Why (at Least Some) Processes Matter

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As is well known, the philosophical debate on processes and mechanisms, as key concepts to grasp causal relations, has undergone several shifts over the past four decades or so. Moving from processes to mechanisms, and back again, philosophers of science have explored various disciplinary fields, searching for convincing and well-justified theoretical tools to, on the one hand, address causation, and, on the one hand, make sense of the actual use of causal concepts into scientific practice. While claiming that the notions of causal process and mechanism are compatible, the contribution argues for the relevance of the former for epistemological purposes. To support such a view, a specific example from the biomedical sciences is analyzed: cancers of unknown primary origin. Drawing on current scientific research on this distinctive class of pathologies, and to some of the open questions it is addressing, it is argued that a processual approach is particularly well suited to explaining the search for explanations of the origin, trajectories and dynamics of such oncological occurrences.

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— PROCESSES — MECHANISMS — CANCER STUDIES

1. Setting Some Context: on Processes, Mechanisms and All That

The notion of process has undoubtedly a long, intense and articulated history in philosophy of science, where it has been largely related to causation and causal explanation, with changing fortunes, but, de facto, never disappearing from the scene. Let us start by recalling just a few crucial stages of such a story, to underscore their significance for philosophy of science and highlight some turning points in the recent debate. This will allow us to then consider some roles processes can be currently held to play and stress their merits – also with respect to views that set some preference over mechanisms instead.

Views on processes have been advocated by various prominent authors, driven by different concerns and aimed at different uses. Among the most authoritative names, Bertrand Russell (1948) claims that «A *causal line* may always be regarded as the persistence of something – a person, a table, a photon, or what not. Throughout a given causal line, there may be *constancy of quality*, *constancy of structure*, or *gradual change* in either, but *not sudden change* of any considerable magnitude. I should consider the process from speaker to listener in broadcasting one causal line» (475). Although previously highly critical of causation – which, as is well-known, he maintains to be «a relic of a bygone age» (1912), erroneously regarded as useless, like the monarchy, whereas it is actually detrimental – Russell believes that causal lines play an essential role, insofar as they preserve identity over time by maintaining certain relevant properties in a continuous manner.

Continuity is the key-notion into one of the most successful philosophical views on processes in the Eighties and Nineties, i.e. Wesley Salmon's, who promoted a genuine revival of causation, by interpreting it probabilistically (1984). According to Salmon, causation has often been criticized by philosophers and tentatively excluded from what is considered as soundly justified scientific reasoning because it has been conceived incorrectly. Rather than relying on an entity ontology, which leaves the problem of causal connections open and somewhat mysterious, Salmon maintains that a *process ontology* is perfectly suited for the task. Causal processes are to be conceived as spatio-temporal continuous lines, which are responsible for links across the world. They are capable of transmitting causal influence, by virtue of being continuous and able to retain and transmit a modification (mark) once it is imposed on them. The interaction of two or more causal processes brings about change; change is propagated along causal processes. Processes that transmit their own structure are capable of *transmitting marks*, *signals*, *information*, *energy*, *and causal influence*: «causal interactions are the agents of production: they produce changes in processes that intersect one another. Causal processes are the agents of propagation; they transmit causal influence throughout the universe» (Salmon 1998, 206). Causal processes do not behave deterministically: «the concepts of which [Salmon] is speaking are probabilistic. Therefore, when two causal processes intersect, there is a distribution of probabilities over the different possible results, including the possibility of no interaction at all» (*ibidem*). Salmon thus supports *probabilistic mechanism*, where mechanisms are networks of causal processes, underlying phenomena and operating in genuinely *stochastic* ways. To explain

amounts to exhibit the explananda as occupying their places in the causal patterns structuring the world, by identifying the network of causal processes responsible for their occurrence and/or their features. Processes and the mechanisms they constitute are held to *objectively* exist and *ontic* explanations exhibit them, opening the "black box of nature". In principle, this account is intended to apply both in the natural and in the social sciences, even if spatio-temporal continuity imposes a rather strong constraint on explanations of, for instance, social, anthropological or psychological phenomena, as well as those found in quantum mechanics ones. [1]

Although not immune to criticisms, Salmon's view met large consensus, fostering the debate on probabilistic causation and on mechanistic explanation. The latter has been extremely extensively discussed since the late Nineties, so much so that a whole philosophical movement has been shaped, so-called New Mechanism, which has elaborated on the notion of mechanism as a suitable conceptual tool to address scientific explanations of complex systems across various fields, and – from some perspectives – to grasp ontological features too. Neo-mechanists have significantly developed, articulated and deepened this approach. Whereas Salmon had started from processes, making them the fundamental constituents of mechanisms, authors as Stuart Glennan, William Bechtel, Carl Craver, Lindley Darden, Peter Machamer, and others, have been arguing for an entity-based ontology, with entities being the building blocks of mechanisms, acting and interacting in bringing about their overall behavior, by virtue of some configuration. New mechanists' views differ from one another, but they share the idea that causation has got to do with *organized* production. Let us just recall a few of the most successful definitions of mechanism, which clearly show that a few common tenets hold:

[1] Phil Dowe (2000) has formulated a view of causal processes which is meant to overcome Salmon's limits (especially those related to the formulation in counterfactual terms of causal processes) and, strictly referring to physics and chemistry, to take the presence and transmission of conserved quantities as the distinctive features of causal processes. Its core definitions are: 1) a causal interaction is an intersection of world lines which involves exchange of a conserved quantity; 2) a causal process is a world line of an object which manifests a conserved quantity, where "a world line is collection of points in a spatio-temporal diagram representing the history of an object. An object is anything found in the ontology of science ... or common sense" and "it is required that the object have identity over time" (91).

MDC (2000): «Mechanisms are *entities* and *activities organized* such that they are *productive* of regular changes from start-up to finish or termination conditions» (1).

Bechtel and Richardson (2005): «A mechanism is a structure performing a function in virtue of its component parts, component operations and their *organization*. The *orchestrated functioning* of the mechanism is responsible for one or more phenomena» (423).

Illari and Williamson (2012): «A mechanism for a phenomenon consists of *entities and activities organized* in such a way that they are responsible for the phenomenon» (119).

Glennan (2017): «A mechanism for a phenomenon consists of entities (or parts) whose *activities and interactions* are *organized* so as to be responsible for the phenomenon» (13).

As these definitions show, the dominant philosophical trend in the first couple of decades of the XXI century has been to promote a shift from processes to mechanisms, from a focus on *the causal structure of the world* to the promotion of *the new mechanical philosophy*. Whereas Salmon and his followers did not present processes and mechanisms as alternative options, but, rather, as fully compatible notions, with the

former constituting components of the latter, the new mechanists have been stressing that entities and activities, rather than processes, are the conceptual tools needed to address both natural and social phenomena, which are multi-layered, complex and significantly dependent on the contexts and their transformations.

The shift from processes to mechanisms supported by new mechanism brought about also a different sensitivity with respect to the criteria to be respected in deeming something as genuinely "causal". Whereas one of the major concerns in Salmon's work was to find *strict criteria* to discriminate genuinely causal from non-causal processes (or pseudo-processes), new mechanists are inclined to include the largest possible set of settings in their mechanistic views. Varieties of entities and activities are admitted, which are stated to be field-relative, and the range of mechanistic accounts which are deemed as endowed with some explanatory power is large, with the admission of, e.g., mechanisms' sketches or schemata, or how-possibly, how-plausibly, how-actually explanatory models. New mechanism advocates a much more inclusive conception of mechanisms and mechanistic explanations. Rather than being driven by the need to determine in a clear-cut and unequivocable way what counts as causal from what does not, new mechanism aims at having some notion which can work for mechanisms across the sciences (Illari and Williamson 2012), and which is grounded in the details of scientific practice (Machamer, Darden and Craver 2000). To do so, an expansive conception of mechanism is embraced, with the identification of a variety of kinds of mechanisms, understood permissively (Glennan 2017), and the admission that, in order to effectively explain mechanistically in different field, we need to accept to be dealing with mechanistic diversity, with more or less paradigmatic definitions of a mechanism, defined along a continuum by different parameters (e.g. Skillings 2015). This goes together with the recognition of contextual factors in the assessment of causal links and elaboration of causal explanations, [2] and with a strong interest not only in the causal structure of the world as such, but in how we can get access to it, *how the search for mechanisms works*. The discovery of mechanisms, explanatory strategies, different approaches to modelling, abstraction, idealization, incompleteness, have been increasingly discussed, together with the different standpoints that can orient mechanistic understanding and the recognition that describing an item's mechanistic role involves some *perspectival aspect* (see e.g. Craver 2001; Darden 2008).

The success of new mechanism has been partly due to the same reasons that have also been considered as its drawbacks. The attempt to embrace with one single view – the mechanistic one – the largest possible amount of phenomena, both in the natural and in the social realms, by elaborating an extremely flexible notion has both widen the applicability of mechanism and, on the other hand, made it vulnerable: the view has been accused to run the risk, in the end, of being so comprehensive as to become utterly vague, and not genuinely representative of the ways in which actual scientists conceive of the phenomena they

[2] As a matter of fact, the latest Salmon – including some posthumous works – already stresses that the context does actually play a role in causal explanations. For example: "statements about the relations between causes and effects are usually highly selective, and they are typically context-dependent" (Salmon 2002, "A Realist Account of Causation"); "the 'cause-effect' terminology is heavily context-dependent – involving human background knowledge, interests, and purposes" (Salmon 2010, "The Causal Structure of the World"). This perspective does not imply any stepping back from the ontic conception of explanation: according to Salmon, although how we explain is affected by the context, the contents of the explanations grasp objective features of the world.

address. Criticisms have paved the way to a revival of processes, which as a matter of fact had been – as stressed above – the starting point of reflections on mechanisms themselves back in the late Seventies/early Eighties.

2. Why (at Least Some) Processes Still (and Probably Will) Matter: on Processual Views in the Biological and Biomedical Sciences

After almost four decades of focus on mechanisms, processual theories have returned to the forefront in philosophy of science, prominently, although not exclusively, through the work of John Dupré. His processual conception (see e.g. Nicholson and Dupré 2018), which is explicitly and robustly metaphysical, has been particularly influential in relation to the life sciences, whose objects of inquiry are distinctively characterized by continuity and development in space-time.

Processual views do not focus on entities as such, but on the *dynamic patterns* of the processes of life, devoting special attention to the relationships between energy, time, movement and environment at different scales (molecular, cellular and organismal). Priority in addressing phenomena is given to their dynamic character, to occurrences and change, where stability is taken to be derived, as sorts of snapshots onto a continuous flow. According to contemporary processual views, «organisms are best conceptualized as spatio-temporally extended entities whose mereological composition is fundamentally contingent and whose essence consists in changeability. […] the identity of an organism is grounded not in certain collections of privileged properties, or features which it could not fail to possess, but in the succession of diachronic relations by which it persists, or 'perdures' as one entity over time» (Austin 2020, 13).

A rigorous and consistent processual view requires embracing quite a few wide-ranging tenets. According to Nicholson and Duprè, «the world—at least insofar as living beings are concerned—is made up not of substantial particles or things, as philosophers have overwhelmingly supposed, but of processes. It is dynamic through and through» (2018, 3), and «change is essential to the identity and persistence of any process» (12). Persistence and identity are thus held to require causal continuity: that a given process occurs at all and that that same process continues to occur over time depend upon the occurrence and causal continuity of certain underlying activities or changes (see Skrzypek 2023).

A processual account for living beings is suggested, stressing that organisms are in thermodynamic disequilibrium with their environments, have life cycles, and are typically dependent on many features of the environment. Life itself is characterized as a *hierarchy of processes* and dynamic at all levels (molecules, cells, tissues, organisms, lineages), as opposed to things, «i.e., entities the identities of which can be defined independently of change, and which are neatly separated from one another» (Meincke 2019, 5). Identity is not given as such; it is derived frow a continuous flow. Against a conception of reality which is understood in terms of its components, and against any mechanist tenet on decomposition or agenda on reduction, stability is taken to be derivable from change: «any stability to be observed in living systems is the result of continuous process and change. […] The identity of a living system cannot be reduced to the identity of its parts insofar as the identity

of the parts is itself dependent on the production of the identity of the living system as a whole. It is therefore impossible to treat an organism as a thing that is composed of smaller things» (13). Accordingly, stability itself is only provisional and can be achieved only by acknowledging, first of all, that *everything flows*. Organisms are complex hierarchies of biological processes that are continuously interacting with one another and with environmental processes as well. As a result, the system as a whole is maintained into a far-from equilibrium state and is continuously subject to change. Accordingly, if we want to make sense of the identity of biological dynamical systems, we have to think of it as a hard-won achievement, constantly constituted and sustained by the system itself, through a regulated exchange of matter and energy with the environment (see Meincke and Duprè 2020).

This view presents a clear metaphysical stance, but can also be used as a lens to address scientific practice, and some strictly conceptual and methodological issues within it. Cell division and differentiation are all the more effectively described if in terms of processes and change. To live, keep its features, grow, age, and finally die, an organism must keep a peculiar equilibrium between all cells' activities; it is a balance between different forms of continuous mutations, at different scales, that grants the persistence of a given individual organism across time. This perspective allows us to conceive effectively pathologies as well, and has been employed, for instance, in addressing cancer. Once health is conceived of as depending on the highly regulated intertwinement of different organismic processes, a processual view appears highly suitable to define and explain carcinogenesis. Bertolaso and Dupré (2018) have specifically applied it to cancer studies, insofar as the latter – as is well known – tackle very complex conditions. Although all different from one another, cancers share the fact that they arise from some failures in the processes that regulate the production and destruction of cells. To explain the stability of a multicellular organism and its destabilization following the onset of cancer, it is held that we should appeal to the dynamic relationships among parts at different levels of the organizational hierarchy, that are causally more relevant than the intrinsic properties of those parts. Carcinogenesis is the disruption of processes at multiple levels of organization, which mutually regulate and stabilize each other. Not only is hence *spatiotemporal* continuity to be investigated, but *organizational* continuity too (see e.g. Di Frisco and Mossio 2020): organizational continuity requires a causal structure, constraining possible transformations, determining the thermodynamic flow within a system, and thus allowing a properly organized system to persist through time – or to be ruptured, turning into a pathological condition.

Boniolo and Campaner (2018) too have focused on the notion of process in cancer studies, highlighting how it plays a crucial role in actual scientific practice. Databases in cancer studies de facto use processual notions. In particular, Gene Ontology holds that biological process are pathways made up of the activities of multiple gene products (http://www.geneontology.org/), and the Dictionary of Cancer Terms of the National Cancer Institute offers a precise and unambiguous definition of molecular pathway as «a series of actions among molecules in a cell that leads to a certain end point or cell function» (https://www.cancer.gov/publications/

dictionaries/cancer-terms?cdrid=561605). A molecular pathway can be conceived as a continuous series of *n* causal bonding steps, starting from one molecule and leading to a molecular outcome with a certain function, which is determined by the entire pathway itself. It is thus by means of processual notions that molecular behaviors are to be understood.

In the next section we will consider a particular case from cancer studies which can be taken to show some epistemological benefit a processual account can have in addressing, specifically, *explanatory* issues.

3. An Example from Cancer Studies

So-labelled "cancers of unknown primary" (CUP) are cancers which, while presenting metastatic features, are not such that they can be related to primary ones at diagnosis: patients diagnosed with cancer of unknown primary site present with histologically confirmed metastatic cancer for which clinicians are unable to identify a primary tumor after a standard diagnostic approach. In other terms, such tumors appear as metastatic from the very beginning. Most cases of CUP are carcinomas, divided into: adenocarcinomas of well or moderate differentiation (60%), undifferentiated or poorly differentiated adenocarcinomas (30%), squamous-cell carcinomas (5%), and undifferentiated neoplasms (5%). From a clinical standpoint, they share some fundamental characteristics: they tend to have short history, with symptoms and signs associated with metastatic sites; to be invasive, with an aggressive clinical course and an unpredictable metastatic pattern; to disseminate quickly in the absence of a primary tumor. Their development is unusual: CUP do not follow a standard from a pre-malignant lesion to malignant type of progression and patients usually present more than one metastatic site at the diagnosis (with three or more organs involved at time of diagnosis in a third of patients). The incidence of cancers of unknown primary makes them relevant, and the severity very relevant from a clinical standpoint: CUP account for 3–5% of all human cancers, are reported to be the seventh to eighth most frequent malignant tumors, and the fourth most common cause of cancer death in both sexes. Median age at presentation is 65–90 years, the disorder is slightly more common in men than in women and predominantly affects late adults (although it is not confined to them).

Diagnosis can follow different routes and take into account different elements, brought to light through different techniques. Among them, histopathology, analysis of clinical and laboratory information on medical history and different current parameters (e.g. full blood count, urinalysis, occult blood testing, …), imaging (e.g. chest X-ray, computed tomography of the thorax, abdomen and pelvis, mammography, etc.). Prognosis is typically worse than that for primary tumors and, given the still limited knowledge, therapeutic options for CUP are basically combinations of therapies used for primary tumors. Clinically, there are two main subtypes: a) A favourable (less frequent) subtype, based on a basic resemblance of CUP with a similar primary tumour; hence, patients are treated according to the therapy used for the most similar tumour; b) an unfavourable (more frequent) subtype, with no resemblance with any known primary tumour, a median survival ranging from 6 to 10 months, and a therapy consisting of just some combinations of already used chemotherapy (usually based on

platinum non-selective treatment) and palliative care.

Research progress on CUP is clinically relevant not only per se, but also potentially for all patients with cancers prone to metastatic dissemination (see e.g. Laprovitera et al. 2021). Research questions focus on their origin: CUP follow an aggressive biological and clinical course, without there being clear evidence of etiological or risk factors that contribute to the pathogenesis of the syndrome. Is there some distinctive and unique nature of CUP? Is there any specific natural history of cancer in CUP patients? Two main theories are proposed. According to the first one, the metastatic cells develop very early and spread to other, distant sites. When the metastasis is observed, though, the primary tumour is either too small to be detected or has essentially regressed and disappeared from the organism. This might explain why sometimes, when post-mortem examination is done, the primary tumour can be found; other times, the primary tumour finally grows when the patient is still alive and becomes detectable. According to the second theory, there are specific cell-types that become malignant; they could be sorts of stem-cells, at different stages of differentiation. When this sort of stem-cells become malignant, they do not follow the normal pathway toward metastasis - that is, through the development of primary tumours. Rather, they begin to migrate and give origin to metastasis before they give origin to a primary tumour. In this scenario, the primary tumour does not exist, nor will it ever exist. Etiological issues remain open: CUP might either harbor primaries that cannot be detected by the standardized diagnostic investigations, or carry distinct genetic and epigenetic aberrations. Hence, the clinical and pathological enigma of CUP, which has to do with its peculiar (or not …) nature: "The unique biology of these tumours remains almost unknown. Nonetheless, current data suggest that metastatic dissemination can occur in the absence of growth of a primary tumour by virtue of inherent metastatic aggressiveness of cancer cells" (Fizazi et al. 2015, 133) [3]. What relationships do we need to focus on? What epistemological approach best fits actual research trends aimed at grasping the pathophysiology of CUP? And – this is the crucial point – is the primary tumour unknown, or truly non-existent? Are we dealing with «a missing primary site, or with a missing biology»? (Pentheroudakis et al. 2007).

[3] Although rapid advances have been made in some areas of oncology, management of CUP continues to be challenging. Nearly 90% of patients have a unique pattern of molecular abnormalities that differ from each other. See e.g. Kato et al. (2021).

Currently, a given set of tumors are classified as CUP, with no clear and univocal understanding of their origin and stages. The answer to the questions above makes all the difference for the development of research – its directions, methods and tools – and, consequently, for therapeutic strategies. Does a processual account help? We believe it does, for (at least) a couple of reasons. First, it places a strong emphasis on the temporal dimension: processes unfold over time, rely on sequential properties and depend on elements of continuity. "The concept of cancer of unknown primary origin comes from the limitation of present methods to identify cancer origin" (Rosenfeld et al. 2008, 462). Ways of tracing the origin back in time — unravelling the actual causal processes at play, the occurrences and critical turning points that alter the situation and exert varying influence on what follows —are expected to shed light on the origin of CUP. By investigating explanatorily relevant temporal processes, scholars might either get to examine the causal impacts of possible various key

moments in processes over time, hence reconstructing the temporal structure of CUP, or discover that there is no such a sequence of relevant causal impacts in the "historical scenario" leading to the disease, thus paving the way to different narratives on what CUP actually are. In this sense, a processual approach can foster a different ontological understanding and classification of the pathology.

Secondly, and by no means less important, a processual approach is fully aligned with relevant research trends, focusing on microRNA expression and the ways in which they are expressed in the tumours. MicroRNA changes when the tumour metastasises, but researchers also noticed that there are some microRNA that do not change and maintain a sort of signature of the tissues they come from. «Multi gene expression profiling seems to be a potentially excellent approach for tissue-of-origin identification, and microRNAs seem to be very important markers in cancer. Indeed, also if specific microRNAs modulated during the metastatic process have been identified, both mRNA and microRNA expression assays proved their ability to reveal the tissue of origin by using cancer-specific genes retained by metastasis, which led to the recent development of molecular tests based on microarray» (Ferracin et al. 2011, 44). The core idea here is that there can be cases where the expression of microRNA is very similar in the primary and in the metastatic tumour. For this reason, it is possible to look at microRNA profiles to infer origin of the tumour, by assessing whether a sort of transmitted signature of microRNA has been retained in the metastatic tumour. Research is pursued using microRNA technologies looking for a signature that, given a non-primary, belongs to a range of different primary sites. In other words, a search for a "tissue of origin" is implemented. This approach is grounded on the idea of some "signature passing through", and cannot but recall Salmon's concept of "mark", as a feature that persists and is transmitted along processes. If identified, the "cancer-type-specific microRNA signature" (see e.g. Ferracin et al. 2011; Laprovitera et al. 2021) is highly explanatorily relevant and can play an extremely important role in shedding light on etiological processes. The presence and persistence of a microRNA mark – understood as a perduring sign, in Salmon's terms – can support a different way of carving life processes into distinct entities – in line with what recent processualists have proposed.

«There is now increasing evidence that CUP represents a group of heterogeneous, unrelated site-specific tumors which happen to share the property of having a primary site that escapes detection. […] As genomic characterization of CUP is refined, the assigned 'unknown' term is being challenged» (Enconomopolou et al. 2015, 598). Different views on CUP are still debated, in the effort of opening the – so-to-speak – "dark box of cancer". «It looks as if CUPs were further classifiable into two different groups, one that retains more clearly features of the primary tumor, and one which is also more undifferentiated and difficult to predict. […] Each CUP entity *is probably unique*» (Ferracin, 8 March 2023, oral communication). In cases like the one at stake, a processual approach can contribute to effectively tackle puzzles and enhance epistemological progress. The appropriate focus of research for understanding the phenomenon under investigation is not on individual entities, but rather on reconstructing trajectories of development of a pathological condition, believing that

this is going to reveal what the pathology is ultimately like – and, in the end, whether it constitutes a distinctive kind of pathology or not. A focus on processes, signatures/marks can be taken as a way of determining on determining whether something should be identified as one of the primary units in the set of oncological pathologies, or not. Unlike neo-mechanist accounts, where the focus lies on interacting entities and their mutual organization, a processual view – while not opposed to such an approach – allows for a better grasp of the continuity of transmission and of what can be etiologically inferred from it. In light of CUP, both Salmon's processual view and more recent forms of processualism can prove insightful. Salmon assigns considerable explanatory significance to continuous propagation of change (the mark imposed): "it may be possible to argue that scientific understanding can be achieved most efficiently […] by searching for spatio-temporally continuous processes capable of transmitting marks" (Salmon 1998, 122). More recent processualist accounts, in turn, replace the idea that systems should be conceived as mechanisms, whose constituent parts are discrete entities with certain intrinsic properties, with the idea that processes and change are ontologically primary. That things are derived from processes, that "change is constitutive of identity through time" and "identity [is] to be understood as genuinely processual" (Meincke 2019, 3) better suits epistemological contexts such as the present, in which we are dealing with an entity currently "lacking sharp boundaries" (*ibidem*).

4. Concluding Remarks

Relations between mechanistic and processual accounts have been extensively – and at times vividly – discussed. Are we compelled to choose between them, or, rather, can they, to varying degrees, be reconciled? Is a genuine reconciliation even required, or has the supposed conflict been largely illusory?

The previous sections have shown that, while acknowledging the strengths of a mechanistic account, a processual approach offers researchers with a conceptual apparatus particularly well suited to tackling issues in the biomedical sciences. In the specific example considered, attempts to trace a still opaque disorder back to its precise origins rely on the search of a "signature" that might persist through metastasis over time. A processual perspective brings to the forefront spatio-temporal continuity and marking – which can play a significant epistemological role, even without addressing ontological or metaphysical stances. *Whether or not a mark can be found and is shown to be transmitted sets the boundaries between different interpretations of CUP*. A processual approach aligns closely to the notions and expressions used in specific contexts in scientific practice, guiding us to focus on continuous dynamic behaviour, and, in doing so, prompting reflections on whether something may be established as a separate, distinct entity by virtue of properties it maintains over time, or not.

«Everything changes. Substance does not have any effect without process. If something does not dynamically interact with any other thing, it is inert and hence irrelevant. […] Finally, while nothing is perceivable without process, there are many processes that are not things:

a thunderstorm, for example, or a burning flame, or a disease running through a population. […] These phenomena involve entities— molecules, viral particles or electrochemical potentials in our nerve cells—but these entities are exchangeable; they come and go during the lifetime of a process. What defines and characterizes a process are *the dynamical interactions among constituents, not the constituents per se*" (Jaeger & Monk 2015, 1064, italics added). Accordingly, a processual account highlights the lack of discreteness, the absence of permanent boundaries and the centrality of relatedness and interconnection, with *becoming* taking precedence over *being*, and the emphasis falling not on constituents per se, but on dynamic interactions.

May CUP constitute a distinctive cancer entity, or not? The pathology can be regarded as a (genuine or otherwise) form of CUP by virtue of its relation (or the lack thereof) to something preceding it (a primary cancer). To address this issue, a processual approach can fare better than starting from an already established entity, or some set of mechanistic entities. However, this does not entail any actual opposition to a mechanistic account. «Organisms are entities for the identity of which change, including exchange with the environment, is essential, which is to say that they are processes» (Meincke 2019, 5), and undoubtedly mechanists too recognize the role of interaction and exchanges between the mechanistic systems and the environment, and their sensitivity to changes in environmental contexts. Mechanistic notions can and do play a role; yet they are unlikely to be always the unique and best epistemological option. When persistence and identity through time, change and continuity are epistemologically crucial, processes matter (see e.g. Boniolo & Campaner 2018; Campaner 2022); at the same time, processes can be rephrased as interacting networks constituting, along Salmon's lines, mechanisms.

«Overall the [*classic*] process account has limited applicability, for at least two reasons. One is that it restricts to just one question, namely the distinction between causal and pseudo-processes. Another is that it is tailored to physics contexts. […] The characterization of causal processes and interactions of the original process account is too specific to cover cases of causal production, beyond classical physics» (Russo 2022, 254). On the one hand, a strict understanding of processes in physics-related terms is surely of limited applicability; on the other hand, however, the epistemological issues raised by cases like the one under consideration can be fruitfully addressed in terms of processes and marks, especially in the light of the work of process advocates over the last couple of decades. Some of this work argues for the compatibility of processes and mechanisms. For instance, «mark transmission as in *sending a signal* would be a good description for what is going on in etiological processes. At the etiological level, a cause is that first step in the *causation process* that initiates the pathomechanism, and the pathomechanism is the *biological mechanism* that initiates the disease process» (Dammann 2020, 107). Ultimately, we should focus on marks as "signature" to settle the "U" in CUP – where the latter might also be read, epistemologically, as "Cancers of Unknown Processes".

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