Electronic Journal of Qualitative Theory of Differential Equations
2017, No. **6**, 1–12; doi: 10.14232/ejqtde.2017.1.6 http://www.math.u-szeged.hu/ejqtde/

A stochastic model of nosocomial epidemics in hospital intensive care units

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Received 3 October 2016, appeared 25 January 2017
Communicated by Mihály Kovács

Abstract. A stochastic differential equation model is developed to portray an epidemic of antibiotic resistant infections in a hospital intensive care unit. The dynamical behaviors of the solutions of this model are analyzed and numerical simulations are given to illustrate the dynamics of the solutions.

Keywords: stochastic differential equation, nosocomial infection, asymptotic behavior.

2010 Mathematics Subject Classification: 92D30, 60H10, 92C60.

1 Introduction

Nosocomial (hospital-acquired) infections caused by antibiotic resistant bacteria are a major global public health problem. Numerous factors contribute to the emergence and spread of these bacterial infections in hospital settings. To fully understand the impact of different factors, various mathematical models have been developed [3,4,6,8,13,14]. Many of these models are formulated as ordinary differential equations (ODEs). These models divide patients and health care workers (HCW) into different compartments, such as infected or uninfected patients and contaminated or uncontaminated HCW. The rate of change of each compartment is described by an ODE under the assumption that the interactions among different groups are deterministic. These models have been applied to the population-level analysis of the spread of nosocomial epidemics [4,5,14].

One drawback of ODE models is that they cannot directly reflect randomness in epidemic events. For instance, the parameters in ODE models should be viewed as averages. Consequently, ODE models can only describe average behavior. Hence there is a need to formulate randomness more precisely in nosocomial models. This is especially true for nosocomial models in hospital subunits, such as an intensive care unit (ICU), which are usually very small, and where randomness may have large influence. Thus, continuous-time Markov chain models (CTMC) and individual based models (IBM) have been used to model nosocomial

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infections in many studies [11, 12, 14]. Despite the utility of simulations of CTMC and IBM, analytical results are lacking due to the inherent complexity of these systems.

A modeling framework closer to ODE, which incorporates randomness and offers analytic tractability, are stochastic differential equations (SDEs). SDEs are useful for modeling biological phenomena, and have been applied to many investigations [2, 7, 10, 15]. However, to the best of our knowledge, little work has been done on modeling nosocomial infections with SDE. Motivated by this problem, we will develop and analyze SDE models of nosocomial epidemics in an ICU.

This paper is organized as follows: in Section 2 we formulate the SDE model, in Section 3 we analyze the model, in Section 4 we provide numerical simulations of the model, and in Section 5 we discuss conclusions derived from the model.

2 Derivation of the stochastic model

In [13] an antibiotic resistant infection epidemic in an ICU is treated with both IBM and ODE approaches. The epidemic population was divided into the following seven compartments:

- uninfected patients (P_U);
- patients infected with a nonresistant bacterial strain not on antibiotics specific to this strain $(P_{N_{\text{off}}})$;
- patients infected with a nonresistant bacterial strain on antibiotics specific to this strain $(P_{N_{\text{on}}})$;
- patients infected with the resistant strain of this bacteria (P_R);
- uncontaminated HCW (H_U);
- HCW contaminated with the nonresistant bacterial strain (H_N);
- and HCW contaminated with the resistant strain (H_R).

Then a system involving seven ODEs was derived; see [13, Eq. (1)–(7)]. That system was further simplified based on certain assumptions and reduced to a model involving three ODEs; the reader is referred to [13, Section 3] for the details.

In this section, we first use the idea similar to [13] to build an ODE model. To simplify the problem, we combine $P_{N_{\text{off}}}$ and $P_{N_{\text{on}}}$ defined above as a single compartment: patients infected with a nonresistant bacterial strain (P_N). All other compartments remain the same. The transmission among the compartments is described by Figure 2.1.

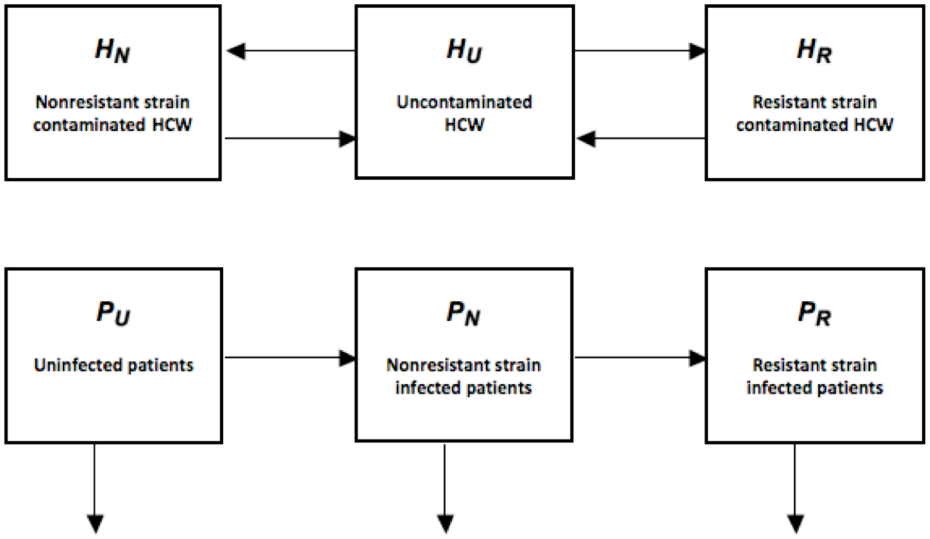


Figure 2.1: Schematic diagram of the model compartments.

Based on Figure 2.1, a system involving six ODEs is derived as follows:

$$P'_U(t) = \frac{1}{T_N}P_N(t) + \frac{1}{T_R}P_R(t) - \frac{N_H\pi_N H_N(t)}{N_P T_V N_H}P_U(t), \tag{2.1}$$

$$P'_N(t) = \frac{N_H\pi_N H_N(t)}{N_P T_V N_H}P_U(t) - \frac{N_H\pi_R H_R(t)}{N_P T_V N_H}P_N(t) - \frac{1}{T_N}P_N(t), \tag{2.2}$$

$$P'_R(t) = \frac{N_H\pi_R H_R(t)}{N_P T_V N_H}P_N(t) - \frac{1}{T_R}P_R(t), \tag{2.3}$$

$$H'_U(t) = \frac{1}{T_V}H_N(t) + \frac{1}{T_V}H_R(t) - \frac{\omega_N P_N(t)}{T_V N_P}H_U(t) - \frac{\omega_R P_R(t)}{T_V N_P}H_U(t), \tag{2.4}$$

$$H'_N(t) = \frac{\omega_N P_N(t)}{T_V N_P}H_U(t) - \frac{1}{T_V}H_N(t), \tag{2.5}$$

$$H'_R(t) = \frac{\omega_R P_R(t)}{T_V N_P}H_U(t) - \frac{1}{T_V}H_R(t), \tag{2.6}$$

where N_P, N_H, T_V, T_N, T_R, ω_N, ω_R, π_N, π_R, are all positive constant parameters. The model assumptions and meanings of parameters may be summarized as follows (the reader is referred to [13] for the details).

1. There are N_P patients and N_H HCWs in the ICU. The units of time are days.

2. All patients who exit the ICU are immediately replaced by uninfected patients. The exit rate of an uninfected patient is not specified as another uninfected patient replaces such a patient immediately.

3. T_N is the average time of the length of stay (LOS) of a patient infected with the nonresistant strain. It is assumed this value is additional to any time already spent in the ICU as an uninfected patient. $1/T_N$ is interpreted as the exit rate of a patient infected with the nonresistant strain.

4. T_R is the average time of the LOS of a patient infected with the resistant strain. It is assumed this value is additional to any time already spent in the ICU as a patient

uninfected plus time spent infected with the nonresistant strain. $1/T_R$ is interpreted as the exit rate of a patient infected with the resistant strain.

5. T_V is the average time (in days) of a patient-HCW visit. $N_H/(N_P T_V)$ is the average number of visits received by a patient per day.

6. During each visit of a patient by an uncontaminated HCW there is a probability ω_N of HCW contamination by a patient infected with a nonresistant strain and a probability ω_R of HCW contamination by a patient infected with a resistant strain. A contaminated HCW remains contaminated only for the subsequent next visit to a patient.

7. During each visit of an uninfected patient by a HCW contaminated with the nonresistant strain, there is a probability π_N that the patient is infected with the nonresistant strain. During each visit of a patient infected with the nonresistant strain by a HCW contaminated with the resistant strain, there is a probability π_R that the patient is infected with the resistant strain.

Implicitly assumed in the model is that patients infected with the non-resistant strain, $P_N(t)$, are prescribed antibiotics and the resistant strain can only infect patients on antibiotics. The justification for this assumption is that antibiotics provide a favorable environment for the resistant strain to infect a patient and, in the absence of antibiotics, the resistant strain cannot establish an infection. Additionally, within-host mutation from the non-resistant strain to the resistant strain is assumed to be sufficiently rare, so that infected patients (on antibiotics) only become resistant through exposure to the circulating resistant strain via contaminated HCW. Since the populations of patients and HCW remain constant in time, equations (2.1) and (2.4) can be eliminated, and the following system is obtained:

$$P_N'(t) = \frac{\pi_N H_N(t)}{N_P T_V}(N_P - P_N(t) - P_R(t)) - \frac{\pi_R H_R(t)}{N_P T_V} P_N(t) - \frac{P_N(t)}{T_N}, \tag{2.7}$$

$$P_R'(t) = \frac{\pi_R H_R(t)}{N_P T_V} P_N(t) - \frac{P_R(t)}{T_R}, \tag{2.8}$$

$$H_N'(t) = \frac{\omega_N P_N(t)}{T_V N_P}(N_H - H_N(t) - H_R(t)) - \frac{H_N(t)}{T_V}, \tag{2.9}$$

$$H_R'(t) = \frac{\omega_R P_R(t)}{T_V N_P}(N_H - H_N(t) - H_R(t)) - \frac{H_R(t)}{T_V}, \tag{2.10}$$

Further since the time-scale of patient-HCW visits is much faster than patient turnover, it is assumed in [13] that

(H1) the HCW compartments are in a quasi-steady state, i.e.,

$$H_N'(t) = H_R'(t) \equiv 0, \qquad t \geq 0.$$

Then, by (2.5), (2.6), and (H1),

$$\begin{cases} H_N(t) = \dfrac{\omega_N N_H P_N(t)}{N_P + \omega_N P_N(t) + \omega_R P_R(t)}, \\ H_R(t) = \dfrac{\omega_R N_H P_R(t)}{N_P + \omega_N P_N(t) + \omega_R P_R(t)}. \end{cases} \tag{2.11}$$

Hence, System (2.7)–(2.10) is simplified to two equations:

$$P_N'(t) = \frac{N_H\pi_N\omega_N P_N(t)(N_P - P_N(t) - P_R(t))}{N_P T_V(N_P + \omega_N P_N(t) + \omega_R P_R(t))} - \frac{N_H\pi_R\omega_R P_R(t)P_N(t)}{N_P T_V(N_P + \omega_N P_N(t) + \omega_R P_R(t))} - \frac{P_N(t)}{T_N}, \tag{2.12}$$

$$P_R'(t) = \frac{N_H\pi_R\omega_R P_R(t)P_N(t)}{N_P T_V(N_P + \omega_N P_N(t) + \omega_R P_R(t))} - \frac{P_R(t)}{T_R}. \tag{2.13}$$

It is clear that (H1) plays an important role to derive System (2.12), (2.13). However, (H1) is a simplification of large scale uncertainty in random events. Thus, it is more realistic to allow H_N and H_R to vary from their quasi-steady states. We therefore weaken assumption (H1) by introducing random perturbations into (2.11):

$$\begin{cases} H_N(t) = \dfrac{\omega_N N_H P_N(t)}{N_P + \omega_N P_N(t) + \omega_R P_R(t)}(1 + \sigma_1\dot{B}(t)), \\ H_R(t) = \dfrac{\omega_R N_H P_R(t)}{N_P + \omega_N P_N(t) + \omega_R P_R(t)}(1 + \sigma_2\dot{B}(t)), \end{cases} \tag{2.14}$$

where $\dot{B}$ is a white noise, and $\sigma_1 \geq 0$ and $\sigma_2 \geq 0$ are the intensities of the noise. Thus, by (2.7), (2.8), and (2.14), we obtain the following SDE model:

$$dP_N(t) = f_1(P_N(t), P_R(t))dt + g_1(P_N(t), P_R(t))dB(t), \tag{2.15}$$

$$dP_R(t) = f_2(P_N(t), P_R(t))dt + g_2(P_N(t), P_R(t))dB(t), \tag{2.16}$$

where

$$f_1(x,y) = \frac{N_H\pi_N\omega_N x(N_P - x - y)}{N_P T_V(N_P + \omega_N x + \omega_R y)} - \frac{N_H\pi_R\omega_R xy}{N_P T_V(N_P + \omega_N x + \omega_R y)} - \frac{x}{T_N}, \tag{2.17}$$

$$f_2(x,y) = \frac{N_H\pi_R\omega_R xy}{N_P T_V(N_P + \omega_N x + \omega_R y)} - \frac{y}{T_R}, \tag{2.18}$$

$$g_1(x,y) = \frac{\sigma_1 N_H\pi_N\omega_N x(N_P - x - y)}{N_P T_V(N_P + \omega_N x + \omega_R y)} - \frac{\sigma_2 N_H\pi_R\omega_R xy}{N_P T_V(N_P + \omega_N x + \omega_R y)}, \tag{2.19}$$

$$g_2(x,y) = \frac{\sigma_2 N_H\pi_R\omega_R xy}{N_P T_V(N_P + \omega_N x + \omega_R y)}, \tag{2.20}$$

and $B(t)$ is a standard Brownian motion.

Remark 2.1. The solutions P_N and P_R of System (2.15), (2.16) are two continuous stochastic processes defined on a probability space $(\Omega, \mathcal{A}, \mathcal{P})$. Let $\mathbb{T}$ be an interval in time. Then both $P_N : \mathbb{T} \times \Omega \to \mathbb{R}$ and $P_R : \mathbb{T} \times \Omega \to \mathbb{R}$ are functions of two variables $t \in \mathbb{T}$ and $\omega \in \Omega$. The normal convention is that the variable ω is often suppressed; see for example [1] for the details. In the sequel, we will use $P_N(t)$ and $P_R(t)$ to denote the solutions of System (2.15), (2.16). ω is only included as needed.

Other parameters in the model, such as transmission probabilities, contact or removal rates, may also vary randomly. However, we leave this for future research and only consider random perturbations of the quasi-steady states for contaminated HCW. The inclusion of random perturbations in these terms reflects the inherent uncertainty in the quasi-steady state assumption. The fast dynamics associated with HCW contamination and decontamination

which allow for the quasi-steady state assumption, also can lead to high-frequency noise when stochasticity is included. Indeed, in multiple types of stochastic models of nosocomial infections, HCW contamination is highly variable on small intervals of time [11,12,14]. Thus, it seems that equations in (2.14) are an effective way to introduce random perturbations, while also allowing for analysis of a reduced model afforded by the quasi-steady state assumption.

3 Analysis of the solutions

We first consider the positivity of solutions of System (2.15), (2.16). Using an idea similar to [7, Theorem 4.1], we can prove the following theorem:

Theorem 3.1. *Let* (P_N, P_R) *be the solution of* (2.15), (2.16) *starting from the initial value* $(P_N^{[0]}, P_R^{[0]}) \in \mathbb{R}^2_{++}$ *with* $\mathbb{R}_{++} = (0,\infty)$. *Then* $(P_N(t), P_R(t))$ *remains in* $\mathbb{R}^2_{++}$ *with probability* 1, *i.e.,* $P_N(t) > 0$ *and* $P_R(t) > 0$ *for all* $t \geq 0$ *almost surely (a.s.).*

Proof. Since f_1, f_2, g_1, and g_2 are locally Lipschitz continuous, for any initial value $(P_N^{[0]}, P_R^{[0]}) \in \mathbb{R}^2_{++}$, there exists a unique local solution $(P_N(t), P_R(t))$ on $[0, \tau_e)$, where τ_e is the explosion time. Let $k_0 > 0$ be large enough so that $P_N^{[0]} \in (1/k_0, k_0)$ and $P_R^{[0]} \in (1/k_0, k_0)$. For any $k \geq k_0$, define the stopping time by

$$\tau_k = \inf\{t \in [0,\tau_e) \mid P_N(t) \notin (1/k,k) \text{ or } P_R(t) \notin (1/k,k)\}.$$

Note that if $\tau_e < \infty$, then $\{t \in [0,\tau_e) \mid P_N(t) \notin (1/k,k) \text{ or } P_R(t) \notin (1/k,k)\} \neq \emptyset$. Clearly, for any $k \geq k_0$, $\tau_k \leq \tau_e$, and τ_k is increasing. Let $\tau_\infty = \lim_{k\to\infty} \tau_k$. Then we have $\tau_\infty \leq \tau_e$. If we can prove that $\tau_\infty = \infty$ a.s., so is τ_e. Hence System (2.15), (2.16) has a unique global solution which remains in $\mathbb{R}^2_{++}$ a.s.

Now we will prove $\tau_\infty = \infty$ a.s. Assume the contrary. There exist $T > 0$ and $\varepsilon \in (0,1)$ such that

$$\mathcal{P}\{\tau_\infty \leq T\} > \varepsilon.$$

Hence there exists $k_1 \geq k_0$ such that

$$\mathcal{P}\{\tau_k \leq T\} \geq \varepsilon \quad \text{for all} \quad k \geq k_1.$$

Let $\Omega_k = \{\tau_k \leq T\}$. For any $\omega \in \Omega_k$, at least one of the follows must hold:

$$\begin{aligned} P_N(\tau_k,\omega) &= k, \qquad P_N(\tau_k,\omega) = 1/k, \\ P_R(\tau_k,\omega) &= k, \qquad P_R(\tau_k,\omega) = 1/k. \end{aligned} \tag{3.1}$$

Define $V_1 : \mathbb{R}^2_{++} \to \mathbb{R}_{++}$ by

$$V_1(x,y) = x + 1 - \ln(x) + y + 1 - \ln(y).$$

It is easy to see that $V_1(x,y) \geq 0$ on $\mathbb{R}^2_{++}$. Furthermore, (3.1) implies that

$$V_1(P_N(\tau_k,\omega), P_R(\tau_k,\omega)) \geq \min\{k + 1 - \ln(k),\ 1/k + 1 - \ln(1/k)\}. \tag{3.2}$$

By (2.15), (2.16), and Itô's formula,

$$dV_1(P_N(t),P_R(t)) = F(P_N(t), P_R(t))dt + G(P_N(t), P_R(t))dB(t),$$

where F and G are defined by

$$F(x,y) = \left(1-\frac{1}{x}\right) f_1(x,y) + \left(1-\frac{1}{y}\right) f_2(x,y) + \frac{g_1^2(x,y)}{2x^2} + \frac{g_2^2(x,y)}{2y^2},$$
$$G(x,y) = \left(1-\frac{1}{x}\right) g_1(x,y) + \left(1-\frac{1}{y}\right) g_2(x,y),$$

with f_1, f_2, g_1, and g_2 defined by (2.17)–(2.20).

After some computation, we have

$$dV_1(P_N(t), P_R(t)) \le (C_0 + C_1(P_N(t) + P_R(t)))\, dt + G(P_N(t), P_R(t))dB(t),$$

where

$$\begin{aligned} C_0 = {} & \frac{N_H\pi_N}{T_V} + \frac{N_H\pi_N}{N_P T_V} + \frac{N_H\pi_N\omega_N}{N_P T_V\omega_R} + \frac{N_H\pi_R}{N_P T_V} + \frac{1}{T_N} + \frac{1}{T_R} + \frac{3}{2}\left(\frac{\sigma_1 N_H\pi_N\omega_N}{N_P T_V}\right)^2 \\ & + \frac{3}{2}\left(\frac{\sigma_1 N_H\pi_N}{N_P T_V}\right)^2 + \frac{3}{2}\left(\frac{\sigma_1 N_H\pi_N\omega_N}{N_P T_V\omega_R}\right)^2 + \frac{1}{2}\left(\frac{\sigma_2 N_H\pi_R}{N_P T_V}\right)^2 \\ & + \frac{1}{2}\left(\frac{\sigma_2 N_H\pi_R\omega_R}{N_P T_V\omega_N}\right)^2 + \frac{\sigma_1\sigma_2 N_H^2\pi_N\pi_R}{(N_P T_V)^2} + \frac{\sigma_1\sigma_2 N_H^2\pi_N\pi_R\omega_N}{(N_P T_V)^2\omega_R}, \\ C_1 = {} & \frac{N_H\pi_R}{N_P T_V}. \end{aligned}$$

By using the fact that $x \le 2(x+1-\ln(x))$, we have

$$\begin{aligned} dV_1(P_N(t), P_R(t)) \le {} & [C_0 + 2C_1(P_N(t) + 1 - \ln(P_N(t)) + P_R(t) + 1 - \ln(P_R(t)))]\, dt \\ & + G(P_N(t), P_R(t))dB(t) \\ \le {} & C_2\,(1 + V_1(P_N(t), P_R(t)))\, dt + G(P_N(t), P_R(t))dB(t), \end{aligned}$$

where $C_2 = \max\{C_0,\ 2C_1\}$. Then for any $t_1 \le T$, we have

$$\int_0^{\tau_k\wedge t_1} dV_1(P_N(t), P_R(t)) \le \int_0^{\tau_k\wedge t_1} C_2\,(1 + V_1(P_N(t), P_R(t)))\, dt + \int_0^{\tau_k\wedge t_1} G(P_N(t), P_R(t))dB(t),$$

where $a \wedge b := \min\{a, b\}$. Hence,

$$\begin{aligned} V_1(P_N(\tau_k\wedge t_1), P_R(\tau_k t_1)) \le {} & V_1(P_N^{[0]}, P_R^{[0]}) + \int_0^{\tau_k\wedge t_1} C_2\,(1 + V_1(P_N(t), P_R(t)))\, dt \\ & + \int_0^{\tau_k\wedge t_1} G(P_N(t), P_R(t))dB(t). \end{aligned}$$

Taking the expectation on both sides, we have

$$\begin{aligned} & E[V_1(P_N(\tau_k\wedge t_1), P_R(\tau_k t_1))] \\ & \le V_1(P_N^{[0]}, P_R^{[0]}) + E\left[\int_0^{\tau_k\wedge t_1} C_2\,(1 + V_1(P_N(t), P_R(t)))\, dt\right] \\ & \le V_1(P_N^{[0]}, P_R^{[0]}) + C_2 T + C_2 E\left[\int_0^{\tau_k\wedge t_1} V_1(P_N(t), P_R(t))dt\right] \\ & \le V_1(P_N^{[0]}, P_R^{[0]}) + C_2 T + C_2 E\left[\int_0^{t_1} V_1(P_N(\tau_k\wedge t), P_R(\tau_k\wedge t))dt\right] \\ & = V_1(P_N^{[0]}, P_R^{[0]}) + C_2 T + C_2\int_0^{t_1} E[V_1(P_N(\tau_k\wedge t), P_R(\tau_k\wedge t))]dt. \end{aligned}$$

Then by the Gronwall inequality, we have

$$E[V_1(P_N(\tau_k \wedge t_1), P_R(\tau_k t_1))] \leq (V_1(P_N^{[0]}, P_R^{[0]}) + C_2 T)\exp(C_2 t_1) \leq C_3 \tag{3.3}$$

with $C_3 := (V_1(P_N^{[0]}, P_R^{[0]}) + C_2 T)\exp(C_2 T)$.

By (3.2) and (3.3), for $k \geq k_1$, we have

$$\begin{aligned} C_3 &\geq E[1_{\Omega_k(\omega)} V_1(P_N(\tau_k, \omega), P_R(\tau_k, \omega))] \\ &\geq \varepsilon([k+1-\ln(k)] \wedge [1/k+1-\ln(1/k)]), \end{aligned}$$

where 1_{Ω_k} is the indicator function. It is easy to see that $[k+1-\ln(k)] \wedge [1/k+1-\ln(1/k)] \to \infty$ as $k \to \infty$, which contradicts $C_3 < \infty$. Therefore, $\tau_\infty = \infty$ a.s. □

Next, we consider the stability of the trivial solution $(0,0)$ of (2.15), (2.16). In the sequel, let $P_N(t) = P_N(t; P_N^{[0]})$ and $P_R(t) = P_R(t; P_R^{[0]})$ be the solutions of (2.15) and (2.16) starting from the initial value $(P_N^{[0]}, P_R^{[0]})$. Define

$$R_0 = \frac{N_H T_N \pi_N \omega_N}{N_P T_V}. \tag{3.4}$$

Theorem 3.2. *When $R_0 < 1$, the trivial solution of (2.15), (2.16) is almost surely exponentially stable in probability, i.e.,*

$$\limsup_{t\to\infty} \frac{\ln|P_N(t; P_N^{[0]}) + P_R(t; P_R^{[0]})|}{t} < 0 \quad a.s.$$

for any $(P_N^{[0]}, P_R^{[0]}) \in \mathbb{R}^2_{++}$.

Proof. For any initial value $(P_N^{[0]}, P_R^{[0]}) \in \mathbb{R}^2_{++}$, by Theorem 3.1, System (2.15), (2.16) has a unique solution (P_N, P_R) that remains in $\mathbb{R}_{++}$ with probability 1. By (2.15), (2.16), we have

$$d(P_N(t) + P_R(t)) = f_3(P_N(t), P_R(t))dt + g_3(P_N(t), P_R(t))dB(t), \tag{3.5}$$

where

$$f_3(x,y) = \frac{N_H \pi_N \omega_N x(N_P - x - y)}{N_P T_V (N_P + \omega_N x + \omega_R y)} - \frac{x}{T_N} - \frac{y}{T_R}, \tag{3.6}$$

$$g_3(x,y) = \frac{\sigma_1 N_H \pi_N \omega_N x(N_P - x - y)}{N_P T_V (N_P + \omega_N x + \omega_R y)}. \tag{3.7}$$

Define $V_2 : \mathbb{R}^2_{++} \to \mathbb{R}$ by $V_2(x,y) = \ln(x+y)$. Then by (3.4)–(3.7) and Itô's formula,

$$\begin{aligned} dV_2(P_N(t), P_R(t)) &= \left[\frac{f_3(P_N(t), P_R(t))}{P_N(t) + P_R(t)} - \frac{1}{2}\left(\frac{g_3(P_N(t), P_R(t))}{P_N(t) + P_R(t)}\right)^2\right]dt + \frac{g_3(P_N(t), P_R(t))}{P_N(t) + P_R(t)}dB(t) \\ &= \left[\frac{1}{P_N(t) + P_R(t)}\left(\frac{R_0 P_N(t) N_P}{T_N(N_P + \omega_N P_N(t) + \omega_R P_R(t))}\right.\right. \\ &\quad \left. - \frac{N_H \pi_N \omega_N P_N(t)(P_N(t) + P_R(t))}{N_P T_V (N_P + \omega_N P_N(t) + \omega_R P_R(t))} - \frac{P_N(t)}{T_N} - \frac{P_R(t)}{T_R}\right) \\ &\quad \left. - \frac{1}{2}\left(\frac{g_3(P_N(t), P_R(t))}{P_N(t) + P_R(t)}\right)^2\right]dt + \frac{g_3(P_N(t), P_R(t))}{P_N(t) + P_R(t)}dB(t). \end{aligned}$$

Since $R_0 < 1$, P_N and P_R are positive with probability 1, we have

$$\begin{aligned} dV_2(P_N(t), P_R(t)) \leq & \left[\frac{1}{P_N(t)+P_R(t)}\left(R_0\frac{P_N(t)}{T_N} - \frac{P_N(t)}{T_N} - \frac{P_R(t)}{T_R}\right)\right]dt + \frac{g_3(P_N(t),P_R(t))}{P_N(t)+P_R(t)}dB(t) \\ \leq & \left[\frac{1}{P_N(t)+P_R(t)}\left(-C_4P_N(t) - C_4P_R(t)\right)\right]dt + \frac{g_3(P_N(t),P_R(t))}{P_N(t)+P_R(t)}dB(t) \\ = & -C_4dt + \frac{g_3(P_N(t),P_R(t))}{P_N(t)+P_R(t)}dB(t), \end{aligned}$$

where $C_4 = \min\{(1-R_0)/T_N, 1/T_R\} > 0$. By the definition of V_2, we have

$$d(\ln(P_N(t)+P_R(t))) \leq -C_4dt + \frac{g_3(P_N(t),P_R(t))}{P_N(t)+P_R(t)}dB(t). \tag{3.8}$$

Note that by the law of the iterated logarithm (see for example, [9, Theorem 1.4.2]),

$$\limsup_{t\to\infty}\frac{|B(t)|}{t} = 0 \quad a.s.$$

Then by (3.8), we have

$$\limsup_{t\to\infty}\frac{\ln(P_N(t)+P_R(t))}{t} \leq -C_4 < 0 \quad a.s.,$$

i.e., $(0,0)$ is almost surely exponentially stable. □

Remark 3.3. By the summary of parameters given in Section 2,

- T_N is the average time of LOS of a patient infected with the nonresistant strain;
- $N_H/(N_PT_V)$ is the average number of visits received by a patient per day;
- ω_N is the probability of an uncontaminated HCW contamination by a patient infected with a nonresistant strain during each visit;
- π_N is the probability that an uninfected patient is infected with the nonresistant strain during each visit by a HCW contaminated with the nonresistant strain.

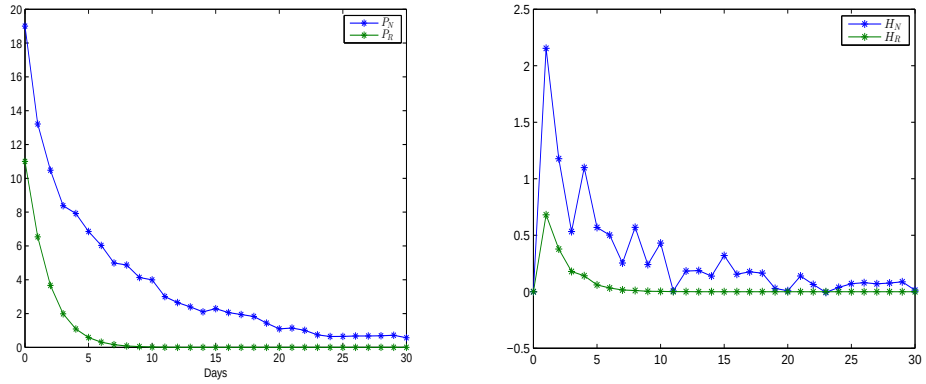
Therefore by (3.4), R_0 relates to these 4 factors. Indeed, R_0 can be interpreted as the number of contacts between HCW and a patient infected with nonresistant strain during the infectious period, $T_NN_H/(N_PT_V)$, multiplied by the probability HCW contamination and subsequent transmission during visit with next patient in wholly susceptible population, $\omega_N\pi_N$. Furthermore, Theorem 3.2 enlightens us that one way to control the spread of the epidemic in an ICU is to reduce the values of these four factors, especially the probabilities ω_N and π_N.

Remark 3.4. By Theorems 3.1 and 3.2 and their proofs, we know that the noise intensities σ_1 and σ_2 do not affect the positivity of solutions and the almost surely exponential stability of the trivial solution of (2.15), (2.16) when $R_0 < 1$.

4 Numerical simulations

In this section, we use numerical simulations to verify the results obtained in Section 3. The values of the parameters of (2.15), (2.16) and the initial values in the following examples are chosen for illustration purpose and are not from actual ICU data.

Example 4.1. Let $N_P = 30$, $N_H = 10$, $T_V = 1/12$, $\pi_N = 0.2$, $\omega_N = 0.3$, $\omega_R = 0.2$, $T_N = 4$, $T_R = 2$, $\sigma_1 = 0.5$, and $\sigma_2 = 0.2$. It is easy to see that $R_0 = 0.96 < 1$. Then by Theorems 3.1 and 3.2, all the solutions of System (2.15), (2.16) remain in $\mathbb{R}^2_{++}$ and the trivial solution is almost surely exponentially stable in probability. Simulation is performed by Matlab. A sample path with the initial condition $(19, 11)$ is given in Figure 4.1. Phase portraits of 12 solutions with different initial conditions are given in Figure 4.2.



(a) (b)

Figure 4.1: (a) Sample path of $P_N(t)$ (blue) and $P_R(t)$ (green) with the initial condition $(19, 11)$ when $R_0 < 1$. (b) Plot of the random perturbations about the HCW quasi-steady state for this example, i.e. $H_N(t)$ (blue) and $H_R(t)$ (green) in equation 2.14. The parameter values are stated in the text for Example 4.1.

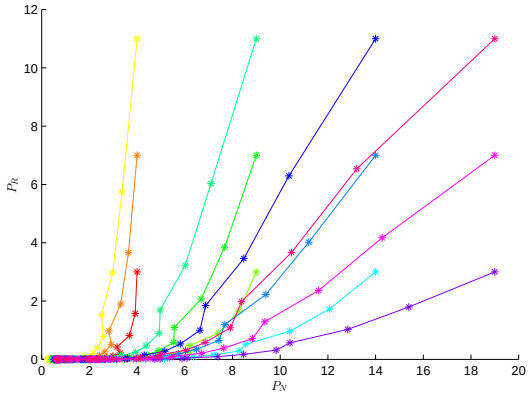
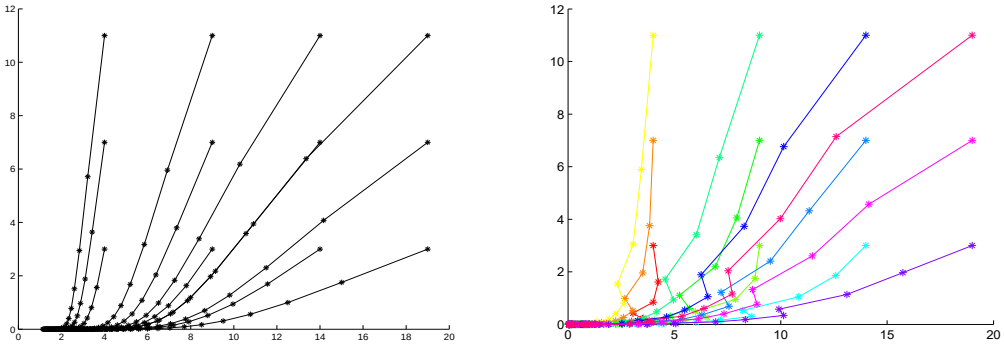


Figure 4.2: Phase portraits of solutions with different initial conditions when $R_0 < 1$.

Example 4.2. We also investigate the effect of varying the intensities σ_1 and σ_2 when $R_0 < 1$ in Figure 4.3. By Theorems 3.1 and 3.2, the positivity and convergence to the disease-free equilibrium are not affected, but observe in the figures that the amplitude of random oscillations in the transient dynamics increases with σ_1 and σ_2.



(a) (b)

Figure 4.3: Phase portraits of solutions with different initial conditions when $R_0 < 1$ and (a) $\sigma_1 = 0.01$ and $\sigma_2 = 0.01$, (b) $\sigma_1 = 1.1$ and $\sigma_2 = 1.0$. The other parameter values are as in Figure 4.2.

We have also carried out numerical simulations when $R_0 > 1$. Results show that the solutions will approach certain stationary solutions, which depend on another reproduction number R_{01}. This work will appear in another paper.

5 Conclusions

In this paper we derive a SDE model of an antibiotic resistant infection epidemic in a hospital ICU. The positivity of solutions and almost surely exponential stability of the trivial solution are proved, when the reproduction number $R_0 < 1$. These results are then illustrated by numerical simulations. These behaviors are consistent with the results obtained in [13]. This concurrence suggests that we may control the spread of nosocomial epidemics by adjusting parameters such as π_N, π_R (the probabilities of patient infection due to patient-HCW visits) or ω_N, ω_R (the probabilities of HCW contamination due to patient-HCW visits). Our work demonstrates that SDE models are useful for investigating nosocomial epidemics, since SDE models can better reflect the uncertainty and randomness that occur in actual ICU settings.

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