SELF-ORGANIZATION OF A COMPLEX SYSTEM: A HYPOTHESIS OF HOMEOSTATIC PATTERN OF PAIN

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ABSTRACT

The concept of homeostasis has expanded: while initially its application used to be bound to the field of classical organ physiology, apparatus or system (eg.: circulation, endocrine system, excretory system), it now appears that there is homeostasis at other levels, both at the cellular and molecular level (eg.: ion concentrations in the cytoplasm, speed the catalysis of an enzyme, etc..) that in terms of systems and functions that control the integrity and quality of biologically significant information (eg.: immune system, neurobiology, the NoPain/Pain system). The NP/P is a structured system for hierarchical architecture, consisting of 3 subsystems: sensory-discriminative, motivational-affective and cognitive-evaluative. In basal and physiological conditions, the whole system is organized with a high degree of modularization, with an activity which favors, especially in the responses to low frequency, the *intra*-rather than the *inter*-modular interactions. Its dynamic behavior is subject to regulatory processes according to a homeostatic model: it is basically a regulatory not linear system, in multiple circuits of feedback/ feedforward control. The homeostatic system is represented by a feedback loop (*feedback*) in which the information on the result of a transformation or an oscillation of activity is postponed, revised and corrected, at the entrance of the cycle. Always interpreted as a linear phenomenon, NP/P system shows on the other hand, in modeling complexity, the ability to compress the regularities identified in a scheme, in an internal model, that is a behavior and understanding of reality model, which is far from being linear.

Keywords: *homeostasis, complex systems, non-linear dynamics, pain and complexity, self-organization.*

1. INTRODUCTION

The impressive success of molecular biology in the last decades has led some authors to state that the only biological investigations truly worthy of scientific status are those able to explain biological phenomena in terms of basic components and the underlying physical and chemical processes. The expectations of these authors go up to the ideal of being able to comprehensively explain the behavior of entire systems based on advanced laws in order to clarify the behavior of atoms and molecules that compose it. I do not want to delve further into, in this context, theoretical disputes of biological reductionism. We believe that the only criterion for the validity of a search strategy is its success. Namely, the analytical methods as well as synthetic ones, ie, the study of living phenomena at higher or lower levels of complexity, are justified if they increase our understanding of a phenomenon, which in medicine always translates into effective, or as more effective than currently available, therapeutic strategies. Beyond extreme positions, we recognize the validity of different levels of scientific description (from quarks to whole societies analysis), each of which is not logically reducible to the other: every reading level has its own laws, and, from the time being none can be brought back to a basic science that includes all the others. It seems reasonable and inevitable to advance the significance and the need to highlight:

1. The existence of separate layers (quark-atoms-molecules-cell-organ-systems-agencies-company) all lawful for investigation;
2. The need to link these levels through: a) an upward motion (summary) that looks for how it happened; b) a downward motion (analysis) that looks for the reason why it happened.

The level of scientific description upon which this work will be placed is that of complex systems, aimed to investigate the background of "non-linear" dynamics, that is, more complicated energy background than those corresponding to the models of Newton-Laplace physical order. This "non-linear" dynamics is the basis of apparition, within systems of well-defined deterministic time evolution of chaos: unpredictable deviations from the ideal trajectory (or behavior), which in the long term will change scenarios (configurations) and expectations (evolution). This non-linearity is also the explanatory basis of self-organization phenomenon, by which, in biological systems, starting from a messy situation spontaneously evolves towards a more ordered state, through the organization (schemes), via feedback mechanisms (homeostasis), of various sub-systems interacting at multiple levels. The unusual conceptual framework that will carry out our reflections is the study of complexity laws as such, and not only complex systems in their specific composition.

2. PAIN AND COMPLEXITY

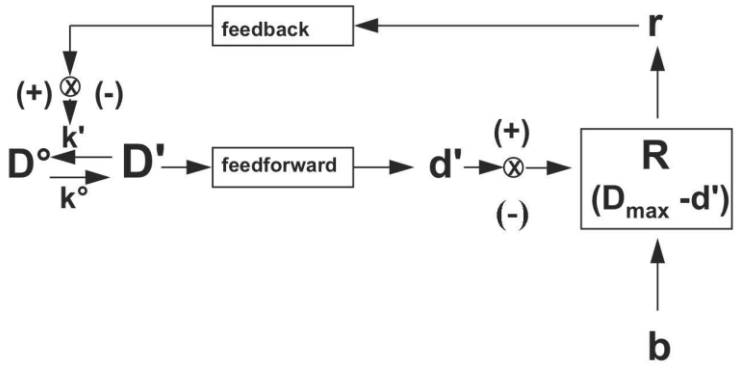
In general, we can say that the core of the problem, or rather, the observation that has led the system of knowledge and interpretation of natural phenomena to be upset, is that according to which, in a well defined "determistic" temporal evolution complex system (which is to say, dynamic systems), the interaction of its sub-components on a scale of observation, leads to a complex global behavior on a larger scale, which in general cannot be predicted by the knowledge of individual components. Furthermore, such unpredictability is not due to lack of information on the system itself, it cannot be filled by the acquisition of new information, but it is an intrinsic property of physical systems, which is manifested in a more or less evident way, depending on the internal or external conditions to the system itself (the so-called phenomenon of "sensitive dependence on initial conditions"). Life has been succinctly described as a "controlled disequilibrium" (Guidotti, 1990). The particular characteristics of this imbalance can be captured in a particularly obvious way, reflecting on the complexity of biological homeostasis to which the NoPain/Pain system (NP/P) fully belongs. As the complexity of systems assigned to such purposes has turned out to become, more evident thanks to biomedical sciences progress, the concept of homeostasis itself has expanded: while initially its application used to be bound to the field of classical organ physiology, apparatus or system (eg.: circulation, endocrine system, excretory system), it now appears that there is homeostasis at other levels, both at the cellular and molecular level (eg.: ion concentrations in the cytoplasm, speed the catalysis of an enzyme, etc..) that in terms of systems and functions that control the integrity and quality of biologically significant information (eg.: immune system, neurobiology, the NP/P system).

3. HYPOTHESIS OF HOMEOSTATIC PATTERN OF PAIN

Despite the fact that a way for a series of studies revealing an increasing number of internal systems for modulation of painful sensory input has been opened since 1965, the "pain" phenomenon continues to be understood only in terms of linear sensory function. The resulting and undeniable, therapeutic advances have mainly benefited from the expression of the acute symptoms, leaving extensive sectors of chronic pain in the grip of enigmatic and not comforting results. In this context, the analytical method has always moved outside of any descriptive and predictive model, if not partial reference. It should definitely be emphasized that no mathematical formula can accurately simulate the behavior of a living system, and that any other model is only an estimate which facilitates the description and understanding of reality, without, however, being able to run out of the variability and complexity. Even within the already observed limits, the modeling that is going to be outlined, will allow us to enclose an area in which the phenomenology of pain will receive unexpected characterizations, although for the time being they will only be analogical and qualitative. Its deriving findings, in fact, have the value of claims, surely of a general nature, being able to encompass the painful expression with interpretive keys appropriate to the complexity of the phenomenon. The NP/P is a structured system for hierarchical architecture, consisting of 3 subsystems: sensory-discriminative, motivational-affective and cognitive-evaluative. The painful event determines, over the subject in whom it occurs, a complex and diversified experience (Melzack and Casey 1968), which includes:

- Identification of the sensory stimulus in terms of location and physical properties (sensory-discriminative subsystem);
- Activation of supraspinal autonomic reflexes (ventilation, circulation, neuroendocrine functions), and motivational unpleasant affective tone of the organism to react (motivational-affective subsystem);
- Processing of painful stimulation (nociception) in terms of storage, comparison with past experiences, learning, capacity for abstraction (interpretation and meaning), attention and vigilance, judgment, intellectual, cultural, ability to verbalization (cognitive-evaluative subsystem) .

In basal and physiological conditions, the whole system is organized with a high degree of modularization, with an activity which favors, especially in the responses to low frequency, the *intra*- rather than the *inter*-modular interactions. Its dynamic behavior is subject to regulatory processes according to a homeostatic model, which can essentially be described as follows:



It is basically a regulatory not linear system, in multiple circuits of feedback/ feedforward control: there exists the considered variable (in this case the variable **D°-D'**), which may change in a reversible way, thanks to the existence of mechanisms that push the reaction or transformation in the two directions (in considered case, **D°--->D'** and **D'---> D°**). We will call "effector systems" these mechanisms, since they are able to make the transformation or modification of the considered parameter. The state of **D** and **D'** depends on the relative imbalance in the activity of the two opposing effector systems (called, respectively, **k°** and **k'**). The homeostatic system is represented here by a feedback loop (*feedback*) in which the information on the result of a transformation or an oscillation of activity is postponed, revised and corrected, at the entrance of the cycle. There are not only negative feedback loops (which guarantee the stability), but also positive, of self-amplification, rings, in which the product of the reaction helps to accelerate the transformation. The human processing of pain is also reinforced by the feedforward control ("advance information" - in our case one of these circuits is given by the "central control trigger", specialized system of large diameter fibers and rapid conduction, formed by ways of projection of the dorsal columns and the post-synaptic system of dorsal columns), which provides for the possible consequences of pain and painful experiences, speaking to plan ahead alternative scenarios. The learning, in fact, as primary component of pain, also explains the individuality of its effects on equal physical intensity, on different people. In order to ensure the normal homeostasis, the activity of effector systems does not occur without mutual checks and without coordination with other systems: for this purpose, one or more regulatory systems (**R**) are inserted in each homeostatic system, playing the role of determining which disequilibrium **D°/D'** should be reached or maintained at all times, by integrating the status of **D°/D'** with the needs of the rest of the organism. In order to do this, the system controller must "monitor" the state of **D°/D'**, receiving from them adequate warning (**d'**), and it must produce a return signal (**r**) that is incorporated in the stimulatory or inhibitory sense by effectors systems. The controller system is then able to control the effector systems being connected to other systems from which it receives information useful to the choice of the control to be carried out (**b**). An intrinsic control is also combined with regulatory system, which could be said to be the memory of the "normal" values of **D'**. The "normal" values are the maximum and minimum limits of the variable **D'**, above and below of which the controller system is mobilized by emitting a signal that influences the activity of effector systems, in the sense of bringing the values back to standard, that is **D°**. In diagram this concept is expressed with the formula (**Dmax-d'**), meaning by this the fact that the controller system operates according to the comparison between the maximum value of tolerable **D'** (**Dmax**) and the signal that indicates the current or potential situation (**d'**). In this scheme, the higher **d'** will be in respect to **Dmax**, the more intense will be the **r** production and then the inhibition of the effector system (**k°) D°--->D'** or the stimulation of the effector (**k') D'--->D°** will be. The lower and the upper limits herein referred are given by the intrinsic structural conditions of the controller system, they are not invariable for all systems, in fact many homeostatic systems fit on different response thresholds when appearing chronic diseases, or in front of repetitive stimulus. Regulatory systems are therefore "plastic": at this level you are experiencing various regulatory events such as hypersensitivity (eg.: Increase of receptors, "priming") or adaptation (eg.: "Down-regulation", contact inhibition, etc.).

4. CONCLUSIONS

In the criticism of the reductionist dogmas we have opposed subsystems that move in an ideal space (non-linear dynamics), to individual elementary particles that move in real space (mechanism), noting that in the case of complex systems requires effective laws other than the microscopic ones are required in order to give a description of the macroscopic behaviour. The NP/P is certainly evidence. Always interpreted as a linear phenomenon, it shows on the other hand, in modeling complexity, the ability to compress the regularities identified in a scheme, in an

internal model, that is a behavior and understanding of reality model, which is far from being linear. This non-linearity is also the explanatory basis of self-organization, phenomenon by which, in biological systems, starting from a messy situation, it spontaneously evolves towards a more ordered state, through the organization (schemes), via feedback mechanisms (homeostasis), of various sub-systems interacting at multiple levels. Guarantor, together with the immune system of our identity, it turns out to be a complex adaptive system that collects information about its surroundings, about himself and about his behavior, so that this monitoring activity, although apparently stationary in effects is actually changing in the course of time according to models that carry the system and its environment to be co-evolutionary.

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