

2002; Longini et al. 2005) and large population sizes (Ferguson et al. 2005, Ferguson et al. 2006). One practical limitation of these models is the difficulty with which we can assess the sensitivity of their predictions to perturbations in the social network structure. Instead, it is often plausible to assume random mixing within a localized community and reduced mixing between the communities—a so-called metapopulation model. We may, for example, wish to subdivide the population by town/city, by county, or by state, depending upon our level of knowledge and the detail of results required (see, for example, Viboud et al. 2006).

Finally, for diseases of wildlife or plants, such as tuberculosis (TB) in badgers (Shirley et al. 2003), rabies in foxes (Murray et al. 1986) or raccoons (Smith et al. 2002), Dutch elm disease (Swinton and Gilligan 1996), or Sudden Oak Death (Kelly and Meentemeyer 2002), there may not be a natural partitioning of the host population. Instead, it is frequently assumed that individuals are either uniformly or randomly distributed, with their density reflecting landscape and environmental factors. In such cases, continuous-space models, phrased as partial differential equations (PDEs) or integro differential equations (IDEs), can be used (Kot 2001). Again, it would be unfeasible to model every badger sett within the United Kingdom or every raccoon in the United States, and naive to assume that either creature respects county or state boundaries. However, due to limitations arising from the spatial resolution of empirical data, which may be aggregated at the county or state level, it may be necessary to model the host population at a similarly coarse scale (Smith et al. 2002).

The type of model used is directly dependent on the host organism, our degree of knowledge about its behavior, and the scale we wish to consider.



7.1. CONCEPTS

A variety of models can be used to study the spatial spread of pathogens, and although each has its own specific aspects, a range of concepts are shared. We first discuss these elements, so that the similarities and differences between the models will be more apparent, and to introduce the language of spatial processes.

7.1.1. Heterogeneity

Spatial heterogeneity refers to differences between populations or individuals at different geographical locations. Such heterogeneities can arise from two sources. Underlying (environmental) heterogeneities describe spatial differences in the fundamental forces governing the population dynamics. For example, wildlife populations in different locations may experience differing habitat conditions that may affect demographic rates, or different human populations may have different social structures leading to variation in disease transmission rates (Finkenstädt and Grenfell 1998; Grenfell and Bolker 1998; van Buskirk and Ostfeld 1998; Auvert 2000). Such underlying heterogeneities are common in the real world, but are frequently ignored in models due to the extra complexity they introduce and due to a lack of available data. If quantitatively precise predictions are required from models, however, it is often vitally important that such underlying heterogeneities are considered (Keeling et al. 2001b; Smith et al. 2002). The second form

of heterogeneity is emergent and describes observed differences in population structures arising from dynamical processes, such as stochasticity, or differences in movement between populations (Hassell et al. 1991; Rhodes and Anderson 1996; Green and Sadedin 2005). In general, this second form of heterogeneity is greatest between populations that experience large amounts of stochasticity, have very different underlying parameters, and have little transfer of infection between them.

Heterogeneity can describe either the underlying differences between two populations, or the emerging dynamic differences in the population levels (such as the proportion of the population that are infectious).

A convenient measure of observed heterogeneity is provided by estimating *correlations*—they quantify the degree to which the dynamics in two (or more) populations behave in the same manner. Simply put, correlations help to establish whether epidemics in different populations are synchronized or out of phase (Grenfell and Bolker 1998; Rohani et al. 1999; Grenfell et al. 2001). If we let I_i denote the time series documenting the prevalence of an infection in population i , then the correlation between epidemics in two populations is calculated as:

$$C_{12} = \frac{(I_1(t) - \bar{I}_1)(I_2(t) - \bar{I}_2)}{\sqrt{\text{var}(I_1)\text{var}(I_2)}}. \quad (7.1)$$

Here, \bar{I}_i refers to the mean infection prevalence (averaged over time) in population i . If the fluctuations in prevalence over time in the two populations are either identical or directly proportional ($I_1 \propto I_2$), then the correlation attains its maximum value of 1. If epidemics in the two populations are independent, then the correlation is zero. If the outbreaks are out of phase, then C_{12} is negative. Given time-series data on the number of cases in two populations, we are predominately interested in the average correlation over a given period, rather than the instantaneous value that is subject to short-term stochastic fluctuations. The correlation cannot be defined for deterministic populations at their equilibrium values (because both population levels are constant and the variance is zero), and therefore, in general, correlations are usually associated with stochastic or seasonally forced systems.

Correlations provide a quantitative measure of the differences between populations: A positive/negative correlation indicates that epidemics are spatially synchronous/asynchronous.

Although the standard correlation (equation (7.1)) measures the heterogeneity generally derived from the stochastic nature of the epidemic process, heterogeneities can also arise due to *traveling-waves*. Consider the spread of West Nile virus across the United States from New York in 1999 to the West Coast in 2003 (see Chapter 4 for a more detailed description of West Nile virus). The observed heterogeneities in incidence on the East and West Coast are unlikely to be a result of either inherent habitat differences, or due to stochasticity. They simply reflect the fact that the disease emerged in the east and travelled west. To quantify this traveling-wave type of heterogeneity we need

to use *lagged correlations*:

$$C_{12}^{\tau} = \frac{(I_1(t + \tau) - \bar{I}_1)(I_2(t) - \bar{I}_2)}{\sqrt{\text{var}(I_1)\text{var}(I_2)}}. \quad (7.2)$$

If a traveling wave is observed, then the value of τ that maximizes the lagged correlation, C_{12}^{τ} , should increase with the separation, d , between two populations. If the traveling wave moves with constant velocity, c , then $\tau_{max} = d/c$, which can be derived from the fact that the time taken for the wave to travel a distance, d , is the distance divided by the velocity. More advanced versions of this approach have been successfully used by Grenfell et al. (2001) to identify traveling waves of measles infection in England and Wales spreading from large population centers like London to the surrounding smaller communities.

7.1.2. Interaction

Consider the behavior of an infectious disease within several human populations. If there is no interaction (movement) between the populations, then their dynamics will be independent and hence the correlation between them will be zero (assuming no other synchronizing mechanisms, such as seasonal forcing or climatic factors). However, movement of hosts between populations, with the associated risk of disease transmission, can couple dynamics. The way in which we choose to model this interaction should reflect the behavior of the host and the scale at which our model operates.

One of the simplest means of modeling the interaction between (for example) two populations is for susceptible individuals at one location to experience an additional force of infection due to infectious individuals at the other. This would represent a phenomenological approach to spatial modeling and we frequently refer to the strength of such interactions as the level of *coupling* between the populations. The greater the coupling, the more each population is impacted by the transmission dynamics of the other and the higher the level of correlation and synchrony.

Interaction or coupling between different spatial locations allows infection to spread and acts to synchronize the epidemic dynamics at the two locations.

It is intuitive that in many situations the interaction between two populations should decrease with the distance, d , between them. This type of behavior can be captured by introducing a *transmission kernel*, K , which modifies the coupling term and is a function of the distance between two populations. Common examples of transmission kernels include exponential ($K \propto \exp(-Ad)$), Gaussian ($K \propto \exp(-Ad^2)$), or power-law ($K \propto d^{-4}$) (Erlander and Stewart 1990; Gibson 1997a,b; Keeling et al. 2004b; Xia et al. 2004), with the precise form chosen determined by the observed dynamics. Estimating the kernel form and parameters is a very difficult but important problem; although the more common, short-distance transmission events determine the basic reproductive ratio, it is the long-distance tail of the kernel that determines the eventual speed of a traveling wave of invading pathogen (Diekmann 1978; van den Bosch et al. 1990; Mollison 1991; Shaw 1995; Lewis 2000; Xia et al. 2004). However, at long distances the kernel is usually very small, so there will be only limited amounts of data for the estimation processes. These rare jumps to new areas cannot be ignored, however, because they are often vitally important to the invasion process.





The reduction in transmission risk with distance is captured by a transmission kernel, which is frequently assumed to be either exponential, Gaussian, or power-law.

7.1.3. Isolation

Isolation is another factor that is common in a wide range of models and real scenarios. It simply refers to the situation when a group of hosts is protected from the risk of transmission due to their spatial separation from an infectious source. For example, we might consider communities that have few contacts with the outside world as being isolated from the general pool of infectious individuals. Alternatively, animal populations that are separated by large distances can be epidemiologically isolated from other populations. The existence of isolated populations can have a profound impact on parameterization; if isolated populations are included in an estimate of disease parameters, their rarity of transmission will bias the results.

7.1.4. Localized Extinction

In any stochastic population model, there is always the risk that the disease will, by chance, become extinct and this risk increases as the host population size gets smaller (see Chapter 6). This is where the spatial resolution of study becomes important. For example, if we consider the aggregate epidemics of an infectious disease like measles in the prevaccine era in the whole of England and Wales, then the probability of witnessing a fade out is almost zero. However, as we examine case reports in increasingly smaller cities and towns, the frequency of local extinctions increases, with the smallest population centers experiencing fade outs in between epidemics sparked by the introduction of infection from cities where it is endemic. The likelihood of such “recolonization events” is influenced by the synchrony of measles epidemics and the coupling between subpopulations (Bolker and Grenfell 1996; Earn et al. 1998; Rohani et al. 1999; Keeling 2000b; Hagenaars et al. 2004). As a result, overall population persistence is determined by a key relationship between the subpopulation size, the degree of interaction, and the strength of asynchrony. The precise details of this relationship remain largely unclear, but some of the complexities are discussed below when metapopulations are described (Section 7.2.3).



Due to the smaller subpopulation sizes often involved in spatial models, localized extinctions are common. Large-scale eradication is prevented by coupling between subpopulations leading to the reintroduction of infection into disease-free areas.

7.1.5. Scale

Two forms of scale are important for spatial models: (1) the scale of interaction, and the (2) the scale of simulation.

The majority of spatial models make some assumption about the spatial scale of interaction and the scale at which the population can be subdivided. Although there is rarely a “correct” scale, it is clear that using too fine a scale and hence creating many subpopulations can be computationally prohibitive, whereas aggregating at too large a scale