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Spot the difference: Causal contrasts in scientific diagrams

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ABSTRACT

An important function of scientific diagrams is to identify causal relationships. This commonly relies on contrasts that highlight the effects of specific difference-makers. However, causal contrast diagrams are not an obvious and easy to recognize category because they appear in many guises. In this paper, four case studies are presented to examine how causal contrast diagrams appear in a wide range of scientific reports, from experimental to observational and even purely theoretical studies. It is shown that causal contrasts can be expressed in starkly different formats, including photographs of complexly visualized macromolecules as well as line graphs, bar graphs, or plots of state spaces. Despite surface differences, however, there is a measure of conceptual unity among such diagrams. In empirical studies they often serve not only to infer and communicate specific causal claims, but also as evidence for them. The key data of some studies is given nowhere except in the diagrams. Many diagrams show multiple causal contrasts in order to demonstrate both that an effect exists and that the effect is specific – that is, to narrowly circumscribe the phenomenon to be explained. In a large range of scientific reports, causal contrast diagrams reflect the core epistemic claims of the researchers.

1. Introduction

Biology is littered with visuals. Some of them are well known even in popular culture, for instance the DNA double helix or evolutionary trees. But beyond these iconic representations we find an extensive visual practice of workaday scientific diagrams. They appear copiously in laboratory meetings and conference talks, and almost all publications include them. An indication of the fact that diagrams are essential rather than decorative is that scientists often advise their students to start reading a paper by looking at the figures. In addition to generating understanding, scientific diagrams appear to be linked with core issues in the philosophy of science such as confirmation, explanation and representation.

Philosophers of science have yet to develop an adequate systematic understanding of scientific diagrams. There exists no standard corpus of works that give a connected view of the functions that scientific diagrams have, how they perform these functions, and how they relate to the established topics in the history and philosophy of science. However, the analysis of scientific diagrams has advanced in the past decade: there is now enough of a literature to frame the debate and to delineate at least some of the key issues that are at stake.[1]

Recently, Bechtel and Abrahamsen (2015) outlined three main functions of diagrams in mechanistic research: diagrams are used, first, to delineate phenomena to be explained; second, to identify causal or explanatory relations between variables; and third, to construct and revise mechanistic models. Even a cursory study shows that each of these functions has many instances in actual science.

The present paper will look in detail at the second of Bechtel's and Abrahamsen's diagram functions, the identification of causal relationships. Many diagrams serve this goal by highlighting difference-makers: they create appropriate contrasts to show changes in an effect under particular interventions. Such diagrams

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[1] Laura Perini has argued that visual representations express claims, like linguistic representations (Perini, 2005b). Her studies address the role of visual representations in biological explanation (Perini, 2005a) and confirmation (Perini, 2005c). Goodwin (2009) has challenged Perini's view that visual representations are apt for truth and falsity, arguing that they should be understood more along the lines of scientific models (for a reply, see Perini, 2012). A tradition in cognitive science asks how reasoning is facilitated by visual representations (see for instance Larkin & Simon, 1987; Hegarty, Just, & Morrison, 1988; Hegarty, 2004, 2011). Finally, the state of the art was advanced in recent years by the Working Group On Diagrams in Science (WORGODS) at the University of California at San Diego. In addition to the discussion in the main text, see Bechtel and Abrahamsen (2012), Sheredos, Burnston, Abrahamsen, and Bechtel (2013), Bechtel, Burnston, Sheredos, and Abrahamsen (2014), Burnston et al. (2014) and Burnston (2016).

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are thus closely tied both to philosophical accounts of causation and to the practice of causal inference. In the 19th century, John Stuart Mill considered the "method of difference" to be the most reliable of his methods of experimental inquiry (Mill, 1843, III.VIII). Its core idea is that if we compare two instances where an effect occurs in one but not in the other, and whose antecedents differ in only one condition, then we can infer that the sole antecedent difference is causally related to the effect. Although it is an early and highly idealized formulation, the method gives a credible first-pass description of many experiments in science. Major philosophical accounts of causation in the 20th century also try to capture the difference-making nature of causes. Arguing for a counterfactual theory of causation, David Lewis writes: "We think of a cause as something that makes a difference, and the difference it makes must be a difference from what would have happened without it. Had it been absent, its effects […] would have been absent as well" (Lewis, 1974, p. 557). Similarly, probabilistic theories of causality use conditional probabilities to represent difference-making. Christopher Hitchcock (2012): "Probabilistic theories of causation capture [the] notion of making a difference by requiring that a cause make a difference for the probability of its effect." Difference-making is also an important component of the interventionist account of causation. Woodward (2013) writes that "the most natural way of defining the notion of causal effect is in terms of the *difference* made to the value of Y by a change or difference in the value of X" (emphasis in original; see also Woodward, 2003b). Finally, in the mechanistic framework, Craver and Darden (2013) note that mechanisms operate because the entities and activities at one stage make a difference to the entities and activities at a later stage. This leads to a natural view of experimental practice: "Experiments that test for causal relevance test whether a given entity, property, activity, or organizational feature makes a difference to what happens at a later stage in the mechanism" (chapter 8). The authors then offer a detailed and useful discussion of kinds of difference-makers and of the methods used to study them. Thus, the notion of difference-making is widespread both in theoretical accounts of causation and in methodological discussions of causal inference.

How causal contrast diagrams are used to learn and reason about difference-makers will be the subject of four case studies from the life sciences, spanning a wide range of different styles of research. The breadth of cases will show that causal contrasts can be found in many superficially very different scientific diagrams and at many levels of inquiry, including research where mechanistic understanding is not yet in sight.

The first case study concerns the molecular and experimental investigation of post-transcriptional gene silencing, where the ubiquity of diagrams showing results from difference-making experiments may be unsurprising (Section 2.1). We then proceed to a non-molecular but still experimental case in ecology: Gause's tests of the Lotka-Volterra predator prey model (Section 2.2). The third case is neither molecular nor experimental: Doll's and Hill's work on the association of smoking and lung cancer (Section 2.3). Finally, the fourth case is a purely theoretical contribution by Alberch on the interaction of development and natural selection in evolutionary processes (Section 2.4).

In order to facilitate thinking about causal contrast diagrams, it will be useful to import a number of notions from Woodward's interventionist framework. Among the accounts of causation currently on offer, interventionism is particularly well developed with regard to biological practice (see among others Woodward, 2003b, 2010; Waters, 2007; and the already cited Craver & Darden, 2013, chapter 8). A causal relationship between C and E will be understood as one where an intervention I on C results in a change in E in at least some background circumstances B. Scientists learn about such relationships either by performing the relevant interventions or by searching for "natural experiments" in which C is changed by an unmanipulated cause I^* that nevertheless has the *properties* of an intervention – most importantly, I^* must not cause a change in E by any causal paths that do not lead through C (Scheines, 2005; Woodward, 2003a, p. 94). Instances of both types of inferences will be discussed below: Section 2.1 (on post-transcriptional gene silencing) and Section 2.2 (on experimental tests of the predator-prey model) present cases in which manipulation occurs, while Section 2.3 (on the relationship between tobacco consumption and lung cancer) discusses an observational study. Crucially, the study of interventions gives knowledge of "partial" rather than "total" causes: interventions demonstrate causal relevance of C to E under circumstances B, but other variables will also be relevant to E either in conjunction with C or by different causal pathways. It remains for further research to discover the range of background conditions B under which the relationship between C and E remains invariant. Some relationships will be stable over a small range of invariance, while others will be stable over a very wide range (Woodward, 2010, pp. 291–296). Scientists sometimes prize stability: Section 2.1 tells the story of the discovery of a causal relationship that proved to be important but quite unstable; a later, similar discovery of a more stable relationship quickly won its discoverers a Nobel Prize. Finally, causal relationships may be more or less specific in the sense that varying the state of the cause C allows us to modulate the state of the effect E in a more or less fine-grained way (Woodward, 2010, 301–314). For instance, we would speak of a specific effect when a carefully targeted chemotherapeutic agent affects only the growth of cancer cells rather than the growth of all cells, as an unspecific spindle poison would. We will see in Sections 2.1 and 2.3 that diagrams are often used to demonstrate that causal relationships are specific.

Before we proceed, a note on terminology is in order. The term "diagram" will be understood broadly to include most visual representations in science. For present purposes I exclude only strictly depictive photographs and drawings (e.g. of a bird's plumage). The term will be used to cover not only line graphs, bar graphs, and scatterplots in state spaces, but also photographs that are used to detect (rather than depict) radioactive markers and fluorescent macromolecules.

2. Causal contrasts in scientific diagrams

2.1. Molecular biology: post-transcriptional gene silencing

One way to change the activity of a gene is to intervene on the DNA sequence of the gene itself or on the sequence of the promotor regions that regulate the gene's transcription. However, it is usually easier to intervene after transcription has occurred – that is, to intervene on the mRNA transcript of the gene before it is translated into a protein. Thanks to research conducted from the early 1980s and culminating in a Nobel Prize awarded in 2006, it is now a key tool of molecular biology to downregulate specific mRNAs by so-called small interfering RNA. In this section we will look at two publications from the history of post-transcriptional gene silencing in order to see how the effects of small RNAs were established. We will see that diagrams played a crucial epistemic and evidential role.

In the 1980s, a number of researchers explored the effects of single-stranded anti-sense RNAs on the levels of complementary mRNA and its translation. The anti-sense RNAs were thought to hybridize with the endogenous mRNA and thereby either to prevent translation or to elicit the destruction of the double-stranded RNA. A representative instance of this research is the work by Crowley, Nellen, Gomer, and Firtel (1985) at the University of California at San Diego.