Organicist and Mechanistic Metaphors in the Early Days of Neuroscience*

Metáforas organicistas y mecanicistas en los comienzos de la Neurociencia

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Abstract

In his work, Michael Ruse underscores the significance of metaphors in science, with a particular focus on the "abyss" between mechanistic and organicist metaphors in the history and practice of biology. Ruse posits that the Darwinian revolution involved a radical "metaphor shift" in biology, transitioning from organicism to mechanism. In this article, I set out several objectives (i) to assess whether the neuronist revolution, pivotal in the inception of neuroscience, involved a shift from an organicist metaphor to a mechanistic one; (ii) to highlight the indispensable influences of organicist metaphors in Cajal's neuron doctrine; and, consequently, (iii) to challenge the idea of an abyss between mechanistic and organicist metaphors, at least, in neuroscience.

Keywords: metaphor - organicism - mechanism - neuron doctrine - Santiago Ramón y Cajal - evolution

Resumen

En sus investigaciones, Michael Ruse destaca la relevancia de las metáforas en la ciencia, centrándose en el "abismo" entre las metáforas mecanicistas y organicistas en la historia y práctica de la biología. Ruse argumenta que la revolución darwiniana representó un cambio radical de metáfora en biología, pasando del organicismo al mecanicismo. En este artículo me propongo: (i) evaluar si la revolución neuronista, crucial en el surgimiento de la neurociencia moderna, implicó un cambio de una metáfora organicista a una metáfora mecanicista; (ii) destacar las influencias esenciales de las metáforas organicistas en la doctrina de la neurona de Cajal; y, en consecuencia, (iii) cuestionar la noción de un abismo entre metáforas mecanicistas y organicistas, al menos en el ámbito de la neurociencia.

Palabras clave: metáfora - organicismo - mecanismo - doctrina de la neurona - Santiago Ramón y Cajal - evolución

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1. Introduction

In several papers and books, Michael Ruse has argued for the importance (even the centrality) of metaphors in the history and practice of science. He has praised Thomas Kuhn's idea that scientific revolutions involve a change in metaphor (Kuhn 1993, Ruse 2021). He has insisted that the Scientific Revolution from the 17th century was a change in root metaphors, from organicism (world-as-an-organism), to mechanism (world-as-a-mechanism). Despite rejecting Kuhn's elucidation of scientific revolutions as world changes, Ruse has endorsed a rather strong version of the incommensurability thesis, namely, that there is a "total breakdown in understanding and sympathy", "an abyss", between alternative root metaphors (Ruse 2021). Since "metaphors are like the blinkers on horses", endorsing one metaphor over another would be a matter of faith commitment, since the relevant topics would be "out of the realm of discourse or understanding" (Reiss & Ruse 2023). Concerning the history of biology, in particular, Ruse (2004) defends the idea that the Darwinian revolution involved a radical change of metaphor, again, from organicism to mechanism. At the same time, he has recently interpreted the "new" biology (i.e., evo-devo) as a swing of the pendulum towards the organicist metaphor (Reiss & Ruse 2023).[1]

Contrary to the early logical empiricist emphasis on the definitional conception of theoretical concepts, some philosophers have considered most scientific concepts to be not definable because they have an "open-texture" (Waismann 1945), meaning that there is no set of empirical methods for determining the concept that provide necessary and sufficient conditions for the application of the concept. Concepts are not delimited in all possible directions, the set of methods for determining the extension of the concept is not established in advance. Similarly, many philosophers that studied metaphor in science noticed that metaphors are "in-explicit" (Kuhn 1993) or "open-ended" (Boyd 1993), in that they do not admit substitution by any exhaustive list of similarities and analogies between features of the primary and secondary subjects; some analogies are not yet discovered, others are not fully understood. Furthermore, at different times in the history of a scientific discipline, different senses, or semantic aspects of a metaphor might be emphasized.

That is the case with the organicist and the mechanistic metaphors in biology. There are many different understandings of organicism and mechanism, and it would be futile to attempt a definition of them. Ruse (2021) traces the genealogy of organicism back to Plato's *Timaeus* and the thought of Aristotle. In a more relevant sense, organicism has its first articulation in Kant's *Critique of Judgment* (1790), and its reception in the natural philosophies of Schelling, Goethe, Haeckel and Spencer. Robert Richards (2004) has argued that this romantic, organicist tradition had a great influence on Darwin's thought, via the influence of Alexander von Humboldt. Ruse (2004, 2005) has denied Richard's interpretation, and argued that Darwin's work striked a key blow for mechanism. In the Darwinian Revolution, the machine metaphor has, at least, two senses: "the world as a whole as a machine" and "individual parts as mechanical contrivances". The first sense was vindicated by Darwin

[1] The concept of metaphor and the role metaphors play in science have been extensively studied in the philosophy of science (Black 1962, Hesse 1966). A common element in various characterizations of metaphors in science is the core intuition of Black's interactive conception of metaphor (1962), wherein a metaphor neither assumes nor provides an exhaustive list of the respects in which the subjects juxtaposed by the metaphor are similar. Expanding on the interactive view, Hesse (1966, p. 192) notes that as long as a model or metaphor is under active consideration as a component in an explanation, the extent of the comparison remains uncertain; it is precisely in this extension that the fecundity of the metaphor or model may reside. According to Boyd (1993), this "openness" or "lack of explicitness" in metaphor bears a significant parallel to the process by which scientific terms like "mass," "electricity," or "heat," are introduced and subsequently employed, as it is uncommon to acquire a list of necessary and sufficient criteria to determine the referents of the corresponding terms. Kuhn (1993) acknowledges this open-textured nature of metaphors in science, and Michael Ruse utilizes the metaphor concept synonymously with Kuhnian paradigm. In this work, we will address metaphors in the sense proposed by Ruse.

by showing how organisms could evolve by blind, unguided, causal laws. The second sense was vindicated in Darwin's functional biology, for example, in his analysis of fertilization of orchids (Darwin 1862, Ginnobili 2011).

In this article, I would like to draw attention to an episode in the early history of modern neuroscience, namely, the neuronist revolution, and to ask whether it also involved a shift from an organicist metaphor to a mechanistic one. In this paper, "neuronist revolution" refers to an episode of late 19th century controversy in histology or microscopic anatomy of the nervous system between reticularists (von Gerlach, Golgi, early Kôlliker) and neuronists (His, Forel, Ramón y Cajal, van Geguchten, Waldeyer, late Kôlliker), that led to the foundation of the neuron doctrine in modern neuroscience (Shepherd 2015, Mazzarello 2018, Parker 2018). To answer this question, at least two typical but different senses of the organicist metaphor in the 19th century are relevant.

1. *Holism*: The organism as a whole explains (because it precedes) the presence and activities of the parts.
2. *Internalism*: Biological change (ontogeny and phylogeny of the organism) is internally guided and progressive, in the direction of increasing complexity, and the arrival point of this progress is the adult human being.

The neuronist revolution appears to exemplify Ruse's thesis regarding the Scientific and Darwinian revolutions—specifically, the shift from organicism to mechanism through a change in metaphor. However, I would like to point out the indispensable presence and influence of organicist themes in Cajal's neuron doctrine. In particular, Cajal, like most of his Spanish colleagues, was an evolutionist under the influence of Ernst Haeckel and Herbert Spencer. In particular, Cajal endorsed a very strong version of *Internalism,* to the point of an explicit commitment to Haeckel's recapitulation principle, or biogenetic law, according to which the ontogenetic development of an organism recapitulates its phylogenetic evolution.

In fact, once you realize it, Cajal's organicism becomes evident in many of his methodological decisions, his drawings of neuronal forests, and, of course, in his metaphors concerning neuron organization and function. This much is enough to call into question the idea that the neuronist revolution, at the dawn of neuroscience, was an all-or-none, win-or-defeat change from organicism to mechanism. While some aspects of the organicist metaphor were abandoned, other aspects were decisive for the revolution.

In this paper, I will proceed as follows. In section 2, I argue that the neuronist revolution required the rejection of a version of Holism. In section 3, I show that Cajal was fully committed to Internalism by analyzing Chapter 1 of the first volume of Cajal's main work, *Textura del sistema nervioso del hombre y de los vertebrados* (Cajal 1899). Finally, I conclude that the idea that scientific revolutions involve a change from organicism to mechanistic worldviews is historically inaccurate, at least for the history of neuroscience.

2. The Neuronist Revolution and Holism

Numerous philosophers, historians, and neuroscientists concur that modern neuroscience embodies a mechanistic perspective when explaining the nervous system (Machamer, Darden & Craver 2000, Craver 2007, Bechtel 2008). In contemporary mechanistic neuroscience, scientific explanations are required to delineate mechanisms that operate across various levels of organization (Craver 2007). To accurately describe a mechanism, a scientific model must initially identify the phenomenon the mechanism underpins (Glennan 2017). Typically, this mechanistic phenomenon is a combination of a target system and specific behaviors in which the target system is involved. Subsequently, the model must depict the constituent entities, their activities, and the organizational features of the target system, all of which constitute the underlying mechanism driving the phenomenon of interest. These entities and activities often span multiple levels of organization in nature, ranging from the atomic and molecular scales to the intricate networks within the brain and entire organisms. Consequently, the quest for mechanisms and their components necessitates the integration of experimental methods, empirical findings, and conceptual resources from diverse scientific fields, such as molecular and cellular biology, neurophysiology, computational neuroscience, experimental psychology, and the cognitive sciences.

Surprisingly, mechanistic philosophers and historians seldom cite the scientific contributions of Cajal as a case study in modern mechanistic neuroscience. Patricia Churchland (1989, 29) argues that Cajal was fundamentally "mechanistic," rejecting the notion of "vitalism," and instead proposing that electrical induction (rather than "mystical forces and substances") could explain all communication between neurons. In their review, Malanowski & Craver (2014) highlight Cajal's groundbreaking assertion that dendritic spines were genuine entities, not mere artifacts of the Golgi's staining technique. This finding posed a clear, teleological question: "Why do neurons have spines?" that significantly advanced the quest for understanding neural mechanisms. Catherine Stinson & Jacqueline Sullivan (2018) praise Cajal's work as "an excellent example of the decomposition strategy at work": the brain is made up of anatomically discrete cellular units, or neurons, and different types of neurons construct different organized patterns in the nervous system.[2]

Are there compelling reasons to consider the neuronist revolution in neuroscience, as a significant triumph of the mechanistic metaphor over the organicist metaphor, akin to the Darwinian revolution in Ruse's perspective? It is quite established that the neuronist revolution required the abandonment of a version of *Holism* about the explanation of the nervous system (Cimino 1999, Mazzarello 2018). By 1860, it became apparent that nervous tissue comprised cell bodies and nerve fibers. However, the precise relationship between these components remained elusive. Nerve cells exhibit a branching structure, with some branches emanating from the cell body and extending considerable distances, intricately intertwining with branches from neighboring cells. During this phase of microscopic exploration of the nervous system's intricacies, the challenge lay in developing a staining technique for nervous tissue that could facilitate a clear and precise visualization of its constituent elements under the microscope. This endeavor necessitated the comprehensive visualization of the entire nerve cell, encompassing even the termination points of its most remote branches. Simultaneously, it entailed the ability to differentiate each individual cell amidst the intricate web of cellular structures (DeFelipe & Jones 1992, Mazzarello 2010, Fiorentini 2011).

The pivotal advancement in understanding the nervous system occurred through the introduction of a staining method for nervous tissue by the Italian histologist Camillo Golgi. Golgi's technique, based on silver nitrate and famously known as the 'reazione nera' or black reaction, marked a turning point in the field of histology. This innovative method, often regarded as "revolutionary" by numerous science historians (Cimino 1999, Shepherd 2015, Bentivoglio *et al.* 2019), selectively stained cell bodies, dendrites, and axons of a few cells at a time, rendering them black against an amber background. Golgi first outlined this method and its initial results in a concise description published in the Italian Medical Gazette (Golgi 1873). Subsequently, in an article, he delved into the cellular morphology of the olfactory bulb in dogs, presenting an extraordinary plate that provided the inaugural visualization of the complete architecture of a cerebral region (Golgi 1875).

Equipped with the black reaction, Golgi made a groundbreaking discovery: cell dendrites terminated freely, lacking anastomosis and continuity with those of neighboring cells. This observation

[2] Stinson & Sullivan (2018) represents the best mechanistic analysis of Cajal's contribution to modern neuroscience. For a recent, critical review of their mechanistic interpretation of Cajal, see Barberis (2018).

challenged the concept of a *dendritic network*, advocated by former reticularist Joseph von Gerlach. However, Golgi approached this discovery conservatively. If dendrites couldn't form a network, he concluded, they likely didn't serve a neural function. This inference was rooted in the reticularist metaphor of the network, that is, that only a network could generate nervous function. Golgi proposed an alternative role for dendrites: they had a trophic function, akin to roots sustaining the cell. Golgi made a second discovery: the axon of a nerve cell doesn't proceed uniformly but bifurcates at a distance from the cell body, giving rise to collateral branches at right angles. For Golgi, this finding offered an elegant, yet conservative, resolution to the reticularist dilemma. The core of the nervous system undeniably formed a continuous and intricate network; there was no other possibility. However, this network comprised terminal ramifications of cellular axons. Hence, Golgi suggested a network of axons instead of dendrites. Golgi thoroughly expounded on this concept in his acclaimed atlas of nervous system anatomy, published in (1885), establishing a cornerstone in the understanding of neurophysiology.

From a physiological standpoint, Golgi advocated a form of *Holism* according to which the diverse 'provinces' of the nervous system shared a singular structure—a diffuse, continuous, and intricate *network* formed by the anastomosis of axons from distinct cells (Mazzarello 2018). This comprehensive neural network, in its entirety, constituted the genuine organ of perception, thought, and action. Golgi's reticularist hypothesis, which posits that the nervous system forms a multinucleated syncytium, a diffuse network of axo-axonal connections, suggests that functional locations and privileged directions for the nervous impulse cannot be distinguished. In his 1906 Nobel speech, Golgi stated: "I have never been able to abandon the idea of the unitary action of the nervous system." He acknowledged his debt to Marie-Jean-Pierre Flourens (1824), who stated that "the cerebral cortex functions as an indivisible whole, housing an essentially single faculty of perception, judgment, and will, the last refuge of the soul." This idea is taken up by Flourens, ultimately, in Cuvier's principle of the conditions of existence, according to which, since all parts of an organized body exert "mutual action upon each other and cooperate toward a common end, which is the maintenance of life" (Cuvier 1798, p. 5), then the true condition of existence of a living being is that its parts work together for the good of the whole (Caponi 2004).

Spanish anatomist Santiago Ramón y Cajal embraced both Golgi's histological methods and anatomical discoveries and consequently absorbed the impact of the reticularist crisis but interpreted those discoveries through a revolutionary conceptual framework. Part of Cajal's criticism was metascientific in nature, and attacked explanatory *Holism* directly:

> The hypothesis of the network once being accepted, nothing is easier than the objective study of a group of neurons or of the behaviour of the terminations of a bundle of fibres; the whole matter is reduced to taking for granted that the final axonic branch lets, after several dichotomies, are lost or disappear in the aforesaid interstitial network; in that sort of unfathomable physiological sea, into which, on the one hand, were supposed to pour the streams arriving from the sense organs, and from which, on the other hand the motor or centrifugal conductors were supposed to spring like rivers originating in mountain lakes. This was admirably convenient, since it did away with all need for the analytical effort involved in determining in each case the course through the gray matter followed by the nervous impulse. It has rightly been said that the reticular hypothesis, by dint of pretending to explain everything easily and simply, explains absolutely nothing; and, what is more serious, it hinders and almost makes superfluous future inquiries regarding the intimate organization of the centres. (Cajal 1923, p. 336; my emphasis)

Despite the reality of axon collaterals, Cajal remained uncertain about whether they eventually lose their individuality in a diffuse network. Having mastered and improved the black reaction, he never observed anastomosis or tissue continuity between axon terminations of nerve cells in any cerebral region, species, or developmental stage (Cajal 1888). Hence, by the principle of parsimony, it is necessary to conclude that axons can fulfill their neural transmission function even when terminating freely, without forming a network. Secondly, and for the same reasons, dendrites can serve a neural function, despite Golgi's discovery that they terminate freely. This delineated the contour and main anatomical components of the nerve cell, or *neuron,* in Waldeyer's (1891) terms: a cell body from which both dendrites and axons emerge in various configurations, all serving a neural function, and communicating with other cells through contact points.

Finally, the microscopic examination of how axon terminals were positioned in relation to dendrites or the cell body of neighboring cells, such as the way stellate cells' tufts in the cerebellum envelop the bodies of Purkinje cells like a basket, inspired Cajal (1891) to propose a physiological generalization concerning the direction of nerve impulse communication within and between cells, known as the "law of functional polarity" (Cajal 1893). According to this principle, the nerve impulse consistently travels from the dendrite, serving as the input mechanism, to the axon terminal, acting as the output; subsequently, the impulse is transmitted to the dendrite or cell body of the next neuron. This principle of functional polarity provides an algorithm for translating morphology into function (Mazzarello 2018).

Even if the metaphor of the cell as a machine is much more predominant in the 20th century, especially following developments in molecular biology, Cajal is particularly organicist in his understanding of cell theory in general. Sherrington, remembering Cajal's *Croonian Lectures* (Cajal 1894), had already noted that:

> [a] trait very noticeable in him was that in describing what the microscope showed he spoke habitually as though it were a living scene. (…) The intense anthropomorphism of his descriptions of what the preparations showed was at first startling to accept. He treated the microscopic scene as though it were alive and were inhabited by beings which felt and did and hoped and tried even as we do. It was personification of natural forces as unlimited as that of Goethe's Faust, Part 2. A nerve-cell by its emergent fibre "groped to find another"! We must, if we would enter adequately into Cajal's thought in this field, suppose his entrance, through his microscope, into a world populated by tiny beings actuated by motives and strivings and satisfactions not very remotely different from our own. He would envisage the sperm-cells as activated by a sort of passionate urge in their rivalry for penetration into the ovum-cell. Listening to him I asked myself how far this capacity for anthropomorphizing might not contribute to his success as an investigator I never met anyone else in whom it was so marked. (Sherrington 1949, pp. xiii-xiv)

Reynolds (2018), analyzing the role of metaphor in the creation of modern cell biology, correctly argues that the concept of the cell has been associated with various metaphors throughout its history and that, since Schwann (1839), many have conceived the cell as an elementary organism. In his *Elementos de Histología Normal y Técnica Micrográfica* (Cajal 1895), Chapter III, that deals with the concept of cell and cell theory in general, Cajal states that: "The cell is a miniature organism, a being endowed with its own life and in charge of the performance of a particular activity in the vast federation of the body of plants and animals."

3. The Neuronist Revolution and Internalism

Although Cajal rejected Holism, there are compelling reasons to argue that his approach is inherently organicist, specifically in his wholehearted endorsement of another organicist concept: Internalism. This second sense of organicism is related to biological change, development and evolution. Several historians of neuroscience consider that Darwin's influence on Cajal is evidenced in the evolutionary approach that he develops in "Structural plan of Neural Centers in the Animal Series", chapter 1 of *Textura del sistema nervioso del hombre y de los vertebrados* (Cajal 1899). Thus, Monte Ferreira, Nogueira and DeFelipe (2014) hold that "[…] one of the most interesting aspects of [Cajal's] studies was his innovative capacity to interpret structure as being the result of evolutionary mechanisms, i.e., natural selection." Furthermore, Swanson (2007, p. 356; my emphasis) claims that:

> The first chapter of Santiago Ramón y Cajal's greatest work […] is a brilliant manifesto for modern neuroscience—crystallizing the paradigm shift that allowed a deep cellular explanation of macrostructure—that has been refined and modified extensively during the last century with advances in cell and molecular biology, but not replaced by a qualitatively new and more powerful global systems model.

However, Cajal was not precisely Darwinian in Ruse's mechanistic interpretation of Darwinism. He marveled at the complexity and sophistication of design features in human (and non-human) neuroanatomy, leading him to believe that evolution could not solely result from blind, non-teleological causes and forces (Cajal 1899). He found anomalies to natural selection mechanisms, for example, in the evolution of paired eyes in worms:

> We must agree, however, that it is almost impossible to conceive the concurrence or formative mode of certain initial variations which represent the starting point of evolution. Thus, for example, it is difficult to understand why the pigmented spots or rudimentary eyes of worms (Turbellaria, Trematoda, Hirudinea, etc.) are round, paired, and residing precisely over the skin that covers the supra- esophageal ganglion, and not other ganglia. Or why a lenticular epidermic thickening appeared, during that period, in front of the pigmented spot with a radius, refractive index, etc. seemingly calculated to project a distinct image on the expansion of the optic nerve. We must confess that, even applying the principle of natural selection, it is impossible to explain satisfactorily these marvelous devices of relation with the environment which are, as we have said, the probable efficient cause of the superior dynamic hierarchy and directing role of the cephaloid ganglion, over all other ganglionic foci. (Cajal 1899, pp. 6-7; my emphasis)

It is worth noting that, in his work "Reglas y Consejos sobre Investigación Científica" published in 1897, Cajal vividly recalls the sensation he experienced upon observing the phenomenon of blood circulation for the first time, which fueled mechanistic inclinations in his youth:

> I was in my junior year of medical studies and had learned about the details of this phenomenon from various books, although my interest had not been aroused particularly, and I had given it little thought. However, one of my friends, Mr. Borao (a physiology assistant), was kind enough to demonstrate the circulation in the frog's mesentery to me. During the sublime spectacle, I felt as though I were witnessing a revelation. Enraptured and tremendously moved on seeing the red and white blood cells move about like pebbles caught up in the force of a torrent; on seeing how the elastic properties of red corpuscles allowed them suddenly to regain their shape like a spring after laboriously passing through the finest capillaries; on observing that the slightest obstruction in the stream converted potential spaces between endothelial cells into actual spaces providing the opportunity for minor hemorrhage and edema; and finally, on noticing how the cardiac beat weakened by curare slowly propelled the obstructing red corpuscles, it seemed as though a veil had been lifted from my soul, and my beliefs in I know not what mysterious forces I had attributed the phenomena of life receded and vanished. In my enthusiasm I exclaimed the following, not knowing that many others, including Descartes especially, had done so centuries before: "Life seems to be pure mechanism. Living bodies are hydraulic machines that are so perfect they can repair the damage caused by the force of the torrent moving them, and even produce other similar hydraulic machines through the mechanism of reproduction." I am absolutely convinced that the vivid impression caused by this direct observation of life's internal machinery was one of the deciding factors in my inclination to biological research. (Cajal 1897, pp. 63-64)

However, the mature Cajal immediately clarifies that:

> Today I do not subscribe unreservedly to this mechanistic concept, nor do I adhere strictly to the physicochemical interpretation of life. The origin and morphology of cells and organs, heredity,

> evolution, and so on include phenomena that depend on incomprehensible absolute causes, notwithstanding the vaunted promise of Darwinism and the postulates of Loeb's school of biochemistry. (Cajal 1897, p. 75; my emphasis)

Thus, while it is true that Cajal's doctrine in *Textura…* is committed to evolutionism, it is also true that it presupposes several ideas of 19th century biological thought that are not exactly Darwinian. Despite being a crystallization of the paradigm shift that leads to modern neuroscience, Cajal's textbook is also a creative reception of several 19th century evolutionary, organicist approaches and metaphors. There is a 40 y-old tradition in historiography concerning the peculiar diffusion of evolutionary thought in the academic/scientific Spanish milieu (Glick 1982). Evolutionism was introduced in Spain not only through the works of Darwin (1859, 1872), but mainly through the syntheses of organicist thinkers like Ernst Haeckel (1866) and Herbert Spencer (1864).

Cajal's "*Textura…*" endorses the idea of the phylogenetic scale as a scale of complexity, i.e. the idea that there is a universal trend in evolution from simple ("homogeneous") to complex ("heterogeneous") when comparing "lower" with "higher" animals. The first unequivocal manifestation of a nervous system is present already in polyps, comprising two classes of neurons: motor and sensory cells. Some progress occurs in the nervous system of worms, which is also formed by the two fundamental neurons, sensory and motor, but a new component intervenes here for the first time, the intermediate or association neuron, that propagates the impulse to neurons residing in other ganglia. Thus, the animal is able to react to the excitation received at any site on the skin by activating the totality of the locomotor apparatus. On ascending the animal scale, a new link appears intercalated between sensory and motor neurons in the vertebrate nervous system: the psychomotor neuron. Memory, voluntary action and intelligence emerge with it.

This trend towards complexity in the animal series leads Cajal (1899, p. 8) to the formulation of two laws of nature that apparently have presided over the evolution and perfecting of the nervous system.

First Law: *Multiplication* of neurons or processes, with the goal of increasing the associations among various organs and tissues.

Second Law: Morphological and structural *differentiation* of neurons to better adapt them to their transmitting role.

Cajal's first and second laws of morphological progress (Multiplication and Morphological Differentiation) are explicitly taken from Spencer's (1863) *Principles of Biology*. Remember that Ruse considered that Herbert Spencer is "the perfect exemplar" of the organicist kind of thinking, according to which "Just as an organism grows fueled by its own internal causes, so Romantic evolutionism saw a kind of internal force or pressure driving the developmental process" (Ruse 2021). Cajal's first law of multiplication is related to "the progressive increase in the number of epidermic, muscle and gland cells as we ascend in the animal series" (Cajal 1899, 8). The second law of morphologic differentiation explains the diversification of neuronal morphologies (unipolar, bipolar, multipolar) and, thus, of interneuronal connections.

One of Cajal's most original contributions in *Textura…* is his *Third Law of Economy*, which is purported to explain some evolutionary trends towards simplicity (instead of complexity) that Cajal found in the animal series.

> Third Law. Unification or concentration of neural masses, or law of economy of the transmitting protoplasm, and conduction time. […] According to a good doctrine of evolution, and even more, accepting the principle of natural selection as the efficient cause of morphologic and functional progress, it is mandatory to justify all structural phenomena appearing in the phylogenetic and

> ontogenetic series, by the actual usefulness to the organism. The utilitarian goal pursued by Nature [in the third Law] is simply economizing protoplasm [combined with the economy of space provided by the development of large cavities destined to lodge the viscera]. (Cajal 1899, p. 8)

The Law of Economy constitutes an insight into the governing factors behind the vast array of forms, sizes, positions, and directions of neurons and nerve fibers. It provides potential explanation for the seemingly arbitrary variations in the emergence points of axons (such as in crook-shaped cells of the optic lobe of birds) and for the displacement or migration of cell bodies during evolution and development (as observed by Cajal in sensitive ganglion cells). Additionally, the Third Law shed light on phenomena such as the clustering of sensitive and motor neurons in ganglia, the Y-shaped bifurcations (rather than T-shaped) of nerve fibers upon reaching the posterior cord, and the origin points of axons within the dendritic arborizations of cerebellar grains.

Let's reconsider the vertebrate ganglion cell. Cajal studied the changes in placement and morphology of sensitive ganglion cells in the animal series. In ontogenetic and phylogenetic evolution, sensitive ganglion cells shifted from a bipolar shape to a monopolar configuration, indicating a transition from a relatively complex morphology to a simpler form (Fig. 1).

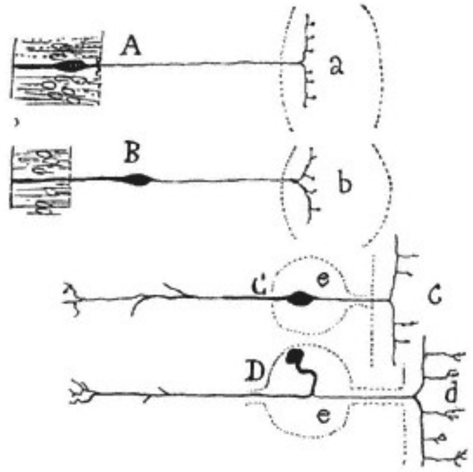

Figure 1. A scheme that shows the changes in placement and morphology of sensitive ganglion cells in the animal series. (A) Sensitive cells of the earthworm; (B) sensitive cells from mollusks; (C) sensitive cells from fish; (D) sensitive cells from mammals, birds, reptiles, and frogs. Taken from Cajal (1929, p. 388).

A comparison between the schemes in Figure 2 reveals disparities in wiring length and, consequently, conduction time, between the ganglion cells of fish and those of higher vertebrates (mammals). The bipolar form of neurons in scheme 2A necessitates winding paths for nerve and peripheral expansions across cell bodies, prolonging the excitation route. In Figure 2B, representing a mammal, cell bodies have relocated to the periphery, distancing themselves from the ganglion's central region, where sensitive conduits are organized in straight bundles.

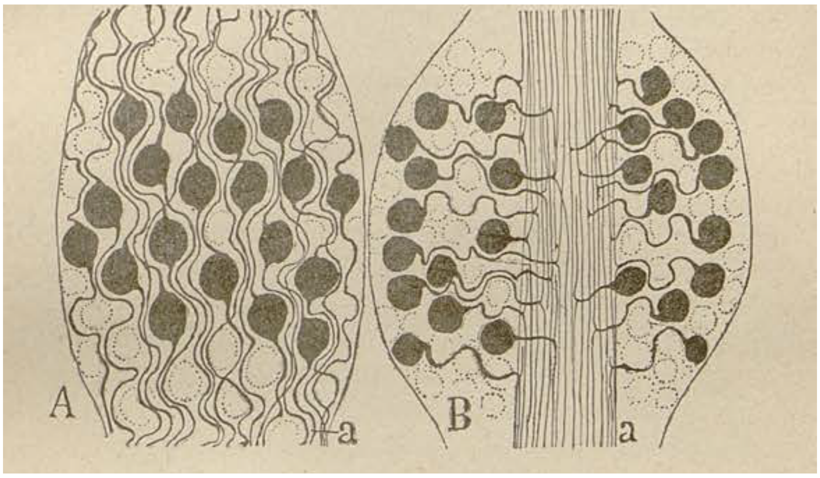

Figure 2. Diagrams of the structure of the spinal ganglia.—A, spinal ganglion of a fish (stingray); B, spinal ganglion of a mammal (cat); a, path followed by sensory excitation. Taken from Cajal (1891, p. 11).

The arrangement in Fig. 2, according to Cajal, represents the most comprehensive and ingenious application of the law of economy of conduction time. Such a disposition benefits animals, given the evident advantage of high-speed conduction of tactile and painful sensations, crucial in the struggle for survival among higher vertebrates.

To add another organicist dimension, Cajal's ontogenetic method, arguably his most significant technical contribution, is rooted in Haeckel's theory of recapitulation, also known as the 'biogenetic law' (1866), according to which "the ontogeny of nervous tissue reproduces, in abbreviated form, with some simplifications and leaps, its phylogeny, and that both in relation to the neuroglia and the nervous cell" (Cajal 1923). Recall that, according to Ruse (2021), Haeckel's biogenetic law stressed the organicist nature of his thinking. Furthermore, in Haeckel's tree of life, human beings are the supreme point of the evolutionary process. With sophistication or complexity as a criterion, we humans are of greater value than any of the other organisms, an idea that, according to Ruse (2021), "is the whole point and purpose" of the organicist metaphor.

Crucial to Cajal's success was his concept of pairing his "double impregnation" technique, involving silver nitrate and potassium dichromate, with a more intellectually driven approach he termed the "ontogenetic or embryological method." This method involved studying young embryos, which he recognized as more favorable subjects. Cajal got acquainted with Haeckel's fundamental biogenetic law while preparing for his second Anatomy chair examinations (Laín Entralgo 1949). Another possible source is Luis Simarro, who was surely the introducer of evolutionary theses in Spanish histology, especially after his time in Paris where he studied with Mathias Duval (Puig-Samper *et al.* 2017). After attending a course by Duval on "the embryogenesis of the brain", Luis Simarro took the following note: "the embryonic development of each organ system offers in its successive phases an exact correspondence with the defined forms of the adult animals of the species inferior that of the embryo" (in Salá Catalá 1987). Already in 1885 the work of Camilo Golgi had appeared in which he explained his staining method. Simarro incorporated the black reaction into the laboratory of his private home located at 41 Arco de Santa María Street in Madrid (Salá Catalá 1987). In 1887, Cajal visited Simarro and learned the Golgi staining method. Cajal's decision to focus on young embryos was grounded in the notion that these organisms represented stages where the nervous system's organization was still in the process of constitution.

The idea that the ontogenetic series recapitulates the phylogenetic series was criticized in the first edition of Darwin's *Origin* (1859), who was aware of von Baer's objections to the recapitulation theory.

Cajal did not attend to those caveats and in *Textura*… Vol 2, part 2, chapt. 47, explicitly endorses the "Parallelism in the Phylogenic and Ontogenic Development [of the cells of the Cerebrum]".

> From the study we have just concluded on the development of the cerebral cortex in the animal series and in the embryonic and youthful stages of mammals, it is deduced that ontogeny of the cerebral pyramid or psychic cell (as we have designated it in deference to the dignity of its activities) corresponds to the stages of the phylogeny. In [Figure 3], taken from a work of ourselves on the subject, the said similarity is displayed. Observe how the neuroblast phase reproduces, grosso modo, the adult disposition of the neurons of invertebrates, and how the forms that the neuron goes through human ontogeny closely resemble the adult [neurons] of batrachians and reptiles. In spite of everything, some ontogenetic phases remain without phylogenetic representation, such as the bipolar, but we already know that individual development is richer in transition forms than are existing species, because the former represents a continuous serial progression, while the latter represents a discontinuous process - on account of the elimination of intermediate forms? The same parallelism is observed in the neuroglial cells. In the fishes, batrachians, and reptiles, the only epithelial or ependymal cells, which, in the birds and mammals, correspond to a fleeting and very early ontogenetic phase. (Cajal 1904, pp. 1119-1120)

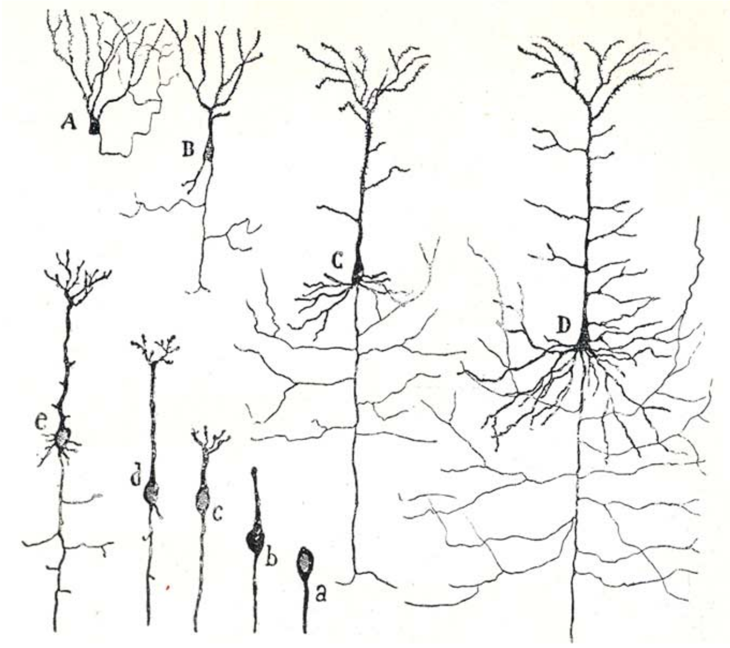

Figure 3. Double diagram where the phylogenetic and ontogenetic evolution of the psychic cell or brain pyramid is shown. A, pyramidal cell of a batrachian; B, of a reptile; C, of the rabbit; D, of man; a, b, c, d, evolutionary phases of the psychic cell in the mammalian embryo.

Cajal's initial research on neuronal morphology in the retina, cerebellum, and medulla cannot be fully comprehended without considering the law of dynamic polarity, which enabled him, by applying Haeckel's biogenetic principle, to infer the evolutionary patterns of vertebrate neurons (Salá Catalá 1987).Thus, the distinctive explanatory pattern of the Spanish Histological School was established (adapted from Salá Catalá, 1987): (i) Develop a staining method that reveals the histological structure under investigation and enables a comprehensive description of it; (ii) investigate the functional significance of the identified structure by examining it in various conditions, such as disease or anatomical injury; (iii) explore the ontogeny of the structure across vertebrate species to deduce its appropriate phylogenetic significance, considering its different components; (iv) formulate hypotheses, considering steps (ii) and (iii), regarding the laws of morphological evolution; (v) if applicable, make recommendations based on these laws, especially in areas related to human beings, such as clinical diagnosis, education, and health legislation.

In summary, Cajal's *Textura…* offers an evolutionary doctrine, albeit not exclusively Darwinian. Spencer's influence is evident in Cajal's laws of morphological progress (multiplication, differentiation, and economy). Haeckel's influence on Cajal is also significant, as the biogenetic law plays a central role in the development of Cajal's embryological method and the formation of both the Spanish Histological School and the modern neuron doctrine. Seen this way, Cajal's contributions can be interpreted as belonging to the organicist tradition, even though he extends the cell approach to nervous tissue.

4. Conclusions

Michael Ruse's version of the incommensurability thesis, positing "an abyss" between organicist and mechanistic metaphors in biology, is called into question. The neuronist revolution, which marked the origin of modern neuroscience, challenges the notion of a straightforward metaphor shift from organicism to mechanism. At least two distinct yet relevant senses of the organicist metaphor in the 19th century should be considered. According to the Holism thesis, the organism as a whole explains the presence and activities of its parts. Meanwhile, the Internalism thesis asserts that biological transitions are internally guided and progressive, leading toward increasing complexity, with the adult human being as the ultimate endpoint of this progress. I have argued that Cajal rejected a version of Holism found in the works of Camillo Golgi. Crucially, I also contend that Cajal explicitly advocated for Internalism. Even if we acknowledge Santiago Ramón y Cajal's evolutionary approach and consider Darwin as primarily mechanistic (as Ruse suggests), it remains a fact that the main evolutionary authors influencing Cajal were staunch organicists. From Spencer, Cajal adopted the idea that evolution is internally guided by principles of multiplication and differentiation, progressing from polyps to human beings. Additionally, from Haeckel, Cajal embraced the biogenetic law, positing that ontogeny recapitulates phylogeny. This concept played a pivotal role in the development of the "ontogenetic method," characteristic of Cajal's revolutionary micrographical studies and the broader Spanish Histological School. In conclusion, Cajal's groundbreaking contribution to the foundation of modern neuroscience undeniably incorporates elements of the organicist metaphor.[3]

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