Causes that Make a Difference *

C. Kenneth Waters

Minnesota Center for Philosophy of Science,
Department of Philosophy,
University of Minnesota

1. A Puzzle and Two Questions

The best theories of causation do a better job clarifying what it means to identify a cause than specifying what it means to pick out the cause that made the difference. For instance, counterfactual theories can explain what it means to say "Mary's striking the match caused the match to light", but they do not explain what it could mean to specify "Mary's striking the match, rather than the presence of oxygen, caused the match to light." Mary's striking the match counts as a cause on counterfactual accounts because if Mary had not struck the match, then the match would not have lit. But the same reasoning leads to the conclusion that the presence of oxygen was also a cause; if oxygen had not been present, then the match would not have lit.[1] There is no denying that oxygen was a real cause. Nevertheless, in ordinary contexts, observers would identify Mary's striking the

* Thanks to Jeff Barrett, Mark Borrello, Richard Creath, Norman Dahl, Richard Grandy, Bill Hanson, Susan Hawthorne, Toben Lafrancois, Roberta Millstein, Bart Moffat, Jane Maienschein, Sandy Mitchell, Katie Plaisance, Chuck Stieg, Marcel Weber, Beyong-Uk Yi, and especially to, Helen Longino, Jay Odenbaugh, Michael Strevens, Jim Woodward, and referees of this journal for constructive comments on various versions of this paper.

[1] Some might say that Mary's striking the match is the "triggering cause" because it explains the timing of the event and that other causes, including the presence of oxygen, are "structural". But this distinction breaks down under a counterfactual analysis of causation. For example, under a counterfactual analysis, the timing of the match lighting was also due to the fact that oxygen was not removed just before the match was struck and then reintroduced with a torch just after the match was struck. In this case, the match would have lit at a later time. Hence, one might argue that the timing of the match lighting was caused by such a series of events not occurring. The distinction between triggering and structural causes, or something much like it, can be sustained by analyzing it in terms of actual difference making causes, rather than mere causes.

match, and not the presence of oxygen, as the factor that made the difference. And in an important sense they would be right. The puzzle is, in what sense?

There is a distinction to be drawn between identifying the causes of an actual phenomenon, such as the presence of oxygen, and picking out the cause that actually made the difference, such as Mary's striking the match. This distinction is elusive, and it is tempting to dismiss it as illusory. On this view, there is an ontological difference between causes and non-causes, but there is no ontological difference among causes. This was the position taken by Mill who argued that the capricious manner in which we select causes from conditions indicates that there is no scientific ground for a distinction.[2] Subsequent attempts to explain the selection of "the cause" from many causes (or from many "conditions") have generally centered on interest-laden factors that depend on the context of inquiry. For example, Hart and Honoré's say that the selection depends on principles that vary "both with the type of causal question at issue and the circumstances in which causal questions arise"[3]. As Mackie explained:

> *. . . since even the choice of a field is relative to a purpose or a point of view, and since even apart from this what we recognize as a cause, rather than a mere condition, commonly depends on what we know – or what we knew first – or what is closely related to our interests, there is much to be said for Mill's refusal to distinguish 'philosophically speaking' between causes and conditions. As an analysis of ordinary language, this would be wrong; but from a theoretical point of view, as an account of causal processes themselves, it would be right."*[4]

Mackie's claim has not been seriously challenged. According to the received philosophical wisdom, the causes we select as "the cause" are the causes that are most relevant to whatever interests we happen to have. Selected causes do not share some ontological feature that non-selected causes lack. What selected causes share is our interest. And our interests, as Hart and Honoré's analysis of the contextual factors underlying the selection of causes reveals, vary from one epistemic context to the next. Ontologically speaking, causes are causes. This view suggests that seeking the one cause among many that actually made the difference would be a fool's errand. Although this is the dominant view in the philosophical literature, it is difficult to sustain when attention is turned to scientists' concrete efforts to identify which cause among a set of causes is actually making the difference.

Nowhere is the practice of picking out actual difference makers more real than in biologists' account of the role of DNA in the development and

---

[2] John Stuart Mill, *A System of Logic*, (New York, NY: Macmillan Press, 1950), p. 244.

[3] H. L. A. Hart and A. M. Honoré, *Causation in the Law* (Oxford: Clarendon Press, 1985), p. 31.

[4] J. L. Mackie, *The Cement of the Universe* (Oxford: Oxford University Press), p. 120.

functioning of cells and organisms. Biologists agree that DNA exercises its roles through the production of RNA and polypeptide molecules. Given the mechanisms of RNA and polypeptide syntheses, DNA is obviously a cause of linear sequences of nucleotides and amino acids comprising these molecules. But, just as obviously, DNA is only one of many causes. Although biologists and philosophers often talk as if DNA "produces" RNA and polypeptides, everyone knows that many different molecules and cellular structures play necessary roles in the *in vivo* syntheses of these important molecules. Even in the simplest case, the production of RNA molecules in prokaryotes, the syntheses causally depend on RNA polymerase. This has led some philosophers to argue for "parity" and against the "reductionistic bias" of biologists who center so much attention on the role of genes and DNA.[5] But perhaps biologists are right, perhaps there is an ontological feature that distinguishes DNA as the actual difference maker. Determining whether biologists are right requires solving the conceptual puzzle about the difference between what it means to be a cause and what it means to be a cause that actually makes a difference. The aim of this paper is to solve this conceptual puzzle and address two related questions about causal reasoning in biology.

The first question concerns arguments for causal parity in complex biological systems. These arguments typically start with the premise that the kind of element emphasized by scientists as the cause of a given process is actually *just* one of many causes of the process. Parity arguments then claim that picking out one cause, when in fact there are many, cannot be justified on ontological grounds because, after all, causes are causes. Some proponents of parity acknowledge that picking out one cause among many might be a useful short-term heuristic.[6] Others argue that it represents an unjustifiable bias that "privileges" false reductive accounts of complex processes over true holistic ones.[7] Either way, if the basic pattern of reasoning in parity arguments is sound, then picking out DNA as the actual difference making cause of the linear sequences of nucleotides in RNA and amino acids in polypeptides cannot be justified on ontological grounds. Biologists, however, have been quick to identify DNA (in most contexts) as the cause of these linear sequences. My first question about causal reasoning in biology is 'does the existence of multiple causes in the complex processes of biological development imply that there cannot be an ontological difference that justifies focusing attention on genes and DNA?'

---

[5] For a number of essays and references to essays arguing for "parity" see Susan Oyama, Paul E. Griffiths, and Russel D. Gray, eds., *Cycles of Contingency*, (Cambridge, MA: Bradford Books, MIT Press, 2001).

[6] For example, see Susan Oyama, *Evolution's Eye* (Durham, NC: Duke University Press, 2000).

[7] For example, see Lenny Moss, *What Genes Can't Do* (Cambridge, MA: Bradford Books, MIT Press, 2003) and Jason Scott Roberts, *Embryology, Epigenesis, and Evolution: Taking Development Seriously* (Cambridge, MA: Cambridge University Press, 2004).

The second question concerns how causal generalizations in biological sciences, such as molecular biology, differ from causal generalizations in many physical sciences. In physical sciences, investigators often prize causal generalizations that hold over as wide a range of conditions as possible. Indeed, many philosophers of science claim that physical scientists seek causal generalizations which hold over all possible conditions. There is an active debate concerning whether such universality is an appropriate ideal for physical sciences, but probably everyone, or at least nearly everyone, would concede that physical scientists are seldom satisfied with generalizations that do not hold under a wide variety of artificial and natural conditions and continuously seek generalizations with ever broader ranges of application. Biologists are also concerned about the range of conditions under which their causal generalizations hold. But in contrast to physicists, they seem *perfectly* satisfied with causal generalizations that are highly sensitive (that is, those which do not hold over a wide range of conditions). Why is the ideal of universality so much less important to biologists than to physical scientists? Have biologists set their sights too low as some philosophers contend? And if these philosophers are wrong (as almost every philosopher of biology claims), that is, if universality is not an appropriate ideal for biological sciences, then what ideal is? My second question about causal reasoning in biology is, 'what kind of causal generality matters in the context of biology?'

I will solve the conceptual puzzle about actual difference making and address the questions about causal reasoning in biology by analyzing causal concepts that have not been adequately analyzed, namely, the concepts of *potential difference maker*, *the actual difference maker*, and *an actual difference maker*. These concepts, and my explications of them, are derivative in the sense that they presuppose an underlying notion of cause. My explications are based on James Woodward's manipulability theory of causation, which provides a useful philosophical framework for getting clear about causal reasoning in science. I will not address the question of whether my analysis could be preserved under alternatives to this theory. I contend, however, that if a theory of causation cannot preserve my analysis of the difference between actual versus potential difference making, then it cannot be adequate for understanding causal reasoning in biology.

It is worth emphasizing that I will not claim that the selection of causes is always based on identifying actual difference makers. As I have said, Hart and Honoré's analysis reveals factors behind the selection of causes that vary from one epistemic context to the next. But I will argue against the notion that all causes are on an ontological par. Some causes are actual difference makers while others are not (regardless of epistemic context), and solving the puzzle of what it is to be an actual difference maker provides a basis for shedding new light on causal reasoning in the sciences. I believe it can also shed light on the selection of causes more generally, but that is a topic for another occasion.

This paper is organized as follows. In section 2, I examine causal reasoning in classical genetics to substantiate my claim that there is a genuine distinction between identifying a mere cause (a potential difference maker) and identifying the cause that makes the actual difference (the actual difference maker). In sections 3 and 4, I review the basics of Woodward's manipulability theory and explain why his theory does not solve the puzzle about the difference between potential and actual difference makers. I formulate the concept of *the* actual difference maker in section 5. This concept, which is missing from Woodward's account, explains why it made sense for classical geneticists (and continues to make sense for contemporary geneticists) to identify one gene as "the cause" of a particular phenotypic effect even though it was already known that many genes are involved in bringing about such an effect. In section 6, I explain how this analysis resolves the puzzle about what it means to identify one cause among many as the actual difference maker. I address the question about parity arguments, which requires specifying the concept of *an* actual difference maker as well invoking ideas about causal specificity in sections 7 and 8. Finally, in section 9, I use my account of the ontology of difference makers to specify what kind of causal generality is relevant in biology.

2. Genes as causes in classical genetics

Classical geneticists routinely identified one gene as *the* cause of a particular phenotype while explicitly acknowledging that any phenotype was brought about by many genes, not just one. Hence, this science is a good place to begin investigating how it makes sense to identify one cause among many as the actual difference maker. The philosophical literature contains many inflated claims about the causal powers classical geneticists allegedly attributed to genes. It is sometimes said, for instance, that Morgan and his collaborators were preformationists and believed that genes were active causal agents that individually brought about distinctive phenotypes.[8] One might try to substantiate such interpretations by searching for highly theoretical passages in which geneticists speculated on epigenesis or preformationism.[9] But classical genetics was largely an experimental science, and we gain a better understanding of its basic causal reasoning by examining how geneticists explained their experimental results, not how they speculated about phenomena they could not actually explain.

---

[8] See Lenny Moss, *What Genes Can't Do* (Cambridge, MA: Bradford Books, MIT Press, 2003).

[9] Alternatively, one might perform a linguistic analysis of the terms (such as 'gene action') or a comparative analysis of metaphors (for example, see Evelyn Fox Keller, *Century of the Gene* (Cambridge, MA: Harvard University Press, 2000). While such approaches identify biases of classical geneticists, they do not necessarily identify the concepts doing the work in explanations of concrete phenomena. My aim here is to reconstruct the reasoning that made the experimental science work in the laboratory and might reasonably be extended beyond the laboratory.

Experimentation in classical genetics involved carefully orchestrated breeding regimens that resulted in distinctive inheritance patterns. Reasoning about these experiments invoked a conceptual division between the internal genetic make-up of an organism, called its *genotype*, and its outward character, called its *phenotype*. What classical geneticists explained were the inheritance patterns formed by the transmission of phenotypic differences from one generation to another. Geneticists explained these patterns by following the transmission of genotypic differences from generation to generation and attributing the presence of alternative phenotypic traits to the presence of alternative genotypes, that is, to the presence of alternative forms of genes.

The classical mode of explanatory reasoning can be illustrated by examining a fragment of experimentation involving Morgan's favored model organism, the fruit fly *Drosophila melanogaster*. It is worth emphasizing that the mode of reasoning illustrated by this historical example is still an important mode of reasoning in genetics today. The experiment I examine below, reported in 1919, entailed breeding flies for several successive generations to produce distinctive inheritance patterns involving several different phenotypic traits, each of which was associated with a different gene. The basic aim of the experiment was to investigate the precise locations of the underlying genes with respect to one another. But it is not necessary for my purposes here to describe the investigative reasoning or the intricate explanation of the complex inheritance patterns involving the transmission of the several traits over half a dozen generations. It suffices to examine only the fragment of the explanation involving the transmission of one of the traits over a single generation. I will examine how Morgan explained the transmission of eye-color from one of the experimental generations to the next.

The parental generation consisted of females with red eyes, the so-called "wild-type" character, and males with purple eyes, the mutant character. When these flies were crossed, all offspring had red eyes. So the resulting inheritance pattern was that red-eyed females crossed with purple-eyed males produced all red-eyed offspring.

Explanations of inheritance patterns in classical genetics proceeded in two stages: the first stage accounted for the transmission of genes; the second stage explained the phenotypic appearances of offspring by drawing connections between genetic make-up and phenotypic appearance. [10] With regard to the first stage, geneticists identified two alleles of the purple gene: the wild-type allele, designated as "+", and the mutant, purple allele, designated as "*pr*". On the basis

[10] I describe this experiment more fully, establish the typicality of the explanatory reasoning examined here, and discuss the larger context of investigative reasoning in which this experiment was conducted in C. Kenneth Waters, "What Was Classical Genetics?", *Studies in History and Philosophy of Science, section A 35* (2004)*:* 783-809.

of prior experiments, geneticists knew that the purple gene was located on chromosome II.

The first stage of the explanation began with the premise, established on the basis of prior experiments (which yielded the flies used as parents in the cross discussed here), that the female parents were homozygous for the wild-type allele (+ / +) and that the male parents were homozygous for the purple allele (*pr* / *pr*). Each offspring received one copy of chromosome II from its mother and one copy from its father via the processes of meiosis and gamete combination. The maternally derived chromosome II in every case must have contained the wild-type allele (since both second-chromosomes of every female parent contained the wild-type allele) and the paternally derived chromosome II must have contained the purple allele (since both second-chromosomes of every male parent contained the purple allele). Hence, all offspring were heterozygous (*pr* / +). The genetic makeup of the progeny was thus explained by tracing the transmission of genes from parents to offspring, which marks the completion of the first stage of the explanation.

The second stage of the explanation drew inferences about phenotypic appearances. The purple allele was known to be *recessive* to wild-type. This means that in relevant contexts, heterozygote flies (*pr* / +) have the same phenotypic appearance as flies homozygous for the wild-type allele. Since the offspring in this cross were all heterozygous, as explained by the first stage of this explanation, and since purple is recessive to wild-type in the context of this experiment, all offspring must have the wild-type character. This completed the explanation of the transmission of red-eye color from mothers to offspring.

The explanatory reasoning here does not depend on identifying the material make-up, mode of action, or general function of the underlying purple gene. It depends only on the ideas that copies of the gene are located in chromosomes that are passed on from generation to generation and that the difference in the gene (that is, the difference between *pr* and +), whatever this difference is, causes the differences in phenotypes.[11] The idea that the gene is the difference maker needs to be qualified: differences in the gene cause phenotypic differences in particular genetic and environmental contexts.

> *Difference principle*: differences in a gene cause uniform phenotypic differences in particular genetic and environmental contexts.

---

[11] For further argumentation on this point and the difference principle stated below, see C. Kenneth Waters, "Genes Made Molecular", *Philosophy of Science, 61* (1994), 163-185. Fred Gifford and Lisa Gannett also stress the importance of difference making in the context of genetics, see F. Gifford, "Genetic Trait" *Biology and Philosophy, 5* (1990), 327-347 and L. Gannet "What's in a Cause? The Pragmatic Dimensions of Genetic Explanations", *Biology & Philosophy 14* (1999), 349–374.

The difference principle is easily applied to experimental contexts because geneticists deliberately simplified the causal situation by standardizing environmental conditions and removing genetic differences that might affect the phenotypes under study (other than the genetic differences being investigated in the experiment). Their strategy was to construct an experimental situation so that only those gene differences being investigated were causing differences in the phenotypic appearances under study.

The fact that classical geneticists routinely constructed experimental situations so that the difference principle would apply undermines the notion that they naively believed that each of the phenotypic characters they studied were preformed in single genes or even gene complexes. They were well aware of the fact that differences in many different genes *could* affect any given trait, and they therefore set up their experiments so the difference in a particular phenotype would be caused by a difference in one gene (or a very few genes), not many. Notice that reasoning in this experimental context naturally invokes an ontological distinction between the general causes of a phenotypic trait (for example, eye color) and the cause of an actual difference in the trait (for example, the difference between red and purple eye color). Many genes are potential difference makers with respect to eye color, but in this experiment genes were controlled via breeding regimens so that only one of these genes (the purple gene) actually differed, and hence only one of these genes actually caused eye color to differ in the experiment.

This interpretation, which invokes an ontological distinction between a cause and the actual difference making cause, is born out by Morgan's own discussion of the causal relationship between genes and phenotypes. Morgan, trained as an embryologist, distinguished between the point in development where geneticists typically observe a difference and the point at which the developmental process was altered to bring about the observed difference:

> . . . the study of embryology shows that every organ of the body is the end-result, the culmination of a long series of processes. A change that affects any step in the process may be expected often to affect a change in end result. It is the final visible effect that we see, not the point at which the effect was brought about.[12]

The next quotation shows, as my analysis implies, that Morgan did not presume a simplistic one-gene one-character type view. He was well aware that particular characters such as eye-color are caused by many different genes. He even speculated that every organ in the body might be affected by each and every gene in the organism's genome:

---

[12] Thomas H. Morgan, *The Theory of the Gene* (New Haven, CT: Yale, 1926), p. 305–306.

> Suppose, for instance, to take perhaps an extreme case, all the genes are instrumental in producing each organ of the body. This may only mean that they all produce chemical substances essential for the normal course of development. [13]

Now, the conceptual puzzle makes its appearance:

> If now one gene is changed so that it produces some substance different from that which it produced before, the end-result may be affected, and if the change affects one organ predominatingly [sic] it may appear the one gene alone has produced this effect. In a strictly causal sense this is true, but the effect is produced only in conjunction with all the other genes. In other words, they are all still contributing, as before, to the end-result which is different in so far as one of them is different.[14]

This passages implies a distinction between two causal concepts. It emphasizes that the end result of development is affected by, that is, caused by, all the genes working in conjunction. But it also acknowledges that in another sense, in what Morgan called the "strictly causal sense", "one gene alone has produced this effect." Morgan's unanalyzed distinction corresponds to the difference between what I am calling "a cause" and what I am calling "the actual difference making cause" (or "the actual difference maker"). His science entailed, as do biological sciences in general, identifying one or a few elements as the "actual cause(s)" in situations that necessarily involve many causes. The problem of explaining what it means to pick out one cause among many as the actual difference maker is indeed a genuine philosophical puzzle.

3. Woodward's manipulability theory of causation and causal explanation

Woodward's manipulability theory of causation does not solve this puzzle, but it provides conceptual tools for constructing concepts of difference making that can explain what it means to pick out the actual difference maker. His theory is based on the idea that causal relationships involve patterns of counterfactual dependencies concerning what would happen if certain properties were manipulated. To say there is a causal relationship between two properties, on this account, is to say that one can change the value of one property by manipulating the other property. The idea that causal relationships are those that could be used for the purposes of manipulation have been developed by a number of scientists

---

[13] See previous footnote.

[14] See previous footnote.

as well as philosophers.[15] Philosophers developing this idea have generally tried to construct reductive theories of causation, that is, theories that describe causal relationships in non-causal terms. But Woodward, following the lead of scientists and statisticians, upon whose work he generously draws, does not aim to provide a reductive analysis of cause (as will become evident below). Instead, he assumes a basic counterfactual notion of cause, and then uses ideas about manipulations developed in the scientific and statistical literatures to construct a general theory about causal relationships and an account of various ways scientist reason about them.

Although Woodward's account includes interesting ideas about causal inference and explanation, I will not describe them here because my argumentation centers on ontological, not epistemological, considerations. In addition, I will not review how Woodward responds to various criticisms of manipulability theories. But it is worth pointing out that since Woodward's theory is not reductive, it avoids difficulties that vex traditional manipulability theories of causation.[16]

Woodward motivates the stress on manipulability by pointing out that human interest in causal relationships began with practical interests in manipulation and control. This motivation certainly resonates with the history of biology. A central theme in the history of experimental biology (and genetics in particular) is that persistent interest in manipulating and controlling life, both on the part of scientists and those providing scientists with resources, has exerted a tremendous impact on the course of research. Even in the cases of evolutionary biology and ecology, which are often pursued in non-experimental venues, research has often

---

[15] Prominent philosophical accounts include R. Collingwood, *An Essay on Metaphysics* (Oxford: Clarendon Press 1940), D. Gasking: "Causation and Recipes", Mind, 64, (1955), 479–487, G. von Wright, *Explanation and Understanding* (Ithica, New York: Cornell University Press, 1971), and Menzies, P. and Price, H. "Causation as a Secondary Quality", *British Journal for the Philosophy of Science, 44* (1993), 187–203. Accounts developed by non-philosophers include T. Cook and D. Campbell, D., *Quasi-Experimentation: Design and Analysis Issues for Field Settings* (Boston: Houghton Mifflin Company, 1979), and J. Pearl, *Causality*. New York: Cambridge University Press, New York, 2000).

[16] For example, a common criticism of manipulability accounts of causation is that by reducing statements about causal relationships to statements about the possibilities of changing effects by manipulating causes, they seem to assume that causes can in fact be manipulated. But Woodward's theory makes no such assumption; rather, it assumes that there is a truth to the matter of what would happen if it were technologically (or otherwise) possible to manipulate the relevant properties and the properties were manipulated. On Woodward's theory, nothing prevents reading both instances of 'were' in this sentence as possibly counter-to-fact. A critic might respond that with respect to some phenomena, such as quantum phenomena, the very notion of manipulation ceases to make sense. If this is indeed the case, then one might defend a manipulability theory like Woodward's on the ground that quantum phenomena are (therefore) not causal. See note 16 for further discussion of how Woodward's theory avoids, or critics might say "postpones", difficulties confronting reductive theories of causation.

been inspired, even driven, by human interests in manipulation and control. Hence, even though Woodward developed his theory of causation largely in the context of physics and economics, the motivation for causal reasoning made salient by his theory is very relevant to causal reasoning in biology.

Woodward, following the practice of many scientists and statisticians, takes the relata of causal relationships to be properties (rather than events). To say that there is a causal relationship between *X* and *Y*, on his account, is to say that *X* and *Y* are properties and that manipulating one property would change the other. Woodward conceives of causal relationships as relationships between variables, so he would express this idea by saying that the value of the effect variable, say *Y*, can be changed by manipulating the value of a causal variable, say *X*. Variables in this context designate properties that take on two or more mutually exclusive values. The variable of temperature, for example, designates a magnitude that can take values such as 20 degrees or 100 degrees and the phenotypic variable of eye-color designates a property that can take on values such as red or purple. These values are possessed by or instantiated in particular entities. So, for example, the water in a kettle might be 20 degrees or the eyes of a fruit fly might be red. So, according to Woodward's theory, causal relationships are relationships between values of distinct properties that can be represented as values of different variables.

Roughly speaking, Woodward writes, a causal relationship exists between two variables, *X* and *Y*, when:

> for at least some individuals there is a possible manipulation of some value of *X* that they possess which, given other appropriate conditions (perhaps including manipulations that fix other variables distinct from *X* at certain values), will change the value of *Y* or the probability distribution of *Y* for those individuals.[17]

The inclusion of the causal term 'change' in the above passage reflects the fact, already mentioned, that Woodward's theory is not reductive. It does not account for cause in non-causal terms.[18] It is a non-reductive, counterfactual theory, potentially consistent with different reductive theories, including counterfactual

---

[17] James Woodward, *Making Things Happen* (Oxford: Oxford, 2003), p. 40.

[18] Woodward's theory, because it is not reductive, cannot solve certain fundamental puzzles about causation, including the problem of coincidence. Because the theory is not reductive, it contains no ultimate answer to those who would ask of the quoted passage: but what distinguishes the claim that the intervention in *X* changes the value of *Y* from the claim that the intervention was merely a coincidence? Woodward's theory provides answers that are useful for understanding how to clarify causal ideas or empirically test them, but its answers presuppose a basic counterfactual notion of cause that is not itself explained. Insofar as puzzles relate directly to this notion, Woodward's theory will not solve them. But this does not imply that his theory is false; rather, it reflects the fact that his theory is not reductive.

theories such as David Lewis'. While some metaphysicians will not be satisfied until they have a reductive theory, perhaps they would be willing to concede that Woodward's theory provides a useful way to think about causes in the meantime. In any case, this is the modest premise upon which the analysis that follows is based.

Two technical concepts are important for understanding the gist of Woodward's theory: intervention and invariance. When Woodward refers to "a possible manipulation of *X*" he has in mind a special kind of manipulation. It is not the case that any manipulation of the value of *X* that subsequently changes the value of *Y* implies that that *X* causes *Y*. For example, a manipulation of the thermometer reading brought about by decreasing temperature would change the phase state of water, but this does not mean that thermometer readings cause water to freeze. To say that the thermometer reading causes water to freeze is to say that a special kind of manipulation of the thermometer reading, a manipulation that did not independently affect other causal variables such as temperature, would change the phase state from liquid to solid. The technical term for the relevant kind of manipulation is "intervention". A manipulation counts as an *intervention on X with respect to Y* if and only if the manipulation changes the value of *X* without changing, independently of the change in value of *X,* the value of any causes of *Y*.[19] "*X* causes *Y*" means that an intervention on *X* with respect to *Y* would change the value of *Y*. Notice that Woodward's account does not require that *all* interventions on *X* would change *Y*, and this brings us to the second technical concept of his theory: invariance.

On Woodward's account, causal relationships are not necessarily universal. *X* can cause *Y* even if intervening on the value of *X* within many ranges of the variables *X* and *Y* would not change the value of *Y*. For example, there is a causal relationship between temperature and the phase state of water even though increasing the temperature of water from 22° C to 95° C will not change its phase state. In addition, *X* can cause *Y* even if intervening on the value of *X* has no effect on the value of *Y* when the value of certain variables not identified in the expression '*X* causes *Y*' is outside some range. For example, the claim that raising the temperature of water from 22° C to 100° C causes water to boil is not contradicted by the fact that increasing the temperature of water from 22° C to 100° C will not change the phase state of water when the atmospheric pressure is significantly greater than standard atmospheric pressure. An advantage of Woodward's theory is that it accounts for the intuitively plausible idea that scientists typically explain phenomena by identifying causal dependencies that do not obtain under all conditions. The thermodynamical explanation of why a flask of water boiled over the flame of a Bunsen burner does not depend on identifying

[19] This is my description of Woodward's concept of intervention. He carefully sets out a technical definition that deals with subtleties that can be ignored for present purposes.

a totally invariant relationship. Identifying a change in water temperature as the cause of the change in phase state under the laboratory conditions suffices.

Woodward says that scientists identify genuine causal relationships even though these relationships (for example, the ones specified in textbooks) are almost always "sensitive" to the values of variables that figure into the specified relationships and/or to the values of variables that do not figure into the specified relationships. According to his account, the expression '*X* causes *Y*' just means there are *at least two* different values of *X*, x_1 and x_2, and *at least one* set of values for the variables specified in the expression and the variables not specified in the expression, such that if one intervened to change the value of variable *X* from x_1 to x_2, the value of *Y* would change. The *invariance* of a causal relationship concerns ranges of values under which the relationship holds. Since causal relationships can be sensitive to the values of many different variables, and since the sensitivity with respect to one variable can depend on the values of other variables, the relevant 'ranges of values' refers to a space (or set of spaces) in a n-dimensional array of variables (where n is the number of variables to which the relationship *X* causes *Y* is sensitive). Hence, it is more accurate to speak of "spaces of invariance" than "a range of invariance."

According to this account, causal explanations in science cite causal relationships exhibiting various amounts of invariance. Any such relationship must be at least *minimally invariant* in the sense that it must hold for at least two different values of the causal variable (a very weak condition). And it may be *maximally invariant* in the sense that it holds for all values of all variables whether they explicitly figure into the specification of the causal relationship or not (a very strong condition). But scientific explanations typically cite causal relationships that fall somewhere between these two extremes. Woodward reserves the term 'law' for maximally invariant causal relationships. A virtue of his account is that it explains what is special about scientific laws (that is, maximal invariance) without implying that this special feature is required for scientific explanation.

Woodward's theory provides a natural framework for expressing the causal relationships identified by classical geneticists. The difference principle, discussed in section 2, can be reformulated in terms of the manipulability theory:

> Differences in a gene cause uniform phenotypic differences in particular genetic and environmental contexts.
>
> ⇓
>
> For at least some organisms, a manipulation of the form of a gene they possessed as a zygote, given other appropriate conditions (such as genetic background and environmental conditions), would change the phenotypes of those individuals.

This reformulation makes salient features of the causal relationship expressed by the difference principle that were crucial for the practice of classical genetics. Experimentation in classical genetics entailed controlling the genetic background and environmental conditions. Geneticists bred model organisms to "clean up" their genetic backgrounds so phenotypic effects of particular mutations would not be masked. They also standardized environmental conditions in the laboratory. These efforts resulted in regular and repeatable patterns of inheritance. Woodward's theory emphasizes the fact that causal relationships, such as those expressed by the difference principle, are context sensitive.

4. A lacuna in the manipulability theory

Woodward's theory provides insights concerning many philosophical questions about causation and causal explanations, but it does not solve the problem about what it means to pick out the cause that makes an actual difference. This lacuna can be illustrated by returning to the experiment discussed in section 2. In this experiment, the purple gene (the gene that takes on one of two contrasting values, + or *pr*) was identified as the cause of red eye-color in the offspring even though this phenotypic end-result was known to depend on a number of different genes and environmental factors. According to Woodward's manipulability theory, the purple gene was indeed a cause because the eye color of offspring could have been manipulated by intervening on this gene (for example, by changing the + allele in heterozygous offspring embryos to a *pr* allele). This idea is an *instantiation of the difference principle*.

> For the offspring in the experiment, a manipulation of the maternally derived gene from + to *pr*, given other appropriate conditions (such as the genetic background and environment), would change the phenotypes of the offspring from red-eyed to purple-eyed.

But Morgan and his collaborators knew that eye color could be manipulated by intervening on a number of different genes (by 1919 they had identified mutations in at least 16 different genes located at separate loci that affected eye color). For example, just as eye-color of the offspring in the experiment could have been manipulated by intervening on the purple gene, eye-color could have been manipulated by intervening on the vermilion gene (for example, by changing the wild-type alleles in the offspring, which were homozygous for the vermilion wild-type allele, to the vermilion mutant allele). Hence, according to Woodward's theory, the vermilion gene was just as much a cause of red eye-color in these offspring as was the purple gene.[20] So Woodward's theory clarifies what it means

[20] Readers might think this problem could be easily resolved since the vermilion mutation results in a different phenotype than that the purple mutation. But there are other examples where

to identify the purple gene as a cause of red eyes, but it implies that the vermilion gene is just as much a cause.

Woodward tries to address the issue of why some causal factors are more significant in particular cases than others when he discusses token causation, where the problem is to pick out "*the* cause" of a single event.[21] But Woodward's analysis of token causation, which he presents only tentatively, does not provide a basis for elucidating the "strict" sense of cause that Morgan alluded to when he wrote: "it may appear the one gene alone has produced this effect. In a strictly causal sense this is true, but the effect is produced only in conjunction with all the other genes."[22]

5. The concept of the actual difference maker

The concept missing from Woodward's theory of cause and causal explanation, and indeed missing from the philosophical literature in general, is that of an actual difference making cause. This concept captures Morgan's "strict" sense of cause, the sense in which the purple gene, and not the vermilion gene, was "the cause" of eye-color in the experiment. Causation is often thought of as difference making. What is typically overlooked, however, is the fact that in order for there to be a difference maker there must be a difference. And in order for there to be an *actual* difference maker, there must be an *actual* difference. This raises the question: an actual difference among what things? The actual difference might be a difference among different entities, that is, among different actual entities, or it might be a difference in the same entity at different actual times.

The first step in identifying an actual difference making cause, or an actual difference maker, is to specify an actual difference among actual entities (or an actual difference in the same entity at different actual times). If there is no actual difference, then there is no actual difference maker. In the classical genetics experiment discussed earlier, there was an actual difference; it was a difference in eye color among mother, father, and offspring flies in the experiment. The actual

---

different mutations (or different combinations of mutations) bring about phenotypic effects that are indistinguishable from one another. My account will explain why, in even these cases, it can make sense to say that one gene and not the other (or one set of genes and not the other set) is the actual difference maker.

[21] See Woodward, *Making Things Happen* (Oxford: Oxford, 2003), pp. 74–86).

[22] Quoted from Thomas H. Morgan, *The Theory of the Gene* (New Haven, CT: Yale, 1926), p. 305–306. Woodward takes readers through a complicated attempt to deal with examples of actual causation, which fails because he tries to identify "the" in the context of singleton causal events. I discuss the problem with such attempts later in this paper. My aim here is to show that the problem of picking out *the actual difference making cause* arises within his theoretical framework. I prefer to offer a solution within his framework that works rather than present a detailed argument about why his tentative analysis of a similar problem will not do the job.

difference maker was the purple gene because it was the cause that actually differed and whose difference led to the actual difference in eye color (red versus purple). The other genes, including the vermilion gene, were causes, but they were not actual difference makers in the experimental population of flies. The other genes that cause differences in eye color could not have been actual difference makers in the experimental population for the simple reason that they did not actually differ and hence it was not differences in them that brought about the actual differences in the population.

The concept of the actual difference maker can be specified as follows.

X is *the actual difference maker with respect to Y in population p* if and only if

i. *X* causes *Y* (in the sense of Woodward's manipulability theory).

ii. The value of *Y* actually varies among individuals in p.

iii. The relationship expressed by '*X* causes *Y*' is invariant with respect to the variables that actually vary in p (over the spaces of values those variables actually take in p).

iv. Actual variation in the value of *X* fully accounts for the actual variation of *Y* values in population p (via the relationship *X* causes *Y*).

Notice that this concept applies only to causes in actual populations. It makes no sense to identify something as the actual difference maker without identifying either a population with at least two entities that actually differ with respect to the effect variable *Y* or a population of one or more entities that exhibit different *Y* values at different actual times. It is worth stressing that the actual effect is not a single property in a single token, it is a difference of a property in a population.[23]

Woodward's theory provides the tools to specify condition iv more fully. Consider what it means to say, for instance, that variations in the purple gene fully accounted for the actual variation in red versus purple eye color in the experimental population. It means that the phenotypic value was a function of the genotypic value in this population and that the generalization '*X* causes *Y*' produced the correlation. Or more concretely: (a) there was an actual difference in eye color among flies in the population; (b) flies in the population with the same genotypic values (with respect to this gene) had the same eye color; and (c) if the flies in the experiment had been intervened on such that they all had the

[23] I am using "population" in a statistical rather than biological sense: a population is either a set of entities or possibly the set of instances of an entity at different times.

same genotypic value (either + / +, + / *pr* or *pr* / *pr*), then this difference in eye color would not have existed. Or more generally:

> *Actual variation in the value of X fully accounts for the actual variation of Y values in population p* (via the generalization '*X* causes *Y*') if and only if conditions i – iii above hold and
>
> > (a) Individuals with the same *X* values in p have the same *Y* values.
> >
> > (b) An intervention on *X* with respect to *Y* that changed the *X* value of all individuals in p to the *X* value that one and the same individual had sans intervention would change *Y* values in p such that they no longer differed.
> >
> > (c) There is no variable *Z*, distinct from *X*, such that an intervention on *Z* with respect to *Y* that changed *Z* values in one or more individuals in p to the *Z* value that one of the individuals had sans intervention would change *Y* values in p.

6. Solving the puzzle about what it means for one cause among many to be the actual difference maker

The concept of the actual difference maker clarifies the idea that there is an ontological difference between being a cause and being the cause that actually made a difference. Being a cause only entails that something is a potential difference maker, not the actual difference maker. To be a *potential difference maker*, that is, to be a causal variable, it suffices to satisfy the counterfactual patterns specified by the manipulability theory. It does not matter whether the causal variable actually varies in any actual population and whether this variation brings about actual differences. But to be the actual difference making cause of an actual difference in a population, the value of the variable must actually differ and this variation must bring about the actual differences among the entities in the population. This is how to make sense of the idea, invoked by Morgan, that it is one thing to be a cause and another thing to be the cause strictly speaking. Seeking the one cause among many that actually made the difference is no fool's errand. It entails picking out the actual difference maker among potential difference makers in an actual population. The philosophical puzzle with which we began is solved.

In fact, the puzzle with which we began does not seem to be much of a puzzle at all. Picking out the actual difference making causes among many causes simply involves picking out the causes that actually differ and whose differences account for the actual differences of interest. It turns out that what makes the conceptual

situation puzzling is not so much a puzzling concept, but puzzling applications, such as the application with which I began, the lighting of the match. To apply the concept to this situation, to say that Mary's striking the match is the actual difference making cause whereas the presence of oxygen was merely a cause, requires identifying an actual difference in an actual population. If Mary took the match from a box, then the matches contained in the box were an actual population and the difference between having lit versus not having lit was an actual difference. With respect to this actual effect (that is, the actual difference in this actual population), it is obvious that Mary's striking the match was the actual difference making cause and that the presence of oxygen was merely a cause. The presence of oxygen was not the cause that made the actual difference in this actual population of matches because, after all, oxygen was present for all the matches.[24]

Before proceeding to the next section, which considers more complex causal situations, it is helpful to consider two possible objections, one concerning whether my resolution of the puzzle is ontological, and the other concerning my use of the terms 'actual' and 'potential'. Readers might question whether this account identifies an ontological feature. After all, the selection of a difference making cause depends on the prior identification of a population. Can populations be identified, or specified, independently of our interest? If not, then applying the distinction between potential and actual difference makers seems to depend on more than ontology. But this line of questioning conflates the identification of a cause with the specification of an effect. Of course, being interested in one effect rather than another depends on more than the ontology of causal processes. Our interests lead us to inquire about the causes of some things and not others. The question here is whether the cause(s) of an effect are fixed by ontology. This account of difference making takes an effect to be an actual difference in an actual population. My claim is that the subset of causes that are the actual difference makers of such an effect is fixed entirely by the ontology of causation in the actual population, not by a mix of ontology and interests as recent writers have maintained.[25] This is not to say that the selection of some causes among many is not based on interest or that it is based on a universal interest to pick out actual difference makers. But interests often are based on an interest to pick out actual difference makers in one or another actual population, and when they are, the issue reduces to ontology: the variety of epistemic factors detailed by Hart and Honoré are irrelevant and the features of real populations specified in this analysis determine which causes are the actual difference makers.

---

[24] This analysis might be extended to singleton cases as well. If there were no other matches, then one could consider the effect to be the difference in the population made up of instances of the match before, during, and immediately after it was struck.

[25] Even Jonathan Schaffer, who comes closest to offering an ontological account, appeals to pragmatic factors to resolve the selection problem. See J. Schaffer, "Contrastive Causation," *Philosophical Review 114* (2005), 297–328.

The error of this possible objection is to infer from the fact that the selection of effect in an epistemic context involves pragmatics to the mistaken idea that what counts as the cause of that effect must also depend on pragmatics. My point is that once the effect is fully specified as an actual difference in a real population, the issue of which causes are the actual difference makers is an ontological one.

Readers might also object that my use of the terms 'actual' and 'potential' is misleading because all causes, even what I call potential difference making causes, are actual in the sense that the actual differences causally depend on them. It is easiest to clarify this point by using the terminology of variables. An actual effect, on my account, is the actual difference in values of an effect variable in an actual population. In the situations examined thus far, one causal variable plays a differentiating role in the sense that actual differences in its value explain the actual differences in values of the effect variable. Other causal variables do not play this role because they exhibit uniform values in the actual population. They are, however, potential difference makers because if, counter to fact, their values varied in the population then this variation could result in an increase in the differentiation of the values of the effect variable. In addition, however, a counter-to-fact variation in the values of a potential difference making variable might result in a reduction of the differentiation of the values of the effect variable (compared to the values of this variable in the actual population). Hence, the difference in values of the effect variable in the actual population depends not just on the different values taken by what I'm calling the actual difference making variable, but also on the uniform values taken by what I'm calling the potential difference making variables. So, one might say all causal variables are "actual" difference makers in the sense that the actual differences depend on all their values. Nevertheless, the fact that the values of some causal variables actually differ and the values of other variables do not is a feature of the causal structure of an actual population. I am choosing to reserve 'actual' to designate the causal variables whose values actually differ and 'potential' to designate the causal variables whose values do not actually differ. This terminology comes very naturally in the contexts of causal reasoning in the special sciences, which will become evident when we turn our attention to the complex biological processes such as development.

In summary, the key to solving the conceptual puzzle, the key to understanding what it means to select an actual difference making cause from a plethora of mere causes, is to see that the selection involves picking out the causal property, differences in which produce an actual difference in a population.

7. The concept of an actual difference maker

In many biological situations, there is not just one actual difference maker, there are many. That is, actual variations in two or more variables in an actual

population account for actual differences in an effect variable. In such situations, the operative concept is *an* actual difference maker, not *the* actual difference maker.

> *X* is *an actual difference maker with respect to Y in population p* if and only if
>
> > i. *X* causes *Y*.
> >
> > ii. The value of *Y* actually varies among individuals in p.
> >
> > iii. The relationship *X* causes *Y* is invariant over at least parts of the space(s) of values that other variables actually take in p. (In other words, it is invariant with respect to a portion of the combinations of values the variables actually take in p.)
> >
> > iv. Actual variation in the value of *X* partially accounts for the actual variation of *Y* values in population p (via the relationship *X* causes *Y*).

As in the case of the actual difference maker concept, the fourth condition in this construction can be specified by using Woodward's concept of intervention.

> *X partially accounts for the actual variation of Y values in population p* (via the relationship X causes Y) if and only if conditions i – iii above are satisfied and
>
> > An intervention on *X* with respect to *Y* that changed the *X* values in one or more individuals in p to the *X* value that one of the individuals had sans intervention would change *Y* values in p.

The statistical relationship between *X* and *Y* values in the case of *an* actual difference maker is far messier than in the case of *the* actual difference maker. In the latter case, the value of *Y* is a function of *X*. But in the case of *an* actual difference maker, the individuals in the population with the same *X* value might have different *Y* values.

The causal relationship underlying an actual difference maker claim is also more complicated. In the case of the actual difference maker, eliminating the variation in *X* values (by intervening on *X* with respect to *Y* in p) would eliminate the variation in *Y* values. In the case of an actual difference maker, eliminating the variation in *X* values (by intervening on *X* with respect to *Y* in p) does not necessarily eliminate the variation in *Y* values. It only changes the variation in *Y* values. In fact, eliminating the variation in the value of *an* actual difference maker might actually increase, rather than decrease, variation in the value of *Y* in p. So, it would be more accurate to use the term "an actual difference maker" with "an actual difference changer" and to specify that an actual different changer might be

"an actual difference increaser" or "an actual difference reducer" in the population. This fine conceptual point has important implications in real science, for example, in quantitative genetics.

Quantitative genetics involves a number of subtleties of actual difference making. While analyzing these subtleties is a topic for another paper, some intuitively plausible connections between actual difference making relationships in different populations can be specified quickly. Suppose there are three populations, p_1, p_2, and p_3, that p_1 and p_2 are mutually exclusive, and that p_1 is a proper subset of p_3. If *X* is the actual difference maker with respect to *Y* in p_1, it is not necessarily the actual difference maker with respect to *Y* in p_2. In fact, it is not necessarily an actual difference maker with respect to *Y* in p_2. But if *X* is the actual difference maker in population p_1, then *X* is at least an actual difference maker in p_3. Furthermore, if *X* is an actual difference maker in p_1, then it is not necessarily an actual difference maker in p_2, but it is necessarily an actual difference maker in p_3.

8. Does the existence of multiple causes indicate that there is no ontological basis for centering attention on genes and DNA?

My solution to the conceptual puzzle about the difference between what it means to be a cause and what it means to make an actual difference reveals the fallacy of causal parity arguments. The fact that there are many causes does imply that there is ontological parity among them. DNA is one cause among many, but in some contexts it might be the actual difference maker while other causes are only potential difference makers. My aim in this section is to identify situations in which DNA is an ontologically distinctive cause, and to clarify the nature of its causal distinctiveness in these situations. It turns out that understanding why DNA is a distinctive cause requires invoking a concept of causal specificity as well as concepts of actual difference making.

As readers will see, the situation I identify is a small part of the developmental process and hence my analysis does not provide the basis for making sweeping claims against all theses of causal parity. But by challenging the basic logic of causal parity arguments, and by showing that parity breaks down in certain contexts, my account reveals important clues for understanding why so much research attention in developmental biology is centered on DNA.[26]

---

[26] Other aspects relevant to a fuller account of this issue are in C. Kenneth Waters, "What Was Classical Genetics", *Studies in History and Philosophy of Science, section A 35* (2004)*:* 783–809, Waters, "A Pluralist Interpretation of Gene-centered Biology" in Stephen Kellert, Helen Longino, and C. Kenneth Waters, eds., *Scientific Pluralism, volume XIX of the Minnesota Studies in the Philosophy of Science* (Minneapolis: University of Minnesota Press, (2006), 190–214, and Waters "Beyond Theoretical

Recall that the first step for identifying the (or an) actual difference maker is identifying an actual difference in an actual population. An important actual difference in cells is the difference in the nucleotide sequences of RNA molecules synthesized in a cell. This is not the only important actual difference in a cell, but it is an important difference. Consider a relatively simple example, the population of RNA molecules synthesized in a bacterium. Synthesis of any RNA molecule in a bacterium depends on the presence of an activated gene (a segment of nucleotides in a DNA molecule), RNA polymerase, and several additional accessory proteins. All of these molecules are causes, so they are all potential difference makers. Intervening on any of the activated DNA segments could alter the sequence of nucleotides in the resulting RNA molecules, and intervening on any of the others (for example, RNA polymerase) could stop RNA synthesis altogether. They are all potential difference makers.

But only the activated DNA segments (the genes) are actual difference makers of RNA sequences in a bacterium. Let *G* be the variable representing the nucleotide sequences in the activated genes, *P* be the variable representing the structure of RNA polymerase molecules, $P_1 - P_n$ designate variables representing structures for each of the accessory proteins, and *R* designate the variable representing the nucleotide sequences in the RNA molecules. Each of the variables *G*, *P*, $P_1, \ldots P_n$ represent causes of *R,* so each satisfies the first condition for being the actual difference maker. But among these potential difference makers, only *G* takes on different values. Hence, only *G* satisfies the second condition for being the actual difference maker. Since the other variables do not take on different values, the causal relationship between *G* and *R* is invariant with respect to the differences in the bacterial cell. So the third condition for being the actual difference maker is satisfied. Furthermore, actual variation in the value of *G* completely accounts for actual variation in *R* values in the sense spelled out in the fourth condition of the actual difference maker concept. That is, individual RNA molecules synthesized from the same gene have the same *R* values and if the activated genes in the cell had been intervened on so that each had the same *G* value (the same nucleotide sequence), then the synthesized RNA molecules would have had the same *R* value as well (the same nucleotide sequence). With respect to the differences in the linear sequences of the population of RNA molecules in a bacterial cell, current evidence indicates that DNA is the actual difference making cause.

RNA synthesis in eukaryotic cells is more complicated. It involves three different kinds of RNA polymerase molecules and many dozens of accessory proteins. The different kinds of polymerase molecules are involved with the

---

Reductionism and Layer-cake Antireductionism: How DNA Retooled Genetics and Transformed Biological Practice", forthcoming in Michael Ruse and David Hull (eds.) *Oxford Handbook to the Philosophy of Biology.*

synthesis of different classes of RNA molecules (for example, RNA polymerase I catalyzes the synthesis of rRNA and RNA polymerase II catalyzes the synthesis of mRNA). Presumably, different accessory molecules are also associated with the synthesis of different RNA molecules. In this situation, DNA is not the only actual difference maker because it is not the only cause that actually differs among the synthesis events in a cell. For example, consider the difference in linear structures of the population of mRNA and rRNA molecules in a eukaryotic cell. The genes involved in the syntheses differ, but so do the RNA polymerases. Intervening on polymerase II could stop synthesis of mRNA altogether, and this would affect the structures of the resulting RNA molecules. Intervening on polymerase I could have a parallel effect, as could intervening on accessory molecules. Hence, DNA is *an* actual difference maker, not *the* actual difference maker. RNA polymerase and accessory proteins could also be actual difference makers. Nevertheless, many other background constituents necessary for the synthesis to occur (for example, water) do not differ. So the logic of the parity argument does not hold. But this does not fully resolve the issue about parity because the different actual difference making causes, say genes versus polymerases, do not seem to be on an ontological par.

Further resolution of the alleged parity requires an additional causal concept, one of causal specificity. The concept I have in mind is similar to Lewis' concept of causal influence, and can be sketched by example.[27] DNA is a *specific difference maker* in the sense that different changes in the sequence of nucleotides in DNA would change the linear sequence in RNA molecules in many different and very specific ways. RNA polymerase does not have this specificity. Intervening on RNA polymerase might slow down or stop synthesis of a broad class of RNA molecules, but it is not the case that many different kinds of interventions on RNA polymerase would change the linear sequence in RNA molecules in many different and very specific ways. This shows that DNA is a causally specific potential difference maker. The fact that many such differences in DNA do actually exist and these differences actually explain the specific differences among RNA molecules indicates that DNA is the causally specific actual difference maker with respect to the population of RNA molecules first synthesized in eukaryotic cells.

As readers familiar with contemporary molecular biology know, RNA production in eukaryotes is often complicated by processes that change RNA molecules after they are synthesized. If we consider the wider population of RNA molecules in a eukaryotic cell (not the subset of those first synthesized), then we need to consider processes such as RNA splicing. RNA splicing changes the

---

[27] David Lewis, "Causation as Influence", *Journal of Philosophy*, XCVII (97), no. 4, (April 2000): 182–97. Conversations with Chris Hitchcock and Jim Woodward helped me to develop this idea. Woodward points out that my ideas about causal specificity had a lot in common with Lewis's ideas about causal influence.

linear sequence of an RNA molecule by removing certain internal segments in the RNA molecule and 'splicing' the remaining pieces together. RNA splicing is causally specific. Often, one and the same RNA molecule is spliced in different ways by different splicing agents. In these situations, the splicing agents are causally specific actual difference makers. They actually differ and the actual differences lead to specific changes in the nucleotide sequence of the mature DNA molecule. In the production of these molecules, DNA is not the only causally specific actual difference maker.[28] We might say that the structure of these mature RNA molecules are determined by DNA (that is, the activated gene) and the splicing agent. In the case of RNA synthesis in eukaryotes the problem of causal parity is resolved, not by showing that DNA is the only causally specific actual difference maker, but by showing that it is one of a several.[29]

Explanations in molecular biology do not rest on the premise that genes are the only causally specific actual difference makers with respect to the linear sequence of nucleotides in primary RNA, processed RNA, and polypeptides, but they do deny the idea that all causal factors involved in the production of RNA and polypeptide molecules are on a causal par. Such a parity thesis is false. If true, it would indicate that emphasizing DNA and splicing agents in explanations of mRNA synthesis has no ontological basis. But current evidence indicates otherwise. The initial synthesis of RNA in prokaryotes and eukaryotes involves many causes including polymerases and accessory proteins, but only DNA is the causally specific actual difference maker. Apparently that is the end of the story for prokaryotes. In eukaryotes, some very important RNA molecules (and perhaps many) are differentially processed, so splicing agents are also causally specific actual difference makers. The linear sequence of nucleotides in mRNA are determined by the linear sequence of nucleotides in DNA, and in cases of differential splicing also by other molecules such as alternative splicing agents.[30]

9. What kind of causal generality matters in biology?

Biologists seek a special kind of generality in causal statements. Whereas physical scientists often try to establish generalizations that express causal relationships that hold over conditions that have not and will not be actualized (to their knowledge), biologists typically care only about whether a relationship holds

---

[28] But as Marcel Weber has pointed out to me, DNA has a greater degree of causal specificity than the other actual difference makers.

[29] I have limited discussion here to one of the apparently several kinds of causally specific actual difference makers involved with the synthesis of RNA in eukaryotes. Discussing more examples would simply belabor my philosophical point that not all causes are on a par because some are causally specific actual difference makers (for example, genes and splicing agents) and others are not (for example, RNA polymerases I and III).

[30] See previous footnote.

under conditions actualized in organisms and their environments (or in the laboratory).[31] Biologists do not care whether causal generalizations linking sequences in mRNA to sequences in polypeptides in the causal processes of polypeptide synthesis would still hold if the cellular conditions were quite different than cellular conditions actually are. For instance, if the form of tRNA molecules were different, then an mRNA molecule that now causes a particular amino acid sequence would cause a very different amino acid sequence. The fact that different tRNA could render the current causal generalizations about polypeptide synthesis false does not matter to biologists unless different tRNA has actually existed or is likely to actually exist in the future. We are now in a position to clarify the kind of causal generality that matters in biology.

The difference can be articulated in terms of invariance space. Recall that a causal relationship is not necessarily maximally invariant; it can hold under some combinations of variable values and not under others. I introduced the term *invariance space* to refer to the set of value combinations under which a causal relationship holds. The observation mentioned above can be expressed this way: physical scientists often aim to identify causal relationships whose invariance space includes combinations of variable values that are not, as far as humans know, ever actualized. The fact that a portion of invariance space is never occupied does not seem to render the question of whether the relationship holds in that portion of invariance space less interesting or important in fundamental physics. But in the case of biology, the fact that a combination of variable values is never actualized does render the question of whether a relationship holds under that set of variable values less interesting and perhaps even altogether irrelevant. Consider the variable of tRNA forms. If the values of this variable were different than they actually are, that is, if actual tRNA molecules had different forms than they actually have, then the causal generalizations associating sequences in RNA and sequences in polypeptides could be strikingly different. And biologists are intensely interested in whether the values of this variable actually differ in certain mitochondria and chloroplast organelles. But if the values do not actually differ, then it does not much matter to biologists whether the invariance space of their generalizations include the non-actualized values.

The reason biologists do not care whether the invariance space of a causal relationship includes combinations of variable values that are not actualized is because they are much more interested in the actual than the possible. Biologists are more interested in explaining actual differences than possible differences, and explaining actual changes over developmental and evolutionary time than possible differences. This is why they are more interested in identifying actual difference

---

[31] This claim needs to be qualified. Biologists interests in manipulating causal processes in organisms sometimes motivates them to seek causal generalizations that hold under conditions that could be artificially brought about in organisms and their environments. See final paragraph in this section.

makers than potential difference makers.[32] This also explains why they are satisfied with highly sensitive causal generalizations about actual difference makers. Whether a property is an actual difference maker depends on whether it makes the difference under the conditions that actually obtain in the actual biological world. Whether it would make that difference if the conditions were different is irrelevant to understanding the difference the property makes in the actual world. Hence, seeking causal generalizations that are invariant over combinations of variable values that have not existed will not, directly at least, further the project of identifying the causal relationships relevant to explaining the actual differences in nature or the actual changes in complex biological processes such as ontological development.

The last claim is qualified ("directly at least") because biologists' interests include manipulating biological entities. This interest stems not just from the motivation to improve conditions for humans (for example, to cure diseases, to increase agricultural yields, to enhance the aesthetic value of plants and animals), but also from the motivation to investigate processes and mechanisms in living systems. A chief strategy of investigation in biology is to manipulate basic biological processes and mechanisms to learn how they work.[33] Hence, it is relevant whether causal generalizations will hold under conditions that could be made actual even if they are not currently actual. With this important qualification in mind, we can say that with respect to the goal of explaining the processes of life such as physiological functioning, ontological development, and evolutionary change, it is irrelevant whether the specified causal relationships extend to invariance spaces that include non-actualized combinations of variable values. This explains why biologists' interest in the actual leads them to be perfectly satisfied with causal generalizations that are highly sensitive even if physical scientists are not.

10. Conclusion

The philosophical literature on causation includes attempts to bring one or another theory of causation into accord with intuitions about what was "the cause" of an event. The literature seems to take it for granted that our intuitions

---

[32] I thank Michael Strevens for emphasizing the idea that biologists are interested in actual difference making because they are interested in the actual, and not the other way around.

[33] See C. Kenneth Waters, "What Was Classical Genetics", *Studies in History and Philosophy of Science, section A 35* (2004)*:* 783–809, Waters, "A Pluralist Interpretation of Gene-centered Biology" in Stephen Kellert, Helen Longino, and Waters, eds., *Scientific Pluralism, volume XIX of the Minnesota Studies in the Philosophy of Science* (Minneapolis: University of Minnesota Press, 2006), and Waters, "Beyond Theoretical Reductionism and Layer-cake Antireductionism: How DNA Retooled Genetics and Transformed Biological Practice" forthcoming in Michael Ruse and David Hull (eds.) *Oxford Handbook to the Philosophy of Biology*, Oxford: Oxford University Press.

are distinguishing causes from non-causes. But the analysis of this paper suggests that intuitions about what was "the cause" in an actual situation might stem from a natural inclination to pick out actual difference making causes, not an inclination to pick out causes simpliciter. Psychological research on causal reasoning in humans supports this idea. Recent empirical findings indicate that which factors are picked out as causes is indeed influenced by whether a candidate causal variable actually takes different values in the entities under observation.[34] The possible relevance of actual variation in the values of causal variables goes unnoticed in the philosophical literature when effects such as the lighting of a match are described as a singular actual outcome in a singleton rather than as a difference in actual outcomes in a multiplicity. Hence, the ontological contexts in which the actual difference making causes are actually making a difference are removed from consideration and it is therefore impossible to identify which cause is the actual difference making cause. Our intuitive judgments about what cause is making an actual difference ends up being based on tacit hunches about what is missing from the descriptions. If biologists were similarly limited to considering the causal synthesis of a single polypeptide molecule, they would have no basis for saying that the polypeptide's linear sequence was determined by DNA, and not by RNA polymerase. In fact, if restricted to considering a single instance (or a population of identical outcomes), it might appear that DNA was merely scaffolding for the synthesis of RNA. The causal distinctiveness of DNA is in the population. It is only in the context where polypeptide molecules with different amino acid sequences are being synthesized that it makes sense for biologists to say that DNA is not on a causal par with many of the other molecules that play causally necessary roles in the synthesis of RNA and polypeptides. Likewise, I suspect, focusing attention on singleton situations about a single lighting of a match, a single breaking of a vase, or the single catastrophic dropping of a boulder obscures important features of causation. Much light could be shed on causal reasoning by shifting attention to causes in populations.

---

[34] Patricia W. Cheng, "From Covariation to Causation: A Causal Power Theory", *Psychological Review 104*, No. 2 (1997): 367–405.