-glycemic, high-fiber diets modulate IGF-1 in acne; omega-3s and polyphenols balance psoriasis microbiota.
4. **Fecal microbiota transplantation (FMT):** Helps restore gut microbial diversity in conditions like AD and psoriasis, reducing TH17-driven inflammation.[66]

However, the skin maintains its independent microbial environments owing to the skin's anatomy and physiology, which creates distinct microenvironments that control microbial growth patterns. Sebaceous areas like the face and scalp support lipid-dependent *Cutibacterium* acnes, which thrives in the oily environment of hair follicles. Moist regions such as the armpits and elbow creases foster the growth of Corynebacterium and Staphylococcus species, while drier areas like the forearm harbor a more diverse microbial community because sebum production is low. These variations stem from differences in pH, moisture, and lipid content, which favor specific microbial populations. For example, eccrine sweat glands secrete salt, acidifying the skin's surface and making it less hospitable to pH-sensitive pathogens.[67]

The skin microbiome plays a critical role in maintaining barrier function and defending against environmental stressors. Beneficial bacteria such as Staphylococcus epidermidis help reinforce the stratum corneum by breaking down sebum into free fatty acids (FFAs), which strengthen the skin's lipid barrier and possess antimicrobial properties. These FFAs also trigger keratinocytes to produce human β-defensin 2 (hBD2), an antimicrobial peptide (AMP) that helps fight Staphylococcus aureus infections. SCFAs, which originate from microbial fermentation, work to lower skin surface pH, which stops pathogen attachment and supports the growth of helpful microorganisms.[68-69]

Microbial metabolism of host-derived compounds generates bioactive metabolites with systemic effects. For instance, *Cutibacterium* acnes converts sebum triglycerides into propionic acid, an SCFA that regulates melanogenesis and reduces UV-induced inflammation via the FFAR2 signaling pathway.[68,70] However, an overgrowth of S. aureus can produce proteases that break down tight junction proteins, weakening the skin barrier and increasing transepidermal water loss (TEWL). This highlights the microbiome's dual role as both a guardian and a sensor of skin homeostasis.[71]

Environmental factors such as UV radiation and pollution cause oxidative stress, reducing Lactobacillus populations that help protect against photoaging. Wearing occlusive clothing increases skin humidity, promoting Candida overgrowth and intertrigo.[72] On the other hand, topical probiotics containing *Lactobacillus* and *Bifidobacterium* improve UV resistance by neutralizing reactive oxygen species (ROS) and stimulating collagen production.[68]

Disruptive skincare practices, such as over-washing and alkaline cleansers, disturb the skin's natural acidity, reducing *Cutibacterium* populations and allowing Staphylococcus colonization. Probiotic-based skincare helps restore microbial balance by introducing beneficial strains like *S. epidermidis* or *Vitreoscilla filiformis*, which compete with harmful bacteria and boost AMP production.[73]

7.2. Microbes in space

Extremophiles have developed new perspectives about microbial survival limits on Earth while establishing potential signs of life across space. In astrobiology, the study of extremophiles has become increasingly relevant as scientists explore whether microorganisms from Earth could endure the harsh conditions of space. The development of human space exploration requires a deep comprehension of extraterrestrial microbial behaviors since it serves protective functions for space infrastructure alongside long-duration space explorations.[74]

The need for stringent sterilization practices exists to minimize microbial interference in scientific testing, but scientists cannot eliminate spacecraft-life microbial links because human-linked microorganisms naturally sustain their existence, as humans have their own set of microbial flora. The survival and adaptability of microorganisms, together with their dispersion possibilities, create concerns about their propagation outside the International Space Station.[74-77]

The ISS External Microorganisms experiment functions as a vital space research project that investigates microbial distributions as well as microorganism transport and survival mechanisms in harsh space environments. Notably, certain microorganisms, such as *Deinococcus radiodurans*, have demonstrated exceptional resilience to high radiation levels, extreme temperatures, and desiccation. These findings not only contribute to planetary protection strategies but also hold promising applications in biotechnology, pharmaceuticals, and agriculture industries.[78]

Investigating microbial survival and transmission in space has profound implications for planetary exploration. The progress of lunar and Martian space missions demands an absolute focus on preventing extraterrestrial environment contamination, especially within regions that might have supported life in the past. Research about space microbiology enables the enhancement of spacecraft cleansing methods, together with improved microbe containment systems and modified protective spacesuit designs. By studying the survival and adaptability of microorganisms in space, scientists are not only preparing for sustained human presence beyond Earth but also ensuring the integrity of potential extraterrestrial ecosystems.[79]

8. Applications of Microorganisms in Space

8.1. Microbial fuel cells (MFCs) in space

NASA's Controlled Ecological Life Support System (CELSS) and ESA's MELiSSA project have explored microbial systems for life support since the 1950s. The concept of using MFCs for electricity generation from human waste was introduced in the 1960s, but research was halted due to limited understanding. Advances now allow MFCs to support long-term space missions, such as Mars expeditions, by generating electricity from onboard organic waste. Future innovations may include miniature MFCs inside the human body to power medical implants.[80]

8.2. Microbial proteins and molecules in space

Genetically engineered proteins such as piezoelectric proteins (Prestin), photoactive proteins, and rhodopsins have potential applications in MFC technology for space missions. Concepts like "Power Skin" integrate electroactive proteins into thin, self-assembling biomolecular layers for power generation in spacesuits. Linking power suits to MFCs could reduce reliance on hazardous nuclear energy in space missions. The BugNRG experiment aboard the ISS demonstrated microbial electricity production using *Rhodoferax ferrireducens*, highlighting the potential of MFCs for future space power systems.[80]

8.3. Microbial diversity and planetary protection

Studying microbial diversity in spacecraft assembly rooms is crucial for preventing contamination of extraterrestrial environments. Planetary protection policies, maintained by COSPAR under the UN Outer Space Treaty (1967), aim to safeguard celestial bodies and Earth from biological contamination. Techniques such as DNA microarrays, bioassays, and omics-based methods help detect microbial presence on spacecraft. Preventing forward contamination is vital for preserving the integrity of missions searching for life on Mars, Europa, and Enceladus.[80]

Table 2: Summary of key microbial applications in space research, sustainable agriculture, and mental-health interventions.

Domain	**Key Microbes**	**Main Function**	**Potential Impact**	**References**
Space Missions	Technologies			
	Rhodoferax ferrireducens(MFC)	Electricity from waste	Life-support power generation	80
	BioRock consortium	REE bioleaching in microgravity	In-space resource	80,82
Agriculture	Rhizobium, Azotobacter Pseudomonas, Bacillus	Biological nitrogen fixation Biocontrol & soil remediation	Reduced synthetic fertilizer Sustainable crop protection	29,30
Mental Health	Lactobacillus rhamnosus, B. longum	Modulation of GABA, SCFA production	Anxiety/ depression relief	30,31,50,30,31,50,52,56

8.4. Microorganisms in bio-mining

Bio-mining utilizes microbes to extract minerals from extraterrestrial materials, such as basalt on Mars or the Moon. The ESA BioRock experiment on the ISS studied rare earth element (REE) bioleaching using Sphingomonas desiccabilis, Bacillus subtilis, and Cupriavidus metallidurans. These studies demonstrated enhanced bioleaching efficiency in microgravity, supporting future in-space resource utilization for settlements.[80,82]

8.5. Microbial secondary metabolite production in space

Microbial secondary metabolites, such as antibiotics, play essential ecological roles and can be influenced by space conditions. The ISS has been used to study spaceflight's effects on microbial metabolism. *Streptomyces plicatus* demonstrated increased actinomycin production in microgravity, offering insights for commercial antibiotic production on Earth. Understanding microbial biosynthetic pathways in space may lead to novel bioproducts and medical advancements.[80]

These applications showcase the vast potential of microorganisms in supporting sustainable space missions, from power generation and planetary protection to biomining and pharmaceutical production.

9. Conclusions

Microbes have played an essential role in shaping life on Earth, from the planet's earliest ecosystems to its most advanced technologies. As research continues to uncover the complexity of microbial interactions, new opportunities are emerging to harness these organisms across health, agriculture, and space exploration.

10. Future Directions

In human health, future efforts should focus on developing precision microbiome-based therapies tailored to individual profiles. This includes engineering gut microbes to produce therapeutic compounds, creating next-generation probiotics, and integrating microbiome-informed approaches into pharmacology and mental health care.

In sustainable agriculture, microbial strategies can help reduce dependence on synthetic fertilizers and restore degraded soils. Enhancing our understanding of soil microbial networks will be key to improving plant resilience, increasing yields, and promoting climate-adaptive farming systems.

In the realm of space exploration, microbes are not only biological passengers but vital tools. Their roles in life-support systems, bioremediation, resource extraction, and planetary protection make them indispensable to future missions. Designing space-compatible microbial technologies will support long-duration habitation while preserving the integrity of extraterrestrial environments.

11. Final Outlook

Microorganisms are more than the foundation of life—they are catalysts for innovation. As we face growing challenges related to health, food security, and planetary sustainability, microbes offer powerful, adaptable solutions. From ancient roots to interplanetary futures, unlocking the potential of the microbial world will be central to designing a resilient, bio-informed, and sustainable future.

12. Source of Funding

None.

13. Conflict of Interest

None.

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