

Rewriting the rules of discovery: Why negative results are essential for AI-driven science and global equity

Eduardo Buxaderas,^a David Díaz Díaz^{b,c,*}

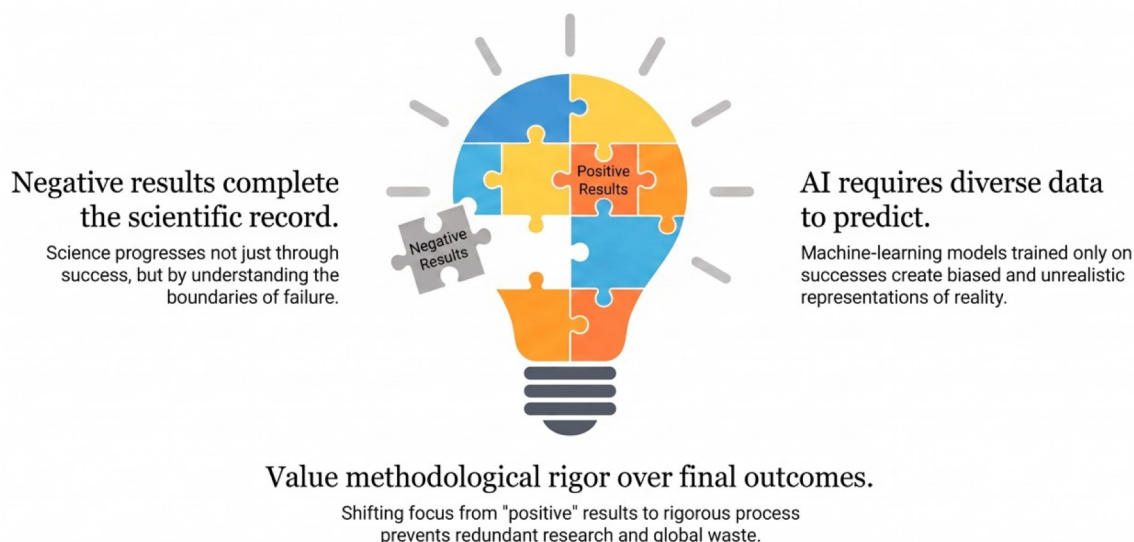
^a Instituto de Química del Sur, INQUISUR (CONICET-UNS), Departamento de Química, Universidad Nacional del Sur, Av. Alem 1253, 8000 Bahía Blanca, Argentina.

^b AFM-NANO, Instituto Universitario de Bio-Organica Antonio González (IUBO-AG), Universidad de La Laguna, Avda. Astrofísico Francisco Sánchez 2, La Laguna 38206, Spain.

^c Departamento de Química Orgánica, Universidad de La Laguna, Avda. Astrofísico Francisco Sánchez 3, La Laguna 38206, Spain.

*Corresponding author: Dr. David Díaz Díaz, AFM-NANO, Instituto Universitario de Bio-Organica Antonio González (IUBO-AG), Universidad de La Laguna, Avda. Astrofísico Francisco Sánchez 2, La Laguna 38206, Spain. Tel.: +34 922318584. E-mail address: ddiazdiaz@ull.es (D.D.D.).

Graphical Abstract



Abstract: Scientific progress depends not only on successful experiments but also on the rigorous documentation of those that fail or produce null or inconclusive outcomes. However, the current publishing system continues to favor positive findings, creating publication bias, limiting reproducibility, and wasting valuable scientific effort. In the era of artificial intelligence (AI), this imbalance has acquired new significance, as machine-learning models trained predominantly on successful outcomes risk learning an incomplete and systematically biased representation of scientific reality. This opinion article argues that negative results should be recognized as an essential component of the scientific record and as a critical resource for AI-driven discovery. We discuss the cultural, methodological, and structural barriers that discourage their dissemination, examine their implications for scientific integrity and global equity, and propose practical measures to promote their systematic reporting, including dedicated publication formats, standardized reporting practices, curated databases, and transparent integration of AI into scientific workflows. We argue that valuing rigor over outcome will not only improve reproducibility and accelerate discovery but also contribute to a more inclusive, ethical, and reliable scientific ecosystem.

Keywords: *Negative results, publication bias, artificial intelligence, scientific integrity, open science, global equity.*

Introduction: A Paradigm Shift in Science

Science is often romanticized as a series of brilliant successes, but its true nature lies in a much messier reality, one filled with trial and error. In most experimental fields, such as chemistry, biology and physics, failed experiments far outnumber successful ones. Yet, the publishing landscape paints an incomplete picture, prioritizing positive results over the wealth of knowledge embedded in so-called failures. As Eddington pointed out nearly a century ago, it is often by pushing theories to failure that we uncover their hidden limitations and gain deeper insight.¹ Indeed, science does not progress despite failure, but through it.

Moreover, the current scientific landscape is increasingly defined by a relentless pursuit of groundbreaking results. This cultural emphasis creates a dangerous distortion: a system where work, dedication, and meticulous methodological rigor are frequently undervalued, overshadowed by the allure of high-impact publications. This pressure not only affects the quality of research but also contributes to a systemic imbalance worldwide, an environment that is fundamentally unfair.

The omission of “negative” results within the academic publishing system has significant consequences for scientific progress, particularly in the era of artificial intelligence (AI). AI systems depend on diverse datasets to generate reliable predictions, and the absence of negative results leaves these models blind to the lessons of failure. In fields like chemical sciences, this gap risks perpetuating inefficiencies and slowing innovation. Could a cultural shift toward publishing negative results unlock AI’s full potential while also advancing science as a whole?

The Hidden Costs of Ignoring Negative Results

A scientific system that does not preserve its failures is condemned to reproduce them. Moreover, when the rationale behind past decisions is lost, methods risk becoming dogma rather than knowledge. In this context, the current publishing culture marginalizes negative results, sidelining valuable data about what doesn’t work. This practice not only wastes resources but also creates blind spots in the scientific record. For instance, in organic synthesis, knowing why a reaction fails, whether due to incompatible reagents or environmental constraints, provides critical insights that guide future experiments.

Without access to such data, researchers often repeat unproductive experiments, and AI models trained exclusively on successful reactions struggle to predict real-world

outcomes. A 2021 study by Schwaller et al.² highlighted how this bias limits the generalizability of AI in chemistry, as models fed only positive results are prone to overfitting and unrealistic expectations. Including negative results could prevent these pitfalls, offering a more accurate and nuanced understanding of chemical systems.

AI thrives on data diversity. To maximize its utility, datasets must include both successes and failures. Negative results are not just data points; they are essential markers that delineate the boundaries of feasibility. From chemical reactivity to drug development and materials science, the exclusion of failed experiments means AI models cannot learn why certain experiments fail, leading to wasted resources and missed opportunities.³ Including such data would allow AI to suggest alternative paths and refine predictions, thereby improving the likelihood of success.

Cultural Barriers: Why Scientists Don’t Share Failures

The reluctance to publish negative results stems from systemic issues in academia. Metrics like journal impact factors and citation counts reward groundbreaking discoveries, not methodical rigor. Publishing failures is often seen as risky, with concerns about reputation and perceived competence discouraging researchers from sharing their “less successful” work. This has a painful emotional impact on many researchers, especially those from younger generations who are taking their first steps in science believing that only positive results will push them to recognized positions, which ultimately would provide them with a successful and meaningful career. Let’s consider the following self-criticism: Are we ready to fairly evaluate, for instance, doctoral research that has not generated publications? In that situation, would many pages holding a substantial amount of work without “positive” results be fairly evaluated by funding agencies and academic institutions in ways that impact career promotion?

Thus, reframing negative results as integral components of scientific progress, not as personal shortcomings, could dismantle these barriers. A significant conceptual extension of this argument is the framework of *Strong Inference*,⁴ which encourages formulating and testing multiple working hypotheses to prevent premature or emotionally driven commitment to a single explanatory model. This methodological viewpoint inherently mitigates confirmation bias and counters the structural incentives that privilege positive outcomes over rigorously obtained null or negative findings. In this context, the systematic publication of negative results is not merely a matter of transparency but a mechanism for preserving cognitive discipline: it broadens

the analytical landscape against which hypotheses are evaluated and safeguards the scientific process from the cognitive narrowing that emerges when only confirmatory evidence is valorized. By doing so, it reinforces a more honest and resilient research culture, one that recognizes that progress often comes from understanding why a hypothesis does not hold. Incorporating such results into the scientific record thus strengthens both methodological robustness and the cumulative reliability of data-driven discovery, ensuring that each experimental outcome, even those that challenge expectations, contributes meaningfully to scientific advancement. Historical examples underscore the importance of this shift. Alexander Fleming's discovery of penicillin was serendipitous, arising from what might have been dismissed as a failed experiment. Had Fleming not recognized its significance, perhaps another researcher would eventually have realized its importance for humanity. Imagine the breakthroughs lost to history because "failures" were never documented or shared. The problem is not that scientists make mistakes, but that the system discourages them from acknowledging them.

Overcoming Challenges: Practical Solutions

Although several initiatives have begun to address these challenges, progress remains fragmented and insufficient. Efforts such as the Journal of Trial and Error (JOTE),⁵ Access Microbiology,⁶ and the increasing openness of preprint platforms like ChemRxiv or BioRxiv, which allow the dissemination of inconclusive or negative outcomes, represent important steps toward normalizing the value of non-positive data. However, while these initiatives mark an important conceptual shift, they rarely address a critical dimension of the issue: the profound economic and geographic inequalities that shape who is able to publish negative results in the first place. The barriers to disseminating non-positive data are not only cultural but also structural, disproportionately affecting researchers working in underfunded institutions or regions with limited resources. In this article, we aim to place this neglected dimension at the center of the discussion, arguing that any meaningful reform must confront the injustices embedded in the global scientific ecosystem.

These platforms demonstrate that the scientific community is slowly acknowledging the need for a more complete and honest research record. However, despite their promise, these efforts are still limited in scale, adoption, and cultural impact. We remain far from a scenario in which negative results are routinely published, properly evaluated, and fully integrated into the scientific workflow.

Adopting a culture of transparency requires systemic changes:

1. **Curated Databases:** Platforms like the Open Database are pioneering efforts to include both positive and negative results. Expanding such initiatives could provide AI with richer datasets.^[7]
2. **Dedicated Journal Sections:** To restore methodological integrity, publishers have a responsibility to lead the change. They should mandate or create dedicated sections for non-reproducible protocols and negative findings. In this context, a viable measure would be the implementation of standardized templates that enable the rigorous and efficient reporting of negative results, while also supporting a more efficient and consistent evaluation process by reviewers. This is not a lowering of standards, but a recognition that all well-founded hypotheses, tested with scientific rigor, hold intrinsic value. It is an ethical imperative to stop rewarding only the *outcome* and start validating the *process*. Therefore, we should also keep in mind that without rigor, negative results risk becoming noise rather than knowledge.
3. **AI-Assisted Analysis:** Machine learning could be used to organize and analyze negative results, extracting valuable insights and identifying trends across datasets. A rigorous protocol that fails to confirm a hypothesis is a success for science; it clearly delineates a path that does not work, thereby saving subsequent researchers time and resources, while potentially avoiding ethical concerns. Because the reality is that the appropriate utilization of AI for tasks like complex data analysis, literature review, or drafting support is a powerful tool for accelerating progress and democratizing access to research, particularly for individuals with limited staffing or funding.

In this context, there is also another worrying aspect. The fear of losing academic credibility, of being seen as less genuine or dedicated, fuels a taboo against acknowledging the use of AI. We need to shift the focus from avoiding AI to transparently and ethically integrating it. Declaring AI assistance is not a sign of weakness; it is a demonstration of competence in using modern scientific tools. By being honest about its use, the researcher can dedicate more time to the unique tasks that require human ingenuity: critical thinking, experimental design, and interpretive reflection. Hiding its use only perpetuates the culture of unrealistic perfection.

The Unjust Geography of Scientific Output

The global scientific community must urgently confront the stark reality of inequality driven by geography and economic status. The path of a researcher operating in a resource-constrained laboratory in a remote part of Africa is intrinsically more demanding and less visible than that of a counterpart in a well-funded European or North American institution. This is a fact which must not be ignored. The lack of access to cutting-edge equipment, reliable power grids, or expensive subscription databases creates colossal barriers entirely unrelated to intellectual capacity.

We must advocate for justice and fairer standards of evaluation. The simple fact of having more wealth or the “luck” of one’s birthplace should not be mistaken for a proxy for superior scientific ethics. In fact, institutions in disadvantaged locations often display extraordinary ingenuity and heightened ethical awareness due to the necessity of maximizing limited resources.

Scientific integrity lies in the rigor and honesty of the work itself, not in its geopolitical origin. To achieve true global science, we must acknowledge and actively mitigate these geographic biases. This acquires even more relevance in the era of AI, where access to the most powerful AI tools is already heavily dependent on economic resources.

Conclusion and Vision for the Future

The benefits of publishing negative results extend far beyond AI. By fostering a culture that values every experimental outcome, we can reduce redundancy, accelerate discovery, and inspire a new generation of scientists. This shift is particularly urgent in addressing global challenges such as climate change, where the stakes are too high for inefficiency.

To build a future where AI realizes its full potential, we must redefine what we consider valuable knowledge. Publishing negative results isn’t about admitting failure; it’s about advancing science as a collective endeavor. As we stand on the brink of unprecedented innovation, let us ensure that every experiment, success or failure, contributes to the pursuit of truth, and therefore the integrity of all results.

The foundational strength of the scientific method rests on honesty and objectivity. Yet, a prevalent bias toward publishing only statistically significant, positive outcomes persists. The notorious “file drawer problem” is crippling collective knowledge. We are wasting valuable research hours globally because well-designed studies yielding null or negative results are often deemed worthless and suppressed. The future of science depends on our ability to look beyond the spectacle of a single, striking result. The true measure of a robust scientific culture is its commitment to transparency, global equity, and unwavering rigor. By valuing the

dedication behind every result (positive or negative), confronting systemic geographic bias, and embracing technological assistance with honesty, we can ensure the scientific method remains a universal, just, and reliable engine for human progress. Let’s be brave and go beyond the spectacle of only “positive” results in publications. Overall, this is a call for global equity, rigor, and ethical transparency in science. In summary, honesty in science should be measured by methodological rigor, not by the positivity of the outcome. We should train scientists not only to succeed, but to fail rigorously and report it transparently. Failing better may not be a weakness of science, but one of its greatest strengths.

Perhaps this vision is idealistic, but scientific progress has always depended on challenging what is considered realistic.

As Confucius said, “When you know what you know and what you don’t know, that is true knowledge”.

Acknowledgments

D.D.D. acknowledges the Ministry of Science and Innovation (PID2022-142118OB I00/MCIN/AEI/10.13039/501100011033/UE), Cátedra de Medioambiente y Sostenibilidad (Cabildo de Tenerife-ULL) (MADS26.L1.04), and Fundación Ramón Areces for financial support. D.D.D. also thanks Nanotec, INTech, Cabildo de Tenerife and ULL for laboratory facilities.

References

1. Eddington, A. S. *Stars and Atoms*. Oxford: Clarendon Press, 1927.
2. Schwaller, P., Vaucher, A. C., Laino, T., Reymond, J.-L. *Mach. Learn. Sci. Technol.*, **2021**, 2, 015016. <https://doi.org/10.1088/2632-2153/abc81d>
3. Kant, S., Deepika, Roy, S. *Discov. Pharm. Sci.*, **2025**, 1, 7. <https://doi.org/10.1007/s44395-025-00007-3>
4. Platt, J. R. *Science*, **1964**, 146, 347-353. <https://doi.org/10.1126/science.146.3642.347>
5. Devine, S., Bautista Perpinyà, M., Delrue, V., Gaillard, S., Jorna, T. F. K., Meer, M. van der, Millett, L., Pozzebon, C., Visser, J. **2020**, 1, 1. <https://doi.org/10.36850/ed1>
6. Bik, E. M. *Access Microbiol.*, **2024**, 6, 4:000792. <https://doi.org/10.1099/acmi.0.000792>
7. Open Reaction Database: <https://open-reaction-database.org>