

Philosophy of Medicine

Book Review

Anya Plutynski's *Explaining Cancer: Finding Order in Disorder*

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1. Introduction

“What does it mean to ‘explain’ cancer?” (Plutynski 2018, 12) It means to find order in the disorder of cancer. Indeed, cancer results from both a breakdown of the normal functions of some tissue in the body—a *disorderly* growth—and from natural selection inside this tissue—the very principle of the *order* of life. The point is not simply that cancer, like any other disease, is both the disruption of a (normal) mechanism and a (pathological) mechanism of its own (Nervi 2010; Moghaddam-Taaheri 2011). Neither a contrast with normal tissue growth regulation nor a stepwise description of the natural development of cancer is sufficient to explain this intrinsically irregular, unpredictable, and highly variable disease.

The guiding thread is evolution. *In evolution*, cancer appears as both the breakdown of selected effects and the very result of some of these selected effects. As Anya Plutynski puts it: “Current function *and dysfunction* are products of our evolutionary and life history” (2018, 3). *In cancer*, evolution proceeds by natural selection of abnormally proliferative cells that break the rules of multicellularity and feed on the very mechanisms that probably evolved as defenses against cancer.

If this were the only factor involved, understanding cancer would still not be easy but it would at least be straightforward. Plutynski’s central idea seems to be that cancer is “interactionally complex” (2018, 11). Interactional complexity happens when interactions between subsystems cannot be understood as interactions of their ultimate outputs alone, without also considering the interactions of their components. It is the necessary result of evolution being a tinkerer (16); that is, trying whatever is available to a new purpose, at the same time as conserving the original functions. Cancer happens in an interactionally complex organism and is interactionally complex itself. For that reason, a multiplicity of theoretical approaches is required to understand cancer (16).

Considering cancer science seriously would certainly shake the orderly view of nested functions and systems inherited by philosophers of medicine from Robert Cummins (1975) via Christopher Boorse (1977). Questioning this view is one example of what makes Plutynski’s book a landmark in the development of philosophy of medicine.



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2. Is Cancer a Natural Kind?

The first question is: why should a phenomenon be considered and explained as “cancer”? In fact, cancer is often depicted as the accumulation, with time, of mutations that provide individual cells with the abnormal capacities described as the “hallmarks of cancer” (Hanahan and Weinberg 2011). Is this a correct *definition* for all cancers? Or is there no significant property that all cancers share? Or do properties come in clusters and predict how cancers behave, based on generalizations that are not exceptionless (Plutynski 2018, 20)?

Plutynski frames this question in terms of whether cancer is (or is not) a “natural kind.” In philosophy of medicine, this question is traditionally understood as a dilemma: are disease entity categories based on natural facts (realism) or are they based on human interests (constructivism) (Simon 2017)? By acknowledging that categories inspired by human interests need not ignore natural facts, Plutynski rightly discards this question. Instead, the question is whether cancer is a kind because of properties common to all cancers or an aggregation of diseases that admit many equally valid subdivisions. The first chapter of Plutynski’s book rejects various versions of the first hypothesis based on different philosophical interpretations of what natural kinds can be and finally claims: “There are a variety of equally satisfactory (or, if you like, ‘natural’) ways of classifying and, indeed, cross-classifying cancers” (Plutynski 2018, 19). In turn, cross-classification entails a form of pragmatism, in the sense that among many natural classifications, researchers or clinicians will have to choose one, depending on their goals or interests.

Plutynski is correct in avoiding the predicament of mutual exclusivity of “practical” and “natural” kinds. The case for pluralism as a faithful description of the field of oncology is also compelling. However, two different questions are in fact present in the question “is cancer one or many?” The first is whether all cancers have common properties that define them as cancers. Although Plutynski raises this question at the beginning of the first chapter, she does not really address it. The second is whether there is one correct subdivision of cancer. Philosophers of medicine have clearly distinguished the two questions about disease in general. “No common properties to all cancers” does not follow from “no correct subdivision of cancer” (and Plutynski does not claim it does). The second question is rarely treated in cancer science and remains unresolved in this book.

3. Cancer or Not Cancer?

Another way to determine whether cancers share properties is to contrast cancer with noncancer. The most relevant and difficult question is to contrast cancer with precancer; that is, a state of a tissue with increased risk of carcinogenesis.

Although Chapter 2 is not explicit about it, this question is raised at two levels. One is cancer *science*. Scientists look for the best possible predictive criteria of the evolution of a precancerous tissue. These criteria concretely define cancer as opposed to noncancer. However, they are imperfect. Another level is cancer *care*. Here, practitioners have to make do with these imperfect criteria and take a decision to treat (or not). When treated, a bet is made that this is *de facto* cancer, even if it is not *de jure*. Chapter 2 raises this practitioners’ problem and shows that “naturalism” in philosophy of medicine both focuses on that problem and fails to solve it.

Few have noticed that the naturalists are indeed making a point about *judgments* in medical practice, rather than *facts* in medical science: “their goal is to avoid confusing

evaluative judgments with empirical ones” (Plutynski 2018, 69). Paradoxically enough, naturalists are not interested in the conceptual problems raised by a correct description of the phenomenon of disease, only in defending the claim that it provides some value-free criterion of disease for the practitioner to judge objectively.

For Plutynski, the problem is rather that at a general level, a definition of disease should be relative to a specific goal, as one definition in terms of necessary and sufficient conditions is “unlikely to both capture the variety of legitimate ways in which this concept is deployed and be normatively guiding” (2018, 67). This important point has already been made (Schwartz 2004) but is rarely taken seriously in philosophy of medicine, resulting in much confusion. The case of cancer shows that some problems of definition are more pressing than others—determining whether an invasive tumor that metastasizes is a disease is not a pressing problem; determining whether a noninvasive lesion is cancer at an early stage is one. This is where a definition of disease would help.

Unfortunately, as Plutynski argues, the naturalistic account does not help. The very problem that it should help to solve, that of the “precise line between health and disease,” is discarded as “academic” by Boorse (cited in Plutynski 2018, 76). More precisely, she explains that the naturalist is only interested in whether an objective line exists while the pressing matter is “*how and why* we choose to draw the line at one place versus another” (78). Plutynski defends the argument that such a decision should rely on a reasonable appreciation of risk—a view close to Peter Schwartz (2014) and Élodie Giroux (2015).

Daniel Hausman critiques Plutynski by arguing that Boorse does in fact make a distinction between “pathological” and “diagnostically abnormal”/“therapeutically abnormal” and that Boorse would be happy to admit that “diagnosis and treatment decisions depend in part on evaluative considerations,” which is, according to Hausman, exactly Plutynski’s point (Hausman 2019, 783). However, her point is not that naturalism is *wrong* but that it is *useless* in the cases where a distinction really matters. If the goal is really to show that the line is drawn based on facts, rather than values, it is a failure. If it is to show that, *in theory*, it could be based on facts rather than on values, naturalism does not solve the practitioner’s problem that it itself raises.

In my view, the problem with naturalism is that it is a position in a debate about values in medical practice, not about facts in medical science. In this perspective, one may also regret that Plutynski does not examine the scientist’s problem—thus developing an alternative form of naturalism, more interested in the conceptual issues around a correct description of cancer. Indeed, the case could have been made, for instance, that interactional complexity explains why cancer is intrinsically impossible to predict in many cases. An interesting question would then be why some predictions or explanations of cancer are more reliable than others—are there properties of cancer that depend more on interactional complexity than others? Another question is whether the difficulty in predicting and explaining cancer depends on stochasticity—the existence of random processes like the accumulation of mutations—or complexity—multiple interactions between multiple pathways. This question can be solved (at least in part) by examining which transitions, in the process of cancer, are more difficult to predict. In the end, all this points toward properties that are distinctive of cancer, as opposed to precancer, and toward important hypotheses about the distinction between “benign” and “malignant.”

4. Do Genes Explain Cancer?

It is true that cancer researchers may sometimes make simplistic causal claims about genes causing cancer and cancer being a genetic disease. However, it would be naïve to take them at face value. Plutynski considers, rightly in my view, that the “mechanistic research program” of cancer genocentrism has been largely successful in identifying important nodes of a complex, unstable, and contextual process. In very inspiring pages, she even sketches a personal view of how concepts such as “generative entrenchment,” “molecular epigenesis,” and “robustness” may help to frame the complexity of cancer and show how the emphasis on mutations as the explicans of cancer is both relevant and limited in scope (Plutynski 2018, 104–108).

Most of chapter 3, however, is dedicated to articulating the case of genes causing cancer with philosophical discussions of cause and causation. It is a balanced presentation of what scientists mean by “cancer is a genetic disease.” Obviously, this does not mean that it is an inherited disease but, rather, that genes play a role in cancer. Yet the imperative of “causal parity” states that when conditions are equally necessary for an effect, none should be considered more explanatory than another, except when asymmetry can be shown; that is, against the background of a large set of necessary but variable consequences, one condition is invariable—a “specific” cause or a “difference maker” (Plutynski 2018, 116). More specifically, scientists do not focus on *actual* but on *possible* difference makers (119)—difference makers that also depend on background conditions. Cancer researchers are interested in genes that make a difference to cancer risk in given conditions but also in conditions where these genes do not make any difference. Genocentrism does not therefore suggest that genetic mutations trigger cancer but, rather, that they will be central in any picture of the causation of cancer.

Curiously enough, chapter 3 focuses on philosophical controversies over causality and misunderstandings of science, rather than on the actual question it itself raises. Anyone who has taught future cancer scientists will testify that these simplistic beliefs philosophers sometimes reproach scientists with really exist, at least in the beginning of a scientist’s career. These ideas are also to be found among philosophers. Yet, is not the primary question about the specific role of genes in cancer, as opposed to many other diseases where they are involved? The chapter provides elements of an answer but does not examine the question.

5. Does Exposure to Carcinogens Explain Cancer?

The other family of causal factors of cancer is carcinogens. Cancer care is full of controversies over the classification of components as carcinogenic. Chapter 4 is a good introduction to these controversies, as well as to the basics of epidemiology and philosophy of epidemiology.

However, the philosophical position here is less elaborated or original than in other chapters. Plutynski adds her name to the list of philosophers that endorse the Hill’s criteria for causation as the best guidelines we have. More specifically, she sides with Julian Reiss (2015) and Alex Broadbent (2011) in the claim that epidemiological studies can suffice to establish causality, insofar as it is a pragmatic question: when does enough evidence justify action? The requirement of mechanistic evidence, she says, bears the risk of delaying decisions—in particular, precautionary measures. In principle, this is defensible. However, given potential collateral risks, as the DDT controversy illustrated so well (Conis 2010),

taking a position in a debate on principles hardly helps to solve practical problems. Is not the practitioner's question *when* and *how* to intervene, as Plutynski herself states in Chapter 3? A philosopher should perhaps propose more than a neat summary of the difficulties that deciders know all too well.

6. Cancer As an Instance of Multilevel Selection

Chapter 5 is arguably the most important chapter in this book. It is the closest we get to a tentative picture of cancer itself. The key to understanding cancer is evolution. The first part of the chapter is structured as a list of evolutionary mechanisms that cast a certain light on cancer, with simple and relevant examples of where in cancer science they have been used at their best.

Cancer is certainly a special case. Neurodegenerative diseases suppose a nervous system, asthma requires lungs, and so on. But cancer only requires multicellularity. Apart from infectious diseases, which are probably strictly universal diseases across the tree of life, cancer has been documented in many forms of multicellular life (Aktipis et al. 2015; Albuquerque et al. 2018), although the exact extension depends on the definition of cancer.

In an interactionally complex organism with “a high degree of plasticity, redundancy, and modularity” (Plutynski 2018, 165), some fundamental dysfunctions transform the normal mode of cooperation between cells into a competition—what Peter Godfrey-Smith calls “re-Darwinization” (Godfrey-Smith 2013). This makes cancer not only the result of evolution but also an evolutionary process in itself. For that reason, besides evolutionary medicine, two other research programs have yielded results on cancer; more specifically, mathematical biology of cancer evolutionary dynamics and evolutionary developmental biology.

In this light, cancer appears as a case of multilevel selection. Cells are selected inside a tumor, a tumor is selected inside an organism, and an organism is itself the result of natural selection. Plutynski explains: “In a ‘multilevel’ selection situation, selection is acting on more than one level simultaneously. Selection at one level may increase or decrease the frequency of traits in a population, which in turn may affect what is available to selection at another level of analysis” (2018, 168).

This is where the book takes a different turn. Instead of simply describing pluralism and pragmatism in cancer science, Plutynski actually proposes a more original view on cancer (2018, 166–179). She draws from a proposed distinction by John Damuth and I. Lorraine Heisler between two forms of multilevel selection: multilevel selection 1 (MLS1), where individuals in a group are the unit of selection and have more or less fit traits within the group, thus making the group itself more or less likely to survive, and multilevel selection 2 (MLS2), where groups are the unit of selection and can be more or less fit in “reproducing” into new groups (traits of such groups can, for instance, be a level of genetic heterogeneity). The result is a recapitulation of the mechanisms of selection involved in the different stages of cancer progression (173). The most original part of this hypothesis is the proposal that invasion and metastasis explain cases of MLS2—a view Plutynski has written about elsewhere (Lean and Plutynski 2016).

The last part of the chapter focuses on an interesting problem with modeling cancer within such an evolutionary framework: it draws from a form of necessity that is ambiguously causal or analytic (that is, mathematical). Plutynski defends the view that such cancer models are based on “would promote” claims—a point emphasized by Elliott Sober

to express how some theoretical models dare assert that X will cause Y, given certain conditions, even before it is known whether X does cause Y. Exposure to mutagenic factors and the size of the organism would promote the frequency of cancer; genetic instability would promote the evolvability of cancer while genetic stability would promote the robustness of cancer; genetic heterogeneity would promote resistance to cancer treatment, and so on.

A limitation of this fascinating chapter is that it embraces a very marginal part of the literature in cancer research. This corpus is orders of magnitude below most significant research programs—decomposing and exploiting the pathways of p53, immunotherapies, tumor sequencing, and so on. So, is this literature simply representative of cancer research? Some philosophers have even denied that natural selection plays a major role in cancer (Germain 2012). In part, the problem seems to be that while cancer research has indeed largely endorsed mathematical modeling of evolutionary processes, it does not seem to come with any strong commitment to the view that cancer really is a process of evolution by natural selection. Philosophers, on the other hand, naturally tend to develop the implicit assumptions attached to such models and draw conclusions about cancer.

7. Does Cancer Research Solve Puzzles without a Theory?

Chapter 6 expresses Plutynski's conviction that cancer research aims at solving specific puzzles of prediction and control much more than at "arriving at 'general theories' of carcinogenesis" (2018, 192). These conclusions echo Harold Kincaid's view that cancer scientists borrow theories from other fields, do not have theories of cancer, and, should they have such a theory, would not need it (Kincaid 2008).

However, as Marie Darrason has noted, this relies on how developed a "theory" must be, and how much it should achieve, to deserve a philosopher of science calling it a medical "theory" (Darrason 2014). Why should a philosopher refuse the denomination when scientists themselves use it? This objection also goes for Plutynski. She first takes two "theories" of cancer—the so-called multistage theory of cancer and the oncogene paradigm—and presents them as solutions to various puzzles; she then takes the example of a puzzle that has found partial solutions, seemingly without any theory—why do we not get cancer more often? However, she never says what is required for a view to stand as a theory in the field of cancer, or which prediction and control can be successful without some explanation. Moreover, why should this be solving a puzzle rather than finding a theory, and why prediction and control rather than explanation? A last ambiguity is whether a theory remains a theory no matter how many difficulties it does not solve, as long as it is still used by scientists to solve puzzles.

That said, there is a difference between Kincaid's claim that medicine does not *need* theories of its own and Plutynski's pointing out that cancer research does not *look* for theories. However, the primary question is how much cancer research can reach in terms of generalization. Although touched on in many places, the question is avoided in the first three chapters, as I have already made clear. The conclusions in Chapter 6 seem to ignore the best of what Chapter 5 develops—no less than preparing the ground for an evolutionary theory of carcinogenesis. Such a theory is certainly neither useless nor inopportune in cancer research.

8. Conclusion

Plutynski's book does much to advance the philosophy of medicine by bridging philosophy of medicine and philosophy of biology beyond their original shared question of the definition of "function" and "dysfunction." It also shows how limited philosophy of medicine remains if it ignores biomedical science. Moreover, it is true that in focusing on claims by philosophers of science, Plutynski sometimes misses original questions that could renew the field of philosophy of science, in particular philosophy of medicine (for a similar conclusion, see Laplane 2019). However, even if the picture of cancer that Plutynski provides cannot do full justice to the complexity of the disease, it is not prisoner to a simplistic philosophical framework. This book is a must-read for philosophers of medicine, not to find illustrations or developments of a familiar debate but to learn about cancer itself and to question a major presupposition of their field: that philosophy of medicine can ignore the details of the mechanisms of diseases and that any disease can simply be treated as an instance of "disease in general."

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References

Aktipis, C. Athena, Amy M. Boddy, Gunther Jansen, Urszula Hibner, Michael E. Hochberg, Carlo C. Maley, and Gerald S. Wilkinson. 2015. "Cancer across the Tree of Life: Cooperation and Cheating in Multicellularity." *Philosophical Transactions of the Royal Society B: Biological Sciences* 370, no. 1673, 20140219. <https://doi.org/10.1098/rstb.2014.0219>.

Albuquerque, Thales A.F., Luisa Drummond do Val, Aoife Doherty, and João Pedro de Magalhães. 2018. "From Humans to Hydra: Patterns of Cancer across the Tree of Life." *Biological Reviews of the Cambridge Philosophical Society* 93, no. 3: 1715–1734. <https://doi.org/10.1111/brv.12415>.

Boorse, Christopher. 1977. "Health as a Theoretical Concept." *Philosophy of Science* 44, no. 4: 542–573. <https://doi.org/10.1086/288768>.

Broadbent, Alex. 2011. "Inferring Causation in Epidemiology: Mechanisms, Black Boxes, and Contrasts." In *Causality in the Sciences*, edited by Phyllis McKay Illari, Federica Russo, and Jon Williamson, 45–69. Oxford: Oxford University Press.

Conis, Elena. 2010. "Debating the Health Effects of DDT: Thomas Jukes, Charles Wurster, and the Fate of an Environmental Pollutant." *Public Health Reports* 125, no. 2: 337–342. <https://doi.org/10.1177/003335491012500224>.

Cummins, Robert C. 1975. "Functional Analysis." *Journal of Philosophy* 72, no. 20: 741–764. <https://doi.org/10.2307/2024640>.

Darrason, Marie. 2014. "Y a-t-il une théorie génétique de la maladie?" PhD diss., Panthéon-Sorbonne.

Germain, Pierre-Luc. 2012. "Cancer Cells and Adaptive Explanations." *Biology & Philosophy* 27, no. 6: 785–810. <https://doi.org/10.1007/s10539-012-9334-2>.

- Giroux, Élodie. 2015. "Epidemiology and the Bio-statistical Theory of Disease: A Challenging Perspective." *Theoretical Medicine and Bioethics* 36, no. 3: 175–195. <https://dx.doi.org/10.1007/s11017-015-9327-7>.
- Godfrey-Smith, Peter. 2013. *Darwinian Populations and Natural Selection*. New York: Oxford University Press.
- Hanahan, Douglas and Robert A. Weinberg. 2011. "Hallmarks of Cancer: The Next Generation." *Cell* 144, no. 5: 646–674. <https://doi.org/10.1016/j.cell.2011.02.013>.
- Hausman, Daniel M. 2019. "What Is Cancer?" *Perspectives in Biology and Medicine* 62, no. 4: 778–784. <https://doi.org/10.1353/pbm.2019.0046>.
- Kincaid, Harold. 2008. "Do We Need Theory to Study Disease? Lessons from Cancer Research and Their Implications for Mental Illness." *Perspectives in Biology and Medicine* 51, no. 3: 367–378. <https://doi.org/10.1353/pbm.o.0019>.
- Laplane, Lucie. 2019. "Anya Plutynski, *Explaining Cancer: Finding Order in Disorder*, Oxford: Oxford University Press, 2018, 280pp., £47.99." *History and Philosophy of the Life Sciences* 41, no. 4, 43. <https://doi.org/10.1007/s40656-019-0284-8>.
- Lean, Christopher and Anya Plutynski. 2016. "The Evolution of Failure: Explaining Cancer As an Evolutionary Process." *Biology & Philosophy* 31, no. 1: 39–57. <https://doi.org/10.1007/S10539-015-9511-1>.
- Moghaddam-Taaheri, Sara. 2011. "Understanding Pathology in the Context of Physiological Mechanisms: The Practicality of a Broken-Normal View." *Biology & Philosophy* 26, no. 4: 603–611. <https://doi.org/10.1007/s10539-011-9258-2>.
- Nervi, Mauro. 2010. "Mechanisms, Malfunctions and Explanation in Medicine." *Biology & Philosophy* 25, no. 2: 215–228. <http://dx.doi.org/10.1007/s10539-009-9190-x>.
- Plutynski, Anya. 2018. *Explaining Cancer: Finding Order in Disorder*. New York: Oxford University Press.
- Reiss, Julian. 2015. "A Pragmatist Theory of Evidence." *Philosophy of Science* 82, no. 3: 341–362. <https://doi.org/10.1086/681643>.
- Schwartz, Peter H. 2004. "An Alternative to Conceptual Analysis in the Function Debate." *The Monist* 87, no. 1: 136–153. <https://doi.org/10.5840/monist20048713>.
- . 2014. "Small Tumors As Risk Factors Not Disease." *Philosophy of Science* 81, no. 5: 986–998. <https://doi.org/10.1086/678280>.
- Simon, Jeremy R. 2017. "Realism and Constructivism in Medicine." In *The Routledge Companion to Philosophy of Medicine*, edited by Miriam Solomon, Jeremy R. Simon, and Harold Kincaid, 90–100. New York: Routledge.