

The Evolution of the Algorithms for Collective Behavior

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Collective behavior is the outcome of a network of local interactions. Here, I consider collective behavior as the result of algorithms that have evolved to operate in response to a particular environment and physiological context. I discuss how algorithms are shaped by the costs of operating under the constraints that the environment imposes, the extent to which the environment is stable, and the distribution, in space and time, of resources. I suggest that a focus on the dynamics of the environment may provide new hypotheses for elucidating the algorithms that produce the collective behavior of cellular systems.

Collective behavior is a process without central control that brings together multiple participants to achieve some outcome. We see the outcomes of collective behavior everywhere in nature: flocks of starlings turn in the sky, groups of T cells find their prey and initiate an immune response, new tissues take form in a developing embryo. Social insects have always been a focal point in the study of collective behavior. At least since the author of Proverbs 6:6 (“Look to the ant, thou sluggard! Consider her ways and be wise”) wondered how “without chief, ruler, or overseer,” an ant colony manages to harvest and store food, it has been apparent that the difficult task of deciphering the behavior of social insects might lead us to understand more generally how natural systems work without central control. Here, I will draw on what I have learned from my research on ants to propose a general framework for investigating collective behavior.

Thinking about collective behavior generates sticky questions about the relation between behavior at the level of the individual participants and at the level of the group or system. For example, we could say that brains think when neurons fire or that the ant colony forages when the ants follow chemical cues. The attempt to distinguish what the neurons do from what the brain does leads to the idea of “emergence,” the behavior of the group that seems to rise above an explanation of what the individuals are doing. But a brain is merely a lot of neurons, and a colony is nothing other than some ants, and the behavior of the brain or the colony comes from the neurons or the ants. It seems to me that the best way to deal with this philosophical quagmire is to step around it. My goal is to explain what may seem, before we understand it, to be emergent and mysterious: how the individual actions produce the collective behavior of the system

Collective behavior is the outcome of interactions among individuals. These interactions are the mechanism or means by which one participant influences and responds to the behavior of another. Cells interact through molecular mechanisms, for example, when a hormone binds to a receptor on a mammalian cell, or when bacteria respond to chemicals secreted into the medium by other bacteria. Neurons use electrical stimulation and the transfer of neurotransmitters. Ants interact with each other through olfaction, assessing the odors on another’s body or deposited by another ant (Gordon, 2010).

The outcomes are what we see: starling flocks turning or the formation of differentiated tissues. There are countless examples of collective behavior, each the outcome of interactions among individual participants. How an ant colony forages is the outcome of olfactory interactions among ants. The formation and pruning of synapses is an outcome of chemical and electrical interactions among neurons. Metastasis from tumors is an outcome of chemical interactions among cells. Even inside cells, the outcomes of interactions among organelles, or of molecules within transcription networks, could be considered to be collective behavior.

Algorithms for Collective Behavior

The fundamental question in the study of collective behavior is how do the interactions among individuals—that is, the means by which one participant influences and responds to the behavior of another—produce the outcome that we see? How do ants use olfactory interactions to organize their foraging? How do cancer cells use hormones and growth factors produced by other cells to metastasize and form tumors? The goal of this essay is to point out that an ecological perspective can help provide a general framework for answering this question.

The quantitative study of collective behavior began with insights from sociology (Granovetter, 1978) and physics (Hopfield, 1982); early studies focused on social insects (e.g., Deneubourg et al., 1986) and animal movement (Okubo, 1986). All were mathematical models that describe how local interactions between individuals produce a collective outcome. These efforts showed that it is possible, in principle, for a mathematical model to describe a process that leads to what seemed to be “emergent” behavior. As a shorthand for “the process that generates collective outcomes from the interactions among individuals,” I will borrow the term “algorithm” from computer science. There are many examples of such algorithms in Sumpter (2010); other specific examples are equation 1 in Rosenthal et al. (2015) or equations 3 and 4 in Prabhakar et al. (2012). By now, it is very clear that such approaches can explain behavior that has been identified in many diverse systems. This quantitative approach has often been embedded in a search for a general mathematical theory, variously called a theory of emergent behavior, complexity, or self-organization; it is based on the hope that a

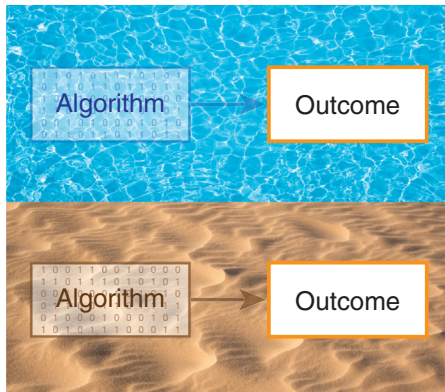


Figure 1. The Fit between Algorithm and Environment
Each large rectangle represents a particular environment with characteristic dynamics. The algorithm that produces a collective outcome is likely to fit the environment in which it evolves. Thus, outcomes that resemble each other may be based on very different algorithms.

general class of models of collective behavior will apply to all systems.

But the proliferating examples of collective behavior now offer a new challenge. The evidence is growing that the processes that generate collective behavior are, like everything else in nature, extremely diverse. For example, there are many different processes that might cause a group of wildebeest, ants, or cells to move as a group from one place to another. Here, I suggest that, like any other phenotypic traits, the rules that produce collective behavior evolve in response to the dynamics of the environment. This ecological perspective may help us to discover, for particular systems, how collective behavior arises from interactions among individuals.

An example from computer science shows why different algorithms can evolve to produce the same outcome. There are many different algorithms that a computer could use for sorting a list of numbers so that they are in ordinal sequence. One algorithm is based on selection; it chooses the smallest value from some subset of the list, and then it chooses the smallest of the remaining ones, and so on. Another algorithm is based on insertion: it chooses the first number in the list, then it moves the number until it comes after another number with a lower value, and so on. Both algorithms ultimately produce the same outcome, an ordered list of numbers. However, because they differ in how they proceed over time, they might differ in the conditions in which they are most likely to generate a complete ordinal sequence and, therefore, are most appropriate. For example, if the first algorithm is interrupted, the beginning of the list will already be in the correct order, while this is not true of the second algorithm. Under some circumstances, it may be useful to have at least the beginning of the list in the correct order. Imagine that the algorithm is a biological process, and that a list in the correct order is the collective behavior that is ecologically important. In an unstable environment with frequent interruptions, the first algorithm might be more likely than the second to evolve.

This example above suggests one of the reasons why, in natural systems, similar outcomes can be produced by different algorithms (Figure 1). In response to unpredictable disruptions in the environment, the intermediate states generated by different

algorithms can themselves be very different, even if the outcomes are similar. Intermediate states, as well as outcomes, are subject to natural selection, and so intermediate states can be the target of selective pressure in environments that are often disrupted. More generally, I argue here that algorithms are likely to evolve to fit environmental conditions.

Because I am using “algorithm,” a term from computer science, to describe a biological process, it is important to note the difference between algorithms implemented by computers and those implemented in nature. The algorithms in computer programs are written by a programmer with the intention to solve a particular problem, but in nature, there is no master programmer acting with intent. However, the specter of a programmer distracts from an important similarity between the two cases: in both computer science and biology, the algorithm itself does not have any intention. The logic gates in the computer merely accept inputs and configure their outputs as 1’s and 0’s, and the way the outputs are linked produces an outcome. The algorithms that generate the collective behavior of ant colonies arose through evolution, not the effort of a master programmer, and the ants themselves are like the computer’s logic gates. An ant responds to interactions with other ants without any intention or desire to create a bridge, foraging trail, or tunnel. Thus, the participants that use an algorithm to provide a collective outcome need not know its goals; in fact, they do not even need to have identical goals (Farine et al., 2015).

Ants provide many opportunities for us to see the fit between the algorithms that produce collective behavior and the dynamics of the environment. More than 14,000 species of ants have evolved collective behavior in an enormous range of environments over the past 130 million years. For example, all ant species engage in some form of collective search to find and retrieve resources. Some species collect patchy resources, those that occur in clusters in space or time or both. A picnic is a patchy resource for ants in both space and time; abundant food appears in a specific place and lasts for a short time until the picnickers and the ants are both done with it. The foraging behavior of ant species that specialize on patchy resources tends to use algorithms that include spatial information in interactions among individuals, with the outcome that additional individuals are recruited from the nest back to the patch of food.

By contrast, some ant species forage for resources that are scattered or distributed at random, appearing unpredictably in space and time. These species use an algorithm to find and retrieve resources that does not include any spatial information. This makes sense when an ant can retrieve a food item on its own, and the presence of an item in a certain location does not mean that others are likely to find more food in the same place. For example, harvester ants collect seeds that are scattered by wind and flooding, not clustered in patches (Gordon, 1993). Interactions between individuals depend on the rate at which food is found, not its location. Each ant leaves the nest to search for food in response to the rate at which it meets returning foragers with food (Pinter-Wollman et al., 2013). Since the more food is available, the more quickly foragers find it and return, the rate of forager return is, in effect, a measure of food availability. Positive feedback that links the rate of ants that leave the nest to the rate at which they return with food allows the colony to adjust its foraging activity to fluctuations in food availability.

When less food is available, fewer foragers return, and this decreases the rate at which foragers leave the nest (Prabhakar et al., 2012).

Feedback is important in many biological systems (e.g., Ferrell, 2016). The algorithms that produce collective behavior specify how interactions among participants create feedback (Åstrom and Murray, 2009). Feedback can be positive, which tends to amplify response to an input signal, or negative, which can dampen the response to an input signal. Types of feedback often operate in combination. In ant recruitment, trail pheromone creates positive feedback, and then, when the food runs out, the pheromone fades away, which shuts down the recruitment process. In cellular systems, there are many examples of circuits involving both positive and negative feedback (e.g., Youk and Lim, 2014) that generate diverse outcomes.

Subtle differences in algorithm can also lead to important differences in outcome. Different regimes of positive and negative feedback based on simple signaling interactions can generate diverse outcomes, such as quorum sensing or paracrine signaling (Maire and Youk, 2015). Migrating groups of cells tend to use chemical and tactile interactions that generate a gradient. The gradient produces feedback that results in a particular direction of movement (Mayor and Etienne-Manneville, 2016). Different types of feedback result when the forward and rear have distinct edges that react differently, while others gather cells passively behind a moving front. These two processes have very different outcomes in the specificity of the shapes formed: for example, whether they fill a gap, as in wound-healing, or create interdigitating layers of tissue, as in the zebrafish neural crest.

Despite this diversity, the algorithms used to regulate collective behavior do have some characteristics in common. They tend to be distributed processes (Gordon, 2015). In a distributed process, the role or behavior of an individual or component is determined by its interactions with others rather than its inherent attributes. Some important advantages of distributed processes, flexibility and resilience to disturbance, arise because different participants in the collective outcome are able to respond to changing conditions (Gordon, 2015). For example, task allocation in an ant colony, the distributed process that determines which ant performs which task at a given time, uses an algorithm based on the rate of interaction between ants. An individual ant assesses interactions by detecting the cuticular hydrocarbon profile of each ant it meets (Greene and Gordon, 2003). An ant's cuticular hydrocarbon profile provides information about its task because the conditions in which an ant works change the chemistry of the hydrocarbons on its body surface. For example, when harvester ant foragers are out in the sun, the proportion of n-alkanes in their hydrocarbon profiles increases, leading a forager to smell recognizably different from an ant that works inside the nest (Wagner et al., 2001). An ant uses its recent experience of interactions with other ants in its decisions about what task to perform and whether to perform it actively (Gordon, 2015). Collectively, this allows the colony to regulate the numbers of ants currently engaged in each task in response to the availability and flow of resources and external conditions. For example, when extra food is available, ants engaged in other tasks switch tasks to foraging as a result of increased interactions with other ants that found food (Gordon 1989).

Distributed algorithms often employ stochasticity to achieve an outcome (Lewontin, 2000; Gerhart and Kirschner, 1997). For example, the algorithm that harvester ants use to regulate foraging activity relies on the variable rate at which foragers find seeds and return to the nest (Prabhakar et al., 2012). There are many examples of the use of stochasticity in nature; it provides information in visual neural circuits (Tkačik et al., 2010), helps to initiate spindle formation (Farhadifar et al., 2015), or regulates the response to disturbance of a swarm of midges (Ni et al., 2015). One simple example is the collective searching of space. If all searchers always remain on the same path, none of them will find anything off the path; random movement increases the probability that a searcher will encounter something novel. This can be seen in the “run-and-tumble” behavior of individual cells during bacterial chemotaxis (Berg and Purcell, 1977). This behavior, combined with interaction between cells, enables efficient search. Another example of the use of stochasticity is the search of conformational space during protein folding; the jostling around of amino acid polymers allows certain sites to find and bind to each other, which changes the probability that neighboring amino acids will interact (McLaughlin et al., 2012). A third example of the use of stochasticity is the role of unpredictable obstacles in the formation of patterns. An instance of this is the aggregation phase of the life cycle of the slime mold *Dicyostelium*, which requires that cells form spiral waves. The spiral wave arises when a wavefront is interrupted by some obstacle. Thus, randomly encountered obstacles are necessary for the algorithm that produces the collective outcome of aggregation (Grace and Hütt, 2015).

For most of the collective behavior that we see in nature, the algorithm is unknown. To learn what the algorithm is, the first step is to find out how the participants interact. This is the investigation of molecular mechanisms, and much of cell biology is engaged in this project. The next step is to understand how the mechanisms come together to create dynamic outcomes. This search for algorithms is the project of systems biology. I suggest here that, to derive hypotheses about what are the algorithms of particular collective behavior, the best place to start is to consider how the collective behavior functions in its environment. This is an ecological question.

Ecological Context: The Environment and Its Dynamics

A system's “environment” is everything it uses and influences. Environments keep changing, and collective behavior changes in response. It is important to remember that environments do not exist independently of organisms; what the environment is depends on how the organisms are linked to it. For example, the macroenvironment of a cell consists of whatever chemical and tactile stimuli it can receive and use. Ethologists referred to this relation for an animal as its “Umwelt,” the aspects of the world that its sensory systems can receive and that its actions can influence.

The most important reason that organisms and environments cannot be considered to be independent is that they are always changing each other (Lewontin, 2000; Sultan, 2015). All living entities engage in “niche construction,” (Odling-Smee et al., 2003) constantly modifying their environments as they are responding to them. Plant roots host mycorrhizae that modify the nitrogen content of soil from which the plants collect nitrogen. Birds build

Table 1. Correspondence between Environmental Conditions and the Dynamics of Collective Behavior

Environment	Dynamics
Energy flow	Feedback
Spend faster than acquire	Stop unless activated
Acquire faster than spend	Go unless stopped
Stability	Rate
High	Slow and steady
Low	Fast or sporadic
Distribution of resources	Rate
Patchy	Accelerating, non-linear
Uniform	Linear

necks, and beavers build dams. Bacteria secrete substances that kill competitors, modify the available nutrients, and allow them to infect new hosts (McNally et al., 2014). In the microenvironment inside the cell, the products of metabolism influence the signaling pathways that regulate metabolism (Agathocleous and Harris, 2013). Cell movement can depend on local modification of the environment: for example, groups of melanoma cells move toward a gradient of lysophosphatidic acid that they create by degrading it as they move along (Muinonen-Martin et al., 2014).

Because collective behavior deals with a changing world, the algorithms of collective behavior must enable it to change appropriately. I suggest here that those algorithms are shaped by the selective pressures of a changing environment.

The dynamical fit between how organisms change and how their environments change is a central theme of evolutionary biology (Mangel and Clark, 1988; Sultan, 2015). The relation of phenotype and environment determines which variants are favored in the turbulent process of natural selection, on the time-scale of generations, that shifts the proportion of a population with particular traits. The relation of organisms and environment determines which variants are favored by natural selection. Ecology is the study of this relation, and this is why ecology can inform our understanding of the algorithms governing collective behavior.

Levins modeled the action of selection in response to a changing environment beautifully in *Evolution in Changing Environments* (Levins, 1968), describing the tradeoff between the cost of flexibility, producing a range of phenotypes for different conditions, and the cost of inflexibility, having the wrong phenotype in particular conditions. Levins (1968) pointed out that the scale of changing phenotypes evolves in relation to what he called the “grain” of the environment—that is, how quickly it changes in time and space.

In previous work (Gordon, 2014), I adapted these ideas to consider the evolution of collective behavior. Collective behavior is a phenotype that has dynamics and evolves in response to the dynamics or grain of the environment. Specifically, I outlined three basic challenges that characterize the dynamics of an environment and constrain how collective behavior functions in particular environmental contexts:

- 1) Operating costs: the relation between the rates of spending and acquiring the energy that keeps the system

going. When spending and acquiring occur at similar rates or when spending is faster than acquiring, the system is under stress. When acquiring is much faster than spending, activity is easier.

- 2) Threat of rupture: how stable the environment is, or how likely conditions are to change, and how likely changes are to interrupt the network of interactions that allows the system to function.
- 3) Distribution of resources: whether some condition, such as the amount of a resource, is patchy, concentrated in time, space, both, or is uniform.

Operating costs, stability, and the distribution of resources are overlapping features of an environment and could occur in any combination. For example, harvester ants live in a stable environment in which they must spend water to obtain it due to water loss while out foraging, and they forage for scattered, uniformly distributed resources. In this environment, natural selection shapes interactions between foragers to create feedback that keeps foragers inactive unless they are stimulated to leave the nest foragers returning with food (Gordon, 2013). Changes in foraging behavior are slow, on the scale of hours, and they do not use recruitment. By contrast, the tropical arboreal turtle ant lives in a rapidly changing environment in which resources can be gained more rapidly than energy is spent because the air is humid. The turtle ants use a system of feedback in which interactions allow the system to continue unless inhibited. They lay pheromone trails as they go, using chemical interactions to maintain a constant activity on the trail. The ants forage for patchy, ephemeral resources to which they recruit quickly, with the numbers at the food increasing at an accelerating rate (Gordon, 2012).

Considering each of these types of dynamics separately suggests how the algorithms for collective behavior may correspond to environmental or physiological context. This, in turn, generates hypotheses about the selective pressures that shape the algorithm. There are likely to be correspondences between algorithm, the feedback regime that regulates the collective outcome, and the ecological situation. I suggest that these correspondences will appear across systems, and that this can provide a unified framework for the investigation of the algorithms that generate collective behavior. The following section outlines some hypotheses about such correspondences, summarized in Table 1.

Algorithms Shaped by Operating Costs **High Operating Costs: Spend Faster than Obtain**

When operating costs are high, the rate of spending energy is higher than the rate of obtaining it, so life is tough. In this situation, activity may be regulated so as to avoid unnecessary costs. This suggests the hypothesis that in such a system, activity occurs only when feedback activates it. If this is true, systems in which a process is inhibited unless activated may indicate a high rate of energy expenditure relative to energy gain.

For example, the system of nestmate recognition in ants appears to operate using the absence of aggression as the default. In many species, ants repel intruders and sometimes attack ants of another colony when they meet outside their nests. Attacking nestmates would have a high cost: wasting time and energy in

fighting and leading to the loss of colony members. Nestmate recognition appears to be a distributed process (Esponda and Gordon, 2015) in which colony identity is defined collectively by all of the ants in the colony. Each ant responds to the odor of another ant by reference to its own unique and shifting boundary in odor space between what it identifies as a nestmate and what it identifies as an outsider. This boundary changes as a result of its experience of encounters with other ants. Early in its life, an ant works inside the nest and encounters only nestmates, but later, while foraging, it may meet an ant from another colony and experience aggression from it. In response to this experience, the ant places the odor of that other ant on the foreign side of its decision boundary. This adverse experience thus “inoculates” the ant against passively allowing future intrusions by a foreigner that smells like the aggressive ant it met. This is analogous to the mammalian immune system: T cells acquire antibodies through experience with the outside world. Both ants and T cells are using similar collective algorithms. The default is not to attack self; the system has evolved to actively keep the “attack” system inhibited. This system requires feedback from the outside world to instigate aggression. The algorithm may have evolved to use active inhibition as the default because the cost of attacking nestmates or launching an autoimmune response is high.

Low Operating Costs: Acquire Faster than Spend

When operating costs are low, activity is not expensive, and feedback can be used to maintain the status quo in activity. This suggests the hypothesis that in conditions of low operating costs, interactions between participants will perpetuate the activity unless something happens to inhibit it. For example, in some ant species, the ants lay trail pheromone everywhere that they walk, with the outcome that other ants follow them, and the trail continues to move forward even in the absence of resources. This creates a highway system from which temporary recruitment trails to new food sources are formed (Flanagan et al., 2013).

In cellular systems, feedback that supports the *status quo* physiological state may be associated with low operating costs. An example of feedback that allows a process to continue, possibly because operating costs are low, occurs in groups of astrocytes. They create cables at the edge of wounds, using adherens in a “treadmilling” process that recycles adherens along a directional gradient such that forward movement promotes further forward movement (Peglion et al., 2014).

Algorithms Shaped by Stability or the Threat of Rupture

Environments differ in stability. Stability is high when change is unlikely, or the magnitude of change is low, or both. One hypothesis about the relation between the dynamics of collective behavior and environmental stability is that high stability is associated with slow, steady responses. By contrast, in unstable environments where the probability of change is high and the magnitude of change can be extreme, response is likely to be more rapid or else to involve a period of waiting out very unfavorable conditions (Balaban et al., 2004). For example, harvester ants forage in a stable resource environment, searching for seeds that can stay in place on the ground for months and that are distributed by wind and flooding in

small increments. Their searching behavior is slow and responds slowly to a change in food availability. The opportunistic, invasive ant species that we meet in our kitchens are able to find sudden windfalls of food, such as crumbs, cat food, and sticky fingerprints very quickly and to recruit their nestmates rapidly to collect it. There are many cases in ecology of the association between environmental stability and the rate of response. One is reproductive allocation: in many organisms, the number of offspring produced and the timing of reproduction depend on the stability of the environment, which sets the probability of success. One of many examples of reproductive allocation is widespread in plants. In unstable conditions, they tend to produce more and smaller seeds rather than a few larger and more costly ones that might not succeed (Westoby et al., 2002).

At the cellular level, there are probably many examples of an association between the algorithm for collective behavior and the stability of the environment. Epithelial cells respond quickly to wounds in an environment, the skin, where invasion and rupture are likely in mammalian bodies (Clark, 1996). By contrast, brains are stable environments in which physical rupture is rare, and the collective behavior of neurons is not regulated to provide rapid repair to traumatic injury. The activation of stem cells involved in hair growth is tuned to very slow oscillations, lasting weeks or months, of morphogenetic proteins (Plikus et al., 2008). This slow rate suggests that environmental conditions changing very slowly on the timescale of months, such as seasonal changes of temperature, may have influenced the evolution of the regulation of hair growth.

Algorithms Shaped by the Distribution of Resources

The distribution of resources or targets can range from patchy or clustered to uniformly distributed and scattered. Response to patchy resources may deploy accelerating or nonlinear dynamics, such as the foraging trails that bring increasing numbers of ants to a picnic. Resources that occur in patches are available only at a certain time and in a certain location, so an accelerating response makes it possible to capture the resource at the place and time when it is still available. By contrast, when resources are uniformly distributed, then there may be no recruitment. Instead, the rate of food intake is linear, as each ant searches independently and each ant takes about the same amount of time to find food.

Accelerating responses to patchy resources are common. Desert plants accelerate soil respiration in response to brief episodes of rainfall (Potts et al., 2014). Cytokines create chemical interactions that T cells follow, with the outcome that numbers of T cells increase at a location where pathogens are patchy and concentrated in time and space (Fricke et al., 2015; Chao et al., 2004). An interesting question is whether the reverse is also true. As the collection of a patchy resource can require an accelerating response, does the observation of an accelerating process indicate a reliance on patchy resources? A classic example of accelerating response is cell proliferation in both metazoan tumors and within populations of microbes; numbers of cells increase at a higher-than-linear rate. Considering whether environmental resources are patchy may allow us to better understand the algorithms that govern cell growth and division both in normal and diseased cells.

Ecology and the Evolution of Algorithms for Collective Behavior

The prediction that the dynamics of the algorithms are likely to fit the dynamics of the environment draws on the idea that natural selection, on the timescale of many generations, shapes the relation between traits and their environments. This relation is based on the response to the environment that an individual organism experiences on the timescale in which it lives and reproduces.

Collective behavior depends on the capacity of the individual participants to engage in the interactions that produce that behavior. For example, how a bird flock turns is the result of the responses of individual birds to the moment-to-moment behavior of their neighbors. On the evolutionary timescale, over many generations, the sensory systems that produce these responses are shaped by the ecological importance of the ability to turn the flock. The algorithm that produces turning thus draws on the sensory systems that have evolved so as to allow the flock to turn. A similar evolutionary process can be traced in transcription regulatory networks as evolutionary changes in signaling pathways: for example, the incorporation of new regulators must allow the entire network to function (Sorrells and Johnson, 2015).

Selection acts on how the collective behavior affects the survival and reproductive success of organisms: how the bird flock can turn to avoid obstacles, or how the transcription regulatory network produces the right proteins at the right time. Perhaps the most familiar example of an evolutionary process in cell biology is cancer. Early studies described cancers as uncontrolled clones of founder cells harboring discrete mutations, and it is becoming clear that these mutations allow cancer cells to engage in destructive collective behavior. As populations of cancer cells evolve over many generations of cells from ancestral healthy cells, the cancer cells acquire new capacities to participate in interactions with other cells. These interactions produce collective outcomes, such as tumors that are able to harness otherwise healthy vasculature. The characteristics of particular cells, such as the receptors they are expressing, are the equipment for playing a game, for joining in a set of relations with certain dynamics; in other words, for following the algorithm that generates cancer. When and where tumors appear depends on selection for cells with the genetic lesions that provide the capacity to interact with other cells, cancerous and healthy, in tumor-forming ways.

To look for the algorithms of collective behavior, the first step is to consider how they operate in relation to environments. For example, we know that animals in cold places have traits that help to deal with the cold, such as thick fur and hibernation, while animals in hot places have traits that help to deal with the heat, such as sweating and dilation of blood vessels. A scientist interested in learning about the physiology of a newly discovered animal that lives in the desert would look for heat dissipation, not for fur. I am suggesting we do the same to discover the algorithms for collective behavior: look for a fit between the algorithm and the environment.

Asking how the algorithms that produce collective outcomes correspond to the relevant ecological dynamics can generate new hypotheses about collective behavior in systems we do not yet understand. There is no single way to accomplish a particular outcome, such as search or migration; each of these

outcomes is regulated differently in particular ecological situations. The way to learn how collective behavior works is to look at its dynamical relation with the system around it: what are the operating costs to keep the process going, how stable is its situation, and how the resources it uses are distributed? For example, among systems that search for and collect resources, do the ones that deal with rapidly changing resources work differently from those that filter stable ones? Do systems that regulate growth in situations of high energy expenditure tend to use characteristic feedback regimes?

Collective behavior, from tumor metastasis to wildebeest migration, is a response to the surrounding environment. Ecology, the study of the layers of overlapping interactions that regulate natural systems in response to changing conditions, is the next frontier for systems biology. To approach collective behavior from an ecological perspective is to extend the fundamental question about evolution, the relation of changing phenotype and changing environment, from the study of whole organisms to the rest of biology.

For cell and systems biology, the answers to these questions may be hiding in plain sight. As Gibson (1986) studies of vision show, the world presents itself to organisms in particular ways, which he called “affordances.” One consequence of this obvious fact, that biological entities respond to the subset of the world that they can perceive, is that it is easier for us to take into account the ecology of entities whose Umwelt is similar to our own. This may explain why we know more about how wildebeest act collectively in response to changing environments than we do about cells; it is easier for us to see what is happening around a wildebeest than around a cell. Growing interest in the collective behavior of cells is due to amazing advances in imaging that makes it possible to observe cells acting. Now, we need to learn to see the world where they are living.

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