Optimal control of diffusion processes pertaining to an opioid epidemic dynamical model with random perturbations

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Abstract
In this paper, we consider the problem of controlling a diffusion process pertaining to an opioid epidemic dynamical model with random perturbation so as to prevent it from leaving a given bounded open domain. In particular, we assume that the random perturbation enters only through the dynamics of the susceptible group in the compartmental model of the opioid epidemic dynamics and, as a result of this, the corresponding diffusion is degenerate, for which we further assume that the associated diffusion operator is hypoelliptic, i.e., such a hypoellipticity assumption also implies that the corresponding diffusion process has a transition probability density function with strong Feller property. Here, we minimize the asymptotic exit rate of such a controlled-diffusion process from the given bounded open domain and we derive the Hamilton–Jacobi–Bellman equation for the corresponding optimal control problem, which is closely related to a nonlinear eigenvalue problem. Finally, we also prove a verification theorem that provides a sufficient condition for optimal control.

Keywords Diffusion processes · Exit probability · Epidemiology · SIR compartmental model · Prescription drug addiction · Markov controls · Minimum exit rates · Principal eigenvalues · Optimal control problem

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1 Introduction

The opioid drug-related problem has recently reached crisis levels worthy of declaring a public health emergency in the United States. For example, more than 53,000 people in the United States died from an opioid overdose in 2016—more than double the figure in 2010—and the increasing use, misuse and abuse of heroin, fentanyl and other opiates, including prescription drugs, shows no signs of slowing [e.g., see Rudd et al. (2016) and Office of the Assistant Secretary for Planning and Evaluation (2015) for additional discussions]. In response to this, a number of federal and state agencies throughout the United States have implemented a wide range of opioid-related policies1 that are primarily aimed at curbing prescription opioid abuse, establishing guidelines to prevent inappropriate prescribing practices, developing abuse deterrents or preventing drug diversion mechanisms (Centers for Disease Control and Prevention 2018; Volkow and McLellan 2016; Frieden and Houry 2016). On the other hand, only a few studies have been reported on the need for effective intervention strategies, based on mathematical optimal control theory of epidemiology for infectious diseases, with the intent of better understanding the dynamics of the current serious opioid epidemic [e.g., see Battista et al. (2018), Njagarah and Nyabadza (2013) and Befekadu and Zhu (2018) in context of exploring the dynamics of drug abuse epidemics, focusing on the interplay between the different opioid user groups and the process of rehabilitation and treatment from addiction; see also Kermack and McKendrick (1927), Samanta (2011) or Ma et al. (2017) for additional studies, but in the context of heroin epidemics that resembling the classic susceptible-infected-recovered (SIR) model, based on the work of White and Comiskey (2007)]. Here, we would like to point out that the roots to opioid crisis are complex and tangled with social and political issues; and therefore, only systemic research and evidence-based strategies can identify the most effective ways for intervention of the current opioid crisis.

In this paper, we consider optimal control of an opioid epidemic dynamical model, when there is a random perturbation that enters through the dynamics of the susceptible group in the compartmental model of the opioid epidemic dynamics. Note that the random noise enters only through a particular subsystem in the compartmental model, and then its effect is subsequently propagated to the other subsystems. As a consequence, the corresponding diffusion is degenerate, for which we also assume that the associated diffusion operator is hypoelliptic, where such an assumption also implies that the corresponding diffusion process has a transition probability density function with strong Feller property. Note that the hypoellipticity assumption is in general concerned with the accessibility property of controllable nonlinear systems that are driven by white noise [e.g., see Sussmann and Jurdjevic (1972) concerning the controllability of nonlinear systems, which is closely related to Stroock and Varadhan (1972) and Ichihara and Kunita (1974); see also Elliott (1973), Sect. 3 and Amano (1979) for additional discussions from the view point of the control theory]. Here, our main objective is to prevent the controlled-diffusion process pertaining to the randomly

1 Including the Ryan Haight Online Pharmacy Consumer Protection Act of 2008 which prohibited the Internet distribution of controlled substances without a valid prescription (Ryan Haight Online Consumer Protection Act 2008); see also Dowell et al. (2016) for CDC guideline for prescribing opioids for chronic pain—United States, 2016.
perturbed opioid epidemic dynamics from leaving a given bounded open domain. To this end, we minimize the asymptotic exit rate (as opposed to maximizing the mean exit-time) with which the controlled-diffusion process exits from the given bounded open domain, and we further derive the Hamilton–Jacobi–Bellman (HJB) equation for the corresponding optimal control problem, which is also closely related to a nonlinear eigenvalue problem. Moreover, we also prove a verification theorem that provides a sufficient condition for the solution of optimal control.

The remainder of this paper is organized as follows. In Sect. 2, we present the problem formulation for optimal control of a diffusion process pertaining to an opioid epidemic dynamical model with random perturbation. The problem we focus on is to minimize the asymptotic exit rate with which the controlled-diffusion process exits from the given bounded open domain. In Sect. 3, we provide our main results—where we derive the HJB equation for the corresponding optimal control problem. In this section, we also provide a verification theorem for the optimal control. Finally, Sect. 4 provides further remarks.

2 Problem formulation

In this section, we present the problem formulation for optimal control of a diffusion process pertaining to an opioid epidemic dynamical model with random perturbation. In particular, the problem we focus on is to minimize the asymptotic exit rate with which the controlled-diffusion process exits from the given bounded open domain and we further establish a connection with a nonlinear eigenvalue problem.

2.1 Mathematical model

In this subsection, we consider an opioid epidemic dynamical model that describes the interplay between regular prescription opioid use, addictive use, and the process of rehabilitation and relapsing into opioid drug use [e.g., see Battista et al. (2018) for a detailed discussion]. To this end, we introduce the following population groups

(i) **Susceptible group—S**: This group in the compartmental model includes those who are susceptible to opioid addiction, but they are not currently using opioids. In the compartmental model, everyone who is not in addiction treatment, already an addict, or using opioids as medically prescribed is classified as “susceptible.”

(ii) **Prescribed user group—P**: This group in the compartmental model is composed of individuals who have health related concerns and also have access to opioids through a proper physician’s prescription, but they are not addicted to opioids. Members of this group have some inherent tendency of becoming addicted to their prescribed opioids.

(iii) **Addiction user group—A**: This group in the compartmental model is composed of people who are addicted to opioids. There are multiple interaction routes to this group in the compartmental model, including those routes that are bypassing the prescribed user group \(P\) (see also Fig. 1 that shows the relationships between the different groups).
(iv) Treatment/rehabilitation—R: This group in the compartmental model contains individuals who are in treatment for their addiction. Here, we include an inherent rate of falling back into addiction as well as a typical process of relapsing due to general availability of the drug. Moreover, we also assume that some of the members from the recovering group who have completed their treatment may return to being susceptible. That is, we assume that successful treatment does not imply permanent immunity to addiction (i.e., in general, an assumption based on the balance of increased risk of addiction verses increased awareness and avoidance).

Then, using the basic remarks made above, we specify the following SIR compartmental model for the opioid epidemic dynamics described by the following four continuous-time differential equations

\[
\begin{align*}
\dot{S}(t) &= -\alpha S(t) - \beta (1 - \xi) S(t) A(t) - \beta \xi S(t) P(t) + \epsilon P(t) + \delta R(t) + \mu (P(t) + R(t)) + \mu^* A(t), \\
\dot{P}(t) &= \alpha S(t) - (\epsilon + \gamma + \mu) P(t), \\
\dot{A}(t) &= \gamma P(t) + \sigma R(t) + \beta (1 - \xi) S(t) A(t) + \beta \xi S(t) P(t) + \nu R(t) A(t) - (\zeta + \mu) A(t) \\
\dot{R}(t) &= \zeta A(t) - \nu R(t) A(t) - (\delta + \sigma + \mu) R(t),
\end{align*}
\]

and

\[
\dot{A}(t) = (1 - \xi) S(t) A(t) - \beta \xi S(t) P(t) - \beta (1 - \xi) S(t) A(t).
\]
where the normalized overall population is assumed to be constant, i.e., \( 1 = A(t) + S(t) + R(t) + P(t) \), since the number of mortality due to opioid-related overdose is very small, when compared to the change in the total population numbers in the short term. Notice that, in Eq. (3) above, the terms \( \beta(1 - \xi)S(t)A(t) \) and \( \beta \xi S(t)P(t) \) are, respectively, due to the interactions with addicted users/drug dealers and due to the interactions with opioid patients, for example, through unsecured or extra drugs [e.g., see also Bicket et al. (2017); and cf. Eq. (1)]. Similarly, the term \( \nu R(t)A(t) \) in Eq. (4) takes into account the process of relapsing due to widespread availability of opioid drugs. Moreover, the followings are brief description for the parameters in the above system of equations, i.e., the system parameters in Eqs. (1)–(4),

- \( \alpha \): the rate at which new people start getting prescription opioid drugs.
- \( \beta \): the total probability of becoming addicted to opioids other than by prescription.
- \( \beta(1 - \xi) \): the proportion of \( \beta \) caused by black market drugs or other addicts.
- \( \beta \xi \): the proportion of \( \beta \) where the non-prescribed, susceptible population begins abusing opioids due to the accessibility of extra prescription opioids, e.g., new addicts obtained drugs from a friend or relative’s prescription.
- \( \epsilon \): the rate at which people come back to the susceptible group after being prescribed opioids.
- \( \delta \): the rate at which people come back to the susceptible group after successfully finishing treatment. Despite having completed rehabilitation, we assume people are susceptible to addiction for life.
- \( \mu \): the natural death rate.
- \( \mu^* \): the enhanced death rate for addicts (i.e., \( \mu \) plus overdose rate).
- \( \gamma \): the rate at which the prescribed opioid users fall into addiction.
- \( \zeta \): the rate at which addicted/dependent opioid users enter the treatment/rehabilitation process.
- \( \nu \): the rate at which users during the treatment fall back into addictive drug use due to the availability of prescribed painkillers from friends or relatives.

Note that the normalized overall population is assumed constant (which is set to unity). Then, with \( P(t) = 1 - S(t) - A(t) - R(t) \), we can reduce the above system of equations in Eqs. (1)–(4) as follows

\[
\begin{align*}
\dot{S}(t) &= -\alpha S(t) - \beta(1 - \xi)S(t)A(t) - \beta \xi S(t)(1 - S(t) - A(t) - R(t)) \\
&\quad + (\epsilon + \mu)(1 - S(t) - A(t) - R(t)) + (\delta + \mu)R(t) + \mu^* A(t) \\
\dot{A}(t) &= \gamma(1 - S(t) - A(t) - R(t)) + \sigma R(t) + \beta(1 - \xi)S(t)A(t) \\
&\quad + \beta \xi S(t)(1 - S(t) - A(t) - R(t)) + \nu RA - (\zeta + \mu^*) A(t) \\
\dot{R}(t) &= \zeta A(t) - \nu R(t)A(t) - (\delta + \sigma + \mu)R(t)
\end{align*}
\] (5)

In order to facilitate our presentation, we adopt the following change of variables: \( S \rightarrow x_1, A \rightarrow x_2 \) and \( R \rightarrow x_3 \). Then, the system of equations in Eq. (5) can be further rewritten as follows
\[
\begin{align*}
\dot{x}_1(t) &= f_1(x_1(t), x_2(t), x_3(t)) \\
\dot{x}_2(t) &= f_2(x_1(t), x_2(t), x_3(t)) \\
\dot{x}_3(t) &= f_3(x_2(t), x_3(t))
\end{align*}
\]  

where the functions \(f_1, f_2\) and \(f_3\) are given by
\[
\begin{align*}
f_1(x_1(t), x_2(t), x_3(t)) &= -\alpha x_1(t) - \beta (1 - \xi)x_1(t)x_2(t) \\
&\quad - \beta \xi x_1(t)(1 - x_1(t) - x_2(t) - x_3(t)) \\
&\quad + (\epsilon + \mu)(1 - x_1(t) - x_2(t) - x_3(t)) \\
&\quad + (\delta + \mu)x_3(t) + \mu^*x_2(t), \\
f_2(x_1(t), x_2(t), x_3(t)) &= \gamma(1 - x_1(t) - x_2(t) - x_3(t)) + \sigma x_3(t) + \beta (1 - \xi)x_1(t)x_2(t) \\
&\quad + \beta \xi x_1(t)(1 - x_1(t) - x_2(t) - x_3(t)) \\
&\quad + \nu x_3(t)x_2(t) - (\zeta + \mu^*)x_2(t)
\end{align*}
\]

and
\[
f_3(x_2(t), x_3(t)) = \xi x_2(t) - \nu x_3(t)x_2(t) - (\delta + \sigma + \mu)x_3(t),
\]
respectively.

In what follows, we assume that a random noise enters only through the dynamics of the susceptible group in Eq. (5) and is then subsequently propagated to the other groups in the compartmental model (see also in Fig. 1). To this end, we consider the corresponding system of stochastic differential equations (SDEs), i.e.,
\[
\begin{align*}
dX_1(t) &= f_1(X_1(t), X_2(t), X_3(t))dt + \sigma_1(X_1(t), X_2(t), X_3(t))dW(t) \\
dX_2(t) &= f_2(X_1(t), X_2(t), X_3(t))dt \\
dX_3(t) &= f_3(X_2(t), X_3(t))dt
\end{align*}
\]  

where \((W(t))_{t \geq 0}\) is a one-dimensional Brownian motion, \((X_1(t), X_2(t), X_3(t))_{t \geq 0}\) being an \(\mathbb{R}^3\)-valued degenerate diffusion process, and \(\sigma_1\) and \(\sigma^{-1}_1\) are assumed to be bounded functions. Moreover, if we denote by a bold letter a quantity in \(\mathbb{R}^3\), for example, the solution in Eq. (7) is denoted by \(\{X(t)\}_{t \geq 0} = (X_1(t), X_2(t), X_3(t))_{t \geq 0}\), then we can rewrite Eq. (7) as follows
\[
dX(t) = F(X(t))dt + B\hat{\sigma}(X(t))dW(t),
\]
where \(F = [f_1, f_2, f_3]^T\) is an \(\mathbb{R}^3\)-valued function and \(B\) stands for a column vector that embeds \(\mathbb{R}\) into \(\mathbb{R}^3\), i.e., \(B = [1, 0, 0]^T\). Note that the corresponding degenerate elliptic operator for the diffusion process \(X(t)\) is given by
\[
\mathcal{L}(\cdot)(\cdot) = \frac{1}{2} \text{tr} \left\{ a(x) D_{x_1}^2(\cdot) \right\} + \sum_{i=1}^3 f_i(x) D_{x_i}(\cdot),
\]
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where \( a(x) = \hat{\sigma}(x) \hat{\sigma}^T(x) \), \( D_{x_i} \) and \( D_{x_1}^2 \) (with \( D_{x_1}^2 = (\partial^2 / \partial x_1 \partial x_1) \)) are the gradient and the Hessian (w.r.t. the variable \( x_i \), for \( i \in \{1, 2, 3\} \)), respectively.

Let \( D \subset \mathbb{R}^3 \) be a given bounded open domain, with smooth boundary \( \partial D \) (i.e., \( \partial D \) is a manifold of class \( C^2 \)), and let us denote by \( C^\infty(D) \) the spaces of infinitely differentiable functions on \( D \).

The following statements are standing assumptions that hold throughout the paper.

**Assumption 1** (a) The functions \( \hat{\sigma}(x) \) and \( \hat{\sigma}^{-1}(x) \) are bounded \( C^\infty(\mathbb{R}^3) \)-functions, with bounded first derivatives. Moreover, the least eigenvalue of \( a(x) \) is uniformly bounded away from zero, i.e.,

\[
y^T a(x) y \geq \lambda |y|^2, \quad \forall x, y \in \mathbb{R}^3, \quad \forall t \geq 0,
\]

for some \( \lambda > 0 \).

(b) The operator in Eq. (9) is hypoelliptic in \( C^\infty(D) \) [e.g., see Hörmander (1967) or Elliott (1973)].

Note that the hypoellipticity assumption is in general related to a strong accessibility property of controllable nonlinear systems that are driven by white noises [e.g., see Sussmann and Jurdjevic (1972) concerning the controllability of nonlinear systems, which is closely related to Stroock and Varadhan (1972) and Ichihara and Kunita (1974); see also Elliott (1973, Sect. 3) and Amano (1979, Theorem 2)]. That is, the hypoellipticity assumption further implies that the diffusion process \( X(t) \) has a transition probability density function with strong Feller property.

### 2.2 Minimum exit rates and principal eigenvalues

In this subsection, we consider the following controlled version of SDE in Eq. (8), with the corresponding controlled-diffusion process \( (X_{0,x}(t))_{t \geq 0} \), i.e.,

\[
dX_{0,x}(t) = \left[ F(X_{0,x}(t)) + Bu(t) \right] dt + B\hat{\sigma}(X_{0,x}(t))dW(t), \quad X_{0,x}(0) = x, \quad (10)
\]

where \( u(\cdot) \) is a measurable control process from a set \( \mathcal{U} \) which is \( \mathbb{R} \)-valued progressively measurable processes (i.e., a family of nonanticipative processes, for all \( t > s \), \( W(t) - W(s) \) is independent of \( u(r) \) for \( r \leq s \)) and such that

\[
\mathbb{E} \int_0^\infty |u(t)|^2 dt < \infty.
\]

Here, our main objective is to minimize the asymptotic exit rate with which the controlled-diffusion process \( X_{0,x}^u(t) \) exits from the given bounded open domain \( D \).

In what follows, we specifically consider a stationary Markov control \( u(t) = v(X_{0,x}^u(t)) \in \mathcal{U}, \) for \( t \geq 0 \), with some measurable map \( v: \mathbb{R}^3 \to \mathcal{U} \). Then, we suppose that the controlled-SDE in Eq. (10) is composed with an admissible Markov control \( v \). Furthermore, let \( \tau_D \) be the first exit-time for the controlled-diffusion process \( X_{0,x}^v(t) \) from the given bounded domain \( D \), i.e.,

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\[ \tau_D = \inf \{ t > 0 \mid X_{0,x}^v(t) \in \partial D \}. \quad (11) \]

Notice that the extended generator for the controlled-diffusion process \( X_{0,x}^v(t) \) is given by
\[
\mathcal{L}_v(f)(x) = \frac{1}{2} \text{tr} \left( a(x)D^2_x f(\cdot) \right) + \langle F(x) + B_v(x), D_x f(\cdot) \rangle, \quad (12)
\]
where \( D_x f(\cdot) \) denotes the gradient operator with respect to \( x \) (i.e., \( D_x \equiv [D_{x_1}(\cdot), D_{x_2}(\cdot), D_{x_3}(\cdot)]^T \)).

Next, let us consider the following eigenvalue problem
\[
-\mathcal{L}_v \psi_v(x) = \lambda_v \psi_v(x) \quad \text{in } D
\]
\[
\psi_v(x) = 0 \quad \text{on } \partial D \quad (13)
\]
where the extended generator \( \mathcal{L}_v \) is given in the above Eq. (12).

In the following section, i.e., Sect. 3, using Theorems 1.1, 1.2 and 1.4 from Quaas and Sirakov (2008) [see also Befekadu and Antsaklis (2015, Proposition 3.2)], we provide a condition for the existence of a unique principal eigenvalue \( \lambda_v > 0 \) and an eigenfunction \( \psi_v \in W^{2,p}_{\text{loc}}(D) \cap C(\bar{D}) \) pairs for the eigenvalue problem in Eq. (13), with zero boundary condition on \( \partial D \). Notice that such an eigenvalue \( \lambda_v \) is also related to the minimum asymptotic exit rate with which the controlled-diffusion process \( X_{0,x}^v(t) \) exits from the bounded domain \( D \), when the controlled-SDE in Eq. (10) is composed with an admissible Markov control \( v \).

### 3 Main results

In this section, we present our main results (i.e., Propositions 1 and 2) that characterize admissible solutions to the optimal control problem in Eq. (13).

The following proposition establishes a connection between the minimum exit rate and with that of the principal eigenvalue for the extended generator \( \mathcal{L}_v \) in Eq. (12).

**Proposition 1** Suppose that an admissible Markov control \( v \) is given. Then, the principal eigenvalue \( \lambda_v \) for the extended generator \( \mathcal{L}_v \), with zero boundary condition on \( \partial D \), is given by
\[
\lambda_v = -\limsup_{t \to \infty} \frac{1}{t} \log \mathbb{P}_x \{ \tau_D > t \}, \quad (14)
\]
where \( \tau_D \) is the first exit-time for the controlled-diffusion process \( X_{0,x}^v(t) \) from the given bounded domain \( D \), i.e., \( \tau_D = \inf \{ t > 0 \mid X_{0,x}^v(t) \in \partial D \} \); while the probability \( \mathbb{P}_x \{ \cdot \} \) in Eq. (14) is conditioned on the initial condition \( x \in D \) as well as on the admissible Markov control \( v(X_{0,x}^v(t)) \), for \( t \in [0, \tau_D) \).
Proof For $\delta > 0$, let $D^\delta \subset D$ (with $D^\delta \cup \partial D^\delta \subset D$) be a bounded domain with smooth boundary, increasing to $D$ as $\delta \to 0$. Let

$$\tau_{D^\delta} = \inf\{ t > 0 \mid \mathbf{X}^v_{0,x}(t) \in \partial D^\delta \}.$$ 

Then, applying Krylov’s extension of the Itô’s formula valid for any continuous functions from $W^{2,p}_{loc}(D)$, with $p \geq 2$ [e.g., see Borkar (1989, Chapter 2); cf. Krylov (1980, Sect. 10, pp. 121–128)] and the optional sampling theorem

$$\psi_v(\hat{x}) = E_x\left\{ \exp(\lambda_v(t \wedge \tau_{D^\delta})) \psi_v(\mathbf{X}^v_{0,x}(t \wedge \tau_{D^\delta})) \right\},$$

for some $\hat{x} \in D$.

Letting $\delta \to 0$, then we have $\tau_{D^\delta} \to \tau_D$, almost surely, and

$$\psi_v(\hat{x}) = E_x\left\{ \exp(\lambda_v(t \wedge \tau_D)) \psi_v(\mathbf{X}^v_{0,x}(t \wedge \tau_D)) \right\}$$

$$= E_x\left\{ \exp(\lambda_v t) \psi_v(\mathbf{X}^v_{0,x}(t)) 1\{\tau_D > t\} \right\}$$

$$\leq \|\psi_v(\mathbf{X}^v_{0,x}(t))\|_\infty \exp(\lambda_v t) P_x\{\tau_D > t\}.$$ 

If we take the logarithm and divide both sides by $t$, then, further let $t \to \infty$, we have

$$\lambda_v \geq -\liminf_{t \to \infty} \frac{1}{t} \log P_x\{\tau_D > t\} \geq -\limsup_{t \to \infty} \frac{1}{t} \log P_x\{\tau_D > t\},$$

(15)

with $\delta \to 0$ (since $\tau_{D^\delta} \to \tau_D$, when $\delta \to 0$).

On the other hand, let $B_k \supset \bar{D} \equiv D \cup \partial D$ be an open domain with smooth boundary and let $\tau_{B_k}$ be the first exit-time for the controlled-diffusion process $\mathbf{X}^v_{0,x}(t)$ from the domain $B_k$. Furthermore, let $\psi_{v,B_k}$ and $\lambda_{v,B_k}$ be the principal eigenfunction-eigenvalue pairs for the eigenvalue problem of $\mathcal{L}_v$ on $B_k$, with $\psi_{v,B_k}(\check{x}) = 1$, for some $\check{x} \in D$.

Then, we have the following

$$\psi_{v,B_k}(\hat{x}) = E_x\left\{ \exp(\lambda_{v,B_k} t) \psi_{v,B_k}(\mathbf{X}^v_{0,x}(t)) 1\{\tau_{B_k} > t\} \right\}$$

$$\geq \inf_{y \in \bar{D}} \left| \psi_{v,B_k}(y) \right| \exp(\lambda_{v,B_k} t) P_x\{\tau_{B_k} > t\}.$$ 

Thus, from Eq. (15), we have the following

$$\lambda_{v,B_k} \leq -\limsup_{t \to \infty} \frac{1}{t} \log P_x\{\tau_D > t\} \leq -\liminf_{t \to \infty} \frac{1}{t} \log P_x\{\tau_D > t\}.$$ 

Then, using Proposition 4.10 of Quaas and Sirakov (2008), we have $\lambda_{v,B_k} \to \lambda_v$ and $\tau_{B_k} \to \tau_D$ as $B_k \to \bar{D}$. This completes the proof of Proposition 1. \qed
Remark 1 In order to confine the controlled-diffusion process $X^v_{0,x}(t)$ for a longer duration in a given bounded domain $D$, a standard approach is to maximize the mean exit-time, i.e., $\max_{u \in U} \mathbb{E}_x\{\tau_D\}$, from the bounded domain $D$. Note that, in general, it is difficult to get effective information about a minimum exit probability and, at the same time, a set of admissible Markov controls in this way. On the other hand, we also observe that a more suitable objective would be to minimize the asymptotic exit rate with which the controlled-diffusion process $X^v_{0,x}(t)$ exits from the bounded domain $D$, where we argued that the corresponding optimal control problem can be closely identified with a nonlinear eigenvalue problem.

In what follows, let us define the following HJB equation

$$L_u(\cdot)(x, u) = \frac{1}{2} \text{tr}\left\{a(x)D^2_{x_1}(\cdot)\right\} + \left\{F(x) + Bu, D_x(\cdot)\right\},$$

with $D_x(\cdot) = [D_{x_1}(\cdot), D_{x_2}(\cdot), D_{x_3}(\cdot)]^T$.

Note that we can also associate the above HJB equation with the following optimal control problem

$$\max_{u \in \mathbb{R}} \left\{L_u\psi(x, u) + \lambda\psi(x)\right\}.$$

Then, we have the following result that provides a sufficient condition for admissible optimal Markov control.

Proposition 2 There exist a unique $\lambda^* > 0$ (which is the minimum exit rate) and $\psi^* \in C^2(D) \cap C(\overline{D})$, with $\psi^* > 0$ on $D$, that satisfies the optimal control problem in Eq. (17). Moreover, the admissible Markov control $v^*$ is optimal if and only if $v^*$ is a measurable selector for

$$\arg \max \left\{L_u\psi^*(x, \cdot)\right\}, \quad x \in D.$$

Proof The first claim for $\psi^* \in W^{2,p}_{loc}(D) \cap C(\overline{D})$, with $p > 2$, follows from Eq. (13) [cf. Quaas and Sirakov (2008, Theorems 1.1, 1.2 and 1.4)]. Notice that if $v^*$ is measurable selector of $\arg \max \left\{L_u\psi^*(x, \cdot)\right\}$, with $x \in D$ [e.g., see also Beneš (1970) on the measurable selection theorem based on specified information about the state trajectories]. Then, by the uniqueness claim for eigenvalue problem in Eq. (13), we have

$$\lambda_{v^*} = -\limsup_{t \to \infty} \frac{1}{t} \log \mathbb{P}_x\{\tau_D > t\},$$

where the probability $\mathbb{P}_x\{\cdot\}$ is conditioned with respect to $x$ and $v^*$. Then, for any other admissible control $u$, we have

$$L_u\psi^*(x, u) + \lambda_{v^*}\psi^*(x) \leq 0, \quad \forall t \geq 0.$$
Let $Q \subset \mathbb{R}^3$ be a smooth bounded open domain containing $\bar{D}$. Let $\hat{\psi}$ and $\hat{\lambda}$ be the principal eigenfunction-eigenvalue pairs for the eigenvalue problem of $L_u$ on $\partial Q$.

Let $\tau_Q = \inf \left\{ t > 0 \mid X_{0,x}^u(t) \in \partial Q \right\}$.

Then, under $u$, we have

$$\hat{\psi}(x) \geq \mathbb{E}_x \left\{ \exp(\hat{\lambda} t) \hat{\psi}(X_{0,x}^u(t)) \mathbf{1}_{\{\tau_Q > t\}} \right\} \geq \inf_{y \in D} \left| \hat{\psi}(y) \right| \exp(\hat{\lambda} t) \mathbb{P}_x \left\{ \tau_Q > t \right\}.$$ 

Leading to

$$\hat{\lambda} \leq - \limsup_{t \to \infty} \frac{1}{t} \log \mathbb{P}_x \left\{ \tau_D > t \right\}.$$ 

Letting $Q$ shrink to $D$ and using Proposition 4.10 of Quaas and Sirakov (2008), then we have $\hat{\lambda} \to \lambda_{v^*}$. Then, we have

$$\lambda_{v^*} = - \limsup_{t \to \infty} \frac{1}{t} \log \mathbb{P}_x \left\{ \tau_D > t \right\},$$

which establishes the optimality of $v^*$ and the fact that $\lambda_{v^*}$ is the minimum exit rate. Conversely, let $\hat{v}^*$ be any optimal Markov control. Then, we have

$$L_{\hat{v}^*} \hat{\psi}(x, \hat{v}^*(x)) + \hat{\lambda}_{\hat{v}^*} \hat{\psi}(x) = 0$$

and

$$L_{v^*} \psi^*(x, \hat{v}^*(x)) + \lambda_{v^*} \psi^*(x) \leq 0, \quad \forall t > 0,$$

with $\hat{\lambda}_{\hat{v}^*} = \lambda_{v^*}$.

Furthermore, notice that $\psi^*$ is a scalar multiple of $\hat{\psi}$ and, at $x \in D$ [cf. Quaas and Sirakov (2008, Theorem 1.4(a))]. Then, we see that $\hat{v}^*$ is also a maximizing measurable selector in Eq. (17). This completes the proof of Proposition 2. □

**Remark 2** Note that the above proposition (which is a verification theorem) is useful for selecting the most appropriate admissible Markov control that confines the controlled-diffusion process $X_{0,x}^u(t)$ to the prescribed bounded domain $D$ for a longer duration.

### 4 Further remarks

This paper briefly considered the problem of controlling a diffusion process pertaining to an opioid epidemic dynamical model with random perturbation so as to prevent
it from leaving a given bounded open domain. Here, we specifically argued that the problem can be posed as minimizing the asymptotic exit rate (as opposed to maximizing the mean exit-time) with which the controlled-diffusional process exits from the given bounded domain; and we further established a connection with a nonlinear eigenvalue problem. Moreover, we also proved a verification theorem that provides a sufficient condition for the solution of the corresponding HJB equation and minimizing admissible controls.

Here, it is worth remarking that there are many possible directions for extensions, for example, one obvious extension would be to consider a risk-sensitive version of the mean escape time criterion in the sense of Dupuis and McEneaney (1997), when the randomly perturbed opioid epidemic dynamics obeys a controlled-SDE with coefficients depending on a small parameter $\epsilon \ll 1$ (cf. Eq. (10)), i.e.,

$$dX^{\epsilon, u}(t) = \left[ F(X^{\epsilon, u}(t)) + Bu(t) \right] dt + \sqrt{\epsilon} B\hat{\sigma}(X^{\epsilon, u}(t)) dW(t), \quad X^{\epsilon, u}(0) = x.$$ 

Note that the natural optimization criterion is to minimize the exponential function of the escape time to a critical loss threshold, i.e.,

$$\mathbb{E}_x^{\epsilon} \exp \left\{ -\frac{\theta \tau_D^{\epsilon}}{\epsilon} \right\},$$

where $\theta$ is a positive design parameter, $\tau_D^{\epsilon} = \inf \{ t > 0 | X^{\epsilon, u}(t) \in \partial D \}$, and $\mathbb{E}_x^{\epsilon} \{ \cdot \}$ denotes the expectation conditioned on $X^{\epsilon, u}(t)$. Equivalently, we can also consider maximizing the following criterion

$$-\epsilon \log \mathbb{E}_x^{\epsilon} \exp \left\{ -\frac{\theta \tau_D^{\epsilon}}{\epsilon} \right\},$$

where the risk-sensitive problem is to obtain an admissible optimal control for the following value

$$\max_{u \in U} -\epsilon \log \mathbb{E}_x^{\epsilon} \exp \left\{ -\frac{\theta \tau_D^{\epsilon}}{\epsilon} \right\} \quad \text{as} \quad \epsilon \to 0,$$

which is also averse to any rapid escapes from the given bounded domain $D$. Moreover, along this direction, one could also exploit the connection between viscosity solutions and that of the theory of large deviations, where the escape time control can be posed as a stochastic differential game [e.g., see Boué and Dupuis (2001) for additional discussions related to time-consistency of such admissible optimal controls]. Another possible extension is to consider a general class of opioid epidemic models described by stochastic differential equations that are driven by a Poisson process [e.g., see Kratz and Pardoux (2018), Pardoux and Samegni-Kepgnou (2017) or Pardoux and Samegni-Kepgnou (2018) for related discussions] and then apply large deviation theory to study the qualitative behavior of such general opioid epidemic models, for example, by providing sufficient information on the probabilistic characteristic of the most probable population trajectory when exiting from the domain of interest, where such
additional information could be useful for interpreting outcome-results from opioid-related intervention policies.

Finally, we emphasize that obtaining qualitative information on the asymptotic exit rate (including the first-exit time from $D$ and the first-exit location on $\partial D$) for the diffusion process pertaining to an opioid epidemic dynamics with random perturbation could be useful for developing evidence-based strategies that aim at curbing opioid epidemics or assisting in interpreting outcome results from opioid-related policies. Moreover, results—based on such qualitative information—are more practical for characterizing typical sample paths of regular prescription opioid users, opioid addicts or the process of rehabilitation and relapsing into opioid drug uses.

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