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A Mathematical Model for the Spatial Spread of HIV in a Heterogeneous Population

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Abstract

An important factor in the dynamic transmission of HIV is the spatio-temporal mobility of the host population. One key challenge in HIV epidemiology therefore, is determining how the spatial structure of the host population influences disease transmission. The aim of this paper is to study how the movement of individuals impacts the spatial spread of HIV. We constructed a deterministic reaction-diffusion equation model for the spread of HIV in a heterosexually mobile population, under the assumption of a varying population size to study the dynamics of HIV spread in a spatially structured population and obtained the minimal wave speed. Then we considered the existence of traveling waves and the influences of parameters on HIV prevalence and the minimal wave speed. Numerical simulation showed that a stationary labyrinthine pattern emerges in the distribution of the infection population density in the two high-risk groups as a result of diffusion.

Keywords: Spatial distribution, HIV, reaction-diffusion, epidemiology.

1. INTRODUCTION

In the epidemiology, one of the central goals of mathematical epidemiology is to predict disease transmission patterns in populations (Liu and Jin, 2013). For instance, the spread of HIV/AIDS have been studied extensively since the first cases were recognized in the late 80' s with the aim of predicting its spread in diverse populations. However, this area of study is still challenging, since so many factors affect the transmission of HIV. Most of the articles have only focused on a single homosexual population, whereas in much of the world, heterosexual contact is the predominant mode of transmission. Finally, the spatial aspect of the epidemic and related with this, mobility of the population is often ignored. All these assumptions might limit the application of such models in describing the complex dynamics of the epidemic (Sani et al., 2006). This article addresses the questions of how diffusion affect the formation of the spatial patterns on the HIV spatial epidemic model by reaction-diffusion mechanisms.

Spatial spread of HIV disease is closely related to the spatial heterogeneity of the environment and the spatial-temporal movement of the hosts. HIV/AIDS epidemic is usually not homogeneous within geographical regions. Some areas are more affected than others. At a country level for instance, there are often wide variations in infection levels between different provinces, states or districts, and between urban and rural areas. In reality, the national picture is made up of a series of epidemics with their own characteristics and dynamics. In modeling HIV and other infectious disease spread, the starting point is the transmission dynamics within a population which is homogeneous in terms of host structures and environmental variation, and then follows by the examination of the impact on the transmission dynamics of the refined and detailed biological/epidemiological structures and patterns of spatial dispersal of the hosts (Ruan and Wu, 2006).

Epidemic theory for homogeneous populations has shown that the basic reproductive number, which may be considered as the fitness of a pathogen in a given population, must be greater than unity for the pathogen to invade a susceptible population (Anderson and May, 1991; Brauer and Castillo-Chavez, 2000; Diekmann and Heesterbeek, 2000; Murray, 2003). It is natural to ask how spatial movement of the hosts affects the spatio-temporal spread pattern of the disease if the basic reproduction number for an otherwise homogeneous population exceeds unity.

Answers to the above question obviously depend on the manner in which hosts move into, out of, and within the considered geographical region. For example, adding an immigration term so that infective individuals enter the system at a constant rate clearly allows the persistence of the disease, because if it dies out in one region then the arrival of an infective from elsewhere can trigger another epidemic. Indeed, a constant immigration term has a mildly stabilizing effect on the dynamics and tends to increase the minimum number of

infective individuals observed in the models (Bolker and Grenfell, 1995). Spread of diseases in a heterogeneous population has also been intensively studied using patchy or metapopulation models. These models are formulated under the assumption that the host population under consideration can be divided into multi-patches so that the host population within a patch is considered as homogeneous, and the heterogeneity is associated with the rates with which individuals move from one patch to another (Arino and van den Dreissche, 2006).

Another popular way to incorporate the spatial movement of hosts into epidemic models is to assume local diffusion of host population, leading to reaction-diffusion equations. One characteristic feature of such models is the appearance of traveling waves. With initial conditions corresponding to a spatially localized introduction, such models predict the eventual establishment of a well-defined invasion front which divides the invaded and un-invaded regions and moves into the un-invaded region with a constant velocity. The velocity at which an infection wave moves is set by the rate of divergence from the (unstable) disease-free state and can be determined by linear methods (Murray, 2003). Most reaction-diffusion epidemic models are space-dependent extensions of the classical Kermack-McKendrik (Kermack and McKendrik 1927) deterministic compartmental model for a directly transmitted viral or bacterial agent in a closed population consisting of susceptibles, infectives, and recovereds. Their model leads to a nonlinear integral equation which has been studied extensively. The deterministic model of Bartlett (1956) predicts a wave of infection moving out from the initial source of infection. Kendall (1957) generalized the Kermack-McKendrik model to a space-dependent integro-differential equation. Aronson (1977) argued that the three-component Kendall model can be reduced to a scalar one and extended the concept of asymptotic speed of propagation developed in Aronson and Weinberger (1975) to the scalar epidemic model.

The Kendall model assumes that the infected individuals become immediately infectious
and does not take into account the fact that most infectious diseases have an incubation period.

Despite these studies on reaction-diffusion epidemic models, however, there are very few studies on modeling spatial spread of specific diseases using partial differential equation models. Hussaini (2010) used an spatial diffusion to model the HIV spread incorporating nonlinear and non-smooth treatment rates. They constructed travelling front solutions whose profiles are heteroclinic orbits which connect either the disease-free state to an infected state or two endemic states with each other.

This paper addresses the question of how both diffusive contacts and diffusive movement
effect the formation of the spatial patterns the population of two groups: the female sex workers and male high-risk groups. We adopted a similar approach of Hussaini(2010) and Zhang *et al*(2012) to model the spatio-temporal spread of HIV in these two groups within Nigeria.

2. MODEL EQUATIONS

In this section we consider a reaction-diffusion model, which use a partial differential equation (PDE) formalism, assume local transmission of infection and rely on spatial diffusion of host to spread the infection to answer the question. We start with the basic equations together with host diffusion.

$$\frac{\partial S_f}{\partial t} = (m+r_f)N_f - (\mu + r_f)S_f - b_{mf}n_m\frac{I_m}{N_m}S_f + d_f\nabla^2 S_f \quad (1a)$$

$$\frac{\partial S_m}{\partial t} = (m+r_m)N_m - (\mu + r_m)S_m - b_{fm}n_f\frac{I_f}{N_f}S_m + d_m\nabla^2 S_m \quad (1b)$$

$$\frac{\partial I_f}{\partial t} = b_{mf}n_m\frac{I_m}{N_m}S_f - (g+\mu + r_f)I_f + d_f\nabla^2 I_f \quad (1c)$$

$$\frac{\partial I_m}{\partial t} = b_{fm}n_f\frac{I_f}{N_f}S_m - (g+\mu + r_m)I_m + d_m\nabla^2 I_m. \quad (1d)$$

where S_f, S_m, I_f and I_m are functions of both space and time, and represent the local density of susceptible female, susceptible male, infectious female and males respectively, as always $N_f = S_f + I_f$ and $N_m = S_m + I_m$. $S_f(x,t)$ is the density of susceptible female at location x at time t, whereas $S_f(x,y,t)$ is the density of susceptible female sex workers at location (x, y) at time t. m is the natural death rate of the population, g is the rate of progression to AIDS, n_f (n_m)is

fraction of all adult female (male) that are female sex workers (high-risk male groups), b_{fm} is the rate at which female sex workers infect high-risk males per susceptible high-risk male and b_{mf} is the rate at which high-risk males infect female sex workers per female sex worker. r_m and r_f are the retirement rates of female sex workers and male high-risk groups respectively whereas d_f and d_m are the female and male diffusion constants.

We now have to specify the rates of change with partial derivatives because our variables are now multi-dimensional, being functions of both space and time. The term ∇^2 is introduced to model the local diffusion of individuals through space. Note that

$$\nabla^2 S_f = \frac{\partial^2 S_f}{\partial x^2} \text{ and } \nabla^2 S_f = \frac{\partial^2 S_f}{\partial x^2} + \frac{\partial^2 S_f}{\partial y^2},$$

for one and two dimensional space respectively. The inclusion of these partial derivatives mimics the diffusion of individuals across the environment. Here, susceptible and infected males diffuse at the same rate d_m, whereas susceptible and infected females diffuse at the rate d_f, reflecting the fact that the two risk groups move at different rates. We do not need to think that the individuals are actually diffusing; we can imagine them as fixed on a lattice with contacts to their nearest neighbours through which the disease propagates.
An equation for $S_f(x,t)$ is unnecessary because $S_f = N_f - I_f$. A similar thing goes for S_m. Mathematically, this translates into the following equations: It is convenient to reformulate the model equations (1a), (1b), (1c) and (1d), in terms of $X(x,t) = \frac{I_f}{N_f}$ and $Y(x,t) = \frac{I_m}{N_m}$ which are the fractions of female and male infectives respectively, at location x in time t. It is easy to verify that $X(x,t)$ and $Y(x,t)$ satisfy the system of partial differential equations:

$$\frac{\partial X}{\partial t} = b_{mf} n_m Y(1 - X) - (g + m + r_f)X + gX^2 + d_f(1 - X)\nabla^2 X, \quad (2a)$$

$$\frac{\partial Y}{\partial t} = b_{mf} n_m X(1 - Y) - (g + m + r_f)Y + gY^2 + d_m(1 - Y)\nabla^2 Y, \quad (2b)$$

$t > 0$ $x \in \Omega$, with null Neumann conditions

$$\frac{\partial X}{\partial x} = \frac{\partial Y}{\partial x} = 0, \quad t > 0, x \in \Omega,$$

where d_m and d_f are the non-negative diffusion rates.

The dynamics of model equations (2a) and (2b) without the diffusion can be summarized as follows: The disease-free equilibrium of system is $E_0 = (0,0)$. The basic reproduction number is

$$R_0 = \sqrt{\frac{\beta_{mf} \nu_m \beta_{fm} \nu_f}{(\gamma + \mu + \rho_m)(\gamma + \mu + \rho_f)}} \quad .$$

This is the threshold value to determine whether HIV can invade a susceptible population and is important for designing control strategies.
If $R_0 > 1$, we can derive the unique endemic equilibrium:

$$X^* = \frac{1}{2\gamma}(A \pm B) \quad and \quad Y^* = \frac{1}{2\gamma}(C \pm D),$$

where $A = b_{mf} n_m Y^* + g + m + r_f$,

$$B = b_{mf}^2 n_m^2 Y^{*2} - 2gb_{mf} n_m Y^* + 2mb_{mf} n_m Y^* + 2r_f b_{mf} n_m Y^* + g^2 + 2gm + 2gr_f + m^2 + 2mr_f + r_f^2,$$

$C = b_{fm} \nu_f X^* + g + m + r_m$ and

$$D = b_{fm}^2 n_f^2 X^{*2} - 2\gamma b_{fm} n_f X^* + 2\mu b_{fm} n_f X^* + 2r_m b_{fm} n_f X^* + \gamma^2 + 2\gamma\mu + 2\gamma r_m + \mu^2 + 2\mu r_m + r_m^2.$$

One key question is, under what circumstance can the introduction of few infected individuals at one end of linear habitat for instance, which is initially uniformly saturated with susceptible individuals at the carrying capacity of the environment, may result in a wave of propagation of infected individuals. Therefore, a zone of transition from one equilibrium point to another is possible and the traveling wave profiles occurs when this transition zone moves across the population (Dunbar, 1983).

In order to investigate such traveling waves, equations (2a and 2b) is written in terms of a coordinate frame to the right with speed c. Let $z = x - ct$ we can rewrite equations (2a and 2b) as the following form:

$$\frac{dX}{dz} = -\frac{1}{c}\left[b_{mf} n_m Y(1-X) - (\gamma + \mu + r_f)X + \gamma X^2 + d_f(1-X)\frac{d^2X}{dz^2}\right], \quad (3a)$$

$$\frac{dY}{dz} = -\frac{1}{c}\left[b_{mf} n_m X(1-Y) - (\gamma + \mu + r_f)Y + \gamma Y^2 + d_m(1-Y)\frac{d^2Y}{dz^2}\right]. \quad (3b)$$

We have the corresponding first order ordinary differential equations with respect to the variable z of the above system:

$$\frac{dX}{dz} = X_f, \quad (4)$$

$$\frac{dX}{dz} = \frac{1}{d_f(1-X)}\left[-cX_f - b_{mf} n_m Y(1-X) - (\gamma + \mu + r_f)X + \gamma X^2\right], \quad (5)$$

$$\frac{dY}{dz} = Y_m, \quad (6)$$

$$\frac{dY}{dz} = \frac{1}{d_m(1-Y)}\left[-cY_m - b_{mf} n_m X(1-Y) - (\gamma + \mu + r_f)Y + \gamma Y^2\right]. \quad (7)$$

We will study this system in the next section:

3. THE MINIMUM WAVE SPEED

A typical wave front solution is where X at one say, as $z \to -\infty$ is at one steady state and as $z \to +\infty$, it is at the other so here we have an eigen-value problem to determine the value, or values, of c, so that a non-negative solution exist which satisfies

$$\lim_{x \to -\infty} (X(z), X_f(z), Y(z), Y_m(z)) = (0, 0, 0, 0)$$

and

$$\lim_{x \to \infty} (X(z), X_f(z), Y(z), Y_m(z)) = (X^*, 0, Y^*, 0).$$

In order to obtain the minimum wave speed for traveling waves for system of equations (4), (5), (6) and (7) we need to find the eigenvalues of its Jacobian matrix at the equilibrium E_0.

$$J(E_0)=\begin{pmatrix} 0 & 1 & 0 & 0 \\ \frac{m+g+r_f}{d_f} & -\frac{c}{d_f} & -\frac{b_{mf}v_m}{d_f} & 0 \\ 0 & 0 & 0 & 1 \\ -\frac{b_{fm}v_f}{d_m} & 0 & \frac{m+g+r_m}{d_m} & -\frac{c}{d_m} \end{pmatrix}$$

The eigenvalues are roots of the polynomial of the fourth degree

$$p(\lambda)=\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_4=0 \qquad (8)$$

where

$$a_1=c(d_f+d_m)/d_fd_m,$$

$$a_2=\frac{c^2-d_fm-d_fg-d_fr_m-d_mm-d_mg-d_mr_f}{d_fd_m},$$

$$a_3=-c(2m+2g+r_f+r_m)/d_fd_m$$

and

$$a_4=(m^2+2mg+mr_f+g^2+gr_f+2mr_m+gr_m+r_fr_m-b_{mf}v_mb_{fm}v_f)/d_fd_m.$$

Since the variables are population, we constrain to the dynamical system the fact that the solution must not oscillate around the origin, i.e., the eigenvalues must assume real values. Since the quartic expression has at least one negative coefficient, it means that there is an eigenvalue with a positive real part. Thus, the disease free equilibrium is unstable.

The minimum traveling waves velocity is obtained from the polynomial $p(\lambda)$, denoted c^*. The condition $R_0>1$implies that $p(0)>0$. Beside, we must have

$$\lim_{\lambda\to\infty} p(\lambda)=\pm\infty, \qquad \frac{dp(\lambda)}{d\lambda}\Big|_{\lambda=0}<0, \qquad (9)$$

in order for p (λ) to always have negative real root. To determine the maxima and minima of the roots of (8), we differentiate with respect to λ and set $\frac{dp}{d\lambda}=0$ which gives

$$\lambda^3+\tfrac{3}{4}a_1\lambda^2+\tfrac{1}{4}a_2\lambda-\tfrac{1}{4}a_3=0 \qquad (10)$$

Applying Cardano's method for solving cubic equation we reduce (10) to its resolvent cubic equation:

$$y^3+by=d \qquad (11)$$

where $b=\frac{1}{2}a_2-\frac{3}{16}a_1^2$ and

$$d=\frac{1}{16}a_1a_2+\frac{1}{4}a_3-\frac{1}{32}a_1^3,$$

which reduces to the quadratic equation,

$$(w^3)^2-dw^3-\frac{1}{27}b^3=0. \qquad (12)$$

The roots of (12) are given by

$$w^3 = \frac{1}{2}\left(d \pm \sqrt{\frac{1}{4}d^2 + \frac{1}{27}b^3}\right) \qquad (13)$$

There are therefore six solutions for (two corresponding to each sign for each root of w^3). Plugging back w into (11) gives three pairs of solutions, but each pair is equal, so there are three solutions to the cubic equation.

By equating the discriminant of equation (13) to zero and putting the values of parameters in Table 1, we obtain the formula,

$$3.327546296 \times 10^9 c^6 + 5.613715278 \times 10^7 c^4 + 2.252996962 \times 10^5 c^2 - 74.97350463 = 0$$

from where it can be seen that the minimum wave speed: $c^* = 0.01756723940.$

4. NUMERICAL SIMULATION

To investigate how the movement of susceptible and infective lead to and impacts the spatial spread of HIV, we carry out a numerical simulation to determine the effects of space on the spread of the disease. We use the year 1992 as the initial time for our simulation. This corresponds to the year in that we have complete data on the prevalence of HIV in the populations. Figure 1(a) and (b) shows the graphical representation of the simulated output. From figure 1(a) it shows that it will take 100 years for the prevalence of HIV to attain ninety percent in the population of female sex workers assuming there is no any form of intervention. Similarly it will take the same period to achieve a prevalence of 65 percent in the high-risk male population (see figure 2(b)).

Table 1

Description of parameters for the spatial model

Parameter	Description	Values	Source
d_f	diffusion coefficient for females	0.01	Assumed
d_m	diffusion coefficient for males	0.01	Assumed
γ	Rate of progression to AIDS	0.116	Hyman (1999)
μ	Mortality rate	0.002	WHO
$b_{mf}v_m$	Combined parameters for male	1.5	Estimated
$\beta_{mf}v_m$	Combined parameters males	0.385	Estimated
ρ_m	turnover rates of high-risks males	0.002	Estimated
ρ_f	turnover rates of high-risk females	0. 015	Estimated

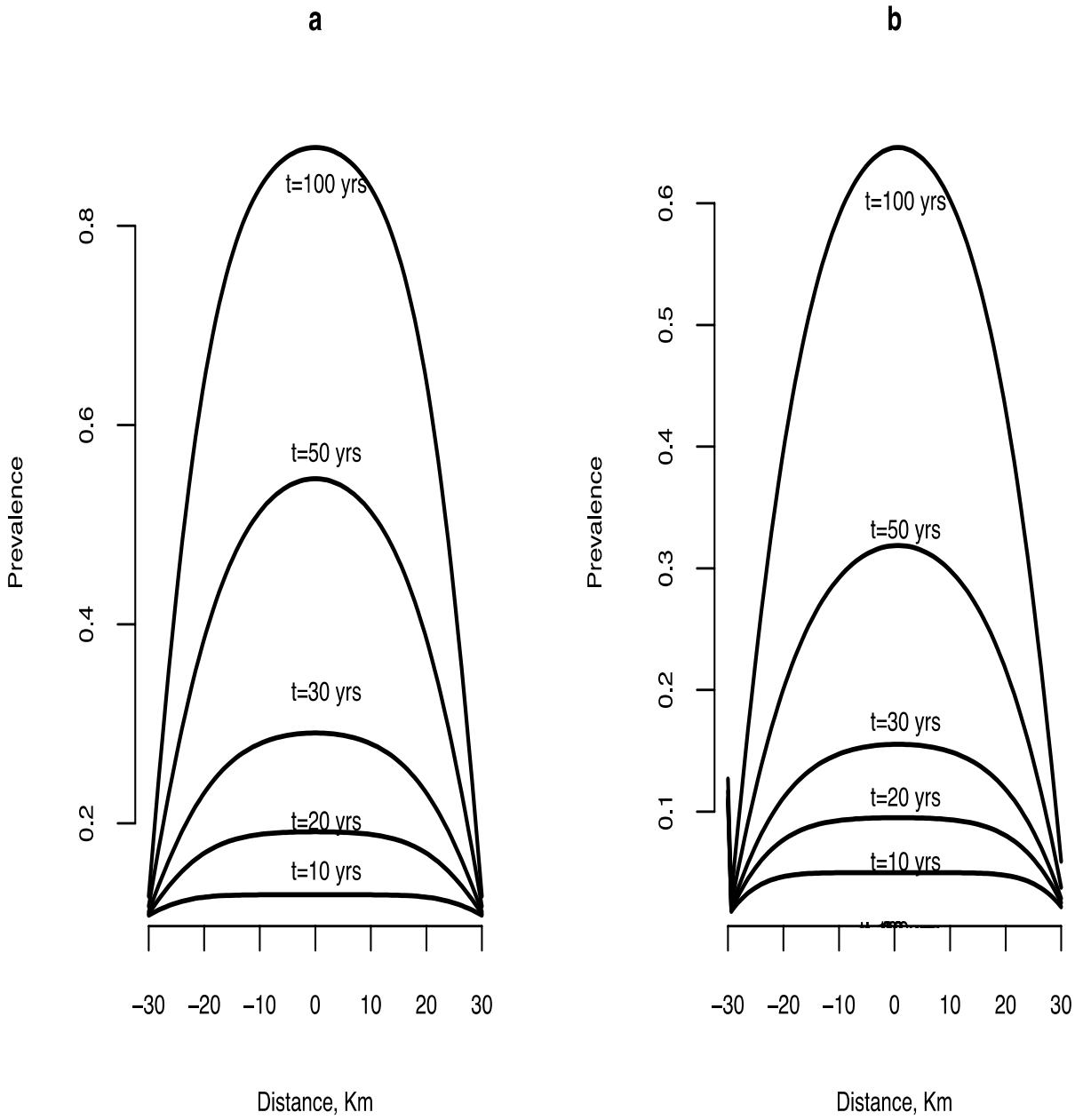

Figure 1: (a) Spatial distribution of prevalence of infected FSW at different time points (b)Infected male high-risks groups at different time points.

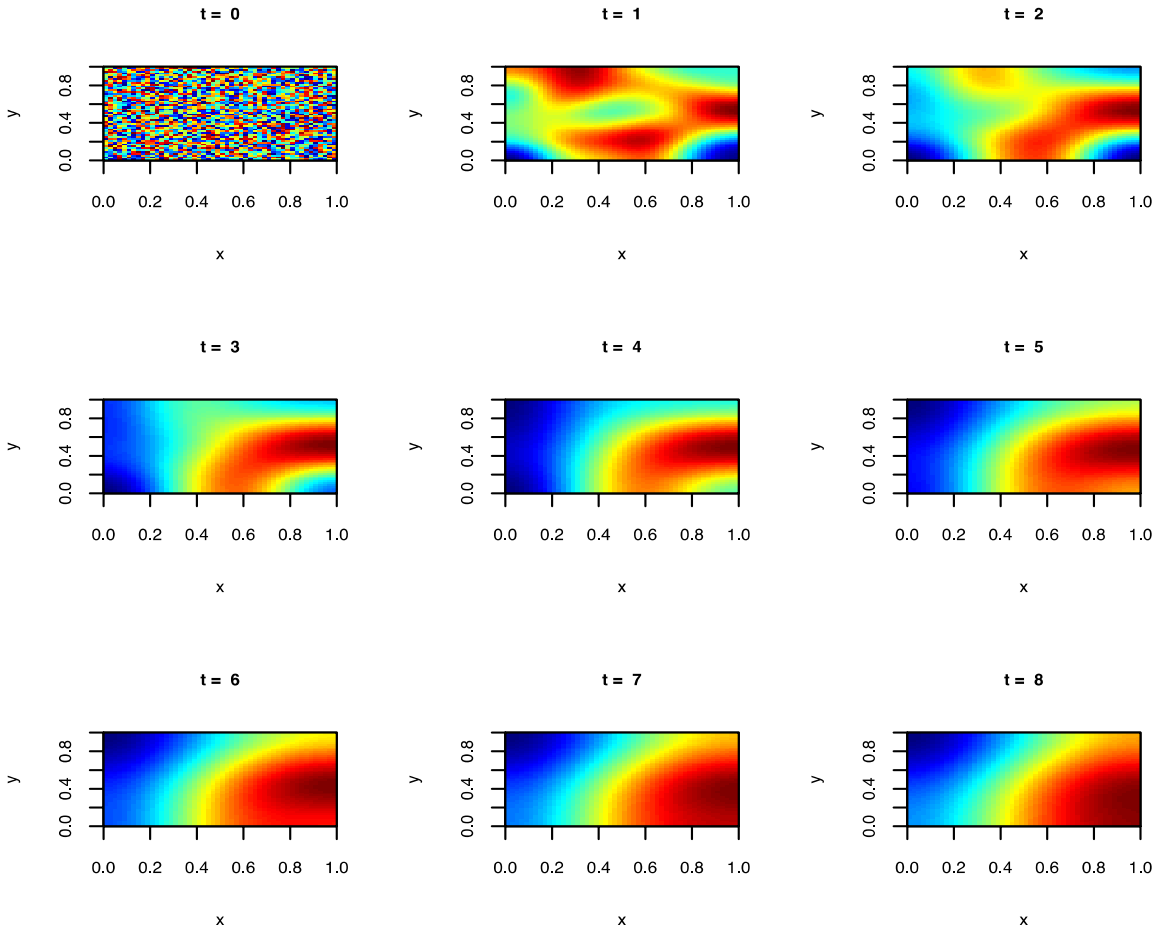

Figure 2: Snapshots of contour pictures of the time evolution of X (x, y, t) at different instants.

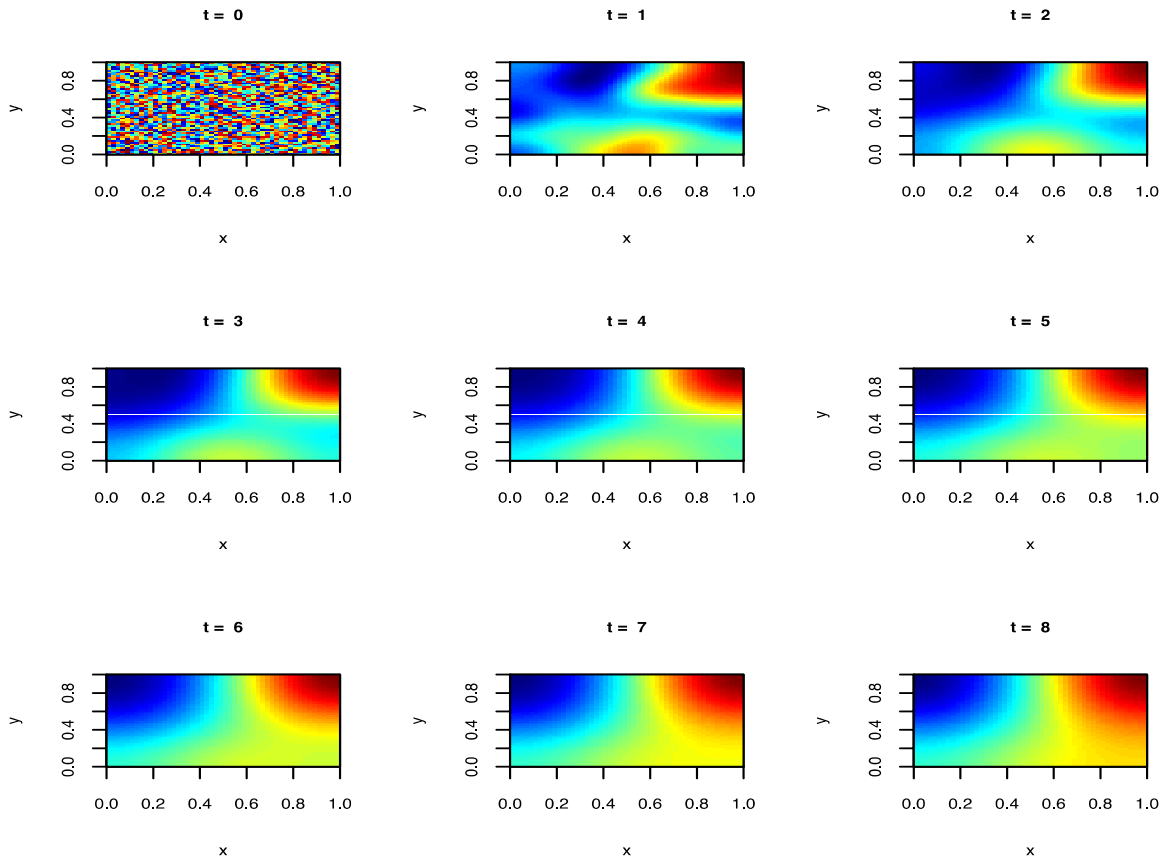

Figure 3: Snapshots of contour pictures of the time evolution of Y (x, y, t) at different instants.

5. CONCLUSION

In this paper, we have presented and tested a theoretical analysis for diffusion-driven spatial pattern in the spatial epidemic model, involving diffusion-driven mechanisms. The spatial epidemic model comes from the classic SI model. We analyzed the role of spatial distribution of HIV in a reaction-diffusion model of biological invasion. The results showed that the minimum traveling wave speed required for successful invasion is c_ = 0. 01756723940. The traveling waves solution connects the steady states $E_0 = (0, 0)$ and $E_1 = (X^* = 0.9732440339,\ Y^* = 0.9240105133)$. Thus, when there are infected individuals in the region, the disease begins to propagate. Results in figure 1 shows the density of the infected populations for different time points. Figures 2 and 3 show that a stationary labyrinthine pattern emerges in the distribution of the infection population density in the two high-risk groups. These figures show the development of a labyrinthine patterns from two different initial conditions. This may explain the prevalence of disease in large-scale geophysics.

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