Chapter 7
Infectious Disease in Wild Animal Populations: Examining Transmission and Control with Mathematical Models

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Abstract The mathematical modeling of ecological interactions is an essential tool in predicting the behavior of complex systems across landscapes. The scientific literature is growing with examples of models used to explore predator-prey interactions, resource selection, population growth, and dynamics of disease transmission. These models provide managers with an efficient alternative means of testing new management and control strategies without resorting to empirical testing that is often costly, time-consuming, and impractical. This chapter presents a review of four types of mathematical models used to understand and predict the spread of infectious diseases in wild animals: compartmental, metapopulation, spatial, and contact network models. Descriptions of each model's uses and limitations are used to provide a look at the complexities involved in modeling the spread of diseases and the trade-offs that accompany selecting one modeling approach over another. Potential avenues for the improvement and use of these models in future studies are also discussed, as are specific examples of how each type of model has improved our understanding of infectious diseases in populations of wild animals.

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7.1 Introduction

Infectious diseases of both humans and animals have played a large role in shaping the world as it is today, from the role of smallpox in the fall of the Aztec (McNeil 1998) to the 2001 foot-and-mouth disease epidemic that cost the United Kingdom over $6 billion (Thompson et al. 2002), and will continue to do so in the future. Although most research into this topic has focused on human and domesticated animals as hosts, the study of wildlife diseases has been growing rapidly since the 1980s (Anderson et al. 1981; Kawata 2010; McCallum 2016). This interest has been driven by desires to minimize risks to human health (e.g., zoonotic diseases such as leptospirosis; Munoz-Zanzi et al. 2014), decrease loss of livestock [e.g., transmission of brucellosis from elk (*Cervus canadensis*) to cattle (*Bos taurus*); Xie and Horan 2009], and preserve either native or endangered species [e.g., canine distemper in the black-footed ferret (*Mustela nigripes*); Thorne and William 1988].

Mathematical models have been a useful tool in the study of wildlife infectious diseases. These models have been used for tasks as varied as predicting the spatial spread of rabies in Eastern Europe (Källen et al. 1985), comparing the benefits of vaccination versus culling in eradicating bovine tuberculosis from England (Smith and Cheeseman 2002), investigating the role of bird feeders in promoting the spread of conjunctivitis in house finches (*Carpodacus mexicanus*) in North America (Hosseini et al. 2004), and even to show that flea-borne transmission is insufficient to maintain plague epizootics in Colorado prairie dogs (*Cynomys ludovicianus*; Webb et al. 2006). Here we present a review of four types of models used in studies of wildlife infectious diseases—compartmental, metapopulation, spatial, and contact network—and discuss their uses, limitations, and contributions to the understanding of infectious diseases. It is important to note that although we present these four models as separate for the purpose of this review, there is in fact substantial overlap between these categories (e.g., a metapopulation model can also exhibit properties of a spatial model).

7.2 Compartmental Models

The majority of disease models are based on categorizing hosts within a population based on their disease status. The most basic form of such a model describes the proportions of the population that are susceptible to (S), infected with (I), and recovered from (R) a particular disease (a complete list of model variables and parameters used in this chapter is provided in Table 7.1). For a pathogen that confers lifelong immunity from future infections, this compartmentalization results in the following set of differential equations that describe how individuals transition between different disease categories:

Table 7.1 Description of variables and parameters commonly used in mathematical models of infectious diseases

Symbol	Definition
S	Proportion of the population that is susceptible to a particular disease
I	Proportion of the population that is infected with a particular disease
R	Proportion of the population that is recovered from a particular disease
υ	Influx of new susceptible into the population through births
μ	Removal of individuals from the population through deaths
β	The product of contact rate and transmission probability for a particular disease
γ	Rate of recovery from a particular disease
X	Number of individuals that are susceptible to a particular disease
Y	Number of individuals that are infected with a particular disease
Z	Number of individuals that are recovered from a particular disease
N	Total number of individuals in the population
R_0	Basic reproductive ratio
λ	The force of infection for a particular disease
ρ_{ij}	The relative strength of transmission from one subpopulation, i, to a different subpopulation, j
P	The proportion of subpopulations infected with a particular disease
r	The reinfection (coupling) rate from an infected subpopulation to an uninfected subpopulation
e	The rate of local extinction for a subpopulation
D_X	Diffusion rate for individuals that are susceptible to a particular disease
D_Y	Diffusion rate for individuals that are infected with a particular disease
D_Z	Diffusion rate for individuals that are recovered from a particular disease
∇^2	Local diffusion rate of individuals through space
$\boldsymbol{G}$	Adjacency matrix that represents the presence, duration, or frequency of contact between individuals

$$\frac{dS}{dt} = \upsilon - \beta SI - \mu S, \tag{7.1}$$

$$\frac{dI}{dt} = \beta SI - \gamma I - \mu I, \tag{7.2}$$

$$\frac{dR}{dt} = \gamma I - \mu R, \tag{7.3}$$

where υ is the influx of new susceptible individuals through births, μ represents the removal of individuals through death, β is the product of contact rate and transmission probability, and γ is the recovery rate (Keeling and Rohani 2008). This formulation is known as the susceptible-infected-recovered (SIR) model, which was originally proposed by Kermack and McKendrick (1927). A slightly different version of these equations can be used to model the *number* of individuals in each disease category:

$$\frac{dX}{dt} = \upsilon - \beta XY/N - \mu X, \tag{7.4}$$

$$\frac{dY}{dt} = \beta XY/N - \gamma Y - \mu Y, \tag{7.5}$$

$$\frac{dZ}{dt} = \gamma Y - \mu Z, \tag{7.6}$$

where X, Y, and Z are the number of susceptible, infectious, and recovered individuals and N is the total number of individuals ($N = X + Y + Z$). Such compartmentalization ignores many details of the progression of the disease, as well as heterogeneity in individual responses and contact probabilities (i.e., all individuals have the same probability of contacting every other individual in the entire population), but nonetheless provides some very important insights into disease dynamics (Keeling and Eames 2005; Keeling and Rohani 2008; Kawata 2010).

Many modifications have been made to this basic framework, usually involving further subdivision of the disease classifications to reflect either more complex pathogen biology (e.g., waning immunity, fatal infection, or the presence of a latent period), multiple pathogens [e.g., canine distemper and sarcoptic mange in fishers (*Martes pennanti*); Keller et al. 2012], multiple hosts [e.g., louping ill virus in red grouse (*Lagopus lagopus scotica*), mountain hare (*Lepus timidus*), and red deer (*Cervus elaphus*); Gilbert et al. 2001], or greater structure within the host population (e.g., age, sex, or social status). These modifications include the susceptible-infectious (SI) and susceptible-exposed-infectious-recovered (SEIR) models, among others. For structured host populations, differences in contact rates between different subgroups often become important, replacing the single parameter β with a matrix that describes the transmission of infection between and within different groups. It is important to note that the assumption of random mixing still remains despite these modifications, although now it is limited to transmission within each subgroup (Keeling and Eames 2005; Keeling and Rohani 2008).

7.2.1 Uses and Limitations

Some of the first and most influential uses of compartmental models involved establishing the conditions necessary to ensure either disease persistence or eradication (Smith and Cheeseman 2002; Keeling and Rohani 2008). Two of the most important quantities in epidemiology emerged from such analyses. The first, R_0, defines the average number of secondary cases that would arise from an average primary case in an entirely susceptible population. The exact formulation of this variable depends on the type of model used (i.e., SIR versus SEIR); however, for the SIR model described above, it is given by $R_0 = \frac{\beta}{\gamma+\mu}$. The force of infection, λ, on the other hand, defines the per capita rate at which susceptible individuals contract the infection, and is equal to βI and $\beta Y/N$, for the proportions and number of individuals formulations, respectively. The values that these quantities take in different host-pathogen systems can determine

the final outcome of the disease (e.g., R_0 must be greater than unity for a disease to spread and less than unity to ensure eventual disease eradication; Keeling and Eames 2005; Keeling and Rohani 2008; Kawata 2010).

Anderson et al. (1981), for example, used a compartmental model to demonstrate that vaccinating at random at least a proportion $p = 1 - 1/R_0$ of the population ensures the eventual eradication of rabies from foxes. Although numerous methods have been devised to improve the calculation of this value (e.g., incorporating age or transmission heterogeneity), the original formulation remains one of the most fundamental and often-used discoveries in epidemiology (Keeling et al. 2003; Garnett 2005; Yip et al. 2007). Multi-host models, on the other hand, have been used to investigate the effects of multiple hosts on maintaining infections in situations where a single host is insufficient to sustain the ongoing spread of the disease (e.g., Dobson and Meagher 1996; Gilbert et al. 2001).

The main limitation of these models is the mean-field assumption, wherein all individuals in the population contact each other with equal probability. Although certain modifications have been devised to address this concern (e.g., introducing host structure such that certain groups mix more preferentially with each other), it still remains the main drawback of compartmental models. Additionally, because such models are aspatial, they cannot be used to investigate the dynamics of host populations that exhibit significant spatial heterogeneity or to model the *spatial* spread of an invading disease (Keeling and Eames 2005; Keeling and Rohani 2008; Kawata 2010).

Another issue with compartmental models has centered on how best to model the transmission between susceptible and infectious individuals. For most of the field's history, density-dependent transmission was used because of its clear analogy to how the rate of interaction between two types of molecules is directly proportional to their densities. While this framework, which yields the familiar βSI transmission term, has been applied with some success, certain populations may not display such a characteristic. For a sexually transmitted disease in humans, for example, the number of transmissible contacts (i.e., sexual partners) is often independent of population density (Lloyd-Smith et al. 2004; Ryder et al. 2007). In these situations, a frequency-dependent rate of transmission is required, which alters the transmission term to $\beta SI/N$ (McCallum et al. 2001; Begon et al. 2002; Keeling and Rohani 2008).

Although these examples may give the impression that transmission operates only at two extremes (i.e., either independent or as a function of host density), in most situations, it is in fact a continuum of values and may even change throughout the course of an epidemic. Antonovics et al. (1995), for example, modeled this continuum based on the Type II Holling functional response curve, wherein contacts at low densities are proportional to the host density but eventually reach a maximum at higher densities. Because the exact formulation of the transmission term is crucial to a model's predictive and descriptive capabilities, as well as the qualitative behavior of the system itself, the relationship of contact rates to density is still an area of active research. In general, however, frequency-dependent transmission is used primarily in models of vector-borne pathogens and human populations, while density-dependent transmission is generally considered to be more applicable to

plant and animal diseases (McCallum et al. 2001; Begon et al. 2002; Keeling and Rohani 2008).

Another common use of compartmental models has been to investigate the role of seasonality in producing either annual, semiannual, or even chaotic patterns of disease prevalence. Many wildlife populations, for example, experience significant changes in transmission rates throughout the year as a result of either flocking behavior (Hosseini et al. 2004), seasonal migration (Bradley and Altizer 2005), or congregation during the breeding and molting season (Swinton et al. 1998). An additional source of seasonality that is almost exclusive to wildlife populations arises from birth pulses which recruit a large number of susceptible individuals into the population at approximately the same time each year (Gremillion-Smith and Woolf 1988; Keeling and Rohani 2008). If a time-dependent component is incorporated into the transmission term, then increasing the amplitude of seasonality can increase the number of prevalence peaks throughout the year, eventually resulting in chaotic dynamics (Ireland et al. 2004).

7.2.2 Specific Applications

The earliest application of compartmental models to infectious diseases in wildlife was presented in the seminal work of Anderson et al. (1981), who developed a deterministic SEI (susceptible-exposed-infectious) model for the fatal rabies virus in European red foxes (*Vulpes vulpes*; Kawata 2010). This model demonstrated that the latent period of rabies could act as a time-delayed density-dependent regulator of fox population growth and result in the 4-year oscillations in population size and disease prevalence observed in fox populations throughout Europe. The authors also concluded that culling alone was unlikely to be effective once rabies becomes established within a fox population. Vaccination, on the other hand, significantly increased the odds of disease eradication, especially when combined with culling in regions with low fox density (Anderson et al. 1981).

Gilbert et al. (2001) used a multi-host approach to investigate how the persistence of a tick-borne virus (louping ill virus) is affected by the presence of grouse, hare, and deer in upland Britain. This model demonstrated that neither deer nor grouse alone could sustain such a virus, but that the combination of the two could and that the inclusion of hare into this system greatly increased the likelihood of virus persistence (Gilbert et al. 2001). These results were later used by Laurenson et al. (2003) to investigate whether decreasing hare density could be used as a strategy to decrease virus prevalence in grouse. They discovered that not only would this strategy decrease infections in grouse, but it would also increase their fecundity as a consequence of increased life expectancy. The authors concluded that mountain

hares serve as a reservoir species that can maintain the virus as long as hare density remains above five individuals km^{-2}.

Packer et al. (2003) used a simple compartmental SI model to demonstrate a very interesting principle—that predator control programs aimed at increasing prey abundance could prove harmful to prey populations that are regulated by infectious diseases rather than by predation. The authors showed that because infected prey live longer in the absence of predators, they are able to infect many more susceptible animals than they would be able to otherwise. Although this effect is more pronounced when predators selectively remove infected prey (e.g., if the infection makes prey easier to capture or locate), nonselective predation is still beneficial to host populations by reducing the life span of infectious individuals. This principle was used to retroactively explain how the introduction of private gamekeepers (who removed predators) in red grouse habitats destabilized the grouse population in North Yorkshire, England (Packer et al. 2003).

7.2.3 Future Directions

As illustrated above, mean-field compartmental models have been used in a wide variety of settings and have provided the foundation for much of the epidemiological literature and theory. Unfortunately, the mean-field assumption and the aspatial nature of these models limit their ability to provide accurate predictions of the likely spread of a disease through a wildlife population. This limitation has led to the development of several more sophisticated methods to describe the spread of infectious diseases, which are detailed throughout the remainder of this chapter. Despite these advances in infectious disease modeling, there are still several aspects of disease ecology that can be best investigated with compartmental models.

For example, compartmental models can be used to explore the role of seasonal variation in mortality rates in the spread of infectious diseases. Previous research has investigated the role of seasonality in births (e.g., Ireland et al. 2004), demonstrating how increases and decreases to the magnitude of this seasonality can have profound consequences to the spread of the disease. Unfortunately, similar theory does not yet exist for the effects of altering the magnitude of seasonality in mortality rates. This avenue for future research would be particularly appealing because, unlike for births, newly developed theory could be tested by manipulating the timing, extent, and demographic characteristics of mortality through changes to harvest regulations. Because harvest constitutes a substantial portion of deaths in many wildlife populations (e.g., Erb et al. 2013; Ramsey et al. 2014), understanding how changes in harvest intensity will impact the spread of disease could prove to be a powerful tool for wildlife managers.

7.3 Metapopulation Models

Although the spread of infectious diseases is predominantly a localized process (i.e., between individuals in the same location), the movement of individuals between aggregate groups can help to facilitate the geographical spread of the disease. Metapopulation models, originally developed for application in ecology (Levins 1969; Hanski 1999), provide a simple but powerful means of capturing this spatial structure by subdividing the entire population into distinct groups known as subpopulations. These models typically assume that transmissible contacts will occur at a higher rate between individuals of the same group than between individuals of different groups, allowing each subpopulation to exhibit largely independent dynamics (Jesse et al. 2008; Ball et al. 2015).

In such a framework, the original SIR equations can be modified as

$$\frac{dX_i}{dt} = \upsilon_i N_i - \lambda_i X_i - \mu_i X_i, \tag{7.7}$$

$$\frac{dY_i}{dt} = \lambda_i X_i - \gamma_i Y_i - \mu_i Y_i, \tag{7.8}$$

$$\frac{dZ_i}{dt} = \gamma_i Y_i - \mu_i Z_i, \tag{7.9}$$

where i refers to parameters that are particular to subpopulation i and may vary substantially between subpopulations due to differences in the local environment (Broadfoot et al. 2001; Langlois et al. 2001; Keeling and Rohani 2008). Although most of the useful quantities derived from mean-field compartmental models still apply, they must now incorporate, ρ_{ij}, the relative strength of transmission from one subpopulation, i, to a different subpopulation, j (e.g., $\lambda_i = \beta_i \sum_j \rho_{ij} Y_j / N_i$ vs. $\lambda = \beta Y/N$; Keeling and Rohani 2008).

Although metapopulation structure is inherently based on the host population of interest, these models usually fall into one of three categories. Wind- and vector-borne transmission models, for example, assume that subpopulations are epidemiologically sessile, forcing coupling (i.e., the strength of transmission) to decrease with distance. These models have been used extensively to model the spatial dynamics of livestock diseases by treating each farm as a sessile subpopulation (e.g., Ferguson et al. 2001; Keeling 2001). Commuter models, which are most commonly used for human population, are instead based on the premise that permanent relocation between subpopulations is rare but temporary travel between them is sufficient for disease spread (Keeling and Rohani 2008). Finally, most models of animal diseases rely on either the migration or permanent movement of individuals to spread the pathogen (Keeling and Rohani 2008).

Once the appropriate relations are defined, the system of equations can be solved in either a deterministic or stochastic manner. Because this framework is able to capture the spatial clustering of the host population, it has been used extensively not only for the study of infectious diseases but also in the ecological literature to derive

such concepts as the extinction-colonization balance, rescue effect, and isolation paradigm (Hanski 1998, 1999).

7.3.1 Uses and Limitation

One of the most common uses of metapopulation models is to investigate the influence of substructure on disease thresholds and persistence. Group size heterogeneity, for example, can increase disease persistence by allowing smaller subpopulations, where the pathogen would normally be unable to persist, to continually become reinfected from larger ones where the disease is maintained (Broadfoot et al. 2001). The level of substructure has also been shown to be an important consideration, with higher numbers of subdivision (e.g., dividing subpopulations into smaller groups) leading to longer disease outbreaks and increased persistence (Swinton et al. 1998). Similar approaches have also been used to understand the rate and heterogeneity of the spatial spread of a pathogen (e.g., Langlois et al. 2001; López et al. 2009).

A general trend that has emerged from this modeling framework is that given certain levels of aggregation and coupling, a pathogen can persist within the host population for much longer than would be predicted by a mean-field compartmental model (Swinton et al. 1998; Fulford et al. 2002; Keeling and Rohani 2008). Although many modeling studies have concluded that persistence increases with the intergroup connectivity, Jesse et al. (2008) demonstrated that the relationship is strongly nonlinear. More specifically, a peak in epidemic duration appears at small movement rates (due to asynchrony in the disease dynamics between subpopulations), followed by a global maximum at larger rates (when the pathogen "perceives" the metapopulation as a single well-mixed population). These results are particularly applicable to outbreak management because they demonstrated that while restricting animal movement (a common response to disease outbreaks in cattle farms) will reduce the total *number* of subpopulations that experience infection, it may also prolong epidemic duration instead of decreasing it. At these lower movement rates, any infectious animal that does move between subpopulations has a large probability of encountering a fully susceptible subpopulation, thereby preventing the disease from dying out for an increased length of time (similar to the rescue effect in ecology). Another important conclusion is that although increasing mixing between subpopulations via habitat corridors is an effective means of species conservation (Hanski 1999), their potential as conduits for the spread of infectious diseases should be carefully considered before implementation (Hess 1994, 1996).

Metapopulation models have also been used to evaluate the benefits of different control strategies that take into account the local nature of spatial transmission. Beyer et al. (2012), for example, demonstrated that rabies fade-out in Tanzania became increasingly more likely once vaccination reduced the number of susceptible dogs in each village subpopulation below 150. Fulford et al. (2002) used a similar

approach to show that for subpopulations that occur in a chain configuration (e.g., along rivers or roads), limited culling applied to alternate patches was significantly more effective in reducing disease prevalence than extensive culling applied in large batches along the chain.

Apart from the fact that metapopulation models still assume homogeneous mixing (although at the intra-subpopulation level), their main limitation is that they require detailed information on the number of individuals in each subpopulation, which can be difficult to collect and computationally intensive to explicitly model (Keeling and Rohani 2008). An alternative approach, originally proposed by Levins (1969), models each subpopulation as being either pathologically empty (disease-free) or occupied (having infection). The intuitive way to conceptualize this is to assume that localized extinctions and successful recolonizations are extremely rare, so that each subpopulation spends the vast majority of its time either disease-free or close to the endemic equilibrium. For a large number of subpopulations with equal probabilities of infecting each other, the proportion of infected subpopulations, P, is governed by

$$\frac{dP}{dt} = r(1 - P)P - eP, \tag{7.10}$$

where r measures the reinfection (coupling) rate from an infected subpopulation to an uninfected one and e is the rate of local extinction (Keeling and Rohani 2008). Although this approach has been used much less extensively than the previously described standard approach, it has nonetheless been used to derive some interesting results [e.g., see Smith et al. (2002) below].

7.3.2 *Specific Applications*

Plowright et al. (2011) created a metapopulation model to provide a mechanistic understanding of the causal links between anthropogenic change and emergence of new zoonoses from wildlife in Australia. As urbanization destroyed most of the contiguous forest cover on the eastern coast, fruit bats (*Pteropus* spp.) began switching their diet from the more patchily distributed nectar and fruit sources to urban gardens that provide abundant food year-round. Unlike the old diet that required long-distance foraging and migration, the new one required minimal migration, which decreased the connectivity between subpopulations (identified by the location of their daytime roosts). By incorporating data on within- and between-camp transmission, the authors demonstrated that the decreased migration led to increased epidemic sizes and divergence in both amplitude and frequency from epidemics in rural camps. This was due to the fact that as fewer individuals migrated, the probability of infected hosts moving between camps decreased, which lowered the probability of camps becoming reinfected after local viral extinction and increased the time over which subpopulations could recruit susceptible individuals via births. This resulting decline in herd immunity across the metapopulation shifted disease

dynamics toward sporadic, shorter, and more intense local epidemics with larger numbers of infected individuals. However, if this connectivity were to drop below a certain threshold level, then the resulting movement would become insufficient to reinfect distant camps. Thus, the same conditions that are currently responsible for large and sporadic epidemics could eventually lead to viral extinction, rendering the entire population vulnerable to a large synchronized outbreak (Plowright et al. 2011).

Another application of this modeling framework was recently employed by Pons-Salort et al. (2014) to explore the role of four different species of bats in the persistence of rabies across three cave-dwelling colonies on the Balearic Islands in Spain. By successively removing each of the four species from the transmission cycle, they were able to demonstrate that the common bent-wing bat (*Miniopterus schreibersii*) is the only species essential for the persistence of the virus, because it serves as a regional reservoir in the system. In fact, if this species were removed, then even increased contact rates and interisland exchanges between the remaining three species would be insufficient to maintain rabies infections. Additionally, Pons-Salort et al. (2014) demonstrated that contrary to expectation, the most abundant species of bat on the islands, the greater mouse-eared bat (*Myotis myotis*), plays a relatively minor role in the persistence of the virus.

A large wave of rabies infections began on the Virginia-West Virginia border in the mid-1970s and generated interest in how landscape structure (e.g., the location of roads, bodies of water, and human population centers) affects the spread of disease. Smith et al. (2002) used a Levins-type metapopulation model to study a small portion of this wave as it traveled through raccoons (*Procyon lotor*) in 169 townships across Connecticut from 1991 to 1996, concentrating on the underlying spatial heterogeneity of the habitat. A spatial SI model (used instead of an SIR because there is no recovery from infection at the township level) was compared to the observed data of reported rabies outbreaks and resulted in a best fit model where rivers reduced transmission by 87% compared to land boundaries; local transmission accounted for most but not all of the spatial spread; and human population density played a small but positive role in transmission (Smith et al. 2002). Although this formulation ignored within-subpopulation dynamics (i.e., a newly infected township can transmit infection as strongly as when endemic equilibrium is reached), it allowed for far richer parameterization without the need to estimate the number of raccoons in each township.

7.3.3 Future Directions

As illustrated above, metapopulation models have provided important insights into the complexities and spatial variation observed in disease prevalence and outbreaks. Despite the progress that has been made in the development and application of these models, however, there are a number of limitations that still require improvement.

For example, there is substantial interest in devising a practical framework for ascertaining the optimum timing and duration of vaccination pulses to promote the extinction of a pathogen at the population level. Although theoretical research has

demonstrated that pulsed vaccination has the ability to synchronize epidemic behavior and thereby limit pathogen rescue effects, understanding how this benefit interacts with the resulting buildup of susceptibles between pulses can have enormous public and animal health consequences (Keeling and Rohani 2008).

Another exciting avenue for future research is to develop a method for using data from the first phase of an epidemic to accurately parameterize all aspects of a metapopulation model (Ball et al. 2015). Unfortunately, data collected during this phase are prone to a number of biases that are not yet fully understood (e.g., underestimation of fatality rates due to the time delay from disease onset to death; Nishiura et al. 2009). Overcoming these challenges could greatly improve the capability of metapopulation models to accurately predict the likely progression of an outbreak and the efficacy of different control strategies.

Finally, several studies have noted that assuming homogeneous mixing within subpopulations tends to overestimate the spatial spread, time to peak incidence, and the peak number of cases of epidemics when compared to more refined models (Ajelli et al. 2010; Keeling et al. 2010). Identifying situations where these differences are most prominent and devising methods to adjust model predictions accordingly still remains a major challenge in metapopulation modeling theory (Ball et al. 2015).

7.4 Spatial Models

Spatial models subdivide the area occupied by the host species into a grid and thus provide a way to model the spatial structure of a population without dividing it into distinct social groups. The most common approach is to model interactions as occurring only between individuals occupying either the same or neighboring grid cells while allowing individuals to move between them. These spatial lattice-based models can be thought of as a special case of metapopulation models (where each cell represents its own subpopulation) and as such are governed by a very similar set of equations:

$$\frac{dX_i}{dt} = \upsilon - \beta X_i \frac{\left(1 - \sum_j \rho_{ji}\right) Y_i + \sum_j \rho_{ij} Y_j}{\left(1 - \sum_j \rho_{ji}\right) N_i + \sum_j \rho_{ij} N_j} - \mu X_i, \tag{7.11}$$

$$\frac{dY_i}{dt} = \beta X_i \frac{\left(1 - \sum_j \rho_{ji}\right) Y_i + \sum_j \rho_{ij} Y_j}{\left(1 - \sum_j \rho_{ji}\right) N_i + \sum_j \rho_{ij} N_j} - \gamma Y_i - \mu Y_i, \tag{7.12}$$

$$\frac{dZ_i}{dt} = \gamma Y_i - \mu Z_i, \tag{7.13}$$

where ρ_{ij} is equal to one if i and j are neighbors and zero otherwise.

An alternative approach is to treat each grid cell as being large enough to only contain a single individual (i.e., a subpopulation of one). This results in a finite number of states for these subpopulations, wherein each cell is either empty or

occupied by a susceptible, infectious, or recovered individual (Keeling and Rohani 2008; Miksch et al. 2013). This formulation follows a fire ecology framework originally developed by Bak et al. (1990), where each cell was either empty or occupied by a healthy or burning tree (reflecting a recovered, susceptible, and infectious host, respectively). Burned trees that died left empty spaces that could then be colonized (reflecting recovery and births), and fire (reflecting infection) could spread between neighboring trees. Although this framework makes a number of simplifying assumptions (e.g., trees do not always die from fire), it has nonetheless been used as the foundation for some interesting spatial models of infectious diseases [e.g., see Tischendorf et al. (1998) below].

7.4.1 Uses and Limitations

Like all mathematical models, lattice-based spatial models are a clear abstraction of reality because, except for agricultural settings such as orchards (e.g., Gibson 1997; Poggi et al. 2013), individuals do not exist on a regular grid. Thus, spatial models are mainly used to investigate how the effects of spatial separation and nonrandom mixing cause disease dynamics to deviate from mean-field approximations in a spatial framework. For example, these models have demonstrated that an invading infection is characterized by a clear wave-like spread because the disease must first spread to neighboring sites before reaching the rest of the population. Similar to metapopulation models, spatial models have also been used to evaluate the broad-scale consequences of different control efforts including vaccination (e.g., Tischendorf et al. 1998) and culling (e.g., White and Harris 1995; Deal et al. 2004).

Although spatial models are a clear abstraction of the spatial structure of most host populations, certain types of wildlife populations actually lend themselves very naturally to be modeled using such an approach. Populations that occur in either a one-dimensional chain (e.g., along a river) or loop (e.g., surrounding an impassable urban center) can be thought of as having only nearest-neighbor connectivity and as such can easily be modeled using a lattice-based approach.

Despite these uses, the separation of populations into a lattice framework has several drawbacks. Imposing a square grid onto a habitat, for example, forces interactions in particular directions (e.g., north, south, east, and west) to play a disproportionately larger role in disease transmission than interactions in other directions. The use of a hexagonal grid, however, helps to alleviate this problem and often better recreates observed spatial patterns (Anneville et al. 1998; Van Baalen and Rand 1998; Kao 2003; Birch et al. 2007). A more general issue is that the discretization of space forces intracell interactions to be far stronger than intercell ones, regardless of the actual distance between individuals in each cell. Two individuals that occupy adjacent corners of two separate cells, for example, would have weaker interactions than two who occupy the same cell but are at opposite ends, despite the fact that the former are closer to each other than the latter (Keeling and Rohani 2008).

Another disadvantage of this lattice-based approach is that dividing the space occupied by a population into discrete cells limits how precisely we can model the location of each individual (i.e., we only know which cell an individual is in but not where inside the cell they are). An alternative approach is to treat this space as continuous, which allows us to model the *exact* location of each individual in the population. This approach is essentially an extension of the lattice-based framework, where the size of each cell has become infinitely small, and is the foundation of reaction-diffusion models (Keeling and Rohani 2008). The standard reaction-diffusion model assumes that individuals move randomly throughout the landscape and that infections are only transmitted between individuals sharing the same location (Källen et al. 1985; Murray et al. 1986; Yachi et al. 1989; Kawata 2010), resulting in the following set of equations:

$$\frac{\partial X}{\partial t} = \upsilon - \beta XY/N - \mu X + D_X \nabla^2 \mathrm{X}, \tag{7.14}$$

$$\frac{\partial Y}{\partial t} = \beta XY/N - \gamma Y - \mu Y + D_Y \nabla^2 \mathrm{Y}, \tag{7.15}$$

$$\frac{\partial Z}{\partial t} = \gamma Y - \mu Z + D_Z \nabla^2 \mathrm{Z}, \tag{7.16}$$

where X, Y, and Z are now functions of both space and time, ∇^2 describes the local diffusion of individuals through space, and D_X, D_Y, and D_Z, are the diffusion rates for the three classes of individuals (Keeling and Rohani 2008; Kawata 2010).

An extension of this approach is to incorporate a transmission kernel that models how transmission risk decreases with distance. This kernel acts to relax the assumption that transmission is solely a localized process, allowing individuals not in the immediate vicinity of an infectious individual to still become infected, albeit at a significantly lower rate (Schofield 2002; Keeling and Rohani 2008). Because reaction-diffusion models provide a very broad-scale view of disease outbreaks, their application has mostly been limited to investigating either epidemics that span large spatial scales (Conner and Miller 2004) or the presence and role of rare but long-range disease transmission (e.g., dispersing animals) in accelerating the spatial diffusion of a newly introduced pathogen (Schofield 2002; Keeling and Rohani 2008).

7.4.2 Specific Applications

In 1997, a large-scale and long-term immunization of European foxes against rabies was under consideration to be either terminated or cut back due to diminishing returns and despite lasting sporadic incidences. Tischendorf et al. (1998) used a spatial model to investigate the effectiveness of this program and assess the consequences of either reducing or eliminating it on the persistence of rabies. This approach involved simulating the mating, dispersal, and vaccination of fox social groups across a lattice grid, as well as the contact between and within groups. Unlike the traditional approach, each grid was able to hold one of six possible states—the

three "simple" states of infectious, empty, and susceptible and three new "mixed" states of susceptible plus immune, infectious plus immune, and empty plus immune (meaning that only immune foxes are present). The results of this model showed that even in a highly immunized fox population such as the one throughout Europe, rabies can still persist in the form of moving clusters of infection. The probability of disease eradication rises sharply after a mean immunization rate of 70% is reached, although a further 6 years of maintaining this level was required to guarantee rabies eradication (Tischendorf et al. 1998).

In South West England, efforts to eradicate bovine tuberculosis from cattle were complicated by the presence of a wildlife reservoir for the disease in European badgers (*Meles meles*). White and Harris (1995) developed a stochastic lattice-based model that incorporated density-dependent fecundity and cub survival and used badger social groups as the basic unit of measurement. The major result of this model showed that although bovine tuberculosis could persist for a long time in populations with a disease-free equilibrium group size of only four individuals, a group size threshold of six was required for the disease to become endemic. Additionally, increasing intergroup contact rates significantly improved the probability and rate of spread of infection and lowered the group size threshold required for endemicity. As such, perturbations of badger social groups caused by control operations could actually increase the probability of persistence (or spread) of an infection instead of preventing it (White and Harris 1995).

In 1977, a single rabies-positive raccoon was identified in Pennsylvania and determined to be a by-product of a restocking program that transported raccoons from Florida to Virginia and West Virginia in the mid-1970s. By 1996, the rabies virus spread to almost all counties in Pennsylvania, resulting in 3912 confirmed cases of infected raccoons and a further 2137 cases in other animals. Moore (1999) used the timing of first cases in each county to construct a reaction-diffusion model for the entire state and explore what factors influenced the speed and direction of the spread. The resulting contours revealed that the infection first spread northward along the corridors of the Appalachian Mountain and Great Valley sections of the state, before twisting to the west once it reached the high plateau areas in the north. These results differed from the homogeneous point diffusion process originally proposed for the rabies outbreak and were used to inform a strategic oral-bait vaccination strategy (Moore 1999).

Sayers et al. (1985) used a similar approach to investigate how geographic features influenced the diffusion of fox rabies through cities in Germany. The derived pathogen velocity vectors demonstrated that propagation was fastest along a broad range of limestone with elevations up to 600 m and diverse land cover and vegetation. These results were later used by Källen et al. (1985) to design a deterministic model for the spread of this epizootic front westward across Europe that helped identify the width of a control barrier that would prevent the disease from entering the rabies-free United Kingdom. This model predicted a front wave speed of 50 km year^{-1}, consistent with empirical data from the German-Polish border, and resulted in an estimated barrier width of 15 km (Källen et al. 1985). This westward spread was eventually halted through the delivery of a highly effective oral vaccine (Jackson and Wunner 2002).

7.4.3 Future Directions

As illustrated above, the use of spatial models has provided managers with not only the tools to evaluate different control strategies but also with explanations for observed disease distributions. However, there are still many interesting aspects of spatial disease models that warrant additional research.

For example, there is interest in exploring how spatial structure influences basic epidemiological characteristics such as R_0 and the epidemic threshold (Riley et al. 2015). Although calculating these values is relatively simple in models that exhibit homogeneous mixing (i.e., compartmental and metapopulation models), the clumping of individuals in spatial models substantially complicates the calculations. Mollison and Kuulasmaa (1985), for example, demonstrated that the epidemic threshold (i.e., the value of R_0 required for the disease to spread through the population) for a nearest-neighbor lattice-based model is between 2 and 2.4, compared to the usual value of 1. A better understanding of how clumping and other spatial characteristics of a population influence this and other aspects of disease spread can greatly improve the use of spatial models.

Another exciting avenue for future research is to investigate the effects of spatial and temporal resolution on the accuracy of spatial models. Although it may be tempting, for example, to select the finest scale possible based on the available data, it may be more helpful to model the spread of the disease at the same scale as that used for control and management (e.g., counties or townships; Riley et al. 2015). Finer temporal scales may also be tempting, but require substantially more data on all aspects of animal behavior that could contribute to disease spread. Kjaer (2010), for example, used a 2-hour time step to model the spread of chronic wasting disease in a hypothetical population of white-tailed deer (*Odocoileus virginianus*). Berg (2016), on the other hand, modeled a similar system using a 1-week time step. Although this later approach allowed for far richer parameterization of the progress of the disease in individual animals, it came at the expense of being unable to include events that occurred at time intervals shorter than 1 week (e.g., occasional daylong excursions made by deer outside of their home range). Developing generalities about how different spatial and temporal scales influence the modeled spread of a disease can greatly improve the use of spatial models in the management and control of wildlife diseases.

7.5 Network Models

Although many infectious disease models assume random mixing either within the host population as a whole or within each subpopulation or grid cell separately, the number of contacts each individual has in a real population is significantly smaller than the (sub)population size and is highly heterogeneous between individuals. The contact network approach, originally developed for application in statistical physics,

provides another means of studying disease dynamics in these heterogeneous populations (Keeling and Eames 2005; Keeling and Rohani 2008; Craft and Caillaud 2011). In this framework, individuals (or groups of individuals) are represented as nodes, and connections between them are referred to as edges. These edges can represent transmission events, contact through which infections could spread, and even movement of animals between groups (Pellis et al. 2015), and can be either undirected (for infections that can pass in both directions with equal probability) or directed (for infections that can pass better in one direction than the other; Keeling and Eames 2005). These connections may also be either binary (representing whether any contact has occurred or not) or weighted (representing the duration or frequency of contact) depending on the host-pathogen system of interest (Godfrey 2013).

The simplest way to represent a contact network is to construct a $N \times N$ adjacency matrix, $\boldsymbol{G}$, where N is the number of individuals in the study population and $\boldsymbol{G_{ij}}$ represents either the presence, duration, or frequency of contact between individual i and individual j. Although this matrix is usually symmetric (i.e., $\boldsymbol{G_{ij}} = \boldsymbol{G_{ji}}$), directed networks yield nonsymmetric matrices (i.e., $\boldsymbol{G_{ij}} \neq \boldsymbol{G_{ji}}$; Keeling and Eames 2005). A number of useful quantities have been derived using adjacency matrices to describe how connections within a network are structured. These include individual-level metrics such as degree (number of edges connected to a single node) and centrality (how important and influential a node is within the network; White et al. 2015), alongside population-level metrics such as clustering coefficient (the extent to which an individual's neighbors are connected to each other; Godfrey 2013) and "small-world-ness" (i.e., the interaction of local clustering and average path length; Humphries and Gurney 2008).

Once the appropriate contact network and associated adjacency matrix are constructed, transitions between disease states are evaluated in discrete time steps (e.g., once every 3 months) on an individual basis using predetermined probabilities (e.g., a susceptible individual who is in contact with an infectious one has a 0.4 probability of becoming infected, while the infectious individual has a 0.2 probability of recovering; Keeling and Rohani 2008). This framework is able to capture complex individual-level structure and heterogeneity in a relatively simple manner and as such has been used not only for animal diseases but also for a variety of human ones such as HIV (Sloot et al. 2008) and SARS (Small and Tse 2005). Network models have also been used in other disciplines, such as sociology, to measure actor prestige (Korfiatis and Sicilia 2007) and to investigate dynamics of rumor spreading (Moreno et al. 2004).

7.5.1 Uses and Limitation

One of the most common uses of network models is to investigate the role of degree heterogeneity and well-connected individuals (i.e., super-spreaders) in driving disease dynamics (Böhm et al. 2009; Hamede et al. 2012; White et al. 2015). For

example, because these super-spreaders can have a disproportionately high impact on the basic reproductive ratio and the epidemic threshold, network models are often used to evaluate how either vaccinating or quarantining super-spreaders will influence disease spread (Craft and Caillaud 2011; Tompkins et al. 2011). Normally, such well-connected individuals would be considered to be at highest risk of infection (Godfrey 2013). However, while this relationship does exist for many wildlife populations [e.g., brushtail possums (*Trichosurus vulpecula*); Corner et al. 2003], it appears to be absent in others [e.g., meerkats (*Suricata suricatta*); Drewe 2009]. It is also important to remember that although super-spreaders have been identified in many wildlife populations, they appear to be absent in others [e.g., Tasmanian devils (*Sarcophilus harrisii*); Hamede et al. 2009].

A general trend that has emerged from analyzing network models is that high variation in the degree distribution tends to lower the epidemic threshold and increase the basic reproductive ratio when compared to mean-field compartmental models that use the average degree as a proxy for transmission rates (Bansal et al. 2007). Although several researchers have proposed methods to account for this heterogeneity in mean-field models (e.g., Anderson et al. 1986; Newman 2002), their explicit inclusion via network modeling still provides the best predictor of disease spread (Hamede et al. 2012).

Comparing alternative networks, on the other hand, has been used to gain insights into the importance of different types of animal behavior in disease transmission and to evaluate support for alternative working hypotheses (Godfrey 2013). Drewe (2009), for example, developed separate networks for grooming and aggressive interactions in meerkats and found that not only are the two highly directional (e.g., groomers had a higher risk of tuberculosis infection than groomees), but that grooming was the most important type of social interaction. Fenner et al. (2011) used a similar approach to demonstrate that connectivity to dispersers was more important than connectivity to resident individuals in predicting nematode loads in pygmy blue-tongue lizards (*Tiliqua adelaidensis*).

Networks have also been used to show that group size alone does not necessarily reflect transmission rates. For example, there appears to be no relationship between group size and risk of infection in gidgee skinks (*Egernia stokesii*; Godfrey et al. 2009). Larger primate groups, on the other hand, offset the increased parasite risk associated with group size by imposing within-group substructure (Griffin and Nunn 2011). Network models have been used to show that social interactions are often more important in disease spread than either spatial proximity or home-range overlap (Bull et al. 2012), address the issue of using different spatial scales (Davis et al. 2008), and investigate if density influences contact rates (Ji et al. 2005). Alongside these more specific applications, network models have also been used in much the same way as earlier model types—to evaluate a wide range of disease control measures such as oral vaccines (Delahay et al. 2009) and culling (Ramsey et al. 2002).

As has been illustrated above, one of the main advantages of network models is their versatility, allowing them to be applied to most host-pathogen systems (e.g., both directly and indirectly transmitted viruses, bacteria, and parasites; Godfrey 2013). In

fact, they can be parameterized to recreate almost any other model type (e.g., a compartmental model is simply a fully connected network, while a lattice-based model can be replaced by a lattice network with nearest-neighbor connectivity; Craft and Caillaud 2011). The main limitation of these models, however, is that accurate parameterization requires detailed data on the contact and movement patterns of every individual within the study population at a time scale appropriate for the transmission process (Godfrey 2013). Although ongoing advances in GPS and proximity sensor technology are helping to alleviate this problem (e.g., Leu et al. 2010; Hamede et al. 2012; Reynolds et al. 2015), accurate sampling of every individual is still neither financially nor logistically feasible except for the smallest of wildlife populations (Tompkins et al. 2011; Godfrey 2013). Because of this, most studies (e.g., Craft et al. 2010; Hamede et al. 2012; Reynolds et al. 2015) use a "representative" subset of the population to generate contact networks that recreate observed measures of connectivity (e.g., average number of contacts, degree distribution, or amount of clustering).

Another challenge in using contact networks is defining what constitutes a transmissible contact (e.g., what proximity or duration is required to transmit an aerosol pathogen; Craft and Caillaud 2011; Tompkins et al. 2011). Because it is often impossible to determine exactly how transmission occurs without resorting to controlled transmission experiments that are often infeasible, most studies use either spatial proximity (e.g., Fenner et al. 2011) or home-range overlap (e.g., Godfrey et al. 2010) as proxies of contact and transmissible events. Additionally, wildlife networks often, if not always, exhibit temporal variation (e.g., higher contact rates while females are in estrous; Rushmore et al. 2013) that can drastically alter disease dynamics, requiring long-term observations for accurate parameterization (Volz and Meyers 2007, 2009; Hamede et al. 2012).

7.5.2 Specific Applications

Although most contact networks are extrapolated from a supposedly representative subset of the study population, certain situations (e.g., endangered or very large animals) may still allow researchers to explicitly capture the full network of contacts. Leu et al. (2010), for example, constructed a directed transmission network for a subpopulation of sleepy lizards (*Tiliqua rugosa*) to determine whether asynchronous use of overnight refuges (a form of indirect and directional transmissible contact) could account for observed ectoparasite loads in individual lizards. Simulating disease spread on this network provided a powerful predictor of ectoparasite loads and revealed that individuals who use many refuges had significantly lower loads as a result of a lower probability of using a previously occupied refuge. This study helped to not only identify increasing the number of available refuges as the optimum strategy for reducing disease in sleepy lizards but also provided one of the first frameworks for using contact networks to investigate the dynamics of indirectly transmitted diseases (Leu et al. 2010).

Network models have been used to demonstrate that heterogeneity in either the connectivity or degree of individuals can have important consequences for the epidemic threshold and rate of spread of a disease. However, it is important to realize that a population's contact structure often operates on multiple hierarchical scales (i.e., individuals form groups that exhibit their own heterogeneous contact network; Craft and Caillaud 2011). Caillaud et al. (2013) constructed an undirected, two-level (i.e., individuals interacting within groups alongside intergroup connectivity) hierarchical model for a hypothetical infectious disease to demonstrate that variation in group size significantly reduces the epidemic thresholds, as well as increases the mean and variance of small outbreak sizes. This suggests that incorporating group size heterogeneity into disease models can greatly improve their predictive capabilities, much like the incorporation of degree heterogeneity described above. The authors also introduced the concept of an epidemiological effective group size, defined as the group size in a homogeneous population that would result in the same epidemic thresholds as the heterogeneous one. By applying this concept to lions (*Panthera leo*) in the Serengeti National Park, Caillaud et al. (2013) demonstrated that the observed network, which exhibited highly variable pride sizes, is comparable to a homogeneous population with approximately 10–20% larger prides.

Recognizing the importance of temporal variation in contact structure, Hamede et al. (2012) used proximity-sensing radio collars to derive seasonal patterns of contact in a distinct population of Tasmanian devils. These patterns were then used to generate sets of contact networks with suitable characteristics (e.g., mean degree and transitivity) that regenerated associations once every 3 months. By stochastically simulating the spread of devil facial tumor disease through these dynamic contact networks, the authors demonstrated that failure to account for seasonal contact structure significantly overestimated the time to host extinction as well as the transmissibility threshold necessary for an epidemic to occur. Interestingly, the differences in time to host extinction between network and compartmental models became negligible for transmission rates close to either zero or one, suggesting that contact heterogeneity has little effect on the dynamics of host extinction from diseases with either very low or very high transmissibility. Unfortunately, because transmission rates are likely to be intermediate for most wildlife diseases, ignoring contact structure can have negative consequences for wildlife conservation (Hamede et al. 2012).

7.5.3 Future Directions

As illustrated above, the use of network models to study the patterns of and driving forces behind disease spread has been growing in the wildlife literature despite many challenges (Craft 2015). As technological advances continue to lessen these challenges, network models will undoubtedly provide the means to investigate many new facets of disease ecology.

For example, Pellis et al. (2015) suggest investigating how specific network characteristics influence the spread of an infectious disease through a system. Previous research has demonstrated the effect of degree and group size heterogeneity on the epidemic threshold and basic reproductive ratio (Hamede et al. 2012; Caillaud et al. 2013). Similar research is needed to investigate other effects such as the impact of clustering and degree correlation on R_0 and the likely size and duration of an outbreak. The role of the distribution and correlation of weights in weighted networks deserves similar attention. A better understanding of the epidemiological consequences of these and other characteristics can greatly improve the use of network models in controlling the spread of infectious diseases (Pellis et al. 2015).

Another exciting avenue for future research is to consider how infections themselves alter the topography and characteristics of a network. Croft et al. (2011), for example, found that the presence of infection in female guppies (*Poecilia reticulata*) decreased the duration of contact between individuals and significantly lowered the clustering of the network. Although this study demonstrated a mechanism by which individuals modified their contact structure in a way that depressed the spread of a disease, other infections may instead alter behavior and the corresponding network in a way that promotes disease spread. Identifying and understanding the consequences of these alterations to the likely spread of a disease is an important step in improving the predictive capabilities of network models.

There is also a need to develop more tractable and realistic methods of incorporating the dynamic nature of real-life contact structures into network models (Pellis et al. 2015). The presence, strength, and direction of contacts between individual animals are neither stagnant nor permanent, but instead change over time due to a variety of intrinsic and extrinsic factors (e.g., resource abundance, migration, or injury). Properly modeling the formation and dissolution of these contacts remains a major challenge in accurately parameterizing dynamic network models of wild animal populations.

Finally, network models can be used to explore how infections have influenced the evolution of social organization in wild animals (Godfrey 2013). One hypothesized cost of this evolution is the increased risk of infection caused by higher contact rates and local population densities (Moller et al. 1993; Altizer et al. 2003). Using network models to investigate how these costs are offset by social behavior (e.g., the use of alternate sleeping or roosting sites) can greatly improve our understanding of social structures and the evolution of certain behaviors in a variety of animals (Godfrey 2013).

7.6 Conclusion

The use of epidemiological models in the study of wildlife diseases began in the early 1980s and has since then grown to be a major component of the wildlife disease literature. Although mean-field compartmental models laid much of the foundation for current epidemiological practices (e.g., the basic reproductive ratio and

vaccination threshold), their inability to capture spatial dynamics led to the use of metapopulation and spatial models (Keeling and Rohani 2008; Kawata 2010). More recently, the use of contact networks has emerged as an intuitive and versatile means of studying disease dynamics. As ongoing advances in GPS and proximity sensor technology make it more feasible to capture the level of data required to more accurately parameterize contact structure, network modeling will continue to provide useful insights into infectious diseases of wild animals (Keeling and Eames 2005; Tompkins et al. 2011; Godfrey 2013).

Although much research has evaluated the uses, limitations, and dynamics of different infectious disease models, many potential avenues for future research still exist for each one. For example, although previous research using compartmental models has assessed the role of birth and transmission seasonality in producing annual, semiannual, and even chaotic patterns of disease prevalence (Ireland et al. 2004; Hosseini et al. 2004), little research investigating the role of seasonal patterns of mortality has been undertaken. The development of generalities about what ecological variables (e.g., resource or predator distribution) govern the establishment of contact structures is also of high priority (Craft and Caillaud 2011; Tompkins et al. 2011).

Several more general concerns also exist. For example, there is a substantial need to improve the analytical and computational tools available to infectious disease modelers; emerging methods developed for the analysis of "big data" are particularly intriguing for discerning the contact structure within populations of wild animals (Pellis et al. 2015). These tools include accurate and computationally efficient methods of calculating the basic reproductive ratio, epidemic threshold, and other epidemiologically important quantities from complex model structures (Ball et al. 2015). Identifying ways to combine two or more of the modeling approaches discussed in this chapter (Ball et al. 2015; Pellis et al. 2015), or to combine these models with other tools such as pathogen phylogenies (Frost et al. 2015), to provide a more realistic representation of the complexities involved in the spread of infectious diseases also deserves additional attention.

The ultimate goal of epidemiological models such as those discussed in this chapter is to allow scientists to understand the mechanisms behind and predict the future course of the spread of infectious diseases. As the use and advancement of these models continue, they will undoubtedly continue to aid efforts to minimize risks to human health, decrease loss of livestock, and preserve native and endangered species of wildlife.

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Compliance with Ethical Standards

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