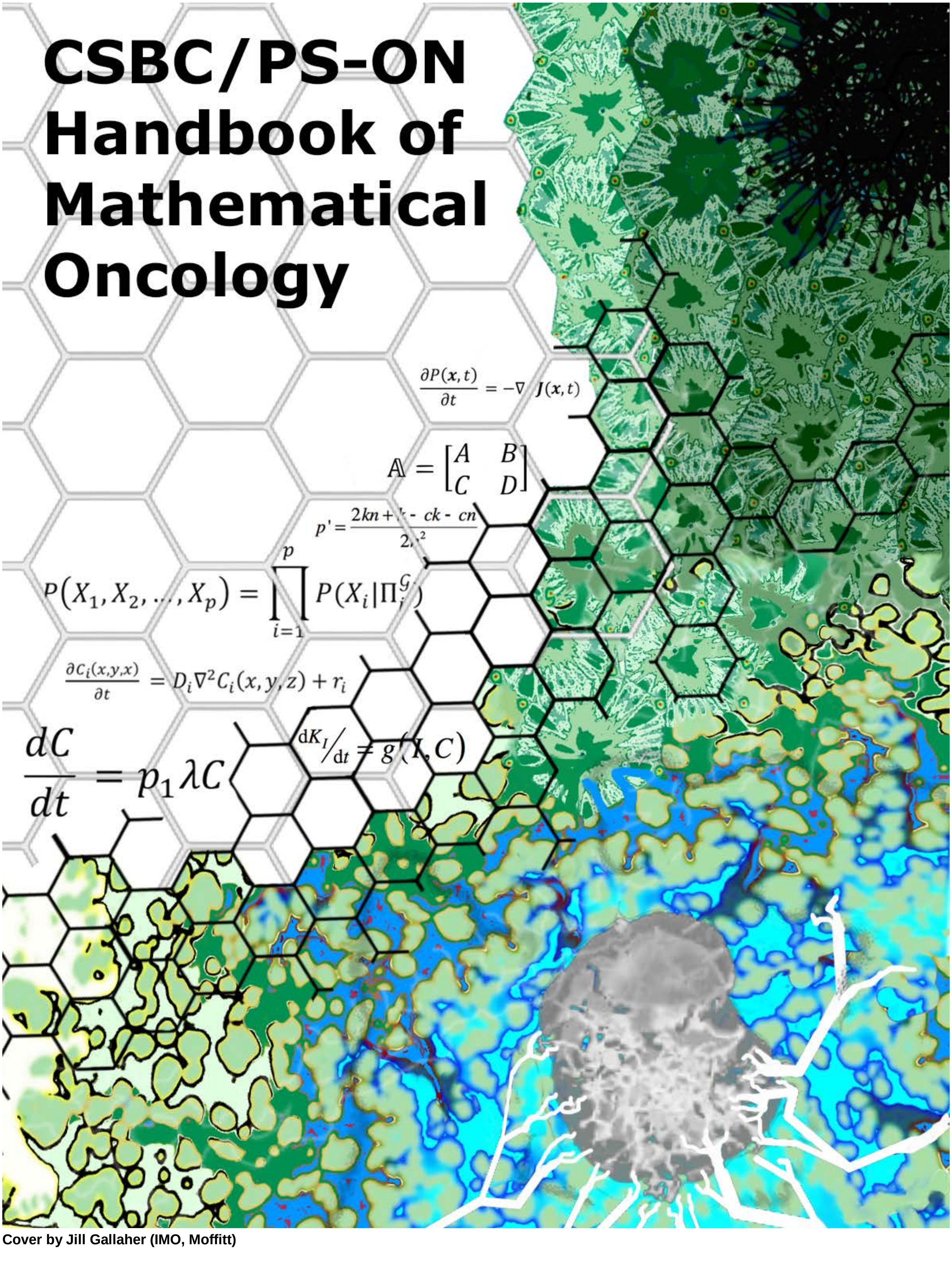
CSBC/PS-ON Handbook of Mathematical Oncology



Cover by Jill Gallaher (IMO, Moffitt)

Mathematical Oncology: Birthing A New Discipline

History of mathematical modeling in cancer biology research

Cancer modeling has a storied history with more than a half century of theoretical and computational models of cancer that seek to explain oncologic phenomena. (Figure 1). Early efforts in mathematical oncology were challenged by the inherent divide between ivy-towered defined disciplines, with discoveries being driven from either the mathematical and physical sciences side or from the biomedical side without a strong integrating tie between these effectively independent silos. Transformative progress in traversing these hurdles was hindered by many obstacles, arguably the largest of which was a lack of team-science-focused funding which resulted in few projects integrating expertise from both the physical sciences and the biomedical perspective. Relatedly, there was (and some would say is) a lack of academic rewards (promotion in the academic setting) for work at such a scientific interface. In addition, there were very few outlets to publish truly integrated research since most journals specialized in only one discipline and research at the interface rarely satisfied reviewers.

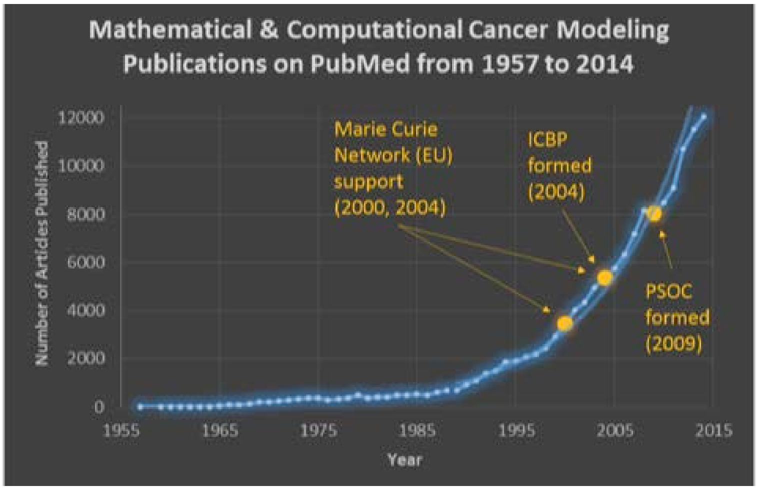


Figure 1: Exponential growth in cancer modeling publications from PubMed (1957-2014).

Despite these and other challenges, a growing passion for improving our understanding of cancer and oncology, led to a slow but steady progress and a provided a few notable successes that caught the attention of the greater cancer community. Many of those successes are outlined in the sets of mini-articles included in this resource, but several key review papers independently document this progress (12540881; 17629503; 18273038; 20179714; 23565501; 24511383; 24607841; 26597528) to name but a few.

A central effort that has enabled the growth of Mathematical Oncology was the engagement of federal funding agencies including those in the European Union and the US. These funding initiatives included, but were not limited to, the Marie Curie Research Training network in the EU (2000) and both the Integrative Cancer Biology Program (ICBP, 2005) (now known as the Center for Systems Biology of Cancer, CSBC, 2010) and the Physical Sciences-Oncology Centers (PS-OC, 2009) (now known as the Physical Sciences-Oncology Network, PS-ON, 2015) funded by the NCI in the US. Acknowledging that mathematical and physical sciences can provide a unifying language for quantifying and understanding cancer systems, these programs helped bridge the divide between disciplines. Promotion through these programs helped crystalize the Mathematical Oncology field to be more data-driven and biologically and clinically relevant. Particularly, these programs reinforced the value of data-driven models that truly integrate across disciplines to provide biologically relevant results that are both testable and clinically relevant. Further, these programs emphasized that there was no single correct model of cancer but that different quantitative tools could elucidate different aspects of the complex adaptive cancer system. As a result, key journals in field began to embrace more integrated approaches (e.g. Cancer Research added a Mathematical Oncology section) and new journals were developed specifically for this purpose (e.g. Integrative Biology, Royal Society Interface, Physical Biology, Convergent Science Physical Oncology). Bridging disciplines was now considered much more of a strength, rather than a risk, for prospective employers which has led to a new generation of integrated scientist that embraces both theoretical and experimental tools.

Current practices in mathematical oncology cover the spectrum from basic sciences through clinical practice. Obviously, such a wide breadth requires an analogously wide tool set. On the basic sciences end, the focus is on understanding and discovering new biological mechanisms through quantitative methods. The complexity of these models is limited by the types of information that can be collected and tested in the experimental setting. Generally speaking, one can measure more elements of interest in the experimental setting, which leads to more complex models. In the clinical setting, however, data is often much more limited and, by necessity, models are simpler. The end goal is the development of quantitative or predictive models that describe the patient's pathology in terms of component parts contributing to the complex system. While, acknowledging the multiple scales of complexity at play within the cell, within the tumor, within the patient and within the population, the ability of models to bridge these scales cannot be underestimated. In fact, a major contributing factor to the greater acceptance of integrated approaches has been the realization that the reductionist paradigm had limitations when it came to understanding how the component parts work together as a system. Further, the growth in data-driven and quantitative cancer biology and medicine discovery has been a central driver in our pursuit to go from genotype to phenotype, from mouse to human and from bench to bedside.

Why this resource is needed

The biannual Mathematics of the PS-OC and ICBP workshops were held in Berkeley (2010), Tampa (2012) and again in Tampa (2014) and were designed to help nurture the developing mathematical oncology community. They primarily served as a key forum for theoretical modelers of cancer to meet and discuss the computational and mathematical challenges faced, the creative solutions to those challenges, work in progress, and opportunities for sharing and collaboration across programs. These meetings also provided an opportunity for participants to go into much more depth concerning the theoretical tools and approaches than is normally possible in the context of the larger annual program meetings. A direct product of these meetings was a desire to create a shared resource of cancer models and modeling approaches in the form of short and succinct mini-papers with the intention to act as a broader resource that would be enduring for the entire community. This resource is intended to provide an underpinning of key methods, concepts and approaches underlying state-of-the-art mathematics and physical sciences in oncology. It is by no means exhaustive, but intended to organically grow as new innovative methods are developed and applied both within and eventually outwith the CSBC and PS-OC programs. Metrics defining the ongoing success of these federal initiatives include items like this resource/booklet. Additionally, this resource provides a central home for those interested in learning more about the field of mathematical oncology.

How to find and contribute to the resource

The Mathematical Oncology bioRχiv channel: http://connect.biorxiv.org/relate/summary.php?col=1

Our plan is to initially grow this resource through additional contributions from the PS-ON and CSBC initiatives. Eventually, through appropriate governance, we will open this completely to the greater mathematical and computational cancer modeling community.

On Behalf of the Organizing Committee,

Alexander R. A. Anderson, Jennifer Couch, Dan Gallahan, Nicole Moore, Kristin R. Swanson & Claire Tomlin.