

Review

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[Yixian Sun](#)^{*}, Qiwei Gao, Chenling Su, [Xia Wang](#)^{*}

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Review

Gut Microbiota Under Microgravity: Current Advances, Challenges, and Future Directions

Yixian Sun ¹, Qiwei Gao, Chenling Su and Xia Wang ^{2,*}

¹ Class 3, Grade 12, Shanghai Jinshan World Foreign Language School, Jinshan District, Shanghai 200540, China

² Shanghai Jinshan World Foreign Language School, Jinshan District, Shanghai 200540, China

* Correspondence: 18037658083@163.com

Abstract

Gut microbiota play a crucial role in maintaining human health by regulating digestion, metabolism, and immune functions. Microgravity during spaceflight has been shown to significantly alter gut microbiota composition and function, posing potential risks to astronaut health on long-duration missions. Recent studies have revealed shifts in microbial diversity, changes in community structure, alterations in metabolic activity, and increased prevalence of stress-tolerant species under spaceflight and simulated microgravity conditions. Specific markers, such as the Firmicutes/Bacteroidetes (F/B) ratio and short-chain fatty acid (SCFA) production, have been linked to metabolic disorders and immune dysfunction, while decreases in beneficial species like *Lactobacillus* and *Bifidobacterium* may compromise gut barrier integrity. These findings highlight the importance of developing targeted interventions, including probiotic supplementation, prebiotic or synbiotic formulations, and dietary modifications, to mitigate gut microbiota dysbiosis in space. Despite advances in culture systems and multi-omics approaches, challenges remain in replicating complex gut dynamics and ensuring astronaut safety during prolonged missions. Future research integrating advanced biotechnology, systems biology, and international collaborations, such as NASA's GeneLab and ESA's MELiSSA projects, is critical to deepen mechanistic understanding and translate findings into practical countermeasures. Overall, this review underscores the translational value of gut microbiota research under microgravity for both space health management and terrestrial medicine.

Keywords: gut microbiota; microgravity; astronaut health; probiotics; Firmicutes/Bacteroidetes ratio; short-chain fatty acids; space medicine

1. Introduction

As human space missions extend in duration and complexity, maintaining astronaut health under microgravity conditions has become an essential research priority. The gut microbiota is a key component of human health, influencing nutrient absorption, immune regulation, and host metabolism. Previous studies have demonstrated that spaceflight induces marked alterations in gut microbial composition and diversity, including reduced diversity and altered metabolic activity [1,2]. These changes are associated with gastrointestinal dysfunction, impaired immunity, and increased inflammation, which pose risks for astronaut well-being during missions.

Notably, research on the International Space Station (ISS) has revealed significant restructuring of gut microbial communities under spaceflight conditions, affecting both beneficial and potentially pathogenic taxa [3]. Probiotic genera such as *Bifidobacterium* and *Lactobacillus* have been highlighted for their role in maintaining gastrointestinal stability and mitigating spaceflight-related symptoms such as constipation [4].

This review systematically examines the impact of microgravity on gut microbiota composition and function, emphasizing microbial diversity, metabolic alterations, and adaptive responses. We also discuss the translational potential of these findings, focusing on probiotic or dietary

countermeasures for astronaut health, as well as implications for terrestrial gastrointestinal disorders [5,6].

2. Current Advances in Gut Microbiota Research Under Microgravity

Recent research has provided valuable insights into how microgravity alters the composition and function of the gut microbiota. One of the most prominent changes is the alteration in the Firmicutes/Bacteroidetes (F/B) ratio, a critical marker of gut health. Studies have shown that microgravity tends to increase the F/B ratio, which has been linked to obesity and metabolic dysfunction [1,2]. In parallel, elevated lipopolysaccharide (LPS) levels, associated with intestinal permeability and systemic inflammation, have been observed [3]. Furthermore, beneficial taxa such as *Akkermansia muciniphila*, essential for maintaining mucosal barrier integrity, are significantly reduced in microgravity [4].

Simulated microgravity models, including rotating wall vessel bioreactors and space-based experiments, demonstrated that *Lactobacillus* and *Bifidobacterium* experience changes in growth kinetics, stress tolerance, and metabolic activity [5]. These studies also revealed decreased production of short-chain fatty acids (SCFAs), such as acetate and butyrate, which play critical roles in maintaining gut epithelial integrity and immune modulation [6].

Notably, *Pseudomonas aeruginosa* exhibited transcriptional and proteomic reprogramming under spaceflight conditions, with increased expression of genes associated with quorum sensing, biofilm formation, and virulence [7]. Such findings highlight the dual effects of microgravity: reducing beneficial microbial diversity while promoting the dominance of stress-tolerant or pathogenic species.

Table 1 summarizes key studies investigating the effects of microgravity on gut microbiota, including alterations in diversity, community structure, and metabolic activity, as well as their implications for astronaut health.

Table 1. Summary of major studies on the effects of microgravity on gut microbiota. The table includes study references, key findings, methodological approaches, and health implications. Abbreviations: SCFA, short-chain fatty acid; F/B ratio, Firmicutes/Bacteroidetes ratio.

| Study | Key Findings | Methodology | Implications |
|----------------------------|--|--|---|
| Estevez et al. (2020) [1] | Reduced microbial diversity, dominance of stress-tolerant species | Fluid Processing Apparatus | Highlights need for nutritional interventions to preserve diversity |
| Crabbé et al. (2011) [2] | Altered community behavior and metabolic reprogramming in <i>P. aeruginosa</i> | Transcriptomics and proteomics | Suggests increased virulence and biofilm potential in space |
| Voorhies et al. (2019) [5] | Reduction in beneficial commensals | 16S rRNA sequencing | Indicates potential astronaut health risks |
| Tsuchiya et al. (2022) [7] | Altered microbial diversity and oxidative stress markers | Metabolomics and oxidative stress assays | Suggests risk of instability and metabolic imbalance |
| Kumar et al. (2023) [8] | Reduced SCFA production capacity | SCFA analysis | Highlights dietary interventions needed to support gut barrier |
| Crabbé et al. (2023) [9] | Increased stress resistance and biofilm capacity | Biofilm assays | Adds complexity to astronaut risk management due to pathogens |

The conceptual overview of how microgravity influences gut microbiota composition and function is shown in Figure 1, highlighting changes in microbial diversity, community structure, and metabolic activity, as well as potential health consequences such as inflammation and gastrointestinal dysfunction.

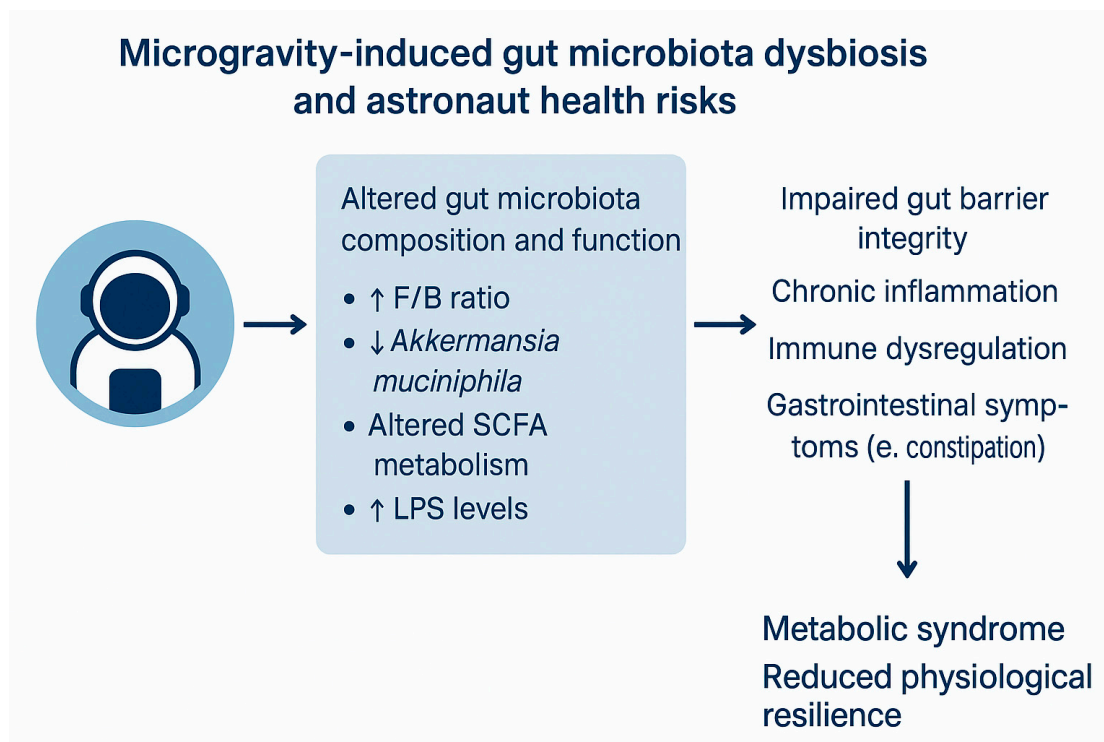


Figure 1. Conceptual illustration of microgravity effects on gut microbiota composition and function. The figure highlights changes in microbial diversity, community structure, and metabolic activity, as well as potential health consequences such as inflammation and gastrointestinal dysfunction.

Spaceflight studies and ground-based simulations have demonstrated consistent patterns. For instance, Estevez et al. (2020) [1] reported reduced microbial diversity and a shift toward stress-tolerant species under microgravity, while Crabbé et al. (2011) [2] showed metabolic reprogramming of *Pseudomonas aeruginosa* with increased virulence potential. Additionally, research by Voorhies et al. (2019) [5] and Turrone et al. (2020) [6] further revealed declines in commensal species such as *Bacteroides*, which are essential for gut homeostasis. These findings illustrate the profound effects of microgravity on both the taxonomic and functional landscape of the gut microbiota.

An integrated summary of F/B ratio shifts, SCFA metabolism changes, and downstream health implications is presented in Figure 2. The left panel provides tabulated data summarizing microbiota and metabolic changes, while the right schematic illustrates health impacts on astronauts, including immune suppression, increased inflammation, and gastrointestinal dysfunction.

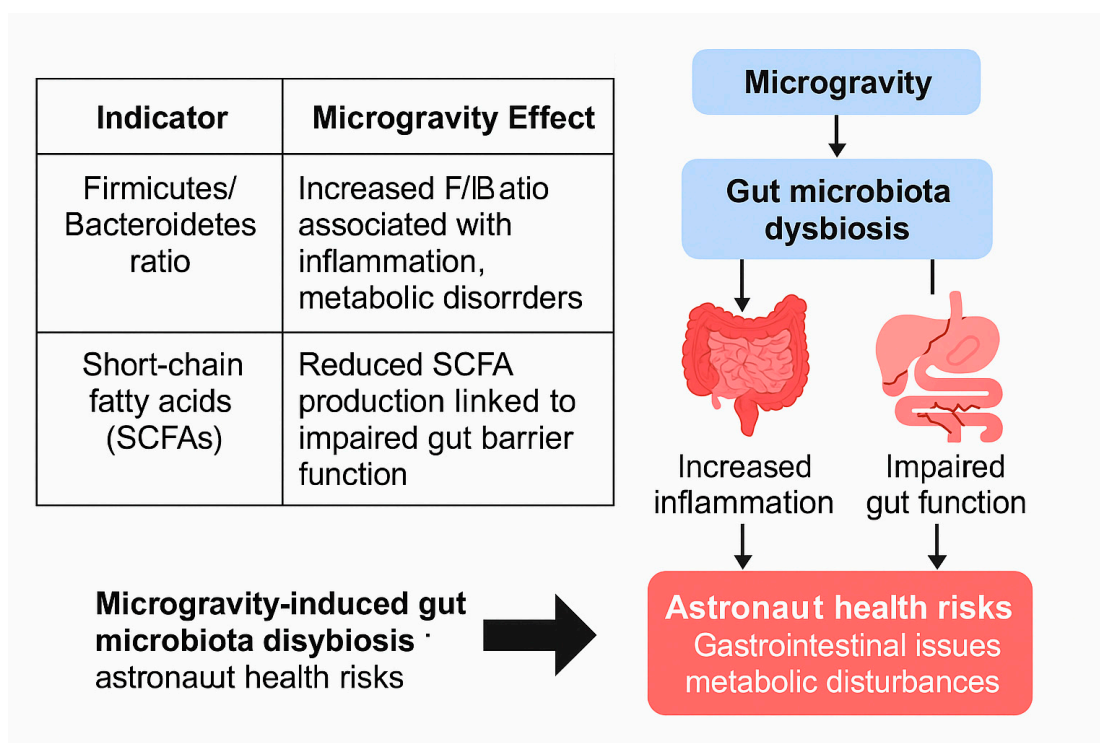


Figure 2. Integrated summary of gut microbiota changes under microgravity. The figure combines tabulated data (left) summarizing alterations in the F/B ratio and SCFA metabolism with a schematic diagram (right) illustrating downstream health implications for astronauts, including immune suppression, increased inflammation, and gastrointestinal issues.

3. Significance of Research Advances

Understanding how microgravity reshapes gut microbial diversity and metabolism is crucial for safeguarding astronaut health during long-duration missions. Dysbiosis under microgravity can result in gastrointestinal problems, impaired immunity, and heightened systemic inflammation [8]. The documented reduction of beneficial species and SCFA production underscores the importance of nutritional and microbial interventions in spaceflight.

Probiotic-based strategies have been increasingly investigated as countermeasures. Specific strains such as *Lactobacillus rhamnosus* GG and *Bifidobacterium longum* have shown promise in stabilizing gut homeostasis, reducing inflammation, and improving barrier function under stress conditions [9,10]. Synbiotic approaches, combining probiotics with prebiotic fibers, further enhance colonization and metabolic activity of beneficial microbes [11]. These targeted interventions provide a practical and feasible strategy for preventing constipation, immune suppression, and metabolic disorders in astronauts.

Beyond space applications, these findings also have translational significance for terrestrial health. Insights into microgravity-induced dysbiosis may inform strategies for managing conditions such as irritable bowel syndrome, metabolic syndrome, and inflammatory bowel disease [12].

4. Challenges

Despite significant progress, several challenges remain in translating microbiome research into operational countermeasures for space health. First, inter-individual variability in microbiome composition complicates the development of standardized probiotic or dietary interventions [13]. Second, most current studies rely on simulated microgravity systems, which only partially replicate real spaceflight conditions [14]. Third, limitations in onboard experimental facilities constrain the depth of in situ microbiome analysis during missions [15].

To address these issues, efforts are underway to integrate real-time omics technologies and miniaturized sequencing platforms aboard space missions [16]. Additionally, personalized approaches based on pre-flight microbiome profiling may allow customized countermeasures tailored to individual astronauts [17]. Ongoing international projects such as NASA's GeneLab and ESA's MELiSSA provide collaborative platforms to overcome technical and methodological barriers [18].

5. Future Research Directions

Future studies should focus on multi-omics integration, including metagenomics, transcriptomics, metabolomics, and proteomics, to provide a holistic understanding of microbial adaptation in space. These approaches can uncover biomarkers of dysbiosis and targets for intervention [19].

Technological innovations such as lab-on-a-chip systems and portable sequencing devices (e.g., MinION) could enable real-time monitoring of microbial shifts during missions [20]. In addition, ground-based analogs such as long-term bed rest studies and Antarctic isolation experiments provide complementary models for testing interventions under extreme conditions [21].

International collaboration will remain key to advancing this field. Programs like NASA's GeneLab and ESA's MELiSSA not only enhance data sharing but also facilitate the validation of probiotic-based countermeasures across different mission profiles [18]. Expanding these networks to involve Asian research consortia could further accelerate discovery and application.

6. Conclusions

Microgravity induces profound changes in gut microbiota diversity, community structure, and metabolic activity, with implications for astronaut gastrointestinal and immune health. Advances in probiotic and dietary countermeasures highlight promising strategies to mitigate dysbiosis and related risks during long-duration spaceflight. Importantly, the translational potential of these findings extends to terrestrial medicine, offering insights into managing metabolic and inflammatory diseases.

This review emphasizes the urgent need for integrated omics, space-compatible culture systems, and international collaboration to ensure astronaut health. By bridging microbiome science and space medicine, this field holds substantial promise for both **future space missions and ground-based disease interventions** [22].

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