Chapter 15
Changing Framework in Explaining Complex Dynamics: Convergences on Systemic Accounts from Two Different Case Studies

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1 Introduction

Systems that continuously acquire new, multiple, superimposed and often delocalized coherent sequences of properties show a complexity that cannot be grasped by traditional approaches that focus on fixed systemic properties. Properties in the latter approach can be grasped, for example, through explanatory concepts like self-organization and emergence, while in the former approach the history of the system has to be taken into account as well. That is, the dynamic inter-change of the systems and of their physiological environment has to be considered at once. There is, therefore, a shift in the explanatory focus that requires both a reformulation of problems and a post-reductionist trans-disciplinarity precisely related to the study of such reformulations and their properties.

In this paper we compare two case studies—music perception and cancer—by looking at how interpretative models evolve while trying to explain the dynamic features of the underling process. In middle Sects. 2 and 3 we introduce cancer case and music perception case. In Sect. 4 follows a discussion of the dimension which can be differently grasped by apparently divergent models and of the peculiar context-dependency of such properties, that will be called embodied-context-dependency. Finally, we explicit a potential outlook in term of transdisciplinarity of the analytic dimension outlined in this paper, for a deeper comprehension of the understanding process of complex dynamics in biological systems.

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2 Cancer Explanatory Theories

2.1 The Discrete: Gene Centered Models

Some cancer explanatory models tend to focus on the cellular component, whose abnormal behavior is due to genetic and epigenetic factors (we will refer to them as "genetic centered perspectives" or GCP). In GCP, cells mainly act as autonomous units that can eventually fully account for cancer. GCP explains cancer in terms of a sequence of mutations of genes, or epigenetic alteration that mimic genetic mutation transforming normal cells in cancer cells. To a first approximation, tumors' properties are explained by the properties entailed in the cell and its components. Tumor cells' properties are traditionally described as follow [7]: self-sufficiency in growth signals; insensitivity to antigrowth signals; evasion of apoptosis; limitless replicative potential; sustained angiogenesis; invasion and metastasis. These hallmarks of cancer focus on the autonomy of tumor cells from other cells and from their environment. They might characterize all tumor cells. Yet this is not the case. Tumor cells are not completely autonomous, and tumors' cells heterogeneity leaves open the question about the explanatory role of cancer cells characterized in those terms. Even attributing to cancer cells the capability to develop all features of a neoplastic phenotype, GCP has difficulties in accounting for tumor heterogeneity. By definition parts should be homogeneous but, in fact, they are not.

2.2 The Continuous: Cell Centered Models

In the last 50 years, however, the general emphasis has changed more and more from considering cancer as the progressive result of genetic mutations producing defects in the regulatory circuits, that regulate proliferation of normal cells, to considering cancer as "a disease of cell differentiation rather than multiplication" [8]. The discovery of Tumor Suppressor Genes (TSGs) integrated the Somatic Mutation Theories universally agreed-upon model of cancer origin and progression. In those years, experimental observations called attention to a different dimension of carcinogenesis other than cell proliferation. The fact that normal mouse cells showed a dominant behavior over cancer cells when the two cell types were merged [9], suggested that the former had to carry genes that were opposed to tumourgenesis, thus showing a tumor-suppressor function. This and other data suggested that carcinogenesis does not require an acquisition of function (assumption that was behind the definition of oncogenes), but rather the loss of it, perhaps through damage of some pattern of cellular differentiation. This step, which is conceptually very simple, technically called for a major research effort to demonstrate that the dominance of oncogenes was not the general rule, casting the foundations of subsequent theories of the cancer cell. From an explanatory point of view, the Clonal Genetic Model of Cancer integrated the knowledge we had till then on oncogenes (ONGs)

and tumor suppressor genes (TSGs) within a unified picture. At its simplest, the model predicts the functional impairment of these genes as the origin of a tumor cell's development, by clonal reproduction into the cells that constitute the tumor mass and ultimately trigger metastases.

It was Bert Vogelstein who shed light on the role of ONG and TSG in describing how different mutations were related and connected in the origin and progression of tumors. The idea of the clonal evolution of tumor cells was reinforced through the description of a coherent and sequential tumorigenic process, consisting of a series of stages of molecular events. This Multigenic and Multiphasic Model of Cancer [5] was widely accepted by the scientific community and provided the scientific basis for the initiation, promotion, transformation and cancer progression, which until then were based on purely theoretical hypothesis. What's new in this model is the emphasis on the fact that the total accumulation of molecular changes were more important for tumor progression than their sequence or even identity, concluding that five or more genetic alterations were probably required for the development of carcinomas, while a lesser number of mutations would be required for benign tumorgenesis [16]. Pointing to this much more relevant aspect of carcinogenesis, Vogelstein had the merit to conceptualize tumor genes in a different and epistemologically relevant way with respect to the kind of classifications that had been adopted since then.

2.3 The Context Dependency: Tissue Centered Models

Organism Centered Perspective (OCP) sees cancer as a problem of tissue organization so that cells lose their contextual control. From 1999 [13], some authors developed the idea that cancer has to be addressed in terms of tissue organization. Interactions between stroma and epithelium when compromised by the action of hormones or other chemical or physical factors become crucial in carcinogenesis. Hence, the study of complex phenomena, such as cancer, can be better analyzed from the perspective of higher hierarchical levels of organization than from the pure cellular level. Epistemological presuppositions assume the hierarchical organization of a multicellular organism system as default. Cancer is thus viewed as a problem of development, an organogenesis that goes awry. It is studied in terms of the three-dimensional structure of tissues and of how intercellular communication takes place within them. The cellular components, once integrated into the tissue, are meant to interact in a way that presents a new and unique feature of intrinsic reciprocity of relationship among cells in the tissue. Heterogeneity is better understood here, but anyway these models have difficulties to grasp the epistemological meaning of the multilevel phenomenology of cancer, i.e. the causal relevance of different levels of the biological organization. OCP reflects organizational systems (i.e. non-aggregative systems like in the antireductionist philosophical accounts). When we artificially separate the components of the tissue cells that form the epithelium and

the underlying stroma, they stop carrying out the functions performed when they were assembled in their unique three-dimensional organization. Once recombined, instead, they form a tissue similar to that of their origin [14].

3 Musical Consonance and Dissonance

We now move to the second case study by briefly introducing a particular aspect of music perception (for consonance and dissonance case see also Di Stefano and Bertolaso [4]). Consonance and dissonance are musical notions, which have been widely studied from the ancient Greek philosophy to nowadays. Without going any further in their historical evolution, we can consider consonance as the relation that links two or more sounds sounding pleasant together, while dissonance as the relation that links two or more sounds sounding unpleasant or rough together [15, 17]. From arithmetic to physics, from psychology to physiology, different explanation of the same phenomenon have been given.

3.1 The Discrete: Frequency Ratio of Intervals

Pythagoras, in the sixth century BC, discovered that the simpler the frequency ratio, the more consonant the interval: the most consonant interval is the octave, which is expressed by frequency ratio of 2:1; frequency ratio of 3:2 gives fifths and frequency ratio of 4:3 gives fourths and so on decreasing in consonance. Thus, the Pythagorean "tetractys", composed by 1-2-3-4, gives reason for all the perfect consonances [3]. Since Pythagoras' mathematics, far from being empirical, is metaphysic, numbers are the deepest reasons of reality. That's the reason why the frequency ratio has so fundamental importance in consonance and dissonance phenomena:

> The issue of consonance and dissonance was for the Pythagoreans not a matter of devising a theory that was harmonious with their hearing, but rather one of hearing the numerical truth that they discovered to be inherent to nature [1, p. 216].

The arithmetical model considers sounds in abstract, and thus enlighten the discrete dimension of the phenomenon. If the *explanandum* is consonance and dissonance, integers ratios are the *explanans*.

3.2 The Continuous: Waves Matching

Frequency ratio is anything else than the arithmetical expression of how the two sound waves match. Consider, for example, an octave: frequency 2 is frequency 1 doubled. So, in physical terms, this means that every two peaks of the upper the

two tones beat together. Since acoustics considers complex sounds, composed by several harmonics, a single tone results from different partial waves matching in different ways. Therefore, the way they match is crucial for the perceptual effect on listener [11, 12]. This represents an essential perspective's change, which leads to the notion of sounds as compound. Physics emerges as a new explanatory level able to capture the continuous dimension of consonance and dissonance perception. In such account, a sound is no more adequately represented by frequency ratios, but better represented by a continuous entity as a wave. However, as arithmetic does, neither physic pays much attention to the physiological/psychological structures of the perceiving body.

3.3 The Relevance of the Context: Regularity of Beating and Cochlea's Properties

Since consonance and dissonance are always perceived by human being, there is the need to shift to the body and to its structures. This can be considered a physiological approach, in which human component (anatomy of hearing apparatus) and physical wave properties are considered together from a unitary perspective. In this perspective, consonant intervals are associated to most regular beating of tympanic membrane. Regular means more synchronized. Helmholtz discovered that the elasticity of the basilar membrane in the cochlea is non-homogeneous, so that sounds at different frequencies have different effects on the perceiving human system [6, 10]. At this level, the physiological one, dynamic features become fundamental and therefore context starts to be relevant. If consonance and dissonance phenomenon is the *explanandum*, now embodied dynamics are the *explanans* [4]. This shift implies a deep change in perspective that highlights a fundamental property of music perception (as happened above for cancer pathology): its context dependency (see Table 1). Such context dependency lies on the fact that living structures are not homogenous neither discrete. In arithmetical terms, all fifths C-G are identical because their frequency ratio is always 2:3. But when listening to consonance, arithmetic no more describes the phenomenon adequately: hearing a fifth at 16 Hz is really different from hearing the same interval at 16 kHz, because the basilar membrane response to the same interval changes at different frequencies.

4 Analytical Dimension of the Phenomenon: The Relevance of the Context

It is, therefore, increasingly clear that the understanding of the processes evoked in the two case studies exceeds a mere psychological upshot or acquisition of knowledge of facts although a kind of relationship between understanding, explanation

and contextual factors have to be hold. In particular, the focus of all these issues remains the question about how such relationship should be understood in explanatory and in conceptual terms [4].

When the context becomes relevant the relationship between the system and environment start to be semantic, and their dynamic interaction become essential. At discrete and continuous level yet no interaction is necessary. Semantic, here, means that something became significant in different ways as it differently interacts with the context. Clear examples of such dependency are offered by the OCP we referred to above. For example, when skin cells are placed in a culture dish, they form a uniform layer of tissue very different from the original, although, if they are placed on a surface previously covered with basement membrane proteins, they tend to associate among themselves and recover the original three-dimensional structure of the epithelium from which they came. However, they often undergo genetic transformation and imbalance when cultured for a long time in vitro so that the real future challenge can be nicely summarized in a title like this: 'Decoding the language of form' [2].

Similarly, in music, the same orchestral excerpts played by different instruments (i.e. within different context) would give totally different result in terms of perception. In arithmetical terms, the original version and the altered one are exactly the same (same frequency ratio). From the physics perspective, they are different because sounds' matching is different, and corresponding waves are different. From the physiological/psychological perspective, they are different not only because sounds matching is different but also because human perception reacts differently.

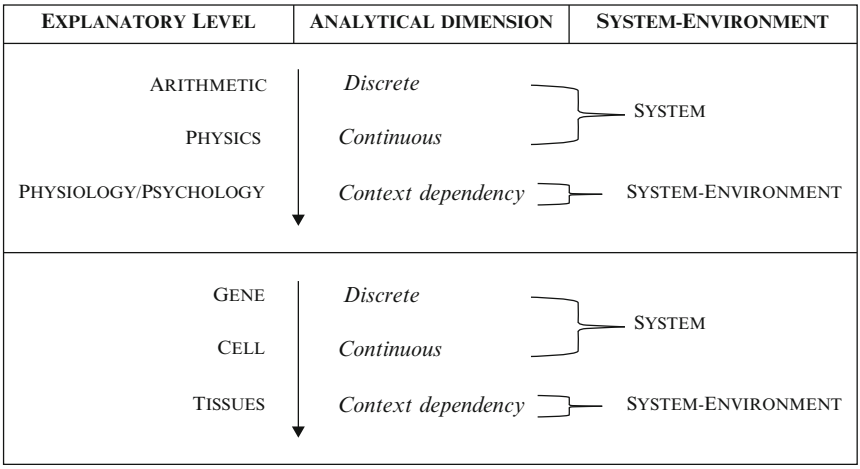

Fig. 15.1: Relationship between explanatory accounts and analytical dimension in the studied cases (cancer and musical consonance and dissonance). Modified version of Table 1 in [4]

The relevance of the context and its properties is evident, for example, in Baroque music, where we often assist to the introduction of a dissonance creating a sort of a new coherence which guides the perceptual and cognitive activity of the listener.

The emergent character of phenomena considered appears, in epistemological terms, when the context dependency becomes relevant (see Fig. 15.1). At the same time, context dependent levels of explanations are more comprehensive than the discrete and continuous ones and such emergent character might have some explanatory priority over the phenomena considered. In fact, phenomena can be distinguished and not separated in all accounts, though it is in the context dependent level that their inter-relationship and their unitary outcome (whether cancer or music perception) actually becomes the very object of inquiry. In this sense, systemic perspective and trans-disciplinarity, as previously explained, become necessary and unavoidable.

Therefore, we cannot definitely choose which is the privileged level the phenomenon should be explained at: there is no chance for any *experimentum crucis*, neither in cancer nor in consonance and dissonance perception, because there is no unique privileged causal level. Systemic approach widen the perspective to the living context, where arithmetic, physics, biology and physiology are fused in a complex and dynamic process. Every attempt to find the definite reason or cause only in one of this partial aspect loses the unity of the whole. Moreover, as happens for more complex biological dynamic behaviors, systemic approach avoids the risk of making methodological recommendations about the ontological restrictions—frequent in epistemological or ontological reductionism—and also avoids deriving methodological indications from holistic principles.

5 Conclusions: Levels of Understanding Process

Facing problems like cancer pathogenesis or musical consonance and dissonance we have to manage a complexity growing up from the biological ground. Correctly understanding what the problem is, or at least what the problem is not, implies, in some cases, a shift within the same discipline, like in cancer case, and in other cases a shift between different disciplines. In the first case we need intradisciplinary shift, in the latter, we need interdisciplinarity. Every authentic widening of perspective really represents an advantage in understanding, though the result of the match between different disciplines can be very different. Multidisciplinarity is the way several disciplines study the same problem, each one maintaining its peculiar basilar concepts. The results are in this case merely combined and their sum is weak. Interdisciplinarity happens when disciplines learn from each other's approaches, concepts, theories, methods. Though, in this case, there is real dialogue between disciplines, it lacks the creation of a new point of view.

Transdisciplinarity is the creation of a new theoretical framework, potentially opened to the emergence of a new discipline. This is the strongest approach and the only one that really leads to a new phase in problem understanding, which may

bring to the redefinition of the object of inquiry in more adequate terms. Transdisciplinarity manages every account as a whole-dependent level and not as something concluded in itself: approaching multidimensional phenomena, accuracy of an explanatory account depends not only on the level of details gained through different methodologies, but also on interplay and reciprocal dependence between the scientific question and the phenomenon under inquiry. Transdisciplinarity, bringing back into the same inquiry the system and its context, allows to distinguish and clarify the epistemological relevance of what we have defined analytical dimensions of phenomena. It also explains how the emergence of what is explanatory relevant structures the process of understanding embodied dynamics. A systemic perspective, therefore, allows us to avoid excessive simplifications driven by mere pluralistic accounts of human understanding and scientific knowledge. Depending on the explanatory contexts, meanings can change and require different epistemologies. The novelty of a systemic and transdisciplinary approach lies not on its object but on the way the object is approached.

Contextual factors in the process of identifying the explanatory level and the relational principles of organization structure the process of understanding. The discovery of new explanatory relationships characterizes such process, i.e. different kinds of understanding emerge as different levels of comprehension of explanatory relevant relationships.

Therefore, the irreducibility of understanding is not an obstacle but rather a condition of the integration of different kinds of human understanding. What might eventually emerge is an epistemology able to ground real interdisciplinary or—more precisely—transdisciplinary approaches which overcome the epistemological tensions on causal and explanatory notions still affecting the philosophical consideration on the understanding of multi-level and systemic dynamics.

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