**Guglielmo Militello, *Functional Integration. A Theoretical Enquiry into the Biological Unit of the Individual*, Springer Nature, Cham 2025, pp. 207, € 109.99, ISBN 9783031947438**

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The concept of 'functional integration' has long been hidden in plain sight. In *Functional Integration*, Guglielmo Militello demonstrates how this concept is a pervasive presence in many longstanding debates in biology and the philosophy of biology, yet it has never been explicitly addressed. For decades, it has been invoked as a seemingly solid foundation for other theoretical concepts across disparate schools of thought, while remaining largely unthematized. For its pivotal role, 'functional integration' calls for a more robust and specific definition. By explicitly adopting an organizational approach, Militello seeks to fill this gap. The primary objectives are to examine the organizational conditions for the cell's functional integration, distinguish differences between prokaryotes and eukaryotes, and propose a theoretical framework for their transition. For these reasons, the book has a twofold structure. The first half emphasizes the need for an investigation into the concept of 'functional integration' and its conditions (ch. 1-2). The second half develops this inquiry through several biological examples (ch. 3-8). The conclusion proposes a definition and highlights its implications in relation to other biological concepts.

In the first two chapters, the author focuses on the interconnections between 'functional integration' and other well-studied biological concepts. Militello provides an overview of life sciences and philosophical debates to investigate the role of 'biological integration' within them. It appears central in physiology, and, more recently, it has been introduced in molecular biology and evolutionary biology discourses, without being conceptualized as such. The same holds in philosophical debates, despite the well-established connection to discussions on biological functions, mechanisms, and individuality. For the author, such pervasiveness requires an explicit analysis. On the one hand, many of these fields accept an unquestioned and

indeterminate conception of functional integration as explanans; on the other hand, these discourses highlight several issues, such as how distinct mechanisms and functions are integrated and how physiological individuals become evolutionary unities. The second chapter demonstrates the necessity of 'functional integration' in conceiving living systems as autonomous. Militello analyzes conceptions from two perspectives, the autopoietic and the organizational ones. Despite its merits, the former, mostly focused on the system's self-reproduction, does not adequately explore the effective integration of mechanisms, nor does it address the relationship between physiological and evolutionary dimensions. The organizational framework conceives biological self-maintaining organization as closure of constraints, that is, characterized by interdependence among entities acting as constraints on each other's process of constitution. Militello notes that closure cannot overlap with 'functional integration', because the individual integration is not a mere coordination of biological functions. However, this framework elucidates how autonomy requires an integration of constitutive – i.e., metabolism, gene expression, and regulation – and interactive dimensions – i.e., minimal agency. Militello argues for the necessity of «complement[ing] the framework» (p. 43). He aims to directly thematize the 'functional integration' necessary for a system to be autonomous and at once a physiological and evolutionary individual.

The upcoming chapters address more biological content. Each begins with a review of the relevant philosophical and biological debates, followed by an analysis of how 'functional integration' is involved in real biological cases. The third chapter focuses on biological regulation, revealing its functional integration with the constitutive regime (C) analyzed above. Once activated, the regulatory mechanisms (R) play a functional role in shifting between Cs to adapt to new conditions, thereby enabling robustness. Conversely, second-order constraints, R, are influenced by constraints and signals produced by C. R and C must work in an integrated manner with signaling subsystems (S) – the signal transduction machinery and intra- and extracellular signals – in a causal loop describable as closure of constraints, as shown by key examples in prokaryotes. This interdependence enables co-evolution, as in eukaryogenesis, which requires increasing complexity in

both subsystem structure and their functional integration. The next chapter further develops this topic. Eukaryogenesis is a major evolutionary transition that entails the emergence of a new form of individuality. There is no consensus on the sequence of events or which competing explanations have been proposed. However, all proposed accounts agree on the thesis of engulfment of mitochondria and chloroplasts through metabolic mutualism. Militello notes that the evolution of proto-eukaryotic cells into both physiological and selective units required mitigation of conflicts. At the physiological level, metabolism, gene expression, and signaling mechanisms had to become functionally integrated. At the evolutionary level, the new individuality required an integrated reproductive system, made possible by mitosis. Furthermore, a new autonomous system emerges in this transition. In this case, the organizational framework helps in revealing the structural constraint that underpins both constitutive and interactive autonomy.

The last four chapters analyze in parallel biological phenomena involving prokaryotes and eukaryotes to understand the organizational conditions for eukaryogenesis. By contrasting the cases of biofilms and endosymbiosis, the fifth chapter focuses on the constraints and mechanisms involved in achieving functional integration. Biofilms exhibit a certain degree of physiological integration enabled by constraints such as the extracellular matrix. Militello argues that engulfment is required for the capability of reproducing as a unit, as in endosymbiosis. For instance, in the endosymbiotic relationship between *Tremblaya* and *Moranella*, the unique selective boundary and central control constrain the metabolic activities of both, introducing functional differentiation and collective reproduction. Although more demanding than biofilms, engulfment entails a reorganization that reduces the autonomy of each component but opens possibilities for structural and organizational novelties. The following chapter zooms in on internal spatial compartmentalization, comparing prokaryotes and eukaryotes. Compartments in prokaryotes create intracellular metabolic niches, permitting the isolation and transformation of toxic intermediates. These are closely connected to genetic and metabolic processes, being crucial for the cell's physiology. However, microcompartments contribute very little to C and do not require reorganizing the closure

between C, R, and S. Conversely, eukaryotic organelles elicit a deeper reorganization of the closure due to the level of functional integration and coordination. Organelles are involved in constitutive processes, their regulation, and several signaling pathways, requiring inter-organelle communication. If a closure is realized in both types of cells, in the eukaryotes, R, S, and C are distributed across various organelles, while in prokaryotes, they occur predominantly within the cytoplasm. Thus, eukaryotes need more complex intracellular communication mechanisms, which emerged with the development of intracellular membranes.

Chapter seven focuses on motility. By comparing symbiotic associations and eukaryotes, Militello examines how collective identity emerges from higher-level control of the interactive autonomy of the parts. Inhibition of component movement is realized in association. However, control of motility is crucial in the transformation of proto-organelles, enabling the system to adapt to different conditions from those of free-living organisms. In the transition to eukaryotes, organelles lose autonomy to allow the functional integration of the whole. Indeed, cytoskeletal-driven displacement plays a distinctive organizational role in the whole constitutive regime and intracellular communication. The eighth chapter compares binary fission in bacteria with unicellular mitosis. It aims to elucidate the degree of functional integration required for the reproduction of an evolutionary individual. Specifically, nutrient availability, metabolic control, and spatiotemporal coordination appear to influence bacterial reproduction. Although in a more complex way, analogous factors can be found in mitosis. Thus, for Militello, an organizational closure among system-level reproduction, metabolic, and developmental processes is required to count as an evolutionary unit.

In conclusion, Militello proposes a definition of 'functional integration' that rejects pluralism in accounts of individuality. The starting point is the reference to a degree of functional interdependence among the parts enabling systemic behaviors. Previous reflections have shown that collective individuals and new cohesive individualities differ in specific spatial constraints, system-level regulation, spatiotemporal coordination, and system-level reproduction. These are the four dimensions in which one can evaluate functional

integration. Furthermore, these can be seen as parameters that can underlie the definition and evaluation of both biological individuality and autonomy.

Militello puts the spotlight on the concept of 'functional integration' and does so effectively. He maintains a clear commitment to the organizational perspective while engaging with the most influential views in the debate. By addressing most of the open questions, he skillfully sets the conceptual issue within both philosophy and biology. The comparative analysis of concrete biological cases strengthens his framework and connects it directly to current scientific research. With its clear organization into chapters focused on specific concepts and issues, *Functional Integration* serves as a practical and valuable resource that has the potential to significantly impact biological research. Thanks to Militello's conceptual clarification, the degree of the system's functional integration can be treated as something comparatively evaluable. However, the book is mostly focused on prokaryotes and unicellular eukaryotes. This narrow scope is justified by the scientific significance and richness of the extensive research body on these organisms and eukaryogenesis (p. xiv). Such a strategy allows the author to examine functional integration both as explanans and as explanandum through precise case studies. These cases effectively clarify distinct concepts in biological descriptions, highlight the role of functional integration, and reveal further implications.

Nevertheless, the conceptual framework needs to be applied beyond unicellular organisms. It is not just a matter of completeness. The cell is defined as the «fundamental unit of life» (p. xiii) that exhibits functional integration. How to relate this principle to other major evolutionary transitions? The framework needs to be tested in these higher-level cases. Multicellularity could challenge the distinction between internal and external environments or constitutive and interactive dimensions of autonomy. The four dimensions identified by Militello (p. 199) as those within which functional integration can be evaluated are displayed both by nested cells and by higher-level systems. The framework, therefore, provides a promising guide for this comparison, though the task still lies ahead. This is not a deficiency, but the next necessary step, in which the same book can be a helpful tool beyond organizational approaches.