**Causal selection in context: specificity, interdependence, and genetic causation**

**Abstract**

Causal selection is the decision one makes when giving a causal explanation to emphasize some causes of a phenomenon as relevant for explanation while backgrounding the rest. Contemporary philosophers agree that causal selection in scientific causal explanation must have something to do with the interests of scientists, though they disagree over whether or how this makes causal selection capricious. They study successful or well-regarded scientific explanations for commonalities that might underlie scientific causal selection decisions. Some accounts hold that once scientists’ pragmatic explanatory aims are fixed, causal selection can follow without further influence of idiosyncratic interests. In this paper, I argue that explanatory aims and selected causal properties or selected causes are interdependent. Further, I argue that this interdependence imposes a limitation on the usual philosophical strategies for understanding scientific causal selection.

**Introduction**

When giving a causal explanation of a phenomenon that has multiple causes, it is typical to pick out some of those causes as explanatory and background others as irrelevant to explanation. This is the process of causal selection, which has been of interest to philosophers of causation and causal explanation at least since John Stuart Mill. Philosophical accounts of causation and causal explanation that are concerned with identifying what is or is not a cause do not necessarily address the question of distinguishing among causes for the purposes of explanation. Most philosophical discussions of causal selection conclude that the choice of explanatory cause is pragmatic in one sense or another. Disagreement persists regarding how causal selection happens, in what sense it is pragmatic, and whether it is therefore arbitrary, capricious, or idiosyncratic. This makes causal selection a problem for philosophers of science. It does not seem that scientists identify explanatory causes capriciously, and if we were to find that they do, this would seem to threaten the integrity of scientific explanation. On what basis or bases, then, do scientists make justified decisions about causal selection?

Contemporary philosophers typically approach the problem of causal selection in scientific explanation by identifying exemplary scientific explanations and looking for commonalities among the causes that are cited in those explanations. They resist the idea that scientists prefer to emphasize certain causes for capricious reasons, so they typically look for features of causes that make them valuable by our existing explanatory standards. For example, some accounts identify shared properties of the causal relationships in exemplary explanations, such as specificity, stability, or proportionality (Waters, 2007; Woodward, 2010). On views like these, while causal selection does involve pragmatic interests in some ways, causal properties can serve as the basis for scientifically justified causal selection because they are general dimensions along which causal relationships can vary, rather than idiosyncratic features of the identity of particular causes.

One such property is fine-grained causal specificity(hereafter “causal specificity”[[1]](#footnote-1)), proposed by C. Kenneth Waters (2007)*.* A maximally specific cause is one which takes several states, and for each distinct state of the cause, one or close to one distinct effect state is produced. Waters’s proposal has been influential in the philosophical literature on causal selection. It has been criticized for its limitations, but the core of the account – that causal properties that we can identify can be the basis of justified causal selection – has been taken up by subsequent proposals. One such proposal that has implications for the scientific justification of causal selection comes from Lauren Ross, who argues that causal selection has two components: one pragmatic and one objective[[2]](#footnote-2) (Ross, 2019).On her view, while scientists do set their explanatory aims based on their interests (the pragmatic component), their aims do not dictate which causal properties will be conducive to those aims, nor do they predetermine which causes happen to have that property (the objective component).

Waters gives his account in the context of biological explanations of cellular processes of transcription and translation. Indeed much of the discussion about causal selection among philosophers of causal explanation taken place in the context of biology, especially genetics and development (Baxter, 2019, 2021; Franklin-Hall, 2015; Ross, 2019; Weber, 2017c, 2017a, 2017b). This has happened for a few reasons (in addition to the fact that much subsequent debate responds to Waters). Biology is causally complex, so they see it as a good context for studying causal explanation when there are many potentially relevant causes at work (Franklin-Hall, 2015). Also, there are causes in biology that biologists, philosophers, and people in general are very interested in comparing – (in)famously, genetic and non-genetic causes of phenotypic trait development. Thus, the case of genetic causation in the growth and development of phenotypic traits has become a kind of anchoring point for philosophical discussion about causal selection. The case is indeed useful for identifying some properties that play a role in causal selection, but it is also apt for my focus in this paper: I will show that the fact that explanatory aims depend upon the entrenched theorists and practices of research programs has important implications for the philosophical study of scientific causal selection.

I will argue for two conclusions. The first is that because explanatory aims depend on, among other things, the causal properties and causes highlighted by past research, these two components of causal selection are interdependent, rather than the causal properties and causes constituting an objective component that takes over once pragmatic aims are set. The features we should use to pick out the explanatory causes of a phenomenon do not follow neatly and separately from our explanatory aims, because those aims are dependent on the sorts of causes contemporary research practices are equipped to identify. While it is conceptually possible that explanatory aims could be set without consideration of the kind of causal control that scientists expect to access (nor the causes expected to facilitate that control) this is not guaranteed, and the structure of scientific practice suggests that the two are instead typically interdependent. The second conclusion is that, partially as a result of this interdependence, the philosophical strategy of surveying exemplary explanations for causal selection solutions is subject to a kind of sampling bias.

The paper is structured as follows: In Section 1, I introduce the problem of causal selection. In Section 2, I introduce C. Kenneth Waters’s account of causal selection, which will also introduce the case of genetic explanation for growth and development. I then show in Section 3 some cases that complicate Waters’s account as well as its implications for understanding the broad popularity of genetic research and genetic explanations. In Section 4 I argue that, contrary to accounts of principled causal selection like Waters’s and Ross’s, explanatory aims cannot be neatly separated from the causal properties scientists favor nor the identity of particular selected causes.

**1. Causal selection**

In this section, I introduce the problem of causal selection. Causal selection, as I mentioned above, is the decision that one makes when stating a causal explanation to designate one or more causes as explanatory while backgrounding (or not mentioning) others. The problem of causal selection is that it is not obvious how one could legitimately designate a cause as more important to cite in an explanation aside from idiosyncratic preferences. In an early articulation of the problem of causal selection, J.S. Mill wrote that there could be no “scientific ground for the distinction between the cause of a phenomenon and its conditions” (Mill, 1884, p. 401). Philosophers agree that causal selection is pragmatic in some sense, because explanation of course depends on what we choose to explain, but they disagree about whether this means it must be capricious or arbitrary in a way that threatens the integrity of scientific causal explanation.

The problem of causal selection arises for any account of causal explanation. In particular, on a minimal interventionist account of causation and causal explanation like that of James Woodward, no effect truly has a singular cause (Woodward, 2003). If causes explain their effects, and an effect has multiple causes, it should follow that each of those causes feature equally and necessarily in the explanation of that effect. But scientists and non-scientists alike routinely cite only one or a few causes as explanatory. If someone drops a burning cigarette on the forest floor, it may cause a fire. While the oxygen in the surrounding air is just as necessary to the fire, intuitively the dropped cigarette, not the oxygen, *explains* the presence of the fire (Hart & Honoré, 1959).

This case is usually resolved by appealing to a notion of structuring versus triggering causes – the oxygen structures the environment in which the cigarette triggers a fire (c.f. Mackie 1974; Dretske 1988; 2004; 2010). But is there some property that distinguishes these types of causes that can be systematically applied across contexts to determine non-arbitrarily which causes are explanatorily relevant? If so, then we can say that causal selection is *principled* in that it is governed by the explanatory value of such a property – whatever it is that makes a cause a structuring cause, for example. If not, then causal selection seems to depend on our (or scientists’) idiosyncratic preference for one or a few particular causal factors over the others. It is traditionally held that causal selection must be pragmatic (Mackie, 1974; Mill, 1884). Causal selection must, of course, have something to do with our explanatory aims, since we (or scientists) must decide what it is that we want to explain in the first place. So it will always be pragmatic in some sense. But if scientists favor one cause over another in their explanations simply because of their idiosyncratic preferences for one factor over another, this would seem to make causal explanation, a major epistemic goal of science, not only pragmatic but alarmingly capricious. Fortunately, scientists do not seem to be making entirely arbitrary decisions in their explanations, and so philosophers of science have looked to the explanatory practices of scientists to understand what guides their causal selection.

One of the sciences that philosophers study for exemplary explanations is biology – for one thing, because of its causal complexity.Biological systems are extraordinarily complex, so they provide many examples of successful explanations despite high causal complexity. This makes them, in the words of Laura Franklin-Hall, a “gold mine for those wanting to identify the selective patterns to which a philosophical account [of causal selection] is responsible” (Franklin-Hall, 2015, p. 18). In her view, searching successful causal explanations is the best way to identify causal selection criteria, and biological explanations offer a good sample. Franklin-Hall and other contemporary philosophers are interested in finding causal selection criteria based on intrinsic features of the relationship between causes and effects, rather than the particular identities of causal factors. Woodward’s causal properties of stability, proportionality, and specificity are examples of such properties (Woodward, 2010). Different explanatory aims might dictate that scientist prefer the, e.g., most proportional cause, and there are objective facts that can support the selection of one cause as the most proportional.

Another reason that philosophers have looked to biology to study causal selection is that philosophers have taken the properties identified in those criteria to constitute an important distinction between genetic and non-genetic causes. It is now generally recognized that the growth and development of phenotypic traits within organisms is brought about by the complex interaction of many genetic and environmental factors. But this “interactionist consensus” has opened further questions in the explanation of development – even though both genetic and environmental factors are causally relevant, there is plenty of room for important distinctions among those causes, and these differences have implications for explanatory practice. Further, genetics has been a hugely influential and productive research program, whereas the influence of non-genetic factors in biological studies of growth and development has received less attention overall. Perhaps the same properties that underlie causal selection can also help to explain the overall popularity of genetic research and genetic explanation. As we will see in the next section, this expectation is one reason that Waters uses the case of genetic causation in his account of causal selection. He suggests that identifying these distinctions can help to explain why “so much research attention is centered on DNA” (Waters, 2007, p. 21). Although I will show that the causal properties underlying causal selection do not go very far in explaining this overall research focus, doing so helps to show the relationship between explanatory aims and selected causes that I argue has implications for philosophical approaches to causal selection.

Building upon the idea of using inherent causal properties to differentiate among causes, Lauren Ross aims to make sense of the intuitively interest-dependent parts of causal selection while maintaining the integrity of scientific causal explanation (Ross, 2019). She argues that causal selection within a particular domain is supported by a context-dependent rationale that incorporates “objective” reasons but also depends upon the interests of investigators (Ross, 2019, p. 3). Our explanatory aims dictate *which* causal property is explanatorily valuable. This is the pragmatic component. Ross writes that, “causal selection for disease is pragmatic in the sense that it is relative to the practical goal of control” (Ross, 2019, p. 13). But the property itself belongs to the causal relationship itself; it is measurable and independent of our explanatory aims. Thus there is an objective component to causal selection: “…once the goal of control is specified, there are objective facts and considerations about what means conduce to it” (Ross, 2019, p. 13). The causes of a phenomenon present themselves with a variety of causal properties to a variety of degrees, and there are objective facts about which of those properties is best suited to our explanatory aims. While our aims tell us which property to prefer (the pragmatic component), the world tells us what the causal factors are, and which causal factor(s) is(are) most relevant (the objective component). On Ross’s view, this dual-component structure – explanatory aims on one side and objective causal features on the other – gives us a *principled* account of causal selection.

But Ross’s account promises too clean of a separation between explanatory aims and selected causal properties (and the causes that exhibit them). Ross argues that once explanatory aims are fixed, scientists’ interests have no further influence over which causal properties are conducive to those aims nor over which causes will exhibit those properties. But as I will show, explanatory aims are not independent of selected causal properties or the causes that exhibit them. This has consequences both for the proposed separation between objective and pragmatic components of causal selection as well as for the more general philosophical approach to causal selection of surveying exemplary explanations for common causal properties.

**2. Fine-grained specificity: a criterion for the objective component of causal selection in genetics?**

In this section I introduce an account of causal selection in order to show both how philosophers go about studying causal selection, and also to introduce the case of genetic explanation for growth and development as an exemplary explanation for understanding causal selection. I present and critique the account of causal selection from C. Kenneth Waters, who argues that scientists select causes that are what he calls *actual* as opposed to *potential* difference makers, that they sometimes further select causes on the basis of a property he calls “fine-grained specificity,” and that this helps to explain why, in biology, there is a relatively large focus of research and attention on genetics and genetic explanations. Genes in cellular processes have these properties of actual difference-making and fine-grained specificity that are explanatorily valuable.

In his 2007 paper, “Causes that make a difference,” C. Kenneth Waters helps to establish the connection between intrinsic features of causal relationships, like specificity, and causal selection, upon which Ross’s later dual-component account is built (Waters, 2007). He introduces concepts of *actual difference making* and *fine-grained causal specificity* as intrinsic properties of causal relationships that scientists use to make causal selection decisions. Waters makes this argument in the context of causal explanation in molecular genetics and consequently connects the general question of causal selection with discussions in the philosophy of biology about genetic causation. This connection was based on one interpretation of the causal parity arguments offered by proponents of Developmental Systems Theory (DST), an interpretation that Stegmann (2012) has called “Millean parity,” for its similarity to Mill’s claim that there are no metaphysical distinctions among causes.[[3]](#footnote-3) DST proponents were critical of attempts to conceive of genes as a distinct class of cause with some kind of privileged epistemic position. Waters intended to show that (1) in contrast to Millean parity, that there are indeed intrinsic differences among causal relationships, namely actual difference making and fine-grained specificity, (2) that these differences can be legitimate bases for causal selection, and (3) that the properties of actual difference making and fine-grained specificity can help to explain why so much research attention in biology has been focused on the activity of genes.

Waters develops his account within Woodward’s interventionist framework for causation and causal explanation, in which causes and effects are represented as variables that are systematically related to one another under intervention on the causal variable (Woodward, 2003). Actual difference making can be summarized as follows: in a given population and with respect to a fixed explanatory target, many causal variables may be identified, but only some of those causal variables take on different values among the members of that population. Others take the same value in each member of the population. Waters argues that DNA sequence is an actual difference maker with respect to MRNA sequence in the process of transcription in protein synthesis. In contrast, the enzyme RNA polymerase (which is present in the cellular environment) is only a *potential* difference maker with respect to mRNA primary sequence in the population of protein products. RNA polymerase is present in the cellular environment uniformly throughout the population of protein products; to vary its presence or character *would* affect the resulting mRNA sequence, but no such variation occurs in typical cells.

In cases in which there are multiple actual difference makers, as there are in protein synthesis in eukaryotic cells, Waters contends that while DNA is only *an* actual difference maker rather than *the* actual difference maker, it has an additional property of fine-grained causal specificity. Waters develops this notion by combining features from David Lewis’s account of causal influence and Woodward’s account of causal explanation: in a causal relationship in which *X* causes *Y, X* causes *Y* with fine-grained specificity if *X* takes many finely-incremented values and these values produce correspondingly fine differences in the value of *Y* (Lewis, 2000; Waters, 2007; Woodward, 2010). DNA sequence is a causally specific difference maker because “changes in the sequence of nucleotides in DNA would change the linear sequence of RNA molecules in many different and very specific ways” (Waters, 2007, p. 23).[[4]](#footnote-4)

The fact that genes alone among the many other causes present in the cellular environment possess *both* these features makes them an appropriate causal factor to single out as explanatory. Scientists do not cite genes as explanatory simply because they are genes, but because scientists’ explanatory goals direct them to pick out the specific actual difference makers in the population of interest, and in organismal development, this happens to be genes. Waters argues that this also helps to explain why biologists are so focused on genes more generally.

On Waters’s view, given biologists’ explanatory aims, the specific actual difference makers are the causes that scientists cite as explanatory, and because that decision is based on an intrinsic causal property and not simply idiosyncratic preference for the particular identity of a causal factor, we can say that causal selection of genetic causes is principled. Thus, for Waters, the general process of causal selection in explanation can be principled when it is based on the properties of actual difference making and fine-grained specificity, and in particular causal selection of genetic causes when explaining organismal development is principled for the same reasons. His account fits neatly within Ross’s framework: there is an objective component to the selection of genetic causes, which is that they possess the properties of actual difference making and fine-grained specificity which are conducive to the explanatory aims of scientists, as well as a pragmatic side, which is our preexisting explanatory aims.

Waters does not claim that fine-grained specificity is unique to DNA outside the context of protein synthesis, nor does he claim that it is the only factor that explains the general popularity of genetic research and genetic explanation.[[5]](#footnote-5) However, Waters’ view that causal specificity is a significant property of genes is taken to be the received view among philosophers (Griffiths & Stotz, 2013; Neal, 2019; Planer, 2015; Weber, 2017c). And it is an example of the kind of implications that are sometimes drawn from examining exemplary explanations for causal selection criteria.

**3. Complications for fine-grained specificity and genetic causes**

Although actual difference-making and fine-grained causal specificity are important for understanding causal selection, they cannot, separately or together, account for the explanatory decisions of scientists studying growth and development. In this section, I discuss several examples in which Waters’ notion of causal specificity either fails to identify the selected genetic cause in a biological explanation, or it successfully identifies the selected cause, but that cause is not genetic. Cases of the former type challenge the generality of the idea that the aims of biologists call for specific causes, while cases of the latter type challenge the idea that genes just happen to have the causal properties that happen to be conducive to biologists’ explanatory aims. These challenges complicate the idea that a solution to the problem of causal selection can also explain the more general focus on genes and genetic explanation. They also suggest that there is something else influencing causal selection besides the initial pragmatic determination of explanatory aims, identification of the most conducive causal property, and identification of the causal factor(s) that maximize(s) that property.

I will discuss explanatory targets of varying proximity to DNA sequence to show that causal specificity and causal selection come apart in explanations of growth and development. Waters uses examples from the immediate intracellular environment to argue for actual difference making and causal specificity. This explanatory target is proximate to DNA sequence because there are relatively few causal steps (in this case, molecular processes) between the cause (DNA sequence) and the effect of interest (RNA sequence). While molecular biologists have shown these processes to be highly complex (which I will discuss further in the next subsection), there are even more steps between DNA sequence and a developed trait than there are between DNA and RNA sequence. In contrast to e.g., the sequence of RNA molecules or even the identity of protein products of genes, developed traits include things like eye color or adult body size. It is worth considering these downstream explanatory targets because the broad popularity of genetic explanation, of course, encompasses much more than the proximate cellular environment of DNA molecules.[[6]](#footnote-6) And so I will discuss examples from the intracellular environment, the slightly ‘zoomed out’ environment of gene expression in, e.g., tissues, and finally to the developed phenotypic trait. Traits are the focus of the paradigmatic works of DST, which are some of Waters’ primary targets (e.g., Oyama et al. (2001), Oyama (1998), Griffiths and Gray (1994)) and notably they are also the original target of the study of heredity, as some biologists have recently pointed out, e.g., Orgogozo, Morizot, and Martin (2015)). In the sections that follow, I will give several examples that help to decouple causal specificity from genetic causes in growth and development by considering explanatory targets causally far downstream of DNA sequence.

*3.1 Specificity, protein synthesis, and gene expression*

Within a broader argument for a different conception of specificity in genetics, Paul Griffiths and Karola Stotz provide reason to think that DNA exhibits Waters-style causal specificity in relatively few contexts within cells (Griffiths & Stotz, 2013). They argue that DNA is not the “sole source of specificity” for gene products (Griffiths & Stotz, 2013, p. 78). Griffiths and Stotz aim to clarify the role and character of specificity in biological development. Their argument is a broader presentation of specificity in genetics but is aimed partly at Waters. They begin with a reconceptualization of the gene in modern biology – the *postgenomic gene*, identified not by particular segments of DNA at particular loci but by the “collection of sequence elements” that collaborate to build a functional product (Griffiths & Stotz, 2013, p. 75). They present specificity is a feature of the gene product – the sequence of RNA nucleotides in a functional RNA molecule, or the primary structure (amino acid sequence) of functional proteins. These products are instances of an enormous variety of possible sequences. Rather than a relationship between a cause and an effect (as Waters uses the notion), specificity, for Griffiths and Stotz, is an explanatory target of its own – what molecular geneticists need to figure out is how the particular identity (sequence) of the gene product is determined. This conception of specificity follows Francis Crick’s sequence hypothesis, in which specificity is also treated as a feature of a piece of a nucleic acid (Griffiths & Stotz, 2013, p. 40). Griffiths and Stotz elaborate this within the framework of information science, which, as they show, neatly captures the idea represented in the sequence hypothesis: there is a certain amount of specific information in the gene product, and that information must come from somewhere – precisely *that* information, or else it would be a different product. The sequence specificity of the gene product underlies its specificity in the historical, stereochemical sense: it interacts with only very particular substrates (Griffiths & Stotz, 2013, pp. 33–40).[[7]](#footnote-7)

Their foundational claim about specificity is that the information that determines the precise identity of a gene product is not contained within only one contributing causal factor – instead, that information is distributed among many causal factors. To capture this idea, they introduce a concept of *distributed specificity* – the cell can precisely control which gene products are made, but only through the action of several causal factors brought together in the right arrangement. They demonstrate this through a careful examination of the processes by which cells actually build gene products. In these processes it is typical, not exceptional, for cells to use a wide range of regulatory factors to determine the particular sequence of a gene product, including but not limited to *cis*-acting sequences, *trans*-acting regulators, and environmental signals. Cells use this process of “regulated recruitment and combinatorial control,” not nucleotide-level variation, to control which gene products are produced (Griffiths & Stotz, 2013, p. 49).

The implications of their argument for Waters’ notion of causal specificity and its role in causal selection, however, need explication. Griffiths and Stotz intend for their argument to respond directly to Waters. They position Waters as holding essentially the same view as Crick in the sequence hypothesis – on their view, when Waters claims that DNA sequence is the only specific actual-difference maker with respect to gene product, he is claiming that DNA is the “sole source of specificity” for the mRNA sequence (Griffiths & Stotz, 2013, p. 78). But this is a subtle reinterpretation of Waters’ view. Waters’ notion of causal specificity differs from both stereochemical and Griffiths and Stotz’s informational specificity in that it is a property of causal *relationships*. Distributed specificity, in contrast, does not describe a relationshipbetween any one cause and the effect. On Griffiths and Stotz’s view, specificity of a gene product is a kind of achievement, which the cell uses “combinatorial control” to attain. Specificity is a feature of the product that needs explanation (where does it come from? how is it achieved?), not a feature of a causal relationship that produces it. Waters’ notion of causal specificity is a property of the mapping between a causal variable and an effect variable; on his view it is incoherent to say that there is a “source” for causal specificity. The Waters picture would certainly allow that many factors contribute to the *particular* identity of a gene product, but he would maintain that only (or most often), DNA sequence is the only cause that has this special relationship of fine-grained specificity with respect to the product. Griffiths and Stotz are, for the most part, making a positive claim by means of their conceptual shift in ‘specificity’ — theirs is the notion of specificity that matters, because Waters’ causal specificity does not feature in the typical activity of cells. But at some points they equivocate, rather than shift. For example, shortly after claiming that the specificity of a gene product is distributed among “*cis*-acting sequences, *trans*-acting regulators, environmental signals, and contingent history of the cell,” they claim that “…all the factors just listed are causally specific difference makers” (Griffiths & Stotz, 2013, p. 99). This is not so — none of these is necessarily a causally specific difference maker. In fact, each of these may have varying degrees of *causal* specificity with respect to the sequence gene products, depending on the product of interest. These factors may have relatively few states that correspond to relatively few differences in the gene product, which is only to the cell’s benefit, if that is the sort of control required to produce the product in question.

Contrary to their stated aims, however, they do not show that there exist other *causally* specific actual difference makers in protein synthesis; they instead show that there often are no causally specific actual difference makers to be found, because there are not particular causal factors that ‘concentrate’ variation into one factor (it is instead distributed among many). Griffiths and Stotz show convincingly that cells do not typically achieve the particular identities of their gene products by modulating the nucleotide sequence and instead do so by recruiting different sets of causal factors (regulated recruitment and combinatorial control); which does imply that the cell is not exploiting the causally specific relationship between DNA and RNA sequence to regularly produce the actual variety of gene products that it produces. More accurately, then, they show that there typically *are no* specific causes for the gene product.[[8]](#footnote-8) The negative conclusion that cells do not typically exploit DNA sequence variation in the way that Waters claims is important for our purposes here, because it implies that the causes selected in explanations of biological development at the intracellular level are not marked by causal specificity. Some arguments against causal specificity in proximate processes extend beyond protein synthesis; other philosophers have made claims similar to those of Griffiths and Stotz about broader gene regulatory networks (DiFrisco & Jaeger, 2020). It will be helpful, however, to consider further cases that support the separation of causal specificity, causal selection, and genetic causes.

Another argument that extends from proximate contexts to more distal ones comes from Janella Baxter, who argues that gene *expression* *levels*, not DNA sequence, control phenotypes at the proximity of tissues and beyond, and these are *often* the relevant feature for causal selection in explanations of developmental biology. Gene expression level might have fine-grained control over a phenotype, but it might instead have a threshold effect (Baxter, 2021). Gene *knockdown* experiments finely modulate the level of a gene’s expression, while gene *knockout* experiments prevent its expression entirely. This latter type of control is not causally specific in Waters’ sense, but both types feature prominently in genetic research.

Actual difference making and specificity are neither unique to DNA nor a ubiquitous property of selected causes in growth and development, even for the targets that interested Waters and others that are found at similar proximity to DNA sequence. But biologists interested in the causes of growth and development are often interested in targets further causally downstream, like phenotypic traits of developed organisms, so it is worthwhile to see whether and how specificity features in those explanations.

*3.2 Specificity and phenotypic traits*

Recall that by “developed phenotypic trait,” I am referring to traits like eye color or body size – phenotypic features that lie far causally downstream of genetic causes, but for which genetic factors are routinely investigated by scientists. The following examples concern specificity and causal selection at this relatively distal scale.

*3.2.1. Some selected causes are specific but not genetic*

Consider the phenomenon of developmental phenotypic plasticity. This is the ability to develop different forms of a trait in response to environmental stimuli. Recent work has uncovered phenotypic traits with dosage-dependent responses to environmental factors. In these cases, incremental changes in the value of a non-genetic cause result in similarly incremental changes in the value of a phenotypic trait, meaning that such non-genetic causes have fine-grained causal specificity.

Griffiths and Stotz (2013) use developmental plasticity as an example to demonstrate that environmental factors can be present among the causes of a developmental outcome – they characterize it as one of the locations of distributed specificity. But again, this is to say that an environmental factor is one of the causes of the particular identity of the gene product; it does not necessarily mean that the environmental factor is itself a cause with fine-grained specificity. On their view, environmental factors may be binary switches and yet maintain their membership to the “distributed specificity” of the gene product. Because the example I give here describes a continuous, dosage-dependent morphological response to an environmental factor, it shows that an environmental factor – a single causal variable – can have fine-grained specificity of just the same kind that Waters attributes to DNA sequence.

Ecologists Nancy Schoeppner and Rick Relyea have shown evidence that fine incremental increases in the density of predators in an organism’s environment causes size differences in prey that are also finely incremented (Schoeppner & Relyea, 2008, 2009). This means that predator density is a specific cause in the same sense that Waters describes for DNA sequence causing RNA sequence. Schoeppner and Relyea use a model organism, larval anuran (wood frog tadpoles, species *Rana sylvatica*). The tadpoles were exposed to an “increasing gradient of predation risk,” to “determine how organisms respond to small environmental changes.” Predator presence was manipulated in two ways: “by altering the amount of prey consumed by a constant number of predators (*Dysticus sp.*) and by altering the number of predators that consume a constant amount of prey.” They found that morphological traits, e.g., various measures of body size, all exhibited a fine-grained response to incremental increases in predator density.On an interventionist account of causation, predator density is clearly a cause of body size, because interventions on predator density reliably produce changes in body size. Predator density is also a *specific* actual difference making cause: it is the fine-grained increases in predator density that produce fine-grained, graded responses in body size. From this example, we can see that biologists select causes which are specific, though non-genetic. Developmentally plastic traits like body size are sometimes explained by a specific, though non-genetic, actual-difference maker.[[9]](#footnote-9)[[10]](#footnote-10)

*3.2.2. Some selected causes are genetic but not specific*

Often when a gene appears to be the only actual difference making cause of a trait, it is not causally specific for its target. There are further cases in which a genetic cause is not specific, yet it is selected over other, non-genetic, specific, actual difference making causes. In the former category, several paradigmatic genetic diseases are said to be explained by a genetic causal factor, where the mutated gene is the only actual difference making cause. One prominent example is Huntington’s Disease, which is caused by mutation in the HTT gene. Huntington’s Disease, along with others like Tay-Sachs’s Disease and sickle-cell anemia are common even in biology textbooks as exemplars of genetic disease. But in such cases the genetic cause is not specific in Waters’ sense. The presence or absence of the mutation is binary, and the disease phenotype is also binary, so it is not the case that many fine-grained changes to the causal variable produce correspondingly many fine-grained differences in the effect. However, these are decidedly genetic diseases – their phenotype is explained by the genetic mutation that causes them.

More powerful are examples of the second type – in which genes are among several actual difference making causes, they are not specific, and they are still the primarily selected cause. I will use the example of the genetic disease Phenylketonuria (PKU) here for its familiarity, but in fact the phenotype of *any* genetic disorder involving the inability to process some metabolic substance will have at least a mutated allele and a metabolite as actual difference making causes of symptom severity (Galactosemia is another example). PKU is characterized by an inability to break down the amino acid phenylalanine when it is consumed in the diet. The disease phenotype includes severe cognitive impairment, organ damage, unusual posture and severely compromised pregnancy (Cederbaum, 2002). It is caused by mutated alleles of the PAH gene that prevent the body from producing enzymes needed to break down phenylalanine.

Consider the explanatory target of symptom severity. Symptom severity varies in fine degrees with the amount of phenylalanine consumed. The amount of phenylalanine consumed is a specific, actual difference making cause. Different mutations in the PAH gene can contribute to symptom severity, but the relationship appears heterogenous and unspecific: “…the notion of genotype-phenotype correlation [in PKU] has been shown to be relatively unhelpful or relatively incomplete, and…substantial genetic heterogeneity is known” (Cederbaum, 2002, p. 702).[[11]](#footnote-11) Much morevariation in much finer degrees of symptom severity are explained by consumption of phenylalanine. Indeed, PKU is primarily treated with a restricted diet in which one does not consume phenylalanine. The level of phenylalanine consumption is, then, a specific, actual difference making cause. Moreover, phenylalanine consumption is a more specific cause than the PAH variant. In this case, the genetic cause is selected over another specific, actual difference making cause.

These examples show that non-genetic causal factors and non-specific causal factors are cited by biologists as explanatory. Taken together, these cases help to separate causal specificity from genetic causes and from selected causes for downstream explanatory targets. Specificity, even in combination with actual difference making, does not account for causal selection in biology, and consequently cannot account for a general focus on genes in causal explanation.One might object that the fact that some selected causes are not specific, or are specific but not genetic, is not relevant to Water’s original argument. For example, Janella Baxter argues that to present counterexamples as objections to the scope of actual difference making and causal specificity is just to miss Waters’ larger point, which is that actual difference making is a solution to causal selection (Baxter, 2021). The fact that this property is not unique to DNA sequence, she argues, does not threaten actual difference making as a refutation of the causal parity thesis. But it is important here that Baxter, following Waters, is interpreting the parity thesis as Millean parity and therefore identifying the parity thesis with the general philosophical problem of causal selection. Recall that Waters makes clear that his aim is not only to distinguish among causes, but also to explain why “so much research attention is centered on DNA” (Waters, 2007, p. 21). Actual difference making is a counterexample to Millean causal parity – the claim that there exist no objective or inherent differences among causes as causes. But it is of limited generality in providing a solution to causal selection and cannot account for the broader research focus on genes and genetic explanation.

**4. Interdependence and the sample of exemplary explanations**

In this section, I argue that explanatory aims and selected causes and causal properties are interdependent, and that this interdependence imposes limitations on philosophers’ strategy of surveying exemplary explanations for causal selection solutions. Ross’s alleviates some of the challenges to Waters’s account posed in the previous section, because she points out that scientists desire different kinds of causal control depending on their explanatory aims. Thus, Ross proposes a more general account of causal selection that explicitly builds in the idea that many causal properties may be relevant. It does not tell us about any connection between the causal properties that scientists select and a focus on one sort of entity as an explanatory cause, i.e., genes – if biologists just desire all different types of causal control depending on the context, how might biologists end up with a relatively large focus on genetic explanation? Recall that on Ross’s view, once explanatory aims are set, the criterion for causal selection should be an intrinsic feature of the cause that serves the explanatory aim. But explanatory aims depend on the framework of investigation available – when causal specificity (in the complementary relationship between DNA and RNA) strands is available to exploit, our explanatory aims are influenced by this availability. This is a particular instance of the more general ideal that successful output from a research area supports subsequent, similar research. Consider two ways in which this kind of support manifests.

First, Waters argues more recently that that biologists focus on genes because genes are uniquely *useful* in biological practice, and that genetics progresses by extension of its techniques, rather than by fleshing out a central organizing theory (Waters, 2004, 2019). What makes genes useful? Perhaps causal specificity underlies causal selection for explanatory targets in the proximate molecular environment of DNA, and then, because genetics was so successful there, its explanatory scope expanded outward, to include targets further downstream. If so, causal specificity would directly explain the success of genetic approaches to the molecular environment of cells and indirectly explain the breadth of the explanatory scope of genetics. It would also mean that selection of genetic causes follows from the more general utility of causal specificity. However, the idea that genes are popular as useful tools in fact contributes more support to the biasing of successful explanations than to the idea of an inherent useful property that genes have.

First, the molecular genetic tools developed for the manipulation of causal relationships proximate to DNA sequence sometimes exploit causal specificity, though not always. They do often exploit the complementarity of DNA and RNA strands. But they do not always exploit *causal specificity with respect to RNA product*, and certainly not to more downstream targets*.* Recall Baxter’s example above – gene knockout and gene knockdown experiments both exploit the DNA sequence associated with a product expression level, but not necessarily the causal specificity of the DNA sequence with respect to the RNA product. And of course, like any tool, genes are not useful solely because of their properties, but because we have the means to take advantage of those properties. Even if causal specificity is useful, it cannot on its own explain why genes are useful tools in contrast to other factors; its utility also depends upon the framework that has already been developed to exploit it.

Second, consider Helen Longino’s work that shows the compartmentalization of research approaches in studying human behavior. In her book, *Studying Human Behavior* Longino shows empirically that among the approaches to studying behaviors, research uptake is clustered within groups of researchers working on the same approach, with the same investigative tools, methods, etc. (Longino, 2013). That is, researchers that are committed to some approach tend to take up, modify, and extend the questions (and answers) afforded by that approach. This, she argues, has partially to do with the incommensurability among some of the different approaches to studying behavior – that they are simply working in different causal spaces. That is to say, they are building the fact that the cause is genetic into their explanatory aims. Scientists often effectively choose their explanatory aims effectively by choosing causes to investigate. Pointing this out also draws attention to the fact that individual scientific studies set up as controlled experiments isolate one variable to determine whether it is a cause. There is therefore a disconnect between the causal explanations offered by individual studies and the more synthetic causal explanations that include multiple factors already confirmed as causes that philosophers might study for causal selection.

What this means for causal selection is that our explanatory aims depend on the kind of control we expect that we can have, based on the technology, theory, and infrastructure that scientists have access to, or even the kind of causes we want to identify in the first place. And the reasons that scientists focus (overall) on one sort of approach are many; not only do they depend on the existing research framework but on other sociological, historical, and public interest factors.

Then it is not the case that explanatory aims are independently set first and then tell us what causal properties to prefer. Rather, the two are *interdependent*. It is not the case that there is a causal property that happens to serve our independently set pragmatic goals. Rather, our pragmatic goals are partially determined by the accessibility of that causal property (or the causes we expect to exhibit that property). Our explanatory aims were affected by the discovery that some genes were specific for certain effects. Moving from a causal property like causal specificity to the conclusion that it is explanatorily significant implicitly invokes the idea that what we can access is explanatorily significant for our aims – maybe it is reasonable or otherwise acceptable that our explanatory ideals depend in part on what we can access, but it does not imply inherent epistemic superiority.

Further support for this claim can be found in Marcel Weber’s responses to Waters. Marcel Weber argues that causal specificity alone does not single out genes in explanation; rather, an additional, precisely defined criterion of *biological normality* is required to sort out which specific actual difference makers matter for explanation and which do not (Weber, 2017c, 2017a). The relevant causes are accessible via biologically normal interventions. These are interventions in Woodward’s sense, with two additional criteria:

(1) the intervention may also be due to natural processes such as spontaneous mutation, replication error, transposition, etc. (the *cetera* includes all known natural causes of genetic variation)

(2) the intervention is compatible with the continued persistence of the biological entity that is being considered (Weber, 2017a).

That is to say, in order to single out genetic causes as explanatory, we need a criterion of causal *relevance*. Once defined, we should be able to apply the criterion of biological normality across explanatory contexts. However, Janella Baxter responds to Weber by arguing that geneticists often pursue decidedly *abnormal* interventions in the laboratory, and it is often these that produce new genetic technologies (Baxter, 2019). The causal variables manipulated by these abnormal interventions are both useful and explanatory. Here, we can see that the ‘objective’ feature of biological normality is dependent upon the experimental framework that geneticists develop.

In addition to the other sociological and historical features that impact what research is pursued and what explanations are produced and shared, this interdependence has implications for the philosopher searching for common properties of selected explanatory causes. For finding a common causal property does not tell us about the relative explanatory value of other properties less represented, for they may be absent for reasons other than explanatory value. If a variety of historical factors explain the broad popularity of genetic explanation as well as the fact that successful explanations in genetics often feature specific causes, and these are the explanations that we search in order to develop causal selection solutions, then we are subject to a kind of sampling bias. If the research choices are constrained by tools that take advantage of causal specificity, then we should expect explanations of targets whose causes can be accessed via that tool. For far downstream phenotypic targets, this may only be a small subset of the things we might otherwise be interested in explaining. Philosophers cannot examine successful explanations that we do not have. Approaches to causal selection like the one followed by, e.g., Waters in his 2007 work and Laura Franklin-Hall are limited in the generality that they can achieve regarding the causal properties or principles that scientists use to make causal selection decisions. Descriptively, of course, one could identify the bases that these explanations have for the causes they highlight, but this alone cannot explain why that property is used for causal selection, nor justify that it is in principle an important explanatorily valuable property compared to others.

**Summary**

Although philosophers agree that causal selection is pragmatic in *some* sense, they take that not to mean that causal explanation is entirely arbitrary or capricious. My first conclusion was that is that this vindication of scientific causal selection cannot be supported by isolating explanatory aims from selected causal properties. Although I have shown that causal selection is not isolated from interests and protected from capriciousness in the way that Ross describes, I have not argued that causal selection in genetics nor the general popularity of genetic explanation is itself unjustified or capricious. This idea that causal properties are limited in their ability to explain the success of the genetic approach is broadly consistent with Waters’ other views about pluralism and the varied roles of genes in biology.

My second conclusion was a consequence of that interdependence relevant to philosophical approaches to causal selection – it is simply that we must be careful not to overgeneralize when mining successful explanations in biology for solutions to causal selection. This sample is partially determined by the explanatory aims of biologists, which are not independent of causal properties. Therefore, the connection between causal selection and the popularity of genetic explanation is, in a sense, in the opposite direction than philosophers expected. It is not that the properties underlying causal selection will account for a broad focus on genes, but rather that the presence and pervasiveness of that focus explain why we have identified particularly those solutions to causal selection.

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1. There are, as we will see, other notions of specificity relevant to this discussion. [↑](#footnote-ref-1)
2. The sense of ‘objective’ used in Ross’s Water’s work on this topic is minimal and only means insensitive to an agent’s wishes or desires. [↑](#footnote-ref-2)
3. Waters appears to draw this interpretation of ‘parity’ primarily from *Cycles of Contingency* (Oyama et al., 2003; Waters, 2007, p. 3). Oyama and Griffiths have separately responded to the interpretation of DST parity as Millean parity. Griffiths maintains that there is a limited ‘parity thesis’ stating the symmetry of causal information among genes, environmental factors, and phenotype, which is informational, rather than Millean parity, c.f., (Griffiths & Stotz, 2013). Griffiths, Oyama, and Gray elsewhere describe the parity thesis as a rejection of a dichotomy between genes and environment – that such a division is only one possible division, helpful in some cases and not necessarily in others (Oyama, 1998; Oyama et al., 2001). Waters’ interpretation here therefore simplifies the DST parity thesis. But it does motivate the idea of distinctions among *causal properties*, not only among the identities of different causes, and if DNA does have a particularly valuable property, this does challenge the claim that the gene-environment division is only one of many choices of equal explanatory potential. Noting that Waters sets up his causal selection account in contrast to DST and Millean Parity is important for my discussion here, but because my argument and its implications are not directed at DST, I refrain from further discussion of Waters’s accuracy to DST texts. [↑](#footnote-ref-3)
4. Woodward (Woodward, 2010) describes two notions of specificity – one is fine-grained influence (where cause and effect variables each have finely-incremented domains) and the other is the extent to which a causal relationship approximates a one-cause, one-effect relationship (and a causal relationship could have both kinds of specificity). Fine-grained influence seems to be the relevant notion here; I have treated this notion in Waters as roughly the same notion that Woodward describes. [↑](#footnote-ref-4)
5. As is clear both in his 2007 paper and influential body of work in the history and philosophy of genetics, e.g., Waters (2004, 2006, 2007). [↑](#footnote-ref-5)
6. Waters, more recently, points out that genetic explanations that rely on causal specificity are extremely limited to the "temporally" and "biologically" close effects within the cell though he uses a concept of temporalproximity to DNA sequence rather than causal proximity. (Waters, 2019). [↑](#footnote-ref-6)
7. This is the sense of biological specificity that structured much of the work in biochemistry and molecular biology that preceded molecular genetics (Morange 1998; 2020). [↑](#footnote-ref-7)
8. Planer (2015) makes another observation along these lines but does not pursue implications for Waters’ account. [↑](#footnote-ref-8)
9. Regarding such specific causal relationships in natural populations, Schoeppner and Relyea note that *Rama sylvatica* are likely to experience variation in predator density year over year due to the fact that both species colonize new, seasonally available environments (vernal pools), suggesting that some experimental conditions will regularly appear in natural populations. However, the specificity of the causal relationship could be compromised by other variation that occurs in natural populations, e.g., prey food availability (Schoeppner & Relyea, 2009, p. 592). [↑](#footnote-ref-9)
10. Regarding the generality or frequency with which we should expect such fine-grained environmental influences on morphology, Schoeppner and Relyea note that their findings are consistent with a number of similar studies, citing examples in both plant and animal studies and writing, “While this study focuses on the effects of variability per se on inducible defences, it is in accordance with the findings of previous work examining the effects of temporal variation in resources on an individual’s phenotype. In all studies to date that have manipulated fine-scaled variation while holding the average environment constant, at least one trait was affected by environmental variability” (Schoeppner & Relyea, 2009, p. 592). [↑](#footnote-ref-10)
11. A more recent review from Hillert et al. (2020) presents a broad study of PAH alleles and finds a similarly unspecific relationship between allelic variant and disease severity. [↑](#footnote-ref-11)