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Modeling Paradigms and Analysis of Disease Transmission Models

Abba B. Gumel
Suzanne Lenhart
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American Mathematical Society

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and Theoretical Computer Science
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This DIMACS volume presents selected papers from the U.S.–Africa Advanced Study Institute on Mathematical Modeling of Infectious Diseases in Africa, held at the African Institute for Mathematical Sciences, Muizenberg, South Africa, from June 11–22, 2007, and the DIMACS Workshop of the same name, hosted by the South Africa Centre for Epidemiological Modeling and Analysis, Stellenbosch, South Africa, from June 25–27, 2007.

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Foreword

In recent years, mathematical modeling of infectious diseases has had an increasing influence on the theory and practice of disease management and control with such diseases as HIV/AIDS, foot-and-mouth disease, and H1N1 virus, and this is increasingly the case with diseases of Africa. In order to understand and prevent the spread of infectious diseases endemic to or emanating from Africa, it is vitally important to train a cadre of workers who are both knowledgeable about modeling and about disease contexts and data gathering in Africa. The success of recent joint US-African modeling studies points to the major advantages of such collaborations while at the same time pointing to the vital need for more trained researchers from both sides. To address the issue of training researchers knowledgeable about African diseases and expert in mathematical modeling of disease, DIMACS, in collaboration with the South African DST/NRF Centre of Excellence in Epidemiological Modeling and Analysis (SACEMA) and the African Institute for Mathematical Sciences (AIMS), held a two-week advanced study institute (ASI) on mathematical modeling and infectious diseases in Africa, culminating in a subsequent 3-day "capstone" workshop at which ASI students and researchers from both the US and Africa interacted and established collaborations. The ASI and workshop gave rise to this volume, though it is by no means a proceedings of those two events and, in fact, is aimed at laying out in an organized way some of the major themes of infectious disease modeling, with special emphasis on infectious diseases of Africa.

The ASI, held at AIMS in Cape Town, South Africa, on June 11-22, 2007, was aimed at training junior US and African participants (graduate students and postdoctoral fellows) in mathematical epidemiology and the control of emerging and re-emerging diseases. The capstone workshop, held at Stellenbosch University, Stellenbosch, South Africa, on June 25-27, 2007, was a culmination of the ASI, enabling ASI students to participate fully in a workshop involving active US and African researchers and aimed at furthering research on the modeling of diseases in Africa. The ASI emphasized basic mathematical techniques used in modeling and reviewed key diseases of Africa. It then introduced the basic ideas of epidemiological modeling, including classical epidemic models such as SIR, SIS, and SEIR; structured modeling; deterministic vs. stochastic models; and uncertainty and sensitivity analysis. It went on to more advanced topics such as meta-population modeling; continuous vs. discrete-time stochastic models; models with vertical transmission; spatial and individual-based models; age structure; and optimal allocation of disease control resources such as vaccine and antiviral doses.

Speakers at the capstone workshop discussed the design and evaluation of cost-effective and sustainable strategies for combating disease spread in Africa, with emphasis on modern statistical tools for surveillance, network methods to elucidate patterns of spread, and evolutionary aspects of endemic African diseases. Challenges from and opportunities arising from increasing availability of data from African studies were discussed. A second theme involved the potential consequences of emerging and re-emerging diseases, in the context of shortage of resources. Speakers addressed drug resistance to tuberculosis, challenges from HIV and malaria, and alternative interventions for pandemic flu, including vaccination, targeted antiviral prophylaxis, and quarantines. Finally, a special session introduced the rapidly-emerging topic of "economic epidemiology," with its emphasis on health economics and the economic aspects of disease burden.

These activities were part of the DIMACS Special Focus on Computational and Mathematical Epidemiology. One specific special focus workshop was instrumental in leading us to develop this DIMACS activity. This was a workshop on "Evolutionary Aspects of Vaccine Use," organized at DIMACS in June 2005, and stemming from the work of the DIMACS working group on Methodologies for Comparing Vaccination Strategies. The special problems of vaccination strategies in Africa that arose in this workshop were one of the primary motivations that led Abba Gumel, one of the editors of this volume, to propose that DIMACS sponsor a workshop that would directly focus on mathematical modeling of infectious diseases in Africa.

A second activity that led to the DIMACS African activities was the summer research conference on "Modeling Dynamics of Human Diseases: Emerging Paradigms and Challenges," held at Snowbird in Utah July 17-21, 2005. One notable feature of the conference was the recognition of the central role of developing nations in the emergence of novel pathogens, and the need to involve researchers from these nations in addressing problems of the spread of disease. This recognition was central in motivating meeting participant Simon Levin, a major leader of the DIMACS Special Focus, to suggest that we pursue ways to more directly engage US researchers and students with African researchers and students.

In turn, the DIMACS African activities that led to this volume have led to a major US-African-Canadian Bio-Mathematics Initiative that includes ASIs and workshops in Uganda, Kenya, and Madagascar, modeled after those in South Africa.

DIMACS thanks Professors Gumel and Levin for their efforts in promoting the ASI and workshop on Mathematical Modeling and Infectious Diseases in Africa. Special thanks go to the Directors of SACEMA and AIMS, John Hargrove and Fritz Hahne, respectively, for their scientific, administrative, and financial support. Brenda Latka of DIMACS played a major role in helping to administer the ASI and workshop and Latka, Wayne Getz, Gumel, Hahne, Hargrove, Levin, Edward Lungu, and Alex Welte helped to organize it. Others who played an important role in developing the concept and scope of the ASI and workshop were Dominic Clemence, Ronald Mickens, Asamoah Nkwanta, and Abdul-Aziz Yakubu. DIMACS is extremely grateful to all of these people for their involvement and support in its African initiatives. Finally, DIMACS thanks Gumel and Suzanne Lenhart for their efforts in putting this volume together.

DIMACS gratefully acknowledges the generous support that makes its programs possible. Special thanks go to the National Science Foundation, under grant 0629720 to Rutgers University, which made the ASI and workshop that led to this book possible. Thanks also go to the DIMACS partners at Rutgers, Princeton, AT&T Labs - Research, Alcatel-Lucent Bell Labs, NEC Laboratories America,

and Telcordia Technologies, and affiliate partners Avaya Labs, Georgia Institute of Technology, HP Labs, IBM Research, Microsoft Research, Rensselaer Polytechnic Institute, and Stevens Institute of Technology.

Fred S. Roberts
DIMACS Director

Preface

This volume is a product of two activities under the auspices of DIMACS Special Focus on Computational and Mathematical Epidemiology, namely the U.S.-Africa Advanced Study Institute (ASI) on Mathematical Modeling of Infectious Diseases in Africa, which took place at the African Institute for Mathematical Sciences (AIMS), Muizenberg, South Africa, June 11-22, 2007, and the DIMACS Workshop on Mathematical Modeling of Infectious Diseases in Africa, hosted by the South Africa Centre for Epidemiological Modeling and Analysis (SACEMA), Stellenbosch, South Africa, on June 25-27, 2007. About 50 graduate students, from across Africa and the USA, attended the ASI, and a total of about 80 people attended the workshop.

The volume consists of two types of papers: tutorial papers and research papers. While the tutorial papers introduce the basic and general principles, concepts, challenges and types of disease modeling, the research papers focus on advanced topics associated with the mathematical modeling (and analysis) of diseases relevant to Africa.

The tutorial-type papers cover topics such as basic principles and framework for modeling diseases, classical (Kermack-McKendrick type) epidemic models, modeling challenges, basic methods of analysis, epidemiological thresholds, uncertainty and sensitivity analysis and the interpretation of the analytical and simulation results obtained. In addition to the aforementioned basic topics, the volume also contains papers on more advanced topics. These include papers on optimal control techniques in disease modeling, design and analysis of discrete-time models, the role of stochasticity in disease modeling, economic aspects of disease modeling and control (including the use of greedy algorithms to obtain optimal solutions) and some advanced dynamical systems techniques for qualitatively analyzing relatively large disease transmission models. Some of these papers address the problem of the transmission dynamics and control of some diseases that inflict major socio-economic and public health burden in Africa, notably HIV and HIV-TB co-infection.

The Editors are very grateful to all those who contributed papers to the volume (S. Shrestha, J. O. Lloyd-Smith, E. M. Lungu, M. Kgosimore, F. Nyabadza, R. Miller Neilan, S. Lenhart, A.-A Yakubu, W. Ding, J. Dushoff, M. S. Sánchez, B. G. Williams, W. Getz, S. D. Hove-Musekwa, V. Runyowa, Z. Mukandavire, O. Sharomi, A. B. Gumel and F. Roberts). In addition to the great scholarly contributions of the authors, this volume would not have been possible without the support of the sponsors of the ASI and the workshop in Stellenbosch, namely AIMS, DIMACS, The U.S. National Science Foundation and SACEMA.

The Editors are immensely grateful to Fred Roberts, who made the whole U.S.-Africa program possible. We are thankful to the DIMACS staff (notably, Margaret Barry Cozzens, Gene Fiorini, Brenda Latka, Christine Spassione and Ricardo Collado) and Ms. Christine Thivierge (Editorial Assistant, AMS) for their support. Finally, we are very grateful to the many anonymous reviewers who helped in reviewing the contributed papers. The Editors are also very thankful to Simon Levin for writing the Prologue to this volume.

Abba Gumel and Suzanne Lenhart
January 23, 2010

Prologue

In recent years, computational biology has become one of the hottest areas in science, spawning new journals, new scientific societies, new departments, and new training programs for undergraduates and graduates. The challenges of genomics and systems biology have attracted leading scientists from other disciplines—in particular physics, computer science and mathematics—who have been motivated to bring their skills to bear on some of the most important and fundamental problems facing humanity. Indeed, the excitement of the advances in genomics, and in certain branches of systems biology, has to some made these applications synonymous with the field of "computational biology." It therefore often comes as a surprise when people learn that computational biology is a very old field, tracing back more than a century, and with roots firmly planted in population genetics and in epidemiology.

The mathematical description of the dynamics of infectious diseases is one of the oldest and most successful branches of quantitative science, tracing back at least a century to the landmark malaria models of the Nobel Laureate, Sir Ronald Ross. It has remained a vibrant area of research since Ross, a subdiscipline with a rigorous theoretical foundation, a highly developed mathematical and statistical framework, and strong contact with data and with management. The concepts of theoretical epidemiology have played fundamental roles in understanding disease dynamics, and in the optimal application of vaccination and other management strategies. This volume continues that tradition, with papers by some of the leading researchers of the subject.

Infectious diseases kill millions of people worldwide every year, and sicken billions of others. Africa has always been a cauldron of devastating diseases, and malaria remains one of the world's greatest killers. Despite the heroic efforts of Ross and others, malaria remains at the top of the world's public health agenda, developing resistance to wonder drugs and frustrating public health workers. Charitable foundations, like the Gates Foundation, have thus placed the elimination or control of malaria and other diseases, especially in Africa, at the tops of their agendas; but money alone cannot solve the problems. We need new approaches, new insights, and new methodologies. The quantitative study of infectious diseases has made remarkable advances in the years since Ross, and powerful new mathematical, statistical and computational tools are available; but much more needs to be done.

It is thus urgent that quantitative biologists increase their efforts to attack the problems of infectious diseases in the African subcontinent, and that has led DIMACS to sponsor a variety of ongoing efforts to address the scientific challenges and to train African scientists in the modern methods of the theory of infectious diseases. This volume is one product of that effort, and will help to strengthen the foundations and the partnerships that have been initiated. It is a mixture of pedagogy and research, building from the foundations of the subject to recent mathematical advances, including especially the application of modern control theory. Most impressively, through a mixture of contributions from U.S., Canadian and African scientists, it is testimony to the vision of Fred Roberts in sponsoring these activities, and to the success of his efforts.

Simon Levin
Princeton University
October 14, 2009

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This volume stems from two DIMACS activities, the U.S.–Africa Advanced Study Institute and the DIMACS Workshop, both on Mathematical Modeling of Infectious Diseases in Africa, held in South Africa in the summer of 2007. It contains both tutorial papers and research papers.

Students and researchers should find the papers on modeling and analyzing certain diseases currently affecting Africa very informative. In particular, they can learn basic principles of disease modeling and stability from the tutorial papers where continuous and discrete time models, optimal control, and stochastic features are introduced.

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