

Stochastic Viral Dynamics with Beddington-DeAngelis Functional Response

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Outline

1. Stochastic SIR model with the functional response
2. Positive invariant region
3. Stationary distribution
4. Pathwise and moment bounds
5. Moment Lyapunov exponent
6. Persistence and extinction

1. Stochastic Model Equations

$$\begin{aligned}dx &= \left(\lambda - \delta x - \frac{\beta xy}{1 + ax + by} \right) dt + \sigma_1 x dB_1(t), \\dy &= \left(\frac{\beta xy}{1 + ax + by} - qy \right) dt + \sigma_2 y dB_2(t), \\dz &= (ky - \gamma z) dt + \sigma_3 z dB_3(t),\end{aligned}\tag{1}$$

where the **susceptible cells** with density $x(t)$ are generated at a constant rate λ , die at a density-proportional rate δx , and become **infective cells** $y(t)$ at a rate $\beta xy / (1 + ax + by)$ called Beddington-DeAngelis functional response. The density of **recovered cells** is $z(t)$.

Beddington-DeAngelis Response

Classical infectious and epidemic disease models use bilinear incidence or interaction terms such as βxy .

The nonlinear incidence rate with this **Holling type II response** $\beta xy / (1 + ax + by)$ was introduced separately by Beddington (1975) and DeAngelis (1975) in ecology.

It was also used in the study of the interaction dynamics of HIV-1 virus and uninfected CD4⁺T cells, cf. Huang et al. (2009).

Deterministic Dynamics and Stability

If the comprehensive reproduction ratio of the virus,

$$R_0 = \frac{k\beta\lambda}{\delta q\gamma + aq\gamma\lambda} \leq 1,$$

the disease-free equilibrium $E_0 = (\lambda/\delta, 0, 0)$ is asymptotically stable. — **Disease Extinction**.

If $R_0 > 1$, the endemic equilibrium $E_1 = (x_0, y_0, z_0)$ in \mathbb{R}_+^3 is globally asymptotically stable — **Persistence**, where

$$\begin{aligned}x_0 &= \frac{q\gamma + kb\lambda}{k\beta - aq\gamma + bk\delta}, \\y_0 &= \frac{k\beta\lambda - a\lambda q\gamma - \delta q\gamma}{q(k\beta - aq\gamma + bk\delta)}, \\z_0 &= \frac{k(k\beta\lambda - a\lambda q\gamma - \delta q\gamma)}{q\gamma(k\beta - aq\gamma + bk\delta)}.\end{aligned}$$

cf. Huang-Ma-Takeuch (2009)

Related Models and Researches

- Quite a few research work on stochastic population dynamics, in particular **Lotka-Volterra type equations for predator-prey models** whose growth/death rates perturbed by noise and adding various functional responses: *bilibear response*, *ratio-dependent response*, *Leslie-Gower response*, and *Beddington-DeAngelis response* on many topics:

Khasminskii and Klebaner (2001), Rudnicki (2003), Rudnicki-Pichor (2007), Deng et al (2008), Ji-Jiang-Li (2011), Mao (2011), Ton-Yagi (2011), Li-Shuang (2013), Zou-Fan-Wang (2013), etc.

- Diffusive predator-prey Model with Bedington-DeAngelis response: Chen-Wang (2005).

Findings by Shown Results

- With stochastic perturbation, there will be no positive **equilibrium** points. Instead one can try to prove that (open problem) there exists a **stationary distribution** on the positive invariant region \mathbb{R}_+^n , which can be viewed as a counterpart in the stochastic dynamics arena.

- If **intensity of noise is relatively small**, hopefully (not always) one can show that stochastic asymptotic dynamics "imitates" the corresponding deterministic dynamics in some way, almost surely, in moment, or in time average.

- If **noise is sufficiently large**, something dramatic and/or unexpected in dynamics may occur: **extinction of all species**, suppress or express exponential growth or explosion.

Large random environment, weather, or epidemic diseases effect seems to be the decisive responsible for the extinction of some species in the nature.

Preliminaries

Assume that $B_i(t)$ are independent standard Brownian motion defined on the canonical probability space (Ω, \mathcal{F}, P) .

$$\mathbb{R}_+^n = \{x \in \mathbb{R}^n : x_i > 0 \text{ for all } 1 \leq i \leq n\}.$$

Itô formula: For $V \in C^{2,1}(\mathbb{R}^n \times [0, \infty), \mathbb{R}_+)$,

$$dV(X(t), t) = LV(X, t) dt + V_x(X, t)g(X, t) dB,$$

for a SDE $dX = f(X, t) dt + g(X, t) dB$, and

$$LV(X(t), t) = V_t(X, t) + V_x(X, t)f(X, t) + \frac{1}{2} \text{Trace} [g^T(X, t)V_{xx}(X, t)g(X, t)].$$

2. Global Existence of Positive Solutions

Theorem

Under the condition $q \geq k$, for any positive initial data (x_0, y_0, z_0) , there is a unique positive solution $(x(t), y(t), z(t))$ of the model SDE (1) such that the solution will remain in \mathbb{R}_+^3 for all $t \geq 0$ with probability one.

- It shows that \mathbb{R}_+^3 is a positive invariant region for the model system. The solution $X(t) = (x(t), y(t), z(t))$ is a time-homogeneous Markov process.

- Let the maximal existence interval of a unique local pathwise positive solution be τ_e . We show $\tau_e = \infty$ a.s.

$$V(x, y, z) = (x - 1 - \log x) + (y - 1 - \log y) + (z - 1 - \log z).$$

Sketch of Proof

$$dV \leq Kdt + \sigma_1(x-1)dB_1 + \sigma_2(y-1)dB_2 + \sigma_3(z-1)dB_3,$$

$$K = \frac{1}{2}(\sigma_1^2 + \sigma_2^2 + \sigma_3^2) + \lambda + \delta + q + \gamma + \frac{\beta}{b}.$$

It suffices to prove $\tau_\infty = \lim_{m \rightarrow \infty} \tau_m = \infty$ a.s.

$$\tau_m = \inf \left\{ t \in [0, \tau_e) : (x(t), y(t), z(t)) \notin \left(\frac{1}{m}, m \right)^3 \right\}.$$

Otherwise, if $\tau_\infty < \infty$, then $P\{\tau_\infty \leq T\} > \varepsilon$. It leads to

$$\begin{aligned} \infty &> V(x_0, y_0, z_0) + KT \\ &\geq \varepsilon \left[(m-1 - \log m) \wedge \left(\frac{1}{m} - 1 + \log m \right) \right] \rightarrow \infty. \end{aligned}$$

3. Stationary Distribution

Definition

Let $P_{X_0,t}(\cdot)$ be the probability measure induced by a stochastic process $\{X(t)\}_{t \geq 0}$ in \mathbb{R}_+^n (or \mathbb{R}^n) over $(\Omega, \mathcal{F}, \mathbb{P})$ with $X(0) = X_0$,

$$P_{X_0,t}(S) = \mathbb{P}\{\omega \in \Omega : X(t, \omega) \in S\}, \quad S \in \mathcal{B}(\mathbb{R}_+^n),$$

If there is a probability measure $\mu(\cdot)$ on the measurable space $(\mathbb{R}_+^n, \mathcal{B}(\mathbb{R}_+^n))$ such that

$$P_{X_0,t}(\cdot) \longrightarrow \mu(\cdot) \quad \text{as } t \rightarrow \infty,$$

in distribution for any $X_0 \in \mathbb{R}_+^n$, then we say that $X(t)$ has a **stationary distribution** $\mu(\cdot)$.

Khasminskii Assumption

Assumption: There is a bounded open set $U \subset \mathbb{R}_+^n$ with regular boundary and the following properties:

1. In a neighborhood of U , the smallest eigenvalue of the diffusion matrix $g(x)$ is uniformly bounded away from zero.
2. For any $x \in \mathbb{R}_+^n \setminus U$, the mean time τ at which a path from x reaches the set U satisfies $\sup_{x \in K} E_x[\tau] < \infty$, for every compact set $K \subset \mathbb{R}_+^n$.

Khasminskii Lemma

Lemma

Under the Khasminskii Assumption, the Markov process $X(t)$ has a stationary distribution $\mu(\cdot)$, $\mu(\mathbb{R}^n \setminus \mathbb{R}_+^n) = 0$. For any bounded continuous function $Q(\xi)$, it holds that

$$\int_{\mathbb{R}_+^n} E[Q(X(t, \xi))] d\mu(\xi) = \int_{\mathbb{R}_+^n} Q(\xi) d\mu(\xi), \quad t \geq 0.$$

For any integrable function $F(X)$ with respect to μ , the ergodic property holds,

$$P \left\{ \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T F(X(t, \xi)) dt = \int_{\mathbb{R}_+^n} F(\xi) d\mu(\xi) \right\} = 1.$$

The Existence of Stationary Distribution

Theorem

If there is a positive equilibrium point $(x_0, y_0, z_0) \in \mathbb{R}_+^3$ for the corresponding deterministic system of ODE, then there exists a *stationary distribution* with respect to the Markov process generated by the positive solutions $(x(t), y(t), z(t))$ of the system of SDE (1).

Proof. Construct another V -function

$$V(x, y, z) = \frac{1 + by_0}{1 + ax_0 + by_0} \left(x - x_0 - x_0 \log \frac{x}{x_0} \right) + y - y_0 - y_0 \log \frac{y}{y_0} + \frac{q}{k} \left(z - z_0 - z_0 \log \frac{z}{z_0} \right).$$

Sketch of Proof

By the equilibrium condition we have

$$LV(x(t), y(t), z(t)) = -Q(x(t), x(t), z(t)) + \sigma$$

where

$$\sigma = \frac{(1 + by_0)x_0\sigma_1^2}{2(1 + ax_0 + by_0)} + \frac{y_0\sigma_2^2}{2} + \frac{qz_0\sigma_3^2}{2k} > 0,$$

$$-Q(x, y, z) = -\frac{\delta(1 + by_0)}{x(1 + ax_0 + by_0)}(x - x_0)^2 - \frac{qy_0b(1 + ax)(y - y_0)^2}{z_0(1 + ax + by)(1 + ax + by_0)} + qy_0R(x, y, z) \leq 0,$$

and

$$R(x, y, z) = 4 - \frac{(1 + ax + by_0)x_0}{(1 + ax_0 + by_0)x} - \frac{(1 + ax_0 + by_0)xy_0z}{(1 + ax + by)x_0yz_0} - \frac{yz_0}{y_0z} - \frac{(1 + ax + by)}{(1 + ax + by_0)} \leq 0.$$

Continued

- $Q(x, y, z) = 0$, iff $(x, y, z) = (x_0, y_0, z_0)$.
- $Q(x, y, z) > 0$, if otherwise in \mathbb{R}_+^3 .
- $Q(x, y, z) \rightarrow \infty$ as $(x, y, z) \rightarrow \infty$.

The diffusion matrix $g(x, y, z) = \text{diag}(\sigma_1^2 x^2, \sigma_2^2 y^2, \sigma_3^2 z^2)$ has the smallest eigenvalue uniformly bounded from zero, on a nbhd of any compact set in $\mathbb{R}_+^3 \setminus U$.

The two conditions in Khasminskii Assumption are satisfied for the bounded open set

$$U = \{(x, y, z) : Q(x, y, z) < \sigma\} \cap \mathbb{R}_+^3.$$

By Khasminskii Lemma, the system of SDE (1) has a unique stationary distribution $\mu(\cdot)$ on \mathbb{R}_+^3 .

4. Moment and Pathwise Estimates

Lemma

For $p > 1$, the solution of the Bernoulli equation

$$\frac{dv}{dt} = p v(t) \left[- \left(\delta - \frac{\sigma^2}{2}(p-1) \right) + \lambda v^{-\frac{1}{p}}(t) \right],$$
$$v(0) = v_0,$$

is given by

$$v(t) = \left[v_0^{\frac{1}{p}} e^{-\theta_p t} + \frac{\lambda}{\theta_p} (1 - e^{-\theta_p t}) \right]^p,$$

where

$$\theta_p = \delta - \frac{\sigma^2}{2}(p-1).$$

Uniform bounds of the p -th Moments

Theorem

Suppose the following condition is satisfied,

$$\delta - \frac{\sigma_1^2}{2}(p-1) > 0, \quad q - \frac{\sigma_2^2}{2}(p-1) > 0, \quad \gamma - \frac{\sigma_3^2}{2}(p-1) > 0.$$

Then for $p > 1$ and all positive solution of the stochastic viral equations (1) with $(x_0, y_0, z_0) \in R_+^3$,

$$\limsup_{t \rightarrow \infty} E[x^p(t)] \leq L_1(p),$$

$$\limsup_{t \rightarrow \infty} E[y^p(t)] \leq L_2(p),$$

$$\limsup_{t \rightarrow \infty} E[z^p(t)] \leq L_3(p).$$

Remark. For $p = 1$, bounds are given thru linear equations.

Uniform Moment Bounds

$$L_1(p) = \left(\frac{\lambda}{\delta - \frac{\sigma_1^2}{2}(p-1)} \right)^p$$

$$L_2(p) = \left(\frac{4\beta b\lambda}{b(2\delta - \sigma_1^2(p-1))(2q - \sigma_2^2(p-1))} \right)^p$$

$$L_3(p) = \left(\frac{8k\beta\lambda}{b(2\delta - \sigma_1^2(p-1))(2q - \sigma_2^2(p-1))(2\gamma - \sigma_3^2(p-1))} \right)^p$$

where δ, q, γ are **death rates**, λ, β, k are **production or growth rates**, and $\sigma_1, \sigma_2, \sigma_3$ are **noise intensities**.

Sketch of Proof

For positive solutions,

$$d(x^p) \leq px^{p-1} \left(\lambda - \delta x + \frac{\sigma_1^2}{2}(p-1)x \right) dt + px^p \sigma_1 dB_1(t).$$

$$\frac{dE[x^p(t)]}{dt} \leq -p \left(\delta - \frac{\sigma_1^2}{2}(p-1) \right) E[x^p] + p\lambda E[x^p]^{1-\frac{1}{p}}.$$

Use Lemma for Bernoulli equations and comparison theorem.
For the y -equation, the nonlinear term of functional response

$$\frac{\beta xy}{1 + ax + by} \leq \frac{\beta x}{b}.$$

Pathwise Upper/Lower Bounds

Theorem

Every positive solution $(x(t), y(t), z(t))$ of the system (1) with $(x_0, y_0, z_0) \in \mathbb{R}_+^3$ satisfies

$$\Phi_l(t) \leq x(t) \leq \Phi_u(t),$$

$$\Psi_l(t) \leq y(t) \leq \Psi_u(t),$$

$$\Gamma_l(t) \leq z(t) \leq \Gamma_u(t), \quad t \geq 0, \text{ a.s.}$$

where

$$\begin{aligned} \Phi_u(t) = & \lambda \int_0^t \exp \left\{ - \left(\delta + \frac{\beta}{b} + \frac{\sigma_1^2}{2} \right) (t-s) + \sigma_1 (B_1(t) - B_1(s)) \right\} ds \\ & + x_0 \exp \left\{ - \left(\delta + \frac{\beta}{b} + \frac{\sigma_1^2}{2} \right) t + \sigma_1 B_1(t) \right\} \end{aligned}$$

Continued

$$\Psi_u(t) = \frac{\beta}{b} \int_0^t \Phi_u(s) e^{-\left(q + \frac{\sigma_2^2}{2}\right)(t-s) + \sigma_2(B_2(t) - B_2(s))} ds$$
$$+ y_0 e^{-\left(q + \frac{\sigma_2^2}{2}\right)t + \sigma_2 B_2(t)},$$

$$\Gamma_u(t) = k \int_0^t \Psi_u(s) e^{-\left(\gamma + \frac{\sigma_3^2}{2}\right)(t-s) + \sigma_3(B_3(t) - B_3(s))} ds$$
$$+ z_0 e^{-\left(\gamma + \frac{\sigma_3^2}{2}\right)t + \sigma_3 B_3(t)}.$$

Absorbing Property in Time Average

Theorem

Under the same condition that the noise intensities are relatively small,

$$\delta - \frac{\sigma_1^2}{2}(p-1) > 0, \quad q - \frac{\sigma_2^2}{2}(p-1) > 0, \quad \gamma - \frac{\sigma_3^2}{2}(p-1) > 0,$$

all the positive solutions has the property a.s.

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t x^p(s) ds = \int_{R_+^3} \xi^p d\mu(\xi, \eta, \zeta) \leq L_1(p),$$

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t y^p(s) ds = \int_{R_+^3} \eta^p d\mu(\xi, \eta, \zeta) \leq L_2(p),$$

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t z^p(s) ds = \int_{R_+^3} \zeta^p d\mu(\xi, \eta, \zeta) \leq L_3(p).$$

5. Moment Lyapunov Exponent

Definition

The p -th moment Lyapunov exponent of a pathwise solution $X(t, X_0)$ of the SDE (1) is defined by

$$\Lambda(p) = \limsup_{t \rightarrow \infty} \frac{1}{t} \log E|X(t, X_0)|^p, \quad p \geq 1.$$

Theorem

Under the same assumption as above, for $p \geq 1$,

$$\Lambda(p) = \limsup_{t \rightarrow \infty} \frac{1}{t} \log E\|X(t, X_0)\|_{\mathbb{R}_+^3}^p \leq 0,$$

for any positive solution $X(t, X_0) = (x(t, x_0), y(t, y_0), z(t, z_0))$ of the stochastic viral equations (1) with $X_0 \in \mathbb{R}_+^3$.

Sketch of Proof

The p -th moment of the geometric Brownian motion

$$dS = -\delta S(t) dt + \sigma S(t) dB$$

for $p > 1$ is given by

$$E|S(t)|^p = |S(0)|^p \exp \left[p \left(\frac{(p-1)}{2} \sigma^2 - \delta \right) t \right].$$

Directly estimate: in view of $\log(1+x) \leq x$ for $x > 0$,

$$\begin{aligned} \limsup_{t \rightarrow \infty} \frac{1}{t} \log (E|x(t, x_0)|^2) &\leq \limsup_{t \rightarrow \infty} \frac{1}{t} \log (E|\Phi_u(t)|^2) \\ &\leq \limsup_{t \rightarrow \infty} \frac{1}{t} \log \left(1 + \frac{x_0^2(2\delta - \sigma_1^2)}{\lambda^2} \exp\{(\sigma_1^2 - 2\delta)t\} \right) \\ &\quad + \limsup_{t \rightarrow \infty} \frac{1}{t} \log \frac{2\lambda^2}{2\delta - \sigma_1^2} = 0. \end{aligned}$$

when $p = 2$. Then bootstrap for the y and z components.

6. Persistence and Extinction

For a deterministic or stochastic model in **population dynamics** for ecology or **viral and epidemic dynamics** for disease control, the two most important questions are the analysis and prediction of persistence and extinction.

Definition

A component $x(t)$ of the system is said to be persistent in mean, if

$$\liminf_{t \rightarrow \infty} E[x(t)] > 0,$$

or persistent a.s. if

$$\liminf_{t \rightarrow \infty} x(t) > 0.$$

Other types of persistence and extinction can be defined.

Useful Lemma for Stochastic Predator-Prey Eqns

Lemma

Consider a one-dimensional SDE

$$dX = X(t)(a - bX(t)) dt + \sigma X(t) dB.$$

If $a > \frac{\sigma^2}{2}$, then for any solution $X(t)$ with $X_0 > 0$, one has

$$\lim_{t \rightarrow \infty} \frac{1}{t} \log X(t) = 0, \text{ a.s.}$$

and

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t X(s) ds = \frac{a - \frac{\sigma^2}{2}}{b}, \text{ a.s.}$$

Thus the solutions are persistent in time mean.

But this does not work for the stochastic SIR model with the Beddington-DeAngelis functional response.

Lemma $\lim_{t \rightarrow \infty} \frac{1}{t} \log x(t) = 0$

$$x(t) \leq \Phi_u(t) \leq \frac{\lambda}{\delta + \frac{\beta}{b} + \frac{\sigma_1^2}{2}} \exp \left[\sigma_1 \left(B_1(t) - \min_{0 \leq s \leq t} B_1(s) \right) \right] \\ + x_0 \exp \left[- \left(\delta + \frac{\beta}{b} + \frac{\sigma_1^2}{2} \right) t + \sigma_1 B_1(t) \right]$$

The running max of BM, $B_1(t) - \min_{0 \leq s \leq t} B_1(s) = |B_1(t)|$ in **distribution**, and $\log(1+x) < x$ lead to

$$\limsup_{t \rightarrow \infty} \frac{1}{t} \log \Phi_u(t) \leq \limsup_{t \rightarrow \infty} \frac{1}{t} \left[\sigma_1 \left(B_1(t) - \min_{0 \leq s \leq t} B_1(s) \right) \right] \\ + \limsup_{t \rightarrow \infty} \frac{1}{t} \log \left[1 + \frac{x_0(\delta + \beta/b + \sigma_1^2/2)}{\lambda} \exp(\text{Ratio}) \right] = 0.$$

The Exponential Transformation

Let $x(t) = e^{u(t)}$, $y(t) = u^{v(t)}$, $z(t) = e^{w(t)}$. The SDE of this stochastic viral model is converted to

$$du = \left(- \left(\delta + \frac{\sigma_1^2}{2} \right) + \lambda e^{-u} - \frac{\beta e^v}{1 + a e^u + b e^v} \right) dt + \sigma_1 dB_1,$$

$$dv = \left(- \left(q + \frac{\sigma_2^2}{2} \right) + \frac{\beta e^u}{1 + a e^u + b e^v} \right) dt + \sigma_2 dB_2,$$

$$dw = \left(k e^{v-w} - \left(\gamma + \frac{\sigma_3^2}{2} \right) \right) dt + \sigma_3 dB_3.$$

Here we see

$$dv \leq \left(\frac{\beta}{a} - \left(q + \frac{\sigma_2^2}{2} \right) \right) dt + \sigma_2 dB_2.$$

Extinction of the Infectives

Proposition

If $\beta/a < q + \sigma_2^2/2$, then $\lim_{t \rightarrow \infty} y(t) = 0$. The infective cells tends to extinction.

By the stochastic comparison theorem, cf. Ikeda and Watanabe (1981), p. 352,

$$\begin{aligned}v(t) &\leq v_0 + \left(\frac{\beta}{a} - \left(q + \frac{\sigma_2^2}{2} \right) \right) t + \sigma_2 B_2(t) \\ &= v_0 + \left(\frac{\beta}{a} - \left(q + \frac{\sigma_2^2}{2} \right) \right) t \left[1 + \frac{\sigma_2 B_2(t)}{\left(\frac{\beta}{a} - \left(q + \frac{\sigma_2^2}{2} \right) \right) t} \right] \rightarrow -\infty.\end{aligned}$$

by SLLN for Brownian motion. Then $\lim y(t) = \lim e^{v(t)} = 0$.

Persistence of the Susceptible

From the u -equation,

$$\begin{aligned} du &= \left(- \left(\delta + \frac{\sigma_1^2}{2} \right) + \lambda e^{-u} - \frac{\beta e^v}{1 + a e^u + b e^v} \right) dt + \sigma_1 dB_1, \\ &\geq \left(\lambda e^{-u} - \left(\delta + \frac{\sigma_1^2}{2} + \frac{\beta}{b} \right) \right) dt + \sigma_1 dB_1, \end{aligned}$$

and $d\tilde{u} = (\lambda e^{-u} - \theta) dt + \sigma_1 dB_1$, $\theta = \delta + \sigma_1^2/2 + \beta/b$, has a unique stationary distribution whose probability density is a solution of the stationary Fokker-Planck equation

$$\frac{1}{2} \sigma_1^2 \frac{d^2 p}{d\xi^2} - \frac{d}{d\xi} [(\lambda e^{-\xi} - \theta) p] = 0.$$

The solution is

$$p(\xi) = C \exp \left\{ -\frac{2\theta}{\sigma_1^2} \xi + \frac{2\lambda}{\sigma_1^2} e^{-\xi} \right\},$$

where C is the normalizing const.

Persistence of the Susceptible

Accordingly, cf. Rudnicki (2003), Skorokhod (1987),

$$u(t) \geq \tilde{u}(t)$$

which converges in distribution to a stationary solution \tilde{u}_* whose probability density is $p(\xi)$, as $t \rightarrow \infty$.

Proposition

The susceptible cells will be persistent in mean and

$$\begin{aligned} \liminf_{t \rightarrow \infty} E[x(t)] &\geq \int_0^{\infty} e^{\xi} p(\xi) d\xi \\ &= C \int_0^{\infty} \exp \left\{ \left(1 - \frac{2\theta}{\sigma_1^2} \right) \xi + \frac{2\lambda}{\sigma_1^2} e^{-\xi} \right\} d\xi \\ &\geq \frac{C\sigma_1^2}{\sigma_1^2 - 2\theta} = \frac{C\sigma_1^2}{2(\delta + \beta/b)} > 0. \end{aligned}$$

Persistence of the Recovered

Proposition

Under the condition $\beta/a < q + \sigma_2^2/2$, The recovered cells will be persistent in mean.

From the w -equation

$$dw = \left(ke^{v-w} - \left(\gamma + \frac{\sigma_3^2}{2} \right) \right) dt + \sigma_3 dB_3$$

with $y(t) = e^{v(t)} \rightarrow 0$ under the condition, the proof is similar.

- **Many questions** still unanswered: stability, bifurcation, stochastic pattern formation for SPDE models, etc.

Conclusion

- The study shows that under the condition $q \geq k$ the positive cone \mathbb{R}_+^3 is invariant with probability one for the pathwise solutions of this model of stochastic viral dynamics.
- Construction of Lyapunov functions shows that there is a unique stationary distribution whose probability density function is a steady state of the Fokker-Planck equation.
- Moments and pathwise upper/lower bounds and some asymptotic estimates are obtained, which make possible to discuss the persistence and extinction of the virus diseases.

All these can be used for better reveal of features of models of stochastic SIR equations with different functional responses and for better understanding of medical/epidemic incident events.

THANKS