Journal of Statistical Physics (2023) 190:144
https://doi.org/10.1007/s10955-023-03157-9

Stochastic Modeling of Bacterial Population Growth with Antimicrobial Resistance

Mahmoud B. A. Mansour[1]

Received: 16 November 2022 / Accepted: 3 August 2023 / Published online: 18 August 2023

Abstract
In this paper we consider a stochastic model of bacterial population growth with antimicrobial resistance under the influence of random fluctuations. We analyze the model for the problem of persistence and extinction of bacterial cells. This analysis shows asymptotic extinction and conditional persistence for growing population. Moreover, we perform computer simulations in order to illustrate the model behavior. The model results have important implications for the eradication of bacterial cells and the emergence of resistance.

Keywords Stochastic model · Bacterial growth · Persistence · Extinction

1 Introduction

The dynamics of growth of bacteria and other microbes treated with antibiotic drugs is complex and multifaced. For a recent study see [1], in which the authors used a compartmental model to explore three scenarios by which bacteria develop antimicrobial resistance: point mutations, plasmid mediated horizontal gene transfer via conjugation, and either mutation or horizontal gene transfer resulting in resistance to the same class of antibiotic, using examples motivated by a study of *Escherichia coli*. Other studies can be found in [2, 3]. Authors of [2] characterized and built a model of the inoculum effect in *E. coli* cultures using a large variety of antimicrobials, where the outcome of a antibiotic treatment on the growth capacity of bacteria is largely dependent on the inoculum effect. In [3], the authors used a theoretical model to predict the dynamical response of a bacterial cell to a time-dependent dose of ribosome-targeting antibiotic.

Besides, it was found that bactericidal drugs induce demographic and environmental stochasticity, and thus the population size fluctuates over time [4, 5]. Authors of [4] used the Markovian birth-and-death model to demonstrate the stochastic nature of eradicating bacteria with antibiotics. In [5], stochastic response of bacterial cells to antibiotics was justified and its mechanisms and implications for population and evolutionary dynamics were shown. Also, in

Communicated by Lei-Han Tang.

✉ Mahmoud B. A. Mansour
m.mansour4@hotmail.com

[1] Department of Mathematics, Faculty of Science, South Valley University, Qena 83523, Egypt

[6], the emergence of drug resistance both in bacterial colonies and in malignant tumors was discussed. Particularly, it was shown that individual resistant mutants emerge randomly during the birth events of an exponentially growing sensitive population. Overall, many factors can affect bacterial susceptibility to antibiotics such as cell-to-cell heterogeneity as well as mutations, which lead to the stochastic growth and stochastic fluctuations in population size. These fluctuations have important implications for the extinction and persistence of bacterial cells. Also, stochastic influences were justified in various population growth models. Some examples can be found in [7–18]. With such different models, the effect of the stochastic noise in the growth dynamics has been studied analytically and numerically. In such models, the stochastic characters have been found and discussed, such as the stationary probability distribution, mean first passage time, resonant activation, noise enhanced stability, stochastic resonance. Also, other stochastic growth models can be found in [19, 20].

In this paper, we study a stochastic bacterial population growth model under the influence of random fluctuations. Such a model is a simplified form of the model presented in [1] and describes the growth dynamics of bacterial population with antibiotic resistance. We mainly investigate the effect of multiplicative random noise on the growth dynamics especially extinction and persistence of bacterial cells. Similar models have also been considered by different authors can be found in [21–23]. Authors of [21] formulated continuous time Markov chain models using ODE models and analyzed the extinction probability for a cancer cell. They also used computer simulations to examine the effect of chemotherapy when applied to the different growth models. In [22] the authors derived and analyzed the time-dependent probability density function for the number of individuals in a population at a given time in a general logistic population model with harvesting effort using the Fokker–Planck equation. Authors of [23] studied the stochastic logistic-harvest population model with and without the Allee effect. With the help of the associated Fokker–Planck equation, they analyzed the population extinction probability and the probability of reaching a large population size and studied analytically and numerically the impact of the harvest rate, noise intensity, and the Allee effect on population evolution. In the case considered here we focus on long time behavior of the process solution.

The significance and novelty of this research work are follows.

- We proposed this stochastic model based on the deterministic within-host model [1] of antibiotic resistance, which consists of the two/three equations for the strains of bacteria.
- This simple model is able to capture the stochastic dynamics of bacterial population with antimicrobial resistance. Also, of that mentioned above, it is different from that for instance in [4] where the Markovian birth-and-death model has been used to demonstrate the stochastic nature of eradicating bacteria with antibiotics using the master equation.
- Here, we studied the longtime behavior to obtain a threshold for extinction and persistence of bacterial cells.

The advantages of this model are (i) it demonstrate the stochastic effect of eradicating bacteria with antibiotics and (ii) it has significant implications for the prediction of treatment outcomes.

In practice, the results obtained enable us to understand the stochastic dynamics of the bacterial cells and effects of the anti-microbial treatments, which also gives us insights on how to eliminate bacterial cells. As a result, for instance we obtain a threshold which depends on the intrinsic growth rate, the antimicrobial rate and the noise intensity rate. Regarding the threshold, we find that decreasing the intrinsic growth rate of bacterial cells or increasing the noise intensity rate or the antimicrobial rate lead to the elimination of bacterial cells.

The rest of this paper is organized as follows. In Sect. 2, we introduce the stochastic differential equation model. In Sect. 3, we analyze the steady probability distribution. In Sect. 4, we analyze the extinction and persistence of bacterial cells. In Sect. 5 we verify and illustrate the model behavior by computer simulations. Section 6 contains a conclusion.

2 The Stochastic Differential Equation Model

In this section we introduce a stochastic model for bacterial growth with antibiotics. Different deterministic differential equation models for bacterial growth have been proposed and studied. Commonly used are logistic type growth models

$$\frac{dx}{dt} = (\alpha - \beta x)\, x, \tag{1}$$

where x denotes the bacterial population density at time t, α is the per capita maximum fertility rate of population, β denotes the strength of intra-competition of population. During antimicrobial resistance the bacterial growth kinetics is perturbed by the antibiotic drug, which can be described by a loss term $-\gamma x$, where γ is the antimicrobial rate. Taking into account the effect of antimicrobial resistance leads to the model

$$\frac{dx}{dt} = (\alpha - \beta x)\, x - \gamma x. \tag{2}$$

To study the bacterial evolution in stochastic environment, we assume that random fluctuations, such as rapid environmental changes, affect the system through external parameters. In this case, we suppose that, as random perturbations, the intrinsic growth parameter α in model (2) is regarded as a random variable in the form

$$\tilde{\alpha} = \alpha + \sigma \xi(t), \tag{3}$$

where α is the mean intrinsic growth rate, ξ is Gaussian white noise, and σ is the intensity of the noise. Then, equation (2) is replaced by stochastic differential equation for the random process X in the form

$$dX = ((\alpha - \beta X)\, X - \gamma X)\, dt + \sigma X dW(t),\, X(0) = x_0, \tag{4}$$

where $dW(t) = \xi(t)dt$. Here, W is defined on complete probability space $(\Omega, \mathcal{F}, P)$ equipped with the natural filtration $(\mathcal{F}_t)_{t\geq 0}$ associated to the Wiener process. It is assumed that the variable x is dimensionless, i.e., the equation describes changes in relative bacterial population size.

3 Analysis for Steady Probability Distribution

In this section we analyze the steady state probability density of bacterial cells. First, we observe that the deterministic model can be written

$$\frac{dx}{dt} = -\frac{\partial V}{\partial x},$$

where V is the potential function defined by

$$V(x) = -\frac{\eta}{2}x^2 + \frac{\beta}{3}x^3,$$

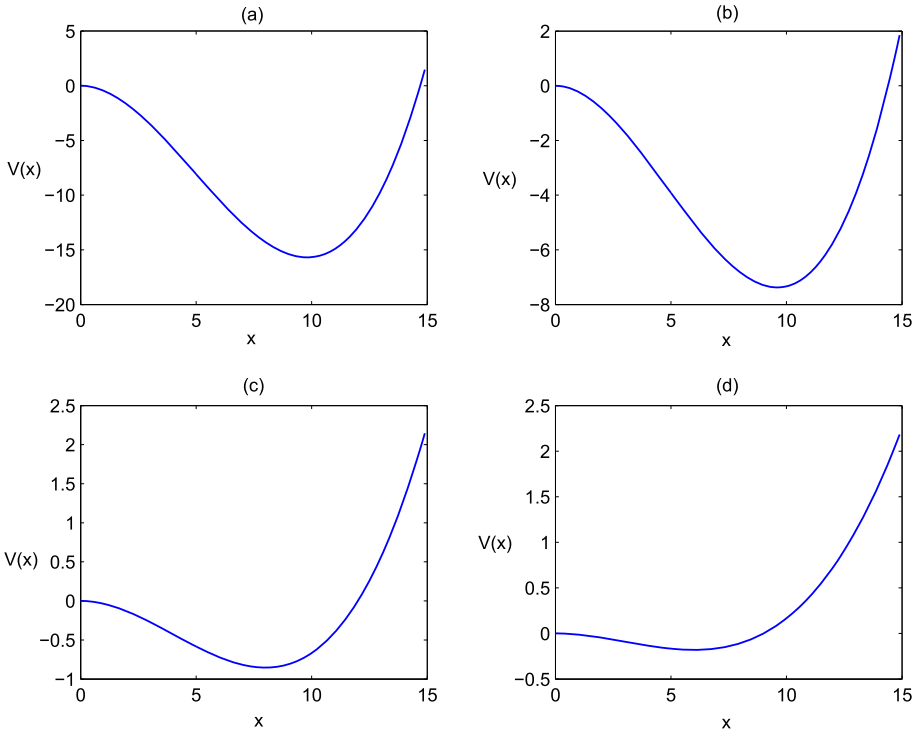

Fig. 1 Plot of the effective potential V as a function of the population size x, where **a** $\alpha = 1.0$, $\beta = 0.1$, **b** $\alpha = 0.50$, $\beta = 0.05$, **c** $\alpha = 0.1$, $\beta = 0.01$, **d** $\alpha = 0.05$, $\beta = 0.005$ and $\gamma = 0.02$

where $\eta = \alpha - \gamma$, see Fig. 1. The potential function has a local minimum corresponding to the stable equilibrium and a local maximum at $x = 0$, which is an unstable equilibrium if $\alpha - \gamma > 0$. For $\alpha - \gamma > 0$, the bacterial population converges to the stable equilibrium $x_s = (\alpha - \gamma)/\beta$. We observe that the population $x(t)$ tends to 0, the state of extinction, namely there is not bacterial cells, if and only if $\alpha/\gamma \leq 1$; while in the stable state $\alpha/\gamma > 1$, namely the bacterial cells exist and stay at a certain level. Thus, the system is bistable and the bistable feature of system depends on the parameter γ.

Now, the transitional probability density $P(x, t)$ satisfies the corresponding Fokker-Planck equation

$$\frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x} f(x) P(x,t) + \frac{\sigma^2}{2} x^2 P(x,t), \tag{5}$$

where $f(x) = (\eta - \beta x)x$. Then, the steady state probability $P_s(x)$ density can be obtained from (5) as in [24] and can be written as

$$P_s(x) = N_s x^{2\left((\alpha-\gamma)/\sigma^2 - 1\right)} \exp\left(-\frac{2\beta x}{\sigma^2}\right), \tag{6}$$

where N_s is a normalizing constant. Note that the probability density (6) is normalized for $\eta => \sigma^2/2$. At $\sigma^2/2 < \eta < \sigma^2$ the probability density is divergent at $x = 0$, and we have a nose induced phase transition at the point $\eta = \sigma^2$, see Fig. 2.

Next, we simulate the steady-state probability $P_s(x)$ density of bacterial cells for different noise intensities σ^2 and antimicrobial parameter γ. In Fig. 2, we plot the steady-state proba-

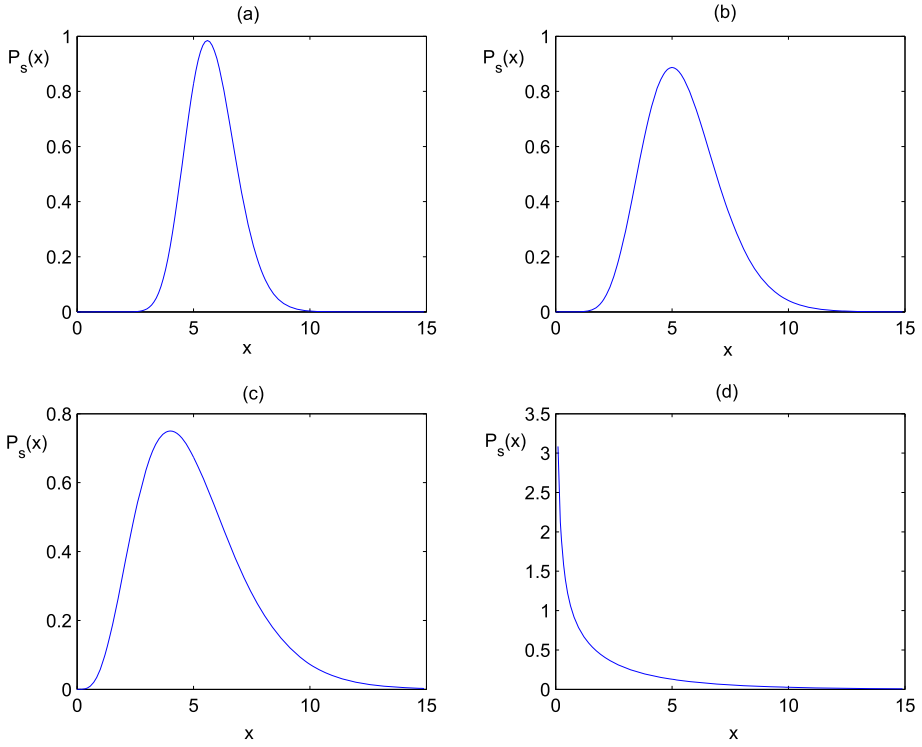

Fig. 2 This figure shows the steady probability probability $P_s(x)$ density of bacterial cells $X(t)$ for $\alpha = 0.05$, $\beta = 0.005$, $\gamma = 0.02$ and different values of σ^2: **a** $\sigma^2 = 0.002$, **b** $\sigma^2 = 0.005$, **c** $\sigma^2 = 0.01$, and **d** $\sigma^2 = 0.04$

bility $P_s(x)$ density for given parameters α, β, γ and different noise intensities σ^2. In Fig. 3, we plot the steady-state probability $P_s(x)$ density varying with antimicrobial parameter and fixed σ^2. Clearly, the extinction of bacterial cells increases with increase of γ and is the more probable for large σ^2.

4 Analysis for Extinction and Persistence

In this section we analyze longtime behavior using methods in [25] and present analytical results concerning the extinction and persistence for the model Eq. (4).

4.1 Extinction

In this subsection we will discus the extinction of the system (4).

Theorem 1 *If*

$$\frac{\alpha}{\gamma} - \frac{\sigma^2}{2\gamma} < 1 \ \textit{and} \ \sigma^2 \leq \alpha, \tag{7}$$

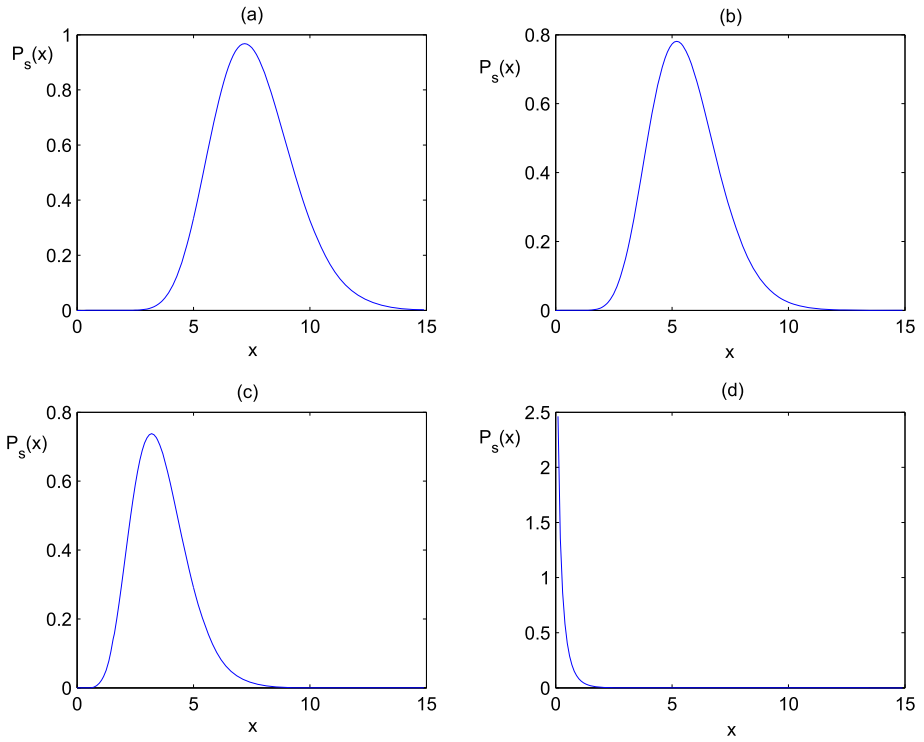

Fig. 3 This figure shows the steady probability probability $P_s(x)$ density of bacterial cells $X(t)$ for the same parameters in figure 1 except $\sigma^2 = 0.004$ and different values of γ: **a** $\gamma = 0.01$, **b** $\gamma = 0.02$, **c** $\gamma = 0.03$, and **d** $\gamma = 0.047$

then for any given initial values $X(0) = X_0 \in (0, \alpha)$*, the solution of the model (2) obeys*

$$\limsup_{t\to\infty} \frac{1}{t} \log(X(t)) \leq \alpha - \gamma - \frac{\sigma^2}{2} < 0 \ \ a.s, \tag{8}$$

namely, $X(t)$ *tends to zero exponentially almost surely.*

Proof From the Ito formula, we have

$$\log(X(t)) = \log(X_0) + \int_0^t f(X(s))ds + \int_0^t \sigma dW(s), \tag{9}$$

where $f : \mathbb{R} \to \mathbb{R}$ is defined by

$$f(x) = \alpha - \gamma - \beta x - \frac{\sigma^2}{2}. \tag{10}$$

However, under condition (7), we have

$$\begin{aligned} f(X(s)) &= \alpha - \gamma - \frac{\sigma^2}{2} - \beta X(s) \\ &\leq \alpha - \gamma - \frac{\sigma^2}{2}, \end{aligned}$$

for $X(s) \in (0, \alpha)$. It then follows from (9) that

$$\log(X(t)) \leq \log(X_0) + \left(\alpha - \gamma - \frac{\sigma^2}{2}\right)t + \int_0^t \sigma dW(s). \tag{11}$$

This implies

$$\limsup_{t\to\infty} \frac{1}{t}\log(X(t)) \leq \alpha - \gamma - \frac{\sigma^2}{2} + \limsup_{t\to\infty} \frac{1}{t}\int_0^t \sigma dW(s) \ \ a.s. \tag{12}$$

But by the larger number theorem for martingales, we have

$$\limsup_{t\to\infty} \frac{1}{t}\int_0^t \sigma dW(s) = 0 \ \ a.s.$$

We therefore obtain the desired assertion (8) from (12).

The following theorem cover the case when $\sigma^2 > 2(\alpha - \gamma)$. □

Theorem 2 *If*

$$\sigma^2 > 2(\alpha - \gamma), \tag{13}$$

then for any given initial values $X(0) = X_0 \in (0, \alpha)$, the solution of the model (2) obeys

$$\limsup_{t\to\infty} \frac{1}{t}\log(X(t)) \leq \alpha - \gamma - \frac{\sigma^2}{2} < 0 \ \ a.s, \tag{14}$$

namely, $X(t)$ tends to zero exponentially almost surely.

Proof From the Ito formula, we have

$$\log(X(t)) = \log(X_0) + \int_0^t f(X(s))ds + \int_0^t \sigma dW(s), \tag{15}$$

It then follows that

$$\log(X(t)) \leq \log(X_0) + \left(\alpha - \gamma - \frac{\sigma^2}{2}\right)t + \int_0^t \sigma dW(s). \tag{16}$$

In the same way as in the proof of Theorem 1, this implies that

$$\limsup_{t\to\infty} \frac{1}{t}\log(X(t)) \leq \alpha - \gamma - \frac{\sigma^2}{2} \ \ a.s., \tag{17}$$

Hence, the proof is complete. □

4.2 Persistence

In this subsection we will discus the persistence of the model system (4).

Theorem 3 *If*

$$\frac{\alpha}{\gamma} - \frac{\sigma^2}{2\gamma} > 1, \tag{18}$$

then for any given initial values $X(0) = X_0 \in (0, \alpha)$, the solution of the model (2) obeys

$$\limsup_{t\to\infty} X(t) \geq \xi \ \ a.s., \tag{19}$$

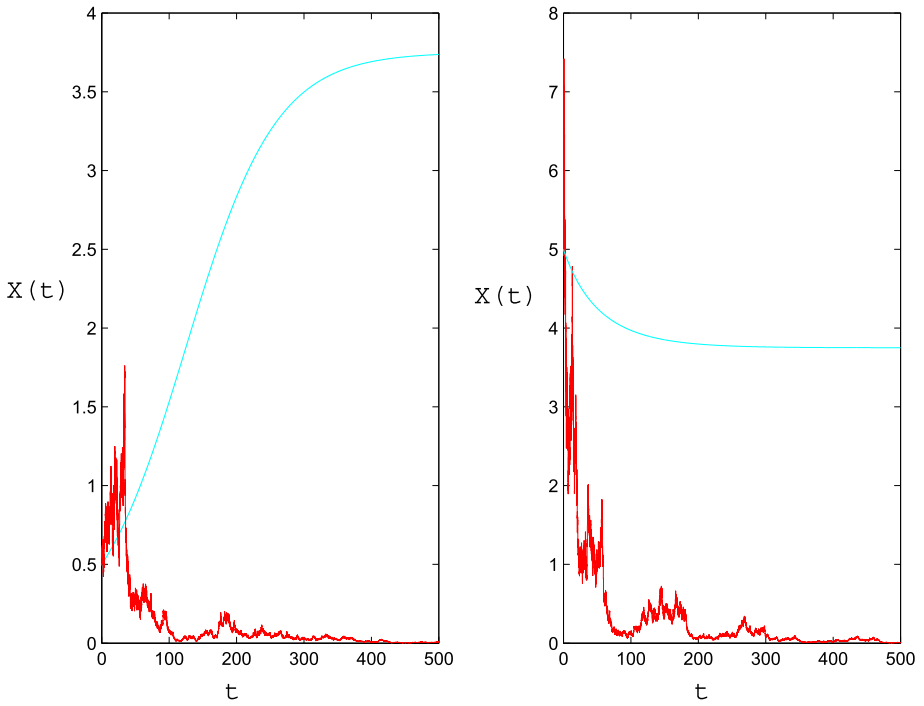

Fig. 4 This figure shows computer simulation of the sample path $X(t)$ for the model equation (4) (cyan) and its corresponding deterministic model Eq. (2) (red) with given parameters, using initial values in the left $X(0) = 0.5$ and in the right $X(0) = 5$

and

$$\liminf_{t\to\infty} X(t) \leq \xi \quad a.s., \tag{20}$$

where

$$\xi = \frac{2(\alpha - \gamma) - \sigma^2}{2\beta}, \tag{21}$$

which is the unique root in $(0, \alpha)$ *of*

$$\alpha - \gamma - \beta x - \frac{\sigma^2}{2} = 0. \tag{22}$$

That is, $X(t)$ *will rise to or above the level* ξ *infinitely often with probability one.*

Proof We begin to prove assertion (19). If it is not true, then there is a sufficiently small $\epsilon \in (0, 1)$ such that

$$\mathbb{P}(\Omega_1) > \epsilon, \tag{23}$$

where $\Omega_1 = \left\{\limsup_{t\to\infty} X(t) \leq \xi - 2\epsilon\right\}$. Hence, for every $\omega \in \Omega_1$, there is a $T = T(\omega) > 0$ such that

$$X(t, \omega) \leq \xi - \epsilon \quad whenever \quad t \geq T(\omega). \tag{24}$$

It therefore follows from (24) that

$$f(X(t, \omega)) \geq f(\xi - \epsilon) \quad whenever \quad t \geq T(\omega). \tag{25}$$

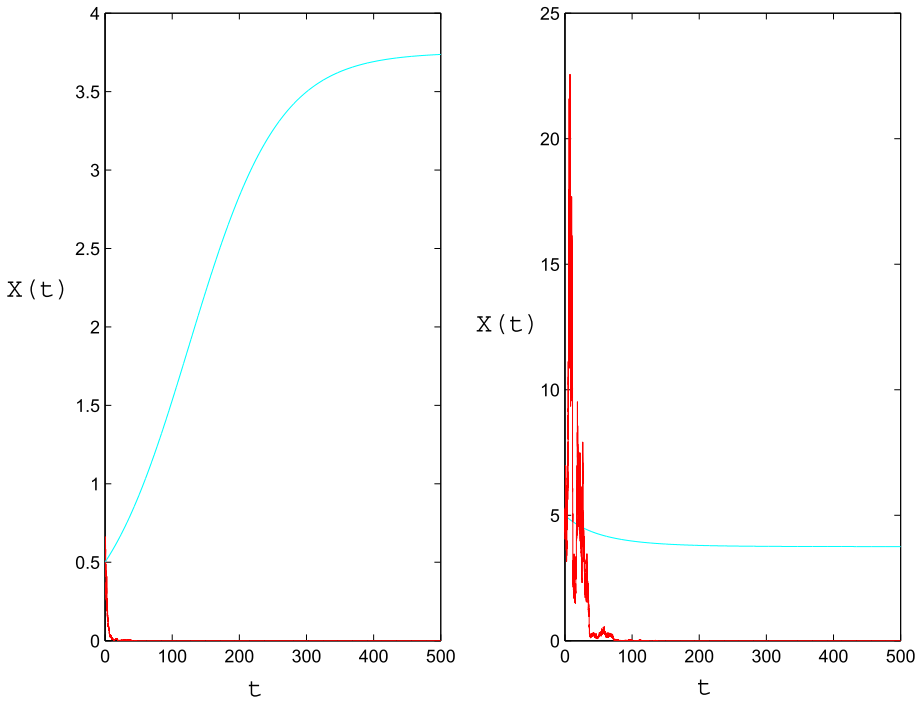

Fig. 5 This figure shows computer simulation of the sample path $X(t)$ for the model equation (4) (cyan) and its corresponding deterministic model Eq. (2) (red) with given parameters, using initial values in the left $X(0) = 0.5$ and in the right $X(0) = 5$

Moreover, by the large number theorem for martingales, there is a $\Omega_2 \subset \Omega$ with $\mathbb{P}(\Omega_2) = 1$ such that for every $\omega \in \Omega_2$,

$$\lim_{t\to\infty} \frac{1}{t} \int_0^t \sigma dW(s,\omega) = 0. \tag{26}$$

Now, fix any $\omega \in \Omega_1 \cap \Omega_2$. It then follows from the Ito formula and (25) that, for $t \geq T(\omega)$,

$$\begin{aligned} \log(X(t,\omega)) \geq \log(X_0) + \int_0^{T(\omega)} f(X(s,\omega))ds + f(\xi-\epsilon)(t-T(\omega)) \\ + \int_0^t \sigma dW(s,\omega). \end{aligned} \tag{27}$$

This yields

$$\liminf_{t\to\infty} \frac{1}{t} \log(X(t,\omega)) \geq f(\xi-\epsilon) > 0,$$

whence

$$\lim_{t\to\infty} X(t,\omega) = \infty.$$

But this contradicts (24). We therefore must have the desired assertion (19).

Next we prove assertion (20). If it is not true, then there is a sufficiently small $\delta \in (0,1)$ such that

$$\mathbb{P}(\Omega_3) > \delta, \tag{28}$$

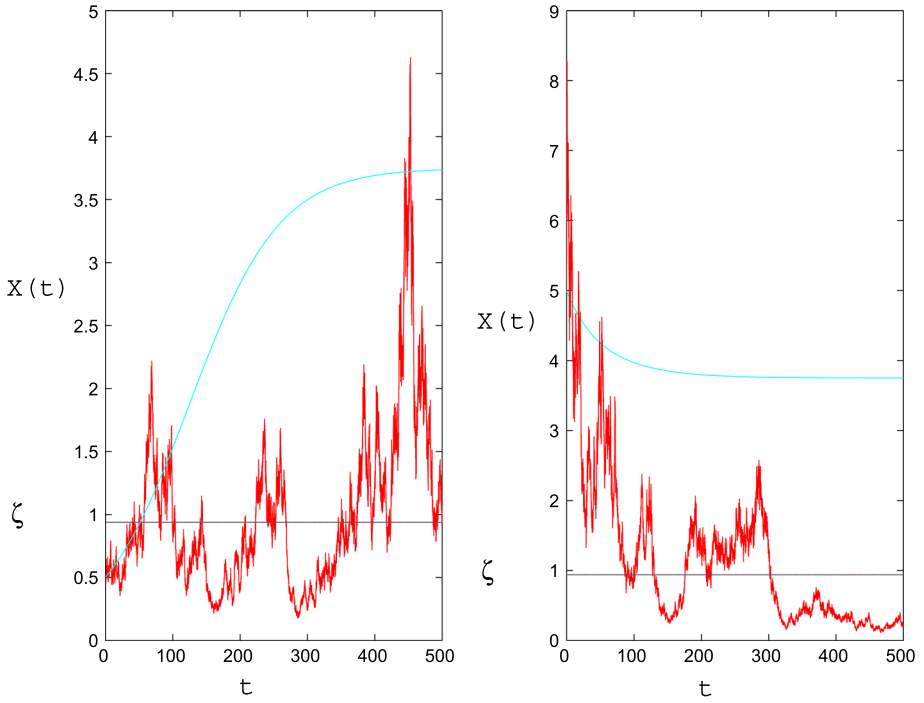

Fig. 6 This figure shows computer simulation of the sample path $X(t)$ for the model equation (4) (cyan) and its corresponding deterministic model Eq. (2) (red) with given parameters, using initial values in the left $X(0) = 0.5$ and in the right $X(0) = 5$

where $\Omega_3 = \{\liminf_{t\to\infty} X(t) \geq \xi + 2\delta\}$. Hence, for every $\omega \in \Omega_3$, there is a $\tau = \tau(\omega) > 0$ such that

$$X(t,\omega) \geq \xi + \delta \quad whenever \quad t \geq \tau(\omega). \tag{29}$$

Now, fix any $\omega \in \Omega_3 \cap \Omega_2$. It then follows from the Ito formula that, for $t \geq \tau(\omega)$,

$$\begin{aligned} \log(X(t,\omega)) \leq \log(X_0) + \int_0^{\tau(\omega)} f(X(s,\omega))ds + f(\xi+\delta)(t-\tau(\omega)) \\ + \int_0^t \sigma_i dW(s,\omega). \end{aligned} \tag{30}$$

This, together with (26), yields

$$\limsup_{t\to\infty} \frac{1}{t} \log(X(t,\omega)) \leq f(\xi+\delta) < 0,$$

whence

$$\lim_{t\to\infty} X(t,\omega) = 0.$$

But this contradicts (28). We therefore obtain the desired assertion (20). Hence, the proof is complete. □

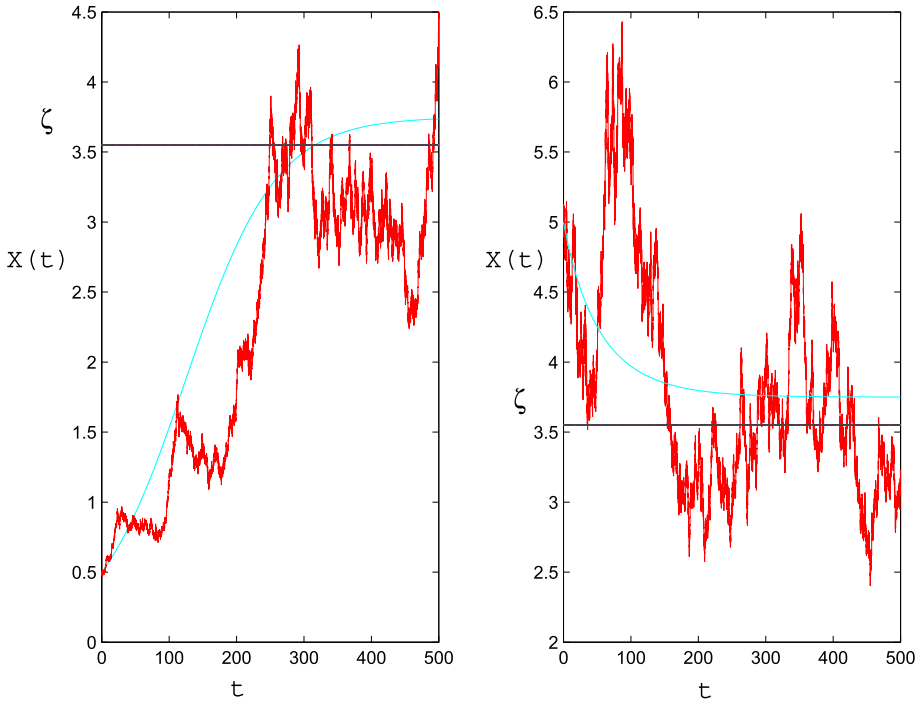

Fig. 7 This figure shows computer simulation of the sample path $X(t)$ for the model equation (4) (cyan) and its corresponding deterministic model Eq. (2) (red) with given parameters, using initial values in the left $X(0) = 0.5$ and in the right $X(0) = 5$

5 Computer Simulations

In this section we use the Euler-Maruyama method [26] with the time step 10^{-2} and present computer simulations in order to illustrate the model behavior particularly for the extinction and persistence of the bacterial cells. According to the conditions in Theorems 1, 2 and 3, the extinction and persistence of bacterial cells rely on the parameter space σ and γ. Figure 4 shows the extinction of bacterial cells according to the conditions in Theorem 1 for the parameters $\alpha = 0.05, \beta = 0.004, \gamma = 0.035$ and $\sigma = 0.2$. Figure 5 shows the same result according to the conditions in Theorem 2, with keeping the parameters the same but let $\sigma = 0.4$.

To illustrate the result in Theorem 3, we keep the same parameter values except σ is reduced to 0.15 from 0.2. The computer simulation in Fig. 6 shows this result, showing clearly fluctuation around the level $\zeta = 0.9375$. To further illustrate the effect of the noise intensity, we keep all the parameter values unchanged but reduce σ to $\sigma = 0.04$. In Fig. 7, we show the resulting computation simulation, illustrating clearly the increase of the level $\zeta = 3.55$ and persistence. Figure 8 shows a computer simulation of the distribution of the solution $X(t)$ in the persistent case for higher and lower σ. In this figure we plot histograms, showing the distribution of $X(t)$ in the case of $\sigma = 0.15, 0.1, 0.05$ and 0.025.

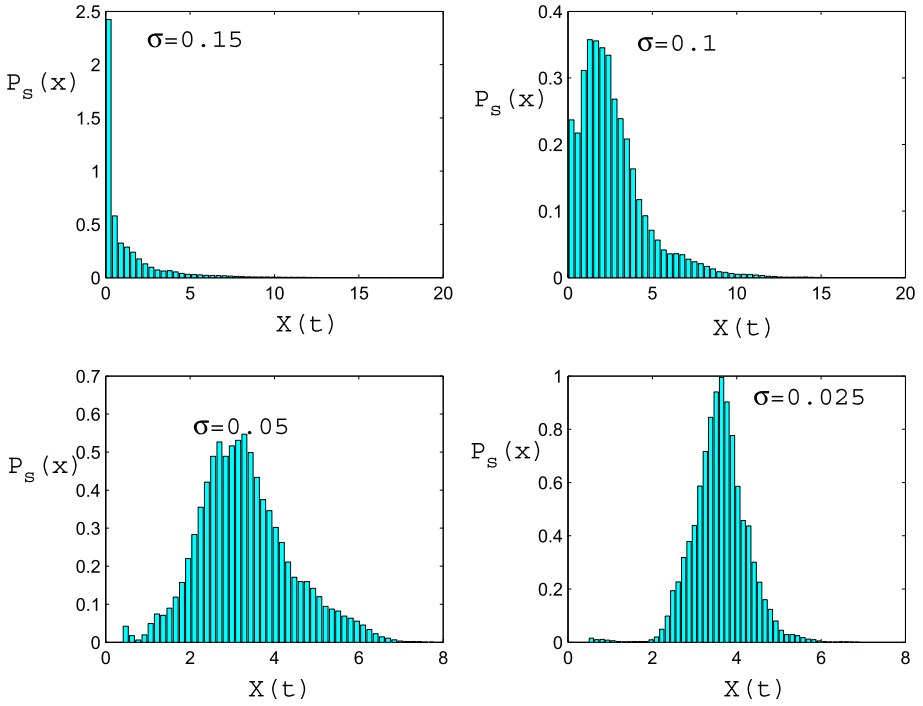

Fig. 8 This figure shows histograms of the values of the path $X(t)$ for given parameter values with $X(0) = 0.5$, and different values of σ

6 Conclusion

In this paper, based on the deterministic model equations in [1], we have considered a stochastic model for the dynamics of bacterial population with antimicrobial resistance under the influence of random fluctuations. We have used the technique of parameter perturbation and investigated the effect of multiplicative noise on the evolutionary dynamics. We first have evaluated the steady state probability density of bacterial cells for different noise intensities and antimicrobial intensities. Then, we have studied the longtime behavior and obtained necessary conditions (a threshold) for extinction and persistence of bacterial cells. Further, the model behaviors ware illustrated by computer simulations. The obtained results demonstrate the growth dynamics of the bacterial population which was controlled by the antimicrobial rate and the noise strength rate. Regarding the results of the threshold, it can be used to analyze the drug resistance observed in evolving and variable bacterial cell population.

Overall, the principal theoretical implication of this study is that the stochastic model is capable to define the macroscale properties of the dynamics of bacteria with antimicrobial resistance, capturing stochastic growth, and identifying the specific response to antibiotic treatment. This may be important for the use of therapeutic purposes.

Author Contributions I contribute this work.

Funding Open access funding provided by The Science, Technology & Innovation Funding Authority (STDF) in cooperation with The Egyptian Knowledge Bank (EKB). This research did not receive any funding.

Data Availability Not applicable.

Declarations

Conflict of interest The author declares no conflict of interest concerning the publication of this manuscript.

Ethical Approval Not applicable.

References

1. Roberts, M.G., Burgess, S., Toombs-Ruane, L.J., Benschop, J., Marshall, J.C., French, N.P.: Combining mutation and horizontal gene transfer in a within-host model of antibiotic resistance. Math. Biosci. **339**, 108656 (2021)
2. Frenkel, N., Dover, R.S., Titon, E., Shai, Y., Kedar, V.R.: Bistable bacterial growth dynamics in the presence of antimicrobial agents. Antibiotics **10**, 87 (2021)
3. Greulich, P., Dolezal, J., Scott, M., Evans, M.R., Allen, R.J.: Predicting the dynamics of bacterial growth inhibition by ribosome-targeting antibiotics. Phys. Biol. **14**, 065005 (2017)
4. Coates, J., Park, Bo. R., Le, D., Simsek, E., Chaudhry, W., Kim, M.: Antibiotic-induced population fluctuations and stochastic clearance of bacteria. eLife **7**, e32976 (2018)
5. Akiyama, T., Kim, M.: Stochastic response of bacterial cells to antibiotics: its mechanisms and implications for population and evolutionary dynamics. Courr. Opin. Microbiol. **63**, 104–108 (2021)
6. Kessler, D.A., Levine, H.: Scaling solution in the large population limit of the general asymmetric stochastic Luria-Delbruck evolution process. J. Stat. Phys. **158**, 783–805 (2015)
7. Arranz, F.J., Peinado, J.M.: A mesoscopic stochastic model for the specific consumption rate in substrate-limited microbial growth. PLoS ONE **12**(2), e0171717 (2017)
8. Ai, B.-Q., Wang, X.-J., Lui, G.-T., Lui, L.-G.: Fluctuation of parameters in tumor cell growth model. Commun. Theor. Phys. **40**, 120–122 (2003)
9. Braumann, C.A.: Growth and extinction in randomly varying populations. Comput. Math. Appl. **56**, 631–644 (2008)
10. Drakos, S.: On stochastic model for the growth of cancer tumor based on the finite element method. Am. J. Biomed. Eng. **6**, 166–169 (2016)
11. Golec, J., Sathananthan, S.: Stability analysis of a stochastic logistic model. Math. Comput. Modell. **38**, 585–593 (2003)
12. Krstic, M., Jovanovic, M.: On stochastic population model with the Allee effect. Math. Comput. Modell. **52**, 370–379 (2010)
13. Soboleva, T.K., Pleasants, A.B.: Population growth as nonlinear stochastic prosess. Math. Comput. Modell. **38**, 1437–1442 (2003)
14. Wang, C.-J., Li, D., Mei, D.-C.: Pure multiplcaative noises induced population extinction in an anti-tumor model under immune surveillance. Commun. Theor. Phys. **52**, 463–467 (2009)
15. Schlomann, B.H.: Stationary moments, diffusion limits, and extinction times for logistic growth with random catastrophes. J. Theor. Biol. **454**, 154–163 (2018)
16. Dorini, F.A., Bobko, N., Dorini, L.B.: A note on the logistic equation subject to uncertainties in parameters. Comput. Appl. Math. **37**, 1496–1506 (2018)
17. Sau, A., Saha, B., Bhattacharya, S.: An extended stochastic Allee model with harvesting and the risk of extinction of the herring population. J. Theor. Biol. **503**, 110375 (2020)
18. Calatayud, J., Cortes, J.-C., Dorini, F.A., Jornet, M.: On a stochastic logistic population model with time-varying carrying capacity. Comput. Appl. Math. **39**, 1–16 (2020)
19. Caceres, M.O.: Passage time statistics in a stochastic Verhulst model. J. Stat. Phys. **132**, 487–500 (2008)

20. Marathe, R., Bierbaum, V., Gomez, D., Klumpp, S.: Determinstic and stochastic descriptions of gene expression dynamics. J. Stat. Phys. **148**, 608–627 (2012)
21. Sharpe, S., Dobrovolny, H.M.: Predicting the effectiveness of chemotherapy using stochastic ODE models of tumor growth. Commun. Nonlinear Sci. Num. Simul. **101**, 105883 (2021)
22. Otunuga, O.M.: Time-dependent probability density function for general stochastic logistic population model with harvesting effort. Phys. A **573**, 125931 (2021)
23. Tesfay, A., Tesfay, D., Brannan, J., Duan, J.: A logistic-harvest model with Allee effect under multiplicative noise. Stoch. Dyn. **21**, 2150044 (2021)
24. Gardiner, C.W.: Handbook of Stochastic Methods. Springer, Berlin (1990)
25. Gray, A., et al.: A stochastic differential equation SIS epidemic model. SIAM J. Appl. Math. **71**, 876–902 (2011)
26. Kloeden, P.E., Platen, E.: Numerical Solution of Stochastic Differential Equations. Springer, Berlin (2010)