Epistolution: A Possible Structuring Principle for the Human Superorganism

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Abstract. The genes-first view of life explains physiological function from the perspective of replicators coevolving in a multicellular organism. But this explanation fits awkwardly with the view of a human as a superorganism composed of many types of biota. If the coordinating principles of life are contained in unified genomes that have evolved as sets, how are the actions of microbiotic partners coordinated into functional systems? How are genes selected for expression, in either the host or in the microbiota? I propose a principle of downward causation by which the niche, rather than the genes, provides the final cause of organismic activity. Since this principle unites the activity of all living cells under a form of what might be called intelligence, its name reflects *epistemology*, the sources of knowledge, and *evolution* united — "epist-olution" offers a testable synthesis. Perhaps a superorganism is a set of networks that synchronize to their niche using the formula: *if used, then reinforce; else mutate stochastically*.

Keywords: Epistolution, Superorganism, Microbiome, Sleep, Synchrony, Niche, Homeostasis, Allostasis, Artificial General Intelligence.

1 The Intractability of Neo-Darwinian Gene Expression

DNA appears to be the prime causative agent in biology. Seen as a genetic program, the functional adaptative traits that organisms express fit them to their environments in a special way, namely in a way that allows the DNA that apparently causes those traits to be replicated. But this logic is tautological. Natural selection, viewed in this way, is a claim that Nature provides survival to those that survive, and replication to those that replicate. It does not provide a mechanistic link between what DNA does, which is to provide templates to build proteins, and the traits upon which natural selection must exert itself. How do we get from a protein to a trait? Even more mysteriously, how does the cell determine which genes to express, and when? We still have not worked out the logic of physiological function well enough to explain, in any animal, what precisely triggers the expression of one gene rather than another at a given time and place in embryonic development. It is true that DNA sequences are often held in such a way as to make them easier or harder to express given the architecture of regulatory networks, and expression levels can often be partially predicted from such positioning [1]. This

does not isolate causation because the regulatory networks are themselves never isolated from their environment, and that environment also partially predicts gene expression, for example in the sex determination of crocodilians through egg temperature [2]. A gene has never expressed itself; it requires a cell and a regulatory network. The production level of a given protein in adjacent cells of the same type can vary by as much as three orders of magnitude [3]. Assuming that protein to be part of the functional process that results in adaptive traits for the whole organism, what makes one cell overexpress the protein and the adjacent one underexpress it? How do the cells communicate with one another to determine the right average level of production?

In order to work together as a coordinated multicellular organism, the cells must exert influence on one another. A cell must interact with others in a way that promotes the survival of the organism as a whole and not its destruction from, say, cancer. But the nature of this causal influence is still murky. The possibilities of gene expression are nearly endless. If a trait can arise from any number of genes, the number of ways that the 30,000 or so genes in human cells could be combined to produce traits amounts to a number near 2×10^{72403} [4, 5]. But the total number of particles in the universe is estimated at only 3.28×10^{80} [6]. This shows that it is impossible, even in the long history of life, for evolution to have explored even a tiny fraction of all traits. Instead, the cell is exercising what a naïve observer would be tempted to call "choice" in deciding what genes to express.

None of these facts fit the "blueprint" metaphor which has sometimes been used in biology. If life is an emergent consequence of DNA, why are organisms not *systematically* interpreting their DNA codes one by one, like a carpenter with a blueprint? Or alternately, why are cells not *randomly* exploring these possibilities for gene expression? If a trait can arise from any combination of genes, then there must be some systematic logic at work that selects combinations of genes. As the math I've just shown suggests, the possibilities for expression are far too vast to be unguided.

If this logic of gene expression were encoded quite prescriptively in the genes, then it would be interpreted inflexibly whatever the conditions. This would provide no leeway for cells to influence one another at all, so that can't be the case. If it were encoded in a set number of permutations, so that it might be expressed in many different ways given certain external triggers, then a finite number of triggers would suffice to cause the expression of every functional pattern. I presume that this is the working assumption of many biologists today. In this case the physiological logic of gene expression is an almost incomprehensively vast field of meta-instructions, one for each condition each set of DNA may face. In this case, in order for us to fully understand the logic of the human body, we would have to map out the set of all the possible cues for gene expression that might come from any of the internal states of each cell, and then map all the physical conditions faced by each cell that might lead to these internal states. We would have to do this in all the 35 trillion or so human cells in the body. Bear in mind these cells diversify into roughly 200 cell types…skin, blood, neurons, bones, muscle, and so on, as they undergo all the phases of growth, development, and senescence. If we missed just a few of these meta-instructions in building our map, it seems possible that these unaccounted-for codes might throw the whole model off.

But the combinatorial explosion of complexity does not end there. In fact, research over the past two decades has revealed that the human body is really a superorganism, composed not only of human cells but also of trillions of prokaryotes, viruses, and very small eukaryotes that comprise its microbiota. Many estimates show that the cells in this microbiota are more numerous than the human cells, and that they are vital for our survival in the environment we inhabit. This microbiota functions not only as a digestive organ and regulator of metabolism, but as an integral part of a healthy immune system, and as a component of the cognitive process [7-11]. This community of foreign cells with foreign genes is not acquired along with the germ cell from the parent, but acquired from the environment after birth in a somewhat haphazard way, resulting in significant differences in microbiota even in identical twins [12]. Dethlefsen et al. write that "at the species and strain level the microbiota of an individual can be as unique as a fingerprint [13]." There *are* internal organelles in eukaryotic cells with their own genetic material that are acquired from the germ cell, but the symbiogenesis thesis suggests that these were once separate organisms that have been incorporated [14]. There is evidence that this flexible partnership with external cells with foreign DNA is not only very ancient indeed, but that it is nearly ubiquitous among eukaryotes, and is vital to normal function [15].

The existence of a microbiome means trouble for the promise of understanding physiological function through the genes-first view of life. If it were correct that gene expression was determined by a meta-program that was encoded in the DNA, then that program would have to be also encoded reliably in the trillions of diverse cells of the microbiota as well. These prokaryotes that are wildly different from human cells and from one another might be expected to contain wildly different meta-instructions as well. Somehow the bulk of them would have to contain sets of codes that just so happened to be intimately tuned not only to the local conditions where they might seek their own survival, but also to macroconditions that supported the survival of the host. And if this theory of gene expression were true, then in order to understand that host and its survival, we would have to map all these microbiotic meta-instructions just as precisely as the host cell meta-instructions. These populations of microbiota are remarkably stable over long time spans [16], but also shifting from minute to minute in their host based on diet, sleep, exercise, and other variables [17]. The fact that the microbiome of an individual is reorganized by diet and yet maintains its long-term stability is a strong indication that a community-level logic must be present.

Occasionally, DNA from one species can be viably transferred into an enucleated egg cell of another. When this happens, the resulting organism develops into a mixture of both parent species. In one case, Sun et al. transplanted carp DNA into a goldfish egg, and the resulting trans-species hybrid had an intermediate number of vertebrae that was between those of the two parents. This experiment proves that at least in one case, the germ cell can successfully build a functioning organism with a set of DNA that is evolved for an entirely different purpose, that of making a different creature [18]. If the proposed meta-instructions were the only cause of gene expression, this experiment shows that at the very least, the number of permutations covered by these meta-instructions must be vast enough to cover not only all the conditions faced by cells in one species, but occasionally vast enough to cover those faced by cells in related species as

well. This gives an indication of just how intractably enormous this hypothetical set of meta-instructions would have to be.

2 Finding A Niche

There is no way out of this combinatorial problem from the perspective of Neo-Darwinism. Locating all the causal responsibility for the gene expression patterning of an organism within the DNA leaves no way for us to plausibly compute the logic of physiology. Perhaps this may be the reason why no researcher has computed that logic yet. Even simple single-celled organisms present us with a complex process that is still far beyond our abilities to understand and replicate with non-biological material. Trying to build a robotic device that could perform all the functions of, say, a fruit fly, is still firmly in the realm of science fiction. But what alternatives might there be?

There is one plausible alternative, testable in principle, that might suffice. Unfortunately in order to understand it one has to rearrange most of the philosophical furniture of Western civilization. This is the idea that ecological niches may structure the interactions of organisms directly. In order to entertain this hypothesis, we have to set aside the aversion to downward causation that has accompanied serious biology since the nineteenth century. I should say that this is *not* an argument for intelligent design. This idea is compatible with a materialistic cosmology, and with the empirical observations that have underpinned Neo-Darwinism. I have no doubt that DNA evolves by natural selection, and that having the right DNA is vital for life. I am only suggesting that on the level of physiology, organisms may be sets of interlocking networks that are sensitive enough to their niches that they take their instructions from those niches. Just as the upward logic of Neo-Darwinism requires only mutation and differential selection, this downward logic may only require a similar basic set of universal rules to guide living systems into a form of synchrony with their environments.

Aristotle separated four types of causes: material cause, formal cause, efficient cause, and final cause. There is no doubt that DNA is a material cause of life; without it cells would not be able to store templates for making proteins. DNA has no replacement. And many of the essential nutrients that build a cell are irreplaceable. Likewise not just any cells will work to build a given superorganism. Many are maladaptive, such as cancer cells or infectious parasites. Life has many requirements. But still the body can work with a surprisingly broad array of materials to accomplish its goals on a higher level, because it has an internal logic which selects the right building blocks, puts them in the right place, and makes them behave a certain way. We can ingest a broad array of foods and host a broad array of commensal microbes, meanwhile excreting non-nutrients, waste, and poisons, and excluding the many trillions of maladaptive microbes that might harm us. But how does all this selection occur?

Perhaps the question of what is the final cause of a living system, so long banished from biology, could be useful in working out this puzzle. Final cause means purpose, or teleology. To know this is to know what role each part of the system plays in the whole system. In a system with teleology, each level structures the behavior of the level

below it. For example, in a musical concert the composer writes the score, the conductor interprets it, the musicians play, and the instruments sound. If you ask why a given violin is playing a B flat at a particular moment and not another, an answer makes no sense without reference to the levels above. My suggestion is that in a living system it may be the niche that is the composer, and the DNA sequences that are the instruments.

What is a niche, exactly? A niche is a set of orderly physical patterns that allow an organism to remain intact and living. A human can live only in a narrow band of conditions, in air with sufficient oxygen, at mild temperatures, in regular cycles of light and dark, with gravity of a certain strength, with fresh water, nutritional solids, and places to sleep, in areas free from large predators, parasites, viruses, storms, and excessive radiation. All these conditions are vital for our survival and are not ubiquitous in the universe but highly concentrated in a very delicate area between the sea, land, and sky of one particular planet. How do we know where a niche is and where it is not? We can guess, but we do not know precisely, because we cannot see niches directly…the only niche-detection device ever invented *is* an organism. There may be many more niches than there are organisms to fill them. Jakob von Uexküll called it the *Umwelt* [19]. A niche is a place with a special form of order; a niche is not just *anywhere*.

How do we stay in this niche and not drown in a puddle or fall out of a window? We do this by our *actions*. It is intuitive for us to see ourselves as independent intelligent agents in the world we live in. When we reflect on ourselves, we see a loose part, an "I", that drives the whole system by our choices, rather than being driven by it. But of course all our actions are also reactions. When we attempt to investigate this empirically, we get caught in an infinite regress trying to find the "I" in the neurons. It's as if we are asking of a clock, "What part of the clock keeps the time?" We are looking at each spring and gear, noticing which of them impairs timekeeping most when removed, and deriving from this a reductive account of where the essential timekeeping function lives. Conventionally, describing an action as *purposive* is to say it works at the level of the organism. A person *chooses* to act. If you go down to the level of brain cells or up to the level of the biosphere as a whole, the description no longer applies. But our body system is not causally isolated from its environment, it is completely enmeshed in interaction with both the environment and with itself at all times. The whole clock mechanism keeps the time, of course.

This illusion of agency is reinforced by the fact that we can see that there are a tremendous number of possible ways a human organism *could* interact with its niche. Many of the features of the environment can change markedly without impacting the health of the organism, a fact which suggests they have little causal influence. But surprisingly, research suggests that many of the genes in the genome can also be deleted with no harmful effect. For example, 80% of roughly 6000 gene knockouts in an entire yeast genome were found to be silent under normal conditions [20]. So there appears to be considerable buffering in either direction. One possible conclusion we can draw from this is that the causal chain in an organism runs from the DNA up to the niche and back down again, in a continual loop. This is what the authors of the Santiago theory of cognition called "a circular form of organization [21]." In this case the organism could be seen as a process *mediating* between its genes and its niche.

3 Niche Synchrony

If the logic of an organism's physiology is not encoded precisely in its DNA, it nevertheless still must operate according to an orderly method. But where can this order be found? The niche is very orderly in a sense, but it is not a physically precise envelope of predictable stimuli like a video game. It is the real world, where myriad unpredictable effects happen all the time. The alarm clock goes haywire, the coffee spills, the door jams. And just as organisms can withstand the deletion of most single genes, organisms can withstand these routine perturbations in their niches. The wide variety of conditions that an organism can tolerate, just like the intractable number of combinations of genes possible to generate traits, suggests that there could be no precise instructional code embedded in the niche, either.

One natural physical process that takes imperfect materials and assembles them into orderly structures, even in the face of chaotic conditions, is synchrony [22]. This process has proved devilishly difficult to study, perhaps because mathematical models of the nonlinear phenomena involved are too sensitive to the initial conditions of the variables to be reliable. Sometimes the models vary wildly based on small tweaks. But nevertheless the phenomenon exists in many forms in Nature, from the rings of Saturn to the chirping of crickets to the formation of crystals. Synchrony brings chaotic energy and matter into orderly or rhythmic motion. Many metronomes, placed on a tabletop but set to different rhythms, gradually synchronize [23]. In this example, it is easy to see that there are only two directions possible for each pendulum to move in time, either toward synchrony or away from synchrony. I call these the "cardinal directions."

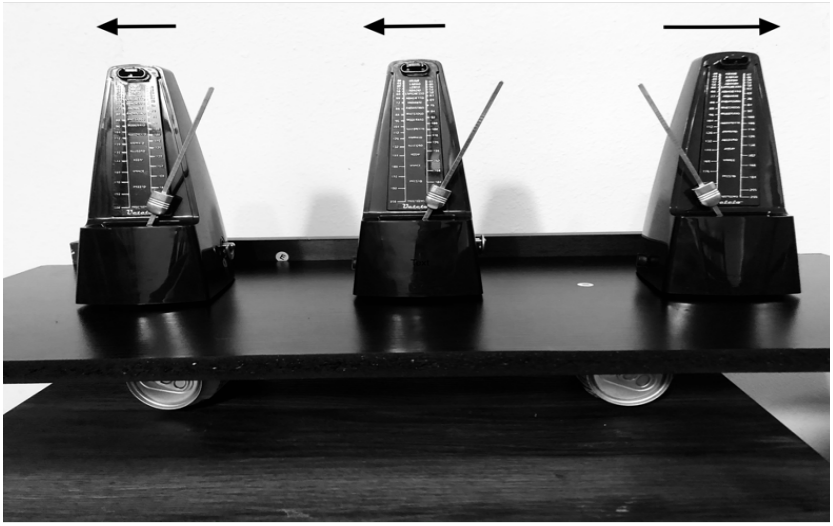

Fig. 1. Positive and negative feedback drives synchronization of connected networks

The pressure of the metronomes on the left as they swing in time exert a strong pull on the metronome on the right, which gradually forces it to accede to their same rhythm. In this case, and in all cases of synchrony, an object caught in the synchronizing system only has two directions to move, either away from the system's rhythm or towards it. The physical dynamics of synchrony simply make it just a bit harder for the object to move away from synchrony and a bit easier to move towards it. This is what gives synchrony its eerie "drift" that can be so beautiful to observe. The result is the coordination of forces that seemed disconnected into a seamless dance of elegant fluid motion.

Perhaps organisms do much the same through homeostasis or allostasis. Homeostasis is the process by which organisms maintain their physiology within certain parameters…salinity, temperature, pH, and so forth, by interacting with their environment, and allostasis is a term which recognizes that there is a "drift" to this process. These are the actions that every living cell carries out that solve its problems by selecting genes for expression. Perhaps we can think of the allostatic process as a form of intelligent "agency," keeping the organism inside its niche. At a basic level, all matter is a network of dynamic energy quanta held in a certain pattern by physical interactions. This means that everything living, too, is made of networks. Organic molecules are networks, proteins are networks, organs are networks, and whole animals are networks. Matter-energy passes in and out of these networks, but the networks cycle and reconfigure themselves somehow to maintain their integrity through changing conditions to remain alive. In other words, it brings itself into approximate synchrony with its niche.

So how does each network in a living cell or organism "know" whether it is approaching niche synchrony or departing from it? What makes it behave correctly given changing circumstances? This problem on its face appears as difficult as the question of gene expression. There appear to be no fixed detailed instructions that we can decipher in the cellular structures themselves, in the cytoplasm or the organelles or the cell membrane or anywhere else. Instead, living organisms possess a tremendous diversity of forms, from tiny spirochetes to enormous whales, and each of them interacts with its surroundings quite differently. Surely the niches available for life are vastly more diverse and numerous than the actual organisms on Earth, but since we cannot detect niches directly we do not know.

If we keep in mind that there are two cardinal directions in a synchronizing system, then it follows that the only thing necessary to produce approximate synchrony would be some process active in each network that distinguished between them. If a network is moving toward synchrony it must take some form of reinforcement, and if it is moving away from synchrony it must take discouragement or undergo degradation or mutation or some kind. What cue would there be when a network is approaching synchrony? The network would be stimulated or triggered by the niche. It would be *used*. If it remained unused, then it could be presumed to be departing from synchrony over time. As a general rule, all structures in the body experience some breakdown or atrophy if they are both unused and alive for a long period of time. With disuse tendons, muscles, even organs like the heart and brain become gradually weaker and shrink in size [24]. Structures that are used vigorously, on the other hand, become stronger. We can keep ourselves more physically fit through exercise, a fact that is hard to explain from the perspective of Neo-Darwinism. Likewise, neural pathways that are exercised

become more active, and those that are disused fall into degradation more rapidly. We forget far more than we remember. The formula for adjusting the networks to drive niche synchrony might be: ***If used, then reinforce; else mutate stochastically***.

4 General Intelligence

One way to experimentally refute the Neo-Darwinian theory of genetic causation would be to show that lifelike behavior could be produced without DNA. We know that naked DNA alone in a petri dish remains inert forever; it never produces life. But perhaps it might be possible to activate a biological niche without an organism inside it.

How would we know if an experimental device was interacting with a niche in a lifelike way? If we made the device as small as a cell, we would be required to use molecules for its construction that were functionally identical to the molecules of a living cell, but these molecules would have to be nonliving. Finding nonliving surrogates for all the molecules of a cell and assembling them into a cell-like form that would interact as a cell does is hard to imagine. It is hard enough to manipulate the real materials of a living cell; this approach seems a non-starter. On the other hand, if the niche and the device were created in a computer simulation, the niche itself would be highly artificial and bear little resemblance to the chaotic conditions of the real world. It would be impossible to tell if the device was really behaving as a living cell would, solving problems, or instead in a way that just superficially resembled problem-solving. How would we determine what comprised real problems for this simulated device?

In practice the easiest niche to examine empirically may be the niche of the entire human organism, simply because this is the niche of the examiner. Behavior that is lifelike, if it appeared in a nonhuman or artificial niche, would be hard to recognize as lifelike. This is because, if this conjecture is correct, the key feature of lifelike behavior is not any particular set of actions but rather the quality of using actions to solve problems using creativity. This quality could only really be recognized by an observer who was himself sensitive to the contextual problems of a similar niche, which would equip him to judge whether or not the actions of the device represented creative adaptive solutions to them. Since the device would have, in many particulars, slightly different problems than a biological organism no matter how carefully it was constructed, the evaluation of those solutions by the examiner would always be a matter of some intuitive judgement. We recognize intelligence when we see it, for example in an octopus, though we can't currently say precisely what intelligence *is*.

The premise that intelligence consists in exquisite sensitivity to a niche is supported by the observation that higher intelligence seems to require organisms to sleep. The function of sleep is no longer considered to be a period of rest, or torpor, but rather one of comprehensive repair [25]. Why should maintenance of the networks of higher animals require a holistic repair cycle in which the animal is often prone, unconscious, and vulnerable for hours at a time? Why can we not repair on-the-go? Evolution should have surely selected against this dangerous adaptation unless there were a tremendous

benefit involved. Sleep has convergently evolved both in bilaterians like us (fish, reptiles, mammals) and also in intelligent mollusks, further suggesting that it is indispensable to intelligence [26, 27]. The primary symptom of sleep loss is cognitive impairment. Without any sleep at all, cognition eventually becomes impossible.

I propose that sleep may be the cycle within which highly complex multicellular organisms make a concerted effort to apply the first command of the epistolution formula to their networks: *if used, reinforce*. Stochastic mutation can happen in many ways, including the passive degradation of complex particles at body temperature, but repair and reinforcement requires coordinated effort. This might explain the strange cyclical nature of the physiological routines of sleep which subvert consciousness and overtake many bodily processes to accomplish functions which are still obscure.

5 Testing Downward Causation

If an artificial network could be designed which was a) complex enough to store as much knowledge as the human body, b) adjustable according to the epistolution formula, and c) sensitive to many of the same stimuli with which a human body interacts, the device might serve as an empirical test both of Neo-Darwinist causation and of inductivist epistemology. Inductivism holds that learning occurs by building theories from examples, but the physicist David Deutsch has recently refuted this claim, advancing the view of Karl Popper that knowledge is built through conjecture and refutation [28]. A Popperian view of the body might suggest that our thoughts could be considered anticipatory hallucinations, punctuated by corrections from our world. For example, one might never notice the skin on the outside of one's left pinky for years until one day one finds that a glove has a hole in it in just that tiny location. The skin in that little patch had been sending sensory signals continually for years, but they only reached one's awareness and influenced one's behavior when those signals violated a hallucinatory set of expectations about temperature and pressure.

Advances in hardware and software have only recently brought this test into the range of technical feasibility. In order for a human-like niche to be engaged, it would be necessary for the test device to possess the robotic equivalent of arms and fingers to handle objects, temperature, vibration and pressure sensors, and robotic eyes, ears and larynx. It is our general body design that activates the human niche. This provides the frame of reference within which our individual problems make sense to one another as humans, allowing communication and coordinated problem-solving.

To model a human nervous system in software, a complex set of nodes might be linked to sensory input and to motor output. A flow of energy moving down a pathway between nodes could serve both as anticipation of the patterns of excitement coming from the niche and also as an impulse to motor action. Since motor action would cause sensory input to change, the flows of energy through the system would be causally linked to the rhythms of the niche. They would be both expectations and actions, or

"expect-actions." When these flows were in sync, no new motions would be triggered; only when surprises occurred would new expect-actions take place.

The timing of these flows of energy would be essential to the ability to generate meaning from them. Each of the nodes must possess, like neurons, both a set of adjustable connections to other nodes and an adjustable endogenous clock that allows the system as a whole to synchronize. Like a neuron, each node would have its own configuration of firing properties, and these properties would be adjusted in periodic "sleep" phases, based on the results of continuous waking activity. If a node or connection was used, the sleep phase should reinforce it, and if was unused for long period, it should mutate. Though imprecise at first, over time this type of network should evolve into a better anticipation of the environmental stimuli in the niche. If this conjecture is correct, this rhythmic anticipation would comprise lifelike creativity.

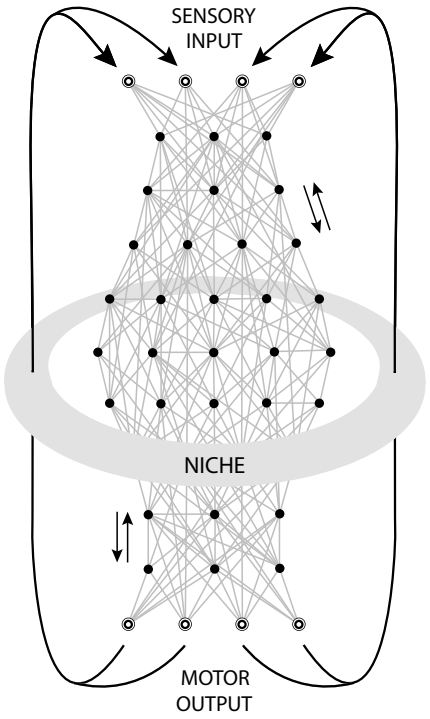

Figure 2. Expect-actions take on the rhythms of a niche because they are causally connected.

In this network, problems would arise from surprises to the hallucinatory expectations embedded in the pattern of connections and their rhythmic firing. If we throw a ball into the air, we expect (and expecting includes moving our bodies to anticipate) the return of that ball on a certain schedule. If it does not return on schedule or appears at an unexpected place, we have learned something by the experiment. If we successfully consolidate that lesson through sleep, the next time we conduct a similar experiment we have a slightly easier time catching the ball. That type of re-adjustment may be how organisms of any sort learn to respond appropriately to their context.

Would this device have motivations? Yes. It would have mismatches between its hallucinatory anticipations and the flow of its sensory input, and these would drive new interactions to develop. These may be the same sort of contextual problems that we experience in trying to understand our world. The evolution of new interactions that more correctly anticipate those problems may be the source of creativity in all higher animals. If this robotic niche synchrony worked approximately at a high level in the human niche, this would provide one possible explanation for the physiological logic of gene expression in all living organisms.

Possibly no organism finds itself in a niche that perfectly matches in every physical detail the ancestral niches that selected its DNA. There may always be a mismatch, therefore an epistemological struggle, to the acts of life. In this view, an organism would be a mediator that adjusts between two vast reservoirs of possibility, one above and one below, by applying the epistolution formula to its networks in cycles of periodic adjustment. In more complex intelligent creatures, this process may be so invasive and thoroughgoing that it requires the complete physiological dedication of a comprehensive cycle, sleep. This experiment might illustrate a possible adaptive purpose for a costly and dangerous process that appears perverse given current theories. If it worked, it would point the way toward a new, more comprehensive theory of life.

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