2025, 65(3): 898-915
CSTR: 32112.14.j.AMS.20240586
DOI: 10.13343/j.cnki.wsxb.20240586

微生物学报
Acta Microbiologica Sinica
http://journals.im.ac.cn/actamicrocn

Review 综述

蜜蜂肠道微生物的时空特性和功能研究进展

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刘建辉, 陈敬, 胡越洋, 吴小波 . 蜜蜂肠道微生物的时空特性和功能研究进展[J]. 微生物学报, 2025, 65(3): 898-915.
LIU Jianhui, CHEN Jing, HU Yueyang, WU Xiaobo. Research progress in temporospatial characteristics and functions of gut microbiota in honeybees[J]. Acta Microbiologica Sinica, 2025, 65(3): 898-915.

摘　要：蜜蜂(*Apis mellifera*)是全球范围内至关重要的授粉昆虫，同时也是研究发育与行为模式的重要生物模型，兼具显著的经济、生态及科研价值。蜜蜂肠道微生物，作为其生存的“共生体”，借助社会行为互动传播，对蜜蜂的发育与健康发挥着关键作用。这些微生物不仅助力蜜蜂消化吸收营养物质，还能有效抵御病原体侵袭，增强宿主免疫力。近年来，蜜蜂已成为肠道微生物研究的热门模型。科研人员不仅深入分析了蜜蜂肠道微生物群的组成与功能，还积极探索了菌株的多样性与特定功能。本文综述了蜜蜂肠道微生物群的时空动态变化特性、影响微生物群落结构的因素、微生物群对蜜蜂生物学特性及健康的影响，以及微生物的功能性应用，旨在为蜜蜂肠道微生物的研究与实践应用提供有价值的参考。

关键词：蜜蜂；肠道微生物；时空特性；功能研究

资助项目：国家自然科学基金(32372942)
This work was supported by the National Natural Science Foundation of China (32372942).
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Received: 2024-09-23; Accepted: 2024-12-23; Published online: 2025-02-05

Research progress in temporospatial characteristics and functions of gut microbiota in honeybees

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Abstract: Honeybees (*Apis mellifera*) are important pollinators worldwide and models for the research on development and behaviors, showcasing great economic, environmental, and scientific benefits. As the symbiont of honeybees, the gut microbiota is transmitted through social behavioral interactions and plays a crucial role in the development and health of honeybees. It not only helps honeybees digest and absorb nutrients but also helps resist pathogen invasion and enhance immunity. Recently, honeybees have emerged as the models for studying gut microbiota. Researchers not only analyzed the composition and function of the gut microbiota in honeybees but also explored the diversity and functions of strains. This paper reviews the temporospatial dynamics of the gut microbiota in honeybees, the factors affecting the gut microbiota, the influences of the gut microbiota on the biological characteristics and health of honeybees, and the functional applications of the gut microbiota, providing references for the research and application of the gut microbiota in honeybees.

Keywords: honeybee; gut microbiota; temporospatial characteristics; functional research

蜜蜂(*Apis mellifera*)作为一种不可或缺的传粉昆虫，在推动全球农业的可持续发展和维护生态系统的整体健康中扮演着至关重要的角色。然而，近年来的统计显示，全球蜜蜂种群正遭受寄生虫侵袭、化学杀虫剂污染及营养不良等多重挑战，导致种群数量大幅下降[1-3]。这一现象不仅直接导致经济作物产量的显著减少，更对生态平衡的稳定造成了严重威胁[4]。蜜蜂肠道中的微生物在促进食物消化、清除有毒物质、供应必需营养、防御病原体与寄生虫侵害，以及调控生长发育和免疫等多方面发挥着重要作用，深刻影响着宿主的生存状态和行为表现[5-6]。在过去的 20 年里，科研人员对蜜蜂肠道微生物群的组成和功能有了实质性的认识进步。测序技术的进步使得研究者能够在物种和菌株水平上更深入地探索蜜蜂肠道微生物群。此外，蜜蜂已成为研究肠道微生物相互作用及其进化机制的理想模型，通过构建无菌蜜蜂并定殖特定细菌菌株的实验方法，可以探索这些微生物如何单独或协同作用，进而影响宿主的健康状态及宿主-微生物的共演化机制[5]。本文综述了蜜蜂肠道菌群的组成、时空动态特征、影响因素及其在功能应用层面的研究进展，同时探讨了现有研究的局限性，并对未来的研究方向进行展望。

1 蜜蜂肠道菌群组成与时空特征

1.1 蜜蜂肠道微生物的组成

肠道作为肠道微生物栖息和繁衍的核心区域，其微环境对微生物的组成、结构和功能具有显著影响，其中，不同性别和级型的蜜蜂，其肠道微生物组成存在明显区别(表 1)。蜂王肠道的优势菌群包括大黄蜂菌(*Bombella*)、共生杆菌(*Commensalibacter*)、吉列姆氏菌(*Gilliamella*)、蜂鸣乳杆菌(*Bombilactobacillus*)和乳杆菌(*Lactobacillus*)；雄蜂肠道内，*Bombilactobacillus* 和 *Lactobacillus* 则占据主导地位；至于工蜂，其肠道微生物群落更为丰富多样，包括斯诺德氏菌(*Snodgrassella*)、*Gilliamella*、双歧杆菌(*Bifidobacterium*)、*Bombilactobacillus*、*Lactobacillus* 等 5 个核心菌群，以及弗里希氏菌(*Frischella*)、巴尔通氏体(*Bartonella)*、蜜蜂杆菌(*Apibacter*)和 *Commensalibacter* 等普遍存在的菌群[5,8-9]。此外，蜜蜂体内还存在一些环境细菌(如蜜蜂乳杆菌(*Apilactobacillus*)、*Bombella* 和果糖乳杆菌(*Fructobacillus*))以及一些机会性致病菌(如沙雷氏菌(*Serratia*)和哈夫尼菌(*Hafnia*))等，尽管它们的丰度较低，但却对蜜蜂的生存和健康产生影响[6]。这些微生物的存在和互动，共同维系着蜜蜂体内微生态的平衡与稳定。

1.2 蜜蜂肠道微生物的时空特征

1.2.1 蜜蜂肠道微生物的时间分布特性

蜜蜂肠道微生物群落的结构与多样性深受其个体发育阶段、年龄增长及社会分工的复杂影响。作为完全变态发育的昆虫，蜜蜂的个体发育过程需经历卵、幼虫、蛹和成虫 4 个阶段[4]。新孵化的蜜蜂幼虫肠道内近乎无菌[10-11]，依赖哺育蜂的精心喂养。在 1–2 日龄时，蜜蜂幼虫肠道的优势菌群为醋杆菌科(*Acetobacteraceae*)；而从 3 日龄起，这一主导地位逐渐被厚壁菌门(*Firmicutes*)所取代，在此阶段幼虫肠道微生物的组成和丰度表现出显著的不稳定性[10,12-14]。化蛹期间，蜜蜂体内经历剧烈的生理变化与器官重构，同时与外界环境的交流大幅减少，导致体内细菌数量锐减，值得注意的是，在化蛹后期，后肠壁发生脱落，进一步加剧了新羽化成虫肠道内细菌的匮乏状态，使新出房的蜜蜂肠道近乎无菌[15-16]。

蜂王在其生命周期的不同阶段，肠道内的优势菌群也发生显著变化。幼虫期及新出房时的蜂王，肠道优势菌为埃希氏菌属(*Escherichia*)、吉列姆氏菌属(*Gilliamella*)，而随蜂龄增长和生理状态变化，成熟蜂王的肠道内则主要由共生杆菌属(*Commensalibacter*)、大黄蜂菌属(*Bombella*)、乳杆菌属 *Lactobacillus*) Firm-4 和 *Lactobacillus* Firm-5 等菌种占据主导地位，这一变化归因于蜂王自身的生理发育、饮食变化以及与工蜂间复杂的互动关系[17-19]。相较于蜂王，雄蜂的肠道微生物群落则展现出不同的特征，其核心菌群为 *Lactobacillus* Firm-4 和 *Lactobacillus* Firm-5[13,20]。工蜂在羽化后的 4–6 d 内，通过取食、接触粪便及与蜂巢环境的相互作用等一系列复杂行为获得肠道微生物，并迅速建立起稳定的成虫肠道微生物群落。工蜂体内的核心优势菌为蜜蜂肠斯诺德氏菌(*Snodgrassella alvi*) wkB2、栖蜜蜂吉列姆氏菌(*Gilliamella apicola*) wkB1、星状双歧杆菌(*Bifidobacterium asteroides*) ATCC 25910、*Lactobacillus* Firm-4 和 *Lactobacillus* Firm-5[15,21]。随着工蜂年龄的增长，其肠道内的 *Lactobacillus* 和 *Bifidobacterium* 的相对丰度减少，而变形菌门(*Proteobacteria*)的相对丰度增加[22]。

此外，蜂群内部的劳动分工也对蜜蜂的肠道微生物群落产生深远影响[23]。幼蜂在羽化出

表1 蜜蜂肠道中的细菌种类(引自文献[7])

Table 1 Species of bacteria in the bee’s gut (quoted from literature [7])

Phylum	Phylotype	Species	Primary gut location
Core bacteria			
Proteobacteria	*Gilliamella* (Gamma-1)	*Gilliamella apicola*	Adult ileum lumen and queen guts
		Gilliamella apis	Adult pylorus
Proteobacteria	*Snodgrassella* (Beta)	*Snodgrassella alvi*	Adult ileum wall
Firmicutes	*Lactobacillus* (*Lactobacillus* Firm-5)	*Lactobacillus apis* *Lactobacillus helsinborgensis* *Lactobacillus huangpiensis* *Lactobacillus juensis* *Lactobacillus kimbladii* *Lactobacillus kullabergensis* *Lactobacillus laiwuensis* *Lactobacillus melliventris* *Lactobacillus rizhaonensis*	Adult ileum and rectum, queen, and drone guts
Firmicutes	*Bombilactobacillus* (*Lactobacillus* Firm-4)	*Bombilactobacillus mellifer* *Bombilactobacillus mellis*	Adult rectum, queen, and drone guts
Actinobacteria	*Bifidobacterium*	*Bifidobacterium apousia* *Bifidobacterium asteroides* *Bifidobacterium choladohabitans* *Bifidobacterium coryneforme* *Bifidobacterium indicum* *Bifidobacterium mellis* *Bifidobacterium mizhiense* *Bifidobacterium polysaccharolyticum*	Adult rectum
Non-core gut-restricted bacteria			
Proteobacteria	*Frischella* (Gamma-2)	*Frischella perrara*	Adult pylorus and ileum
Proteobacteria	*Bartonella* (Alpha-1)	*Bartonella apis* *Bartonella apihabitans* *Bartonella choladocola*	Adult hindgut
Proteobacteria	*Commensalibacter* (Alpha-2.1)	*Commensalibacter* sp.	Adult hindgut and queen guts
Bacteroidetes	*Apibacter*	*Apibacter adventoris*	Adult hindgut
Environmental bacteria			
Proteobacteria	*Bombella* (Alpha-2.2)	*Bombella apis* *Parasaccharibacter apium* *Saccharibacter* sp.	Adult crop, larval and queen guts, and hive
Firmicutes	*Apilactobacillus*	*Apilactobacillus apinorum* *Lactobacillus apinorum* *Apilactobacillus kunkeei* *Apilactobacillus nanyangensis* *Apilactobacillus xinyiensis* *Apilactobacillus zhangqiuensis*	Adult crop, larval gut, nectar, honey, hive for *Apil. kunkeei*, and adult gut for other species
Firmicutes	*Fructobacillus*	*Fructobacillus apis* *Fructobacillus fructosus*	Adult gut for *Fru. apis*, larval and adult guts, and hive for *Fru. fructosus*
Pathogens			
Proteobacteria	*Hafnia*	*Hafnia alvei*	Adult gut
Proteobacteria	*Serratia*	*Serratia marcescens*	Adult gut

房后初期主要负责蜂巢内的哺育工作，3 周后则转变为采集蜂[24]。这一转变伴随着肠道微生物群落的显著变化：哺育蜂相较于采集蜂，肠道内的 *Lactobacillus* 的比例更高，且两者间的微生物群落组成存在显著差异[20,25-27]。在东方蜜蜂中，哺育蜂还展现出更高的 *Gilliamella* 和 *Snodgrassella* 丰度[28]。内勤蜂肠道的 *Lactobacillus* Firm4 和双歧杆菌科(*Bifidobacteriaceae*)的丰度高于外勤蜂[20,27]。值得注意的是，蜜蜂肠道微生物群落的变化还与其体内生物胺水平密切相关，这些生物胺在蜜蜂劳动分工的调控中发挥着重要作用[29]。

1.2.2 蜜蜂肠道中微生物的空间分布特性

蜜蜂肠道细菌的分布在其复杂的消化系统中展现出鲜明的空间特异性，这一现象不仅揭示了微生物与宿主间的紧密互作关系，也体现了它们在肠道内独特的生态位(图 1)[5]。蜜蜂的消化道由蜜囊、中肠、幽门和后肠(包含回肠和直肠)等部分组成，每一区域都承担着特定的消化与吸收功能[8]。

蜜囊是蜜蜂体内用于暂时储存花蜜的器官，其内部细菌丰度相对较低，主要栖息着一些随花蜜进入或通过接触蜂箱等蜂具而引入的微生物，如 *Apilactobacillus* 和 *Bombella*，它们与花蜜的初步处理过程相伴而生[30]。中肠是蜜蜂最大的消化器官，细菌群落在此展现出其重要性，*Gilliamella* 和 *Snodgrassella* 等细菌在此占据主导地位，它们靠近幽门区域(一个连接中肠和后肠的小区域)，积极参与食物的消化与营养的吸收过程[9]。幽门作为中肠与后肠的桥梁，其内的非核心菌株 *Frischella* 可能在中肠物质向后肠传递的过程中扮演特殊角色[31]。

相比之下，蜜蜂的后肠成为了细菌聚集的主要场所。这一区域由稳定的角质层保护肠壁，确保了内部环境的相对稳定，同时，那些未能在中肠被完全消化的膳食化合物在此累积，为栖息于此的微生物群提供了丰富的碳源与氮源，进一步促进了这些微生物的生长与繁殖[32]。回肠具有深邃繁复的内折结构，这扩大了细菌与其的接触面积，进一步促进了营养的吸收。因此，虽然回肠的长度比中肠短，但细菌数量远高于中肠。回肠拥有 *Gilliamella apicola* 和 *Snodgrassella alvi* 这 2 类核心菌群，相比之下，直肠作为后肠的终端，其营养丰富的环境吸引

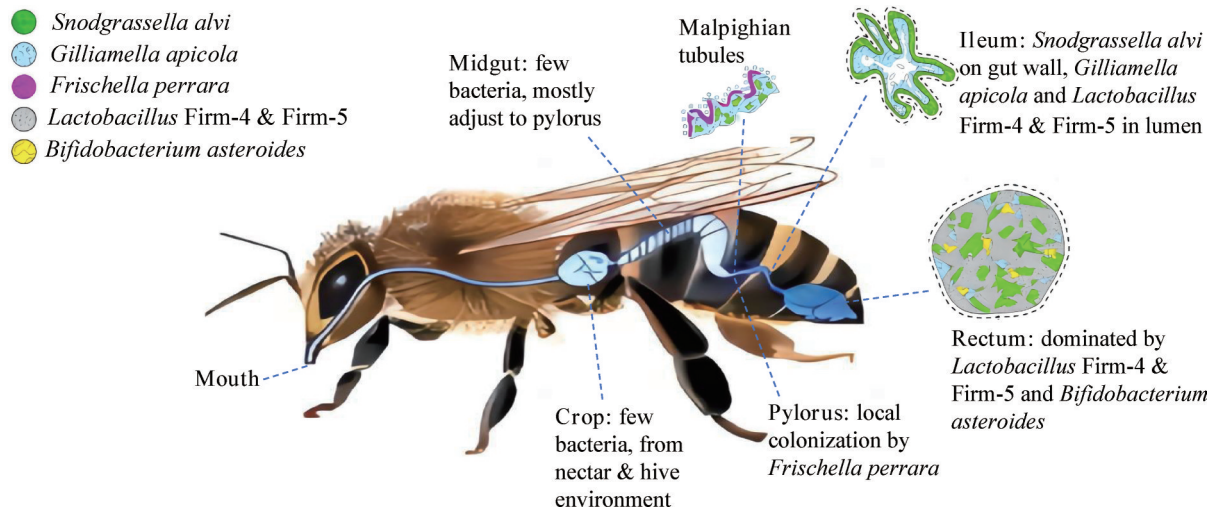

图1 蜜蜂肠道微生物的空间位置分布(改自文献[8])

Figure 1 Spatial location distribution of honeybee gut microbes (adapted from literature [8]).

了绝大部分稳定的微生物栖息，其中 *Lactobacillus* Firm-4、*Lactobacillus* Firm-5 和 *Bifidobacterium asteroides* 等优势菌种在此占据主导地位，它们不仅丰富了肠道微生物的多样性，还可能对蜜蜂的肠道健康与整体生理功能产生重要影响[33]。

2 影响蜜蜂肠道微生物群的因素

蜜蜂为全球农业带来了显著的生态与经济效益。然而，蜜蜂的生存面临着遗传、营养、农药暴露和病原体侵袭等多重威胁，这些因素不仅严重影响蜜蜂的健康状况，同时也深刻改变着蜜蜂肠道微生物群落的构成和丰度。

2.1 宿主遗传的调控

蜜蜂的遗传多样性是塑造其肠道微生物群多样性的关键因素之一[34]。Mattila 等[35]研究发现，与单雄授精蜂王的蜂群相比，多雄蜂王蜂群展现出更为丰富的遗传背景和肠道微生物多样性，其中 *Bifidobacterium* 的相对丰度显著提升，而潜在病原体的数量则显著减少。尽管在个体蜜蜂或蜂群层面，遗传相似性与肠道细菌组成的相似性之间并未发现直接联系，但 Bridson 等[36]的研究揭示了遗传多样性与肠道细菌群落多样性之间的正相关关系。Su 等[37]分析了来自中国 13 个省份的东方蜜蜂肠道宏基因组，发现花粉饮食与肠道微生物组的组成和功能之间存在显著相关性，但他们并未发现蜜蜂基因组位点变异会直接影响细菌组成。

2.2 食物和营养的双重驱动

在蜂群中，花蜜作为碳水化合物的来源，与富含多样化营养成分如碳水化合物、氨基酸、脂类及维生素的花粉相辅相成，共同为蜂群提供必需的营养物质[38]。尤为特别的是，花粉壁所包裹的多糖虽然不能被蜜蜂直接消化，但却是其肠道微生物群落的重要食物来源[39]。研究表明，蜜蜂对花粉的摄取显著促进了其后肠中总细菌和核心细菌群落的繁荣[26,40]。相反，缺乏花粉会导致蜜蜂直肠中总细菌和核心细菌群落的衰退[41]。花粉摄入还激发了蜜蜂消化道内糖苷水解酶的活性，其代谢产物如有机酸等有助于蜜蜂宿主的健康[40-41]。

花粉在维持蜜蜂健康肠道菌群生态平衡中发挥着重要作用，其质量和新鲜度在塑造蜜蜂肠道微生物群中起着至关重要的作用。摄入低营养价值的桉树花粉不仅减少了 *Lactobacillus* Firm-4、*Bifidobacterium* spp. 等有益菌的数量，还促进了非核心菌如蜜蜂巴尔通氏体(*Bartonella apis*) DSM 29779 的滋生，进而削弱蜜蜂的免疫系统，这为致病菌、微孢子虫等病原体的入侵提供了可乘之机[42]。食用不新鲜的花粉也会破坏肠道细菌的平衡，对蜜蜂的发育和生存构成潜在威胁[43]。以蛋白质代替花粉作为食物来源，同样会导致肠道内有益细菌多样性的减少和丰度的下降，增加蜜蜂患病风险[44]。Su 等[37]通过饲养和接种生物试验，进一步揭示了花粉多糖成分的变化对 *Gilliamella* 与 *Lactobacillus* 间拮抗关系的调控作用。

当蜜源植物稀缺时，养蜂人常通过补充糖源来保障蜜蜂的能量需求，然而这一举措也会微妙地影响蜜蜂肠道菌群的结构。例如，夏季短期饲喂蔗糖能改变消化道内根瘤菌科(*Rhizobiaceae*)、醋杆菌科(*Acetobacteraceae*)、昆基氏蜜蜂乳杆菌(*Apilactobacillus kunkeei*) ATCC 700308 和稀罕弗里希氏菌(*Frischella perrara*) ATCC BAA-2450 的相对丰度[45]。然而，在越冬期，不同糖源(如小麦淀粉糖浆、蔗糖糖浆或花蜜)对蜜蜂胃肠道微生物群及寄生虫水平的影响则相对有限[5]。此外，不同糖源还显著影响了东方蜜蜂的寿命、学习记忆能力[46]，这可能与糖源

中特定成分对肠道菌群的差异化调节有关，进而强调了在蜜蜂食物资源匮乏时，合理补充蜜源或蜂蜜水溶液对于保护其健康发育的重要性。

2.3 病原体的侵袭

病原体的侵袭显著扰乱了蜜蜂肠道内微妙的微生物生态平衡。与健康蜜蜂幼虫相比，感染欧洲幼虫腐臭病(European foulbrood, EFB)和蜜蜂囊状幼虫病病毒(sacbrood virus, SBV)的蜜蜂幼虫肠道微生物数量会显著降低[47]。Erban等[48]研究发现，感染欧洲幼虫腐臭病会重塑蜜蜂肠道菌群的结构，而感染美洲幼虫腐臭病(American foulbrood, AFB)会特异性地影响*Lactobacillus*的丰度。作为全球蜜蜂种群生存的主要威胁之一，狄斯瓦螨(*Varroa destructor*)的寄生不仅影响了蜜蜂的生存，还改变了其宿主蜜蜂肠道微生物的构成[49]。Hubert等[50]的研究表明，狄斯瓦螨寄生会导致蜜蜂肠道微生物群中*Bartonella apis*相对丰度的增加和*Snodgrassella alvi*的减少，同时扰乱了*Lactobacillus*菌群的平衡。此外，蜜蜂感染东方蜜蜂微孢子虫(*Nosema ceranae*)会导致*Gilliamella*的相对丰度增加[51]，在重度感染情况下还会表现出*Proteobacteria*相对丰度的增加和*Firmicute*相对丰度的减少的特征[52]。病原体感染会导致蜜蜂肠道微生物群落生态失调，为病原体入侵提供了可乘之机。在此期间，由于病原体对宿主防御的抵抗力更强，并且能更好地利用肠道营养环境，因此可以迅速胜过共生菌，从而影响宿主的群落结构和功能。

2.4 农药化学品的挑战

蜜蜂健康状况的下滑与杀虫剂和抗生素的过度使用、环境污染密切相关[53-55]。不同健康状态的蜜蜂，其肠道菌群展现出明显的差异性[56-57]。然而，这种多样性对蜂群整体健康的影响却呈现出复杂性，既有正面关联也有负面效应，其核心在于有益菌与致病菌之间的动态博弈[35]。Daisley等[58]揭示了肠道生态失调的2个阶段，即肠道微生物群失衡和受损。在肠道微生物群失衡情况下，肠道菌群出现暂时波动，免疫系统减弱，*Firmicutes*的相对丰度下降，*Proteobacteria*的相对丰度增加；而在肠道微生物群受损后，肠道菌群的组成发生了显著变化，蜜蜂处于免疫功能低下状态，*Firmicutes*急剧减少，*Proteobacteria*显著增加，放线菌门(*Actinobacteria*)减少，非核心细菌增加[58]。

Hotchkiss等[59]详尽列举了多种农药及相关化合物对蜜蜂肠道微生物群的影响，其中包括多种杀虫剂(如香豆磷、氟虫腈、吡虫啉、烯啶虫胺、多杀菌素、氟胺氰菊酯、噻虫啉和噻虫嗪等)、杀菌剂(如啶酰菌胺、吡唑醚菌酯和百菌清等)以及除草剂(如草甘膦及其代谢物氨基甲基膦酸)等。此外，杀虫剂(如啶虫脒、氟吡呋喃酮、乙虫腈和氟啶虫胺腈)、杀菌剂(嘧菌酯)和杀螨剂(氟氯苯氰菊酯)也被证明对蜜蜂的肠道微生物群具有潜在威胁[1,6,54,60-64]。接触杀虫剂后最常见的变化是*Bifidobacterium*和*Lactobacillus*的相对丰度下降[59]。

四环素作为养蜂业中的常用抗生素，其使用虽旨在防治疾病，但却悄然削弱了蜜蜂的肠道健康[65]。经四环素处理的蜜蜂会影响其对后代的饲养[66]，此外，高剂量的四环素处理可导致蜜蜂肠道菌群失调，并在蜂群中具有传递效应[67]。使用诊断PCR、肠道细菌基因组分析和肠道宏基因组学的研究表明，长期接触抗生素还促进了蜜蜂肠道内耐药基因[如药物外排泵基因(*tetB*、*tetC*、*tetD*、*tetH*、*tetL*和*tetY*)以及核糖体保护基因(*tetM*和*tetW*)]的积累，同时研究还发现西方蜜蜂(*A. mellifera*)中抗生素抗性基因(antibiotics resistance genes, ARGs)含量较高，而在东方蜜蜂(*A. cerana*)中也发现了几个核心ARG组的普遍存在，这些基因主要由蜜蜂特异性肠

道成员 *Gilliamella* 和 *Snodgrassella* 所携带[68-70]，这些发现强调了抗生素使用的长远风险。

除农药与抗生素外，纳米塑料(nano-plastics, NPs)、微塑料(micro-plastics, MPs)及重金属等环境污染物也被发现能够破坏蜜蜂的肠道微生物群。100 nm 聚苯乙烯颗粒(polystyrene particles, PS)处理降低了肠道中 *Lactobacillus* 和 *Bifidobacterium* 的相对丰度，使得蜜蜂更易感染致病菌蜂房哈夫尼菌(*Hafnia alvei*) ATCC 13337，从而增加死亡率[71]。聚乙烯微塑料(polyethylene microplastics, PE-MPs)扰乱蜜蜂的肠道微生物群落，尤其是核心菌 *Snodgrassella*，导致蜜蜂死亡率升高并增加它们对病原体的易感性[72]。在长期亚致死浓度的重金属镉(Cd)暴露下，中华蜜蜂(*Apis cerana cerana*)的抗氧化基因(如 *AccSOD1*、*AccTPx3* 和 *AccTPx4*)的转录本数量和超氧化物歧化酶活性显著降低，同时改变了肠道中细菌和真菌群落的结构，破坏了微生物群落的平衡，导致蜜蜂死亡率增加[73]。

3 蜜蜂肠道微生物群的功能

蜜蜂肠道微生物群已成为肠道微生物学领域内一个极具吸引力和前瞻性的研究模型[74]，这一发现极大地推动了蜜蜂微生物功能特性的广泛探索。研究表明，蜜蜂肠道内的微生物不仅参与植物多糖的消化过程，还在抵御病原体、外源物质解毒、促进发育、增强免疫以及调节行为等方面发挥关键作用[6,23,39,75-77]，对蜜蜂的整体健康至关重要(图 2)。

3.1 肠道微生物对病原体防护的影响

Raymann 等[78]的研究表明，蜜蜂的肠道菌群是蜜蜂免受病原体侵袭的重要防线。这些菌群不仅能有效抵抗机会性致病菌[75,79]和真菌病原体[80-81]，还展现出对 RNA 病毒的潜在抗性[82]。具体而言，蜜蜂乳杆菌(*Lactobacillus apis*) CCM 8403 能够通过诱导调节 Toll 通路的基因表达，促进宿主抗菌肽(antimicrobial peptides AMPs)(如 abaecin、apidaecin、defensin 和 hymenoptaecin)的合成，从而抑制 *Hafnia alvei* 的增殖[83]。蜜蜂肠道菌群也能通过刺激宿主免疫系统和增强宿主对东方蜜蜂微孢子虫的抵抗力来促进宿主健康[84]。*Apilactobacillus kunkeei* 有助于抵御美洲幼虫腐臭病和欧洲幼虫腐臭病的威胁[5,85]。*Snodgrassella alvi* 和 *Gilliamella* spp. 在回肠中定

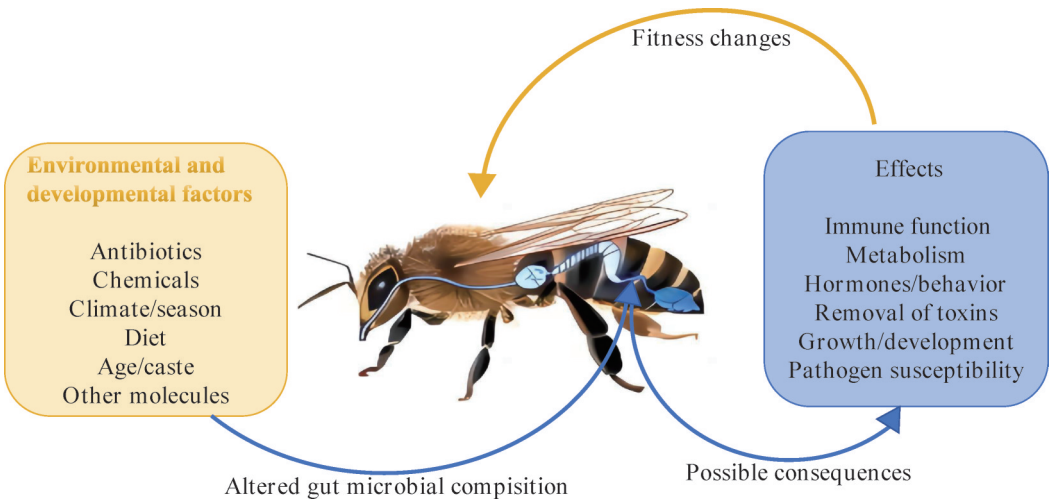

图2 肠道微生物在蜜蜂健康中的作用概述图

Figure 2 Overview of roles of the gut microbiome in honey bee health.

殖，通过形成生物膜，构建一道物理屏障，有效降低了蜜蜂感染锥虫(*Crithidia bomb*)的风险[86-87]。同时，部分 *Lactobacillus* 也能够分泌特定代谢物，直接抑制锥虫的增殖[88-89]。蜜蜂大黄蜂菌(*Bombella apis*) JCM 31623 是一种与蜜蜂幼虫相关的细菌共生体，在体外实验中成功抑制了球孢白僵菌[*Beauveria bassiana* (Bals.-Criv.) Vuill]和黄曲霉(*Aspergillus flavus*)的生长，并有效保护了幼虫免受黄曲霉的侵害[80]。

抗生素的滥用则对蜜蜂肠道微生物群造成了严重破坏，导致微孢子虫数量激增[90]，进一步加剧了蜜蜂肠道微生物生态的失衡[51]。然而，通过引入 *Snodgrassella alvi* 进行定殖，能够在一定程度上减少蜜蜂肠道微孢子虫的含量[91]，并显著提升蜜蜂的存活率[81]。此外，与拥有正常菌群的蜜蜂相比，无菌蜜蜂在感染残翅病毒后的存活率显著降低[82]，这进一步证实了肠道微生物群在蜜蜂抗病毒防御中的重要作用。其他研究也揭示了病毒感染与蜜蜂肠道微生物群组成或多样性之间的紧密联系[5,82]。

3.2 肠道微生物对蜜蜂发育和行为的影响

蜜蜂肠道内的微生物群落对蜜蜂的生长发育和学习记忆行为具有重要的作用。具体而言，一个健全完整的微生物群落与卵黄素及胰岛素信号通路基因表达的上调、嗅觉功能的增强、行为模式的转变、神经系统的成熟与突触传递效率的提升，以及肠道、血淋巴和脑组织中氨基酸、甘油磷脂、激素和短链脂肪酸含量的增加有关[66,92-95]。值得注意的是，当蜜蜂体内缺乏 *Snodgrassella alvi* 和 *Gilliamella* spp. 等关键微生物，以及这些微生物与其他发酵剂产生的短链脂肪酸时，蜜蜂在成年早期会表现出体重增加减缓和肠道异常的现象[92,96]。此外，肠道微生物的缺乏也会抑制蜜蜂体内发育相关基因(如胰岛素信号传导基因和卵黄素基因)在蜜蜂体内各组织部位的表达[92,97]。保幼激素 III 作为昆虫生长、发育和繁殖的关键调节因子[98]，在蜜蜂中控制着蜜蜂从哺育蜂到采集蜂的转变[99-101]，而 *Bifidobacterium asteroides* 在肠道内的定殖能够提高保幼激素 III 衍生物的肠道浓度[93]，进而影响肠道的整体功能[102]。

肠道菌群对蜜蜂行为的影响同样不容忽视。通过伸吻反应试验，科研人员观察到肠道微生物群在调节蜜蜂对蔗糖的敏感性以及嗅觉学习记忆能力方面发挥着重要作用，拥有丰富且多样菌株的肠道微生物群促进了蜜蜂正常的味觉行为反应，使其对低浓度蔗糖更为敏感[92,94]。进一步的研究表明，与无菌蜜蜂或经抗生素处理的蜜蜂相比，体内定殖有完整菌群或特定菌株的蜜蜂展现出了更高的学习效率[5,66]。更深层次的研究揭示了蜜蜂肠道微生物群可能通过影响大脑功能来调控行为。例如，*Lactobacillus apis* 菌株可能通过将色氨酸转化为吲哚衍生物，激活宿主芳烃受体，从而促进蜜蜂的记忆形成[66]。此外，肠道微生物群还参与调节血淋巴中的碳水化合物和甘油磷脂代谢，单一定殖 *Bombilactobacillus*、*Gilliamella* 或 *Lactobacillus* 菌株会导致蜜蜂大脑中多巴胺和血清素的水平下调[94]，而特定菌株如 *Bifidobacterium*、*Bombilactobacillus* 或 *Lactobacillus* 的定殖则能够上调与嗅觉、学习记忆能力相关的基因表达[66,94-95]。值得注意的是，蜜蜂的肠道微生物群还通过调节染色质的可及性和氨基酸的生物合成，在蜂巢内同伴间的社会网络构建中发挥关键作用[95]。

3.3 肠道微生物对蜜蜂营养代谢的影响

蜜蜂依赖富含糖分的花蜜以及富含氨基酸、脂质和维生素的花粉作为其主要食物来源[103]，在这一复杂的食物代谢过程中，蜜蜂肠道内的

微生物群落扮演着至关重要的角色[40,104]。一些容易获得的营养物质(如花蜜中的糖、花粉中的氨基酸、脂质和维生素)在中肠中被加工和吸收，而其他一些多糖如纤维素、半纤维素和果胶等，则在蜜蜂肠道微生物酶的作用下被降解和发酵，从而产生短链脂肪酸供宿主使用[39]。工蜂肠道内的益生菌如 *Bifidobacterium*、*Bombilactobacillus*、*Gilliamella* 和 *Lactobacillus*，含有多种促进碳水化合物降解的酶，如果胶降解酶、糖苷酶、多糖水解酶，有助于增强蜜蜂的营养吸收和健康保护[39,105-106]。这些特定菌株能够代谢包括甘露糖、阿拉伯糖、木糖在内的多种糖类，甚至能处理对蜜蜂具有潜在毒性的鼠李糖，从而提升了蜜蜂对不良食物的耐受性及资源利用效率[107-108]。此外，蜜蜂饮食中的蛋白质含量通常有限[5]，*Snodgrassella alvi* 和蜜蜂吉列姆氏菌(*Gilliamella apis*) NO3 等微生物通过循环利用马氏管中的含氮废物，为蜜蜂提供了额外的氮源，间接促进了蛋白质的合成与补充，这对于维持蜜蜂的生理健康及生存至关重要[109]。蜜蜂肠道微生物不仅促进了营养的吸收与转化，还增强了蜜蜂对复杂环境的适应能力和生存竞争力。

4 蜜蜂益生菌的潜力

近年来，抗生素在动物养殖中的广泛应用引发了多重问题，包括抗药性的出现、动物产品中抗生素残留超标以及环境污染加剧，这些问题在一定程度上阻碍了产业的发展并降低了动物产品的质量。鉴于益生菌的稳定性、无致病性、易于扩增及适应肠道微生态等特性，其作为抗生素的替代方案在饲料添加剂领域展现出了广阔的应用潜力。在养蜂业中，益生菌的应用已不仅限于预防和治疗蜂巢内的微生物感染，更成为维护蜜蜂健康的重要手段。然而，当前市面上多数蜜蜂益生菌产品并非源自蜜蜂自身的原生微生物群落，而是来自食品工业的细菌和真菌。尽管这些外来菌种在一定程度上能够保护蜜蜂健康，但它们往往难以在蜜蜂体内稳定定殖[5,97]。为解决这一问题，科学家尝试通过口服肠道匀浆将健康工蜂中提取的肠道细菌转移到患病或微生物群失衡的蜜蜂体内，实现了在实验室条件下幼蜂的稳定定殖。然而，该方法也伴随着引入病原体的风险[97]。此外，研究表明，采用特定天然核心菌定殖蜜蜂的策略，能够有效抵消农用化学品及环境压力对蜜蜂肠道稳态的破坏，进而阻止机会性病原体的入侵[5,75,110-111]。然而，这些研究多局限于实验室环境，因此需要开展蜂群田间水平的实证研究，以全面评估益生菌在养蜂实践中的实际效果。

针对蜜蜂美洲幼虫臭病等特定疾病，益生菌的应用研究也取得了积极进展，Daisley 等[112]研究表明，联合使用 *Apilactobacillus kunkeei*、植物乳植杆菌(*Lactiplantibacillus plantarum*) ATCC 14917 和鼠李糖乳酪杆菌(*Lacticaseibacillus rhamnosus*) ATCC 7469 能够上调蜜蜂免疫基因表达，降低病原菌载量，从而提高幼虫被病毒感染后的存活率并减轻免疫失调。然而，也有研究指出，*Lactobacillus* 和 *Bifidobacterium* 混合物的使用并未显著改善感染美洲幼虫腐臭病蜂群的健康状况[113-114]。这些研究的不同结果反映了实验设计、操作细节、给药方法以及蜂群条件对益生菌效果的影响[115]。蜜蜂肠道细菌工程改造为改善蜜蜂健康提供了另一种策略，*Snodgrassella alvi* 转基因工程菌具有激活瓦螨体内 RNA 干扰(RNA interference, RNAi)反应的能力，其能够显著降低寄生在蜜蜂身上的瓦螨的存活率，并减少蜜蜂感染病毒的风险[116]。

尽管一些结果很有希望，但在蜜蜂中使用益生菌的潜力仍不清楚，尤其是在田间条件下。然而，益生菌及其相关技术的研究与应用正逐

步改变着养蜂业的面貌，为蜜蜂健康与产业可持续发展注入了新的活力。

5 蜜蜂肠道微生物的功能研究技术手段

在研究蜜蜂肠道共生菌与宿主之间的相互作用时，科学家们发现蜜蜂与人类的肠道存在诸多相似之处，这一发现使得蜜蜂成为研究肠道微生物的重要模式生物，对于医学、农业以及生态学等多个领域都具有深远的意义[117]。因此，深入探究蜜蜂肠道菌群的种类及其功能，并通过基因编辑等技术构建具有抗逆性的菌群，不仅有望为改善蜜蜂的健康状况提供新的策略，同时也可能为人类的健康改善开辟全新的思路。

蜜蜂在抵抗病毒侵袭时，主要依赖于自身的免疫反应，其中 RNAi 是昆虫(包括蜜蜂在内)的一种至关重要的抗病毒防御机制。通过运用 CRISPR-Cas9 这一先进的基因编辑技术，能够精准地编辑蜜蜂肠道内的共生菌，从而实现靶向性地对抗病原物的目的，蜜蜂肠道核心菌群参与抵御寄生疾病，对原生肠道共生体的基因工程改造为蜜蜂疾病防控开辟了新途径[118-119]。通过改造 *Snodgrassella alvi* 等共生菌，科学家们成功实现了其在蜜蜂体内的稳定定殖，并利用这些工程菌生产双链 RNA 以激活 RNAi 机制，从而抑制病原体基因表达，提高蜜蜂对感染残翅病毒、微孢子虫等疾病的抵抗力[81,91,116]。此外，某些昆虫体内的肠道微生物还具备降解农药的独特能力。以主要危害豆科植物的点蜂缘蝽[*Riptortus pedestris* (Fabricius)]为例，其体内的共生菌 *Burkholderia* 能够降解杀螟硫磷这一农药[120-121]。农药降解功能基因的发现，为通过基因编辑手段提升蜜蜂的抗药性提供了可能。

除了使用基因工程改造肠道菌群外，还能通过一些其他的科研技术研究肠道菌群的潜在价值。例如，通过微流控单细胞液滴培养蜜蜂肠道菌，能够研究蜜蜂肠道微生物群的多样性以及蜜蜂肠道共生菌存在的宿主特异性适应机制，这有助于寻找一些难以捉摸的细菌[122]。针对全球气候变化导致的传粉昆虫适生范围变化，Zhang 等[123]的研究揭示，共生菌 *Buchnera* 的热敏感性能够影响宿主的耐热性能，这意味着可以通过调整内共生菌来提升昆虫的耐热性。使用纳米换能器进行肠道工程菌磁热时空感应调控，能够帮助治疗大黄蜂肠道寄生虫疾病和消除农药残留[124]。此外，使用工程菌进行精确热调节可以帮助治疗一些神经疾病[125]。在蜜蜂体内，众多共生菌均具备巨大的潜力，通过相关技术探索研究其功能，在不破坏菌群平衡的前提下，为保护蜜蜂的健康提供了新的途径。

6 展望

近年来，随着公众对蜜蜂健康问题的日益关注，蜜蜂肠道微生物的研究与应用也迎来了前所未有的增长。截至目前，研究表明蜜蜂肠道微生物群对宿主的消化、解毒、行为、病原体防御和免疫系统都具有实质性影响。被剥夺正常微生物群的蜜蜂和微生物群被化学物质破坏的蜜蜂表现出一系列健康缺陷，包括摄食行为的变化、对病原体的更易感性，以及蜂群整体的高死亡率。相比之下，对无菌蜜蜂进行单菌或混菌定殖可以帮助其微生物群恢复部分功能[6,126-128]。

尽管大量证据表明肠道共生体对蜜蜂有好处，但这些影响背后的分子机制在很大程度上是未知的。例如，肠道微生物群的特定成员已被证明可以防止病原体增殖并保护宿主免受病原体诱导的死亡，但尚不清楚保护是来自宿主免疫反应和/或微生物之间的直接相互作用[76,129]。关于蜜蜂微生物群在毒素代谢中的作

用的研究仍处于起步阶段。尽管一些研究调查了外源性生物(包括农用化学品和特定的植物次生代谢物)是如何代谢的，但这种代谢对蜜蜂健康的影响在很大程度上是未知的[5-6]。农用化学品对肠道微生物群落的影响可能源于蜜蜂机制(如细胞色素 P450)或特定肠道共生体的代谢能力(如水解酶)[76,130]。

最近的另一个研究方向涉及脑-肠轴。长期以来，蜜蜂一直被用作研究行为的模型，从认知到社会互动，行为分析已经非常成熟。最近的研究利用这些行为分析和无菌蜜蜂来探索微生物群在味觉、嗅觉学习和蜂群社交网络中的作用，并研究它们在蜜蜂身体不同区域发挥的转录和代谢功能，结果表明，原生微生物群的共同作用塑造了蜜蜂的行为[95]。将微生物群对行为的影响与血淋巴和脑组织中基因表达和代谢物的变化联系起来，有望填补这一新兴领域的空白。

蜜蜂的肠道稳态与其健康状态之间存在着微妙的平衡，一旦这一平衡被打破，病原体便可能乘虚而入，对蜜蜂健康构成严重威胁。在面对环境压力源时，蜜蜂的肠道微生物群往往首当其冲，受到显著影响。遗憾的是，当前多数研究仍局限于分析肠道微生物群的相对丰度或采用定量 PCR 等方法测定其绝对丰度[65,131]，以解释压力源下的群落变化，却鲜少深入探讨这些变化如何影响蜜蜂的蜂群恢复力，即蜂群在遭受扰动后，其负面效应能持续多久。显然，若不进一步揭示这些变化对蜜蜂健康的深远影响，单纯地研究肠道微生物群变动将显得苍白无力。

此外，随着研究的深入，科学家们的视野已不再局限于蜜蜂本身，而是拓展至大黄蜂及其他野生蜜蜂的肠道微生物群，这一转变不仅有助于更全面地保护多样的传粉媒介，还极大地丰富了对于宿主-细菌相互作用及其进化历程的认识。因此，深入研究蜜蜂肠道微生物群的动态变化，不仅对于促进蜜蜂健康具有直接而重要的实际意义，更有助于透过蜜蜂这一独特视角，洞察社会性动物间复杂的跨物种相互作用机制。通过揭示蜜蜂与其肠道细菌之间错综复杂的关系与进化历程，能够为保护这些生态系统中不可或缺的传粉者提供更为坚实的科学支撑。

作者贡献声明

刘建辉：论文构思和设计、资料检索、论文撰写和修订；陈敬：论文资料检索与修订；胡越洋：论文审阅与修订；吴小波：论文构思和设计、论文审阅与修订。

作者利益冲突公开声明

作者声明不存在任何可能会影响本文所报告工作的已知经济利益或个人关系。

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