A New Biology: A Modern Perspective on the Challenge of Closing the Gap between the Islands of Knowledge

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Abstract. This paper discusses the rebirth of the old quest for the principles of biology along the discourse line of *machine-organism disanalogy* and within the context of biocomputation from a modern perspective. It reviews some new attempts to revise the existing body of research and enhance it with new developments in some promising fields of mathematics and computation. The major challenge is that the latter are expected to also answer the need for a new framework, a new language and a new methodology capable of closing the existing gap between the different levels of complex system organization.

Keywords: biological mathematics, biocomputation, interactions, events.

1 Introduction: The Quest

The domain of self-organization is common to physical and life sciences, to social sciences, economy and engineering. There has been a lot of research carried out in this field during the past 50 years and we have attained some progress. However, we still cannot pass a distinct boundary with our current state of science, methodology and technology. This is because we still cannot well understand complex natural systems and the processing of events within them.

The ultimate goal of modern science and engineering is to understand matters and to develop sustainable technologies emulating the building and organization principles of complex natural systems. However, before developing a technology we need to provide the basics, the formalisms, models and theories required to make this happen.

Basically, we have three questions to answer in this discussion round. First, what is the quest we are going for, second what needs to be done, i.e. our ambition and mission, and third, what are the next steps, i.e. our approach.

For the first question, we set out in the direction of reviving the final quest for discovering the principles of biology known from the works of Rashevsky [1,2] and Rosen [3,4] as topological biology, relational biology or complex systems biology along the focused discourse line of Michael Conrad's *machine-organism disanalogy* [5,6] within the technological context of biocomputation [7,8]. Despite these efforts to re-think theoretical biology by means of mathematics failing in practice, because the experimentalists simply did not understand and hence did not know how to implement the mathematical abstractions and the biological generalizations [9], these early attempts provide a good base to start from by revising and enhancing them with new methods and approaches from a modern perspective.

2 The Miss(ion)

Now, let us turn to the second question: what is being missed? When doing research in these areas we can easily observe a certain gap between big and small, a gap between machinery and cells, a gap between individuals and society from many perspectives. One of the major questions here is the complexity of interactions in living systems which are organized at multiple levels and at multiple timescales. These interactions are fairly well known at each single level.

However, what we do not know well is the view of the system and its operation as a whole. The top level and the lower levels of a complex natural system have been well studied in the past. For instance, in macro economy we have such models as fiscal and monetary policies involving a few basic parameters such as taxation or interest rates, whereas in micro economy we have economic models of individuals or classes of individuals, studied as individual decision-making units in a rather idealistic way. In neuroscience and psychology we have behaviors of the overall system and neurons, groups of neurons and their biochemical activity at the micro level correspondingly.

Yet, the big gap remains between these two dimensions: at the *mesoscopic* level. We still do not know how structures, processes and events trigger and organize (themselves) in between. An analogy for this gap could be found in the difference between the impact and interpretation of decision making processes using current models in psychology and sociology associated to the micro and macro levels organization, i.e. individuals vs. communities, societies, nations, etc.

Therefore, we need *a universal and extensible formal approach to explain the dynamics of hierarchical organization of biosocial phenomena at multiple levels and timescales along with the interactions between them.*

In summary, we are missing something very fundamental at the junction between the micro, macro and mesoscopic levels. We need to tackle what is missed in order to explain this gap between the levels of complex system organization. Whether it is a new framework, a new tool, a new language or maybe a new methodology, this needs to be explored.

Paradoxically, a similar phenomenon can be observed within the historical and epistemological framework of scientific development. This interdependence between the different disciplines in science has been shown as a series of the illustrations in a survey about Integral Biomathics [10] where the relationship between the natural sciences and formal models and theories was represented as a set of interdependent hierarchies within the spiral development of science. This model was recently formally represented using Memory Evolutive Systems (MES), a technique based on dynamic category theory to model evolutionary multi-scale adaptive self-organized systems [11,12]. The latter promises to be a well suited technique we can use to start our quest.

3 The Approach

What kind of *language* could be used to achieve the goals defined in the previous section? What kind of theory and what kind of models are suitable for our mission?

An emphasis on events [13], and in particular on *extreme events* (a term that is being explored in complex themes such as climate change and financial markets), may lead us to establish principles that may guide our research, such as the multiplicity principle [11] or the four Wandering Network principles [14].

As soon as we accept both *dynamics* and the *multiplicity principle*, we can move forward towards devising this new model framework and language for expressing the evolutionary dynamics of complex biosocial systems. Whereas expressing dynamics leads towards the integration of various temporal parameters into the model, the multiplicity principle allows us to account for the emergence of more and more complex individual levels of interaction and organization.

Another issue to solve on the way is the controversy between internal and external viewpoint of system description. Scientific models in natural sciences, such as physics and biology are usually external, done from a third person perspective which is not involved in the system processes and is not part of the model, the Observer. We need, however, also the so-called protobiological [15] and endophysical models [16] in our approach, which while being based on complex systems hierarchies [17], development and evolution [18] are capable to integrate the internal view at the system as part of it beyond synthesis [19] and “beyond the flat earth perspective in systems biology” [20].

Thus, the *coregulator* (CR) hierarchical organization construct of the MES theory [11] is a completely *internal* representation of e.g. neuro-cognitive system. It is real, i.e. related to the parts of the system, evolutionary and non-artificial formation, for instance explaining that we may observe some kind of virtualization and regenerative post-traumatic functional substitution of damaged brain segments by other ones, such as those in the visual or motor cortex [21]. This conclusion comes from the different links which arrive to the CRs allocated by observation. In this way, the individual CRs represent internal (hence partial) views of the system itself according to MES.

Nevertheless, category theory alone cannot take account of supplementary mathematical structures. In addition to hierarchy and dynamics using the CR construct, the MES formalism could be with additional capabilities from other domains in mathematics and computer science by replacing the categories by categories *enriched* in topology, higher order categories, stochastic maps or Bayesian networks, this in a similar way that Petri Nets developed diverse offsprings associated with such properties and functionalities as color, priority/weight, time, vector addition with states, stochastic states, degrees of liveness, etc. Thus, MES evolve to an 'enriched' MES integrating another kind of structure.

We can also describe a "Science" MES, in which each single CR can represent a whole formal theory. This MES provides the base for the integration of multiple domains of knowledge with their interactions In this way, we are able to express the development of science at successive moments of time within an evolving model of science [22], the emergence of a new theory, model or language based on two different domains of knowledge being expressed in this MES by a higher level CR And the links/interfaces between two different knowledge domains can be studied, possibly ensuring the correct transformation of data from the one domain into the other. Furthermore, a good practical approach to implement categories is the object-oriented paradigm in computer languages. Another complementary aspect of this implementation is the usage of functional (process-oriented) programming.

4 The Protomodel

In particular, we identify the following central question when modeling an evolving complex system: how many dimensions has the quality vector of a non-monolitic complex system? In our current view they are at least seven:

1. objects/components
2. functions/procedures
3. behaviours
4. relations/topology
5. patterns/categories
6. subsumption and composition hierarchy
7. hierarchy of the structural, temporal and procedural organization

However, in order to develop a new mathematical construction we need to identify first the problem at hand. What are we going to solve? Which examples can be used to develop and test the new approach? The *multiplicity principle* which generalizes the degeneracy property of the neural code is exactly what explains the possibility of multiple causes for the emergence and development of a natural phenomenon, such as the formation of more and more complex mental objects based on the neural activity. Another interesting approach is to use the capabilities of *fractals* in shaping and modulating the activity of biosocial systems.

Basically, there are two criteria for evaluating such approaches and principles: i) the level of complexity with its multiple temporalities leading to cascades of events backfiring between levels, and ii) the level of modeling uncertainty (where the multiplicity principle plays a role). They can be used as base for investigating the applicability of the novel mathematical formalisms to real world problems such as tumor development, theory of aging, global climate change, pandemic developments and stock market crashes.

The above domains have in common the emergence of *extreme events* in self-organizing systems characterized by nonlinear dynamics. Linear systems analysis is arguably one the major achievements of 20th century mathematics. However, it is questionable that linear analysis is a suitable strategy in the domains mentioned above. For example, complex phenomena such as the self-sustaining activity of the brain cannot be entirely explained in linear analysis basis.

5 The Challenges

We meet many challenges on the way towards discovering the principles of biomathematics and biocomputation. For the moment, we have identified the need of developing specialized mathematical theories and models and computational toolsets/solutions in the following areas:

- Mathematical models such as MES [11] of multi-scale systems and of their self-organization through the 'interplay' between their different regulatory processes accounting for their different complexities and rhythms.
- Computer simulation of MES or bridging Theoretical Neuroscience and Computational neuroscience.
    - MES does not explain how the patterns of neurons are formed, or how the categories of neurons of higher complexity are created, but it does provide fresh theoretical insights that deserve to be explored by either empirical tests or computational simulations.
    - Another issue is to reconcile the different aspects of CR modeling.
- Mathematics of non-linear processes (Are Platonic forms non-linear?)
    - Complexity science aims to investigate nonlinear systems where the relevant features are both local and global in a way that is intrinsically not reducible. Thus nonlinearity is the chief factor in complexity science.
- 3D VR/AR (virtual/augmented reality) and 3D TV from molecular and system biology to computational medicine.
- Dynamic computer graphics for compositions of 3D curves: development of mathematical algorithms and software for computer graphics imaging of rotated 3D curves and fractals.
    - Fractals of 2D curves show interesting geometry. Fractals or compositions of 3D curves show much more complex 3D geometry exhibiting interesting features. Their properties, however, could not be demonstrated with static views only. They need to be rotated. The preferable mathematical expression of a 3D curve is by parametric equations with 3 variables and a few parameters.

Herewith the development of precise standard languages to support the theory deserves a special attention. The expressive capabilities e.g. of BPMN, a language for business processes management is currently very purely for use in its own domain [23], not to mention biology.

Hence, we need

1. to pay attention to the grounding problem when using a particular language and a methodology capable to fuse or at least interconnect the different languages and models.
2. to develop dynamically extensible semantic meta-models of both object-oriented and functional languages and their combinations completing the models with the holistic view of the system.
3. to extend and redesign the available languages for system biology and to construct new ones that precisely define the concepts of *state* and *event* including their taxonomy (origin, occurrence, duration, frequency, etc.), [23].

In summary, we need to devise a playful environment for mathematics where one theory can be substituted with another in order to achieve creative discovery. It is time to develop new alternatives to those short-term strategies and conceptions of the past and present. One way to be pursued aims to track down the underlying principles, written in formal-mathematical terms that explain the organization of complex biological systems such as the cortex and other major areas in the brain. Anticipation and autonomy are other two issues that need to be addressed within this context.

6 The Outlook: On Interactions and Events

Everything that happens in (living) Nature is based on entropically driven interactions and self-assembly reactions. Their common characteristics are events. Interactions are continuous and everywhere; they are ubiquitous. An important aspect of interactions is their organization on a multiplicity of scales/viewpoints within the same context/location with different complexity levels and rhythms.

Yet, continuity itself depends on the timescale where it is observed. Generally, matters which appear discrete at small timescales can appear continuous at larger timescales. Hence, we have to do with scales and relativity here or perhaps even with scale relativity [24,25]. Another aspect of such complex irregular systems is the event-triggered emergence and development of abstract heterarchies (i.e. dynamical hierarchical systems inheriting logical inconsistencies between levels) in terms of time/state-scale re-entrant forms which are very difficult to formalize as dynamical systems because of their intrinsic inconsistencies [26]. Finally, there are interactions between heterogeneous viewpoints (models), modes or development stages of such systems (in a timeline that extrapolates to evolution), while their self-organization depends on the cooperation/competition between a net of internal regulatory processes executed by physical entities (organs) or CoRegulators (CR's) each operating in an internalistic, endophysical manner [16] at its own complexity level and with its own temporality [11]. Thus, events can result from the interactions between CoRegulators [13]. This interdependence can be observed at all scales in (living) Nature. Ultimately, multiscale interactions and their nonlocal characteristics at the deepest quantum level lead to the question and hypotheses about the emergence and evolution of consciousness [27].

In summary, human beings, being large lumps of matter (made up of large numbers of cells, each made up of large numbers of complex molecules, atoms, etc.) comprehend the world as interactions. Given the scale at which they see things and processes, these events are made up of very large numbers of superposed interactions between entities at lower levels of organization.

Can the new software engineering paradigm of event-driven architectures and complex event processing for large enterprise systems [28] and a projected vision of computational socio-genomics [29] gain ground as model and technology bridging and automating research in the life science disciplines? This is a question we hope to answer in the course of our quest. Each time human thought has crossed a tenet's border allowing a new assumption, new tools were developed to prove the new hypothesis and advanced our understanding of the world. Real events, however, such as those we perceive, single or in the structures we perceive (companies, families, nation-states, flocks of birds, etc.) are more complex, and are made up of lower-level structures which are not indefinitely characterisable, and which probably do not need to be [30].

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