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Microbiology COMMENTARY

A new microbial iron-sulfur coupled metabolism: Ecological and environmental implications

Hong Zhang,[1] Huanbao Sun,[1] Yaqing Liu,[2] Caiyun Jiao,[1] Wenzhao Liu,[1] Hans Hermann Richnow,[3] Rubing Zhang,[4] and Manman Wei[1,*]

[1]College of Biological Engineering, Qingdao University of Science and Technology, Qingdao 266042, China

[2]College of Light Industry and Food Engineering, Guangxi University, Nanning 530004, China

[3]Leibniz Institute for Tropospheric Research, Leipzig 04318, Germany

[4]CAS Key Laboratory of Bio-based Materials, Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences, Qingdao 266101, China

*Correspondence: manman.wei@qust.edu.cn

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The biogeochemical cycling of sulfur and iron is fundamental to Earth's ecosystems, exerting profound impacts on the global elemental cycle and climate. Microbial metabolism governs sulfur species transformations through oxidation, reduction, and disproportionation reactions, among which dissimilatory sulfate reduction serves as a cornerstone process responsible for sulfide generation in anoxic environments. Traditionally, sulfides re-oxidation to sulfate is believed to rely on oxygen or nitrate as electron acceptors. However, complete sulfide oxidation and substantial sulfate accumulation are frequently observed in anoxic, iron-rich habitats where these canonical electron acceptors are depleted.[1] For decades, the reaction between sulfide and iron(III) oxides in such environments was considered predominantly abiotic, described as spontaneous chemical reactions producing elemental sulfur (S^0) and iron monosulfide (FeS). This purely chemical view, however, could not adequately explain the rapid sulfide oxidation rates and substantial sulfate accumulation measured in oxygen/nitrate-depleted environments. While early geochemical investigations suggested potential microbial involvement,[2] no microorganism had been definitively shown to completely oxidize sulfide to sulfate using iron(III) oxides as a terminal electron acceptor, leaving a critical conceptual gap in our understanding of metabolic links between the sulfur and iron cycling. This gap has now been filled by a groundbreaking study published in *Nature* by Chen et al., which revealed a novel microbial metabolism termed MISO (microbial iron oxide respiration coupled to sulfide oxidation).[3]

The delayed discovery of this pathway can be attributed to a series of the methodological and conceptual challenges that long obscured its detection. A major conceptual blind spot arose from the prevailing view that sulfide-iron(III) oxide interactions are predominantly abiotic and that insoluble iron(III) oxides cannot support complete microbial sulfide oxidation. Indeed, the abiotic reaction between sulfide and iron(III) oxide is thermodynamically favorable and kinetically efficient under numerous environmental conditions, often overshadowing the biological contribution. Moreover, organisms capable of MISO (e.g., *Desulfurivibrio alkaliphilus*) are typically slow-growing chemolithoautotrophs that are readily outcompeted in conventional incubation experiments. Even when a microbial role was hypothesized, obtaining definitive experimental validation has proven exceptionally challenging. The complexity of sulfur transformation processes due to the wide range of sulfur oxidation states and chemical forms, as well as the dynamic interactions between abiotic and biotic reactions, poses a significant barrier to precise characterization, quantification, and pathway identification. Disentangling biotic contributions from dominant abiotic reactions thus remained a major technical limitation that hindered early investigations.

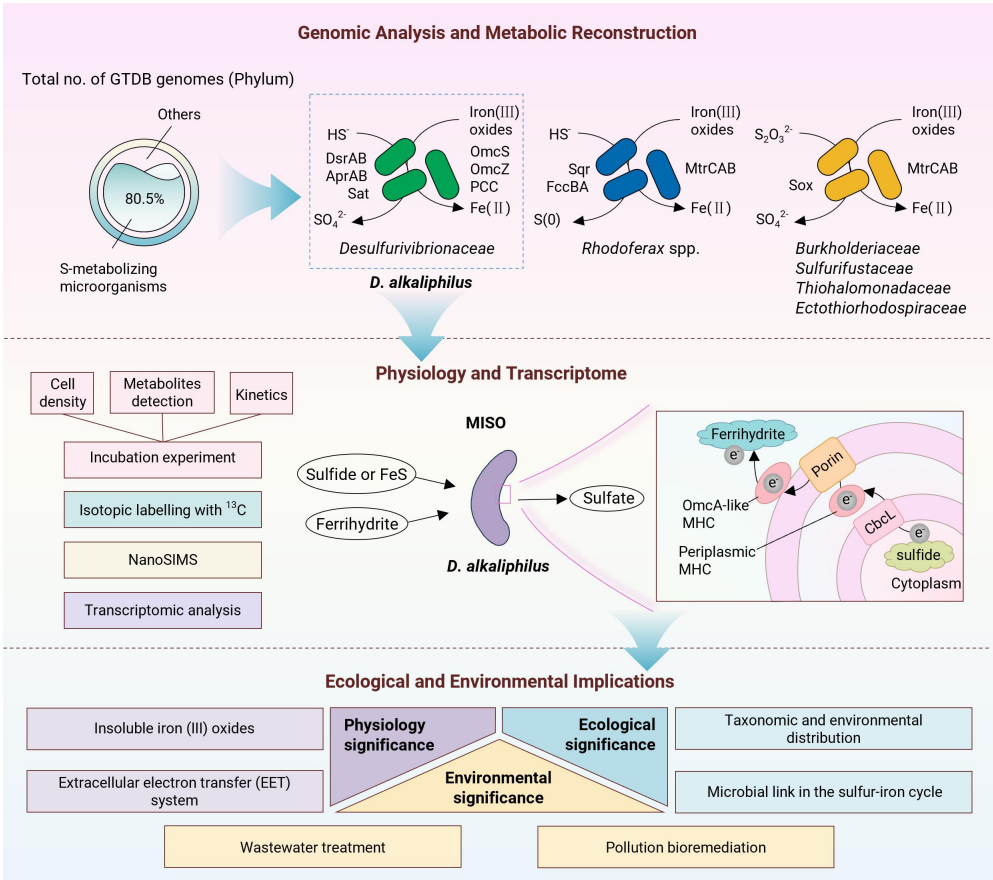

Figure 1. Mechanistic overview of microbial iron oxide respiration coupled to sulfide oxidation.

Chen et al. successfully overcame these challenges using an integrative strategy combining comparative genomics, stable isotope labeling, and transcriptomics. Through large-scale genomic analysis and metabolic reconstruction, they revealed broad taxonomic potential for sulfur transformations across 80.5% of bacterial and archaeal phyla (120 out of 149) and identified co-occurring genetic signatures for sulfide oxidation and extracellular iron(III) oxide reduction in 37 prokaryotic phyla.[3] Gibbs free energy calculations further confirmed the thermodynamic feasibility of MISO metabolic pathways, with energy yields sufficient to support microbial growth, thereby establishing MISO as both mechanistically plausible and energetically favorable under natural conditions.

To experimentally validate this metabolism, the authors ingeniously designed incubation experiments featuring periodic supply of sulfide at environmentally relevant low concentrations (~50 μM), using *Desulfurivibrio alkaliphilus* as a model organism. Isotopic labeling with ^{13}C-bicarbonate combined with nanoscale secondary ion mass spectrometry

(NanoSIMS) analysis revealed ^{13}C enrichment in individual microbial cells, directly demonstrating that inorganic carbon was assimilated into biomass and that this autotrophic carbon fixation was coupled to MISO metabolism. These experiments successfully disentangled microbial contribution from abiotic reactions, demonstrating that *D. alkaliphilus* can outcompete purely chemical sulfide oxidation with iron(III) oxide and providing definitive evidence for MISO. Further transcriptomic analysis and qPCR validation indicated that sulfide oxidation proceeds via a reversed dissimilatory sulfate reduction pathway, with electrons transferred directly to iron(III) oxides via multiheme cytochromes. This multi-layered approach, integrating microbial cultivation, genomics, isotopic tracing, transcriptomics, and thermodynamic modeling, offers compelling evidence for a previously unrecognized metabolic linkage between sulfide oxidation and iron(III) oxide respiration (Figure 1).

Undoubtedly, MISO represents a paradigm shift in microbial physiology and ecological function. Unlike traditional sulfur oxidizers that rely on soluble electron acceptors (e.g., oxygen, nitrate), MISO bacteria utilize insoluble iron(III) oxides, which are the most abundant oxidant pool in anoxic environments.[4] This widespread substrate availability implies broad taxonomic and environmental distribution across diverse anoxic habitats, including marine sediments, freshwater wetlands, hydrothermal vents, and subsurface aquifers. Chen et al. estimated that MISO contributes 1-7% of total sulfide oxidation to sulfate in global marine sediments, thereby playing a significant role in alleviating toxic sulfide accumulation. Critically, MISO establishes a direct metabolic bridge between the sulfur and iron cycles. By coupling sulfide oxidation to iron(III) reduction, this pathway forms a closed biogeochemical loop in which sulfide generated from dissimilatory sulfate reduction is re-oxidized to sulfate with negligible S^0 accumulation. This coupling provides an elegant explanation for the long-standing puzzle of sulfate accumulation in anoxic, iron-rich ecosystems where traditional electron acceptors are unavailable. Furthermore, MISO links these two elemental cycles with the global carbon cycle. MISO bacteria assimilate inorganic carbon (CO_2/HCO_3^-) into biomass using energy derived from sulfide oxidation coupled with iron(III) oxide reduction. This chemoautotrophic carbon fixation converts inorganic carbon into microbial organic carbon, which enters anoxic food webs and drives downstream carbon cycling processes. By uncovering this previously unknown biological mechanism that links sulfur, iron, and carbon cycling, the discovery of MISO fundamentally reshapes our understanding of anoxic biogeochemistry and its contributions to global elemental cycling.

Beyond its fundamental significance, MISO holds substantial promise for environmental biotechnology, especially for the development of efficient and sustainable approaches for wastewater treatment and pollution bioremediation. The capability to completely oxidize toxic sulfide to sulfate using low-cost, naturally abundant iron(III) oxides offers an attractive alternative to conventional chemical treatment methods for sulfidic effluents generated by mining, oil refining, and pulp manufacturing industries. Unlike chemical oxidation or energy-intensive aeration, MISO produces soluble sulfate and recyclable ferrous iron (Fe(II)) as metabolic end products. Beyond sulfide removal, the Fe(II) generated during MISO enables synergistic bioremediation of complex industrial effluents containing both sulfide and heavy metals. Fe(II) can react with heavy metal contaminants (e.g., Pb^{2+}, Cd^{2+}, Cr^{6+}) to form insoluble metal sulfides or hydroxides, which can be efficiently removed through sedimentation or filtration. Notably, MISO microorganisms possess a sophisticated extracellular electron transfer (EET) system, functionally analogous to those characterized in well-studied electroactive bacteria such as *Geobacter sulfurreducens*.[5] This EET mechanism supports efficient electron transfer from sulfide to solid-phase iron oxides, revealing promising biotechnological avenues. For instance, MISO could be potentially integrated into microbial fuel cells (MFCs) or bioelectrochemical systems (BESs) to generate electricity directly from sulfide oxidation, converting waste treatment into energy recovery. Furthermore, the EET capacity may facilitate direct interspecies electron transfer to methanogens in anaerobic digesters, potentially enhancing methane production from sulfide-rich organic waste streams. MISO thus represents not merely a biogeochemically interesting phenomenon but a versatile platform for developing next-generation sustainable environmental technologies.

As a newly discovered microbial metabolism, MISO remains far from fully understood at a mechanistic level. To date, the physiological and molecular mechanisms of MISO have only been validated in a single model organism under controlled laboratory conditions. Whether this metabolism operates similarly across the 37 prokaryotic phyla with MISO genetic potential, and how these microorganisms function within complex microbial communities, requires further investigation. Beyond mechanistic characterization, the quantitative contribution of MISO to global biogeochemical cycles remains preliminary, and the fundamental mechanisms governing MISO microbe-mineral interactions during extracellular electron transfer are still poorly understood. Addressing these knowledge gaps will require integrated approaches combining multi-omics technologies, stable isotope labeling, environmental physiology, biogeochemical modeling, and high-resolution microscopy. From a biotechnological perspective, translating MISO from laboratory discovery into practical application faces considerable challenges related to scalability and field validation. Future research will require to optimize operational parameters, engineer synthetic microbial consortia, and conduct pilot-scale investigations to evaluate performance under real-world conditions, including potential environmental impacts such as acidification or downstream sulfate reduction resulting from soluble sulfate production. Integrating this previously cryptic metabolism into global biogeochemical models and unlocking its potential for sustainable environmental technologies will be essential for advancing both fundamental biogeochemistry and practical environmental applications.

REFERENCES

1. Silva-Caceres M., Bond T. and Vriens B. (2023). Incomplete sulfide oxidation under suboxic conditions: Rates and aqueous sulfur speciation. *Appl. Geochem.* **159**:105848. DOI:10.1016/j.apgeochem.2023.105848
2. Fernandes-Martins M. C., Colman D. R. and Boyd E. S. (2024). Sulfide oxidation by members of the Sulfolobales. *PNAS Nexus* **3**:201. DOI:10.1093/pnasnexus/pgae201
3. Chen S. C., Li X. M., Battisti N., et al. (2025). Microbial iron oxide respiration coupled to sulfide oxidation. *Nature* **646**:925–933. DOI:10.1038/s41586-025-09467-0
4. Zhou Z., Tran P. Q., Cowley E. S., et al., (2025). Diversity and ecology of microbial sulfur metabolism. *Nat. Rev. Microbiol.* **23**:122-140. DOI: 10.1038/s41579-024-01104-3
5. Hu Y., Han X., Luo Y., et al., (2024). All roads lead to Rome: Cyclic di-GMP differentially regulates extracellular electron transfer in *Geobacter* biofilms. *Innov. Life* **2**: 100052. DOI: 10.59717/j.xinn-life.2024.100052

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AUTHOR CONTRIBUTIONS

All authors conceived the original idea. Hong Zhang wrote the draft. Yaqing Liu, Huanbao Sun, Caiyun Jiao, Wenzhao Liu, Hans H. Richnow and Manman Wei provided critical revisions. All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.

DATA AND CODE AVAILABILITY

No new data were created or analyzed in this study.