PART I

Overview

CHAPTER 1

Introduction to Analyzing and Modeling Spatial and Temporal Dynamics of Infectious Diseases

Dongmei Chen
Department of Geography, Faculty of Arts and Science, Queen's University, Kingston, ON, Canada

Bernard Moulin
Department of Computer Science and Software Engineering, Faculty of Science and Engineering, Laval University, Québec City, QC, Canada

Jianhong Wu
Department of Mathematics and Statistics, Faculty of Science, York University, Toronto, ON, Canada

1.1 BACKGROUND

Infectious disease spread is a major threat to public health and economy. Based on the statistics of the World Health Organization (WHO), 25% of human death is caused by infectious diseases. The spread of an infectious disease involves characteristics of the agent such as virus and bacteria, the host, and the environment in which transmissions take place. Appropriately modeling and actually predicting the outcome of disease spread over time and across space is a critical step toward informed development of effective strategies for public health intervention (Day et al. 2006; Moghadas et al. 2008; Arino et al. 2011).

Given the ongoing risk of infectious diseases worldwide, it is important to develop appropriate analysis methods, models, and tools to assess and predict the disease

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spread and evaluate the disease risk. In order to ensure better understanding and to design more effective strategies for responding to existing and future disease outbreaks, questions such as the following are often asked:

(a) What are the distributions of diseases across space and how do they interact with their environment? What are their origins, destinations, and spreading channels?

(b) What are the potential spreading patterns of a disease across space and over time given the potential habitats of its host and its environment?

(c) Which diseases will be spread around the globe successfully via global traveling and trading as well as wildlife movement (e.g., bird migration)?

(d) Which parts of regions (or cities) are at the greatest risk of being exposed to a disease given urban and regional host habitats and population distributions as well as intercity and regional transportation networks?

(e) Which population groups are most vulnerable to a disease?

Understanding the spatiotemporal patterns of disease spread is the key to identifying effective prevention, control, and support of infectious diseases. Recognizing the conditions under which an epidemic may occur and how a particular disease spreads is critical to designing and implementing appropriate and effective public health control measures.

Methods and tools are needed to help answer aforementioned questions involving the spatiotemporal patterns, their relevance and implications to humans and ecosystems, their impact on the vulnerability of different populations, and to develop public health policy decisions on disease prevention issues. Multidisciplinary collaboration among experts on different aspects of these diseases is important to develop and utilize these tools.

Advances in geographic information system (GIS), global positioning system (GPS), and other location-based technologies have greatly increased the availability of spatial and temporal disease and environmental data during the past 30 years. These data provide unprecedented spatial and temporal details on potential disease spreads and wildlife/human movements. While this offers many new opportunities to analyze, model, predict, and understand the spread of diseases, it also poses a great challenge on traditional disease analysis and modeling methods, which usually are not designed to handle these detailed spatial–temporal disease data. The development of different approaches to analyze and model the complicated process of disease spread that can take advantage of these spatial–temporal data and high computing performance is becoming urgent.

Through a research project jointly funded by the Canadian Network of Centers of Excellence on Geomatics for Informed Decision (GEOIDE), Mathematics of Information Technology and Complex Systems (MITACS), Public Health Agency of Canada (PHAC), and Institut national de santé publique du Québec, a network of more than 30 researchers coming from academics, government agencies, and

industry in Canada, the United States, France, China, India, and other countries was established in 2008 and has since been conducting collaborative projects in selected diseases representing different modes of transmission dynamics. This network has also organized several workshops on spatial and temporal dynamics of infectious diseases.

This book represents a collection of most recent research progresses and collaboration results from this network of researchers and their collaborators. Twenty chapters contributed by fifty researchers in academic and government agencies from seven countries have been included in this book. As such, the book aims to capture the state-of-art methods and techniques for monitoring, analyzing, and modeling spatial and temporal dynamics of infectious diseases and showcasing a broad range of these methods and techniques in different infectious disease studies.

In the following, we give a brief overview of infectious diseases and the transmission mechanisms of different infectious diseases covered in this book, followed by outlining the structure and contents of this book.

1.2 INFECTIOUS DISEASES, THEIR TRANSMISSION AND RESEARCH NEEDS

Infectious diseases are also known as *transmissible* diseases or *communicable* diseases. The illness of infectious diseases is caused by the infection, presence, and growth of pathogenic biological agents (known as *pathogens*) in an individual host organism. Pathogen is the microorganism (or microbe) that causes illness. Infectious pathogens include viruses, bacteria, fungi, protozoa, multicellular parasites, and aberrant proteins known as prions. These pathogens are the cause of disease epidemics, in the sense that without the pathogen, no infectious epidemic occurs. The organism that a pathogen infects is called the *host*. In the human host, a pathogen causes illness by either disrupting a vital body process or stimulating the immune system to mount a defensive reaction (www.metrohealth.org). Based on the frequency of occurrence, infectious diseases can be classified as *sporadic* (occurs occasionally), *endemic* (constantly present in a population), *epidemic* (many cases in a region in short period), and *pandemic* (worldwide epidemic).

An infectious disease is termed *contagious* if it is easily transmitted from one person to another. The transmission mechanisms of infectious diseases can be categorized as *contact transmission*, *vehicle transmission*, and *vector transmission*. *Contact transmission* can occur by direct contact (person-to-person) between the source of the disease and a susceptible host, indirect contact through inanimate objects (such as contaminated soils), or droplet contact via mucus droplets in coughing, sneezing, laughing or talking. *Vehicle transmission* involves a media. Based on the media type in transmission, the infectious diseases can be categorized as airborne (diseases transmitted through the air such as influenza, anthrax, measles), foodborne (diseases transmitted through the foods such as Hepatitis A and E), and waterborne (diseases transmitted through the water such as Cholera).

A large proportion of infectious diseases are spread through *vector transmission*. A vector is the agent that carries and transmits an infectious pathogen from one host to another (James 2001). Vectors may be mechanical or biological. A mechanical vector picks up infectious pathogens outside of its body and transports them in a passive manner through its movement (such as housefly). The pathogen never enters or impacts the body of the vector. On the contrary, a biological vector lets the pathogen reproduce in its body. Most commonly known biological vectors are arthropods such as mosquitoes, ticks, flies, and bugs. Many biological vectors feed on blood at some or all stages of their life cycles. During the blood feeding, the pathogens enter the body of the host and cause the illness.

Understanding the disease transmission mechanism is important for infectious disease control and prevention. Many factors can influence the spreading patterns of infectious diseases. For diseases with different transmission mechanisms, factors that can impact the disease spread vary. Human mobility and social networks can greatly impact the spread of infectious diseases with contact transmission. Climate and environmental conditions can significantly impact the habitat suitability, distribution, and abundance of vectors. Climate change can influence survival and reproduction rates of vectors and pathogens within them, as well as intensity and temporal pattern of vector activity throughout the year. Human activities such as land use change, habitat disruption, pesticide use can significantly change the vector habitat and media condition, and thus impact the spread of diseases.

Quantitatively analyzing and modeling spreading of infectious diseases under different environmental and climate conditions is not new. Many methods and approaches have been developed to simulate infection process, investigate observed disease patterns, and predict future trends (see Chapter 2 in this book). Much of the past effort on disease modeling has been devoted to mathematical modeling at population level assuming various kinds of homogeneity. However, possible spatial–temporal spread and outcomes of a disease outbreak at different communities and environments usually play even more important roles in determining public health interventions. Spatial analysis, modeling, and simulation of infectious disease transmission provide a plausible experimental system in which information of hosts and vectors and their typical movement patterns can be combined with a quantitative description of the infection process and disease natural history to investigate observed patterns and to evaluate alternative intervention options (Riley 2007).

There are roughly three stages in predicating the transmission of an infectious disease (Rogers and Randolph 2006): (1) identification of the pathogen, its host, and its pathway of transmission among the hosts; (2) determining the spatial transmission pattern of infectious diseases and their environment; (3) understanding the dynamic process of the transmission of the disease using models. However, each of these stages involves significant challenge. The first stage requires effective diagnostic tools and initial exploration of the disease. The second stage involves the survey and quantitative description of the spatial and temporal pattern of the disease, followed by analyzing the relationship of the disease with its environment. The goal of the third stage is to establish quantitative models calibrated with field measurements and surveys.

1.3 DISEASES COVERED IN THIS BOOK AND THEIR TRANSMISSION MECHANISM

In this book several diseases with different disease spread mechanisms, including West Nile virus, Lyme disease, influenza, schistosomiasis, malaria, sexually transmitted diseases, have been used for various analyzing, modeling, and simulation applications in different chapters. Here we briefly outline the transmission process, pathogen, host, and main vectors for each disease.

1.3.1 West Nile Virus

West Nile virus (WNV) is a vector-borne disease with the virus belonging to the genus *Flavivirus* in family Flaviviridae. WNV is known to be transmitted to humans through the bite of an infected mosquito. It was first identified in Uganda in East Africa in 1937 and had been a *sporadic* disease before the mid-1990s. The first large outbreak of WNV was in Romania in 1996. Since then WNV has spread globally and becomes endemic in Africa, Europe, West Asia, North America, and the Middle East. WNV first appeared in the United States in 1999 (Nash et al. 2001) and had spread from New York State to all the 48 continental states of the United States between 1999 and 2005. In Canada, WNV was first detected in Ontario and Québec in 2001 and had spread to seven provinces of Canada by 2003. WNV can cause neurological disease and death in humans. In 2012 alone, the United States had 5674 WNV human cases reported (CDC 2013a), in which 92% cases had illness on-site and 5% (286) died.

WNV is commonly transmitted to humans by female mosquitoes, the prime vector, and it is maintained in nature through a cycle involving transmission between birds and mosquitoes (see the picture at http://www.westnile.state.pa.us/animals/transmission.htm for WNV's transmission cycle). Birds are primary reservoir for WNV. In North America, there are over 17 native bird species that can carry WNV. The WNV-carrying mosquito species vary at different geographical areas. On the east coast of North America, *Culex pipiens* is the main source, while the main species in the Midwest and West are *Culex tarsalis* and *Culex quinquefasciatus* in the Southeast (Hayes et al. 2005). Humans, horses, and other mammals can be infected. When a mosquito bites an infected bird, the virus enters the mosquito's bloodstream. When an infected mosquito bites an animal or a human, the virus is passed into the host's bloodstream and causes serious illness of the host. About 20% of people who become infected with WNV will develop West Nile fever.

1.3.2 Lyme Disease

Lyme borreliosis, more commonly referred to as Lyme disease, is a tick-borne disease caused by the bacterium belong to the genus *Borrelia* (Samuels and Radolf 2010). *Borrelia burgdorferi* is the main bacteria type of Lyme disease in North America. This disease can be transmitted to humans by the bite of certain infected ixodid ticks. Unlike mosquitoes that can transfer WNV to humans with a single bite, the tick has to be attached to the body for at least 24–36 hours. One of the most prominent symptoms

of Lyme is a skin lesion, known as *erythema migrans*. Closely resembling a bull's-eye, this rash can expand up to the width of a person's back from the site of the tick bite. This disease can also cause flu-like symptoms such as fever, headache, and muscle pain at its early stages. Without proper treatment, the bacterium can disseminate to other tissues, affecting joints, neurologic, and cardiac systems (PHAC 2014). Lyme borreliosis has become endemic in many areas of Asia, Europe, and North America and is the most commonly reported vector-borne illness in the United States with a total number of 22,014 confirmed cases in 2012 (http://www.cdc.gov/Lyme/stats/).

The life cycle of the tick undergoes three main developmental stages consisting of larva, nymph, and adult (see Figure 18.1). The life span of the tick range from approximately 2 to 4 years and their development rate depends on the time it takes for the tick to find a host to feed on as a larva or nymph. While ticks may acquire the bacterium at any time during their life cycle and transfer the disease from one developmental stage to the next (Spielman et al. 1985), studies have shown that the tick will not transfer the bacterium vertically via egg from an infected female (Magnarelli et al. 1987). Adult ticks tend to feed and mate on medium- to large-sized mammals, such as humans, white-tailed deer (*Odocoileus virginianus*), dogs, cats, raccoons, bears, and horses (Morshed et al. 2006). As the tick depends on a variety of mammalian hosts for their method of transportation, the spatial distribution of Lyme disease is highly dependent on the spatial variation of its hosts such as small rodents, white-tailed deer, and migratory birds to expand their range (Odgen et al. 2008).

1.3.3 Avian and Human Influenza

Influenza (commonly known as the flu) is a common respiratory disease for birds and mammals caused by RNA (ribonucleic acid) viruses. For humans, the flu virus can be easily passed from person to person and affects the nose, throat, and lungs. The common flu symptoms include fever, runny nose, headaches, coughing, fatigue, muscle pain, and other illness (Eccles 2005).

There are three main types of influenza viruses (A, B, and C), in which A is the main cause of influenza in humans and can cause severe human pandemic (MacKellar 2007). Most influenza virus that caused human pandemic deaths in the history are type A virus, such as H1N1 (which caused Spanish flu in 1918 and Swine flu in 2009), H2N2 (which caused Asian flu in1957), and H7N9 (2013 in China). Wild aquatic birds are the natural hosts for a large variety of influenza A strains. Influenza is transmitted through the air. When an infected person coughs or sneezes, infected droplets containing the virus get into the air and another person can breathe them in and get exposed. The virus can also be spread by hands infected with the virus. Influenza can also be transmitted by direct contact with bird droppings or nasal secretions containing the virus, or through contact with contaminated surfaces.

RNA viruses have been recognized as highly mutable since the earliest studies, and responsible for a variety of medically and economically important diseases of man, plants, and animals (Steinhauer and Holland 1987). Based on the WHO's report, seasonal influenza cause about 3–5 million cases severe illness and about 250,000–500,000 deaths each year. A deadly human influenza pandemic would cause

2–7.4 million deaths worldwide over the course of around 3 months (WHO 2009), and the World Bank estimated that the potential economic cost of a pandemic of human influenza would be as much as US$2 trillion in damages.

All birds are thought to be susceptible to infection with bird flu (or avian) influenza viruses. Depending on the virus strain type, influenza virus can also cause devastating outbreaks in domestic poultry or wild birds. For example, highly pathogenic H5N1 bird-flu virus had hit 53 countries since 2003, caused over 3200 million domestic and wild birds to be killed at a cost of well over US$20 billion, and ruined the livelihood of millions of smallholder farmers. To date (October 2013), H5N1 also caused 641 human illnesses in which 380 died (WHO 2013d).

1.3.4 Schistosomiasis

Schistosomiasis is a water-borne parasitic disease caused by blood flukes (trematode worms) of the genus *Schistosoma*. There are two major forms of schistosomiasis (intestinal and urogenital) caused by five main species of blood fluke, impacting different geographical regions of the world (WHO 2013b). *Schistosomiasis* often causes chronic illness that can damage internal organs. Intestinal schistosomiasis can result in abdominal pain, diarrhea, and blood in the stool. Liver enlargement is common in advanced cases. The classic sign of urogenital schistosomiasis is hematuria (blood in urine). Fibrosis of the bladder and ureter and kidney damage are sometimes seen in advanced cases (WHO 2013b).

Schistosomiasis is transmitted through snails in the water as the intermediary agent with humans being the definitive host (see its life cycle at http://commons.wikimedia.org/wiki/File:Schistosomiasis_Life_Cycle.jpeg). Fresh water contaminated by parasites is the main media of *Schistosomais* spreading. Larval forms of the parasite released by snails in the freshwater can penetrate the human skin when people contact infested water. *Schistosomiasis* is the second most socioeconomically devastating parasitic disease after malaria and has been reported in 78 countries. There were about 28.1 million of people reported to have been treated for schistosomiasis in 2011 (WHO 2013b).

1.3.5 Malaria

Malaria is a vector-borne infectious disease caused by the *protozoan* parasites of the genus *Plasmodium*. The malaria parasite is transmitted to humans via the bites of infected female mosquitoes of the genus *Anopheles*. Of the hundreds of Anopheles species described, approximately 70 have been shown to be competent vectors of human malaria (Hayes et al. 2005). Mosquitoes can become infected when they feed on the blood of infected humans. Thus, the infection goes back and forth between humans and mosquitoes. Malaria causes symptoms that typically include fever and headache, which in severe cases can progress to coma or death. The disease is widespread in more than 100 countries in Africa, Southeast Asia, the Eastern Mediterranean, Western Pacific, Americas, and Europe, in which most are in tropical and subtropical regions around the equator.

Malaria can cause significant economic loss and enormous public health problems. Half of the world population is at risk of malaria (WHO 2013a). In 2010 there were an estimated 219 million malaria cases, with an estimated 660,000 deaths, of which 90% occurred in sub-Saharan Africa and the majority were children under five in Sub-Saharan Africa (WHO 2013a).

1.3.6 Sexually Transmitted Diseases

Sexually transmitted diseases (STDs) are also referred to as sexually transmitted infections (STIs) and venereal diseases (VDs). There are more than 20 types of STDs caused by 30 different bacterial, fungal, viral, or parasitic pathogens (CDC 2013b). STD transmission in human population is mainly caused by person-to-person sexual contact. Some STIs can also be transmitted via IV drug needles used by an infected person, as well as through childbirth or breastfeeding.

STDs have a major negative impact on sexual and reproductive health worldwide. STDs are an important cause of infertility in men and women. According to WHO, 499 million new cases of curable STIs (which do not include non-curable STDs such as HIV) occur annually throughout the world in adults aged 15–49 years (WHO 2013c). In the United States about 20 million new STD infections occur each year, in which half occur among young people aged 15–24 (CDC 2013b).

1.4 THE ORGANIZATION AND OUTLINE OF THIS BOOK

This book is organized into four parts with 20 chapters. It starts with an overview chapter on various spatial modeling methods of infectious diseases, followed with three sections of different mathematical, statistical, spatial modeling, and geosimulation techniques.

Part I begins with a brief overview of the background of infectious diseases, diseases covered in this book, and research needs of modeling and analyzing the spatial and temporal dynamics of infectious diseases. The second chapter, written by Chen, provides a general review of different methods of modeling spatial and spatial–temporal dynamics of infectious diseases. The advantages and limitations of different methods are compared, and issues and challenges in disease modeling are highlighted.

1.4.1 Mathematical Modeling of Infectious Diseases

This part starts with Chapter 3 on a narrative about bioinformatics and mathematical modeling studies to understand the infection dynamics and spatial spread of WNV. Although WNV was isolated in 1937 and several outbreaks in different regions have been reported since then, this mosquito-borne disease has become a major public health issue in North America since its identification in New York City in 1999. The narrative provided by Murty, Banerjee, and Wu started with a brief review about the epidemiology, disease transmission, viral genomics, and bioinformatics

progress toward therapeutic treatments and supporting dynamic model development. This chapter then uses some popular mathematical models to illustrate the iterative intellectual cycle toward modeling formulation and applications, assisted by surveillance, guided by public health issues, and contributing to the understanding of disease spread mechanisms and the optimal design of effective intervention to alter the spatiotemporal patterns of WNV spread for the purpose of control.

One of the potential applications of disease modeling is to provide qualified risk assessment and forecasting, which constitutes the core of Chapter 4 by Abdelrazec, Cao, Gao, Proctor, Zhu, and Zheng. This chapter describes some recent results of an interdisciplinary team on a novel statistical model to predict the minimal infection rate, and on a new index based on compartmental models to measure the WNV risk. The developed dynamical minimal infection rate provides a first attempt to test and forecast the weekly risk of WNV by explicitly considering the temperature impact on the mosquito abundance. This was tested using regional surveillance data.

Chapter 5 is coauthored by two leading scientists, Arino and Khan, of the renowned Bio.Diaspora, a major project for the spread of infectious diseases that is dedicated to understanding the global airline transportation network and leveraging knowledge of this complex "living" system to better prepare for and respond to global infectious disease threats. Modern disease surveillance systems such as the Global Public Health Intelligence Network (GPHIN) generate alerts by continuously monitoring internet news sources for the occurrence of keywords related to infectious diseases. However, all of these alerts do not carry the same potential to generate infectious disease outbreaks in distant locations. In this chapter, Arino and Khan discuss how modeling can help bridge knowledge about health conditions in the locations where the alerts are being generated and the global air transportation network. This serves to assess the potential for an emerging or reemerging disease to quickly spread across large distances and to quantify the risk represented to a given public health district by an alert generated elsewhere in the world. The work of Arino and Khan's team, reflected in this chapter, has been dealing with the relationship between the movement of populations and the spread of infectious diseases using mathematical modeling and information about the global air transportation network, driven by such data as the International Air Transport Association (IATA).

Two modeling templates for disease spread in a spatially heterogeneous environment—patch models and reaction diffusion systems are then introduced by Gao and Ruan in Chapter 6, in the context of spatial spread of malaria between humans and mosquitoes. These spatial models are also used to examine the complication due to the multi-strain nature of malaria. Future directions relevant to temporal heterogeneity, latency delay, and environmental factors are discussed.

The final chapter in this part is based on an ongoing collaboration between Bourouiba (MIT), Gourley (University of Surrey), Liu (University of Wyoming), Takekawa (USGS Western Ecological Research Center), and Wu (York University Centre for Disease Modelling). Their focus has been on the spatial dynamics of migratory birds and the interaction of ecology and epidemiology and its consequence in terms of global spread of avian influenza along wild birds' migration routes. Among a few other goals, the authors hope to demonstrate that "modeling benefits from

surveillance (satellite tracking and GIS technologies) and modeling may contribute to surveillance design."

1.4.2 Spatial Analysis and Statistical Modeling of Infectious Diseases

Part III provides several reviews and examples of spatial analysis and statistical modeling methods in order to take account of the spatiotemporal dynamics of infectious disease spread. Determining the spatial transmission pattern of infectious diseases and its environmental impacting factors is one of key steps in vector-borne infectious disease modeling and control. Spatial and temporal analysis of disease incidence and prevalence is commonly used in order to gain insights on disease spreading pattern and trend and to explore the relationship between disease spread and environment, climate and other factors. Part III starts with a chapter coauthored by Richardson and Chen on analyzing the global spread of H5N1 from 2007 to 2011 using spatiotemporal mapping methods. In order to determine whether the global spread of H5N1 has similar spreading paths as bird migration processes, a spatial–temporal query tool was developed to find the temporal difference of start dates and distance between each pair of outbreaks. The spatiotemporal characteristics of the outbreaks were mapped to determine outbreak clusters. These clusters were joined chronologically by polylines that are compared with potential bird migration paths.

Detecting potential spatial and temporal disease aberration and clustering are important for disease control, especially for early warning of disease outbreaks (Chen et al. 2011). Spatial scan statistics are commonly used for detecting clusters of disease and other public health threats. Chapter 9 coauthored by Belanger and Moore presents two challenges identified in spatial scan statistics: determining appropriate circular scanning window size and dealing with high requirements on computational resources in order to detect both circular and arbitrarily shaped spatial clusters. These challenges are more obvious in detecting clusters in real-time syndromic surveillance systems where each new observation necessitates at least a partial rescan of potentially affected areas of the study window. This chapter discusses recent advances in cloud computing technologies and platforms to test for emergent spatial clusters of sexually transmitted infections across the province of Ontario, Canada. Cloud computing facilitates the ability to detect flexibly shaped clusters of disease in real time (or near real time) and to do so cost-effectively.

The dynamics of vector-borne diseases (VBDs) are greatly influenced by extrinsic environmental factors, such as temperature and rainfall. Much research has gone into improving our understanding of how the dynamic of VBDs depends on these environmental factors, and how this translates to spatiotemporal distributions of disease. In Chapter 10 Johnson and her colleagues review various approaches being used for analyzing the spreading dynamics of malaria. Modeling efforts can be loosely grouped into process-based models that explicitly link vector and parasite biology to transmission and tactically oriented models that aim to link climate factors with areas of current transmission in order to understand drivers of the disease. Although current models have significantly improved our understanding of the factors influencing malaria transmission, there are still areas that would benefit from more attention.

This chapter highlights these areas, and suggests new methodologies to tackle these factors and integrate new data with models.

Individual-level models (ILMs) are a flexible class of discrete-time infectious disease models that can be used to model data from such systems. They allow for the inclusion of covariates, such as geographical location, at the level of the individuals within the population. Chapter 11, coauthored by Deardon and his students, reviews a class of ILMs and how they are used in the modeling of spatiotemporal dynamics of infectious disease transmission process. They address the issue of statistical analysis of infectious disease data using such models. A Bayesian statistical framework using Markov Chain Monte Carlo techniques is proposed in order to fit the models to data. This chapter examines how this can be done, how results can be interpreted, and how models can be compared and validated. However, this type of ILM is usually computationally intensive. This chapter also presents a novel method of reducing the computational costs.

Geostatistical models have been widely used in disease studies. The following three chapters present different studies of using geostatistical methods and models to deal with different problems in mapping the risk of three infectious diseases. In Chapter 12, Zhang presents a Bayesian spatiotemporal geostatistical approach for detecting the distribution and dynamics of schistosomiasis risk in regions of China. Environmental, topographic, and human behavioral factors were included in the model. The results give clear indications of high risk regions for future schistosomiasis control, and provide useful hints for improving the national surveillance network of schistosomiasis and possible methods to utilize surveillance data more efficiently.

Chapter 13, coauthored by Wen, Chen, and Majury, provides an example of how spatial analysis and geostatistical models can be used to analyze disease risks at the urban scale. Urban scale disease risk analysis is practically crucial for controlling and managing a potential disease pandemic due to the large number of people living there. Chapter 13 presents a study of understanding the dynamics of the 2009 H1N1 outbreak at Greater Toronto Area (GTA) of Canada. This study develops a procedure framework by integrating exploratory data analysis and geostatistical models for estimating the spatial dynamics of a human pandemic.

Missing data is a common problem in health and environmental surveillance data in which outcomes are absent over many spatial units or locations in the study area. In Chapter 14, Yoo, Chen, and Russel investigate the associations of environmental and weather conditions with the underlying (latent) process that is assumed to generate the observed mosquito counts. They present a geostatistical spatiotemporal prediction model for missing WNV mosquito data in the mosquito surveillance system by introducing a spatiotemporal correlation. The proposed model takes account of the nature of count data explicitly using a Poisson generalized linear model. This model tackles the nonstationarity in WNV mosquito abundance data by restricting the decision of stationarity to a local neighborhood surrounding the target prediction point.

Chapter 15, coauthored by Feng and Dean, deals with another important data issue: zero-inflated count data in disease analysis. In many disease studies zero-inflated count data are spatially correlated. Considering the similar spatial structures of impacting factors, variables measured at the same spatial locations may be

correlated in space and time, indicating that they may be characterized by a common spatial risk surface. This chapter describes a zero-inflated common spatial factor model and a multivariate conditional autoregressive (MCAR) model. These models are applied to a study of comandra blister rust (CBR), a disease of lodgepole pine trees caused by a fungus. The authors demonstrate how joint outcome modeling of multivariate spatial disease data can be used to improve the predictive accuracy of disease incidence over space.

1.4.3 Geosimulation and Tools for Analyzing and Simulating Spreads of Infectious Diseases

In Part IV, authors discuss important challenges and propose solutions to model and simulate the spread of infectious diseases in georeferenced virtual environments, using either population- or agent-based models (ABMs). In Chapter 16, Moulin and his colleagues present a large literature review on existing epidemiological models and approaches of VDBs in which the spatial/geographic dimension is either missing or quite limited. They also review various modeling and simulation techniques such as System Dynamic, Cellular Automata, and agent-based approaches, emphasizing their advantages and limitations when it comes to modeling the spatial and mobility dimensions of disease spread. Then, the authors propose an approach integrating multispecies population modeling and patch modeling, as well as mechanisms to simulate the populations' evolution, interactions, and mobility, using georeferenced data structured in an Informed Virtual Geographic Environment (IVGE) in which the geosimulations take place. The authors also present the foundations of ZoonosisMAGS, their geosimulation software, which fully implements the proposed approach and enables the exploration of various scenarios on the simulated phenomena (temperature evolution, influence of landscape characteristics, variation of biological and epidemiological parameters of the different evolution and interaction models of the involved species, study of displacement behaviors of mobile species). In Chapter 17 the authors provide more technical details on the ZoonosisMAGS Platform, which is composed of several pieces of software: the IVGE creator; a prototyping tool programmed in MATLAB® to rapidly create and explore new simulation models; and the ZoonosisMAGS software coded in C++ to develop full-scale geosimulations of VDB spread. Several examples are provided for the modeling and simulation of Lyme disease spread and the advantages and limits of the proposed approach and software are discussed.

In Chapter 18, Haddad and his colleagues explore the important issue of proposing simulation and analysis tools to assess the risk of VDB for humans, taking into account the behavior patterns of people in recreational areas. The case of Lyme disease threat for visitors in the Sénart Forest (France) is used to illustrate the proposed approach. In this project described in the chapter, the authors developed different ways to collect data about human activities (traditional questionnaires and online questionnaires coupled with a web-mapping tool) in recreational areas. They present their approach to analyze the collected data in order to identify and formalize activity patterns of people in the study area. These patterns can be used to create a virtual population

of persons (i.e., forest visitors) to simulate their behaviors in a virtual geographic environment in which risky areas can be located in relation to the presence of VBD vectors.

In Chapter 19, Haddad, Moulin, and Thériault propose an innovative GIS-based spatial–temporal simulation approach and a software, which fully integrates disease epidemiology, human mobility, and public intervention models in a GIS system. Their system allows for the rapid exploration of intervention scenarios in the first days of an infectious disease outbreak. The full integration of the simulator in a commercial GIS allows a public health decision maker to simply set intervention scenarios (i.e., vaccination, closure of different types of establishments, public transit) to visualize and assess the spread of a contagious disease in a geographic area displayed in a GIS.

In Chapter 20, Friesen and McLeod study how smartphone trajectories' data can provide useful input for the simulation of infection spread using agent-based modeling tools. The authors assess different types of cellular network data available from a telecommunications service provider and demonstrate their utility in estimating agent behavior patterns as suitable inputs into an ABM of contact-based infection spread. Two ABMs of infection spread have been developed using the cell phone trajectory data: a province-wide simulation of infection spread and a more detailed simulation of infection spread between two proximate rural towns. A third ABM illustrates the proposed validation process, comparing mobility patterns extracted from cellular data to actual traffic survey data.

1.5 CONCLUSION

We have tried in this open chapter to introduce the basics of infectious diseases and their transmission mechanisms, to elaborate on the role of geospatial analysis, mathematical modeling, statistical methods, and geosimulation in understanding spatial and temporal dynamics of infectious diseases. In this book, various methods and techniques are proposed to analyze and model the dynamics of infectious diseases, including mathematical modeling, statistical analysis and modeling, spatial and temporal pattern analysis, geovisualization, GIS, remotely sensed data, system dynamic modeling, geocomputation, and simulation techniques. Authors also discuss issues and challenges such as missing data, underreporting, modeling validation, and uncertainty.

Throughout this book, ample examples are provided from different angles to show how advances in GIS and computing technology in general, and geographic positional systems and remotely sensed data in particular, have been evolving in their capabilities to capture detailed information on time and location of disease incidence, population and other hosts' mobility, environmental and weather conditions. Such detailed data provides a significant improved source for tracking, monitoring, analyzing, and modeling dynamics of infectious diseases. Increasing availability of geospatial information through positioning technology, geosensor networks, and human volunteers will add enormous challenges as well as provide new opportunities in spatial–temporal disease analysis and modeling in the future.

This book is aimed to serve as a guide or reference for researchers/scientists and students who use, manage, or analyze infectious disease data, or professionals who manage infectious disease-related projects. It can also be used as a reference or important supplement to understand the various traditional and advanced analysis methods and modeling techniques, as well as different issues and challenges in infectious disease applications. We hope that this book will further promote a better use of infectious disease data collected by various sources and promote interdisciplinary collaboration in analysis/modeling technology.

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