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RESEARCH ARTICLE

A Stochastic Impulsive Competition Model for Tumor Evolution under Intermittent Androgen Deprivation Therapy

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Abstract

In prostate cancer treatment, intermittent androgen deprivation therapy can delay the emergence of drug resistance, yet its efficacy is influenced by environmental fluctuations, treatment parameters, and competition among tumor cell populations. To investigate the mechanisms underlying resistance during intermittent therapy, we developed a stochastic impulsive differential equation model. First, a global analysis of the model without environmental noise is conducted. Subsequently, sufficient conditions for tumor extinction and persistence are established based on stochastic stability theory. Numerical simulations further demonstrate that moderate noise suppresses tumor growth, and an optimal treatment intensity exists beyond which excessive intervention accelerates drug resistance. Moreover, excessively high treatment frequency impairs the recovery of androgen-dependent cells, thereby compromising resistance control.

Keywords: prostate cancer, intermittent androgen suppression, stochastic impulsive model, drug resistance.

1 Introduction

Prostate cancer ranks among the most common and life-threatening malignancies in men globally, with an incidence second only to all male cancers and a mortality rate fifth among cancer-related deaths, making it a critical public health issue [1, 2]. With the accelerated aging of populations and the widespread adoption of early screening, the diagnosis rate of prostate cancer has been increasing annually [3–5]. Extensive research has demonstrated that the development and progression of prostate cancer are highly dependent on the androgen signaling pathway, where androgens play a pivotal regulatory role in tumor cell proliferation and survival [6]. Based on this biological characteristic, androgen deprivation therapy (ADT) has long been established as the standard endocrine treatment strategy for advanced and metastatic prostate cancer [7, 8].

Clinically, ADT is primarily administered in two forms: continuous androgen deprivation (CAD)

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and intermittent androgen deprivation (IAD) [9]. CAD typically involves surgical or pharmacological castration to maintain serum androgen levels persistently within the castration range, thereby suppressing the proliferation of androgen-dependent (AD) cancer cells. However, under sustained strong selective pressure, a fraction of AD cells may undergo molecular mutations or activate alternative signaling pathways, enabling them to proliferate without exogenous androgen. This evolutionary adaptation facilitates the emergence of androgen-independent (AI) cancer cells, ultimately driving disease progression to metastatic castration-resistant prostate cancer (mCRPC), and leading to treatment failure [15, 17]. In contrast, IAD regulates androgen levels in a cyclic manner: during treatment periods, androgens are temporarily reduced to inhibit AD-cell growth, and therapy is suspended once prostate-specific antigen (PSA) levels fall below a predefined threshold, allowing endogenous androgen levels to recover. Such periodic modulation of the hormonal environment can attenuate the strong and continuous selective pressure imposed by CAD, thus reducing the likelihood of rapid phenotypic conversion of AD to AI cells under long-term androgen deprivation. Meanwhile, restoring androgen during the off-treatment period helps maintain a sufficient population of AD cells and weakens the fitness advantage of certain AI subclones, enabling ecological competition to suppress AI expansion and delay the onset of mCRPC under a manageable tumor burden. Moreover, intermittent recovery of androgen levels can alleviate adverse effects associated with prolonged hypoandrogenism, including sexual dysfunction, osteoporosis, and cognitive decline [18–20].

Extensive dynamical modeling efforts have been devoted to studying ADT and its combination strategies, providing important insights into how key regulatory factors influence disease progression. Ideta et al. [10] developed a PSA-threshold–based switching model to compare CAD and IAD, demonstrating that, under certain biological assumptions, the persistent strong selective pressure imposed by CAD is more likely to drive the system toward relapse, while IAD, through PSA-regulated switching, periodically modulates the androgen environment and therefore can delay or even prevent disease recurrence [28, 29]. In parallel, tumor growth is inevitably affected by fluctuations in environmental factors such as temperature, radiation, chemical exposure, oxygen availability, and nutrient supply [21–24]. These stochastic perturbations alter cellular proliferation and apoptosis rates and may also influence the cumulative effect of therapeutic selective pressures. To more accurately capture such uncertainties, Zazoua and Wang formulated a stochastic model under a continuous-deprivation setting, incorporating differential competition coefficients between AD and AI cells. Their analysis highlights how noise intensity and competitive interactions jointly determine cancer cell extinction or persistence [13]. Building on this direction, Tanaka et al. [11] introduced stochastic disturbances into an IAD framework and fitted the model to clinical data, quantifying how AI growth parameters and initial androgen levels shape treatment-cycle duration and relapse timing, thereby underscoring the role of random fluctuations in tumor evolution. Moreover, modeling studies have been extended to combined therapeutic strategies. Rutter integrated ADT with dendritic cell (DC) vaccination and showed that more frequent DC administration, under equivalent total dosage, can delay the onset of mCRPC. Yang further developed a stochastic model coupling ADT with pulsed DC immunotherapy, demonstrating that high-noise environments and high-frequency immunization can effectively suppress tumor progression [12, 14].

Compared with a constant castration environment, the periodic alternation of androgen levels in prostate cancer treatment helps avoid subjecting AD cells to sustained strong selection pressure, which could otherwise accelerate their transformation into the AI cells phenotype. The recovery of androgen during off-treatment periods can both reduce the proliferative advantage of certain AI clones and preserve a sufficient population of AD cells, enabling ecological competition to suppress AI expansion. These combined effects may delay the emergence of resistance while maintaining overall tumor burden at manageable levels. Although existing studies have revealed several clinical features of IAD through data fitting and numerical simulation, theoretical understanding remains limited, particularly regarding how pulse amplitude and frequency interact with the competitive strength between cancer cell subpopulations to determine long-term disease outcomes. Motivated by this gap, the present study develops a stochastic impulsive dynamical model describing tumor evolution under IAD, while retaining the asymmetric competitive interactions between AD and AI cells. Using analytical conditions together with systematic numerical experiments, we investigate how the periodicity and intensity of IAD, along with cellular competition structure, jointly regulate resistance dynamics and shape the long-term fate of prostate cancer.

This paper is structured as follows: Section 2 begins by introducing the stochastic model used in the study and the relevant theoretical foundations. Subsequently, Section 3 analyzes the stability of the deterministic system of the model. Section 4 derives the threshold conditions for the mean persistence and extinction of cells. To verify the theoretical results, Section 5 provides multiple sets of numerical simulations. Finally, Section 6 summarizes the research content of the entire paper and presents several conclusions and future research prospects.

2 Mathematical model

2.1 Model formation

Zazoua and Wang [13] considered distinct competition coefficients between AD and AI cancer cells and established the following stochastic differential equations for CAD.

$$\begin{cases} dx_1(t) = \left[r_1 x_1 A\left(1 - \dfrac{x_1 + \alpha x_2}{K}\right) \right. \\ \qquad \left. - (d_1 + m_1)\left(1 - \dfrac{A}{a_0}\right) x_1 \right] dt \\ \qquad + \sigma_1 x_1 dB_1(t), \\ dx_2(t) = \left[r_2 x_2 \left(1 - \dfrac{\beta x_1 + x_2}{K}\right) \right. \\ \qquad \left. + m_1 \left(1 - \dfrac{A}{a_0}\right) x_1 \right] dt \\ \qquad + \sigma_2 x_2 dB_2(t), \\ dA(t) = \big[-\gamma(a_0 - A) - \gamma a_0 u \big] dt. \end{cases} \tag{1}$$

where x_1 , x_2 and A are the concentrations of AD cancer cells, AI cancer cells and androgen, r_1 and r_2 are the proliferation death rate of AD and AI cancer cells, respectively, d_1 is the death rate of AD cells. a_0 is the normal androgen concentration, α and β are the positive competition coefficients between two types of tumor cells, m_1 is the maximum mutation rate from AD to AI cancer cells, u is the efficacy of ADT, K is the carrying capacity of these cells, γ is the androgen clearance and production rate.

To delay prostate cancer recurrence and optimize the androgen deprivation therapy regimen, we modified the continuous androgen deprivation model proposed by Wang into a pulsed intermittent androgen deprivation model.

$$\begin{cases} \left.\begin{aligned} dX_1(t) &= [r_1 A(1 - \frac{X_1 + \alpha X_2}{K}) \\ &\quad - (d_1 + m_1)(1 - \frac{A}{a_0})] X_1 dt \\ &\quad + \sigma_1 X_1 dB_1(t), \\ dX_2(t) &= [r_2 X_2 (1 - \frac{\beta X_1 + X_2}{K}) \\ &\quad + m_1 (1 - \frac{A}{a_0}) X_1] dt \\ &\quad + \sigma_2 X_2 dB_2(t), \\ dA(t) &= -\gamma(A - a_0) dt, \end{aligned}\right\} \quad t \neq nT, \\ A(nT^+) = (1 - \delta) A(nT), \quad t = nT. \end{cases} \tag{2}$$

where δ is the intensity of treatment of IAD , σ_1 *and* σ_2 are the intensities of the white noise influencing X_1 *and* X_2. In addition we keep the meaning of other parameters consistent with (1) and note that all the parameters in (2) are positive.

Through a simple calculation, we obtain the T-periodic solution of $A^T(t)$ of system (2),

$$A^T(t) = a_0 + \frac{-\delta a_0 e^{-\gamma(t - nT)}}{1 - (1 - \delta) e^{-\gamma T}},$$

Replace $A(t)$ with $A^T(t)$, then we get the reduced system of system (2),

$$\begin{cases} dX_1(t) = \{P(1 - \frac{X_1 + \alpha X_2}{K}) \\ \qquad - (Q_1 + Q_2)\} X_1 dt + \sigma_1 X_1 dB_1(t), \\ dX_2(t) = \{r_2 X_2 (1 - \frac{\beta X_1 + X_2}{K}) + Q_2 X_1\} dt \\ \qquad + \sigma_2 X_2 dB_2(t). \end{cases} \tag{3}$$

where $P = r_1 A^T$, $Q_1 = d_1(1 - \frac{A^T}{a_0})$, $Q_2 = m_1(1 - \frac{A^T}{a_0})$. Next, we analyze the global dynamics of the equivalent system (3). To this end, we first introduce some essential definitions and lemmas.

2.2 Preliminaries

In this section, we give following notations, lemmas and definitions of this paper. Assumed that $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\geq 0}, \mathbb{P})$ is a complete probability space equipped with a filtration $\{\mathcal{F}_t\}_{t\geq 0}$ that is right-continuous. In this probability space, we define $B_i(t)$ $(i = 1, \dots, n)$ as independent Brownian motions.

If the number of factors in a product is zero, we assume the product equals 1.

For convenience, we give some notations,

$$\langle f(t)\rangle^* = \limsup_{t\to+\infty} f(t),$$

$$\langle f(t)\rangle_* = \liminf_{t\to+\infty} f(t),$$

$$\langle f(t)\rangle_t = \frac{1}{t}\int_0^t f(s)ds.$$

Definition 1. [14] The population $X_i(t)$ becomes extinct if

$$\lim_{t\to+\infty} X_i(t) = 0 \quad \text{a.s.}$$

The population $X_i(t)$ becomes persistent in mean if

$$\limsup_{t\to+\infty} \frac{1}{t}\int_0^t X_i(s)ds > 0 \quad \text{a.s.}$$

Definition 2. [13] The solution is said to be stochastically ultimately bounded if for any $\varepsilon \in (0,1)$, there exists a positive constant $M = M(\varepsilon)$ such that for any initial value $X(0) = (X_1(0), X_2(0)) \in \mathbb{R}_+^2$, the corresponding solution $X(t) = (X_1(t), X_2(t))$ satisfies,

$$\limsup_{t\to+\infty} \mathbb{P}\{|X(t)| > M\} < \varepsilon.$$

Lemma 1 [14] *Let* $M = \{M_t\}_{t\geq 0}$ *be a real-valued continuous local martingale with* $M_0 = 0$. *If*

$$\limsup_{t\to+\infty} \frac{\langle M, M\rangle_t}{t} < \infty \quad \text{a.s.}$$

then

$$\lim_{t\to+\infty} \frac{M_t}{t} = 0 \quad \text{a.s.}$$

The Brownian motion $B(t)$ *is a continuous square integrable martingale, and its quadratic variation is* $\langle B(t), B(t)\rangle_t = t \quad (t \geq 0)$. *Therefore, from Lemma 1,*

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

and for any small $\varepsilon \in (0,1)$, *there exists a large* T *such that*

$$\left|\frac{B(t)-B(s)}{t-s}\right| < \varepsilon, \quad t-s > T \quad a.s.$$

Lemma 2 [25] *Suppose* $X(t) \in C[\Omega \times R_+, R_+]$,

1. *If there exist constants* $\lambda_0 > 0$, $t_1 > 0$ *and* $\lambda \geq 0$ *such that,*

$$\ln X(t) \leq \lambda t - \lambda_0 \int_0^t X(s)ds + \sum_{i=1}^n \sigma_i B_i(t),$$

for any $t > t_1$, *where* σ_i *is a constant,* $1 \leq i \leq n$, *then*

$$\langle X(t)\rangle^* \leq \frac{\lambda}{\lambda_0} \quad \text{a.s.}$$

2. *If there exist constants* $\lambda_0 > 0$, $t_1 > 0$ *and* $\lambda \geq 0$ *such that*

$$\ln X(t) \geq \lambda t - \lambda_0 \int_0^t X(s)ds + \sum_{i=1}^n \sigma_i B_i(t),$$

for any $t > t_1$, *where* σ_i *is a constant,* $1 \leq i \leq n$, *then*

$$\langle X(t)\rangle_* \geq \frac{\lambda}{\lambda_0} \quad \text{a.s.}$$

3 Analysis of deterministic model

As a preliminary analysis, we first consider the deterministic version of model (3). Then we set $\sigma_1 = \sigma_2 = 0$ in system (3), we obtain the following deterministic system:

$$\begin{cases} \frac{dX_1}{dt} = PX_1\left(1 - \frac{X_1+\alpha X_2}{K}\right) - (Q_1+Q_2)X_1, \\ \frac{dX_2}{dt} = r_2X_2\left(1 - \frac{\beta X_1 + X_2}{K}\right) + Q_2X_1. \end{cases} \tag{4}$$

Then the following three theorems establish the existence of equilibrias and analyze their stability properties for the system (4).

Theorem 1
(1) *The trivial equilibrium point* $E_0 = (0,0)$ *and the boundary equilibrium point* $E_1 = (0, K)$ *always exist.*

(2) *Assume that*

$$1 - \frac{Q_1+Q_2}{P} > \alpha \tag{5}$$

holds. Then there exists a unique positive equilibrium point $E_2 = (X_1^*, X_2^*)$ *in* (4). *In addition, system* (4) *has two positive equilibria* $E^1 = (X_1^1, X_2^1)$ *and* $E^2 = (X_1^2, X_2^2)$ *if conditions*

$$\begin{aligned} &0 < 1 - \frac{Q_1+Q_2}{P} < \alpha, \\ &0 < -\frac{b}{2a} < \frac{K}{\alpha}\left(1 - \frac{Q_1+Q_2}{P}\right), \\ &f\left(-\frac{b}{2a}\right) < 0 \end{aligned} \tag{6}$$

holds.

Proof (2) We consider the case where both $X_1^*$and X_2^* are non-zero and setting $\frac{dX_1}{dt}=0$, $\frac{dX_2}{dt}=0$, get

$$X_1 = K\left(1-\frac{Q_1+Q_2}{P}\right)-\alpha X_2. \tag{7}$$

Substitute (7) into the first equation of (4), obtaining a quadratic equation in X_2:

$$f(X_2)=aX_2^2+bX_2+c, \tag{8}$$

where $a=\frac{r_2(\alpha\beta-1)}{K}$, $c=Q_2K\left(1-\frac{Q_1+Q_2}{P}\right)$, and $b=r_2\left[1-\beta\left(1-\frac{Q_1+Q_2}{P}\right)\right]-\alpha Q_2$.

First, if condition (5) holds ,It can be calculated that

$$f\left(\frac{K}{\alpha}(1-\frac{Q_1+Q_2}{P})\right)<0, \quad f(0)=c>0.$$

Therefore, equation (8) has exactly one positive root X_2^* in the interval $\left(0,\frac{K}{\alpha}(1-\frac{Q_1+Q_2}{P})\right)$. Thus, system (4) has a unique positive equilibrium point (X_1^*,X_2^*), where $X_1^*=K\left(1-\frac{Q_1+Q_2}{P}\right)-\alpha X_2^*>0$.

If condition (6) holds, then it can be calculated that

$$f\left(\frac{K}{\alpha}(1-\frac{Q_1+Q_2}{P})\right)>0, \quad f(0)=c>0.$$

Besides, we also have $f(-\frac{b}{2a})<0$,thus equation (8) has a positive root in $(0,-\frac{b}{2a})$ and another positive root in $\left(-\frac{b}{2a},\frac{K}{\alpha}(1-\frac{Q_1+Q_2}{P})\right)$. Thus, the system (4) has two positive equilibrium points $E^1(X_1^1,X_2^1)$ and $E^2(X_1^2,X_2^2)$.

Theorem 2
(1) The trivial equilibrium point $E_0(0,0)$ is unstable.

(2) $E_1(0,K)$ is locally asymptotically stable if

$$1-\frac{Q_1+Q_2}{P}<\alpha.$$

(3) $E_2(X_1^*,X_2^*)$ is locally asymptotically stable if

$$1-\frac{Q_1+Q_2}{P}>\alpha.$$

(4) If condition (6) is satisfied, then $E^1(X_1^1,X_2^1)$ is locally asymptotically stable and $E^2(X_1^2,X_2^2)$ is a saddle point.

Proof (1) We can obtain the Jacobian matrix at the equilibrium point as follows.

$$J=\begin{pmatrix} P(1-\dfrac{2X_1^*+\alpha X_2^*}{K}) - (Q_1+Q_2) & -\frac{\alpha P}{K}X_1^* \\ -\frac{\beta r_2}{K}X_2^*+Q_2 & r_2(1-\dfrac{\beta X_1^*+2X_2^*}{K}) \end{pmatrix}$$

At the equilibrium point E_0, the Jacobian matrix J_0 is

$$J_0=\begin{pmatrix} P-(Q_1+Q_2) & 0 \\ Q_2 & r_2 \end{pmatrix}.$$

Since $r_2>0$, so the equilibrium point E_0 is unstable.
(2) At the equilibrium point E_1, the Jacobian matrix J_1 is

$$J_1=\begin{pmatrix} P(1-\alpha)-(Q_1+Q_2) & 0 \\ -\beta r_2+Q_2 & -r_2 \end{pmatrix}.$$

Thus, if $1-\frac{Q_1+Q_2}{p}<\alpha$ holds,the equilibrium point E_1 is locally asymptotically stable.

(3) At the equilibrium point E_2, the Jacobian matrix is J ,and we have

$$Q_1+Q_2=P(1-\frac{X_1^*+\alpha X_2^*}{K}),$$
$$r_2(1-\frac{\beta X_1^*+2X_2^*}{K})=-Q_2\frac{X_1^*}{X_2^*}<0$$

Thus,

$$trJ=-\frac{P}{K}X_1^*-Q_2\frac{X_1^*}{X_2^*}<0, \tag{9}$$

Furthermore, when $\alpha\beta\le 1$,

$$\begin{aligned} D := \det J &= -\frac{P}{K}X_1^*r_2(1-\frac{\beta X_1^*+2X_2^*}{K}) \\ &+\frac{\alpha P}{K}X_1^*Q_2-\frac{\alpha\beta P r_2}{K^2}X_1^*X_2^* \\ &=\frac{PX_1^*}{K^2}(r_2(2-\alpha\beta)X_2^* \\ &+KQ_2\alpha-r_2K+r_2\beta X_1^*) \\ &>0. \end{aligned} \tag{10}$$

If $\alpha\beta>1$, the sign of the D is determined by

$$D_1=r_2(2-\alpha\beta)X_2^*+KQ_2\alpha-r_2K+r_2\beta X_1^*, \tag{11}$$

Substituting equation (7) into equation (11), we obtain:

$$\begin{aligned} D_1 &= 2r_2X_2^*(1-\alpha) \\ &-K\left[r_2(1-\beta(1-\frac{Q_1+Q_2}{P}))+\alpha Q_2\right] \\ &=-2Ka\left(X_2^*+\frac{b}{2a}\right). \end{aligned} \tag{12}$$

Since $\alpha\beta>1$, according to Theorem 3.1, there exists one positive root for the input value curve, so $X_2^*<-\frac{b}{2a}$. From equation (12), we get $D_1>0$. Therefore, from Hurwitz criterion indicates we know that all eigenvalues have negative real parts, and consequently, the equilibrium point is locally asymptotically stable. Similarly, we can obtain that the Jacobian determinant at equilibrium point $E^1(X_1^1, X_2^1)$ is positive, while at equilibrium point $E^2(X_1^2, X_2^2)$ it is negative.Hence, Theorem 2 is proved.

Theorem 3
(1) $E_1(0, K)$ is globally asymptotically stable if

$$1 - \frac{Q_1 + Q_2}{P} < \alpha.$$

(2) $E_2(X_1^*, X_2^*)$ is globally asymptotically stable if

$$1 - \frac{Q_1 + Q_2}{P} > \alpha.$$

Proof Let

$$f(X_1, X_2) = PX_1\left(1 - \frac{X_1 + \alpha X_2}{K}\right) - (Q_1 + Q_2)X_1,$$

$$g(X_1, X_2) = r_2X_2\left(1 - \frac{\beta X_1 + X_2}{K}\right) + Q_2X_1.$$

Taking the Dulac function $D(X_1, X_2) = \frac{1}{X_1X_2}$, then

$$\begin{aligned}
&\frac{\partial(Df)}{\partial X_1} + \frac{\partial(Dg)}{\partial X_2}\\
&= -\frac{1}{X_1^2X_2}\left[PX_1\left(1 - \frac{X_1 + \alpha X_2}{K}\right) - (Q_1 + Q_2)X_1\right]\\
&\quad + \frac{1}{X_1X_2}\left[P\left(1 - \frac{2X_1 + \alpha X_2}{K}\right) - (Q_1 + Q_2)\right]\\
&\quad - \frac{1}{X_1X_2^2}\left[r_2X_2\left(1 - \frac{\beta X_1 + X_2}{K}\right) + Q_2X_1\right]\\
&\quad + \frac{1}{X_1X_2}\left[r_2\left(1 - \frac{\beta X_1 + 2X_2}{K}\right)\right]\\
&= -\left(\frac{P}{KX_2} + \frac{Q}{X_2^2} + \frac{r_2}{KX_1}\right) < 0.
\end{aligned}$$

By the Dulac criterion, system (4) has no closed orbits, According to the Poincaré-Bendixson theorem and the local stability of the these equilibrium points, we can conclude that if $1 - \frac{Q_1+Q_2}{P} < \alpha$, then E_1 is globally stable. If $1 - \frac{Q_1+Q_2}{P} > \alpha$, then E_2 is globally stable. This completes the proof.

4 Analysis of stochastic model

4.1 Existence and uniqueness of the solution

Theorem 4 *For any initial value $(X_1(0), X_2(0)) \in \mathbb{R}_+^2$, system (3)has a unique global positive solution: $(X_1(t), X_2(t)) \in \mathbb{R}_+^2$ a.s.*

Proof First , let us show that model (3) has a unique local positive solution.Consider the following equations:

$$\begin{cases}
dx(t) = \Big[P\Big(1 - \dfrac{e^{x(t)} + \alpha e^{y(t)}}{K}\Big)\\
\qquad - (Q_1 + Q_2) - \dfrac{1}{2}\sigma_1^2\Big]dt + \sigma_1 dB_1(t),\\
dy(t) = \Big[r_2\Big(1 - \dfrac{\beta e^{x(t)} + e^{y(t)}}{K}\Big) + Q_2\dfrac{e^{x(t)}}{e^{y(t)}}\\
\qquad - \dfrac{1}{2}\sigma_2^2\Big]dt + \sigma_2 dB_2(t).
\end{cases} \tag{13}$$

with initial data $x(0) = \ln X_1(0)$, $y(0) = \ln X_2(0)$. Clearly, the coefficients of model (13) satisfy the local Lipschitz condition, therefore (13) has a unique local solution $(x(t), y(t))^T$ on $[0, \tau_c)$, where τ_c represents the explosion time. According to Itô's formula, $\big(X_1(t) = e^{x(t)}, X_2(t) = e^{y(t)}\big)$ is the unique local positive solution to (3). Now let us verify that $\tau_c = +\infty$. Consider the following auxiliary systems:

$$\begin{aligned}
dn(t) &= n(t)[P - Q_1 - Q_2 - \frac{P}{K}n(t)\\
&\quad - \frac{\alpha P}{K}M(t)]dt + \sigma_1 n(t)dB_1(t), && (14)\\
dN(t) &= N(t)\left[P - Q_1 - Q_2 - \frac{P}{K}N(t)\right]dt\\
&\quad + \sigma_1 N(t)dB_1(t), && (15)\\
dm(t) &= m(t)\left(r_2 - \frac{\beta r_2 N(t)}{K} - \frac{r_2 m(t)}{K}\right)dt\\
&\quad + \sigma_2 m(t)dB_2(t), && (16)\\
dM(t) &= M(t)\left(r_2 + \frac{Q_2 N(t)}{m(t)} - \frac{r_2 M(t)}{K}\right)dt\\
&\quad + \sigma_2 M(t)dB_2(t). && (17)
\end{aligned}$$

According to the comparison theorem of stochastic differential equations [26], for $t \in [0, \tau_c)$,

$$n(t) \le X_1(t) \le N(t), m(t) \le X_2(t) \le M(t) \ a.s. \tag{18}$$

Inspired by Theorem 2.2 in Jiang [16], we get

$$\begin{aligned} N(t) &= \exp\left[(P - Q_1 - Q_2 - \tfrac{1}{2}\sigma_1^2)t + \sigma_1 B_1(t)\right] \\ &\times \left\{\frac{1}{N(0)} + \frac{P}{K}\int_0^t \exp[\sigma_1 B_1(s)] \right. \\ &\qquad \left. \times \exp[(P - Q_1 - Q_2 - \tfrac{1}{2}\sigma_1^2)s]ds\right\}^{-1}, \quad (19) \end{aligned}$$

$$\begin{aligned} n(t) &= \exp\Big[\int_0^t (P - Q_1 - Q_2 - \tfrac{\alpha M(s)}{K}P - \tfrac{1}{2}\sigma_1^2)ds\Big] \\ &\times \exp\left[\sigma_1 B_1(t)\right]\Big\{\frac{1}{n(0)} + \frac{P}{K}\int_0^t e^{\sigma_1 B_1(v)} \\ &\times \exp\Big[\int_0^v (P - Q_1 - Q_2 - \tfrac{\alpha M(s)}{K}P \\ &\quad - \tfrac{1}{2}\sigma_1^2)ds\Big]dv\Big\}^{-1}, \quad (20) \end{aligned}$$

$$\begin{aligned} m(t) &= \exp\Big[\int_0^t (r_2 - \tfrac{\beta r_2 N(s)}{K} - \tfrac{1}{2}\sigma_1^2)ds + \sigma_2 B_2(t)\Big] \\ &\times \Big\{\frac{1}{m(0)} + \frac{r_2}{K}\int_0^t \exp\Big[\int_0^v (r_2 - \tfrac{\beta r_2 N(s)}{K} \\ &- \tfrac{1}{2}\sigma_1^2)ds\Big]\exp\left[\sigma_2 B_2(v)\right]dv\Big\}^{-1}, \quad (21) \end{aligned}$$

$$\begin{aligned} M(t) &= \exp\Big[\int_0^t (r_2 + \tfrac{Q_2 N(s)}{m(s)} - \tfrac{1}{2}\sigma_2^2)ds + \sigma_2 B_2(t)\Big] \\ &\times \Big\{\frac{1}{M(0)} + \frac{r_2}{K}\int_0^t \exp\Big[\int_0^v (r_2 + \tfrac{Q_2 N(s)}{m(s)} \\ &- \tfrac{1}{2}\sigma_2^2)ds\Big]\exp\left[\sigma_2 B_2(v)\right]dv\Big\}^{-1}. \quad (22) \end{aligned}$$

Note that $N(t) > n(t) > 0$, $m(t) > 0$, and $M(t) > 0$ hold for all $t > 0$, so $t_c = +\infty$.

Theorem 5 *The positive solutions $X(t) = (X_1(t), X_2(t))$ of system (3) are stochastically ultimately bounded.*

Proof Let $V(t_1, X_2, X_2) = e^t(X_1^q + X_2^q)$, where $p > 1$. By applying Itô's formula we obtain,

$$\begin{aligned} & dV(t, X_1, X_2) \\ &= e^t(X_1^q + X_2^q)dt + qe^t(X_1^{q-1}dX_1 + X_2^{q-1}dX_2) \\ &\quad + \frac{1}{2}q(q-1)e^t[X_1^{q-2}(dX_1)^2 + X_2^{q-2}(dX_2)^2] \\ &\le e^t[(1 + q(P + \frac{1}{2}(q-1)\sigma_1^2))X_1^q - \frac{qP}{K}X_1^{q+1}] \\ &\quad + e^t[qQ_2X_1X_2^{q-1} + (1 + q(r_2 + \frac{q-1}{2}\sigma_2^2))X_2^q \\ &\quad - \frac{qr_2}{K}X_2^{q+1}]dt + qe^t\sum_{i=1}^{2}\sigma_i X_i^q dB_i(t) \\ &\le e^t(Q_1 + Q_2)dt + qe^t\sum_{i=1}^{2}\sigma_i X_i^q dB_i(t), \end{aligned} \quad (23)$$

where $Q_1, Q_2 > 0$ and denote $H = Q_1 + Q_2$, Integrating both sides of equation (23) from 0 to t and taking expectation yields,

$$\mathbb{E}\left[e^t\left(X_1^q(t) + X_2^q(t)\right)\right] \le X_1^q(0) + X_2^q(0) + H(e^t - 1).$$

Hence,

$$\mathbb{E}\left[X_1^q(t) + X_2^q(t)\right] \le e^{-t}\left(X_1^q(0) + X_2^q(0)\right) + H(1 - e^{-t}),$$

$$\limsup_{t\to+\infty}\mathbb{E}\left[X_1^q(t) + X_2^q(t)\right] \le H. \quad (24)$$

Note that,

$$|X|^q = \left(X_1^2 + X_2^2\right)^{\frac{q}{2}} \le 2^{\frac{q}{2}}\left(X_1^q + X_2^q\right). \quad (25)$$

Therefore, from (24) and (25) , it follows that

$$\limsup_{t\to+\infty}\mathbb{E}\left[|X|^q\right] < 2^{\frac{q}{2}}H.$$

For $\forall\, \varepsilon \in (0, 1)$, let $M_1 = \sqrt{2}\left(\frac{H}{\varepsilon}\right)^{\frac{1}{q}}$, By Chebyshev's inequality,

$$\begin{aligned} \limsup_{t\to+\infty}\mathbb{P}\left\{|X| > M_1\right\} &= \limsup_{t\to+\infty}\mathbb{P}\left\{|X|^q > M_1^q\right\} \\ &< \frac{2^{\frac{q}{2}}H}{[\sqrt{2}(\frac{H}{\varepsilon})^{\frac{1}{q}}]^q} = \varepsilon. \end{aligned}$$

Thus, the solution of this model is stochastically ultimately bounded.

4.2 Persistence in mean and extinction

Theorem 6 *Assume*

$$P - (Q_1 + Q_2) < \frac{1}{2}\sigma_1^2, \quad (26)$$

Then we have the following assertions:

(1) *Androgen-dependent cells X_1 go to extinction.*

(2) *If*

$$r_2 - \frac{\sigma_2^2}{2} < 0, \quad (27)$$

then androgen-independent cells X_2 go to extinction.

(3) *If*

$$r_2 - \frac{\sigma_2^2}{2} > 0, \quad (28)$$

then androgen-independent cells X_2 are persistent in mean.

Proof (1) First,we prove the extinction of AD cells X_1 under condition (26). Applying Itô's formula to $\ln X_1(t)$ and integrate it from 0 to t, we obtain

$$\begin{aligned}&\frac{1}{t}(\ln X_1(t) - \ln X_1(0))\\ &= (P - Q_1 - Q_2 - \frac{1}{2}\sigma_1^2) - \frac{P}{K}\langle X_1(t)\rangle \\ &- \frac{\alpha P}{K}\langle X_2(t)\rangle + \sigma_1 \frac{B_1(t)}{t}\end{aligned} \tag{29}$$

Taking the upper limit of (29) yields

$$\limsup_{t\to+\infty} \frac{1}{t} \ln \frac{X_1(t)}{X_1(0)} \leq P - Q_1 - Q_2 - \frac{1}{2}\sigma_1^2 < 0 \quad \text{a.s.}$$

Therefore,

$$\lim_{t\to+\infty} X_1(t) = 0 \quad \text{a.s.}$$

That is to say , $P(\Omega_1) = 1$ holds, where $\Omega_1 = \{\omega_1 \in \Omega : \lim_{t\to\infty} X_1(t, \omega_1) = 0\}$. As a consequence, for any $\omega_1 \in \Omega_1$ and any small $\varepsilon_1 > 0$, there exists a constant $T_1(\varepsilon_1, \omega_1) > 0$ such that

$$X_1(t, \omega_1) < \varepsilon_1 \quad \text{for } t \geq T_1. \tag{30}$$

(2) We now proceed to prove the extinction of androgen-independent cells X_2 under condition (26) and (27) .

$$\begin{aligned}dX_2 &= \left[r_2 X_2 \left(1 - \frac{\beta X_1 + X_2}{K}\right) + Q_2 X_1\right] dt \\ &\quad + \sigma_2 X_2 dB_2(t) \\ &\leq (Q_2 X_1 + r_2 X_2)dt + \sigma_2 X_2 dB_2(t).\end{aligned}$$

Recalling the equation (30) ,for $t > T_1$, and $\omega_1 \in \Omega_1$, we have:

$$\begin{aligned}dX_2(t, \omega_1) &\leq [Q_2\varepsilon_1 + r_2 X_2(t, \omega_1)]dt \\ &\quad + \sigma_2 X_2(t, \omega_1) dB_2(t, \omega_1),\end{aligned}$$

Set

$$\begin{aligned}d\varphi(t, \omega_1) &= [Q_2\varepsilon_1 + r_2\varphi(t, \omega_1)]dt \\ &\quad + \sigma_2\varphi(t, \omega_1) dB_2(t, \omega_1),\end{aligned} \tag{31}$$

with initial value $\varphi(0, \omega_1) = X_2(0, \omega_1)$. The solution of (31) is

$$\begin{aligned}\varphi(t, \omega_1) &= \varphi(0, \omega_1) \exp\left[(r_2 - \frac{1}{2}\sigma_2^2)t + \sigma_2 B_2(t, \omega_1)\right] \\ &+ Q_2\varepsilon_1 \int_0^t \exp\Big[(r_2 - \frac{1}{2}\sigma_2^2)(t - s) \\ &+ \sigma_2(B_2(t, \omega_1) - B_2(s, \omega_1))\Big] ds,\end{aligned} \tag{32}$$

According to Lemma 1, for any $\varepsilon_1 \in (0, 1)$, there exists a large T_2 such that

$$\left|\frac{B_2(t, \omega_1) - B_2(s, \omega_1)}{t - s}\right| < \varepsilon_1, \quad \forall \quad t - s > T_2 \tag{33}$$

Without losing generality, we assume that equation (33) is valid for any $\omega_1 \in \Omega_1$.Hence, for all $t > T_2$,

$$\varphi(t, \omega_1) \leq \varphi(0, \omega_1) e^{L_1 t} + \varepsilon_1 Q_2 (I_1 + \frac{e^{L_1 t} - e^{L_1 T_2}}{L_1}) \tag{34}$$

where

$$\begin{aligned}L_1 &= r_2 - \frac{1}{2}\sigma_2^2 + \sigma_2\varepsilon_1 < 0 \\ I_1 &= \int_0^{T_2} e^{\left[(r_2 - \frac{1}{2}\sigma_2^2)v + \sigma_2(B_2(t,\omega_1) - B_2(t-v,\omega_1))\right]} dv\end{aligned}$$

According to Kolmogorov theorem [27], for all $t \geq T_2$,there is a positive constant M_2 such that,

$$I_1 \leq M_2 \quad a.s \tag{35}$$

Taking the superior limit of (34) we obtain that,

$$\limsup_{t\to+\infty} \varphi(t, \omega_1) \leq Q_2\varepsilon_1 (M_2 - \frac{e^{L_1 T_2}}{L_1}),$$

The arbitrariness of ε_1 leads to

$$\limsup_{t\to+\infty} \varphi(t, \omega_1) = 0.$$

From the comparison theorem, we obtain that for all $\omega_1 \in \Omega_1$,

$$\limsup_{t\to+\infty} X_2(t, \omega_1) = 0,$$

In view of $P(\Omega_1) = 1$,we conclude that

$$\lim_{t\to+\infty} X_2(t) = 0 \quad a.s.$$

(3) Now, we show that androgen-independent cells X_2 will be persistent in mean when (26) and (28) holds. Applying Itô's formula to $\ln X_2(t)$ and integrate it from 0 to t.

$$\begin{aligned}&\ln X_2(t) - \ln X_2(0) \\ &= (r_2 - \tfrac{1}{2}\sigma_2^2)t - \frac{r_2\beta}{K}\int_0^t X_1(s)\, ds \\ &\quad - \frac{r_2}{K}\int_0^t X_2(s)\, ds + Q_2\int_0^t \frac{X_1(s)}{X_2(s)} ds + \sigma_2 B_2(t)\end{aligned}$$

According to equation (30), we can obtain that for any $\omega_1 \in \Omega_1$ and $t > T_1$

$$\ln \frac{X_2(t,\omega_1)}{X_2(0,\omega_1)} \geq (r_2 - \tfrac{1}{2}\sigma_2^2 - \tfrac{r_2\beta\varepsilon_1}{K})t - \tfrac{r_2}{K}\int_0^t X_2(s)ds + \sigma_2 B_2(t),$$

From Lemma 2 and (28), we have

$$\liminf_{t\to+\infty} \frac{1}{t}\int_0^t X_2(s,\omega_1)\mathrm{d}s \geq \frac{K}{r_2}(r_2 - \frac{r_2\beta\varepsilon_1}{K} - \frac{1}{2}\sigma_2^2),$$

By the arbitrariness of ε_1 and $P(\Omega_1) = 1$, we obtain

$$\limsup_{t\to+\infty} \frac{1}{t}\int_0^t X_2(s)ds > 0. \quad a.s.$$

This completes the proof.

Theorem 7 *Assume*

$$P - (Q_1 + Q_2) > \frac{1}{2}\sigma_1^2, \tag{36}$$

Then we have the following assertions:
(i) Androgen-independent cells X_2 are persistent in mean.

(ii)

$$r_2 - \frac{\sigma_2^2}{2} \neq 0, P - (Q_1 + Q_2) - \frac{\sigma_1^2}{2} > \frac{P\alpha}{r_2}(r_2 - \frac{\sigma_2^2}{2}), \tag{37}$$

then androgen-dependent cells X_1 are persistent in mean.
(iii) If one of the following two conditions is satisfied,

$$(a)\alpha\beta \leq 1, \quad P - (Q_1 + Q_2) - \frac{\sigma_2^2}{2} < \frac{P\alpha}{r_2}(r_2 - \frac{\sigma_2^2}{2}), \tag{38}$$

$$(b)\alpha\beta > 1, \quad P - (Q_1 + Q_2) - \frac{\sigma_2^2}{2} < \frac{P}{\beta r_2}(r_2 - \frac{\sigma_2^2}{2}), \tag{39}$$

then androgen-dependent cells X_1 will go to extinction.

Proof (i) Now, let us proof the persistence of AI cells X_2 by contradiction. Assume that X_2 are not persistent in mean, which means for $\Omega_2 = \{\omega_1 \in \Omega_2 : \langle X_2(\omega_1)\rangle^* = 0\}, P(\Omega_2) > 0$ holds. Let $\omega_1 \in \Omega_2$, for any $\varepsilon_2 > 0$, there exist a large $T_3 > 0$ such that:

$$\langle X_2(\omega_1)\rangle_t < \varepsilon_2, \quad for\ all\ \ t \geq T_3 \tag{40}$$

From the solution of the first equation in (3), we can obtain that

$$\begin{aligned}\frac{1}{X_1(t,\omega_1)} = \frac{1}{X_1(0)}\exp\Big[&- t(P - \frac{P\alpha}{K}\langle X_2(\omega_1)\rangle_t \\ &- (Q_1+Q_2) - \frac{1}{2}\sigma_1^2 + \sigma_1\frac{B_1(t,\omega_1)}{t})\Big] \\ &+ \frac{P}{K}\int_0^t \exp\Big[(t-s)(-P + Q_1 + Q_2 \\ &+ \frac{\sigma_1^2}{2} + \sigma_1\frac{B_1(s,\omega_1) - B_1(t,\omega_1)}{t-s}) \\ &+ \frac{P\alpha}{K}\int_s^t X_2(\tau,\omega_1)d\tau\Big]ds\end{aligned} \tag{41}$$

According to Lemma 1, for the $\varepsilon_2 > 0$, there is a large T_4 such that

$$\left|\frac{B_1(t,\omega_1) - B_1(s,\omega_1)}{t-s}\right| < \varepsilon_2 \quad for\ all \quad t - s > T_4, \tag{42}$$

Without loss of generality, assume that (42) holds for all $\omega_1 \in \Omega_2$, using the inequality (40), we see that for all $t > \mathscr{T}_1 := T_3 \vee T_4$,

$$\frac{1}{X_1(t,\omega_1)} \leq \frac{1}{X(0)}e^{L_2 t} + \frac{P}{K}[I_2 + \frac{e^{L_2 t} - e^{L_2\mathscr{T}_1}}{L_2}] \tag{43}$$

where

$$L_2 = Q_1 - P + Q_2 + \frac{1}{2}\sigma_1^2 + \left(\sigma_1 + \frac{P\alpha}{K}\right)\varepsilon_2 < 0,$$

$$\begin{aligned}I_2 = \int_0^{\mathscr{T}_1} \exp\Bigg[v\Bigg(&-P + Q_1 + Q_2 + \frac{1}{2}\sigma_1^2 \\ &+ \sigma_1\frac{B_1(t-v,\omega_1) - B_1(t,\omega_1)}{v}\Bigg) \\ &+ \frac{P\alpha}{K}\int_0^v X_2(\theta,\omega_1)d\theta\Bigg]dv\end{aligned}$$

Applying the Kolmogorov Theorem [27], we obtain that there exists a constant $M_3 > 0$, such that

$$I_2 \leq M_3, \quad t > \mathscr{T}_1$$

thus ,from (43) we obtain

$$\limsup_{t\to+\infty} \frac{1}{X_1(t,\omega_1)} \leq \frac{P}{K}(M_3 - \frac{1}{L_2}e^{L_2\mathscr{T}_1})$$

That is to say, there is a positive constant $\xi_1$such that

$$X_1(t,\omega_1) \geq \xi_1, \quad t > \mathscr{T}_1. \tag{44}$$

In addition, from Theorem 2, we see that there exists positive constant M_4 and T_5 such that for all $t \geq T_5$, $X_1(t) \leq M_4 \, and \, X_2(t) \leq M_4 \quad a.s.$

Consequently, for all $t \geq \mathscr{T}_2 := T_5 \vee \mathscr{T}_1$ and $\omega_1 \in \Omega_2$, we obtain

$$dX_2(t,\omega_1) \geq [r_2 X_2(1 - \frac{\beta M_4}{K} - \frac{M_4}{K}) + Q_2\xi_1]dt \\ + \sigma_2 X_2 dB_2(t)$$

As a result,

$$X_2(t,\omega_1) \geq X_2(0)e^{t\left[r_2\left(1-\frac{\beta M_4+M_4}{K}\right)-\frac{1}{2}\sigma_2^2+\sigma_2\frac{B_2(t,\omega_1)}{t}\right]} \\ + Q_2\xi_1\int_0^t e^{\sigma_2\left(B_2(t,\omega_1)-B_2(s,\omega_1)\right)} \\ \cdot e^{(t-s)\left(r_2\left(1-\frac{\beta M_4+M_4}{K}\right)-\frac{1}{2}\sigma_2^2\right)}ds \tag{45}$$

According to Lemma 1, we see for any $\varepsilon_3 > 0$, there exists a large T_6 such that

$$\left|\frac{B_2(t,\omega_1) - B_2(s,\omega_1)}{t-s}\right| < \varepsilon_3, \forall t-s > T_6 \quad a.s. \tag{46}$$

In general, we assumed that (46) holds for all $\omega_1 \in \Omega_2$, we see that for all $t > \mathscr{T}_3 := T_6 \vee \mathscr{T}_2$,

$$X_2(t,\omega_1) \geq Q_2\xi_1 \int_{\mathscr{T}_3}^t e^{L_3 v}dv$$

where

$$L_3 := r_2(1 - \frac{\beta M_4 + M_4}{K}) - \frac{\sigma_2^2}{2} + \sigma_2\varepsilon_3$$

If $L_3 \neq 0$, then for all $t \geq \mathscr{T}_3$,

$$X_2(t,\omega_1) \geq \frac{Q_2\xi_1}{L_3}(e^{L_3 t} - e^{L_3\mathscr{T}_3}).$$

If $L_3 = 0$, then for all $t \geq \mathscr{T}_3$,

$$X_2(t,\omega_1) \geq Q_2\xi_1(t - \mathscr{T}_3).$$

Thus,

$$\liminf_{t\to+\infty} X_2(t,\omega_1) = +\infty, \; L_3 \geq 0,$$

$$\liminf_{t\to+\infty} X_2(t,\omega_1) \geq -\frac{Q_2\xi_1}{L_3}e^{L_3\mathscr{T}_3} > 0, \; L_3 < 0,$$

which contradicts the previous hypothesis, thus X_2 are persistent in mean.

(ii) Next, we employ the method of proof by contradiction, assuming that the AD cells X_1 are not persistent in mean. Thus there exists $\Omega_3 = \{\omega_1, < X_1(\omega_1) >_t^* = 0\}$ with $P(\Omega_3) > 0$. Let $\omega_1 \in \Omega_3$, for any $\varepsilon_4 > 0$, there exists $T_7 > 0$ such that

$$\langle X_1(\omega)\rangle^* < \varepsilon_4, \; t > T_7. \tag{47}$$

We now discuss the following two cases separately. For the first case: $r_2 - \frac{\sigma_2^2}{2} > 0$, from the second equation of (3) we get:

$$dX_2 \geq (r_2 - \frac{r_2\beta}{K}X_1 - \frac{r_2}{K}X_2)X_2dt \\ + \sigma_2 X_2 dB_2(t), \; for \; all \; t \geq 0 \quad a.s.$$

Thus,

$$\frac{1}{X_2(t)} \leq \frac{1}{X_2(0)}e^{-t\left(r_2-\frac{\sigma_2^2}{2}-\frac{r_2\beta}{K}\langle X_1\rangle_t+\frac{\sigma_2 B_2(t)}{t}\right)} \\ + \frac{r_2}{K}\int_0^t e^{(t-s)\left(-r_2+\frac{\sigma_2^2}{2}-\sigma_2\frac{B_2(s)-B_2(t)}{t-s}\right)} \\ \cdot e^{\frac{r_2\beta}{K}\int_s^t X_1(v)dv}ds \tag{48}$$

we noticed that for the $\varepsilon_4 > 0$, there is a large $T_8 > 0$ such that

$$\left|\frac{B_2(t,\omega_1) - B_2(s,\omega_1)}{t-s}\right| < \varepsilon_4, \quad \forall t-s > T_8. \tag{49}$$

It is supposed that (49) is valid for any $\omega_1 \in \Omega_3$ in general. Substituting (49) and (47) into (48),we see that for all $t > \mathscr{T}_4 := T_7 \vee T_8$,

$$\frac{1}{X_2(t,\omega_1)} \leq \frac{1}{X_2(0)}e^{tL_4} + \frac{r_2}{K}(I_3 + \frac{e^{L_4 t} - e^{L_4\mathscr{T}_4}}{L_4}) \tag{50}$$

where

$$L_4 = -r_2 + \frac{\sigma_2^2}{2} + \left(\frac{r_2\beta}{K} + \sigma_2\right)\varepsilon_4$$

$$I_3 = \int_0^{\mathscr{T}_4} e^{v\left(-r_2+\frac{\sigma_2^2}{2}\right)+\sigma_2\left(B_2(t-v,\omega_1)-B_2(t,\omega_1)\right)} \\ \cdot e^{\frac{r_2\beta}{K}\int_0^v X_1(\theta,\omega_1)d\theta}dv$$

From the Kolmogorov Theorem, there exists a $M_5 > 0$ such that

$$I_3 \leq M_5, \; t > \mathscr{T}_4$$

then for all $\omega_1 \in \Omega_3$, we obtain

$$\limsup_{t\to+\infty} \frac{1}{X_2(t,\omega_1)} \leq \frac{r_2}{K}(M_5 - \frac{e^{L_4\mathscr{T}_4}}{L_4})$$

Thus, there is a $\eta_1 > 0$ such that,

$$X_2(t,\omega_1) \geq \eta_1, \ for\ all\ t \geq \mathscr{T}_4. \tag{51}$$

Besides, from the equation (3) we have

$$\begin{aligned}
&t^{-1}\big(\ln X_1(t) - \ln X_1(0)\big)\\
&\quad = P - Q_1 - Q_2 - \frac{\sigma_1^2}{2} - \frac{P}{K}\langle X_1\rangle_t\\
&\qquad - \frac{P\alpha}{K}\langle X_2\rangle_t + \frac{\sigma_1 B_1(t)}{t} \qquad (52)\\
&t^{-1}\big(\ln X_2(t) - \ln X_2(0)\big)\\
&\quad = r_2 - \frac{\sigma_2^2}{2} - \frac{r_2\beta}{K}\langle X_1\rangle_t - \frac{r_2}{K}\langle X_2\rangle_t\\
&\qquad + Q_2\Big\langle \frac{X_1}{X_2}\Big\rangle_t + \frac{\sigma_2 B_2(t)}{t} \qquad (53)
\end{aligned}$$

From (52) and (53) we see for all $\omega_1 \in \Omega_3$, $t \geq \mathscr{T}_4$

$$\begin{aligned}
&t^{-1}\left(\ln X_1(t,\omega_1) - \frac{P\alpha}{r_2}\ln X_2(t,\omega_1)\right)\\
&\quad = t^{-1}\left(\ln X_1(0) - \frac{P\alpha}{r_2}\ln X_2(0)\right) + P - Q_1 - Q_2\\
&\qquad - \frac{\sigma_1^2}{2} - \frac{P}{K}(1-\alpha\beta)\langle X_1\rangle_t - \frac{P\alpha}{r_2}\left(r_2 - \frac{\sigma_2^2}{2}\right)\\
&\qquad + \frac{\sigma_1 B_1(t)}{t} + \frac{PQ_2\alpha}{r_2}\left\langle \frac{X_1}{X_2}\right\rangle_t - \frac{P\alpha}{r_2}\frac{\sigma_2 B_2(t)}{t}\\
&\quad \geq t^{-1}\left(\ln X_1(0) - \frac{P\alpha}{r_2}\ln X_2(0)\right) + P - Q_1 - Q_2\\
&\qquad - \frac{\sigma_1^2}{2} - \frac{P\alpha}{r_2}\left(r_2 - \frac{\sigma_2^2}{2}\right) - \frac{P\alpha}{r_2}\frac{\sigma_2 B_2(t)}{t}\\
&\qquad + \frac{\sigma_1 B_1(t)}{t} - \frac{P}{K}\left(1 - \alpha\beta + \frac{K\alpha Q_2}{r_2\eta_1}\right)\langle X_1(\omega_1)\rangle_t
\end{aligned} \tag{54}$$

From (51) and the boundedness of $X_2(t)$, we get

$$\lim_{t\to+\infty}\frac{\ln X_2(t)}{t} = 0, \quad \limsup_{t\to+\infty}\frac{\ln X_1(t)}{t} \leq 0\ ,$$

Moreover, taking the limit on both sides of (54) we get

$$0 \geq P - Q_1 - Q_2 - \frac{\sigma_1^2}{2} - \frac{\alpha P}{r_2}(r_2 - \frac{\sigma_2^2}{2}) > 0.$$

Thus, we led to a contradiction, X_1 is persistent in mean.

Under the condition that $r_2 - \frac{\sigma_2^2}{2} < 0$, from the second equation of (3) we have

$$\begin{aligned}
X_2(t) \leq{}& X_2(0)\exp\left[t\left(r_2 - \frac{\sigma_2^2}{2} + \frac{B_2(t)}{t}\right)\right]\\
&+ Q_2\int_0^t e^{(t-s)(r_2 - \frac{\sigma_2^2}{2}) + B_2(t) - B_2(s)}X_1(s)ds
\end{aligned}$$

Thus,

$$\int_0^t X_2(\tau)d\tau \leq X_2(0)I_4 + Q_2L_5 \tag{55}$$

where

$$I_4 = \int_0^t e^{\tau(r_2 - \frac{\sigma_2^2}{2} + \frac{B_2(\tau)}{\tau})}d\tau,$$

$$L_5 = \int_0^t\int_0^\tau e^{(\tau-s)(r_2 - \frac{\sigma_2^2}{2}) + B_2(\tau) - B_2(s)}X_1(s)dsd\tau.$$

Let us choose ε_4 such that

$$r_2 - \frac{1}{2}\sigma_2^2 + \varepsilon_4 < 0. \tag{56}$$

For all $\omega_1 \in \Omega_3$, $t \geq \mathscr{T}_4$, using equation (49)and the properties of Brownian motion, there exists a positive constant S_1 such that

$$\begin{aligned}
I_4(t,\omega_1) &= \int_0^t e^{\tau(r_2 - \frac{\sigma_2^2}{2} + \frac{B_2(\tau,\omega_1)}{\tau})}d\tau\\
&\leq \int_0^{\mathscr{T}_4} e^{\tau(r_2 - \frac{\sigma_2^2}{2}) + B_2(\tau,\omega_1)}d\tau\\
&\quad + \int_{\mathscr{T}_4}^t e^{\tau(r_2 - \frac{1}{2}\sigma_2^2 + \varepsilon_4)}d\tau\\
&= \int_0^{\mathscr{T}_4} e^{\tau(r_2 - \frac{\sigma_2^2}{2}) + B_2(\tau,\omega_1)}d\tau\\
&\quad - (r_2 - \frac{1}{2}\sigma_2^2 + \varepsilon_4)^{-1}e^{(r_2 - \frac{1}{2}\sigma_2^2 + \varepsilon_4)\mathscr{T}_4}d\tau ds\\
&\leq S_1
\end{aligned}$$

Reversing the order of integration in L_5 and using equation (56), we see

$$
\begin{aligned}
L_5(t,\omega_1) = &\int_0^{\mathscr{T}_4} e^{-s\left(r_2-\frac{\sigma_2^2}{2}\right)-B_2(s,\omega_1)} X_1(s,\omega_1) \\
&\times \int_s^{\mathscr{T}_4} e^{\tau\left(r_2-\frac{\sigma_2^2}{2}\right)+B_2(\tau,\omega_1)} d\tau\, ds \\
&+ \int_0^{\mathscr{T}_4} e^{-s\left(r_2-\frac{\sigma_2^2}{2}\right)-B_2(s,\omega_1)} X_1(s,\omega_1) \\
&\times \int_{\mathscr{T}_4}^t e^{\tau\left(r_2-\frac{\sigma_2^2}{2}\right)+B_2(\tau,\omega_1)} d\tau\, ds \\
&+ \int_{\mathscr{T}_4}^t e^{-s\left(r_2-\frac{\sigma_2^2}{2}\right)-B_2(s,\omega_1)} X_1(s,\omega_1) \\
&\times \int_s^t e^{\tau\left(r_2-\frac{\sigma_2^2}{2}\right)+B_2(\tau,\omega_1)} d\tau\, ds \qquad (57)
\end{aligned}
$$

We know that the integration intervals of the first and second terms on the right-hand side of the expression are finite, and their integrands are bounded. Therefore, they are both bounded by some positive constant S_2. Furthermore, from (46), it follows that the third term on the right-hand side has the upper bound. Thus, we have

$$
\begin{aligned}
\frac{1}{t}\int_0^t X_2(\tau,\omega_1)d\tau \le X_2(0,\omega_1)\frac{S_1}{t} + Q_2\Big(\frac{2S_2}{t} \\
- \frac{e^{2\varepsilon_4}}{\left(r_2-\frac{\sigma_2^2}{2}+\varepsilon_4\right)}\langle X_1(\omega_1)\rangle_t\Big)
\end{aligned}
\tag{58}
$$

which holds for $for\ all \quad t \ge \mathscr{T}_4$ and $\omega_1 \in \Omega_3$. Taking the superior limit on both sides of (58), we get

$$
\langle X_2(\omega_1)\rangle^* \le \frac{Q_2 e^{2\varepsilon_4}}{-(r_2-\frac{\sigma_2^2}{2}+\varepsilon_4)}\langle X_1(\omega_1)\rangle^*, \quad \forall\, \omega_1 \in \Omega_3. \tag{59}
$$

Since for $\forall\, \omega_1 \in \Omega_3$ we have

$$
\langle X_1(\omega_1)\rangle^* = 0.
$$

From (59) we get, $\langle X_2(\omega_1)\rangle^* = 0, \quad \forall\, \omega_1 \in \Omega_3$

This contradicts the mean persistence of X_1 stated in (i). Hence, X_1 is persistent in mean.

(iii) From the two equations (52) and (53), we obtain

$$
\begin{aligned}
&t^{-1}\left(\ln X_1(t) - \frac{P\alpha}{r_2}\ln X_2(t)\right) \\
&\le t^{-1}\left(\ln X_1(0) - \frac{P\alpha}{r_2}\ln X_2(0)\right) + P - Q_1 - Q_2 \\
&-\frac{1}{2}\sigma_1^2 - \frac{P\alpha}{r_2}\left(r_2-\frac{1}{2}\sigma_2^2\right) - \frac{P}{K}(1-\alpha\beta)\langle X_1\rangle_t \\
&+\sigma_1\frac{B_1(t)}{t} - \frac{P\alpha}{r_2}\sigma_2\frac{B_2(t)}{t}
\end{aligned}
\tag{60}
$$

Taking the superior limit on both sides of equation (60) and when condition (a) holds, we get

$$
\begin{aligned}
&\limsup_{t\to+\infty}\left[t^{-1}\left(\ln X_1(t) - \frac{P\alpha}{r_2}\ln X_2(t)\right)\right] \\
&\le P - Q_1 - Q_2 - \frac{1}{2}\sigma_1^2 - \frac{P\alpha}{r_2}\left(r_2-\frac{1}{2}\sigma_2^2\right) < 0
\end{aligned}
$$

Therefore,

$$
\limsup_{t\to+\infty}\frac{X_1(t)}{X_2(t)^{\frac{P\alpha}{r_2}}} = 0
$$

Since Theorem 2 shows that $X_2(t)$ has an upper bound G, then

$$
0 \le \frac{X_1(t)}{G^{\frac{P\alpha}{r_2}}} \le \frac{X_1(t)}{X_2(t)^{\frac{P\alpha}{r_2}}} \quad \text{a.s.}
$$

Taking the superior limit on both sides of the above inequality yields

$$
\limsup_{t\to+\infty}\frac{X_1(t)}{G^{\frac{P\alpha}{r_2}}} = 0 \quad \text{a.s.} \tag{61}
$$

Using the two equations (52) and (53), we obtain

$$
\begin{aligned}
&t^{-1}\left(\ln X_1(t) - \frac{P}{\beta r_2}\ln X_2(t)\right) \\
&\le t^{-1}\left(\ln X_1(0) - \frac{P}{\beta r_2}\ln X_2(0)\right) + P \\
&\quad - Q_1 - Q_2 - \frac{1}{2}\sigma_1^2 - \frac{P}{\beta r_2}\left(r_2-\frac{1}{2}\sigma_2^2\right) \\
&\quad + \frac{P}{K\beta}(1-\alpha\beta)\langle X_2\rangle_t + \sigma_1\frac{B_1(t)}{t} - \sigma_2\frac{P}{\beta r_2}\frac{B_2(t)}{t},
\end{aligned}
\tag{62}
$$

Taking the superior limit on both sides of the above equation gives

$$
\begin{aligned}
&\limsup_{t\to+\infty}\left[t^{-1}\left(\ln X_1(t) - \frac{P}{\beta r_2}\ln X_2(t)\right)\right] \\
&\le P - Q_1 - Q_2 - \frac{1}{2}\sigma_1^2 - \frac{P}{\beta r_2}\left(r_2-\frac{1}{2}\sigma_2^2\right) < 0.
\end{aligned}
$$

Table 1. Main parameters values.

Parameter	Biological Meaning	Value	Source
r_1	Proliferation rate of AD cells	0.025/day	[12]
d_1	AD cancer cell death rate	0.064/day	[12]
m_1	Maximum mutation rate (AD → AI cells)	0.00005/day	[12]
r_2	Net proliferation rate of AI cells	0.006/day	[12]
K	Cancer cells carrying capacity	11×10^6	[12]
a_0	Basal level androgen concentration	20 nmol/L	[10]
γ	Androgen clearance/production rate	0.08/day	[12]

Using the same method, we obtain

$$\limsup_{t\to+\infty} \frac{X_1(t)}{G^{\frac{P}{\beta r_2}}} = 0, \tag{63}$$

From the above conclusions, it follows that

$$\lim_{t\to+\infty} X_1(t) = 0 \quad \text{a.s.}$$

5 Numerical simulations

In this section, we investigate the combined effects of random perturbations and treatment strategies on tumor dynamics, we perform a numerical simulation analysis of model (2). Table 1 lists the main parameters of our model and their sources.

In Figure 1, the initial values of the solution were fixed as $X_1(0) = 15 \times 10^6, X_2(0) = 0.1 \times 10^6$, and the other parameter values are as follows: $\alpha = 0.9,\ \beta = 0.8$ and $T = 100$. We set $\sigma_1 = 0.2,\ \sigma_2 = 0.9$, by simple calculation gets $P - (Q_1 + Q_2) - \frac{\sigma_1^2}{2} > \frac{P\alpha}{r_2}(r_2 - \frac{\sigma_1^2}{2}),\ P - (Q_1 + Q_2) > \frac{\sigma_1^2}{2}$, from Theorem 7, the AD cells become persistent in the mean (Figure 1(a)). If we set $\sigma_1 = 0.9,\ \sigma_2 = 0.1$, then $P - (Q_1 + Q_2) < \frac{\sigma_1^2}{2},\ r_2 - \frac{\sigma_2^2}{2} > 0$. Conditions (3) of Theorem 6 show that AI cancer cells are persistent (Figure 1(b)); If we set $\sigma_1 = 0.9,\ \sigma_2 = 0.02$, then $P - (Q_1 + Q_2) < \frac{\sigma_1^2}{2}$, as shown by Condition (1) of Theorem 6, AD cells tend to extinction (Figure 1(c)); If we set $\sigma_1 = 0.9,\ \sigma_2 = 0.7$, then we get $P - (Q_1 + Q_2) < \frac{\sigma_1^2}{2},\ r_2 - \frac{\sigma_2^2}{2} < 0$, Theorem 6 (2) states that androgen-independent cells go to extinction. A comparison of the four subfigures in Figure 1 reveals that when the random perturbation intensity reaches a certain threshold, the proliferation of both AD and AI cells will be effectively suppressed and ultimately lead to their complete eradication.

In Figure 2, we fix $\alpha = 0.7, \beta = 0.9, \sigma_1 = 0.03$ and $\sigma_2 = 0.02$, the other parameter we set as same as Figure 1, then modified the parameter δ to assess its influence on the progression of AD and AI cells under IAD therapy. The condition $r_2 - \frac{\sigma_2^2}{2} > 0$ guaranteed by this parameter set, together with the analytical results from Theorems 6(3) , implies that AI cells persist regardless of the chosen δ, confirming that complete tumor eradication via IAD is unattainable in this scenario. The simulations reveal a critical dependence of tumor severity and controllability on δ. For $0.1 \leq \delta \leq 0.5$, both AD and AI cells coexist. In this regime, AD cells act as stronger competitors, suppressing AI cells to a manageable level and maintaining the tumor in a controllable state. In contrast, for $\delta > 0.5$, a drastic shift occurs: AD cells tend toward extinction, while AI cells proliferate rapidly. This transition signifies the progression to a more lethal, treatment-resistant form of the disease: metastatic castration-resistant prostate cancer. Therefore, the simulations identify $\delta = 0.5$ as the approximate optimal value to control AD and AI cells. A treatment strategy with $\delta \leq 0.5$ produces superior results by leveraging competitive suppression to delay AI dominance, thereby extending the window of disease controllability.

In Figure 3, we fix $\sigma_1 = 0.03,\ \sigma_2 = 0.02,\ \delta = 0.5$ and the other parameters as set in Figure 1. By comparing the two subgraphs in Figure 3, we find that when T is very small (i.e., androgen deprivation is performed with high frequency), the average hormone level within the cycle decreases. The net growth rate of AD cells turns negative and is continuously converted to AI cells, leading to rapid decline and eventual extinction. However, once AD cells are almost extinct, the pressure of resource competition eases and AI cells will quickly approach the carrying capacity limit, occupy a dominant position, and ultimately result

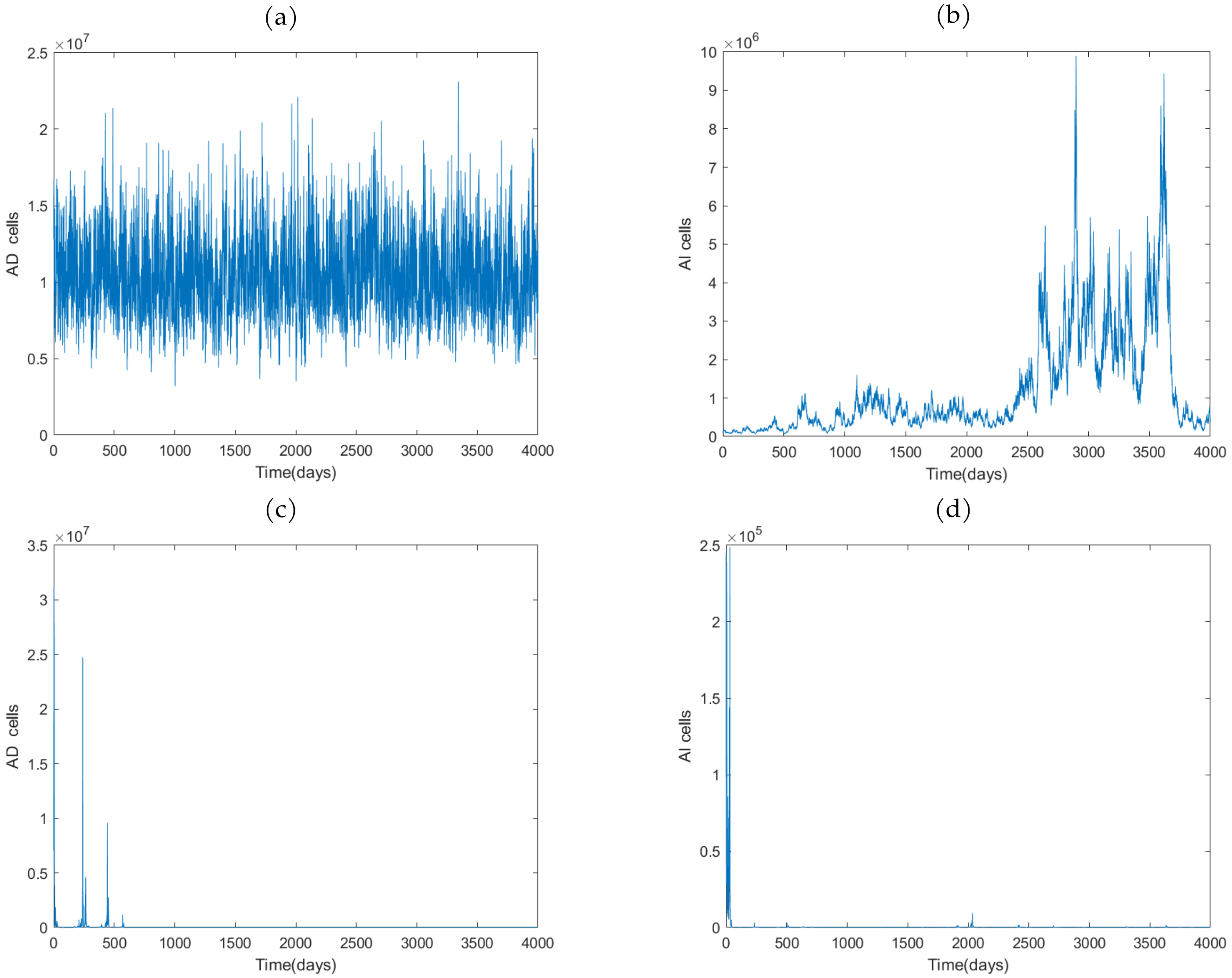
(a) (b) (c) (d)

Figure 1. The effects of white noise on AD and AI cells.

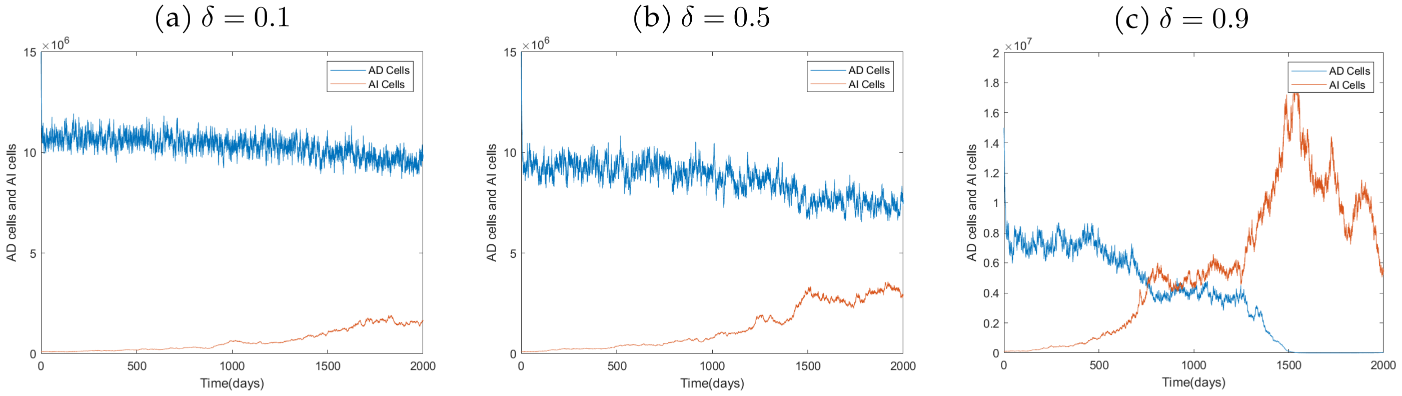
(a) $\delta = 0.1$ (b) $\delta = 0.5$ (c) $\delta = 0.9$

Figure 2. Treatment effects under different IAD efficacy levels.

in the progression of cancer to mCPRC. In contrast, when the interval T of androgen deprivation is long, AD cells can be maintained and AI cells suppressed through competition. Although AI cells accumulate slowly, they are difficult to surpass, and eventually AD cells and AI cells coexist. It can be seen that an excessively high deprivation frequency will accelerate the emergence of AI cells, while the appropriate

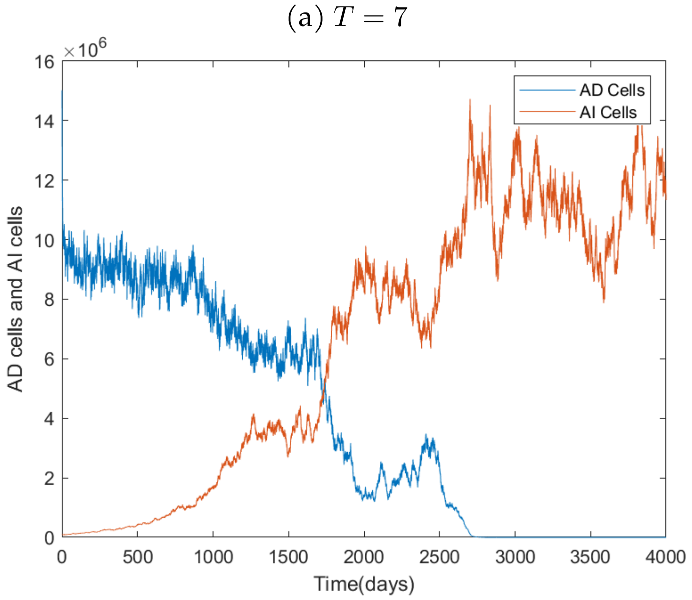

Figure 3. Effect of Pulse Frequency on AD and AI Cells.

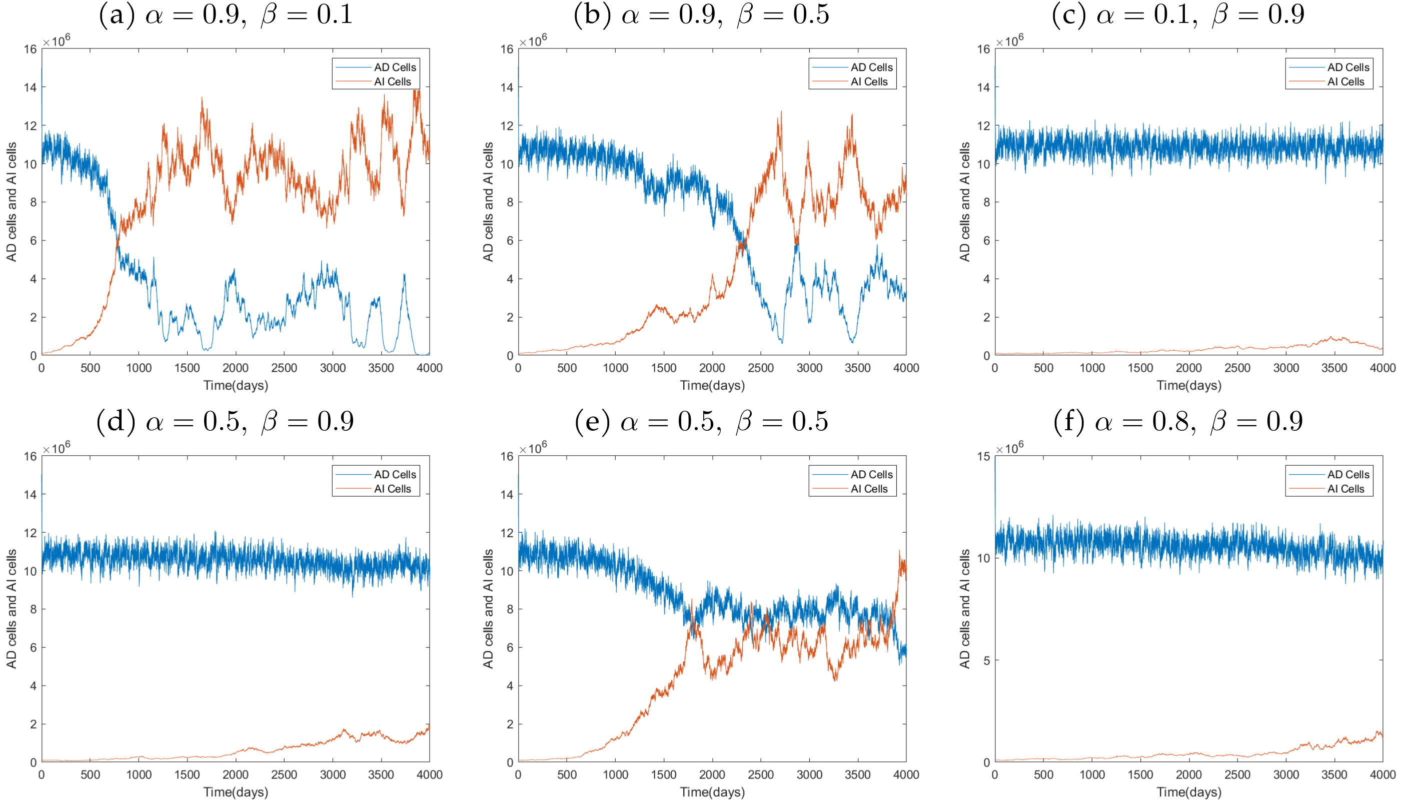

Figure 4. Population dynamics of AD and AI cells under different competition coefficients(α, β).

prolongation or adaptive adjustment of the deprivation frequency to retain a certain population of AD cells is expected to use ecological competition to delay drug resistance and manage the total cell load in a more controllable manner.

In Figure 4, we clearly reveal three typical outcomes of the competition between AD and AI cells through random dynamical simulations under six different parameter sets: When $\alpha/\beta > 1$, AI cells ultimately dominate and induce resistance; when α is significantly smaller than β, AD cells can maintain a long-term advantage, effectively delaying disease progression and when the competition strengths of both are comparable, the system exhibits long-term coexistence. Therefore, the competition ratio α/β is a key factor in determining the fate of cancer cells and the onset of clinical resistance. Thus, increasing β and decreasing α is a core therapeutic strategy for delaying the onset of mCRPC.

6 Discussion

This study develops a stochastic pulsed dynamical model to elucidate the synergistic regulatory mechanisms of noise perturbations, therapeutic parameters and cellular competition on the evolution of prostate cancer under intermittent androgen deprivation therapy. We first prove the existence and uniqueness of a global positive solution for the stochastic system and analyze its stochastic ultimate boundedness. The results indicate that both types of cancer cells can be effectively controlled within a finite range without unlimited growth during prostate cancer treatment.

Using Itô's formula and the strong law of large numbers for local martingales, we establish precise threshold conditions for the extinction and mean persistence of both AD and AI cells. Theoretical analysis shows that when the conditions $P - (Q_1 + Q_2) < \sigma_1^2/2$ and $r_2 < \sigma_2^2/2$ are satisfied, both types of cancer cells tend toward extinction. Conversely, when $P - (Q_1 + Q_2) > \sigma_1^2/2$ and specific competition conditions are met, the system may exhibit a coexistent state. These threshold conditions clearly delineate the dual role of stochastic noise in tumor evolution: appropriate noise intensity can promote tumor regression, whereas insufficient noise may lead to drug resistance.

Compared to existing studies, the theoretical innovation of this work lies in simultaneously considering pulsed therapeutic effects and stochastic noise disturbances, for the first time establishing analytical threshold conditions for cell survival and extinction, providing a quantitative basis for understanding the evolution of tumor drug resistance. The study finds that stochastic noise intensity exhibits a critical threshold effect. When noise exceeds a critical value, both AD and AI cells can be driven to extinction, offering a novel perspective for utilizing therapy-induced stochastic fluctuations to achieve tumor eradication and breaking through the traditional cognition of deterministic models.

Furthermore, the competition coefficient ratio α/β is identified as a core factor determining therapeutic outcomes. When $\alpha/\beta < 1$, AD cells can persistently suppress AI cells through ecological competition, significantly delaying the onset of drug resistance. This finding suggests that therapeutic strategies should not only focus on androgen suppression but also pay attention to modulating the competitive balance between cell populations.

The parameter δ also emerges as another key modulator of tumor controllability. Simulations in Figure 2 identify $\delta = 0.5$ as the approximate optimal value. Below this threshold, AD cells persist and competitively suppress AI populations, maintaining the tumor in a manageable state. Conversely, when $\delta > 0.5$, AD cells are rapidly driven to extinction, releasing AI cells from competitive pressure and accelerating progression to mCRPC. This nonlinear response underscores the risk of over-treatment and aligns with clinical observations that excessive androgen suppression may hasten drug resistance.

This study has initially revealed the stochastic dynamic characteristics of prostate cancer under intermittent androgen suppression, yet limitations remain, which also point out directions for future in-depth research. Future studies should focus on integrating the metabolic interaction mechanisms between AD and AI cells, and quantifying the role of the resource compensation effect in tumor evolution. Meanwhile, it is necessary to construct a multi-dimensional model that incorporates immune cell infiltration and treatment heterogeneity to simulate the efficacy of combined ADT and immune checkpoint inhibitors. Such integrated models will serve as a key bridge for translating theories into the practice of precise combined therapy.

7 Conclusion

This study proposed and analyzed a stochastic impulsive model for prostate cancer under intermittent androgen deprivation therapy, incorporating environmental noise, periodic treatment pulses, and asymmetric competition between AD and AI cells. We established the existence and uniqueness of a global positive solution and derived sufficient conditions for cell extinction and mean persistence. Theoretical analysis reveals that stochastic noise exhibits a threshold effect: when intensities exceed critical values, both cell types can be driven to extinction, suggesting that appropriately harnessed fluctuations may contribute to tumor control. Numerical simulations yield key clinical insights: (i) moderate noise suppresses tumor growth; (ii) treatment intensity δ exhibits nonlinear effects—moderate suppression ($\delta \leq 0.5$) preserves AD cells to competitively delay AI dominance, while over-treatment ($\delta > 0.5$) accelerates AD depletion and hastens castration-resistant progression; (iii) excessively high-frequency deprivation impairs AD recovery and promotes AI outgrowth; (iv) the competition ratio α/β is decisive—lower values favor AD persistence and delay resistance. These findings provide a quantitative framework linking IAD parameters, stochastic fluctuations, and intercellular competition to prostate cancer outcomes, suggesting that moderate, well-timed androgen suppression may be more effective than maximal continuous blockade.

Future work should incorporate immune dynamics, metabolic interactions, and combination therapies to enhance translational potential toward personalized, evolution-informed cancer treatment.

Data Availability Statement

Data will be made available on request.

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Conflicts of Interest

The authors declare no conflicts of interest.

AI Use Statement

The authors declare that no generative AI was used in the preparation of this manuscript.

Ethical Approval and Consent to Participate

Not applicable.

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