Title: Epistolution: A New Principle of Life

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Abstract: Our predominant fundamental theories of biology assume that the organized appearance of life and the reliable recurrence of ontogeny are due to heritable influences. In this view, inheritance even carries responsibility for producing learning. Learning is thought to be enabled by complex structures like brains, and it is assumed to be aimed at solving problems related to survival and reproduction. I propose that this is wrong on all three counts. Genetic selection cannot happen without phenotypes and phenotypes may require intentional learning to generate. The theory of life may only make sense if full-blown agency, involving beliefs, intentions, and desires, motivates every living cell rather than an inherited program or set of instructions. Both cells and organisms appear to learn to use genes for their own contingent, adaptive ends; I propose that biological inheritance may be impossible without this top-down control. I have named this form of learning "epistolution," combining "epistemology" and "evolution," to distinguish the idea from other concepts. Although all ontogeny requires epistolution, especially clear examples include embryonic development, wound healing, regeneration, cancer, memory, dreaming, creativity, swarm intelligence, epigenetic inheritance, and the placebo effect. I propose that the principles of epistolution, once known, will be generalizable and can be used to build artificial devices that create genuine subjective knowledge. This paper is an attempt to clarify epistolution to allow researchers to test models of it in laboratories, perhaps uncovering principles that can give us engineering ability over life, and cognition, for the first time.

All adaptive plasticity as learning

Claims that all organisms have some form of "agency," that they make choices and pursue their own goals, are now commonplace in biological discourse [1, 2]. How could these claims be compatible with the assumption that ontogeny is organized by a comprehensive inherited program that aims at survival and reproduction? Goals cannot be both spontaneously self-created and also wholly inherited. In contrast to mere teleonomy, *agency* seems to require a genuine purposefulness, involving beliefs, desires, and intentions.

Biological agency could be more coherently defined as the ability to form new, independent, individual goals through learning. Learning is often viewed as an evolved trait, but gene expression is controlled by the interaction between the phenotype and the environment [3, 4]. This makes genomic function a consequence of learning as well as a cause of it. This means that learning cannot be merely an evolved trait under genomic control [5].

It requires at least some goal-seeking plasticity to get from any genotype to any phenotype. Adaptation to changing conditions is a basic feature of all embryonic development, even the development and reproduction of single cells [6]. For example, if we take E. coli clones and put them in slightly different environments, they adapt in modest ways metabolically, behaviorally, or morphologically to accommodate different conditions, and that adaptation has consequences for their gene expression patterns [7-10]. If we simply classify all this goal-oriented plasticity as "learning," then it becomes a basic principle of life that is continuous from very simple to very complex organisms.

Intention before inheritance

This modest form of purposeful physiological learning featuring inter- and intracellular signaling, adaptive plasticity, and gene regulation may be a feature of all living systems no matter how simple. If so, it raises the possibility that this feature is not an evolved character, rather it may be a necessary prerequisite for ontogeny. It may be prohibitively unlikely, in environments that change significantly and unpredictably, for a surviving phenotype to develop *unintentionally*. If it is present in all life, it would appear that under the conditions on our planet biological natural selection might not be possible without it. This would mean some form of purposeful physiological learning was already present in the first life form and has been present in all life ever since. Such a universal "mental" function in all cells is ruled out if we insist on a firm boundary between what type of cells can give rise to mental functions and which cannot, but if so, where does this boundary lie? Are neurons alone sufficient? Neurons and glial cells? Neurons, glial cells, peripheral nerves, and gut microbiota[11]?

It is tautological that without survival and reproduction a lineage could not persist, but this doesn't prove that life must be exclusively dedicated to seeking it out; it is also logically possible that it could happen as a byproduct of pursuing another agenda. If we accept that organisms can have experiences, accumulate memories, and gain knowledge, we have to recognize that these cannot possibly be "about" survival and reproduction because individual organisms never experience nonsurvival or alternative rates of reproduction. A universal form of purposeful physiological learning presents a motive, an organizing principle for life, that could theoretically supercede survival and reproduction. Survival and reproduction could thus be seen as an incidental byproduct in some subset of the systems that pursued this teleological aim.

Problem-finding, not problem-solving

Learning is currently defined and tested in terms of problem-solving ability, or identified in incipient forms of the same such as sensitization, habituation, or associative learning [12-14]. This project was implicitly based on the assumption that learning is an evolved trait which arose to solve problems related to survival and reproduction. We have established above that this is likely not the case. Fundamentally, problems must be identified before they can be solved. Because all organisms develop in responsive interaction with their environments, we cannot presuppose that inheritance defines the problems that are addressed by plasticity. As every struggling student knows, intelligence tests occur not in the cognitive domain of the subject but rather in the domain of the observer, which is a very different space indeed. Instead of simply reading out heritable solutions to problems encountered by their ancestors, all organisms may be trying to actually understand the world themselves, which means finding their own problems in their own domains[15].

Unlike problem-solving, which presupposes a goal implanted by natural selection, *understanding* means open-ended experimentation to develop a sense of what entities and causal forces exist in one's surroundings [16, 17]. This would mean that all life, every living cell and also every whole organism, would contain within its phenotype some representation of the world that conflicts, in some respect, with experience. The urge to understand the world could thus serve as an intrinsic motivation for all living behavior, even morphological development. As strange as it may seem, this would mean for example that a lineage of cells in a developing embryo, as they differentiate into distinct somatic cells with specific functions, would be in effect forming stable *opinions* about how they each should live and behave as individuals and collectively, opinions based on experience, learning, and memory.

Understanding as the aim of life

The ability to contain a representation of the world inside one's phenotype and act on it is not necessarily a matter of consciousness. Consciousness in humans, for example, is largely extinguished during sleep even though sleep is considered critical for learning[18]. Although consciousness and focused attention certainly plays a role in the formation of new knowledge for humans, it would be hard to rule out the possibility that knowledge could form in biological structures incapable of consciousness, or the possibility that some rudimentary form of consciousness, though greatly attenuated in single cells, is coterminous with life[19]. As for consciousness, although we know that some biological structures (humans) contain representations of an umwelt, there is currently no empirical test to determine whether this is true of all organisms, therefore it is impossible to rule this out on experimental grounds.

If some life forms can develop perspectives, why not all of them? Understanding-seeking systems would be easy to mistake for survival-seeking genetic programs because the only such systems that can persist for long must incidentally be compatible with a successful chain of material inheritance. It has become easy to manipulate DNA, document phenotypic difference, and conduct statistical analyses which ignore the exact nature of the causal relationship. It is quite difficult, on the other hand, to imagine the world from the point of view of another life form, and yet this is exactly what may be required to adequately explain a specific organism's actual development and behavior.

There must be a set of principles, though they are still unknown, that keeps life more organized than nonlife, far from thermodynamic equilibrium. Our predominant theories of biology assume that this organized appearance is due to heritable (read genetic or cytoplasmic) material influences. In its extreme form, this view sees control exerted by a plan or code received from evolution by natural selection as a form of transcendent intelligence [5, 20]. Since what is inherited is a matter of contingent historical accident compounded over trillions of generations, according to this account there is no reason to believe that any general principle could be extracted that might elucidate how learning (and thereby ontogeny) occurs. Life would be intractably complex and inscrutable because "the system and its historical antecedents are mechanistically and causally inseparable [20]".

If, however, we conclude that no inheritance would have been possible without some purposeful physiological learning, then there must be a relatively simple, general, endogenous mechanism according to which all living beings learn because it has been shared with all the ancestors of the first living cell. It may in fact be that *this is what has allowed particulate inheritance to proceed*. If there were no such learning then life might have been doomed to remain a simple, invariant self-replicating system like an ice crystal, dependent on a constellation of very specific environmental conditions for its existence and, like such crystals, unable to project reproductions of its morphology into the future beyond these very narrow confines. If this were true then genetic material, instead of being a condensed structure confined to a particular region and deployed in a highly selective, flexible way during ontogeny, would be in effect the entire morphology of the organism, again as it is for a crystal. Instead, the genome appears to be a specialized replicated tool, a library of templates for making RNA whose use is regulated, maintained, and reproduced by the entire cell[21].

The search for a mechanism

So what could be the mechanism, common to all cell types on earth, that might produce this purposeful physiological learning, this *epistolution*? Could it be oscillators and servomechanisms? In cybernetics, life was conceived of as a set of servos and oscillators driven by the genome, but in my account it is interactions with the umwelt that drives them. As we stated in point #2, gene expression (and everything that it leads to, including self-organization, development, and cognition) is controlled by an interaction between the phenotype and the environment. An organism is a system with an open-ended constitution that makes it capable of informing its own internal organization by reading its external surroundings and incorporating them into itself functionally and purposefully, by *understanding its world*, in other words. In light of this new insight, principles might be discovered to instantiate epistolution in a network of oscillators linked by adjustable connections. A set of rules for such a configuration might be found that interprets novel data and finds new problems rather than acting simply as a readout of evolved, inherited signals. This type of algorithm, unlike all existing evolutionary algorithms, would have no intrinsic genotype-phenotype map and no preprogrammed survival or reproductive instinct, but might instead develop its form and its behavior strictly according to what it learned about the world. This would resolve the question of why and how biological genotypes lead to phenotypes.

A formalized model of epistolution might serve as a general principle explaining life. If so, this conceptual breakthrough would lead to more effective medical intervention, regenerative therapies, and eventually to the ability to design and build whole organisms fit for therapeutic, commercial, or creative purposes. In contrast to the current statistical mimicry termed "artificial intelligence [22]," machines programmed according to the (still currently unknown) principles of epistolution could gain causal understanding by inventing and testing their own subjective theories of what entities and forces exist in the world. Though not necessarily conscious, they would be the first artificial systems with the ability to develop their own subjective cognitive perspectives, their own *agency*. This might comprise a powerful new technology amplifying scientific, technological, aesthetic, and moral progress in many intellectual domains.

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