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Single Cell Sequencing Techniques and Biological Explanation

Caroline Angleraux[a*]

[a] *UMR 1253, iBrain, Université de Tours, Inserm, Tours, France*

***Corresponding author:** Caroline Angleraux, Email: Caroline.Angleraux@univ-paris1.fr

Abstract

The aim of this paper is to examine the type of biological explanation implied by single-cell sequencing, using established frameworks in the philosophy of biology, particularly those of new mechanical and systems biology. While investigating the extent to which new mechanistic philosophy or systems biology represent theoretical frameworks that align with single-cell sequencing, a part of -omics sequencing techniques, I claim that the objective of single-cell sequencing corresponds with the *zeitgeist* in theoretical philosophies of biology. The *zeitgeist* is a stance that advocates for a broader perspective on living organisms and that rejects reductionism. However, there remains a disparity between the scientific narrative and the practical capabilities of single-cell sequencing. Consequently, the conclusion drawn in this paper is that while single-cell sequencing aligns with the *zeitgeist* in certain theoretical philosophies of biology, it also acknowledges their theoretical limitations.

Keywords: ontology, cell type, cell classification, single-cell technology

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1. Introduction

Single-cell sequencing involves sequencing the genetic material of each cell individually. This technique offers high resolution at the genetic level and highlights the heterogeneity present within cell populations of tissue samples. Consequently, it facilitates the identification of distinct cell types and the composition of various cell populations. Additionally, by adapting to various levels of resolution, it also illuminates the dynamic nature of cellular structures. It not only underscores tissue development and microenvironments but also enables the tracking of cell lineages and specifications. As synthesized by Wang and Navin, several common applications have emerged from single cell sequencing methods over the last decade: "(1) delineating population diversity, (2) tracing cell lineages, (3) classifying cell types, and (4) genomic profiling of rare cells" (Wang and Navin 2015, p. 606). These diverse applications explain why single-cell techniques are employed across a broad spectrum of research and clinical contexts, including neurobiology, tissue mosaicism, microbiology, germline transmission, embryogenesis, organogenesis, prenatal diagnosis, immunology, and cancer research.

In the past decade, the use of single-cell techniques has experienced significant growth, emerging as both a valuable and trendy method of sequencing. Moreover, its capability to merge and integrate data from other sequencing techniques led to the recognition of single-cell multimodal -omics as the "method of the year 2019" by *Nature Methods* (2020). This acknowledgment underscores the unprecedented precision of the data obtained and the integration possibilities these techniques offer. In essence, single-cell sequencing facilitates the production and the combination of diverse datasets, which helps with the elucidation of complex patterns.

The approach of single-cell sequencing, as part of multimodal -omics, seeks to foster a more integrated understanding of biological phenomena, striving for a comprehensive perspective. By preserving and managing the complexity of collected data, single-cell multimodal -omics aims for complete data integration, thereby facilitating a holistic view of biological structures (cf. for instance Lähnemann *et al.* 2020, p. 22).

In this regard, as I will show, single-cell multimodal omics aligns closely with prevailing trends in philosophies of biology, which elaborate on the theoretical foundations of biology and which advocate for a broader understanding of living organisms. In other words, various theoretical philosophies of biology, such as systems biology or new mechanistic approaches, are deeply committed to incorporating explanations of complex biological phenomena into their frameworks. And by complex biological phenomena, they mean nonlinear effects or emergent properties. As we will develop further, their will to take into account complex biological phenomena is part of an ambition to embrace a holistic approach (Bechtel 2016). Then, as a shared inclination to consider complex biological phenomena within a holistic approach, single-cell multimodal omics mainly matches with the philosophical *zeitgeist*. As Tseng and Santra write: "Over the last two decades, there has been a significant shift towards studying biological cell function in a holistic manner, rather than adhering to a reductionist scientific paradigm, thus establishing the approach known as 'systems biology' or 'systomics'" (Tseng and Santra 2016, p. IV).

While both scientific and philosophical narratives advocate for a holistic perspective on biological phenomena, in practice, their explanations typically rely on the analysis of components and their qualities, following a bottom-up approach. While there is a tendency to integrate data from various levels and construct networks within systems to provide explanations, this integration seldom involves top-down approaches, and thus does not necessarily result in a holistic view being achieved. Upon closer examination of its epistemological framework, a mismatch becomes apparent between the scientific narrative (what it is aimed at doing – Morgan and Norton Wise 2017) and actual practices (what it actually does for now). This gap underscores the disparity between theoretical aspirations and practical implementation.

2. A Mismatch Between the Scientific Narrative and Practices

Single cell sequencing techniques are used for performing crucial tasks, mainly for identifying precise cell types or cell profiles and tracing cell lineages. The way of performing these tasks varies widely, depending on the context of experiment and on available equipment. For instance, in order to isolate a cell within a sample, methods include, among others, serial dilution, laser capture microdissection (LCM), or microfluidics (Wang and Song 2017). There are also different sequencing methods, depending on what is targeted (*e.g.* genome, epigenome or transcriptome; Wang and Song 2017, p. 3). And the way of organizing and integrating data in the libraries also depends on the kinds of biological samples that have been analyzed[a]. In essence, single cell sequencing can be applied to a wide range of objects and comprises a plurality of methods. Beyond the wide spectrum of techniques and methods it encompasses, the main steps involve isolating cells, sequencing genetic material, cataloging data, and analyzing it. Single-cell sequencing generates large and dense datasets, prompting many studies to attempt combining and integrating data obtained from genomic, epigenomic, or transcriptomic layers. As Kashima *et al.* (2020) list them, different computational methods have been developed to provide an overview of single cell data sets and to achieve multiomic analyses.

In this process, from isolating samples to combining datasets, each step is shaped by a technical context as well as driven by epistemic choices. For instance, in an experimental design aimed at identifying different cell populations within a multicellular tissue sample for cancer research, different granular level used to cluster cells ends up providing different number of cell populations within the sample. Within these cell populations, the pursuit of cell types or states (cf. Gross 2023 and Trapnell 2015) influences the selection of keywords in datasets. In another example, when the objective of an experimental design is to better understand transcription processes in bacteria, making decisions such as distinguishing between technical noise and lack of gene expression, or structuring databases to integrate data from samples of different species (cf. Zhang, Gao and Wang 2018)

[a] "Different types of measurements from multiple experiments need to be obtained and integrated. Depending on the actual research question, such experiments can be different time points, tissues, or organisms. For their integration, we need flexible but rigorous statistical and computational frameworks" (Lähnemann & *al.* 2020, p. 21).

is necessary. Their decisions are epistemic choices that shape the interpretation of results. As Leonelli argues in the context of scientific datasets: "The choice and definition of keywords used to classify and retrieve data matters enormously to their subsequent interpretation. Linking diverse datasets means making decisions about the concepts through which nature is best represented and investigated." (Leonelli 2019, p. 2). Technicians and scientists conducting experiments can justify the epistemic reasons behind their experimental designs, and data scientists can explain how and why datasets are elaborated or combined in specific ways. However, scientists who use bioinformatic data without generating them often overlook the underlying epistemic choices that shape the overall design and outputs. Published papers rarely make these assumptions explicit.

As a consequence, many single-cell sequencing studies exhibit a mismatch between the experimental approach and the overarching scientific narrative. In practice, research teams often rely on genome sequencing to infer specific cellular mechanisms or, more broadly, organic processes. However, within the narrative, these same works are presented as offering a holistic understanding of the given process. As a general but accurate example of this popular call for a holistic understanding, the article by *Nature Methods* (2020) that recognizes single-cell multimodal omics as the method of the year 2019 develops claims in its subtitle that single-cell multimodal omics measurement "offers opportunities for gaining holistic views of cells one by one". Then, while *de facto* the majority of single-cell sequencing studies are grounded in a reductionist approach with bottom-up explanations, they also advocate for a holistic view of their subject of study. In this context, "reductionism" is an epistemological approach that deduces processes, behaviors, or qualities of a system from the qualities or combinations of its components; it employs a bottom-up explanation, as higher levels of the biological system are explained by properties from the lower ones. Moreover, the use of the term "holistic" implies a comprehensive yet precise understanding of the mechanism, contextualized within a specific tissue; it often involves combining data from different levels of analysis as well (one can explicit this characterization from Polychronidou and *al.* 2023 for instance). However, it seldom involves top-down explanations, which consider the impact of structural properties or functional states of the whole system on subsystems. It also rarely addresses supra-cellular levels or combines datasets from sub- and supra-cellular analyses. (On these classical distinctions, cf. for instance Gilbert and Sarkar 2000; Mazzochi 2012 or Soto and Sonnenschein 2018).

This difference between the actual practice and the narrative is quite common in the literature. For instance, Mujal and *al.* (2022) investigated the differentiation from monocyte to macrophage in kidney cancer using mouse and human tissues. They employed single-cell RNA-sequencing analysis of tumors and discovered, among other findings, that immune cell differentiation was correlated with the amount of regulatory T cells in the mouse model. They also demonstrated that heterogeneity in macrophages cancer was correlated with regulatory T cell density. They asserted: "In this way, holistic analysis of monocyte-to-macrophage differentiation creates a framework for critically different immune states." In other words, this study highlights correlations between certain types of cells, their quantities, and certain physiological characteristics (such as density) based on RNA analysis. While the authors characterize their approach as holistic (perhaps because they identify correlations and integrate various analyses), their study, in practice, remains within a reductionist framework, drawing inferences from sequencing data.

In a similar vein, Park and *al.* (2021) try to enlighten how transcriptomic landscape of individual hepatocytes is altered in response to a high-fat diet, aiming for a "holistic characterization" of hepatocytes. While single-cell transcriptome studies have revealed that hepatocyte gene expression and function vary widely across their metabolic zonation, this paper emphasizes that the patterns of transcriptome alteration depend on the metabolic zones, with some responses being independent of the zonation profile. Thus, this study relies on a single-cell RNA-sequencing dataset and uses specific markers to define metabolic zonation profiles, employing a bottom-up explanatory approach. In this context, a holistic characterization entails deducing metabolic states from transcriptomic data, even though it struggles to account for the complex structure of liver tissue. As the authors themselves acknowledge: "it is possible that this [the given method] is an oversimplification of the complex histological architecture of the liver" (Park *et al.* 2021).

Single-cell practices include the description of molecular processes and clustering, and they predominantly employ bottom-up approaches without incorporating top-down perspectives. Then, single-cell practices do not meet their narrative, their advocacy of holism. This limitation to meet this goal is mainly understood by those who use these techniques as a technical limitation. And it is

the reason why corporations like 10x which produce single-cell tools develop new sequencing and analysis techniques in order to integrate and combine better data from different biological levels. As an example, they advertise a "Visium Spatial Gene Expression" that integrates total mRNA analysis for intact tissues sections with morphological context. The point is to better identify the connection between gene expression and morphological context, which means to better correlate the connection between different biological levels. It aims to better fulfil the holistic narrative, which entails a broader intention to combine and integrate data from various biological levels of analysis, to better justify the complex structures of biological organization.

Nevertheless, the mismatch between the narrative and actual practices persists for now. While technical development plays a part, the persistence of this mismatch may also be explained by a gap between practices and the conceptual framework in which experimental results are understood. In other words, single cell practices, *de facto*, take place in a reductionist approach but develop a "holistic" narrative that targets a comprehensive approach to living processes. Then, the mismatch between practices and narrative may also result from the underdevelopment of a conceptual framework that could read data results in a theoretical context that matches the narrative. Indeed, as it currently stands, this mismatch is epistemologically questionable because it results in a situation where, in practice, data continue to accumulate, yet the theoretical framework guiding their interpretation does not align with the intended narrative of holism.

Consequently, while experimental outputs must be analyzed within a conceptual framework to provide meaningful insights and achieve a comprehensive biological explanation – not merely an accumulation of data – this conceptual framework still appears to be under development. As Krohs and Callebaut elaborate: "The huge amounts of data produced by the genome projects were in fact collected almost free of any theoretical burden; as could have been expected, they turned out to explain next to nothing". A few pages later, they add: "'Omics', however, lack a theoretical framework that would allow to use these data sets as such (rather than just tiny bits that are extracted by advanced data-mining techniques) to build explanatory models that help understand physiological processes." (Krohs and Callebaut 2007, p. 184 and p. 208). In the case of omics studies, including single-cell analysis, the general framework for attributing meaning to data and contextualizing a biological explanation is not yet fully developed. This tension can also be perceived in Lähnemann and *al.* (2020): while this paper lists challenges that single cell data science must overcome and presents them as technical issues, it actually lists epistemological challenges to overcome (*e.g.*, how to deal with errors and missing data in the identification of variation from sequencing data, how to map single cells to a reference atlas, or how to integrate data across samples, experiments and types of measurement). Consequently, the gap between practices and the scientific narrative can be attributed to the fact that the theoretical framework that provides meaning to these practices is still in development. Moreover, as we will see in the next section, this theoretical framework itself seems to exhibit the same kind of mismatch.

3. Systems Biology as a Theoretical Approach to Single Cell Practices?

Systems biology seems to be the theoretical framework favored by users of single-cell analysis. As mentioned in the introduction, Tseng and Santra (2016) assert that systems biology represents the best theoretical approach for examining biological processes in single-cell analysis and, more broadly, omics. Similarly, Veenstra (2021) elaborates on how single-cell data are employed within a systems biology approach and how omics advances within a systems biology framework.

Systems biology seeks to explore how the functional properties of a living system, such as a cell or an entire organism, are brought about by the interactions among its components or parts (Boogerd *et al.* 2007). For instance, at a cellular level, systems biology examines the relationship between molecules and cells in two ways. Firstly, cells are viewed as organizing molecular systems to understand how functional properties arise from specific interactions between molecular processes. Secondly, cells are examined through their molecular properties to explain and predict cellular behavior. Thus, systems biology seeks to integrate bottom-up and top-down approaches in studying living systems. In a top-down approach, the focus is placed on molecular behaviors within living systems, regarded as wholes. In a bottom-up approach, emphasis is on molecular properties to understand how parts of the system interact (Boogerd *et al.* 2007). This combination of both approaches aims to apprehend biological phenomena on a broad basis, assuming that component behaviors within a living system are involved in nonlinear interactions. And yet, "in nonlinear interactions, qualitatively

new properties can arise, depending on the state the system is in, as the strength of the interactions vary with that state" (Boogerd *et al.* 2007, p. 11). Then, one may study molecular properties and behaviors in relation to the overall state of the system to gain a clearer picture of emergent and non-emergent properties of the living system.

In the narrative of systems biology, we observe that understanding living systems begins with decomposing and identifying parts of the system; the aim is to identify components and then observe how they interact. Veenstra describes the research progression in systems biology as akin to assembling a jigsaw puzzle. He outlines a three-step methodology, which involves identifying the pieces, organizing them into manageable parts, and finally assembling them to reveal the complete picture of the system operation (Veenstra 2021, p. 9). The method primarily focuses on the pieces and their assembly, often overlooking the examination of the constraints of the whole system or processes that involve entities at different levels of the system – as instantiated by Cornish-Bowden and *al.* (2004) with the example of metabolism. Consequently, this focus helps explain why, in practice, works claiming to be in systems biology often prefer bottom-up approaches. As Cornish-Bowden and *al.* assert: "Despite the current vogue for 'systems biology', this term is often little more than a euphemism for gathering ever more details on an ever larger scale, and not, as it should be, the study of biological systems as systems rather than collections of components" (Cornish-Bowden *et al.* 2004, p. 713).

Moreover, the narrative of systems biology strongly emphasizes molecular analysis. Whether employing a bottom-up or a top-down approach, the focus remains on studying molecular properties or behaviors to better define the relationship between molecular structures and functions. Molecular analysis is deeply entrenched in a well-established tradition that typically employs the bottom-up approach to study biological phenomena. This way of explaining biological phenomena based on molecular analysis often raises questions regarding whether these phenomena are epistemologically reducible to physiochemical phenomena (cf. Mossio and Umerez 2014). As a result, it explains why, in practice, works claiming to be in the realm of systems biology often favor bottom-up approaches.

Thus, systems biology does not fully achieve what its scientific narrative claims. There is a mismatch within the theoretical framework intended to support single-cell analysis, single-cell omics. In other words, just as the technique and method of single-cell analysis have not yet achieved what researchers set out to do according to their own narrative, similarly, systems biology has not yet fully addressed its objectives, despite being perceived as the privileged theoretical framework for single-cell analysis. Consequently, this is a situation in which the theoretical framework evolves alongside the techniques it supports. Additionally, due to this ongoing development simultaneously, the gap between usage and narrative may be perceived as resulting from a technical obstacle: if the gap remains unabridged, it is because omics technologies continue to evolve, particularly in elucidating the evolutions of biological processes in their spatiotemporal context. This is the argument put forward by Veenstra (2021, p. 7), who subsequently adds nuances:

> "While the progress made in omics research is exciting, a complete systems biology view that enables us to accurately predict how cells and organisms respond to either internal (e.g., gene mutations) or external (e.g., drug treatment) events is still in the distant future. Sometimes it appears this capability is beyond our reach. As we learn more about known components of the cell, new classes of biological molecules are discovered that have profound effects on how the cell functions." (Veenstra 2021, p. 9)

The promise of deeper understanding in biology appears to hinge on technological advancements, particularly in the detailed analysis of genetic material. It is therefore coherent that a bottom-up approach is still preferred, given the correlation between systems biology development and technological advancements. However, while the inability to fully implement a systems biology framework is often described resulting from technical obstacles, the underlying issue may be more theoretical in nature. As Callebaut claims, relying on Cornish-Bowden, "most papers in which the words 'systems biology' appear 'have surprisingly little to do with older notions of biological systems' such as the systems theory advocated by von Bertalanffy (1969) or the work of Robert Rosen (1934-1998)" (Callebaut 2012, p. 72). While advocating for a greater emphasis on functional aspects when theorizing biological phenomena, systems biology, in practice, still closely resembles traditional ways of doing biology. Functional and organismic perspectives, as previously emphasized by early pioneers of living systems biology, are still not as extensively incorporated as might be expected.

In summary, systems biology is presented as an operational theoretical framework for single-cell omics. Systems biology includes a variety of perspectives, yet the overarching aim is generally to

integrate both bottom-up and top-down approaches. This integration seeks to consider both organismic context and system decomposition, ultimately leading to a more comprehensive understanding of biological phenomena. However, the theoretical proposals applied in practice often fall short of the ambitious claims made by systems biology. This discrepancy is one reason why Callebaut advocates for "scientific perspectivism" which integrates different perspectives to enhance scientific practice and theoretical understanding. He also suggests that his scientific perspectivism could align with the principles of new mechanistic philosophy[b]. Building on this premise, could new mechanistic philosophy offer another theoretical framework for single-cell omics?

4. New Mechanistic Philosophy as a Theoretical Approach to Single Cell Practices?

New mechanistic philosophy originates from the classical mechanistic views of the 17th century, developed by figures such as Galileo and Descartes. This approach aimed to elucidate complex phenomena by breaking them down into interactions among their constituent parts, explainable by principles of motion. While this model is suitable for reducing various phenomena to physical laws, its application to biology raises questions about the reduction from biology to biochemical processes. To avoid such reductions while maintaining mechanistic views of biological systems, new mechanistic philosophy has emerged to provide a distinct explanatory framework inferred from the conceptual underpinnings of everyday biological practice. New mechanistic philosophy is advocated by scholars such as Craver, Darden, Bechtel, or Richardson; it encompasses a diverse range of research, and not all proponents share identical claims.

However, in general, new mechanistic philosophy regards living beings as natural systems organized into subnetworks of parts. The point is to identify parts of the system and how they are organized in order to understand how the activity of the whole system results from the activity of its organized parts. In other words, by adopting mereological perspective, a mechanistic approach considers that a living system is structured into parts and the performance of the system functions and subfunctions result from the way these parts interact. Bechtel and Richardson (1993) highlight two strategies employed in biology: decomposition, which involves physically or conceptually separating system components; and by localization, which entails precisely identifying the parts and their interactions that give rise to biological phenomena. These descriptive strategies are what new mechanistic philosophy consider to be explanations, which amount to the analysis of the constitutive parts of a system. This kind of explanation allows the prediction of future behavior, thereby facilitating anticipation of potential experimental modifications.

While classical views about mechanism vouch for reductionist explanations of living beings, Bechtel and Richardson advocate for non-reductionist ones. They contend that, in light of the complex and non-linear effects observed in living systems, it is essential to consider how these effects emerge from the interactions among their components. Living systems are viewed as integrated systems with emergent effects[c] and a multi-level explanation is necessary to properly justify the identification of complex causal mechanisms in living organisms. Moreover, since component parts and operations can be modified by elements both within and outside the system, mechanistic explanations may also incorporate a study of the system's environment and the top-down constraints that impact the system, particularly during development. Then, in these new mechanistic approaches that attempt to depict the complexity of natural systems from a non-reductionist perspective, explanation involves describing how a biological process works and determining the causal networks that enable the process to operate (cf. Bechtel 2006, p. 34). A phenomenon is considered explained when distinguishing features are identified within specific sections of the natural system and when these features are connected through a particular causal network. As such, new mechanistic philosophy appears like a suitable theoretical framework for single-cell omics to rely on.

However, opting for new mechanistic philosophy as a theoretical framework of single cell approaches would also lead to tensions. Considering that new mechanistic philosophy is based on how biological research works, addressing issues through the mechanistic approach would equate, in a certain way, to addressing issues about how biology, as a

[b] "Scientific perspectivism inaugurates 'a methodological victory for Leibnizian organicism over a one-sided Cartesian mechanicism" (Toulmin, 1982, p. 138) – while I simultaneously believe the former can be fully cashed out in terms of the "New Mechanistic Philosophy of Science" developed by Bechtel, Darden, Glennan, and others" (Callebaut 2012, p. 75).

[c] "We suggested that such behavior could be seen as 'emergent' at least insofar as the organization of the system, rather than distinctive contributions of its constituent components, determines systemic function" (Bechtel and Richardson 1993, p. xxxv).

way of experimenting, works. In this regard, a key epistemological consideration regarding mechanisms is their relation to reductionism. To what extent does new mechanistic philosophy truly integrate bottom-up and top-down approaches? Indeed, in mechanistic explanations, the integration of the different levels of organization sometimes remains problematic, particularly as the smaller component explanatory level remains the main level of analysis. As Nicholson explains: "This heuristic fragmentation of the organism into causal mechanisms, despite being necessary for its investigation, often comes at the expense of neglecting the way in which the organism as a whole influences the behaviour of its parts" (Nicholson 2012, p. 159). In other words, while new mechanistic philosophy claims to integrate the different levels of organization for explanation, *de facto*, the focus remains primarily on the more basic parts of the natural system. Additionally, the method of decomposing the natural network depends mainly on the structural properties of the system rather than its functional properties.

Consequently, new mechanistic philosophy may also exhibit a mismatch between what they aim to achieve conceptually and their actual conceptual limitations. At least, they often present ambiguities regarding reductionism and the integration of top-down and bottom-up approaches, mirroring challenges encountered in single-cell omics. Given that new mechanistic philosophy is grounded in biological practices and highlights their theoretical foundations, it only makes sense that they encounter similar theoretical uncertainties as some of those found in systems biology.

5. Conclusion

Single-cell analysis represents an unprecedented advancement in omics research. By elucidating the heterogeneity of cell populations or lineages within a sample, they enable a unique level of inference, facilitating comprehensive studies of biological phenomena. However, upon closer examination, a mismatch emerges between the aspirations of single-cell omics—such as achieving a framework that integrates data from different levels of analysis—and their actual experimental procedures. In particular, the scientific narrative of single-cell analysis advocates for a holistic view of biological processes, emphasizing the broader intention to integrate databases across various biological levels. However, in practice, it primarily involves the description of molecular processes and clustering and predominantly relies on a bottom-up approach, neglecting to incorporate a top-down perspective. As a result, a mismatch persists between the intended narrative and the current practices in single-cell analysis.

This mismatch calls for an explanation of the theoretical background of single-cell analysis. From a biologist's perspective, this gap between practice and narrative primarily arises because of technical challenges that need to be overcome. Despite the emergence of new technical methods for processing data, such as improved integration of morphological context, dynamic views of cell specialization, and enhanced sample preservation in microbiological sequencing, the theoretical framework and its underlying assumptions remain inadequately implicit. Some authors have suggested that systems biology is perceived as a suitable theoretical framework for understanding single-cell omics. However, both systems biology new mechanistic philosophy – which has been examined as potential suitable theoretical contexts – exhibit a similar mismatch to the one observed in single-cell omics. Overall, the emphasis on holism in narratives of omics and systems biology, along with the specific attention given to nonlinear properties in systems biology and new mechanistic philosophy, primarily reflect a principled opposition to reductionism. From this initial stance against reductionism, theoretical positions are still under development.

To question the mismatch and advance the development of a suitable framework for single-cell studies, it is imperative to explicit background assumptions. From an epistemic standpoint, the goal is to delineate these assumptions to justify the level of detail to be included and to clarify its relevance to the organismic context of explanation. Explicitly stating the theoretical background and, consequently, constructing a theoretical framework that incorporates organismic and functional perspectives are crucial endeavors aimed at achieving the comprehensive biological explanations that single-cell omics seek to provide. Additionally, from a philosophical perspective, there is a need to further develop conceptual mappings of reductionism, emergentism, and organicism to continually refine the narrative aimed at comprehensively explaining biological phenomena. There are also reasons to think that this kind of gap may be a recurrent phenomenon in science. The analysis realized in this paper therefore represents a high potential of generalization that could help improve understanding of scientific dynamics beyond the boundaries of single-cell omics.

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