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Determinism and probability in the development of the cell theory

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ABSTRACT

A return to Claude Bernard's original use of the concept of 'determinism' displays the fact that natural laws were presumed to rule over all natural processes. In a more restricted sense, the term boiled down to a mere presupposition of constant determinant causes for those processes, leaving aside any particular ontological principle, even stochastic. The history of the cell theory until around 1900 was dominated by a twofold conception of determinant causes. Along a reductionist trend, cells' structures and processes were supposed to be accounted for through their analysis into detailed partial mechanisms. But a more holistic approach tended to subsume those analytic means and the mechanism involved under a program of global functional determinations. When mitotic and meiotic sequences in nuclear replication were being unveiled and that neo-Mendelian genetics was being grafted onto cytology and embryology, a conception of strict determinism at the nuclear level, principally represented by Wilhelm Roux and August Weismann, would seem to rule unilaterally over the mosaic interpretation of the cleavage of blastomeres. But, as shown by E.B. Wilson, in developmental processes there occur contingent outcomes of cell division which observations and experiments reveal. This induces the need to admit 'epigenetic' determinants and relativize the presumed 'preformation' of thedevelopmental phases by making room for an emergent order which the accidental circumstances of gene replication would trigger on.

It can be felt appropriate to verify what meaning the concept of determinism conveyed in its original application to biology by Claude Bernard at the very time he was annexing and interpreting fundamental tenets of the cell theory. The cell theory itself in its transformations from mid-nineteenth century on had oscillated between analytic and holistic notions of cell functional processes and of their structural bases. But cytologists had to meet a considerable epistemic challenge when attempting to design a synthesis of cell physiology with neo-Mendelian genetics and analytic approaches to embryological development. Though deterministic in its outline, such a synthetic theoretical design, exemplified for instance in the latest edition of E.B. Wilson's *The Cell in Development and Heredity* (Wilson, 1925), deserves reassessment with regard to the relativity and "plasticity" of its explanatory framework. In the more recent period, the quasi-hegemony of deterministic molecular genetics has tended to undermine or at least rigidify the multi-factor, multi-level approach at the heart of the attempted earlier cytological syntheses. From a methodological point of view, it may prove relevant to investigate some elements of the historical pathway that led to contemporary alternatives to strict genetic determinism.

1. Reflections about the original meanings of "determinism"

The term "determinism" originally stemmed from a misinterpretation of Leibniz's principle of determining (or sufficient) reason. In that context, as Jean Gayon clearly established, in the early 19th century, the term determinism began to be used, mainly by philosophers, to refer to a kind of metaphysical fatalism (Gayon, 1998).

But I shall skip that interesting story of origins and turn briefly to Claude Bernard's view of determinism as applicable to the life sciences. The epistemic use of the term is essentially due to Claude Bernard's *Introduction à l'étude de la médecine expérimentale* (1865). Significantly, Bernard oscillated between two meanings of the term. On the one hand, the "determinism of phenomena" refers to a fundamental principle of physiology as of all natural science, stating that "the conditions of existence of all phenomena are absolutely fixed." (Bernard, 1865, p. 116). The principle of the conditions of existence was in fact inherited from Auguste Comte's positivism. It was equivalent to an epistemic presupposition that the laws ruling over organic as well as inorganic bodies are constant and rule over phenomena in such a way that they follow necessarily (by conditional necessity, so to speak) from the setting wherein they come about (i.e. from a manifold of determining factors). In this general phrasing, the principle states a constant legal

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connection between causally linked empirical data, and it affords a general methodological requirement applying to scientific explanations.

The other meaning is a more limited one. The determinism of a phenomenon is its proximal cause as a determining cause in the production of that phenomenon. Although this cause may not be sufficient per se for producing that effect, it comes in as a necessary condition, failing which the process will not materialize. Indeed, the best would be for experimental analysis to reach causes at once necessary and sufficient, but the complexity of most physiological processes is such that this would be too much to be hoped for. There is a significant pragmatic dimension to the unveiling of these determinisms, since their identification is directly linked to the experimenter's operative interventions in modifying the conditions of existence for a given phenomenon. I may not know the full set of conditions that combine to produce a physiological process of some kind, but insofar as I am able to alter the phenomenon by reasoned analytic interventions on a specific factor under given *ceteris paribus* clauses, I get an effective hold of the causal chain. As a result, I may infer some limited predictions on the basis of acknowledged empirical regularities. But this imposes no constraint on ontology such that it would exclude the option of considering stochastic processes as being one of nature's possible ways of making things happen, provided stochastic processes are seen as conformable to a general notion of what is a determinant, that is to say, a necessary causal condition among a manifold of potentialities.

2. Analytic vs. functional determinism in 19th century cell theory

Upon its invention by Matthias Schleiden and Theodor Schwann in 1838–39, the cell theory started influencing the framing-up of causal analyses (Schleiden, 1838; Schwann, 1839). The demonstration undertaken by Schwann was to the purpose of proving that the organic structures of animals, according to botanical analogies provided by Schleiden, were cells or transformed cells and that the formation and transformation of cells could account for all organic operations, including higher level ones. His erroneous view about cell formation and reproduction by cytoblastemic crystallization was, for Schwann, part of a reductionist approach that went much farther than the mere idea that cells constitute the elementary parts of organisms and that every living structure derives from cells through assignable transformations. It implied indeed that the cell is the true archetype of the organism and that the organism in all its achieved complexity should be analyzed into cell interactions, from the physiological viewpoint of metabolic processes, as well as from the morphological viewpoint of structure building. This new explanatory mode was thus presented:

> "[…] growth does not ensue from a power resident in the entire organism, but […] each separate elementary part is possessed of an independent power, an independent life, so to speak in other words, the molecules in each separate part are so combined as to set free a power by which it is capable of attracting new molecules, and so increasing, and the whole organism subsists only by means of the reciprocal actions of the single elementary parts. So that here the single elementary parts only exert an active influence on nutrition, and totality of the organism may indeed be a condition, but is not in this view a cause." (Schwann, 1847, p. 191)

The *Theorie der Zellen*, at once a speculative hypothesis and a heuristic model, inflects cellular histology toward resuming the physiological problem *par excellence*: what does functional integration rest on? The new approach to this question was intended to reinforce the rights of an analysis grounded in the morphological and metabolic properties of the cell; correlatively, physiologists should from then on renounce all idea of causation linked with the functional integration of the organism as a whole. Concerning the plastic, that is morphogenetic, phenomena, Schwann reinterprets the formation sequence: *nucleolus* → *nucleus* → *membrane* as resulting from a stratified sedimentation determined by molecular attractions. Metabolic phenomena would be subject to the same type of representation as formative processes: cells modify chemically the organic fluids they absorb and they modify their own structures by the same occasion. Metabolic processes would determine the structural organization of multi-cellular organisms. And the analysis of metabolic processes would fit alterations resulting from mechanical or chemical interactions in and among cells along a scale of growing complexity in the structures and operations produced. In sum, and pending a more thorough survey, extending research to the phenomena of cell life, whether plastic or metabolic, would present the 'epistemic' merit of remaining within the limits of what can be 'deduced from phenomena' (an equivalent of causal determinism).

In *Genèse de la théorie cellulaire* (Duchesneau, 1987), I aimed to show how this theory was transformed, after Schwann's attempt at a deterministic 'histogenetic' demonstration, through its merging with a physiology that opposed the reductionism advocated in Schwann's *Mikroskopische Untersuchungen*: this reversal in methodology was the noteworthy contribution of Johannes Müller (1801–1858), Schwann's teacher, in the late editions of his *Handbuch der Physiologie des Menschen* (2nd edition of volume II, 1840; 3rd edition of volume I, 1844). The revision then went on with the rejection of the formation of cells from cytoblastema as layered and nested membranes. To Robert Remak and Rudolph Virchow, also disciples of Müller, the cell theory owed from 1855 on its second principle *Omnis cellula e cellula*, but equally remarkable demonstrations about embryogenesis as the mode of development of multi-cellular organisms and about the dynamics of change in pathological cell replication (Remak, 1855; Virchow, 1855). Then, during the last decades of the 19th century, developments came about concerning protoplasmic structures and the discoveries of mitosis and meiosis as processes determining nucleus replication. I will not enter any details about those various points (Baker, 1988). I shall be content with indicating some typical causal interpretations of functions and processes that emerged from canonical expositions of the cell theory with significant effect on the views concerning organic development when genetics came to the fore.

I shall start with Müller's revised *Handbuch*. The Prolegomena evoke a notion of organism which sounds somewhat Kantian. Müller asserts:

> "Organized bodies do not differ from inorganic bodies only by the manner in which the elements that constitute them are arranged; but the continuous activity that deploys itself in living organic matter is also endowed with a creative power subject to the laws of a reasonable plan, of harmony, for the parts are so disposed that they respond to the end for the sake of which the whole exists; and this is precisely what makes the organism distinct." (Müller, 1851; I, p. 16)

This statement is developed into assertions about the primordial role of the notion of a structural, but more fundamentally dynamic, whole in the explanation of organs, including cells as elementary organs, but also in the explanation of functional arrangements resulting from combinations of organs. "There is therefore, writes Müller, in the organism the unity of the whole which hovers above the manifold of parts and towers over it." (Müller, 1851; I, p. 17) By contrast with crystals, "[…] the form of animals and of organs testifies that the whole is disposed in a rational manner for the action of forces, and that there is a pre-established harmony