

PREFACE:
**SPECIAL ISSUE ON CANCER MODELING,
ANALYSIS AND CONTROL**

This special issue of Discrete and Continuous Dynamical Systems Series B in *Cancer Modeling, Analysis and Control* originated as a result of the Casablanca International Workshop on Mathematical Biology, held in Casablanca, Morocco from June 20-24, 2011. This five-day workshop was aimed at: (1) bringing together US, international, and African experts in the field of mathematical biology to exchange ideas, (2) advancing the state of research in the field of mathematical modeling of infectious and in host diseases, and (3) providing a platform for the participants to explore opportunities for collaboration across disciplinary boundaries, as well as across countries and continents. The general themes of the workshop were the modeling and analysis of infectious diseases in Africa such as HIV, tuberculosis, influenza, malaria, cholera, and within-host diseases such as cancer. A particular focus of this workshop was on the analysis and control of cancer models.

This volume brings together a range of articles by some of the invited participants of the workshop as well as other mathematicians and applied scientists who were not able to attend the workshop, but were very happy to contribute to this special issue. A total of eleven papers were contributed to this special issue of the DCDS-B as follows:

N. Bellomo, A. Bellouquid, J. Nieto, and J. Soler, “Modeling Chemotaxis from L^2 -Closure Moments in Kinetic Theory of Active Particles.” The authors propose a methodological approach to derive macroscopic models of biological tissues from the underlying description at the microscopic scale, as delivered by the kinetic theory for active particles. The approach is specifically focused on the modeling of chemotaxis phenomena by the Keller-Segel approximation which incorporate flux-limited terms. They can be specifically applied to model different types of biological phenomena where pattern formation occurs, such as angiogenesis and vascular morphogenesis.

F. Bill, and J. Clairambault, “Designing Proliferating Cell Population Models with Functional Targets for Control by Anti-Cancer Drugs.” The authors present a survey of mathematical models of proliferating cell population dynamics designed to theoretically solve problems of therapeutic optimization encountered in the clinic of cancers. As review, this paper provides a comprehensive survey of the literature and summarizes the “state-of-the-art” in the field.

L. de Pillis, T. Caldwell, E. Sarapata, and H. Williams, “Mathematical Modeling of Regulatory T-Cell Effects on Renal Cell Carcinoma Treatment.” The authors formulate a mathematical model describing the dynamics of the interactions between tumor cells, T-regulatory (T_{reg}) cells and other immune cells, including the inhibitory effect of sunitinib on T_{reg} , and how these interactions might vary according to patient-specific immune strength. They demonstrate that the model with the chosen parameter set can give simulated results that qualitatively and quantitatively reflect clinical data.

M. Delitala, and T. Lorenzi, “Recognition and Learning in a Mathematical Model for Immune Response Against Cancer.” The authors describe a mathematical model for the immune response against cancer. This model outlines the evolution of cancer cells characterized by heterogeneous antigenic expressions and exposed to the action of antigen presenting cells and T-cells. The proposed modeling approach takes into account mutation, proliferation and competition phenomena involving tumor cells as well as tumor-immune interactions.

H. Jain, and A. Friedman, “Modeling Prostate Cancer Response to Continuous Versus Intermittent Androgen Ablation Therapy.” The authors formulate and analyze a mathematical model of prostate cancer progression based on detailed intracellular androgen-mediated signaling, with the aim of predicting optimal treatment protocols based on individual patient characteristics. The model predicts that, while a cure is not possible for androgen-independent castration-resistant cells, continuous therapy results in longer disease-free survival periods.

Y. Kim, and S. Roh, “A Hybrid Model for Cell Proliferation and Migration in Glioblastoma.” The authors develop a hybrid model of glioblastoma that identifies a key mechanism behind the molecular switches between proliferative phase and migratory mode in response to metabolic stress and biophysical interaction between cells. They show that cell migration not only depends on glucose availability but also on mechanical constraints between cells. The mathematical analysis of the core system predicts that periodic injection of glucose will lead to the periodic transition between the migratory and proliferative modes. The authors also indicate several directions for further development of in vivo and/or in vitro glucose-assisted invasion hybrid models.

Y. Kogan, Z. Agur, and M. Elishmereni, “A Mathematical Model for The Immunotherapeutic Control of The Th1/Th2 Imbalance in Melanoma.” The authors develop a model for the Th1/Th2 imbalance in melanoma patients and its regulation via IL-12 treatment. Their results suggest that in melanoma, the cellular arm of the immune system cannot reverse tumor immunotolerance naturally, and that immunotherapy may be the only way to overturn tumor dominance. These results can help to understand the role of cytokines in such immune reactions, and therefore to propose better treatment protocols in the future.

S. Nanda, L.G. dePillis, A. Radunskaya, “B Cell Chronic Lymphocytic Leukemia: A Model with Immune Response.” The authors present a mathematical model of B cell chronic Lymphocytic Leukemia (B-CLL) with immune response, that can capture both rapid and slow disease progression. They show that the immune system plays an important role in the progression of B-CLL observed in the clinic. The compartmentalized form of the model presented in this paper, which separates out NK, T and helper-T cell dynamics, provides a useful starting point to modeling treatments that target these specific populations.

V. M. Savage, A. B. Herman, G. B. West, and K. Leu, “Using Fractal Geometry and Universal Growth Curves as Diagnostics for Comparing Tumor Vasculature and Metabolic Rate with Healthy Tissue and for Predicting Responses to Drug Therapies.” The authors provide a fractal analysis of existing vascular data, and present a new mathematical framework for predicting tumor growth trajectories by coupling: (1) the fractal geometric properties of tumor vascular networks, (2) metabolic properties of tumor cells and host vascular systems, and (3) spatial gradients in resources and metabolic states within the tumor. Taken together, this new

integrated mathematical framework will help to anticipate and understand growth trajectories across tumor types and drug treatments.

H. Schattler, U. Ledzewicz, and M. Faraji, “Optimal Protocols for a Mathematical Model of Tumor-Immune Interactions under Chemotherapy with Immune Boost.” The authors formulate an optimal control problem that combines the cancer chemotherapy agent with the immunotherapy in form of a boost to the immune system as a multi-input optimal control problem. The analytical and numerical results about the structures of optimal controls provide some insights into the structure of optimal protocols, i.e., the dose rates and sequencing of the drugs in these combination treatments.

X. Zheng, G.Y. Koh, T. Jackson, “A Continuous Model of Angiogenesis: Initiation, Extension, and Maturation of New Blood Vessels Modulated by Vascular Endothelial Growth Factor, Angiopoietins, Platelet-Derived Growth Factor-B, and Pericytes.” The authors propose a continuous model of angiogenesis, which addresses all three initial stages of new blood vessel growth: initiation, extension, and maturation. The mathematical analysis and numerical simulations of the model presented in this paper successfully capture the experimental observations in corneal angiogenesis.

We thank all of the contributing authors for their hard work that made this DCDS-B special issue a reality. We also thank the reviewers for their dedicated efforts and valuable comments. We sincerely thank the excellent DCDS-B editorial team for their professional help, patience, guidance, and skillful editing of this special issue.

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Guest Editors:

Amina Eladdadi
The College of Saint Rose
Albany, NY, 12203, USA
eladdada@strose.edu

Noura Yousfi
Hassan II-University
Faculty Des Sciences, Ben M’Sik
Casablanca, Morocco
nourayousfi@gmail.com

Abdessamad Tridane
School of Letters and Sciences
Arizona State University
Mesa, AZ, 85212, USA
atridan@asu.edu

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