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SPOTLIGHT

Symbiosis of disciplines: how can developmental biologists join conservationists in sustaining and restoring earth's biodiversity?

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ABSTRACT

What can developmental biology contribute toward mitigating the consequences of anthropogenic assaults on the environment and climate change? In this Spotlight article, we advocate a developmental biology that takes seriously Lynn Margulis' claim that 'the environment is part of the body'. We believe this to be a pre-condition for developmental biology playing important roles in conservation and environmental restoration. We need to forge a developmental biology of the holobiont – the multi-genomic physiologically integrated organism that is also a functional biome. To this end, we highlight how developmental biology needs to explore more deeply the interactions between developing organisms, and their chemical, physical and biotic environments.

KEY WORDS: Developmental biology, Restoration ecology, Sustainability, Holobiont, Symbiosis

Introduction

In the 1800s, embryology was an outdoor discipline. Indeed, the person who invented the term 'ecology', Ernst Haeckel, was an embryologist. But changes in techniques (microtome sectioning, staining and experimentation) and academic reforms (pressure to publish) brought embryology inside. In 1880, Haeckel despaired that the next generation of embryologists 'will only know cross-sections and colored tissues, but neither the entire animal nor its mode of life'. Reviewing this transformation of embryology, historian Lynn Nyhart concluded, 'A curious and unintended result of this line of research was an increasing neglect of the living organism, which caused a de facto separation of the study of development from the consideration of its relation to the conditions of existence' (Nyhart, 1994). The life cycle and its ecological context would be largely ignored by embryologists for generations to come.

Presently, biology has changed, and the planet has changed. Just as the microtome and Romanowsky staining techniques altered the directions of embryology in the late 19th century, the more recent inventions of PCR and high-throughput RNA analyses have informed us of biological relations that had previously been unknown and unstudied. Moreover, the planet is now experiencing its 6th major extinction: a deterioration of biodiversity caused by our technological matrix. Global temperatures are rising, the ocean is becoming more acidic, habitats for animal and plant life are being destroyed, and monocultures and the poisons that sustain them are replacing natural environments. Nature has been so transformed that between 75 and 95% of terrestrial biomes have been reshaped by humans (Ellis, 2010).

With biology and the planet so changed, we wish to advocate for our field's return to the environment with our molecular knowledge and visualization techniques. We wish to advocate a developmental biology that takes seriously Lynn Margulis' claim that 'the environment is part of the body' (Margulis, 2006). If this statement is true, then developmental biology – the science of body construction – must expand. It must become much more ecological in scope, embracing developmental plasticity and developmental symbiosis as whole-heartedly as it does developmental genetics. Similarly, ecology must become more developmental in its questions, embracing whole life-cycle developmental processes. This view of life changes our perspective on environmental agency and on how biodiversity is to be conserved.

Our goals in this paper are: (1) to convince developmental biologists that they need to pay more attention to the environment; and (2) to explain why developmental biology is important for addressing the impacts of environmental degradation and climate change, particularly on loss of biodiversity. We begin by presenting five new principles and some evidence for them. We then highlight how development biology and ecology could come together to become scientific allies in conservation and restoration biology.

Organismal development is regulated by the interactions of zygotic cells and acquired symbionts

Developmental symbiosis, 'sympoiesis', is almost universal (Gilbert et al., 2012; McFall-Ngai et al., 2013; Bosch and Hadfield, 2021). The cow is not born with a functional rumen. The rumen is formed when the bacteria residing in that area of the gut acquire plant fiber when the calf is weaned (Chiu and Gilbert,

Advocating developmental biology
This article is part of Development's Advocacy collection – a series of review articles that make compelling arguments for the field's importance. The series is split into two: one set of articles addresses the question 'What has developmental biology ever done for us?' We want to illustrate how discoveries in developmental biology have had a wider scientific and societal impact, and thus both celebrate our field's history and argue for its continuing place as a core biological discipline. In a complementary set of articles, we asked authors to explore 'What are the big open questions in the field?' Together, the articles will provide a collection of case studies that look back on the field's achievements and forwards to its potential, a resource for students, educators, advocates and researchers alike. To see the full collection as it grows, go to: https://journals.biologists.com/dev/collection/59/Advocacy.

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2020). Then, metabolites from the bacteria induce new gene expression in the gut, forming a rumen. Similarly, a *Euprymna* squid is not born with a functional light organ. The interaction of appendages on the squid ventrum with *Vibrio* bacteria causes the morphogenesis from an embryonic state to a fully functional light organ (Essock-Burns et al., 2021). In mice, *Bacteroides* bacteria acquired during birth activate angiogenin 4 gene expression in Paneth cells of the newborn mouse gut, causing the mesenchyme surrounding the gut to form blood vessels (Stappenbeck et al., 2002). In the nematode *Bugia malayi*, *Wolbachia* bacteria are responsible for the polarity of the second mitotic division of the embryo (Landmann et al., 2014). We literally become one with others (Haraway, 2016). Symbiotic cooperation between organisms is as much a 'co-author' of evolution as natural selection (Zook, 2015; Carrier and Bosch, 2022).

The organism is a holobiont, a consortium of zygote-derived cells plus its symbiotic microbes (Margulis, 1991; Theis et al., 2016). The microbes are integrated into the physiology of an organism in a complete way. Such 'co-metabolism' between symbiotic partners (both microbes and the eukaryotes within which they live) is well-documented in mammals, arthropods, mollusks and even hydrothermal vent worms. For example, most of the serotonin in the mammalian body is produced by the intestinal epithelium when it is induced by short-chain fatty acids produced by gut microbes. This serotonin is crucial for maturing the enteric neurons that enable peristalsis. Other microbes are crucial for bone stability, endocrine regulation and even neuronal function (Gilbert and Epel, 2015; Sultan, 2015; De Vadder et al., 2018). Each pore is an ecosystem, and we are biomes as well as organisms. Symbiotic bacteria are crucial for forming the immune systems of both mammals and arthropods. Indeed, immunity can now be considered a holobiont property, and not merely that of the larger 'host' (Gilbert and Tauber, 2016). The innate immune system, characteristic of all animals, very likely arose as a communication system between eukaryote hosts and microbial symbionts.

But we are unaware of how we become holobionts. We are just starting to become aware of the ways that plants and animals decide which bacteria to take into their bodies and which to avoid or expel. These symbiotic microbes, whether bacteria, fungi or algae, are environmental entities that literally become parts of our bodies. Developmental biology must explain how the environment becomes part of the body.

The environment must not be seen as a 'stage' upon which living things metabolize, reproduce and evolve

Life is constantly helping build its environment. Earth science studies have shown that the chemical composition of the earth is constructed through remarkably intricate feedback mechanisms between organisms and their physical substrates. Foremost among the organismal interactions are the nitrogen fixation processes that evolved as symbioses between plants and microbes, the soil-forming symbioses forged between plants and fungi, the coral symbioses formed between plants and cnidarians, the carbon dioxide/oxygen exchange between animals and plants, and the root-extending interactions between fungi and plants that enabled plants to expand onto land and embed into newly formed soil (Pirozynski and Malloch, 1975; Lenton et al., 2020). These are processes at the shoreline where developmental biology meets the environment. The holobiont develops, incorporating different species into its body in ways that change the characteristics of all partners.

The alteration of the environment by organisms is an ongoing process and is the central feature of niche construction. On a small level, the reciprocity of a developing organism and its niche is exemplified by goldenrod gallflies and mammalian placentation. The female gallfly lays her eggs on the goldenrod. When the caterpillars hatch, they eat the goldenrod stem and larval salivary proteins induce plant cell proliferation to form a gall. The larva enters the gall and continues eating from within it. As winter approaches, the gall desiccates, producing volatile chemicals that instruct the larvae to produce sorbitol and trehalose: two sugars that act as antifreeze (Williams and Lee, 2005). Here, we see reciprocal induction on the ecological level. In mammals, the embryo constructs a habitat for itself, inducing the uterus to alter its cell cycles, adhesion proteins, immune architecture and vasculature (Chavan et al., 2021).

Larvae, eggs and embryos can alter the environment by their mere presence, as most larvae provide nutrition for other organisms. The billions of invertebrate larvae found in oceans are crucial for the marine ecosystem, being components of the great plankton webs that are critical to the food chains of the ocean. Indeed, as the adults of most of these species are benthic and sessile, the exploiting of new habitats and genetic intermixing are brought about by these very small larvae, the eventual destinations of which are determined by prevailing tides and currents. On land, hatchlings of blue tits demand over 100 caterpillars per day to sustain their growth, the juvenile stages of one organism being the environment for the juvenile stages of another (Visser et al., 2006). Turtle eggs provide minerals and nitrogen for dune vegetation, helping restore ecosystems on the beaches where they're laid. Thus, the environment is, in large part, produced by developing bodies.

Developmental plasticity is universal

The genome does not encode a unique phenotype. Rather, each genome encodes a repertoire of phenotypes that can be called forth by specific environmental conditions. Such developmental plasticity is the ability of an immature organism to react to an environmental input with a change in form, physiology or behavior. It is probable that all organisms use some form of developmental plasticity in generating their phenotypes. In some cases, these environmentally induced differences are obvious. The queen bee, ant or termite differs remarkably in morphology, physiology and behavior from workers sharing the same genome. Here, caste is determined by factors (mostly nutrition) that regulate juvenile hormone levels in the larva (Nijhout, 1999; Pfennig, 2021; Hanna and Abouheif, 2021).

Predators can also induce developmental changes. When gravid *Daphnia* recognize lipids from the saliva of predatory fly larvae, their offspring develop defensive weaponry that prevent their being swallowed by the predator (Weiss et al., 2018). The mammalian immune system is another example of predator-induced plasticity. Here, different clones of lymphocytes are expanded when encountering antigens of particular predators (viruses, bacteria and fungi).

Temperature is another powerful developmental signal. Sex determination in many fish and reptilian species is determined by the temperature at a particular time of gestation and, as a result of global climate change, there is now the danger of several turtle species becoming extinct through becoming monosexual (Jensenn et al., 2018). In some species of insects and plants, the microbial symbiont provides the thermoregulatory response proteins enabling survival or fecundity at high temperatures (Gilbert et al., 2010).

Touch and pressure are also powerful agents in altering phenotypes. Grasshoppers can transform from local sedentary

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herbivores into migratory plague locusts when the densities of their populations cause them to brush against one another. This happened recently in the plagues that wiped out agricultural production in eastern Africa in 2018-2019, when global warming caused storms whose moisture exacerbated locust proliferation (Gililand, 2020). Young rats can become anxious adults when they do not receive the hormonal stimuli produced by the licking and grooming of the mother rat (Weaver et al., 2004). Interestingly, in both cases, serotonin mediates the touch signal. The environment not only selects phenotypes, it helps create them. Thus, the developing body responds to its external environment.

The organism is a life cycle

John Bonner, following Darwin's colleague Thomas Huxley, wrote that an organism does not have a life cycle; rather, the organism is the life cycle (Bonner, 1965). The view taken here is that the life cycle is the central unit in biology. The notion of the organism is used in this sense, rather than that of the individual at a moment in time, such as the adult at maturity.

Moreover, Bonner saw an organism being constructed by both the division of an existing cell into many cells and also by the coming together of many cells into one individual. His work pushes us to look at the development of the holobiont life cycle. This perspective circumvents our mammalian bias to look at adults as the cornerstone of life. For most organisms, especially insects, independent life is the larval stage, and the adult is a very transient form that often exists solely for mating and dispersal. Male mosquitoes are but mobile gonads, and though the adult mayfly might live for but a day, its embryos and nymphs live the other 364.

Most life cycles are coordinated by the environment, especially abiotic environmental factors; this is the topic of phenology. The timing of flower opening, the emergence of butterflies from their chrysalides, the falling of deciduous leaves, the egg-laying of numerous organisms and the timing of the developmental cycle of honeybees are examples of this regulation. The warming of the climate has caused changes in phenology, and these changes can be disastrous. Recent studies on British birds show that the differences between peak hatching time and peak caterpillar abundance have diverged by nearly 2 weeks for some species. For sanderlings, the hatching time of which is regulated by photoperiod, but whose food source is regulated by temperature, the divergence has been 1.3 days per year for the 17 years since 1995 (Reneerkens et al., 2016). However, phenology has largely been seen as an ecological science, not a developmental one. A recent review by forest ecologists (Chmura et al., 2019) ends by saying, ‘We are optimistic about opportunities to continue developing a more mechanistic and predictive understanding of phenological shifts in an age of global climate change’. Such mechanisms are what developmental biology can offer.

Temperature also plays roles in limiting life cycles. The life cycle of the coral holobiont is abrogated by heat, which causes the coral cells to release their endogenous algal symbionts. This ‘bleaching’ of the corals has destroyed over 50% of the Great Barrier Reef within the past decade (Morton and Redfearn, 2020). And symbionts can be pathogenic as well as mutualistic. Heat expands the life cycles of many pathogenic fungi, nematodes and arthropods into new areas. Moose populations are declining in Minnesota due to brain worms, nematode parasites brought by white-tailed deer as their range moves northward due to climate change. The brain worm has a complex life cycle that becomes interrupted by moose, who are killed by it. In addition, higher temperatures have allowed tick eggs to survive in more northerly climates. Moose have been found with thousands of ticks in their fur, and the itching is so intense that the moose rub much of their fur off. This makes them more susceptible to harsh winter weather. One way of keeping the deer separate from the moose may involve restoring wolf populations to the region (Oliveira-Santos et al., 2021).

In addition, many life cycles are dependent upon other organisms. Biofilms induce larval settlement and metamorphosis for numerous species of sponges, cnidarians, crustaceans, annelids, echinoderms, mollusks and urochordates (Hadfield, 2011; see Box 1). The metamorphosis of *Amphimedon* sponges depends on chemical cues produced by an endogenous bacterial symbiont, while the metamorphosis of *Crassostrea* oysters depends on the biofilms accumulated on shells on the benthos (Fig. 1). Wandering coral larvae are attracted to reefs by the sound of snapping shrimp, and some coral larvae attract their algal symbionts through green fluorescent protein (see Freckelton et al., 2017; Gilbert, 2021; Song et al., 2021). Thus, the holobiont life cycle incorporates biotic and abiotic factors of the environment.

Box 1. The role of environmental bacteria in inducing metamorphosis in invertebrate larvae – a personal case study by Michael G. Hadfield

The point in the life cycles of most marine invertebrates where they must transition from a swimming larva to a benthic juvenile is largely dictated by interactions with specific bacteria residing in surface biofilms, the compositions of which are largely determined by the physical and chemical environment of the habitat (Hadfield, 2011). These interactions are so important for the continued development of these organisms that most can remain for long periods as competent larvae in the plankton until stimulatory bacteria are contacted. If the surface-bacterial community in a habitat changes only slightly, the animal communities living there will also change.

In our laboratory, we focus on how bacteria can induce larvae of the tube-dwelling polychaete worm *Hydroides elegans* to settle and undergo metamorphosis. Larvae of this circumglobally distributed warm-water worm, although competent to undergo metamorphosis 5 days after fertilization, can feed and survive for months if the right bacterial biofilms are not encountered. Having isolated pure cultures of various metamorphosis-inducing bacterial species, we asked whether all the inductive bacteria provide the same cues, what their signaling molecules might be and whether these cues are environmentally specific. We learned that some inductive bacteria are habitat specific at the level of bacterial strain. That is, cultures of the species *Pseudoalteromonas luteoviolacia* are inductive when isolated from a typical *Hydroides* habitat, such as the estuary of Pearl Harbor on the island of O'ahu, Hawai'i, but strains isolated from Kane'ohe Bay coral reefs, on the opposite side of O'ahu, do not induce metamorphosis.

Signaling molecules from specific bacteria interact with neurosensory cells on the surface of larvae to stimulate a cascade of developmental events, including attachment to the substrate, primary tube secretion, loss of locomotory/feeding cilia and some cells, tissue migration, and cell differentiation. These mechanisms, which are typical of the mechanisms involved in the embryonic development of all animals, lead us to ask: what is the nature of the bacterial cue? The cue from the biofilm bacterium *Cellulophaga lytica* is the lipopolysaccharide (LPS) that forms the outer coat of all gram-negative bacteria (Freckelton et al., 2022). We are now determining which component, the lipid or the polysaccharide, provides the cue, and what the mechanisms are by which the larvae are induced to undergo their morphological, physiological and ecological metamorphic events. Environmental bacteria are as integral a part of this process as the endocrine and neuroendocrine factors that are integral to vertebrate and arthropod development.

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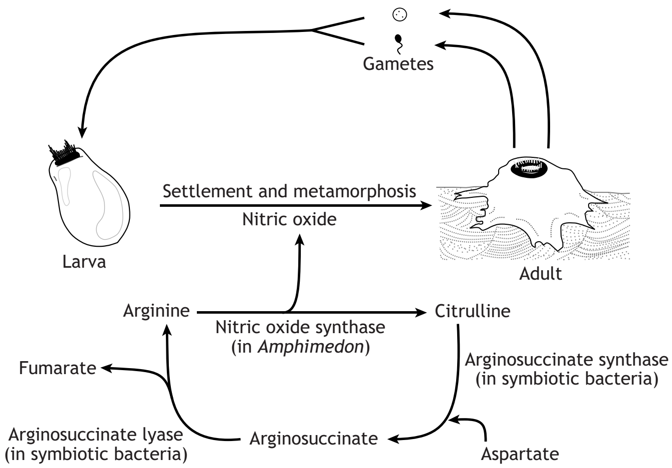

Fig. 1. Bridging of larval to adult stages of the *Amphimedon* life cycle by symbiotic bacteria living within the sponge. Nitric oxide, the signal for settlement and metamorphosis, is generated by enzymes encoded by both the sponge genome (nitric oxide synthase) and the genomes of bacterial symbionts (arginosuccinate synthase and arginosuccinate lyase) living within the interior cells of the larva. Based on Song et al. (2021).

Every physical and chemical aspect of the environment impacts the developing organism

Biologists have been long aware that animal physiology is impacted by the temperature of the environment of an organism, as well as by its oxygen and carbon dioxide concentrations, and, especially for marine organisms, by its pH and hydrostatic pressure. Because of increasing environmental temperatures brought about by the grossly excessive fossil fuel exploitation and forest destruction by humans, greenhouse gases are accumulating in the atmosphere at an unprecedented rate, causing increased global temperatures, changes in the frequency of rainfall and the occurrence of catastrophic storms. Although all these changes greatly impact life across the planet, the impacts are perhaps even greater in the oceans where increasing temperatures cause declining oxygen concentrations (Penn and Deutsch, 2022) and increased carbon dioxide uptake is causing acidification. Together, these environmental alterations produce unprecedented challenges for developing organisms. Because many marine animals (sponges, corals, mollusks, worms, tunicates and fishes) spawn their gametes directly into the sea where fertilization takes place, very small and naked cells are faced with environments to which it is extremely difficult to rapidly adapt. Even very small downward shifts in pH make calcification difficult, negatively impacting bivalve mollusks throughout their life cycles (Miller et al., 2009; Hettinger et al., 2012; Barros et al., 2013; Waldbusser et al., 2013). Indeed, the impacts of these environmental assaults has been demonstrated to affect gene expression patterns in different oysters (Liu et al., 2012, 2020). Epigenetic alterations in gene expression resulting from environmental changes should also be expected. Relatively unexplored are the impacts of ocean warming, acidification and oxygen deprivation on the microbes that are necessary as essential symbionts (see Fig. 1) or habitat cues (see Box 1) for many marine animals (Das and Mangwani, 2015; Espinel-Velasco et al., 2018; Nelson et al., 2020). All of these changes should be foci for developmental biologists who must first study the phenomena and measure their magnitude before advancing ideas to mitigate the worst consequences and prevent extinctions (see Pinsky and Fredston, 2022). The developing organism is impacted by every part of the climate in which it develops, especially those millions of animals that spawn naked gametes into the sea.

Taking action: development biology and ecology should become scientific allies in conservation and restoration biology

Three quotations provide the context to the structure of this section.

> *Learn what is true, in order to do what is right' is the summing up of the whole duty of man.*
>
> Thomas Huxley (1870)

If we of the industrialized world are to restore or even sustain nature, we must first know how nature operates. Without knowledge of larvae, life cycles and symbionts, we have made poor decisions. In trying to allow adult salmon free access to streams, we have made it impossible for salmon to breed properly; industrial fertilizers are creating plants that no longer can attach mycorrhizal symbionts to extend their roots; we are spraying crops with insecticides and herbicides such that 98% of the honey produced in Canada contains glyphosate (Kokkoris et al., 2019; Martín-Robles et al., 2019; Thompson et al., 2019). The knowledge we need, as suggested above, is often found where developmental biology meets ecology, specifically where eco-devo meets restoration ecology. So, our first duty is to know what is true, to the best of our abilities.

> *It's easier to imagine an end of the world than to imagine the end of capitalism.*
>
> Frederick Jameson (1994)

Even if we know what is true, we still need to do what is right. This involves politics and economics. So, our second duty is to understand that global climate change is a social problem and that capitalism is not necessarily the best way to run economies or ecosystems. This gets into the problems of funding and regulation of research (Reardon, 2017; Hadfield and Haraway, 2019; Stengers, 2018). Evaluating scientific 'excellence' must consider how a research program might lead to ecosystem stability or the safety of salamanders and honeybees now. And 'doing what is right' extends to regulatory agencies, wherein moneyed industrial powers have decided that fracking is legal and fracking corporations cannot be sued for damages, that phthalates are safe for pregnant women, and that bisphenol A and glyphosate do not cause cancer. Capitalism must take a back-seat to science.

> *Anthropogenic explanations of climate change spell the collapse of the age-old humanist distinction between natural history and human history.*
>
> Dipesh Chakrabarty (2009)

In this brief article, we have presented scientific evidence that Margulis' adage that 'the environment is part of our body' must be taken literally. This, of course, has enormous consequences for public health; a healthy body must include a healthy environment. But this must be considered the priority for every animal and plant (Sariola and Gilbert 2020).

There are, of course, definite research projects that are highlighted in this new paradigm. The foremost is: how do organisms evolve and develop symbioses? What allows some algae entry into coral and other not? What allows certain bacteria to become human 'self' while others are actively destroyed or expelled? How do changes in microbiomes reshape developmental, including behavioral, processes for different species?

Moreover, the fusion of natural history and human history reveals that political and natural economies co-construct one another in intimate ways. The big problem is still how do nature and humans win back the planet together? Given that there will not likely be an international agency that would distribute research funds equitably (or, as Kim Stanley Robinson has recently suggested, a black ops movement to sabotage the infrastructure supporting global demise;

Robinson, 2020), we need a redefinition of scientific excellence and of national defense. In this task we may learn from holobionts, who are able to incorporate the environment into their bodies as part of their immune defense networks. Over 90% of technoscientific research in the USA ($649 billion dollars in 2018) is funneled through its military (Lindee, 2020). Imagine climate change as bombs that would destroy cities and cause many deaths and large migrations. Then imagine those funds substantially redirected for real planetary defense.

There will have to be radical changes in what we consider scientific excellence and scientific worth. So here is another problem: how do you restructure scientific priorities? Grants would be awarded based on how well their conclusions would serve to preserve and restore species and natural-social ecosystems. Developmental biology would shift to have an ecological focus, while professional ecology would relinquish the 'ecosystem services' paradigm where nature is given monetary values according to its value to human society. This is a worldwide problem, and the solution must be a world-wide solution. And developmental biology should not be sitting on the sidelines, thinking that it's all up the ecologists and politicians. They need us. Thus, we advocate an alliance between developmental biology and ecology, with emergency funding and the channeling of resources – scientific, political and economic – for deflecting the magnitude of the sixth extinction of planetary life and for understanding how communities – holobionts, biomes and civilizations – emerge.

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