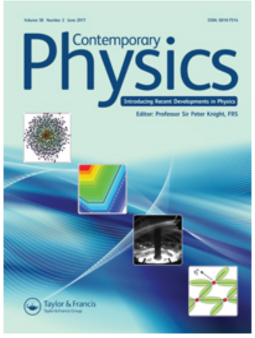


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# Physics of cancer: the new adventure of physicists against cancer

Miguel A. F. Sanjuán

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ESSAY REVIEW

# Physics of cancer: the new adventure of physicists against cancer

A review of **Physics of cancer**, by Claudia Tanja Mierke, Bristol, Institute of Physics, 2015, 449 pp., £99 (hardback), ISBN 978-0-7503-1135-9. Scope: monograph. Level: postgraduate, early career researcher, researcher.

Physics of Cancer is a recent catchword reflecting the current efforts on the relationship of physics and cancer research. Certainly, this relationship is not new. Broadly speaking, there have been many attempts for years to use physics referred to cancer treatments, diagnosis or even image techniques by using X-rays, magnetic fields, protons or even other subatomic particle therapies. All these techniques have been used in the past and are being used excellently mainly by radiation physicists or medical physicists with wonderful results.

But when we talk about physics of cancer, we refer mainly to the endeavour adopted by physicists in recent years to face problems related to cancer research, from a physical point of view. The traditional approach to the growth and proliferation of cancer comes from a biological perspective. However, physical ideas and concepts can illuminate the mechanisms and processes related to the development of cancer cells and tumours. From this point of view, doubtless more conceptual, there is a stronger challenge in understanding what part of life connects with cancer, what makes it so resistant and oftentimes indestructible. Perhaps a stronger and more difficult challenge consists of ascertaining what physical laws or mathematical models might explain this phenomenology. A key idea is that this challenge is somehow similar to what physicists face in their attempt to search for the laws of nature.

This investigation will definitely help us to better understand what is life and different ways to fight cancer. This is probably what the physicist Paul Davies felt when he received a phone call from Anna Barker [1], the then deputy director of the US National Cancer Institute (NCI), asking for help in the war against cancer. Among other things, Anna Barker told him that in the last 40 years the survival rates of cancer had barely changed despite the large investments of millions of dollars.

The purpose was indeed to provoke physicists to intervene with new, fresh and radical ideas. Paul Davies replied that he did not know anything about cancer, but he accepted the challenge anyway. Perhaps if the proposal had been to keep working on the areas already mentioned where physicists have been working, he would probably not have accepted. This proposal was so insightful and interesting that he could not resist being involved in this new great challenge.

After that, the NCI decided to create in 2009 a network of 12 Physical Sciences-Oncology Centres (PS-OCs) [2], and in June 2015 the NCI announced the creation of 4 new centres spread over the US. Most of these centres are located in university and oncological centres with a large tradition in basic and clinical research. And right now, Davies is the principal investigator of one of them. The initiative, of course, has spread to Europe, where new activities are being developed. And the methodology precisely focused on searching for new problems in cancer, to look at them from different viewpoints and to attempt to investigate the underlying physical and dynamical principles.

This research will help as a byproduct to improve oncological treatments and also to improve the prediction and earlier diagnosis of metastasis, taking into account the physical interactions of cancer cells with their microenvironment, as well as the influence of external mechanical forces.

This new perspective has been called the Physics of Cancer, including ideas of many scientists that have been involved in this new research field. From this viewpoint, I also wish to mention the eminent biologist, Nobel Prize in Medicine 2001, and ex-President of the Royal Society, Sir Paul Nurse. In some talks and writings, he has put forward the "Great Ideas in Biology" [3], which consists of the cell, the gene, evolution, life as chemistry, and finally the idea of biology as an organised system with information. Many biological systems can be described as complex systems interacting among themselves that can be understood in terms of the information processes acting among them. Furthermore, they operate at all scales, from neurons to complex ecosystems. In short, he declares that the sciences of complexity can bring biology to a new theoretical and abstract setting similar to those already occupied by physics and chemistry.

Furthermore, ideas very familiar to physicists such as phase transitions have also been used to conceptualise certain phenomena associated with the dynamics of cancer [4]. This is just an example of the application of concepts from statistical physics to the initiation and development of cancer. Many internal and external factors are responsible for the evolution and spread of tumours. And many of these factors are created by feedback mechanisms and nonlinear behaviour involved in the dynamics of the processes affecting them. This is another reason why nonlinear science and the science of complex systems have also much to do with this new approach in cancer research.

The ultimate goal of this approach consists of giving a quantitative description of the initiation and progress of cancer, using tools coming from physics and mathematical modelling and using particular experimental, computational and theoretical tools and skills. Needless to say, these are useful complements to experimental and clinical studies. Moreover, they reveal unknown physical principles, which might have been overlooked when only a biological approach has been considered.

A deep question might be necessary: Does cancer research need physics at all? The relationship between physics and mathematics with biology and medicine is not new. There has been a long-standing tradition of interaction between these subjects, where the famous physicist Erwin Schrödinger contributed to the development of molecular biology with his *What is Life?* [5]. A very interesting and recommendable essay review on the book has been written recently by Peter V.E. McClintock [6]. Identifying the simplicity in complexity is an important goal, where an intelligent understanding of the relationship between theory and data is required. Perhaps a quantitative modelling of biological data is not the only task to be carried out by physicists. One more important challenge would be working together with cancer biologists to develop a theory of cancer.

An important goal is to identify some key questions that, if tackled in an interdisciplinary manner, could lead to fundamental advances in our understanding of cancer. Some are related to quantitative modelling using population genetics and evolutionary game theory to parameterize patterns of progression, whereas others relate to the development of mathematical models that can be validated using clinical observations. There are also physical considerations centred on the application of mechanobiology to metastasis, and the application of thermodynamics to understand cancer cell biology. It would be necessary to establish bridges between the typical viewpoint of biologists and the particular viewpoint of theoretical physicists. A stronger dialogue between biologists and physicists is needed, and this challenging effort would certainly be highly beneficial to cancer research. Physicists working in cancer might help by their particular way of thinking, offering both tools and concepts that can contribute to a better understanding of the complex disease that is cancer.

Furthermore, many interesting review papers [7–9], special issues in physics journals [10], articles in physics magazines [11], new books, new research groups, and scientific meetings have been developed in this direction all over the world. In fact, the American Physical Society March meeting has organised sessions to introduce the subject to interested attendees.

Though there are very good reviews and many research articles showing the role of physics in the war against cancer, there are very few books and monographs on this nascent field. The book *Physics of Cancer* [12] by Claudia Tanja Mierke is one of the first attempts to introduce the application of current biophysical research to cancer. When one sees the title of this book, one might think that this is the kind of book one would need to read to acquire a general overview of the field of physics of cancer. However, I do not think this is the case. The author is a biophysics professor with a background in biology and molecular biology. She has been working in the field in the past few years and she has even organised numerous activities around the subject at the University of Leipzig, where she is currently working. Her background is strongly reflected throughout the monograph, as well as her research, which is mainly focussed on mechanical properties of cells. Definitely, the style used in the writing is not the expected style in a physics textbook or monograph.

I do not think that there is any regulation to catalogue a book as a physics book, but there is something extremely surprising in this case. It is composed of 12 chapters occupying a total of 449 pages; out of them there are only 10 figures and 8 equations (6 appear in one chapter and the remaining 2 in another). Including what the author defines as *further reading* and *references* that appear at the end of each chapter, you can find an amount of more than 2500 references. Most physics texts are not like that. Some chapters contain mainly references specific to some very specialised topics like mechanical properties of cells and elasticity, cell biology and experimental methods, medical journals and cancer biology. The reader can easily understand that most of the chapters are in essence a review paper on a rather specific field at a rather specialised level.

The back cover of the book clearly emphasises the focus on the mechanical properties of cancer cells and their role in cancer disease and metastasis, highlighting the importance of the mechanical properties of cancer cells and their microenvironment. From this point of view, perhaps it would have been fair to have introduced these keywords in the title, thereby avoiding any sort of confusion with the term physics of cancer.

I do not doubt that this book could be useful for those interested in the physical aspects of cancer, but I would say that it can be of much more use for those especially interested in the mechanical properties of cells for the understanding of cancer disease. A strong background in cancer biology is also assumed.

There are other books of interest which have been recently released for a better understanding of the current efforts of the applications of the physical sciences in oncology. Among them, there is one edited book by a physicist bearing the name physics of cancer in the title and two textbooks bearing the name of mathematical oncology or mathematical foundations of oncology. *Mathematical oncology* is the preferred term in the applied mathematics community, while *physics of cancer* is commonly preferred in the physics community. Both of them share a similar approach as the one we have described earlier, though perhaps one of them uses more extensively mathematical modelling and computational techniques.

Needless to say, physics of cancer is a research field in its infancy, which explains why the term is not widely used and, more importantly, why there is not yet a consensus on the main contents of the field. This clearly explains why in the few books existing so far, the contents are different depending of course on the choice of the authors.

Bernard Gerstman is a physicist with a background in theoretical and computational biophysics, currently the chairman of the Department of Physics of Florida International University. His approach in *Research on the Physics of Cancer: A Global Perspective* [13] fits perfectly with the ideas previously described at the beginning of this essay. The book contains 12 chapters devoted to different topics and written by physicists and mathematicians from all over the world. The chapters describe research work carried out in various domains of the field of physics of cancer providing a rich overview including mathematical modelling, computational biophysics, statistical physics, experimental data and radiation biophysics. The book can be of interest for all those researchers that would like to enter the field or those who are simply interested in it, and would like to have an overview of some of the problems typically tackled in the physics of cancer community.

The textbook *Dynamics of Cancer: Mathematical Foundations of Oncology* [14] is written by a professor of theoretical and computational biology and a professor of mathematics with a background in physics. This is truly a textbook, which even includes some teaching aids. It deals with both deterministic and stochastic mathematical models, and the use of ordinary differential equations, partial differential equations or cellular automata. The book is divided into three parts. The first part Basic Growth Dynamics and Deterministic Models deals with concepts coming from population dynamics which are used to explain basic models of tumour growth. The second part, Evolutionary Dynamics and Stochastic Models, describes the evolutionary dynamics of tumour initiation in different situations, and a stochastic modelling of cancer growth, treatment and resistance generation. A final part on Advanced Topics concludes with chapters on immune responses, tumour growth and therapy; evolutionary dynamics of stem cell-driven tumour growth; and some other more specialised topics. This book can be useful as an introduction to some of the mathematical techniques commonly used in the physics of cancer research. I believe that this textbook can be very beneficial for many people, including advanced undergraduate and in particular graduate students and early researchers, providing a broad picture of the subject of dynamics of cancer and its mathematical aspects.

The last textbook *Introduction to Mathematical Oncology* [15] is written by a mathematician, a biologist with a background in mathematical biology and a biomedical engineer. The textbook has been tested by the authors in lectures with students and is clearly written for pedagogical purposes. It contains 13 chapters covering introductory cancer modelling and models of tumour growth, evolutionary ecology of cancer, models of chemotherapy, radiation therapy and chemical kinetics. Furthermore, it also contains exercises, projects and open questions, and even mathematical open questions, all of them very helpful for the students to learn about cancer dynamics. Consequently, it can be used for an undergraduate or a graduate course in mathematical modelling on cancer dynamics. It also includes some MATLAB computer codes to reproduce some figures and to solve some exercises. I also consider that this textbook can be very useful for advanced undergraduate, graduate students and young researchers, and professionals interested in having a background in the mathematical modelling aspects of cancer dynamics.

Physicists and mathematicians are working together and meetings are being organised along with cancer biologists. The physics of cancer is one of the true challenges of our time. Physics of cancer will hopefully become a useful research line and a challenge in the advancement of the contribution of physics to cancer research.

Cancer is a very complex and heterogeneous disease from all different viewpoints. An integration of all sciences, including physics, biology and mathematical modelling along with medicine, is needed to definitively confront the war against cancer.

Sir William Osler, one of the fathers of modern medicine, stated at the turn of the nineteenth century that "Medicine is a science of uncertainty and an art of probability". The familiarity of physicists with uncertainties and probabilities will undoubtedly mean that medicine will be enriched by physicists' contributions.

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Miguel A. F. Sanjuán
*Department of Physics, Universidad Rey Juan Carlos, Móstoles, Spain*
miguel.sanjuan@urjc.es http://orcid.org/0000-0003-3515-0837


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