Title: Biologic Relativity: Who is the observer and what is observed?

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Abstract

When quantum physics and biological phenomena are analogously explored, it emerges that biologic causation must also be understood independently of its overt appearance. This is similar to the manner in which Bohm characterized the explicate versus the implicate order as overlapping frames of ambiguity. Placed in this context, the variables affecting epigenetic inheritance can be properly assessed as a key mechanistic principle of evolution that significantly alters our understanding of homeostasis, pleiotropy, and heterochrony, and the purposes of sexual reproduction. Each of these become differing manifestations of a new biological relativity in which biologic space-time becomes its own frame. In such relativistic cellular contexts, it is proper to question exactly who has observer status, and who and what are being observed. Consideration within this frame reduces biology to cellular information sharing through cell-cell communication to resolve ambiguities at every scope and scale. In consequence, it becomes implicit that eukaryotic evolution derives from the unicellular state, remaining consistently adherent to it in a continuous evolutionary arc based upon elemental, non-stochastic physiologic first principles. Furthermore, the entire cell including its cytoskeletal apparatus and membranes that participate in the resolution of biological uncertainties must be considered as having equivalent primacy with genomes in evolutionary terms.

Key Words: quantum physics, thought experiment, implicate order, physiologic first principles, biologic relativity theory, cell-cell communication, unicell, evolution

"The most curious part of the thing was, that the trees and the other things round them never changed their places at all: however fast they went, they never seemed to pass anything. "I wonder if all the things move along with us?" thought poor puzzled Alice. And the Queen seemed to guess her thoughts, for she cried, "Faster! Don't try to talk!"

Lewis Carroll, *Through the Looking Glass*

Introduction

An instinctive human frame of reference governs our perception of the life cycle of macro organisms as an arc, initiated with birth, extending across development and maturity, ultimately leading to death. The result is a natural impression of a clock-like progression. This is consistent with the general terms of directionality that Newtonian mechanics imposed upon physics with respect to space and time. Darwinism is entirely rooted in a causal model that is in conformity with this conceptualization of biological space-time as absolute. Within those terms, evolutionary motion proceeds by natural selection based upon the accumulation of gradual internal genetic modifications that continue by direct vertical descent, yielding differential reproductive fitness. In such a macro-organic frame, it is not surprising that reproduction became the centerpiece for the standard narrative of Darwinian evolution (Koonin, 2009). However, contradictory evidence suggests that the cellular constituencies of macro-organisms rather than the whole are of greatest importance (Shapiro, 2011; Miller, 2013). In this biological frame, perceptions of space and time need not be co-aligned with macro-organic priorities. When re-appraised in this manner, eukaryotic evolution becomes a fractal reiteration of basic physiologic first principles established in the unicellular form to which it maintains perpetual fidelity (Torday, 2013). In consequence, evolutionary development can no longer be considered within any Newtonian conception of space-time as an absolute, and must be reconsidered instead in new terms of biological

relativity.

A genome in motion

This differing perspective is driven by the intersection of several critical and well-substantiated factors. First principles of physiology have been identified that can be shown to extend forward from the unicellular form throughout eukaryotic macroevolution in unbroken linkages (Torday and Rehan, 2012). The critical role of epigenetics in evolution is now being acknowledged. Further, it is clear that all cells are cognitive entities and decision-making capacity is invested at every scope and scale in biological forms. Lastly, all macro-organic entities are holobionts [the inherent community of innate cells of any eukaryotic macro-organism and all of its symbiotic microbes], not biological singularities. The crux of that intersection is at the level of the eukaryotic, unicellular zygotic phase- all eukaryotic life undergoes an obligatory recapitulation through it. Moreover, it is now becoming clear that all eukaryotic life remains deeply anchored to it, and adherent to that phase throughout the ensuing life cycle despite outward appearances through biological first principles that resonate from it (Petrov et al., 2015). In consequence, biological and evolutionary development can be appropriately re-appraised as always remaining centered within cellular rather than macro-organic mechanisms that unfurl according to a consistent set of principles in fractal reiterations. It becomes evident then that any absolute terms for biologic space and time that have been traditionally imposed as implicit to the macro-organic form need not apply to the cellular constituencies that compose those organisms. This perspective shifts our perceptions of the means by which biologic organisms react to environmental stress and settle ambiguities in biological terms. Consequently, a re-ordered understanding of biological causation is impelled. A central question then emerges: in biological

terms, who is doing the observing and exactly what is being observed?

Determining an answer is aided by abundant research that has identified an ever-greater role for epigenetic factors in biology (Rapp and Wendell, 2005; Jablonka and Raz, 2009; Bossdorf et al., 2008; Upham and Trosko, 2009). This Lamarckian form of inheritance of acquired characteristics is both horizontal and vertical (Brody, 1973; Potter, 1974). These environmental impacts are now understood to have significant evolutionary implications (Jablonka and Lamb, 2014). Environmentally acquired epigenetic marks are heritable, transferring to the next generation through egg and sperm as germ line cells (Gapp et al., 2014). Yet, not all epigenetic impacts yield heritable changes. Some, such as terminal differentiation or apoptosis of stem cells are not inherited somatically, and others are only “transient” in progenitor and differentiated cells, such as those needed for cell division. The extent to which some are retained and others rejected during meiosis, at fertilization, or in the post-zygotic stage is only now being actively determined (Daxinger and Whitelaw, 2012; Grossniklaus et al., 2013). It is clear that epigenetic marks are processed at multiple stages during embryogenesis, centered upon homeostatic principles during morphogenesis (Feng et al., 2010; Morgan et al., 2005). The life cycle itself may play a role in this epigenetic selection process since the timing and duration of its stages from infancy to senescence are all determined by the endocrine system, which is under epigenetic control by the environment (Zhang and Ho, 2011). However, basic research is indicating that a dominant locus of that discriminatory process lies within the zygotic unicell, through which all eukaryotic organisms must recapitulate (Reik et al., 2003; Jahnke and Scholten, 2009; Wossidlo et al., 2011; Rousseaux et al., 2008). In this context, it is worthwhile citing a comment about cancer made by Potter (1973)- “The biochemistry of cancer is a problem

that obligates the investigator to combine the reductionalist approaches of the molecular biologist with the wholistic approaches of the holistic requirements of hierarchies within the organism. The cancer problem is not merely a cell problem, it is a problem of cell interaction, not within tissues, but with distal cells in other tissues. But in stressing the whole organism, we must also remember that the integration of normal cells with the welfare of the whole organism is brought about entirely by molecular messengers acting on molecular receptors.”

It is also now understood that the end products of all eukaryotic biological development are holobionic organisms. On a cellular basis, we and all other eukaryotic organisms are as much or more microbe than innate cellular material (Turnbaugh et al., 2007; Peterson et al., 2009, Hoffmann et al., 2015). Macro-organisms are now being understood as complex linked cellular ecologies (Miller, 2013). Imperatively though, the continued existence in any macro form remains an exclusive path through the unicellular zygote. There are no exceptions in eukaryotic biology. Therefore, any stage in which there is significant assortment of epiphenomena as they intersect with any innate genome must be assessed as having significant dominion. That express stage is the always-recapitulating unicellular phase. { While this statement is correct, newer evidence points to that “unicellular phase” is encapsulated in the germinal & somatic stem cells”. It is not necessary to bring concept into any modification of the original text, as this point has been made : Trosko, J.E. and Kang, K.-S., “Evolution of energy metabolism, stem cells and cancer stem cells: How the Warburg and Barker hypotheses might be linked. *Internatl. J. Stem Cells* 5: 39-56, 2012.} Duly noted; we thank the Reviewer for pointing this out.

When considered in this fashion, embryological development can be reduced to the fundamental ubiquity of cell-cell communications at every scope and scale, preceding and enabling the recapitulated unicellular form, and then continuing through it towards its macro-organic elaboration (Trosko, 2007; Trosko, 2011a).

Several implications then follow. A straightforward dynamic underscores all eukaryotic development: cell-cell communication is a sender-receiver operation necessitating cellular cognition. When that faculty is honored as inherent to all the cellular constituents of holobionts, both those that are innate cellular constituents and our ubiquitous microbial partners, then the fundamental principles of development consequently shift into a focused concentration upon the cellular domain in all evolutionary development (Trosko et al., 1990; Trosko, 2011b; Trosko, 2011c; Trosko, 2014). When considered in this manner, first principles of physiology become evident (Torday and Rehan, 2012). For example, fundamental links between the evolution of the lung can be traced backwards in time through its development and phylogeny using the cellular interactions for the synthesis of lung surfactant phospholipid at a level of adaptation that is centered at the cellular level rather than a macro organic one (Torday and Rehan, 2004). The basic principles of vertebrate evolution can be understood as always leading back to the advent of cholesterol at its first insertion into the cell membrane of single celled eukaryotes, thereby facilitating oxygenation, metabolism and locomotion (Torday and Rehan, 2012). As the most primitive of surfactants, the role of cholesterol can be understood to form a crucial aspect of the continuous arc from the unicellular state and its cell membrane towards the emergence of the mammalian lung in order to facilitate cellular oxygenation. It can be appreciated then that eukaryotic development is not invested in the alluring macro-organic forms that our senses

readily appraise (Bohm, 1980). Instead, that development is directed towards hologenomic networks of mixed cellular constituencies that co-exist along invisible threads of collaboration, co-dependency and competition, yet always remaining bound to their unicellular origins (Torday and Rehan, 2013).

If the centrality of the cellular constituencies that compose holobionts become the focus of biological development instead of the macro-organic whole, how might that impact evolutionary theory? It is clear that it would do so critically and on multiple levels (Torday, 2013). For example, it would offer an explanation for why sexual reproduction is so much more robust than asexual reproduction. It is obvious that sexual reproduction per se cannot give rise to novelty from a stable genome that does not already have that evident flexibility within its pre-existing capacity. Merely recombining the haploid parental gene pools does not, in and of itself, give rise to emergent and contingent traits that extend beyond the genetic complement that is already present. However, when epigenetic mechanisms are included, the role of sexual reproduction as a means of making the contributions more robust emerges. For example, males and females have different life cycle histories and experiences that enrich the reproductive component of evolution. This has been researched through the study of the sexual dimorphism of lung development, largely focused on the timing of lung surfactant production by the developing fetus ((Torday and Nielsen, 1987). The development of chick embryonic lungs is an effective model because the genetic determinants of zygosity in birds and mammals are inversely related in mammals and birds, i.e., XX/XY and ZW/ZZ (female, male) respectively. Since the overall sexual dimorphism of bird and mammal biology, including secondary sex characteristics, adult size, disease susceptibility, longevity are also reciprocal, an opportunity is provided to determine the deeper

significance of this phenomenon. It has been found that the homozygotic sex is at an advantage for the timing of lung surfactant production and lung development in preparation for birth. This finding is consistent with the theory that the heterozygotic sex is derived from the homozygotic sex for increasing the biodiversity of the species. Although a conventional explanation is that the heterogametic sex is more vulnerable to selection pressure by the absence of balancing genetic alleles on their sex chromosomes (Brockdorff and Turner, 2015), research suggests that the better explanation is that the dimorphic phenotype offers greater opportunity for sex differential accumulation of epigenetic marks, rendering the species much more sensitive to its environment. Furthermore, there is added evidence at other levels for the advantage of sexual reproduction over clonal lineages. Bananas and other cultivars are produced via clonal lineages through human intervention. In the 1950's, Panama disease caused by a fungus, *Fusarium oxysporium* led to the extinction of a particular banana cultivar, the *Fors Michel*, that had been the dominant cultivar of that era (Pérez-Vicente, 2004). Clonal lineages have proved to be less vigorous and are immunologically less capable of meeting environmental stresses than those that reproduce sexually over many generations (Zhang et al., 2013).

In this new frame, how does phenotypic variation result?

Darwin (1859) offered this perspective at the conclusion of his *On the Origin of Species*: “There is grandeur in this view of life, with its several powers, having been originally breathed into a few forms or into one; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved.” This, he adduced was attributable to “... the war of nature, from famine and death, the most exalted object which we are capable of conceiving,

namely, the production of the higher animals, directly follows". From this highly charged Victorian perspective, a conventional wisdom emerged that phenotypic variation is the result of natural selection and adaptation through descent with modification (Margulis and Sagan, 2002) within a frame in which causality is generally considered direct, just as our senses suggest.

However, it was the physicist David Bohm who pointed out the systematic bias of our human perceptions (Bohm, 1980). He concluded that perceptions formed through our evolved senses are only an 'explicate' realm in a larger state that includes a vast range of 'implicates'. All simultaneously co-exist. The difference is quantum in nature and not trivial, as it affects our understanding of biology and thereby, evolutionary development. Therefore, an analogy can be advanced that a change of frame in biological terms about relative observer status is merited whose difference from the normative frame is similar to the relinquished concepts of Newtonian absolute space-time compared to the acceptance of Relativity Theory. The crux of this differentiation is the dramatic impact it has on any understanding of the emergence of phenotype. In a frame of biological relativity, phenotype radiates from within the purposes of the cell and the reciprocal interactions of cellular networks directed towards local problem solving as opposed to any conventional Darwinist macro-organic model. Within this new biologic frame, phenotypic variation is the result of epigenetic inheritance in coordination with any central genome, as well as with other vital intracellular structures. Importantly, this is all purposed through cellular aims and necessities, and directed to the maintenance of cellular homeostasis rather than resulting as a simple product of reproductive frequencies. Although it remains true that variation is in service to any organism as extracted information from the environment, the central importance of those epigenetic impacts and the object of that service crucially change from the macro-organic level to that of the cell and its local and extended networks. While it

remains certain that by modifying the phenotype, macro-organisms are able to extend themselves into environments and cope with the stresses attendant to them, the deployment of epigenetic marks still remains focused within the matrices of the linked cellular ecologies that constitute holobionts rather than exclusively at the scale of the macro-organic whole as Darwinism has long presumed. Each generation learns about its environment, and sustains itself within it, but it is a product of the success in doing so at the cellular level through the active filtering of acquired epigenetic information that affects evolutionary development, rather than the simplistic notion of reproductive fitness at the level of the macro-organic whole.

Within this frame, in an inversion of normative assumptions, any phenotype is not merely adaptive per se, but has its present form by remaining consonant with the existing environment and its exerted stresses. If there is congruence, no evolutionary change will occur. However, if changes are needed, novel epigenetic marks will be detected during meiosis, and either will be merged with the gene pool or rejected either by germ line cells, at the stage of the zygotic unicell, or through subsequent fetal developmental mechanisms. Critically, this epigenetic process is adjudicated at the cellular network level of macro-organisms that represents its primary locus of acquisition, and then must undergo obligatory processing at the unicellular zygotic level and multiple post-zygotic stages (Trosko, 2011d). Furthermore, and necessarily then, this is a deterministic process that extends forward through cellular awareness according to homeostatic needs through both competitive and collaborative cellular interactions (Miller, 2013; Torday 2013).

Discussion:

In his book “The Structure of Scientific Revolutions” Thomas Kuhn said that the hallmark

of change in science is marked by a change in its descriptive language. In light of any new biological frame, it would be desirable to change the manner by which certain well known concepts have been defined. There are many interlocking aspects of physiology and development that must necessarily mesh to sustain any eukaryotic life form. Therefore, when the primacy of the unicellular form and the inherency of cellular purposes and proscriptions are asserted as the proper epigenetic frame for understanding eukaryotic macro-organic life, then the dynamical features that elaborate cellular life as they overlap evolutionary development must also be reconsidered. Consequently, concepts of homeostasis, pleiotropy, heterochrony, and the primacy of the entirety of the cellular apparatus as opposed to the central genome of any cell all require reconsideration.

In conventional terms, homeostasis is considered as a synchronic (same time) servo-mechanism for maintaining the status of organismal physiology. In that manner, it might be no different from any home thermostat. However, if properly regarded from the perspective of developmental physiology, homeostasis is a robust, dynamic, intergenerational, diachronic (across-time) mechanism for maintaining, sustaining and modifying physiologic structure and function. Cell-cell signaling underscores embryogenesis and provides for physiology and repair based upon homeostatic preferences. The cellular nature of such processes are thereby emphasized in a manner that provides insights into the scale-free universality of the homeostatic principle. In such circumstances, the maintenance of homeostasis becomes a relativistic frame as an ever-shifting dynamic, retaining continual responsiveness to the outward environment even as it sustains the cellular boundaries through which it is enacted. Homeostasis is a cellular phenomenon that yields macro-organic form only as its outward manifestation. However, the homeostatic principle that underscores life is very much anchored as a cellular faculty (Trosko,

1998). Homeostasis has its frame of reference within individual cells in communication with others that then amplify within tissues as cellular ecologies to support and sustain any macro-organic whole (Torday and Rehan, 2012; Miller 2013). Certainly, beyond the cellular level, homeostasis is sustained in any individual macro-organism from the inception of life through meiotic reproduction, reiterated time and again through ontogeny and phylogeny via mitosis, and is continually expressed as organismal physiology and its limits. However, in this new frame, this functional path is the means by which individual cells and those in collaborative networks sustain their responsiveness to the stresses of the outward environment and adapt to it according to a developmental plan that is directed towards the reproduction of linked cellular ecologies according to an inherently cellular arc of life.

Pleiotropy, too, changes when understood within a relativistic biological frame (Torday, 2015). In conventional terms, pleiotropy is considered to be the random expression of individual genes that might generate phenotypic traits. However, when the epicenter of adaptation is reconsidered to be at the cellular level based upon cellular purposes as opposed to the macro-organism, an interesting shift in perspective can be proposed. Pleiotropy becomes problem solving at the cellular level as enacted through networked cellular necessities and the advantages of epigenetic stimulation. Consequently then, evolution transmutes from simply stochastic phenomenon to a deterministic consequence of complex physiology from the unicellular state extending forward from unicellular roots as the process of cellular problem solving towards environmental stresses. Pleiotropic novelties can then emerge through recombination and permutation of pre-existing genetic capacities reiterating through reproduction based on past and present physical and physiologic conditions. This phenomenon is now substantiated by the known process of “splice variants” of gene products caused by environmental signals and micro-RNA epigenetic

regulation of gene expression (Zhou et al., 2014). This is continually in adaptive service to the immediate and future needs of the organism for its enduring survival as impacted by a continuous stream of epiphenomena. The advantage of this mechanism is that functional homologies that link lung to kidney, skin to brain, or thyroid to pituitary become examples of pleiotropy as a problem solving mechanistic evolutionary strategy towards problem solving for cells and the cellular networks that comprise hologenomes.

Similarly then, heterochrony, or the timing of pleiotropic events in an organism due to an unspecified change in the timing or rate of developmental events, can be appraised differently when viewed from within cellular metrics. In traditional evolution theory, it is supposed that novel structures and functions can evolve through random events. Plainly though, within a cellular frame, cell-cell signaling processes for embryogenesis are merged with epigenetic mechanisms of inheritance and then applied to cellular mechanisms for problem solving. In this circumstance, novel adaptations are invoked that pertain to cellular needs rather than macro forms. This is particularly true when underpinned by physiologic stress, causing microvascular shear stress, which is known to cause genetic mutations and duplications (Storr et al., 2013). It should be borne in mind that the Radical Oxygen Species that mediate such effects are themselves signaling mechanisms (Upham and Trosko, 2009; Trosko and Kang, 2012), but if their down-stream effects are not adaptive, mutations and duplications will ultimately prevail within the 'context' of any given biologic structure or function (Storr et al., 2013). In other words, what is typically referred to as internal selection can be better understood as a derivative of cellular imperatives fostering that which otherwise appears as heterochrony.

When the primacy of cellular mechanisms is fully considered, then all aspects of the cell must be

acknowledged to participate. Yet, once the genetic code was revealed, evolutionary biologists fully embraced the genome as the centrality of evolution for reproduction and variation.

However, there is a growing body of evidence that the singular concentration within evolutionary development on genes disregards other vital cellular structures. For example, the cytoskeleton is far more than just the supportive infrastructure of the cell. That role is better understood when its functions under microgravitational conditions are observed. In studies of lung and bone cells, (Torday, 2003) it has been discovered that in 'zero G' conditions, expression of Parathyroid Hormone-related Protein mRNA decreases dramatically, only to be reinstated under eugravitational conditions. This effect is of both physiologic and pathophysiologic interest because PTHrP signaling is necessary for the development and maintenance of lung and bone alike, going all the way back to the water-land transition some 300 million years ago (Torday, 2013). PTHrP is necessary for the formation of alveoli in the lung, and calcification of cartilage. Beyond that, the homeostatic control of lung and bone physiology are equally dependent on PTHrP signaling.

But the role of the cytoskeleton goes much deeper in vertebrate evolution than that, as revealed by the effect of microgravity on yeast (Purevdorj-Gage et al., 2006), the most primitive of eukaryotes. These organisms lose both their ability to regulate calcium flux and to bud, the fundamentals of integrated physiology and reproduction, respectively. In other words, these organisms are highly attuned to gravitational force, referring all the way back to their biologic origins, and the cytoskeleton is necessary for that sensitivity. In the amoeba *Dictyostelium*, the ultimate purpose of the cytoskeleton is further clarified. When deprived of nutrients, the free-swimming form of *Dictyostelium* reverts to the sessile colonial phenotype. The determinant of

this phenotypic change is the Target of Rapamycin (TOR) gene (Sasaki and Firtel, 2006), whose regulation is determined by the cytoskeleton. Hence the cytoskeleton, under the influence of TOR, also functions critically to determine the phenotype of any organism and therefore, phenotypic variation is not simply occurring at the genetic level. The influence of the cytoskeleton extends much further and is highly broad-based since that same TOR signaling complex is involved in vertebrate physiologic regulation of ions, nutrients, physical forces, oxygen, and controls cell growth.

New observational techniques emphasize the surprising role of the cytoskeleton. It has been shown that the trafficking of proteins that make cellulose in the formation of the plant cell wall is governed by microtubules and enzymes. This interaction governs the thickness and strength of secondary plant cell walls, and forms a continuum with the movement of plant life from sea to land. In this process, the microtubule cytoskeleton actively directs the synthesis of the new cell wall through the action of multiple individual enzymes (Watanabe et al., 2015). Further yet, the cytoskeleton is central to the processes of meiosis and mitosis. Therefore, the cytoskeleton is either actively or indirectly involved in nearly all cellular processes that reverberate throughout any macro-organism. This includes the maintenance of homeostasis within the physical environment and the most fundamental aspects of cell function. Moreover, the microtubules of both plants and animals are under hormonal control, forming a functionally-integrated property of the organism. Hameroff and Penrose have invoked the microtubule in the integration of the brain, functionally integrating body and mind (2014). Such details over an expansive range of cellular properties reveals an important reality: the cytoskeleton becomes a consequential player in the determination of phenotypic status, heterochrony, and pleiotropy as all cellular structures fully participate in cellular actions. In such circumstances, it is no longer clear that the genome,

though necessarily extremely important, is actually at the center of cellular life and purposes.

Therefore, 'who' is the observer and 'what' exactly is being observed are deeply context dependent, whether within the confines of any cell or as it is reiterated layer upon layer to enact any macro-organism.

Conclusion

The virtual thought experiments of Einstein's General Relativity Theory completely reshaped our modern understanding of the physical world and opened the unfamiliar domain of a counter-intuitive observer-dependent space-time continuum. His monumental predecessor, Isaac Newton, had believed in absolute space and time. In Newton's view, objects move through absolute space. Time and gravity are real. Einstein deduced otherwise; gravity is due to the physical distortion of the fabric of space-time, and there are no absolutes.

Certainly, many have tried to provide a steady link between the physical and organic realms. Famous among these were Prigogine (1984) and Polanyi (1968) in their attempts to apply the principles of physics to biology. Both admitted to failing to make the connection between the seemingly disparate disciplines of Physics and Biology since they used Newtonian notions of space-time rather than considering any possibility of biological relativity.

However, if cues from this latter path are fully considered, then such a transition can be achieved even when applied within biological constraints (Lowenstein, 2000). That progress is dependent upon an open exploration of the relative relationships of the status of individual constituent cells in which ambiguity is settled in biological organisms through abundant cell-cell communication in their own complex skein of interaction rather than at the level of the macro-organic aggregate as previously assumed. Such a transition requires the same flexibility of thought that permitted

the displacement of the seemingly common sense notions of Newton's mechanics for the disquieting realities of Einstein's relativity.

Contemporary understanding of the full range of cellular faculties finally charts an integration of biology into an analogous yet differing frame as distant from Darwinism as Einstein was from Newton. In both instances, fixed coordinates become relative points according to the frame of the observer. In the biological realm, two differing realities of observer status collide with our prior normative understanding of evolutionary development, where the drama has been presumed to be ensconced at the level of the macro form. An alternate focus is now permitted that rests upon two essential differences from the past: any evaluation of the eukaryotic macro organic form requires its proper deconstruction into its linked cellular constituencies, and significant regulatory oversight of the macro form resides within its obligatory unicellular zygotic stage. In such terms, it becomes necessary to re-consider where the central action of observation in any evolutionary narrative is actually embodied. Is it the macro-organic form presumed under Darwinism? Might it be that the actual observer status lies elsewhere..... perhaps within and among the cellular constituencies that constitute those macro organisms? Or even further yet, might it rest within the unicellular zygotic phase through which all macro organic life must recapitulate? Crucially though, contemporary knowledge has revealed realities that prior conventional theory insufficiently accommodates. It is exactly this differential that impels a reexamination of our perceptions of the exact terms of biological relativity, placing its central context as a continual shift permitting the settlement of biological ambiguities that necessarily arise from an unrelenting stream of epiphenomena impacting the layered cellular constituencies that enact macro-organisms. Importantly though, even as observer status continually transforms, there is a perceptual core of cellular First Principles that obviates space-

time in the biologic sense just as it does in physics (Torday 2013). This transition is underpinned through re-conceptualizing evolution as always dwelling within the unseen world of cells rather than the macro-organic forms upon which evolutionary development has previously concentrated. In this new frame, each macro-organic form is better understood as cellular objects in motion, forming self-similar fractals (Torday 2013). It is their cellular constituents that define them in an evolutionary sense. Necessarily then, understanding how these networks develop from the zygotic unicell, elaborate as holobionts, and then recapitulate once again through another zygotic unicell, requires further investigation within this fresh frame of reference—perhaps Samuel Butler was right when he said that “a hen is only an egg’s way of making another hen” (2009). Consequently, the shape of the whole changes into a thoroughly contemporary perspective in the same manner that Einstein’s reconceptualization of gravity and velocity opened an unfamiliar realm: space-time as a continuum, ... capable of deformation where subjective experience relates to the status of the observer. As such, physics was then according new rules in which measurements are no longer absolute and are critically dependent upon the status of that observer. In the physics of quantum realities, it is the observer that collapses the superimposition of states that suspend the implicate from the explicate (Atmanspacher, 2012; Woolf and Hameroff, 2001). Therefore, an opportunity exists to append biology through its own new frame. That route extends through a deeper understanding of the full capacities of the cell. Within an updated biology that emphasizes cellular mechanisms at its core, the site of observer status dramatically changes. Eukaryotic evolution remains fixed within cellular roots through its perpetual reiteration through the unicellular form, and thereby always remains permanently embedded within that frame through all successive generations. This constancy is united within cellular purposes by cognitive players utilizing cell-cell

communication as information to produce non-stochastic solutions to cellular problems. In consequence, our human notions of biologic space and time based upon our apprehension of our corporeal selves are forced to yield as merely biased observer status. It resembles the gulf in perspective between the Red Queen and Alice in Lewis Carroll's *Through the Looking Glass*. The Queen, in her realm, asserts that she must run just as fast as she can to simply stay in place. Might we not then be a confounded Alice imagining that we run alongside the Queen (and her ova) yet perpetually separated from the actual reality of our innate unicellular embodiment by our differing perception of space-time? Our conscious subjective reality need not be nearly the same as that of our cells. Yet, before such an atypical concept is resisted, it is best to recollect that our constituent cells are the actual means by which we survive and through which our lives are sustained? When our biological imaginings enlarge to accept an unsettling deconstruction of ourselves as cognitive cellular networks that exist within mutually co-existent yet differing spheres, an unusual biologic reality unfurls. In this new realm, objective and subjective become one, as both implicates and explicates dependent upon the frame of reference, remaining intimately entwined within their own strange dimension as a special case of Relativity Theory.

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