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Modeling the Spread of Infectious Diseases in Global Transport Systems

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Historical Background

Infectious diseases currently present serious public-health threats worldwide, concerning health systems, governments, industry, and society in general. Prior to the existence of modern transportation networks, natural barriers limited certain diseases to specific geographic regions. However, contemporary global transport systems have connected previously isolated regions, providing a means for pathogens to move around the globe faster and further than ever before. Additionally, a rise in the volume of international air travel has resulted in an increased likelihood of imported infections among travelers into new regions. For these reasons, it is imperative to develop models which quantify the risk of importing infected passengers and vectors into a new region, as well as predict the expected impact an infectious disease may have on a given region once introduced. Furthermore, the extensive range of GIS tools now available offers a means for researchers and public-health authorities to understand and visualize spatial databases including outbreak locations, human mobility networks, and ecological and environmental conditions. Given the spatial and temporal component of infectious disease outbreaks, GIS tools can and should be exploited to develop new and improved prediction models. Such models should be robust, meaning they can be applied to a range of newly emerging outbreaks, and parameterizable, thus adaptable for real-time implementation. If designed properly, these models can be used to aid decision makers in designing optimal public-health policies, such as prioritizing specific travel routes and locations (origin cities, destination airports, etc.) on which to implement passenger surveillance and control strategies.

To accurately model risk of disease spread through global transport systems, there are substantial data requirements and multiple critical components which must be considered. As will become evident from this chapter, a wide range of approaches have been implemented. The best choice of model is highly dependent on the disease type (contact based or vector borne), the objective sought, and the level of available data. The remainder of this chapter will outline some of the current modeling approaches as well as their strengths and weaknesses.

The remainder of this chapter is broken into the following sections: "Scientific Fundamentals," "Key Applications," and "Future Directions." "Scientific Fundamentals" contains

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an overview of the traditional mathematical models (i.e., compartmental models) used to represent the spread of an infectious disease within a human population. Compartmental models are presented for two different types of infectious diseases, contact based and vector borne, which vary based on their spreading dynamics. Subsequently, species distribution models (SDMs), which are relevant for modeling vector-borne diseases, are briefly discussed. The "Key Applications" section focuses on disease-spreading models at the global scale. Various papers from the literature are reviewed, and a selection of risk models (varying by their methodology) are presented. The "Future Directions" section highlights existing gaps in the literature where further research would be of value.

Scientific Fundamentals

To model the risk of disease spread at a global scale, network analysis and optimization tools can be utilized. In a mathematical modeling context, a network structure is defined by a set of nodes and links. For example, the air traffic network can be represented by a set of nodes which correspond to airports and links which correspond to air travel routes between airports. The maritime freight network can analogously be defined by the set of port and shipping movements between them. For a given mobility network structure, link weights can be defined to represent the risk posed by a given travel route, as either numerical values or a function of network attributes. Link weights can have very simple definitions, such as the volume of passengers using a given air traffic link or volume of sea cargo movements, or they can take a more complex functional form which accounts for both link-specific attributes such as travel volume and distance, as well as node-specific attributes such as regional population, local environmental conditions, the presence of pathogens, regional economic indicators, outbreak size, etc. However, defining route-level risk functions in real time to accurately model emerging epidemics is not a simple task. For a model to be useful to planners, it must be validated, which is in itself a challenging task and highly dependent on available data.

Published methods which identify the risk of infection associated with travel vary from simple patient-based surveys to complex mathematical models. The surveys generally rely on evaluating patient travel histories after they are diagnosed with a specific illness, whereas the mathematical models seek to predict the future epidemic dynamics based on assumptions about the human population, mobility patterns, and characteristics of the disease itself.

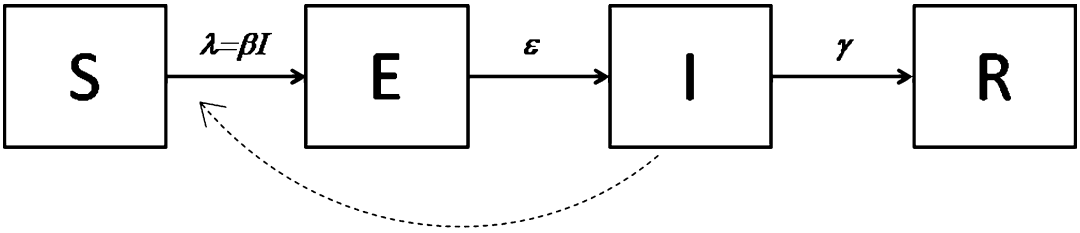
This chapter will introduce a subset of the methodologies used to model the spread of disease, which will be further classified as either contact-based or vector-borne disease models. The two classes of diseases display distinctly different dynamics due to the presence of the third-party spreading agent in the vector-borne diseases, and for this reason, modeling them requires different methodological approaches.

Compartmental Models

The stochastic nature of infectious disease transmission poses a significant challenge to predicting the impact that a new disease might have on a population. Over the last 100 years, significant research efforts have focused on predicting the expected spreading behavior of infectious diseases, which exploit characteristics of both population dynamics and the disease itself.

While the focus of this chapter is modeling risk at a global scale, the epidemic dynamics of infectious diseases at a regional scale has a direct impact on the risk posed at the national and global scale. That is, if a disease is highly transmissible, it is more likely to pose a global risk because travelers are more likely to be infected and will also pose greater harm at their travel destination. For these reasons, models which can characterize local outbreak behavior are highly relevant to global risk modeling and will therefore be introduced first.

For diseases which are transmitted through direct human-to-human contact, the progress of an epidemic in a large population can be mathematically represented using a generic compart-



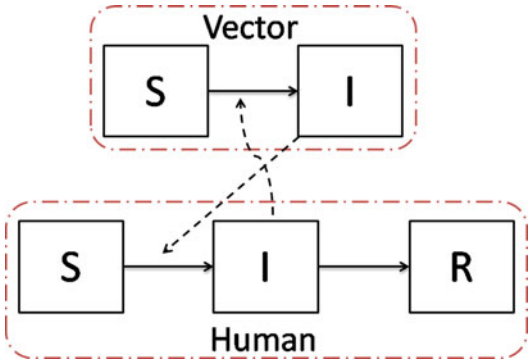
Modeling the Spread of Infectious Diseases in Global Transport Systems, Fig. 1 An SEIR compartmental model illustrating the force of infection, $\boldsymbol{\lambda}$, which is a function of the transmission rate; $\boldsymbol{\beta}$ and proportion of the population infected, *I;* the incubation rate, $\boldsymbol{\varepsilon}$; and recovery rate, $\boldsymbol{\gamma}$

mental model. The first compartmental models date back to the 1920s, proposed by Kermack and McKendrick (1927), the simplest of which included two main health states, susceptible (S), or previously unexposed to the pathogen, and infected (I), currently colonized by the pathogen. The SI model has since been expanded to include additional states such as recovered (R), or successfully cleared of the infection, and exposed (E), infected but not yet infectious. The flowchart in Fig. 1 illustrates the four compartmental states, the transitional state rates, and corresponding direction of flow through the states for an acute infectious disease, that is, those diseases where the immune system responds "rapidly" to remove pathogens within a short period after infection (days or weeks).

In traditional compartmental modeling, S, E, I, and R are defined as the *proportion* of the total population, N, in each disease state. The transition from S to E depends on the number of infected in the population (relationship is denoted by the dotted line) and can be defined as the force of infection, λ, which is the per capita rate at which susceptible people contact the infection. The force of infection, λ, is equal to the product of I and β, and β is the product of the transmission probability of the pathogen and the contact rate in the population. The transition rate from E to I can be simply defined as ε, the inverse of the average duration of the latent period or the number of days after an individual is infected and before they are infectious. The state change from I to R is based on the recovery rate or the average amount of time spent in the infectious state. The transitional rate of change is often assumed to be a constant, γ, the inverse of the "infectious period." It is important to note that this rate of change is actually variable, and a function of changes in the pathogen itself, as well as various intervention policies. The transitional rates from E to I and I to R can generally be estimated using clinical data, while the rate of change from S to E is much more complex and a function of the epidemic dynamics. Given predefined state transition rates between compartments, the state of the population (number of people falling into each compartment) at any time, t, can be defined using a set of ordinary differential equations.

A compartmental model can also be applied for the local transmission of vector-borne diseases, where a vector is any agent that carries and transmits an infectious pathogen to another living organism and includes mosquitoes, flies, sand flies, lice, fleas, ticks, and mites. Due to the role of the vector in the transmission process, the compartmental models which are used for contact-based diseases cannot be directly applied to vector-borne diseases. A compartmental model representing the infection dynamics of vector-borne diseases (such as a disease spread by mosquitoes) is illustrated by the flowchart in Fig. 2, where the top compartments refer to the states of the vectors and the bottom compartments refer to the states of humans. The transitional rate of change from S to I for both the human and vector is codependent and increases with the proportion of infected humans and vectors in the region. The dependency is a function of the mean rate of bites by a particular vector and the vector-to-human transmission probability per bite.

The use of compartmental models allows one to quantify the statistical properties of epidemic patterns by analytically predicting pathogen spread over time. Specific metrics of interest are the prevalence and duration of the epidemic. Additionally, these models can be applied to evaluate potential intervention strategies such as vaccination schemes, which can be accomplished by reducing the number of susceptibles in the population and comparing the epidemic metrics. For more on compartmental models, see May and Anderson (1991).

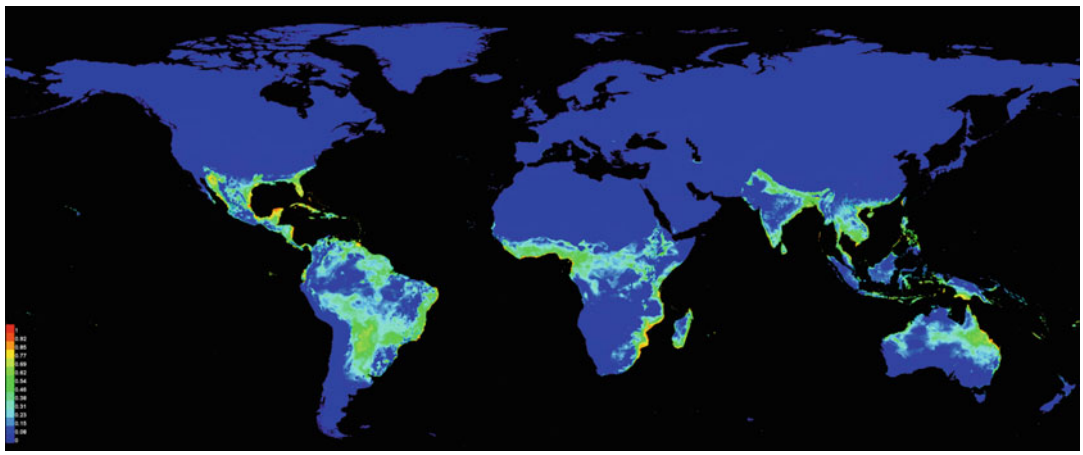


Modeling the Spread of Infectious Diseases in Global Transport Systems, Fig. 2 An example of a compartmental model for vector-borne diseases, illustrating the relationship between the infection dynamics of the human and vector populations

Species Distribution Models (SDMs)

In addition to the biting rate, a critical component of a vector-borne disease risk model is the likelihood of vector presence in a region. This is because a vector-borne disease cannot spread directly between humans; it must be passed through the vector. The probability of a given vector's presence in a region can be estimated using species distribution models (SDMs). SDMs predict the potential geographical distribution of a species based on occurrence points of a species and environmental data (i.e., climatic and topographic features). SDMs are sometimes interpreted as approximating the ecological niche for a species and can provide a robust framework to analyze the biogeographical determinants of vectorborne diseases (Peterson 2008). The output of SDMs can be interpreted as the probabilistic expectation of vector presence of a species in a given spatial cell. SDM outputs are a critical component in modeling the risk of arbovirus importation and establishment.

For the last decade, SDMs have typically been constructed using machinelearning algorithms, including a maximum entropy-based software package (Maxent) (Phillips et al. 2006, 2008; Campbell et al. 2015) and boosted regression tree (BRT) models (Kraemer et al. 2015), GARP and BIOCLIM. An example of a global SDM is illustrated in Fig. 3 for the yellow fever mosquito



Modeling the Spread of Infectious Diseases in Global Transport Systems, Fig. 3 Example of species distribution models for the yellow fever mosquito

Aedes Aegypti, one of the known spreading vectors of dengue and Zika virus. SDMs can correctly predict the known traditional ranges of the species, though they need to be continually validated and refined with updated data on the spread of these species.

Vector presence at both the travel origin and destination is a significant factor in estimating the risk of introduction and establishment of a disease into a region. For example, consider the case where there is an outbreak of dengue on a small island in the Caribbean. Assume, for simplification, there are only two departing travel routes with equal travel volumes; one route departs to New Orleans, LA, in the southern USA where the dengue vector is well established, and the other route departs to Toronto, ON in Canada, where the local conditions are unsuitable for harboring the same vector species. In this example, there is significantly less harm posed to Toronto because it is unlikely an individual infected with dengue will arrive in Toronto and further spread the disease. In contrast, a dengue-infected passenger arriving in New Orleans could be bitten by a local mosquito which could then spread the infection to other humans. Furthermore, if there is a large enough influx of infected cases in a given region at once, an autochthonous cycle could result. Thus, the inclusion of SDM data in disease models is critical for estimating the harm posed to a region.

Key Applications

So far, the focus of this chapter has been on modeling the infection dynamics between humans (and vectors) at a local scale. The local-level models are necessary, but not sufficient to model the risk of disease spread and establishment at a global scale. As was the case with the local-level models, contact-based and vector-borne diseases require separate modeling approaches at the global scale. Various methodologies have been proposed for each type of disease; a subset of which will be introduced in the following sections. The examples introduced are intended to provide the reader with a basic understanding of the critical components of the problem and some possible methodological approaches that have been used. It is however important for the reader to recognize that the models presented here represent a limited selection from a rapidly evolving field of literature. A comprehensive review of the literature is beyond the scope of this work.

The Global Spread of Contact-Based Diseases

In efforts to encapsulate the spread of disease through global transport systems in conjunction with ongoing disease propagation within a local population, compartmental models have been applied within a multilayer framework where the layers represent different levels of human mobility, such as air travel and daily commuting patterns. These models allow for a global-level analysis of future outbreaks and the ability to evaluate relevant intervention strategies such as closing airports, reducing air travel, closing schools, and limiting the number of people going to work, among other quarantine efforts.

Global-scale compartmental models have been applied in both an analytical and simulation-based framework. Analytical models are appealing because they require minimal computation efforts and can provide quantitative metrics about outbreak dynamics (Rvachev and Longini 1985; Balcan et al. 2009; Colizza et al. 2006). However, analytical models require simplifying assumptions to be made about the population structure and interaction dynamics and are therefore unable to incorporate information about explicit network structure properties.

Agent-based simulation, or individual-based models (IBMs), on the other hand, can incorporate specific network structure properties, i.e., contacts links between individual nodes, into their models, and utilizes agent-based simulation to recreate outbreak scenarios. The most advanced IBMs incorporate social contact data, as well as regional and international travel data in efforts to replicate interaction dynamics among "connected" populations at a global scale. The value of IBMs is they are able to replicate multiple possible spreading

scenarios, predict average spreading behavior, and analyze various intervention strategies for a given network structure and disease. However, while they can capture a greater degree of detail in their predictions and analysis compared with analytical models, they require a highly detailed set of input data and significant computational resources (Balcan et al. 2010; Eubank et al. 2004; Broeck et al. 2011; Ajelli et al. 2010). Furthermore, due to the inherently stochastic nature of a disease outbreak, multiple simulations are required to compute *expected* outcomes. Given the data requirements and required run time, IBMs can be expensive and computationally taxing, but they have the potential to provide a greater degree of realism, and a means to evaluate very specific control strategies, and are therefore an invaluable tool for planning.

In addition to analytical models and IBMs, which provide insights into the expected spreading behavior of an outbreak, there currently exists a growing demand for a new paradigm of models which exploit the increasingly available real-time epidemiological, spatial, and clinical data in order to evaluate an ongoing outbreak and advise on real-time control strategies. Recent advances in scenario-based modeling have begun addressing this issue. For example, there are various models which use genetic sequence data to analytically infer the geographic history of a given virus' migration (Drummond and Rambaut 2007; Haydon et al. 2003; Jombart et al. 2009). A methodology presented by Gardner et al. (2014) was designed to infer outbreak patterns in social contact networks using case-report data and disease-specific properties by identifying the maximum probability spanning tree (MPST), and further extended in Fajardo and Gardner (2013) and Rey et al. (2015), to consider the case of partial case information availability. A similar model was implemented on a global air traffic network by Gardner et al. (2012) to infer the most likely air travel routes responsible for spreading the 2009 H1N1 (swine) influenza pandemic within the USA. These works represent a growing field of research which seeks to exploit network optimization tools and the types of real-time infection data and are becoming increasingly available during the onset of outbreaks.

The Global Spread of Vector-Borne Diseases

To model vector-borne disease spread at a global scale, analysis of surveillance and monitoring policies must consider the possible infection pathways of locally established vector populations becoming infected from new hosts (e.g., infected air travelers) and subsequently spreading the virus. Furthermore, the sustained presence of an arbovirus (a virus which is spread by arthropod vectors) in a (destination) region is dependent on the local ecological and environmental conditions, specifically existing populations of the spreading vector.

Both transport systems and climate change have contributed to the introduction and expansion of new disease carrying vector populations into previously uninhabited regions. Transport systems such as international air travel and maritime freight provide new intercontinental pathways for vectors, while climate change and urbanization result in extended transmission seasons and more suitable environments for the vectors. Furthermore, a greater likelihood of imported vector-borne infections among travelers returning to previously unexposed regions is expected in the near future due to a warming climate, increased arboviral activity in Asian and Pacific nations, in conjunction with increased travel to and from these regions.

Two different methodological approaches to estimate the global risk model of vector-borne disease spread are presented below. The first approach defines the link-level risk a priori as a function of variables and estimates the risk of disease spread on a relative scale across the network. The second approach is optimization based and instead seeks to calibrate a functional form that represents the link-level risk. Both models utilize data on the transport system, regional economic attributes, SDMs, and/or ecological and environmental factors.

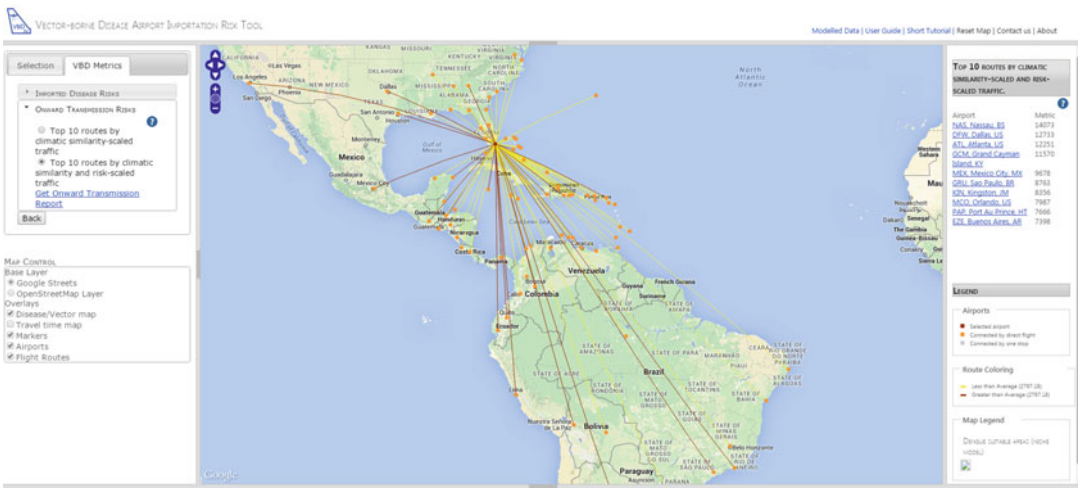
Relative Risk Models

One approach to quantify travel risk (at a route level) utilizing the type of data noted previously is to define the link-level risk as a product of variables. An example of such a relative risk model is the Vector-Borne Disease Airline Importation Risk Tool (VBD-AIR: http://www.vbd-air.com/), which is a web-based GIS tool for defining the role of airports and airlines in the transmission and spread of vector-borne diseases, including malaria, dengue, yellow fever, and chikungunya (Huang 2012). In this tool, the total volume of travel was determined by the passenger volume for air travel, and the climatic similarity was calculated as a distance-based vector. The risk of imported infections, imported vectors, and onward transmission is computed as the product of the *climate Euclidean distance* (CED – defined below), traffic capacity, and disease/vector prevalence at origin locations, which serves as an estimate for the relative risks between scheduled routes of incoming flights between origin i and destination j bringing exotic disease vectors and their consequent establishment. The risk function is computed as shown in Eq. (1):

$$R_{ij} = \frac{1}{(r_i - r_j)^2 + (t_i - t_j)^2 + (h_i - h_j)^2} v_{ij}\ e_i \tag{1}$$

where R_{ij} is the relative risk between origin i and destination j; r, t, and h are the monthly rainfall levels, temperature, and humidity, respectively, at the corresponding airport; v_{ij} is the air traffic capacity between i and j; and e_i is the endemicity at the origin or probability of vector presence. The first part of the function is referred to as the climate Euclidean distance (CED). Each of the three parts is individually normalized before being multiplied to compute the relative risk (Huang 2012); thus, R_{ij} always falls between 0 and 1. These results can be used to identify the set of travel routes entering a given airport which pose the highest risk to that airport and more generally to aid planners and decision makers responsible for allocating limited surveillance resources. An example of the tool visualization is presented in Fig. 4. This screenshot identifies all direct travel routes into Miami International Airport originating in dengue-endemic regions, as well as a list of the top ten routes which pose the highest risk.

Another global risk model was published by Gardner and Sarkar (2013), with the objective of quantifying the relative risk of vector-borne disease spread by infected travelers arriving at or traveling through any given world airport. Similar to the network definitions in the previously introduced models, airports are represented as nodes,



Modeling the Spread of Infectious Diseases in Global Transport Systems, Fig. 4 Screenshot of the VBA-AIR tool, identifying all direct travel routes into Miami International Airport originating in dengue-endemic regions and a list of the top ten highest risk routes (http://www.vbd-air.com/)

and the links in the network represent directed air travel connections between airports. One major difference between this model and the model previously introduced by Huang et al. (2012) is the inclusion of vector suitability data from SDM outputs at both the travel origin and destination. In the model proposed by Gardner and Sarkar (2013), the harm posed to a destination airport j from travel originating at airport i is defined in Eq. (2):

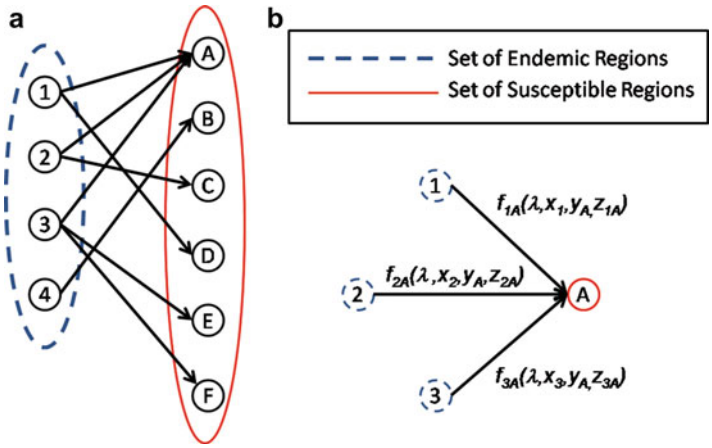
$$u_{ij} = \frac{\varepsilon_i s_i \sigma_i v_{ij} \alpha_j s_j}{D_{ij}}. \tag{2}$$

Equation (2) is specific to the origin-destination (OD) pair i, j, and is dependent on the origin being in an endemic region (this is disease specific), the outbreak intensity at the origin (σ_i), the suitability at the origin (s_i), the total passenger volume (v_{ij}) traveling between i, j, the population at the destination (α_j), the suitability at the destination (s_j), and the travel distance (D_{ij}). The binary variable, ε_i, is set to 1 for all airports in endemic regions. The origin suitability, s_i, represents the relative ecological risk of the spreading vector (e.g., *Aedes aegypti* or *Aedes albopictus* – the Asian tiger mosquito) being present at the origin, provides a measure of the likelihood of an outgoing traveler being infected, and is computed from SDM models. The destination suitability, s_j, is included because, in order for a disease to spread further after introduction into a new region by an infected traveler, the destination habitat must be ecologically suitable for an insect vector population to establish itself. In the model presented in the paper, the expectations were aggregated to the city level by averaging overall the cells in each geographical unit to define the relative ecological risk in each city. The outbreak intensity, σ_i, is a function of the outbreak size and population density at the origin, which is assumed to be correlated with the probabilistic expectation that an outgoing traveler would be infected. The passenger flow variable, v_{ij}, or the total passenger volume originating at airport i and traveling to airport j captures the potential dispersal for the disease and includes travel on both direct routes and indirect routes with stopovers. The population at the destination, α_j, is a measure of the threat posed to a given region from the disease. The risks are normalized by dividing the highest value computed over all i, j combinations; thus, what is being estimated is the *relative expected harm* posed to a destination airport j from travel originating at airport i. A similar model was proposed in the same paper to quantify the harm posed to stopover airports through traffic. Similar models are applied to estimate the relative risk of dengue spread posed by travelers out of the Philippines after Typhoon Haiyan (Gardner and Sarkar 2015) and to estimate the relative risk of Zika spread from Latin America in the 2015–2016 epidemic (Gardner et al. 2016).

Optimization-Based Modeling Framework

Optimization-based modeling frameworks are increasingly being applied to the field of epidemiology. As an alternative to the relative risk models discussed prior, which define the risk functions a priori, optimization methods can be applied to estimate risk functions for a given network (Gardner et al. 2012; Bóta et al. 2014). These models utilize available spatial-temporal case data and network properties to estimate risk functions, which can then be used to predict the likelihood of further disease spread in the network. (Optimization methods can also be applied in a planning context (Chen et al. 2016) to help make real-time control decisions at early stages in an outbreak, with limited information. However, this is a topic beyond the scope of this chapter.)

An optimization-based methodology which estimates risk functions for air travel routes likely to spread dengue into new regions is presented in Gardner et al. (2012). The outcome of the network model provides the expected number of dengue cases in each non-endemic region that can be attributed to a particular endemic region connected to it. In the proposed network structure, geographic areas are represented as nodes, belonging to either the set N of endemic nodes or the set G of susceptible nodes. The links in the network represent directed air travel connections between geographic areas (originating from G), while the measure P_{ji} represents the number of predicted infections at



Modeling the Spread of Infectious Diseases in Global Transport Systems, Fig. 5 (**a**) Bipartite network connecting endemic regions to susceptible regions: the susceptible US and Europe nodes represent mutually exclusive sets. (**b**) Link-based functions: these predict the number of infections at susceptible node A, attributed to each adjacent endemic region (1, 2, and 3)

a susceptible node i attributed to an endemic node j. A directed bipartite network structure is used to connect the endemic countries to susceptible regions through directed arcs. Figure 5a provides an illustration of the bipartite network structure. Figure 5b illustrates a four-node extraction from the network to illustrate the generalized link-based functional form used in the model. The function $f_{ji}\ (\lambda, x_j, y_i, z_{ji})$ represents the number of cases observed at i for which j is responsible, where λ represents a vector of *calibrated* parameters, x_j represents the characteristics of origin j, y_i represents the characteristics of destination i, and z_{ji} represents the vector of parameters specific to directed link (j, i). The total predicted number of infections at i is given by

$$P_i = \Sigma_{\forall j \in A\ (i)}\ f_{ji}\ (\lambda, x_j, y_i, z_{ji}),$$

where $A(i)$ represents the set of endemic nodes adjacent to i.

The model seeks to find the unknown parameter vector λ. Attributes included in the function are travel volumes, outbreak data at the origin of travel, destination population size, and habitat suitability for the spreading vector (e.g., based on SDMs) at both ends of the route. The generic problem formulation is as follows:

$$\min_{\lambda} \sum_{\forall i \in N} (I_i - P_i)^2$$

s.t.

$$P_{ji} = f_{ji}\ (\lambda, x_j, y_i, z_{ji}) \quad \forall\ i \in N\ \forall j \in G \tag{3}$$

$$P_i = \Sigma_{\forall j \in A\ (i)}\ P_{ji} \qquad \forall\ i \in N \tag{4}$$

This type of model can be easily extended to model risk posed by maritime trade, as well as extended to model the risk posed by alternative vectors and diseases. The model is quantitatively calibrated using actual infection reports, thus providing a more reliable estimate of risk. However, the dependency on case data also represents the main limitation of this type of model; without complete infection data, the model cannot be properly calibrated. In addition to calibration, an additional challenge faced by this model as well as all the models presented in this chapter is validation. Proper validation of risk estimates would require comprehensive infection data on the actual transmission paths of the disease (i.e., travel routes which infected individuals were on and scenarios which resulted in further spread at the destination). Continued model development

can help to provide guidance to public health authorities on the most valuable type of data collection which will in turn enhance the predictive accuracy of such models.

Future Directions

Increased international air travel volumes have increased the risk of introducing infectious diseases into new regions and thus increased the demand for quantifiable models to accurately predict disease-spreading behavior at the global scale. Typically, epidemiological models are used as a planning tool in preparation for possible pandemics, before an emerging infection event, and often rely on assumptions which cannot always be verified prior to the event. However, the inherent stochasticity of disease spreading makes it impossible to anticipate all outbreak scenarios. Experiences from the 2009 H1N1 pandemic, H5N1 and H7N9 avian influenzas, SARS, MERS-CoV, and Ebola, among others, have heightened concerns about possible severe global outbreaks of emerging infectious diseases and have highlighted the need for models which can be used in implementation of real-time containment and control strategies.

As illustrated in this chapter, network-based mathematical models can be prepared to aid in analysis and understanding of emerging infectious outbreaks. However, new methodologies are required which can be efficiently implemented during the acute phase of epidemics. Specifically, models which exploit the types of information now available from organizations such as the World Health Organization (WHO) and the International Health Regulations (IHR) including case reports, epidemiological and clinical characteristics, and laboratory testing, are in high demand and necessary to inform disease control and surveillance efforts in real time.

Future research should aim to further strengthen mathematical modeling of epidemiological risk assessment by developing an integrated risk model for real-time spatial and temporal tracking of infectious diseases. Such models should utilize real-time case reports and simultaneously incorporate contact networks, spatial networks, species distribution models, and multimodal transport systems, in efforts to capture the interaction between global transport systems and local transmission risk. The development of real-time predictive models are necessary to inform policy and practice through identifying infectious disease control needs and mitigate the burden of infectious diseases imported through travel.

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