

Scale-dependent approaches to modeling spatial epidemiology of chronic wasting disease

(e.g., birth, mortality, etc.) are often included, particularly for diseases where on a similar timescale as birth and death. In addition to the effect of disease on population performance, the model may explicitly limit population size via density dependence, harvest, and/or density independent processes. Data required to reliably estimate model parameters are more often available at the level of a single population or finer scale and are rarely available at broader spatial scales.

COMPARTMENT MODELS



At a variety of scales, many models of disease dynamics will divide the host population into categories of susceptible, infected, and recovered (SIR) (e.g., Anderson and May 1979, Anderson and

May 1991, Hudson et al., 2001), where recovered can indicate removal from the susceptible pool through acquired immunity (Figure 3.1A). We note that for CWD, the appropriate compartment model is a SI (Figure 3.1B) because animals do not recover. SIR-type models have led to a broad range of important insights to disease dynamics and control strategies during the last 80 years (Kermack and McKendrick 1927, Bartlett 1957, May and Anderson 1978, Anderson 1979, Hudson et al. 2001). The basic SIR model structure has been expanded to accommodate many complex details, including latent periods between infection and infectiousness, age and sex structure, individual variation in susceptibility and infectiousness, and spatial/social structure (Figure 3.2). Moreover, for modeling CWD, an environmental reservoir can easily be included in these SIR-type models (Figure 3.1B). Compartmental

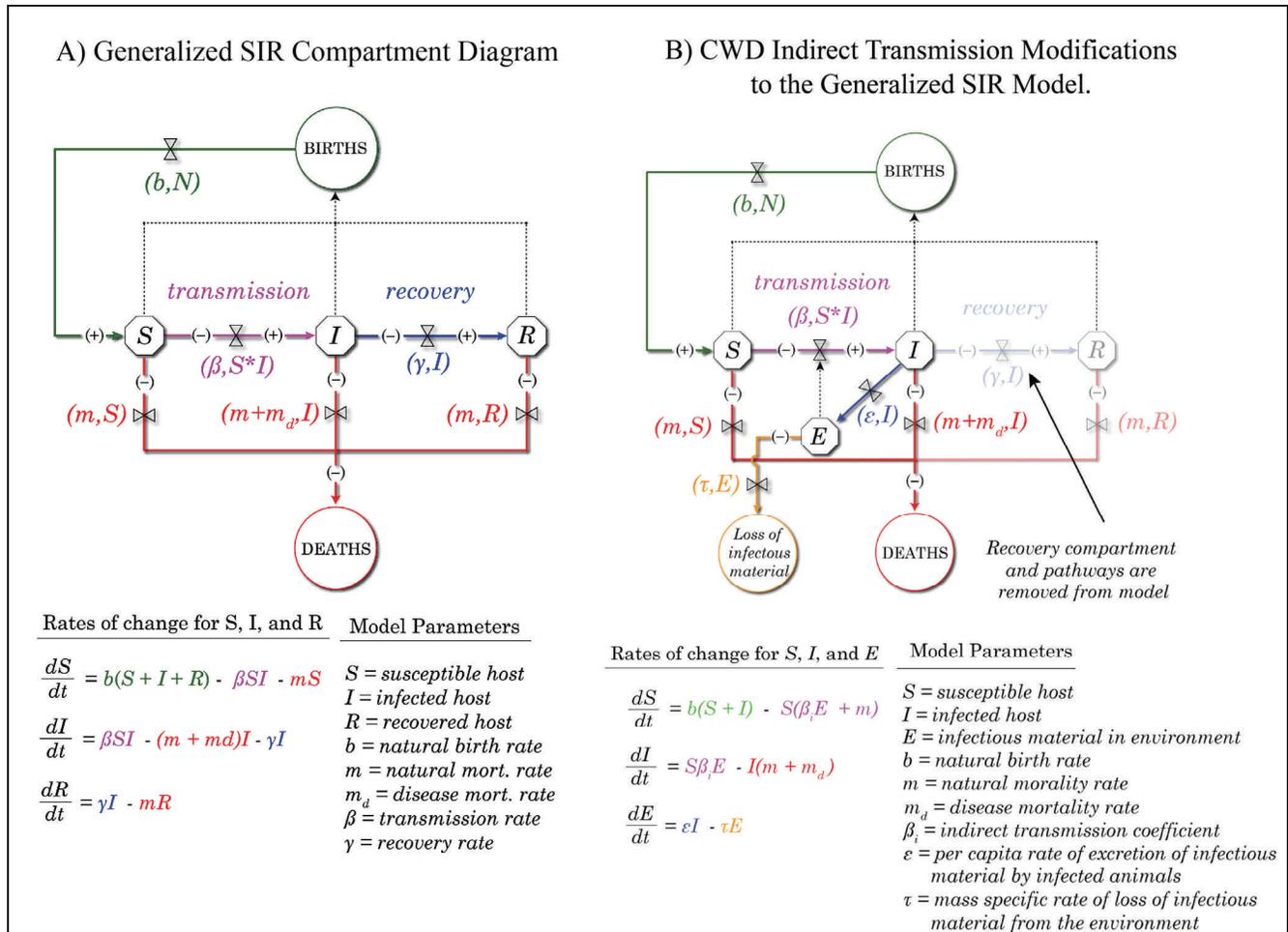


Figure 3.1 Compartments and traditional differential equations for (A) generalized SIR model and (B) CWD adaptation.

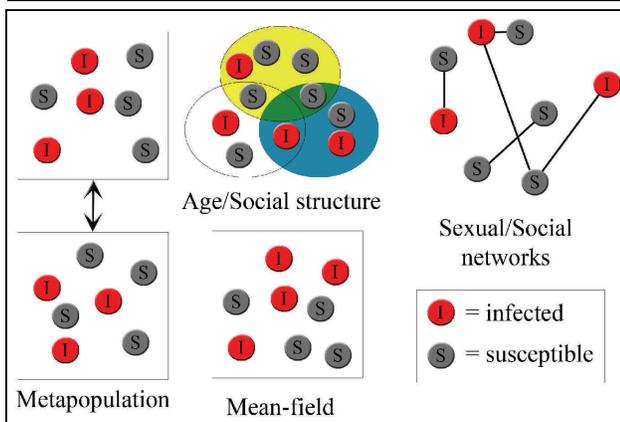


Figure 3.2. Elaborations of traditional SIR models of disease transmission. Adapted from Ferguson et al. (2003).

SIR models can be deterministic or stochastic, spatial or non-spatial, and composed of difference or differential equations. Statistical estimation via likelihood theory can be used to estimate model parameters, while model selection methods, such as Akaike's Information Criterion or Bayesian Information Criterion, can be used to compare and evaluate support for competing SIR model structures. SIR models that are composed of a relatively small number of differential equations may be solved using analytical tools. When additional details are added to SIR models, it quickly becomes more difficult to find analytical solutions, estimate model parameters, and evaluate the level of support for different model structures. As a result, researchers usually explore more complicated model structures via computer simulation. Simulation and randomization techniques can be used to model more complicated structures or to evaluate the effects of stochasticity in various model parameters.

Compartment models have been used to evaluate potential control and transmission of CWD. Hobbs (2006) constructed a relatively simple compartment model to explore the potential of a predator (e.g., large carnivore) that selectively fed on CWD-infected elk to control or eradicate the disease. The model showed that under circumstances thought to be within the bounds of realistic parameter estimates, a small positive selection for infected elk would have a large influence on prevalence of CWD.

In another example, Miller et al. (2006) constructed a set of six compartment models that varied in complexity and in potential routes of transmission. Beyond the basic SIR structure, model complexity varied by including (or not including) a latent period, indirect transmission, and an incubation period. They fitted model parameters to observations from two epidemics in captive herds of mule deer, using information criteria to identify the models that best matched observation. Model results for the two epidemics in captive herds best supported a model that included only indirect transmission, substantiating empirical evidence for environmental transmission of CWD in mule deer (Miller et al. 2006). Transmission rates estimated by Miller et al. (2006) are likely much greater than those in free-ranging deer, and they thus provide an upper bound for modeling CWD transmission and spread over larger spatial scales. Results from this and several other studies suggest the role of an environmental reservoir of infection. This environmental reservoir should be considered in the construction of SIR-type models of CWD as well as several of the other modeling methods we discuss in this text.

Compartmental models cover an exceptionally broad range of model types, as evidenced by Anderson and May's (1991) 700 page book, which focuses on models based on SIR-type structures. It is thus neither possible nor useful to describe all the kinds of questions that can be addressed with these models. In general, compartmental models are most suited to large populations, where aggregate behaviors adequately account for disease and population dynamics. Problems with demographic and/or disease stochasticity may arise when host populations are small or disease is uncommon. Compartmental models that are not individual-based and assume that all individuals are equal within their particular disease category are often not suited to simulating dynamics where the attributes or behavior of individuals are important (e.g., where there are socially dominant animals, or where movement patterns are highly heterogeneous). Compartment models

may need to be individual-based where the number of infectious individuals is small, the spatial scale is small, or where there is considerable and important heterogeneity between individuals.

Questions addressed / model predictions:

1. Predicts R_0 , (the average number of secondary cases that arise from a single case at the start of a disease outbreak) and associated disease dynamics, including rates of flux between groups of susceptible, infected, and recovered (or dead).
2. Depending on model detail, compartmental models can address dynamics of disease with latent periods.
3. Estimates rates of spatial spread of disease.
4. Facilitates evaluation of types and relative importance of models and mechanisms of transmission.
5. Estimates threshold population size for persistence of disease.

Data required:

1. Data requirements are highly dependent on model structure and level of detail. Minimal requirements would include data on the proportion of the population in each class (susceptible, infected, or recovered) over time.
2. For highly detailed compartment models, additional data may be required on movement rates, sex and age composition, disease state, on social contacts, effects of infection on vital rates, factors related to disease resistance, effects of environmental contamination levels, and population demographic processes.

Output:

1. A minimal set of outputs would be the number of individuals in each disease class of susceptible, infected, and recovered or dead at each time step. With further embellishment, parameters can be fit to data to estimate such things as latency period, number of infectious contacts, mode of transmission, a threshold population size below which the disease cannot persist (if

any), rate of spread, and many other attributes.

General usefulness:

Compartment models provide a versatile and well understood approach to modeling diseases, especially at a fine scale. Mathematical techniques for estimating parameters and analyzing model behaviors are generally known, and this knowledge greatly facilitates model construction and evaluation. The ability to use analytical mathematical techniques to fully understand model dynamics makes these models particularly suitable for exploring the potential effects of management actions.

Usefulness to CWD modeling and/or management:

Compartment models can be extremely useful for modeling transmission and dynamics of CWD. In particular, simple models can be quickly and easily constructed to simulate and evaluate the effects of assumptions such as transmission mode and rate, control or eradication strategies, and population processes. Anderson and May (1991) provide a compendium of compartment model structures and a wide range of applications.

INDIVIDUAL-BASED MODELS



Individual based models (IBM) explicitly represent each individual in one or more populations. In an IBM, individuals are typically characterized by their sex, age, disease status, and other relevant characteristics that can include physiological state, genetic constitution, reproductive condition, resistance to disease, membership in a social group, propensity to migrate, etc. Bonabeau (2002) noted that individual, or agent-based, models are likely to be appropriate when:

- Individual attributes likely to affect disease dynamics are highly heterogeneous.

- Transitions are non-linear and may be characterized by threshold of behavior (e.g., sudden long-range jumps).
- The focus is on initial stages of disease invasion, or when the disease is at low prevalence such that the discrete nature of individuals and stochasticity are important to the ultimate dynamics of the disease.
- Interactions between individuals are heterogeneous (e.g., via social or mating structure) and these interactions result in large deviations from a predicted aggregate behavior.
- Averages are inappropriate and exceptional or rare events are important (e.g., a rare infection that leads to an epidemic).

These traits are characteristic of most natural animal populations, and they may be very important at some spatial scales. A key advantage of IBMs over many state-variable models (i.e., models that aggregate individual into large, homogeneous classes such as females and males) is the potential ability to model the attributes of individuals and the mechanisms by which individuals interact with their environment. By so doing, IBMs do not require simplifying assumptions that we know are false. By contrast, many state-variable models require estimation of parameters that operate over broad spatial and temporal scales – measurements that are frequently difficult and expensive, to obtain, and that are estimated with wide confidence intervals. Model structure and model parameters in IBMs are generally easy to interpret, and to explain to non-technical audiences. Huston et al. (1988), DeAngelis and Gross (1992), and Grimm and Railsback (2005) provide more comprehensive descriptions of IBMs and their applications.

By concept, IBMs can be very simple and require only a few easily-measured parameters. However, it is very easy for modelers to construct highly detailed IBMs and there is often a tendency to do so. Highly detailed IBMs of CWD may be useful for scenario analyses, but they may also be impossible to validate because they will likely require estimating a large

number of poorly known parameters. With complex IBMs, interactions between functions and individuals can lead to substantial difficulties in attempts to directly relate changes in inputs to changes in model behavior. IBMs are generally not suitable for analytical analyses, and a key step in model development is to conduct a comprehensive sensitivity analysis.

As both the spatial scale and number of animals increase, simpler models may adequately mimic system dynamics. Recent research, however, has shown the importance of individual variation in disease dynamics (Lloyd-Smith et al. 2005a). Many disease models, particularly those of microparasitic infections (e.g. bacteria and viruses), assume that all individuals are the same with respect to their infectiousness and susceptibility. For sexually-transmitted and vector-borne infections there have been many studies illustrating wide variation in individual contact rates (Kretzschmar 2000, Liljeros et al. 2001, Eames and Keeling 2004).

This led to the concept of a general 80-20 rule, whereby 80% of infections are likely to be caused by only 20% of the infectious individuals (Woolhouse et al. 1997, Woolhouse et al. 2005). Lloyd-Smith et al. (2005b) showed that for human microparasitic diseases, a large skew in the number of infections caused by different individuals was common and even more skewed than what would be expected from the 80-20 rule. These highly infectious individuals, the superspreaders, are likely to play a large role in the disease dynamics, and this individual heterogeneity is easily incorporated into IBMs. Theoretical modeling suggests that disease systems with a large degree of heterogeneity in individual infectiousness are more likely to go extinct, but if they do persist they tend to have more explosive dynamics. Furthermore, control efforts focused on superspreaders are much more effective than control measures that are broadly applied to the entire host population (Lloyd-Smith et al. 2005b). At this point, there are no data on contact rates and the infectiousness of different

individuals for CWD. However, the variation in prevalence among different sex and age groups (Miller et al. 2000, Miller and Conner 2005), as well as potential differences in genetic susceptibility (Jewel et al. 2005), suggest that substantial individual variation may also exist in CWD systems.

Gross and Miller (2001) and Cary (2004) constructed IBMs to explore dynamics of CWD in deer populations, the former in Colorado mule deer and the later in Wisconsin white-tailed deer. The Colorado model was non-spatial and simulated CWD dynamics in a single, closed population, whereas the Wisconsin model included a high degree of detail on small-scale movements of deer in an agricultural landscape. These differences in model detail reflected the relative availability of data from the two regions and the types of questions the models were designed to address. Both models were developed to evaluate the effects of a range of potential management options to control or eradicate CWD.

A comparison of the IBMs developed by Gross and Miller (2001; hereafter G-M) and Cary (2004; hereafter Cary) is a useful illustration of alternative approaches to model development. The G-M model was specifically developed to examine potential impacts of CWD on mule deer populations in the endemic areas of Colorado. Relatively good data on the individual epidemiology of CWD were available from captive animal studies, but similar to many wildlife disease systems few data were available on naturally infected populations and individuals. Model construction and parameter estimation and evaluation reflected the paucity of data and the need to broadly explore model behavior. The non-spatial IBM simulated a single population, and incorporated a simple frequency-dependent, random-mixing social structure for disease transmission, to broadly explore model behavior. Results were presented for a wide, but realistic, range of parameter values, and only general (versus specific) model dynamics were discussed. Simulations showed that all realistic sets of parame-

ters eventually caused dramatic declines in deer populations, and that all disease control strategies would require intensive, long-term commitments and resource investments.

By contrast, the Cary model included a highly detailed spatial representation of the study area, and estimates of model parameters were based on a broader range of studies of deer biology, harvest data, and a very detailed land classification map. Nonetheless, the level of detail in this model required estimating many parameters for which there was relatively little data. The spatial extent of the model was explicit and consisted of 20736 grid cells, each representing 0.65 km² (i.e., 0.25 mi² or 160 acres). During simulations, the position (grid cell) of each individual was tracked, and deer were anchored to specific home ranges, which could shift in response to winter feeding. Cary's model was constructed to evaluate a series of specific management actions, on a very specific population inhabiting a well-defined landscape. Cary examined a variety of alternative transmission functions, and showed that "... many combinations of transmission functions, latency time, and transmission coefficient were successful in reproducing the details of a cluster of CWD cases ...".

Based on existing data and assumptions on disease transmission and animal movements, the Cary model estimated the time of establishment of CWD prior to observation (7 to 15 years), and projected specific rates of spatial spread of the disease (1.6 to 3.7 miles per year). Under a range of model assumptions, the Cary model concluded that harvest of sufficient intensity to remove the majority of infected animals prior to death by disease could effectively stem the spread of CWD, and perhaps eventually result in disease eradication. Such specific conclusions could not be derived from the more general structure of the G-M model, but these conclusions also required assumptions on animal and disease behavior that still need to be verified.

Questions addressed / model predictions:

Box 3.1 Density Dependent vs. Frequency Dependent Transmission

A major challenge in modeling disease is determining the functional form of the equations that most appropriately represent disease transmission. Until fairly recently, most disease models represented interactions between hosts and pathogens as random encounters, where the likelihood of contact was directly proportional to host density (McCallum et al. 2001), also called mass-action transmission (de Jong et al. 1995 propose alternate terminology). This ‘random mixing’ model is generally described as a density-dependent (DD) transmission, and the rate of disease transmission increases with host density. By contrast, another large class of models treats disease transmission as a function of the proportion of infected individuals in the population (the disease prevalence) rather than host density. This mode of transmission has often been described as frequency-dependent transmission (FD). This distinction has implications for disease control (Anderson and May 1991; Lloyd-Smith et al. 2005a, b).

The choice of DD or FD disease transmission can lead to key differences in the behavior of models under some conditions. A particularly important difference is that simple models with DD transmission exhibit a population threshold density, below which a disease cannot invade or persist (Anderson and May 1979). This model prediction is the theoretical basis for using population reductions be used to control or eradicate disease.

In contrast, the efficiency of disease transmission in FD models can remain high even when population densities are low, and simple FD models generally do not exhibit a lower population threshold below which disease fails to persist (Getz and Pickering 1983). FD models better represent disease transmission in social animals, where group size and contact rate between individuals is determined more by social behavior than by random encounters between individuals. Among published studies, FD models were most often used to model sexually transmitted diseases.

It seems likely that many diseases, including CWD, will exhibit behaviors consistent with DD transmission, at least at extremely high and low densities. However, as Swinton et al. (2002) noted, predictions from DD and FD models are identical when host densities remain the same. In addition, McCallum et al. (2001) concluded that there is little support for DD transmission among wildlife studies. Field observations of CWD prevalence, and estimates of host density, are currently too imprecise to distinguish predictions from models with DD or FD transmission.

Nonetheless, Schaubert and Woolf (2003) criticized Gross and Miller’s (2001) CWD model and model interpretations, focusing on the sole representation of FD disease transmission by Gross and Miller. Under conditions more relevant to management of cervid populations (i.e., moderate to high population densities and low to moderate disease prevalence), the behavior of models with DD and FD transmission will be indistinguishable when compared to field data. We constructed a set of simple disease models suitable for simulating CWD to demonstrate this point. Following Anderson and May (1979), we represented a population as consisting of susceptible (S) and infected (I) individuals. In this case, a S individual has not been infected and is neither influenced by disease nor can they transmit disease. Animals infected (I) with disease can transmit the disease and exhibit a higher death rate.

Following Anderson and May (1979, 1991), both population dynamics and disease dynamics can be represented by a simple set of equations:

$$\frac{dS}{dt} = b(S + (1 - e)I) - \alpha S - mS$$

$$\frac{dI}{dt} = \alpha S - (m + \mu)I + beI$$

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Box 3.1 Density Dependent vs. Frequency Dependent Transmission
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with the variable definitions and initial values as shown in the table below.

Parameter	Initial value	Description
b	0.4	Offspring per individual per year
α		Transmission rate (see functions below)
m	0.10	Proportion of population dying each year
μ	(fit)	Proportion of infected individuals dying from disease each year
β	(fit)	Transmission parameter (see functions below)
S	800	Number of susceptible animals
I	10	Number of infected animals
N	810	Total number of animals ($S + I$)
K	2000	Number of animals where birth rate is zero (density-dependent population parameter)

α = transmission rate, where:

$\alpha_{DD} = \beta I$ for density-dependent transmission,

$\alpha_{FD} = \beta I / N$ for basic frequency-dependent transmission, and a form (α_{MM}) proposed by McCarty and Miller (1998) and used by Gross and Miller (2001) in their CWD model.

$$\alpha_{MM} = 1 - \left(1 - \frac{1}{N}\right)^{\beta I}$$

For the purposes of the simulations, parameters are per year and as above.

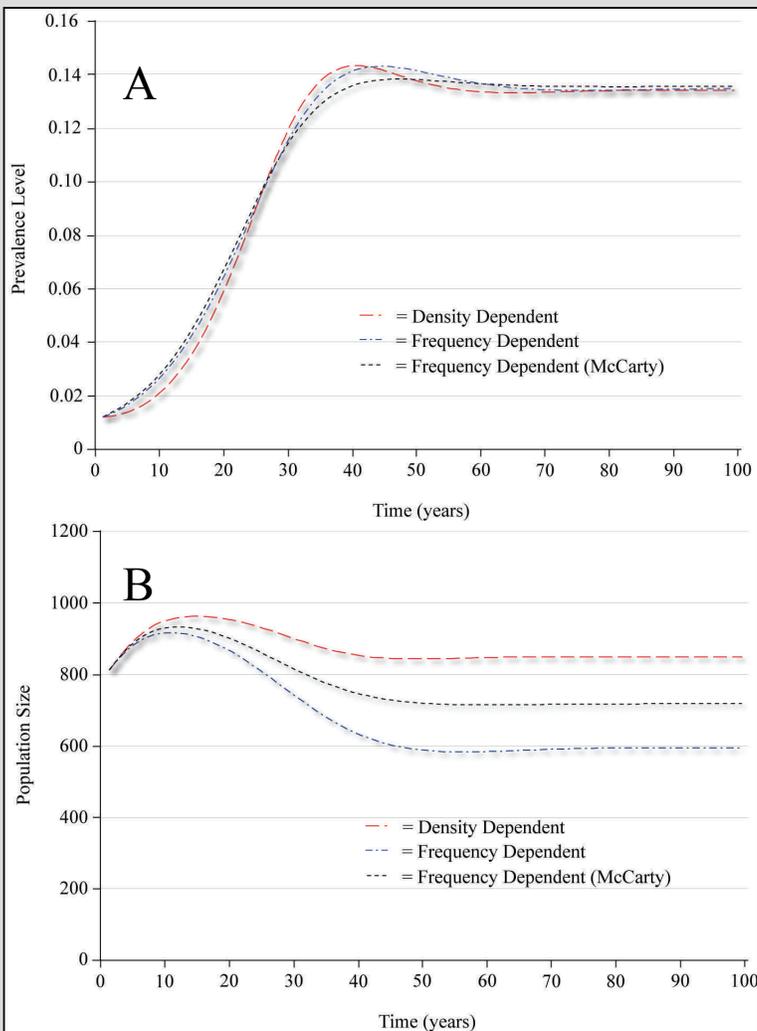
To control population size, density dependence in reproduction was represented in the form of $1 - (N/K)$, thus the final equations are:

$$\frac{dS}{dt} = b \left(1 - \frac{S + I}{K}\right) (S + I) - \alpha S - mS$$

$$\frac{dI}{dt} = \alpha S - (m + \mu)I$$

* Note: vertical transmission rate (e) was set to zero and hence eliminated from the above equations.

No field studies have unambiguously documented the existence of host population thresholds (Lloyd-Smith et al. 2005a). While the existence of a lower population threshold is of theoretical interest, many models of wildlife disease exhibit very similar behavior over a broad range of host densities. Field observations from free-



Comparison of (A) prevalence and (B) population size for density dependent, density independent, and McCarty and Miller (1998) density dependent functions of CWD transmission rates.

Box 3.1 Density Dependent vs. Frequency Dependent Transmission
(continued from last page)

ranging populations are simply not adequate to distinguish dynamics produced by frequency- or density-dependent transmission over broad (realistic) ranges of host density. Key differences in disease dynamics related to mode of transmission occur when host population density declines below the threshold in a DD model, and these dynamics have very important implications on the ability of a control strategy (especially population reduction) to eradicate disease. Additional data on transmission dynamics are required to realistically evaluate the likely effectiveness of intensive culling as a management strategy for CWD (Gross and Miller 2001, Schaubert and Woolf 2003). We encourage future modeling efforts evaluate the sensitivity of their results and conclusions to this assumption.

1. Predicts disease dynamics, (e.g., rates of change in infection and duration of epidemic) within a population through time.
2. Predicts effects of population sex and age structure on disease dynamics.
3. Predicts effects of control strategies, which may include test and cull, population reduction, habitat manipulation, harvest strategies, and/or vaccination.
4. Predicts effect of individual variation on factors such as genetic resistance, transmission rates, and movement.
5. Predicts effects of spatial structure of the environment on disease transmission and/or persistence.
6. Predicts effects of social structure on disease dynamics and the effectiveness of control strategies.

Data required:

The data required varies with level of detail and intent of the model. For a theoretical model, existing observations of population structure (e.g., proportion in observable age-sex categories) and disease prevalence may all that is required. For a highly complex model with population and spatial structure, detailed data on population age and sex composition, disease prevalence, and on animal movement and contact rates may be necessary before there is sufficient confidence in model results to influence management decisions. It is very easy to construct overly-complex IBMs. Considerable thought should be directed toward constructing simple, tractable models; that is, models with the smallest possible number of estimated parameters.

Output:

Model outputs vary with model structure and level of detail, but virtually all IBMs will simulate population structure and disease state (e.g., susceptible, infected, infectious) through time for defined sex and age classes. Model outputs will typically include harvest and treatment variables, such as the number of animals vaccinated, tested and culled, or harvested. Outputs of spatially explicit models will include the location of all animals, which are usually used to estimate animal densities across the landscape. Any other simulated variables of interest can also be produced, including physiological state, genetic composition, and number of offspring. These variables permit calculation of many other factors of ecological interest such as generation time, indices of genetic diversity, gene flow rates, etc.

General usefulness:

IBMs have proven to be highly useful for simulating a wide variety of situations in animal ecology. They are routinely used in applications that share many characteristics that apply to CWD: where migration or dispersal of individuals is important to establishing new populations or transmitting disease, for simulating changes in genetic composition, and for evaluating the consequences of behavioral differences of individuals and species. Grimm and Railsback (2005) provide many other examples. Although run separately here, IBMs have often been run on top of a grid, where the environment is described by the attributes of the grid cells as is discussed in the Spatial Stochastic Model section below.

Usefulness to CWD modeling and/or management:

This approach has great potential and the first CWD models constructed were IBMs (Gross and Miller 2001; Cary 2004). The level of detail is easily varied to accommodate species or site-specific characteristics. A drawback to using an IBM is that the models must be evaluated using numerical rather than analytical techniques, which can be quite time consuming. Model evaluation should include a carefully conducted sensitivity analysis. Complex IBMs can generate very large quantities of output – sometimes measured in giga-bytes – in which case data reduction, analysis, interpretation, and communication can be significant challenges.

There are a number of CWD-specific questions that individual-based model are particularly well suited to addressing. For example,

- How does individual variation in propensity to disperse affect the efficiency of management activities to control CWD?
- How do individual social behaviors (e.g., fidelity to a family or other social group) affect disease dynamics and CWD control strategies?
- How does genetic variation in resistance to CWD affect disease and population processes, including changes in gene frequencies, disease dynamics and population growth and persistence?

Fulford et al. 2002, Hess et al. 2002, Keeling and Rohani 2002, Cross et al. 2004, Hagenaars et al. 2004). Network models represent a very flexible method of capturing different social/spatial structures (Keeling 1999, Watts 1999, Newman 2002, Cross et al. 2004, Ferrari et al. 2006). Traditional models typically assume that an individual’s risk of infection depends upon the prevalence or density of infectious individuals in the local (or global) population. Network models, on the other hand, explicitly incorporate information about who is connected to whom and then assess each individual’s infection risk according to the number of contacts they have with infectious individuals. These models have been primarily used for sexually-transmitted infections where the contacts among individuals may be limited and variable. The strength of the network modeling approach is its flexibility to represent a wide range of social or spatial structures. Contact networks may change over time, but due to the lack of empirical data on network structure and how it changes over time, most network models have been static (Keeling 1999, Watts 1999, Read and Keeling, 2003). Ferrari et al. (2006), however, illustrated how the contact network could evolve over time as individuals become infected and removed by a disease. In particular, the most well-connected individuals are infected first, leaving a much more sparsely connected network of susceptible individuals that are less likely to be contacted and infected.

NETWORK MODELS



Early models of disease often assumed that the host population was homogeneously mixed (Anderson and May 1991). In other words, each individual was equally likely to contact every other individual within a single unit of time. Because this assumption obviously does not hold for many human or wildlife situations, many studies have used different methods of accounting for spatial or social structure (e.g., Swinton 1998, Keeling 1999, Keeling and Gilligan 2000a, b, Thrall et al. 2000, Park et al. 2001,

A matrix of pairwise contact probabilities often underlies these models. This association matrix is filled with association indices (a_{ij}), which describe the amount of contact between individual i and individual j . These association indices can then be multiplied by infection rates or probabilities to simulate the disease dynamics. Keeling (1999), and Keeling and Grenfell (2000) used contact networks to extend SIR models to structured populations. They found that inclusion of spatial heterogeneity and social structure provided predictions of R_0 that were more concordant with empirically derived estimates than models that excluded these factors.

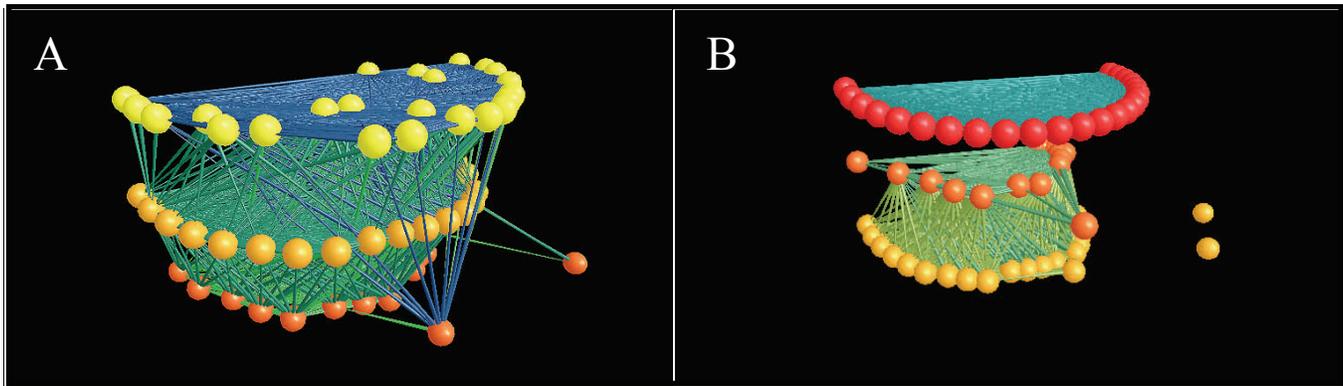


Figure 3.3. Network graphs of African buffalo association data for (A) November 2001 through October 2003 and (B) May 2002. Balls represent radio-collared buffalo and lines indicate that two individuals spent some portion of the time interval within the same group. Note that the data collected over a short window of time indicates that one herd was completely separated from the others (B). Over the course of the study, however, movement among herds creates a well-connected network (A). Figure from Cross et al. (2004).

The study by Cross et al. (2004) was primarily for heuristic purposes, but to our knowledge, is the only study in a wildlife system to use a dynamic network modeling approach based on associations between individuals from different population groups (Figure 3.3). The study showed that the dynamic properties of the network were particularly important for acute infections where the disease may go extinct within a local group prior to any connections forming between groups. For chronic diseases like CWD, the network structure connecting different groups may be of minor importance because disease persists for a long time relative to the frequency of new connections developing between groups. Consequently, disease could readily move from one group to another regardless of the network structure. The major hurdle to applying this approach is the difficulty of estimating associations between individuals and then scaling those estimates up to create an appropriate network structure that accurately reflects the entire population of interest.

Spatial heterogeneity or social structure in a population will reduce the spread of a disease when the number of long-distance connections is relatively low. The existence of either factor violates the assumption of homogeneous mixing and this invalidates the estimation of R_0 by many epidemiology models. If populations are

not homogeneous, then theoretical estimates of R_0 exceed, often greatly, the observed R_0 (Keeling 1999). R_0 is often a very poor predictor of disease invasion in spatially or socially structured populations where the local group size is small (Figure 3.4) (Ball et al 1997, Cross et al 2005a). Even if R_0 is high and the disease easily invades the local group of individuals, R_0 does not inform us about the likelihood of continued spread of the disease to other groups. Group-to-group transmission of a disease depends upon the movement rate of hosts and parasites and the persistence of the parasite within the local group (Cross et al 2005a, b), assuming no environmental transmission.

Questions addressed / model predictions:

1. Predicts R_0 and R_t and ensuing disease dynamics (speed and duration of epidemic) within a population through time.
2. Estimates effects of population structure on disease dynamics during the duration of the infection.
3. Indicates “core groups” that are likely to harbor disease and where management efforts may be focused.

Data required:

1. Estimates of interconnectedness or association of individuals or small groups, such as territory members, (i.e., population struc-

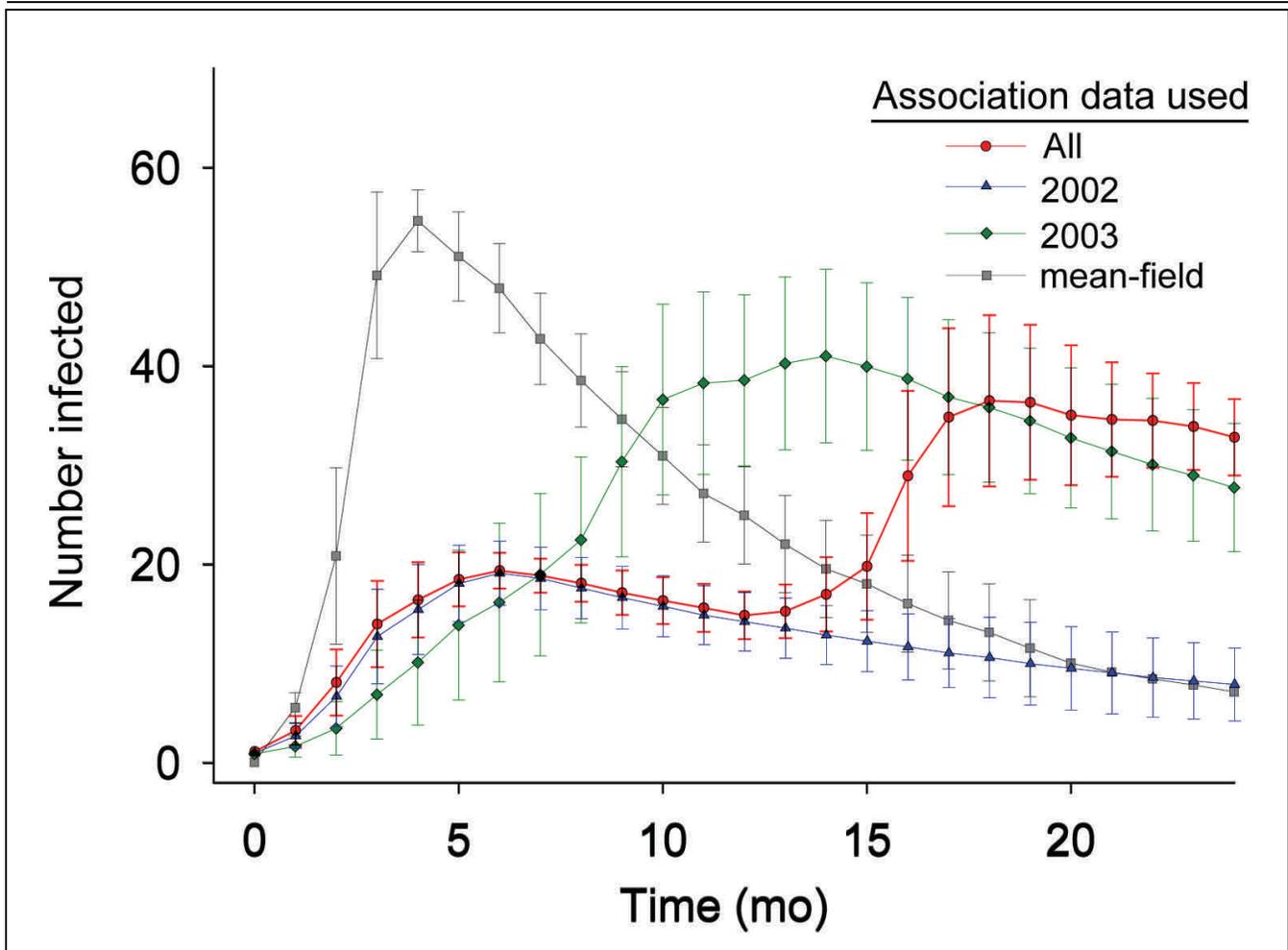


Figure 3.4. Mean and standard deviations of the number of infected individuals over 50 runs of the disease model using monthly association data from the entire study period (red circles), 2002 (black triangles), 2003 (white squares), or a mean-field model (blue circles) where all individuals were connected but the monthly force of infection was the same. All simulations used a transmission coefficient β of 0.03 and a recovery probability γ of 0.1. Figure from Cross et al. (2004).

ture), preferably at each time step of interest.

2. Infection status of study individuals (susceptible, infected, or recovered) at each time step of interest.

Output:

1. Predicts total number of individuals that will become infected during the course of an epidemic and number of individuals infected through time (time trace of the epidemic).
2. If data is collected through time, estimates of variance in population structure.

General usefulness:

This approach has great potential because of its flexibility to simulate many different spatial/social structures. However, its utility is likely to be limited in many wildlife disease systems by the lack of individual data on associations between individuals. Continued improvements in radio-tracking and GPS technology will make these data more available, but several questions remain that limit the general utility of contact network modeling. This approach can uniquely address questions such as: “How do we efficiently sample a network?” Then, given that sampling, “How do we scale up the sample so that it represents the entire network of interest?” To the authors’ knowledge, these questions, crucial to network mod-

eling, have not yet been answered for any human or wildlife disease system.

Usefulness to CWD management:

Given the potential for environmental transmission and chronic nature of CWD, network modeling may be of limited utility for CWD management. In the case of CWD it will be very difficult to define who contacts whom, particularly when the infectious agent may persist in the environment for several years (Pálsson 1979, Miller et al. 2004). When environmental contamination is significant, the network of contacts between live individuals may be far less important in determining disease dynamics.

SPATIAL STOCHASTIC MODELS
(FOLLOWING SMITH ET AL. 2002)



Spatial stochastic models are called spatial

because each individual is explicitly located in space, usually on a grid cell representing a small (e.g., territory) to large (e.g., county) area, and stochastic because rules of movement and vital rates are chosen randomly from a distribution or bootstrapped from the data. Spatial stochastic models can operate at a variety of scales; at a landscape scale space may represent the summary of disease cases or prevalence throughout an area, such as a wildlife management unit, or for an entire population (for details, see the landscape-level section on cellular automata models). However, at a fine scale, grid-based spatial stochastic models are used to model disease epidemiology within a single population, or in a relatively small area, such as winter range. Grid-based spatial stochastic models can incorporate characteristics of other model types, and the size of grid cells can be defined to represent an area that might contain one or a few animals (perhaps a family or social group), or an entire population. At the fine scale the data is usually more intensive and at finer resolution. Birth and death rates, gene frequencies, and rules for movements between cells are often required,

while at larger scales data such as time of first infection in an area can suffice. The question of interest and biology and ecology of the relevant animals dictate the scale of the model.

More complicated grid-based models can be designed to directly ingest information from a GIS to characterize cell properties that can include elevation, vegetation type, food availability, or cover. These attributes can then be used to estimate habitat quality or the ability of areas, represented by cells, to support growth or persistence of organisms. Grid cells can be organized into multi-cell units to represent territories, and population densities based on areas (e.g., contiguous grid cells or ‘patches’) that contain a suitable mix of habitat types. Models to simulate population processes (e.g., birth, death, movement, etc.) and disease dynamics are run over the grid of cells, and suitable metrics can be extracted at any desired level – by cell, groups of cells, across a given area, or for the entire population. Model results can be interpreted as non-spatial (e.g., total number of individuals), but the strength of the approach is to investigate the effects and consequences of spatial patterns or heterogeneity.

Cary’s (2004) CWD model is an example of a spatial stochastic model. However, because it was described in detail in the IBM section we do not discuss it here. Instead, we discuss 2 other spatial stochastic models used to model disease spatial epidemiology. Smith and Harris (1991) used this approach to evaluate the efficacy of different control strategies on the spread of rabies in urban foxes in a city in southern England. They subsequently applied their model to several other cities in southern England. They did not use underlying habitat or environmental factors to predict population density, but rather modeled a range of typical fox densities based on data from similar areas in southern England. Although this model was spatial, it was not explicit in that fox densities/territories were not related to particular physical locations. Fox territories were represented by an appropriate number of grid cells; territo-

ries were smaller at high densities and larger at low densities. Similar to a cellular automata approach, for every time step the density of foxes in and near each cell determined dispersal rules, probability of encounter, and home range size at the next time step. These model outputs were then used to calculate the number of foxes infected with rabies and ultimately to depict the spatiotemporal dynamics of the disease under various control strategies. Note that rules were not static, but they varied with fox biological season.

In their model of the spatial dynamics of parapoxvirus disease in red and grey squirrels, Rushton et al. (2000) provide a good example of the nexus of an explicit spatial and individual based model approach. In this spatially stochastic model, the landscape was represented by 25 m² cells, where each cell was classified by proportion of different habitat type that was relevant to squirrels. Remote sensing data was used to define the habitat type of each cell, for a particular location in England, making this an explicitly spatial model. From the amount of contiguous habitats, potential densities of red and grey squirrels were calculated, and then dispersal and competition rules determined the relative densities of the two species for each cell or group of cells. An individual based epidemiologic model was run on top of this spatially explicit population model in which population density determined rates of encounter with infected individuals and the likelihood of becoming infected. These dynamics predicted the number of infected individuals of each species, for each cell and time step.

Because the class of spatial stochastic models includes models that are very general to those that are highly detailed and complex, models of this type can be used to address a huge range of questions. The level of detail, spatial and temporal resolution, and inputs and outputs can be adapted to the specific questions of interest. Because this class of models includes such a broad range applications, we do not address these categories below.

General usefulness:

Spatial stochastic models are useful for evaluating population dynamics where spatial heterogeneity is important. In general, they are used for scenario, or ‘what-if’, analyses because the amount of data required to accurately estimate model parameters usually exceeds what is available. Consequently, error propagation is a serious issue, and confidence intervals on outputs may be so large that estimates are not useful in themselves. The primary value of highly detailed spatial models is usually the ability to compare the relative value of various management scenarios. Any model validation that does occur is usually at the scale of “was the disease present in this group of cells or not”, with observed values compared to predicted values. Finally, it is relatively easy to construct grid-based spatial models using off-the-shelf software.

Usefulness to CWD management:

Spatial stochastic models are useful for modeling CWD and evaluating management strategies where adequate data exists. Cary (2004) used a grid-based representation, over which individuals moved, to simulate CWD in a Wisconsin landscape. For CWD, different movement rules or transmission functions could be included in a spatial stochastic model and results compared to observed patterns of prevalence. This type of approach may provide insight into the function and influence of these types of factors at the scale at which adequate data could be collected.

FOCAL APPROACH:

INDIVIDUAL-BASED MODELS

Individual-based models (IBMs) will clearly contribute to our understanding of the dynamics of CWD and they will likely play an increasingly important role in modeling a wide variety of diseases. We thus present this as a focal method for fine-scale modeling of CWD. As described above, the range of problems that can be addressed by IBMs is vast, and this translates into a similarly large range in the

level of detail and complexity that can be included in any particular model.

We describe the general stages or tasks that a ‘typical’ IBM project will require. While these steps are described as if they are accomplished sequentially, model development is rarely a linear process. One needs to simultaneously consider model objectives, the types and quality of data available, and there is usually a need to continuously evaluate model objectives, model structure, and model performance.

Step #1: Define model objectives

The first stages of model development are the same for virtually all models, including IBMs. Step one is to clearly define the objectives for the modeling exercise. Model objectives need to articulate the questions that must be addressed, features that are desirable, and the scales of space and time that are relevant to the questions. Will the model be used to support decisions in a specific management area, or is the primary use of the model to understand more general system behaviors? What data are available to estimate model parameters, and to compare to model results? The answers to these questions will help determine model structure and the required types of model outputs. At this stage, it is usually important to consider the tradeoff between model parsimony and realism, and the position along this gradient will likely be constrained by the availability of data.

Common uses for IBMs are to compare the relative consequences of competing management actions, which can include factors that might affect disease transmission or prevalence. One may wish to examine the potential effects of supplemental feeding in harsh years, habitat manipulations, harvest regimes, or test-and-cull of diseased animals. The main purpose of modeling may be to determine the likelihood of achieving a specific management goal or target, or to project population changes or prevalence rates over time and compare results to those in the absence of disease man-

agement. If the intent is to evaluate management actions, the best objectives are quantitative, specific, time-bound, and results are reflected by variables that can reasonably be simulated by an IBM and measured and compared to field observations. In the case of CWD, models can be constructed with specific objectives (1) to evaluate whether our hypotheses about the epidemiology of CWD, as codified in mathematical equations, were consistent with observed disease dynamics (Miller et al. 2006), and (2) to investigate the likely consequences of typical actions to control disease (e.g., Gross and Miller 2001; Cary 2004).

Step #2: Define model experiments

After the key objectives for the model are identified, a related set of model simulations should be defined. For most IBMs, these model ‘experiments’ will consist of scenarios, based on input variables that define the initial model conditions and the ‘treatments’ that are to be applied. The universe of potential model scenarios for any IBM is huge and one must define a limited number of experiments that are to be conducted, and the analyses that will be used to evaluate results. For IBMs of CWD, model experiment scenarios might include the proportion of a population examined each year in a test-and-cull program (say, 10%, 25%, 50%, 75%, and 100%), or the harvest rates of adult does and bucks. Because ‘treatments’ are usually nested and crossed, the potential number of experiments can rapidly become unmanageable. Thus, one should start with clearly defined and listed scenarios.

Step #3: Develop conceptual model

As early as possible, the modelers should develop a conceptual model of the entire system to be simulated (Jackson et al. 2000). A conceptual model generally consists of one or more diagrams of the system, and a narrative that describes key processes and functions. Development of the conceptual model usually helps all involved to more fully identify, articulate, and understand what processes and functions the model needs to include, and, more importantly, what can be left out. In the

process of constructing a conceptual model, knowledge gaps are almost always identified as well as parts of the IBM most likely to be problematic. When developing the conceptual model, it is helpful to very carefully document potential sources of information that can inform model construction and evaluation, from published and other sources.

Many problems with simulation models can be traced to errors in the scheduling of model events. A common error is to produce outputs at an inappropriate time for comparing to field observations. For example, errors in model evaluation can occur when observed prevalence rates of CWD are estimated from animals harvested in the fall, but the model produces prevalence estimates just after birth, a time equivalent to late spring. A well-constructed and detailed conceptual model can help avoid these sorts of errors.

In general, the model development process is to first implement a very simple host demographic population model that includes simple functions for birth and death, as well as an appropriate level of detail on the individuals in the model (typically, the sex and age of each individual). For CWD, approximate vital rates can readily be obtained from the literature for deer (and elk and moose), and population performance of the IBM can be compared and calibrated to observations. Once the basic population model is functioning, more detailed processes can be implemented. Harvest and/or density-dependent reproduction (and perhaps mortality) is typically added next to restrict population size. After this, disease control treatments, genetic inheritance, movement, infection dynamics, or other more complex functions may be incorporated. Additional species may be added so that predation (selective or random) can be simulated, or animal-habitat interactions may be incorporated. Regardless of which features are implemented, it is critical to very carefully examine model performance as each new function is added.

Step #4: Estimate model parameters

Throughout the process of model development, the process of parameter estimation will usually be going on simultaneously. The science and art of parameter estimation is well beyond the scope of this handbook; Hilborn and Mangel (1997) provide an outstanding introduction to the subject.

Step #5: Validate model

Once the model is running, robust, and appears to be operating correctly, it is important to conduct a thorough verification process before proceeding with what are likely to be time-consuming model experiments. Because most IBMs incorporate both stochasticity and complex interactions, model verification can be a difficult and time-consuming process. Interested readers should refer to examples of IBM and more comprehensive treatises (e.g., DeAngelis and Gross 1992; Grimm and Railsback 2005).

Step #6: Run model experiments

For most models, an almost infinite number of model experiments could be conducted. It is necessary to carefully prioritize a limited number of model scenarios that will effectively address the management or heuristic questions. Even with a limited number of scenarios, IBMs are usually capable of producing huge quantities of model output. A core challenge is to reduce and summarize model outputs, and to develop graphics or other summaries that concisely and effectively communicate results to key audiences. The analysis and communication challenges posed by output from IBMs are usually underestimated.

GENERAL CONCLUSIONS ABOUT FINE-SCALE APPROACHES FOR CWD MODELING

There are several key assumptions often made in modeling analyses at the fine scale that, in part, determine model results and conclusions. Of particular importance to disease control and management is the relationship between transmission and host density and/or populations size (McCallum et al. 2001,

Schauber and Woolf 2003). There are few data available to estimate the relationship between host density and CWD transmission, or other factors thought to significantly influence transmission of CWD in free-ranging populations. Data from Caley et al. (1998) and Joly et al. (2006) provide data sets suitable for estimating or inferring changes in contact with variation in host density. Because data on transmission rates are typically sparse, modeling analyses are often forced to assume a particular relationship between host density and transmission rates (Box 3.1). With respect to CWD, key differences in disease dynamics result from the assumed mode of transmission when host population density declines below the threshold, and these dynamics have very important implications on the ability of a control strategy (especially population reduction) to eradicate a disease. Our current understanding of CWD transmission in free-ranging populations is not adequate to unambiguously distinguish dynamics produced by frequency- or density-dependent transmission over broad (realistic) ranges of host density and disease prevalence. Recent studies (Joly et al. 2006) observed patterns of CWD prevalence consistent with density-dependent disease transmission, but the relative roles of different transmission modes are unknown. Additional data on this relationship are critical to determining the likely effectiveness of management strategies for CWD (Gross and Miller 2001, Schauber and Woolf 2003), and we encourage future modeling and field efforts to better understand the epidemiology of CWD and to evaluate the sensitivity of model results to transmission functions.

In addition, several studies suggest a strong role of an environmental reservoir of infection for CWD (Miller and Williams 2003, Miller et al. 2004, Miller et al. 2006). This environmental reservoir should be considered in SIR-type models of CWD as well as several of the other modeling methods we discuss in this text. To do so requires adding an additional compartment or variables to track the amount of infectious material, which could be increased by the presence and death of infectious individuals,

and decreased by the degradation of the prion proteins over time. The inclusion of an environmental reservoir of CWD can have important implications for the effectiveness of different management strategies and the duration required to achieve management objectives.

Finally and most importantly, demographic data for CWD infected versus uninfected free-ranging deer are needed for all methods operating at the fine scale. It is at a fine scale that the basic biology of CWD transmission and its true effects on the vital rates and dynamics of deer populations will be revealed. Consequently, field studies designed to estimate survival and fecundity rates of CWD infected and uninfected deer are needed to ultimately determine the effect of CWD on population growth rate. This, along with field studies of transmission dynamics, including effects of environmental contamination and social structure, are needed to determine the spatial epidemiology and functions of transmission of CWD within and between deer populations. Although we chose IBMs for the focal approach, data needs outlined here will support most of the methods in this section. Used individually or together, compartment models, IBMs, and spatial stochastic models are all needed to fully understand the nature of the spread of CWD and its ultimate effects on deer population dynamics.

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