EPISTEMOLOGY IN LIFE SCIENCES. AN INTEGRATIVE APPROACH TO A COMPLEX SYSTEM LIKE CANCER

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In the introduction to his book *Hierarchy Theory*, H. Pattee notes that: "increasing complexity of organization is always accompanied by new levels of hierarchical controls. The loss of these controls at any level is usually malignant for the organization under that level" (Pattee 1973). This is clear in cancer research and it is also evident in society and in the social and political aspects of scientific activity. When the amount of information and the complexity of the interaction in networks increases within any kind of dynamic process of knowledge, a new level of regulation is necessary if the system is to function reliably. My point is that what specifies this systemic approach is the integrative dimension of complex systems hierarchically organized, and that considering this dimension is possible to find a parallelism between the principles that govern the unitary behavior of an organism and the need to work interdisciplinarily in scientific practice when dealing with complex biological systems (Bertolaso 2012). Integration is possible not only for practical reasons, but because the intrinsic way the natural world is and how we know it. Let us learn from cancer research.

Cancer is commonly recognized as a phenomenon that leads to a general disorganization of organs and tissues, and it is becoming clear that various elements and different levels of biological organization are involved in the neoplastic process: from genes to the cells and the tissues. The structure of biological complexity itself, then, justifies the trend towards integrative explanatory models of cancer. What is certain, in fact, is that it is not possible to causally explain tumors' origin and progression just in molecular terms. A dynamic aspect has to be taken into account. This dynamic dimension is clearly related with the loss of hierarchical organization, thus making impossible to reduce the specific functionality and activity of the neoplastic cells solely the to genes' activity. This is why systemic approaches are almost commonly used now in cancer research, although held by different epistemological perspectives (Bertolaso 2011).

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Some are explaining cancer and its origin in terms of genes' pathways and cells activity. Others are instead looking at cancer in terms of organization of the tissue and of the principles that allow cellular differentiation and morphogenesis. The biology of cancer, thus, implies reasoning on the specific relationships between molecular elements and cells, through different levels of organizational functionality. Similarly, cancer research increasingly requires collaboration among different areas of biomedicine and biophysics, in order to elaborate systemic models able to capture the complexity of the phenomenon and to elaborate a more comprehensive explanatory theory for its account (Soto and Sonnenschein 2011). This movement towards systemic models that describe cancer's behavior opens an interesting reflection on the philosophical presuppositions of the systemic approaches and to interdisciplinary projects in life sciences as well.

The choice of the right epistemic categories for the study of a phenomenon has important implications for the understanding and setting of the entire research program. The same has to be said for any process of knowledge that regards a dynamic system and its features. In understanding cancer from a biological and philosophical point of view, relationships have become crucial as well and analytic approaches; the challenge has become to confront concepts and vocabulary to make our discourse un derstandable and useful for different disciplines. The former was a need; the latter is still a dream. A system, in fact, is a plurality of elements that become a unity due to the properties that characterize the overall complexity of the whole. A new unity is integrated through functional cooperation. This notion of system obviously opens to an antireductionist position and asks for a deeper reflection on the nature of this integration. By reacting to a simplistic methodology and a reductionist vision in life sciences, one that supposes that the existence of pure experiential data will probably give rise by induction to general laws, the epistemology of contemporary cancer research has made it clear that the scientific theories are our own elaborations so that the procedures of experimental science are always interpretative. They combine experimental observations with theoretical considerations, using concepts that contain dimensions that are already systemic, such as those related to the notion of function (Bertolaso 2009). Systemic categories inherently require collaboration from different disciplines and skills, different points of view. It is the systemic approach, thus, that opens the possibility of an interdisciplinary and transdisciplinary work and not the other way around. It is the very feature of a systemic behavior, i.e., integration of parts into a whole when performing a higher unified behavior, which grounds the possibility of this approach. Verifying how a systemic approach can be applied not only at different disciplinary fields, but also to account for the original complexity, avoiding in this way useless reductionisms, makes an interesting point. It opens new perspectives and helps us to consider why systemic properties may be theoretically universal, i.e., general although not generic. This is also why Marcos states, in an interesting analysis of science in society: "If we accept the systemic stance, it is not enough to consider only the epistemological aspects of science, other values are also at stake when we do science and we reflect on it" (Marcos 2010, 32).

The integration of knowledge and methodology from different disciplines, often represented by different colleagues, requires the awareness of being part of a system acknowledging the beauty and the risk of unity, i.e., positioning ourselves into a whole new identified system by bringing all participants together. Experience shows that a real dialogue can be possible if there is a common and previously shared goal. This common objective, in fact, helps to understand how a specific behavior can be realized in different ways and through compatible paths. Reformulating problems and finding new solutions is a common challenge, not a private one. Systems due their dynamicity to their (interchangeable) parts, while their organization to their unity (Lenoci 2011). What determines, in fact, the shift from a group to a system is organization with an identity, i.e., a common strategy supported by a network of interactions among elements; from its part, structure of interactions constitutes one of the potential application and output of the organization itself. From this point of view, a system is characterized by a relational structure, where the identity of its elements is determined by the system. The interdisciplinarity I am talking about is thus not just the sum of disciplines, it is not enough to find common language and methodology, but implies sharing a common objective that drives a focused research. Cooperation is more than aggregation and its output is not to hold the capacities of the component parts; it depends on the dynamic properties of the network and, then, its capability to generate new ideas that were not there before. Like in an organism, parts, once entangled in a unity, perform new activities and behavior. Systemic perspective thus allows recovering a new perspective any time it is required, listening to different disciplines and looking back to the already done research. In this way, their track is made clear, better suited to lead in a further research program.

By shifting our attention from observations to their theoretical coherence, scientific discovery performs as an act of integration. This act may require sustained efforts guided by exceptional gifts, but its logic serves as a model for the logic of discovery. Bringing this implicit dimension of discovery to awareness, and thus helping the construction of more comprehensive theories is, in my opinion, one of the merits of controversy and eventually integration of a pluralist approach to a biological phenomenon. Of course, this implies an ontological claim about the reality of the known entity and an epistemological one that overcome the structural limit of any

form of Cartesian dualism (cf. also Polanyi 1969). Moreover, the original intention of Logical Positivism was to establish all knowledge in terms of explicit relations between sensory data. Nevertheless, usefulness and success in integrating different disciplines and fields of scientific research shows that this positivist attitude is doomed to failure when facing biological phenomena. Cancer research seems to show us that this dynamic making explicit an implicit presupposition and its structure has its counterpart in the way the principles determining the stability of an organism exercise its control over its parts. An integrative approach is thus necessary to complete the work of organizing the data now at our disposal, in accordance with a combined systemic, unitary and relational view of the phenomenon under study, that is, the living organism.

Acting bio-logically requires such attitude towards unification and skills to endorse it. Limits in cancer research, in fact, are often related with the intrinsic limits of a reductionist approach that is not able to capture the whole picture, or being unable to change perspective when the complexity of the phenomenon so requires. Integration as an intrinsic dimension of a systemic perspective is crucial. Integration is then an epistemic challenge and a methodological tool. Integrative Pluralism, as developed by Sandra Mitchell (2009), stresses this position: pluralism of approaches, i.e., the possibility and relevance of admitting different ways to look at the same phenomenon. It is not just to explain it, but that it can be explained in different ways/models. The recognition of the limits of reductionism can then favor a methodological pluralism, which, in turn, prevents the identification between ontology and methodology. Reductionism, in fact, at least as a methodology, has led to important discoveries and continues to be necessary within the experimental method (Buzzoni 2007). It is rather the transformation of methodological directives into ontological restrictions that has become the serious defect of modern scientific thought.

It is the systemic dimension, therefore, that requires an interdisciplinary approach and not vice versa. It is also needed in its integrative component, characteristic of interdisciplinary work. The system opens an interdisciplinary and transdisciplinary horizon. Even if this necessity often arises for pragmatic reasons, the underlying epistemological questions must be taken seriously to the extent of our ability to know the world and describe it, and the reflection on the ontological properties of the living organisms which they can trigger. In the end, principles that govern the unitary behavior of an organism seem to constitute a condition of the possibility of the integration of different disciplines in scientific practice, as well as when dealing with complex biological systems. Integration is thus possible and needed not just for practical reasons, that are nevertheless good reasons in many cases, but because the intrinsic way the natural world is and how we know it. A remarkable conclusion for an interdisciplinary and

systemic approach in life sciences can be finally borrowed from Urbani Ulivi: "Referring to ordered reports what has often seemed a maze of contingencies, all the diversity, behavior, expressions are fleeting and changeable, as parts, but they are deeply and inextricably linked to that stable and invariant relational pattern, proper and exclusive of the 'human'" (Urbani Ulivi 2011, 247).

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