Review

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Sympoietic View of Life

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Review

A Sympoietic View of Life: Gaia as a Holobiont Community

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Abstract: A view of life, based on sympoiesis, metabolism, and the second law of thermodynamics is proposed. Sympoiesis is the notion that organisms develop as teams, and that symbionts play roles in forming their partners. Metabolism is seen to occur not only within these developmental symbionts, but between them, as well. This occurs through thermodynamic principles of finding the lowest free energy states. Once one accepts the thermodynamics of metabolism and that holobionts emerge through sympoiesis, Gaia becomes readily understood. New ethical principles flow from these considerations.

Keywords: sympoiesis; Gaia; thermodynamics; metabolism; ethics

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The concept of organism has evolved rapidly in the past century. Indeed, if the twentieth century has been characterized as "the century of the gene" (Keller 2002), the twenty-first century may become characterized as the century of the holobiont relationship. Increasingly, we are becoming cognizant that organisms are not (and have never been) biological individuals. Rather than being the read-out or epiphenomena of genes, our anatomy, physiology, immunity, development, mental health, and evolution appear to be generated in concert with other symbiotic organisms. I will argue that conceiving organisms as holobionts (the organism as including its persistent symbionts) has deep consequences for modeling life and ethics.

This essay will attempt to show that if one understands that (1) organisms are holobionts that are constructed through symbiotic interactions (sympoiesis) and (2) that metabolism acts to form cells, organisms, and ecosystems through the same thermodynamic principles, then (3) Gaia becomes a logical biological outcome. In fact, Gaia can be modeled as a holobiont organism that is the integration of its numerous enmeshed metabolic systems. This leads to new modes of biological thinking, scientific practices, and ethical actions.

This essay will expound the following principles for modeling and discussing living beings:

First, the organism should be considered as *being* a life cycle, not merely *having* a life cycle (Bonner 1965; DiFrisco 2019; Gilbert 2019). These life cycles interact and entangle, such that the life cycle of one organism may be essential for the continuation of the life cycle of another organism.

Second, a holobiont is both an organism and a collection of ecological communities (Gilbert 2019, 2020; Suarez and Stencel 2020). These communities change as an organism develops, such that the development of an organism involves both embryological development and ecological succession.

Third, there is a dialectic between an organism and "its" metabolism. Metabolism i usually defined as the set of chemical processes that sustain life within an organism. These processes include the conversion of food into energy-storing compounds and structural compounds (proteins, fats, etc) , as well as the elimination of waste from the cell. However, while metabolism can be seen as a function of the organism, the organism can also be seen as function of its metabolism. Indeed, metabolic flows exist between organisms and help distinguish between the organism and its environment.

Fourth, interactive matter seeks the thermodynamically least energetic, most stable, local conformation (Prigogine and Stengers 1984; Kauffman 2020). This "seeking" can be seen in the formation of molecular compounds and crystals, in the folding of proteins, in the gene regulatory networks that characterize different cell types, in the formation of organs from such cells, in the metabolic networks that generate holobionts, in the communities of holobionts that organize into ecosystems, and finally in Gaia, wherein the different community metabolisms find a thermodynamic equilibrium within the framework of the planet that they helped create.

The remainder of the essay will discuss how this integrated view of life promotes particular types of ethical and scientific questions and practices.

I. Our holobiont heritage and the entanglement of sympoiesis

"Organisms are holobionts, and life is sympoietic," is a statement that could not have been made from twentieth century biology. "Holobiont" refers to the scientific conclusion that organisms are integrated consortia of a host organism plus numerous species of other symbiotic organisms[1]. In the adult human body, approximately half the cells are symbiotic microbes. Moreover, these bacteria, fungi, protists, and archaea are not merely fellow travelers who share our food with us. They are critical for our healthy physiology, development, and immunity (Gilbert et al, 2012; McFall-Ngai et al, 2013). Cows may be herbivores, but they have no genes in their nuclei that encode for grass-digesting enzymes. These cellulose-digesting enzymes come from the set of microbes living within the rumen of their guts (Moraïs and Mizrahi 2019). Similarly, the ability of a termite to digest wood is conferred by its gut symbionts. The termite's genome, alone, contains no genes for the digestion of cellulose or lignin (Margulis and Sagan 2001). In coral, most of the animal's carbon resources come from the photosynthesis of its algal symbionts (Muscatine et al 1984). Fungi extend the roots of plants and may have made it possible for plants to adapt to land (Pirozynski and Malloch 1975), and microbes are critical for normal mammalian bone growth, endocrine function, heart function, and respiration (McFall-Ngai et al 2013). We exist as multi-species consortia.

Even "unicellular organisms" are not really unicellular. Rather, protists such as amoebae and diatoms are holobionts associated with other microbial symbionts (Vincent et al 2018; Kanso et al 2021; Colp and Archibald 2021). The protist *Mixotricha paradoxa* is responsible for synthesizing the enzymes that permit certain termites to digest wood. Only, this *Mixotricha* is not a single protist, but a protist whose cell is associated with thousands of bacteria, comprising at least four different species (Margulis and Sagan 2001). With few (if any) exceptions, animals and plants are holobionts, integrated partnerships of several species that function together to make a healthy organism[2] (Zilber-Rosenberg et al 2008; Theis et al 2016; Roughgarden et al 2017). An organism is not a monoculture of genetically identical cells.

But more fundamentally, such symbioses are not just between mutually consenting adults. Symbiosis takes place during development to *generate* the adult. This functioning together in ongoing development is more accurately called, "sympoiesis," a “making-with” partnership, rather than autopoesis, “self-formation.” Sympoiesis refers to the observation that multicellular eukaryotic organisms use symbiotic microbes to co-construct organs (Dempster 1998; Haraway 2016; Clarke and Gilbert 2022). Mammals first receive their microbiomes as they pass through the birth canal, and our human bodies become seeded by

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[1] As we will see, Haraway (2016) has pointed out that the host is also in a symbiotic relationship and is therefore another symbiont. It's just larger.

[2] Some animals have been reported to lack symbiotic partners. While rare, these would not be unexpected. In many instances, horizontal gene transfer has given animals the genes that had made their symbionts essential.
Two groups of beetles, for instance, have acquired fungal genes whose protein products digest plant cell walls (Kirsch et al 2014). In at least one instance of an animal devoid of internal symbionts, external bacteria are critical in propelling the organism from the larval to adult stages of its life cycle (Vijayan et al 2019; Freckelton et al 2022).

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specific microbes as we leave our mothers (Koren et al 2012; Funkhauser and Bordenstein 2013). Immediately after birth, mother's milk contains nutrients that feed the infant, while a second compartment of mother's milk feeds the species of bacteria (primarily *Bifidobacteria*) that help mature the gut and its neurons (Zivkovic et al 2011; de Muinck & Trosvik 2018).

Animal (and plant) development is predicated on such symbioses. The nerves that promote peristalsis and hearing, the lymphocytes that constitute the immune system, the intestinal capillaries that take nutrients to the body, and even portions of the mammalian brain are matured by microbial symbionts (Steppenbach et al 2002; see Gilbert and Epel 2015). Indeed, the cow rumen is constructed in response to signals from the bacteria whose progeny will dwell within it (Sander et al 1959; Baldwin and Conner 2017). *Wolbachia* bacteria are responsible for the proper orientation of the second mitotic division of the nematode *Brugia malayi* (Landman et al 2014), and they are needed for the formation of ovaries in the *Asobara* wasp (Dedeine et al 2001). Almost all animals are co-created through interactions between their zygotically derived cells and their environmentally derived microbes[3].

Symbiotic microbes are important partners in the development of mammalian immune and nervous systems, the major cognitive interfaces that allow us to interact with our environments (Tauber 2013). For instance, germ-free mice (rendered symbiont-deficient for experimental research) have serious neurological and immunological syndromes. The immune systems of germ-free mice have fewer lymphocytes, less active intestinal macrophages, reduced vascularity, lower cytokine production, and lower titers of serum immunoglobulin (Dobber et al, 1992; Ratsika et al, 2022). Indeed, symbiotic gut microbes are needed for generating the B-cells and T-cells of the gut-associated lymphoid tissue (Rhee et al, 2004). These microbes appear to promote this immune competence by changing the T cell populations (Kieper et al, 2005; Mazmanian et al, 2005) and by inducing blood cell development (Erny et al 2021; Khosravi et al, 2017; Theis et al 2016). Therefore, immunity is not merely a function of the host. Rather, the immune system is a holobiont property made through sympoiesis (Pradeu 2019; Gilbert and Tauber 2016; Schneider 2021).

Symbiotic bacteria also stimulate the fetal and postnatal development of the mammalian brain (Cryan et al, 2019; Morais et al, 2021; Nagpal & Cryan 2021). Compared to conventionally bred mice, germ-free mice have lower levels of the mRNAs for transcription factor Egr1 and the paracrine factor BDNF in relevant portions of their brains, while having elevated levels of the neural hormone serotonin (Diaz Heijtz et al, 2011; Clarke et al, 2013). These changes correlate with behavioral differences between the germ-free and conventionally raised mice, leading Diaz Heijtz and colleagues (2011, p 3047) to conclude that "during evolution, the colonization of gut microbiota has become integrated into the programming of brain development, affecting motor control and anxiety-like behavior."

Although mammalian embryos are thought to develop within a sterile amnion (Kennedy et al 2023), about 30% of the small molecules carried in the maternal bloodstream of a pregnant mouse arise directly or indirectly from symbiotic microbes (Nicholson et al, 2012). In this way, the microbes in the maternal gut can create compounds that circulate throughout the body, cross the placenta, and affect the developing fetus. When the gut microbes of a pregnant mouse digest plant fiber, they produce short-chain fatty acids (such as butyrate and propionate) that enter the maternal bloodstream, pass into the fetal circulation, and reach the organs of her developing embryos. Here, these bacterial products activate particular genes in the embryonic pancreas, nervous system, and intestines. These changes in gene expression generate proteins that mature the sympathetic neurons and confer life-long obesity-resisting metabolic phenotypes to the

[3] *Sympoiesis* is a concept in developmental biology referring to developmental inputs from several sources. We are not merely the products of the zygotic cells; we are created "together" with the help of other species. This has been confused with the notion of *symbiogenesis*, which is a concept in evolutionary biology meaning that evolutionary events such as speciation and the formation of the first cells arose through the acquisition of new genomes (rather than by the mutation of existing ones).

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offspring (Kimura et al, 2020). Other soluble products of the maternal gut microbiome (especially hippurate and trimethyl-5-aminovalerate) stimulate the maturation of auditory neurons in the fetal mouse brain (Vuong et al, 2020). If these latter metabolites are not produced by the microbiome of the pregnant mouse, the resulting adult progeny have hearing deficiencies.

Gut microbes are also critical for the development of new neurons in adult mice. Neural stem cells generate new neurons in the adult mouse hippocampus. In the adult mouse, indole, synthesized from dietary tryptophan by the mother's gut microbiome, is carried through the blood to the hippocampus. Here, it activates the aryl hydrocarbon receptor of the neural stem cells, converting the receptor into a functional transcription factor that activates the genes responsible for neuron production. Since these are the neurons thought to be critical for memory and learning, the bacteria are truly a part of "who" one is. As Wei and colleagues (2021, p. 2) claim, "Gut microbes are an evolving, prokaryotic component of the meta-organismal self."

If the microbes of mammalian guts are critical for "basic neurogenerative processes such as the formation of the blood-brain barrier, myelination, neurogenesis, and microglia maturation" (Sharon et al, 2016, p. 915), then could such microbes also be critical for normal mental functioning? There is now evidence that by helping generate the brain, the microbiome may also be stimulating mammalian social behaviors (Stilling et al, 2018; Sherwin et al, 2019). Germ-free mice have abnormal behaviors, including excessive time spent in repetitive self-grooming, social avoidance, and very little time spent in social investigation. Desbonnet and colleagues (2014) remarked that these traits appeared to be similar to those of autistic children. Moreover, many of these behavioral traits can be normalized by providing the germ-free mice with gut bacteria early in post-natal life. Wu and colleagues (2021) have discovered that these "socializing" bacteria (especially *Enterococcus faecalis)* can act, in part, by suppressing the release of corticosterone from the paraventricular region of the brain. This might make socializing with other mice a less stressful experience. The asocial behavior of germ-free mice may also be due to the paucity of oxytocin-releasing signals from the vagus nerve, which can be reversed by providing the germ-free mice with *Lactobacillus reuteri* or with microbes from normal mice or even from neurotypical humans (but not with microbes from some autistic patients; Sgritta et al, 2019; Sharon et al, 2019).) *Lactobacillus* has been reported to help regulate emotional behavior in mice through a vagus nerve-dependent regulation of GABA receptors (Bravo et al, 2011)[4].

Therefore, the microbiome appears to be critical for normal animal development. In mammals, the gut, pancreas, immune system, and brain form from the interactions of microbial cells with zygote-derived cells. Animals develop sympoietically, in partnership at every level. Indeed, if bacteria help make us into healthy and social animals, perhaps we animals are the bacteria's way of making more environments for their descendants (Gilbert, 2018, 2021). In helping make our bodies and our social behaviors, both animals and microbes benefit.

Since these sympoieses contribute to physical development and to the development of social behaviors, they are critical to the completion of life-cycles. The crucial role of sympoiesis to the life cycle can be seen starkly in many invertebrates, where the metamorphosis from larva to adult is itself mediated by microbes. In the life cycle of the sponge *Amphimedon*, for instance, bacteria are needed to supply the arginine that is utilized to make the nitric oxide cue for settlement of the larvae and their metamorphosis into the adult sponge (Song et al 2021). Similarly, lipopolysaccharide from the biofilm-forming bacterium *Cellulophaga lytica* is needed for the settlement and subsequent metamorphic events of *Hydroides elegans*, the common tube worm (Freckelton et al 2022).

[4] Although human autism spectrum anomalies probably have many causes, pilot studies have shown that replacing the gut bacteria of severely autistic children with those of neurotypical children can dramatically enhance the sociability of many patients (Kang et al 2019, Puricelli et al, 2022).

The ability of symbionts to mediate life-cycles can be seen as a subset of a larger entanglement of life cycles that has long been recognized. The life cycles of birds, insects, and plants, for instance are often mutually dependent and synchronized. For instance, the flower develops and opens at the same time that the adult insect has emerged from its pupal cuticle and is able to pollinate it. Moreover, the birds have evolved so that their young are born at the same time as the insect caterpillars are plentiful, so the young birds could eat as many as a hundred caterpillars each day. This is the way evolution works--by the allowing the development of each organism to synchronize with the life cycles of other organisms[5].

Sympoiesis must be foregrounded as a crucial parameter for the conception of life. First, sympoiesis means the end of our thinking of ourselves and other organisms as monogenomic, self-contained, self-making individuals (Haraway, 2016; Gilbert et al 2015; Demster 1998). As Donna Haraway noted, we literally "become one with others." We receive 22,000 genes from the zygote; we receive over 8 million different genes from our symbionts (Funkhauser and Bordenstein 2013). Life cannot, therefore, be considered as mere readouts of the zygotic genome, and if precision genetic medicine is to be more than a promise, it would have to include (at least) the genes of the holobiont's microbes, which encode proteins that can inhibit or augment drug treatment (Weersma et al 2020; Sariola and Gilbert 2020).

If organisms are to be perceived as individuals, we are individual teams. And just like teams, organisms are formed through a mixture of cooperative and competitive processes. One competes to become part of a cooperating team, and "making the team" can be intensely competitive, whether it be for the Chicago Bears or for an ursine holobiont. The *Euprymna* squid needs *Vibrio fisheri* bacteria to help form its light organ. To get these bacteria, the newborn squid absorbs environmental microbes onto its ventral surface, selectively winnows away gram-positive bacteria, and then kills all the gram-negative bacteria that are not *Vibrio fisheri* (Koehler et al 2018). As novelist Richard Powers (2018, p. 142) has concluded, "Competition cannot be separated from numerous flavors of cooperation."

Second, for almost all animals (and probably plants and fungi, as well) there is no autonomy, and autopoiesis (*sensu* Maturana and Varela,1980) is confined to cellular self-maintenance. Rather, animals are created by sympoiesis, which is an entangled integration of embryology and ecology. The co-symbionts mutually scaffold and provide affordances for each other's existence (Clark and Gilbert 2022; Chiu and Gilbert 2020). The symbionts in the rumen allow the existence and propagation of cows; the cows allow the existence and propagation of their ruminal bacteria. There is no "host" in the symbiotic relationship (Haraway 2016). Animals constitute the environment of bacteria, as bacteria constitute the environment of the animals (Formosinho et al 2022.) [6]

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[5] The warming of the climate has disrupted this synchrony, and these changes can be disastrous. Differences between peak hatching time and peak caterpillar abundance in several European birds have diverged by nearly 2 weeks for some species. For sanderlings, the hatching time (which is regulated by photoperiod), and their major food source (which is regulated by temperature) have diverged 1.3 days per year for the 17 years since 1995 (Reneerkens et al., 2016).

[6] Although Lynn Margulis was a major supporter of the notion of autopoiesis, she did not know of sympoiesis (a term coined by Dempster in 1998), and her views regarding the "operational closure" of autopoietic systems would presently create a problem for her theories of linked, symbiotic associations in a holobiont (Clarke and Gilbert 2022). Rather, for Sagan and Margulis (1991), symbiosis was a conglomeration of *adult* organisms. "What is remarkable," they postulate "is the tendency of autopoietic entities to interact with other recognizable autopoietic entities. … Such mergers (fertilization, partner-integration in symbiosis) lead to autopoietic entities of still greater complexity." This view harkens back to that of Maturana and Varela (1980; xxvi-xxvii) who postulated that social units were consortia of pre-existing autopoietic entities. This view of symbiosis as unions of adult organisms is also seen in Margulis' championing of Donald Williamson's hypothesis that metamorphosis from juvenile to adult was the union of two adult life cycle stages. Margulis had not envisioned the entangled sympoietic networks that would co-construct the symbiotic entities during their development. The developmental biology of Maturana and Varela is predicated on a genetic determinism

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Third, evolutionary speciation often occurs, as Lynn Margulis and Dorian Sagan (2002) announced, through "acquiring genomes." Indeed, what gets selected in evolution may be the "team" of organisms, not the individual players (Roughgarden et al 2017; Osmanovic et al 2018; Roughgarden 2020). On the microevolutionary level, new combinations of symbionts have given rise to new phenotypes. Whether a pea aphid is green or red, thermotolerant or thermolabile, immune or susceptible to parasitoid wasp infection, depends on the bacteria associated sympoietically with the developing aphid body (Dunbar et al 2007; Oliver et al 2009; Tsushida et al 2010). The acquisition of new symbionts has enabled the red turpentine beetle to become a major killer of Chinese pine trees (Sun et al 2013; Taerum et al 2013) and has allowed the *Riptortus* bean bug to acquire the resistance to insecticides (Kikuchi et al 2012; Kim et al 2016; Lee 2019).

In addition, major evolutionary innovations made through new sympoietic pathways may include multicellularity (Dayel et al 2011), meiosis (Woznica et al 2017), herbivory (Gilbert 2020), and the mammalian uterus (Emera and Wagner 2012). Each appears to have arisen through new combinations of animals and symbiotic microbes (Gilbert 2019). Even the animal nervous system may have evolved partly out of a need to orchestrate the complex interactions between animals and their associated micro-organisms (Augustin et al. 2017; Klimovich and Bosch 2018). Thus, symbionts add a new modular dimension to evolution, and these symbiotic modules can be tightly tied to an animal's physiology and development (such the pea aphid's needing microbial symbionts in order to have complete nutrition; Monnin et al 2020; Bennett and Moran 2015) or loosely tied to an animal's development (as in the above-mentioned cases for color, thermotolerance, and parasitoid resistance in pea aphids). As Žukauskaitė (2020) points out, "sympoietic systems carry different bits of information in their components …This makes sympoietic systems more flexible and adaptive, in the sense that they can easily adapt to changing environments, and also create something new, produce new forms of organization (in this regard they are allopoetic)."

Fourth, there is neither closure nor a self-defined boundary to the symbiotic team. Sagan and Margulis had opined (1991), "In order to qualify as an autopoietic entity … material-metabolizing entities must be bounded by membranes made by their own metabolism." This follows from Matura and Varela (1980, p. 20) who claim, "The organism ends at the boundary that its self-referring organization defines in the maintenance of its identity." Varela would define this as the cell membrane, that construction of cellular metabolism that permits the bounded metabolic network that create it (Varela 1997, p. 75). However, the membranes, which decide what is permitted to enter the cell, are not autopoietically constructed. During symbioses, "host lipids serve as building blocks for bacterial membrane formation and as an energy source" (Vromman and Subtil 2014). Moreover, membranes can be regulated by symbionts or by other environmental agents. Temperature, for instance, determines sex in turtles by regulating cell membrane calcium ion channels (Weber et al 2020), microbial symbionts are critical in regulating the membrane permeability of epithelia (*e.g.*, François-Étienne et al 2023), and maternal licking alters the ability of rat pups' hippocampal neurons to respond to glucocorticoid hormones (Weaver et al 2004; Hellstrom et al 2012). Neither a cell nor the nervous system in self-contained. Closure and autopoiesis can no longer characterize eukaryotic organisms. Autopoiesis does not form new organisms, it sustains and repairs them. Rather, different species act together sympoietically to continually construct each other. While the holobiont body has a "tendency to closure" (Montévil and Mossio 2015), closure can never complete, even operationally.

So what is the boundary of the holobiont? Gilbert and Tauber (2016) have proposed that the boundary is the immune system, a system created through the interactions of host and symbionts. This system defines "self" in a dynamic manner, changing constantly as new microbes and new meals are encountered.

that can no longer be accepted. "The goal state (in the language of the observer) that controls the development of an organism is, except for mutations, determined by the genome of the parent organism." (Maturana and Varela 1980, p. 27). Such a perspective preclude sympoiesis, and we have just shown that this isn't the case.

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> "Whatever these interactions are between microbe and host, the holobiont is being continuously constructed. Harmony is not something given, but rather something that requires interactive agency throughout the lifespan of the organism."

The holobiont body can appear and function as an individual, even as it changes and develops its parts[7]. However, there is no autonomy except as a team. Organisms are holobionts, continually developing through sympoiesis.

II. Thermodynamic drives

It seems that whenever one contemplates parts integrating into a whole, the key constraint (both constructive and restrictive) turns out to be the second law of thermodynamics. The second law of thermodynamics (the asymmetry of energetic processes in the universe such that interactions proceed in the direction that produces the highest entropy) characterizes both the living and non-living world (see Mossio and Bich 2017). It describes movement toward randomness and uniformity. However, life can build and maintain order by making use of the sun's energy, temporarily delaying the decay into death. Life will use this combination of entropic movement and solar energy to fold proteins, generate cells, build organisms, assemble holobionts, construct communities, and create Gaia. Within the general cosmological framework of entropic decay, attractor wells of stable interactions can persist in which order could develop.

The second law of thermodynamics is not a principle that "reduces" biology to physics. Rather, the second law is a constraint, like that of gravity, which can promote creativity. Think, for instance, of all the means of locomotion that have evolved to counteract and simultaneously use gravity. For most living beings (the exceptions being those organisms clustered around deep sea thermal vents), solar energy absorbed by plants, algal protists, and cyanobacteria is used to convert water and carbon dioxide into glucose. Energy is lost in this process; but enough is stored locally such that the glucose molecules can be transformed by the organism's mitochondria (or by the microbial organism, itself) into energy-storing ATP molecules. These small phosphorylated compounds will provide the energy that can build and maintain the organism. When these ATP molecules are split to release energy, more energy is made than is used. The rule of thermodynamics--that local order is created and maintained by the loss of order elsewhere--is never broken. As Schneider (2004) has concluded, "Life never violates the second law, and thermodynamic gradient reduction provides living systems with a 'final cause,' their 'go,' their 'direction.'"

Indeed, most of chemistry is based on the interactions of charged substances seeking their lowest possible energy states. Electron orbitals "seek" to be filled. (How many nerdy wedding toasts have likened the marriage partners to sodium and chloride ions?) While this thermodynamic principle is the basis of classical physical chemistry, its ramifications on the macroscopic world are enormous. The nascent planet, itself, found a thermodynamically favorable state wherein its water, metal core, and atmosphere could exist simultaneously (rather than meld into a homogeneous mush). Indeed, the hydrogen-rich envelope that surrounded the rocky proto-planet may have been critical in providing a temporary thermodynamic affordance whereby the "earth's water, core density, and overall oxidation state can all be sourced to

[7] Perhaps, as suggested by Béatrice de Montera (personal communication), a sympoietic reading of Gilbert Simondon (2009) is appropriate. Here, the organism is continually becoming a new individual. As it seeks relationships with its environment, it constructs a "theater of individuation...a perpetuated individuation, which is life itself, according to the fundamental mode of becoming: *the living conserves within itself a permanent activity of individuation.*" Reading this sympoietically, Simondson's "pre-individual" (or more appropriately "pre-individual field") can be the organism that can constantly change its symbionts, and which can become many things, depending on its microorganisms. It is in a "metastable state."

equilibrium between hydrogen rich primary atmospheres and underlying magma oceans in its primary planetary embryos" (Young et al 2023)[8].

A. Protein folding

Every structural and physiological event in a cell depends upon protein folding. Enzymes need a particular shape to bind to their substrates; antibodies must fold to accommodate their antigens, hormones must have a form recognizable by their specific receptors, and sperm and egg must mutually recognize one another by the complementary shapes of their protein ligands and receptors (Gilbert and Greenberg 1984). Signaling pathways, DNA replication, and protein synthesis are each based on the interlocking shapes formed by protein folding. Protein folding attempts to place the charged amino acids into the lowest-energy stable structures, with the hydrophobic residues placed inward. Each polypeptide chain consists of a string of amino acids, and interactions between these amino acids determine the pathways by which the proteins fold. There is much trial and error, as the protein folds and unfolds in nanoseconds to "find" the lowest free energy state. Each polypeptide chain has configurations that take it to the lowest free energy, and there are paths that funnel each protein into such a low-energy structure (Levinthal 1969; Jacobs and Shakhnovich 2018). Indeed, the landscape of protein folding is that of energy basins (Dill et al 1997) whose topology "is represented by an energy ordinate and funnel-like curve whose width roughly represents the number of configurations for each energy state. Within the present model, this figure resembles an inverted binomial distribution" (Martinez 2014). These interactions allow peptide domains to coalesce, such that folding results into one or a few stable structures.

Moreover, "The dynamic network occurring during folding determines not only the protein's structure but its function, and the directions in which its structure will vary by mutation" (Salazar-Ciudad and Cano-Fernandez 2023). In some cases, a mutation causes a change in the folding such that the protein loses its function. In other cases (such as sickle cell hemoglobin and neo-beta-galactosidase; Hall 1976) new phenotypes emerge from the new pattern of folding. Proteins fold to fall into their minimal energetic state, and this determines their function.

B. Epigenetic landscapes

Similarly, in the formation of particular cell types, the interactive networks of proteins and nucleic acids allows for a single genome to produce multiple types of cells. Each cell type can be considered a stabilized local low-energy configuration. This concept was first proposed by C. H. Waddington in his model of the epigenetic landscape (1940) Like the model of protein folding, it consists of a series of low-energy funnels separated by high-energy barriers of instability. For Waddington (Waddington 1940; Gilbert 1991a, 1991b), the specification of a cell takes place through a series of steps, each of which can be considered a bifurcation wherein numerous genes and their products interact to generate a sequence of changes which can be called "the epigenetic path."

In a normal or "wild type" embryo, these pathways to a specific cell type are usually quite distinct (and often mutually inhibitory), such that once a cell goes down a particular path, that decision is irrevocable. Moreover, once cells have entered into a specific path of development, their final condition can be affected by sets of genes that act to further specify the cell into a more stable state. Finally each pathway is 'canalised', or buffered, so that even if the path is mildly disturbed, the cell will regulate its development to re-enter that pathway. The synergistic action of many genes "whose operations interact in such a way to define a pathway of change in a multi-dimensional phase space" provide a stability to the path to which the developing system tends to return after disturbance (Waddington 1973: 502). Waddington put these

[8] For reasons of brevity, this paper has to limit the discussion of thermodynamic equilibria to ongoing biological phenomena. The origin of life is another important story for which the second law of thermodynamics may provide a crucial context (Goldenfeld and Woese 2011; Kauffman 1993; England 2020).

epigenetic paths onto a landscape where gravity represented the thermodynamic force pushing these pluripotent cells into particular channels of development (see Gilbert 2011).

This dynamic has been confirmed in numerous organs. The insulin-secreting beta-cells of the pancreas, for instance, proceed down a path where they are sequentially specified as inner cell mass cells (as opposed to trophoblast cells), embryonic disc cells (as opposed to amnion cells), endomesodermal cells (as apart from ectodermal precursors), endoderm cells (as opposed to mesoderm cells), foregut endoderm (as opposed to intestinal progenitors), pancreatic foregut endoderm (as opposed to liver precursors), endocrine pancreas progenitor cells (as opposed to exocrine pancreatic cells), beta/delta progenitor cells (as opposed to alpha progenitor cells), and finally to beta-pancreatic cells (rather than delta cells). This trajectory can be replicated with pluripotential stem cells in culture (Zhou et al 2011; Pagliuca et al 2014; Rezania et al 2014).

Sui Huang and co-workers (2009) have re-interpreted Waddington's epigenetic landscape such that these final cell types represent "attractor states" wherein the feedback loops between the genes and proteins become stabilized through their mutual interactions, forming a low-energy thermodynamic configuration. Moreover, Huang (2012) explicitly relates this propensity to the potential energy wells that allow protein folding.

> Since network states have distinct stabilities, one needs to know the relative stability of each state S, which is a consequence of the particular 'wiring' of the regulatory interactions; this will allow one to predict a phenotype change… Thus, the specific network interactions impart on each state S the urge to move on a specified trajectory towards a more stable state until all regulatory influences are satisfied. In such a balanced, 'force-free' state S, the gene expression pattern is stationary and also 'locally stable'. Such stability implies that it is surrounded by less stable states – thus, it will re-establish its characteristic gene expression pattern when slightly perturbed and displaced to a close neighbourhood. A stable state S is called 'attractor state' as it attracts the nearby, less-stable states that are in its 'basin of attraction'. Trajectories within a basin of attraction converge to the attractor state of that respective basin – the state where the quasipotential U exhibits a local minimum – akin to being at the bottom of a 'potential energy well' in classical physics."

Thus, like the amino acids folding in a protein, the cells have an "urge to move" towards a stable state. Further modeling (Torres-Sosa et al 2012) has shown that such attractor states can be stabilized or converted to another attractor state through mutation and selection.

C. Organ formation

One of the first applications of thermodynamic principles to embryonic development concerned organ formation. The notion that embryonic cells may align themselves based on their thermodynamic properties can be traced back to D'Arcy Thompson, who noted that embryonic cell clusters often resembled soap bubbles, whose configurations are governed by minimizing the surface free energy (Thompson 1917; Heisenberg 2017). In 1964, Malcolm Steinberg used thermodynamic principles to construct his differential adhesion hypothesis for organ formation. Using dissociated cells derived from embryonic tissues, Steinberg showed that certain cell types migrate to the center of an aggregate when combined with some cell types, but migrate peripherally when combined with others. These interactions followed a behavioral hierarchy (Steinberg 1970). Pigmented retina cells, for example migrate internally to neural retina cells, and heart cells migrate internally to pigmented retina cells. Moreover, heart cells migrated internally to neural retina cells. These observations led Steinberg to propose that cells interact to form an aggregate with the smallest interfacial free energy (*i.e.,* like the soap bubbles).

Cells could rearrange themselves into the most thermodynamically stable pattern if the cell types differed in their strengths of their adhesions. Therefore, the early cleavage embryo can be considered as being in an equilibrium state until there is a change in the adhesive properties of the cell membranes (such as those generated by the production of new cell membrane proteins). Then, movement would be needed to restore the cells to a new equilibrium configuration. These movements would be continued as intercellular interactions caused new cell membrane proteins to be synthesized.

As distinct cell layers form in the embryo, they separate from one another due to such differential affinities (Townes and Holtfreter 1955). Davis and colleagues (1997) found that the tissue surface tensions of the individual germ layers were precisely those required for this type of sorting, and numerous experiments confirmed that cell types that had greater surface cohesion migrated centrally when combined with cell types that had less surface tension (Foty et al. 1996; Krens and Heisenberg 2011). Evidence now shows that boundaries between tissues can indeed be created by different cell types having both different types and different amounts of cell adhesion molecules, primarily, cadherin proteins (Steinberg and Takeichi 1994; Foty and Steinberg 2005), and that such cell sorting is directly correlated with cadherin-mediated surface tension (Foty and Steinberg 2013). The importance of thermodynamic free energy at the site of boundary formation has been shown in the development of numerous species throughout the animal kingdom (*e.g.,* Fiero-Gonzalez et al 2013; Iijima et al 2020; Polanco et al 2021)

D. Ecological succession

In ecological succession, a set of transitory communities proceeds through intermediate stages to become a set of organisms whose interactions form a stable equilibrium under specific conditions (Lindeman, 1942). Bare rock, for instance, is colonized by lichens and other "pioneer species", leading to conditions that favor (given certain conditions) grasses and perennials. These create soil conditions favorable for intermediate species such as shade-intolerant trees and shrubs. These, in turn, will cause the soils to be able to support an interactive community[9] of shade-tolerant trees (such as oaks).

The ecological succession leading to different types of stabilized communities is modelled similarly to that of cell specification through an epigenetic landscape. Whereas embryonic development usually takes weeks or months, ecological succession takes centuries; but the models are remarkably similar. According to Würtz and Annila (2010), "Ecological succession is described by the 2nd law of thermodynamics. According to the universal law of the maximal energy dispersal, an ecosystem evolves toward a stationary state in its surroundings by consuming free energy via diverse mechanisms."

As in the embryo, ecological succession concerns the multistability of a dynamic system, critically poised between maintaining its identity and changing its dynamics to become something different. Attractor basins and the resilience of attractors to resist perturbation are similarly modeled (Hollings 1973; Pimm 1984.) Mitra and colleagues (2015), for instance, have modelled the conditions of community ecology wherein a community might go from one basin of attraction into another one. Like the epigenetic landscape model, these mathematical models involve bistable discrete dynamic systems that are separated by an energy barrier.

These models take on importance when describing ecological disturbances that would lower that energy barrier between such discrete states, such that one ecosystem would become a different one. These constitute the so-called "tipping points" discussed by conservation biologists. As in the epigenetic or protein-folding landscapes, the tipping points can be overcome either by lowering the height of the barrier or raising the height of the basin. Coral-dominated reef ecosystems can be converted into algae-dominated reef ecosystems, for instance, (a) if predators that eat algae are eliminated, (b) if chemicals that promote the

[9] Such end-states of ecological succession have traditionally been called "climax communities." Indeed, Blaser and Kirschner (2007) refer to the human holobiont as resembling a climax community. However, this term has been questioned due to the observations that disturbances are more common than previously expected and the concept that local abiotic factors are critically important. For instance, different communities become prevalent at different elevations of a mountain, and even the water drainage due to the slope of the land can alter the community that stabilizes there.

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growth of algae are introduced; or (c) if conditions that destroy coral are introduced. In such models, the stable ecosystems are often represented as basins separated by cliffs, just as in the epigenetic landscape models (Ocean Tipping Points 2023; Chemello et al 2018).

E. Holobionts

While embryonic development and organismal succession are usually studied in the separate fields of developmental biology and ecology, respectively, they are united in the holobiont. If we take seriously the idea that organisms are both individuals and collections of ecological communities (Gilbert 2019; Sariola and Gilbert 2020; Suarez and Stencel 2020), then we have to realize that animals are simultaneously the products of embryological development and ecological succession. Indeed, Skillings (2016) maintains that “most holobionts share more affinities with communities than they do with organisms...”

Ley and colleagues (2007, p. 3) note, "When a new human being emerges from its mother, a new island pops up in microbial space." And if we are islands popping up in microbial space, then the colonization and succession patterns of island biogeography prevail. We should therefore look at mammalian development in terms of dispersal, local diversification, environmental selection, and ecological drift (Costello et al, 2012). Indeed, the mammalian microbiome develops ecologically upon and within an infant that has so far developed embryologically, forming the infant into an organism with the abilities (such as herbivory and peristalsis) that allow it to become part of a larger ecosystem. Our various microbiomes have ecological succession (Gonzales et al 2011; Bordenstein and Theis 2015; Ratsika et al 2022), resulting from a combobulation of several factors (Milani et al 2017), including the bacteria available for colonization (Wampach et al, 2018; Shao et al, 2019), the diet that preferentially enables the proliferation of certain microbes (Carmody et al, 2015; Rothschild et al, 2018), and the genotype of the organisms that provide the environment for the microbes[10] (Goodrich et al, 2014; Kurilshikov et al, 2021;Brooks et al 2016).

Breast-fed and formula-fed macaque monkeys, for instance, generate different communities of gut microbiota, and the microbiota of such breast-fed monkeys are more capable of producing the lymphocytes responsible for eliminating opportunistic pathogens (Ardeshir et al 2014). Here, diet produces two alternative equilibrium states with different capacities. In other cases, different populations of microbes act to perform similar functions (Doolittle and Inkpen 2018). Different herds of cattle have different symbiotic populations of microbes in their rumen. Although each of these microbial communities allow sympoiesis and nutritional symbiosis, they can have different phenotypes. Some of these communities, for instance, produce higher level of methane gas than do others (Moraïs and Mizrahi 2019b). Some microbes are generalists and will colonize numerous species, whereas other microbes are specialists that recognize species-specific genetic markers on particular hosts (Theis et al 2016; Lim and Bordenstein 2020).

Thus, we see a minimal "goal-directness" in the life, where protein folding, cell specification, organ formation, ecological succession, and holobiont development are each fabricated by entities seeking their respective stable thermodynamic minima. This goal-directedness is pervasive throughout living matter, even though (and because) life is far from an equilibrium condition (Schrödinger 1944; Prigogine 1967). This allows for the possibility of lower equilibrium states that are nowhere close to the final resting equilibrium of death, whether it be the death of a cell, an organism, or an ecosystem[11].

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[10] This could be the cell surfaces of the "host" or the community of other microbes that support the membership of a bacterium within a biofilm. Blaser and Kirshner (2013) propose that cross-signaling relationships between humans and their microbes constitute evolutionary stable strategies for holobiont development.

[11] Perhaps fluorescence provides a metaphor of such activation. In many materials, ultraviolet light will be absorbed by an electron, activating it to a higher energy level. It cannot maintain that high energy, and so it releases light energy (fluorescence) as it returns to its baseline state. Chlorophyl is activated by the wavelengths of light that send it into a higher energy state. It transfers this energy to various compounds that allow the construction of the cells, tissues, and organs of organisms. , Moreover, fluorescence can be made to persist by a constant bath of UV light, just as chlorophyl

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III. Metabolism

In such a view, thermodynamics allows attractor basins of local stability at energy levels far from final equilibrium. Here, we entertain a perspective wherein "life does not tend toward self-preservation, as we have almost always thought, but toward the manifestation of the world." (Barbaras, 2008). Life manifests itself in the world as metabolism. As Hans Jonas realized, "The exchange of matter with the environment is not a peripheral activity engaged by a persistent core: it is the total mode of continuity (self-continuation) of the subject of life itself."

Life, for Jonas, is the set of relationships wherein the only way to retain one's individuality is by changing one's parts. This is the meaning of metabolism. An organism "is never the same materially and yet persists as its same self, *by* not remaining the same matter." (Jonas 1966, 76; see Gilbert 1982; Landecker 2017). Thus, the living organism is characterized by what Jonas (1966, p. 80) has called "a needful freedom," as metabolism constitutes both the identity of the organism and, simultaneously, its dependence on its environment. On one hand, " the organism must appear as a function of metabolism rather than metabolism as a function of the organism." But on the other hand, " life not as a property of an already constituted living being, but as the act by which it constitutes itself and individuates." As Anne Sophie Meincke (2022) has expounded, this dialectic allows one to perceive an organism as an identity-maintaining individual unit as well as part of a homogeneous and non-individualistic world of metabolism. Indeed, "the very opposite of isolation emerges from the isolation of the organic self" (Jonas 2001, p. 85). This dialectic is critical for perceiving holobionts and Gaia as co-metabolizing wholes.

This current view of metabolism, wherein all the components of an organism are in a constant state of chemical renewal, was formulated by Rudolf Schoenheimer. He was the first investigator to tag nutrients with radioactive chemicals and watch their transformation as they became different molecules and different body parts. (Schoenheimer 1935, Schoenheimer 1942; Guggenheim 1991; Landecker 2013). These insights were formulated into metabolic pathways by Schoenheimer and several other professors, many who had fled Hitler to come to Great Britain or the USA[12] (Kennedy 2001; Holmes 2001). Hans Krebs, Otto Meyerhoff, and Fritz Lipmann, for instance, helped elucidate the schema whereby oxygen, the byproduct of photosynthesis, served as the receptor for electrons from dietary nutrients, allowing cells to make the energy-storing ATP molecules that allowed life to persist against entropic gradients. As Schoenheimer (1942, p. 65) wrote,

> The new results suggest that all constituents of living matter, whether functional or structural, of simple or of complex constitution, are in a steady state of rapid flux. The finding of the rapid molecular regeneration...suggests that the biological system represents one great cycle of closely linked chemical reactions.

This view that the parts of the body were in flux and constituted the organism had a history prior to biochemistry. Cuvier had written that "The living being is a whirlpool… in which matter is less essential than form," and Thomas Huxley celebrated that remarkable "transubstantiation" by which lobster could be turned into Huxley, and if shipwrecked, Huxley could be reciprocally transformed into lobster (Huxley 1868; Gilbert 1982). Metabolism became the basis of Claude Bernard's physiology (Bernard 1866), wherein cells maintained a "milieu interior" consisting of metabolic processes. In 1896, embryologist E. B. Wilson

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re-activates after transferring energy when bathed in an appropriate light. Eventually, the organisms die, returning (literally) to their ground state..

[12] Hans Jonas was also a Jewish professor who fled Hitler's Germany, emigrating to Great Britain in 1933 and moving to British Palestine a year later. He returned to England in 1940 to enlist in a British military brigade to fight Hitler in Italy and Germany, and he later fought for Israeli independence. He could have learned of Schoenheimer's work either directly or from his friend Ludwig von Bertalanffy (Landecker 2013).

(1896, 431), concluded, "Inheritance is the recurrence, in successive generations, of like forms of metabolism." He would later (Wilson 1905) link this ability of directing metabolism to the chromosomes.

Holobiont co-metabolism

We now understand, however, that whereas metabolism was originally defined as a cellular phenomenon, metabolism is a communal enterprise (Dupré and O'Malley 2009; Kelty and Landecker 2019). In holobionts, the set of symbiotic organisms (including the "host") participate in each other's metabolisms. In the mealy bug *Planococcus*, the production of the amino acid phenylalanine begins with enzymes encoded by the bug's symbionts, *Tremblaya* bacteria. The metabolites generated by these enzymes then travel into another bacterial species, *Moranella*, which are symbionts within the *Tremblaya* bacteria. The newly made metabolites from *Moranella* then return to the *Tremblaya* bacteria, where they are converted into a product that can be metabolized into phenylalanine by enzymes encoded by the *Planococcus* genome (McCutcheon and von Dohlen 2011).

In mammals, bacterial products, especially the short chain fatty acids, are sent through the circulation of the body, where they sustain the digestive system, the circulatory system, bone growth, and other physiological functions (Kelty and Landecker, 2019; McFall-Ngai et al 2013). As mentioned earlier, gut microbes are critical for producing new neurons in adult mice. Here, enzymes from the pancreas release the amino acid tryptophan from proteins. The gut microbes can take this amino acid and convert it into indole, which circulates through the blood and can activate the genes responsible for embryonic hippocampal neuron production. In 2013, Smith and colleagues coined the term "co-metabolism" to indicate that foods are being metabolized by both host enzymes and microbial enzymes, and that the products of one are often substrates for the other. We have an entangled metabolism.

Holobiont co-metabolism: Gaia

Hannah Landecker (2013) has pointed out that perceiving organisms as a function of metabolism reverses the way we separate organisms from their respective environments.

> Metabolism, in this analysis, was not a boundary between two things, but a dynamic production of there being two things at all: without metabolism, there would be no need to have inside and outside, organism and environment, animal and world. In other words, there are not two entities which then enter into exchange with one another, requiring a boundary to keep them distinct, but a third thing – a metabolism – which produce the two-ness of organism and environment.

Metabolism is a global process whereby organism and environment are co-constructed, and Gaia is characterized (Margulis and Sagan 2000, 78) by its "incessant self-organizing metabolism." As Bruno Latour (2017, 142) noted, "Gaia is only the name proposed for all the intermingled and unpredictable consequences of the agents, each of which is pursuing its own interests by manipulating the environment." This idea that organisms, as well as organs, were enmeshed in metabolic webs was first appreciated in community ecology. G. Evelyn Hutchinson (1940) proposed that a community of living organisms could be regarded as a single organism, and it should "therefore be possible to study the metabolism of that organism." And here we have the beginnings of the Gaia hypothesis, which arose by name from James Lovelock's consideration that the world might indeed be an entire organism. In this view, geology didn't make a "stage" for life, and Earth wasn't a "Goldilocks planet" where water, oxygen, and the temperature were perfect for life. Rather (in a way that resembles Niche Construction writ large), Life was the agent that terraformed the planet[13].

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[13] The capitalization of "Life" is a recognition of its agency by Bruno Latour (2020): "Lovelock from space, taking the question as globally as possible; Margulis from bacteria, taking the question from the other end, both realizing that Life, capital L, has managed to engineer its own conditions of existence." Remarkably, our biosphere is still being

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First, Life is responsible for the strange composition of Earth's atmosphere (Lenton and Dutreuil 2020; Lenton et al 2020). Without certain living species, oxygen would be 1 atom in 10^{12} rather than one atom in five. Methane is 10^{30} times more abundant on earth than it would be at an abiotic equilibrium. Archaea originally made the methane, and Cyanobacteria originally made the oxygen. Second, Life is responsible for the strange composition of the ground. We have soil, not regolith[14]. The flux of phosphorus through living systems is probably 1000-fold over what might be expected geologically, and animals are critical in hydrating the earth's crust. Much of earth's minerals are oxygen-containing carbonates or silicates, made from Life's excess oxygen. And third, Earth without Life would probably be a pressure cooker with a temperature of 50°C. Photosynthetically derived oxygen created the ozone layer and induces a cold trap to form in the upper atmosphere, preventing water and hydrogen from escaping. The world's ecosystems are, like the symbionts on our bodies, both contained and interacting. Phosphorus, nitrogen, calcium, and atmospheric gasses are cycled between organisms in food webs that encompass planetary proportions. In Canada's Great Bear Rainforest (the largest temperate rainforest on the planet), for instance, "eighty percent of the nitrogen in the forest's trees comes from the salmon" (Wagner and Reynolds 2019; Muller 2022). And 100% of the carbon in their trunk and branches come from the carbon dioxide expelled by organisms and fossil fuels.

Lynn Margulis (1995) would argue, "Lovelock would say that Earth is an organism. I disagree with this phraseology….I prefer to say that Earth is an ecosystem, one continuous enormous ecosystem composed of many component ecosystems." Interestingly, that was also the characteristic of another one of her conceptions, the holobiont (Margulis 1991). Gaia is an autotrophic (photosynthetic) holobiont whose symbiotic components are in constant co-metabolism (Matyssek and Lüttge 2013; Gilbert 2020b). Gaia's existence, like that of all holobionts, is sympoietic, not autopoietic (see Gilbert 2019b; Clarke and Gilbert 2022). Indeed, Margulis (Margulis, 1990, p. 866) characterized Gaia as not being in a state of physiological homeostasis, but in an embryological state of "homeorhesis." This was Waddington's (1957) term for the crucial observation that embryonic cells changed as they interacted with other cells, eventually differentiating into the component cells of integrated organisms (Matsushita and Kaneko 2020). And like the embryonic cells that interact in order to mutually differentiate, and like the organism that uses metabolism to remain the same while changing its components, Gaia, too, has to maintain itself as its component organisms evolve. There is always change, and Gaia is constantly changing. Unlike machines, an organism has to function as it develops.

The holobiont body, as we have seen, is an interconnected temporally changing web of ecosystems, where the mouth, gut, fingers, and reproductive orifices each support different communities of organisms. The holobiont is thus a *team* of organisms, a consortium expressing an integrated, enmeshed, and distributed development and metabolism. Patrice Manglier (2021;67-71), following Bruno Latour, has argued that a key characteristic of Gaia, perhaps its most important feature, is that it is the "continuity of entanglements." Once one accepts the reality of metabolism and holobionts, Gaia is neither magical nor

manufactured by the descendants of microbes, and the cycling of material between them constitute the basis of our ecosystems and the energy that sustains our bodies. Oxygen is produced by photosynthesis, which is accomplished through the plant's chloroplasts. These chloroplasts are believed to have once been cyanobacteria. Similarly, the oxygen is utilized by the plant and animal's mitochondria to produce the energy needed to sustain life. The mitochondria are also believed to have once been symbiotic bacteria. The waste product of this combustion is carbon dioxide, which plants use to make sugars, starches, and the wood of trees.

[14] Lewis Thomas (1974, p. 145) , reflecting on the June 1969 photograph of the earth as seen from the moon, stated, "The astonishing thing about the earth, catching the breath, is that it is alive. The photograph shows the dry, pounded surface of the moon in the foreground, dead as an old bone."

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extraordinary; or perhaps no more magical or extraordinary than any other form of life. Gaia can be modeled as a holobiont[15]. But Gaia should have been named for her daughter, Rhea, the goddess of flux.

Moreover, Gaia, like any other ecosystem or holobiont, is an attractor basin. The atmosphere, lithosphere, hydrosphere (and especially the soil rhizosphere around roots) are each their own attractor, and they are integrated into Gaia, which is a metabolic attractor state whose component parts are in dynamic stable relationships with each other. It is a realm of Leibnitzian "compossibility." Whereas all things may be possible, they are not possible together. Gaffney and Steffan (2016) have modeled Gaia as an attractor basin and have pointed out that there have been (and still are) other attractors. There is the attractor of "snowball earth" (which was experienced during the ice-ages) and the attractor of "hothouse earth" (which would be the result of catastrophic global climate change.) In this latter attractor, temperatures would be beyond the limits of human viability, and neither attractor would be habitable for *Homo sapiens* and the food we now grow. There are other attractors that can be imagined, as well. These include "plantationocene earth" (Haraway et al 2015), where some human beings' extractive management has diminished biodiversity solely to capitalistic Western humans and their (often coerced) companion species, and "techno-earth" (Ellul 1964; Hawking and Cellan-Jones 2014) where nature has vanished, and humans, if existing at all, are the fleshy workers maintaining an integrated technological matrix of artificially intelligent entities that assign functions to living beings.

While these different dystopian attractors emphasize the fragility and potential mortality of Gaia, there may also be also be (e)utopian attractors, where humans may actually help increase the dynamic interactivity and health of the biosphere. Latour's (2018) "terrestrial attractor," seeking a balance between the importance of physical (local) habituation and access to the global world, is depicted as a sane alternative to other, more pathological, attractors. A "polyphonic" earth is envisioned by Robinson (2020 p. 562) and is championed by authors as diverse as Haraway (2016) and Kimmerer (2013b). In this Gaia, economic well-being has been decoupled from planetary exploitation, and it inhabitants "would not cease the layered, curious practice of becoming-with others for a habitable, flourishing world" (Haraway 2016, p. 168). While the dystopian attractors can be easily reached through inaction, there would have to be many new policy decisions to reach these eutopian states. This is why imagining such possibilities is crucially important. "How can we begin to move towards ecological sustainability," writes Kimmerer (2013, p.6), "if we cannot even imagine what the path feels like?" Indeed, "utopian thinking regarding sustainable development could result in more integrated and holistic visions of future society in climate science and policy" (Hjerpe and Linnér 2009, p. 234). It may be more productive to envision joyful futures than to envision escapes from horrific ones.

Changing attractor states has happened in earth's history. Roughly 2.3 billion years ago, Cyanobacteria evolved photosynthesis and poisoned the air with oxygen. This "Great Oxidation Event" caused the mass extinction of the anaerobic microbes that had thrived in the Gaian attractor basin having a reducing (hydrogen-abundant) atmosphere (Lyons et al 2014; Aiyer 2022). This massive elevation in oxygen created a new equilibrium, producing the planet as we know it, a planet full of metabolisms/organisms that evolved to use oxidative phosphorylation (the use of oxygen to manufacture ATP) as a means of accumulating energy. Certain bacteria originally possessed this ability. Later, through symbiotic pathways, some of these bacteria became incorporated into Archean cells and became the mitochondria of eukaryotic organisms--the protists, plants, animals, and fungi (Margulis 1996). Thus, the cyanobacteria changed the attractor basin into the present form of Gaia. We would not be the first species to cause mass extinctions by changing the atmosphere.

[15] The forest may be considered as a transition, spanning between the holobiont and Gaia (Matyssek and Lüttge 2013). Its separate trees (indeed trees of different species and ages) can be linked together metabolically through symbiotic fungi and bacteria. Here, nutrients from one tree can pass into the bodies of other trees. Such interactions alter plant competition, facilitate seedling growth, and stabilize the biome (Simard et al 1997; Selosse et al 2006).

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Gaia is also a holobiont in the sense that it has an "exosymbiont," the moon, which has significantly helped form the evolution of life on earth. First, the moon's gravity set in motion the tidal ecosystems (enabling coral reefs, littoral zones, and wetlands) that encompass some of the most critical sites for evolution and biodiversity. Second, periodic lunar light serves as the critical timekeeper for many physiological events, especially reproductive synchrony and life-cycle changes (Kaiser and Neumann 2021; Lin et al 2021, Zurl et al 2022). And third, the moon provides locational cues and challenges as part of the environment (Thums et al 2016; Nyholm and McFall-Ngai 2021). Luna has changed and is still changing the evolutionary path of the Earth. Thus, the Gaia holobiont is defined, sympoietically, by its organismal endosymbiotic components and by its major partner, the moon.

IV. Ethical imperatives for holobionts

"*'Learn what is true, in order to do what is right' is the summing up of the whole duty of man*."

-Thomas Huxley, 1870

Metabolism sustains living beings by allowing "some new principle of refreshment," for it is able "to preserve order amid change and to preserve change amid order" (see Whitehead 1929, 399). The goal of thermodynamic striving is not an end-state (which is death), but rather the maintenance of form through metabolic processes mediated by thermodynamics[16]. Life exists far from equilibrium, which allows local energy minima such as catalytic proteins, stable cell types, holobiont organisms, and ecologically stable communities, culminating in the Gaian attractor that includes ourselves. Gaia, and so we, is/are thermodynamically mortal and constantly changing; and that makes life's developmental creativity, tied to the moon and the sun, possible and meaningful.

Hans Jonas (1966) insisted, "Ontology, as the ground of ethics, was the original tenet of philosophy," and we are constructing a new ontology. Whitehead (1929) concluded that "Morality of outlook is inseparably conjoined with generality of outlook," and we are constructing a new outlook. And David Graeber and David Wengrow (2021 p. 525) have recently concluded, "What is the purpose of all this new knowledge, if not to reshape our conceptions of who we are and what we might become."

Given that life "seeks" thermodynamic equilibria, we find ourselves in a world of desire that is neither top-down nor bottom-up; rather, it is permeating the universe at all scales (see Tsing 2012, Latour and Schultz 2022, p. 72; Kauffman 2020). Gaia is then the result of Whitehead's "Divine Eros," that balances and integrates the separate individualities into a "harmony of harmonies" (Whitehead 1933; 264, 265, 277, 281, 296.) It generates a Spinozan *Deus sive Gaia* that we both inhabit and exemplify[17]. The planet-making, protein-folding, embryo-generating, holobiont-forming, ecosystem-constructing thermodynamic processes generate us and Gaia. All life turns out to be a single clade (Hermida 2016; Mariscan and Doolittle 2018), so there is nothing truly "other" to confront. Each plant, fungus, soil microbe, or animal is but another part of the metabolism of Gaia, and therefore another part of us.

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[16] See Kauffman, 2002. As mentioned above, Waddington (1957) and Margulis (Margulis, 1990, p. 866), viewed such a commitment as "homeorhesis" rather than "homeostasis." A good example of a local commitment is our relation to gravity. Our local attractor is the center of the earth, and our feet point there, even though the sun is a much more potent gravitational force.

[17] This may sound like the panentheist statement that we are all parts of God. One could accept this if one posits Gaia as both the creator and the created. Indeed, we (and all holobiont organisms) would be created "in its image." However, if one believes in the existence of a creator outside of nature/Gaia, one can follow the precept of the rabbi and physician Maimonides (1190/1956; see Seidenberg 2015), who saw "the entire globe as one individual being endowed with life, motion, and a soul." Maimonides also saw the agency of matter quite clearly: "A pious man of my time would say that an angel of God had to enter the womb of a pregnant woman to mold the organs of the fetus…This would constitute a miracle. But how much *more* of a miracle would it be if God had so empowered matter to be able to create the organs of a fetus without having to employ an angel for each pregnancy?"

This should alter our notion of ethics. Western notions (and language) of individual ethical responsibility are still based on conceptions of individuality, power, and property that had been codified into Roman law two millennia ago. Here, the powerful had the right to claim individuality and to use their property (land, slaves, family) as they saw fit. Our views of nature are still those of ownership, even if couched in terms of stewardship (which is, after all, a royal hierarchical relationship.) If the basic questions of ethics depend, as Alasdair MacIntyre (2007) claimed, upon "who are we" and what vulnerabilities our nature accords us, then our holobiont biology becomes central. We are not who we thought we were, and the notion of human flourishing becomes physically bound to the flourishing of Gaia.

What does it mean, for instance, when we are always the nature that is being destroyed? What is our responsibility to nature when "do not ask for whom the bell tolls; it tolls for thee" refers to our vulnerability when a species of soil bacteria or salamander perishes? Just as "anthropogenic explanations of climate change spell the collapse of the age-old humanist distinction between natural history and human history," (Chakrabarty 2009), so do they collapse the distinction between anthropocentric and nature-centered environmental ethics. The ethical questions from a holobiont/Gaian perspective are no longer merely exacerbations of older problems of maldistribution of wealth or resources. MacIntyre (2007,p. 216) asks, "In what does the unity of an individual life consist?" His answer is that it is the narrative conflation of the questions, "What is good for me?" and "What is good for man?" However, biology has changed the notion of our having an "individual life," as well as our sufficiency of existing outside of nature. We have new ethical questions, some of which will be outlined here.

If life is to continue proliferating, with organisms generating new offspring, we must include the concept that our holobiont metabolism reciprocally entangles us with others such that Gaia helps form us (as we help form Gaia). Margulis' (2006) dictum that "the environment is part of the body," is seconded by Barad's (2007) insisting that "we are of the world in its ongoing intra-activity." In such a case, a healthy holobiont body *requires* a healthy environment. A healthy body would have to interact/intra-act with its "environment" to maintain the health of the environment in order to maintain its own health.

While this interpenetration of organism and environment persists for all organisms, it is particularly relevant for humans. "We need," write Matyssek and Lüttge (2013), "global world ethics for maintaining the equilibrium of Gaia." And here we return to the philosopher of metabolism, Hans Jonas, who ended *The Phenomenon of Life* (1966, p. 282) claiming that "through the continuity of mind with organism and organism with nature, ethics becomes part of the philosophy of nature." In 1984, Jonas wrote such a new ethical theory, mandating that we take the environment as something essential for being human. Moreover, since humans are creatures of nature, and since nature is involved in forming the human, then anthropogenic damage to nature damages humankind. His claim is that we are now living in an age where, by degrading nature, we are simultaneously degrading, and perhaps exterminating, the human. Therefore, Jonas (1984 p. 139) pointed out that all philosophy must "stand back behind the bare saving of the precondition, namely the existence of mankind in a sufficient natural environment." He decides that humans are worth preserving (for their remarkable potential), and that the only way for future generations of humans to be saved is to save nature. He contrasts this non-separatist view of the interests of humanity and nature with the "narrow anthropocentric view...which is ready to sacrifice the rest of nature to his purported needs." The realization of the latter view, says Jonas (1984, p. 137), "can only result in the dehumanization of man, the atrophy of his essence even in the lucky case of biological survival."

That leads to the second "goal" of organismal development: to become a healthy partner in the ecosystem. Like the cells reciprocally specifying each other in an embryo, organisms are each other's environments. The ability to respond, response/ability (Haraway 2016), is the basis for, and is enabled by, entanglement. Viewing evolution as a negotiation between the "egoism of each species and the overall symbiotic balance," Jonas claims (Jonas 1984, p.136,-137) that humans are enmeshed in nature and that nature promotes our becoming human[18]. In a world where humans have expanded such that non-human nature is placed in jeopardy, we must consider "care for the future of all nature on this planet as a necessary condition of man's own." For Jonas, we have a "solidarity of interest with the organic world."

> But even if the prerogative of man were still insisted upon as absolute, it would now have to include a duty toward nature as both a condition of its own survival and an integral component of his unstunted being. We have intimated that one may go further and say that the common destiny of man and nature, newly discovered in the common danger, makes us rediscover nature's own dignity and commands us to care for her integrity over and above the utilitarian aspect.

Jonas (1984, p. 11) rephrases Kant's ethical imperative to become, "Act so that the effects of your action are compatible with the permanence of genuine human life." Or, as Marian Wright Edelman, the founder and president of the Children's Defense Fund, summarized, "Be a good ancestor."

That Gaia is an attractor state containing interacting human tissues is not merely a metaphor, but a physical reality that has been quantified and measured. A recent paper in *Nature* (Rockström et al 2023) reports that "the stability and resilience of the Earth system and human well-being are inseparably linked, yet their interdependencies are generally under-recognized; consequently they are often treated independently." These scientists have measured the parameters of the attractor basin (surface temperatures, underground water flows, nitrogen cycling, etc.) and warn that we are falling out of the stable Holocene basin that has sustained us for 12,000 years.

Moreover, these researchers (Rockström et al 2023; Gupta et al 2023) have claimed that in some parts of the planet, we have already passed the thresholds where the earth can provide environments that will permit sufficient conditions for justice. They claim that keeping earth's ambient temperature 1.5°C above the average of pre-industrial times might enable the world's affluent people to protect themselves (and maintain their exploitative lifestyles), but it would expose nearly 200 million people to dangerous and unprecedented temperature increases. The authors of these papers suggest that to provide the minimal conditions of environmental justice, the global temperature rise needs to be kept below 1°C. It has already surpassed this point (Masters and Henson 2023). This enmeshes us in questions of responsibility that had not asked previously.

Another parameter of the Gaian attractor basin concerns the extent of "natural ecosystem areas." In a sympoietic organism, be it a holobiont or Gaia, there must be checks and balances to population growth. The cells of an organ continue to communicate with each other, and one of their most important functions is to regulate the proliferation of neighboring cells. Overproduction of microbial cells beyond their normal limits is called "infection." Overproduction of zygotically derived cells beyond their normal limits is called "cancer." Proliferation is a "default" state of cells, and each cell has to be actively prevented from multiplying (Sonnenschein and Soto 1999; Soto and Sonnenschein 2021). If we are to enjoy a dynamically

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[18] Jonas is explicit that we not do any act that might call into question the continued existence of humanity. This certainly includes not degrading nature and not using nuclear weapons; but after the publication of his book, three other existential threats emerged that would fall under this caveat. The first concern the potentially suicidal positive feedback forged between extractive technologies, socioeconomic systems, and values (Mitchell 2013; Ghosh 2021; Wellum 2023). The second is Artificial Intelligence, as it is "a domain of agnostic and free-floating function," much like organic evolution (Halpern 2018; Amoore 2023). It is a "truly other" form of intelligence, a new clade that has the potential for causing human (and other organismal) extinctions (CAIS 2023), and which can potentially fight back against attacks. Another clade that could cause human extinction would be viruses (Lederberg 1989), and gain-of-function virology studies should also be placed under that *caveat* (Evans et al 2015; Brouillette 2023). Perhaps the closest analogy to both AI and viruses may be the origin of photosynthesis, an information-gathering and transducing mechanism that caused the first and largest mass extinction event.

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stable holobiont-like Gaia, we need to control human proliferation (A. E. Clarke and Haraway 2018), for humans, especially those of the "Western civilazations, are the cause of our contemporary climate change. Less than 5% of the globe can be considered "natural" (Ellis 2021), and it is estimated that recent capitalistic human activity has destroyed over 80% of the world's mammals (Bar-On et al 2018). Currently, the biomass of domesticated mammals now outweighs wild land mammals 30 to 1 (Greenspoon et al 2023).

Indeed, in the epigenetic landscape of the developing body modeled by Huang and colleagues (2009), cancer is itself an attractor. The notion of humans as the cancer of the earth is itself widely disseminated[19]. Moreover, cancers generate their own niche (Huch and Rawlins 2017), producing dividing cells (the cancer stem cells on which most researchers have been focusing), as well as non-dividing cells that become niches that allow the cancer stem cells to survive. Humans secrete such a supportive niche, our exploitive and extractive technological environment, allowing human numbers to expand so rapidly while poisoning and replacing other organisms (Gilbert 2020b). Jonas (1984, p. 137) had also pointed out that while life "is on the whole symbiotic but not static," it is maintained by "mutual limiting interferences."

Being a healthy partner in the ecosystem also means that a goal of normal development is to make an organism physically and morally capable of proliferating, diversifying, and transmitting microbes. Microbes are the basis of soil and marine ecosystems (see Moran 2015; Mueller et al 2019), and bacteria help make us who we are. However, medical and agricultural applications of our scientific knowledge have caused large-scale changes in the composition of microbial communities in humans (Blaser 2018) and on the planet (Bell and Tylianakis 2016; Rappuoli et al 2023), and these alterations are associated with disease and the loss of resilience in plants and humans (Blaser 2014; Sariola and Gilbert 2020; Berg and Cernava 2022). To remain "fully human," we must be responsible propagators of microbes for the health of the earth and our human progeny.

A third, and related goal of human development, is to help Gaia maintain a stable low-energy basin with the biodiversity similar to that which it had prior to the accelerated phase of capitalism and the industrial revolution. As Lenton and Latour (2018) propose, "A central goal for this century is surely to achieve a flourishing future for all life on this planet." As mentioned above, alternative, pathological, attractors are possible. This means that the world should not be valued according to human wants or needs, for the planet is a single process/entity of interpermeable and interpenetrating stuffs. What is good is that which is good for the planet which we help form. Karen Barad's ethics (2007) is congruent with Gaia: "Ethics is therefore not about right responsibility for a radically exteriorized other, but about responsibility and accountability for the lively relationalities of becoming, of which we are a part." This means that humans should use their human-specific traits--our bipedal stance, our opposable thumbs, our enormous brains--for the care and nurturing of Gaia (Tronto 2013; Stengers 2015; Puig de la Bellacasa 2017; Flower and Hamington 2022) . Whether one views it as the stewardship of God's creation or the preservation of evolved interactive biodiversity doesn't matter.

And it must be remembered that "climate change" is nothing less than Gaia's attempts to maintain thermodynamic equilibrium. For billions of years, the earth has balanced its heat gains and losses. With each major disturbance, new equilibria have been achieved. The Holocene epoch, whose climate enabled the flourishing of human societies, is a product of one such equilibration (Bova et al 2021). Only within the past century, when industrial byproducts such as carbon dioxide and methane ("natural gas") have been raised to precariously high levels, is excess solar heat trapped in the soil, air, and oceans. The storms, droughts, floods, and forest fires are not the wrath of a vengeful God or gods. Neither the earth, Gaia, nor

[19] One can purchase "Humans are the cancer of the Earth" t-shirts from the web. Cancer is a disease from within the body politic, not from outside it (such as infection; Gilbert 1979, 2020) and the metaphor has recently been publicized by Hern (2022). Jacques Ellul (1964) called the mechanical takeover of humanity "La Technique," (translated as "technosphere.") It is the "second nature" in which we live, our supporting environment that has allowed us to propagate beyond nature's capacity.

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Nemesis is seeking revenge. Climate change is simply the thermodynamic cause-and-effect consequence of our planet's accumulation of more heat than it is able to dissipate[20].

The material connections of Gaia, just like the material connections of our cells, have evolved to equilibrate and adapt. The two major corollaries of the second law of thermodynamics are: (1) Heat is the energy transferred between systems due to a temperature difference, (2) Heat cannot pass from a cooler body to a hotter body. Rather, hotter bodies transfer heat to colder ones. And such is happening. More heat in the atmosphere and oceans means more energy to be released as prolonged heat domes, forest fires, and torrential rain (Zhang et al 2020; Masters and Henson 2023). The heat in the ocean also prevents atmospheric oxygen to be absorbed by water. Cold water holds much more oxygen than warm water, and as the oceans warm, less oxygen is available for fish. The heat also causes the symbiotic algae to be expelled from their coral, leaving the coral to starve. Since the beginning of the Anthropocene in the 1950s, the world has lost half of its coral population (Eddy et al 2021). And this isn't yet "the new normal." Industry, including the military, has not stopped putting carbon dioxide and methane into the air. We have yet to see the new normal. This has been the hottest year in human history, and it may be the coolest year for the next several centuries.

V. Expanding science beyond the West: Towards a new vocabulary

Contemporary biology is in a transition state of irritation and doubt (Soto et al 2018). Its fixities have become unmoored, as the reductionist program of biology has discovered that biology is actually a study of relationships, not entities (Gilbert 2017; Nicholson and Dupré 2018; Dupré 2020). We have discovered the radical co-dependency of life--co-evolution, co-metabolism, and co-development-- and we are entering a new biology whose ideas of nature are not easily expressed in the vocabulary or stories inherited from Western civilization. However, notions of reciprocity and contextual coming-into-being are integral to many indigenous and non-Western societies. Western science has always made it a point of acknowledging its forebears, and we would be wrong in claiming these "new" ideas to be Western inventions.

Several Asian cultures, for instance, have longstanding scientific traditions emphasizing notions of change and context. First, the Buddhist principle of co-dependent origination, *Pratityasamutpada*, emphasizes that what appears to be an individual entity comes into existence though interdependent relationships that create one another, in a process of continual arising and ceasing. This is what contemporary Indian cultural theorist, Lata Mani (2022) has translated as "co-dependent co-arising." The 14th century sage Tsongkhapa celebrated this concept, concluding, "No *dharma* ('thing') has an existence of its own, but always comes into existence in dependence on other *dharmas*"(Valentine 2018). Things *do* exist conventionally, but ultimately everything is dependently arisen, and therefore void of inherent existence. "Since objects do not exist through their own nature, they are established as existing through the force of convention." (Tsongkhapa 2006).

In the ontology of many American indigenous cultures, reciprocity is central to the maintenance of the planet (Agapakis et al 2022) and the various animals, plants, mountains, and rivers are kin to humans (Deloria 19992; LaDuke 1999). Robin Wall Kimmerer (2013a), a botanical scientist and faithkeeper of her Potawatami tribe, relates this to feedback lops and thermodynamics:

> *Reciprocity—returning the gift—is* not just good manners; it is how the biophysical world works. Balance in ecological systems arises from negative feedback loops, from cycles of giving and taking. Reciprocity among parts of the living Earth produces equilibrium, in which life as we

[20] The lay Black lesbian Quaker minister, O, of Philadelphia contends that is worth re-reading the blessings and curses in Deuteronomy 28-30, not as a story of God's potential wrath, but as a cause-and-effect narrative about morality and climate. For ideas concerning the Bible as a record of indigenous Jewish wisdom concerning climate, see Seidenberg, 2020).

> know it can flourish. When the gift is in motion, it can last forever. Positive feedback loops, in which interactions spur one another away from balance, produce radical change, often to a point of no return.

Western science is not the only narrative context in which to frame data, and Kimmerer states (2013b, 346)," I dream of a world guided by a lens of stories rooted in the revelations of science and framed with an indigenous worldview." As theologian Terra Rowe (2017) has explicated, the gift relationship in the Western world view has not been reciprocity, but grace--a gift that needs no reciprocation. And this has had "damning consequences."

> The widespread influence of a Protestant theological doctrine might be rather quaint if it were not also tied to such damning consequences. The problem with this definition of gift—particularly from an ecological and climate concerned perspective—is that, when defined as an exclusion of exchange or reciprocity, the "free" gift is not only free of obligation, but also of the intradependent relations that we now understand to make up the fabric of every level of existence. If the earth gives freely and unconditionally, nothing ties us to the world. We are free to do what we please, free of demands, free of responsibility, and free to separate ourselves and see the earth as something "other"—an expendable, usable "resource."

However, "reciprocity" is too weak a word, as it fails to denote the mutual dependency of those who give and receive. "Reciprocity" does not imply the "needful freedom" of Jonas and the "reciprocal capture" of Stengers (2010), where encounter leads to mutual transformation. We need a word that brings to mind an interdependency so vital that when such relationships unravel, "dependence becomes a peril rather than a blessing" (Rose 2017). Perhaps these notions of reciprocity need to encounter Buddhist notions of *Pratityasamutpada* and an interspecies extension of the pan-African notions of *Ubuntu*--"I am because we are" (Mugumbate and Nyanguru 2013; Le Grange 2023.) Such views of life, remarks James Tully (2018) "brings to awareness the interdependent ecological self, in contrast to the independent ego-self of our dominant way of life." Moreover, such symbiotic ways of thinking are "neither altruistic not egoistic, for that debilitating distinction rests on the presupposition that organisms are independent and self-sufficient to begin with." Certainly, this concept of reciprocity is readily extended to the more-than-human through Jonas' and Margulis' notions that humans are co-constructed with their environments. We need a word that can distinguish a mutualistic symbiosis (returning a gift, which can be between two adult relatively stable organisms) and sympoiesis, wherein the organisms are changed and matured through these interactions.

Such identity-forming reciprocity is a critical factor during embryological development, and notions of receptivity and mutual maturation of cells relate directly to of *Pratityasamutpada* (Gilbert and Epel 2015; Gilbert 2016; Denver 2022). For example, when a bulge of cells from each side of the developing brain contacts the ectoderm that would otherwise form the epidermis of the head, it calls to those ectoderm cells to become lens. But these chemicals are not commands. The chemicals (*e.g.*, BMP4, Fgf8) that tell the ectoderm to become lens are those same proteins that will tell the limb skeleton to grow outward from the body and regulate oocyte formation in the ovary. How the cells interpret the signals depends on their history and their neighbors. Moreover, once the lens cells start forming, they reciprocally call to the brain bulge cells to become the retina. Thus, the retina and lens co-construct each other sympoietically, in a series of calls and responces.

But there is more to this notion of *Pratityasamutpada*. There are "pay-it-forward" mechanisms, as well. When the lens cells develop, they invaginate into the body, and they put forth signals that induce not only the brain cells beneath them, but also the ectoderm cells that collect above them. As the lens develops, it calls to these upper ectoderm cells to become the cornea. In this way, the eye develops through a combination of reciprocal feedback loops and pay-forward loops. The cornea is because of the lens-retina relationship. Such feed-forward loops are responsible for numerous organ systems and ecosystem formation. In the cultural context, pay-it-forward is an indirect reciprocity mechanism, and it appears to be sustained only by social cues, that is, if a person earns a good reputation through such cooperation (Horita et al 2016). It is therefore incumbent on societies to reward such cooperators with reputational tokens that make such behaviors desirable and normative.

This vocabulary from more than Western sources can enrich our perceptions of nature. We should critically and constructively introduce these concepts into our current biological thinking. Not to do so would risk having biological science becoming (or remaining) a Western ethnoscience wherein data are forced into the Procrustean notions of an existing religious or social contexts (Gilbert 2022). We should also bring in concerns from other regions and peoples of the world[21].

Biology has changed and has become a science of context-dependent relationships that integrate our agency with the agencies of other organisms and even with thermodynamically directed non-living matter. A Gaian perspective should be able to integrate local and global ecosystems in a way that can celebrate local nature-cultures without promoting the ecological fascism that has often accompanied such environmentalism (see Kantor 2007; Latour 2018; Ghosh 2021; Treuer 2021) Moreover, we may be at the point where the maintenance of the current incarnation of Gaia, with all its conjoined metabolic pathways, ground waters, oceans, predators and prey, microbes, cabbages, and kings, demands radical sociopoliticalchanges to prevent the radical reordering of life on this planet.

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