TOPICAL REVIEW

Situating physiology within evolutionary theory

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Abstract Traditionally defined as the science of the living, or as the field that beyond anatomical structure and bodily form studies functional organization and behaviour, physiology has long been excluded from evolutionary research. The main reason for this exclusion is that physiology has a presential and futuristic outlook on life, while evolutionary theory is traditionally defined as the study of natural history. In this paper, I re-evaluate these classic science divisions and situate physiology within the history of the evolutionary sciences, as well as within debates on the Extended Evolutionary Synthesis and the need for a Third Way of Evolution. I then briefly point

out how evolutionary physiology in particular contributes to research on function, causation, teleonomy, agency and cognition.

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Abstract figure legend The evolution of evolutionary thinking can be depicted as a flower, each petal of which represents a specific school that in turn is made up of particular research cells that interconnect with one another through a complex network similar to how cells connect in a beehive. The schools of Darwinism and the Modern Synthesis together underlie the Neodarwinian paradigm that has been dividing into the micro-, meso- and macroevolutionary oriented research schools, which respectively study evolution below, at and above the organismal level. In recent years, the Neodarwinian paradigm has been subject of both expansion and critique. Expansion of the Neodarwinian paradigm has mainly come from scholars who call for an eco-evo-devo approach that joins theories on evolution with development and ecology. Critique has mostly come from scholars who call for the need for an independent study of reticulate evolution as it occurs by means of symbiosis, symbiogenesis, lateral gene transfer, infective heredity and hybridization. Physiology is a mesoevolutionary research field because it is focused on the living organism and the functionality of its systems and subsystems. It is represented in the diagram by an adaptation of Leonardo da Vinci's *Vitruvian Man*, as a reference to the field's traditional association with the biomedical sciences. Physiology today is furthermore one of the sciences that enables collaboration between micro-, meso- and macroevolutionary oriented fields on the one hand, and ecological and reticulate evolution research on the other.

Introduction

Physiology, from the ancient Greek for nature (*phúsis*) and reason (*lógos*), involves the study of nature in its living form (*phuō*), as it becomes or generates in natural history (Fletcher, 1837). Classical divisions make physiology traditionally differ from, on the one hand, metaphysics, that beyond the ever-changing natural world seeks out above-natural, ontological constants (*epistêmê* or true knowledge), and on the other hand, technological studies (*tékhnē*, practical skills, craft or art), that inquire into un-natural, crafted and artificial entities. These old divisions, however, are nowadays more fluent, as the field of physiology advances in tandem with progress made in the more practical, technological and engineering sciences, which in turn enable the acquisition of knowledge on life's fundamental physiological structures.

As the science of the living, physiology has mostly evolved in association with advances made in the health and biological sciences. In the biological sciences, physiology was one of the first fields to examine organized complexity at and below the organismal level by focusing on what Bernard in the 19th century called the '*milieu Intérieur*', the internal milieu of the organism (Holmes, 1986). Within this internal milieu, physiologists have consistently sought the reasons why organisms demonstrate self-sustaining and self-perpetuating properties such as metabolism, sensibility, mobility, autonomy or agency.

An investigation of how the organism maintains itself internally by necessity also incorporates research on how the organism and its various components differ from, and interact with, the external, abiotic and biotic world. Physiology therefore has kept close ties with ecological research on the one hand, as well as epigenetic, behavioural, neurological and even sociocultural research on the other.

Physiology distinguishes itself from these sciences by primarily linking results of research on the role of

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the internal and external environment on organismal functionality to health and disease. Physiology has played a crucial role in the biomedical sciences by helping to shape the fields of internal medicine and pharmaceutics. Physiology here has an applied component to it, one that links remediation, therapeutics, technology and even engineering, artificial intelligence, and robotics to the shaping of present and future life. Advances in both areas of physiological research, biological and medical, have come to be recorded in two different Nobel Prize categories, the Nobel Prize for Physiology or Medicine, and the Nobel Prize for Chemistry.

The focus on health or the proper functioning of organs and systems has made physiology's research outlook be either on the present or, with the goal to eradicate disease, on the future. Such an outlook differs from evolutionary research that has traditionally focused on the past. When writing on cause and effect in biology, Ernst Mayr (1961: 1502), for example, could still easily distinguish between functional and evolutionary biologists. The former, he argued, investigate the proximate causes of organismal form and behaviour, the latter study the ultimate causes. As a consequence, evolutionary-historical or phylogenetically oriented research has long advanced by excluding ontogenetically (Gould, 1977) and ecologically (Lewontin, 1982) oriented research, and it is in association with these fields that physiology developed. Today, epigenetics, eco-evo-devo and reticulate evolution research is enabling past barriers to be lifted and this enables physiology to be placed under evolutionary scrutiny.

This paper investigates where physiology can be located inside the evolving fields of evolutionary science, how it contributes to ongoing pleas for an Extended Evolutionary Synthesis and a Third Way of Evolution, and how Evolutionary Physiology differs from its traditional counterparts.

Situating physiology within the Flower of Evolution

The growth of evolutionary thinking can be characterized by a flower (Gontier, 2023). The petals of the flower represent the seven major research schools that have evolved since the introduction of Darwin's theory of evolution. These include the schools of Darwinism, the Modern Synthesis, Micro-, Meso- and Macroevolution, Ecology, and Reticulate Evolution (Figure 1). In what follows, the major research areas and contributions of these schools are briefly reviewed.

Darwinism. The school of Darwinism commences with the introduction of the theory of evolution by means of natural selection as formulated by Charles Darwin (1859). The premises of Darwin's theory include that organisms possess variation in inheritable traits that can be harmful, neutral or beneficial to the organism in a hypothesized struggle for existence over scarce environmental resources as well as a hypothesized battle between the sexes over reproductive mates. In such a scenario, beneficial or adaptive traits that help the organism to survive and reproduce will be naturally and sexually 'favoured' or selected, either by the environment or through mate choice. As a consequence, organisms with adaptive traits will be more likely to survive and pass on their traits through reproduction while organisms with maladaptive traits will naturally become weeded out. This results in a shift at the population level where over generations through time, surviving and reproducing organisms will come to demonstrate gradual descent with modification from their ancestors, so much so that varying populations and eventually new species will be formed.

Darwin's probabilistic account of how evolution can possibly occur under a set of hypothesized conditions received immediate adherence in the 19th century school of Darwinism that subsequently applied selection theory not only to biological but also to linguistic and sociocultural change through time. Biological Darwinism, however, relied on ill-informed ideas on the sources of variation, and Social Darwinism often synthesized with false racial and progressivist ideas, either of which were later considered scientifically and politically incorrect. Darwinism therefore became temporarily eclipsed (Bowler, 2005) by the, at the time, rising schools of embryology and epigenetics (Peterson, 2014).

The Modern Synthesis. The founders of the Modern Synthesis (Huxley, 1942) reappraised and synthesized the tenets of Darwinian selection theory with Mendelian 'factor' or genetic inheritance theory (Ford, 1931) and genetic mutation theories (de Vries, 1901–03) leading to the rise of theoretical population genetics (Fisher, 1930; Haldane, 1932; Wright, 1932). While Darwin had mostly focused on organismal variation, the Modern Synthesis helped in the theoretical conceptualization of genes (Fox Keller, 2002), genetic selection and genetic drift theory on the one hand (Wright, 1932), and species and speciation concepts (Jepsen et al., 1949) as well as large-scale evolutionary trends (Simpson, 1944) on the other. These theories were subsequently tested through artificially induced mutation and selection experiments conducted on a variety of organisms (Dobzhansky, 1937; Morgan, 1932; Muller & Painter, 1929) that proved that genetic mutations can induce phenotypic variation that indeed can impact an organism's survival and reproductive chances. These outcomes were taken as foundational for the Neodarwinian paradigm that states that micro-evolution, or small and random genetic mutations, suffice

Figure 1. The Flower of Evolution
The flower represents the seven major schools of evolution that have evolved since the introduction of Darwin's theory of evolution. Although pre-Darwinian ideas exist that can genuinely be designated as evolutionary, many of which would later be rediscovered and integrated into existing research, modern evolutionary thinking is generally recognized to have started with the school of Darwinism and the later reinterpretation of some of its basic tenets by the founders of the Modern Synthesis. Darwinism and the Modern Synthesis together form the Neodarwinian paradigm that subsequently expanded into the micro (genetic)-, meso- (organismal)- and macro- (species) oriented evolution schools. All three schools have additionally brought the school of Ecology to bear on evolutionary theory by examining how genes, organisms and species interact with one another and the abiotic environment. The latter research focus has given way to the rising eco-evo-devo (Ecological Evolutionary Developmental Biology) paradigm, here depicted in the various tones of blue. Eco-evo-devo scholars continue to understand their theories as expansions of Neodarwinian thinking. The Reticulate Evolution school on the other hand studies phenomena that many scholars in the respective fields recognize as non-Darwinian mechanisms and processes of evolution, and they therefore understand their theories to complement rather than expand existing paradigms.

to explain macroevolution, understood as speciation (Mayr, 1961; Mayr & Provine, 1980).

Continuously subject of both expansion and critique, this Neodarwinian paradigm has been differentiating further into the micro-, meso- and macroevolutionary oriented research schools.

Microevolution. In the microevolution school, advances in biochemistry and molecular genetics have enabled scholars to better flesh out the meaning of theoretical concepts such as gene flow or migration, first developed by the founders of the Modern Synthesis. This is largely due to expanding knowledge on the structure of DNA and protein synthesis as well as the increasing ability for gene, protein and eventually whole genome sequencing which enables a molecular-based tracking of variation as well as, via molecular clock theories (Zuckerkandl & Pauling, 1965), new means of estimating divergence and speciation.

Following 'aperiodic crystal' (Schrödinger, 1944), 'information,' 'communication' (Shannon & Weaver, 1949) and 'code' metaphors (Crick et al., 1961; discussed in Gontier, 2021a; Koonin, 2017; Stegmann, 2016), as well as mathematico-theoretical research done on 'self-reproducing automata' (von Neumann, 1966), the genome has long been considered a 'frozen accident' (Crick, 1968) made up of 'selfish replicators' (Dawkins, 1976), some of which translate into amino acids that underlie protein synthesis, most of which is 'non-coding' and therefore traditionally labelled as 'junk DNA' (Ohno, 1972). Accordingly, the 'central dogma' (Crick, 1958: 153) of molecular genetics dictates that 'information' flows from DNA to RNA to protein, or '… that once "information" has passed into protein it cannot get out again. In more detail, the transfer of information from nucleic acid to nucleic acid, or from nucleic acid to protein may be possible, but transfer from protein to protein, or from protein to nucleic acid is impossible. Information means here the precise determination of sequence, either of bases in the nucleic acid or of amino acid residues in the protein.'

This dogma of molecular genetics has, however, proven untrue, because chromosomal arrangements as well as gene structure and expression can be modulated in response to cellular, organismal and environmental cues. Mobile genetic elements (McClintock, 1950), which form part of those genome regions designated as junk, as well as chromatin regulation (Bannister & Kouzarides, 2011), prove that information can flow in the opposite direction. Rather than being frozen accidents subject to random copying errors, or selfish replicators that exploit their 'vehicles', genomes demonstrate mechanisms for self-repair beneficial to both the genome and the organism. Gene mobility, genome inscription or epigenetic formatting enable structural and functional changes to the genome that Shapiro (2022) characterizes as 'Natural Genetic Engineering'. Rather than understanding genomes as 'Read-Only Memory information storages', Shapiro (2013) calls out for understanding them as 'Read-Write data storage systems' subject to cellular modifications. A consequence of such gene and protein alteration mechanisms is that learning and cognition must be present from the cellular level onward (Shapiro, 2021).

Macroevolution. While the school of microevolution has evolved by trying to translate theoretical gene selection theories formulated by the founders of the Modern Synthesis to the molecular level, the macroevolution school has evolved by countering the idea that micro-evolution suffices to explain macroevolution (Gontier, 2015a). Instead, macroevolutionists have professed autonomy of their research field.

Darwin (1859) assumed that evolution by means of natural selection occurs gradually, but he lamented the numerous gaps in the fossil record between species that disproved his idea of intermediates. The idea that nature does not make jumps, however, proved to be a remnant of Greco-Roman and Judeo-Christian worldviews that understand nature as forming a continuous and harmonious chain of being (Lovejoy, 1936). That evolution is necessarily gradual became critiqued by many of Darwin's contemporaries, and also several founders of the Modern Synthesis discussed scenarios whereby evolution proceeded according to different rates and tempos. In the field of botany, Stebbins (1940), for example, pointed toward hybridization in plants and the polyploidy it can lead to as sources for rapid evolutionary change. In palaeontology, Simpson (1944), in his book on *Tempo and Mode of Evolution*, distinguished between slow, medium and rapid tempos of evolution and he raised the possibility of quantum evolution. However, both research areas remained marginalized. Botany therefore mostly evolved outside of the Neodarwinian framework, by finding solace either in the school of ecology or in reticulate evolution studies.

Palaeontology instead has averred for the Neodarwinian paradigm to recognize and account for the presence of different evolutionary rates across diverse time scales, and in so doing palaeontologists have expanded selection theory to species and above-species phenomena (Rensch, 1947; Stanley, 1979). The theory of punctuated equilibria, introduced by Eldredge & Gould (1972), argued that gaps in the fossil record are data. In addition to the pattern of phyletic gradualism, cladogenesis occurs according to a pattern of punctuated equilibria in which long periods of stasis are intermitted by short periods of rapid change. The theory falsifies older

ideas of the incompleteness of the fossil record, and it has sought to show how selection theory (Eldredge, 1985) and evo-devo mechanisms (Gould, 1977) can explain both stasis (Eldredge et al., 2005) and rapid speciation (Gould, 1989). In this regard palaeontology has also introduced investigations into adaptive radiations (e.g. Grant & Grant, 2008), mass extinctions (Alvarez et al., 1980; Benton, 2005; Raup, 1994), their interrelation and dissociation (Hoyal Cuthill et al., 2020; Yoder et al., 2010), and their overall impact on biodiversity (Sarkar, 2005) on the one hand, and on the other, it has helped advance research on how species and higher taxa can be defined from within cladistics (Hennig, 1950) and hierarchy theory (Eldredge & Salthe, 1984). Both areas enable macroevolutionary theory to integrate ecological theories.

Mesoevolution. The mesoevolutionary school is the last of the three expansions of the Neodarwinian paradigm to have occurred, and it has evolved by reaching back to older, sometimes pre-evolutionary theories of organismal development (discussed in Gould, 1977). Mesoevolutionary theory thus integrates evolutionary theory neither below nor above, but at the organismal level, by examining how developmental processes and life-history events impact evolution.

While Darwin understood the organism as the target of selection, the Modern Synthesis reduced the study of the organism to a study of its genes, how they are mutated and how they are passed on to future generations. Both the Weismann barrier (Weismann, 1892) and the Central Dogma of molecular biology caused scholars to understand ontogenetic processes, which include embryological, physiological and gerontological processes, as irrelevant to phylogeny.

Today such is considered antithetical to evo-devo research (Carroll, 2005; Hall, 2012) that has significantly expanded our molecular understanding of processes such as homology and modularity (Wagner, 1996). Evo-devo examines the role played by gene-regulatory networks (Davidson & Erwin, 2006; De Robertis et al., 1990; Gehring, 1996; McGinnis & Kuziora, 1994) in the development of anatomical form, as well as the role played by physiological processes in the development of functional systems (Newman, 2014; Noble, 2013; Noble et al., 2014). It is thus here, in the mesoevolutionary school, that we find the integration of physiology into current evolution research.

Mesoevolutionary research furthermore introduces an ecological dimension to its research outlook by investigating the organism–environment relationship, and here, it links to a study of how epigenetic and altogether extragenetic mechanisms and processes impact life history. Evolution cannot be reduced to a genetic

level and rather involves the reproduction of entire developmental cycles (Oyama, 1985; Oyama et al., 2001), as well as intergenerational transmission through learning so typical of sociocultural evolution (Baldwin, 1896; Jablonka & Lamb, 1995). In fact, increasing insights into genome flexibility through the study of mobile genetic elements or processes such as phenotypic plasticity (West-Eberhard, 2003) demonstrate that learning is present from a molecular level onward.

Advances in micro-, meso- and macroevolution research have therefore given way to the recognition that selection can operate on multiple units at different levels of an evolutionary hierarchy (Brandon, 1982; Lewontin, 1970), leading, on the one hand, to research on multilevel selection theory (Gontier, 2010; Okasha, 2006), and on the other, to complexity research that investigates the major transitions in evolution (Maynard Smith & Szathmáry, 1995).

Ecology. Ecology mostly evolved outside of the framework of the gene-based Modern Synthesis. Instead, this school is rooted in the Darwinian idea of studying organisms and the species they group into in relation to their environment. Ecological research, on the one hand, involves a delineation of the biotic and abiotic environment into organisms, species, communities, ecosystems and biomes (Egerton, 2017; Odum, 1953), and on the other hand, a measuring of the various forms of resource management and energy consumption that occur within and between these entities (Lotka, 1925; Volterra, 1931). Ecology therefore associates, on the one hand, with research on the 'household', 'economy' or 'polity' of nature (Haeckel, 1866; Levins, 1968; Stauffer, 1957), as well as, on the other, with research in biophysics (Prigogine & Stengers, 1984) and investigations of biogeochemical cycles (Butcher, 1993; Lovelock, 1972, 1979; Volk, 1998).

Darwin's portrayal of existence as a struggle over natural resources resulted in theories originally focusing on species competition. An example is the Red Queen Hypothesis (Van Valen, 1973) that originally was introduced to explain interspecies competition between, for example, predator and prey, as a reason for extinction. Later, the hypothesis also served to explain the competitive advantages of sexual reproduction as well as coevolution between host and parasite (Ridley, 2003; Van Valen, 1975).

Ecology has also attempted to explain symbiosis and hybridization research in (Neo)darwinian, competitive and selectionist terms, while adherents of the reticulate evolution school prefer to understand these in more neutral terms, as stand-alone mechanisms and processes that differ from natural selection. Similarly, the classic food chains and cycles that were introduced to make sense of interspecies relationships are now often understood as forming reticulate webs of life (Egerton, 2007)

and the question is whether selection theory (alone) can make sense of them or whether additional explanations are in order. The Darwinian assumptions of competition over natural resources and the characterization of life as a struggle for existence have today additionally been questioned by neutral theories of biodiversity (Hubbell, 2001; MacArthur & Wilson, 1967).

The delineation of the different realms of ecology has furthermore brought forth a reappreciation of the dynamic nature of such realms. While Darwin understood the environment not only as the locus but as the actor of selection, and organisms as passive subjects of selection, niche construction theory (Gould & Lewontin, 1979; Lewontin, 1982) instead recognizes organisms as capable of actively altering their environment into an increasingly hospitable and habitable zone of life. Niche construction, moreover, leaves an ecological footprint which becomes the subject of ecological inheritance (Odling-Smee, 1988), and this extends traditional notions of genetic inheritance. Ecology has thus also contributed to units and levels of selection debates, and such research connects with questions on major transitions as well as system formation or biological individuality. While species today are recognized to form historical individuals (Ghiselin, 1974), the ontological status of communities, ecosystems or biomes continues to be subject of debate (for a discussion see Sukhoverkhov & Gontier, 2021). Nonetheless, ecologists have mostly sought to integrate new, often biophysically inspired thinking into the Neodarwinian synthesis rather than rupturing from it.

Reticulate Evolution. A final school that evolved outside of the dictum of the Modern Synthesis, and whose roots also precede the introduction of Darwinian thinking, is the Reticulate Evolution School. Reticulate Evolution is a container term for evolution as it occurs by means of symbiosis, symbiogenesis, lateral gene transfer, hybridization and infective heredity (Gontier, 2015b). From these, hybridization is mostly studied in plants (Stull et al., 2023; Wissemann, 2007) and to a lesser extent in animals (Arnold, 2009; Goulet et al., 2017; Moran et al., 2021); infective heredity (Watanabe, 1963; Zinder, 1953) is researched by virologists, bacteriologists, physiologists and physicians (Flores et al., 2014; Nasir et al., 2012; Roux et al., 2013); lateral gene transfer is nowadays well studied in molecular genetics (Arnold et al., 2022; Soucy et al., 2015); symbiogenesis research is mostly analysed from within biochemistry and cell studies (Margulis, 1998; Sagan, 1967); and especially symbiosis research is conducted from within the school of ecology (Douglas, 2010; Moran, 2006; Zook, 2015).

Comprising a diverse set of disciplines that study different as well as at times overlapping mechanisms and processes of evolution, all forms of reticulate evolution involve the horizontal or network-like exchange, crossing, or actual merger of distinct evolutionary lineages. Reticulation is a means by which foreign genes, proteins, tissues or entire organisms are exchanged. Such is antithetical to the premises of Darwinism and the Modern Synthesis that understand evolution as an intra- rather than interlineal process, and as a branching and bifurcating rather than net- or web-like process (Doolittle, 1999; Doolittle & Bapteste, 2007).

The consequences of any kind of reticulation amongst different lineages can be positive, neutral or negative. Hybridization in plants, for example, has been recognized to enable genetic rejuvenation, ecological expansion and speciation, but it often comes with a genetic load as it can lead to polyploidy in the hybrid offspring. Adavoudi and Pilot (2021) surveyed 115 studies in mammalian hybridization conducted over the last decade. They found that half of the cases studied had identified negative consequences on the hybridizing taxa, 38% were neutral and the remaining studies found positive effects of hybridization.

Symbiosis research has a long history (Gontier, 2016; Sapp, 1994) of investigating how organisms belonging to different species live in close association with one another, not only ecologically, but also physically, by sometimes living inside or upon one another. Such species interactions can be neutral, commensal, amensal, mutual, parasitic or synnecrotic. None of these symbiotic interactions is per definition selective or competitive, although engaging in any of these interactions can provide competitive and selective advantage or disadvantage for either symbionts or hosts or all. Symbiosis research therefore also forms part of more traditional and selection-focused ecological research, but symbiosis can be described in its own terms.

Symbiosis furthermore expands the classic range of ecological theory because it can become hereditary (Lederberg, 1952) and lead to evolution by symbiogenesis (Carrapiço, 2015; Margulis, 1991, 1998). An evolutionary mechanism in its own right, symbiogenesis has played a critical role in the evolution of eukaryotic cell organelles. Both mitochondria and chloroplasts evolved from prokaryotes that merged with some of the first nucleated cells. These prokaryotes subsequently lost their individuality and evolved into the cell organelles they are today. Such 'individuality through incorporation' as Margulis called it, underlies the formation of new biological individuals called holobionts (Gilbert et al., 2012; Guerrero et al., 2013; Margulis, 1991). In association, Rosenberg and Zilber-Rosenberg (2011) have made a plea to expand genome research typical of population genetics to a study of hologenomes.

Pro- and eukaryotes alike are furthermore prone to viral infections (La Scola et al., 2003) and over the course of eukaryotic evolution, multicellular organisms

have further coevolved with a varying infectious and symbiotic viriome and microbiome that has consistently contributed to organismal health and disease (Moelling, 2020; Roossinck, 2015; Villarreal & Ryan, 2019; Witzany, 2020; Gontier & Sukhoverkhov 2023), and, as recently shown, organismal ageing (Teulière et al., 2023).

Lateral gene transfer (Gontier, 2015b; Shapiro, 2022; Soucy et al., 2015) occurs through a number of mechanisms and processes whereby pro- as well as eukaryotic organisms exchange genes either amongst themselves or amongst gene-carrying entities such as plasmids or viruses. Both bacterial and viral infections and lateral gene transfer blur the boundaries not only with symbiogenetic research but also with epigenetic research, as the movement and incorporation of mobile genetic elements can be understood as a horizontal or reticulate phenomenon occurring within and between distinct lineages (Schaack et al., 2010). Even sexual reproduction, known to occur amongst organisms of distinct lineages during hybridization, can be understood as a means for sperm cells to introduce foreign DNA into eggs (Lavitrano et al., 1989; Spadafora, 2020).

The boundaries between different types of reticulate evolution are thus fuzzy. This is mostly due to the fact that similar phenomena have often been discovered and described in different fields using different terminology. These fields are only now starting to reticulate scientifically, and an encompassing framework that delineates and classifies all forms of reticulate evolution currently remains forthcoming. Certain for most scholars active in this emerging school, however, is that any form of reticulate evolution is inherently non-Darwinian. Such a view neither falsifies selection theories nor excludes the possibility that selection operates upon reticulately evolved entities. In fact, many scholars understand reticulate evolution processes as a source of evolutionary innovation that in a second phase can become subject of selection.

Situating physiology within the Extended Evolutionary Synthesis and the Third Way of Evolution

Today, the rising paradigm of Ecological Evolutionary Developmental Biology or eco-evo-evo (Gilbert & Epel, 2008; Gilbert et al., 1996), depicted in the various shades of blue in Fig. 1, has as its primary goal to integrate advances made in micro-, meso- and macroevolutionary schools with insights from ecology. It is also within this paradigm that we can situate most adherents of an Extended Evolutionary Synthesis or EES (Chiu, 2022; Laland et al., 2015; Pigliucci & Müller, 2010). Associated originally with the reappraisal of a mesoevolutionary outlook on evolution, founders of the EES have engaged primarily in shaping the field of evolutionary developmental theory. It is through the study of the impact that organismal development and life history events have on the future course of evolution that evo-devo scholars began situating the organism within an environmental context, thereby giving the incentive for eco-evo-devo movements.

This explains why topical issues addressed by adherents of this school include phenotypic plasticity, evolvability and evolutionary constraints such as developmental bias, inclusive inheritance, and niche construction. Most of these mechanisms and processes have now been (re)interpreted to complement and extend Neodarwinian thinking. Gould (1977, 1989), for example, understood the existence of selection plateaus as delineating the limits of natural selection in bringing forth evolutionary novelty, and he preferred to interpret the genetic regulation of body plans in terms of homeostasis, which led him to reappraise older embryological, epigenetic and palaeontological research. Adherents of the EES instead have actively sought to reformulate the theoretical and biophysical jargon of systems into a selectionist and adaptationist jargon. Gould & Lewontin (1979) also understood niche construction to counter panadaptationist views in which organisms, in a Popperian sense, are thought to corroborate and fit the environment. The construction of a niche negates the possibility of adaptation understood as such fitting. Adherents of the EES have instead interpreted niche construction formation as adaptive because it is beneficial to the organism and the group (Odling-Smee et al., 1996; Svensson, 2018). Such a view leaves out a consideration of the ontological consequences of niche construction theory (for a discussion see Gontier, 2018).

While evo-devo and epigenetic processes have mostly been understood from an organismal level onward, in relation to body plan formation on the one hand (Davidson & Erwin, 2006; Müller, 2007, Newman, 2006) and organismal learning and the role it plays in the formation of sociocultural niches (Jablonka & Lamb, 2014) on the other, especially scholars active in the Third Way of Evolution (TWE) movement are also looking into how learning occurs from the microevolutionary, molecular genetic (Ho & Saunders, 1979; Shapiro, 2022), chromosomal (Nowacki et al., 2011) and cellular levels (Baverstock & Ronkko, 2008; Miller et al., 2023) onward (Igamberdiev, 2022).

TWE scholars are moving beyond the original focus of the EES to also try and understanding teleonomy, agency, cognition and semiotics as it evolves at, below and above organismal levels (Alexander, 2019; Caporale, 1984; Corning, 2014; Emmeche & Kull, 2011; Shapiro, 2021; Sharov & Tønnessen, 2022; Vane-Wright, 2014; Walsh, 2015; Westling, 2013).

Research on major transitions (Maynard Smith & Szathmáry, 1995), which is associated with EES thinking,

in this regard is becoming more and more reformulated in terms of research on individuality formation that traditionally associates with system (von Bertalanffy, 1951) and hierarchy theories (Eldredge & Salthe, 1984), complexity research (Oyama et al., 2001), and reticulate evolution research (Gilbert et al., 2012; Margulis, 1991). This research area is also leaning more toward TWE approaches but the boundaries are fuzzy, and collaboration and joint publications between the two movements now exist (Corning et al., 2023; Noble et al., 2014; Vane-Wright & Corning, 2023). The binding science that facilitates such dialogue is by and large physiology. This is because physiology is the field that has since long searched for the biochemical and cellular foundations of organismal functions that extend into behaviour and cognition.

A significant number of scholars studying aspects of reticulate evolution also find a home in the TEW rather than in EES movements that try and reduce reticulate evolution processes to ecology and inclusive inheritance theories (e.g. Danchin et al. 2011). Adherents of reticulate evolution do not deny the existence of evolution by means of natural selection or the importance of extending inheritance theory and including ecological theory into mesoevolutionary analyses. However, rather than seeking out integration into an inherently Neodarwinian-focused evolution paradigm, they recognize the uniqueness of mechanisms and processes that underlie reticulate evolution, many of which, especially through holobiont formation, extend above and below the level of the organism. Reticulate evolution theory is demonstrating that variation, adaptation, heredity and fitness, constraints and affordances, speciation and extinction surpass organisms and species and can be caused by mechanisms and processes other than natural selection (Gontier, 2020). TEW scholars therefore plead for a more pluralistic evolutionary biology (Shapiro & Noble, 2021) that recognizes that numerous units, levels, mechanisms and processes are involved in bringing forth evolutionary change in time and space (Gontier, 2010). There is thus no privileged position of one unit, level or mechanism over another, which Noble (2016) and Noble et al. (2019) have characterized as 'biological relativity'.

Traditional *versus* evolutionary physiology

Physiological inquiries can be said to originate with the attempt to maintain life when challenged by sickness, ageing or death. As such, physiology has roots of which we do not know how far they extend back in time. The ancient Greeks are generally recognized to have started inquiries into human health and proper functioning of the body, but medicinal practices extend far before Western cultures and reach back all the way to (Far) Eastern and African healing practices.

The modern science of physiology is estimated to have originated during the 19th century, in congruence with the more general division of the sciences. During these times, physiology received its mark of being a science concerned with the living, characterizable by what Aristotle had called coming and becoming, that is the capacity to generate, live, die and regenerate.

As the science of life or the study of self-sustainability through time, physiology gave way to vitalism which in the 19th century could mean quite a different number of things (Driesch, 1914; Fletcher, 1837). In line with Aristotle's distinction between vegetative (sensible), animalistic (mobile) and intelligent (rational) souls, vitalism could minimally and simply refer to the organismal capacity for 'sensibility,' 'irritability' or 'locomotion' which in turn became studied in terms of electricity in nerve wirings. Or vitalism could more generally refer to the act of living through the 'work', 'activity' or 'hierarchical organization' of a body's organ parts. In this latter regard, the body was conceptualized as a 'factory' or 'machine' where the 'whole' forms a 'unity' that is the result of the 'sum of its parts' and where the parts demonstrate a (harmonious) 'division of labour' (D'Hombres, 2012). Even before evolutionary theory was introduced, Fletcher (1837, book 1, 127–155) had already demonstrated how such research focuses on proximate and ultimate principles of organized beings, that is the presential structure of the organism or the historical process or organization by which the organism is formed.

On the more extreme end of the spectrum, such mechanistic accounts were rejected and vitalism continued to refer to a matter-extending soul or life force (Bergson, 1998). That life itself is substantial rather than processual was opposed by organicist schools of thought (Phillips, 1970) that nonetheless continued the naturalistic study of how 'organized' (instead of living or vital) being evolves over time. The upside of undoing of the requirement of life for organization was that the study of organized being could refer not only to biological organisms (Wolfe, 2014) but also to sociopolitical states or cultures which were soon understood as superorganisms (Spencer, 1876), or to the Earth itself which Hutton already in 1785 had described as both a 'system' and 'machine'. He wrote: 'When we trace the parts of which this terrestrial system is composed, and when we view the general connection of those several parts, the whole presents a machine of a peculiar construction by which it is adapted to a certain end. We perceive a fabric, erected in wisdom, to obtain a purpose worthy of the power that is apparent in the production of it'. (Hutton, 1788: 209).

Over the years, research on 'organized complexity' or how parts and wholes form hierarchical systems that demonstrate emergence (Lewes, 1875; Morgan, 1923) has been studied from within systems theory (von Bertalanffy, 1951), hierarchy theory (Pattee, 1973), complexity

research (Capra, 1996; Prigogine & Stengers, 1984) and most recently by research into biological individuality (Love & Brigandt, 2017). Emergence theory originated in studies of the mind, systems theory traditionally is associated with behavioural studies, hierarchy theory with ecology and macroevolution, complexity research with biophysics (Baverstock, 2013; Igamberdiev, 2022), and biological individuality debates are primarily associated with ecological research on eusocial insects (Wheeler, 1928; Wilson, 1971), symbiogenesis research (Margulis, 1991) and Gaia theory (Lovelock, 1972). It is in the latter regard that they have been taken up in theorizing over major transitions (Clarke, 2010).

Amidst this scholarly theory formation, physiologists have dutifully been mapping how gene–protein complexes, cells, organs and regulatory systems of which the organism is composed function both individually as well as when part of a larger whole, how that whole demonstrates properties irreducible to its parts and how the whole in turn situates itself within the larger environment. Traditionally, physiology's research outlook has thereby been on the present functioning of the parts and wholes that make up the body, or on the future in so far as knowledge of proper functions has been used to remediate and cure disease. However, the fields of evolutionary physiology (Feder et al., 2000; Garland & Carter, 1994) and evolutionary medicine (Trevathan et al., 1999) are now demonstrating how such research also has a bearing on our understanding of evolution.

Evolutionary physiology in this regard is actively helping to (re)introduce and conceptualize function (Noble, 2013; Noble et al., 2014; Roux, 2014), causation (Gontier, 2021b; Noble et al., 2019), teleonomy (Corning et al., 2023; Pross, 2005; Vane-Wright & Corning, 2023), agency (Noble & Noble, 2022; Okasha, 2023; Walsh, 2015) and cognition (Shapiro, 2021; Slijepcevic, 2021; Westling, 2013; Wheeler, 2006) into evolutionary research.

Concluding remarks

This paper has situated physiology within the history of evolutionary science, within ongoing debates over the need for an Extended Evolutionary Synthesis and Third Way of Evolution, and within the transition from traditional to evolutionary physiology. Physiology has a long history of associating on the one hand with biochemistry and the biomedical sciences, and on the other with the behavioural and neuro-cognitive sciences. Both sides are now integrating with eco-evo-devo research and reticulate evolution studies. Accordingly, physiologists have been key players in larger debates held in the evolutionary and biomedical sciences over reductionism *versus* holism, mechanism *versus* emergentism, structure *versus* function, proximate *versus* ultimate causes of behaviour, ontogeny *versus* phylogeny, and gene-determinism *versus* epigenetics. The repeating pinnacle of debate has thereby been whether the organism equals the sum of its parts and functions somewhat like a harmonious unity or machine, or whether there exists some sort of transcendence or emergentism from the parts that make up living beings, in the form of functionality, organizing complexity, behaviour, autonomy, agency, cognition or free will. If the latter, the question follows if any or all of these emergent traits enable self-causing directionality to one's developmental or evolutionary faith. Answers continue to be sought.

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Additional supporting information can be found online in the Supporting Information section at the end of the HTML view of the article. Supporting information files available:

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