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Microbial Science: The Hidden Cost of Null Result Bias in Fermentation and Translational Research

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Abstract

The field of microbial biotechnology, which includes areas like precise fermentation and synthetic biology, is experiencing groundbreaking innovations with a market size projected to reach $400 billion by 2030. Despite these advances, the systematic undervaluing of well-conducted publications that report null or negative results has become a significant obstacle to research progress, investments, and integrity. In areas such as fermentation, biomanufacturing, or metabolic engineering, important negative findings, such as the failure of a productive strain to scale up under shear stress, are often kept unpublished. Similarly, failures in food microbial interventions, like producing unwanted flavor byproducts, are frequently confirmed in labs worldwide. This repetition holds back microbial innovation. The current economic impact, which is often overlooked and not properly measured, is substantial, estimated at around $28 billion annually, due to wasted research efforts caused by irreproducibility issues in preclinical science research. To counteract this bias against publishing valuable "null results," all scientific journals should broaden their scope and policies, with funding agencies validating negative research outcomes, and academic programs teaching the importance of reporting null results to uphold research integrity.

The field of microbial biotechnology stands at a pivotal moment. Biomass and precision fermentation are revolutionizing alternative protein production [1–3], engineered microbial consortia are transforming bioprocessing [4], and synthetic biology continues to expand the metabolic boundaries for sustainable applications[5]. The projected total market size for microbial products is $400 billion by 2030[6]. However, despite this notable progress, innovation, and commercial impact, a significant issue persists within science and this specific discipline in particular: the systematic neglect of methodologically rigorous null and negative results. Null result bias represents not merely a cultural preference or publication bias, but rather a burden on translational research efficiency, capital allocation, and scientific integrity across microbial and food science communities [7–11].

In fermentation and bio-manufacturing, a critical null result carries substantial practical implications. This showcases an unexpected limitation or reveals a critical systemic effect that cannot be easily modeled or predicted. Although such data are often regarded as failures or disappointing outcomes, it provides important information that could prevent redundant experimental efforts, optimize the process, and accelerate timelines. However, these findings rarely appear in peer-reviewed literature [7,12]. Instead, they remain in internal reports and proprietary industrial datasets, making them inaccessible to the broader scientific community that could benefit from them.

One important issue in this field is scaling up fermentation and bio-manufacturing from lab to pilot or commercial-scale, where success often lies in scalable process parameters. A classic null result is the failure of a lab-productive strain to successfully scaleup to large, high-density bioreactors from bench to 50-liter pilot fermentation despite promising performance in 5-liter batches. This failure often results from the strain's extreme sensitivity to non-

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genetic, physical factors, such as intolerance to agitator-dependent shear stress or cell damage caused by aeration[13]. These null results regarding a strain's shear-stress tolerance or optimal gassing rate are essential for developing future scale-up protocols[13]. However, because such outcomes are perceived as lacking novelty, they are rarely published, resulting in other researchers needing to independently rediscover this information through processes that are both time-consuming and costly.

For synthetic biology, metabolic engineering frequently involves targeted genetic interventions, such as gene knockouts, overexpression, or non-native insertions, designed to redirect metabolite production toward a desired product[14,15]. However, these interventions often fail due to pleiotropic metabolic effects [16]. The desired genotype can lead to adverse effects, such as reduced growth rates or a complete disruption of essential metabolic pathways [14]. Publishing those null results that document the specific failures helps to better delineate the physiological limits within the metabolic network. This critical negative data prevents wasting unnecessary time to replicate those results and expedites simulations for new genetic designs.

In the rapidly advancing field of microbial food technology, interventions designed to improve nutrition, preservation, or texture often fail due to unforeseen quality issues [16]. For instance, it may unintentionally generate undesirable volatile organic compounds (VOCs) or off-flavors that render the product commercially untenable[15]. Such outcomes are rarely published, and this effect is even more pronounced in industry-led studies, where all findings are often kept confidential. As a result, other researchers often repeat similar experiments with recurrent failures.

The non-publication of a methodologically sound null result guarantees that months or years of high-skilled researchers' and students' time are spent repeating the same failed metabolic engineering strategy, media formulation, or scale-up setting. This redundancy slows the pace of microbial innovation. The research community should operate as a communicative group project where every result contributes to collective understanding. The current system prevents this collective action. For instance, when this time is aggregated across the numerous labs worldwide working on synthetic biology and fermentation, the total cost in lost time and effort keeps accumulating. While it is challenging to calculate the precise monetary burden of not publishing null results in the microbial sector, established benchmarks underscore the scope of the problem. Broader analyses of irreproducible research in the US preclinical life sciences suggest a financial burden of approximately $28 billion annually[17]. This cost comes from factors related to publication bias and the resulting incentives, such as poor study design, insufficient analysis, and inadequate reporting, the very flaws that arise when researchers selectively present findings to meet publication criteria [9,17]. At this scale, every replicated failure represents billions in lost opportunity, compromising market share and slowing the commercialization of essential technologies. The financial burden associated with redundant research and development remains substantial and continues to slow down scientific advancement. To tackle this issue of commonly discrediting null or negative results in the field of microbiology, we need fundamental cultural change. Journals serving the microbial science and food technology communities must expand their editorial mandates, establishing dedicated sections or companion platforms specifically for null result submissions. Several leading initiatives have already established the feasibility of publishing studies with negative or null results[11]. For example, Access Microbiology has introduced a dedicated collection for negative findings[18]. Journals such as PLOS One and Microbiology Spectrum, along with broad journals focusing on null and negative outcomes, including the International Journal of Negative Results (IJNR) and Null Scientific, explicitly encourage the submission of methodologically sound research regardless of the directionality of the results. Funding bodies must recognize negative result publications as legitimate research outputs deserving of performance credit and career advancement consideration. Collaborative consortia bridging academia and industry can pioneer shared negative data repositories that preserve commercial confidentiality while preventing redundant experimental waste. Critically, graduate training programs in microbiology, fermentation science, and bioprocess engineering should explicitly teach the analytical and ethical importance of reporting null or negative outcomes.

Addressing the systemic null result bias in microbial science requires a coordinated effort. Journals should expand their editorial policies, and funding agencies are encouraged to view such publications as valuable research outcomes that are part of career development. Additionally, academic programs must integrate the importance of null results reporting into their curricula. By breaking down the cultural disincentive against publishing "failures," the microbial and food science communities can move beyond repetitive experimentation. Through this comprehensive approach, we can accelerate innovation and more effectively turn the potential of microbial biotechnology into commercial benefits that are efficient, scalable, and sustainable

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References

1. Eastham JL, Leman AR. Precision fermentation for food proteins: ingredient innovations, bioprocess considerations, and outlook—a mini-review. *Curr Opin Food Sci.* 2024 Aug;58:101194.

2. Knychala MM, Boing LA, Ienczak JL, Trichez D, Stambuk BU. Precision fermentation as an alternative to animal protein: a review. *Fermentation.* 2024 Jun 14;10(6):315.

3. Molfetta M, Morais EG, Barreira L, Bruno GL, Porcelli F, Dugat-Bony E, et al. Protein sources alternative to meat: state of the art and involvement of fermentation. *Foods.* 2022 Jul 12;11(14):2065.

4. Kumar P, Chitara D, Sengupta S, Banerjee P, Rai SN. Microbial consortia in biotechnology: applications and challenges in industrial processes. *3 Biotech.* 2025 Nov;15(11):386.

5. Jones EM, Marken JP, Silver PA. Synthetic microbiology in sustainability applications. *Nat Rev Microbiol.* 2024 Jun;22(6):345–59.

6. Arshad M, Arshad I, Aslam H, Sukmawati D, Anvar AH, Shakir HA, et al. Microbial bioproducts: current advances, industrial applications, and future perspectives. *J Umm Al-Qura Univ Appl Sci.* 2025 Sep;11(3):545–60.

7. Springer Nature. *The state of null results: Insights from 11,000 researchers on negative or inconclusive results* [white paper]. London: Springer Nature; 2025. Available from: https://stories.springernature.com/the-state-of-null-results-white-paper/index.html

8. Chopra F, Haaland I, Roth C, Stegmann A. The null result penalty. *Econ J.* 2023;134. Available from: https://doi.org/10.1093/ej/uead060

9. Curry S, Mercado-Lara E, Arechavala-Gomeza V, Begley CG, Bernard C, Bernard R, et al. Ending publication bias: a values-based approach to surface null and negative results. *PLoS Biol.* 2025 Sep 24;23(9):e3003368.

10. Knight J. Null and void. *Nature.* 2003;422. Available from: https://doi.org/10.1038/422554a

11. Nimpf S, Keays DA. Why (and how) we should publish negative data. *EMBO Rep.* 2020 Jan 7;21(1):e49775.

12. Santiago Vispo N. Redefining scientific success: how null results foster open research. *Bionatura Journal.* 2025 Sep 15;2(3):1.

13. De Mello AFM, De Souza Vandenberghe LP, Herrmann LW, Letti LAJ, Burgos WJM, Scapini T, et al. Strategies and engineering aspects on the scale-up of bioreactors for different bioprocesses. *Syst Microbiol Biomanuf.* 2024 Apr;4(2):365–85.

14. Montaño López J, Duran L, Avalos JL. Physiological limitations and opportunities in microbial metabolic engineering. *Nat Rev Microbiol.* 2022 Jan;20(1):35–48.

15. Volk MJ, Tran VG, Tan SI, Mishra S, Fatma Z, Boob A, et al. Metabolic engineering: methodologies and applications. *Chem Rev.* 2023 May 10;123(9):5521–70.

16. Graham AE, Ledesma-Amaro R. The microbial food revolution. *Nat Commun.* 2023 Apr 19;14(1):2231.

17. Freedman LP, Cockburn IM, Simcoe TS. The economics of reproducibility in preclinical research. *PLoS Biol.* 2015 Jun 9;13(6):e1002165.

18. Bik EM. Publishing negative results is good for science: This article is part of the Negative Results collection. *Access Microbiol.* 2024 Apr 2 [cited 2025 Nov 17];6(4). Available from: https://www.microbiologyresearch.org/content/journal/acmi/10.1099/acmi.0.000792