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Review 综述

多组学技术揭示嗜甲烷菌代谢调控与生态功能的研究进展

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摘　要：甲烷作为仅次于二氧化碳的全球第二大温室气体，是缓解气候变暖的减排重点。嗜甲烷菌凭借独特的甲烷代谢能力，在温室气体控制与低碳生物合成领域得到广泛关注，其代谢机制与生态功能探索已成为国内外研究热点。近年来，高通量组学技术的快速发展与多组学整合分析加速推动了嗜甲烷菌的研究变革，实现了从单一基因功能鉴定向系统代谢过程解析的深度演进。本文系统总结了基因组学、转录组学、蛋白质组学及代谢组学在嗜甲烷菌领域的应用进展，重点探讨了组学技术在解析好氧嗜甲烷菌碳同化通量分配、揭示厌氧甲烷氧化新型代谢路径以及破解菌群间跨界互作与电子传递机制中的决定性作用。围绕嗜甲烷菌在工业生物技术应用中面临的环境适应机理复杂、底盘细胞代谢通量失衡及气液传质效率受限等核心瓶颈，本文提出从描述性组学向功能驱动与精准干预转变，通过单细胞多组学及人工智能深度融合，构建高效的人工嗜甲烷菌细胞工厂与合成微生物组，为全球碳中和目标的实现提供创新的生物学解决方案。

关键词：组学技术；嗜甲烷菌；代谢机制；生态功能；甲烷

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Research progress in metabolic regulatory and ecological functions of methanotrophs driven by multi-omics

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Abstract: Methane, the second most abundant greenhouse gas after carbon dioxide, represents a critical target in climate change mitigation efforts. Owing to their unique ability to utilize methane, methanotrophs have received substantial attention in greenhouse gas mitigation and low-carbon biomanufacturing, making the understanding of their metabolic pathways and ecological functions a vibrant research area worldwide. In recent years, the rapid development of high-throughput omics technologies and the integration of multi-omics analysis have accelerated a paradigm shift in methanotroph research, enabling the deep evolution from the identification of single gene functions to the elucidation of systemic metabolic processes. This review systematically summarizes the progress in the application of genomics, transcriptomics, proteomics, and metabolomics in methanotroph research, highlighting the decisive roles of omics technologies in elucidating carbon assimilation flux distribution in aerobic methanotrophs, uncovering novel metabolic pathways of anaerobic methane oxidation, and deciphering cross-domain interactions and electron transfer mechanisms within microbial consortia. To address current bottlenecks in the industrial application of methanotrophs, including poorly understood environmental adaptation mechanisms, imbalanced metabolic flux in chassis cells, and limited gas-liquid mass transfer efficiency, this review proposes a shift from descriptive omics toward function-driven and precision-intervention research. By integrating single-cell multi-omics and artificial intelligence-enhanced modeling, future studies may construct efficient artificial methanotrophic cell factories and synthetic microbial communities, thereby providing innovative biological solutions for achieving the global carbon neutrality goal.

Keywords: omics technology; methanotrophs; metabolic mechanism; ecological function; methane

甲烷是仅次于二氧化碳(CO_2)的第二大温室气体，以百年期计算，甲烷单位质量温室效应约为 CO_2 的 28 倍，对全球变暖影响显著，已成为温室气体减排的重点目标[1]。除永久冻土融化、湿地缺氧环境中的微生物活动自然释放外，广泛存在于偏远矿区、小型垃圾填埋场及畜禽养殖场等场景的分散式甲烷，因分布零散、能量密度低且收集难度大，长期以来是全球甲烷减排治理工作中的薄弱环节[2-5]。相较于集中式排放甲烷，这些分散式甲烷若直接排入大气，不仅加剧了区域性的气候风险，更造成了宝贵碳资源的严重浪费。针对这些难以并网或集中利用的分散式甲烷，开发极具针对性的原位转化技术已成为国际共识[6]。因此，探索低能耗、高效率的转化路径，将这种零星分布的温室气体在源头转化为性质稳定的高附加值产物，是实现碳捕集与资源循环利用协同发展的关键突破口[7]。

在应对上述挑战的过程中，嗜甲烷菌(methanotrophs，也称甲烷氧化菌)在全球甲烷循环及碳平衡调控中发挥着核心作用[8]。嗜甲烷菌依据是否以氧气为终端电子受体，可分为好氧嗜甲烷菌与厌氧嗜甲烷菌两大类。好氧嗜甲烷菌根据系统进化和细胞特征可进一步分为 I 型、II 型、X 型及其他类型四大类，其中 I 型与 X 型属于伽玛变形菌纲(*Gammaproteobacteria*)，II 型属于阿尔法变形菌纲(*Alphaproteobacteria*)，疣微菌门(*Verrucomicrobiota*)则包含部分其他类型的嗜甲烷菌[8]。好氧嗜甲烷菌的核心特征为依赖特有的甲烷单加氧酶(methane monooxygenase, MMO)将甲烷氧化为甲醇，并通过不同碳同化途径完成固碳循环[8]。厌氧嗜甲烷菌则通过与硫酸盐、硝酸盐、金属离子等电子受体发生氧化还原反应实现厌氧甲烷氧化(anaerobic oxidation of methane, AOM)，主要包括厌氧甲烷氧化古菌(anaerobic methanotrophic archaea, ANME)与依赖亚硝酸盐的 NC10 细菌等类型[9]，具体分类与特征代谢过程如表 1 所示。尽管嗜甲烷菌在分散式甲烷治理中展现出巨大潜力，但将这一甲烷天然代谢能力转化为实际应用仍面临诸多认知瓶颈。具体而言，针对嗜甲烷菌在复杂自然环境中的代谢调控网络、能量分配策略、环境响应机制及菌群协同关系等尚缺乏系统性认知，尤其是在低甲烷浓度、多胁迫共存环境中的适应机制尚不明确。与此同时，传统研究手段多聚焦于单基因或单通路的功能解析，难以从系统层面揭示嗜甲烷菌多层次代谢调控网络与生态功能的整体框架，从而在一定程度上制约了该菌株的深入发展。

以基因组学、转录组学、蛋白质组学、代谢组学为代表的组学技术，依托高通量检测和生物信息学方法，能够系统刻画细胞在 DNA、RNA、蛋白质及代谢物等分子层面的动态规律与互作关系，突破了传统研究范式的局限，为深入揭示嗜甲烷菌的复杂代谢机制提供了核心支撑[10-11]。随着测序技术与质谱分析能力的不断提升，组学技术已从生命科学基础研究广泛扩展至医学、农学、环境微生物学等多个应用领域，并彻底改变了嗜甲烷菌的研究版图，使嗜甲烷菌研究从依赖纯培养的狭窄范畴拓展至广阔的自然环境[12]。依托宏基因组学与单细胞测序技术，研究人员打破了传统分离培养的局限，相继发现并鉴定了大量具有独特代谢特征的代表性菌株(表 2)。在好氧环境中，组学技术应用不仅深化了对甲基弯曲菌属(*Methylosinus*)等经典属种的认知，更揭示了极端环境下嗜酸嗜甲基菌(*Methylacidiphilum*)等嗜酸嗜热嗜甲烷菌的特殊生存策略[18]；在厌氧环境中，组学技

表1 嗜甲烷菌的分类及特征代谢过程

Table 1 Classification and characteristic metabolic processes of methanotrophic bacteria

Classification	Type	Phylum	Characteristic metabolic process
Aerobic methanotrophs	Type I	*Gammaproteobacteria*	Intracellular formaldehyde assimilation *via* the ribulose monophosphate (RuMP) pathway
	Type X		Intracellular formaldehyde assimilation *via* the RuMP pathway, with partial enzymatic activity of the serine cycle, as well as RuBisCO-mediated carbon fixation *via* the Calvin-Benson-Bassham (CBB) cycle
	Type II	*Alphaproteobacteria*	Formaldehyde assimilation *via* the serine cycle, occurring on the intracytoplasmic membrane and in the matrix
	Others	*Verrucomicrobiota*	Carbon assimilation *via* CO_2 fixation using the CBB cycle
Anaerobic methanotrophs	Archaea	ANME	Anaerobic oxidation of methane coupled to sulfate, nitrate, or metal ion reduction
	Bacteria	NC10	Nitrite-dependent anaerobic oxidation of methane

表2 嗜甲烷菌代表性菌株的分类与特征

Table 2 Classification and characteristics of representative methanotrophs

Classification	Type	Representative model strains	Key metabolic features	Research significance	References
Aerobic methanotrophs	Type I	*Methylomonas* sp.; *Methylobacter* sp.; *Methylomicrobium buryatense*	Methane oxidation *via* particulate methane monooxygenase (pMMO); carbon assimilation through the RuMP pathway; high growth rate and carbon conversion efficiency	Canonical C1 chassis organisms for methane bioconversion, metabolic engineering, and systems biology studies	[13-14]
	Type II	*Methylosinus trichosporium*; *Methylocystis* sp.	Methane oxidation by pMMO and/or soluble methane monooxygenase (sMMO); carbon assimilation *via* the serine cycle; strong stress tolerance and polyhydroxybutyrate (PHB) accumulation capacity	Important models for methane biofixation, carbon storage, and plant-microbe interaction studies	
	Type X	*Methylococcus capsulatus* Bath	Multiple carbon assimilation strategies combining RuMP, CBB cycle, and partial serine pathways; expression of both pMMO and sMMO; high metabolic flexibility	Benchmark model for studying methane oxidation regulation, nitrogen metabolism coupling, and environmental adaptation	
	Verrucomicrobiota	*Methylacidiphilum* spp.	Methane oxidation under extremely acidic and thermophilic conditions; carbon fixation *via* the CBB cycle	Expansion of methanotrophic diversity and ecological niches beyond *Pseudomonadota*	
Anaerobic methanotrophs	ANME archaea	ANME-1; ANME-2; ANME-3	Anaerobic methane oxidation *via* reverse methanogenesis; syntrophic association with sulfate-reducing bacteria; extracellular electron transfer mechanisms	Core functional guild driving sulfate-dependent anaerobic methane oxidation (S-AOM) in marine sediments	[15-16]
	NC10	*Candidatus* Methylomirabilis oxyfera	Nitrite-dependent anaerobic methane oxidation; intracellular oxygen production *via* nitric oxide dismutation; pMMO-driven methane oxidation	Paradigm-shifting discovery revealing oxygen-independent methane oxidation and tight carbon-nitrogen coupling	[17]

术界定了厌氧甲烷氧化的 ANME-1、2、3 古菌类群以及具有产氧产氮潜力的 NC10 门细菌(如 *Candidatus* Methylomirabilis oxyfera)[19]。这些新物种的发现不仅填补了极端环境与缺氧环境中甲烷氧化微生物多样性及代谢机制的研究空白，更重塑了人们对微生物跨界电子传递及产氧产氮耦合代谢的认知，为构建人工甲烷转化体系提供了全新的生物底盘与代谢模块[14,20]。

基因组学不仅揭示了嗜甲烷菌潜在的代谢能力与进化适应基础，还结合转录组学解析了嗜甲烷菌对环境变化的动态响应机制；蛋白质组学进一步鉴定了关键酶与调控蛋白在代谢网络中的功能执行过程；而代谢组学则直接反映了代谢流的实时分配。这些多组学信息的整合使相关研究从单点描述迈向系统认知[20-22]。然而，多组学数据的整合分析仍存在不足、嗜甲烷菌代谢与环境响应动态变化的解析能力有限，以及环境样本自身的复杂性仍是当前研究面临的主要挑战[23]。基于上述背景，本文系统综述了组学技术在嗜甲烷菌细胞代谢与生态功能研究中的最新进展，重点梳理了组学技术在碳代谢、氮代谢、能量代谢、金属离子响应、环境适应性及菌群互作等方面的应用现状。在此基础上，进一步展望了组学技术在深度解析甲烷代谢途径的调控机制和生态意义中的应用前景，讨论了该领域面临的主要挑战与亟待解决的问题。

1 组学技术在嗜甲烷菌细胞代谢功能解析中的应用

1.1 碳代谢

从进化尺度看，嗜甲烷菌的分型与地球大气演变深度耦合。基于组学数据的系统发育分析表明，嗜甲烷菌的演化历程与地球大气从厌氧到好氧的转变过程高度吻合。太古宙时期，大气呈强还原性且极度缺氧，厌氧甲烷氧化古菌通过反向产甲烷途径占据碳循环核心[24]。随着“大氧化事件”爆发，氧气浓度的剧增产生了巨大的选择压力。在此背景下，以甲烷单加氧酶为核心的好氧嗜甲烷菌逐步演化兴起并在有氧生态位中占据主导地位，而厌氧甲烷氧化古菌则退居至缺氧环境延续至今[25]。

1.1.1 好氧嗜甲烷菌的碳代谢路径

组学技术为从极端环境中发现和挖掘具有非典型碳代谢能力的嗜甲烷菌新物种提供了重要工具，有效拓宽了好氧嗜甲烷菌碳代谢多样性的认知边界。长期以来，疣微菌门嗜甲烷菌被认为是专性利用单碳底物的类群。然而，转录组学研究颠覆了这一认知。分离自强酸性火山口(pH 低至 2.7，温度高达 55 ℃)的 *Methylacidiphilum fumariolicum* SolV，不仅能够共代谢甲烷以外的气态烷烃，最新转录图谱更揭示了该菌株对丙酮、丙醇等 C3 化合物的利用能力，即通过灵活调节卡尔文循环(Calvin-Benson-Bassham cycle, CBB)与三羧酸循环(tricarboxylic acid cycle, TCA)之间的通量分配实现单碳向多碳代谢的快速切换[18,26]。与此同时，基因组学在极端嗜酸菌株待定嗜酸嗜甲基菌(*Candidatus* Methylacidiphilum) YNP IV 中锁定了多个与甲烷氧化密切相关的 *pmo* 基因簇及保守铜结合基序，阐明了颗粒型甲烷单加氧酶(particulate methane monooxygenase, pMMO)在极端环境下的遗传基础和激活机制[27]。上述新物种的发现，不仅重新定义了疣微菌门的生态生理特征，更为在酸性矿山废气、高温工业尾气等特殊工业场景中开发耐极端环境菌株提供了关键菌种资源[28]。然而，当前极端环境嗜甲烷菌的功能验证仍在很大程度上依赖可培养体系，深海热液口、永冻土等环境中潜在功能类群的系统鉴定仍是未解决的前沿问题。

在新物种发现的基础上，多组学技术进一步系统鉴定了好氧嗜甲烷菌中碳同化路径的多样性，并厘清了不同功能类型在核心代谢骨架上的本质差异，如图 1 所示。针对 I 型嗜甲烷菌，多组学联用以布里亚特甲基微菌(*Methylomicrobium buryatense*) 5GB1 为代表菌株，确立了以甲烷氧化、核酮糖单磷酸(ribulose monophosphate, RuMP)循环及 TCA 循环为核心骨架的碳代谢路径，并通过 ^{13}C 代谢流分析与转录组学联用，锁定 RuMP 循环中特定调控基因作为营养诱导调控的关键节点[29-30]。针对 II 型嗜甲烷菌，以发孢甲基弯曲菌(*Methylosinus trichosporium*) OB3b 为核心对象，多组学分析确

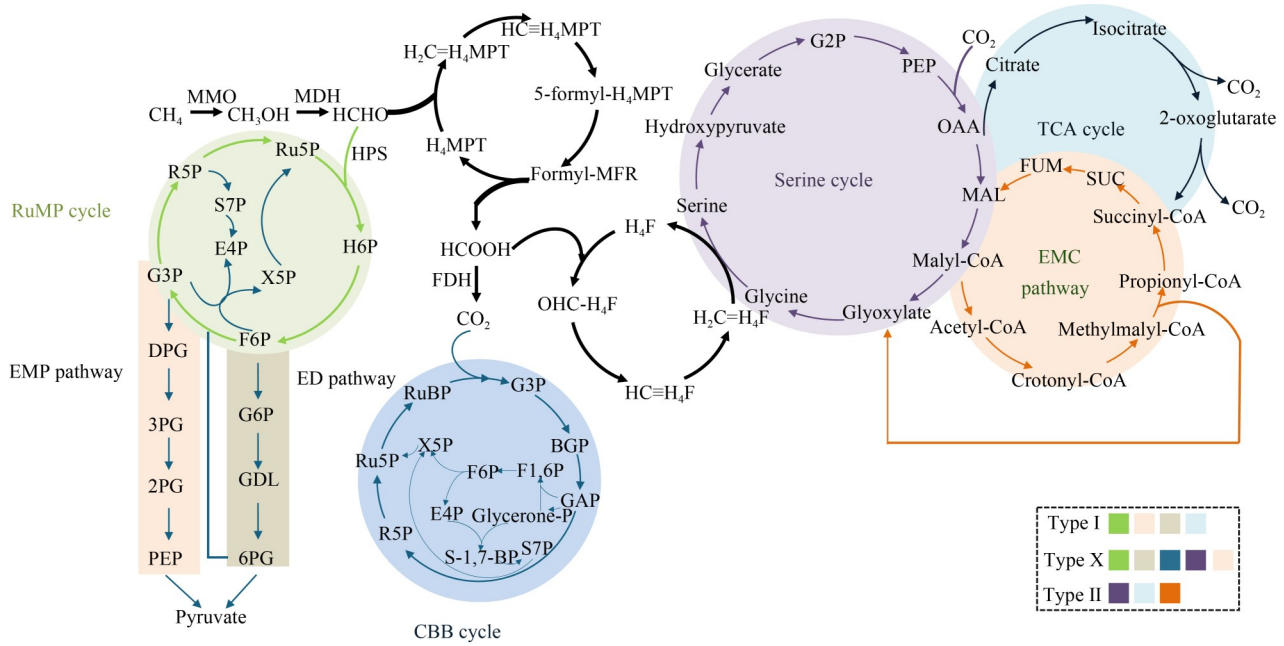

图1 好氧嗜甲烷菌的碳代谢路径图[8]

Figure 1 Carbon metabolic pathway of aerobic methanotrophic bacteria[8]. RuMP cycle: Ribulose monophosphate cycle; EMP pathway: Embden-Meyerhof-Parnas pathway; ED pathway: Entner-Doudoroff pathway; CBB cycle: Calvin-Benson-Bassham cycle; TCA cycle: Tricarboxylic acid cycle; EMC cycle: Ethylmalonyl-CoA cycle; pMMO: Particulate methane monooxygenase; sMMO: Soluble methane monooxygenase; MDH: Methanol dehydrogenase; FDH: Formate dehydrogenase; Ru5P: Ribulose-5-phosphate; H6P: Hexulose-6-phosphate; F6P: Fructose-6-phosphate; G3P: Glyceraldehyde-3-phosphate; R5P: Ribose-5-phosphate; X5P: Xylulose-5-phosphate; E4P: Erythrose 4-phosphate; S7P: Sedoheptulose-7-phosphate; DPG: Diphosphoglycerate; 3PG: 3-phosphoglycerate; 2PG: 2-phosphoglycerate; PEP: Phosphoenolpyruvic acid; G6P: Glucose-6-phosphate; GDL: Glucaric acid lactone; 6PG: 6-phosphogluconate; $H_2C=H_4MPT$: 2-dehydropentanoyl-4-phosphooctanoate; $HC\equiv H_4MPT$: 4-hydroxybut-3-yn-2-yl-4-methyl-3-oxopentanoyl-4-phosphooctanoate; Formyl-MFR: Formyl-methanofuran; H_4MPT: 4-methyl-3-oxopentanoyl-4-phosphooctanoate; H_4F: Tetrahydrofolate; $H_2C=H_4F$: Dihydrofolate; $HC\equiv H_4F$: 5,6,7,8-tetrahydrofolate; $OHC-H_4F$: 10-formyltetrahydrofolate; RuBP: Ribulose-1,5-bisphosphate; BGP: 1,6-bisphosphoglycerate; F1, 6P: Fructose-1, 6-bisphosphate; Glycerone-P: Glycerone-phosphate; S-1,7-BP: 1,7-bisphosphoheptulose; MAL: Malate; OAA: Oxobutanedioic acid; FUM: Fumarate; SUC: Succinate.

立了以丝氨酸循环(serine cycle)与乙基丙二酰辅酶 A (ethylmalonyl-CoA, EMC)途径为特征的独特同化策略，并明确了可溶性甲烷单加氧酶(soluble methane monooxygenase, sMMO)在该类群特定菌株中的特异性分布规律[31-32]。针对 X 型嗜甲烷菌，通过全基因组规模代谢模型与转录组学联用确立了荚膜甲基球菌(*Methylococcus capsulatus*) str. Bath 兼具 RuMP 循环、CBB 循环与丝氨酸循环的代谢路径特征，从分子机制层面证实了核酮糖 1,5-二磷酸羧化酶/加氧酶(ribulose-1, 5-bisphosphate carboxylase/oxygenase, RubisCO)在维持氧化还原平衡中的不可替代作用[33-34]。上述 3 类菌型在碳同化路径上的本质差异决定了它们在不同营养环境条件下的竞争

优势，进而驱动了各自生态位的分化。I 型菌凭借 RuMP 途径的高碳转化率，适合作为单细胞蛋白与有机酸合成的工业底盘；II 型菌通过丝氨酸循环更易积累聚羟基丁酸酯(polyhydroxybutyrate, PHB)等聚合物，EMC 途径为合成长链高值化学品提供前体；X 型菌的双重代谢路径则赋予其在工业废气浓度波动环境下更高的代谢鲁棒性[14,35]。

鉴定出碳同化路径的骨架结构后，解析代谢节点对环境扰动的响应机制，是实现代谢工程定向改造的前提。在 I 型菌 *M. buryatense* 5GB1 中，甲烷/氧气进气比的改变会直接触发转录水平的应激响应，揭示了菌株通过重分配能量流实现环境适应的调控本质[29]；基于此机制，研究人员成功实现了代谢通路从生物量积累向目标营养物质合成的定向切换，并克服了碳同化限速瓶颈，实现甲烷与 CO_2 协同增效合成琥珀酸等高附加值产品[36]，进一步耦合光催化还原策略，在 *M. buryatense* 5GB1C 工程菌株中完成了从 CO_2 到蔗糖、α-法尼烯等长链化合物的高效生物合成[37]。在 II 型菌中，转录组学解析了 *M. trichosporium* OB3b 关键酶系统的精细响应机制，该菌株能通过下调甲醇脱氢酶表达来协调甲醇氧化速率与同化循环间的碳通量平衡[31]；利用该调控线索，研究人员通过阻断内源性 PHB 合成路径并引入异源变位酶模块成功将 EMC 循环中间体重定向至高价值产物合成通路，实现了由甲烷到 2-羟基异丁酸、1,3-丁二醇及(*R*)-1,2-丙二醇等商业化化学品的直接转化[38-40]。在 X 型菌中，多组学证据揭示了非典型环境下的能量适应机制，即通过上调 TCA 循环通量协同驱动渗透调节物质生物合成[41]；定量蛋白质组学与生物信息学联用，进一步实现了从 *M. capsulatus* 蛋白组中精准识别高性能乳化肽等高价值组分[42]。

然而，上述调控机制的解析仍面临若干未突破的科学瓶颈，在不同碳源或混合废气条件下，多路径碳通量的实时动态分配规律尚不清晰；代谢切换的分子开关与上游信号感知系统之间的偶联机制有待阐明。在工程转化层面，针对分散式甲烷废气波动大的特性，如何利用组学技术识别的功能基因开发动态调控元件，实现代谢通路与废气浓度的高效匹配，是提升嗜甲烷菌低浓度甲烷利用的关键。

1.1.2 厌氧嗜甲烷菌的碳代谢路径

厌氧嗜甲烷菌主要包括 ANME 古菌和 NC10 门细菌，代谢涉及硫酸盐依赖型、硝酸盐依赖型、亚硝酸盐依赖型以及金属离子型 4 种耦合方式[43]，广泛存在于湿地、海洋沉积物、土壤以及动物的肠道等缺氧环境中[44]。由于该类菌株极难纯培养，导致代谢路径的系统解析长期滞后，多组学技术的引入有效克服了这一瓶颈[45]。

组学技术持续揭示新的厌氧甲烷氧化功能类群，从根本上修正了对 AOM 驱动力的认知。新谱系 ANME-2d (*Ca*. Methanoperedens nitroreducens)的发现修正了硝酸盐依赖型 AOM 仅由 NC10 门细菌驱动的传统认识[46]。此后，从富碘生境中鉴定的 *Ca*. Methylomirabilis iodofontis 更展现了甲烷氧化耦合产氧反硝化与碘酸盐还原的独特协同模式，将厌氧甲烷氧化细菌的代谢广谱性拓展至多元素耦合领域[19]。这些新物种的持续发现深刻重塑了对厌氧环境多元素循环耦合机理的认知框架。

在获得新物种的基础上，多组学技术系统鉴定了厌氧甲烷氧化与不同电子受体耦合的代谢路径，并揭示了不同功能类群在核心路径上的本质区别。对于硫酸盐依赖型 AOM (sulfate-dependent anaerobic methane oxidation, S-AOM)，宏基因组与宏蛋白质组的整合分析确立了 ANME 通过反向产甲烷路径将甲烷氧化为 CO_2、并与硫酸盐还原过程实现能量耦合的核心机制[47]。对于硝酸盐/亚硝酸盐依赖型 AOM，多组学比较分析界定了两类微生物的路径本质差异，NC10 细菌通过独特的内产氧路径产生分子氧以激活甲烷，而 ANME-2d 古菌则运行反向产

甲烷路径[48]，代谢途径如图 2 所示。对于金属离子介导的 AOM，宏基因组与宏转录组分析锁定了参与锰介导的厌氧甲烷氧化(manganese-dependent anaerobic oxidation of methane, Mn-AOM)的基因簇，并揭示了电子跨越古菌 S 层还原胞外锰离子的电子传递路径[51-53]。除锰离子外，其他高价金属离子同样可作为 AOM 的电子受体。进一步研究证实，磁铁矿等导电矿物通过上调膜结合蛋白及异二硫化物还原酶相关基因加速了电子从内膜向外膜的转移[54]。在矿山废水或高盐湖泊等实际环境中，由 Se^{6+}、Cr^{6+}、As^{5+}等高价金属离子驱动的 AOM 过程[55]兼具温室气体减排与重金属原位生物修复的双重功能。

种间电子传递机制的精准解析，是理解 AOM 热力学可行性与工艺调控的关键。多组学研究推翻了 ANME-2 直接还原硫酸盐的早期假设，转而揭示了由多血红素 c 型细胞色素及胞外电子传递网络介导的跨界电子传递机理，阐明

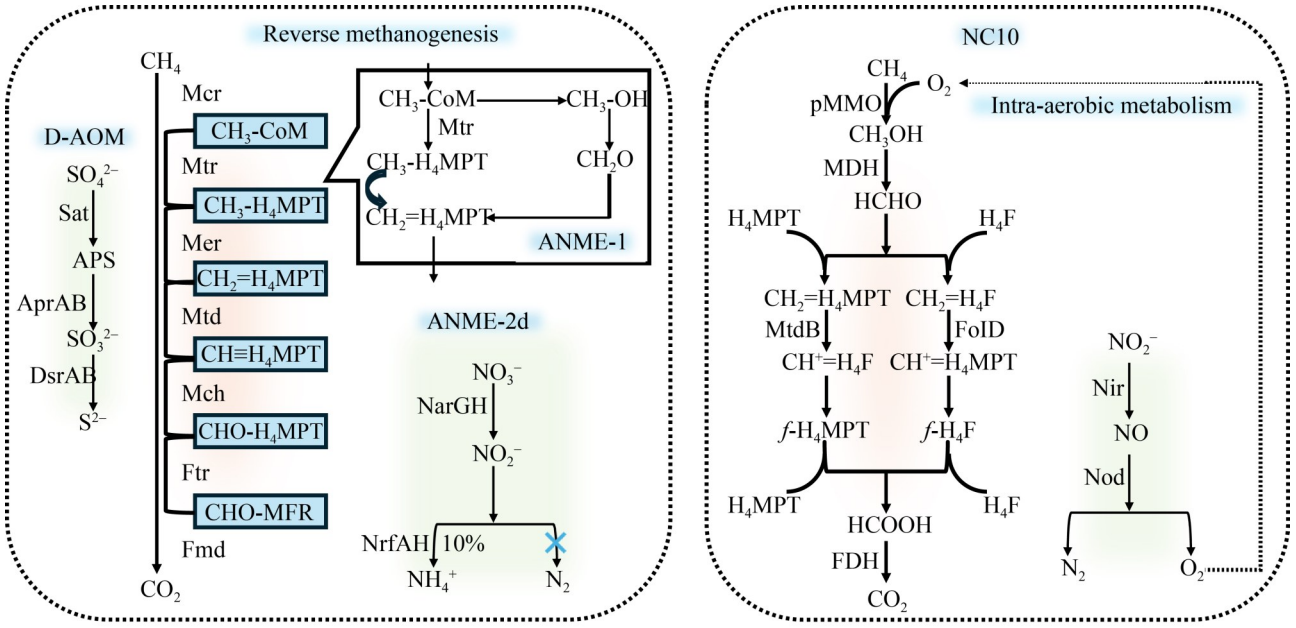

图2　厌氧嗜甲烷菌的碳代谢路径图[49-50]

Figure 2　Carbon metabolism pathway map of anaerobic methanotrophic bacteria[49-50]. Mcr: Methyl-coenzyme M reductase; CH_3-CoM: Methyl-coenzyme M; CH_3-H_4MPT: Methyl-4-methyl-5, 6, 7, 8-tetrahydropteroyl-tetrahydromethanopterin; CH_2=H_4MPT: 2-dehydropentanoyl-4-phosphooctanoate; CH≡H_4MPT: 4-hydroxybut-3-yn-2-yl-4-methyl-3-oxopentanoyl-4-phosphooctanoate; CHO-H_4MPT: Methenyl-tetrahydromethanopterin; CHO-MFR: Formyl-methanofuran; Mtr: Methyl-coenzyme M transferase; Mer: F420-dependent methylene-tetrahydromethanopterin reductase; Mtd: F420-dependent methylene-tetrahydromethanopterin dehydrogenase; Mch: Methenyl-tetrahydromethanopterin cyclohydrolase; Ftr: Formylmethanofuran-tetrahydromethanopterin formyltransferase; Fmd: Formylmethanofuran dehydrogenase; APS: Adenosine-5′-phosphosulfate; Dsr: Dissimilatory sulfite reductase; Apr: Adenosine-5′-phosphosulfate reductase; Sat: Sulfate adenylyltransferase; Nar: Nitrate reductase; Nrf: Cytochrome c nitrite reductase; CH_2=H_4F: Dihydrofolate; CH^+=H_4F: Methenyl-tetrahydrofolate; CH^+=H_4MPT: Methenyl-tetrahydromethanopterin; *f*-H_4MPT: Formyl-tetrahydromethanopterin; *f*-H_4F: Formyl-tetrahydrofolate; Nir: Nitrite reductase; Nod: Nitric oxide dismutase; Mtd: Methylene-tetrahydromethanopterin dehydrogenase; FoID: Quinone oxidoreductase.

了 ANME 与硫酸盐还原菌之间高度协同的代谢分工[44,47]。对 ANME-2a 古菌及其伴生菌群的宏基因组评估进一步证实，这些微生物具备精密的 Fe^{3+}还原相关基因簇，能够通过胞外电子传递实现甲烷氧化与金属还原的直接偶联[56]。上述机制的阐明直接转化为可操作的工艺调控策略，在硫酸盐依赖型体系中，温度适度升高与硫酸盐浓度增加能显著驱动 ANME 类群的优势聚集，在分子水平上强化甲烷氧化与硫酸盐还原的代谢通量[57]；在硝酸盐依赖型体系中，通过施加辅助电压强化功能细菌在阳极表面的代谢优势，可显著提升甲烷氧化与反硝化的协同效率[58]；在金属离子介导型体系中，铁富集环境下的 AOM 速率明显高于单一硫酸盐体系，铁与硫酸盐共存时可额外提升约 10% 的 AOM 活性[59]。

当前厌氧碳代谢机制研究面临的最主要技术瓶颈是纯培养体系的缺失，使得遗传操作与生化验证极难开展，这导致大量基于宏组学的机制推断长期停留在假说层面，难以获得直接的因果性证据。开发针对 ANME 类群的单细胞基因组技术或富集培养体系将是突破这一瓶颈的关键技术路径。

1.2 氮代谢

长期以来，嗜甲烷菌被认为仅以甲烷为能源维持生长，缺乏独立的氮代谢体系[60]。近年来的组学研究改变了这一认识，部分嗜甲烷菌同时具备完整的硝酸盐同化与反硝化通路，甚至具有生物固氮能力[61]。这一认识显著拓展了嗜甲烷菌在自然界碳-氮循环中的生态地位，为系统解析嗜甲烷菌氮代谢机制提供了新的研究视角。

组学技术的群落层面应用，首先在新物种与新功能的氮代谢系统解析上取得了突破。通过整合宏基因组学与比较基因组学，研究人员首次在群落水平上鉴定了由膜结合型硝酸盐还原酶(NarGHI)、同化型硝酸盐还原酶(NasAB)及亚硝酸盐还原酶(NirBD)构成的完整氮代谢通路，构建了嗜甲烷菌硝化与反硝化的功能框架[62]。在固氮功能方面，嗜甲烷菌在湿地根际等贫氮环境中展现出极强的氮固定潜力，通过调节甲烷排放与促进植被生长的协同作用，嗜甲烷菌对总甲烷氧化的贡献率在特定环境下可从 12.1% 显著提升至 33.5%[63]，明确嗜甲烷菌在碳氮耦合循环中的主导生态地位[64]。此外，铁依赖型甲烷氧化固氮新途径的发现进一步丰富了这一认知，甲基胞囊菌属(*Methylocystis*)等类群能够利用 Fe^{3+}作为电子受体、以甲烷或甲醇为电子供体驱动固氮过程[65]，修正了传统固氮过程依赖特定有机底物的认知，展现了嗜甲烷菌固氮代谢的多样性。

在功能类群发现的基础上，多组学技术进一步在分子水平系统解析了嗜甲烷菌氮代谢通路的完整架构。研究表明，嗜甲烷菌能够利用硝酸盐、铵盐和尿素等多种氮源参与生长代谢，氮代谢通路涵盖同化型硝酸盐还原、异化型反硝化和生物固氮 3 条主要支路[66-67]，主要氮代谢通路如图 3 所示。在固氮通路层面，本研究组通过转录组学系统分析了 *M. buryatense* 5GB1 的固氮调控网络，明确 *nifA* 为核心调控因子，*nifA* 缺失导致多条氮同化相关基因显著下调，直接削弱固氮能力，从而为固氮通路的靶向工程改造提供了明确的分子靶点[68]。

在明确氮代谢通路基本架构的基础上，进一步解析嗜甲烷菌对环境扰动的动态响应机制，是实现代谢工程精准调控的关键前提。多组学证据揭示了氮代谢对环境波动的差异化响应，*M. capsulatus* Bath 中硝酸盐利用基因对温度等环境变化表现出高度敏感性，而氨同化过程则维持极强的稳态特征，赋予菌株在多变环境下的生存优势[21]。这种调节灵活性在限氮条件下演变为高效的代谢切换机制，即通过精准控制氮源通量，实现了从生物量积累向糖原等目标产物合成的高效切换[30]，为氮代谢调控服务于工业生产目标提供了概念验证。在工业瓶颈突破层面，Zhang 等[69]通过解析高浓度氨条件下羟

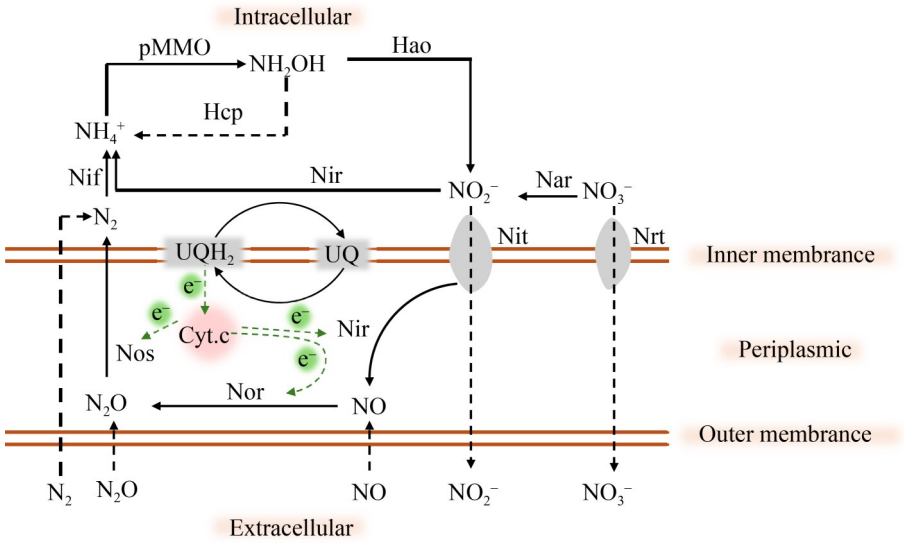

图3 嗜甲烷菌的氮代谢路径图

Figure 3 Nitrogen metabolism pathway of methanotrophic bacteria. Nar: Nitrate reductase; Nir: Nitrite reductase; Hao: Hydroxylamine oxidoreductase; Nor: Nitric oxide reductase; Nif: Nitrogenase; Hcp: Hydroxylamine reductase; Nod: Nitric oxide dismutase; Nrt: Nitrate transporter; Nit: Nitrite transporter; UQH_2: Ubiquinol; UQ: Ubiquinone; Cyt.c: Cytochrome c.

胺异常积累导致能量代谢受阻的毒性机理，开发出精准克服氨抑制的营养诱导与应激调控策略，显著增强了底盘细胞在工业废气等复杂环境下的耐受性与生产稳定性。这标志着嗜甲烷菌氮代谢研究已实现从机理认知向工业应用的实质转化。

然而，当前氮代谢研究仍存在诸多问题，例如，碳氮代谢之间跨通路协同调控的分子信号网络尚不清晰，尤其是固氮过程的能量消耗与甲烷氧化供能之间的平衡关系亟需明确；现有宏组学研究大多在混合群落水平进行，难以将特定氮代谢功能精准归属至具体物种。这些局限性提示，未来应加强单细胞转录组学与原位稳定同位素探针技术的联合应用，以实现对氮代谢调控网络的更精准解析。

1.3 能量代谢与 ATP 合成机制

嗜甲烷菌的碳代谢与氮代谢最终均以能量代谢为核心支撑，通过底物水平磷酸化与氧化磷酸化 2 种方式协同供能。其中，底物水平磷酸化包括糖酵解途径(Embden-Meyerhof-Parnas pathway, EMP)、2-酮-3-脱氧-6-磷酸葡糖酸途径(Entner-Doudoroff pathway, ED)和 TCA 循环，在代谢过程中产生少量 ATP，而氧化磷酸化则是 ATP 合成的主要来源。在电子传递链中，电子流动释放的能量被转化为跨膜质子动力势，最终驱动 ATP 合酶合成 ATP[70]。由于该过程涉及多层级代谢网络与精细调控，传统单通路研究难以揭示这一过程的整体运行机制，而多组学技术为系统解析这一复杂能量网络提供了关键工具。

组学技术首先揭示了嗜甲烷菌在特殊环境下独特的能量获取策略。*Methylomonas denitrificans* FJG1 利用高度多样化的细菌血红蛋白系统精准感应并捕捉极低浓度氧气，从而在极低氧生态位下维持甲烷氧化活性与能量代谢的连续性[71]，揭示了嗜甲烷菌在低氧条件下维持能量代谢连续性的潜在适应机制。这一发现提示，在工业低氧废气处理场景中存在尚未被充分挖掘的耐低氧功能类群。

基因组学与代谢组学的联合分析确立了 I 型

与 II 型嗜甲烷菌在核心能量获取策略上的本质区别，I 型嗜甲烷菌能量代谢以 EMP 途径为主要糖酵解支路，而 II 型嗜甲烷菌则通过更高通量的 TCA 循环强化还原力供给与氧化磷酸化能力，这种能量获取策略的差异决定了它们在不同营养生态位下的竞争优势[70,72-73]。在此基础上，研究人员构建并优化了嗜碱甲烷图瓦微菌(*Methylotuvimicrobium alcaliphilum*) 20Z^{R} 的全基因组规模代谢模型，通过模拟计算系统解析了该菌株在不同氧气与甲烷供应比例下核心碳代谢的通量分配与能量平衡特征[74]，为定量理解能量代谢的环境依赖性提供了可计算框架。

在理解自然能量代谢机制的基础上，多组学研究进一步揭示了嗜甲烷菌能量代谢调控的关键分子节点，并开辟了人工能量增强策略的方向。微量元素铁被证实是驱动碳氮耦合循环的关键分子开关，铁作为电子传递链关键组分，通过调节碳代谢网络的通量分配，显著影响能量流向与生长效率，为通过微量元素干预提升底盘细胞在工业规模化生产中的代谢稳定性提供了精准靶点[75]。在人工能量增强层面，Jiao 等[76]构建了一种自激活的光驱动生物杂化系统，通过在 *M. buryatense* 5GB1 表面自组装光敏剂，利用太阳能驱动将甲烷直接转化为清洁能源氢气，同时产生还原力，为底盘细胞补充能量，打破了 *M. buryatense* 5GB1 天然代谢中的能量供给瓶颈。

然而，目前关于 pMMO 催化过程中“氧化还原臂模型”与“直接耦联模型”等电子传递假说[77-78]仍缺乏统一的实验验证。pMMO 与电子传递链、ATP 合酶之间的空间组织与动态耦合机制，是当前能量代谢研究最关键的未解问题。未来需进一步整合冷冻电镜等结构生物学手段与多组学数据，构建从电子转移到 ATP 合成的完整分子调控网络，为通过能量代谢工程提升甲烷转化效率提供结构层面的靶点。

1.4 金属离子响应机制

大量研究表明，微量金属元素是嗜甲烷菌维持正常生长和能量代谢不可或缺的因子，但此类元素的浓度失衡会抑制微生物生长。MMO 作为甲烷氧化与能量获取的起始酶，本身具有显著的金属依赖性，其中 pMMO 依赖铜离子，sMMO 则依赖铁离子，铜开关机制通过介导 pMMO 与 sMMO 在转录水平上的差异表达，成为微生物应对环境金属波动、优化能量分配的典型调控策略[32]。此外，锰离子(Mn^{2+})、镍离子(Ni^{2+})等也参与调控嗜甲烷菌的代谢活性[79]，因此金属稳态调控直接关系到甲烷氧化效率与整体能量代谢水平。

组学技术在金属响应领域的一个重要贡献是揭示了稀土元素依赖型甲醇脱氢酶的广泛分布。转录组与蛋白质组研究证实，镧等稀土元素可介导甲醇脱氢酶从钙依赖型向稀土依赖型的同工酶切换，这一发现不仅揭示了嗜甲烷菌对稀土元素的生理依赖性，更开辟了利用嗜甲烷菌天然摄取机制从工业废液中生物富集并回收高价值稀土资源的应用路径[80]。

多组学技术系统揭示了嗜甲烷菌中多金属离子响应调控网络的完整架构。早在转录组学应用初期，Nielsen 等[81]发现 sMMO 与 pMMO 的表达受细胞可利用铜浓度精细调控，即当铜浓度低于 1 μmol/L 时诱导 sMMO 表达，而当铜浓度高于 5 μmol/L 时 pMMO 占主导地位，首次从转录层面确立了铜感知代谢切换的基本阈值。随着组学深度的提升，这一金属响应网络的复杂性被进一步揭示。铜氧化物纳米颗粒的存在驱动铜外排泵与周质空间铜结合蛋白相关基因的协同上调[82]，表明铜响应涉及多层级的金属稳态维持机制。在厌氧体系中，宏基因组学研究显示，在亚硝酸盐驱动的厌氧反应体系中补充 Fe^{3+}可显著上调甲烷氧化、氮还原及血红素 c 型细胞色素相关基因表达，协同增强甲烷氧化与亚硝酸盐去除效率[67]；宏转录组学与宏基因组分析进一步揭示了锰介导的铁/锰还原与氮代谢的复杂耦合机制，在硝酸盐依赖型厌氧甲烷氧化过程中锰离子的介入能够驱动异化硝酸盐

还原为铵，改变了氮源转换路径并优化了能量捕获效率[56]。

金属响应调控网络最深层的机制问题在于，不同金属离子的信号如何被整合进核心代谢调控网络，实现跨通路的协同响应。最新转录组研究揭示，铜离子的波动不仅调控 pMMO/sMMO 的表达切换，还显著重塑 *M. trichosporium* OB3b 的整体氧化还原状态，并通过调控铁载体基因簇的表达建立了铜与铁代谢通路之间紧密的交互调控关系[83]。这一发现表明，铜、铁 2 种金属的信号感知与代谢响应并非相互独立，而是通过共享的氧化还原信号节点实现系统整合，从根本上改变了对金属稳态调控逻辑的认知。上述机制认识已被直接转化为环境治理与资源回收应用，部分嗜甲烷菌可在厌氧条件下将 Fe^{3+}还原为 Fe^{2+}，进而与重金属形成稳定络合物，实现污染物固定与去除，结合电化学体系可进一步提升重金属废水处理效率[84-85]；野外与模拟体系研究证实，铁富集环境下的厌氧甲烷氧化速率明显高于硫酸盐体系，铁与硫酸盐共存时可额外提升约 10% 的 AOM 活性[59]。

当前金属组学与转录组学的整合分析尚处于起步阶段，细胞内金属离子的原位分布与动态变化难以被实时捕捉；多种金属共存条件下的竞争性响应逻辑在复杂工业废水场景中尚缺乏系统的实验研究。这些局限提示，未来应加强同步辐射 X 射线荧光等原位金属成像技术与多组学数据的联合应用，以实现对金属响应网络的更精准解析。

2 组学技术在嗜甲烷菌生态功能研究中的应用

2.1 抗逆性与环境适应性

嗜甲烷菌广泛分布于多种自然与人工生态系统中，该类菌株的生长环境通常伴随高温、低温、高盐、低氧、硫化物等多重环境胁迫[55]。长期的环境选择压力促使它们进化出复杂而精细的抗逆性与环境适应机制。系统理解这些机制，需要从基因调控、代谢网络、细胞生理和群落结构等多个层面综合分析，而多组学技术为这种多维度整合分析提供了重要工具。

环境因子变化直接影响嗜甲烷菌的代谢活性与群落结构，其中温度被认为是最具决定性的驱动因素之一。在菌株层面，Zhu 等[86]基于高通量测序对冰川前陆土壤样本进行分析发现，II 型嗜甲烷菌甲基胞囊菌属(*Methylocystis*)在 35 ℃条件下成为主要活性菌群，表明特定菌株具备较强的温度耐受与适应能力。Tveit 等[87]进一步通过转录组学揭示，不同嗜甲烷菌在热驯化过程中采用截然不同的基因调控策略，从转录调控层面阐明了菌株间温度响应差异对甲烷消耗速率的影响；在群落层面，上述菌株间的差异化温度响应策略进一步驱动了群落整体结构的演替重组。Reddy 等[88]的宏基因组研究系统阐明了温度升高引起的群落结构演替规律，30 ℃时甲基杆状菌属(*Methylobacter*)占优势，而 40 ℃时嗜热菌株甲基嗜热菌属(*Methylocaldum*)成为主导种群，揭示了温度梯度对优势功能类群的定向筛选作用。在功能动态层面，Li 等[89]结合稳定同位素示踪与高通量测序技术，解析了南海沉积物中活跃嗜甲烷菌对温度变化的动态响应，发现在 4–37 ℃范围内，甲基单胞菌科(*Methylomonadaceae*)是该海域执行甲烷消纳功能的关键功能类群；进一步地阈值分析表明，低温环境有助于维持特定嗜甲烷类群的代谢活性，而温度升高则显著改变了功能类群的内部多样性与丰度分布。综合上述研究，温度对嗜甲烷菌的影响涵盖从单菌株转录调控到群落结构重组的多个层次，核心机制在于温度通过差异化筛选具有不同热适应策略的功能类群，实现群落整体代谢功能的动态重构。

除温度外，盐度、土壤理化性质等环境因子同样深刻影响嗜甲烷菌的生态分布与功能分工。在宏观环境梯度层面，基于群落网络分析

发现，随着盐度升高，嗜甲烷菌多样性显著下降，II 型菌株甲基弯曲菌属(*Methylosinus*)相对丰度升高，而 I 型菌株甲基球菌属(*Methylococcus*)下降[90]，表明盐度梯度对不同菌型具有差异化的筛选压力。在中观土壤生态位层面，Zheng 等[91]通过跨气候带的宏基因组与代谢分析进一步揭示，不同土壤类型下嗜甲烷菌发生明显生态位分化，暖温带高 pH 稻田中 I 型嗜甲烷菌占优势并通过 RuMP 途径实现更高碳转化效率，而低 pH 热带土壤则更有利于 II 型菌群的生长。这表明土壤 pH 与气候带的协同作用通过筛选不同碳同化策略的功能类群，从根本上驱动了嗜甲烷菌群落的生态位分化，并直接决定了不同农业生态系统中甲烷氧化的整体效率。在微环境梯度层面，Geng 等[92]进一步将分析精度细化至水稻生育期与土层深度，发现 *Methylomirabilis* 细菌的丰度在 10−20 cm 土层和早期生长阶段达到最高水平，体现出该菌株对微环境梯度变化的精细适应能力。在极端环境条件下，上述对氧气、pH 及底物浓度的适应能力进一步延伸至缺氧胁迫场景。部分甲烷氧化菌能够以铁氧化物为替代电子受体，通过重构碳代谢与能量代谢维持甲烷氧化功能[43]，展现出高度的代谢可塑性，揭示了嗜甲烷菌在电子受体匮乏环境中维持核心代谢功能的应急调控策略。

当前全球大气甲烷浓度约为 1 800–1 900 ppb (parts per billion)，远低于嗜甲烷菌高效利用甲烷所需的底物浓度阈值，这在全球尺度上构成了嗜甲烷菌碳源获取的限制[7]。在我国，煤矿乏风气、垃圾填埋场逸散气及分散式养殖场沼气等甲烷排放源高度分散，局部甲烷浓度普遍偏低，进一步加剧了嗜甲烷菌在实际应用场景中的底物获取困难。针对如何在极低底物浓度下维持代谢活性这一尚未完全解答的科学问题，嗜甲烷菌进化出了低底物浓度下的适应机制。例如，在营养匮乏的深海碳酸盐台地中，基因组学分析显示，稀有生物圈中的嗜甲烷菌通过扩充的能量回收基因簇和多样的底物摄取系统，在极低甲烷通量下维持基本生命活动[93]。此外，α-变形菌纲嗜甲烷菌在经历底物丰沛与匮乏交替循环时通过转录组调控迅速降低非生长相关维持能耗，表现出极强的代谢稳态[94]。针对分散式低浓度甲烷治理的工业需求，组学技术在识别与挖掘高亲和力 pMMO 及其调控元件方面发挥了核心作用。同时，多组学联合分析识别出了与高亲和力表型协同表达的强启动子及电子传递模块，为构建低浓度甲烷捕获能力的合成生物底盘提供了关键元件[78,95]。这对于实现煤矿乏风气、垃圾填埋场逸散气等分散式低浓度甲烷的高效减排具有重要应用价值。

借鉴自然演化中的抗逆机制，研究人员进一步探索了嗜甲烷菌在工业特殊环境中的应用潜力。在沼气转化过程中，剧毒杂质硫化氢(H_2S)常通过竞争性结合 MMO 活性位点并阻断电子传递链，对嗜甲烷菌产生强烈的生长抑制，这一毒性效应长期被视为制约粗沼气直接生物转化的核心障碍[96]。针对这一问题，多组学技术的应用使研究人员得以从单菌株与群落 2 个层次系统揭示微生物的防御与代偿机制。在单菌株响应层面，Pei 等[97]利用转录组学手段解析了 *M. capsulatus* Bath 对 H_2S 的响应机制，发现细胞通过上调硫代谢解毒路径以及系统性重塑金属稳态调控网络，以此减轻 H_2S 对呼吸链细胞色素的损伤，揭示了单菌株在面对硫化物胁迫时的主动代谢响应策略。然而，单菌株的耐受能力存在固有上限，构建具有高耐受性的微生物群落成为进一步提升系统稳健性的必要路径。在群落耐受策略层面，Jiang 等[98]通过宏基因组测序分析，从厌氧消化液中富集出可耐受高浓度 H_2S (5.64 g/m^3)的嗜甲烷菌群，证实蓝细菌与嗜甲烷菌之间的互作协同显著增强了系统对 H_2S 的耐受能力，表明种间互作可作为突破单菌株耐受极限的有效补偿机制。上述发现从单菌株与群落 2 个层次修正了此前关于嗜甲烷菌对硫化物高度敏感的认知，也为直接利用粗沼气生物合成甲醇等绿色技术提供了理论依据。

此外，上述机制认知为工程技术转化应用提供了明确的改造靶点。针对分散式甲烷常混有硫化物等杂质的现状，可利用蛋白组学识别的抗性蛋白对底盘细胞进行基因强化或定向进化，培育高鲁棒性菌株，从而减少废气预处理成本，加速技术从实验室向矿井、养殖场等工业现场的实质性转移。

2.2 菌群互作与共生关系

嗜甲烷菌的环境适应性不仅体现在自身代谢调控能力上，更体现在与多类微生物形成的复杂互作与共生网络中。这些互作关系将甲烷代谢与碳、氮、硫及金属循环紧密耦合[99]，在维持生态系统稳定性与温室气体平衡方面发挥核心作用。传统培养与单因素实验难以解析此类复杂群落关系，而转录组学与代谢组学的动态追踪研究则突破了这一局限，揭示了自然菌群在受到外部扰动时群落内不同成员会通过协调转录响应实现代谢互补，维持群落整体功能的稳定性。

嗜甲烷菌与产甲烷菌之间形成稳定的代谢互补共生关系，产甲烷菌产生甲烷作为终产物，而嗜甲烷菌消耗甲烷以获得能量维持生长，从而在生态系统尺度维持甲烷通量平衡[100]。基于多组学的生态研究表明，农业管理措施可通过优化该互作网络的代谢平衡实现甲烷减排。具体而言，施用不同类型有机肥料可改变土壤氧化还原电位，抑制产甲烷菌相关基因的表达，同时激活嗜甲烷菌的甲烷氧化活性，从而在源头减少甲烷排放[101]。Zhang 等[102]通过基因组与转录组联合分析揭示，特定施肥与灌溉方式可同步影响两类菌群的丰度与代谢活性，通过强化甲烷氧化作用与抑制产甲烷过程的协同，显著降低水稻土甲烷排放。此外，季节性气候变化等自然因素同样影响这一互作关系的动态平衡。Wang 等[103]证实，湿地甲烷排放强度取决于该互作关系的季节性动态演替，这种自然波动与人为干预共同决定了陆地生态系统的碳通量特征。

除与产甲烷菌形成碳循环耦合外，嗜甲烷菌在缺氧或微氧环境中还与反硝化菌、硝化菌形成高度协同的氮循环互作网络。湖泊沉积物研究发现，厌氧甲烷氧化古菌位于细胞聚集体核心，而反硝化菌围绕分布，形成空间结构有序的共生体系[104]。反硝化菌以甲烷氧化产生的甲酸盐、甲醇等中间代谢物为碳源，同时向嗜甲烷菌提供硝酸盐等电子受体，实现能量与物质的闭合循环。研究进一步证实，在微氧条件下厌氧甲烷氧化古细菌、好氧嗜甲烷菌与硝化菌可协同共存，由于硝化细菌的氨单加氧酶(ammonia monooxygenase, AMO)与好氧嗜甲烷菌 MMO 在活性位点结构上高度相似，AMO 可在底物浓度较低时交叉催化甲烷氧化，使硝化细菌在甲烷富集的共存环境中获得额外的碳源与能量供给，从而在竞争中形成代谢优势[105]。Nwoba 等[106]通过代谢组与转录组证实，甲酸盐与甲醇是连接甲烷氧化与反硝化的关键代谢枢纽。在更复杂的多菌共存体系中，Wu 等[107]进一步发现，在缺氧条件下好氧嗜甲烷菌甲基八叠球菌属(*Methylosarcina*)与完全氨氧化菌硝化螺菌属(*Nitrospira*)共存，通过代谢耦合促进硝酸盐还原与甲烷氧化协同进行。研究表明，在硝酸盐/亚硝酸盐充足条件下，反硝化驱动的甲烷氧化可成为缺氧环境中主导甲烷汇过程[108]，为通过调控氮循环实现甲烷减排提供了重要理论基础。

除氮循环外，厌氧甲烷氧化古菌还与硫酸盐还原菌形成稳定的外壳型共生体，通过耦合甲烷氧化与硫酸盐还原实现能量互补[109]。尽管目前对该体系的分子互作机制认知仍有限，但已有多组学证据表明这种共生体系在海洋沉积物与缺氧生态系统中广泛存在，并在全球甲烷收支中发挥重要调控作用。上述碳、氮、硫多元素循环的耦合互作，共同构成了嗜甲烷菌在自然生态系统中发挥温室气体调控功能的系统性网络。通过多组学技术的整合应用，研究人员不仅在单菌株水平上揭示了嗜甲烷菌的代谢

潜力，更从群落结构与元素循环耦合的维度阐明了微生物间复杂的代谢分工与协同策略。表 3 对比了嗜甲烷菌中组学技术应用的代表性研究，基于对好氧与厌氧嗜甲烷菌研究进展的系统梳理可以发现二者在生态策略上存在显著差异，好氧类群通过高效的酶促反应与跨物种的代谢产物交换维持群落内碳、氮等元素的持续流通；而厌氧类群则更倾向于形成紧密的物理聚集体，通过种间直接电子传递等精细机制在能量匮乏的环境中生存。

表3　嗜甲烷菌中组学技术应用的代表性研究

Table 3　Recent representative advances in omics applications in methanotrophs

Omics technology	Strain	Function	References
Genomics	*Methylomonas* sp. UP202	Complete genome sequence showing metabolic diversity in methane oxidation and nitrogen compound utilization	[110]
	Methylomonas sp. EFPC1	Complete genome sequence revealing genetic adaptation to mercury-contaminated environments	[111]
	Methylococcus sp. EFPC2		
	Methylococcus capsulatus MIR	Complete genome with the ability to grow on methanol, containing both MxaFI and XoxF methanol dehydrogenases	[112]
	Methylomonas defluvii sp. nov.	Identification of a novel species containing both particulate and soluble methane monooxygenase genes	[113]
	Methylomonas montana sp. nov.	First nonpigmented *Methylomonas* species lacking soluble methane monooxygenase	[114]
	Methylocystis sp. (Amazonian)	First genome of an Amazonian floodplain sediment *Methylocystis*, revealing methane oxidation and nitrogen fixation potential	[115]
	Methylocystis sp. MJC1	Comparative genomic analysis identifying this strain as a platform for PHB biosynthesis	[116]
	Methylocystis parvus OBBP	Complete genome revealing the genetic basis for PHB production	[117]
	Methylocystis suflitae sp. nov.	Identification of a novel species with methane and methanol utilization and nitrogen fixation capabilities	[118]
	ANME-2a enrichment cultures	Genomic analysis revealing Fe(III) reduction mechanisms involving multiheme c-type cytochromes	[119]
	Methylotenera and *Methylobacter*	Metagenomic analyses in an advanced denitrification system coupled with aerobic methane oxidation, identification of synergistic metabolic pathways for methane oxidation and nitrogen removal	[62]
Transcriptomics	Multiple ANME lineages	Transcriptomic evidence showing differential stimulation by sulfate among ANME lineages, with ANME-2a exhibiting higher metabolic activity	[47]
	Methylomicrobium album BG8	RNA biomarker *pmoA* levels universally correlated with methane oxidation activity; transcriptomic analysis revealing regulatory responses to methane and oxygen limitation	[120]
	ANME-2a enrichment cultures	Transcriptomic analysis of Fe(III) reduction-related enrichment cultures involved in anaerobic methane oxidation	[121]
	M. buryatense 5GB1	Utilizing transcriptomics to reveal regulatory mechanisms, and through nutritional induction strategies, redirecting the metabolic flow from biomass accumulation to the synthesis of food components	[30]

(待续)

(续表3)

Omics technology	Strain	Function	References
	M. buryatense 5GB1S	By integrating ^{13}C metabolism, methane and CO_2 were synergistically combined to synthesize succinic acid, leading to a significant advancement in biological upcycling and recycling	[36]
	M. trichosporium OB3b	Transcriptomic analysis revealed the impact of copper on physiology and gene expression during growth on methane or methanol	[83]
	Alphaproteobacterial methanotrophs	Transcriptomics elucidated the resilience and robustness mechanisms of strains under methane feast-famine scenarios	[94]
	Methylomonas sp. ZR1	Genome-scale metabolic analysis revealing a central metabolic network; identification of unique metabolic traits supporting fast growth and high lycopene production on methane, and metabolic imbalance during methanol growth	[122]
	Methylacidiphilum fumariolicum SolV	Metabolic characterization of a thermoacidophilic methanotroph capable of growth on non-methane C3 compounds (2-propanol and acetone), revealing distinct metabolic pathways and growth kinetics	[26]
Proteomics	ANME-2a archaea	Protein landscape analysis revealing integrated system for diazotrophy and membrane fortification, showing functional coupling between AOM machinery and auxiliary modules	[123]
	Multiple ANME lineages	Comparative proteomic analyses revealing differentiation in bioenergetic pathways and conserved roles of multiheme cytochromes	[124]
	Methylomonas	Proteomics analysis revealed changes in the expression of key proteins, particularly the impact on the activity of soluble methane monooxygenase caused by volatile organic compounds and carbon dioxide emissions	[125]
	Methylomonas denitrificans FJG1	Proteomic analysis identified diverse bacteriohemerythrin genes that enable oxygen sensing and capture, supporting survival in low-oxygen ecosystems	[71]
	Ca. M. sinica	Proteomics combined with transcriptomics revealed that iron modulates growth by reprogramming carbon metabolism and nutrient coupling	[75]
Metabolomics	Methanotrophic bacteria (multiple species)	Species-specific secondary metabolite production analyzed by LC-MS and GC-MS; identification of volatile compounds and biosynthetic gene clusters revealing ecological roles and adaptive strategies in methane cycling	[22]

基于上述自然共生网络的组学解析，研究人员进一步将这些发现应用于合成微生物组的理性设计。合成微生物组的设计逻辑直接借鉴天然共生体系中的代谢分工原则，以多组学数据为导向，识别自然群落中维持稳定共存的关键基因与调控元件，明确可供工程化利用的功能模块[126]。在此基础上，通过设计营养缺陷型互补或信号分子依赖型生长等互利依存关系，从基因工程层面将菌株间的协作关系强化为稳定的代谢依存，从而赋予人工群落在外部扰动下的稳定共存能力，为嗜甲烷菌合成微生物组的工业应用奠定了理论基础。

3 总结与展望

组学技术的革新驱动嗜甲烷菌研究从单一物种转向系统级的机理剖析。基于多组学数据整合分析，研究人员以 *M. capsulatus* 等为代表菌株，解析了不同甲烷浓度下该菌株的代谢响应机制，量化了甲醇、甲酸等核心中间产物的代谢通量演变规律，深化了对嗜甲烷菌 C1 代谢机理的认知[127-128]。此外，多组学技术阐明嗜甲烷菌在湿地、海洋等环境中适应 pH 与温度波动

的稳态调节机制，并通过合成微生物组学揭示了复杂环境中的种间互作模式，实现了从分子图谱到生态功能的关联解析，为锁定代谢工程改造的关键靶点及构建人工嗜甲烷菌细胞工厂奠定了理论基础[30,129]。

尽管组学技术已推动了部分代谢路径的解析，但嗜甲烷菌的工业化应用仍面临严峻挑战。在机制认知层面，复杂环境下的适应机制尚未完全破解。现有组学数据多源于单一菌株或受控实验室环境，难以真实还原生态系统中多组分竞争与种间电子传递的复杂性。在使能工具层面，高效遗传操作工具匮乏，限制了对嗜甲烷菌代谢通量的精准调控。相较于大肠杆菌等成熟底盘，嗜甲烷菌的调控元件及信号转导网络研究尚浅，尤其在 MMO 的异源表达与能量代谢优化方面仍存在巨大瓶颈[130]。在工程放大层面，生物反应器内的气液传质限制严重制约了生产强度。此外，脂质组学作为解析膜系统动态变化的重要工具，目前在嗜甲烷菌研究中尚属空白，导致嗜甲烷菌特有内膜系统如何随环境变化调节物理性能进而影响 pMMO 稳定性的问题，目前仍难以从分子层面得到系统解析。因此，如何将组学揭示的代谢机理系统转化为代谢工程策略，突破遗传工具与工程放大的双重瓶颈，仍是推动嗜甲烷菌工业化应用亟待解决的核心问题[20,131]。

未来，组学技术应致力于建立多组学特征与代谢功能的深度关联，实现嗜甲烷菌的理性设计与重塑。在基础研究领域，利用单细胞转录组学破解嗜甲烷菌群落内的细胞异质性[132]，从个体层面揭示特定菌株维持高代谢活性的机理，为筛选高性能工业底盘提供精准依据。通过宏基因组学与系统发育基因组学的联合应用，系统挖掘深海热液口、永冻土等极端环境中保存原始代谢特征的古老嗜甲烷菌谱系，解析 *pmo* 与 *mcr* 等关键功能基因在地球大氧化事件前后的水平转移轨迹与功能分化模式，在分子水平还原嗜甲烷菌与大气甲烷浓度变化的共进化机制[133]。结合表观基因组学，阐明非编码 RNA 等介导的碳、氮代谢转换的多维调控网络；利用时空组学可视化生物膜内部的代谢梯度，解析共生菌群内的电子传递机理[134]。在应用层面，针对矿井乏风气与垃圾填埋场逸散气等典型超低浓度场景，该类技术的开发核心在于利用组学挖掘的高亲和力甲烷单加氧酶及其调控元件[135]，构建具备强捕获能力的合成生物底盘，从源头实现甲烷向微生物蛋白、生物甲醇及长链化合物的高值化转化。然而，目前分散式甲烷成分复杂，硫化物等杂质对关键代谢酶具有显著毒性，亟需通过抗性蛋白强化与定向进化提升菌株的稳定性。通过机器学习辅助的计算预测与实验验证循环迭代系统优化代谢限速步骤，推动嗜甲烷菌技术从实验室向矿井、养殖场等复杂工业现场的实质性转化[136]。此外，在合成微生物组构建层面，通过人工设计具备氮、硫循环耦合能力的定制化菌群可有效解决工业发酵中单一菌株抗污染能力差、代谢负担重的瓶颈问题。总之，组学技术有望从观察工具进化为设计工具，在助力实现甲烷减排目标的同时，开启甲烷生物炼制的新篇章。

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