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Myxozoa in Haeckel's Shadow

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Abstract

The "new" Cnidaria incorporating oligocellular myxozoans with multicellular cnidarians flouts Ernst Haeckel's biogenetic law and challenges contemporary hierarchical preconceptions of evolution, development, and biological structure. Instead of distorting definitions of embryos, tissues, and organs in order to bring once - unicellular eukaryotes under the aegis of Eumetazoa, current molecular, structural, and developmental data should be incorporated into proposals for new evolutionary mechanisms, such as the symbiogeny hypothesis.

Keywords: Myxozoans; Tissue science; Eukaryotes

Introduction

The recent elevation of Myxozoa from a phylum of unicellular eukaryotes to one of multicellular eukaryotes [1–22] offers biologists a rare opportunity to examine some of biology's hidden premises. Several of these are buried in Ernst Haeckel eccentric dogma, the "doctrine of evolution… called the biogenetic law or the law of recapitulation…[That] phylogenesis is the mechanical cause of ontogenesis" [23].

Contemporary biologists hardly ever espouse Haeckel's postulates directly but advance them clandestinely. A patina of evolutionary determinism surreptitiously shades biologists' thinking, including their understanding of the structure, development, and evolution of tissues, organs, and organisms. But the conversion of once-unicellular organisms into oligo- and multicellular organisms is so utterly contrary to Haeckel's dogma that it threatens to overturn the biogenetic law.

Accommodating protistans into the ranks of Metazoa is not simply a matter of contending with "multicellular chauvinism." Placing Myxozoa among the Radiata (or Bilateria as the case may be) is auspicious, because organisms at these ranks have tissues, and myxozoans barely have cells. What, then, are the myxozoan equivalents of tissues? Furthermore, myxozoans generally do not have embryos with gastrulas. What then are the myxozoan equivalents of germ layers, and where do the new cnidarians leave the biogenetic law?

Haeckel's Mark on Biology

Contemporary concepts of tissues' evolutionary origins in embryonic sources reflect Ernst Haeckel's "genius for generalization." He is legitimately credited with supplying biology with the "brilliantly worded aphorisms" [23] that framed his theories of germ layers and the gastraea: Tissue or a "coenobium" occur only in metazoans where they are built up of a number of cells… Hence, further, true germinal layers, and the tissues which are formed from them, are found only in the metazoa… In all the metazoa only two primary layers appear at first, and these have always the same essential significance; from the outer layer the external skin and nervous system are developed; from the inner layer are formed the alimentary canal and all the other organs.… The two cell layers… [are] simple epithelia… all the other organs and tissues are a later and secondary growth from these… In the further development of the various tissue-forming animals from the gastrula we have to distinguish two principal groups. The earlier and lower types (the acoelenteria or acoelomia)… [comprising] the gastraeades, sponges, cnidaria, and platodes… and higher types (the caelomaria or bilateria)… [with] a true body cavity, and generally (the coelenteria or acoelomia… [beginning with] worms and the higher types of animals which were evolved from these later on, the echinodermata, mollusca, articulata, tunicata, and vertebrate" [24].

Historically, Haeckel's germ layer and gastraea theories followed biology's cell theory (that cells are the units of biological structure, function, reproduction, and evolution), but Haeckel's theories overtook the cell theory and replaced cell functions with determined evolutionary trajectories. Thus biological structure became the reflection of what had been; development ceased to be adaptive and became the sequel of evolution; evolution became the cast molding the organism.

At the close of the 19th century, Haeckel (among others) had successfully extended deterministic thinking about the evolution of organisms to their development and biological structure. Epithelial tissue determined a metazoan hierarchy above sponges, but having only "two primary layers" precluded "lower" animals from having any tissue other than a "simple epithelium." Only the gastrula's mesoderm derived from entoderm (aka endoderm) provided the material for advanced tissues. Furthermore, whereas didermic (diploblastic) animals were stuck in radial symmetry, tridermic (triploblastic) embryos blossomed into bilateral larvae and adults that culminated with us (actually, with [hypothetical?] colonial organisms beyond us).

Haeckel's views of evolution determining development were formulated prior to TH Morgan's gene theory (to say nothing of RA Fischer, JBS Haldane, and JS Huxley's "Modern Synthesis"), but even overlooking Haeckel's untimeliness, he might have exercised restraint in view of biology's vast ignorance surrounding the origin of cells, their functions, variations, and adaptations. Consequently, instead of raising questions, he formulated a "natural system of classification [that] gives a true picture of the genealogical relationships of organisms that the smaller and larger classificatory groups correspond

to greater or lesser branches of the genealogical tree" [25]. Regrettably, Haeckel's conceptual medley of maxims remains with biologists still.

Fudging On Gastraeas and Germ Layers

Haeckel's gastraea theory employed his biogenetic law to link his germ layer theory to evolution. The sheer breadth of the law and its resonance for every aspect of biology proved irresistible. Even the great iconoclast, Thomas H. Huxley turned the two "membranes" he discovered in adult medusas (named ectoderm and endoderm by his friend George Allman [26] also Allmann [23]), into embryonic germ layers.

Libbie Hyman, the doyenne of comparative anatomy and keen Haeckel critic, did not escape the allure of the biogenetic law or successfully elude the seductions of the gastraea and germ layer theories. In her monumental, multivolume work, The Invertebrates, she defined tissue morphologically as a "complex of approximately like cells," principally, "epithelial, connective, muscular, nervous, and reproductive" (to which are commonly added blood and lymphatic tissues) adding, "a combination of two or more kinds of cells or tissues into a functioning whole is termed an organ" [23]. But Hyman did not stop there. She went on to place tissues and organs in both evolutionary and developmental contexts.

Hyman asserts that whether or not a germ layer follows some similar plan throughout the animal phyla "it can scarcely be doubted that the later stages of development exhibit a certain similarity especially in the bilateria and that in general each germ layer gives rise to certain definite organs." Thus, Haeckel's germ-layer theory emerges, and "the gastraea… the common ancestor of all the Metazoa… [is] reproduced in their embryology as the gastrula stage" [23]. Hyman thus granted that the gastraea theory "and its corollaries represent a masterly simplification of the embryologic and phylogenetic history of animals and furnish a clear and plausible explanation of the stages by which complex metazoan structure might have been achieved" [23].

Similarly, Edward Stuart Russell, the dean of animal morphology, form, and function, credited Haeckel with giving "evolutionary embryology" a "more precise and more technical formulation." But Russell also criticized Haeckel for postulating "hypothetical ancestral forms… [as] concrete projections or archetypes of the classificatory groups." And Russell challenged the originality of Haeckel's notion that "each stage of ontogeny had its counterpart in an adult ancestral form" citing Charles Darwin and Fritz Müller as originating the "thought that development repeats evolution" [25].

Furthermore, Russell observed "an analogy between the biogenetic law and the law of von Baer, for both assert that development proceeds from the general to the special," and Russell was keen to point to fundamental resemblance "between the biogenetic law and the Meckel-Serres law" that "the higher animals repeat in their ontogeny the adult organization of animals lower in the scale" as also championed by Louis Agassiz. Russell goes on to complain that Haeckel's influence in the post-Darwinian period of "evolutionary speculations" was due to "an evil heritage of detailed and unintelligent work" on "the democratization of morphology which followed upon the facilitation of its means of research… [made possible by] the very great and real advances which technical improvements alone rendered possible" [25].

Otherwise, Russell succumbed to the allure of Haeckelianism and granted legitimacy to the germ-layer and gastraea theories despite their being "crude, dogmatic and extreme." Ultimately, Russell conceded that Haeckel's "historical importance is considerable." Haeckel's notion that "species of one genus must be descended from a generic ancestral form, genera of one family from a single family Urform, and so on for the higher categories" epitomizes Russell's version of the "three-fold parallelism" of "the natural system, embryonic development, and palaeontological succession" [25].

No Need to Quibble

To further quote Hyman: "There is no need to quibble over the word recapitulation" [23]. Unfortunately, there is, notably over Hyman's reflections on the embryonic determinism that led her to fracture the mesoderm. She characterized the Radiata, including Cnidaria and Ctenophora, as "phyla in which the mesoderm is chiefly an ectomesoderm and exclusively mesenchymal…, i.e., presenting a relatively low grade of construction; they have progressed along the lines of cellular differentiation, but organs are lacking, and hence functional systems have remained in a low state of organization" [23].

In contrast, mesoderm, as such, has "entodermal or both entodermal and ectodermal origin in the bilaterial groups… Whereas, it generally holds true that the ectoderm produces the skin and its derivatives, nervous system, and the end sections of the gut, the entoderm becomes midgut and its derivatives… the mesoderm is the source of the connective tissues, muscles, and blood vessels."

Regrettably, and despite Hyman's efforts to make herself clear and avoid misinterpretation, her view was misappropriated to support an evolutionary schism between bilaterians with a true mesoderm derived from endoderm and radiates with an ill-defined mesenchyme and without a proper mesoderm. Contrary to Hyman's stated intention, the Radiata was cast as didermic (diploblastic), having only two of the three germ layers found in the tridermic (triploblastic) Bilateria. Consequently, since all the bilaterians possessed complex tissues and organs, a polarized anterior-posterior axis, and a mid-sagittal plane with mirror-image symmetry the source of all complexity and bilateral symmetry was attributed to the third germ layers, the mesoderm.

Myxozoa Becomes Multicellular

Here then is the muddle caused by "elevating" Myxozoa from a phylum of protists to one of metazoans: Infectious organisms with a modicum of cells, no embryos, and hardly any possibility of having a mesoderm were ironically expected to possess multicellular qualities! How have myxozoans fared?

For decades, specialists had been inching Myxozoa toward recognition as a phylum of multicellular animals [1–17]. Expectations ran so high that Myxozoa's "demise" as a protistan phylum was declared [18–19] even before deciding whether the myxozoans would belong to the Radiata or Bilateria. Molecular evidence ultimately proved decisive: Myxozoan "nematocyst" proteins (nematogalectins and minicollagens) were seen to be akin to cnidarian cnidocysts proteins [20]. Thus, Myxozoa became a member of the Cnidaria [21] and hence of the Radiata (as long as the superphylum lasts) Furthermore, "leveraging cross-referenced transmission electron micrographs… demonstrate homology of the ontogeny of myxosporean polar capsules (aka "nematocysts") with medusozoan atrichous isorhizan nematocysts" [22] (i.e., a type of cnidarian cnidocysts)

Cnidarians have long been said to be at a tissue grade of organization because of qualities attributed to their epithelia or epithelialmuscular cells. In particular, cnidarian epithelia have occluding junctions (septate desmosome and permeability barriers), hemidesmosomes attaching the cells to a supporting basal lamina of microfibrillar or granular condensations above the mesoglea [27–29]), and sometimes spot desmosomes and communicating gap junctions (in Hydrozoa if not Anthrozoa and Schyphozoa [30–31]).

Cnidaria's neighbors on the metazoan tree (ignoring the ambiguous Mesozoa) are also granted tissue status. To the degree that species (?) of modern Trichoplax are informative, placozons have an epithelium, although they lack crucial mesodermal components other than (probably) germ cells. Otherwise, the "placozoan genome harbors representatives of all major genes that are involved in neurogenesis in higher animals… [even if Trichoplax's cells] show not the slightest morphological hint of nerve or sensory cells" [32].

Ctenophores also make the tissue grade, since their surface cells are linked by apical belt junctions and spot desmosomes (albeit not tight junctions or septate desmosomes). These cells are also mounted on a basal lamella (a subcellular electron-lucent [lamina rara]) and a granular fibrillar dense outer and fibrillar mesoglea [33–35].

What about the Myxozoa? Myxosporozoan spores (in contrast to the trophic plasmodial stage or macroscopic nematode-like malacosporeans) contain cells not merely stuck together but functionally differentiated. The homology of myxozoan "nematocyst" and cnidarian cnidocyst proteins does not elevate Myxozoa to the tissue grade, however. In fact, cnidarian cnidocytes and myxozoan "nematocytes," better known as polar capsules, are merely cells containing differentiated organelles consisting of an encapsulated inverted and extrusible thread.

But cnidocytes and polar capsules do not constitute a metazoan tissue. They may be autapomorphies within a Cnidaria/Myxozoa clade, apomorphies independently derived in related groups, or synapomorphies derived from a common ancestor, but cnidocysts and polar capsules are not found in other metazoans (Cnidocysts present in nudibranchs are entirely appropriated from hydroid prey). The most that can be said is that cnidoblasts that make cnidocysts and capsulogenic cells that differentiate as polar capsules behave like mesenchymal cells by way of migrating from internal sites to the spore's surface.

A stronger case for myxozoan tissues can be made for epithelia in myxozoan spores at the cellular infectious stage. The spore's outer enclosing or enveloping cells, pericytes, epispores, endospores, and pansporoblasts give "clear ultrastructural evidence of known metazoan features such as terminal cell differentiation, intercellular septate and desmosomal junctions, intercellular cytoplasmic communication, and cross-linked collagen" [22; also see 66]. Along with valve shells and polar capsules, the enclosing cells may even be considered parts of an infection apparatus (an organ?).

On the other hand, the sources of myxozoan enclosing cells pose problems for the standard definition of tissues: i.e., a complex of similar cells from the same source. The myxozoan "epithelial" cells are not produced by ordinary cell division. In some myxosporidians (Myxobolus), diploid (and polyploid) cells are carved out of a plasmodium, while in others (Aurantiactinomyxon), cells perform meiosis and fusion (fertilization) before giving rise to enveloping and inner cells [2]. Thus, in order to include the enveloping cells as epithelia, the definition of tissues must be expanded to accommodate the cellularization of plasmodia and union of somatic cells. Conceivably, these processes are myxozoan apomorphies, or other metazoans have lost these possibilities for producing somatic cells in the course of evolutionary history.

One may more easily grant the title epithelium to the covering of the saclike malacosporean coelomic parasites of bryozoans. These parasites have an "outer wall of epithelial cells" [36] (aka "mural cells" sometimes spotted with polar capsules: see [66]) "joined by cell-cell junctions and underlain by a basal lamina" [37]. In addition, the malacosporeans have definitive tissue: tetraradial blocks of longitudinally arranged muscle "embedded in the extracellular matrix between inner and outer epithelial tissue layers" [37]. Thus, the malacosporean myxozoans, and by extension, Myxozoa generally would seem to qualify as tissue-grade organisms.

Modifying the "Mesoderm"

The cnidarianists, Katja Seipel and Volker Schmid [38,39] were not been standing idly by while Myxozoa turned Cnidaria upside down in order to accommodate the former protist. They proposed that low locomotory pressure explained the evolutionary reduction of mesodermal differentiation into muscle in the cnidarian planulas of small hydrozoan polyps and in the digestive tube and tentacles of small hydrozoan medusas. Presumably, muscle would not have offered an adaptive advantage following the reduction or loss of the medusa in sessile hydrozoans (One might add that muscle would have little function in the histozoic life style of myxoporozoan myxozoans, albeit muscle would function adaptively in the coelozoic life style of macroscopic malacosporean)

On the other hand, comparative molecular and genomic analyses are not barriers to the view that proto-cnidarians were triploblastic with an incipient mesoderm in the form of amoebic cells. "Based on expressed sequence tag (EST) analyses… and the targeted study of specific gene families: signaling pathways and transcription factors involved in the early patterning and development of bilaterians are present in cnidarian genomes and are active in development… indicating that these pathways and regulatory mechanisms predate the eumetazoan radiation" [34].

In "anthozoan and scyphozoan [polyps]… the presumptive mesodermal elements include amoeboid cells, the mesentery retractor muscles and scleroblasts, all of which are embedded or deeply rooted in the extracellular matrix (mesoglea) and derive from the ectoblastemal cells invading the extracellular matrix from the gastrulation site during or shortly after endoderm formation. These data lend further support to the cnidarian mesodermate hypothesis, whereby cnidarians and bilaterians share a common triploblast ancestor" [39].

Seipel and Schmid's "mesodermate hypothesis" proposes that "both the jellyfish and bilaterian striated muscles are derived from mesoderm-like primordia in a common ancestor established before the Zootype with clustered Hox genes" [39]. In cubozoan and scyphozoan medusas, cross-sections of tentacles show tubular bundles of smooth muscles and nerve cells largely isolated from ectodermal and endodermal layers. Likewise, in hydromedusas, the "swimming bell with a well-developed striated muscle layer… is derived from the entocodon, a mesoderm-like third cell layer established at the onset of medusa formation" [38].

Developmentally, the entocodon is completely separate from both the ectoderm and endoderm by extracellular material. "The entocodon thus forms a compartment of its own and merits mesodermal status" [39]. Indeed "the evolution of striated muscle-based locomotion [in Cnidaria] most likely was based on an integrated anatomy assembled from three germ layers" [39; but see 40].

The "hydrozoan entocodon… has the ability to differentiate both muscle and nerve cells, indicating an evolutionary connection between the two cell types" [39]. Apparently, serial epithelial to mesenchymal transformations (EMTs) take place during cnidarian "mesoderm" formation. Furthermore, "recent gene expression studies on mesodermal/myogenic and patterning genes in the anthozoan Nematostella vectensis do not contradict this conclusion" [39]. Cnidaria, including Myxozoa, should, therefore, be recast at the mesodermal level of complexity and the superphylum Radiata dissolved.

Cnidarian embryos always had mesodermal qualities if not in name, but, ironically, the chasm between mesodermal and non-mesodermal embryos seems to be filled by oligocellular myxozoans. Validating myxozoans station, the anemone Nematostella, "have several clusters of homeobox genes" [34] identified with mesoderm. Not "surprisingly… genes known to be involved in mesoderm development in bilaterians are also enriched among eumetazoan novelties, given that the textbook picture of cnidarians is that they lack mesoderm. Yet we know that many of these genes are associated with basic patterning functions and/or the regulation of cell migration and fate" [34].

Cnidoblasts are also mesodermal-like by way of being "derived from the endoderm" [41], and cnidarians' amoebic cells produce mesodermal-like specialized cells as well as gametes. In addition, nerve (ganglionic cells) and muscle are produced in the presence of the amoebic cells if not, necessarily, by these cells.

Without putting too fine a point on it, myxozoan valve shells and capsulogenic cells might be said to be mesodermal-like by way of arising from the internal sporoblast. The outward movement of these cells, especially capsulogenic cells differentiating as polar capsules, to the spore's surface is also reminiscent of cnidoblasts in cnidarians moving to slots in epidermal battery cells. Cell movement might not ordinarily be listed as one of mesodermal cells' characteristics, but, certainly, mesodermal cells are conspicuous for their movement in embryos and in vertebrate adults. Indeed, the movements of mesenchymally derived lymphocytic cells to specific sites (e.g., thymus, spleen, tonsils, intestinal lymph patches) are quintessentially mesodermal behaviors.

Crucially, cnidarians' distinct amoebic cells perform the rudimentary mesodermal functions of integrating components in hydrozoans' nerve net and other mesodermal-dependent processes such as differentiating as muscle, glandular cells (albeit not present in Scyphozoa [42]), along with germ cells. Nor is it unthinkable to attribute mesodermal qualities to the differentiated shell valves, and ultimately sporogenic cells in addition to capsulogenic cells.

Developing diploblasts and broadening bilaterians

Seidel and Schmid also envisioned diploblastic "cnidarians derived from a triploblast ancestor" [39]. Indeed, they suggested that, "the origin of triploblasty predated the cnidarian-bilaterian divergence" [38; also see 43 and 66]. In fact, characterizing cnidarians as radially symmetrical is inaccurate or, at least, not sufficiently inclusive, since many anemones have bilateral symmetry by way of their polarized oral/aboral axis and a mirror-image mid-sagittal folding plane. In the course of evolution, the definitive step toward bilaterality might well have been "taken before the divergence of Cnidaria" [16], and cnidarians could have been originally bilaterally symmetrical only to acquire radially symmetrical contours secondarily [38–39,44–46]. Clearly, a revision of concepts of axes of symmetry and genes acting on asymmetric expression is overdue [46,47].

Paleontological evidence might be helpful for placing bilateral symmetry in context. Microscopic thin sections of Precambrian fossils in phosphatized Doushantuo formations of China (within the range of 570 ± 20 million years ago) revealed "organisms that produced embryos of bilaterian affinity, as well as clearly differentiated cnidarian forms" [48]. The fossilized bilateral organism, Vernanimalcula guizhouena gen. et sp. nov, that lived some 40 to 55 million years before the Cambrian, "indicates that the genetic tool kit and pattern formation mechanisms required for bilaterian development had already evolved by Doushantuo times… and that the evolutionary appearance of developmental programs required to generate a multilayered bilaterian body plan preceded the entrainment of the growth programs required for macroscopic body size" [49].

Thus, cnidarian-style symmetry and conventional bilaterality would seem to have coexisted and co-evolved in the Ediacara rather than bilaterality evolving from the raidiality. Chen et al's fossils [49] might not, after all, be too far off the trajectory of animal evolution predicted by the notion of bilateral cnidarians with "ParaHoxozoa" [33], "Urmetazoa" [50] or "Planulozoa" [51] as a clade of Placozoa, Cnidaria and Bilateria with Ctenophora its sister group [52].

Haeckel's Legacy

Haeckel's theories may not be au courant, but they cut a wide swath through biology's history, and their traces have not been erased entirely. Biologists puzzle over Haeckel's impact, attributing it to everything from whimsy to the seduction of grand ideas, but Haeckel's continued, if sub-rosa, popularity escapes explanation.

With refreshing candor, D'Arcy Wentworth Thompson, "perhaps the greatest polymath of our century" [53] passed off the gastraea theory somewhat facetiously: "There is… a certain homely phenomenon which goes some way, perhaps a long way, to explain… [the gastrula's] configuration. An ordinary gelatine lozenge, or jujube, has (like the developing gastrula) a more or less spherical form, depressed or dimpled at one side; this is a very noteworthy conformation, and it arises, automatically, by the shrinkage of a sphere" [54].

And Sir Gavin de Beer heaped ridicule on Haeckel who was "led to an erroneous and unfortunate exaggeration of the information which embryology could provide. This was known as the 'biogenetic law' and claimed that embryology was a recapitulation of evolutionary history of its species" [55]. Nevertheless de Beer notes "that the rejection of the 'theory of recapitulation' in no way detracts from the significance for evolution of the information provided by embryology, which demonstrates affinity between different groups and thereby provides the evidence that these groups have descended with modification from common ancestors" [55].

The eminent Oxford cell biologist Henry Harris complained that Haeckel's writings are "permeated with theories that have subsequently been discredited" [56]. But Harris also credited Haeckel

with an "inspired guess" that "the cell nucleus as an indispensable component of a real cell… was responsible for the transmission of hereditary characters; the cytoplasm, he suggested, was concerned with the accommodation of the cell to its environment" [56].

And Stephen Jay Gould, in his famously penetrating fashion, attached an historic explanation to the wide dissemination of Haeckel's "preeminent principle for tracing phylogeny," namely, that biologists incongruously lumped von Baer's "theory of embryonic retention by unaltered inheritance, [to] Haeckel's… theory of active evolutionary change by acceleration of previously adult morphologies into early stages of descendant's ontogenies" [57]. Gould also suggested that Haeckel provided the "central ingredients to [August] Weismann's theory of evolutionary hierarchy" [57].

Rudolf Raff, the well-known evolutionary biologist, provided a scathing review of Haeckel's contribution beginning by condemning Haeckel for doctoring "his drawings [of early stages of vertebrate development] to exaggerate similarities" [58]. Furthermore, according to Raff, the "theoretical idea that phylogeny drives ontogeny was drained of any value by the advent of Mendelian genetics. Garstang argued in 1922 that modifications could be made at any point in development, and that recapitulation has no universal validity. Morgan pointed out explicitly that a new gene could produce its effect at any stage of development. With the escape from strict recapitulation, de Beer proposed that heterochronies of various sorts are the most important engines of evolutionary change" [58]. Nevertheless, Raff admits that Haeckel "remain[s] relevant to us [because w]e need to know the phylogeny of any set of organisms or genes whose evolution we wish to study" [58].

Going Beyond Haeckel

Ultimately, the introduction of Myxozoa into the Metazoa upsets the Haeckelian "apple cart." Arguments over whether myxozoans are primitive cnidarians or degenerate cnidarians spill forth far and wide, but since cnidarians are recognized as metazoans "which came first" (Myxozoa or Cnidaria) becomes academic — evolution has taken care of it. Myxozoans claim to tissue status thus overturns the biogenetic law of recapitulation, the germ-layer theory, and the centrality of the gastrula in metazoan evolution. Indeed, if all the pundits and apologists of Haeckelian versions of development had lived to see the day of Myxozoa's "elevation," they would have to retract their vaunted enthusiasm for Haeckel's sweeping generalizations and may even deign to liberate biology from Haeckel's vaulted rubric.

The first Haeckelian spinoff to be challenged might be the hierarchical concept of tissues. The entry of oligocellular Myxozoa into the ranks of multicellular Eumetazoa challenges notion of the tissue grade of evolution. Refinements on the definition of epithelia (e.g., a requirement for adhesion junctions) once reinforced removing sponges' outer pinacoderm and inner choanoderm from the category of epithelia and separated Porifera (Parazoa) from Eumetazoa (Epitheliozoa [59]), but a maximum likelihood analysis shows that "within the metazoan sub tree, the sponge and ctenophore lineages diverge first, followed by placozoa and cnidarians" [60]. If ctenophores have tissue status, can sponges be far behind? Might Porifera also have broken off the metazoan tree after the creation of "tissue"?

In fact, members of the sponge genus Homoscleromorpha "possess tissue layers resembling true epithelia… [albeit lacking] genuine belt desmosomes" [61], and new molecular data further undermine the distinction between sponges and eumetazoans [62]. Moreover, the mere presence of germ cells would qualify sponges as possessing "tissue," since sponges have spermatozoa and eggs that produce embryos (witness the amphiblastula of Calcarea and parenchymella of Demospongiae). The methods of fertilization may be bizarre, but if apomorphies among cnidarian and myxozoan do not disqualify them from the tissue grade, sponges would also "make the grade." Moreover, sponges' amoebic cells — archeocytes, collencytes, sclerocytes — should qualify as tissue despite their absence from other metazoa.

The tradition of granting tissues to ctenophores [63] would seem based on firmer ground, indeed extending some criteria for tissues [64]. For example, ctenophora's stellate amoebic cells are identified as mesenchymal and said to occupy mesenchyme. These cells lack basal lamellae and are (possibly) linked by gap junctions to each other, amoebic cells and muscle. They produce extracellular material of ctenophore's copious transparent jelly-like substance (mesoglea), and qualify, therefore, as connective tissue, but, unlike typical mesenchymal cells, ctenophora's amoebic cells are multinucleate.

Likewise, ctenophore muscle qualifies as tissue, since it is surrounded by lamina externa and forms a mesenchymal muscle system coming in various sizes, shapes, and types: ribbon-shaped smooth parietal muscle, giant, multinucleated smooth circular, radial mesogleal muscle, and striated tentilla muscles (accessory, entangling tentacles containing colloblasts) And nerves extend into the aboral sensory organ and statocyst and form a subpharyngeal nerve net. Nerves synapse with collaoblasts, the ctenophore-specific cells with eosinophilic granules that glue prey and may have sensory functions. Other specialized tentacle cells include secretory, granular, and spumous, and sensory cells. In addition, photocytes, the source of ctenophores brilliant blue luminescence, are probably stimulated by synaptic contacts. And gonads of both sexes differentiate from endodermal tissue along meridional canals. Gametic tissue as such originates from the gonadal wall lying below the digestive cells.

However, "functional components of the fibroblast growth factor, notch, hedgehog, and the nodal (TGF-β superfamily) pathways, all of which are important in the segregation of mesoderm in different bilaterian forms, are also not observed [in ctenophores]. Other genes known to be involved in bilaterian mesoderm development, such as gli/glis genes, are expressed in neural (but not mesodermal) cells" [33, emphasis added]. One might argue that ctenophore's "mesenchyme" and "muscle" should retain "tissues" status despite their failure to meet criteria based on mesodermal molecules, but how can ctenophore's "nerves" remain nervous tissue having mesodermal molecules instead of ectodermal molecules [64]?

These inconsistencies would seem to place the very notion of tissues "up for grabs." If something as supposedly primitive as a ctenophore tissue is not related molecularly to bilaterian tissue, are biologists to drop the concept of tissue or redefine it in more inclusive terms? Furthermore, the absence of HOX genes would seem to deny ctenophores' claim for a genuine anterior–posterior axis [33]. Must new definitions also be applied to concepts of symmetry? These conundrums presented by claims and counterclaims demand biologists' attention. Clearly premises about tissues and their origins and assertions about kinds of symmetry require reevaluation [46,47].

This reevaluation might begin with Leo Buss' prophetic suggestion for how hereditable variation plays a role in development and the origins of structure: "Cell lineages within a chimeric individual must compete for limited energy resources and for positions in the germ

line. Any activity, such as somatic tissue compatibility, that prevents the invasion or proliferation of such variants serves as a mechanism mediating such competition" [65].

Similarly, Okamura et al. suggested that polar capsules in malacosporean myxozoans "may have arisen by independent incorporation of eukaryotic symbionts into Cnidaria and Myxozoa which then evolved as nematoblasts and capsulogenic cells respectively" [66]. And from a different perspective, I recently suggested [67,68] that symbiogeny, competition, and selection provided a cornucopia of possibilities for the evolutionary departure of tissues and differentiated cells in stem-metazoans with an epithelial/amoeba (mesoderm) construction. Prior to the evolution of mechanisms for self-recognition, cryptozoic multicellular eukaryotes may have formed all sorts of symbiotic, mutualistic, and parasitic relationships some of which later became incorporated into metazoan symbiogens.

But replacing Haeckel's evolutionary determinism with "a chimeric individual" or "metazoan symbiogens" does not preclude evolution's role in development or even the smoothly running drive toward adaptation via the accumulation of mutations. "Science is not confined to a linear temporal succession… [Science proper marks] points of rupture and points of reconnection" [69].

Summary and Conclusion

Integrating Myxozoa in the Metazoa presents a rare opportunity to reevaluate some of biology's ongoing premises. Frequently errors in theory arise from the extension of Haeckel's biogenetic law, germ layers, and the gastraea theories to tissues, organs, and organisms. Despite cogent criticism, Haeckel's theories permeate contemporary versions of the cell theory and inject linear and hierarchical views of evolution into concepts of development and biological structure. Consequently, the presence of tissues is denied to sponges; the mesoderm is fractured with Radiates lacking it and the Bilateria having it; bilateral symmetry is granted to tridermic (triploblastic) animals while denied to didermic (diploblastic) animals. The entry of myxozoan spores to the ranks of Metazoa challenges biologists to remove these inconsistencies, no matter how poetic, from views of evolution, development, and structure. By incorporating Myxozoa into the Metazoa, biologists may finally be forced to forego Haeckelian aphorisms and substitute complexity consonant with contemporary molecular, microscopic, and developmental data.

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