Open Peer Commentaries

on Nelson Vaz and Luiz Andrade's "The Epigenetic Immune Network"

Function vs. Structure: The Immune System as a Case in Point

Jorge Mpodozis Marín
Universidad de Chile, Chile
epistemo/at/uchile.cl

> Upshot • Functional approaches to systems, while of heuristic value in many cases, may lead to a neglect of some fundamental aspects of systemic phenomenology. The adoption of an alternative structural/mechanistic approach can be very enlightening to unveil, and effective to solve, the conceptual and heuristic limitations resulting from the adoption of the functional approach. The epistemic history of immunology, as described in the target article, offers compelling evidences of this situation.

« 39 » The conversations between Francisco Varela and Nelson Vaz, as described in the target article, compose a complex tapestry in which many different conceptual threads become lucidly interwoven. It is therefore impossible, not to say unnecessary, to highlight each of the knots composing this tapestry in a short commentary. Instead, I would like to address only the implicit concepts that form the framework upon which this fabric is based. And by doing so I will also try to clarify a more-or-less implicit question that is present throughout the dialogues between Varela and Vaz, i.e., is it worth treating the immune system as a cognitive system?

Systems

« 40 » Let me start with the question: what is that we call a system? The consensual definition of a system (Maturana, Mpodozis & Letelier 1995), i.e., a definite set of elements interconnected in such a way that the degree of freedom of each of these elements becomes limited by the interconnections it sustains with other elements, seems to provide a sufficiently general answer. However, once one agrees to treat a given entity as a system, such a general notion raises an immediate operational problem: defining the elements and the interconnections. The decomposition of a system implied by the aforementioned consensual notion cannot be deduced from such notion, and requires further specification of the criteria used to define the entity as a system of a certain class. As an example, the answer to the question "Is a living organism composed of cells, molecules or atoms?" requires a prior implicit or explicit definition of what, as a system, a living organism is.

« 41 » Starting from Aristotle on, the overwhelmingly dominant mode of addressing systemic phenomena is one of the functional type, according to which systems are defined by the intended functions and purposes they fulfill, or the goals they pursue. From this perspective, partitions of a system will necessarily bring forth components and interactions defined by their role in the achievement of systemic functions. This perspective, while of heuristic value in many cases, may (and in many cases will) lead to a neglect of all aspects of the systemic phenomenology that do not match the purported functional roles.

« 42 » If, for example, the immune system is defined as a defensive agent of the organism against aggressions from external pathogens, then the focus of the immunological research will be on the interactions of lymphocytes and "antibodies" with pathogens, and on the dynamic of production of lymphocytes and antibodies during infectious processes. The sole fact that immunoglobulins, which are a specific type of protein molecules produced by lymphocytic cells, become designated as "antibodies" indicates that these molecules are defined primarily by their "defensive role" rather than by their constitutive properties, such as their chemical structure. At the same time, focusing research on the defensive role of the immune system leads to a neglect of certain "uncomfortable" aspects of immunological phenomena. One of the most salient neglected phenomenon is "natural immunity," that is, the fact that even when kept from birth in an "antigen-free" environment (i.e., not exposed to macromolecules of any kind, including dietary molecules), each animal produces antibodies (i.e., IgM immunoglobulins) that are able to generate a unique and distinct pattern (profile) of reactivity with a complex mixture of ligands that remains stable during its whole life span (Haury et al. 1997). Equally salient is the scarce attention given to the phenomenon of "oral tolerance," that is, to the fact that highly immunogenic materials when contacting the organism initially by a mucosal (oral) route, e.g., when ingested as food, trigger the operational opposite of immunological memory, i.e., a robust stabilization at levels of responsiveness that are inversely proportional to the

http://constructivist.info/13/1/141.vaz

amount of the ingested antigens (Verdolin et al. 2001). This latter neglect is of a most distressing kind, since, as Vaz has repeatedly claimed over the years, oral tolerance phenomenology encompasses an enormous therapeutic potential that at present remains virtually unexplored (Vaz et al. 1997; Carvalho et al. 2002; Costa et al. 2011).

« 43 » One can say that phenomena such as natural immunity and oral tolerance are neglected by mainstream immunology because they call into question the heuristic and epistemological value of the "defensive" approach. I would like to add that this situation constitutes a sharp, perhaps dramatic (because it is more important than mere scholarly discussions) example of the limitations of the functional approach to systemic phenomena.

« 44 » An alternative, but the least popular, mode of addressing systemic phenomena is one of the structural/mechanistic type, according to which systems are defined as units whose properties result from the deterministic operation of the mechanism entailed in the structure (i.e., components and operational relations between them) that generates them. Consequently, properties of a system are not contained in, nor can they be reduced to, the properties of its components, since the system as a unit and the mechanism that gives rise to it exist in different operational spaces. For example, from a thermodynamic perspective, the properties of a molecular gas (such as pressure, temperature, and volume) are radically different from the properties of its molecular components (kinetic energy). Therefore, from a structural perspective, the purported functions that a system performs, or the goals it pursues, do not belong to the domain of the structural conformation of the system. Thus, the ascription of functions to a system gives no indication of its structural/operational constitution, and in many cases not even a hint about it. For example, consider the acute contrast between the *functional* dictum "the nervous system is a device for grasping and processing relevant environmental information" and the *structural* dictum "the nervous system is an architectonically complex network of synaptic interactions between neurons." The former does not contain indications about how the nervous system is constituted while the latter does.

« 45 » Moreover, the ascription of functions may not only lead to a neglect of relevant structural aspects of the systemic constitution (as we discussed above for the case of the immune system), but may also prove to be heuristically misleading, as it leads to looking into the structural domain searching for properties that belong to the systemic domain (i.e., to looking for pressure in the molecules or thinking in the brain) (Maturana 1985).

« 46 » In the target article, Andrade and Vaz offer several examples of how the abandonment of functional stances in favor of structural stances leads to an enriched understanding of the immunological phenomenology. But, on this basis, what can be said about the conceptual and heuristic value of the "cognitive" stances toward the immune system?

Cognition

« 47 » Let us move to a scenario in which there is a structurally dynamic system that exists in and through continuous interactions with a supporting environment, in other words, an acting system. In the case of such a system, what is it that is usually called cognition? Is it a phenomenon (i.e., something a system does), or it is a purported explanation of a certain phenomenon? Or is it both?

« 48 » As a phenomenon, what is usually called cognition ultimately refers to the fact that the acts (i.e., the changes of the interactional state) of a system in relation to its environment are adequate for maintaining the identity of the system until the system disintegrates. In that sense, it can be said that a living system knows how to live while remaining alive, or a breathing organism knows breathing, until it stops breathing and therefore loses that knowledge. Consequently, any acting system, as long as it exists, exists as a cognitive system. Thus, emphasizing the cognitive character of a given acting system adds nothing to the understanding of the operational constitution of such a system.

« 49 » As an explanation, cognition usually refers to the notion that the "cognitive" acts (in the sense stated above) of a given system arise as a result of particular processes by means of which the system grasps and forms an internal representation of some meaningful environmental features. It is easy to note that this notion is akin to, and consistent with, the functional approach to systems, as it views cognitive acts as resulting from the action of a process whose function is to produce them. But, from the structural/mechanistic perspective this explanation has no operational sense, since

a as long as knowing is understood as a systemic act, it cannot be reduced to, contained in or represented by any element or process taking place in the domain of the structural conformation of the system, and
b the structural changes that a system undergoes in the course of its interaction with the environment can only be triggered but not specified by the environmental agents with whom the system interacts.

(See Maturana et al. 1995 as a general reference for both points.)

« 50 » Also, from this perspective, to suppose that a given system acts as it acts because it knows (i.e., produces or contains an internal representation of) its environment adds nothing to the understanding of the operational constitution of such a system. Therefore, the claim that the immune system is a "cognitive system" does not seem to have any relevant conceptual or experimental value, unless one is able to clarify in operational terms (which acts, which processes, which components) the meaning that such a claim may have.

Conclusion

« 51 » From what was said above, it follows that the adoption of a structural/mechanistic approach can be very enlightening, both conceptually and practically, when confronting the epistemic limitations resulting from the functional approach. Varela was one of the main proponents of the structural/mechanistic approach to systemic phenomena, a conceptual perspective that implicitly or explicitly inspired most of his work. I claim, from all of the above and from my personal knowledge of the history and circumstances, that the encounters between Vaz and Varela (in which the Chilean military coup of 1973 had some responsibility, as, after the coup, leaving Chile was for Varela a wise decision regarding his personal safety) had a most decisive part in requiring

immunology to take the necessary switch from the functional to structural paradigm, and in projecting the scope of this change to deep experimental and conceptual aspects of the immunology.

Jorge Mpodozis Marin holds a PhD in physiology and neurobiology from the University of Chile. He is part of the Council of the Faculty of Sciences, University of Chile, where he teaches regular courses on evolution, neuroethology, and biology of cognition. Jorge is a founding member of the Chilean Society of Evolutionary Biology and the Chilean Society of Neurosciences. He has directed numerous research projects, undergraduate and graduate students, focusing mainly on the anatomy and comparative physiology of the visual system in vertebrates.

Received: 19 October 2017
Accepted: 26 October 2017

Diseases: Loss of Inner Harmonies?

Humberto R. Maturana
Escuela Matriztica de Santiago, Chile
hmr/at/matriztica.org

> Upshot • An organism is a harmonious closed network of molecular and cellular interactions that produce molecular and cellular transformations and replacements in the continuous realization of its molecular autopoiesis. The processes that we call immunity are dynamics of recovery of that harmony when it is lost as a result of the appearance or intrusion of molecules that do not normally pertain to it, which destroy that harmony, giving rise to what is lived as a disease.

« 1 » In my writings, I refer to cognition, saying that when one says that a person or a system knows, what one is saying is that in her opinion that person or system is behaving or operating in an adequate manner according to the circumstance in which one is observing it. When one says that one knows that something is the case, and one is asked, how do you know? The answer that one gives is always a description of the doings that have to be performed for that to happen. It is in that sense that the metaphor "every living system as it lives operates as a cognitive system" is both adequate and misleading. When I said that in the book *The Tree of Knowledge* (Maturana & Varela 1987), I was claiming that knowing is adequate doing according to what the observer thinks is adequate doing in the circumstances of her observation. But metaphors are generally misleading because they mostly obscure the actual processes that the person who uses them wants to evoke, and in this sense the authors of this article are right.

« 2 » I do not consider it adequate to talk about any system as a cognitive system as a metaphor aiming to evoke how it operates. Systems do not exist by themselves as such. When one talks of a system, one wants to refer to a configuration of relations that one abstracts in the flow of interactions and transformations of a collection of elements that one distinguishes in one's daily living: a configuration of relations that we, as observers, distinguish as spontaneously or artificially being conserved in some domain of our concern. A tornado, for example, is not an entity with definite borders, and extends only as far as the observer chooses what must be conserved in its dynamic. The same happens with what is called the immune system, which does not exist by itself, and appears only when we, as observers, distinguish in an organism a configuration of dynamic relations that we think must be conserved in it, so that what we call immune processes appear.

« 3 » An organism exists (regardless of whether it is unicellular or multi-cellular) as a closed network of cellular and molecular processes in which molecules and cells produce and destroy one another in a harmonious manner that continuously results in the organism's self-production through the realization of its molecular autopoiesis. In this process, molecules enter and come out of the organism while the organism remains in its dynamic closure, oblivious to what we, as observers, see as its ecological niche or environment. In the evolutionary history of the different kinds of organism that constitute the biosphere, the different kinds of molecules appearing inside them, either being produced by them or entering into them from the medium that contains them, have fundamentally five different destinies independently of where they come from. They may…

- be incorporated in the normal metabolic processes;
- be destroyed;
- disharmonize the normal metabolic processes;
- be expelled; or
- accumulate in the organism.

« 4 » The manners of dealing with the molecules that appear inside the different kinds of organisms currently living have been transformed and changed along the natural drift of their respective lineages according to the manners of living that have been conserved in them (Maturana 1980; Maturana & Mpodozis 2000). Natural drift is not a history of adaption to a changing medium but a history of conservation of the realization of living of the organism in a transforming and changing ecological niche that does not preexist as such, but arises as it slides in the medium in the tangent of the realization of its living. Therefore, to understand what we obscure by talking of "immune systems" we have to look at what harmonious networks of normal processes of molecular and cellular productions and interactions are conserved by the destruction of the molecules or cells that disrupt them. I cannot answer these questions because I do not study these processes. Yet I feel that when we attend much to what we think is the description of the function of a process with respect to the operation of the organism in its niche, we do not fully see how that process occurs in relation to the realization of its living.

« 5 » In the process of realization of the molecular autopoiesis of an organism there is no "concern" with the environment in which it operates, so there is nothing in the inner operation of the organism other than harmonious metabolic processes that conserve its living, or it dies. Similarly, in the inner dynamics of the operation of the nervous system of an organism there are only changes of configurations of relations of neuronal activities that are adequate for the conservation of its living in the tangent of the historical present in which the organism realizes its molecular autopoiesis, or not and becomes ill and recovers … or does not recover and dies. If we confuse our description of the immune processes thinking in an