

Origins of the Embryo: self-organization through cybernetic regulation

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Abstract

The construction of an embryo from a single cell precursor is a highly complex process. Evolutionary emergence of the first embryos is even more complex, and involves both a transition to multicellularity along with the establishment of developmental mechanisms. In this chapter, we propose that embryogenesis relies on a community of cells conforming to a regulatory model of emergent multicellularity. This model draws together multiple threads in the scientific literature, from complexity theory to cybernetics, and from thermodynamic entropy to artificial life. All of these strands come together to inform a model of goal-oriented regulation for emergent structures in early life. This is an important step in the evolution of early life, as well as the emergence of complex life in the earliest habitats. Our model, called the cybernetic embryo, allows for a systems-level view of the embryogenetic process.

1. The Origin of a Cybernetic Embryo

“Deep understanding of causality sometimes requires the understanding of very large patterns and their abstract relationships and interactions, not just the understanding of microscopic objects interacting in microscopic time intervals.” Douglas Hofstadter, *I am a Strange Loop* (Hofstadter, 2007).

The idea of applying cybernetics to understand embryogenesis has been proposed as an alternative means of understanding the processes of self-reference, collective organization, and differentiation during tissue formation and organogenesis (Gordon and Stone, 2017). According to this view, a series of nested cybernetic (self-regulating) systems are responsible for generating differentiated tissues and multicellular structures. This model exists within a larger, more complex picture of differentiation, which includes experimental work in frogs and sea urchins (Kearl, 2012), theoretical work by Gordon (1999), and even more recent work on electro-chemical signaling networks (Levin and Pezzulo, 2016). The nested structures that result from a cybernetic developmental process includes both hierarchical and heterarchical configurations (Bruni and Giorgi, 2015; von Goldammer et al., 2003). While many biological systems are hierarchical, heterarchies also occur in contexts where the constituent elements of a system can be configured in a number of equivalent ways (McCullough, 1945). These complex systems also utilize signals from outside the embryo, which results in an open thermodynamic system.

How does cybernetics describe highly complex biological systems? Cybernetics is the study of the predictive behavior of systems as they converge upon goal states. As a general theory of systems, cybernetics provides an abstract and holistic view of a biological system’s universal characteristics. It also provides a simplified dynamical description of these biological systems as

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they transition between equilibrium and non-equilibrium states (Weiner, 1961; Ashby, 1963; Pask, 1961). A cybernetic view of embryogenesis suggests an inviolate level at both the top and the bottom of the analysis: at the bottom the origin of organismal complexity, at the top the development of the embryo in successive stages in evolution. Ultimately, the central theme of the cybernetic embryo model is in providing a formal description of how regulatory mechanisms might behave in the regime between order and chaos (Gelens et al., 2015; McIsaac et al., 2011).

In this chapter, we will look beyond the specificity of the biological processes related to processes such as differentiation or induction. Rather, we will ask why groups of totipotent cells that later differentiate in a coordinated fashion are able to produce high degrees of complexity. We will approach this by treating the embryo as an abstract set of processes that represent the deep structure of developmental processes. We will establish a development model based on insights from cybernetics, game theory, computational linguistics, biological information, and physics that can explain the process of developmental history at both the cellular and organismal levels. A developmental model based on the principles of cybernetic regulation could become quite unwieldy. Therefore, we must state the requirements for origination of the cybernetic embryo and its processes. This leads us to two interrelated questions: 1) how do multicellular systems emerge, particularly in a developmental/life-history context, and 2) what is the fundamental unit of regulation in the embryo?

One primary concern of cybernetic embryo origins is the origin of regulative processes themselves, particularly as they relate to the origin of multicellular systems. Broadly speaking, the embryo satisfies two criteria in defining living systems: embryos are self-sustaining (Luisi, 2003) and self-replicating (Schuster and Sigmund, 1983). Whether found within eggs or within seeds, embryos require a supportive environment. In this sense, embryos are not completely self-sustaining. However, Turchin's (1995) definition of metasystems suggests that an embryogenesis embedded in the proper physiochemical environment can create and support the embryo as a self-sustaining entity. The criterion of self-sustenance is also related to the process of autopoiesis (Varela et al., 1974). In Abel (2009), autopoiesis as defined in the embryo consists of three parts: a network of reactions (or interactions) capable of regenerating all of a system's components existing within a self-defined boundary. In the embryo, we have both totipotent and pluripotent cells as well as a directed form of regeneration in which the basic arrangement (e.g. organismal structure) of the parent is recapitulated in the offspring. This recapitulation occurs through a set of feedback mechanisms (Varela et al., 1974) between genome, organism, and environment.

2. Mechanisms of the Cybernetic Embryo

Two ideas that will run through this chapter are the Law of Requisite Variety and the Good Regulator Theorem. Taken collectively, these ideas will provide a link between the cybernetic embryo as a conceptual model and the dynamic aspects of evolution and development. The Law of Requisite Variety, or the first law of cybernetics, defines the role of variation in a regulated system (Ashby, 1963). In an equilibrium system, variation is advantageous in terms of both competition and controllability. Particularly in terms of controllability, variation of the controller must be greater than the number of states controlled (Ashby, 1963). In this way, cybernetic systems can exhibit great robustness without having to predict every possible state in the system. While this is similar to the anticipatory systems of Rosen (1985), we have integrated such an argument with the notion of epigenetic landscapes (Waddington, 1935; Waddington, 1962) to yield a regulatory model that is both dynamic and generative.

In the case of our cybernetic embryo, we propose that the determinant of all developmental trajectories (evolution) produces an infinitely greater variety of possible states than the developmental process can encompass in any one species. In some cases, such as in the nematode *Caenorhabditis elegans*, development is mostly deterministic in terms of pathways taken during the developmental process (Penigault and Felix, 2011). In this case, evolution leaves no room for developmental contingencies, but produces a highly controlled trajectory. In other cases, such as the phenomenon of phenocopying (phenotypic diversity from the same genotype) in mammalian development (Sharma et al., 2016), evolution provides an avenue for robustness by leaving a number of possible contingencies for development that result in the same phenotype. From a cybernetics perspective, evolution has now resulted in a finite set of strategies (Koestler, 1967) expressed in the form of unique developmental trajectories. However, the amount of variation available to the evolutionary process influences what control strategies are available with relation to the developmental system. If the genetic pathway controlling development is highly complex, then we should expect more diversity in the developmental process. Overall, controllability (for definition in complex networks, see Liu et al., 2011) will vary based on the amount of organismal diversity provided by evolution and the number of viable developmental pathways.

Understanding this relationship in terms of the biology of an embryo also requires an appreciation for the Every Good Regulator Theorem (EGRT; see Conant and Ashby, 1970), which states that well-regulated systems must be a model of the system. In other words, regulatory mechanisms are meta-structural, not necessarily linked to specific biological components. We propose that in the embryo, the model of regulation is a discrete combinatorial set of pathways that connect the products of evolution and the instructions of development.

3. Candidate Processes

In a wide range of biological cell types, and even in protocells (Chen and Walde, 2010), we can see that single cells possess many regulatory mechanisms. In fact, the term “regulator” might seem too general given the complexity of cell function. Yet in this case, the term “regulator” is meant to be more general, as in a mechanism that allows for cell lines to replicate and remain self-contained as a living system. While our concern is largely theoretical, it is also related to the transition from a single cell to multiple cells in the same organismal system. In this sense then, we are also interested in how clusters of cells are able to regulate themselves as a single self-contained entity. When control occurs at the global level, it influences all other function in the cellular unit. Depending on the context, the regulatory mechanism can change scope during the process, with the same mode of control occurring at different scales (Lodhi and Muggleton, 2010). We will discuss the possible mechanisms for control later in the chapter. For our present concern, it is important to keep the black box regulator distinct from the theoretical construct.

Related to this is the need to understand what makes for an efficient regulator. Many processes in the cell are efficient, yet in terms of the theoretical regulator, the measure for efficiency is quite different. This is associated with the scale of regulation. Let us use a specific metabolic pathway as an example of a well-defined (non-theoretical) regulator. While this pathway can be considered an efficient regulator, its scale is not relevant to the entirety of the organismal (single or multicell) system. It is the singular course-grained regulator at the macroscale, which must be efficient for our cybernetic embryo to be persistent and self-sustaining.

Upon presenting the case for effective biological regulation, we can now consider the spontaneous order of embryos. More specifically, we can consider emergent order as it relates to the first embryos, which themselves are examples of a single cell to multicell transition in life-history (Kalinka and Tomancak, 2012). In a sense, embryogenesis encodes the evolutionary transition of multicellular complexity into a formal biological process. How exactly does the unfolding of this process become a quasi-repeatable phenomenon? In short, embryogenesis proceeds through a process of instruction resulting from genomic content and the spatial positioning of individual cells. The process is quasi-repeatable because while embryogenesis often yields similar results in embryos of the same species, depending on the species and mode of development there is some room for error and variation. Nevertheless, the answer we are looking for already exists in the epigenetic landscapes of Conrad Waddington (Waddington, 1957; Morris et al., 2016; Goldberg et al., 2007).

The epigenetic landscape is a tree-like structure that favors certain developmental pathways over others. Waddington referred to these favored pathways as canals (Siegal and Bergman, 2002), which when reinforced across individuals and over generations leads to the canalization of the developmental process (Waddington, 1957). The landscape is a discrete possibility space (based on the geometry of a Hamiltonian phase space) representing an exhaustive number of possible developmental outcomes (Goldberg et al., 2007). While Waddington originally meant for the epigenetic landscape to be metaphoric and descriptive in nature, more recent models envision development as a process of self-assembly, driven by free energy minimization and the ability of cells to reproduce a target shape in a collective manner (Friston et al., 2015).

It is our contention that both historical contingency and energetic constraints are responsible for determining the shape of canalization through this landscape. Specific developmental events necessarily lead to a finite number of subsequent events. This presents itself as a form of epigenetic memory, which when combined with specific instructions, can produce a tightly constrained tree topology along this landscape. We can observe this process in the developmental founder cells of *Caenorhabditis elegans* (Rose and Kemphues, 1998) or the establishment of developmental modules in vertebrates (Kuratani, 1998). The epigenetic landscape construct is also useful for understanding contexts in which these developmental constraints no longer act to focus the multicellular system. For example, we can examine the difference between increasing degrees of freedom and reduction of degrees of freedom due to a one-way embryogenetic development (for general concept, see Wissner-Gross and Freer, 2013). In a strictly developmental context, the available degrees of freedom are reduced as the embryo becomes increasingly specified. However, for biological processes such as cancer or aging, the degrees of freedom are increased.

Intuitively, the addition of cells to an organism might suggest a sort of combinatorial explosion of complexity that is biologically intractable. Epigenetic constraints resulting from developmental contingency (Oyama et al., 2003) suggest that the opposite holds true. In the embryo, the establishment of contingency results in part from the hierarchical organization of multicellular complexity and thermodynamic constraints. As a quasi-historical process, embryogenesis is shaped by developmental contingencies, which limit the role of environmental variation and are enforced by the twin phenomena of thermodynamic entropy and genetic information. As part of a more abstract cybernetic process, contingencies serve to shape the unfolding of information itself over time. As closed-ended dynamic systems (such as

embryogenesis) progress, messages are decoded and assembled within an increasingly specific context (Weiner, 1954).

4. Thermodynamics and Complexity

In the middle of 19th century, the irreversible process was first identified as a subject of theoretical interest, and defined a new subdiscipline of physics called thermodynamics. Later, Rudolf Clausius characterized the Second Law of Thermodynamics as the inevitable growth of entropy in any closed system. Ludwig Boltzmann developed a mathematical basis for the Second Law several decades later (Sharp and Matschinsky, 2015). In particular, Boltzmann's H-theorem that allows us to characterize thermodynamic irreversibility using a molecular-kinetic interpretation of heat processes and a comparison of thermodynamic state probabilities. A half-century later, a means to characterize the role of entropy in information was developed by Shannon (1948) and gave birth to a new scientific discipline revolving around the theory of information. Ben-Naim (2015) has remarked thusly on the relationship between the two: "Entropy, as it is now recognized, does not mean 'transformation', or 'change', or 'turn'. It does mean information". While many people accept the congruities between thermodynamic entropy and Shannon information, treating them as equivalent is not appropriate for all types of systems. In the concept of negentropy (Brillouin, 1953), entropy and information are treated as separate entities. According to this view, there is a subtle but important distinction made between entropy and information in cases where entropy works against the growth of complexity. In living systems, negentropy might act to limit the role of entropy but not information during the accumulation of complexity.

One way in which biological complexity might interact with information is by characterizing the information use in the regulation of processes as a form of algorithmic (or descriptive) complexity (Solomonoff, 1964; Kolmogorov; 1965; and Chaitin, 1969). Algorithmic complexity is relatable mathematically to Shannon Information, and reveals direct dependency between a given system's complexity and its total degrees of freedom. Although not equivalent to Shannon information, algorithmic complexity and entropy are mathematically similar. These mathematical interrelationships allow us to generalize the Second Law of Thermodynamic as a general law of complication (Mikhailovsky and Levich, 2015). Taking into account conditional complexity derived through degrees of freedom as indicated above, this law might also be the way in which living systems maximize their freedom.

We see countless examples of complication in the world around us. Complication is seen in a universe developing from simplicity of Big Bang and baryon soup to its current complexity of metagalaxies, galaxies, stars, and planets. It is matter born of quarks, electrons, neutrinos, gluons, etc., and has come up to macromolecules, cells, and living organisms. Perhaps the best example of complication is the evolution of complexity encompassing prokaryotes, eukaryotes, and multicellular organisms. It is characteristic of each organism that develops from fertilized zygote to mature organism. It defines the evolution of humanity, from the simplicity of scattered tribes to complexity of the contemporary world with nations, corporations, and stock markets. These examples are far from being exhaustive. However, these examples clearly contradict the interpretation of complexity as defined by maximum entropic states and randomization (chaos) as simple processes. In fact, these are all complex processes for which the maximum degree of complexity lies on the edge of order and chaos (Lineweaver, 2013). We also see this with the growth of real-world algorithmic complexity in structures that age and/or evolve over time (Papadimitriou, 2014). Yet increases in algorithmic complexity usually do not reach

their maximum values regardless of system.

The reason for this apparent suboptimality is simple: growth in complexity is limited by natural law. Laws of nature lead to a notion of permanent counteraction between the general law of complication and all other laws of nature. These laws are the only entities that do not obey the general law of complication and have not changed, as far as we know, during all the existence of our universe. This counteraction reveals itself at all the levels of hierarchy. Even the maximum entropy of ideal gas considered by Boltzmann in his H-theorem is not a real chaos. Its material points move in straight lines (Newton's First Law), collide elastically (Newton's Third Law), and their average energy, i.e., temperature, is proportional to the square of their velocity (Newton's Second Law). With increasing complexity and diversity, limitations by various laws of nature increase as well (Fuentes, 2014).

However, there is at least one way out that allows complexity to break through local barriers set by the laws of nature. This is called hierarchogenesis, and specific examples of hierarchogenetic events are described in Mikhailovsky and Gordon (2017). In the context of a cybernetic embryo, hierarchogenesis proceeds by systems of a given hierarchical level uniting from individual components. The total information of such a new super-system at a new level of hierarchy will be equal to the sum of information values for each of united systems (due to the additivity of entropy and information) plus information produced by interactions among these systems. This allows systems and their associated complexity to increase to new plateaus over time. While hierarchogenesis provides an emergent basis for the origin of such structures, increasing complexity may also be due to the law of requisite variety and emergent cybernetic control. In the next section, we will consider how this might be so.

5. Information and life

To understand how hierarchogenesis leads to actual biological complexity, we can turn to a process central to embryogenesis called morphogenesis. Morphogenesis is a process of diversifying organs and tissues within an organism to complete its life cycle. During the course of morphogenesis, hierarchical structures are created through processes of regulation. Yet the biology of phenotype and molecules demonstrate these regulatory relationships in an indirect manner. In fact, nature features many mechanisms, chemical, mechanical, electrical, etc., to accomplish this. At their core is the processes of information signaling and utilization.

To abstract this within a cellular automaton, the *Morphozoic* model (Portegys et al., 2017) has shown that tractable rule sets composed of hierarchically nested cellular neighborhoods are capable of producing both local and global information processing effects that can simulate reaction-diffusion morphogenesis (Turing, 1952), gastrulation, axon pathfinding, and other phenomena. Stephen Wolfram (2002) has demonstrated that simple rule sets can produce dynamic patterns within them, and that this complexity can be abstracted into hierarchical graphs (Wolfram, 2015).

We know that complex living systems lie in a middle ground between high and low entropy (Adami and Brown, 1994), and that perhaps regulatory mechanisms are responsible for keeping such systems within a critical set of values. As with the idea of negentropy, there is evidence that natural complex systems become more robust as they grow in complexity, and this robustness enables mechanisms such as self-sustenance and mutability. Even artificial systems seem to show

this property under certain circumstances. For example, variations of circuits that can implement a logical function become more numerous as the number of components grows (Raman and Wagner, 2011). In fact, it may be that the evolvability of a complex biological system and its tendency for innovation are features of the information content itself (Ball, 2015; Eigen and Schuster, 1979).

Continuing along these lines, studies of genetic variations indicates that “fit” configurations tend to be located on particular “paths” in the space of all possible configurations (Kirshner and Gerhart, 2006). This allows one successful genotype to migrate through mutation into other successful ones that could be more complex, and can be taken as a refutation of the oft-cited implausibility of life arising due to its sheer combinatorial complexity (Parter et al., 2008). Ball (2015) demonstrates this in discussing the interconnected nature of organismal complexity at multiple scales in determining fitness. For example, there are pathways in highly dimensional, complex systems that lead to “fit” phenotypes in only a few mutational steps. This is in part a property of combinatorics, where neural networks capable of sorting a very large number of inputs are constrained by a relatively small number of plausible pathways (Lin and Tegmark, 2016). In the biological case, however, greater complexity leads to more paths to fitness instead of making it increasingly less probable. In the context of the evolution of development, this provides a means to find stable paths to embryogenesis.

6. Emergence of Cybernetic Control via Evolutionary Transition and Constraint

In this section of our chapter, we will discuss how cybernetic elements can be put together to demonstrate the emergence of phenotypic complexity. We will mathematically and graphically define cybernetic elements, and then place such systems of elements into both a toy model and evolutionary context. Our toy model of choice for this demonstration is the Vehicle model of nervous system complexity, an approach introduced by Valentino Braitenberg (1984) to synthesize simple embodied nervous systems of varying complexities. To do this, we must represent the components of the vehicles as simple cybernetic elements. We must also consider what these cybernetic elements represent when arrayed in a set of interrelationships. By the end of this section, this will be explained and placed in the context of the cybernetic embryo.

While even the simplest cybernetic elements represent dynamic processes, they can also self-assemble into complex systems. Cybernetic systems can therefore represent changes in complexity of complex systems over time. This process of integration represents interactive processes ranging from symbiotic (Douglas, 2014) to cooperative (Pfeiffer and Bonhoeffer, 2003), and is representative of major evolutionary transitions (Maynard-Smith, 1983; Szathmary and Smith, 1995). In a less-abstract manner, this reintegration can represent the embryogenesis of a Vehicle, or transformation from a set of regulators functioning independently, to a set of autoregulating cells that work together to reproduce and function as higher-level units.

We can begin our discussion of cybernetic element complexity with simple cybernetic elements that can be represented both mathematically and graphically. We can characterize a set of cybernetic elements as an inferential structure, or a graphical model which models a specific hypothesis about regulation at a single biological scale. The simplest cybernetic structure is a first-order feedback loop (Figure 1) over a unit of time, which can be defined with a set of partial differential equations

$$\frac{dx}{dt} = f(y-x) \tag{1}$$

$$\frac{dx}{ds} = f(y-x)$$

where dt is the cybernetic structure over time, and ds is the cybernetic unit across space. The cybernetic structure consists of a unit x that receives a feedback loop (FB), a unit y that receives a feedforward loop (FF). Cybernetic units are used to characterize regulation independently over time (as is the case with serial cell divisions) or across space (as is the case in intercellular signaling).

The cybernetic models introduced here are adapted from models of molecular production and turnover (Alicea, 2014), and has been modified to approximate the regulation of discrete space-time processes. This differs from approaches that treat the embryo purely as a bag of chemical inducers and morphological gradients (Turing, 1952). In application to the cybernetic embryo concept, we combine simple cybernetic elements with pathways to serve as regulators of cellular state. Each set of cybernetic element and pathway combination (examples shown in Figures 1-3) represent idealized motifs, which simplifies the basic regulatory configuration independent of tissue type or even scale. With a focus on process rather than phenomenon, oversimplistic representations provide us with an idealized way to model data related to complex processes.

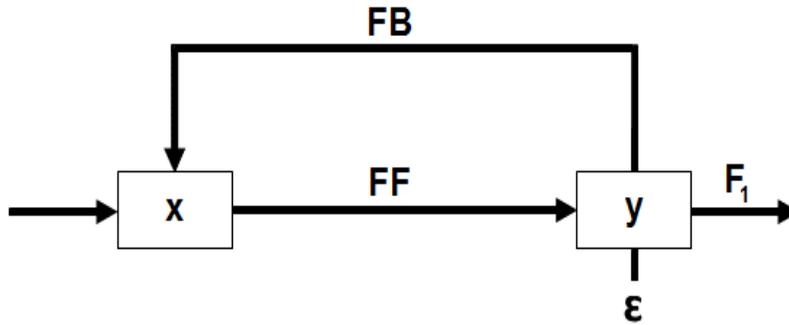


Figure 1. The simplest cybernetic element motif, a first-order feedback loop. Symbols are defined in Equation 1.

Cybernetic elements as introduced here may or may not be implemented in a material fashion. As a purely theoretical tool, networks of cybernetic elements can provide structure to messy systems ranging from the dynamics of transcription in cells to the interactions between cells themselves. The use of cybernetic element as a fundamental unit is broadly applicable, and serve as a problem structuring method (Mingers and Rosenhead, 2004) to make complex biological systems tractable. However, black box cybernetic elements can also be represented as formal replicator systems such as von Neumann self-replicating automata (Sipper, 1998; von Neumann and Burks, 1966).

Therefore, we also propose that cybernetic elements can exist as ensembles, which in this context represent a collection of cells with transient or nonexistent functional interrelationships. Let us now assume that an ensemble of simple cybernetic elements can self-replicate at rate τ , but

with a simple structure that does not interact with any of the other replicators. This results in a hybrid model of first-order regulation (serial) of a set of cybernetic elements with population dynamics. This can be defined using a form of the Quasispecies equation (Eigen and Schuster, 1979), and can be defined in the following manner

$$\dot{s}_m = \sum_j w_{mj} s_j - (b_m \cdot s_m) \quad [2]$$

where \dot{s} is a differential term, w_{mj} is the contribution of replicator s_j to the production of replicator s_m , s_m is a specific replicant at a particular timepoint, s_j is the replicator, and b_m is a coefficient that represents the rate of degradation and/or mortality.

As both feedback in individual units and the size of the population fluctuates, it becomes obvious that systems of increased complexity will only emerge in a highly transient manner. Therefore, a higher level of regulatory control is required. This higher-order control need not be hierarchical, but does need to take advantage of the products resulting from spontaneous organization (Eigen and Schuster, 1979). This results from cooperative effects between cybernetic elements resulting from functional needs. One source of emergent interdependency involves the long-term consequences of regulation for each individual cell. Consider the time-series that result from Equation 1: in cases of either too much (runaway) feedback or too little (dampening) input, a single regulator can become dysregulated quite easily. In these cases, a more elaborate cybernetic element can form, and may result in a larger regulatory system (see Figure 2).

Larger regulatory systems generally result from the inclusion of unit along with corresponding feedforward and feedback connections. An example of this is analogous to the static nervous system design for Vehicle #2 in Braitenberg (1984). In this case (Figure 2), each feedback unit is cross inhibited, while each feedforward unit receives a first-order feedback from the cross-inhibited feedback unit. This is mathematically defined as

$$\frac{dE}{dt} = \frac{y}{x'/x} , \frac{y'}{x/x'} \quad [3]$$

$$\frac{dE}{ds} = \frac{y}{x'/x} , \frac{y'}{x/x'}$$

where dt is the cybernetic structure over time, ds is the cybernetic unit across space, x and x' are parallel feedforward units, y and y' are parallel feedback units, and E is the global systemic (e.g. behavioral) output.

Another form of interdependency resulting from regulatory needs results in the formation of futile (or metabolic) cycles (Qian and Beard, 2006). Futile cycles (see Figure 3) are indefinite first-order feedback loops that utilize two multiplicative noise channels: one in the feedforward loop, and one in the feedback loop (Samoilov et al., 2005). The feedforward noise channel is positive, while the feedback noise channel is negative. Such channels produce no tangible output, but are both energetically active and produce an entropic output. It is not clear whether futile cycles are adaptive, as they consume energy but produce no tangible output. As a part of larger systems, they serve a purely regulatory function (Tu and McKnight, 2006). This can be described mathematically as

$$\frac{dF}{dt} = x(\sigma) + \frac{x}{y(-\sigma)}$$

$$\frac{dF}{ds} = x(\sigma) + \frac{x}{y(-\sigma)}$$

[4]

where dt is the cybernetic structure over time, ds is the cybernetic unit across space, $x(\sigma)$ is the noise-driven feedforward (FF) component, and $y(-\sigma)$ is the noise-driven feedback (FB) component (which result in negative feedback from element y to element x). Futile cycles can evolve from first-order feedback loops as either a support structure for other, more complex regulatory elements, or as a transitive structure from first-order feedback loops to more complex elements. Thus, transitional elements such as the futile cycle may allow for the buildup of complexity amongst a set of cybernetic elements.

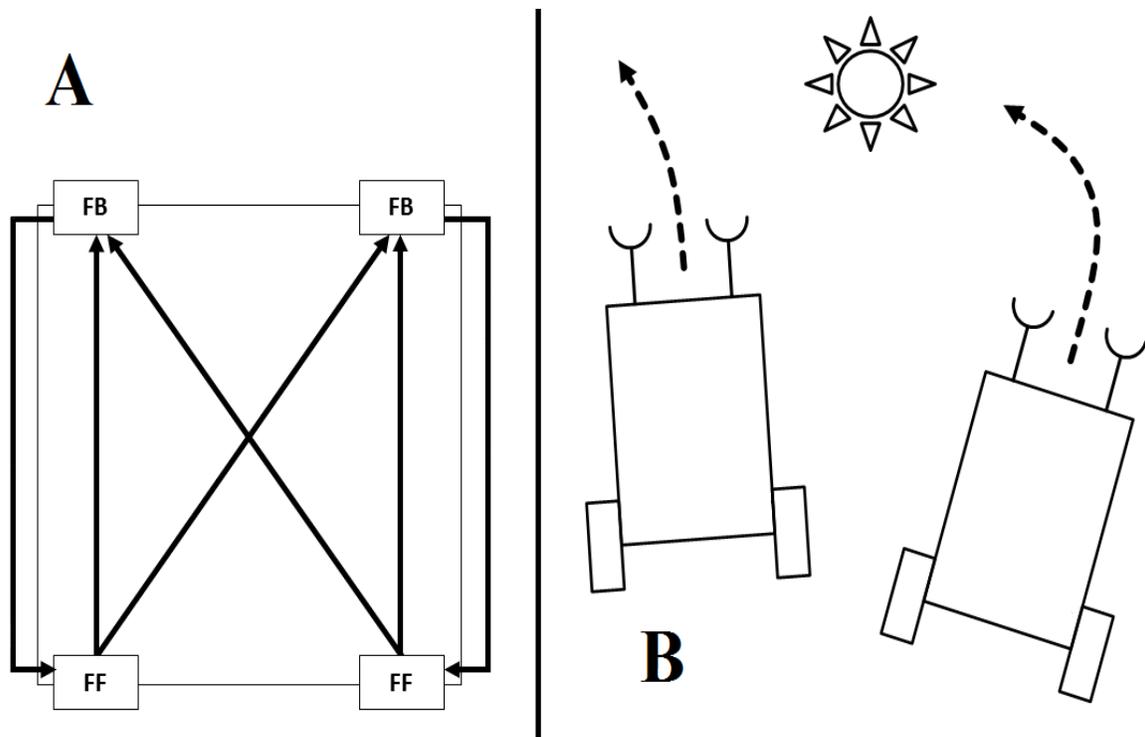


Figure 2. A cybernetic element (cross-feedforward, lateral feedback motif – Panel A) as demonstrated in the form of a Braitenberg Vehicle nervous system (Panel B). Panel A: pathways on the vehicle body show connectivity between sensors (e.g. frontal inputs that provide a feedforward signal, or FB) and effectors (e.g. wheels that provide feedback, or FF). Panel B: Two vehicles orienting their movement behavior relative to a common light source (the vehicle on the left is moving away from the light, while the vehicle on the right is moving towards). Panel B is adapted from https://commons.wikimedia.org/wiki/File:Braitenberg_Vehicle_2ab.png and is under CC-BY-SA license.

Biologically speaking, moving from a collection of simple cybernetic elements to a higher-level system of interacting cybernetic elements is an evolutionary transition (Szathmary and Smith, 1995). While this could be concurrent with the transition from single-cell to multi-cell organisms,

it could also characterize the transition between Prokaryotes and Eukaryotes or the transition from RNA world to genomes containing DNA. We can treat this variety of evolutionary transitions in such a generic fashion because the biological process can be demonstrated both graphically and quantitatively as the expansion of a generic regulatory system.

As cybernetic transitions allow for computational flexibility that scales to multiple problems and hypotheses (Perez-Jimenez, 2014), they also allow for an alternative means of representing the underlying biocomplexity. By viewing biocomplexity as the length of regulatory events (rather than as a genome size or number of cells), we can approximate how biological processes themselves evolve while still remaining active.

The question arises as to how cybernetic units become ordered in a heterogeneous system. This is similar to the topic of disorder-to-order transition (von Forester, 2003) in the realm of complexity theory. Emergent order through interactions can be understood by breaking down the system into individual behaviors ordered in time. In this formulation, the functional organization cybernetic elements will be ordinal with respect to time, which then imposes order through constraint upon the entire system. This can be thought of as a process of addition, where complexity is added to the emerging system as a series of smaller subsystems. In an embryo specifically, this could be instantiated as a series of timed cell division events. One way to model this type of spontaneous behavior is to look at first-mover dynamics, which is derived from game-theoretic Stackleberg competition (Leitmann, 1978).

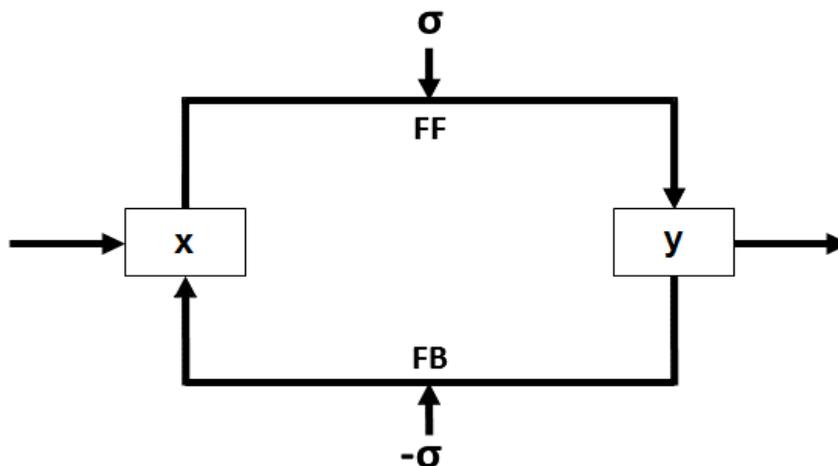


Figure 3. One possible transitional or auxiliary cybernetic element: the futile cycle. All symbols are defined in Equation 4.

The computational mechanism we will propose for the emergence of large-scale sets of cybernetic elements, which comprise complex, multicellular embryos, is the Stackleberg leader-follower game (Hu and Fukushima, 2015). Leader-follower games are generally pairwise, and can be composed of multiple leaders and multiple followers (Sinha et al., 2014). This can occur in as a series of subgames occurring in multiple time-dependent stages, so that each leader-follower subgame can build on the next. A simple demonstration of first-mover dynamics is how the two-player competitive game of tic-tac-toe proceeds according to Stackleberg leader-follower rules, and can be mapped to the early rounds of cell division in embryogenesis (Figure 4). While each

move in the game (playing a character, dividing a cell) represents a local intentionality, the results (pattern in 3x3 grid, whole embryo) at the global scale are quite unintentional.

In Figure 4A, we can see that X chooses first, and the play is to occupy the center square. Assuming each player makes an optimal move in the context of the previous player's move, the result of this first move is to constrain O into a defensive move. This meta-strategy proceeds until the game ends in a tie, and neither party obtains three characters in a row. First-mover dynamics can also be observed for a dividing embryo in Figure 4B, where division at the one-cell stage produces two cells, which constrain the position and orientation of subsequent divisions. As with the tic-tac-toe example, we make several assumptions about optimality with respect to the size/orientation of cells at each round of division.

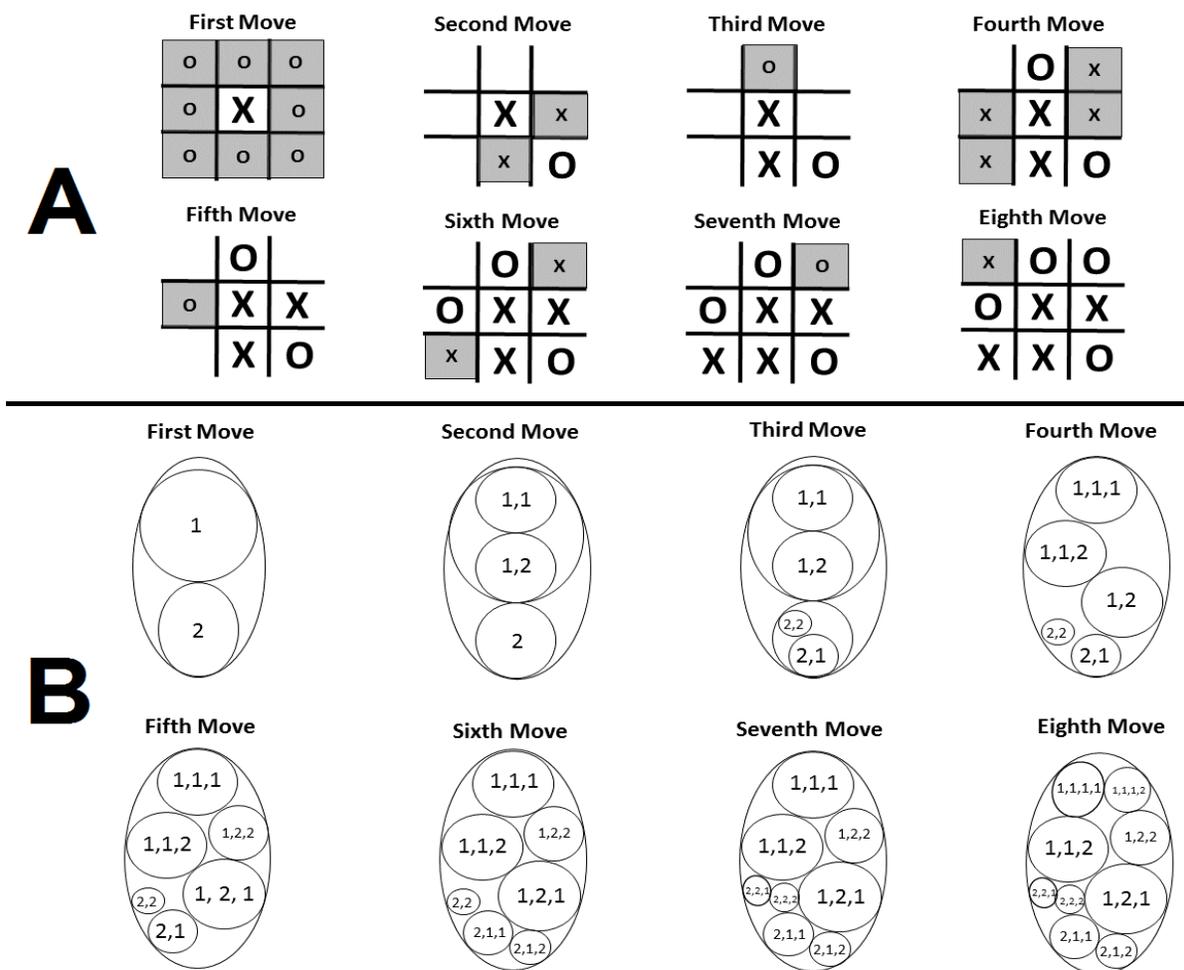


Figure 4. A diagram of how first-mover dynamics proceed in a game of tic-tac-toe. A: a step-by-step analysis of the first-mover tic-tac-toe-game. Gray squares are the number of possible moves in the next turn. B: a step-by-step analysis of how first-mover dynamics proceeds in a dividing embryo, with a cell's position in a lineage tree shown by sequential numbers inside the cell.

Even though most applications of Stackleberg games have involved non-cooperative decision-making (Pita et al., 2010), first-mover dynamics can be achieved through non-cognitive decision-making (Baluska and Levin, 2016). In the tic-tac-toe example, the outcome is determined

solely by the first mover's initial move, and in an evolutionary context can be explained through maximization of individual fitness and evolutionary constraint. In fact, each move tends to constrain the subsequent move, and leads to a generally progressive decrease in the system's degrees of freedom over time. An analysis of the tic-tac-toe game in Figure 4A is shown in Figure 5.

In conclusion, we can consider whether the Vehicles model is suitable for understanding evolutionary variation. In Braitenberg (1984), a variety of Vehicle phenotypes are decomposed using a syllabic network. Syllabic networks are constructed by using common features within a description for each vehicle, and uncover commonalities at the level of syllabic similarity. As each vehicle added to the analysis increases in descriptive complexity, new nodes are required to represent this complexity. Such a result is one of an expanded network, both in the number of connections to a single node and overall connectivity of the network. This is analogous to the production of new cybernetic elements during the course of evolution. An expansion in both the number and variety (Ashby, 1958) of cybernetic elements is necessary to allow for increases in complexity without sacrificing functional losses. Expansion of systemic size and complexity may also provide clues as to the level of selection and fitness criteria that allow for regulatory systems to expand while remaining functionally integrated.

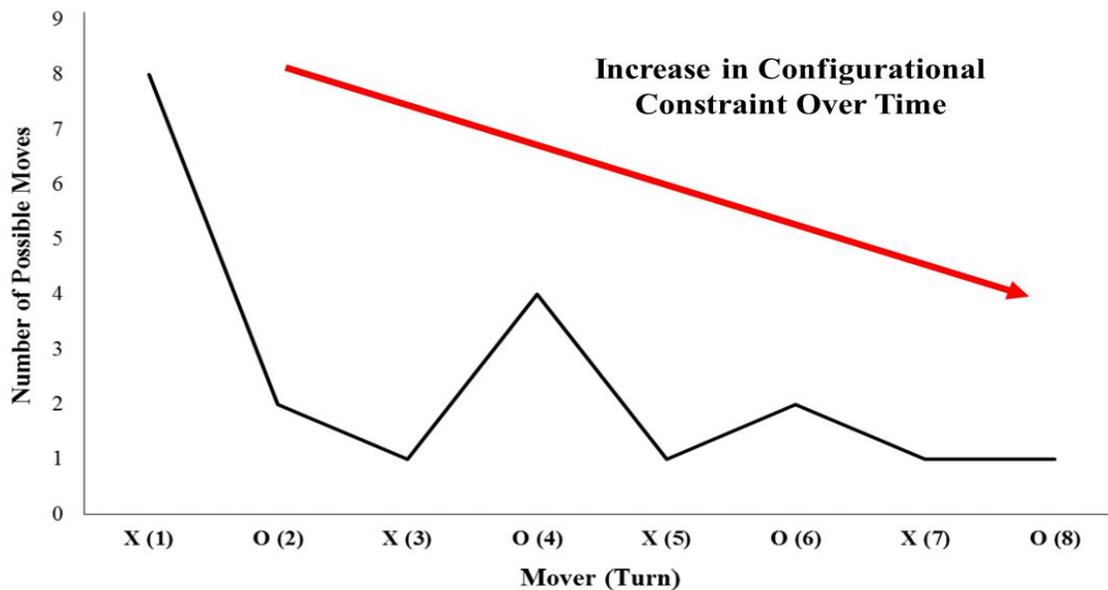


Figure 5. A graph showing an analysis of the tic-tac-toe example of first-mover dynamics (Figure 4A), plotted as the number of possible moves per turn versus the identity of the mover (e.g. X or O) per unit time and sequential turn.

7. Embryogenesis as a Quasi-Reversible Process

Another component of the cybernetic embryo is to understand embryogenesis as a reversible process. Not only do we want to understand what meta-processes aid in constructing the embryo, we also want to identify the essential nature specific combinations of events that guide an embryo through development. In other words, embryogenesis can be both highly deterministic

(reversible) or highly contingent (non-reversible). While the reversibility of embryogenesis and similar processes is limited by thermodynamics (Yuan et al., 2015), it may be reversible enough to discover key features through a process of reverse engineering. While we do not as of yet have a clear methodology, experiments utilizing genetic algorithms (Holland, 1992) can inform our understanding of the complexity and reversibility of embryogenesis.

Genetic algorithms are often used to optimize complex processes in a high dimensional and often rough phase space (Kauffman, 1993) that mimics the combinatorial complexity of biological evolution. These spaces resemble the epigenetic landscapes of development, and thus are also applicable to understanding the relationships between development and evolution (Cortez et al., 2017). It encompasses such biological counterparts as genes, genotypes, and phenotypes that are evaluated by some fitness function. Mutations and genotype mating with gene cross-over are also used to produce fitter offspring within an evolving population of genotypes. Fitter offspring are selected to populate future generations. Genetic algorithms have been found to be capable of finding solutions within large and rough feature spaces.

One striking example of the power of artificial evolution as an optimizer comes from Levin's work on Flatworm regeneration (Lobo et al., 2012; Lobo and Levin, 2015; Graeber, 2016). In this case, an optimization procedure was used to discover a model that would explain regeneration and associated phenotypic characteristics of the flatworm. Finding a series of developmental pathways to describe the cascade of events that leads to a successful recapitulation of the phenotype is an exercise in evaluating whether or not the developmental process is reversible. If so, the optimization process should be relatively easy. This can be done *in silico* in a way that mimics the mechanisms and processes of biological systems (Ray, 1991; Adami and Brown, 1994).

Lobo and Levin (2015) used a genetic algorithm to find the head-trunk-tail configuration in flatworm in order to simulate then length of time it takes to recapitulate the regenerative phenotype using no particular pathway. This required six billion simulated experiments and 26,727 generations of models to converge on the desired result. This requires a very large amount of time in evolutionary terms, so it is clear that many of these pathways must be buffered against by the genotype. This approach also works to characterize connectomics in small nervous systems such as that of the nematode *Caenorhabditis elegans* (302 neurons). In one case (Portegys, 2015), a hybrid genetic algorithm was used to weight synaptic connections in the *C. elegans* nervous system. There are over 3,000 synaptic connections between these neurons. Synapses are weighted such that the activation states of source neurons affect target neurons variably. These weights could also be optimized could be optimized to produce arbitrary input-output sequences, suggesting possible weighting schemes for the actual synapses to produce observed behaviors. This degree of complexity could be achieved using metamorphic code, which is self-editing but preserves the original function by adding code to the program that accomplish a sub-function through alternative means (Rad et al., 2012).

8. Conclusions

The embryo is a complex system that increases its phenotypic complexity during a period of great differentiation and specialization. As a process, embryogenesis seems to be both highly regulated and goal-directed towards entropic optimality. Both of these properties can be described

in the language of cybernetics. In cybernetic terms, goal-directedness is defined as systems with coherent states that are maintained in the face of perturbation (Heylighen and Joslyn, 2001). In this chapter, we demonstrate this by addressing two questions posed in the Introduction. The first question is answered in Section 6 in the form of black box mechanisms. The second answer, however, is more elusive. Based on our argument in this paper, the mechanism is selection on the various degrees of freedom (or developmental pathways) from single cell to fully developed organism. Selection itself is imposed by thermodynamic entropy and information, the details of which are the subject of future work. Nevertheless, a formal structural model of selection has now been proposed as a set of regulatory mechanisms resulting in patterns such as feedback and cross-inhibition (for applications to neuronal systems, see Rutishauser et al., 2015).

Thus, patterns of regulation observed in embryogenesis can be said to be a product of natural selection. Natural selection for goal-directed behavior has a number of consequences. Selection for stability in developmental cognitive systems suggests that positive feedback-driven phase transition serves as the predominant mechanism for the emergence of goal-directedness and even agency (Kelso, 2016). While this example relies on the existence of a formalized nervous system, there is increasing evidence that from a purely information-processing standpoint, such computations can be carried out by other biological circuits and systems (Levin and Baluska, 2016). With respect to embryogenesis, two processes in particular are highly similar to formalized neural systems: bioelectric processing between cells during morphogenesis (Levin et al., 2006) and mechanisms that guide cellular behavior on the basis of past experience (Wang et al., 2009; Balaskas et al., 2012). In other multicellular systems such as the slime mold *Physarum polycephalum*, simple decision-making can occur through cooperativity, positive feedback, and the employment of behavioral heuristics at the organismal level (Reid et al., 2016).

Another way of viewing evolutionary transitions specific to the complexity of embryos involves the concept of metasystem transitions (Heylighen et al., 1995). Metasystem transitions can be defined as emergent processes in associative systems, and consist of composite elements that undergo sudden organizational changes (Francois, 1995). More specifically, metasystem transitions are related to the creation and reorganization of both hierarchical and heterarchical subsystems (Last, 2015). The expected signature of metasystem transitions resembles long periods featuring stable hierarchies and heterarchies interrupted by rapid reorganizations of the relationships between cells (Wake, 1983). In the context of embryos, the "metasystem" allows for collective populations of cells to reorganize both during development and over evolutionary time.

One of our arguments made throughout this chapter involves evolutionary and thermodynamic factors working in concert to direct adaptive processes related to function. This has a conceptual relationship to cybernetics that might inspire future work. Watanabe (1966) has made the connection between Hamiltonian landscapes, the law of requisite variety, and the cybernetic regulation of emergent complexity. Specifically, he cites the inverse H-law as a potential mechanism for the regulation of complexity in emerging multicellular systems. The inverse H-law allows for anti-entropic behavior to guide nonequilibrium systems, or systems that have been perturbed away from equilibrium. This is similar to the argument of Wissner-Gross and Freer (2013), who argue that anti-entropic system behavior is not only expected of the process of entropy maximization in nonequilibrium systems, but leads to the emergence of life and increases in intelligence.

In the case of the cybernetic embryo, the key is how both the regulatory landscape and the epigenetic landscape deal with variation. In the case of the regulatory landscape, the discrete dynamics of a system can account for significant variety if system states are ergodic with respect to a system's dynamics. In other words, control is more or less assured as long as the variation can be anticipated. This might occur if a regulatory system adds components as they are needed in a stepwise fashion (for an example, see Rebeiz et al., 2009). The epigenetic landscape poses a different problem, and requires an additional buffering mechanism (Pujadas and Feinberg, 2012) to "match" the variety encountered as a result of environmental perturbation in a manner consistent with the cybernetic matching and proportional laws of Kompala et al. (1986). In this case, regulatory elements that are in normal times redundant must be evolved to enable ergodicity when variety is encountered. It is likely that if the regulatory system is questioned encounters unanticipated perturbations, then the addition of regulatory elements must be redundant (addition of elements in a non-stepwise fashion).

Aside from the role of evolutionary and thermodynamic processes in maintaining regulation, there is also a case to be made for the emerging embryo as an active modeler of both evolutionary processes and its own dynamics. In Ashby (1963), the notion of a system modeling its own behavior through approximation is relevant, and can be updated to reflect what we see in embryogenesis. Returning to the notion of multicellular systems emerging from single-celled systems, we see that embryos are governed by both spatial scale and the flow of time. In the case of spatial scale, we have so far discussed the bottom-up aspects of biological complexity. However, there is also an element of "wholeness" (Bohm, 1980) in the embryo, particularly when one considers the embryo as a single, discrete entity (Gordon and Gordon, 2016). The flow of time is also a particularly interesting problem that goes beyond the conventional aspects of dynamic regulation. In terms of regulation, one might view the embryo and its constituent parts as having a retrocausal temporal structure (Krasnikov, 1997). Specifically, the component parts (genes, proteins, and individual cells) might change in response to selective pressures at the level of the whole embryo. This rather specialized view of multilevel selection (Krupp, 2016) would allow for changes to unfold in the development and evolution of future embryos, but also allows for selection to act upon lower organizational levels and their own regulatory requirements.

In the case of embryogenesis, the context of developmental contingency could determine whether the process of embryogenesis is either hierarchical or heterarchical. Hierarchical structures (such as found in the lineage tree of the nematode *C. elegans*) may emerge as a response to high degrees of environmental perturbation. This would ensure consistency in the face of unexpected variation. By contrast, heterarchical structures (such as found in Vertebrates) might emerge in systems that have additional regulatory mechanisms to buffer unexpected variation. The cybernetic embryo also provides a critical link between emergence, evolution, and adaptive biological processes. For example, there are also connections that link interactivity and regulatory motifs that are worthy of further study, such as how tic-tac-toe played in Stackleberg equilibrium resembles a futile cycle. In this case, the set of resulting interactions produced thermodynamic entropy without a clearly advantageous outcome for each competitor. While the first mover in a pairwise interaction constrains the second mover, playing the game optimally results in a cancellation of initial advantage that resembles the lack of production in a futile cycle. However,

these interactions do result in one useful outcome: structure potentially used as a scaffold for increasing complexity.

There are many potential criticisms of our approach, particularly as it simultaneously covers much intellectual ground while also claiming great generalizability. The abstract nature of our approach, which is partially reliant on biosemiotic and other symbolic approaches, is also quite unconventional. There have been systems biological critiques of semiotic approaches, particularly as to whether or not natural phenomena can be reduced to natural (or artificial) linguistic forms (Emmeche and Hoffmeyer, 1991). However, there are also two advantages to using such an approach. The first is that a general structuralist approach is a useful heuristic in dealing with the holistic nature of phenotypes (Emmeche, 2011). Additionally, emergentist approaches also help us understand emergent processes (Emmeche and Hoffmeyer, 1991) and act to countervail gene-centric approaches (Alicea and Gordon, 2014). Along with these advantages, our approach provides a formal set of links between the evolution of development and regulatory mechanisms provided by the cybernetic embryo framework is a crucial component to reverse engineering the embryo defined as a multicausal, cascading, nested decision-making system (Gordon and Stone, 2017). In this context, differentiation is the result of the arrival of a networked decision. Feedback signals, across space and time, are a metaphorical 'spooky glue' holding the overall physiochemical system of evolution and development together. Future work might focus on building meta-models of this process that include multiple scales of biological organization.

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