Mechanisms in Practice: A Methodological Approach

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Abstract
In this paper we offer a minimal characterisation of the concept of mechanism in biomedicine, according to which a mechanism is a theoretically described causal pathway. We argue that this conception can be drawn from scientific practice, as illustrated by how a central biological and biomedical mechanism, the mechanism of apoptosis, was first identified and characterised. We will use the example of cytological and biochemical theoretical descriptions of the mechanism of apoptosis to draw lessons about the meaning of the concept of mechanism in biomedical contexts and to contrast our preferred account of mechanism with some prominent accounts within the philosophical literature. The main outcome of our discussion will be that commitment to mechanism is first and foremost a methodological stance.

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1. Introduction

'Mechanism' is a fundamental concept within the life sciences. But what exactly is a mechanism? This question has recently gained much prominence in the philosophical literature, and search for mechanisms and mechanical explanations has been viewed as a main aim of life sciences, and science in general.[1] There exists a widespread consensus among philosophers of science that an adequate philosophical account of the practice of current sciences must be structured around this basic notion.[2] However, philosophers have not yet reached a consensus about what a mechanism is. This lack of a generally accepted account may seem surprising to the outsider, given the prominence of the concept in scientific practice.

Our aim in this paper is to offer an adequate and minimal characterisation of the concept of mechanism as this is used in biomedicine, by discussing how a central biological mechanism, the mechanism of apoptosis, was identified and characterised. We will use this example to draw lessons about the meaning of mechanism in biomedical contexts and also to contrast our preferred account of mechanism with some prominent accounts within the philosophical literature. The main outcome of our discussion will be that commitment to mechanism is first and foremost a methodological stance.

2. Mechanism in practice

If we want to understand what the things that scientists identify as mechanisms are, we had better examine how mechanisms are identified in practice. We shall use the case of apoptosis as a benchmark. There are several reasons why this is a particularly good example for our purposes. The term ‘apoptosis’ was introduced by John F. R. Kerr, Andrew H. Wyllie and Alastair R. Currie in a seminal paper in 1972 as the name of a newly discovered mechanism, and in particular of “a hitherto little recognised mechanism of controlled cell deletion”. [3] It is thus a clear case that can be used to draw lessons about how a new mechanism is identified in biomedicine, and hence about what exactly a mechanism is taken to be. Subsequent research has identified apoptosis as a ubiquitous mechanism for the regulation of cell populations with important clinical relevance and has
offered various levels of description of its workings. As we will see, this provides further insights into the nature of mechanisms in biomedicine.

What did Kerr et al. do to identify the mechanism of apoptosis? Here is a reconstruction of their strategy. First, Kerr et al. offered a theoretical description of what they saw as a distinctive causal process. This was a kind of process that had not been described in detail before and had very specific morphological features. A main aim of their paper was to describe those features. Electron microscopy revealed that this process involved the following morphological changes: condensation of cytoplasm and nucleus, fragmentation of the nucleus, formation of protuberances on the surface of the cell, subsequent breaking of the cell and formation of spherical structures that are membrane-bound and contain cell organelles and nuclei fragments, that are condensed but otherwise functional (Kerr et al. named them ‘apoptotic bodies’), and finally the phagocytation and degradation of apoptotic bodies by other cells.

Second, the authors specified the ubiquitous character of the new process: the morphological changes associated with it occur in many circumstances, both physiological and pathological. For example, it was observed that apoptosis occurs spontaneously in both treated and untreated malignant tumours, and that it is involved in cases of pathological atrophy. But it was also observed in normal involution of tissues, in normal development (e.g. during the development of digits), and in general, in cellular turnover in normal adults. Crucially, in all those types of circumstances the observed morphological changes associated with the apoptotic process were “essentially the same”.[3]

Third, they noted a distinctive feature concerning the new process, viz., its non-disruptive nature. In particular, whereas it was a process resulting in the death of the cell, it did not produce inflammation. This enabled them to discriminate it from necrosis, the process that results in the death of the cell following a toxic stimulus. However, apoptosis was triggered also by physiological stimuli. It thus seemed to have a specific role within the organism. This immediately gives rise to the question: what is a main function of apoptosis?

In order to identify such a function, Kerr et al. noted that a particular kind of process has to exist, namely some form of “physiological cell death” that is at work balancing divisions in cell populations.[3] However, necrosis, due to its
disruptive nature, cannot play that role. Apoptosis, however, precisely because a) it is non-disruptive, b) can be triggered by physiological stimuli, and c) is ubiquitous, is a particularly well-suited candidate to play that role. As Kerr et al. put it, apoptosis “is well suited to a role in tissue homoeostasis, since it can result in extensive deletion of cells with little tissue disruption”.[3] The conclusion, then, is that apoptosis plays a crucial regulatory role in tissue homeostasis.

To sum up, Kerr et al. argued as follows: Since apoptosis is
i) a distinctive morphological process
ii) ubiquitous
iii) non-disruptive, in contrast to necrosis
iv) triggered by physiological stimuli
and given that
v) a form of “physiological cell death” that is at work balancing divisions in cell populations must exist
and since
vi) necrosis cannot play that role
therefore,
vii) apoptosis is well suited to play that role

We can now extract from this case some salient features that are sufficient for the introduction and the characterisation of a new mechanism in biomedicine. First of all, mechanisms are processes, or as we prefer to call them, borrowing a terminology widespread in biomedicine, causal pathways. So, the first task that Kerr et al. had to accomplish in order to introduce the mechanism of apoptosis was to offer a theoretical description of a certain process, which is extended over time and is characterised by specific features. The process can be seen as causal as it is characterised by a regular sequence of events and difference-making relations among its constituents: the formation of apoptotic bodies is dependent on the fragmentation of the nucleus, which depends on the condensation of cytoplasm and nucleus. The recurrence of this succession of events under a variety of conditions offered evidence that this is indeed a causal sequence, with a possible genetic basis. As Kerr et al. put it, “[t]he ultrastructural
features of apoptosis and its initiation and inhibition by a variety of environmental stimuli suggest to us that it is an active, controlled process”.[3]

But the identification of this new type of pathway did not require a full understanding (and hence a full description) of its workings. So, Kerr et al. noted that the mechanism of condensation, a main stage in the apoptotic process, was “still unknown”[3]. Additionally, there was a lot that was not yet known “of the factors that initiate apoptosis or of the nature of the cellular mechanisms activated before the appearance of the characteristic morphological changes”.[3]

And of course, nothing was yet known of the biochemical processes underlying apoptosis or its genetic basis. This shows that it is one thing to identify a mechanism for a certain phenomenon and it is quite another thing to acquire a full description of its workings. Hence, even with limited knowledge about the various causal details, it is possible to identify and initially describe a potentially important new causal pathway.

Descriptions of a mechanism can be made richer by offering more detailed characterisations. This can involve only the ‘horizontal’ dimension, as we may call it, of a process, for example offering further cytological details of apoptosis; more interestingly, it can involve the ‘vertical’ dimension. Describing the “mechanisms of condensation”, for example, can be done at a cytological level by offering further cytological details, perhaps more fine-grained ones, or by offering details in the vertical dimension, for example by giving a biochemical description of what is going on.

Descriptions of biological mechanisms then are always couched in theoretical language, and can be enriched in various ways. In particular, there can be alternative theoretical descriptions of the same mechanism; for example, we now have a cytological and a biochemical description of the apoptotic pathway (see below). Hence, at a minimum, a mechanism is a certain theory-described causal pathway.

The regulatory role of apoptosis was crucial for its identification as a distinctive kind of mechanism. In fact, Kerr himself in earlier work had already observed the process that was to be called apoptosis, but he did not regard it as a new kind of mechanism. Instead, he viewed it as a type of necrosis, i.e., as a type of pathological cell death—‘shrinkage necrosis’, as he called it—that was “non-
degenerative in nature” compared to classical necrosis.[4] But shrinkage necrosis was not viewed as a new kind of mechanism. As he put it, “[s]hrinkage necrosis is a distinct and important type of cell death, which has received relatively little attention in the past. It probably results from noxious stimuli that are insufficiently severe to produce coagulative necrosis”. [5]

It was the fact that apoptosis seemed to have a basic regulatory function within the organism that led, in the 1972 paper, to its identification as a new kind of mechanism. There, the apoptotic process is not taken to be a type of necrosis anymore; it is contrasted with necrosis and constitutes a new and very important kind of regulatory mechanism of cell death. Whereas the various microscopic observations described in the paper are used to establish a new causal pathway, the regulatory argument offered by Kerr establishes that the new causal pathway constitutes a new kind of mechanism, thereby introducing a new taxonomy of types of cell death.

So, the function of a particular theoretically described process, i.e. its role within the organism, is important when introducing a new mechanism. The function serves to further distinguish the process from other similar processes, and it’s crucial for establishing not only a distinct but also a new kind of mechanism. So, in our example, both necrosis and apoptosis are mechanisms for cell death. But they are distinct mechanisms since, first, they are characterised by different cytological features, and second, they play different roles within the organism.1

Apoptosis, then, was introduced as “a distinctive morphological process (...) which plays a complementary but opposite role to mitosis in the regulation of animal cell populations” and thus “subserves a general homeostatic function”. [5] The lesson: what the identification of a new mechanism in the life

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1 Although philosophers agree that mechanisms are always mechanisms for a phenomenon, there is disagreement about the relation between mechanisms and function. See [6] for an overview of the discussion.
2 We thank an anonymous reviewer for making this suggestion.
3 See [11] for a description of the E. coli lac operon regulatory mechanism in terms of difference-making; as noted in [11], difference-making better captures the causal relationships present in negative regulation that is involved in homeostatic mechanisms, which involves cases of so called double prevention that present difficulties to alternative characterisations of within mechanism interactions.
4 It is well recognised in the literature that mechanisms form hierarchies –see [14] for discussion of mechanistic levels. While we agree that a mechanism such as apoptosis can be described at various levels, we do not derive any ontological consequences from such
sciences requires, is a theoretical description of a causal pathway with a certain function.

By the middle 1970s it had already been recognised that “cell death was as much a part of cell biology as mitosis, extension of an axon, the enzymatic sequence of glycolysis, or secretion”.[7] This was a crucial conceptual breakthrough compared to the older way of thinking about cell death; before the 1970s cell death had not been seen as a phenomenon on a par with mitosis or glycolysis, which constitute fundamental biological mechanisms. However, the important point here is that even after the introduction and the wide recognition of apoptosis in the 1970s, research on apoptosis did not gain the importance it has today. But in the 1990s the field was transformed into a fundamental research area within the biomedical sciences. A major reason for this transformation was that the mechanism was understood to such an extent that it was seen as a phenomenon that was medically central. This reflects then a second major breakthrough in the history of apoptosis: by the middle 1990s, cell death was seen as “a highly controlled and medically important element of existence”.[7]

The recognition of the medical importance of apoptosis was based on the discovery that apoptosis played a crucial role in several organismic functions. Central for this realisation were the discoveries that apoptosis is very common, is genetically based, is intimately related to the immune system and is important in cancer research (for example, it has been discovered that it is regulated by the p53 tumor suppressor gene). Thus, in the last decades the clinical relevance of apoptosis became evident.

To illustrate the kind of understanding of the mechanism of apoptosis that we now possess and to compare it to the cytological description outlined earlier, let us briefly review the description of the mechanism at the biochemical level, focusing on the mammalian apoptosis pathway (for details see [8]). A central part of the pathway is a process called the ‘caspase cascade’, which is a positive feedback cascade that involves the activation of caspases, a type of enzymes that when activated perform proteolysis. Apoptosis occurs when some caspases—that normally exist in inactive form in the cytoplasm—are activated. Active caspases in turn activate more caspases that eventually break down the
cell. There are two distinct signalling apoptotic pathways: the intrinsic pathway, where the initial apoptotic signal that ultimately leads to the activation of the cascade cascade comes from inside of the cell, and the extrinsic pathway, where the initial signal comes from outside.

Here is a brief description of the biochemical mechanism underlying the extrinsic pathway of apoptosis: The initial signal of the extrinsic pathway is the binding of a ligand (such as the Fas ligand of T-lymphocytes) to a death receptor (such as the Fas receptor), which is an intermembrane protein that has a domain within the cell. When the ligand binds to the receptor, this domain (FADD in the case of the Fas receptor) is activated and recruits an adaptor protein. Next, procaspase-8 or 10 binds to the adaptor protein. The formation of this complex, known as DISC (death inducing signalling complex), is the signal for the caspase cascade. The procaspases are cleaved and form active caspases 8 and 10. These are the initiator caspases that lead to the activation of effector caspase-3, and so the positive feedback loop of the caspase cascade is activated.

The biochemical mechanism underlying the intrinsic pathway of apoptosis can be summarised as follows: Central component of the intrinsic pathway is the bcl-2 family of proteins, which include pro-apoptotic and anti-apoptotic proteins. Normally, in the cell there is equilibrium between pro-apoptotic bcl-2 proteins and anti-apoptotic ones, and apoptosis via the intrinsic pathway is prevented. This equilibrium can be disrupted when, for example, the DNA of the cell is irreparably damaged, or the cell stops receiving survival signals. When this happens, other pro-apoptotic proteins are synthesised (so called BH3-only proteins), which bind to anti-apoptotic bcl-2 proteins. But then, the pro-apoptotic proteins that normally exist within the cell are not inhibited by the anti-apoptotic ones, and can activate the caspase cascade. This activation happens when the pro-apoptotic proteins form aggregates that create channels in the outer mitochondrial membrane. This causes the release of cytochrome-c, a mitochondrial protein, into the cytoplasm. Subsequently, cytochrome-c binds to Apaf-1 (Apoptotic protease factor 1), which causes Apaf-1 proteins to form a complex called the apoptosome. This in turn activates initiator caspase-9, which then activates effector caspase-3, thereby activating the positive feedback loop of the caspase cascade.
This biochemical description illustrates the point that there may exist different theoretical descriptions of one and the same mechanism. But another important point here is that the description at the biochemical level is richer than the cytological one in a crucial sense: it provides specific causal information, i.e. it identifies difference-making relations among various components of the pathway. Knowing these difference-making relations is important for discovering types of interventions that can be made in order to control the outcome of the process. It is easy to see that the more detailed the description of the causal pathway, the more options for such interventions one has. So, knowing the biochemical description of the apoptosis pathway is important for discovering ways one can intervene to induce apoptosis for therapeutic purposes (for the relations between apoptosis and cancer treatment see for example [9]).

What biomedicine, then, adds to the previous characterisation of a mechanism as a causal pathway, is that theoretical descriptions of causal pathways should be such that they provide specific causal information that makes interventions possible (for a concept of mechanism in medicine along similar lines see also [10]).

Our claim that mechanisms are theoretically described causal pathways should not be taken to imply that mechanisms are not things in the world. Certainly causal pathways are as real as anything. Rather, it is meant to highlight that the best description of the causal pathway (and hence of the mechanism) is given by the relevant theory and not by an abstract metaphysical account. Does it follow that every theoretically described pathway is a mechanism? Not at all. It should be a correctly described causal pathway. Not all theoretical descriptions of causal pathways are on a par. First, a theoretical description might fail to capture the actual causal dependencies in the world—such descriptions cannot pick out mechanisms. Second, some theoretical descriptions of a particular causal pathway might be less detailed compared to others, as shown by cytological and biochemical descriptions of apoptosis. How detailed a theoretical description can be, is something that will be determined by scientific practice itself. In the case of apoptosis, for example, the initial description was quite detailed: it involved the careful description of various cytological features as well as situating the pathway within the overall functioning of the organism. A less
detailed description such as ‘cells die on their own’, for example, is shown by practice to be too meagre to be of interest. Lastly, the actual initial identification of a pathway should be seen as the first step that leads to the further elucidation of the various causal dependencies that are involved in the pathway. The end result is a highly informative theoretical description that embeds the pathway within the known physiological and biochemical functions of the organism.

Might be the case that the features of mechanisms in biomedicine identified here by us are not in fact exemplified in the case of apoptosis? It might be claimed that apoptosis i) is not linear; ii) has no obvious start and end points; iii) involves homeostasis; and iv) is such that spatiotemporal organisation is crucial. Collectively, it might be argued, these features cannot be accounted for without a more metaphysically inflated account of mechanisms. By way of reply, it should be noted that all the above features are compatible with our account of mechanisms as theoretical descriptions of causal pathways. First, pathways are processes; but it does not follow that they have to be ‘linear’ processes. Apoptosis as characterised cytologically might seem ‘linear’, i.e. as a stepwise process with no negative or positive feedback loops. However, its biochemical description is far more complex, with multiple pathways and complex causal cycles. In any case, we still have, ultimately, a web of sequences of events related by difference-making relations. Second, we do not take it as a general requirement that a process has to have well-defined starting and end points; this is something to be determined by biological practice. In the case of the extrinsic pathway of apoptosis, for example, the starting point of the process is specified by the binding of a ligand, such as the Fas ligand, to a death receptor. Third, homeostasis, which itself involves negative feedback loops, can also be described in terms of difference-making relations among the components of the pathways underlying the homeostatic process. Fourth, the spatio-temporal organisation is indeed crucial for the functioning of any causal pathway and because of this it is typically included in the theoretical description of the pathway; a detailed

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3 See [11] for a description of the E. coli lac operon regulatory mechanism in terms of difference-making; as noted in [11], difference-making better captures the causal relationships present in negative regulation that is involved in homeostatic mechanisms, which involves cases of so called double prevention that present difficulties to alternative characterisations of within mechanism interactions.
theoretical description of the causal pathway will state the spatiotemporal
relations among the various components of the pathway that are required for the
proper functioning of the mechanism.

There might be a further worry in the offing: Can we properly describe
something as a mechanism even when it is not acting? If, it might be thought, the
mechanism of apoptosis can be said to function properly, without apoptosis
being initiated, this would seem to be a problem for the present view. Hence,
should mechanisms be thought as always acting, or can there be mechanisms
waiting-to-act? Note that there is no consensus among the new mechanists on
this issue: Illari & Williamson, for example, think that a stopped clock would be
such a non-acting mechanism;[12] for Glennan, on the other hand, mechanisms
are always acting.[13] So, Glennan distinguishes between a mechanical system
and a mechanism, where a mechanical system is “a system that regularly
engages in or is disposed to engage in mechanistic processes”. A mechanical
system then is not strictly speaking the mechanism; “it is rather a thing in which
mechanisms act”. When a system S does something ψ “the mechanism is the
organized activities and interactions of entities within the system that is
responsible for that ψ-ing” and “[i]f mechanisms truly are understood to be
entities acting, the mechanism persists only for the duration of the action”. [13]
While we disagree with Glennan’s general metaphysics of mechanism, we think
that this distinction between mechanisms and systems is essentially correct and
concordant with biomedical practice. In the present case, the cell (or some part
of the cell) can be taken as the system within which the process of apoptosis
occurs. But apoptosis itself, qua a mechanism of regulated cell death, is there
only when the relevant causal pathway is acting.

To sum up. The salient features of mechanisms in biology and
biomedicine are the following: mechanisms are causal pathways described in
theoretical language that have certain functions; these descriptions can be
enriched by offering more detailed or fine-grained descriptions; the same
mechanism can then be described at various levels using different theoretical
vocabularies (e.g. cytological vs biochemical descriptions in the case of
apoptosis); lastly, the descriptions of biomedically important mechanisms are often such that they contain specific causal information that can be used to make interventions for therapeutic purposes.

### 3. Methodological mechanism

In the previous section we used the case of apoptosis to offer a general characterisation of the concept of mechanism as used in biomedicine: identifying mechanisms is equivalent to identifying stable causal pathways, described in the language of theory, which bring about a certain effect and perform a certain function. When it comes to practice, this seems enough for having a general understanding of mechanisms and their role.

Within the recent philosophical literature the issue how best to characterise mechanisms has given rise to a debate that has centred on how to understand mechanisms in science from the point of view of fundamental ontology. This is not the place to discuss in any detail this debate among the so-called new mechanists or its rich historical and philosophical background (for discussion see [15], [16], [17]). Instead, we are going to briefly refer to a couple of key features of ‘New Mechanism’ and contrast them to our preferred methodological account.

New mechanists take ‘mechanisms’ to be entities (complex systems) in their own right which are characterised by a certain ontological structure. In a now famous paper, Peter K. Machamer, Lindley Darden and Carl F. Craver claimed: "Mechanisms are entities and activities organised such that they are productive of regular changes from start or set-up to finish or termination conditions".[18] Other similar general characterisations of a mechanism have appeared in the recent literature, but the following (which Glennan has called ‘minimal mechanism’ [13]) represents a broad consensus: “a mechanism for a phenomenon consists of entities and activities organised in such a way that they are responsible for the phenomenon”.[12]

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1 It is well recognised in the literature that mechanisms form hierarchies – see [14] for discussion of mechanistic levels. While we agree that a mechanism such as apoptosis can be described at various levels, we do not derive any ontological consequences from such talk.
Such accounts invite a number of questions concerning the basic building blocks of mechanisms. For example, consider the claim (which is part of many accounts) that a mechanism consists of two distinct kinds of building blocks—entities (organised in a stable way into a spatio-temporal pattern) and activities. But what grounds the difference between entities and activities? Activities are supposed to ground the causal efficacy of mechanisms (according to Machamer et al. mechanisms require “the productive nature of activities”); they are the ontic correlates of (transitive) verbs.[18] At issue here, then, is the ontological structure that underlies and unites the scientific theoretical descriptions of mechanisms. Significantly, there are alternative, and competing, ways to characterise this ontological structure: instead of having both entities and activities, one can characterise activities in terms of entities and their causal powers (as for example does Stuart Glennan [13]). The question here is: what is added to scientific practice by insisting that a description of a mechanism has to be couched in some preferred philosophical categories, e.g. entities and activities, powers or what not?

Take the case of apoptosis. What clarity (or extra information) would it be added to the cytological characterisation of apoptosis offered by Kerr et al., if we were to add that, for example, in the case of the condensation of cytoplasm and nucleus, condensation is an activity (whatever that means) and cytoplasm and nucleus are entities (whatever that means)? And are the protuberances that form on the surface of the cell and give rise to apoptotic bodies, entities or not? Or, what is the added value of the claim that apoptotic bodies have the power to degrade? Similar questions can be asked for the biochemical description of the apoptotic pathway.

In contrast to such metaphysically inflated accounts of mechanisms, our discussion of apoptosis showed that for the identification of a mechanism, a theoretical description of the causal pathway (and the function performed) is enough; there is no reason to characterise it further in terms of a preferred ontology. But then, what one can say about what a mechanism in general is, is just to say that it is a causal pathway that is theoretically described. Philosophers who characterise mechanisms in general in terms of a preferred ontological
inventory have the burden to justify what this further characterisation adds to the minimal account that can be extracted from biological practice.

The focus on biomedical practice, then, motivates a deflationary approach to mechanistic talk in biology and biomedicine: such talk does not have to be interpreted in a manner that leads to inquiry into how best to characterise the mechanistic ontology of the world. Rather, commitment to mechanism is essentially a methodological (as opposed to an ontological) stance; and mechanism is primarily a methodological concept. We will close with some remarks on this stance, which we have called Methodological Mechanism (MM).[19]

MM consists of two main claims, a negative and a positive. The negative claim is that the concept of mechanism as used in scientific practice need not (and should not) be characterised in abstract ontic terms aiming at ontic unity. The positive claim gives a generic characterisation of mechanism as a concept of practice present in various scientific fields. Let’s examine these two claims in more detail.

The negative claim differentiates MM from many prevalent philosophical accounts of mechanism. MM remains agnostic (or non-committal) concerning the precise ontology underlying a causal process: it does not commit itself to the existence of activities, powers and the like as distinct from entities and their properties. This deflationary stance is a decisive advantage of MM over its rivals. First, as a generic account of mechanism applicable to various scientific fields, it retains the advantages of the recent complex systems accounts over older reductive approaches to mechanism.[20], [21] But second, unlike complex system accounts, it does not read off from scientific practice any views about the ontology of causation (views that do not seem to be supported by the concept of mechanism as used in practice). As noted already, this ontological agnosticism is agnosticism about a ‘deeper’ ontological description of the mechanism, i.e., ‘deeper’ than the one offered by the relevant theory. As such it is far from implying that mechanisms as causal pathways are not things in the world. According to MM, in elucidating ‘mechanism’ as a concept of practice we need not go further and commit ourselves to a certain ontological ground of the difference-making relations. Third, by doing so, it avoids the need to answer
several metaphysical questions that seem not important in scientific practice. In sum, it takes mechanism to be primarily a methodological, rather than an ontological, concept.

MM is thus opposed to views that biomedical practice, in constructing mechanistic explanations, leads to specific consequences about the ontology of a ‘mechanistic’ world. For example, it has been claimed that only a ‘local’ metaphysics of activities or powers can capture the sense in which mechanisms are both ‘real and local’ to the phenomenon they produce [22]. While we take it to be fully consistent with MM to view mechanisms as causal pathways that are both ‘real and local’, in that the identification of a mechanism involves the localisation of the components of the pathway, we resist the further move to a ‘local’ (aka lawless) metaphysics. We have two main disagreements with such a move: first, what one may mean by a ‘local’ metaphysics is far from clear or uncontroversial (see [23]). But second, arguments such as those in [22] take place in the context of a discussion on the ontology of mechanisms, and do not directly aim to characterise mechanism as a concept of practice. At the same time, of course, MM is compatible both with the view that the fundamental ontology of the world is broadly neo-Aristotelian as well as with a more Humean view.

The main idea behind the positive claim of MM is that search for mechanisms improves our understanding of natural phenomena. When scientists look for mechanisms that produce the phenomena, they seek to describe causal pathways that lead from the initial event of the pathway to the resulting state. A mechanism then is some process that shows how exactly the effect is produced⁵. However, to say this is not to make an ontological claim about the structure of the world, but to stress that one of the aims of science should be the discovery of pathways connecting cause and effect, which are regular enough so that they can be relied upon to enhance our understanding of how some effects are brought about, and of how we can intervene in order to prevent unwanted outcomes, or to treat diseases. Mechanisms, then, can be

⁵ The idea that mechanistic explanation enhances understanding by identifying a process that connects cause and effect was central in the context of the emergence of mechanistic philosophy in the 17th century (see for example Robert Boyle’s essay ‘About the Excellency and Grounds of the Mechanical Hypothesis’ in [24]).
viewed as theoretically described stable explanatory structures, whose exact content and scope may well vary with our best conception of the world. In particular, a pathway does not have to be described in some privileged (and maybe reductionist) language; pathways in science are described using the theoretical language of the relevant scientific field. Such a description is enough for the identification of a new mechanism, as we have seen in the case of apoptosis. Hence, viewing mechanism in methodological terms licenses our preferred account of mechanism: a mechanism in the biomedical sciences is a theoretically described causal pathway producing the phenomena of interest.

Let us close with a final worry: is it justified, in offering our general characterisation of mechanism, to generalise from the example of apoptosis to other mechanisms in biomedicine? While further examples will certainly be useful in order to show that the features of mechanisms identified here are typical in biomedicine, we think that such a generalisation is very plausible and the example of apoptosis can be taken as representative. There are two main reasons to be optimistic regarding this.

First, our account does not depend on very specific features of the particular case examined, but on features that are commonly found in many cases of mechanisms described in biomedicine. That mechanisms correspond to causal pathways, that these pathways are described using the theoretical language of a particular field, that there can be more or less detailed descriptions of causal pathways, and that pathways serve a function (or functions), are very minimal requirements for something to count as a mechanism; for example, it can be easily seen that they apply to all kinds of biochemical (and other) pathways (e.g. signalling pathways, metabolic pathways).

The second reason is that we take the main philosophical contrast to be

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6 A reviewer suggested that the following two claims have to be distinguished: (i) that a general account of mechanisms has to be metaphysically agnostic and (ii) that mechanisms should be characterised in terms of causal pathways involving difference-making relations rather than in terms of entities, activities and organisation. It is indeed possible that one may accept (i) without abandoning the minimal characterisation of mechanism, simply by remaining neutral on how to understand entities, activities and organisation from a metaphysical point of view. However, ‘activities’, for example, are typically introduced as a novel ontological category; hence, the elements of the minimal characterisation are too metaphysically loaded and very hard to read in such a neutral way (see Glennan [13] for a recent example of such a non-neutral reading of the minimal characterisation).
between MM and metaphysically inflated accounts of mechanism. But if MM is sufficient to characterise apoptosis, it is doubtful whether other case studies will make a metaphysically inflated account necessary: if that were the case, to make philosophical sense of the mechanism of apoptosis we would similarly need such a metaphysically inflated account. The reason is that the case of apoptosis exemplifies all the characteristics taken to require a metaphysically inflated characterisation of mechanism: for example, the introduction of both entities and activities to capture both the various macromolecules and their interactions. Hence, if MM is sufficient to understand the present case, it is very doubtful that other cases will require to abandon MM.

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