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ORIGINAL PAPER

On the Ehresmann–Vanbremeersch Theory and Mathematical Biology

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Abstract Category theory has been proposed as the ultimate algebraic model for biology. We review the Ehresmann–Vanbremeersch theory in the context of other mathematical approaches.

Keywords Evolutionary systems · Memory · Biological theory · Aging of organic structures · Cognitive coherence

1 Introduction

The Ehresmann–Vanbremeersch work is an abstract theory of biology, continuing and substantially extending the ideas of Rashevsky and Rosen. Before discussing the theory per se, it is fair to ask: Why should one care?

In recent years, technological progress has made it necessary to control multiple sensors and effectors and to utilize common sense and context in carrying out computer operations. These requirements are no longer confined to the laboratory or industrial setting but now permeate daily life. The newest tools in computational mathematics, aimed at addressing these needs, include such fields as *neural networks*, *fuzzy logic*, and *genetic algorithms*, and are explicitly based on biologically inspired ideas. Older methods for handling such problems of "computational intelligence" including operations research and statistics were developed from applications to social and economic problems—insurance, gambling, and military logistics, rather than chemistry and physics.

Thus, a strong motivation for studying biology in the abstract is the possibility of uncovering its mechanisms for coordinating movement, perception, behavior, and resources so that everything appears when and where needed. Even individual cells

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are marvelous examples of "Just-in-time" planning, while the rippling muscles of an orca provide incredibly precise power compared to which conventional maritime science is crude.

Another very good reason to study biology from an abstract point of view is to observe the broad-brush features which otherwise may get lost in the detail. For example, the long-fought "war against cancer" has a huge number of researchers with an enormous budget and yet, according to a recent series of articles in the New York Times, their actual accomplishments are meager. Perhaps one needs to see more than the individual trees to manage a forest.

Still another reason is the increasing age of the populations of the more prosperous countries. Aging puts an emphasis on holistic aspects such as memory and quality of life and yet the corresponding medical specialty of gerontology/geriatrics is notoriously underserved, as those of us with aging parents have discovered. If individual clinical interventions are the experiments, where is the theory to guide them?

A second fair question to ask is: What is special about the Ehresmann–Vanbremeersch theory?

First, there are the authors themselves. Andrée Ehresmann is a mathematician, who studied with Choquet (one of the leading analysts of the twentieth century) and who then worked with and married Charles Ehresmann (a category-theorist of equal status with Choquet). The Ehresmann couple produced seminal papers in category theory; their collected work, which forms a large part of the mathematical foundation of the EV theory, spans several volumes (Ehresmann 1980–1984). Jean-Paul Vanbremeersch, on the other hand, is a physician specializing in gerontology, with substantial clinical experience who in addition currently coordinates a home for the elderly. Thus, his theoretical activities are grounded in actual cases.

The collaboration of these two authors has continued for >20 years. Thus, the EV theory is based on the long-term and thorough cooperation of two first-rate intellects from mathematics and medicine. This is the type of collaboration which Norbert Wiener and Ivan Havel both wrote about, where the practitioners of the separate disciplines don't just transfer data back and forth but actually learn each other's habits of mind and procedures.

Having shown the reader why this book is worth the effort to study, let me be clear about the scope of my review. Due to lack of time and space as well as to my own slowness in comprehending the full depth of the EV-theory, I will say very little about its concluding parts, which deal with memory and neural systems. Subsequent to writing [MES] (we write [MES] to refer to the book under review), Ehresmann and Vanbremeersch have extended their ideas still further in these directions (Ehresmann and Vanbremeersch in press), cf. [MES, Chap. 10, p. 332 et seq.]. However, it is very exciting to learn that their notion of the Archetypal Core, developed purely as a result of the theory, has apparently found corroboration in experimental neuroscience (Hagman 2000). Thus, still another reason for the reader to take the time to study the Ehresmann–Vanbremeersch book is its potential contribution to neuroscience. I also suspect that it may prove useful in the field of cognitive science, where once again basic theory is needed.

The view of biology afforded by *Memory Evolutive Systems* reminds this reviewer of the science fiction stories of Jules Verne, whose resting place is in Amiens, where both authors, Ehresmann and Vanbremeersch, work. While Verne did not have a precise image of the actual technology of the first human flight to the Moon, for example, he did have the basic parameters of the lunar module, including the size of the crew and duration of the voyage, almost exactly right.

My own commentary is of a very different nature, that might be more comparable with R. C. Crumb, the American cartoonist from Cleveland. Cartoons, as Daumier showed so well, can capture the essence of a situation. I hope to draw attention to some interesting connections between biology and mathematics and to suggest some useful extensions of the categorical ideas which underlie the book.

Ehresmann and Vanbremeersch have elaborated a subtle theory of structure, perfectly suited to the complex diagrams of biochemistry and inter- and intra-organic interactions. Using the notion of categories which are layered with respect to both hierarchical structure (levels) and time (evolution and structural components), they present a nuanced theory that even allows them to propose a mechanism to model aging.

In [MES, p. 33], comparing their work to that of others in categorical systems theory, EV assert that in the other work

> the role of categories is … descriptive, and deep results of category theory are not exploited. On the contrary, in our model where we use categories to represent the successive configurations of a system, we make use of fundamental constructions, to give an internal analysis of the structure and the dynamics of the system.

The treatment of time and influence in the EV approach is novel and has a rather biological flavor. The deep categorical results are constructed via the complexification theorems of Chapter 4 and utilize the Multiplicity Principle, which assures the existence of complex links.

In this reviewer's opinion, EV's extensive utilization of limits and colimits of diagrams, based on the earlier work of both Charles and Andrée Ehresmann, is brilliant. Though it is completely impractical as a computational tool (given the limitations of present technology), I think it captures essential aspects of biological organization and may lead to more concrete hypotheses which are capable of being tested. Babbage's idea of the Analytic Engine was also completely theoretical in his day, but it has been quite practical since the advent of digital computers (made possible by way of quite a few unforseeable historically driven technological steps—e.g., the space race leading to semiconductors). In the same way, new developments in optical computing and artificial intelligence may allow actual implementation of their radical program for a mathematical framework for biology.

Certainly, the book is not a complete answer to all these questions. Some issues of coordination and computation are not considered, and the theory does not answer the fundamental questions: What is life and How do organisms successfully anticipate events? These topics are addressed, however; see [MES, pp. 224–230 and Theorem 7, p. 141].

This book is a monumental work which may influence all future research in theoretical biology. I think that Joseph Needham would be delighted!

The review is organized as follows. In the next two sections, we discuss Memory Evolutive Systems and Living Systems. Sections 4 and 5 are on the categorical nature of the model, and the idea of hierarchical categories. Section 6 considers MES in the context of abstract mathematical approaches to biology. Section 7 is an example, while in Sect. 8 we propose some possible explanations for the successful cooperation of the Centers of Regulation which is required by the EV theory. Finally, in Sect. 9 we consider the relationship between biology and physics.

2 Memory Evolutive Systems

The theory of Memory Evolutive Systems (MES) has been developing for more than 20 years. Its creators, Ehresmann and Vanbremeersch, have proposed a unique synthesis of various ideas and concepts, organized around the notion that life is an evolving hierarchical category with a functorial dynamic. Along with Robert Rosen and a few other mathematicians, philosophers, and biologists, EV believe that the formal theory of categories is the correct framework within which to develop a theory of biology.

However, unlike other attempts to establish a categorical framework for biology such as the reviewers own efforts (Kainen 1989, 1991, 1996, 2005), EV allow a detailed role for time, including various scales. They introduce novel concepts of influence, regulation, and memory; and they also admit quantitative measurements for morphisms, so that analysis can be combined with the algebra.

According to [MES, Chap. 6, p. 176],

> A complex hierarchical natural system autonomously maintains its identity over time; it evolves and adapts to changes in its environment, in spite of the multiplicity of its complexity levels, each one with its own structural and temporal constraints…
>
> Because there is no central regulating mechanism, it is necessary that the system have a network of partial regulatory organs, the *co-regulators*…

Co-regulators are subsystems of the natural system whose components act together to perform a specific function.

EV apply their method to create a theory of aging in organic systems. They also consider cognitive and semantic aspects, as well as physiological responses to stimuli.

It is the purpose of this article to comment on their book (Ehresmann and Vanbremeersch 2000), hereafter referred to as [MES]. Some additional or alternative concepts are proposed.

The EV-theory is rather elaborate and the order of its presentation can be varied substantially. It may help the reader to imagine an incomplete picture, waiting for the global view to emerge as with a Gestalt image in experimental psychology.

3 Living Systems

We begin by discussing an older but more succinct presentation which also incorporates some ideas of Jerry Chandler. Living systems are modeled as follows (Vanbremeersch et al. 1986):

(1) A web of *regulations* each coordinated by a particular *Center of Regulation* (CR) with characteristic [spatial and] temporal domain. The regulations may be conflicting or cooperating. "The equilibration process among these CRs is not directed from above but depends on *structural temporal constraints* … which may lead to the emergence of more complex structures."
(2) "An internal memory, which may develop in time, allows for a selection of local operations based on *anticipation* of their results, and for possible repairs in case such an operation cannot be performed in due time."
(3) "Higher level structures have several different lower level implementations (*symmetry-breaking* in the passage from higher to lower levels), thus ensuring structural stability and plasticity." (All italics as in the paper.) **[Square brackets indicate author comments.]**

Organization of the system is described as the family of all its components at all levels and their interactions—e.g., for a cell, the organelles, molecules, atoms, with chemical and topological relations. Change of organization is restricted to the archetypal catastrophes of birth, death, splitting, and fusing, as enumerated by Thom (1993); that is, the emergence of new objects, the destruction of existing objects (e.g., the programmed death of certain neurons), cellular mitosis (when a cell divides into two daughter cells), and the aggregation of separate cells into a new (though transient) organism (as in slime-molds). The process of metabolism, where higher-level components are broken down into lower-order ones, as in digestion of food, is a bit different since it suggests the dissolution of a colimit. Similarly, the obverse metabolic process in which elementary components are bound into something higher as in the synthesis of a protein seems to be the formation of a colimit.

Observing an organism, one sees the interactions among the various components, each organized by a CR with a particular time [and space] scale and acting within the Newtonian world. Each CR consists of a small group of *actors*. The CR operates using a stepwise procedure with a set of *strategies* that can be performed, specific energy-generating or energy-consuming reactions which make or break bindings. The usual result of a strategy can be anticipated by the CR and its application can be determined to have succeeded or failed in creating the usual effect.

The strategies and their results determine part of the memory. While a low-order CR may have only one strategy (a cyclic process), higher order CRs may have a wide range of strategies available. "Higher CRs (e.g. in a neural system) can learn new strategies, thus developing the memory."

The choice of strategy by a CR depends on what information is observable by its actors at that particular time and on the "anticipated memorized result of the strategy." This information forms the *actual landscape* of the CR. Once the strategy

is chosen, prior to its realization, everything unfolds as a simple physical system governed by, e.g., "differential equations satisfied by appropriate variables."

Selected strategies may not have the anticipated results, because of competition with other CRs (this is characteristic of complex systems); hence, their behavior is unpredictable. Though the landscapes of the CRs are "incommensurable" [like Leibnizian monads], the different CRs depend on global resources. At each instant, their strategies influence the system, so there needs to be an equilibration process.

Important structural constraints arise from propagation delays and the span of stability. There is some flexibility but there is a limit to the perturbations which can be tolerated without disrupting the process. This is where the quantification of morphisms is especially useful and leads to a quantitative model of aging based on the different time-scales involved.

Equilibration [when it is needed] discards a strategy of a CR if the constraints aren't satisfied, leaving a *fracture* in the landscape and change of strategy to repair it. This can lead to the emergence of higher-order objects and new properties and is "facilitated by the robustness and plasticity of complex systems."

4 The Categorical Model

The mathematical substance of Memory Evolutive Systems is built using the theory of categories. Category theory is abstractly the "pushout" (i.e., a coherent amalgamation) of the algebraic theory of semigroups and the combinatorial theory of directed graphs—one has arrows between objects and a way to compose some sequences of arrows to produce new arrows, subject to the existence of an identity arrow for each object and associativity for compositions of arrows. To the abstract framework of categories, Ehresmann and Vanbremeersch introduce *quantifications* by means of labeling links with observables such as force or propagation delay.

At time t, EV suppose that there is a category $\mathcal{K}_t$ which has a "layered" structure in the sense that each object at level $n+1$ is the colimit of a diagram in the subcategory formed by all the lower levels. This includes not just the substructures but their ontogenies. The category which describes the system at time t includes all of the structure (objects are the components while morphisms are interactions); it is related to the description at time $t' > t$ by a (level-preserving) *partial* functor, defined only on the objects and morphisms that survive, $F : \mathcal{K}_t \to \mathcal{K}_{t'}$) which "can be generated by *complexification with respect to a strategy*." That is, each object arises in a principled way from it progenitors using some rationale for eliminating old objects and introducing new ones.

In the more fully developed theory presented in the book, the new terms *option* and *procedure* replace "strategy"; "option" refers to the complexification process, while "procedure" refers to selection by a CR.

A key idea, and quite an attractive one, of the EV-approach is to regard diagrams (which are called *patterns*) as collective behavior in a category with colimits representing the most efficient embodiment of the ensemble as an emergent object

with its resulting morphisms. More exactly, there is a *sketch* which is a graph (or underlying diagram scheme) and a homomorphism of the sketch into the underlying graph of a category. One natural way for a category to "grow" is to add new objects and morphisms so that patterns in the original category which did not have colimits now do have them.

In general, colimits are treated far more extensively in the EV-approach than are limits. Of course, a colimit in the opposite category is a limit in the original one, so limits are implicitly already handled. However, within the same category, it is clear that both concepts should have quite different interpretations. In the book [MES, p. 114] the necessary formalisms are given and the idea is advanced that limits correspond to classifications. Limits also occur in the notion of procedural memory [MES, Chap. 8, pp. 256–258].

Describing the different types of complexifications, Thom's four *standard changes* are considered: "birth, death, confluence and scission." For example, within a cell, the following operations on macromolecules correspond: endocytosis, exocytosis, synthesis, and decomposition. These entail the modification of the configuration (components and interactions) around a given time [and place]. "In terms of matter and energy, birth and death relate to exchanges with the outside, while confluence and scission relate to internal exchanges." Thus, "structure-information" consists of the category K while "circulating-information" which depends on the objectives informs the functor which maps the category K to a new category K' in which standard changes are applied to K according to the specified option and "acts like a servo-mechanism to implement them."

The Ehresmann–Vanbremeersch vision is quite detailed; they postulate explicit categorical operations (pp. 117–120). Birth and death introduce new objects or eliminate old ones. Scission permits a complex object in K to dissolve into its separate components, while confluence integrates a pattern in K into a complex object, which may emerge in K' and which binds the pattern by becoming its colimit in K'.

An *option* gives a list of objectives for changing a category in any of these standard ways: (i) A graph U of external elements 'to be absorbed'. (ii) A set V of objects of K 'to be eliminated'. (iii) A set of patterns of K 'to be bound' (by a colimit). A *mixed option* is an option specifying objectives of the previous three types as well as (iv) A set of patterns of K to be classified (by a limit).

The complexification of a category according to such options is achieved by (i) absorption of external graphs, (ii) elimination of objects, (iii) binding and (iv) classifying of patterns. In absorption, the external graph becomes a subgraph of the complexification; in elimination, there is a partial functor defined only on the objects and morphisms of K which don't involve eliminated objects. Each pattern P to be bound is integrated into an object cP which becomes its colimit and if P and P^o are *homologous*, then $cP = cP^o$. Homologous means that their *operating fields* (these are "comma categories" if P consists of a single object) are isomorphic. Elimination presumably also needs $lP = lP^o$ whenever the patterns P and P^o are "pro-homologous", where lP stands for the limit of P.

5 Categorical Hierarchies

Categorical hierarchy is a key notion of the EV-theory. An object of a given level is *complex* with respect to lower levels "if it is the colimit of a pattern representing the organization of its lower level components." For example, a molecule is the colimit of its component atoms, an organism is the colimit of its component cells, and so forth. This is interesting but more detail would be helpful. In molecules, the atoms are not still but move according to the mechanical and electromagnetic forces acting upon them. It has been suggested in the literature that the recognition of antigens may depend on the vibrational state of the molecule. Certainly an atomic nucleus depends not just on its nucleonic components but also on its binding energy and excitational state. These might well be subsumed by the EV-theory, as they represent the morphisms of the diagram from which the higher level object emerges as colimit.

Perhaps language would be a suitable target for the notion of categorical hierarchy, where once again Ehresmann and Vanbremeersch's theory could provide a unifying framework. In fact, language is not discussed in [MES] but semantics is considered [MES, pp. 269–279]; see also Ehresmann and Vanbremeersch (in press, pp. 327–330). It seems to this reviewer that written language has three levels, the second and third emerging from the first and second, respectively: there are alphabets of letters, dictionaries of words, and an infinite ensemble of grammatical sentences.

Chomsky's idea of implicitly given formal and neuro-anatomical constraints might describe the diagrammatic syntax that constrains the sort of word-diagrams from which sentences arise. Puns rather clearly involve complex links. Moreover, while a paragraph is just a string of sentences, there are cognitive aspects which enable humans to derive meaning more easily from one paragraph-parsing rather than another. So one might view paragraphs (or perhaps stories, descriptions, concepts, etc.) as colimits of their constituent sentences. Hence, such units of cognition would also be second-order colimits of their constituent words, and the EV-theory could possibly contribute here to the task of automatically summarizing bodies of text. Moreover, this might allow the construction of *experiments* where various basic and secondary aspects of the theory could be tested and refined.

"We need to analyze how links between complex objects are formed." (p. 73) Let Q and P be two patterns in category K. A *cluster* from Q to P is a maximal set G of links from the components of Q to those of P which correlate with "the distinguished links of both patterns, so that the information transmitted to P by each component of Q is well-coordinated with the constraints imposed by the internal organization of P. Clusters can be composed; that is,

$$\text{if } G : Q \to P \text{ and } G' : P \to Q', \text{ then } GG' : Q \to Q'.$$

A link between two complex objects is called *simple* if it arises from a cluster joining the patterns of which they are the colimits. A *complex* link exists between two complex objects when there are separate links among the lower-level objects of which they are the colimits but these separate links are not directly composable. The notion of complex link is central to the theory and represent a departure from

ordinary category theory. I find this idea extremely "biomorphic"; for example, the relation between the use of the tongue in speech and in sex would represent such a complex link.

The various notions of diagram morphisms in the EV-theory are flexible enough to permit nice descriptions of the evolution of a company, as its goals and personnel change over time, yet retaining a focus on certain products or services. It is rare to find a mathematical structure with such a wide range of applicability, but this is exactly what one might expect from a theory based on categories.

6 Relation to Mathematical Biology

The EV-theory is among other things a *mathematical* theory of biology. As such, it should be compared with other developments in this direction. The very idea of having such a theory is by no means accepted—though the present trend is clearly moving in this direction.

When I first attended Gordon Research Conferences in theoretical biology in the mid-1970s, the biologists with whom I spoke uniformly rejected the very notion that there could be anything mathematical about biology. For them, mathematics was associated with physics and chemistry—something precise and exactly repeatable—which is surely not very biological. The term "Mathematical Biology" meant the use of mathematics to *describe* biological phenomena.

For instance, Rashevsky noted that a spherical shape minimizes surface area so for a cell, it is efficient to maintain an approximately spherical shape. A similar analysis indicates that to dissipate heat a long stringy shape (as in hair and fur) is good. Indeed, this sort of analysis has even been applied to account for distinct physiotypes: the ectomorphic builds of African Watusi versus the round and squat physiques of Esquimaux. Rashevsky had more complex arguments that typical cell sizes were best from a mathematical perspective.

But as Kuhn has noted, paradigms do shift (often with the replacement of one generation by the next). The notion that biology can *compute* is now becoming accepted by most biologists; this seems especially clear in the field of psychophysics. This sympathy to the introduction of mathematical ideas has also been driven by molecular data the implications of which had not yet penetrated 35 years ago.

In fact the idea of an abstract approach to biology is old. Leaving aside the ancients, such as Aristotle, the mystical tradition, and Leibniz's monads, in the twentieth century several eminent scientists and mathematicians attempted to construct a rapprochement. Needham proposed a role for topology in embryology (Needham 1936); he was also prescient in recognizing the essential role of fiber structures in the cell. Today, of course, it is known that topology plays an essential part in cell reproduction and metabolism since DNA must be unknotted for both activities. Cozzarelli invented a basic technique for treating cancer by interfering with the so-called topoisomerases which carry out this unknotting work (e.g., Wasserman and Cozzarelli 1986). This is particularly interesting since these protein

molecules, while not themselves alive, operate with an efficiency that is as yet unexplained.

Rhodes suggested in a parenthetical remark that the interaction of three people who are held together, when no two of them separately would be, could be likened to a famous topological example (beloved of magicians) called the Borromean Rings. Using his fundamental results on the theory of semigroups, Rhodes also proposed an algebraic model of metabolism (Rhodes 1971; Langer et al. 1968). Zeeman (1961) showed the existence of what he called a *stable thought* by means of a fundamental result from topology called the Fixed Point Theorem and he modeled perception using a functor from algebraic topology called "homology" (not the same as homology in molecular biology). Zeeman is also known for his theory of topological unknotting.

Another development in the abstract mathematical exploration of biology was Catastrophe Theory, largely developed by Thom and Zeeman; see Thom (1993). One of the aims of the theory was a way to understand the behavioral split which occurs when an animal is attracted to food but is afraid of some obstacle connected with achieving it. In an explicitly categorical theory (reversing his previous antipathy to the subject), Thom applied diagrams to a theory of significance (Thom 1990).

Both algebraic and combinatorial ideas have appeared in connection with genetics in essays by Gamow and Weyl. Some years ago, Benzer considered the application of interval graphs while biology may have been a partial motivation for the Erdős–Renyí theory of random graphs. More recently, Kaufmann (1993) used Boolean networks and random graph theory in his model of the interactions among separate genes.

Algebraic approaches have arisen in computational linguistics and are related to Latent Semantic Analysis. Smolensky and Legendre (2000) attempt to mathematically characterize the relationship between neural processing and higher-level symbolic computation, including linguistic grammar.

Algebraic and symbolic methods have also entered the general domain of mathematical biology, and a lengthy review article recently appeared (Reed 2000). Among other areas discussed, two examples of mathematics applied to medicine are given. One is the proposal to use simulation of fluid flow (based on MRI data) to analyze surgical interventions, while the second suggests the evaluation of cost-effectiveness of testing procedures and determination of optimal schedules.

Reed points out the incredible complexity of cells, which includes not just their biochemistry but also their organized movements—e.g., in reproduction, the DNA molecule (with two complementary strands) is split and then new complementary strands are formed, the doubled DNA separates, and the two daughter cells are created from the original cell, involving pinching off and various other topological modifications. These are drastic changes to the cell. Yet the cell is also stable, enjoying homeostatic immunity from minor fluctuations in the environment. Reed asks, "How does a cell do all this?" and suggests the answer involves stochastic differential and partial differential equations. Though it is not mentioned in his review, this does lead to algebra through the algebraic analysis of such equations—as

differential operators can be viewed as linear operators and the existence of positive or negative eigenvalues may provide information on the types of solutions.

The energy a cell needs to make the movements that determine its life is provided by individual molecules that must be metabolized. But this can't be a purely analytic activity as the energy must be ready when it is needed. A feedback model doesn't seem to be sufficient. Some sort of essentially algebraic calculation is made which determines when and where the "molecular motors" should be deployed.

In addition to genetics and protein–protein interactions, Reed considers the problem of DNA packing. This very long molecule is coiled into an extremely small space, and so the issues of how it replicates and how proteins are synthesized from the encoded information on the DNA are far from clear when thought of as molecular computations. To solve these problems, his review suggests the need for all of the following: partial differential equations, geometry, combinatorics, and topology (especially knot theory). It is difficult to see how pattern recognition and decision-making can arise from networks of simple neurons and much new theory will be needed.

A sequence of three recent conferences have focused on "algebraic biology" by which they include algebra, combinatorics, and computational intelligence. They have included research in mathematical modeling and system design, analysis, and verification, applied to molecular structure, sequence, and evolution, as well as genomics and proteomics. See, e.g., Barnette (2000).

The Statistical and Applied Mathematical Sciences Institute (SAMSI), based in North Carolina, has organized a 2008–2009 Program on Algebraic Methods in Systems Biology and Statistics: 'In recent years, methods from algebra, algebraic geometry, and discrete mathematics have found new and unexpected applications in systems biology as well as in statistics, leading to the emerging new fields of "algebraic biology" and "algebraic statistics." Furthermore, there are emerging applications of algebraic statistics to problems in biology.'

Thus, the EV-theory is consistent with an evolving trend in theoretical biology.

7 A Naturalistic Scenario

Let us consider an animal in a herd of its kind on the African plain. Each animal on the plain is an object of the category and the morphisms are the messages they send amongst themselves. Most messages are sent from the animal to itself, and these include various forms of identity.

The messengers are of several forms—visual, chemical, tactile, auditory, thermal; they act across physical and temporal distance and can be obstructed. For instance, predators hunt facing the wind.

Already there are interesting hierarchical aspects to this first level of a categorical viewpoint. The insects, for example, can usually be ignored from the perspective of animal-animal interaction (unless the bite of a fly makes a small animal cry out and so attract unwelcome attention from a predator). But insects are in symbiosis with animal and plant species, providing a subtlety to the articulation of nature that would be lacking without them. Indeed, insects provide a means to recycle organic

material that otherwise might be lost. According to the EV-perspective, insects, mammals, higher plants, fungi, bacteria, viruses—i.e., all of current-day life—is the colimit of the diagram of evolutionary history, itself emergent from the day-to-day diagram wars for existence that comprise this categorical view of biology. (It would be interesting to enlarge their theory to include the idea of multiplayer combinatorial and differential games.)

The utility of a categorical perspective is that it can apply at any scale. For instance, there can be intellectual objects (theories and humans) with messages transmitted being (i) human proposing a theory, (ii) humans talking or e-mailing, (iii) human writing a paper (morphism from human to himself), (iv) human reading a paper (not necessarily by herself), (v) papers themselves contain messages (e.g., theory acting on theory and about human dialogues)—so there are messages about messages.

But does this idea explain or predict anything new?

Returning to the animals in the plain, the herd animals attempt to blend in with the crowd, obtaining statistical safety. This enforces certain behavioral patterns that need to be determined to create the unified motion of the herd in flight. Messages are interchanged in a blizzard of rapid onset and decay, and somehow this enhances survival for the species.

Ehresmann and Vanbremeersch explicitly say that they don't give formal rules for the selection of strategies. (See Guitart's review elsewhere in this volume for some ideas on this problem.) However, even with a selection of strategies, there remains the problem of making explicit calculations. As von Neumann asked long ago, how can inexact biological components determine the parameters needed for precise actions?

In contrast, the theory proposed below would provide mathematical reasons for the heuristic success of organisms.

8 Some Mathematical Tools for Biology?

Just as a lever can provide mechanical advantage, mathematics can enable one to calculate solutions to problems with a smaller number of steps or to demonstrate that some property holds if a weaker form of the property is true. In some cases, it is possible to guarantee exact answers using only inexact measurements—just as digital codes allow one to be sure that a particular message was sent even when the channel of transmission is noisy.

I believe that biology opportunistically uses the affordances created by mathematical advantage, and in the subsections below several examples are sketched involving robustness and built-in structures.

8.1 Robustness

Robustness includes phenomena such as the following.

(1) In a finite-dimensional euclidean space **E**, there is an angle $\alpha_{\mathbf{E}} > 0$ such that if errors of less than $\alpha_{\mathbf{E}}$ in measuring the angle between two vectors are ignored, a resulting maximal pairwise approximately orthogonal set of vectors will be a small deformation of an exact pairwise-orthogonal set (Kainen and Kurková 1993). A pairwise approximately-orthogonal set has the same cardinality as a pairwise exactly-orthogonal set when the approximation is sufficiently close.

(2) A mapping between two metric spaces is an *isometry* if it preserves distance. The following says that if a mapping is close enough to preserving distance, then it differs by very little from a mapping which exactly preserves distance. (Metric, here, just means that there is a notion of "distance" which satisfies the usual criteria of non-negativity and the triangle inequality provided that the distance comes from a suitable normed linear space.)

For Banach spaces X, Y and $\varepsilon \geq 0$, $h : X \to Y$ is said to be an ε-isometry if it preserves distance up to an additive distortion of ε—i.e., if

$$\sup_{x,y \in X} \left| \|h(x) - h(y)\|_Y - \|x - y\|_X \right| \leq \varepsilon,$$

where $\|\cdot\|_Z$ denotes norm in $Z = X$ or Y. When $\varepsilon = 0$, this is just an ordinary isometry, also called a strict or true isometry. For $\varepsilon > 0$, any mapping uniformly close to a strict isometry is an ε-isometry; that is, isometries are approximate isometries. Conversely, for $\varepsilon > 0$, it can be shown that many ε-isometries are uniformly close to a true isometry. A special case of the following lovely result was first discovered by Hyers and Ulam (1947). There exists a universal positive constant C such that for every $\varepsilon > 0$, every pair X, Y of Banach spaces, and every ε-isometry $h : X \to Y$ which is onto and continuous, there exists a strict isometry $g : X \to Y$ with

$$\sup_{x \in X} \|h(x) - g(x)\|_Y \leq C\varepsilon;$$

in fact, $C = 2$ is now known to be the best possible constant.

Thus, certain structural features of geometry are robust to sufficiently small errors in measurement. Hence, imperfect senses can nevertheless obtain an exact model of the environment regarding these features.

Logic and algebra can also be robust.

(3) Commutativity of diagrams requires that certain pairs of parallel paths (i.e., paths with common source and target objects) produce the same result. Such a pair of parallel paths is also called a *face* of the diagram. For example, a square composed from four arrows oriented from left to right and top to bottom is commutative if going right then down gives the same morphism as going down then right.

One can view the commutativity of diagrams as a means for representing information. For instance, it is now standard to define structural properties of algebras and co-algebras such as associativity by means of commutative diagrams. The definition of many category-theoretic concepts, such as that of functor or

natural transformation, can be phrased as requiring the commutativity of certain special-form diagrams.

The robustness theorems below imply that commutativity is not as brittle as it might seem and diagrams can be shown to be commutative with increasing efficiency as the dimensionality increases.

For diagrams of a certain type (modeled by the digraph of a hypercube), when the morphisms in the category are all isomorphisms, a small fraction of the squares being commutative can force all other squares to commute. For the 3-dimensional cube, the effect is modest—one can skip one of the six square faces; if the others commute, it must too. But for d dimensions, we proved that (Kainen 2002) a fraction of approximately $4/d$ of the square faces will suffice. While these "forcing" squares must be chosen correctly, this shows that a principled approach to checking the commutativity of a high-dimensional cube gives a return on investment which improves with the dimension.

Moreover, if the total number of squares in the d-dimensional cube which *could* be non-commutative is smaller than $d-1$, then in fact these questionable squares are commutative—when commutativity fails, it must do so on at least $d-1$ squares (Kainen 2002). Thus, no subset of size $d-2$ of the set of all square faces of the d-cube can block the commutativity of the diagram. Hence, statistical sampling which results in a good estimate of the number of possibly non-commutative squares can lead to a robust conclusion regarding commutativity of the entire diagram.

These facts, while restricted to diagrams on the scheme of a hypercube, can be extended to more general diagram schemes by extending the theory of embedding subdivisions of digraphs in hypercubes (Hechler and Kainen 1974).

Thus, algebraically encoded logical information can be efficiently decoded by using a small forcing set of faces (i.e., checking a small set of key facts). And a sufficiently small set of apparent failures can be discounted as errors in the measurement process. In these ways, mathematics can help to maintain a robust model of the environment.

We feel that this last example of robustness of commutativity is supportive of the EV theory which would otherwise depend on the reliability of its components.

8.2 Structures

Another way that mathematics can serve biological purposes is by providing structures. Originally, Rashevsky noted that surface-tension minimization tends to give spherically shaped cells. But structure in a basic mathematical sense can have pervasive and subtle impacts.

Chirality seems to be an organizing principle of the brain and the central nervous system. As is well known, vertebrates process information contralaterally—that is, each side of the brain processes sensory data from the opposite side of the body and controls the muscles on the opposite side as well. Zeeman (1961) reviewed this situation from a topological perspective and noted how the neural representations of object images are placed where they are needed for muscular coordination through the twin reversals of the ocular lens and chiasmatic decussation (crossing of nerve

bundles from the portion of the retinae nearest the nose to the opposite hemisphere of the brain).

This contralateral organization of the nervous system could facilitate the rapid recognition of biological scenarios. The perception of objects which are in peripheral vision (right or left), such as predators, happens in one hemisphere of the brain which also controls the muscles for that side. In contrast, objects in foveal vision could be goal objects such as prey and are mapped to *both* sides of the brain. Thus, crude neurophysiological data immediately discriminates divergent scenarios of biological significance. For a discussion of different theories of contralateral organization, see Capozzoli (1995).

Another fundamental structural feature is the nature of the algebraic substrate. Suppose life, just as we now know to be the case for physics, makes no sense within the "real" numbers, but requires higher-order entities: complex numbers or even hyper-complex. Such ideas originated in physics. For example, one needs complex numbers to explain the phenomenon of polarized light, and quaternions are used in computer image processing and in models of human eye movements.

Changing the underlying scalar division algebra, even just from real to complex, permits new phenomena of a highly biomorphic flavor. For instance, in complex manifolds, boundaries, being of codimension 2, do not separate (as Arnold has observed). This elementary fact reminds one of the mental ability of being able to be simultaneously outside one's head and inside it, too, as when washing one's face. The two sensations (on hands and face) are clearly connected within the mind and the brain, yet they cross a topological boundary. Higher codimensions for the boundary might permit other interesting phenomena, such as unknotting.

The octonions possess the interesting property that they are the first Cayley–Dickson algebra to have a natural lattice of integral elements for which the finite set of unit-magnitude members do not constitute the corners of a fully symmetric platonic solid for that dimension (Kainen 2000). Indeed, Coxeter (1976) describes such a set of size 240. But no platonic solid in eight dimensions has 240 vertices. For physics, this is a codification of symmetry-breaking. The next C-D algebra beyond the octonions has dimension 16 and contains non-trivial zero divisors, and these could be viewed as annihilation and creation operators.

The non-associativity of the octonions is not a drawback for their potential use in biology; rather, it could be an advantage. The learning of an animal plainly depends, not just on the ordinal order-of-occurence of prior experiences, but also on their spacing in time—assuming that events occuring in short succession are associated first, the natural data gives rise to a parenthesized string. Standard models of data as fixed sets are not biomorphic, in my opinion, and while seeming to make problems easier, in fact, these models may be unrealistic, irrelevant, and unnecessarily difficult.

Moreover, the octonions lose their associativity in a rather controlled way. For instance, suppose we write e_i, $i = 0,1,\ldots,7$ for the generators, where $e_0 = 1$; the other e_i, $i = 1,\ldots,7$ are called the pure octonion generators. Of the 35 distinct triples of pure octonion generators, exactly 7 are associative, while the other 28 are anti-associative, i.e., associative up to a factor of -1. And products of three generators are automatically associative when the three generators aren't distinct. Additional

consequences of associativity, called the Moufang identities, remain true (Coxeter 1976).

Thus, if biological computations actually occur in terms of octonionic arithmetic, they would naturally incorporate a perception which depends on the associations within the data, as seems to be the case in biology. One might argue that it is far-fetched that biology should use such sophisticated mathematical developments, but of course all of these abstract algebraic concepts have been invented (or, if you prefer, "discovered") by humans who are certainly biological. Thus, the math of which we know *came* from biology; perhaps it can arise within biology without our intercession. And if this is true, then the structures which are carried by such an evolved algebraic system could give new capabilities to the organisms which utilize them.

9 Relationship between Biology and Physics

What is the structural relationship between biology and the physical world? No theory of biology can ignore this question. There is also the issue of feasibility: How does the phenomenon of life happen? De Chardin invokes the obscurity of sources, but that isn't an answer. Further, once life exists, why isn't it snuffed out by the cataclysms of geologic time?

Ehresmann and Vanbremeersch remark that organisms are only "locally and temporarily" mechanisms (cf. [MES, p. 141 and pp. 226–230]). They differentiate biological systems from purely physical ones, following Rosen (1985), in terms of the relations among the different kinds of causation. According to the EV-theory biological systems result from a large number of complexifications in which "the causal interactions between all the levels are continuously mingled in the dynamic flow" (p. 228). This distinguishes such systems from purely physical ones where material, formal and effective causality are strictly separated. (Aristotle's final causation certainly can't apply to a purely physical system.) The EV-theory shows how the intermixing of causations occurs and thereby makes Rosen's hypothesis rigorous.

EV also support Rosen's idea of life as an *anticipatory* system through their detailed theory of memory. Anticipatory systems, if we knew how to create them, would be of great value in technological applications, and there is a substantial body of work regarding systems which act as though they had knowledge of future events; see, e.g., Dubois (1998). However, it seems to me that memory alone is not sufficient to explain prediction. Indeed, it is difficult to imagine how animals could recognize the danger of fast-moving vehicles without invoking some kind of *simulation*, and this would require explicit calculations. It is not plausible that merely weighting different memory traces would provide the necessary accuracy. Otherwise, neural networks would already be able to solve such problems. Indeed, as with the process of equilibration of CRs, Ehresmann and Vanbremeersch make no claim to having a method to achieve such prediction.

This is where I will put on my cartoonist's cap and suggest a possible solution: **Life is physics running backwards**. To explain this, we need some details of interest in their own right.

The role of quantum-mechanical properties is discussed on pp. 162–163 of [MES], as a consequence of Theorem 7 (A characteristic of Complexity, p. 141), itself resting on Theorem 3 (Iterated Complexification Theorem, pp. 133–134). Theorem 7 proves that the Multiplicity Principle (MP) allows for the emergence, through successive complexification processes over time, of objects with increasing complexity levels, leading to more and more complex systems. Further, on pp. 226–228, EV discuss how the MP leads to the formation of higher order records (with several non-homologous ramifications) in the memory of a MES permitting a richer choice of strategies by the higher CRs and a more flexible interplay among their procedures, whence the development of more and more complex cognitive processes. So quantum mechanics is basic to their theory.

Quantum theory is essential in some biological processes. For instance, the detection of photons by the rhodopsin pigment in the eyes is known to involve direct quantum effects, as is photosynthesis. The biophysics of neuronal microtubules may involve the coherent propagation of energy (Craddock et al. 2000; Del Giudice 1988). In particular, when Planck's constant dominates the product of energetic and temporal uncertainty, i.e., if

$$\Delta E \cdot \Delta t \ll \mathrm{h} = 4 \times 10^{-15} \mathrm{eV\,s},$$

then measurement of time might be reversed. Gamow wrote amusingly about this theoretical possibility in his Mr. Tompkins in Wonderland books for children. A back-of-the-envelope calculation shows that typical biophysical parameters for neurons are within this range.

Let us suppose that such time reversal actually occurs in the neuronal process. Then we would have a mechanism for prediction. In sports, for instance, one knows at the instant of release whether or not the ball is going to go through the hoop. In golf, how is it possible to get a hole-in-one? Somehow, the idea that one imagines the result and works backward from it seems plausible.

But leaving aside fantasy, there are other reasons to believe that biology somehow involves time-reversal. From the standpoint of directed graphs (digraphs for short), physics and biology have exactly the same structure, except that all of the arrows are reversed as I shall explain.

A digraph is called a finite-state machine (FSM) if it has a unique arrow out of every node. It is well-known (and easy to prove) that the connected components of an FSM digraph consist of directed cycles, with trees rooted on the cycle whose branches flow down to the root. One may have several arrows entering a given node but only one points away from it. This conforms to one's intuition that physical systems are deterministic, with only one behavior possible once the initial state is given; that is, such a digraph is thoroughly cartesian.

In biology, no such deterministic behavior can be expected (unless one is absolutely committed to predestination which is as extreme a concept as vitalism). What is the digraph of a living system? A living system, we assert, has a unique

historical development; that is, there can be only one arrow *in*. Hence, living systems do have the structure of an FSMs running backwards, assuming that the reversal of time corresponds to the reversal of arrows.

Finally, there is one more reason to consider time-reversal as a fundamental aspect of biology, and that once again involves category theory, specifically the concept of adjointness. Mac Lane has described adjointness as the central notion in category theory and it occupies a substantial part of his book (Mac Lane 1986). Goguen (1971, 1972) showed that adjointness describes the relationship between behavior and realization of machines, while Lawvere (1963) shows that syntax and semantics are adjoint.

Let F be a functor from some category $\mathcal{S}$ to another category $\mathcal{G}$ and let U be a functor in the reverse direction. One says that F is the *left adjoint* to U (or U is right adjoint to F) provided that there is a natural bijection between the morphisms (in $\mathcal{S}$) from s to Ug and the morphisms (in $\mathcal{G}$) from Fs to g. The standard example is to let $\mathcal{S}$ be the category of sets and functions, G the category of groups and homomorphisms, U the functor that associates to a group its underlying set and to a homomorphism its underlying function, and F the "free group" functor that associates to a set s the group Fs which is generated by the elements in s and their formal inverses, with only the defining conditions of a group as relations. So if x, y, $z \in s$, then

$$(x \cdot y) \cdot z = x \cdot (y \cdot z),$$

and so on.

In the EV-theory, adjointness appears indirectly through the notion of colimit (and limit). My own theory is much more limited in scope than that of Ehresmann and Vanbremeersch, and it is concerned primarily with the relationship between biology and physics (Kainen 1991, 1996). I suppose that there are a pair of adjoint functors—one of "perception" and the other of "action"—that describe the relation of organism to environment. My theory was developed independently of that of EV (and also of Rosen). In fact, it was stimulated by misunderstanding the title of an article by S. Harnad on "categorical perception" (see Harnad 1990), together with a recollection of the work of Goguen and Lawvere.

My theory has perception involving formation of a colimit (gestalt perception is an extreme case) and is consistent with EV's notion of perception. It also includes a dual notion of muscular synergy (Kainen 1989) to account for operations such as signing one's name as a limit of intentions. This also seems to be consistent with the EV-theory, where limits correspond to actions.

This possible connection of biology with adjointness suggests still another reason to take time-reversal seriously. There are certain parallels between abstract systems theory and abstract biology. In a very interesting conference held at Amherst in 1973 on categorical systems theory, Arbib and Manes (1974) showed that adjointness could be regarded as a mechanism for time-reversal.

In fact, even a weaker notion, that of *weak* adjointness (Kainen 1971a, 2005) may give a better model. One can illustrate the idea using algebraic topology, as noted in Kainen (1971b). The universal coefficient theorem for ordinary homology states that

for any topological space X and abelian group G, there is a natural short exact sequence

$$0 \to Ext(H_{n-1}(X), G) \to H^n(X; G) \to \mathrm{Hom}(H_n(X), G) \to 0.$$

But the cohomology group $H^n(X;G)$ is naturally isomorphic to the group $[X,K(G,n)]$ of all homotopy classes of maps from the topological space X to the Eilenberg-MacLane space $K(G,n)$, which has single non-vanishing homotopy group G in dimension n. Accordingly, for every topological space X and every abelian group G, there is a natural *epimorphism*

$$\eta_{X,G} : [X, K(G, n)] \to \mathrm{Hom}(H_n(X), G)$$

In a cartoon view, an element α in $\mathrm{Hom}(H_n(X),G)$ represents a visualization of an imagined future perception of an animal relating to some desired goal G. The elements in $[X,K(G,n)]$ which η sends to α are the actions which the animal can perform now on the representation of G to achieve that visualization. Being epimorphic means that any visualization is achievable but not necessarily in a unique fashion. Choosing the actualization carefully could allow economy and intelligence of behavior.

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