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Tutorials in Mathematical Biosciences III

Cell Cycle, Proliferation, and Cancer

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Preface

This is the third volume in the series "Tutorial in Mathematical Biosciences". These lectures are based on material which was presented in tutorials or developed by visitors and postdoctoral fellows of the Mathematical Biosciences Institute (MBI), at The Ohio State University. The aim of this series is to introduce graduate students and researchers with just a little background in either mathematics or biology to mathematical modeling of biological processes. The first volume was devoted to mathematical neuroscience, which was the focus of the MBI program in 2002–2003. The second volume dealt with mathematical modeling of calcium dynamics and signal transduction, which was the focus of the MBI program in the winter of 2004. Documentation of these activities, including streaming videos of the workshops, can be found on the web site http://mbi.osu.edu.

The present volume is devoted to the topics of cell division cycle, tumor growth, and cancer chemotherapy. These topics were featured in three MBI workshops held during the fall of 2003. The first chapter gives an overview of the modeling of cell division cycle. This is a process of replicating the genetic material as well as other cellular components of the cell. The emphasis here is not on the biochemistry, but rather on the dynamics arising from the topology of the network of molecular interactions.

Chapters 2–4 deal with various aspects of tumor growth. At the early stage of tumor growth, the tumor cells receive nutrients (oxygen, glucose, etc.) from the blood, which circulates in the vasculature. However, as the tumor grows, the blood supply is unable to keep up with the demand: Indeed, cells which reside in the core of the tumor do not receive enough nutrients and they become necrotic. In order to enable its continued growth, the tumor secretes growth factors and, as a result, new blood vessels are formed and move into the tumor in a process called angiogenesis. The mathematical model and analysis of this process are described in Chap. 2. By the time a tumor has grown to a size that can be detected, there is a strong likelihood that it has already reached the vascular growth phase. Chapter 3 deals with this situation by developing a mathematical model exploring the process that enables the

tumor to "soften" the extracellular matrix and invade the neighboring tissue. This invasion may eventually lead to cancer metastasis. Chapter 4 is concerned with the interaction between tumor cells and immune cells. It develops a model of tumor growth which includes tumor-infiltration cytotoxic lymphocytes in a relatively small tumor prior to tumor-induced angiogenesis. The models in Chaps. 2–4 are based on partial differential equations.

Chapter 5 deals with cancer chemotherapy. Two major obstacles to successful chemotherapy of cancer are cell-cycle phase dependence of treatment, and emergence of resistance of cancer cells to cytotoxic agents. The chapter develops optimal control models with the aim of making chemotherapeutic processes more successful.

Finally, Chap. 6 gives an overview of mathematical models of solid tumors and cancer therapy which developed in the last several decades. Here the emphasis is on novel mathematical problems. The models are generally based on partial differential equations in a domain, the tumor region, which is one of the unknowns of the problem. The chapter presents open problems for mathematicians.

I wish to express my appreciation and thanks to Baltazar Aguda, Howard Levine, Marit Nilsen-Hamilton, Mark Chaplain, Anastasios Matzavinos, Marek Kimmel, Georgios Lolas and Andrzej Swierniak for their marvelous contributions. I hope this volume will serve as a useful introduction to those who want to learn about important and exciting problems that arise in modeling of cell division cycle, cell proliferation, and cancer.

Ohio
September 2005 *Avner Friedman*

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