

# Life is determined by its environment

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**Abstract:** A well-developed theory of evolutionary biology requires understanding of the origins of life on Earth. However, the initial conditions (ontology) and causal (epistemology) bases on which physiology proceeded have more recently been called into question, given the teleologic nature of Darwinian evolutionary thinking. When evolutionary development is focused on cellular communication, a distinctly different perspective unfolds. The cellular communicative-molecular approach affords a logical progression for the evolutionary narrative based on the basic physiologic properties of the cell.

Critical to this appraisal is recognition of the cell as a fundamental reiterative unit of reciprocating communication that receives information from and reacts to epiphenomena to solve problems. Following the course of vertebrate physiology from its unicellular origins instead of its overt phenotypic appearances and functional associations provides a robust, predictive picture for the means by which complex physiology evolved from unicellular organisms. With this foreknowledge of physiologic principles, we can determine the fundamentals of Physiology based on cellular first principles using a logical, predictable method. Thus, evolutionary creativity on our planet can be viewed as a paradoxical product of boundary conditions that permit homeostatic moments of varying length and amplitude that can productively absorb a variety of epigenetic impacts to meet environmental challenges.

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## Introduction

Over the course of the last two centuries, great strides have been made in circumscribing evolutionary development (West-Eberhard 2005; Gluckman *et al.* 2009) and phylogeny (Valentine 2004). However, the ontologic and epistemologic underpinnings of physiology have recently been brought into question (Torday & Rehan 2004) given the teleologic and tautologic nature of the conventional Darwinian narrative (Roux 2014). An alternative perspective to that general narrative can now be offered based on cellular patterns of communication and cell–cell signalling mechanisms for morphogenesis (Torday & Rehan 2007a). Such complex, structured communication is enabled by signalling molecules and growth factors, but also through other equally important non-molecular means that directly influence unicellular and multicellular metabolism, growth and development. When evolutionary development is focused on cellular communication, a different narrative unfolds (Torday & Rehan 2009) that uniquely depicts the evolutionary progression towards more nuanced organisms (Torday *et al.* 2010), initiated and determined by environmental factors (Torday & Rehan 2011).

In contrast to the probabilistic Darwinian framework traditionally imposed on the ontogeny and phylogeny of physiologic traits, we hypothesize that a deterministic, cellular communicative-molecular approach affords a logical, progressive evolutionary narrative using basic cell properties and reciprocating interactions between the environment and the organism (Torday & Rehan 2011) that extend beyond random

mutation and selection. According to this model, the cell is a self-similar reiterative unit of activity that reciprocally communicates with and reacts to its environment. It does so, at every scope and scale, by remaining firmly anchored within first principles that are inherent to the unicellular form.

## How do cellular mechanisms drive the evolution of physiology?

The essential component for understanding evolutionary development is gained through insights into cell–cell signalling pathways. For example, Torday & Rehan (2004, 2007b) have exploited the evolution of the lung at the cellular-molecular level as a ploy to reverse-engineer the organ of gas exchange all the way back to its unicellular origins. The premise that eukaryotic calcium homeostasis is counterbalanced by lipid homeostasis at multiple levels, both within (Case *et al.* 2007) and between cells (i.e. lipid rafts) allows an informed perspective for how complex physiology translates into the fundamental homeostatic regulation practiced by unicellular organisms. Similar means can be used for other metabolic pathways within cells. At all levels, from the protocell, to eukaryotes and all complex organisms, similar reciprocating and reiterative patterns are reinforced to enable the diversity of forms and faculties that can be observed. The nature of that end-point has only recently been apprehended (Torday 2013). All complex creatures are collaborations of deep and extensive cellular ecologies as hologenomes (Miller 2013).

## How life progressed

Early in the evolutionary progression, the otherwise toxic ambient calcium concentrations within primitive cells had to be lowered by forming calcium channels, composed of lipids embedded within the cell membrane. This also led to the complementary formation of the endoplasmic reticulum, an internal membrane system for the compartmentalization of intracellular calcium. Ultimately, the advent of cholesterol synthesis led to its incorporation into the cell membrane of eukaryotes, differentiating them (our ancestors) from prokaryotes (bacteria), which are devoid of cholesterol. This process was contingent on an enriched oxygen atmosphere, since it takes 11 atoms of oxygen to synthesize one cholesterol molecule. The cholesterol-containing cell membrane thinned out, critically increasing oxygen transport, enhancing motility through increased cytoplasmic streaming and was also conducive to endocytosis, or cell eating.

All of these processes are the primary characteristics of vertebrate evolution (Perry & Carrier 2006). At some stage in this progression of cellular complexity, impelled by oxygen-promoting metabolic drive, the evolving physiologic load on the system resulted in endoplasmic reticulum stress, periodically causing the release of toxic calcium into the cytoplasm of the cell. The counterbalancing, or epistatic mechanism, was the 'invention' of the peroxisome (de Duve 1969), an organelle that utilizes lipids to buffer excess calcium. That mechanism ultimately became homeostatically constitutive, further promoting the movement of ions into and out of the cell. Importantly, the internalization of the external environment by this mechanism reciprocally conveyed functional biologic information about the external surroundings, and promoted intracellular communication.

Cannon (1932) later formulated the concept that biological systems exist to 'trigger physiological responses to maintain the constancy of the internal environment in face of disturbances of external surroundings,' which he termed homeostasis. He emphasized the need for reassembling the data being amassed for the components of biological systems into the context of whole organism function. Hence, Weibel & Taylor (1991) tested their theory of 'symmorphosis,' the hypothesis that physiology has evolved to optimize the economy of biologic function.

Harold Morowitz (Smith & Morowitz 2004) is a proponent of the concept that the energy that flows through a system also helps organize that system. This is better reformulated to reflect the realm in which cells live; communication flowing through systemic awareness is the essential organizing aspect.

As eukaryotes thrived, they experienced increasing pressure for metabolic efficiency in competing with their prokaryotic cousins. They ingested bacteria via endocytosis, which were assimilated as mitochondria (Margulis *et al.* 2006), providing more bioenergy to the cell for maintaining homeostatic flux. Eventually, eukaryotic metabolic cooperativity between cells gave rise to multi-cellular eukaryotes, which were effectively able to compete with prokaryotes. As Simon Conway Morris has archly noted, 'Look! Once there was bacteria, now there is

New York' (Morris 2011). There are reasons to consider this proposition. The unicellular realm can obviously engineer complex environments through behavioural traits such as Quorum Sensing and biofilm formation. Such actions are purposeful, based on awareness invested within all cells, an ability to act, to react and to communicate reaction and intent to others. In so doing, even at the most primitive stage of our evolutionary path on this planet, the unicellular environment demonstrates characteristics of multicellular organization in an organized confederacy. Communication is the enabling component of that process. And from this more loosely affiliated structural architecture, evolution unfolds in a pattern best characterized as self-similar iteration that is always based upon cellular first principles. The same basic impulses impel each stage. Evolution can best be envisioned as the consequence of cellular growth factors and their signal-mediating receptors in counterbalance to selection at every level, most particularly at that of the collaborative collection of cellular constituents that affects localized ecologies that become hologenomes. Evolutionary development can then be reframed as separate from Darwinian selection, which is strongly based on reproductive fitness of the entire organism towards a differing direction. Evolutionary development is better understood as the product of cognitive cells solving cellular problems at multiple functionally-linked levels through intense communication, which produces both random and deterministic outputs. This is the frame within which our vertebrate ancestors facilitated cell-cell signalling, providing insights to metazoan evolution. It is this same process that is recapitulated each time the organism undergoes embryogenesis.

This cellular focus on the process of evolution serves a number of purposes. First, it regards the mechanism of evolution from its unicellular origins as the epitome of the integrated genotype and phenotype. Multicellular organisms evolved from the starting place of the unicellular cell membrane and its cellular partners as the common origin for all evolved complex traits. Further, it offers a discrete direction for experimentally testing the constituents of evolution based on the ontogeny and phylogeny of cellular precursors. For example, it is commonplace for evolution scientists to emphasize the fact that any given evolved trait had its antecedents in an earlier phylogenetic species as a pre-adapted, or exapted trait. These ancestral traits can subsequently be cobbled together to form a novel structure and/or function. Inescapably, if followed to its logical conclusion, all metazoan traits must have evolved from their unicellular origins. Indeed, King *et al.* (2003) have shown empirically that the entire metazoan 'toolkit' is present in the unicellular form.

## Cellular communication

It is worthwhile now to consider the means by which cells are known to communicate. It was not very long ago that the only mechanism that was considered consisted of cell membrane receptors and molecular signalling. However, it is now known that microorganisms communicate by varied means, and that the communication process is intense. As Visick & Fuqua

(2005) note, 'It is clear that chatter among microorganisms is extensive and pervasive'. It is quantitatively important enough that it is estimated that 6–10% of all genes in the bacterium *Pseudomonas aeruginosa* are devoted to cell–cell signalling systems.

The varied mechanisms by which this communication proceeds are currently being extensively researched, yielding surprising results. Neelson (2010) had documented a previously unknown electrical communication at a distance between bacteria in differing layers of sediment in the Aarhus Bay in Denmark. Dubey & Ben-Yehuda (2011) described sophisticated intercellular nanotubes as pathways of communication between microbes, which permits the interchange of content. Other ready means are now known, including mechanical signals as mechanotransduction (Burkholder 2003, 2007), mechanical load (Urban 1994), or mechano-electrical transmission, as exhibited by hair cells (Howard *et al.*, 1988). However, there are means for cells to communicate with each other without physical contact or the diffusion of molecules that are only beginning to be explored.

For example, a potential higher form of intercellular communication relating to underlying calcium signalling has been demonstrated by cells that are physically separated from one another (Chaban *et al.* 2013). The exact means is not yet understood. Receptor-mediated interactions based on electromagnetic waves have been documented (Mullins *et al.* 1999). Albrecht-Buehler (1994) has proposed that centrosomes are infrared detectors. Farhadi (2014) cites research that supports the conclusion that cells can generate electromagnetic waves and communicate via electromagnetic signals at a distance, as does Trushin (2003). Scholkmann *et al.* (2013), in a comprehensive review discuss a broad range of experiments documenting non-chemical and non-contact cell-to-cell communication. Fels (2009) discusses photons as information carriers as biophotons that are emitted at wavelengths of 200–650 nm, spanning both the ultraviolet and visible spectra (Ruth & Popp 1976). The necessary implication of a means of non-local correlations in animal physiology is well-known (Ho 2008), though the mechanisms involved are not. The instantaneous reaction of groups of tissues to stimuli over widely dispersed tissues and enormously varied scales is incompatible with only a molecular, or even a cell–cell electrically evoked response trigger. Pizzi *et al.* (2004) have presented data that strongly suggest the validity of non-local properties in biologic systems by an as yet undetermined path. Therefore, intercellular communication is vast, and proceeds by a range of mechanisms that are only now being investigated.

This variety of means of communication between cells adds further reasons for why all complex organisms return to the unicellular zygotic state. Fidelity of those patterns of communication in a life cycle that imposes a large number of epigenetic experiences might clearly be considered of paramount importance. In all likelihood, ontogeny takes a path towards the recapitulation of phylogeny in order to vouchsafe the fidelity of all of the homeostatic mechanisms that support communication among the cellular parties that facilitate cellular integrity, on the one hand, and drive development on the

other. Without such a fail-safe mechanism for the foundational principles of life, there would inevitably have been drift from the fundamentals of cellular faculties, putting the core processes of evolution at risk in response to environmental changes.

One implication of this perspective on evolution – starting from the unicellular state phylogenetically, being recapitulated ontogenetically – is the likelihood that it is the unicellular state that is actually the primary level of selection (Torday 2013). The multicellular state – which Gould & Lewontin (1979) called 'Spandrels' – is merely a biologic agent for monitoring the environment between unicellular stages in order to register and facilitate adaptive changes. This consideration can be based on both *a priori* and empiric data. Regarding the former, emerging evidence for epigenetic inheritance demonstrates that the environment can cause heritable changes in the genome, but they only take effect phenotypically in successive generations. This would suggest that selection actually operates at the level of the germ cells of the offspring, which act as the conveyance. There is some observational evidence to support this; for example, the starvation model of metabolic syndrome may illustrate this experimentally. Maternal dietary restriction can cause obesity, hypertension and diabetes in the offspring (Hanson & Gluckman 2014). But the offspring also mature sexually at an earlier stage due to the excess amount of body fat and precocious adrenarche. Though seemingly incongruous findings of a relationship between food deprivation and reproduction, this may represent the primary strategy to accelerate the genetic transfer of information to the next generation (positive selection). This mechanism effectively overarches the expected paucity of food in favour of the probability that the next generation will find itself in a favourable nutrient environment (The latter is a reasonable supposition since it is highly unlikely that organisms originated in a nutrient poor environment). The concomitant obesity, hypertension and diabetes are unfortunate consequences of this otherwise adaptive process in the adults, resulting from enhanced bioenergetics allocated for reproduction (Torday & Rehan 2012). Under these circumstances, one can surmise that it is the germ cells that are the explicit level of selection; in other words, the adults are disposable, as Kirkwood (1977) has opined, the difference being that now there is a testable mechanism.

Hologenomic evolution theory provides yet another mechanism for selection emerging from the unicellular state. According to that theory, all complex organisms actually are vast collaborations of linked, co-dependent, cooperative and competitive localized environments and ecologies functioning as a unitary organism toward the external environment. These co-linked ecologies are comprised of both the innate cells of that organism, and all of the microbial life that is cohabitant with it. The singular function of these ecologies is to maintain the homeostatic preferences of their constituent cells. In this theory, evolutionary development is the further expression of cooperation, competition and connections among the cellular constituents in each of those linked ecologies in successive iterations as they successfully sustain themselves against a hostile external genetic environment. Ontogeny would then recapitulate phylogeny since the integrity of the linked environments

that constitute a fully developed organism can only be maintained by reiterating those environmental ecologies in succession towards their full expression in the organism as a whole.

There is a further justification for thinking that the unicellular state is the actual object of selection. This primacy is focused within calcium signalling as an initiating event for all of biology. There is experimental evidence that the increases in carbon dioxide during the Phanerozoic eon caused acidification of the oceans, causing leaching of calcium from the ocean floor (Kempe & Kazmierczak 2002). The rise in calcium levels can be causally linked to the evolution of the biota, and is intimately involved with nearly all biologic processes. For example, fertilization of the ovum by sperm induces a wave of calcium that triggers embryogenesis (Ciapa & Chiri 2000). The same sorts of processes continue throughout the life cycle (Cullen & Lockyer 2002), until the organism dies (Trewavas 1999). There seems to be a disproportionately high investment in the zygote from a purely biologic perspective. However, given the prevalence of calcium signalling at every stage, on the one hand, and the participation of the gonadocytes in epigenetic inheritance on the other, the reality of the vectorial trajectory of the life cycle becomes apparent – it cannot be static, it must move either toward or away from change – as Wallace Arthur (2004) has taught us, the embryo is ‘biased’.

### Where might we place our emphasis?

This unicellular-centric vantage point provides an impulse to shift our gaze towards our true place in the biologic realm. This is already occurring in medicine, as it is becoming increasingly apparent that our obligate interactions with our immense microbiome require such an adjustment (Miller 2013). It is being learned that the unicellular world has its surprising mechanisms and capacities. The proper understanding is a byway through the ‘Big Bang’ of the cell forward, with all its faculties and strictures. By concentrating on cellular dynamics, an entirely coherent path is empowered. Tennyson’s line about ‘Nature, red in tooth and claw’ is the merest simplification of evolution. We and all other creatures evolved from unicellular organisms through cooperation (Cavalier-Smith 2009), co-dependence (Pratt 2011), collaboration (Chapman & Margulis 1998) and competition (Hummert *et al.* 2014). These are all archetypical cellular capacities. It is not surprising then that we ourselves are only examples of self-similar cellular reiterations extending forward from these base capacities, and thereby embody self-same and similar behaviours.

How might these insights direct us towards any search for extraterrestrial life? By analogy, our inquiry must be centred on awareness, reciprocation and boundary conditions. It is by these means that cellular communication clearly flourishes on our planet. Reciprocal mechanisms that are conclusively enacted as awareness are then epitomized in the cell as the fundamental unit of life. It is likely that the property of awareness is not definitively invested exclusively within the cellular unit insofar as viruses, prions and other proteins also possess a property of awareness and discriminative preference. Therefore, as

any extraterrestrial life could reasonably be expected to be quite different from our own macro-organic sensibilities and faculties, then any exploration of our own inner life, and an inquisitive search for dialog with our own cellular companions would be a fruitful means in uncovering a mode of communication with alien life outside of our own planet.

Cellular mechanisms have not been our focus, since our prior assumption had rested on the belief that cellular communication was based on direct molecular interactions (Cantley Hunter 2014). However, research is proving that alternatives exist. What antennae or radio array has been erected to communicate with our hologenomic cellular partners? Communication among these obligate constituents of ourselves is active and abundant, yet ignored by us. Are they not an alien life form, at least with respect to our own faculties? Do they not have their own means of making their intentions clear to others? How might our search for intelligent life elsewhere be altered if we determined the advantage and had the disposition to communicate with the ‘alien’ life within us and on us? This is life that is so intimately entwined with our own that it enables our survival and reproduction on this planet. However, even as we enthusiastically engage in a broad search for alien life beyond our planetary limits, there is no similar drive to communicate with the alien microbial life with which we are intimately associated.

Life on Earth is likely due to the uniquely combined presence of water and lipids on its surface, and the effects of the sun, moon, gravity, carbon dioxide, oxygen and the availability of polycyclic hydrocarbons. All of these have been put to service by the cell. So the proper focus in the search for a hospitable celestial body might shift towards an exploration of the combinations of physical components that might lead to the formation of micelles that serve as a protected space within which negentropy, chemiosmosis and homeostasis could have occurred. Others have shown, for example, that electromagnetic force can alter the configuration of phospholipid membranes (Madrid & Horswell 2014), and that van der Waals forces will affect the structure of such membranes (Berkowitz & Vácha 2012).

Although self-similar geometric patterns might be likened as a metaphor for biologic mechanisms, any such emergence still requires a further impulse. What then is that iterative means? The answer is that cells communicate within their boundaries and among each other. In the unicellular environment, the reciprocating relationships between lipids, DNA and calcium, are amplified and reinforced within those boundaries. Herein lies a powerful paradox. Boundaries reinforce creativity in biology. Our creativity might be unlocked by looking within our own boundaries based on a thorough understanding of all those mechanisms that exist to enable communications within and among cells.

Frank & Sullivan (2014) have recently explored concepts of a sustainable human civilization in Astrobiological terms using The Drake equation (Burchell 2006) as a vehicle. The Drake equation relates to a series of estimates of the number of civilizations in our galaxy that might support radio communication as a proxy for intelligent life. The probability

determination is based upon a series of assumptions about the numbers of planets that might potentially support life, the number that eventually do so, the fraction of those that might develop technology that release signs of their existence, and the length of life of those civilizations. The case is made that the search for extraterrestrial life could be rewarded by evaluating habitable planets based on an ensemble of markers for Species with Energy-Intensive Technology (SWEIT) on our planet. That trajectory, as appraised on Earth through its impact on climate change, would then bear on both issues of Earthly sustainability and the search for extraterrestrial civilizations. By modelling SWEIT through energy consumption rates, and population and planetary systems, the authors propose that there might be some discrimination between 'natural' and SWEIT-derived consequences on climate on this planet that might be generalized to inform our search for alien life. It is pertinent that emphasis is directed towards the most important variable in the Drake equation, 'L', or the length of time that a civilization survives to emit detectable signals. Although the Drake equation relates to estimates of the probability of intelligent life that employ technologies of our human kind, its underlying principles could be enlarged to include other attributes of the biologic realm. The cellular world utilizes its technologies according to its own capacities. Its substrate is biologic material. Its tools include a wide range of physical phenomena and energy usage that are all forms of communication, including genetic interchange. Its language is perhaps abstruse, but could be made accessible if deeply explored. Importantly, the prokaryotic realm has been continuous on this planet, the only species to be so sustained. There are many scientists that feel that the species divisions that are made among prokaryotes are artificial and that they are in fact only a single species with separable breeding fractions. Therefore, the Drake equation can be further empowered by two means. First, by freeing our imagination about what constitutes technology, and second, by concentrating on the alternate methods by which it is employed for communication by the only continuous biologic set on this planet, and has done so to sustain itself for billions of years. This latter particularly satisfies the consequential 'L' in the equation. This combination then represents a proper supplemental focus for Astrobiological inquiry.

## Conclusion

An evolutionary focus on the cell provides a novel bridge towards devising a means by which extraterrestrial life might be sought, or how communication with it might be achieved. Until recently, the cognitive capacity of unicellular life had not been appreciated. Yet its primacy is apparent. It is the most enduring evolutionary participant on our planet, having been the only life form for the first several billion years, and recapitulates through multicellular organisms for the exploitation of environmental niches to cope with epiphenomena. The mechanisms by which it sustains this success are iterative biologic forces reciprocating with physical phenomena intrinsic to our planet. Understanding the capacities and limitations

of the unicell permits the identification of basic principles of evolutionary development that devolved as a series of coordinate interactions between nucleobases, lipids and calcium within the boundary constraints of semi-permeable membranes. This fortuitous reciprocity yields negentropic self-reinforcement as a First Principle of evolution, from which other fundamental paths radiate. Evolutionary creativity on our planet can then be viewed as a paradoxical product of boundary conditions that permit homeostatic moments of varying length and amplitude that can productively absorb a variety of epigenetic impacts to meet environmental challenges. This is what our planet does too, in its own form and by its own means (Lovelock 2003).

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