BALKAN JOURNAL OF PHILOSOPHY. Vol. 9, Issue 1, 2017

CAUSATION AND EXPLANATION IN PHENOTYPE RESEARCH

Özlem Yılmaz
Sabancı University, Faculty of Engineering and Natural Sciences
Tuzla, İstanbul, Turkey
e-mail: ozlemyilmaz@sabanciuniv.edu

Abstract:

A phenome occurs through the many pathways of the complex net of interaction between the phenome and its environment; therefore researching and understanding how it arises requires investigation into many possible causes that are in constant interaction with each other. The most comprehensive investigations in biology are the ones in which many biologists from different sub-areas—evolutionary biology, developmental biology, molecular biology, physiology, genetics, epigenetics, ecology—have collaborated. Still, biologists do not always need to collaborate or look for the most comprehensive explanations. A more standard investigation in biology occurs within a single subarea, and uses well-defined experiments with very specific conditions. This paper is about causation and related explanation in plant phenome research and its relevance to Aristotle's Theory of Four Causes. I argue that there are causes which resemble Aristotle's formal, material, and efficient causes in phenotype explanation and occurrence; but causes which resemble Aristotle's final causes occur in phenotype explanation only, not in the occurrence.

Key words: Plant Phenome, Causation, Explanation, Complexity, Interaction, Four Causes.

1. Introduction

There are many factors in phenome occurrence, and these are related to each other in such a way that they are constantly affecting each other through a complex net of many processes. This interrelated and complex way of existing together causes the phenotype. Understanding the complex pathways of the interaction net between genotype, phenotype, and environment requires investigation into many possible causes, including ecological, physiological, evolutionary, developmental, molecular, epigenetic, and genetic factors. When scientists reach an explanation of a phenotypic trait, this explanation concerns one of these factors, so they are giving an explanation of one of the phenome's parts. If they want to give a comprehensive explanation of a phenotypic trait, then research into *all* of these factors is required, which likely necessitates collaboration with other scientists. The completeness of this explanation is of course limited by our current scientific knowledge, unless we are asserting new laws.

I think biology as a branch of Natural Sciences has its own specific features and it is different from physics or chemistry in many ways. This is not the subject of this paper, but I would like to mention that I believe these differences are related to the great complexity in phenome occurrence. Biologists usually do very well defined and strictly confined experiments after which they give explanations of some very specific parts of very specific biological phenomena. They do not often conclude generalizations as physicists or chemists usually do. Clearly this does not mean that biology is less powerful than them, it only means that it is a bit different from them or we can say it just how biology is.[1]

Although this paper is about explanation, it is not about the difference between explanation and interpretation in biology. When I use one of these words in this paper, I may sometimes mean both together. I think almost every explanation has some amount of interpretation, because I believe there are usually some values in explanations. I think value-free science is impossible and values may interfere

[1] For some information about pluralism and sciences, see "Chapter 1: The Miracle of Monism" in Dupré, 2012.

with scientific practice at many steps in the process, so I give great importance to having good values in science (respecting human rights, all living things, and the environment).

The main aim of this paper is to give a clear ground of the causation and explanation in plant phenotype research.[2] I argue that its grounding properties are based on two aspects: (1) the complex interactions of processes in phenome[3] ontology, and (2) the complex structures of society and the scientific community. Although these are not new in philosophy of biology, the novelty of my contribution is in examining them specifically in plant research, an area which has received much less attention in philosophy of biology literature than animal research.[4] This paper is also significant due to the recent rise in plant phenomics. The drastic changes in environment (i.e. climate change, fast population growth) and the related need for more hardy, nutritious, and voluminous crop plants has generated new challenges for plant scientists and spurred advancements in phenomics. After giving a detailed explanation of phenome occurrence and research (the second part), the final part of the paper compares current phenotype research and Aristotle's Theory of Four Causes. I believe this attempt is helpful for constructing a stronger ground on the subject, since Aristotle is one of the earliest philosophers of biology, and created very well-organized principles for the scientific study of life (Lennox, 2006). His theory of investigation and explanation of living things still influences many philosophy of biology theories,[5] some of which I refer to in the last part. Although there are many discrepancies between the Four Causes theory and causation and explanation in current phenotype research, I found this comparison useful since these well-organized principles on investigating living things have a structure that emphasizes both multiplicity[6] and strong relatedness of causes.

2. Phenome and Phenome Research

A phenome is the expression of an organism's self in a certain environment; it is everything of the organism except its genome. The important thing to remember about an organism and its environment is that we usually cannot define a clear boundary between them; they are interpenetrating, constantly sending signals back and forth, constantly causing and affecting one another. It is usually very difficult to define the "self" of an individual organism because its environment is so intrinsic to it that we cannot easily say where the organism ends and its environment begins.[7] For example: arbuscular mycorrhiza and plants, or microbiota in animals' intestine. Both the arbuscular mycorrhiza and the microbiota of intestines have different genotypes than the plant's genotype and the animal's genotype, but they are part of the organisms' systems, and every phenotypic trait of the organism has a direct or indirect effect on them. We can even say that a phenotypic trait—one part of the phenome that we decide to measure—of an animal is also a phenotypic trait/environment of its microbiota.

Before proceeding to the occurrence of the phenomes and causation and explanation in phenotype research, I would like to give a few more definitions of "phenotype" for the sake of clarity: "The phenotype is the descriptor of the phenome, the manifest physical properties of the organism, its physiology, morphology and behavior" (Lewontin 2011). "The appearance or characteristics of an organism resulting from both genetic and environmental influences" (Nicotra et al. 2010). A phenome is "The expression of the genome as traits in a given environment" (Furbank and Tester 2011). Lewontin says that phenome to phenotype is like genome to genotype and token to type (Lewontin 2011). For example, having brown hair is a phenotype, but my brown hair is my phenome.

A phenome occurs through the interaction between a plant and its environment. Plants constantly

[2] While this paper is about plant phenotype research, the thesis I am asserting here is coherent with causation and explanation of phenotype research into all the living things.

[3] I would like to acknowledge that my ideas on "the plant phenome" have been developed through my years of research experience in plant biology and physiology laboratories with several groups of colleagues and through reading a great number of biology papers, not all of which I can refer to here. Also, my recent meetings with John Dupré helped me very much in framing my ideas.

[4] Like plants, working on microbes is also a new trend in philosophy of biology.

[5] For instance: Mayr 1961; Short 2002; Pigliucci 2003; Lennox 2006; Anzaldo 2007; Williams 2010; Haig 2014; Mix 2015.

[6] A multiplicity of causes—via mentioning Aristotle—have been pronounced recently, for instance: proximate and ultimate causes in biology (Mayr 1961) and Tinbergen's four questions in ethology: function, phylogeny, mechanism, ontogeny (Tinbergen 1963).

[7] There is some recent literature on the self of the living things. For instance: Pradeu and Vitanza (2012).

receive signals from their environment. These signals are classified according to their physical and chemical properties and quantities, and converted from one form to another and transmitted through the plant's body. During these transmissions, many internal processes are rearranged such that each process affects another (influences one or more other processes) from some specific parts, resulting in changes to these parts and causing ramified cascades. These rearrangements of internal processes are *a response to environment*, as plant scientists call it. *This response is basically the plant itself*. It can be many things, such as opening or closing stomata, doing more or less photosynthetic activity, expressing more or less of a gene, producing more or less of a hormone, etc.

Just like plants, the environment senses signals, too. There is again a signal transmission and response production, but these happen differently in living and non-living parts of the environment. So there is a constant relation: reception → response production → reception of the produced response → again response production → reception → production → reception → production… between a plant and its environment. This interaction can be illustrated though an arrow pointing two ways between plant and environment, but if we want to better illustrate it, we would draw *many* two-way arrows (we do not know for sure how many), and these arrows would usually touch each other as well, constituting a very complex net. The important point is that this net of interaction is not just between plant and its environment; it is also inside both of them. That is also why there is no very clear boundary between a plant and its environment.

Plants (and also their environments) have many parts and levels—with every level having many parts, and every part having many levels—which are constantly affecting each other. Both plants and the environment have complex pathways of interaction in and between every level and part of them. Because of this complexity, in the occurrence of phenotypes there are sets of causes which are interrelated. Therefore, phenotype explanation and research is clearly *context dependent*. Scientists look at this complexity and then decide to research a *single* response of a *single* organism to a *single* change in a *single* environmental parameter or a *single* genome part. So scientists have a clear *purpose* because they carefully define their research parameters. This purpose is also context dependent: it depends on the state of scientific knowledge and the state of society (these are also complex systems—even more complex than phenotype occurrence). When a scientist defines these parameters and designs an experiment, it means that she/he picked a *possible cause* from the complexity of the phenomena. Of course she/he does not pick it randomly; this decision depends on scientific knowledge and society. Then she/he designs an experiment with several groups in which all the values are stable—"natural" conditions (background conditions)—and she/he makes an *intervention* (Woodward 2010) with her/his nominated possible cause in some of the groups. At the end of the experiment, if her/his hypothesis comes up as not false (she/he observes a change in the subject phenotypic trait in different groups), she/he concludes that the possible cause is actually the cause of the subject phenotypic trait. Two very important points here: (1) this is a cause of the phenotypic trait in question in *a specific context* (in her/his experiment context), and (2) she/he *nominated it as a cause* in the first place; so she/he should be aware that there are many other possible causes that may be more important than the subject cause. This is why there is always a very detailed materials-methods section in biology research papers. The specific context of their experiments is given both in resulting explanations (in general terms) and also in materials-methods section (in detail).

Before giving a simple example, I would like to say that from different areas of phenotype research, many very different examples can be given.

For instance, say there is a plant physiology research group that wants to investigate plant responses to rising carbon dioxide (CO_2) levels in the atmosphere. And suppose that the following describes the situation of the society and the scientific community:

- We have climate change problem, and we now know that it is because of greenhouse gases emissions from human activities.
- We have climate change research and action groups.
- CO_2 is one of the greenhouse gases (current concentration is around 400 ppm[8] in the atmosphere).
- We hope to stop or slow climate change (to reduce our greenhouse gases emissions). We also want to be prepared for possible scenarios: until the end of this century, in the best-case scenario the CO_2 concentration will be

[8] pm: parts per million

between 430-480 ppm, and in the worst-case scenario it will be more than 1,000 ppm (IPCC 2014).

- We have a huge food security problem: many people do not have enough food, and many more are suffering from nutrient deficiency related diseases.
- Wheat is one of the main crop plants.
- Plants use CO_2 in photosynthesis. (More CO_2 may be beneficial for production?)

There is a clear need in society for better-adapted and more nutritious crop plants. So this creates a challenge for plant science community[9]: to more thoroughly understand how plants cope with changes in climate (such as elevated levels of CO_2). Let's say the example lab group designs this experiment: research on a durum wheat cultivar's *Triticum durum*, Sarıçanak 98 *(certain organism's)* grain yield, nutrient composition in grain, photosynthesis activity,[10] etc. *(certain responses—certain phenotypic traits)* in response to 500 ppm and 800 ppm *(certain change)* CO_2 concentration *(certain environmental parameter).* They will have three groups: 400 (as current ambient—control group), 500 and 800 ppm (as elevated: possible future concentrations). They will try to hold all the other parameters (parameters that we know: temperature, humidity, soil conditions, light, etc.) at optimum stable values,[11] and measure the traits in question in these three groups. They will use as many replicates as they can in each group so that their results will be more reliable. At the end of the experiment, if they find statistically significant differences between the measured values from each group, they will calculate the probabilities and conclude by explaining how this certain change (100 ppm and 400 ppm difference from current conditions) in this certain environmental parameter (CO_2 concentration) causes a certain phenotypic trait (let's say: bigger grains—and since they are investigating several related phenotypic traits, they may explain some mechanisms) in this durum wheat cultivar (*Triticum durum* Sarıçanak 98). They are totally aware that this result is for *this specific experiment context*.[12]

If they were to extend their research, they may want to get closer to the "real conditions," so they may want to experiment on a combination of changes. According to current scientific knowledge, climate change is causing a combination of changes in the environment. For example, in some parts of the world fields are facing drought and high temperatures, while in some other parts they are faced with floods, etc. So let us suppose that this example research group decided to work on temperature stress as well. When they design an experiment with both elevated CO_2 concentration and high temperature, they will have many more experiment groups,[13] and with replicates in each group they will end up with a very big experiment and a lot of data.[14] This time their explanation will be broader, but still within their experiment context.

3. Aristotle's Theory of Four Causes and Phenome Investigation

In *Physics* book 2, Aristotle begins by stating the difference between things that are natural and things that are not natural (Aristotle, *Physics* 192 b_{8-16}). He emphasizes that natural things have a "*source of change and of stability"* inside them. Later he makes this emphasis clearer by saying:

> The nature of a thing, then, is a certain principle and cause of change and stability in the thing. (Aristotle, *Physics* 192 b_{20-21})

He further says that if we want to have the knowledge of a thing's nature, we must investigate it:

> For the point of our investigation is to acquire knowledge, and a prerequisite for knowing anything is understanding *why* it is as it is – in

[9] Of course the relation between science and society is much more complicated than in this simple example.

[10] As stated before, the decision to choose these phenotypic traits depends on the current state of scientific knowledge and society; in this case, these are agriculturally valuable traits.

[11] This is usually not completely attainable because of the complexity of phenotype occurrence, so it can be done only to some extent. Because of this, resulting data will probably contain a lot of "noise."

[12] Even if only one factor was different in the background conditions, the results could be different.

[13] Let us say that they add two elevated temperature groups (control: 24 ^oC, elevated: 25 and 27 ^oC) to the previous design. They would then have the following groups: 24 ^oC–400 ppm CO_2 concentration; 24–500; 24–800; 25–400; 25–500; 25–800; 27–400; 27–500; 27–800. If they were to add one more parameter to the experiment, say drought stress, they would have many more groups, also in combination with three of the stressors.

[14] They will analyse this data and they will try to explain both sole effects and the interactive effects of the subject possible causes on the subject phenotypic traits.

> other words, grasping its primary cause. (Aristotle, *Physics* 194 b_{18-20})

Then he tells us that there are four ways of using the word *cause*, and these are:

- Material Cause: "from which a thing is made and continues to be made" (Aristotle, *Physics* 194 b_{23-24}). He says that we ask the question "What is it made of?" to investigate the material cause of a thing.
- Formal Cause: "for the form or pattern (i.e. the formula for what a thing is" (Aristotle, *Physics* 194 b_{26-27}), and we ask "What is it?" to investigate the formal cause of a thing. This also gives us the definition of a thing.
- Efficient Cause: "for the original source of change or rest." (Aristotle, *Physics* 194 b_{29}), and we ask "What initiated the change?" to investigate the efficient cause of a thing.
- Final Cause: "for the end. This is what something is for" (Aristotle, *Physics* 194 b_{32}), and we ask "What is it for?" to investigate the final cause of a thing.

He further says:

> So it is clear that there are these causes and there are this many of them. It is the job of the natural scientist, then, to understand all four of these causes; if he refers the question 'Why?' to this set of four causes—matter, form, source of change, purpose—he will be explaining things in the way a natural scientist should. (Aristotle, *Physics* 198 a_{21-23}) (also referred to in Falcon 2012)

I think that when we read the *Physics* we see that there are no *clear boundaries* between causes, that they are very closely related to each other; they sometimes may refer to the same cause (for example: the formal cause may be the final cause), but yet there are also *some* differences, and they are related to each other in different ways. In one part of the book, Aristotle says that formal cause, final cause, and efficient cause are same:

> In many cases, the last three of these causes come to the same thing. What a thing is and its purpose are the same, and the original source of change is, in terms of form, the same as these two. (Aristotle, *Physics* 198 a_{24-26})

He also points out the difference between material cause and formal cause while again stating the sameness of formal—definition—and final—end—causes. He says:

> …the necessity is in the matter, but the end is in the definition. (Aristotle, *Physics* 200 a_{14})

He further says that sometimes having knowledge of three of the causes (or even just one) is enough to have knowledge of a thing, so that if we know a thing's material cause, formal cause, and efficient cause, we have the knowledge of it:

> In short, then, the question 'Why?' is resolved by answering it in terms of a thing's matter, what it is and its original source of change. (Aristotle, *Physics* 198 a_{31-32})

A living thing consists of levels of materials, and without these special materials and their specific features, there cannot be that specific phenotype. Because of this, an explanation of or research into any level or part of an organism (molecules, atoms, subatomic particles, organs, tissues, etc.) is similar to Aristotle's explanation of material cause. Aristotle says: "necessity is in the matter." Today we know necessity is in the matter together with interactions/encounters. We know that each material, for example each atom, has some specific features that necessitate a specific move depending on the moves/features of the neighboring atoms, and the combination of some specific atoms constitutes a molecule (another level) that has some specific features necessitated from its specific parts (features of the atoms that constitute it)[15] and the moves/features of neighboring molecules. In other words: every part of an organism has its specific roles/features according to its features and its surroundings/position within this net, so that if it was in a different place, its roles/features/activities would have been very different. Since any genome, phenome, or environment consists of many kinds of materials (nucleic acids, phosphate groups, sugars, proteins, tissues, soil particles, water, etc.), research on them and explanation of them resembles Aristotle's investigations and explanations of material causes.

Genes carry information that can be transferred between generations, and genotype sometimes defines the organism's species, so we can say: research into and explanation of genotypes is similar to investigations and explanations of formal causes. But I want to emphasize that knowing the genotype of an

[15] The features of the molecule depend on the features of its atoms, but is different than the combination of the features of its atoms.

organism does not mean that we know its phenotype. It means that we have knowledge of one of the causes of the organism's phenotype. Through their phenome, genes interact with the environment to express themselves, and how much and which gene products will be produced depends on environmental signals and the developmental stage. So we can say that research into and explanation of environmental factors is also similar to investigations and explanations of formal causes. But as with genotypes, we cannot say that we have knowledge of the subject phenotype when we only know about environmental factors that affect it. Again we can only say that we "have knowledge of *some* of the causes of the subject phenotype." Phenotype sometimes defines the organism's species and its morphology and appearance, so research into and explanation of phenotypes is also similar to investigations and explanations of formal causes.

There cannot be a phenome without environmental effects. There cannot be organism without an environment, and I think we can even say that environment is intrinsic to living things. The interaction between organism and environment causes changes in living things, so research into and explanation of environmental factors and organisms (phenome+genome) is similar to investigations and explanations of efficient causes.

If we want to compare Aristotle's Theory of Four Causes and current phenotype research, we can say that Aristotle's material, formal, and efficient causes are similar to causes in phenotype research in investigations of phenotype, genotype, and environment (and in investigations of all related parameters: ecological, evolutionary, developmental, molecular, genetic, epigenetic, physiological).[16]

In phenotype occurrence there is both *stability and change* in organisms. Aristotle says these are both in the nature of the natural things. I think this togetherness of stability and change in living things occurs through the interaction between an organism and its environment, and that these are the very basic and essential features of living things. As parts of living things, genotype, phenotype, and environment have both stability and change in them. Speaking very generally, genotype has more stability, while environment has more change, and phenotype has equal parts of both.

Shields (2008) points out that "*some scholars have come to understand four aitia more as explanations rather than as causes*," and also says: "*Aristotle's approach to aitia may be regarded as blurring the canons of causation and explanation*." I think causation and explanation are strongly related to each other, but they are different in the sense that causation is about "what is there" and "what really cause something," while explanation carries both causation and our *intentions* (although causation also carries our intentions in the sense that we choose to give our attention to some specific causal relations rather than others).[17] Still, the causal relation is really there in the phenomena we are investigating.

Because of this, if we compare Aristotle's Theory of Four Causes and current phenotype research, one of the four causes—final cause—has no analogue in contemporary science, since we do not know (and *cannot* know) if it really exists. According to contemporary science, there is no *telos* in biological phenomena. Living things and their parts are not moving toward some specific end. They just happen because of the situation (all the current interactions) and the history of the situation (evolution and the all past interactions). Aristotle says that there is no evolution; he believed that each living thing has a specific form which is also its *telos* (final cause).

Today we know that this is not true. However, in our investigations into the living things we do use functional language: we say that some parts of living things are *for* some other parts or activities, as if they have some specific *telos*. But we speak this way due to the limitations of language, because this is how we inquire into living things (it is in our *explanations*). In attempting to understand how a living system works, we try to systemize a set of norms which operate it. However, we sometimes observe that it does not follow certain norms.[18] For example, if a living thing encounters a very unusual environmental stimuli, it may not act as we expect; it will

[16] Pigliucci (2003) says evolutionary processes are similar to efficient causes. This is coherent with what I am saying, but I think they are not the only processes that are similar to efficient causes. As I have stated, the investigation of the current interaction and the history of interaction between an organism and its environment resembles investigation of efficient causes. Pigliucci also states that ecological niche construction resembles final causation. I may agree with this only in the explanatory sense, not as a causal relation.

[17] And again I would emphasize that in the case of a regular phenome investigation, we leave many other parameters aside and attend to only a few. It is our *choice* to investigate *certain causal relations* rather than others.

[18] This is related to "reasons of indeterminacy in biology" (Mayr, 1961).

interact with the stimuli (probably stretching its phenome),[19] and through this interaction (which happens within the context of many other interacting things) it will rearrange itself and express itself according to this new environment, so its phenome will change. Alternatively, it may simply die (although when a system dies, it turns into another system). It does not have a specific end that it tends to be; it may become a vast number of things—different phenomes—depending on its interactions.

Living things are obviously different than nonliving things, but this does not mean that they have a *telos*. I think the only things that living things possess that resemble a *telos* are the needs *to exist* and *to express themselves*. This expression is always in some specific situation, and depends on all the organism's interactions and the history of all interactions. We cannot say that there is a *specific self* or *end* that living things tend to be. Some philosophers argue that biological organisation is inherently teleological, and that this intrinsic teleology can be grounded in the process of evolution; they say the biological organisation determines itself (Mossio and Bich 2014). I argue that it does not determine itself; rather, it expresses itself in its environment through its interactions. The self is the phenome of the biological organisation at a certain specific point in time (or the collection of the phenomes of it through specific time periods), and its expression is the result of the biological organisation-environment interactions (both the current interaction and the history of all interactions: a biological organization possesses the effects of its ancestral history throughout its genome and epigenome, and also its own history throughout its epigenome and phenome).

As stated above, there is an analogue to final cause in phenotype explanation and research (not in occurrence and not in causation), and we can also say that a *scientist's purpose* resembles a final cause. But the degree of similarity between final cause and a scientist's purpose is much less than the degree of similarity between formal-material-efficient causes and phenotype-genotype-environment parameters. This "final cause analogue" cannot be (and should not be) treated in the same way as the "formal cause analogue" in phenotype research, as are final and formal causes of in Aristotle's Theory, because if they are same, then the scientist's purpose is interfering with the explanation of the experiment.

The gene-centered view can be given as an example: here the scientific value of the experiment's data is still good (a causal relation is revealed), but the scientist's purpose is interfering with the correctness of the explanation. This happens when a scientist sees her/his nominated cause as the most important cause of the subject phenotype, as if there is no complex net, no set of many causes in the occurrence of phenotype. In this case, the scientist's nominated cause becomes like Aristotle's final cause in suggesting that the gene *has a purpose*: to *cause or try to cause a certain phenotype*. We know that genes do not have purposes, and they do not strive toward specific ends; they merely interact with a phenome and environment in a way that causes specific proteins to be produced. I am not saying that in no case is a gene the most important cause of the subject phenotypic trait. In rare cases a gene may be the most important cause,[20] but there are also other causes that altogether constitute the specific situation in which subject phenotype occurs. And in these rare cases in which a gene is the most important cause of the subject phenotype, scientists must investigate many factors to reach this conclusion.

Both "Aristotle's four causes" and "genotype-phenotype-environment" or "genetic, epigenetic, physiological, developmental, molecular, environmental, evolutionary factors" are related to each other very strongly in that they describe a complex net of factors that altogether constitute the organism. We can look for specific causes in specific research plans, depending on the situation and/or the purpose of the investigation, but we should always be aware that this is a way of doing practical research, and that these specific causes may differently affect other contexts, or there might be some other causes which are more important than the subject cause. If our aim is explaining an organism's phenotype as a whole (all the causes of it),[21] we should search for all three causes: formal-material-efficient (or ecological, physiological, developmental, molecular, epigenetic, genetic, and evolutionary) factors in the context of their interrelated state. And whether we are researching one part of the phenotype, or we are researching all parts of it, an awareness of all the interrelated factors and the complexity of the phenotype is very important for attaining a good explana-

[19] This stretching ability (phenotypic plasticity) also depends on all the previous encounters—all interactions the living system had throughout its life, and all interactions of its ancestors.

[20] Maybe we can say that in these cases, genes are "the difference makers" (Waters, 2007).

[21] This is of course still context-dependent.

tion of the phenotype, just as Aristotle's student of nature is aware of the multicausality of nature.

References

Anzaldo A A (2007) Back to the Future: Aristotle and Molecular Biology. *Ludus Vitalis* Vol XV, 28: 195–198.

Aristotle (2008) *Physics*. Oxford World's Classics, Translation: Robin Waterfield.

Dupré J (2012) *Processes of Life*. Oxford: Oxford University Press.

Falcon A (2012) Aristotle on Causality. In *The Stanford Encyclopedia of Philosophy*, ed. Edward N. Zatla.

Furbank R T, Tester M (2011) Phenomics – technologies to relieve the phenotyping bottleneck. *Trends in Plant Science* 16,12: 635–644.

Haig D (2014) Fighting the good cause: meaning, purpose, difference, and choice. *Biol Philos* 29:675–697.

IPCC (2014) Climate Change, Synthesis Report of the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. (eds.) The Core Writing Team, Rajendra K. Pachauri, Leo Meyer (subject to final copy edit and layout).

Lennox J (2006) Aristotle's Biology. In *The Stanford Encyclopedia of Philosophy*, ed. Edward N. Zatla.

Lewontin R (2011) The Genotype/Phenotype Distinction. In The Stanford Encyclopedia of Philosophy, ed. Edward N. Zatla.

Mayr E (1961) Cause and Effect in Biology. *Science* 134:1501–1506.

Mix L (2015) Nested explanation in Aristotle and Mayr. *Synthese* July: 1–16.

Mossio M, Bich L (2014) What makes biological organization teleological. *Synthese* November: 1–26.

Nicotra A B, Atkin O K, Bonser S P, Davidson A M, Finnegan E J, Mathesius U, Poot P, Purugganan M D, Richards C L, Valladares F, van Kleunen M (2010) Plant phenotypic plasticity in a changing climate. *Trends in Plant Science* 15: 684–692.

Pigliucci M (2003) From molecules to phenotypes? The promise and limits of integrative biology. *Basic and Applied Ecology* 4: 297–306.

Pradeu T, Vitanza E (2012) *The Limits of the Self: Immunology and Biological Identity*. Oxford: Oxford University Press.

Shields C (2008) *Aristotle. The Stanford Encyclopedia of Philosophy* (First published 2008; Summer 2012 Edition), Ed.: Edward N. Zatla.

Short T L (2002) Darwin's concept of final cause: neither new nor trivial. *Biology and Philosophy* 17:323–340.

Tinbergen N (1963) On aims and methods of ethology. *Zeitschrift für Tierpsychologie* 20:410–433.

Waters C K (2007) Causes That Make a Difference. *The Journal of Philosophy* 104: 551–579.

Williams N (2010) Aristotle's Lagoon. *Current Biology* 20(3): R84.

Woodward J (2010) Causation in biology: stability, specificity, and the choice of levels of explanation. *Biol Philos* 25:287–318.