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MULTI-PATCH STOCHASTIC EPIDEMIC MODEL: FLUCTUATIONS

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Abstract

It is an important challenge to understand how the geographical dispersion of a population modifies the evolution of epidemics. In this paper, we consider a multipatch SIS model, and analyse the stability of the endemic equilibrium. We consider the classical deterministic model as the law of large numbers limit, as the size of the population tends to infinity, of stochastic models. Moreover, we investigate the effect of the spatial structure on the time taken by the fluctuations of the stochastic model to drive the system from the endemic to the disease free equilibrium. Our conclusion is that, if the parameters of the epidemic are homogeneous over the various patches, the effect of the fluctuations should be comparable to that of a similar homogeneous model. On the contrary, if the parameters of the epidemic model differ from one patch to another, then the situation is quite different, and in the cases which we investigated, the time taken by the fluctuations to drive the system to the disease free equilibrium is significantly larger than in the homogeneous model.

1. Introduction

In this paper, we study the fluctuations of a stochastic SIS multi-patch model around its law of large numbers limit. Our motivation for this work is the following. Provided that the basic reproduction number R_0 is larger than 1, there will typically exist an endemic equilibrium in the deterministic SIS model, which is asymptotically stable. In other words, the deterministic model predicts that the epidemic will last for ever. On the other hand, it is not hard to show that the stochastic model will reach the disease free equilibrium in finite time a.s. That is, the stochastic model predicts that the

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epidemic will stop soon or later. The larger the size N of the population is, the closer the stochastic model is to the deterministic model. Therefore it is intuitive that the larger the population size N is the more one has to wait until the epidemic goes extinct in the stochastic model. As we will see, this is exactly what the mathematics tell us.

Indeed, the central limit theorem tells us that one observes fluctuations of order $N^{-1/2}$ in time of order 1. On the other hand, in the endemic equilibrium the set of infectious individuals constitute a rather small proportion of the total population. If N is not too large so that $N^{-1/2}$ is of the order of the proportion of infectious individuals in the endemic equilibrium, then there is a chance that the epidemic stops quickly. We shall make this more precise below. On the other hand, the theory of "small random perturbation of dynamical systems" due to Wentzell and Freidlin [13], and based upon large deviations theory, predicts that fluctuations of order 1 appears if we wait a time of the order of $\exp(N\overline{V})$, where $\overline{V}$ will be defined below. In between those two extremes, the theory of moderate deviations allows to predict the time one has to wait if one wants to see a deviation of order $N^{-\alpha}$, for any $0 < \alpha < 1/2$. Those results have been presented in the case of the homogeneous model (for the case of the SIS, the SIRS and the SIR model with demography) in Pardoux [19]. For the details of the arguments exploiting the Central Limit Theorem and Large Deviations, see chapter 4 of [5], and for the arguments exploiting moderate deviations, see [20].

The present paper considers the SIS multi-patch model. Our goal is twofold. First we want to show that the above quoted results which hold for homogeneous models, are also valid for the multi-patch SIS model. For a more precise description of how the three approaches apply to the extinction time of the epidemic, depending upon the size N of the population, see the comment after Theorem 6.3 below.

Second, we show that under certain conditions, the asymptotic variance of the limit in the CLT is the same as that in the homogeneous model, the latter being known explicitly. And concerning the results exploiting Large and Moderate Deviations, we show how to compute numerically the rate $\overline{V}$ which appears in the exponent. We also show in one particular example with 2

patches how $\overline{V}$ varies with the parameters of the model. This suggests that if some parameters of the model can be modified, it could be useful to choose those parameters in order to minimize the rate $\overline{V}$.

In the literature, there are some results which discuss the advantage of certain values of certain parameters, based upon an analysis of the deterministic model. In particular, considering a two patches deterministic SIR model, Bailey [4] showed that if the transmission rate of one patch is slightly bigger than 1 and that of the other patch is less than 1, then travel can eventually cause the disease extinction in both patches. He also shows that if the transmission rate of one patch is significantly greater than 1 and that of the other patch is less than 1, then travel can cause the disease to remain endemic in both patches. Studying a SIS patch model, Arino and Driessche [2] showed that mobility can stabilise or destabilise the disease free equilibrium. Using numerical simulations for a SIR model with two patches, Arino et al. [3] showed that by increasing travel rates in both patches, the disease dies out in all patches, in contrast, small travel rates can help the disease to persist. Also, using numerical simulations Wang and Zao [25] showed that travel of individuals can both intensify and reduce the spread of the disease in all patches. Considering on the one hand a SIR model, D. Clancy [6] showed that movement of infectious individuals decreases the spread of the disease. On the other hand, by considering the spread of a carrier-borne-disease, D. Clancy [7] showed that increasing the movement of either infectious or susceptible individuals tends to increase the spread of the infection.

Our contribution opens a different point of view. The question we raise is the following: by modifying the parameters of a multi-patch SIS epidemic model, can one make it easier for the inherent random fluctuations to cause the extinction of an endemic disease?

The paper is organized as follows. In section 2, we describe our multi-patch SIS stochastic model, and its deterministic law of large numbers limit. In section 3, we establish the central limit theorem, and we show that the variance of the proportion of the total population of infectious is equal to the one of the homogeneous model, if all individuals have the same diffusion coefficients and the disease transmission and recovery rates are constant over

the patches. In section 4, we show that our process satisfies the large deviations principle and using numerical computations we analyze the influence of the heterogeneity on the quasi-potential. Finally, in section 6 we study the moderate deviations, and we compute the quasi-potential numerically, which we compare to that of the homogeneous model.

2. The Stochastic Model and its Law of Large Numbers Limit

The population consists of N individuals, where each individual is located at one of ℓ geographically distinct patches. Patches represent human communities in which the disease can diffuse and grow. Individuals in that population can be classified according to their ability to transmit the disease to others. Susceptible individuals are those who do not have the disease and who can get infected. Infectious individuals are those who have been infected and can transmit the disease to susceptible individuals. Infections are local: they are the result of an encounter of a susceptible and an infectious individual, who are located in the same patch. More details on this model can be found in our previous work (N'zi, Pardoux and Yeo [17]). The mathematical model is a random Markov epidemic model, solution of a Poisson process driven stochastic differential equation (SDE), and reads as follows

$$\begin{cases} S_j^N(t) = S_j^N(0) - \frac{1}{N} P_j^{\inf}\left(N\int_0^t \frac{S_j^N(r) I_j^N(r)}{S_j^N(r) + I_j^N(r)}\, dr \right) + \frac{1}{N} P_j^{rec}\left(N\int_0^t \gamma_j I_j^N(r) dr \right) \\ - \sum_{k=1}^{\ell} \frac{1}{N} P_{S,j,k}^{mig}\left(N\int_0^t \nu_S a_{jk} S_j^N(r) dr \right) + \sum_{k=1}^{\ell} P_{S,j,k}^{mig}\left(N\int_0^t \nu_S a_{kj} S_j^N(r) dr \right) \\ I_j^N(t) = I_j^N(0) + \frac{1}{N} P_j^{\inf}\left(N\int_0^t \frac{S_j^N(r) I_j^N(r)}{S_j^N(r) + I_j^N(r)}\, dr \right) + \frac{1}{N} P_j^{rec}\left(\frac{1}{N}\int_0^t \gamma_j I_j^N(r) dr \right) \\ - \sum_{k=1}^{\ell} \frac{1}{N} P_{I,j,k}^{mig}\left(N\int_0^t \nu_S a_{jk} I_j^N(r) dr \right) + \sum_{k=1}^{\ell} P_{S,j,k}^{mig}\left(N\int_0^t \nu_S a_{kj} I_j^N(r) dr \right) \\ t \in [0, T],\ j = 1, \ldots, \ell. \end{cases} \tag{2.1}$$

In this setting

- ℓ is the total number of patches;
- N is the total population size;

- $S_j^N(t)$ (resp. $I_j^N(t)$) denotes the proportion of the total population which is both susceptible (resp. infectious) and located in patch j at time t;
- λ_j and γ_j are nonnegative constants that express the rate of disease transmission and recovery in patch j, respectively;
- ν_S and ν_I are the diffusion coefficients for susceptible and infectious individuals, respectively;
- for all $i, j \in \{1, \ldots, \ell\}$, a_{ij} denotes the rate of migrations from patch i into patch j, with $a_{ii} = 0$;
- the P_j's are mutually independent standard Poisson processes.

– $P_j^{\inf}\left(\int_0^t \lambda_j \frac{S_j^N(r) I_j^N(r)}{S_j^N(r) + I_j^N(r)} dr\right)$ counts the number of transitions of type $S^N \to I^N$ on the patch j between time 0 and time t;

– recovery of an infectious happens at rate γ_j, so $P_j^{rec}\left(\int_0^t \gamma_j I_j^N(r) dr\right)$ counts the number of transitions of type $I^N \to S^N$ on the patch j between time 0 and time t.

– The term $P_{S,j,k}^{mig}\left(N\int_0^t \nu_S a_{jk} S_j^N(r) dr\right)$ counts the number of migrations of susceptible individuals from patch j to k, if we assume that each susceptible migrates from j to k at rate $\nu_S a_{jk}$, and similarly for the compartment I^N, but with ν_S replaced by ν_I.

Note that we have $\sum_{j=1}^{\ell} [S_j^N(t) + I_j^N(t)] = 1$, for all $t \geq 0$, provided the initial condition satisfies that condition at time $t = 0$.

Let us set $\mathcal{Z}^N(t) = \begin{pmatrix} S_1^N(t) \\ I_1^N(t) \\ \dots \\ S_\ell^N(t) \\ I_\ell^N(t) \end{pmatrix}$.

We denote by $\otimes$ the operator defined as follows: for two vectors $u = (u_1, u_2, \dots, u_\ell)$ and $\nu = (\nu_1, \nu_2)$,

$$u \otimes \nu := (u_1\nu_1, u_1\nu_2, u_2\nu_1, u_2\nu_2, \dots, u_\ell\nu_1, u_\ell\nu_2).$$

We set $\mathfrak{h}_1 = \begin{pmatrix} -1 \\ 1 \end{pmatrix}$, $\mathfrak{h}_2 = \begin{pmatrix} 1 \\ -1 \end{pmatrix}$, $\mathfrak{e}_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$ and $\mathfrak{e}_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$. In what follows, $(\mathcal{Z}^N)i$ denotes the restriction of $\mathcal{Z}^N$ to the i-th patch and $(\mathcal{Z}^N)_{im}$ denotes the coordinate of the vector $\mathcal{Z}^N$ of patch i and of type m, where type $m = 1$ is for susceptible individuals and type $m = 2$ for infectious individuals, that is $(\mathcal{Z}^N)_{i1} = S_i^N$ and $(\mathcal{Z}^N)_{i2} = I_i^N$.

We can rewrite the stochastic model in the aggregated form

$$\mathcal{Z}^N(t) = z_N + \frac{1}{N}\sum_{i=1}^{\ell}\sum_{m=1}^{2} e_i \otimes \mathfrak{h}_m P_{im}^{(1)}\left(N\int_0^t \beta_{i,m}((\mathcal{Z}^N(r))_i)dr\right)$$

$$+ \frac{1}{N}\sum_{i=1}^{\ell}\sum_{m=1}^{2} (e_i - e_j) \otimes \mathfrak{e}_m P_{im}^{(1)}\left(N\int_0^t \nu_m a_{ij}(\mathcal{Z}^N(r))_{im}dr\right), \tag{2.2}$$

where $z_N = \mathcal{Z}^N(0)$, e_i is the unit vector of the canonical basis of $\mathbb{R}^\ell$, each $P_{i1}^{(1)}$ (resp. $P_{i2}^{(1)}$) is a Poisson process which counts the infections (resp. the remissions) in patch i, and the $P_{jim}^{(2)}$ are Poisson processes which count the migrations between patches. For all $i \in \{1, \dots, \ell\}$,

$$\beta_{i,1}((\mathcal{Z}^N(r))_i) := \lambda_i \frac{S_j^N(t)I_j^N(t)}{S_j^N(t) + I_j^N(t)} \text{ and } \beta_{i,2}((\mathcal{Z}^N(r))_i) := \gamma_i I_i^N(t).$$

In the sequel u^T denotes the transpose of the matrix u.

If we let the total population size N go to infinity, then the stochastic model converges to a deterministic patch model.

Theorem 2.1 [Law of Large Numbers]**.**

Let $\mathcal{Z}^N$ *denote the solution of the SDEs* (2.2). *Let us fix an arbitrary* $T > 0$ *and assume that* $\mathcal{Z}_N \to \mathcal{Z}(0)$ *a.s., as* $N \to \infty$. *Then* $\mathcal{Z}^N(t) \to \mathcal{Z}(t)$ *a.s. locally uniformly in* t, *where* $\mathcal{Z}(t) := (S_1(t), I_1(t), S_2(t),, I_2(t), \ldots, S_\ell(t), I_\ell(t))^T$ *is the unique solution of the system of ordinary differential equations*

$$\frac{dz}{dt}(t) = b(\mathcal{Z}(t)), \tag{2.3}$$

where $b(Z) = \sum_{i=1}^{\ell}\sum_{m=1}^{2}[e_i \otimes \mathfrak{h}_m]\beta_{i,m}((\mathcal{Z})_i) + \sum_{i,j=1}^{\ell}\sum_{m=1}^{2}\nu_m a_{ij}[(e_j - e_i) \otimes \mathfrak{e}_m](\mathcal{Z})_{im}$.

This theorem is a particular case of a rather old result. It can be found e.g. in chapter 11 of Ethier and Kurtz [12] or in Britton and Pardoux [5].

Let R_0 denote the basic reproduction number of the system (2.3) (the expected number of secondary cases produced, in a fully susceptible population, by a typical infected individual during its entire period of infectiousness). R_0 allows one to determine whether or not a major epidemic may start from the initial infection of a small number of individuals. The next generation matrix approach of Van den Driessche and Watmough [27] is used to compute R_0.

By setting

$$A = diag(\gamma_j)_{1\le j\le \ell},\ B = diag(\gamma_j)_{1\le j\le \ell} \text{ and } D = (d_{ij})_{1\le j\le \ell}$$

with $d_{ij} = \begin{cases} -\sum_{\substack{k=1\\k\neq i}}^{\ell} a_{ik} & \text{if } i = j, \\ a_{ij} & \text{if } i \neq j, \end{cases}$

we have $R_0 = \rho(BV^{-1})$, where $V = \nu_I D - A$.

We shall say that an equilibrium point is a disease free equilibrium if in

that state there is no infected individual, whereas the endemic equilibrium means that the population contains a positive proportion of infected individuals.

It is shown in [1] that if $R_0 < 1$ the disease free equilibrium is globally asymptically stable.

The following theorem, which treats the existence and stability of the endemic equilibrium, is proved in T. Yeo [26].

Theorem 2.2. *Assume that* $\nu_I = \nu_S := \nu$ *and that the basic reproduction number* R_0 *satisfies* $R_0 > 1$. *Then the system* $\frac{dz}{dt}(t) = b(\mathcal{Z}(t))$, *has a unique endemic equilibrium* $\mathcal{Z}^*$ *which is globally asymptotically stable*.

3. Central Limit Theorem

3.1 The convergence result

In this section, we study the fluctuations of the stochastic model around its deterministic law of large numbers limit by a central limit theorem. To this end we introduce the rescaled difference between $\mathcal{Z}^N(t)$ and $\mathcal{Z}(t)$, namely

$$\mathfrak{W}^N(t) = \begin{pmatrix} \sqrt{N}(S_1^N(t) - S_1(t)) \\ \sqrt{N}(I_1^N(t) - I_1(t)) \\ \vdots \\ \sqrt{N}(S_\ell^N(t) - S_\ell(t)) \\ \sqrt{N}(I_\ell^N(t) - I_\ell(t)) \end{pmatrix}.$$

We denote by "$\Rightarrow$" the weak convergence. We have

Theorem 3.1. [Central Limit Theorem]. *Assume that* $\sqrt{N}(\mathcal{Z}_N - \mathcal{Z}(0)) \Rightarrow W(0)$, *as* $N \to \infty$, *where* $W(0)$ *is a random vector*. *Then*, *as* $N \to \infty$, $\{W^N(t), t \geq 0\} \Rightarrow \{W(t), t \geq 0\}$, *for the topology of locally uniform convergence*, *where the limit process* $W(t)$ *satisfies*

$$W(t) =$$

$$W(0) + \sum_{i=1}^{\ell} \int_0^t e_i \otimes (\nabla_Z \beta((Z(r))_i) \cdot (W(r))_i) dr + \sum_{i,j=1}^{\ell} \sum_{m=1}^{2} \nu_m a_{ij} (e_j - e_i) \otimes \mathfrak{e}_m$$

$$\int_0^t (W(r))_{im} dr + \sum_{i=1}^{\ell} \sum_{m=1}^{2} e_i \otimes \mathfrak{h}_m \sqrt{\beta_{i,m}((\mathcal{Z}(r))_i)} dB_{im}^{(1)}(r) + \sum_{i,j=1}^{\ell} \sum_{m=1}^{2} \nu_m a_{ij} (e_j - e_i)$$

$$\otimes \mathfrak{e}_m \int_0^t \sqrt{\beta_{i,m}((\mathcal{Z}(r))_i)} dB_{im}^{(1)}(r),$$

where we set $\beta((\mathcal{Z}(r))_i) = (\beta_{i,1}((\mathcal{Z}(r))_i), \beta_{i,2}((\mathcal{Z}(r))_i))^T$, *and* $\beta_{im}^{(1)}$, $B_{jim}^{(2)} 1 \le i$, $j \le \ell$, $m = 1, 2$ *are mutually independent standard Brownian motions*.

Theorem 3.1 is a special case of Theorem 3.5 of Kurtz [16], and also of Theorem 2.3.2 of Britton and Pardoux [5]. Since

(i) the function $\mathcal{Z} \mapsto b(\mathcal{Z})$ is of class C^1, locally uniformly in t;

(ii) $b(\mathcal{Z})$ is locally Lipschitz as a function of z, locally uniformly in t, the assumptions of Theorem 2.3.2 of Britton and Pardoux [5] are satisfied. □

Theorem 3.1 gives us an explicit expression for the limit of the renormalized time-dependent fluctuations around the deterministic multi-patch model. If the initial condition $\mathcal{Z}(0)$ is chosen to be the endemic equilibrium of the limiting deterministic model, we can derive an explicit formula for the covariance of our Ornstein-Uhlenbeck process (OUP). From the last theorem, we can deduce the following Corollary.

Corollary 3.1. *Assume that* $\nu_I = \nu_S := \nu$, $R_0 > 1$ *and let* $\mathcal{Z}^*$ *be the unique endemic equilibrium of the ODEs* (2.3). *Assume also that* $\sqrt{N}(\mathcal{Z}_N - \mathcal{Z}^*) \Rightarrow W^*(0)$, *as* $N \to \infty$.

$$W^*(t) = W^*(t) + \sum_{i=1}^{\ell} \int_0^t e_i \otimes (\nabla_Z \beta((\mathcal{Z}^*)_i) \cdot (W^*(r))_i) dr$$

$$+\sum_{i,j=1}^{\ell}\sum_{m=1}^{2}\int_0^t \nu a_{ij}(e_j-e_i)\otimes \mathfrak{e}_m(W^*(r))_{im}dr$$

$$+\sum_{i=1}^{\ell}\sum_{m=1}^{2}\int_0^t \sqrt{\beta_{i,m}((\mathcal{Z}^*)_i)}\nu a_{ij}[e_j-\mathfrak{h}_m]dB_{im}^{(1)}(r)$$

$$+\sum_{i,j=1}^{\ell}\sum_{m=1}^{2}\int_0^t \sqrt{\nu a_{ij}(\mathcal{Z}^*)_{im}}[(e_j-e_i)\otimes \mathfrak{e}_m]dB_{im}^{(2)}(r)$$

In particular, $W^*(t)$ *has a normal distribution with covariance matrix*

$$\sum\nolimits_t = e^{tG}\left(\sum\nolimits_0 + \nu\int_0^t e^{-uG}CC^T e^{-uG^T}du\right)e^{tG^T},$$

where $G=\begin{pmatrix} G_1 & G_2 \\ G_3 & G_4\end{pmatrix}\cdot G_1, G_2, G_3$ *and* G_4 *are* $\ell\times\ell$ *matrices, and are given by*

$$G_1(i,j)=\begin{cases} -\lambda_1\left(\dfrac{I_i^*}{S_i^*+I_i^*}\right)^2-\nu\sum\nolimits_{k\neq i}a_{ik}, & \text{if } i=j,\\ \nu a_{ji} & \text{if } i\neq j,\end{cases}$$

$$G_2 = diag\left(-\lambda_j\left(\frac{S_j^*}{S_j^*+I_j^*}\right)^2+\gamma_j\right)_{1\le j\le \ell},$$

$$G_3 = diag\left(\lambda_j\left(\frac{I_j^*}{S_j^*+I_j^*}\right)^2+\gamma_j\right)_{1\le j\le \ell},$$

$$G_4(i,j)=\begin{cases} \lambda_i\left(\dfrac{S_i^*}{S_i^*+I_i^*}\right)^2-\nu\sum\nolimits_{k\neq i}a_{ik}-\gamma_i, & \text{if } i=j,\\ \nu a_{ji}, & \text{if } i\neq j,\end{cases}$$

$$C=\begin{pmatrix} C_1 & C_2 & C_3 & O\\ -C_1 & -C_2 & O & C_4\end{pmatrix},$$

where $C_1 = diag\left(\sqrt{\lambda_j \frac{S_j^* I_j^*}{S_j^* + I_j^*}}\right)_{1\le j\le \ell}$, $C_2 = diag(\sqrt{\gamma_j I_j^*})_{1\le j\le \ell}$

and O *is the null matrix with dimension* $\ell \times \ell(\ell-1)$. $C_3 = (C_3^1, \ldots, C_3^\ell)$ *is a matrix with dimension* $\ell \times \ell(\ell-1)$, *where each* C_3^k *is a block matrix with dimension* $\ell \times (\ell-1)$, *given by*

$$C_3^1 = \begin{pmatrix} \sqrt{a_{12}S_1^*} & \sqrt{a_{13}S_1^*} & \sqrt{a_{14}S_1^*} & \sqrt{a_{15}S_1^*} & \ldots & \sqrt{a_{1\ell}S_1^*} \\ -\sqrt{a_{12}S_1^*} & 0 & 0 & 0 & \ldots & 0 \\ 0 & -\sqrt{a_{13}S_1^*} & 0 & 0 & \ldots & 0 \\ 0 & 0 & -\sqrt{a_{14}S_1^*} & 0 & \ldots & 0 \\ 0 & 0 & 0 & -\sqrt{a_{15}S_1^*} & \ddots & 0 \\ \ldots & \ldots & \ddots & \ddots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \ldots & -\sqrt{a_{1\ell}S_1^*} \end{pmatrix}$$

$$C_3^2 = \begin{pmatrix} -\sqrt{a_{21}S_2^*} & 0 & 0 & 0 & \ldots & 0 \\ \sqrt{a_{22}S_2^*} & \sqrt{a_{23}S_2^*} & \sqrt{a_{24}S_2^*} & \sqrt{a_{25}S_2^*} & \ldots & \sqrt{a_{2\ell}S_2^*} \\ 0 & -\sqrt{a_{23}S_2^*} & 0 & 0 & \ldots & 0 \\ 0 & 0 & -\sqrt{a_{24}S_2^*} & 0 & \ldots & 0 \\ 0 & 0 & 0 & -\sqrt{a_{25}S_2^*} & \ddots & 0 \\ \ldots & \ldots & \ddots & \ddots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \ldots & -\sqrt{a_{2\ell}S_2^*} \end{pmatrix}$$

$$\vdots$$

$$C_3^\ell = \begin{pmatrix} -\sqrt{a_{\ell 1}S_\ell^*} & 0 & 0 & 0 & \ldots & 0 \\ 0 & -\sqrt{a_{\ell 2}S_\ell^*} & 0 & 0 & \ldots & \sqrt{a_{2\ell}S_2^*} \\ 0 & 0 & -\sqrt{a_{\ell 3}S_\ell^*} & 0 & \ldots & 0 \\ 0 & 0 & 0 & -\sqrt{a_{\ell 4}S_\ell^*} & \ldots & 0 \\ 0 & 0 & 0 & 0 & \ddots & 0 \\ \ldots & \ldots & \ddots & \ddots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \ldots & -\sqrt{a_{\ell(\ell-1)}S_\ell^*} \\ \sqrt{a_{\ell 1}S_\ell^*} & \sqrt{a_{\ell 2}S_\ell^*} & \sqrt{a_{\ell 3}S_\ell^*} & \sqrt{a_{\ell 4}S_\ell^*} & \ldots & \sqrt{a_{\ell(\ell-1)}S_\ell^*} \end{pmatrix}.$$

The matrix C_4 *is defined like* C_3 *with* I^* *in place of* S^*.

Proof. From Theorem 3.1, we obtained directly that $\{W^N(t), t \geq 0\}$ converges weakly to an OUP $\{W^*(t), t \geq 0\}$, where W^* is the process W with $\mathcal{Z}^*$ in place of z. Given the matrices G and C as in the Corollary 3.1, we note that W^* satisfied the following stochastic differential equation

$$dW^*(t) = GW^*(t)dt + \sqrt{\nu}Cd\mathcal{B}(t),$$

with $\{\mathcal{B}(t), t \geq 0\}$ being a $2\ell^2$-dimensional Brownian motion, which component are $B^{(1)}_{im}$, $B^{(2)}_{jim}$, $1 \leq i, j \leq \ell$, $m = 1, 2$. Following Karatzas & Shreve [14] (section 5.6), the solution of this SDE is

$$W^*(t) = \Gamma(t, 0)W^*(t) + \int_0^t \Gamma(t, r)\sqrt{\nu}Cd\mathcal{B}(r),$$

where Γ is a $2\ell \times 2\ell$ matrix, with $\Gamma(t, s) = \exp((t - s)G)$. It then follows that $\{W^*(t), t \geq 0\}$ is a Gaussian process, with mean

$$\mathbb{E}(W^*(t)) = \Gamma(t, 0)\mathbb{E}(W^*(0)).$$

If we define $\sum_t Cov(W^*(t))$, we have that

$$\sum\nolimits_t = e^{tG}\left(\sum\nolimits_0 + \nu\int_0^t e^{-rG}CC^T e^{-rG^T}dr\right)e^{tG^T}. \qquad \square$$

Comment 3.1. Although Corollary 3.1 gives us an explicit expression for the covariance matrix Σ_t, it remains difficult to compute this quantity in the general case. Given values to the parameters of the model, we can compute e^G by using a numerical solver. However, there is one particular case where one can derive a simple explicit formula for this covariance matrix, which allows us to find an upper bound for the fluctuations around the endemic equilibrium of the deterministic model. That is the object of the next section.

3.2 The variance of the proportion of the infectious subpopulation

We now assume that the disease transmission and recovery rates are uniform over the patches, that is for all $j = 1, \ldots, \ell$, $\lambda_j = \lambda$ and $\gamma_j = \gamma$. We assume also that infectious and susceptible individuals have the same diffusion coefficients $(\nu_I = \nu_S := \nu)$. In this case, we will find an explicit formula for the asymptotic variance of the fluctuations of the proportion of infectious individuals in the total population. Replacing C by $\sqrt{\nu}C$, we can suppress ν from the above formulas.

Now assume that $\mathcal{Z}_N \to \mathcal{Z}^* = \overbrace{(1, 1, \ldots, 1)}^{\ell terms} \otimes \bar{\mathcal{Z}}$, where $\bar{\mathcal{Z}} = \frac{1}{\ell}\left(\frac{\gamma}{\lambda}, 1 - \frac{\gamma}{\lambda}\right)$.

We extend the operator $\otimes$ to matrices in the following way. If A and B are two matrices with dimensions, respectively, $m \times n$ and $p \times q$,

$$A \otimes B := \begin{pmatrix} a_{11}B & \ldots & a_{1n}B \\ \vdots & \ddots & \vdots \\ a_{m1}B & \ldots & a_{mn}B \end{pmatrix}.$$

We may note in passing that $(A \otimes B) \cdot (C \otimes D) = (A \cdot C) \otimes (B \cdot D)$, for every matrices A, B, C and D. With the above notations, we can express $W^*(t)$ in matrix-vector form as

$$W^*(t) = \int_0^t [(\mathbb{I}_\ell \otimes \nabla_{\mathcal{Z}} b(\bar{\mathcal{Z}})) \cdot W^*(r) + (D \otimes \mathbb{I}_2) \cdot W^*(r)]dr$$

$$+ \int_0^t \mathbb{I}_\ell \otimes \sqrt{\sum(\bar{\mathcal{Z}})} \cdot dB(r) + \int_0^t \tilde{D} \otimes diag(\sqrt{\bar{\mathcal{Z}}}) \cdot d\tilde{B}(r),$$

where we used the notations

$$\sqrt{\sum(\bar{\mathcal{Z}})} := \sqrt{\frac{\gamma}{\ell}\left(1 - \frac{\gamma}{\lambda}\right)}\begin{pmatrix} 1 & -1 \\ -1 & 1 \end{pmatrix},\ diag(\sqrt{\bar{\mathcal{Z}}}) = \begin{pmatrix} \sqrt{\frac{1}{\ell}\frac{\gamma}{\lambda}} & 0 \\ 0 & \sqrt{\frac{1}{\ell}\left(1 - \frac{\gamma}{\lambda}\right)} \end{pmatrix} \text{ and}$$

$b(Z_1, Z_2) = \left(\lambda \frac{Z_1 Z_2}{Z_1 + Z_2} - \gamma Z_2\right)\begin{pmatrix} -1 \\ 1 \end{pmatrix} \cdot \widetilde{D}$ is a $\ell \times \ell(\ell - 1)$ matrix formed by ℓ block matrices, each with dimension $\ell \times \ell(\ell - 1)$. That is $\widetilde{D} = (\widetilde{D}_1 \ \widetilde{D}_2 \ \ldots \widetilde{D}_\ell)$, where

$$\widetilde{D}_1 = \begin{pmatrix} \sqrt{a_{12}} & \sqrt{a_{13}} & \sqrt{a_{14}} & \sqrt{a_{15}} & \ldots & \sqrt{a_{1\ell}} \\ -\sqrt{a_{12}} & 0 & 0 & 0 & \ldots & 0 \\ 0 & -\sqrt{a_{13}} & 0 & 0 & \ldots & 0 \\ 0 & 0 & -\sqrt{a_{14}} & 0 & \ldots & 0 \\ 0 & 0 & 0 & -\sqrt{a_{15}} & \ddots & 0 \\ \ldots & \ldots & \ddots & \ddots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \ldots & -\sqrt{a_{1\ell}} \end{pmatrix}$$

$$\widetilde{D}_2 = \begin{pmatrix} -\sqrt{a_{21}} & 0 & 0 & 0 & \ldots & 0 \\ \sqrt{a_{21}} & \sqrt{a_{23}} & \sqrt{a_{24}} & \sqrt{a_{25}} & \ldots & \sqrt{a_{2\ell}} \\ 0 & -\sqrt{a_{23}} & 0 & 0 & \ldots & 0 \\ 0 & 0 & -\sqrt{a_{24}} & 0 & \ldots & 0 \\ 0 & 0 & 0 & -\sqrt{a_{25}} & \ddots & 0 \\ \ldots & \ldots & \ddots & \ddots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \ldots & -\sqrt{a_{2\ell}} \end{pmatrix}$$

$$\vdots$$

$$\widetilde{D}_\ell = \begin{pmatrix} -\sqrt{a_{\ell 1}} & 0 & 0 & 0 & \ldots & 0 \\ 0 & -\sqrt{a_{\ell 2}} & 0 & 0 & \ldots & \sqrt{a_{2\ell}} \\ 0 & 0 & -\sqrt{a_{\ell 3}} & 0 & \ldots & 0 \\ 0 & 0 & 0 & -\sqrt{a_{\ell 4}} & \ldots & 0 \\ 0 & 0 & 0 & 0 & \ddots & 0 \\ \ldots & \ldots & \ddots & \ddots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \ldots & -\sqrt{a_{\ell(\ell-1)}} \\ \sqrt{a_{\ell 1}} & \sqrt{a_{\ell 2}} & \sqrt{a_{\ell 3}} & \sqrt{a_{\ell 4}} & \ldots & \sqrt{a_{\ell(\ell-1)}} \end{pmatrix}.$$

B (resp. $\widetilde{B}$) is the vector of Brownian motion corresponding to the infections and recoveries (resp. to the migrations). By setting $\mathcal{G} = \mathbb{I}_\ell \otimes \nabla_{\overline{Z}} b(\overline{Z}) + D \otimes \mathbb{I}_2$, then, we have

$$W^*(t) = +\int_0^t e^{(t-r)\mathcal{G}} \cdot \mathbb{I}_\ell \otimes \sqrt{\sum(\overline{\mathcal{Z}})} \cdot dB(r) + \int_0^t e^{(t-e)\mathcal{G}} \cdot \widetilde{D} \otimes diag(\sqrt{\overline{\mathcal{Z}}}) \cdot d\widetilde{B}(r).$$

Since $\mathbb{I}_\ell \otimes \nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})$ and $D \otimes \mathbb{I}_2$ commute, Then $e^{t\mathcal{G}} = e^{t\mathbb{I}_\ell \otimes \nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})} \cdot e^{tD \otimes \mathbb{I}_2}$. We have also

$$(\mathbb{I}_\ell \otimes \nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}}))^n = \mathbb{I}_\ell \otimes (\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}}))^n \text{ and } (D \otimes \mathbb{I}_2)^n = D^n \otimes \mathbb{I}_2, \text{ for all } n \geq 0,$$

from which we deduce that $e^{t\mathbb{I}_\ell \otimes \nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})} = \mathbb{I}_\ell \otimes e^{t\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})}$ and $e^{tD \otimes \mathbb{I}_2} = e^{tD} \otimes \mathbb{I}_2$. Hence the covariance matrix of $W^*(t)$ is given by

$$\begin{aligned}
&Cov(W^*(t)) \\
&= \int_0^t (e^{(t-r)D} \otimes e^{(t-r)\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})}) \cdot (\mathbb{I}_2 \otimes \sqrt{\sum(\overline{\mathcal{Z}})}) \cdot (\mathbb{I}_2 \otimes \sqrt{\sum(\overline{\mathcal{Z}})})^T \\
&\cdot (e^{(t-r)D} \otimes e^{(t-r)(\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}}))^T}) dr \\
&+ \int_0^t (e^{(t-r)D} \otimes e^{(t-r)\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})}) \cdot (\widetilde{D} \otimes diag\sqrt{(\overline{\mathcal{Z}})}) \cdot (\widetilde{D} \otimes diag\sqrt{(\overline{\mathcal{Z}})})^T \\
&\cdot (e^{(t-r)D} \otimes e^{(t-r)(\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}}))^T}) dr \\
&= 2\int_0^t e^{(t-r)D} \cdot e^{(t-r)D^T} \otimes [e^{(t-r)\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})} \cdot \sum(\overline{\mathcal{Z}}) \cdot e^{(t-r)(\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}}))^T}] dr \\
&+ \int_0^t (e^{(t-r)D} \cdot \widetilde{D} \cdot \widetilde{D}^T \cdot e^{(t-r)D^T}) \otimes (e^{(t-r)\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}})} \cdot diag(\overline{\mathcal{Z}}) \cdot e^{(t-r)(\nabla_{\mathcal{Z}} b(\overline{\mathcal{Z}}))^T}) dr,
\end{aligned}$$

with $\sum(\overline{\mathcal{Z}}) := \frac{\gamma}{\ell}\left(1 - \frac{\gamma}{\lambda}\right)\begin{pmatrix} 1 & -1 \\ -1 & 1 \end{pmatrix}$.

Now, to find the variance of the proportion of the total population of infectious, we multiply $Cov(W^*(t))$ from the left by u^T and from the right by u, where $u = (1, 1, \ldots, 1) \otimes \mathfrak{e}_2$.

But, since $D^T\begin{pmatrix}1\\ \vdots\\ 1\end{pmatrix} = D\begin{pmatrix}1\\ \vdots\\ 1\end{pmatrix} = 0$, then $e^{tD^T}\begin{pmatrix}1\\ \vdots\\ 1\end{pmatrix} = e^{tD}\begin{pmatrix}1\\ \vdots\\ 1\end{pmatrix} = \begin{pmatrix}1\\ \vdots\\ 1\end{pmatrix}$. Moreover $\widetilde{D}^T\begin{pmatrix}1\\ \vdots\\ 1\end{pmatrix} = 0$. Then, we deduce that

$$\int_0^t u^T \cdot (e^{(t-r)D} \cdot \widetilde{D} \cdot \widetilde{D}^T \cdot e^{(t-r)D^T})$$

$$\otimes (e^{(t-r)\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}})} \cdot diag(\overline{\mathbb{Z}}) \cdot e^{(t-r)(\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}}))^T}) \cdot u\, dr = 0.$$

Therefore

$$u^T \cdot Cov(W^*(t)) \cdot u$$

$$= 2\int_0^t u^T \cdot e^{(t-r)D} \cdot e^{(t-r)D^T} \otimes [e^{(t-r)\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}})} \cdot \sum(\overline{\mathbb{Z}}) \cdot e^{(t-r)(\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}}))^T}] \cdot u\, dr$$

$$= 2\ell\int_0^t \mathfrak{e}_2^T \cdot [e^{(t-r)\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}})} \cdot \sum(\overline{\mathbb{Z}}) \cdot e^{(t-r)(\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}}))^T}] \cdot \mathfrak{e}_2 dr.$$

We have that $\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}}) = -(\lambda-\gamma)\begin{pmatrix}1-\gamma/\lambda & -\gamma/\lambda\\ -1+\gamma/\lambda & \gamma/\lambda\end{pmatrix}$, and since

$$\begin{pmatrix}1-\gamma/\lambda & -\gamma/\lambda\\ -1+\gamma/\lambda & \gamma/\lambda\end{pmatrix}^2 = \begin{pmatrix}1-\gamma/\lambda & -\gamma/\lambda\\ -1+\gamma/\lambda & \gamma/\lambda\end{pmatrix}, \text{ then}$$

$$e^{t\nabla_{\mathbb{Z}} b(\overline{\mathbb{Z}})} = e^{-t(\lambda-\gamma)}\begin{pmatrix}1-\gamma/\lambda & -\gamma/\lambda\\ -1+\gamma/\lambda & \gamma/\lambda\end{pmatrix}.$$

We then obtain

$$u^T \cdot Cov(W^*(t)) \cdot u$$

$$= 2\gamma\left(1-\frac{\gamma}{\lambda}\right)\int_0^t e^{-2(t-r)(\lambda-\gamma)}\mathfrak{e}_2^T\begin{pmatrix}1-\gamma/\lambda & -\gamma/\lambda\\ -1+\gamma/\lambda & \gamma/\lambda\end{pmatrix}\cdot\begin{pmatrix}1 & -1\\ -1 & 1\end{pmatrix}$$

$$\begin{pmatrix}1-\gamma/\lambda & -1+\gamma/\lambda\\ -\gamma/\lambda & \gamma/\lambda\end{pmatrix}\mathfrak{e}_2 dr$$

$$= \frac{\gamma}{\lambda} \int_0^t 2(\lambda - \gamma) e^{-2(\lambda-\gamma)(t-r)} dr$$

$$= \frac{\gamma}{\lambda} (1 - e^{-2t(\lambda-\gamma)}).$$

Hence, the variance of the proportion of infectious individuals is close to

$$\frac{1}{N} \frac{\gamma}{\lambda} (1 - e^{-2t(\lambda-\gamma)}), \text{ when } N \text{ is large:}$$

We have just proved

Theorem 3.2. *Assume that, for all* $j = 1, \ldots, \ell$, $\lambda_j = \gamma$ *and* $\nu_I = \nu_S = \nu$, *then N times the variance of the proportion of the infectious subpopulation in the multi–patch SIS model converges, as N tends to* $+\infty$, *towards*

$$\frac{\gamma}{\lambda} (1 - e^{-2t(\lambda-\gamma)}).$$

Exactly the same limit is obtained for the variance of the same proportion in the SIS homogeneous model (one patch) with infection rate λ *and recovery rate* γ.

Remark 3.1. (i) From Theorem 3.2, we deduce that, for $\eta > 0$ fixed and any $\delta > 0$, there exist t and N large enough such that we have the following upper bound for the probability of a positive deviation of $\sqrt{N} \sum_{j=1}^{\ell} (I_j^N(t) - I_j^*)$

$$\mathbb{P}\left[\sqrt{N} \sum_{j=1}^{\ell} (I_j^N(t) - I_j^*) \geq \eta \right] \leq \exp\left\{ -\frac{\lambda}{\gamma} \eta^2 + \delta \right\}.$$

(ii) The central limit theorem and Theorem 3.2 tell us that $\sqrt{N} \sum_{j=1}^{\ell} (I_j^N(t) - I_j^*)$ converges to a Gaussian process, whose asymptotic variance can be approximated by γ/λ for large t. This suggests that for large t, the total numbers of the infectious individuals in the population is approximately Gaussian with mean $N \sum_{j=1}^{\ell} I_j^*$ and standard deviation $\sqrt{N\gamma/\lambda}$.

If N is such that this standard deviation is at least the mean divided by 3, then it is likely that $\sum_{j=1}^{\ell} I_j^N(t)$ will hit zero in a time of the order of 1. This gives a critical population size (the minimum number of people required to sustain indefinitely an infectious pathogen) roughly of the order of $N_c \sim \frac{9\gamma/\lambda}{(\sum_{j=1}^{\ell} I_j^*(t))^2}$.

The choice of 3 is somewhat arbitrary, but if we instead choose 2 the process will hit 0 fairly quickly with a probability close to 1, and if we choose 4 it seems extremely unlikely that it will hit extinction within e.g. a lifetime, so 3 seems like a reasonable compromise. The conclusion is that, for a given infectious disease, given g and l, the epidemic might stop quickly in a community of size $N \ll N_c$, whereas an endemic situation will persist for a very long time if $N \gg N_c$. Remember that at equilibrium, in most diseases, the proportion of infectious individuals is rather small, hence N_c is reasonably large.

4. Large Deviations Principle and Extinction of an Endemic Disease

For large N, the stochastic model can be seen as a small random perturbation of the deterministic model. If the starting point of the stochastic process is close to the endemic equilibrium of the ODE, then its solution will be close to that equilibrium. But, based upon Large Deviations, the Freidlin-Wentzell theory tells us not only that sooner or later the small perturbations of the stochastic process will drive it out of the bassin of attraction of the stable equilibrium of the ODE, but it gives an estimate of the time it takes for this to happen. For this reason, we will investigate in this section the Large Deviations Principle (LDP) from the law of large numbers, for our SIS model which is constructed on a finite numbers of patches. We refer to Dembo & Zeitouni [8] for an introduction to Large Deviation theory, and its application to Brownian motion driven SDEs. Large deviations for Poisson processes driven SDEs have been studied in particular by Shwartz and Weiss [23], Dolgoarshinnykh [9], Pardoux and Samegni [18]. The case of Poisson processes with vanishing rates is studied in Shwartz and Weiss [24]. In [9], Dolgoarshinnykh derived the sample path LDP for the SIRS processes from

that for standard Poisson processes. In these studies the difficulty follows from the fact that some of the rates in the stochastic process may vanish, and this makes the estimate delicate since the logarithms of the rates enter the rate function. Then Kratz and Pardoux [15], Pardoux and Samegni [18] and Britton and Pardoux [5] also present an approach for continuous time epidemic models which is adapted to the case where some rates of the process vanish. Our multi-patch model corresponds to that situation. The main application of the LDP is to estimate the time needed for the small random perturbations to drive the system from the stable endemic equilibrium to the disease free equilibrium.

4.1 Useful notions

We start by stating some useful notions.

- The rates $\widetilde{\beta}_k$ are those which appear in the Poisson processes $P_{im}^{(1)}, P_{jm}^{(2)}$. That is a $\widetilde{\beta}_k(\mathcal{Z}^N(t)) \in \{\frac{\lambda_i S_i^N(t) I_i^N(t)}{S_i^N(t) + I_i^N(t)}, \gamma_i I_i^N(t), \nu_S a_{ij} S_i^N(t), \nu_I a_{ij} I_i^N(t), i, j \in \{1, \ldots, \ell\}$

The vectors $h_k \in \{-1, 0, 1\}^{2\ell}$ denote the respective jump directions with jump rates $\widetilde{\beta}_k$. The process $\mathcal{Z}^N$ can be written as follows

$$\mathcal{Z}^N(t) = Z_N + \int_0^t b(\mathcal{Z}^N(r))dr + \frac{1}{N}\sum_{k=1}^{2\ell^2} h_k P_k\left(N\int_0^t \widetilde{\beta}_k(\mathcal{Z}^N(r))dr\right),$$

where $P_k \in \{P_{im}^{(1)}, P_{jim}^{(2)}, 1 \le i, j \le \ell, m = 1, 2\}$.

- $\mathcal{C}([0, T]; \mathbb{R}^{2\ell})$ denotes the set of continuous functions from $[0, T]$ into $\mathbb{R}^{2\ell}$, and $\mathcal{AC}_{T, 2\ell}$ denotes the subset of absolutely continuous functions.
- For $\phi \in \mathcal{AC}_{T, 2\ell}$, $\mathcal{AC}_{2\ell^2}(\phi)$ denotes the set of functions $c \in L^1(0, T; \mathbb{R}_+^{2\ell^2})$ such that for all $1 \le k \le \ell^2$, $c_t^k = 0$ on the set $\{t, \widetilde{\beta}_k(\phi(t)) = 0\}$ and $\frac{d\phi(t)}{dt} = \sum_{k=1}^{2\ell^2} c_t^k(t) h_k$, t a.e.

- We define the following distance between two elements ϕ, ψ of $\mathbb{D}([0, T]; \mathbb{R}^{2\ell}) : \| \phi - \psi \|_T = \sup_{0 \le t \le T} \| \phi(t) - \psi(t) \|$, where $\| \cdot \|$ is the 1-norm of $\mathbb{R}^{2\ell}$.

The rate function

Considering the stochastic process $\{\mathcal{Z}^N, t \ge 0\}$, we want to derive an LDP for the trajectories in $\mathbb{D}([0, T]; \mathbb{R}^{2\ell})$. To this end we first define a rate function as follows

$$I_T(\phi) := \begin{cases} \inf_{c \in A_{2\ell^2}(\phi)} & \text{if } \phi \in \mathcal{AC}_{T,2\ell} \\ +\infty, & \text{otherwise.} \end{cases}$$

where

$$I_T(\phi \mid c) = \int_0^T \sum_{k=1}^{2\ell^2} g(c_t^k, \tilde{\beta}_k(\phi(t)))dt$$

with $g(x, y) = x \log(x/y) - x + y$, where we assume that for all $x > 0$, $\log(x/0) = \infty$ and $0 \log(0/0) = 0 \log(0) = 0$.

The state space in which our process $\mathcal{Z}^N(t)$ evolves is its interior.

$$E = \left\{ \mathcal{Z} \in [0, 1]^{2\ell} : \sum_{i=1}^{2\ell} \mathcal{Z}^i \le 1 \right\}.$$

In what follows ∂E denotes the boundary of the set E and $\mathring{E}$ its interior.

The LDP proved in Pardoux and Samegni [18] used the following two assumptions:

Assumption 4.1. There exists $\mathcal{Z}_0 \in \mathbb{R}^{2\ell}$ such that the collection of mapping $\Phi_a : E \mapsto \mathbb{R}^{2\ell}$ defined by $\Phi_a(\mathcal{Z}) = \mathcal{Z} + a(\mathcal{Z}_0 - \mathcal{Z})$, defined for each $0 < a < 1$, is such that $\mathcal{Z}^a = \Phi_a(\mathcal{Z}) \in E$, for all $\mathcal{Z} \in E$, and moreover for some $0 < c_2 < c_1$ and all $\mathcal{Z} \in E$.

$$| \mathcal{Z} - \mathcal{Z}^a | \leq c_1 a, \; dist(\mathcal{Z}^a, \partial E) \geq c_2 a.$$

Let us define for all $a > 0$

$$B^a = \{\mathcal{Z} \in E : dist(\mathcal{Z}, \partial E) \geq c_2 a\}, \text{ and } C_a = \inf_{1 \leq k \leq 2\ell^2} \inf_{\mathcal{Z} \in B^a} \widetilde{\beta}_k(\mathcal{Z}).$$

Assumption 4.2 (1) The rate $\widetilde{\beta}_k$ are Lipschitz continuous and bounded.

(2) For any $1 \leq k \leq 2\ell^2$, if $\mathcal{Z} \in \overset{\circ}{E}$, $\widetilde{\beta}_k(\mathcal{Z}) > 0$.

(3) There exist two constants η_1, and η_2 such that whenever $\mathcal{Z} \in E$ is such that $\widetilde{\beta}_k(\mathcal{Z}) < \eta_1$, $\widetilde{\beta}_k(\mathcal{Z}^a) > \widetilde{\beta}_k(\mathcal{Z})$ for all $a \in (0, \eta_2)$, and for any $1 \leq k \leq 2\ell^2$.

(4) There exists a constant $\rho \in (0, 1/2)$ such that $\lim_{a \to 0} a^{\rho} \log(C_a) = 0$.

4.2. Large deviations principle of $\mathcal{Z}^N$

Here and below we shall use the following notation concerning the initial condition of $\mathcal{Z}^N$. We fix $\mathfrak{z} \in \mathbb{R}^{2\ell}$ and start $\mathcal{Z}^N$ from the point $\mathcal{Z}^N(0) = \mathcal{Z}_N$, where the i-th coordinate $\mathcal{Z}_N^i$ of $\mathcal{Z}_N$ is given by $\mathcal{Z}_N^i = \frac{[\mathfrak{z}^i N]}{N}$, $[\mathfrak{z}^i N]$ denoting the integer part of $\mathfrak{z}^i N$. We shall denote by $\mathcal{Z}^N_{\mathcal{Z}_N}$ the process $\mathcal{Z}^N$ starting from $\mathcal{Z}_N$.

Using the fact that the state space E is convex, it is easy to see that Assumption 4.1 is satisfied, with some $\mathcal{Z}_0 \in \overset{\circ}{E}$. Moreover, since the rate functions $\widetilde{\beta}_k(\cdot)$ are Lipschitz and bounded, then it is not hard to see that Assumption 4.2 is also satisfied. Then a combination of Theorem 4 and Theorem 5 in Pardoux and Samegni [18] yields the following theorem.

Theorem 4.1. *For every open set* $O \subset \mathbb{D}([0, T]; \mathbb{R}^{2\ell})$

$$\limsup_{N \to \infty} \frac{1}{N} \log \mathbb{P}(\mathcal{Z}^N_{Z_N} \in O) \geq - \inf_{\phi \in O, \, \phi(0) = \mathfrak{z}} I_T(\phi).$$

For every closed set $F \subset \mathbb{D}([0, T]; \mathbb{R}^{2\ell})$, *and any compact subset* $\mathcal{K}$ *of* E

$$\limsup_{N\to\infty} \frac{1}{N} \log \sup_{\mathfrak{z}\in\mathcal{K}} \mathbb{P}(\mathcal{Z}^N_{Z_N} \in F) \leq -\inf_{\mathfrak{z}\in\mathcal{K}} \inf_{\phi\in F,\, \phi(0)=\mathfrak{z}} I_T(\phi).$$

4.3. Time of extinction in the SIS patch model

Let $T^N_{Ext} = \inf\{t \geq 0,\ I^N(t) = 0\}$. In this subsection we want to estimate the time taken by the stochastic process $\{\mathcal{Z}^N\}$ to leave the bassin of attraction of the endemic equilibrium. That will be an application of the large deviations principle. Let

$$V(\mathcal{Z}, \mathcal{Z}', T) = \inf_{\phi,\, D_{T,E},\, \phi(0)=\mathcal{Z},\, \phi_T=\mathcal{Z}'} I_T(\phi),$$

$$V(\mathcal{Z}, \mathcal{Z}') = \inf_{T>0} V(\mathcal{Z}, \mathcal{Z}', T),$$

$$\overline{V}_a = \inf_{\mathcal{Z}\in E\setminus\{\exists\, i: I_i=0\}} V(\mathcal{Z}^*, \mathcal{Z}),$$

Following Pardoux and Samegni [18], Theorem 4.1 implies the following result.

Theorem 4.2. *Let* $T^{N,\mathfrak{z}}_{Ext}$ *be the extinction time in the SIS model starting from* $\mathcal{Z}_N = \frac{[N\mathfrak{z}]}{N}$. *Given* $\eta > 0$, *for all* $\mathfrak{z} \in E$,

$$\lim_{N\to\infty} \mathbb{P}(\exp\{N(\overline{V} - \eta)\} < T^{N,\mathfrak{z}}_{Ext} < \exp\{N(\overline{V} - \eta)\}) = 1, \tag{4.1}$$

and for N large enough,

$$\exp\{N(\overline{V} - \eta)\} \leq \mathbb{E}(T^{N,\mathfrak{z}}_{Ext}) \leq \exp\{N(\overline{V} - \eta)\}. \tag{4.2}$$

We need to evaluate the quantity $\overline{V}$ to obtain an approximation of the extinction time of the epidemic. $\overline{V}$ can be written in the following form

$$\overline{V} = \inf_{T,\, \phi\in\mathcal{AC}_{T,2\ell}:\phi(0)=\mathcal{Z}^*,\ \phi(T)=0} \inf_{c\in\mathcal{A}_{2\ell}2(\phi)} \int_0^T \sum_{k=1}^{2\ell^2} g(c^k_t,\ \widetilde{\beta}_k(\phi(t)))dt,$$

and we note that it is the solution of the following optimal control problem

$$\begin{cases} \underset{c}{Min} \sum_{k=1}^{2\ell^2} \int_0^T g(c_t^k, \widetilde{\beta}_k(\phi(t)))dt, \\ \dfrac{d\phi(t)}{dt} = \sum_{k=1}^{2\ell^2} c_t^k h_k, \\ \phi(0) = \mathcal{Z}^*, \ \phi(T) = 0. \end{cases} \tag{4.3}$$

Let us mention that this quasi-potential has been calculated in the case of the homogeneous model (see Pardoux and Samegni [18]). In that situation,

$$\overline{V} = \log(R_0) + R_0^{-1} - 1,$$

which shows that $\overline{V}$ is a monotone increasing function of R_0 for $R_0 > 1$, and it vanishes if $R_0 = 1$. But in our case, we cannot find an explicit formula for $\overline{V}$. Hence we use again the optimal control software "Bocop" to compute numerically an approximation of the value of $\overline{V}$, in the case $\ell = 2$.

As explained in Britton and Pardoux [5], there is no optimal trajectory from $\mathcal{Z}^*$ to 0. Then we start from a point $\mathcal{Z}^* - \delta$ (where $\delta \ll 1$) which is close to the endemic equilibrium $\mathcal{Z}^*$. Since we have in mind to compare the homogeneous and the heterogeneous case, we compute $\overline{V}$ for a trajectory from $\mathcal{Z}^* - \delta$ to δ in both cases.

4.4 Optimal control problem for the computation of $\overline{V}$

In the case of the homogeneous model, using calculations similar to those of Britton and Pardoux [5], we find

$$\overline{V}(2\delta - 1 + \gamma/\lambda)\log(\gamma/\lambda) + (1-\delta)\log(1-\delta) - 1 + \delta - (\gamma/\lambda + \delta)\log(\gamma/\lambda + \delta) + \gamma/\lambda + \delta.$$

For $\delta = 10^{-2}$, $\lambda = 1.5$ and $\gamma = 1$, we have $\overline{V} \approx 0.0680$.

Here, we aim at discussing how the heterogeneity of the environment influences the value of the quasi-potential $\overline{V}$ and then the extinction time of

the epidemic. Hence, we perform a full-scale sensitivity analysis. We consider the case of two patches, and compute $\overline{V}$ for some values of the parameters.

Table 1

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
1.5	1.5	1	1	0.0007	0.0007	0.06388988
1.5	1.5	1	1	0.005	0.005	0.06389509
1.5	1.5	1	1	0.02	0.02	0.06390584
1.5	1.5	1	1	0.1	0.1	0.06391835
1.5	1.5	1	1	0.1	0.5	0.06391310
1.5	1.5	1	1	0.1	1	0.06391135
1.5	1.5	1	1	0.1	2	0.06391027
1.5	1.5	1	1	0.1	5	0.06390954
1.5	1.5	1	1	0.5	0.1	0.06392426
1.5	1.5	1	1	0.5	0.5	0.06392421
1.5	1.5	1	1	0.5	1	0.06392396
1.5	1.5	1	1	0.5	2	0.06392346
1.5	1.5	1	1	0.5	5	0.06392374
1.5	1.5	1	1	1	0.1	0.06392546
1.5	1.5	1	1	1	0.5	0.06392552
1.5	1.5	1	1	1	5	0.06392531
1.5	1.5	1	1	2	0.1	0.06392618
1.5	1.5	1	1	2	0.5	0.06392621
1.5	1.5	1	1	2	1	0.06392620
1.5	1.5	1	1	2	5	0.06392616
1.5	1.5	1	1	5	0.1	0.06392664

1.5	1.5	1	1	5	0.5	0.06392667
1.5	1.5	1	1	5	1	0.06392266
1.5	1.5	1	1	5	2	0.06392668

In Table 1, both patches have the same rate of infections $\lambda_1 = \lambda_2 = 1.5$, and the same rate of recovery $\gamma_1 = \gamma_2 = 1$. We have the following observations. Firstly the quasi-potential is very little sensitive to the diffusion coefficients ν_S and ν_I. Secondly, when $\nu_S = \nu_I := \nu$, we observe that $\overline{V}$ is a monotone increasing function of n, and its values are close to that of the homogeneous model. Thirdly, when the diffusion coefficient of the infectious individuals is small $(\nu_I < 1)$, we observe that the quasi-potential is a monotone decreasing function of ν_S. Finally, for ν_S fixed, $\overline{V}$ is a monotone increasing function of ν_I.

Table 2

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
1.5	1.5	1.5	0.5	0.1	0.1	0.15834979
1.5	1.5	1.5	0.5	0.1	0.5	0.08646118
1.5	1.5	1.5	0.5	0.1	2	0.06104814
1.5	1.5	1.5	0.5	0.1	5	0.05511921
1.5	1.5	1.5	0.5	0.5	0.1	0.13515130
1.5	1.5	1.5	0.5	0.5	0.5	0.11605712
1.5	1.5	1.5	0.5	0.5	1	0.09329336
1.5	1.5	1.5	0.5	0.5	2	0.07916069
1.5	1.5	1.5	0.5	0.5	5	0.06971181
1.5	1.5	1.5	0.5	1	0.1	0.12493619
1.5	1.5	1.5	0.5	1	0.5	0.11543207
1.5	1.5	1.5	0.5	1	2	0.08134209

1.5	1.5	1.5	0.5	1	5	0.07110322
1.5	1.5	1.5	0.5	2	0.1	0.11931524
1.5	1.5	1.5	0.5	2	0.5	0.11201741
1.5	1.5	1.5	0.5	2	2	0.08198918
1.5	1.5	1.5	0.5	2	5	0.07161757
1.5	1.5	1.5	0.5	5	0.1	0.11440354
1.5	1.5	1.5	0.5	5	0.5	0.10855991
1.5	1.5	1.5	0.5	5	1	0.09398299
1.5	1.5	1.5	0.5	5	2	0.08133421
1.5	1.5	1.5	0.5	5	5	0.07155268

In Table 2, both patches have the same rates of infection $\lambda = 1.5$, and different rates of recovery. In this case, we remark that the quasi-potential is a monotone decreasing function of the diffusion coefficients ν_S. Furthermore, the quasi-potential is sensitive to the diffusion coefficient ν_S and ν_I. Compared with Table 1, it appears that the value of the quasi-potential is greater in the case of Table 2 (except the case $\nu_I = 0.1$). Hence, for the same rate of infection, if the rate of recovery on both patches is different, that can increase the time of extinction of the epidemic.

Table 3

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
2	1	1	1	0.1	0.1	0.13300260
2	1	1	1	0.1	1	0.13948634
2	1	1	1	0.1	2	0.15553404
2	1	1	1	0.1	5	0.15665938
2	1	1	1	0.5	0.1	0.13094946
2	1	1	1	0.5	0.5	0.14922713

2	1	1	1	0.5	1	0.15225154
2	1	1	1	0.5	2	0.19338106
2	1	1	1	1	0.1	0.13007143
2	1	1	1	1	0.5	0.14769450
2	1	1	1	1	1	0.15044565
2	1	1	1	1	2	0.15187630
2	1	1	1	1	5	0.15275238
2	1	1	1	2	0.1	0.12932141
2	1	1	1	2	0.5	0.14631146
2	1	1	1	2	5	0.15088231
2	1	1	1	5	0.5	0.14511235
2	1	1	1	5	1	0.14743955
2	1	1	1	5	5	0.14928123

In Table 3, $\lambda_1 = 2$, $\lambda_2 = 1$, and the infection rate on both patches is $\gamma = 1$. Here, the values of the quasi-potential is greater than the one of the homogeneous case. But it is not much sensitive to the diffusion coefficients. By fixing the diffusion coefficient of the infectious individuals, we observe that $\overline{V}$ is a monotone increasing function of ν_S. Conversely, for ν_S fixed, we observe that $\overline{V}$ is a monotone decreasing function of ν_I when the diffusion coefficient of susceptible individuals is small $(\nu_S < 1)$.

Table 4

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
2	1	1.5	0.5	0.1	0.1	0.09259574
2	1	1.5	0.5	0.1	0.5	0.07566492
2	1	1.5	0.5	0.1	1	0.07143704

2	1	1.5	0.5	0.1	5	0.06741124
2	1	1.5	0.5	0.5	0.1	0.09032259
2	1	1.5	0.5	0.5	0.5	0.06037173
2	1	1.5	0.5	0.5	1	0.07181220
2	1	1.5	0.5	0.5	2	0.06866973
2	1	1.5	0.5	0.5	5	0.06664475
2	1	1.5	0.5	1	0.1	0.08935810
2	1	1.5	0.5	1	0.5	0.07652209
2	1	1.5	0.5	1	1	0.07145629
2	1	1.5	0.5	1	2	0.06828403
2	1	1.5	0.5	2	0.1	0.09788083
2	1	1.5	0.5	2	0.5	0.07615368
2	1	1.5	0.5	2	2	0.06797799
2	1	1.5	0.5	2	5	0.06585038
2	1	1.5	0.5	5	1	0.07090993
2	1	1.5	0.5	5	2	0.06774671

In Table 4, $\lambda_1 = 2$, $\lambda_2 = 1$, $\gamma_1 = 1.5$ and $\gamma_2 = 0.5$ Here $\overline{V}$ is sensitive to the diffusion coefficients. It appears that $\overline{V}$ is a monotone decreasing function of ν_S. Also, by fixing the diffusion coefficient of susceptible individuals, we see that the quasi-potential is a decreasing function of ν_I.

Table 5

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
2	1	0.5	1.5	0.1	0.1	0.219098282
2	1	0.5	1.5	0.1	0.5	0.09113194
2	1	0.5	1.5	0.1	1	0.06445685

2	1	0.5	1.5	0.1	2	0.04955660
2	1	0.5	1.5	0.1	5	0.03992785
2	1	0.5	1.5	0.5	0.1	0.15502270
2	1	0.5	1.5	0.5	0.5	0.17597830
2	1	0.5	1.5	0.5	1	0.11731207
2	1	0.5	1.5	0.5	2	0.09039406
2	1	0.5	1.5	0.5	5	0.07145280
2	1	0.5	1.5	1	0.1	0.12935284
2	1	0.5	1.5	1	0.5	0.15555805
2	1	0.5	1.5	1	2	0.09851895
2	1	0.5	1.5	1	5	0.07706810
2	1	0.5	1.5	2	0.1	0.11249079
2	1	0.5	1.5	2	0.5	0.14521667
2	1	0.5	1.5	2	1	0.12656503
2	1	0.5	1.5	2	2	0.10224187
2	1	0.5	1.5	2	5	0.07976383
2	1	0.5	1.5	5	0.1	0.10041725
2	1	0.5	1.5	5	0.5	0.13399275
2	1	0.5	1.5	5	5	0.08095013

In Table 5, only patch 1 is in an endemic situation, contrary to the case in Table 4. In this case, $\overline{V}$ is very sensitive to the diffusion coefficients. The values of the quasi-potential remain greater than those in Table 4 (where both patches are in an endemic situation). When $\nu_I = \nu_S$ or ν_I is small $(\nu_I < 1)$, $\overline{V}$ is a monotone decreasing function of ν_S. Here the quasi-potential is smaller in the case where the diffusion coefficient of infectious individuals is small and one of the susceptible individuals is large. It is larger in the case where both diffusion coefficients are small.

Table 6

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
2.5	0.5	1	1	0.1	0.1	0.11976635
2.5	0.5	1	1	0.1	0.5	0.06311766
2.5	0.5	1	1	0.1	1	0.05007184
2.5	0.5	1	1	0.1	2	0.04247088
2.5	0.5	1	1	0.1	5	0.03730292
2.5	0.5	1	1	0.5	0.1	0.08896987
2.5	0.5	1	1	0.5	0.5	0.09783242
2.5	0.5	1	1	0.5	1	0.08246158
2.5	0.5	1	1	0.5	2	0.07144443
2.5	0.5	1	1	0.5	5	0.06308287
2.5	0.5	1	1	1	0.1	0.08283626
2.5	0.5	1	1	1	0.5	0.09731332
2.5	0.5	1	1	1	2	0.07679765
2.5	0.5	1	1	1	5	0.06772333
2.5	0.5	1	1	2	0.1	0.07046595
2.5	0.5	1	1	2	0.5	0.09433121
2.5	0.5	1	1	2	2	0.07912119
2.5	0.5	1	1	2	5	0.07006957
2.5	0.5	1	1	5	0.1	0.06498999
2.5	0.5	1	1	5	0.5	0.09077776
2.5	0.5	1	1	5	1	0.08673071
2.5	0.5	1	1	5	2	0.07919208
2.5	0.5	1	1	5	5	0.07112742

In Table 6, both patches have the same recovery rate. Only patch 1 is in an endemic situation. In this case, we remark that the quasi-potential is very sensitive to the diffusion coefficients. When $\nu_I = \nu_S$ or the diffusion coefficient of infectious individuals is small, then $\overline{V}$ is a monotone decreasing function of ν_S. As in the previous case, $\overline{V}$ is small when the diffusion coefficient of infectious individuals is small and the one susceptible is large. But $\overline{V}$ is large in the case where both diffusion coefficients are small. The values of $\overline{V}$ are large in the case of Table 5 than in the case of Table 6. Furthermore, in many cases of Table 6, the values of $\overline{V}$ are large than the ones of the homogeneous case.

Table 7.

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
2.5	0.5	0.5	1.5	0.1	0.1	0.27064807
2.5	0.5	0.5	1.5	0.1	0.5	0.09560663
2.5	0.5	0.5	1.5	0.1	1	0.06092021
2.5	0.5	0.5	1.5	0.1	2	0.04227762
2.5	0.5	0.5	1.5	0.1	5	0.03037407
2.5	0.5	0.5	1.5	0.5	0.1	0.17253833
2.5	0.5	0.5	1.5	0.5	0.5	0.19499598
2.5	0.5	0.5	1.5	0.5	1	0.13866271
2.5	0.5	0.5	1.5	0.5	2	0.10025293
2.5	0.5	0.5	1.5	0.5	5	0.07247470
2.5	0.5	0.5	1.5	1	0.1	0.13055085
2.5	0.5	0.5	1.5	1	0.5	0.19169669
2.5	0.5	0.5	1.5	1	5	0.08340398
2.5	0.5	0.5	1.5	2	0.1	0.10238341
2.5	0.5	0.5	1.5	2	0.5	0.17137155

2.5	0.5	0.5	1.5	2	1	0.15656419
2.5	0.5	0.5	1.5	2	2	0.12492756
2.5	0.5	0.5	1.5	2	5	0.08947044
2.5	0.5	0.5	1.5	5	0.1	0.08170288
2.5	0.5	0.5	1.5	5	1	0.14292825
2.5	0.5	0.5	1.5	5	5	0.09285865

In Table 7, $\overline{V}$ is a monotone decreasing function of ν_S when ν_I is small. Conversely, $\overline{V}$ is a monotone increasing function of ν_I when ν_S is large. As in the previous case, the case where $\overline{V}$ is the largest is the one where both diffusion coefficients are small, and it is small in the case where the diffusion coefficient for susceptible infectious individuals is small and the diffusion coefficient for susceptible individuals is large. Again in the present case, the quasi-potential values are much higher than the homogeneous model's (except the case $\nu_I = 0.1$).

Table 8

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\overline{V}$
2.5	0.5	1.5	0.5	0.1	0.1	0.05626799
2.5	0.5	1.5	0.5	0.1	0.5	0.05585668
2.5	0.5	1.5	0.5	0.1	1	0.05578432
2.5	0.5	1.5	0.5	0.1	2	0.05576527
2.5	0.5	1.5	0.5	0.1	5	0.05575526
2.5	0.5	1.5	0.5	0.5	0.1	0.05775356
2.5	0.5	1.5	0.5	0.5	0.5	0.06183417
2.5	0.5	1.5	0.5	0.5	1	0.06183159
2.5	0.5	1.5	0.5	0.5	2	0.06215810
2.5	0.5	1.5	0.5	0.5	5	0.06235621

2.5	0.5	1.5	0.5	1	0.1	0.06196546
2.5	0.5	1.5	0.5	1	0.5	0.06251847
2.5	0.5	1.5	0.5	1	2	0.06287057
2.5	0.5	1.5	0.5	2	0.1	0.06202028
2.5	0.5	1.5	0.5	2	0.5	0.06282561
2.5	0.5	1.5	0.5	2	1	0.06289555
2.5	0.5	1.5	0.5	2	2	0.06322846
2.5	0.5	1.5	0.5	5	0.1	0.06200597
2.5	0.5	1.5	0.5	5	0.5	0.06299459
2.5	0.5	1.5	0.5	5	1	0.06310545
2.5	0.5	1.5	0.5	5	2	0.06343788

In Table 8, only patch 1 is in an endemic situation. Firstly, we remark that the quasi-potential is less sensitive to the diffusion coefficients. Secondly, when the diffusion coefficients are equal, $\overline{V}$ is a monotone increasing function of ν_S Thirdly, $\overline{V}$ becomes a monotone increasing function of ν_S when the diffusion coefficient for infectious individuals becomes large. For ν_S fixed, $\overline{V}$ is a monotone increasing function of ν_I. Finally, we observe that in this case, the quasi-potential values are less than the homogeneous model's.

From the above observations, it clearly follows that the heterogeneity of the environment influences the quasi-potential and then the time of extinction of the epidemic. These results show that spatial heterogeneity and rates of movement of susceptible and infectious individuals play an important role in disease persistence and extinction. The movement of susceptible or infected can enhance or suppress the spread of disease depending on the heterogeneity and connectivity of the spatial environment. These results have important implications for disease control.

The extensive tables providing the numerical values of $\overline{V}$ for many sets of parameters, although helpful, are not very easy to interpret. Then we

perform a full-scale sensivity analysis by computing the first and total-order indices and to determine the effect of the various parameters on $\overline{V}$.

5. Sensitivity Analysis

To assess to the sensistivity of $\lambda_1, \lambda_2, \gamma_1, \gamma_2, \nu_S, \nu_I$ on $\overline{V}$, we need to write $\overline{V}$ as a function of these parameters, that is $\overline{V} = f(\lambda_1, \lambda_2, \gamma_1, \gamma_2, \nu_S, \nu_I)$. We then use the previous values of $\overline{V}$ computed with the Bocop software to approximate f by using the multiple variate regression technique. Next we compute the Sobol indices.

Sobol indices

Sobol sensitivity analysis determines the contribution of each parameter and their interactions to the overall variance. First-order Sobol indices measure the direct effect of a parameter on the variance of the model output, by isolating the contribution of that parameter individually, while keeping the other parameters fixed at their mean or nominal values. First-order Sobol indices are useful for identifying parameters that have a significant impact on the model.

On the other hand, total indices measure the total effect of a parameter, including its direct effect and its interaction with other parameters. Total indices are important for understanding how a parameter can influence the results of the model when the other parameters also vary. Total-order sensitivity indices take into account both the main, second-order, and higher-order effects. Sensitivity analysis based on both first-order and total-order Sobol indices offers a more complete view of the importance of parameters, as it takes into account both direct effects and interactions. When a parameter has a high first-order Sobol index and a low total index, this indicates a situation where the parameter has a significant direct effect on the variance of the model output, but where its interactions with other parameters have a limited impact on the overall variability of the results. On the other hand, when a parameter has a low first-order Sobol index and a high total index, this indicates a situation where the parameter has a limited direct effect on the variance of the model output, but where its interactions with other parameters have a significant impact on the overall variability of the results.

An overview of Sobol-based sensitivity indices can be found in in A. Puy et al. [22].

Here we use the R package "sensobol" to compute the first order and total order Sobol indices, and find the following.

Table 1. Sobol-based sensitivity indices.

Parameters	First order indices	Total order indices
λ_1	0, 011	0, 221
λ_2	0, 072	0, 233
γ_1	0, 016	0, 032
γ_2	0, 072	0, 163
ν_I	0, 204	0, 335
ν_S	0, 143	0, 558

This shows that the parameters rank in order of influence on V according to their total sensitivities as follows: ν_S, ν_I, λ_1, λ_2, γ_2, γ_1.

This shows that all the coefficients influence the value of $\overline{V}$. Moreover, the quasi-potential is much more influenced by the diffusion coefficients ν_S and ν_I, followed by the infection parameters λ_1 and λ_2.

6. Moderate Deviations and Extinction of an Endemic Disease

Moderate deviations have been studied in Pardoux [20], in the case of homogeneous epidemic models with a constant flux of susceptibles. In this work, the author introduces deterministic and stochastic epidemic models in a homogeneous community, namely the SIS, SIRS and SIR model with demography. He then studies moderate deviations for such models and explains how it can be used to predict the time taken for the stochastic perturbations to stop the epidemic for moderate population sizes. In the case of the SIS model he made comparison between the central limit theorem, moderate deviations and large deviations. Here, we follow [20] and derive

moderate deviations for our process, which models a heterogeneous community. We want to study moderate deviations at scale a of $\mathcal{Z}^N(t)$, where $0 < \alpha < 1/2$. The case $\alpha = 0$ corresponds to the large deviations, and $\alpha = 1/2$ to the central limit theorem. Hence moderate deviations describe a range of fluctuations between those of the central limit theorem and those of the large deviations. Our results relies essentially upon those in [20], which can be applied in our case since the assumptions are satisfied. Then, in what follows we collect several intermediate results which will allow us to conclude the main results. Since $\sum_{j=1}^{\ell}(S_j(t) + I_j(t)) = 1$, the system (2.1) can be reduced to a $(2\ell - 1)$-dimensional SDEs, whose solution will be denoted as $\mathcal{Z}^N(t)$. We shall assume that for $1 \le i \le \ell$, the i-th coordinate of $\mathcal{Z}^N(t)$ stands for $I_i^N(t)$. Let us mention that the two following assumptions are satisfied by our model:

(H.1) the rate $\widetilde{\beta}_k(\mathcal{Z})$ is bounded, $1 \le k \le 2\ell^2$;

(H.2) $b \in \mathcal{C}^1(\mathbb{R}^{2\ell-1}; \mathbb{R}^{2\ell-1})$, and $\nabla_{\mathcal{Z}} b : \mathbb{R}^{2\ell-1} \to \mathbb{R}^{2\ell-1}$ is bounded and Lipschitz.

We define $\mathcal{Z}^{N,\alpha}(t) = N^{\alpha}(\mathcal{Z}^N(t) - \mathcal{Z}^*)$, where $\mathcal{Z}^*$ is the unique endemic equilibrium of the ODE (2.3). Our goal is to study large deviations of $\mathcal{Z}^{N,\alpha}$ at speed $a_N = N^{2\alpha-1}$.

6.1. Set-up

In this subsection, we introduce some notations which will be used in the sequel. First recall that $\mathcal{Z}(t)$, the limit in the law of large numbers, solves the ODE

$$\mathcal{Z}(t) = \mathcal{Z}(0) + \int_0^t b(\mathcal{Z}(r))dr. \tag{6.1}$$

Let $I := (I_1, \ldots, I_\ell)$ be the vector of the proportions of the subpopulation of infectious individuals. In the case $\nu_I = \nu_S$, the system (6.1) has a unique

stable equilibrium point $\mathcal{Z}^*$ (c.f. Yeo [26]), for which $I_j > 0$, $\forall 1 \le j \le \ell$. Let $\{\mathcal{M}_k, 1 \le k \le 2\ell^2\}$ be mutually independent Poisson random measures on R_+^2 with mean measure the Lebesgue measure, and let $\overline{\mathcal{M}}_k(dr, du) = \mathcal{M}_k(dr, du) - drdu$, $1 \le k \le 2\ell^2$. The process $\mathcal{Z}^N$ can be rewritten as follows

$$\mathcal{Z}^N(t) = \mathcal{Z}_N + \int_0^t b(\mathcal{Z}^N(r)) + \frac{1}{N}\sum_{k=1}^{2\ell^2} h_k \int_0^t \int_0^{\tilde{\beta}_k(\mathcal{Z}^*)} \overline{\mathcal{M}}_k(dr, du). \tag{6.2}$$

Concerning the initial condition $\mathcal{Z}_N$, we fix some $\mathcal{Z} \in \mathbb{R}^{2\ell-1}$ and start the process $\mathcal{Z}^N$ from the vector $\{\mathcal{Z}^* + \theta N^{-\alpha}\mathcal{Z}\}_N$, where $\{\mathcal{Z}\}_N := [N\mathcal{Z}]/N$.

We set

$$V^{N,\alpha}(t) = \left(\int_0^t [\nabla_{\mathcal{Z}} b(\mathcal{Z}^* + \theta N^{-\alpha}\mathcal{Z}^{N,\alpha}(t)).\nabla_{\mathcal{Z}} b(\mathcal{Z}^*)]d\theta\right)\mathcal{Z}^{N,\alpha}(t),$$

and define

$$\mathcal{Y}^N(t) = \frac{1}{N}\sum_{k=1}^{2\ell^2} h_k \int_0^t \int_0^{\tilde{\beta}_k(\mathcal{Z}^*)} \overline{\mathcal{M}}_k(dr, du), \text{ and } \mathcal{Y}^{N,\alpha}(t) = N^\alpha \mathcal{Y}^N(t).$$

Then we can rewrite $\mathcal{Z}^{N,\alpha}$ as follows

$$\mathcal{Z}^{N,\alpha}(t) = N^\alpha(\{\mathcal{Z}^* + N^{-\alpha}\mathcal{Z}\}_{N-\mathcal{Z}^*}) + \int_0^t \nabla_{\mathcal{Z}} b(\mathcal{Z}^*)\mathcal{Z}^{N,\alpha}(r)ds + \tilde{\mathcal{Y}}^{N,\alpha}(t). \tag{6.3}$$

where $\mathcal{Y}^{N,\alpha}(t) = \int_0^t V^{N,\alpha}(r)dr + \mathcal{Y}^{N,\alpha}(t)$.

Let $\mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$ denote the set of functions from $[0, T]$ into $\mathbb{R}^{2\ell-1}$ which are right continuous and have left limits at any $t \in [0, T]$. We equip $\mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$ with the topology of uniform convergence. $\mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})^*$ denote the dual space of $\mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$. For $\mathcal{Z} \in \mathbb{R}^{2\ell-1}$, let $\mathfrak{F}_{\mathcal{Z}} : \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1}) \to \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$ be the continuous map which to x

associates y the solution of the ODE

$$y(t) = \mathcal{Z} + \int_0^t \nabla_{\mathcal{Z}} b(\mathcal{Z}^*) y(s) ds + x(t)$$

and for each $N \geq 1$, $\mathfrak{F}_{\mathcal{Z}, N} : \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1}) \to \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$ be the continuous map which to x associates $\mathcal{Y}_N$ solution of the ODE

$$\mathcal{Y}_N(t) = N^{\alpha}(\{\mathcal{Z}^* + N^{-\alpha}\mathcal{Z}\}_{N-\mathcal{Z}^*}) + \int_0^t \nabla_{\mathcal{Z}} b(\mathcal{Z}^*) \mathcal{Y}_N(s) ds + x(t).$$

In what follows, we shall denote by $\mathcal{Z}^{N, \alpha}_{\mathcal{Z}_N}$ the process $\mathcal{Z}^{N, \alpha}$ starting from $\mathcal{Z}^{N, \alpha}(0) = N^{\alpha}(\{\mathcal{Z}^* + N^{-\alpha}\mathcal{Z}\}_{N-\mathcal{Z}^*})$. From (6.3), we have that $\mathcal{Z}^{N, \alpha} = \mathfrak{F}_{\mathcal{Z}, N}(\widetilde{\mathcal{Y}}^{N, \alpha})$. Then from Corollary 4.2.21 in Dembo and Zeitouni [8], large deviations of $\mathcal{Z}^{N, \alpha}$ will follow from whose of $\widetilde{\mathcal{Y}}^{N, \alpha}$. Hence it suffices to show that $\widetilde{\mathcal{Y}}^{N, \alpha}$ satisfies a Large Deviations Principle. First we need to define the rate function for our large deviations principle. Let $Q(t) := \sum_{k=1}^{2\ell^2} h_k \int_0^t \int_0^{\widetilde{\beta}_k(\mathcal{Z}^*)} \overline{\mathcal{M}}_k(dr, du)$, We define the Fenchel-Legendre transform of

$$\Lambda(\upsilon) = \frac{1}{2} \mathbb{E}[\upsilon(Q)^2]$$

$$= \sum_{k=1}^{2\ell^2} \frac{\widetilde{\beta}_k(\mathcal{Z}^*)}{2} \int_{[0, T]^2} r \wedge t \langle h_k, \upsilon \rangle(dr) \langle h_k, \upsilon \rangle(dt),$$

as

$$\Lambda^*(\phi) = \sup_{\upsilon \in (\mathbb{D}([0, T]; \mathbb{R}^{2\ell-1}))^*} \{\upsilon(\phi) - \Lambda(\upsilon)\}, \ \phi \in \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1}),$$

where here and below $\upsilon = (\upsilon_1, \upsilon_2, \ldots, \upsilon_{2\ell-1})$ is a vector of signed measures and $\langle h_k, \upsilon \rangle(dt) := \sum_{i=1}^{2\ell^2} h_k^i \upsilon_i(dt)$, h_k^i denoting the i-th coordinate of the vector h_k.

6.2. The rate function Λ^* and moderate deviations of $\mathcal{Z}^N$

In this subsection we compute the rate function Λ^* and show that the process $\widetilde{\mathcal{Y}}^{N,\alpha}$ and then also $\mathcal{Z}^{N,\alpha}$ satisfies a Large Deviations Principle. Let us set $\mathfrak{M} = \sum_{k=1}^{2\ell^2} \widetilde{\beta}_k(\mathcal{Z}^*) h_k \widetilde{\otimes} h_k$, where

$$h_k \widetilde{\otimes} h_k = \begin{pmatrix} h_k^1 h_k^1 & h_k^1 h_k^2 & \dots & h_k^1 h_k^{2\ell-1} \\ h_k^2 h_k^1 & h_k^2 h_k^2 & \dots & h_k^2 h_k^{2\ell-1} \\ \vdots & \vdots & \ddots & \vdots \\ h_k^{2\ell-1} h_k^1 & \dots & \dots & h_k^{2\ell-1} h_k^{2\ell-1} \end{pmatrix}, \text{ for all } k = 1, \dots, 2\ell^2.$$

Lemma 6.1. *$\mathfrak{M}$ is a symmetric positive definite matrix.*

Proof. For any vector $u = (u^1, u^2, \dots, u^{2\ell-1})$,

$$\begin{aligned} u^T \mathfrak{M} u &= \sum_{k=1}^{2\ell^2} \sum_{i=1}^{2\ell-1} \sum_{m=1}^{2\ell-1} \widetilde{\beta}_k(\mathcal{Z}^*) h_k^i h_k^m u^i u^m \\ &= \sum_{k=1}^{2\ell^2} \widetilde{\beta}_k(\mathcal{Z}^*) \left(\sum_{i=1}^{2\ell-1} h_k^i u^i \right)^2 \\ &\geq 0. \end{aligned} \tag{6.4}$$

Now, if $u^T \mathfrak{M} u = 0$, then $\langle h_k, u \rangle = 0$, for all $k \in \{1, \dots, 2\ell^2\}$. On the one hand, $\forall\, i \in \{1, \dots, \ell - 1\}$ there exists $k \in \{1, \dots, 2\ell^2\}$ such that $\langle h_k, u \rangle = 0$ implies $u^i = u^{\ell+i}$. On the other hand $\forall\, i \in \{1, \dots, 2\ell - 1\}$, there exists $k \in \{1, \dots, 2\ell^2\}$ such that $\langle h_k, u \rangle = 0$ implies $u^i = u^{i+1}$. These two facts implies that all coordinates of the vector u are equal. Moreover, there exists some $k \in \{1, \dots, K\}$ such that $\langle h_k, u \rangle = 0$ implies that $u^{2\ell-1} = 0$. Then $u^i = 0$, $\forall\, i \in \{1, \dots, \ell - 1\}$. □

Lemma 6.2. *For all $\phi \in (\mathcal{C}^2([0, T]))^{2\ell-1}$, such that $\phi(0) = 0$, we have*

$$\Lambda^*(\upsilon) = \frac{1}{2} \int_{[0,T]} \langle \phi'(t), \mathfrak{M}^{-1} \phi'(t) \rangle dt.$$

Proof. Let $\upsilon = (\upsilon_1, \upsilon_2, \ldots, \upsilon_{2\ell-1})$ be a vector of signed measure on $[0, T]$ and $\phi \in (\mathcal{C}^2([0, T]))^{2\ell-1}$ such that $\phi(0) = 0$. First we have

$$\langle \upsilon, \phi \rangle - \Lambda(\upsilon) = \langle \upsilon, \phi \rangle - \frac{1}{2} \int_{[0,T]^2} r \wedge t \langle \mathfrak{M}\upsilon(dr), \upsilon(dt) \rangle.$$

To find $\Lambda^*(\phi)$, we need to take the supremum over the vectors of signed measures u on $[0, T]$ of the above functional. The supremum is achieved at a signed measure u for which the gradient is equal to zero. Computing the gradient of the functional $\langle \upsilon, \phi \rangle - \Lambda(\upsilon)$ with respect to the vector of signed measures u, and equating it to zero yields

$$\phi(t) = \int_{[0,T]} r \wedge t \, \mathfrak{M}\upsilon(dr),$$

$$= \int_{[0,t]} r \, \mathfrak{M}\upsilon(dr) + t \int_{(t,T]} \mathfrak{M}\upsilon(dr), \ \forall \, t \in [0, T]. \quad (6.5)$$

Now, from (6.5), it follows that $\phi'(t) = \int_{(t,T]} \mathfrak{M}_\upsilon(dr)$. Furthermore, since

$$\phi'(T) - \phi'(T) - \int_{(t,T]} \phi''(r) dr,$$

then

$$\phi'(T) - \int_t^T \phi''(r) dr = \int_{(t,T]} \mathfrak{M}_\upsilon(dr),$$

from which we deduce that $\mathfrak{M}(\upsilon)(dt) = -\phi''(t)dt + \phi'(T)\delta_T(dt)$. M Hence

$$\upsilon(dt) = -\mathfrak{M}^{-1}\phi''(t)dt + \mathfrak{M}^{-1}\phi'(T)\delta_T(dt).$$

Substituting this signed measure in the above formula of $\langle \upsilon, \phi \rangle - \Lambda(\upsilon)$, implies that, since $\phi(0) = 0$,

$$\Lambda^*(\phi) = \frac{1}{2}\left(- \int_{[0,T]} \langle \phi(t), \mathfrak{M}^{-1}\phi^n(t) \rangle dt + \langle \phi(T), \mathfrak{M}^{-1}\phi'(T) \rangle \right)$$

$$= \int_{[0,T]} \langle \phi'(t), \mathfrak{M}^{-1}\phi^n(t) \rangle \, dt,$$

as claimed. □

Theorem 6.1. *The sequence* $\{\widetilde{\mathcal{Y}}^{N,\alpha},\ N \geq 1\}$ *satisfies the large deviations principle in* $\mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$, *equipped with the supnorm topology, with the convex, good rate function* Λ^* *and with speed* a_N, *in the sense that for any Borel subset* $\Gamma \subset D([0, T]; \mathbb{R}^{2\ell-1})$,

$$-\inf_{\phi\in\overset{\circ}{\Gamma}} \Lambda^*(\phi) \leq \liminf_{N\to\infty} a_N \log \mathbb{P}(\widetilde{\mathcal{Y}}^{N,\alpha} \in \Gamma)$$

$$\leq \limsup_{N\to\infty} a_N \log \mathbb{P}(\widetilde{\mathcal{Y}}^{N,\alpha} \in \Gamma) \leq -\inf_{\phi\in\overline{\Gamma}} \Lambda^*(\phi),$$

denoting by $\overset{\circ}{\Gamma}$, $\overline{\Gamma}$ *the interior and the closure of the set* Γ, *respectively*.

Since our multipatch stochastic model satisfies the assumptions (H.1) and (H.2), then the assumptions of Theorem 4.7 in Pardoux [20] are satisfied. We then refer the reader to this reference for the proof. □

Finally we can now derive the main result of this section, which is a consequence of Theorem 6.1 and Corollary 4.2.21 from Dembo and Zeitouni [8].

Theorem 6.2. *The collection of processes* $\{\mathcal{Z}^{N,\alpha}(t),\ 0 \leq t \leq T\}$ *satisfies a large deviations principle with speed* $a_N = N^{2\alpha-1}$ *and the good rate function*

$$I_{\mathcal{Z},T}(\phi) = \Lambda^*(\mathfrak{F}_{\mathcal{Z}}^{-1}(\phi))$$

$$= \begin{cases} \Lambda^*\left(\phi(\cdot) - \mathcal{Z} - \nabla_{\mathcal{Z}} b(\mathcal{Z}^*)\int_0^{\cdot} \phi(s)ds\right), & \text{if } \phi(0) = \mathcal{Z}; \\ +\infty, & \text{otherwise.} \end{cases}$$

More precisely, for any closed set $F \subset \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$,

$$\limsup_{N\to\infty} a_N \log \inf_{\mathcal{Z}\in\mathcal{K}} \mathbb{P}(\mathcal{Z}_{\mathcal{Z}_N}^{N,\alpha} \in F) \geq -\inf_{\phi\in F} I_{\mathcal{Z},T}(\phi).$$

For any open set $G \subset \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$,

$$\limsup_{N\to\infty} a_N \log \inf_{\mathcal{Z}\in\mathcal{K}} \mathbb{P}(\mathcal{Z}_{\mathcal{Z}_N}^{N,\alpha} \in G) \geq -\inf_{\phi\in G} I_{\mathcal{Z},T}(\phi).$$

Also, following of Corollary 5.6.15 in Dembo and Zeitouni [8], we deduce from Theorem 6.2 the following corollary.

Corollary 6.1. *Let $\mathcal{K}$ denote an arbitrary compact subset of $\mathbb{R}^{2\ell-1}$*

For any closed set $F \subset \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$,

$$\limsup_{N\to\infty} a_N \log \inf_{\mathcal{Z}\in\mathcal{K}} \mathbb{P}(\mathcal{Z}^{N,\alpha}_{\mathcal{Z}_N} \in F) \geq - \inf_{\phi\in F,\, \mathcal{Z}\in\mathcal{K}} I_{\mathcal{Z},T}(\phi).$$

For any open set $G \subset \mathbb{D}([0, T]; \mathbb{R}^{2\ell-1})$,

$$\limsup_{N\to\infty} a_N \log \inf_{\mathcal{Z}\in\mathcal{K}} \mathbb{P}(\mathcal{Z}^{N,\alpha}_{\mathcal{Z}_N} \in G) \geq - \sup_{\mathcal{Z}\in\mathcal{K}} \inf_{\phi\in G} I_{\mathcal{Z},T}(\phi).$$

6.3 Time of extinction of an epidemic

We shall use moderate deviations to estimate the extinction time of an epidemic. We define

$$V(\mathcal{Z}, \mathcal{Z}', T) = \inf_{\phi,\, \phi(0)=\mathcal{Z},\, \phi(T)=\mathcal{Z}'} I_{\mathcal{Z},T}(\phi),$$

$$V(\mathcal{Z}, \mathcal{Z}') = \inf_{T>0} (\mathcal{Z}, \mathcal{Z}', T),$$

$$\overline{V}_a = \inf_{\{\mathcal{Z}, \mathcal{Z}_{i2}=-\mathfrak{a}_i,\, 1\leq i\leq \ell\}} V(\mathcal{Z}^*, \mathcal{Z}),$$

where $\mathfrak{a} = (\mathfrak{a}_1, \mathfrak{a}_2, \ldots, \mathfrak{a}_\ell)$ in the sense $\mathfrak{a}_i > 0$ for all $i = 1, \ldots, \ell$. Denoting by $\mathcal{Z}^{N,\alpha}_{z,i}(t)$ the i-th component of $\mathcal{Z}^{N,\alpha}_z(t)$, we define

$$T^N_{z,a} := \inf\{t > 0,\, \mathcal{Z}^{N,\alpha}_{z,i}(t) \leq -\mathfrak{a}_i,\, 1 \leq i \leq \ell\}.$$

Theorem 6.3. *For $\mathfrak{a} > 0$, $\mathcal{Z} \in \mathbb{R}^{2\ell-1}$ such that $\mathcal{Z}_i > \mathfrak{a}_i$ $\forall\, i \in \{1, \ldots, \ell\}$ and any $\eta > 0$,*

$$\lim_{N\to\infty} \mathbb{P}(e^{N-2\alpha}(\overline{V}_a - \eta) < T^N_{z,\mathfrak{a}} < e^{N^{1-2\alpha}}(\overline{V}_a - \eta)) = 1$$

and

$$\lim_{N\to\infty} N^{2\alpha-1} \log \mathbb{E}(T^N_{z,a}) = \overline{V}_a.$$

This theorem is a consequence of Corollary 6.1. In fact, as shown in Britton and Pardoux [5], the main conditions are assumptions (H.1) and (H.2), that are also satisfied by our multipatch model. Recalling that $Z^{N,\alpha}(t) = N^{\alpha}(\mathcal{Z}^N(t) - z^*)$, we see that $T^N_{\mathcal{Z},\mathfrak{a}}$ is the time of extinction of the epidemic if $\mathfrak{a} = N^{\alpha}I^*$, where $I^* = (I^*_1, \ldots, I^*_\ell)$ is the vector of proportions of infectious individuals in the various patches at equilibrium.

Roughly speaking, the CLT predicts extinction in time of order 1 in the case where $\sqrt{N}\Sigma_j I^*_j$ is of order 1. According to Theorem 6.3, Moderate Deviations predicts extinction in time of order $\exp(N^{1-2\alpha}\overline{V}_a)$, if $\mathfrak{a} = N^{\alpha}I^*$ is of order 1, for some $0 < \alpha < 1/2$. If none of those is satisfied, then Large Deviations predicts extinction in time of order $\exp(N\overline{V})$, see Theorem 4.2.

If one can evaluate the quantity $\overline{V}_a$, then from Theorem 6.3, we have a good approximation of the extinction time of the epidemic. Hence, it is important to evaluate this quantity.

6.4 Optimal control problem for the computation of $\overline{V}_a$

In the homogeneous case, the deterministic SIS model can be reduced to a one dimensional ODE, and Pontryagin's maximum principle allows to find an explicit expression for $\overline{V}_a$ (see Pardoux [20]). But in our case the dimension is greater than 1, and Pontryagin's maximum principle does not solve explicitly the optimal control problem. However, this quantity can be approximated numerically with a optimal control software. Here we use the optimal control software named "Bocop" to approximate the exact values of $\overline{V}_a$. More information about the Bocop software can be found on the website https://www.bocop.org.

Recall that

$$\overline{V}_a = \inf_{\{\mathcal{Z},\, \mathcal{Z}_{i2} = -\mathfrak{a}_i,\ 1 \le i \le \ell\}} \inf_{T>0} \inf_{\phi:\phi(0)=\mathcal{Z}^*,\ \phi(T)=\mathcal{Z}} I_{\mathcal{Z}^*,\,T}(\phi).$$

The linearized ODE around the endemic equilibrium reads $\dot{\mathcal{Z}}(t) = \nabla_{\mathcal{Z}} b(\mathcal{Z}^*)\mathcal{Z}(t) + u(t)$. We remark that $\overline{V}_a$ is the minimal value of the

following optimal control problem

$$\begin{cases} \underset{u}{Min} \int_0^T \mathfrak{J}(u(t))dt \\ \dfrac{d\phi(t)}{dt} = \nabla_{\mathcal{Z}} b(z^*)\phi(t) + u(t) \\ \phi(0) = \mathcal{Z}^*,\ \phi(T) = \mathcal{Z} : \mathcal{Z}_{i2} = -\mathfrak{a}_i,\ \forall\, i \in \{1, \ldots, \ell\}, \end{cases} \tag{6.6}$$

where $\mathfrak{J}(u(t)) = \dfrac{1}{2}\langle \mathfrak{M}^{-1}u(t),\ u(t)\rangle$.

If the values of the parameters of the model are such that $R_0 > 1$, then there exists a unique globally asymptotically stable endemic equilibrium. In such case we can use the "Bocop" software to compute an approximation of $\overline{V}_a$.

Below, we give the value of $\overline{V}_a$ for some parameters in the case of two patches. For two patches, we have

$$\mathfrak{M} = \begin{pmatrix} \left(\lambda_1 \dfrac{S_1^*}{S_1^* + I_1^*} + \gamma_1 + \nu_I\right) I_2^* + \nu_I I_2^* & -\lambda_1 \dfrac{S_1^* I_1^*}{S_1^* + I_1^*} - \gamma_1 I_1^* & -\nu_1(I_1^* + I_2^*) \\ -\lambda_1 \dfrac{S_1^* I_1^*}{S_1^* + I_1^*} - \gamma_1 I_1^* & \left(\lambda_1 \dfrac{S_1^*}{S_1^* + I_1^*} + \gamma_1 + \nu_S\right) I_2^* + \nu_I(1 - S_1^* - I_2^*) & 0 \\ -\nu_1(I_1^* + I_2^*) & 0 & \lambda_2 \dfrac{I_2^*(1 - S_1^* - I_1^* - I_2^*)}{1 - S_1^* - I_1^*} + (\gamma_2 + \nu_I) I_2^* + \nu_I I_1^* \end{pmatrix}$$

and

$$\nabla_z b(z^*) = \begin{pmatrix} \lambda_1\left(\dfrac{S_1^*}{S_1^* + I_1^*}\right) - \gamma_1 - \nu_I & -\lambda_1\left(\dfrac{S_1^*}{S_1^* + I_1^*}\right)^2 & \nu_S \\ -\lambda_1\left(\dfrac{S_1^*}{S_1^* + I_1^*}\right) - \gamma_1 - \nu_S & \lambda_1\left(\dfrac{S_1^*}{S_1^* + I_1^*}\right)^2 - 2\nu_S & -\nu_S \\ -\lambda_2\left(\dfrac{I_2^*}{1 - S_1^* - I_1^*}\right)^2 + \nu_I & -\lambda_2\left(\dfrac{I_2^*}{1 - S_1^* - I_1^*}\right)^2 & -\lambda_2 \dfrac{I_2^*(1 - S_1^* - I_1^* - I_2^*)}{1 - S_1^* - I_1^*} - \gamma_2 - \nu_I \end{pmatrix}$$

The endemic equilibrium of the ODEs can be computed by using a numerical solver. Here, we used the solver "Wolfram Alpha".

Below, we carry out a sensitivity analysis to highlight the effect of the model parameters on the quasi-potential $\overline{V}_a$.

Table 9

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\mathfrak{a}$	$\overline{V}_a$
1.5	1.5	1	1	0.0007	0.0007	(2, 2)	5.78586
1.5	1.5	1	1	0.005	0.005	(2, 2)	1.85745
1.5	1.5	1	1	0.1	0.1	(2, 2)	0.32162

Table 10

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\mathfrak{a}$	$\overline{V}_a$
2.5	0.5	0.5	1.5	0.0007	0.0007	(2, 0.001)	20.3172
2.5	0.5	0.5	1.5	0.005	0.005	(2, 0.009)	19.9867
2.5	0.5	0.5	1.5	0.1	0.1	(2, 0.1)	15.7859

Table 11

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\mathfrak{a}$	$\overline{V}_a$
2	1	0.5	1.5	0.0007	0.0007	(2, 0.002)	16.8036
2	1	0.5	1.5	0.005	0.005	(2, 0.01)	16.5982
2	1	0.5	1.5	0.1	0.1	(2, 0.2)	13.9578

Table 12

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\mathfrak{a}$	$\overline{V}_a$
1.5	1.5	1	1	0.0007	0.0007	(2, 3)	30.812
1.5	1.5	1	1	0.005	0.005	(2, 3)	30.8086
1.5	1.5	1	1	0.02	0.02	(2, 3)	30.7977
1.5	1.5	1	1	0.1	0.1	(2, 3)	30.7577

Table 13

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\mathfrak{a}$	$\overline{V}_a$
1.5	1.5	1.5	0.5	0.00001	0.00001	(2, 3)	668.789
1.5	1.5	1.5	0.5	0.0003	0.0003	(2, 3)	151.915
1.5	1.5	1.5	0.5	0.002	0.002	(2, 3)	81.4161
1.5	1.5	1.5	0.5	0.1	0.1	(2, 3)	56.8567

Table 14

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\mathfrak{a}$	$\overline{V}_a$
2	1	0.5	1.5	0.00001	0.00001	(2, 3)	31644.7
2	1	0.5	1.5	0.0001	0.0001	(2, 3)	31691.8
2	1	0.5	1.5	0.0005	0.0005	(2, 3)	6380.15
2	1	0.5	1.5	0.01	0.01	(2, 3)	367.836

Table 15

λ_1	λ_2	γ_1	γ_2	ν_I	ν_S	$\mathfrak{a}$	$\overline{V}_a$
2.5	0.5	0.5	1.5	0.00001	0.00001	(2, 3)	86745.8
2.5	0.5	0.5	1.5	0.0001	0.0001	(2, 3)	86812.8
2.5	0.5	0.5	1.5	0.0005	0.0005	(2, 3)	17421.8
2.5	0.5	0.5	1.5	0.01	0.01	(2, 3)	939.331

In Table 9, both patches have the same rate of infection and recovery, and are in an endemic situation. We note that the quasi-potential $\overline{V}_a$ is a monotone decreasing function of $\nu := \nu_1 = \nu_S$, for $\mathfrak{a} = (2, 2)$. Then, in this case, increasing both the movements of susceptible and infectious individuals reduces the value of $\overline{V}_a$. Even if the components of the vector a are not equal, we note from Table 10 and 11 that $\overline{V}_a$ decreases if we increase both the movements of susceptible and infectious individuals. Moreover, infection and recovery rates on the patches are not equal, and only patch 1 is in an endemic

situation. In Table 12, $\lambda_1 = \lambda_2$, $\gamma_1 \neq \gamma_2$ and both patches are in an endemic situation. We note that the quasi-potential takes high values compared to the previous cases, and it is also a monotone decreasing function of $\nu := \nu_1 = \nu_S$. In the Tables 13, 14 and 15, only one patch is in an endemic situation. In this cases, we note that the quasi-potential takes very high values.

These examples show how heterogeneity of the environment and of the rates of movement of individuals can influence the quasi-potential $\overline{V}_a$, and then the time of extinction of the epidemic.

7. Conclusions

In our multi-patch SIS model, it is a fact that sooner or later the random fluctuations will drive the system to the disease free equilibrium, which is an absorbing subset for the stochastic Markov model, of which the deterministic model is the law of large numbers limit. The goal of the present paper was to analyse the effect of the spatial structure on the stability of the endemic equilibrium, measured by the time taken by the fluctuations to drive the system to the disease free equilibrium.

We have shown that the theoretical results (Central Limit Theorem, Large and Moderate Deviations), which allow to quantify the fluctuations around the law of large numbers limit, apply to our multi-patch model similarly as in the case of the homogeneous model. Next, we have tried to compare the fluctuations in the multi-patch model with those in the homogeneous model. We were able to show that, if the two parameters of the stochastic model (the infection and recovery rates) do not differ from one patch to another, then the variance of the limit in the CLT coincides with that in the homogeneous model. Similarly, in the Large Deviations result applied to a two-patch SIS model, the quasi–potential (which is, for large N, close to the logarithm of the extinction time divided by *N*), is close to the quasi-potential of the homogeneous model if both the infection and recovery rates are constant over the patches, and do not vary much with the rates of movements. On the contrary, if the recovery rates differ from one patch to the next, the quasi-potential takes larger values, which are sensitive to the rates of movements, apparently monotone decreasing as a function of those rates. In the moderate deviations regime, the quasi-potential is sensitive to the

rates of movements in all cases (and again monotone decreasing), and it is significantly larger when the infection and recovery rates differ, in such a way that the endemic equilibrium would be stable in one, and unstable in the other patch, would they be isolated.

Those quantitative comparisons should be studied further. In particular, it would be interesting to know how the variance in the CLT is modified when the infection and recovery rates vary from one patch to another. Does it necessarily tend to increase in such situations, compared to the case of homogeneous parameters? This unfortunately can probably be studied only numerically, for a few specific sets of parameters.

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