

Book Review: Azra Raza, *The First Cell: And the Human Costs of Pursuing Cancer to the Last*, Basic Books, 2019, ISBN 9781541699519 - A Philosophical Review, Part One -

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Abstract. This paper is a critical review of the book entitled *The First Cell: And the Human Costs of Pursuing Cancer to the Last*, published in 2019 by Basic Books. Its author, Azra Raza—an oncologist specialized in the diagnosis and treatment of myelodysplastic syndrome—presents “systems biology” as the panacea for the diagnosis and treatment of human malignancies. In addition, Raza holds “reductionism” as the reason for humanity’s inability to defeat cancer. However, these concepts offer a simplistic account which lacks the nuance that the current discussions taking place in the field demand. This review will explore the philosophical basis of the author’s views on why the so-called “War on Cancer” is being lost.

Keywords: cancer, cell, war on cancer, paradigm shift, reductionism, systems biology

JEL Codes: I1.

The “War on Cancer” was officially unleashed when US President Richard Nixon signed the National Cancer Act in December of 1971. In that same year, and in his State of the Union address, President Nixon proposed “an intense campaign to find a cure for cancer (Leaf, 2004). The National Cancer Act mandated the reduction of the “incidence, morbidity and mortality from cancer” through research and the translation of that research into implementable diagnostic and treatment methods (De Vita, 2004). Almost half a century into this war and an annual global investment in the billions of dollars in cancer research and treatment people are still debating whether or not we are winning, or even making a progress, in this fight against one of the staunchest enemies of humanity.

For most forms of cancer, a sustained remission is rare, and cures are even rarer. Cancer therapeutics, especially the new “smart drugs”-targeted therapy, immunotherapy, gene therapy, personalized medicine or customized drugs-are exorbitantly costly, yet provide marginal benefits measured in terms of weeks or months of extended survival. This constitutes a major cost-benefit dilemma for patients, healthcare systems and governments worldwide (Hanahan, 2004).

In the “War on Cancer” debate very few take the position that we have won, or are winning, this fight. In the main, there are two groups in this debate: on the one hand, there are those who maintain that although humanity is still far from announcing victory, we are, nevertheless, making significant progress in the understanding and treatment of different kinds of cancer; on the other hand, there are those who believe that

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not only we are not making any progress in this war, we are actually losing it. Azra Raza, in her book *The First Cell*, belongs to the latter group. Raza thinks that the “cancer winter continues (10).

Azra Raza is an oncologist by training who specializes in the diagnosis and treatment of myelodysplastic syndrome, which is a disease of the bone marrow with high potential for acute leukemic transformation, which ushers in the terminal stage of this disease. In her book, Raza gives an account of her personal experiences with a number of individuals who were afflicted with cancer. Most of whom she treated and cared for and all of whom ultimately succumbed to their illness, including her husband Harvey Preisler, who was a distinguished oncologist and who died of lymphoma in 2002.

The book is composed of seven main chapters; each carries the name of one of those individuals with whom she established more than just a patient-doctor relationship. With Raza, things became very personal and many times she would let those patients into her life. The last of these chapters carries her late husband’s name “Harvey”. But in these chapters, Raza not only described the experience of dealing with those patients, but she also included her views on the current state of cancer research and treatment. There is a lot going on in this book and in this limited space, therefore, one must be selective in what to highlight.

The following lines will focus on the author’s views on the problem of cancer and how she envisages the war on cancer should be conducted moving forward. Despite all the grandiose ideas, some of which verge on the fantastic, the author did not offer a real, or realistic, alternative model for dealing with the cancer problem. She presents the concept of systems biology, which is a relatively new concept and gained prominence and attention in the past couple of decades, as the panacea for the diagnosis and treatment of human malignancies. However, as we shall see later, systems biology is still a discipline in the making and faces several challenges that should be overcome before it becomes a basis for a new approach to the understanding of the malignant process. But before we show how systems biology cannot be the paradigm shift that the author enthusiastically advocates, we will look at the philosophical basis of the author’s view on why we are losing the war on cancer.

Few would dispute the author’s assessment that the current state of cancer research and therapeutics is not bringing humanity anywhere close to defeating this disease. As someone who specializes in treating myelodysplastic syndrome and its acute leukemic phase, known as acute myeloid leukemia, the author maintains that the treatment of this disease has not changed or evolved in any significant way for the past fifty years. The author argues that the same can be said of most common types of cancer. She describes the routine protocol for treating most cancers as “slash-poison-burn” (Raza, 6). This stands for surgery, chemotherapy and radiation therapy.

On the cancer treatment front, the author directs harsh criticism towards those who announce a certain drug as “game changer” while, in fact, it only prolongs life for few weeks or months. On the cancer research front, the author rejects animal models and tissues cultures for investigating carcinogenesis and experimenting with new drugs. She thinks that successes in those animal models and in vitro methods has nothing “to do with treating disease in humans” (Raza, 6). After this assessment, the author proclaims her view on the war on cancer forcefully, unequivocally and without mincing words: “No one is winning the war on cancer. It is mostly hype, the same rhetoric from the same self-important voices for the past half century” (Raza, 6).

The author then goes on to attack the philosophical basis of the current paradigm for understanding the malignant process. The author holds “reductionism” the responsibility for humanity’s inability to deal cancer the long-awaited coup de grace: “The disease [cancer] is fantastically complex. More fantastic is the reductionist conceit that targeting a single genetic abnormality with a single drug will be curative” (Raza, 10). But the author has good tidings to tell readers: “The heyday of reductionism, looking for one culprit

gene at a time and searching for one magic bullet, is over. The era of big data, cloud computing, artificial intelligence...has arrived. The ideal strategy will emerge from harnessing cutting-edge technology for a multidisciplinary *systems biology* through the consilience of scientists with expertise in molecular genetics, imaging, chemistry, physics engineering, mathematics and computer science” (Raza, 244).

Let me note here that introducing concepts such as reductionism and systems biology in a popular book about cancer, which is supposed to be written for the illumination of the lay reader, without providing even a brief history on the development and evolution of those ideas is somewhat problematic. Most of those who pick up this book, I am willing to bet, are hardly versed in the fundamentals of the philosophy of science and biology, let alone aware of the ongoing debates taking place in those fields of inquiry, to be able to judge the author’s assessment of the cancer problem. Many will have no choice but to accept the author’s narrative that reductionism is the culprit and systems biology will save the day. This is a simplistic account and lacks the nuance that the current discussions taking place in the field demand.

But what exactly is reductionism? Is it really, as the author claims, responsible for our failure to defeat cancer? Is molecular biology, which is supposedly the epitome of the reductionist model in biology and against which the author directs her criticism a reductionist explanatory model? Will the new era, the era of systems biology, which the author is so enthusiastic about, witness a paradigm shift in cancer research and treatment? Will this new paradigm, should we accept that characterization, put reductionism finally to rest? In this first part of the article I will attempt to answer the questions pertaining to reductionism. In the second part I will deal with systems biology.

Reductionism has a very long history that dates to the ancient Greeks. But a relatively more recent history of reductionism attributes this explanatory model to Galileo and Newton, who laid down its foundations, and the French philosopher Rene’ Descartes who formulated its philosophical premises (Bazzari, 2013.) In the classical sense, reductionism can be defined as an approach to the understanding of phenomena based on the laws of physics and chemistry. Any phenomenon, according to this explanatory model, can be decomposed into its constituent components. These components can then be understood in terms of the laws of physics and chemistry. By understanding the parts, an account of the whole can be achieved. Reductionism has been the dominant explanatory paradigm in the sciences for the past three centuries.

Reductionism as it pertains to the biological sciences is represented by molecular biology, which the author of “The First Cell” is supposedly attacking when she attacks reductionism. The molecular biological program started its ascension in the 40s and 50s of the past century, especially after the discovery of the double helix structure of the DNA by Francis and Crick in 1953. The role of genes and their products in explaining biological function soon gained significance. Molecular biology reached its apex in the 1970s and 80s. This was enhanced by the development of advanced technologies such as recombinant DNA technology, cloning, mass spectrometry and high-through put platforms for DNA sequencing. These technologies allowed the discovery and elucidation of the roles of different genes and their byproducts; most prominently the identification of the oncogenes, tumor suppressor genes and their proteins. The focus, subsequently, became on the part which each of these genes and proteins played in malignant transformation and growth. Of course, things did not remain that simple and soon cellular signaling pathways and their substrates were discovered and their roles in malignancy became the latest research programs in the study of cancer.

The literature on reductionism in the sciences, especially the biological sciences, is huge. But the idea of reduction is one of the most controversial topics in the biological sciences. It is not the purpose of these lines to outline these debates. However, we will focus on the idea whether molecular biology is a reductionist

program. It is important to note that one of molecular biology's main tenants is to encourage the study of individual molecules in order to understand a more complex biological phenotype (Powell & Dupré, 2009). In this sense molecular biology can be defined as a research program that "looks to the molecular scale for answers to biological questions posed at any scale" (Powell & Dupré, 2009). But molecular biology never engaged in any further reduction. Molecular biology afforded knowledge at the molecular level of organization that opened the possibility for understanding human biology from that level to the level of the whole organism (Hartwell et al., 2008).

It has been argued that those who attack reductionism and advocate the systems biology approach seem to be against a kind of an obsolete form of reductionism, which can be described as classical reductionism. This kind of reductionism calls for the reduction of all phenomena into their physical and chemical properties and tries to explain them in accordance with the laws of physics and chemistry. In other words, classical reductionism entails reducing all biological laws, that supposedly explain biological phenomena, into physical laws (Dupré, 1993). Molecular biology, the quintessence of biological studies, it is argued, has never implemented such a program (Gatherer, 2010).

Further, there are those who think that molecular biology is not a reductionist approach for the study of biological phenomena to begin with. They argue that reduction of a biological complex phenomenon, like cancer, to its molecular property "is not reductive at all...because it is not a reduction of a complex to a simple representation but a reduction of a complex to a complex representation" (Debru, 2002). Thus, the author in her book seems to be totally insensitive to the historical nuances of the reductionist doctrine and its usage in the different domains of scientific study. This lack of historical sensitivity led the author to present her thesis-end of reductionism and the rise of a holistic or systemic understanding of biological phenomena-as a *fait accompli*. A cursory review of the literature on this hotly- debated subject will reveal the inaccuracy of the author's premise.

Raza rightly points out that animal models and in vitro methods (such as tissue cultures) do not recapitulate cancer behavior and its response to therapy in the same way that they take place in the human body. Additionally, she plausibly argues that cancer is a complex disease that cannot be exhaustively explained by a linear model of causation: gene mutation leads to malignant transformation. We now know that there are other factors that play a significant role in the malignant process; most importantly, epigenetic factors and the tumor's microenvironment. Mention should also be of the cellular networks, which are composed of hundreds, sometimes thousands, of interacting elements that need to be mapped and analyzed. The latter is the domain of systems biology.

Indeed, a more holistic or systemic approach to carcinogenesis is needed. But can we say that reductionism, which, according to the author, gave us an incomplete understanding of the malignant process, is the reason why we are losing, or at least not winning, the war on cancer? It is too simplistic a view to claim such a thing. To blame a single factor for our mishandling of this very complex disease is, ironically, a reductionist view. It has been extensively discussed why the fight against cancer has not been going in humanity's favor. However, even if cancer research changes course and fully adopts systems biology as the new paradigm for understanding cancer, a lot must be done on many fronts before cancer research can be said to have changed course. Take for example what is entailed by the implementation of systems biology as the new model for studying cancer. Systems biology is an interdisciplinary approach that requires the collaboration of molecular biologists, mathematicians, information specialists, physicists and computer engineers. Fundamental changes are needed, in both academic and research institutions, to bring all those experts together. This is not an easy challenge to overcome.

There is also the financial aspect. Systems biology, simply defined, is a methodology that aims to integrate biological information. It amasses huge amounts of data and then studies them using mathematical models and computer simulations. Some of the technologies that the author proposes as tools for collecting information, which might signal the first inklings of cancer, hence the title of the book *The First Cell*, sound like they are from a sci-fi movie as the author herself admits: “The above [technologies] are not scenes from *Fantastic Voyage*” (Raza, 237). The author is referring to a 1966 sci-fi movie. Some of the proposed technologies are: a smart bra that is worn for an hour once a week and has biosensors that monitor changes in bodily temperature and texture. The data generated is then captured and interpreted by an accompanying app that detects the first few cancer cells; there is also a machine that scans a person’s body every day while taking their shower (Raza, 237). But the most fantastic of all is a scenario in which individuals are screened from birth to death for any early development of cancer cells. The protein signature of these cells is identified and is used to determine their origin (Raza, 238).

One cannot but ask: Who is going to pay for all this? Is it the government? The insurance companies? Will public policy facilitate, or stand as a barrier to, the wide-spread availability of such technologies? Will the technology be available in, and affordable by, developing nations? Cancer is not a problem for the wealthy and developed countries. Cancer is a global problem. Winning the war on cancer requires more than changing our epistemic model for the study of this disease.

In the second part of this article we will look at systems biology and give a brief overview of this relatively young discipline. We will try to answer the question whether systems biology can be considered a paradigm shift (à la Kuhn) in the study of cancer and other diseases. We will also look at some of the challenges that systems biology still faces.

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