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# Outlook on the Physics of Cancer: A New Interdisciplinary Area

In this book, we have tried to define the expanding boundaries of the relatively new field of the physics of cancer. Traditionally, physicists have contributed to cancer research mostly through the development of novel diagnostic and imaging tools. Things started to change in the last few years when physicists became more and more involved in trying to understand the roots of cancer and its development, bringing to the field their experience with quantitative modeling and data analysis. The basic idea is that cellular processes should ultimately obey the laws of physics: cell migration or mitosis occurs thanks to physical forces; tumors grow into tissues and are thus subject to mechanical and hydrodynamic forces. To understand these issues one needs to perform quantitative measurements and develop theoretical models as physicists have been doing for centuries.

In the last few years, cancer research witnessed the emergence of several promising new avenues deserving further investigation. Biology is currently undergoing a real revolution brought by the sheer growth of readily available quantitative data on all kind of biological processes in general and on cancer in particular. A considerable international effort is currently underway to assemble large databases of genetic mutations, transcriptomes and miRNA for all kinds of tumors from hundreds or sometimes thousands of patients. The ultimate goal of these efforts is to pave the way to a new type of personalized or precision medicine in which treatment will be tailored to the specific genetic and epigenetic features of each patient. Traditional training in biology is, however, often insufficient to deal with the mathematical and computational complexity associated with big data, which are instead the bread-and-butter of physicists. So while these big projects are not driven by physics, many of the people involved were trained in physics.

While genetic, transcriptomic, proteomic and metabolomic data are steadily accumulating in public databases, their interpretation is still a pressing challenge. The first problem stems from the fact that often data in different experiments are recorded using various methods with differences in normalization, formatting and



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notation. Hence it is often hard to treat and compare different data sets at the same time. Efforts are, however, underway to produce and assemble publicly available homogeneous databases for cancer, like TCGA (`https://tcga-data.nci.nih.gov/tcga/`). Studying large data sets could help answer fundamental questions about the emergence of tumors. Cancer is a multifactorial pathology that reflects the complex regulatory network inside the cell. Finding main hubs of this network, and the different ways it can function when perturbed, is a challenging task for the future.

Among the relevant and promising themes where we expect a contribution coming from physical sciences, we would also like to mention the role of chromatin conformations in gene regulation (Risca and Greenleaf, 2015). Cancer cells are characterized by wide chromatin alterations (see section 8.3), suggesting an important, but yet unclear, regulatory role of chromatin conformations (Reddy and Feinberg, 2013). Novel chromosome conformation capture techniques allow a precise map of chromatin topology to be obtained, and in particular of the location of contact points between chromatin domains (Giorgetti et al., 2014). A quantitative interpretation of three-dimensional DNA conformations would require the development of accurate large-scale numerical simulations (Dans et al., 2016). The problem is complex because of the multiple hierarchical scales involved (Gibcus and Dekker, 2013), from the small-scale behavior of single nucleotides that require methods based on quantum mechanics, such as *ab initio* molecular dynamics and quantum Montecarlo, to larger scales that can be approached by classical molecular dynamics or molecular mechanics that can overcome the typical timescale limitations of the former method. Atomistic methods, however, are unable to model large-scale chromatin topological features which require coarse-grained approaches such as polymer models (Dans et al., 2016).

The key role of the immune system in controlling each function of the organism is so important that understanding its regulation could help fight cancer. Indeed, a promising avenue for therapeutic intervention relies on strengthening the immune response against tumors or on weakening the mechanisms by which tumors evade the immune system. These interactions between immunity and cancer are very intriguing and complex topics which could benefit from quantitative methods and models.

This book aims to contribute to the training of a new generation of biologists and cancer researchers who should be able to combine the standard laboratory skills of biochemistry, cell biology and imaging with mathematical and computational tools for analysis and modeling. While we are still far from this goal, we are convinced that future cancer biology should not be completely removed from mathematical theories but should instead embrace them. Experiments will still remain informative but, as the amount of data grows, quantitative modeling and computational

analysis will become imperative to disentangle its complexity. There is an enormous amount of knowledge to be gained from transforming a biological "cartoon" into a mathematical model. As was recently noted by Rob Phillips, in biological papers, theory, if present at all, is currently relegated to the last figure (Phillips, 2015). This is strikingly different in physics, where theory can not only appear in the first figure, but can span entire papers and even research fields. The suspicion against theorists is extraordinarily well rooted in biology: more than a century ago, the Nobel prizewinner Santiago Ramon y Cajal, in his advice to young investigators, warned against theorists, ranked alongside megalomaniacs and contemplators (Ramon y Cajal, 1897). It is slightly ironic that only a few years later, Albert Einstein, a theorist, was revered as the iconic physicist. One century later, it is probably the right time to overcome these distinctions and let theorists and experimentalists work together in biology.

While a physics training can be useful to tackle the complex problems posed by cancer research, it is by no means sufficient. There is an enormous body of sophisticated knowledge on the biological processes ruling cell behavior that cannot be ignored. The present book tries to distill the minimal and essential information needed by physicists to orient themselves in cancer research. We hope that we succeeded in this admittedly complicated endeavor.