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Biological Individuality: A Relational Reading

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Wholes and Parts: Composite Individuals

Reading these essays brought me back to a time decades earlier, when I was reading *Zen and the Art of Motorcycle Maintenance* during a particularly hot Baltimore summer. That was where I was introduced to the dissection of wholes into structural and functional, anatomical and physiological, components. That was a time when I was introduced to wholism in my history of biology courses while performing cell culture for my PhD in biology. It was when I was gripped by the fights between Huxley and Owen, and when I was learning how classification could be used as a political tool. All these things proved useful in reading these essays.

That time, the mid-'70s, was a time of great turmoil of parts and wholes. The "sixties" had been a time when masses of people dared to contest the traditional boundaries and functions of parts and wholes. Did the government have the right to coerce individuals to fight in a war they did not find virtuous? Did the government have the right to coerce states and citizens to afford civil rights to blacks when it went against their values and traditions? What was a family, now that divorce was common? Civil rights, women's liberation, and the ecology movements saw blacks, women, and nature as a triad demanding to be an interactive part of the community, respected as agents, not seen merely as resources (Gilbert 1979).

Parts and wholes are similarly being contested now. Economic globalization has turned nation-states into inconvenient boundaries; electronic media have realized science fiction fantasies of instantaneous communication across the planet; artificial reproductive technologies have totally altered the definition of the family; industry has fused together science, medicine, and education; and gender and religion have become matters of choice. It is not

an accident that during the past few years there have been so many symposia on part/whole relationships.

Some of the most dramatic reappraisals of part/whole dynamics have been in biology. Twenty-first-century biology threatens to subsume twentieth-century biology into a new paradigmatic framework. The biology of anatomic individualism that has been the basis of genetics, anatomy, physiology, developmental biology, and immunology has been shown to be, at best, a weak first approximation of nature (Gilbert et al. 2012; McFall-Ngai et al. 2013). We are neither anatomic nor physiological individuals. This has been shown consistently not only in invertebrates and in vertebrate model organisms, but also in humans. More than half the cells in the human body are bacterial. Moreover, bacterial products comprise over 30% of our blood metabolites (McFall-Ngai et al. 2013), and they are necessary for our normal physiological maintenance. Kwashiorkor, historically thought of as a protein deficiency disease, has been found to be pathological only if certain bacteria reside in the person's gut (Smith et al. 2013). Pregnancy alters the microbiota of the gut, and these microbes induce some of the characteristic metabolic changes of pregnancy when placed into germ-free mice (Koren et al. 2012). Certain gut inflammatory diseases can be cured by altering the types of bacteria in the intestines or by fecal transplants (Bakken et al. 2011; Chow et al. 2010). So we have come to be considered "holobionts," consortia consisting of the eukaryotic cells plus our persistent bacterial communities (Rosenberg et al. 2007; Gilbert et al. 2012). We are multilineage individuals.

Next, it has also been shown that our bacteria are necessary and expected for our normal development (Gilbert et al. 2012; Gilbert 2013). We are not only the product of the fertilized egg, we are also the product of the bacterial consortia that colonize us. Certain sugars in mother's milk are digested not by baby, but by the baby's bacteria. Moreover, the bacteria have evolved ways of colonizing (in the most literal way) the body. In mice, the blood vessels taking food from the intestine don't form properly without bacteria, nor do the gut-associated lymph nodes. The bacteria accomplish this by secreting factors that induce gene expression in the mammalian intestine (Hooper et al. 2001; Becker et al. 2013). This induction is expected and normal. In some genes, 90% of their expression is induced by bacteria. In zebrafish, bacteria induce the normal division of intestinal stem cells. Without these bacteria, not enough stem cells are made, and the intestine lacks many of its most important cell types (Rawls et al. 2004). The life cycle of an organism requires the life cycles of other organisms (Fig. 12.1). We are not individuals by developmental criteria.

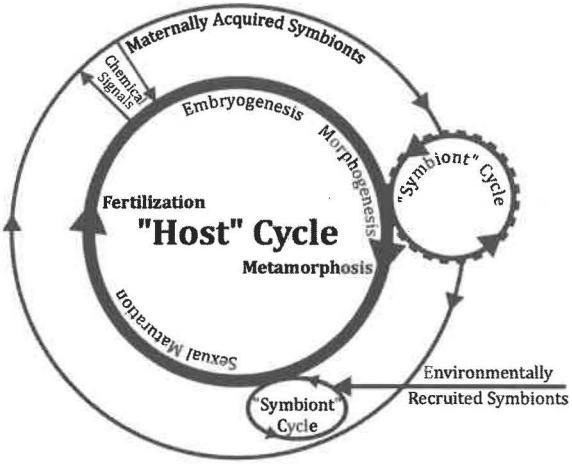

FIGURE 12.1. A holobiont life cycle. The "traditional" life cycle of the animal is shown by the dark black circle. This is supported by the life cycles of symbionts acquired from the egg (thinner circle), and symbionts acquired from the environment. The symbionts can provide chemical signals necessary for early development and protection of the embryo, while the "host" can provide signals to sustain and differentiate these symbionts. Symbionts can be essential for completing host development (as in the mammalian gut) and/or traversing developmental stages such as metamorphosis, as shown by the "gear" form of the symbiont life cycle. They can also provide chemical signals for larval settlement and facultative morphogenesis. (Drawn by David Gilbert after a draft from the 2011 NESCent conference on the origin and evolution of animal-microbe interactions.)

And we are certainly not individuals by genetic criteria. There are about 160 major species of bacteria normally resident on and in our bodies, and the human microbial genome has 150-times more genes than our zygotic genome. In many invertebrates, symbiont genomes are a source of selectable genetic variation. The phenotype of pea aphids—their color, their thermotolerance, and their resistance to parasitoid infections—depends on alleles of their symbionts (Dunbar et al. 2007; Oliver et al. 2009). Many invertebrates receive their symbionts directly from the egg. Indeed, the symbionts are packaged into the egg along with ribosomes, mitochondria, and mRNAs. Mammals and most other vertebrates receive symbionts by infection, primarily from the mother, during pregnancy and parturition (Funkhouser and Bordenstein 2013). We go from one symbiotic system (that of the mother) to another (that of symbionts).[1] Thus, the symbionts must be considered as a third genetic system along with the nucleus and mitochondria (Moran 2007; Gilbert 2011). And birth, which has long been conceived as the creation of a new individual, is actually the continuance of community (Gilbert 2014)! We are not genetic individuals.

In the old paradigm, our genetically pure body was protected against mi-

crobial assault by the immune system. Indeed, we lived in a voracious microbial world that would devour us if it were not for the immune system. This is why we received inoculations and booster shots, and this fact was driven home relentlessly and mercilessly by the AIDS epidemic. The discipline of immunology had been called "the science of self/non-self discrimination" (Klein 1982). In this view, the immune system consists of defensive "weaponry," evolved to protect the body against threats from pathogenic microbes.

In a fascinating inversion of this view of life, recent studies have shown that an individual's immune system is in part created by the newly acquired microbiome (see Pradeu 2012). In vertebrates, the gut-associated lymphoid tissue is specified and organized by bacterial symbionts (Rhee et al. 2004; Lanning et al. 2005). When symbiotic microbes are absent in the gut, the immune system fails to function properly and its repertoire is significantly reduced (Lee and Mazmanian 2010; Round et al. 2010). Similarly, Hill et al. (2012) have shown that microbial symbionts provide developmental signals that limit the proliferation of basophil progenitor cells and thereby prevent basophil-induced allergic responses. Lee and Mazmanian (2010) conclude, "multiple populations of intestinal immune cells require the microbiota for their development and function."

The immune system, therefore, appears to be more of a "passport control agent" or even a "bouncer" rather than a defensive army posted to keep the zoological organism "pure." Indeed, the immune system actively recruits the symbionts. The antibodies produced in the intestinal crypts might actually play a "critical role in establishing a sustainable host-microbial relationship" and might be involved in "the creation of an optimal symbiotic environment on the interior of the PPs [Peyer's patches]" (Peterson et al. 2007; Obata et al. 2010). Thus, the immune system, built, in part, under the supervision of microbes, does not merely guard the body against other hostile organisms in the environment. It also mediates the body's participation in a community of "others" that contribute to its welfare (Tauber 2000, 2008).

Ideologically, this signals a huge change. No longer is biology a matter of "us versus them," "eat or be eaten." The existential and Darwinian mode of defining one's self as "being against all others" has been replaced by a more Harawayan and Deleuzian notion of us "becoming with the other."

So if there is no genetic, developmental, immunological, anatomical, or physiological individual, what is "individual selection" in evolution? Can it be that organisms are selected as multigenomic associations? Is the fittest in life's struggle the multispecies consortium, and not an individual of a single species in that group? This possibility has been raised by Bateson (1988), who

has argued that "the outcome of the joint action of individuals could become a character in its own right." Since it replicates with selectable variation, the holobiont may be an important level of evolutionary selection.

This moves the biological discussion of symbiotic associations into the arena of "group selection." Most discussions of group selection, however, are not germane here, because they assume that the group in question is composed of members of a single species. A holobiont is a team of different species. However, one important concern is relevant to our discussion of the holobiont: cheaters. The major problem for all group selection theories (and the groups, themselves) are potential "cheaters," those lower-level members of the group that would proclaim their own autonomy and that would multiply at the expense of the others. The problem of "cheaters" then has to be solved in such a way that associates in a symbiotic relationship are under the social control of the whole, the holobiont (Stearns 2007).

This strong socializing and unifying force is found in the immune system (see Burnet and Fenner 1949; Tauber 2000, 2009; Ulvestad 2007; Eberl 2010; Pradeu 2010). If the immune system serves as the integrating system, keeping the animal and microbial cells together, then to obey the immune system is to become a citizen of the holobiont. To escape immune control is to become a pathogen or a cancer. Cheaters are destroyed by the immune system. It is now possible to envision selection as more like team competitions than individual competitions. An American football team may have the best quarterback in the league; but it will not get into the playoffs if its other members can't defend him or catch his passes.

Thus, the symbionts are welcomed into the animal body and are regulated by the immune system. As part of the body, the microbes not only help the body develop and remain physiologically intact, they also provide a secondary system of genetic transmission from parent to offspring. They can provide selectable variation from generation to generation. Moreover, in addition to providing this selectable variation, microbial symbionts may have played, and continue to play, other roles in animal evolution as well (Margulis and Fester 1991). Animal speciation may be mediated, in part, through the ability of microbes to induce reproductive isolation. This can be achieved through symbiont-induced cytoplasmic incompatability between hybrids (Brucker and Bordenstein 2012, 2013) or by symbiont-induced mate selection (Sharon et al. 2010).

Last, we may never have been "pure" animals, innocent of symbionts. We must remember not only that eukaryotic protists were created by endosymbiosis, but that the protist world is full of complex symbioses (Margulis 1981;

Margulis and Fester 1991; Sapp 2009). Some of these microbial symbioses may have led to multicellularity. The choanoflagellates are unicellular protists that are the sister group of the animals. However, these unicellular forms can be converted into multicellular entities—complete with an extracellular matrix and cytoplasmic bridges between cells—by a specific bacterium that often coexists with them. If the protists are cultivated in filtered water, they remain unicellular. If the bacteria are added back, they can form multicellular entities (Dayel et al. 2011; Alegado et al. 2012). Thus, bacteria symbionts may have been important in initiating multicellularity, the ultimate part/whole dialectic in biology.

Science News Magazine's December 28, 2013, issue ranked "microbes ascendant"—the holobiont idea of organisms—as the top story in science for 2013. Its next issue had four stories on how bacterial symbiosis is redefining life. The biology of the twenty-first century will have a different perspective on parts and wholes.

And that's only the beginning. Biology is changing in other ways, too, and these changes are renegotiating the parts/whole distinction. Systems biology sees information flow as a common denominator of all biology, seeking to place all biological disciplines under a common rubric. This, of course, has been a common strategy for dominance in biology. However, for several reasons, the boundaries of the biological disciplines have become remarkably porous. Indeed, it's difficult to justify calling anything "interdisciplinary" or "transdisciplinary," because there are no such disciplines. Biology has become—to use a biological word—syncytial. Just as there are several nuclei within the cytoplasm of a syncytium (such as found in certain muscles and placental cells), there are centers of professional power and training within the common cytoplasm that is biology. So there are good reasons for biologists to speak about parts and wholes. The relationships we had learned are being transformed into something new and very different, and perhaps much richer and more profound.

Relations with these Chapters

The chapters in this volume are the constituent "parts" of this book, but reading them collectively allows them to interact with one another and with this new context I have been discussing. I'll discuss them here, not as a review (that would make this another and very large chapter), but as a conversation. If the chapter is meaningful to a reader, then the "reader's portion" is not passive, but rather an actively engaged interaction. One can even say that the reader and text form a system, and that the text has no meaning outside that

system. So I will allow you, the next reader, to selectively eavesdrop on some of the conversations I've been having with these chapters.

And what better place to start than with Scott Lidgard and Lynn Nyhart's discussions in chapter 1 about the contexts framing the part/whole debates. The body politic metaphor acquires new dimensions in our discussions of symbionts. Just as modern immunology was framed during the Franco-Prussian War, where boundaries and defensive weaponry were paramount, symbiosis theory is framed during a time of massive migrations of people across borders. In some instances, the migrations are encouraged (leading, for instance, to Chinese and Indian information technologists coming to northern Finland to work for Nokia); and in other instances, the migrations have been forced by the combination of ecological and political deterioration (leading, for instance, to Islamic populations migrating from Africa and Asia to Europe and the Americas). In such sociopolitical contexts, who is foreign and who is a citizen takes on a particular immediacy. Are symbionts foreigners to a racially pure body (descended from a single cell)? Are the symbionts legal resident aliens, green-card holders whose work visas are checked constantly by an especially sensitive immune system? Or are the symbionts full citizens of a multilineage polity that help generate the body as a normal function? Moreover, the debates about what criteria enable the holobiont to be considered an individual are far from over (Gilbert et al. 2015; Moran and Sloan 2015). The discussion of parts and wholes must be seen as occurring within a sociopolitical context that is evident in our daily lives, in our political rhetoric, and in our front-page headlines.

The chapter on the alternation of generations by Lynn Nyhart and Scott Lidgard (this volume) provides a deeper historical context, showing that those nineteenth-century questions of what constitutes individuality are still with us today. It was Thomas Henry Huxley who (contra Richard Owen, of course) defined the individual as the progeny of the fertilized egg, and it made me wonder if Huxley knew about the work of the embryologist Robert Remak on the origin of cells by division of preexisting cells, being performed at about the same time. Huxley had a penchant for seeing life in its embryological context. He even said that "evolution was not speculation but a fact; and it takes place by epigenesis" (1893), and he instructed Darwin (while the latter was writing the *Origin*) that differences between organisms "result not so much of the development of new parts as of the modification of parts already existing and common to both divergent types." Huxley's relationships of parts to wholes are interesting on many levels, not the least in that they change and remain integrated. This will lead to a notion of homology that is still being hotly debated today.

Once the body was seen as a collection of asexually generated cells, the link could be made to plants not only in terms of cell structure but in terms of reproductive modes. One of the great debates on individuality centered on the alternation of generations, where a sexual generation would produce an asexual generation (often with a different body form), which would produce a new sexual generation. Cnidarian polyps and medusae were discovered to be part of the same life cycle. Here, many biologists considered such an animal not just one distinct "individual," but two, or even more. Steenstrup, Owen, Rudolf Leuckart, Johannes Müller, and others took up the challenge of relating parts to wholes in the complex worlds of colonial plants, jellyfish, and corals, eusocial insects, and parasites. Botanists like Matthias Schleiden, Alexander Braun, and Wilhelm Hofmeister struggled with the nature of plant individuality and alternation of generations. Steenstrup saw that a life cycle comprised multiple generations of "individuals," and Leuckart was particularly adept at making his arguments that no individual of a sexually reproducing species could fulfill all the functions of the species itself (Nyhart and Lidgard 2011). So no animal or plant of that sort was a "perfect" specimen. Leuckart also brought up the notion of "polymorphic" individuals, each with its own task in the division of labor.

Indeed, as we study more organisms and as we see how lineages interact, the questions of individuality are more with us than ever. Take *Mastotermes darwinensis.* Is a worker termite an individual? Or is it the hive, since only the queen is fertile? Or is it even the termite, since it can't digest wood without its bacterial symbiont, *Myxotricha.* But *Myxotricha* is itself a composite of at least five different species, none of which exists except in such an association and in the gut of these termites (Margulis and Sagan 2001). And the "individual" changes as it develops. The notion of the life cycle as the "individual" has returned to evolutionary discussions through the writings of John Tyler Bonner (1995). This has important ramifications if the "life cycle" is that of the holobiont, with its persistent communities of microbes.

In his great synthetic work, *The Cell in Inheritance and Development* (1896), E. B. Wilson wrote, "There is at present no biological question of greater moment than the means by which the individual cell-activities are co-ordinated, and the organic unity of the body maintained; for upon this question hangs not only the problem of transmission of inherited characteristics and the nature of development, but our conception of life itself." The nineteenth-century questions of what constitutes an individual have been recast in twenty-first-century terms and have again moved to the center of biology.

At one end of the symbionts spectrum are the parasites, and Michael Os-

borne (this volume) has provided a fascinating analysis of the evolution of the parasitic idea in both biology and sociology. The formulation and separation of these ideas took place during the Third French Republic by such eminent scientists as Claude Bernard, Edmond Perrier, and Raphaël Blanchard. Originally, the term did not carry negative connotations and denoted a person who ate alongside a more senior person. (Although Darwin would add his barnacles to the debate, it's difficult to describe him as Captain Fitzroy's parasite.) In biology, the usage became restricted to a member of a different species who lacked something that the host provided. In society, though, a parasite became defined as a member of the same species who "leeched off" his conspecifics. The social context is the Third French Republic, where Solidarism undergirded the social contract, where there was debate concerning the status of the French colonial possessions and peoples, and where biological parasites persisted in preventing colonial expansion.

As these studies of symbiosis were being performed, so was the analysis of metabolism; and often by the same people. Hannah Landecker (this volume) provides an elegant analysis of one of the most fundamental notions of what constitutes an organism: metabolism. Metabolism is nothing less than the ability to preserve the identity of the whole by continually changing its component parts. Because metabolism enables the stabilization of an "individual" by permitting the organism to retain constancy while constantly changing its component parts, "individuals" are not just material things, but always relational processes in time as well (Gilbert 1982). That's what distinguishes us from machines, and that's what our machines look for when they go to Mars to determine if there is "life" there. Metabolism is the paradoxical foundation for existence. Levinas (1969) joyfully celebrates this interconversion of one life into another: "Nourishment as a means of invigoration, is the transmutation of the other into the same, which is the essence of enjoyment: an energy that is other, recognized as other . . . becomes, in enjoyment, my own energy, my strength, me."

Thomas Mann (1969 [1924]) viewed metabolism more pessimistically: "What then was life? It was warmth, the warmth generated by a form-preserving instability, a fever of matter, which accompanied the process of ceaseless decay and repair of albumen molecules that were too impossibly complicated, too impossibly ingenious in structure . . . It was not matter and it was not spirit, but something between the two, a phenomenon conveyed by matter, like the rainbow on the waterfall, and like the flame."

In 2013, a new notion has come into being: "co-metabolism." This is the idea that the metabolic flux that enables us to persist is in fact, a flux between us, our diet, and our symbionts (Smith et al. 2013). Co-metabolism is criti-

cal for our physiological homeostasis. Metabolism is now being taken out of the context of "eat or be eaten," where, as Landecker notes, it helped build "commonly held notions of individual organisms as alone in the world." It is presently being placed into a context of messmates. Indeed, the word "commensal" means just that. In the holobiont, we see an incredible play on the historical opposition between life as lineages and life as metabolically self-sustaining wholes (Gilbert 1982; Dupré and O'Malley 2009). The metabolic entity—the holobiont—is made up of several interacting lineages.

Andrew Reynolds's (this volume) sociological perspective on cell-cell communication shows that this idea has become central to the integration of parts and wholes in biology. Indeed, Reynold's chapter on the integration of parts and wholes through communication gives us a vantage point to look at the roles of social metaphors in biology. Endocrine factors are the hormones that act globally (traveling through the blood from one group of cells to the body) to integrate the entirety of the organism/polity. Paracrine factors, influencing nearby cells through the intercellular fluid, act in their local neighborhoods; while juxtacrine factors (on cell membranes) interact only with adjacent cells. Together, these signaling molecules allow cells to act globally or locally to form organs and keep them intact. One of the generalizations that embryologists have made is that cells lead double lives. As "adult" cells, they have a specific function, such as making insulin, pumping fluid, or being transparent to light; but as "young" cells, they are in the construction trades. They produce paracrine factors that build organs from cells. They are both the material and efficient causes of the embryo, and the embryo builds itself from immature cells. In the development of eyes, the cells that induce the lens to form are the cells that will later give rise to the retina.

The embryo as "cell society" has been a critically important metaphor in embryology, and one of the extrapolations of this metaphor concerns who rules this body politic (Gilbert 1988, 1992). Interestingly, the three major types of model organisms in developmental biology reflect the three major models of how the body politic is governed: realist, liberal, and constructivist (see Walt 1998; Copeland 2000). The genetic model systems in developmental biology approximate the "realistic" view of the body politic. The genes are the central authorities running the show. The embryological model systems of developmental biology are like the "liberal" view of the body politic. There are several cellular centers of authority, and interactions between these centers make possible unique and emergent institutions. Last, the evo-devo/eco-devo model systems of developmental biology model are like the "constructivist" model of the body politic. Here, the body is generated not only

by internal factors but also by the interactions of that body with its biotic, cultural, historical, and environmental milieu.

I am particularly drawn to Ingo Brigandt's chapter (this volume) that argues that processes are bodily parts, just as structures are. I think this is a critical point to make, and one that brings the structure/function question squarely into the part/whole controversy. This new perspective on considering functions as parts allows Brigandt to see the intimate relationships between structure and function. It also allows us a new perspective on homology through evolutionary time. I think that one of the reasons we have been distracted from this view is the way that processes are represented graphically: all those arrows. But the arrows, denoting temporal sequence and causation, are actually showing stereocomplementary structural fit (Gilbert and Greenberg 1984). Just like bones fitting together, just like the lungs having a space on the left-hand side for the heart to fit into, the proteins of a signal transduction pathway must bind together in a stereocomplementary pattern. Brigandt is able to relate "activity" and "function" in ways that allow us to see the homology of related activities, independently from their functions.

What constitutes the natural part also becomes a question. The construction units of the body need not be the same as the adult anatomical units. Flies have parasegments, and vertebrates have rhombomeres and medial rib modules. These construction units are not seen in the adult. It may be that what the embryo considers as a natural unit is what the enhancer "perceives." There is an enhancer for gene expression in the medial rib and in each hindbrain rhombomere. And exaptation is the rule. Brigant's view of a homologue as a "unit of morphological evolvability" is a great point for discussion, because it leads to considering exaptations and their roles in evolution.[2]

And like the questions brought up by other chapters in this book, this philosophical chapter is intensely relevant to today's biology. For those of us who work on the origin of the turtle shell, homology is a huge issue, and questions of connectivity, embryological origin, and altered function that Brigant addresses are at the center of these investigations (Lyson et al. 2013; Cebra-Thomas et al. 2013).

And this problem of turtle bone homology has been one that has been discussed brilliantly by Olivier Rieppel (2012), but not here. In this volume, Rieppel discusses a critically important, but much neglected, historical episode in the debates over parts and wholes and their extrapolation from biological entities to social entities. Focusing on Martin Heidenhain's biological notion of nested structural hierarchies, enkapsis, Rieppel analyses the strange history of wholism in Nazi Germany. This was an area where wholism and

Goethe's notion of multiplicity in unity were used both by Jewish mandarin scientists and by Nazis constructing a new German biology for the Third Reich. (*Bildung und Kultur* were the watchwords of the Reform Jewish movement, and Jews swelled the ranks of the Goethe Society [Mosse 1997].)

The use of wholism by the Nazis and the destruction of the scientific infrastructure of central Europe during World War II (including the Prater Vivarium in Vienna) effectively wiped out a tradition of wholistic biology that attempted to counter the reductionist tendencies of Anglophone science. This paper tries to show how important this tradition was to the biology of central Europe. In America, where genetics, cell biology, and an engineering approach to the science predominated, this perspective was seen as a minor variant favored by Nazis. Wholism is a war casualty; and like most refugee communities that fled the Nazi-occupied areas, it never had the same vitality or centrality that it had before "Blut und Boden" became standard-bearers for lineage and environment.

The biological idea that the whole preceded its parts can be found in Kant's Third Critique, and it became a normative part of embryology, which was, after all, a predominantly German discipline. Charles Otis Whitman (who received his PhD in Leipzig) was one of the most influential American embryologists in the early 1900s, and he made this a fundamental principle of the developmental biology he taught at the University of Chicago and at the Marine Biology Laboratories. The notion that the parts form the whole simultaneously with the whole defining the function of the part has been a major paradigm of animal development, and can be seen as a major concept in the work of Hans Spemann and Paul Weiss. This was a doctrine that did not have to be National Socialist, even if extrapolated into society, which Whitman did, on a more republican basis.

But extrapolated into the German *Volksgemeinschaft* by people like August Thienemann, it meant that an individual person would have the moral obligation to sacrifice his life for the greater good of the whole. This was the morality of Nazi Germany, but it can also be said to be the morality of any country during war. It is the role of governments to remind their citizens that their country persists thanks to those who made "the supreme sacrifice." The part/whole dichotomy is at its most existential summit here. E. O. Wilson (2012) recently looked at this part/whole controversy in evolutionary biology. He noted the paradox that within groups, selfish individuals will outcompete altruistic individuals, but that between groups, those groups with altruistic individuals will be favored over those whose individuals do not cooperate. There will be selection, he postulates, on genes promoting both behaviors.

Therefore, "the victory can never be complete; the balance of selection pressures cannot move to either extreme. If individual selection were to dominate, societies would dissolve. If group selection were to dominate, human groups would come to resemble ant colonies." It seems we inherit, as the Talmud declares, a Yetzer Ra impelling us to selfish competitive acts as well as a Yetzer Tov, propelling us to social cooperation. There will always be tension between individuals and society, between love and duty. So we can expect great suffering as well as great literature.

But the genome does not always give the same orders. The directives from the nucleus are modified by information coming from the environment. The genome is not a text to be decoded, but a composition to be interpreted (Gilbert and Bard 2014). Every organism is a performance of the genome, and each performance is a new interpretation. This perspective is particularly appropriate in light of recent research on Predictive Adaptive Responses (PAR). According to the PAR view (Gluckman and Hansen 2004), the genome produces receptors that enable it to monitor the environment. The organism has developmental plasticity such that the phenotype produced is responsive to the environmental signal. However, the signal may or may not be a true signal of the actual environmental change. So a photoperiod getting smaller each day may tell an organism that it should change its pelage from brown to white. Winter is coming. But if it doesn't snow, the white pelage is dangerously sharp against the rocks. Similarly, the mammalian fetus receives signals from maternal nutrition concerning the caloric content of its environment. If provided a poor diet in utero, gene expression in the liver becomes that making a protein suite that stores calories. If there is a "mismatch" and such an infant is born into a well-nourishing world, that infant has a much greater risk of developing obesity, diabetes, and congestive heart failure due to the faulty prediction made in utero.

The notion that predictive testing and planning, from the subatomic to the social level, are the driving forces of sustained individuality is also interesting from the view that humans are planning animals and that fantasy is an important force in human social evolution. Humans can plan strategies by imaging scenarios that never happened and may never happen. We can imagine alternative possibilities and plan to maximize our continuity in the different environments. Our brain can even fool itself by having the body physiologically react to imaginary conditions (Gilbert 2003). This is the basis of entertainment and certainly of sexual fantasy. Humans are self-consciously planning animals. Information theory leaves open the mechanisms by which the modular interactions make possible such long-term exploring, and the

mechanisms would be expected to be different at each level of organization, going from atomic-level constraints (see Deacon 2011) to social planning and campaign strategies.

Beckett Sterner's paper on the mechanisms of cell type inheritance continues the discussion of environmental and internal mechanisms of hereditary control. Here, he introduces the concept of the "demarcator," either a material agent or a causal process that is responsible for integrating the parts or the organism and its life cycle together. Biological entities should be able to be distinguished based on their possession of such demarcators. This concept, Sterner asserts, is still being developed, and it extends the notions of overlap and scaffolding used by Wimsatt and Griesemer (2007). Thus, inheritance could be achieved either by pushes from within (*material overlap* between generations) or influences from without (*scaffolding* directing the phenotypic inheritance). Examples from unicellular organisms—both prokaryotic and eukaryotic—bring together these two modes of inheritance in one scheme. Indeed, it is reminiscent of the "alternation of generations" project that sought to unite asexual and sexual inheritance schemes into a common mode. Indeed, the life cycle is crucial in these discussions of inheritance.

It seems that symbionts use both the scaffolding and material overlap means of propagating phenotype, and that these are not mutually exclusive (Chiu and Gilbert 2015). Many arthropods receive their symbionts primarily through their mother's oocyte, where it has been sequestered. Vertebrates and many invertebrates usually acquire symbionts through infection. This infection can be at the moment of egg laying or parturition; but it is usually from the mother's cache of symbionts, but with contributions from the entire community (Funkhouser and Bordenstein 2013). As mentioned above, symbionts can be the source of hereditable variation as well as reproductive isolation. It will be interesting to see how the demarcator idea plays out in complex symbiotic life cycles where individuality is lost or gained (such as in salamander kleptogenesis [Bogart et al. 2007] and angler fish fusions [Pietsch 2005]).

Some of the most interesting scaffolds, though, involve the inheritance of behavioral phenotypes. Meaney's laboratory has shown that anxiety in rats can be inherited; but only through a complex interaction of what could be interpreted as both material and scaffold. Weaver and his colleagues (2004, 2007) showed that anxious rats had high levels of corticosterone. This was due to the absence of the gluocortocoid receptor in the brains of these rats. This receptor mediates the negative feedback loop, downregulating corticosterone production. The receptor wasn't there because the enhancer regulating that gene's expression in the brain was methylated. And methylation was

permitted in that enhancer only in rats that did not receive adequate maternal care. In the rats that had received maternal care, this same region of DNA was unmethylated, allowing the glucocorticoid receptor gene to be expressed in the brain. So rats without adequate maternal care become more anxious. And what do female rats having this condition do? They give their pups less maternal care. Cross-fostering rats between anxious and non-anxious mothers changes the methylation and the anxious phenotype. Here, behavior controls gene expression, and gene expression helps generate that behavior. The behavior makes the scaffolding.

A similar behavioral-epigenetic scaffolding has been seen in rat sexual behaviors (Champagne et al. 2006; Cameron et al. 2008). Here, high levels of maternal care also cause the demethylation of the regulatory regions of the estrogen receptor genes, enabling their expression in the MPOA region of the brain that is associated with sex-specific behaviors. Those female rats with low estrogen receptors in the MPOA region of the brain have a more receptive sexual phenotype than the rats who had been licked and groomed thoroughly when young. They also do not lick and groom their offspring, thus continuing the inheritance of the trait. These differences, moreover, are not "good and bad," "normal and pathological." Rather, they are variations that may become advantageous in different environments. This is not a pathology, but a norm of reaction. But what is important is that the behaviors are hereditary despite there being no mutational difference in the DNA between the variants. Maternal behavior can create a scaffolding that allows inheritance.

Matthew Herron's paper (this volume) deals directly with one of the major evolutionary transitions, from unicellularity to multicellularity, as shown by the Volvocales. His contribution lays out that there are transitions within the major transitions, and that the progression from one level of individual to another is not a simple binary step. Rather, there are multiple steps, and both genetic and physical parameters appear to be regulating the transitions. In the volvocine algae individuality appears to be partitioned along three levels of the biological hierarchy: cells, colonies, and clones. In each, one sees the principle put forth by Queller and Strassman (2009) that the new individual is characterized by high levels of internal cooperation and low levels of internal conflict. In addition to genetic homogeneity and the single-cell bottleneck of a zygote, *Volvox* "clones" also become individuals through division of labor into distinct soma and germ cells, retention of cytoplasmic bridges between cells, the formation of a common extracellular matrix holding the cells together, and the establishment of organismal polarity through the rotation (on the cellular level) of the basal bodies that produce the flagellum.

In some species, there is even a gastrulation-like movement in which all the cells participate. Clones in different groups of Volvocales have one or more of these marks of individuality.

So is a cancer a "zooid," Huxley's term for parts of colonies that are like individuals but not fully so? There have been some interesting speculations on cancer as an atavistic return to a colonial stage of individuality. Weinberg (2007), for instance, claims that the genes responsible for cellular cooperation during the origins of multicellarity are those whose malfunction causes cancer. Davies and Lineweaver (2011) explicitly claim that cancer is an atavistic condition when genetic or epigenetic instructions "re-establish the dominance of an earlier layer of genes that controlled loose-knit colonies of only partially differentiated cells." Since tumors are often clonal, but develop genetically or epigenetically distinct subclones (for instance, cancer stem cells), it would be interesting to think about a metastasizing cancer as ramets, each having a similar, but distinct genetic or epigenetic identity.

With Snait Gissis' paper (this volume), we come to the nineteenth-century social philosopher (and sometime biological theorist) Herbert Spencer and the explicit analogy of the society being a body politic. But what I am impressed with is what kind of body politic it is. Spencer modeled his society on the embryo. Specifically, he based his views on those of Karl Ernst von Baer, who described development as the change from homogeneity to specialization. "The development of a society as well as the development of man and the development of life generally," said Spencer (1851, 319), "may be described as a tendency to individuate—to become a thing." At the close of *Social Statics*, Spencer wrote, "Yet this phrase of von Baer, expressing the law of individual development, awakened my attention to the fact that the law which holds of the ascending stages of each individual organism is also the law which holds of the ascending grades of organisms of all kinds." And in an 1864 letter to George Lewes, Spencer (1906) claimed, "if anyone says that had von Baer never written, I should not be doing that which I am now, I have nothing to say to the contrary."

I think Spencer prescient in this respect. His people have dual functions—they are parts that make a whole, and they are defined by the whole. Thus, as Gissis notes, Spencer had a hybrid view of individuality, which could be viewed either as "collective individuality" or as a "collectivity of individuals." So it is with the embryo, and the fates of embryonic cells come by their lineage, their interactions with other cells, and their interactions with the environment. The cells make the embryo, and the embryo, in relationship with the environment, makes the cells. Parts and wholes are in relationship from atoms through societies. If societies are like organisms, they are not adults,

they are embryos. If Gaia exists, she's not an adult, either. Without doubt, she is an embryo.

The parts contribute to the whole and the whole determines the parts. The chapters here will interact with each other and with the mind of the beholder in ongoing dialogue. There will be selection and discernment, and there will be the "becoming with," the growth of the whole into a new whole through the interaction with something new. It's been a pleasure and a privilege to be one of the first people who interact with these chapters.

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Notes to Chapter Twelve

1. I wish to thank Martin Jacobs for this observation.

2. So I must tell the story of my favorite exaptation. A year or so ago, I asked the chief science librarian, Meg Spencer, "Why do we have all these rows of *Biological Abstracts*, going back to the 1920s. I'm sure nobody's looked at them since we got internet service." She looked at these rows of unused heavy tomes and said, "Soundproofing. It would take $500 worth of curtains to do what these books do." All the information catalogued in those volumes is now worthless. Rather, the physical properties of the paper have become critical for their preservation in the library. Same object, different pathway of relationships.

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