Catching a wave: on the suitability of traveling-wave solutions in epidemiological modeling

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Abstract

Ordinary differential equation models such as the classical SIR model are widely used in epidemiology to study and predict infectious disease dynamics. However, these models typically assume that populations are homogeneously mixed, disregarding possible variations in disease prevalence due to spatial heterogeneity. To address this issue, reaction-diffusion models have been proposed as an alternative approach for modeling spatially continuous populations in which individuals move in a diffusive manner. In this study, we explore the conditions under which such spatial structure must be explicitly considered to accurately predict disease spread, and when the assumption of homogeneous mixing remains adequate. In particular, we derive a critical threshold for the diffusion coefficient below which disease transmission dynamics display spatial heterogeneity. We validate our analytical results with individual-based simulations of disease transmission across a two-dimensional continuous landscape. Using this framework, we further explore how key epidemiological parameters such as the establishment probability of a disease, its maximal incidence, and its final epidemic size are affected by incorporating spatial structure in SI, SIS, and SIR models. We discuss the implications of our findings for epidemiological modeling and identify design considerations and limitations for spatial simulation models of disease dynamics.

Keywords: ordinary differential equations, diffusion theory, spatial disease modeling, individual-based simulations, SIR model

1. Introduction

A fundamental understanding of how infectious diseases spread across time and space is crucial for predicting the course of epidemics and guiding potential control measures. Compartmental models have provided the workhorse for infectious disease modeling for almost a century [1, 2, 3]. In these models, the population is divided into compartments based on their infection status, such as susceptible (S), infectious (I), and recovered (R) individuals. One of the simplest compartmental models is the so-called SI model, where individuals can only be susceptible or infected [1]. Once infected, an individual perpetually remains in that state. Two classic extensions of this model are the SIS and SIR models [1]: In the former, infected individuals can return to the susceptible class, whereas in the latter they can become recovered, often implying that they are immune to future infections.

Compartmental models are typically studied with ordinary differential equations (ODEs) describing the expected changes in the proportions of the different population compartments over time [1, 2, 4, 5, 3]. For example, consider a simple SI model where individuals come into contact with each other at a constant rate r. Let $i(t)$ specify the fraction of infectious individuals in the population. Whenever a susceptible individual meets an infected one, it contracts the pathogen with probability α (for simplicity, we will use the terms 'pathogen' and 'disease' interchangeably throughout this paper, acknowledging their conceptual distinction). If we assume homogeneous mixing among the individuals, the change in the proportion of infectious individuals over time will be given by:

$$\frac{\partial i}{\partial t} = r\alpha i(1-i) \tag{1}$$

Epidemiological models of this type can be extended to include additional compartments, such as a recovered class, in which case their dynamics may need to be described by a set of ODEs. Over the past century, such models have provided invaluable insights into the factors that shape disease transmission by providing conceptual results and threshold quantities (e.g., herd immunity, basic reproduction number, and replacement number) to anticipate disease spread and the impact of countermeasures, thereby guiding decision-making and public health policies during disease outbreaks [4, 2, 3, 5, 6].

The limitations of ODE models often lie in the underlying assumptions they make of the transmission process. One common assumption of ODE models is that they assume homogeneous mixing among individuals [7]. Yet this is rarely the case for real-world populations, which can be structured in multiple ways [8, 9, 10, 11, 12]. For example, many populations are geographically structured, such that individuals that are close to each other are more likely to come into contact than individuals that are far apart. Besides spatial structure, kinship and social structure can also have a substantial influence on contact patterns [13, 14]. As a result, local disease prevalence can vary substantially between different parts of the population, and this can have a considerable impact on the expected epidemiological dynamics [15, 11, 16]. While classic ODE models have clear advantages for modeling disease transmission, such as their well-understood mathematical properties, computational efficiency, and ability to provide analytical solutions [11], omitting the influence of population structure in these models could lead to inaccurate conclusions about the anticipated disease dynamics.

In this study, we will focus specifically on the potential effects of spatial population structure, which can be incorporated into disease transmission models in several ways. One approach is the use of a meta-population model that divides the population into subpopulations or "patches", each representing a homogeneous host population such as a city. The dynamics within the patches, and the coupling between them, can then be described using a system of ODEs [17, 18, 19]. Such coupling could be based on geographic distance, empirical observations such as mobile phone data [20], or geo-located social media posts, for instance [21]. Alternatively, individual-based or agent-based approaches can be used to model all individuals in the population and their spatial position explicitly [22, 16, 23]. The interactions between individuals (e.g., the rate and strength of contacts) can be regulated by distance-based kernels [5, 24], which can result in a highly variable infection probability across space [11]. Network models represent another class of approaches that allow for very fine-scaled modeling of population structure [25]. In these models, each node usually represents an individual, with edges between nodes representing contacts between individuals. A common assumption of this approach is that a susceptible individual can only contract the disease if an edge connects it to an infectious individual [16, 26]. However, network models are complex and their analysis can require an extensive amount of empirical data to model larger populations [16].

For populations inhabiting a continuous geographic landscape, where individuals primarily move within short distances compared to the overall range of the landscape, reaction-diffusion models can offer an alternative approach for describing spatial disease dynamics [27]. These models were first introduced in the 1930's by Fisher and Kolmogorov to explain the spread of a beneficial allele across a one-dimensional habitat [28, 29]. In such models, the beneficial allele can propagate through the population in the form of a "traveling wave," with a constant and well-defined velocity. Since then, diffusion models have been widely used in mathematical biology to study not only the spread of adaptive alleles but also invasive organisms and infectious diseases [30, 31, 32, 27, 33, 34, 35, 36, 37, 3, 38]. In the context of epidemiology, reaction-diffusion models enable us to describe the proportion of infected individuals as a function of space and time. The diffusion term models the random dispersal of individuals, while the reaction term describes the local rates of disease transmission, in a similar way to a compartmental ODE model [27].

In this paper, we use diffusion theory to study under which scenarios a simple compartmental ODE model is sufficient to capture disease dynamics and when spatial structure has to be taken into account. We derive a simple critical threshold D_c for the diffusion coefficient below which we expect the limited dispersal of individuals to markedly affect disease dynamics. We confirm our results with individual-based simulations conducted in SLiM [39], which allow us to smoothly transition from spatially unstructured to structured populations. Using this framework, we investigate the effect of spatial structure on disease dynamics in three classic compartmental disease transmission models: the SI, SIS, and SIR model [1, 4]. Furthermore, we highlight potential caveats of simulating continuous disease transmission models in a discrete, individual-based, and biologically realistic manner.

2. Results

2.1. ODE model

Consider a simple Susceptible-Infected (SI) model in a closed population of constant size N without birth or death events [1, 5]. There are only susceptible and infectious individuals in the population, and infectious individuals do not recover (i.e., they never leave the infectious compartment). Let $I(t)$

and $S(t) = N - I(t)$ denote the overall counts of susceptible and infectious individuals in the population at time t, and $s(t) = S(t)/N$ and $i(t) = I(t)/N$ their respective population frequencies with $i(t) + s(t) = 1$. If we assume a homogeneously mixing population in which individuals come into contact with each other at a constant contact rate r per time unit, and a disease that establishes in a susceptible individual after contact with an infectious individual with probability α, then the change in the proportion of infectious individuals will be given by Equation (1). The solution to this ODE model is a logistic growth function [40]:

$$i(t) = \frac{1}{1 + [N/I(0) - 1]e^{-r\alpha t}} \tag{2}$$

Whenever $I(0) > 0$, we have $\lim_{t\to\infty} i(t) = 1$, meaning the disease will ultimately spread throughout the entire population. Figure 1A provides an illustration of this logistic spread in the ODE model.

Assuming one infected individual in the beginning ($I(0) = 1$) and a sufficiently large population ($N \gg 1$), the expected time for the disease to reach 50% frequency in the population will be:

$$t_{1/2} \approx \frac{\ln N}{r\alpha} \tag{3}$$

Since $i(t)$ is symmetric around the inflection point at $i(t_{1/2}) = 1/2$, the expected time for the disease to spread through the whole population, which we will call the "fixation time" of the ODE model, is therefore:

$$t_{\text{ODE}} \approx 2t_{1/2} \approx \frac{2\ln N}{r\alpha} \tag{4}$$

2.2. Reaction-diffusion model

ODE models such as the simple compartmental SI model outlined above are widely used in epidemiological modeling [41], yet their underlying assumption of homogeneous mixing makes it difficult to incorporate spatial population structure. For populations that inhabit a continuous landscape, diffusion theory can provide an alternative modeling framework that explicitly includes spatial heterogeneity in disease prevalence [3, 42, 43, 28, 29]. In a diffusion model, the frequency of infected individuals becomes a function not only of time t but also of spatial position x.

Let us consider an SI model in which individuals move randomly according to some dispersal kernel that decays with distance at least as quickly as an exponential function [38]. In such a case, we can model dispersal by a diffusion term [38, 28, 44], while disease transmission can be modeled by a reaction term based on the local compartment frequencies. Together, this yields a second-order partial differential equation for the SI diffusion model of the following form:

$$\frac{\partial i}{\partial t}(x,t) = D\frac{\partial^2}{\partial x^2}i(x,t) + r\alpha i(x,t)[1 - i(x,t)] \tag{5}$$

The diffusion coefficient D accounts for the random dispersal of individuals. In a one-dimensional habitat, $2D = \sigma^2$, where σ^2 is the variance in the expected spatial displacement of individuals per time unit due to their random movement [28, 45]. The reaction term is analogous to the ODE model from Equation (1), except that the frequency of infected individuals now depends on the spatial position x as well. Equation (5) is also known as the Fisher-Kolmogorov or Fisher-KPP equation [28, 29, 3].

One solution to Equation (5) is a so-called "traveling wave" [28, 46, 47, 27, 3, 38, 33] in which the disease spreads outward from an initial introduction point with a constant velocity:

$$v \geq 2\sqrt{Dr\alpha} \tag{6}$$

Figure 1B provides an illustration of these dynamics in a one-dimensional habitat where the disease is introduced at the center and then spreads outward in the form of two symmetric traveling waves to the left and right. The "width" of each wave, i.e., the length of the region between its front (where the frequency of infected individuals is still close to zero) and top (where almost everyone is already infected), is approximately $w \approx 2\sqrt{D/(r\alpha)}$ [28].

It is straightforward to extend this diffusion model to two dimensions. Specifically, let us consider a square habitat of side length 1 with isotropic dispersal. Displacement along the x and y axes can then be treated independently, with each following the one-dimensional model so that the diffusion coefficient now equals half the variance in the displacement in each of the x and y coordinates: $2D = \sigma_x^2 = \sigma_y^2$. Note that the overall displacement in a two-dimensional space, $\Delta = \sqrt{\Delta_x^2 + \Delta_y^2}$, will typically be larger than the

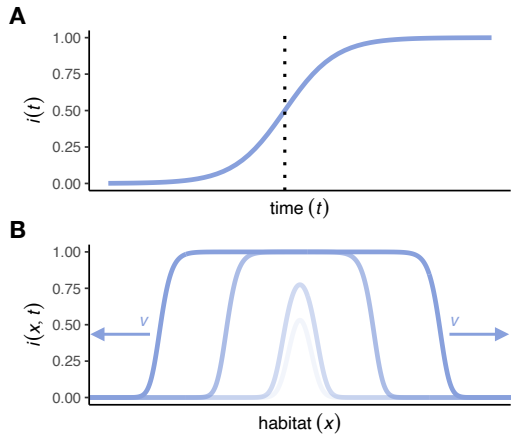

Figure 1: Schematic plots of expected disease spread under the ODE and the reaction-diffusion models. (A) In the ODE model, the frequency of infected individuals, $i(t)$, increases logistically according to Equation (2). The vertical dashed lines represent $t_{1/2}$ as defined in Equation (3). (B) In the diffusion model for a one-dimensional habitat, the disease spreads from an initial release at the center of the habitat via two traveling waves with constant velocity $v = 2\sqrt{Dr\alpha}$ in either direction.

displacement in each individual dimension.

In this two-dimensional diffusion model with isotropic dispersal, the disease will spread from an initial introduction point in the form of a circle with its radius growing at a constant velocity $v = 2\sqrt{Dr\alpha}$, the same speed as a traveling wave in the one-dimensional model [8, 48]. Let us further assume that the habitat size is much larger than the wave width so that the disease is either absent or fixed in most areas of the habitat. This requires $D \ll r\alpha/4$. When the disease is introduced in a small number of individuals at the center of the square habitat, the circle has to grow to a radius $1/\sqrt{2}$ in order to reach all corners of the square. Thus, the expected fixation time of our SI diffusion model in two dimensions will be approximately:

$$t_{\text{DIFF}} \approx \frac{1}{\sqrt{8Dr\alpha}} \tag{7}$$

2.3. Critical threshold

The ODE model assumes a homogeneously mixing population while the diffusion model can explicitly account for spatial heterogeneity in disease transmission due to limited dispersal. Naturally, the question arises of how

the epidemiological dynamics predicted by these models differ, and under which parameters one is more accurate than the other. To answer this question, we can contrast their expected disease fixation times, t_{ODE} and t_{DIFF}. Setting both equal, we obtain a critical value for the diffusion coefficient under which both models predict the same fixation time:

$$t_{\text{ODE}} = t_{\text{DIFF}} \implies D_c = \frac{r\alpha}{32(\ln N)^2} \tag{8}$$

When $D < D_c$ the ODE model predicts a shorter fixation time than the diffusion model because the slow dispersal of individuals becomes a limiting factor for how fast a disease can spread throughout the whole habitat. In this low-dispersal regime, we expect the diffusion model to more accurately describe epidemiological dynamics than the ODE model, which should overestimate the rate of disease spread. By contrast, as D becomes on the order of D_c, the width of the traveling wave in the diffusion model will no longer be much shorter than the habitat size and the disease will no longer spread as a circle with a "sharp" edge. Thus, our calculation of t_{DIFF} in Equation (7) will no longer be accurate and in fact, overestimate the rate of disease spread. Here, the fixation time should begin approaching the prediction of the ODE model. In the high-dispersal regime where $D \gg D_c$, diffusion is strong enough that the population is effectively well mixed over the timescale relevant for the spread of the disease and the ODE model should describe the epidemiological dynamics most accurately.

2.4. Individual-based simulation framework

To test the theoretical predictions derived above, we implemented an individual-based simulation model for disease transmission in SLiM (version 4.0) [39]. By varying the dispersal rates of individuals, our simulation model can smoothly transition from spatially unstructured to highly structured populations, allowing us to investigate disease dynamics across the high and low-dispersal regimes, and to study the predicted transition around the critical diffusion coefficient D_c. We focused on an abstract, directly transmitted disease in a closed population (i.e., no birth or death processes), comprised of $N = 100,000$ individuals. These individuals inhabit a continuous two-dimensional space, modeled as a square arena with a side length of 1 and periodic boundaries to avoid edge effects [49, 15, 5].

The ODE and diffusion models are both continuous-time models, whereas our individual-based simulations in SLiM advance over discrete time steps. We assume that each such "tick" represents one infection cycle. To minimize differences between the discrete-time simulations and the continuous-time mathematical models, we must ensure that $r\alpha \ll 1$ and $D \ll 1$ when rates are measured per tick. However, this requirement does not limit the generality of our models. We can freely choose what period of time in the real world a tick in our simulations corresponds to, such as a year or a millisecond. By choosing a small enough period, we can always ensure that D and $r\alpha$ are sufficiently small.

The disease is transmitted via direct contact between infectious and susceptible individuals. In each tick, we assume that an individual has contact with all individuals that are currently within its interaction distance δ, which we chose such that each individual on average has 15 contacts per tick (i.e., r=15). Note that the average number of contacts per tick is independent of the infection status (i.e., infectious individuals, on average, have as many contacts as susceptible or recovered individuals). For our square landscape of area 1 with 100,000 individuals and toroidal boundary conditions, we found that this corresponds to an interaction radius of $\delta \approx 0.00691$. Each contact between a susceptible individual and an infectious individual results in disease transmission with a probability of α=0.001, yielding $r\alpha = 0.015 \ll 1$. When a susceptible individual has contracted the disease, it will become infectious in the next tick. At the end of each tick, we simulate isotropic dispersal by sampling the x and y displacements for each individual independently from a normal distribution with mean $\mu = 0$ and variance $\sigma^2 = 2D$. The infection status of an individual has no effect on D.

We implemented three compartmental disease transmission models in this simulation framework: (i) the SI model, (ii) the SIS model, and (iii) the SIR model [5]. In the SI model, once an individual is infected, it remains infectious until the end of the simulation. In the SIS model, infected individuals remain infectious for a constant number of n ticks and then reenter the susceptible class. In the SIR model, infected individuals become "recovered" after a constant number of n ticks and cannot become infected again.

Each simulation run is initialized by uniformly distributing 100,000 susceptible individuals across the habitat. At tick 25, the disease is introduced

into the population by infecting the individual closest to the center of the square habitat. For each simulation, we recorded the number of individuals in each compartment at the beginning of each tick until either the disease spread through the whole population, no infectious individuals were left, or the simulation ran for 50,000 ticks. This upper threshold of 50,000 ticks results in a very lenient timeline that is not expected to interfere with the simulated SI disease transmission dynamics. Given our simulation parameters, the disease is expected to fix in the SI model between approximately 1,500 - 14,000 ticks (Equations 4 and 9).

2.4.1. Low-diffusion limit

A key abstraction of the diffusion approach is that it models a continuous density of individuals across the habitat. The relative frequencies of infectious and susceptible individuals are specified at any given position in the habitat and disease transmission can occur exactly at that position. In our individual-based simulation model, however, a finite number of individuals are dispersed across a continuous habitat. It is unlikely that two of them will ever be at exactly the same position. Thus, one has to decide how close two individuals need to be for one to be able to infect the other, which we implemented by defining an interaction radius δ.

Ideally, δ should be very small (i.e., much smaller than the average dispersal distance of individuals) so that the movement of individuals remains the primary driver of disease spread. Yet there is a lower limit on δ for any given contact rate in our model. For example, if we want to ensure that each individual on average has, say, two contacts, this requires a certain minimum interaction radius so that each individual encounters enough individuals within its interaction radius. One important consequence of this is that when D becomes sufficiently small, the spread of the disease will no longer be driven primarily by the dispersal of individuals, but instead by "hopping" between neighboring individuals with overlapping interaction circles. This "hopping" dynamic can lead to disease fixation even when individuals do not move at all, thereby setting an upper bound for the fixation time in the limit $D \to 0$.

We can still describe disease spread under these hopping dynamics by the diffusion model, but we will have to reinterpret the diffusion term. In

particular, we can interpret each transmission event as a "dispersal" step of the disease from the location of the infecting individual to the location of the newly infected individual. To derive a rough estimate of the diffusion coefficient (D_0) of this process, we consider the limiting case where individuals no longer move at all. Starting from the initially infected individual at the center of the habitat, the disease will spread outward in a circular pattern with the traveling wave now driven entirely by the hopping process. The speed of this traveling wave will be given by $\nu = 2\sqrt{D_0 r\alpha}$. One complication is that in the hopping model, D_0 will vary across space because it depends on the occurrence of new transmission events. Thus, D_0 should be zero in areas where either everyone is already infected or everyone is still susceptible. It should be maximal right at the wavefront, where it determines the speed of the wave.

Let us, therefore, consider an infected individual located exactly at the wavefront. We can assume that its neighbors are uniformly distributed across its interaction circle. On average, half of these individuals should already be infected, while the other half are still susceptible. The overall rate at which transmission events from the focal infected individual occur should then be $\Pr(\text{transmission}) = r\alpha/2$. If a transmission event occurs, the variance in the displacement along the x-axis will be $\sigma_x^2 = \delta^2/4$. The effective diffusion coefficient of the hopping process will thus be $2D_0 \approx \Pr(\text{transmission})\sigma_x^2 = r\alpha\delta^2/8$, which according to Eq. (7) yields a fixation time of:

$$t_0 \approx \frac{\sqrt{2}}{r\alpha\delta} \tag{9}$$

This should constitute an approximate upper bound of the fixation time in the limit $D \to 0$, where Equation (7) would predict an infinite fixation time, if only the dispersal of individuals were to be considered.

2.5. SI Model

We initially focused on the SI model to test how well our mathematical predictions describe disease spread in the individual-based simulation model across different dispersal regimes. Qualitatively, we expect that in the low-dispersal regime ($D < D_c = 3.536 \times 10^{-6}$), the disease should spread from its introduction at the center of the habitat as a circle with a steadily growing radius. By contrast, in the high-dispersal regime ($D \gg D_c$), the population should be sufficiently mixed so that the frequency of infected individuals increases in all areas of the habitat at a similar rate. Figure 2 confirms these

qualitative predictions when comparing two simulation runs with $D = 10^{-6}$ (left column) and $D = 10^{-2}$ (right column).

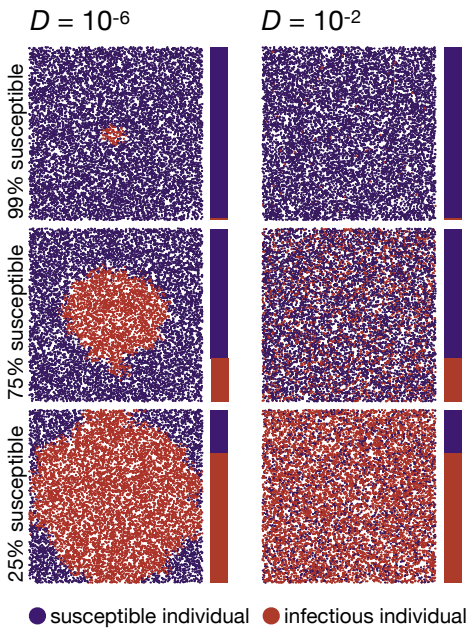

Figure 2: Two exemplary simulation runs in the SI model. The left column shows a run in the low-dispersal regime ($D = 10^{-6}$), while the right column shows a run in the high-dispersal regime ($D = 10^{-2}$). The top, middle, and bottom plots show population snapshots taken when 99%, 75%, and 25% of the population were still susceptible. As predicted, in the low-dispersal regime the disease advances by a growing circle. By contrast, in the high-dispersal regime infectious individuals are homogeneously distributed across space (right column). Data were simulated using the following parameters: $N = 10,000$ (ten-times smaller than our standard model for better visualization), $\alpha = 0.01$, $r = 15$. Videos of simulation runs in the SI model can be found under `https://tinyurl.com/bdddam58`.

We next tested our predictions for the disease fixation time under varying dispersal rates (Figure 3A). In the high-dispersal regime, the observed fixation time t_{sim} is independent of D and well approximated by the predictions from the ODE model given in Equation (4). The time-resolved proportion of infectious individuals follows the predicted logistic growth curve (Figure 3B, bottom panel). When D becomes smaller than D_c, the fixation time starts to increase and becomes inversely proportional to D, as predicted by Equa-

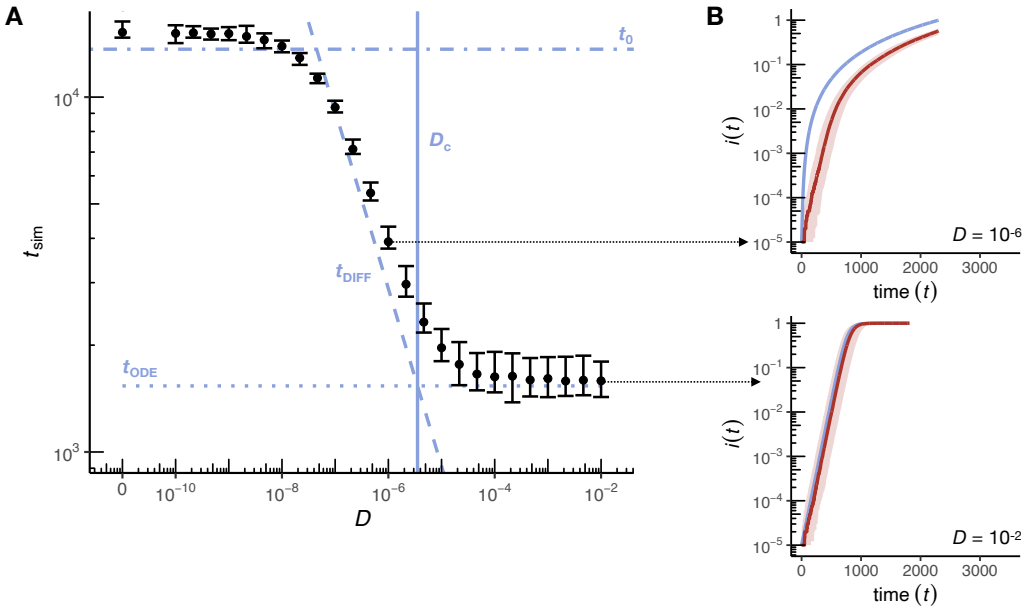

Figure 3: Disease dynamics in the SI model. (A) Time until disease fixation in the simulations (t_{sim}) for varying diffusion coefficients (D). Black dots represent median values and error bars the 2.5 and 97.5 percentiles estimated over 50 simulation runs for each D (for $D = 0$, the spread stagnated in 3 of the 50 runs due to small clusters of susceptible individuals with interaction areas devoid of infectious individuals, which we excluded from the analysis). The vertical solid line indicates the critical threshold D_c according to Equation (8). In the high-dispersal regime ($D \gg D_c$), fixation times converge to the prediction of the ODE model (t_{ODE}, dotted line), whereas in the limit of no dispersal ($D \to 0$), they are bounded by the prediction of the hopping model (t_0, dot-dashed line). In the low-dispersal regime where $D < D_c$, the disease advances as a traveling wave and t_{sim} is well approximated by the prediction of the diffusion model (t_{DIFF}, dashed line). (B) The top panel shows the time-resolved disease dynamics for the low-dispersal regime ($D = 10^{-6}$). Here, the proportion of infectious individuals, $i(t)$, increases approximately as the area of a circle whose radius expands at the predicted wave speed of the diffusion model (blue line). The initial lag between the expected and the observed proportion of infectious individuals is likely caused by the establishment phase of the disease [44, 8]. The bottom panel shows an example from the high-dispersal regime ($D = 10^{-2}$). Here, the proportion of infectious individuals is well approximated by the expected logistic growth function of the ODE model (blue line). Solid red lines represent the median proportion of infectious individuals across 50 simulation runs, and the shaded areas represent the range between the 2.5 and 97.5 percentiles.

tion (7). In this regime, the transmission dynamics are well approximated

by the traveling wave model in which the disease spreads as a circle with a linearly growing radius (Figure 3B, top panel). Once D becomes so small that the fixation time approaches the prediction under the hopping dynamics derived in Equation (9), t_{sim} levels off and again becomes independent of D.

Overall, we observe that fixation times can differ up to one order of magnitude in our simulation model depending on the dispersal rate. This highlights the potential risk of underestimating the expected epidemic duration if predictions are based solely on the ODE model without accounting for population structure.

2.6. SIS Model

In the SI model, infected individuals do not recover from the infection, leading to an inevitable spread and ultimate fixation of the disease as long as $r\alpha > 0$. The SIS model allows infected individuals to transition back to the susceptible state following infection. In a deterministic ODE model of an unstructured population, such a disease is expected to reach an equilibrium frequency of $1 - 1/R_0$ as long as $R_0 > 1$, where R_0 represents the basic reproduction number of the disease (i.e., the average number of secondary infections caused by a single infectious individual when introduced into a completely susceptible population) [50, 5]. If $R_0 < 1$, the disease is typically incapable of establishing in the population and will quickly die out.

To investigate the effects of spatial structure and stochasticity on an SIS model, we modified our individual-based simulations such that infected individuals reenter the susceptible class after a constant number of n infectious ticks, yielding $R_0 = nr\alpha$. Qualitatively, we find that the disease initially still spreads in a circular fashion in the low-dispersal regime and more homogeneously in the high-dispersal regime, similar to the SI model (Figure 4). However, the perpetual reentering of infectious individuals into the susceptible class breaks up this strict circular clustering somewhat more quickly in the SIS model as compared to the SI model. Ultimately, the frequency of infectious individuals reaches the equilibrium frequency of 1-1/R_0 in both the high-dispersal and low-dispersal regimes.

While a deterministic ODE model predicts that any disease with $R_0 > 1$ should successfully establish after introduction, the stochastic fluctuations

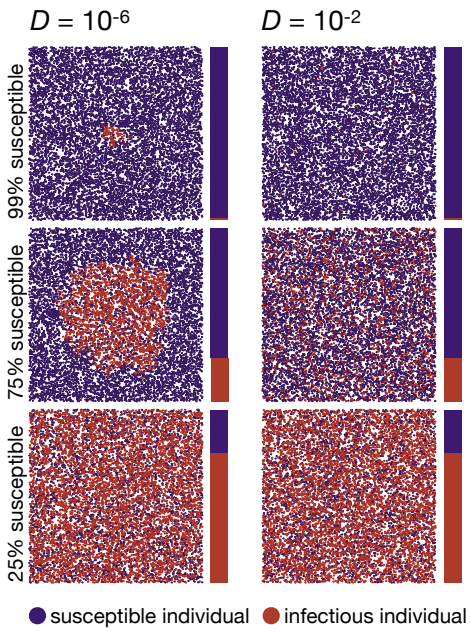

Figure 4: Two exemplary simulation runs in the SIS model. The left column shows a run in the low-dispersal regime ($D = 10^{-6}$), while the right column shows a run in the high-dispersal regime ($D = 10^{-2}$). The top, middle, and bottom plots show population snapshots taken when 99%, 75%, and 25% of the population were still susceptible. As predicted, in the low-dispersal regime the disease initially advances by a growing circle. By contrast, in the high-dispersal regime infectious individuals are homogeneously distributed across space (right column). In contrast to the SI model, infectious individuals hardly cluster in the SIS model late in the simulations even in the low-dispersal regime due to the perpetual reentering of infectious individuals into the susceptible class after n infectious ticks. Data were simulated using the following parameters: $D = [10^{-6}; 10^{-2}]$, $N = 10,000$, $\alpha = 0.01$, $r = 15, n = 30$. Videos of simulation runs in the SIS model can be found under `https://tinyurl.com/bdddam58`.

in our individual-based simulation model can lead to the loss of the disease in certain simulation runs, even for relatively high R_0 values (e.g., approximately 10% of simulation runs with $R_0 = 3$, as shown in Figure 5A). We did not find a strong influence of the dispersal rate on the probability of disease establishment. However, in the high-dispersal regime, the frequency of infected individuals approaches the expected equilibrium frequency more rapidly compared to the low-dispersal regime (Figure 5B-D). Overall, we ob-

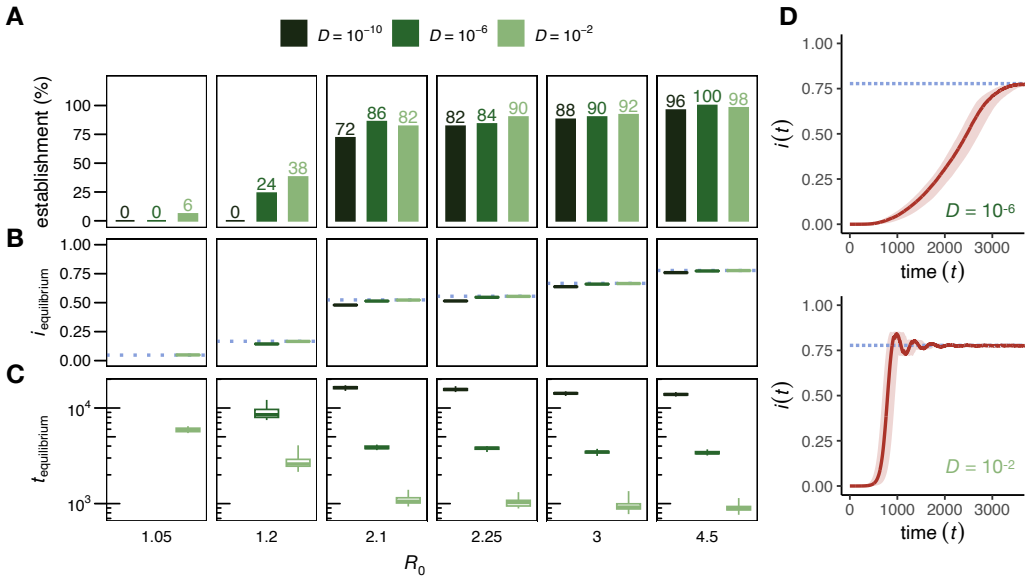

Figure 5: Disease dynamics in the SIS model. (A) Percentage of 50 simulation runs that reached at least a frequency of 1% infectious individuals for varying R_0 values (panels) and three exemplary diffusion coefficients. (B) Observed equilibrium frequencies at the end of the simulations. Boxplots are shown with whiskers indicating the most extreme values within $5 \times IQR$ of the boxes, but the variance among runs was so small that they are not visible. The expected equilibrium frequency for each R_0 value under an ODE model [5] is depicted by the dotted blue line. Simulated disease dynamics in the low-dispersal regime ($D = 10^{-6}$) tend to reach the expected equilibrium at higher R_0 than simulated disease dynamics in the high-dispersal regime ($D = 10^{-2}$). (C) Time of equilibrium onset. We defined the onset of the equilibrium as the first time the frequency of infectious individuals reaches 99% of the observed equilibrium frequency. For large R_0 values, equilibrium establishment in the low-dispersal regime takes almost an order of magnitude longer than in the high-dispersal regime. (D) Time-resolved disease dynamics for $R_0 = 4.5$ and two exemplary diffusion coefficients (top panel: low-dispersal with $D = 10^{-6}$, bottom panel: high-dispersal with $D = 10^{-2}$). The disease spreads faster in the high-dispersal regime and approaches the expected equilibrium frequency earlier (dotted line, [5]). Solid red lines represent the median proportion of infectious individuals across all simulations, and the shaded area represents the range between the 2.5 and 97.5 percentiles.

served that rate of disease spread can again differ by more than an order of magnitude in our simulation model depending on the dispersal rate (Figure 5C).

2.7. SIR Model

In the SIS model, individuals can transition between the susceptible and infectious states but do not acquire resistance to the disease. Conversely, the SIR model incorporates lasting resistance by introducing a "recovered state", to which individuals transition after being infected. Once in the recovered state, individuals cannot return to the susceptible or infectious state. According to a deterministic SIR model, a disease is expected to invade a completely susceptible and unstructured population whenever its basic reproduction number R_0 is larger than one [4]. In such cases, the final epidemic size (e_{final}), representing the overall proportion of individuals who have been infected during the epidemic, can be obtained by solving the transcendental equation $e^{-R_0 e_{\text{final}}} = 1 - e_{\text{final}}$ [3].

To study the SIR model, we modified our simulations of the SIS model such that infected individuals transition to the recovered class after a constant number of n infectious ticks, rather than returning to the susceptible class. It is important to note that this modification does not alter the basic reproduction number of the disease, which remains defined as $R_0 = nr\alpha$. In terms of qualitative behavior, we observed that similar to the SI and SIS models, the high-dispersal regime closely approximates a homogeneously mixed population (Figure 6) whereas in the low-dispersal regime, the disease spreads in a circular pattern across space, as theoretically predicted [51]. However, the traveling wave by which infections spread is now closely followed by another wave describing the emergence of recovered individuals.

The clustering of recovered individuals in close proximity to the wavefront of infectious individuals results in an overall reduction in the rate of disease transmission compared to a homogeneously mixed population and has various implications for disease dynamics: First, in the low-dispersal regime, there is a higher likelihood of the disease being eradicated from the population before it can establish, resulting in a lower establishment probability for smaller diffusion coefficients (Figure 7A). Second, as previously demonstrated [10, 9], higher values of R_0 are required in the low-dispersal regime to approach the theoretically expected final epidemic size (Figure 7B). Third, due to new infections occurring solely at the wavefront in the low-dispersal regime, the maximal disease incidence ($i_{\max}$), representing the maximum proportion of the population ever infected at a single point in time, is smaller compared to the maximal incidence in the high-dispersal regime (Figure 7C). Fourth,

analogous to the SI and SIS models, reduced dispersal slows down disease spread in general. Simulations with a diffusion coefficient of $D = 10^{-6}$ require nearly an order of magnitude more time to reach their respective final epidemic size compared to simulations with $D = 10^{-2}$. Finally, the time-resolved frequency of infectious individuals resembles a bell-shaped curve in the high-dispersal regime, whereas in the low-dispersal regime, it exhibits almost linear growth until late in the simulation (Figure 7D-E).

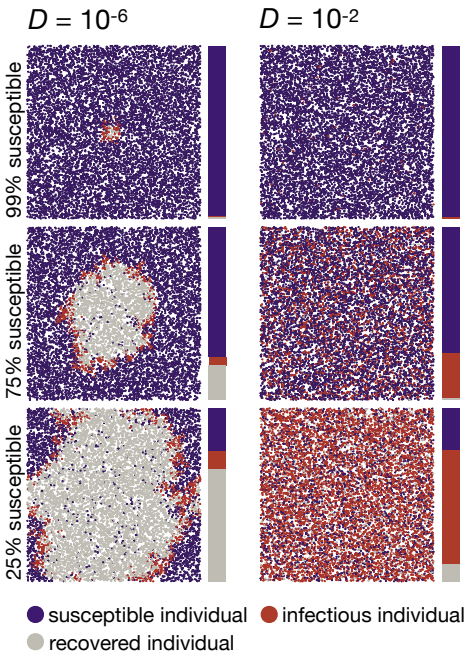

Figure 6: Two exemplary simulation runs in the SIR model. The left column shows a run in the low-dispersal regime ($D = 10^{-6}$), while the right column shows a run in the high-dispersal regime ($D = 10^{-2}$). The top, middle, and bottom plots show population snapshots taken when 99%, 75%, and 25% of the population were still susceptible. As predicted, in the low-dispersal regime the disease advances by a growing circle, with infectious individuals being clustered at the wavefront, and recovered individuals being clustered around the disease origin in the middle of the area. By contrast, in the high-dispersal regime susceptible, infectious, and recovered individuals are homogeneously distributed across space (right column). Data were simulated using the following parameters: $D = [10^{-6}; 10^{-2}]$, $N = 10,000$, $\alpha = 0.01$, $r = 15$, $n = 25$. Videos of simulation runs in the SIR model can be found under `https://tinyurl.com/bdddam58`.

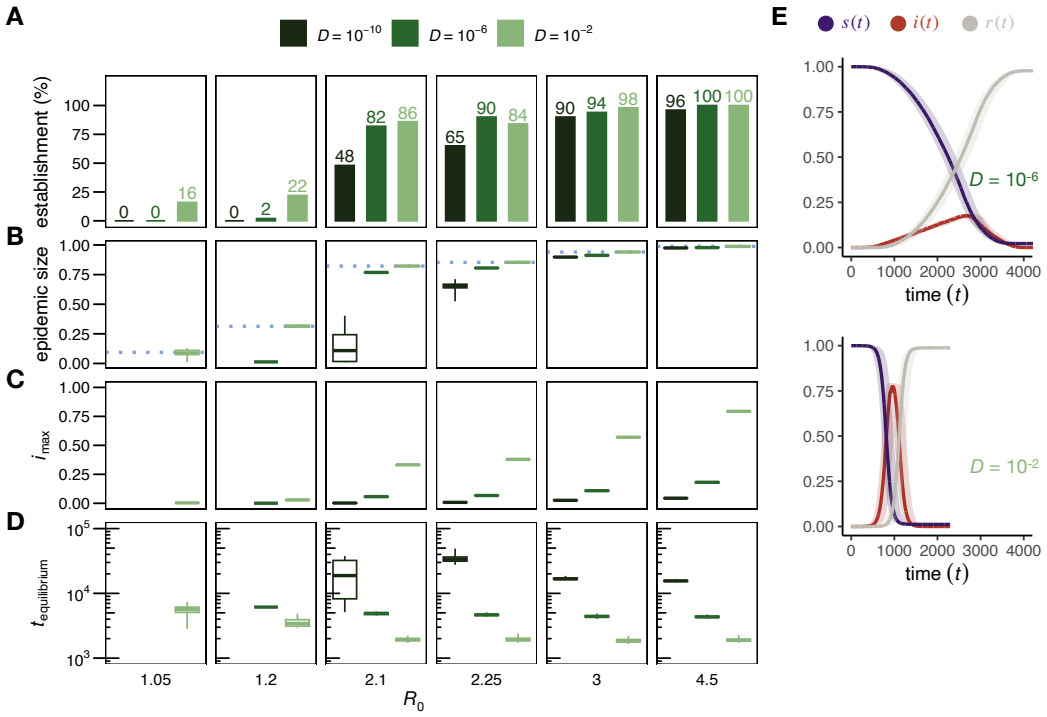

Figure 7: Disease dynamics in the SIR model. (A) Percentage of 50 simulation runs in which the disease reached an epidemic size of at least 1% for varying R_0 values (panels) and three exemplary diffusion coefficients (for $D = 10^{-10}$ and $R_0 = 2.25$, the spread stagnated in 1 of the 50 runs, which was excluded from the analysis). Disease establishment is less likely in the low-dispersal regime. (B) Epidemic size (boxplots are shown with whiskers indicating the most extreme values within $5 \times IQR$ of the boxes). Simulations in the low-dispersal regime require higher R_0 values to approach the theoretically predicted epidemic size. (C) Maximal incidence (the variance among runs was so small that whiskers are not visible). Lower dispersal results in smaller $i_{\max}$ values. (D) Epidemic duration. Simulations in the low-dispersal regime can take an order of magnitude longer than in the high-dispersal regime. (E) Time-resolved disease dynamics for $R_0 = 4.5$ and two exemplary diffusion coefficients (top panel: low-dispersal with $D = 10^{-6}$, bottom panel: high-dispersal with $D = 10^{-2}$). In the high-dispersal regime, the disease spreads rapidly and results in an $i_{\max}$ value of around 0.75. In the low-dispersal regime, on the other hand, infectious individuals are confined to the wavefront, resulting in an $i_{\max}$ value of less than 0.25. Solid lines represent the median proportion of susceptible (blue), infectious (red), and recovered (grey) individuals across all 50 simulations, and the shaded areas represent the ranges between the 2.5 and 97.5 percentiles.

3. Discussion

In this study, we explored the conditions under which it is essential to include spatial structure for precise disease spread predictions when individuals move diffusively across a habitat. We established a critical threshold D_c for the diffusion coefficient, below which disease transmission dynamics is expected to exhibit substantial spatial heterogeneity, while for $D \gg D_c$, the assumption of homogeneous mixing remains adequate. To validate our analytical results, we conducted individual-based simulations on a continuous two-dimensional landscape. Furthermore, we investigated the impact of continuous spatial structure on key epidemiological parameters, including disease establishment probability, maximal incidence, and final epidemic size.

The use of reaction-diffusion models in epidemiology is attractive due to their ability to calculate the expected speed of disease propagation based on measurable life-history traits, such as individual dispersal, average contact rate, and infection risk [36]. However, the applicability of such models hinges on several assumptions. First, a reaction-diffusion model assumes that disease transmission is a highly localized process [25], with long-range pathogen transmission being very rare. Additionally, it assumes uniform individual dispersal across the entire population, disregarding possible variations in movement patterns among individuals. In reality, movement patterns can vary significantly and include processes such as long-range dispersal or preferential movement towards specific locations. Both of these scenarios could profoundly affect disease transmission dynamics and substantially limit the model's accuracy. For example, if a dispersal kernel is not radially symmetric (as assumed in this study), the advancement of the frontal wave will deviate from a spherical shape [8]. If long-distance dispersal is common, the disease can spread from multiple independent locations, where it has been introduced by long-distance migrants [25]. This can ultimately result in a faster spread and accelerating wave speeds over time, as observed for wind-dispersed plant pathogens or avian influenza [44, 27, 33, 52, 25]. In such scenarios, conventional reaction-diffusion models assuming an exponentially bounded dispersal distribution [30, 52, 38] run the risk of significantly underestimating the spread of diseases [44, 52, 53, 33]. This, in turn, can constrain the ability to identify and optimize appropriate disease interventions [54]. Unfortunately, it can be quite challenging to estimate the occurrence of rare long-distance dispersal events in empirical systems [36].

Second, conventional reaction-diffusion models assume that the contact rate and disease establishment proportion are constant for the whole population. However, it is important to recognize that these parameters can exhibit variability among individuals and in response to environmental conditions, which are not explicitly accounted for in our abstract disease model. For instance, the contact rate r can vary significantly among individuals of different age groups [36, 55, 56], the number of contacts can be impeded by complex landscape features such as mountains, rivers, or other barriers [36, 34], and vary with population density or changes in host behavior over time [57]. The disease establishment probability α is often strongly influenced by environmental factors such as temperature, relative humidity, and the level of urbanization [58]. These individual and environmental factors can play a crucial role in shaping the dynamics of disease transmission [59], yet they are not explicitly incorporated into our current model framework.

Third, reaction-diffusion models typically treat space as a continuous and unbounded domain, disregarding edge effects that may exist in real-world habitats with boundaries [5, 49]. To mitigate such edge effects, we implemented periodic boundary conditions in our individual-based framework. This approach ensured that individuals on the boundaries of the simulated population were connected to those on the opposite side, creating a continuous and seamless space. However, one consequence is that susceptible individuals can encounter two disease waves as the disease spreads through the population. Although this may have led to a slight acceleration of disease propagation in scenarios with low dispersal towards the end of the simulations, the overall impact on the rate of disease fixation was relatively small compared to the simulated time frame.

If a biological system meets the assumptions of a reaction-diffusion model, this mathematical framework can provide an appealing approach to studying disease dynamics. For example, Noble used a reaction-diffusion model to study the spread of the Black Death across 14th-century Europe [32], finding that the analytically predicted patterns aligned well with historical records. Disease transmission was treated as a highly localized process with a value of $r\alpha \approx 1-4$ per year and $D \approx 25,900$ km^2 per year, yielding an expected wave "width" of $2\sqrt{D/(r\alpha)} \approx 161 - 322$ km, which is relatively small compared to the investigated habitat (the distance between Messina and Oslo is ap-

proximately 3,200 km). Furthermore, long-distance dispersal was likely very rare in medieval Europe, supporting the suitability of a reaction-diffusion model for studying this particular epidemic. In another study, Murray & Brown used a reaction-diffusion model to study the potential spread of rabies among foxes in the UK [60]. Rabies is transmitted by close contacts and foxes are highly territorial, which limits their individual dispersal. Similar to Noble's work, the $r\alpha$ and D estimates resulted in a relatively small wave "width" when compared to the studied habitat (the southern part of England) [60]. Murray's predictions for a potential spread of rabies in the southern UK were in good agreement with the observed spatial spread of rabies in mainland Europe [60].

While disregarding long-distance dispersal was likely suitable in the aforementioned studies, the scenario should be markedly different for modern human populations. With the growing interconnectedness between human communities, recent epidemics require a comprehensive framework capable of accounting for both short- and long-distance dispersal [61, 52, 38]. Integrating these dispersal mechanisms will be crucial for capturing the realistic dynamics of disease spread and invasion processes [12]. For recent human epidemics, Brockmann *et al.* demonstrated how substituting geographic distances with a probabilistically inspired "effective distance" that accounts for different levels of connectivity between human communities, allows the application of relatively simple diffusion models to study complex disease dynamics [12]. However, one has to be aware that this type of network data are rarely available for non-human species. Furthermore, besides distance and connectivity, individual movement is often influenced by various factors such as behavior, social structures, and environmental conditions [38, 23, 36, 12]. These factors can significantly contribute to the complexity of human movement patterns, making it particularly challenging to robustly integrate them into disease models [62]. If movement patterns are complex, network models or individual-based simulation frameworks might be better suited for studying disease dynamics, although these increasingly complex models may also limit the ability to draw general conclusions [38, 36].

The critical threshold D_c (Equation 8) allows for a back-of-the-envelope calculation of the maximum amount of individual dispersal that would be required to cause a noticeable slowdown in disease spread due to limited dispersal. As an example, consider a simple toy model of a theoretical measles

outbreak in a completely susceptible population. Measles is a highly contagious disease that can cause new infections in up to 90% of close contacts ($\alpha = 0.9$) [63]. Assuming an average of four close contacts per day ($r = 4$) [64], and 979 individuals per km^2 (i.e., the average population density in urbanized areas of the US; $N = 979$) [65], we obtain $D_c = 0.002$ km^2 per day. This means that in order for our theoretical measles outbreak to be substantially slowed down due to limited dispersal, the standard deviation in the expected spatial displacement of individuals in each of the x and y coordinates needs to be less than 69 meters per day on average. This toy example demonstrates that reaction-diffusion models are not suitable to model highly contagious diseases over small habitat ranges. However, they may still be useful for describing the dynamics between larger communities such as individual cities, which has also been done for measles [66, 37].

In order to assess the accuracy of our mathematical predictions derived from diffusion theory, we conducted a comparison with individual-based simulations. This highlighted some important differences and complexities that arise when attempting to simulate a continuous reaction-diffusion process with individual-based simulations. For instance, in our simulation framework, we defined contacts between individuals based on an interaction radius parameter. This approach allowed disease spread to occur by "hopping" between neighboring individuals with overlapping interaction areas even when individuals remained stationary. As a result, there was an upper bound on the fixation time in our individual-based simulations, which may not be immediately evident in other disease models. One might consider mitigating the influence of the interaction radius on disease dynamics by implementing a k-nearest-neighbor approach to model contacts. However, caution should be exercised when using a small value of k (e.g., $k = 1$), in combination with very low dispersal, as this combination could introduce a significant delay in disease spread if the neighbor structure changes only gradually. It is crucial to acknowledge these inherent limitations and potential biases that can arise due to the discretization of spatial and temporal dimensions.

In conclusion, our study highlights the need for careful interpretation and understanding of spatial factors in epidemiological dynamics, while also demonstrating the complexities and design choices that arise in modeling such dynamics.

4. Data Accessibility

The individual-based SI, SIS, and SIR disease transmission models are implemented in the open-source software SLiM (version 4.0) [39] and are available on GitHub under `https://github.com/AnnaMariaL/SpatialDieaseSim`. Videos demonstrating disease spread in structured and unstructured populations are available on YouTube under `https://tinyurl.com/bdddam58`.

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