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ORIGINAL RESEARCH

The hybrid account of activities

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Abstract
According to an influential account of the new mechanistic philosophy of science, entities and activities compose mechanisms. However, the new mechanists have paid too little attention to activities. Critics have charged that accounts of activities in the new mechanism literature are philosophically uninformative and opaque. This paper defends a novel account of causally productive activities, which I call the Hybrid Account, that marries the two dominant philosophical approaches to causation: production and difference-making. The Hybrid Account of Activities (HAA) identifies causally productive activities as robust difference-makers to the next stage of a mechanism. The Hybrid Account provides attractive solutions to causal identification and causal selection problems faced by earlier activities views.

Keywords Activities · Mechanisms · Causation · Explanation · Production · Difference-making

1 Introduction

This paper defends a novel account of causally productive activities. Machamer, Darden, and Craver's [MDC] (2000) influential account of mechanisms, centered on entities and their activities, launched a bourgeoning literature on mechanistic explanation (MDC 2000, 1). These new mechanists characterized an account of explanation that is ubiquitous in sciences such as molecular biology and neuroscience. Their account has since been applied to a variety of scientific fields, and even extended to accounts of metaphysical explanation (Trogdon, 2018). Although this approach has

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become prominent in philosophy of science, a central component of the account has received relatively little philosophical attention, namely activities.

Activities are "producers of change" in the preferred characterization of MDC. This much is agreed upon by all proponents of the activities view of causation. Activities are the causal components of mechanisms. They bring about each stage of the mechanism from start or set up to the explanandum-phenomenon. Examples of activities include binding, transcription, translation, folding, and so on. For instance, the activity of *folding* produces a three-dimensional protein structure from a sequence of amino acids.

Machamer (2004) and Bogen (2008) defend an activities view of causation. However, both doubt there is any unifying characteristic that all activities share beyond being types of causes. This lack of unifying characteristics for activities has opened the activities view to the charge by critics that it is philosophically uninformative. Furthermore, by eschewing counterfactual analysis the activities view does not provide an account of what makes activities *causal* (Woodward, 2002; Psillos, 2004). Franklin-Hall (2016) argues that the activities view fails to distinguish between causes and non-causes that are irrelevant side-effects. I call this the *causal identification problem* of activities. Causal identification, a principled way to tell the causes from the non-causes, is a central task of any causal-explanatory account. Additionally, the new mechanistic philosophy of science needs to account for the special causal-explanatory status of activities. Not all causes have equal explanatory value. Out of an array of causes, some activities are singled out as just those ones that play the role of producers of change. While more recent activities views incorporate a causal identification principle, they have not defended a causal selection principle that justifies the higher explanatory status of activities in a way that distinguishes them from other, less explanatorily relevant causes such as background conditions. I call this the *causal selection problem*. Solving both causal identification and selection problems is essential for activities to serve as an attractive account of causation within mechanisms. Without philosophically informative causal identification and causal selection principles, the activities view risks being a deflationary account of what scientists do.

In order to address the causal identification and causal selection problems, this paper defends an account of activities as productive difference-makers of change, which I call the Hybrid Account of Activities (HAA). On the Hybrid Account, causally productive activities are what make a difference to changes between stages of a mechanism. Causally productive activities engage in a particular kind of difference-making (as specified by the Hybrid Account). The Hybrid Account marries the two dominant philosophical approaches to causation: production and difference-making. Previous activities views typically developed purely productive accounts of activities as causes. Tabery (2004) defended an approach that synthesized earlier activities views, which prioritized production, with Glennan's (1996) interaction view, which prioritized difference-making (Tabery, 2004). The approach defended in this paper is a union of production and difference-making that builds on Tabery's (2004) insight, along with Glennan (2017) and Kaiser (2018), and extends it to offer an attractive solution to the causal identification and causal selection problems.

The Hybrid Account I defend is not a *general* account of causation, or of an activity as such, but about activities as the causally productive components of *mechanisms*. That is, the Hybrid Account specifies the features in virtue of which an activity is causally productive. Some activities may not be causally productive, and not everything that is causally productive is an activity. Furthermore, the account I provide applies to *etiological* mechanisms. I do not discuss constitutive or part/whole mechanisms. My account of activities has two explanatory virtues: (i) it integrates production and difference-making accounts in its characterization of activities, and (ii) it distinguishes between causally productive activities and casual influences that are merely background conditions.

The paper goes as follows: Sect. 2 outlines early activity views of causation defended by MDC (2000), Machamer (2004), and Bogen (2008), and how they suffer from a causal identification problem, and more recent view defended by Glennan (2017) and Kaiser (2018), and how they lack a causal selection principle; Sect. 3 discusses Franklin-Hall's criticism of the activities view of causation that it doesn't distinguish causally irrelevant side-effects from causally productive activities; Sect. 4 briefly discusses Woodward's (1997, 2003) difference-making approach; in Sect. 5, I propose and defend my Hybrid Account of Activities. I develop the case of phosphorylation to highlight the virtues of the account (5.1) and respond to a potential objection (5.2); finally, Sect. 6 concludes.

In what follows (Sect. 2), I outline the activities view of causation. The section is better called the activities *views* of causation since there is a divergence among new mechanists who incorporate activities into their account of mechanisms on how they characterize activities. Nonetheless, the new mechanists discussed in the next section take activities to be the causal components of mechanisms. I discuss these views below and highlight their shortcomings.

2 The activities view

The first activities view was proposed in Machamer, Darden, and Craver's (MDC) (2000) groundbreaking paper in what would become known as the new mechanistic philosophy of science. MDC characterize mechanisms as "entities and activities organized such that they are productive of regular changes from start or set-up to finish or termination conditions" (2000, 3). Mechanisms are not machines. That is, they are not "exclusively mechanical (push-pull) systems" (2000, 2). In order to be a mechanism, it has to be *active*. MDC drew on molecular biology and neuroscience in developing and motivating their account.

The MDC account of mechanisms is dualistic. Their ontology is composed of two irreducible and ontologically equal parts: *entities* and *activities*. Entities are property-bearing objects that engage in activities. Activities are the producers of change. As MDC put it, activities are "types of causes. Terms like 'cause' and 'interact' are abstract terms that need to be specified with a type of activity and are often so specified in typical scientific discourse" (MDC 2000, 6). Entities and activities are organized within mechanisms to produce a phenomenon. "Entities often must be appropriately located, structured, and oriented, and the activities in which they engage must have a temporal order, rate, and duration" (2000, 3). Mechanisms have *regularity* in so far as they operate in more or less the same way under the same conditions. If the description of the mechanism is complete, then there must be *productive continuity* from the start or set-up to the end or termination condition. Consequently, there will be no gap in our knowledge of each step in the production of the phenomenon (2000, 3).

According to MDC, activities are nor merely properties of entities or entities' capacities. If the universe were frozen in time, as if it were an insect encased in amber, all the entities along with their capacities and many of their properties would still be there, but there would be no activities. In the absence of activities, no mechanisms would be operating. Scientists are not merely after what things there are, but "how things work" (Craver, 2007). Mechanistic explanation is well-suited to give us such an account. It is therefore unsurprising that scientists, especially life scientists, appeal to mechanisms in their explanatory work. Entities and activities are therefore irreducible components of mechanisms (Illari & Williamson, 2013).

MDC's (2000) characterization of mechanisms set off a bourgeoning literature on mechanistic explanation.[1] Machamer (2004) expanded on the activities view forwarded in MDC. Consistent with the characterization of mechanism and activities in MDC, Machamer (2004) defended the activities view of causation. Machamer (2004) claims that the criteria for the identification of activities "are specific to kinds of activity that a group, at a time and in a discipline, takes to be fundamental in the sense that they do not feel any need to question their truth or usefulness" (Machamer, 2004, 29). He adds: "It is not clear that they all have any one thing in common or are similar in any significant way, but neither commonality nor similarity are necessary conditions for an adequate category" (Machamer, 2004, 29). While it may be true that we can make do with a category without necessary and sufficient conditions for membership in that category, Machamer's (2004) contention that there is no unifying conception that applies to all activities leaves little justification for the heavy ontological weight MDC place on activities. As Glennan (2017) notes, if activities are what ground our causal claims, "there must be something about activities that makes them what they are" (Glennan, 2017, 31).

Bogen (2008) defends an activities view of causation broadly similar to MDC (2000) and Machamer (2004). On Bogen's account, that activities are causally productive is a further brute fact about activities. He writes that "an activity is causally productive by virtue of facts about the activity, the things that engage in it, and what results from them doing so" (Bogen, 2008, 117). Bogen contends there is no "single, universally applicable criterion" that distinguishes causes from non-causes (Bogen, 2008, 117). Both Machamer (2004) and Bogen (2008) claim activities are discovered and catalogued by scientists, but there is not much further that can be said to unify them. Bogen (2008) endorses the view, first forwarded by Anscombe (1981), that it is a "brute fact" that activities have their effect and that "there is no informative general condition which discriminates causally productive activities from goings on which are not causally productive" (Bogen, 2008, 113). Machamer (2004) is equally skeptical that there is a unifying feature of all activities. He writes of activities that "it is

[1] For the literature on mechanistic constitution see for instance Darden (2002); Craver (2007); Harbecke (2010); Couch (2011); and Gillett (2013). This paper is more narrowly focused on activities.

not clear that they all have any one thing in common or are similar in any significant way…" (Machamer, 2004, 29). For Machamer (2004) and Bogen (2008) then, there is no causal identification principle that picks out activities as causes beyond the work of scientists. As I discuss in Sect. 3, such a view is liable to suffer from a causal identification problem.

In contrast to earlier approaches, more recently Kaiser (2018) and Glennan (2017) have developed activities views that outline conditions for being an activity. Kaiser (2018) develops an activities view by identifying the main features shared by all activities (Table 1). Following MDC (2000), Kaiser (2018) takes "activity" to be how we further analyze "cause" within the context of mechanistic philosophy of science. That is, in order to account for causation and explain causal claims made by scientists, new mechanists develop an account of activities. Activities "produce the changes" (MDC) in a mechanism in virtue of their "active" nature (Machamer, 2004). Following Craver (2007), activities are the "causal components of mechanisms" (Kaiser, 2018, 118). Activities are temporally extended, and therefore they belong to the metaphysical category of occurrents (118). This puts activities in a different metaphysical category from entities (which are continuants), preserving the dualism of entities and activities initially proposed by MDC (2000).

Kaiser claims activities, as the occurrent component of mechanisms, must be *actualized*. Activities are not dispositions or potentialities of entities. They are the actually-occurring producers of change. Activities are always the activities of an entity or entities; that is, without entities to engage in them there would be no activities. Additionally, without activities, entities would not be able to produce changes in themselves or in other entities. Finally, a description of a mechanism (mechanism schema) is complete if it shows the "productive continuity" of the mechanism from beginning to end.

Kaiser provides a helpful analysis of the new mechanist account of activities as causes. Indeed, the Hybrid Account I develop in Sect. 5 assumes K1-K5 as true of activities. However, the K3 condition, that activities are producers of change, is what critics of the activities view challenge as needing philosophical justification. Kaiser (2018) does not tell us what it is about activities that makes them *producers of change* rather than background or enabling conditions, thereby lacking both a causal identification and a causal selection principle. The features Kaiser (2018) highlights do not justify the high explanatory status of activities. The lack of further analysis of production leaves the account without resources to answer the causal selection problem.

Glennan (2017) has an approach that incorporates activities as part of his account of a "minimal mechanism" where "a mechanism for a phenomenon consists of entities (or parts) whose activities and interactions are organized so as to be responsible

Table 1 Kaiser's (2018) list of the main features of activities (Kaiser, 2018, 119 [italics in original])

Kaiser's Main Features of Activities
K1 Activities are *temporally extended* (i.e., occurrents).
K2 Activities are *actualized* (rather than merely potential).
K3 Activities *produce change* (i.e., are types of causes).
K4 Activities require at least one *actively involved entity*.
K5 Activities have *unrestricted arity* (i.e., involve one to many entities).

Table 2 Glennan's list of the necessary conditions for activity-hood (Glennan, 2017, 31)

Glennan's Necessary Conditions for Being an Activity
G1 Activities require entities (parts, components) to act and be acted upon.
G2 Activities produce change in entities (parts, components) that act or are acted upon.
G3 Activities manifest the powers (capacities) of the entities involved in the activity.
G4 Activities are temporally extended processes.
G5 Most or all activities are mechanism-dependent.

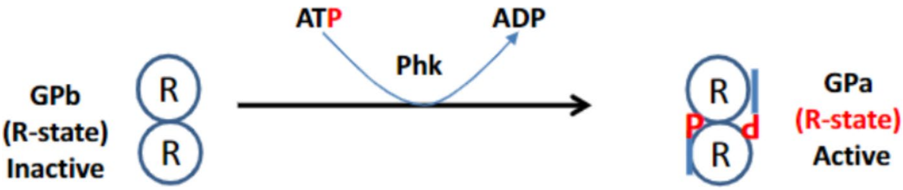

Fig. 1 Phosphorylation of inactive glycogen phosphorylase (GPb) by phosphorylase kinase (Phk) turns it into the active form of the enzyme (GPa). Phosphorylation activity involves taking a phosphate group from another substrate (in this case ATP) and adding it to a binding site of a protein (in this case serine-14 of glycogen phosphorylase) [image adapted from Agius, 2015, 36]

for the phenomenon" (Glennan, 2017, 17). However, unlike earlier activity views, Glennan (2017) still relies on mechanism and not activity as his primary account of causation (more on this below). Glennan (2017) nonetheless provides what he labels the necessary conditions for being an activity (see Table 2).

Glennan's (2017) account goes further than Kaiser's (2018) by grounding the claim that activities are producers of change (G2) in the claim that activities are mechanism-dependent (G5). Activities are productive because there is an underlying mechanism that is responsible for them. For Glennan (2017), "the mechanism-dependence of (all or most) production is a unifying feature of productive activities …" (Glennan, 2017, 33). What makes something causally productive is that there is an underlying mechanism that connects a "causing event" with an "effect event" (Glennan, 2017, 179).

Glennan (2017) goes further than previous activities views by providing a philosophical analysis of production, incorporating a causal identification principle. Activities can be distinguished from non-causes by the presence of an underlying mechanism that accounts for how they bring about the next stage of a mechanism. Something that non-causes lack. However, the mechanism-dependence condition does not provide a causal selection principle. It does not distinguish activities from other causal influences. While activities do have underlying mechanisms that account for how they are able to bring about changes, so do other causal influences such as background or enabling conditions.[2] For instance, pH indicates the concentration of Hydrogen ions, and there is an underlying mechanism by which the activity of Hydrogen ions play a role in folding and binding. Nonetheless, the activities of

[2] As Craver and Kaplan (2020) note, background conditions are difference-makers (Sect. 4).

Hydrogen ion in this mechanism[3] are a background condition and not a causally productive activity. For any given causal influence, there is an underlying mechanism of its action that connects it with an “effect event”. Mechanism-dependence therefore does not provide a selection principle that accounts for activities’ special explanatory status within mechanisms.

In summary, early activities views of causation claimed that it is a further brute fact about activities that they are causal in just those ways scientists who study them claim they are (Bogen, 2008). Glennan (2017) and Kaiser (2018) propose identifying conditions that apply to all activities. Although this advanced the activities view beyond the objection to earlier views’ minimalism, their accounts nonetheless do not solve the causal selection problem. What is needed is a feature or condition of activities that accounts for their causal productivity and justifies their special explanatory status.

In the next section, I outline Franklin-Hall’s (2016) criticism of the activities view of causation. Namely, Franklin-Hall’s charge that activities views of causation fail to distinguish between causal production and causally irrelevant side-effects.

3 Activities and a lack of explanatory constraints

Franklin-Hall (2016) charges that activities are not an explanatorily apt account of causation. More specifically, she argues that the activities view commits a *causation error*. In order to motivate her challenge, Franklin-Hall proposes a mechanistic model, or a mechanism schema in the Craver and Darden (2013) terminology, of a neuron’s release of “neurotransmitters at its axon terminal when its dendrites are exposed to neurotransmitters, and not otherwise” (Franklin-Hall, 2016, 44). The standard model explains this capacity by relating organized macromolecular parts such as axons, dendrites, ion channels and gradients, with “dynamic principles” which causally relate input to outputs. But she proposes a non-standard alternative model which is identical to the standard model,

> except that it appeals to two alternative dynamic principles, one relating neurotransmitter exposure and membrane vibration, and a second relating vibration and any later event genuinely relevant to neurotransmitter release, for example, the entry of calcium into the axon terminal. With these principles and others, such an alternative model might bridge inputs and outputs, stating first that neurotransmitter exposure is followed by membrane vibration, itself followed by cellular calcium entry, eventuating finally in neurotransmitter release (Franklin-Hall, 2016, 46).

[3] While these activities are background conditions within this mechanism, they may very well be causally productive activities in others. See Sect. 5.

However, the "alternative model" commits a causation error. The vibration of a membrane is not part of the productive continuity of neuron depolarization.[4] Yet, Franklin-Hall (2016) contends, it still appeals to "organized parts changing according to dynamic principles" (Franklin-Hall, 2016, 46). Nevertheless, the incorporation of membrane vibration as a part of the mechanism of neuron depolarization is unscientific. It is experimentally known that neuronal membrane vibrations are the result of the wave of ions rushing through the neuron and do not actually produce the depolarization itself (Carlen et al., 1982).

The new mechanists who defended the early activities view do forward a principle that eliminates the "alternative model" in favor of the standard explanation. MDC write of mechanism components, including activities, that the "the components [are those] that are accepted as relatively fundamental or taken to be unproblematic for the purposes of a given scientist, research group, or field" (MDC 2000, 13). Therefore, since no competent scientist would cite membrane vibration as part of the productive continuity of neurotransmitter release, we have reason to pick the standard over the alternative model.

However, Franklin-Hall (2016) argues looking to the sciences to identify and individuate activities is an unsatisfactory way to block the causation error since this ends up being too deflationary. Scientists often identify activities, but we need a philosophically informative account of how they come to correctly identify the parts of mechanisms, including activities. Otherwise, mechanistic explanation is purely a science reporting exercise (Franklin-Hall, 2016, 47). Furthermore, taking the Machamer (2004) and Bogen (2008) position of leaving the causal productivity of activities as an unexplained brute fact "is completely opaque", leaving no room for the view to say why the membrane vibration model is incorrect beyond that it is not what competent scientists would claim in an explanation (Franklin-Hall, 2016, 53).

This opacity is worth resisting for reasons new mechanists will appreciate. It is in tension with the high value new mechanists place on uncovering black boxes to build explanatorily adequate mechanism models. Mechanistic explanation involves turning black boxes into glass boxes by filling in the details necessary to account for the explanandum by describing the mechanism (Craver & Darden, 2013). The task of mechanistic explanation is undermined if one of the two main mechanism components' operations are left a "brute fact" not subject to further philosophical analysis.

Franklin-Hall's (2016) criticism hits upon an important limitation of earlier activities views of causation. A desideratum of any account of causation is that it provides the conditions that enable the identification of causes from a whirl of occurrences. This is no less the case for the activities view. Mechanisms are composed of multiple parts organized such that changes from one stage to the next are accounted for by activities. This requires, both at the scientific and philosophical level, a condition that accounts for activities, out of a panoply of occurrences happening simultaneously,

[4] Of course, the membrane's vibration is an activity of the membrane. It is the result of the properties of the membrane and their interactions. It is however not a *productive* activity as it does not play a causal role in bringing about the next stage of the depolarization mechanism. A causal identification principle is necessary precisely to distinguish *occurrent* activities such as the membrane's depolarization or a heart making lub-dub noises from *productive* activities that are explanatorily relevant.

as the ones productive of the change. In other words, new mechanists need a causal identification principle.

There is a strategy new mechanists can employ to avoid the causal identification problem. Namely, new mechanists can appeal to difference-making as a causal identification principle. Tabery's (2004) account of activities, which synthesized (producing) activities and (difference-making) interactions, avoids the causal identification problem. In a similar vein, I argue that activities are both producers *and* difference-makers (specifically, their production is a special kind of difference-making). The vibration is not a productive activity because it never makes a difference to the occurrence of the next stage of the mechanism. Unifying difference-making and production in the activities view offers an attractive account that addresses the criticisms discussed above and goes beyond Tabery's (2004) by providing a causal selection as well as causal identification principle. In what follows, to motivate my account of activities, I first briefly outline Woodward's influential difference-making approach to causation.

4 Difference-making and causal production

Difference-making approaches to causation and explanation variously propose a way to separate the causal wheat from the non-causal chaff. These approaches to explanation have become dominant in philosophy of science with Woodward (1997, 2003, 2010), Strevens (2004, 2008), Waters (2007), and Weslake (2010) forwarding influential accounts. Difference-making approaches to causation are attractive because they accord with both everyday causal attributions and scientific practice. Difference-making approaches broadly characterize claims about causation as claims about what makes a difference to the occurrence of an effect or explanandum.

An influential difference-making account of causation is Woodward's (1997, 2003) interventionist or manipulability view of causation. For Woodward, to say X explains Y is to say that X causes Y, where X and Y are variables that can have at least two values. Explanations answer what-if-things-had-been-different questions (*w*-questions) that a difference-making approach is well-suited to answer. Woodward takes the relationship between cause and effect to be a form of counterfactual dependence. However, the problem of relevance plagued earlier counterfactual accounts of causation. The joint effects of a cause may counterfactually depend on one another. Nevertheless, they do not provide information about causation. For instance, a barometric reading and a storm counterfactually depend on each other in so far as whenever the barometer displays a reading indicating low air pressure there is a storm and vice versa. However, the barometric display does not cause the storm, neither does the storm cause the barometric display. Rather, both the barometric reading and the storm are the effects of a common cause, namely, low air pressure.

To avoid the problem of irrelevant counterfactuals, Woodward provides an account of which counterfactuals count as causal. According to Woodward, "the counterfactuals that matter for explanation are counterfactuals the antecedents of which are made true by a special sort of exogenous causal process that I call an intervention" (Woodward, 1997, s29).

Woodward defines interventions as follows:

> An *intervention* on *X* with respect to *Y* is an idealized experimental manipulation of *X* which causes a change in *Y* that is of such a character that any change in *Y* occurs only through this change in *X* and not in any other way (Woodward 2010, 290).

Interventions in the account above should be interpreted *heuristically*. That human intervention is not possible does not detract from the view. Suitably characterized natural phenomena may also count as interventions (e.g., a lightning strike). Furthermore, the appeal to intervention, which is itself a causal term, is not viciously circular as Woodward is not providing a reductive account of causation but elucidating how certain causal relationships can be explained in terms of others. This accords with the fact that experiments are widely taken to provide causal information. In other words, "in order to test some causal claims we must assume the truth of others" (Woodward, 1997, s31).

Nevertheless, Woodward's interventionist account of difference-making is too broad to capture causally productive activities while excluding causal influences scientists normally take to be background conditions.[5] Craver and Kaplan (2020) claim they have not yet found a satisfactory way to identify the "differences that make a difference" beyond what can be established by scientific inquiry. They write that "sometimes, we draw a line between foreground and background conditions *(though background conditions often make a big difference)*" (Craver & Kaplan, 2020, 26 [italics added]). However, they have "little of general interest to say about [the] considerations" which lead us to assign to some difference-makers the status of background conditions and to others the status of cause.

New mechanists' more recent incorporation of difference-making blocks worries that the mechanistic approach fails to identify what makes activities causal as opposed to mere irrelevant occurrences. However, that still leaves whether there is a principled way to distinguish the causally productive activities that are taken to be producers of change within mechanisms. As Franklin-Hall (2015) notes, a pragmatic approach to causal selection has been prominent since JS Mill. On the pragmatic view, distinctions drawn between the causes and background conditions are not based on any principled or scientific ground. Causes and background conditions have the same ontological (and even explanatory) status (Franklin-Hall, 2015, 415). The "invidious" distinction drawn between causes is based on the contexts in which the explanation is given and the interests of scientists.

I argue that new mechanists ought to resist a pragmatic causal selection principle. A non-pragmatic causal selection principle vindicates the special explanatory status of activities in new mechanistic accounts advanced by, for instance, Craver and

[5] Woodward (2010) advances causal selection principles such as specificity, proportionality, and stability that narrow the set of relevant difference-makers depending on what's of explanatory interest. These principles nonetheless remain external to the causal account. Waters (2007) also forwards an influential selection principle that distinguishes potential from actual difference-makers. Waters' (2007) account secures a kind of robustness I aim to capture with my second condition of the Hybrid Account discussed in Sect. 5.

Darden (2013) and Krickel (2018). It also better captures what scientists are doing in discovering mechanisms and building mechanism schemas. The Hybrid Account provides a principled causal selection principle that grounds the causal productivity of activities in a way that secures its special mechanistic status.

I now turn to my Hybrid Account of Activities.

5 A hybrid account of activities as productive difference-makers

Activities produce changes within mechanisms, but this fact alone does not tell us how to identify and individuate causally productive activities. Mechanism schemas or models that explain a given target phenomena select just some of the activities, and the entities that engage in them, as worthy of inclusion as mechanism components. The Hybrid Account grounds the causal productivity of activities in robust difference-making. First, causally productive activities are difference-makers to the occurrence of the changes from one stage of a mechanism to the next. This could be the transfer of energy, the transmission of information (for instance the "precise determination of sequence in the DNA-RNA-protein schema), among others. Second, the relation between (causally productive) activities and changes is *robust*. Changes depend on the activities that produce them. It is because of the activities that the changes obtain. For instance, in the well-characterized mechanism of protein synthesis, the entity RNA polymerase transcribes DNA to messenger RNA (mRNA). The activity of transcription produces the next stage of the mechanism (in this case the entity mRNA). By combining these two metaphysical features, difference-making and robustness, the Hybrid Account secures the special explanatory status of activities.

What follows is the Hybrid Account of Activities:

(HAA) Φ-ing is a causally productive activity of a change ψ in the next stage of a regular mechanism if:

i) Φ-ing makes a difference to the occurrence of a change ψ in at least one of the scenarios in which ψ occurs and,
ii) In the highest proportion of the scenarios that Φ-ing occurs, the change ψ occurs.

The first condition (i) incorporates Woodward's interventionist difference-making into an account of activities. This move blocks concerns that the activities view does not distinguish between causation and irrelevant side-effects and occurrences, thereby solving the *causal identification* problem.[6] On my account, we can remove putative causal influences from a mechanism schema if they never make a difference to the production of a type of change in the next stage of the mechanism. If intervening on a variable of a putative causal influence does not change the variable of a given change ψ, then it is not a causally productive activity. We can now discount the membrane vibration in the alternative model proposed by Franklin-Hall (2016) as a causally productive activity in the neurotransmitter release mechanism. The membrane

[6] While I use Woodward's account to specify the first condition, nothing would be lost if an alternative difference-making standard was substituted.

vibration is not an activity, and hence does not belong in the mechanism schema or model, because it does not make a difference to the occurrence of the next stage of the mechanism. An idealized intervention on the membrane vibration would not directly change a variable on the next stage of the neurotransmitter release mechanism.

While the first condition answers the Franklin-Hall (2016) challenge as it eliminates irrelevant side-effects, there are still many difference-makers within a mechanism that are typically not considered causally productive activities although they may still be causal activities that are background conditions. Many causal influences biologists often take to be background conditions, such as temperature and pH, fulfill condition (i) of my account. That is, background conditions are often difference-makers and intervening on them will make a difference to the occurrence of the effect. The second condition answers the *causal selection*[7] problem by providing a selection principle that distinguishes background conditions from causally productive activities.

According to condition (ii), if we take the set of difference-makers to the occurrence of a change (the next stage of a mechanism), the causally productive activity is the member of that set that, in the highest proportion of the scenarios in which it occurs, the change (next stage of a mechanism) occurs. Background conditions fail HAA (ii) because they occur in many more of the scenarios where the change does not occur than the causally productive activity. For instance, if we take changing from an inactive to an active form of an enzyme (i.e., a regulatory protein) as a type of change, the activity *heating at 37 Celsius* makes a difference to that type of change. However, this heating activity occurs in many scenarios where that type of change does not occur. It therefore is a background condition and not a causally productive activity.[8]

Changes within a mechanism can fail to occur because the causally productive activity has been blocked. For example, catalytic activities that activate an enzyme can be blocked by an inhibitor. In this case, the causally productive activity will fail to occur. But it still holds that in the highest proportion of the cases the causally productive activity occurs, the change occurs. This is how the Hybrid Account identifies which difference-maker is *productive* of a type of change. HAA (ii) is a *robustness* condition. Activities are robust causes. Their occurrence reliably leads to the occurrence of the changes that propagate productive continuity across the mechanism. I argue robustness is a defining condition of causally *productive* activities because robustness foregrounds the metaphysical dependence of changes upon activities. Robustness secures the tight modal matching between causally productive activities and the changes they produce within mechanisms. It therefore matches the metaphysical weight activities are taken to have by most new mechanists.

However, while the Hybrid Account marries production and difference-making, it is not a marriage of equals. Production in the Hybrid Account is not as metaphysi-

[7] Franklin-Hall's (2015) causal economy account of explanation incorporates a causal selection principle. See also Waters (2007); Woodward (2010); Strevens (2008); Weslake's (2010) and Ross (2018) for other analyses of causal selection.

[8] Note that while heating remains a background condition within this mechanism, it is possible that it is a causally productive activity within other mechanisms.

cally substantive as earlier production accounts of causation. In this I follow Strevens' (2008) kairetic account, which "represents" causal production as the outcome of "a causal process that made a difference to the occurrence" the explanandum. (Strevens, 2008, 69). Similarly, I represent the causal production relation between activities and mechanistic changes as a particular kind of difference-making,[9] one having the dimension of robustness. Identifying causal production with robustness in turn has epistemic benefit, as it makes certain activity-change relations *expectable*.[10] Although the Hybrid Account has this epistemic benefit, it is not a merely epistemic principle but a metaphysical one. Whether or not causal relations are robust in the way the Hybrid Account requires for causally productive activities is a fact about the world and does not depend on the interests or projects of scientists.

It is also important to keep in mind that HAA is consistent with more than one activity producing a type of change. HAA (ii) merely claims that if Φ-ing is to count as a causally productive activity, then in the highest proportion of the scenarios Φ-ing occurs within a mechanism, the change ψ occurs. It does not follow from this that in all the scenarios that the change ψ occurs, Φ-ing occurs. For instance, methylation (adding a methyl group) may inactivate a given gene X in the cases it occurs. Yet, gene X can be rendered inactive by other activities. As long as those activities also fulfill HAA's conditions, they can be considered causally productive activities. This is an attractive feature of the Hybrid Account since it accords with scientific work on activities that find redundancy in many biological systems. There may be several types of activities that produce the same type of change in different mechanisms.

The Hybrid Account relies on what Craver and Darden (2013) call the "store of types of entities and activities" (Craver & Darden, 2013, 75). These are the types that scientists have characterized and investigated, and which they draw on in the work of proposing and discovering mechanisms. I add to that conception the idea of a type of change. Since many biological mechanism types share the same stages, a type of change from one stage of a mechanism to another is part of that store. The types of changes found in the store enable the *individuation* of causally productive activities. A type of change is potentially found in multiple mechanisms (e.g., activation of an enzyme) and produced by multiple types of activities. It is not only phosphorylation, but also hydroxylation and glycosylation, among other activities, that produce a common type of change (enzyme activation). This individuation procedure, where types of activities are indexed to a type of change, can be applied to the whole "store of types" discussed by Craver and Darden (2013).

These two features of activities highlighted by HAA, that they are difference-makers, that their occurrence, more than any other causal relationship, results in the effect-change, and that they are robust, marks activities as a special type of cause that are well-suited for the life sciences. Not all causes must fulfill these conditions

[9] Glennan (2017) for an alternative account of causal relevance that makes production more fundamental.

[10] Bhogal (2020) defends an account of explanatory goodness whose first dimension, precision, holds that "explanations are better if in more of (that is, a higher proportion of) the physically possible worlds where the explanans is true, the explanans explains the explanandum" (Bhogal, 2020, 18). He notes that the intuitive force behind "precision" is the classic philosophical idea that explanations should make the explanandum expectable. While HAA is not an account of explanatory goodness, HAA (ii) is a condition that is meant to capture the same ideal for the activities view of causation.

in order to be considered causes. But within the mechanistic project, it is *causally productive activities* as specific types of causes that play the causal-explanatory role as producers of change within a mechanism. The advantage of this account lies in its ability to vindicate the selection of some activities, and the entities that engage in them, as the explanatorily privileged elements of mechanism schemas and models. And it does so by grounding the causal productivity of activities in metaphysically robust difference-making that specifies how these activities are the producers of change.

In what follows, I'll motivate my account by showing how it enables identification and individuation of causal productive activities in a molecular and a physiological case. My main illustrative example is the ubiquitous biological activity phosphorylation.

5.1 The case of phosphorylation

To see how the Hybrid Account of Activities works, take for instance the activity "phosphorylating." Phosphorylation is a one of the most important activities in living organisms. It is part of mechanisms ranging from gene regulation to cancer pathogenesis. If we take this activity to be the phenomenon in need of explaining, we find that there is a complex mechanism that underlies it, with multiple steps involving bond-formation, spatial and temporal organization, and ATP (an energy source in cells) metabolism. Phosphorylation produces the changes it does by adding a phosphoryl group to a specific site of a protein. The addition of this phosphoryl group changes the shape of the protein to which it binds. The protein will then have the structure necessary to carry out its activity (Pearlman et al., 2011). Below, I illustrate phosphorylation activity with the case of glycogen phosphorylase.

Glycogen metabolism is a homeostatic mechanism that maintains stable blood glucose levels by synthesizing and degrading glycogen, particularly in the liver. Glycogen is the form carbohydrates take during storage. Liver glycogen is synthesized in response to an increase in the insulin to glucagon ratio as a result of increased glucose concentration in the blood after a meal. Glycogen is degraded between meals and releases as glucose in the blood to maintain blood glucose levels. The synthesis mechanism is mediated by (liver) glycogen synthases.

Human liver glycogen metabolism has four stages:

i) Phosphorylase kinase produces active glycogen phosphorylase by *phosphorylation*.
ii) Glycogen phosphorylase produces glucose 1-phosphate by *phosphorolysis* of glycogen.
iii) Phosphoglucomutase produces glucose 6-phosphate by *phosphorylating* glucose 1-phosphate.
iv) Glucose 6-phosphotase produces glucose by *hydrolyzing* glucose 6-phosphate.

Stage (i) involves change from inactive (GPb) to active (GPa) form of the glycogen phosphorylase enzyme by the *phosphorylation* (adding phosphate group) of the serine 14 region of the GPb form (discussed in detail below). In stage (ii) the active glycogen phosphorylase engages in *phosphorolysis*, which involves using an energetic phosphate group to cleave bonds, to release a glucose 1-phospate from a glycogen chain (glycogen is typically a chain of 1000 glucose molecules). In stage (iii) Phosphoglucomutase *phosphorylates* glucose 1-phosphate to glucose 6-phosphate by transferring a phosphate group from the 1 to 6 position. Finally, in stage (iv), glucose 6-phosphotase *hydrolyzes* glucose 6-phospahate releasing a free glucose molecule that can enter the blood and transport to tissue in need of free glucose (Berg et al., 2002; Adeva-Andany et al., 2016).

As discussed above, (liver) glycogen phosphorylases initiate glycogen degradation (stage i). Importantly for our purposes, "*only the phosphorylated form* of liver phosphorylase (GPa) is catalytically active. Interconversion between GPa and GPb (unphosphorylated) *is dependent on the activities* of phosphorylase kinase and of phosphorylase phosphatase" (Agius, 2015, 33 [italics added]). In other words, phosphorylation is the activity that produces the change from the inactive liver phosphorylase (GPb) to the active form (GPa) of the enzyme, and *in the scenarios* that liver phosphorylases are phosphorylated, they are activated.

Specifically, the serine-14 portion of glycogen phosphorylase enzyme has a binding site for phosphates. Phosphorylase kinases are entities that carry out the phosphorylation activity (Fig. 1). Therefore, we have a type of change, inactive to active form of glycogen phosphorylase, produced by an activity (phosphorylation) that makes a difference to the occurrence of this change in the highest proportion of scenarios this occurs.

As Fig. 1 illustrates, the presence of ATP (an energy molecule that supplies the phosphate) is crucial for the phosphorylase kinase's ability to engage in the phosphorylation activity. Intervening to eliminate ATP would prevent the phosphorylation and subsequently the activation of glycogen phosphorylase. Furthermore, the background temperature, *heating* within a specific range, also makes a difference to the activation of the phosphorylase enzyme. If heating were to exceed or fall short of a certain equilibrium the activation would not occur. Nonetheless, scientists identify the phosphorylation carried out by phosphorylase kinase as the causally productive activity (within this mechanism) and pressure, temperature, and the (presence of a certain concentration of) ATP as background conditions. HAA provides a non-pragmatic justification for this assignment. For instance, heating, while a difference-maker, is present in many of the scenarios where glycogen phosphorylase is in its inactive (GPb) form without the change to the active form (GPa) occurring. That is, the heating activity occurs in many more of the scenarios where the change (from inactive to active) does not occur than phosphorylation. Heating therefore fails to make the change robust in the way the causally productive activity of phosphorylation does. Phosphorylation, however, is the difference-maker that makes a difference to the activation of glycogen phosphorylase in the highest proportion of the scenarios activation occurs. It is therefore appropriately grounds the activity-change relation in a way we are justified in identifying as production.

The Hybrid Account identifies the feature of activities that makes them causally productive. It is not the underlying mechanism of an activity type, such as phosphorylation, that secures its causal productivity. For instance, in eukaryotes and prokaryotes phosphorylation proceeds differently. Different kinds of enzyme complexes, encoded by different genes, engage in phosphorylation. Then why is it that these are all considered the same *type* of activity, even though the underlying mechanisms are different? It is because phosphorylation robustly makes a difference to the realization of the same change type: enzyme activation. It is phosphorylation, adding a phosphoryl group, that productively makes a difference to the occurrence of the next stage in multiple mechanisms ranging from photosynthesis to cell signaling. The causal productivity of phosphorylation as an activity lies in the fact that it makes a difference just in the way outlined by HAA, not in the underlying mechanism that produced it.

To take another example, one of the earliest enzymes where this type of change (from inactive to active) was characterized was tyrosine hydroxylase. This enzyme is important in many neural mechanisms. Active tyrosine hydroxylase is essential in the synthesis of dopamine, an important neurotransmitter in neuro regulation. The activation of tyrosine hydroxylase is a type of change that serves as the start condition of the dopamine synthesis mechanism (Daubner et al., 2011). In their groundbreaking work Joh et al. (1978) characterize how this type of change comes about:

> …the pool of native tyrosine hydroxylase is composed of a mixture of enzyme molecules in both active and probably inactive forms, that the active form is phosphorylated, and that *phosphorylation produces an active form of the enzyme at the expense of an inactive one* (Joh et al., 1978, 4744 [italics added])

This characterization of their discovery illustrates my HAA account. They experimentally identify phosphorylation as the activity that makes a difference in this type of change (from inactive to active tyrosine hydroxylase). They conclude this because they have discovered what Darden (2006) call "activity signatures." Phosphoryl groups, a signature of the phosphorylation activity, was found on all active tyrosine hydroxylases.

Let us take a further, physiological, example to illustrate the Hybrid Account's ability to block the causal identification and causal selection problems. Consider the circulatory system of mammals, an important entity is the heart, and its crucial activity pumping. The fact that blood circulates was an important discovery in the history of anatomy. Within the circulation mechanism, the movement of deoxygenated blood to the lungs and oxygenated blood from the lungs through the rest of the body is enabled by the heart's pumping activity. First, it counts as a causally productive activity on my account because (i) it makes a difference to the change Ψ (movement of blood) and (ii) in the highest proportion of cases pumping occurs, the type of change Ψ occurs. In fact, pumping is the only way organisms with a circulatory system are able to move blood. Even arthropods, which have open circulatory systems where the blood flows freely, have muscles in their abdomen that have pumping-enabling properties. Nonvertebrate animals such as sponges have no blood and move nutrients though a different activity, diffusion.

The pumping activity of the heart illustrates how the Hybrid Account avoids Franklin-Hall's (2016) charge of *causation error* against mechanistic explanation. For instance, one can propose a non-standard mechanism schema for circulation that has the stage contraction of the myocardium, followed by a lub-dub sound, followed by blood leaving the aorta (a major blood vessel). This, of course, contains a non-standard mechanism module (namely the lub-dub sound) that although related by "dynamic principles" to the next stage, nonetheless is not considered part of the production of circulation. Franklin-Hall (2016) charges that new mechanists have not worked out a way to separate non-standard from the standard explanations like the one I gave above. Simply asserting that this non-standard mechanism is not productive of the circulation phenomenon, even though it is correctly describing (at least in part) the behavior of the parts of the standard mechanism, is not philosophically informative.

The Hybrid Account can, however, meet Franklin-Hall's (2016) challenge. The reason the heart's lub-dub sound is not an activity is that it fails condition (i) of my account. It doesn't make a difference to the blood's exiting (or entering) the heart in *any* of the scenarios that type of change occurs in the mechanism of circulation. The lub-dub sound of the heart is a detail that can be abstracted away in our characterization of the mechanism of circulation, while the heart's pumping cannot. In fact, in cases of Still's murmurs, benign heart murmurs that develop in some children, the heart does not make a lub-dub sound at all, even as it continues to produce the next stage in the circulation mechanism. This is more so the case with artificial ECMO (extracorporeal membrane oxygenation) machines that move blood in patients undergoing heart procedures. The machine may make beeping and buzzing noises but not lub-dubs, and what allows it to perform the heart's function in that medical context is its pumping activity. Therefore, one can conclude that lub-dubs do not make a difference to the movement of blood. It is pumping, and not lub-dub sounds, that make a difference and in the scenarios that pumping occurs, movement of blood occurs.

5.2 Causation without robustness

One objection to HAA is that it excludes from the category of causally productive activities causal relationships that lack robustness but that are nonetheless scientifically important. For instance, consider the claim that smoking causes lung cancer or syphilis causes general paresis (i.e., neurosyphilis). Most smokers do not get lung cancer and less than 10% of men infected with syphilis ever developed paresis (Ropper, 2019). This means that there are many more scenarios in which smoking does not result in lung cancer, and syphilis in paresis, than the cases in which they do. Yet the vast majority of people with lung cancer have a history of active smoking (Siegel et al., 2021), and all patients with general paresis had syphilis (Ropper, 2019). Therefore, there is an explanatorily important causal relationship between the causes and effects in these cases. The Hybrid Account would however block appeal to these causes as productive activities since they fail the second condition.

There are two responses to this objection. First, as mentioned above, the Hybrid Account does not set out to be an account of causation or an account of the sole important dimension of causal-explanatory value. There are many causal relationships that are scientifically significant that nonetheless might not be suitable for an activity role within mechanisms. Robustness is one among many dimensions of causal-explanatory value. But securing robustness through HAA ii) allows us to ground the activity-change relation in a way that vindicates the choice of some activities as the components of mechanism schemas over others that are merely background conditions.

Second, causal relationships such as those that obtain between smoking and lung cancer and syphilis and paresis are themselves phenomenal models in need of mechanistic explication. Why is it that some smokers develop lung cancer while many do not? Do smokers that develop lung cancer have higher nicotine metabolism that leads them to smoke more on average? Do they have structural differences in their lung tissue that makes them susceptible to carcinogenic chemicals in cigarettes? Pearl and MacKenzie (2018) discuss the history of research into these questions, including the possibility that there is a "smoking gene" that increases risk of lung cancer in some smokers. Therefore, while the relationship between smoking and lung cancer does lack robustness, it does not mean that the mechanism (or mechanisms) that produce lung cancer in some smokers is not composed of activities which are robust and fulfill both conditions of the Hybrid Account. The new mechanist approach to explanation seeks to fill precisely the kind of black boxes that obtain in cases like smoking—lung cancer and syphilis—paresis. Elucidating the mechanisms, and looking inside those black boxes, can reveal the entities and causally productive activities that explain the phenomena in question.

6 Conclusion

This paper proposes a novel, Hybrid Account of activities (HAA) as productive difference-makers. The Hybrid Account incorporates difference-making into the activities view of causation. The union of production and difference-making in the Hybrid Account has a number of philosophical virtues. First, HAA enables the identification of causally productive activities and their distinction from non-causal side-effects and occurrences. Second, HAA is able to distinguish *productive* difference-makers from mere background conditions. Finally, the Hybrid Account does all of this while preserving the attractive features of the new mechanists' approach, namely, their attention to the actual workings of science and scientific practice. The marriage of production and difference-making in the Hybrid Account forms the basis of the union of scientifically informed philosophy of science and philosophically informed scientific practice that is the ultimate aim of the new mechanists' approach.

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