

具有非线性发生率和时滞的 HIV 感染模型分析

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摘 要: 研究了一类具有 Beddington-DeAngelis 发生率和免疫反应时滞的艾滋病传染模型. 首先通过构造适当的 Lyapunov 泛函并利用 LaSalle 不变原理证明了无病平衡点以及染病无免疫平衡点的全局渐近稳定性; 其次讨论了感染免疫平衡点局部渐近稳定的充分条件, CTL 免疫反应时滞可以改变感染免疫平衡点的稳定性并产生 Hopf 分支现象; 最后利用数值模拟验证了以上结论.

关键词: Beddington-DeAngelis 发生率; CTL 免疫反应; 时滞; 稳定性; Lyapunov 泛函

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近几年, 艾滋病传染模型引起了学界广泛的关注^[1-6]. HIV 能大范围的感染人体细胞, 破坏人体的免疫系统, 使人体成为各种病毒的载体. 适当的模型可以为病毒感染群体动力学提供深刻的见解, 研究此类模型对控制疾病的传播以及艾滋病的防治有重大意义.

从生物学意义和数学角度不难注意到采用更具一般形式的 Beddington-DeAngelis 型功能性反应函数 $\frac{\beta x v}{1 + ax + bv}$ 作为正常细胞被传染的速率可以更为客观地描述病毒与正常细胞之间的动态演化作用. 文献[7-12]均引入了这种功能性反应函数, 并通过构造 Lyapunov 泛函研究了多种病毒动力学模型的全局渐近稳定性. 袁朝晖等人研究了一类具有 Beddington-DeAngelis 发生率及 CTL 免疫反应的艾滋病传染模型^[10]:

$$\begin{cases} \frac{dx}{dt} = s - dx - \frac{\beta x v}{1 + ax + bv} + \delta w, \\ \frac{dw}{dt} = \frac{\beta x v}{1 + ax + bv} - (\delta + \eta + q)w, \\ \frac{dy}{dt} = qw - \alpha y - pyz, \\ \frac{dv}{dt} = Nay - \nu, \\ \frac{dz}{dt} = cyz - rz. \end{cases} \quad (1)$$

其中状态变量 $x(t), w(t), y(t), v(t), z(t)$ 分别表示 t 时刻正常细胞的浓度、处于潜伏期的感染细胞的浓度、病毒感染细胞的浓度、游离病毒粒子的浓度、CTL 免疫细胞的浓度; 参数 $d, \eta, \alpha, \gamma, r$ 分别表示正常细胞、处于潜伏期的感染细胞、病毒感染的细胞、游离病毒粒子、CTL 免疫细胞的死亡速率; s 为产生正常细胞的速率; δ 为处于潜伏期的感染细胞恢复为正常细胞的速率; q 为处于潜伏期的感染细胞变为活性感染细胞的速率; p 为 CTL 免疫细胞反应清除感染细胞的速率; N 为每个活性感染细胞产生病毒粒子的平均个数; c 为已感染细胞激发产生 CTL 免疫细胞的速率; Beddington-DeAngelis 型功能性反应函数 $\frac{\beta x v}{1 + ax + bv}$ 为正常细胞被感染

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的速率. 以上参数均大于零.

为了更准确地描述病毒传染的动力学特征, 可考虑在系统中引入时滞来研究病毒感染细胞的过程^[13-19]. 因此, 本文研究了一个新的带有时滞的病毒感染模型:

$$\begin{cases} \frac{dx}{dt} = s - dx - \frac{\beta x v}{1 + ax + bv} + \delta w, \\ \frac{dw}{dt} = \frac{\beta x v}{1 + ax + bv} - (\delta + \eta + q)w, \\ \frac{dy}{dt} = qw - \alpha y - pyz, \\ \frac{dv}{dt} = N\alpha y - \gamma v, \\ \frac{dz}{dt} = cy(t - \tau)z(t - \tau) - rz, \end{cases} \quad (2)$$

其中 τ 表示从抗原受到刺激到产生 CTL 免疫细胞的时间^[13], 并且 $\tau \geq 0$.

系统(2)的初始条件为

$$\begin{aligned} x(\theta) &= \phi_1(\theta), w(\theta) = \phi_2(\theta), y(\theta) = \phi_3(\theta), v(\theta) = \phi_4(\theta), z(\theta) = \phi_5(\theta), \\ \phi_i(\theta) &\geq 0, \theta \in [-\tau, 0], \phi_i(0) > 0 (i = 1, 2, 3, 4, 5), \end{aligned} \quad (3)$$

这里 $(\phi_1(\theta), \phi_2(\theta), \phi_3(\theta), \phi_4(\theta), \phi_5(\theta)) \in C([-\tau, 0], \mathbf{R}_{+}^5)$, $C([-\tau, 0], \mathbf{R}_{+}^5)$ 为 Banach 空间从 $[-\tau, 0]$ 到 $\mathbf{R}_{+}^5$ 的连续函数映射, 其中 $\mathbf{R}_{+}^5 = \{(x_1, x_2, x_3, x_4, x_5) : x_i \geq 0, i = 1, 2, 3, 4, 5\}$.

1 平衡点的存在性及稳定性

系统(2)的基本再生数和免疫反应再生数分别为

$$R_0 = \frac{Ns\beta q}{\gamma(sa + d)(\delta + \eta + q)}, R_1 = \frac{sqc\gamma(sa + d)(R_0 - 1)}{rsNaqdb + r\alpha\gamma(\eta + q)[dR_0 + as(R_0 - 1)]}.$$

系统(2)存在 3 个平衡点, 其总是存在无病平衡点 $E_0 = (\frac{s}{d}, 0, 0, 0, 0)$.

若 $R_0 > 1$, 则存在染病无免疫平衡点 $E_1 = (x_1, w_1, y_1, v_1, 0)$, 其中

$$\begin{aligned} x_1 &= \frac{s(1 + bv_1)}{dR_0 + sa(R_0 - 1)}, w_1 = \frac{\gamma v_1}{Nq}, y_1 = \frac{\gamma v_1}{Na}, \\ v_1 &= \frac{Nar}{cy} R_1 = \frac{sNq(sa + d)(R_0 - 1)}{sNqdb + \gamma(\eta + q)[dR_0 + as(R_0 - 1)]}. \end{aligned}$$

若 $R_1 > 1$, 则存在感染免疫平衡点 $E_2 = (x_2, w_2, y_2, v_2, z_2)$, 其中

$$w_2 = \frac{s - dx_2}{\eta + q}, y_2 = \frac{r}{c}, v_2 = \frac{Nar}{\gamma c}, z_2 = \frac{cq(s - dx_2)}{(\eta + q)pr} - \frac{\alpha}{p}.$$

x_2 是 $F(x) = 0$ 的一个正根, 其中

$$F(x) = adx^2 + \left[\frac{cd\gamma + bdrNa}{cy} + \frac{\beta Nar(\eta + q)}{cy(\delta + \eta + q)} - sa \right] x - \frac{sc\gamma + bsrNa}{cy}.$$

在研究系统(2)的稳定性前, 先证明系统(2)的解是有界的.

定理 1 对于满足初始条件(3)的系统(2)的解 $x(t), w(t), y(t), v(t), z(t)$, 存在 $\bar{M} > 0$ 使得对于任意大的 t 都有 $x(t) < \bar{M}, w(t) < \bar{M}, y(t) < \bar{M}, v(t) < \bar{M}, z(t) < \bar{M}$.

证明 设 $X(t) = x(t) + w(t) + y(t) + \frac{1}{2N}v(t) + \frac{p}{c}z(t + \tau)$, $\rho = \min\{d, \eta, \frac{\alpha}{2}, \gamma, r\}$, 则 $\frac{dX}{dt} = s - dx(t) - \eta w(t) - \frac{\alpha}{2}y(t) - \frac{\gamma}{2N}v(t) - \frac{pr}{c}z(t + \tau) \leq s - \rho X$, 所以, 对任意大的 t 都有 $X(t) < \frac{s}{\rho} + \epsilon$, 其中 ϵ 是任意小的正常数, 则存在 $\bar{M} > 0$ 使得对于任意大的 t 都有 $x(t) < \bar{M}, w(t) < \bar{M}, y(t) < \bar{M}, v(t) < \bar{M}, z(t) < \bar{M}$. 证毕.

关于 E_0 的稳定性, 有如下结论.

定理 2 若 $R_0 \leq 1$, 则无病平衡点 E_0 是全局渐近稳定的. 若 $R_0 > 1$, E_0 是不稳定的.

证明 定义一个 Lyapunov 泛函如下,

$$L_1(t) = \frac{x_0}{1+ax_0} \left(\frac{x(t)}{x_0} - 1 - \ln \frac{x(t)}{x_0} \right) + \frac{\delta}{2(1+ax_0)(d+\eta+q)x_0} (x(t) - x_0 + w(t))^2 + w(t) + \frac{\delta+\eta+q}{q} y(t) + \frac{(\delta+\eta+q)}{Nq} \nu(t) + \frac{p(\delta+\eta+q)}{cq} z(t) + \frac{p(\delta+\eta+q)}{q} \int_{t-\tau}^t y(\theta) z(\theta) d\theta.$$

由 $s = dx_0$, 可得

$$\begin{aligned} \frac{dL_1}{dt} = & \frac{x_0}{1+ax_0} \left(\frac{1}{x_0} - \frac{1}{x} \right) \left(dx_0 - dx - \frac{\beta x \nu}{1+ax+b\nu} + \delta w \right) + \frac{\delta}{(1+ax_0)(d+\eta+q)x_0} (x - x_0 + w) \\ & [dx_0 - dx - (\eta+q)w] + \frac{\beta x \nu}{1+ax+b\nu} - (\delta+\eta+q)w + \frac{\delta+\eta+q}{q} (qw - ay - pyz) + \\ & \frac{\delta+\eta+q}{Nq} (Nay - \nu) + \frac{p(\delta+\eta+q)}{cq} (cy(t-\tau)z(t-\tau) - rz) + \frac{p(\delta+\eta+q)}{q} (yz - y(t-\tau)z(t-\tau)) = \\ & - \left(\frac{1}{x} + \frac{\delta}{(d+\eta+q)x_0} \right) \frac{d(x-x_0)^2}{1+ax_0} + \frac{\delta w}{1+ax_0} \left(2 - \frac{x_0}{x} - \frac{x}{x_0} \right) - \\ & \frac{\delta(\eta+q)w^2}{(1+ax_0)(d+\eta+q)x_0} + \frac{\gamma(\delta+\eta+q)}{Nq} (R_0 - 1)\nu - \frac{rp(\delta+\eta+q)}{cq} z - \frac{b\beta x_0 \nu^2}{(1+ax_0)(1+ax+b\nu)}. \end{aligned}$$

因为 $R_0 \leq 1$ 并且 $2 - \frac{x_0}{x} - \frac{x}{x_0} \leq 0$, 则 $\frac{dL_1}{dt} \leq 0$, 当且仅当 $x = x_0, w = y = \nu = z = 0$ 时等号成立. 由

LaSalle 不变原理知无病平衡点 E_0 在 $R_0 \leq 1$ 时是全局渐近稳定的.

系统(2)在平衡点 E_0 处的特征方程为

$$(\lambda+r)(\lambda+d) \left\{ [\lambda+(\delta+\eta+q)](\lambda+\alpha)(\lambda+\gamma) - \frac{qNa\beta x_0}{1+ax_0} \right\} = 0,$$

即 $(\lambda+r)(\lambda+d)H_0(\lambda) = 0$, 其中

$$H_0(\lambda) = \lambda^3 + (\delta+\eta+q+\alpha+\gamma)s^2 + [\alpha(\delta+\eta+q+\gamma) + \gamma(\delta+\eta+q)]\lambda + \alpha\gamma(\delta+\eta+q)(1-R_0),$$

若 $R_0 > 1$, 则 $H_0(0) = \alpha\gamma(\delta+\eta+q)(1-R_0) < 0$, 并且 $\lim_{\lambda \rightarrow +\infty} H_0(\lambda) > 0$. 则上述特征方程有正实根. 所以

当 $R_0 > 1$ 时, E_0 是不稳定的. 证毕.

定理 3 当 $1 < R_0 \leq 1 + \frac{bd s N q + d \gamma (\eta + q)}{\delta \gamma (s a + d)}$, 且 $R_1 < 1$ 时, 染病无免疫平衡点 E_1 是全局渐近稳定的.

若 $R_1 > 1$, 则 E_1 是不稳定的.

证明 构造 Lyapunov 泛函如下,

$$\begin{aligned} L_2(t) = & x(t) - x_1 - E \int_{x_1}^x \frac{1+a\theta+b\nu_1}{\beta x \nu_1} d\theta + w(t) - w_1 - w_1 \ln \frac{w(t)}{w_1} + \\ & \frac{\delta(1+b\nu_1)}{2(1+ax_1+b\nu_1)(d+\eta+q)x_1} (x(t) - x_1 + w(t) - w_1)^2 + \frac{E}{qw_1} \left(y(t) - y_1 - \right. \\ & \left. y_1 \ln \frac{y(t)}{y_1} \right) + \frac{E}{Nqw_1} \left(\nu(t) - \nu_1 - \nu_1 \ln \frac{\nu(t)}{\nu_1} \right) + \frac{pE}{cq w_1} z(t) + \frac{pE}{q w_1} \int_{t-\tau}^t y(\theta) z(\theta) d\theta. \end{aligned}$$

其中 $E = \frac{\beta x_1 \nu_1}{(1+mx_1+m\nu_1)}$, 则

$$\begin{aligned} \frac{dL_2}{dt} = & \left[1 - \frac{(1+ax+b\nu_1)E}{\beta x \nu_1} \right] \left(s - dx - \frac{\beta x \nu}{1+ax+b\nu} + \delta w \right) + \frac{E}{qw_1} \left(1 - \frac{y_1}{y} \right) (qw - ay - pyz) + \\ & \left(1 - \frac{w_1}{w} \right) \left[\frac{\beta x \nu}{1+ax+b\nu} - (\delta+\eta+q)w \right] + \frac{E}{Nqw_1} \left(1 - \frac{\nu_1}{\nu} \right) (Nay - \nu) + \\ & \frac{\delta(1+b\nu_1)}{(1+ax_1+b\nu_1)(d+\eta+q)x_1} (x - x_1 + w - w_1) [s - dx - (\eta+q)w] + \\ & \frac{pE}{cq w_1} (cy(t-\tau)z(t-\tau) - rz) + \frac{pE}{q w_1} (yz - y(t-\tau)z(t-\tau)). \end{aligned}$$

因为 $s = dx_1 + E - \delta w_1$, $\frac{E}{w_1} = \delta + \eta + q$, $Nq w_1 = N a y_1 = \gamma_1$, 可得

$$\begin{aligned} \frac{dL_2}{dt} = & - \left(dx_1 - \delta w_1 + \delta w + \frac{d\delta x}{d + \eta + q} \right) \frac{(1 + b_{v_1})(x - x_1)^2}{x x_1 (1 + a x_1 + b_{v_1})} - \frac{\delta(1 + b_{v_1})(\eta + q)(w - w_1)^2}{x_1 (1 + a x_1 + b_{v_1})(d + \eta + q)} - \\ & \frac{Eb(1 + ax)(v - v_1)^2}{v_1(1 + ax + b_{v_1})(1 + ax + b_v)} + \frac{Epr(R_1 - 1)z}{cq w_1} - E \left(\frac{x_1(1 + ax + b_{v_1})}{x(1 + ax_1 + b_{v_1})} + \right. \\ & \left. \frac{x w_1 v(1 + ax_1 + b_{v_1})}{x_1 w v_1 (1 + ax + b_v)} + \frac{1 + ax + b_v}{1 + ax + b_{v_1}} + \frac{y_1 w}{y w_1} + \frac{y v_1}{y_1 v} - 5 \right). \end{aligned}$$

因为 $\frac{x_1(1 + ax + b_{v_1})}{x(1 + ax_1 + b_{v_1})} + \frac{x w_1 v(1 + ax_1 + b_{v_1})}{x_1 w v_1 (1 + ax + b_v)} + \frac{1 + ax + b_v}{1 + ax + b_{v_1}} + \frac{y_1 w}{y w_1} + \frac{y v_1}{y_1 v} - 5 \geq 0$, 当且仅当 $x = x_1$,

$w = w_1, y = y_1, v = v_1$ 时上述不等式的等号成立. 若 $R_1 < 1$ 且 $dx_1 \geq \delta w_1$, 则 $\frac{dL_2}{dt} \leq 0$. 当且仅当 $x = x_1$,

$w = w_1, y = y_1, v = v_1, z = 0$ 时 $\frac{dL_2}{dt} = 0$, 而 $dx_1 \geq \delta w_1$ 等价于 $R_0 \leq 1 + \frac{bdsNq + d\gamma(\eta + q)}{\delta\gamma(sa + d)}$. 由 LaSalle 不

变原理可得无免疫平衡点 E_1 在 $1 < R_0 \leq 1 + \frac{bdsNq + d\gamma(\eta + q)}{\delta\gamma(sa + d)}$ 且 $R_1 < 1$ 时是全局渐近稳定的.

系统(2)在平衡点 E_1 处的特征方程为 $(\lambda + r - cy_1 e^{-\lambda\tau})H_1(\lambda) = 0$, 其中 $H_1(\lambda)$ 是关于 λ 的多项式. 设 $H_2(\lambda) = (\lambda + r - cy_1 e^{-\lambda\tau})$, 则当 $R_1 > 1$ 时, $H_2(0) = r(1 - R_1) < 0$, 且 $\lim_{\lambda \rightarrow +\infty} H_2(\lambda) > 0$. 则上述特征方程有正实根. 所以当 $R_1 > 1$ 时, E_1 是不稳定的. 证毕.

2 正平衡点的稳定性和 Hopf 分支

系统(2)在 E_2 处的线性近似方程为

$$\begin{cases} \frac{dx}{dt} = - \left(\frac{\beta v_2(1 + b_{v_2})}{(1 + ax_2 + b_{v_2})^2} + d \right) x + \delta w - \frac{\beta x_2(1 + ax_2)}{(1 + ax_2 + b_{v_2})^2} v, \\ \frac{dw}{dt} = \frac{\beta v_2(1 + b_{v_2})}{(1 + ax_2 + b_{v_2})^2} x - (\delta + \eta + q)w + \frac{\beta x_2(1 + ax_2)}{(1 + ax_2 + b_{v_2})^2} v, \\ \frac{dy}{dt} = qw - (\alpha + pz_2)y - py_2 z, \\ \frac{dv}{dt} = N a y - \gamma, \\ \frac{dz}{dt} = cz_2 y(t - \tau) + cy_2 z(t - \tau) - rz. \end{cases} \quad (4)$$

系统(4)在零点的特征方程形如

$$G(\lambda) = \lambda^5 + M_1 \lambda^4 + M_2 \lambda^3 + M_3 \lambda^2 + M_4 \lambda + M_5 - (N_1 \lambda^4 + N_2 \lambda^3 + N_3 \lambda^2 + N_4 \lambda + N_5) e^{-\lambda\tau} = 0, \quad (5)$$

其中

$$M_1 = R + P + \gamma + r, M_2 = Q + P(R + \gamma) + r(R + P + \gamma) + \gamma R,$$

$$M_3 = rP\gamma + R[(\gamma + r)P + r\gamma] + Q(P + \gamma + r) - qBN\alpha,$$

$$M_4 = RrP\gamma + Q[(\gamma + r)P + r\gamma] - qBN\alpha(d + r), M_5 = QrP\gamma - rdqBN\alpha,$$

$$N_1 = r, N_2 = r(R + P + \gamma) - cpy_2 z_2, N_3 = r[P\gamma + R(P + \gamma) + Q] - cpy_2 z_2(R + \gamma),$$

$$N_4 = r[RP\gamma + Q(P + \gamma) - qBN\alpha] - cpy_2 z_2(R\gamma + Q),$$

$$N_5 = QrP\gamma - rdqBN\alpha - Q\gamma pcy_2 z_2,$$

$$A = \frac{\beta v_2(1 + b_{v_2})}{(1 + ax_2 + b_{v_2})^2}, B = \frac{\beta x_2(1 + ax_2)}{(1 + ax_2 + b_{v_2})^2}, P = \alpha + pz_2,$$

$$Q = d(\delta + \eta + q) + A(\eta + q), R = d + A + \delta + \eta + q.$$

定理 4 假设 $\tau = 0$, 若 $R_1 > 1$ 且 $\gamma \leq \min\{\alpha, d, \delta + \eta + q\}$, 则感染免疫平衡点 E_2 是局部渐近稳定的.

证明 若 $\tau = 0$, 则(5)变为

$$\lambda^5 + (M_1 - N_1)\lambda^4 + (M_2 - N_2)\lambda^3 + (M_3 - N_3)\lambda^2 + (M_4 - N_4)\lambda + (M_5 - N_5) = 0. \quad (6)$$

因为

$$qBN\alpha = \left(\frac{\beta x_2}{1 + ax_2 + b\nu_2} - \frac{b\beta x_2 \nu_2}{(1 + ax_2 + b\nu_2)^2} \right) qN\alpha < \frac{\beta x_2 \nu_2}{1 + ax_2 + b\nu_2} \cdot \frac{1}{\nu_2} qN\alpha = (\delta + \eta + q)(\alpha + pz_2)\gamma,$$

所以 $qBN\alpha < (\delta + \eta + q)(\alpha + pz_2)\gamma = (\delta + \eta + q)P\gamma$.

又因为 $x_2 > 0, w_2 > 0, y_2 > 0, \nu_2 > 0$ 且 $z_2 > 0$, 所以

$$\Delta_1 = M_1 - N_1 = R + P + \gamma > 0,$$

$$\begin{aligned} \Delta_2 &= (M_1 - N_1)(M_2 - N_2) - (M_3 - N_3) = (R + P + \gamma)[Q + P(R + \gamma) + R\gamma + cp_{y_2}z_2] - \\ &\quad RP\gamma - Q(P + \gamma) - cp_{y_2}z_2(R + \gamma) + qBN\alpha = QR + Pc p_{y_2}z_2 + (R + P + \\ &\quad \gamma)R\gamma + qBN\alpha + (R + P + \gamma)RP + (P + \gamma)P\gamma > 0, \end{aligned}$$

$$\Delta_3 = \{(M_3 - N_3)[(M_1 - N_1)(M_2 - N_2) - (M_3 - N_3)] + (M_1 - N_1)[(M_5 - N_5) - (M_1 - N_1)(M_4 - N_4)] = A_1(pcy_2z_2)^2 + B_1pcy_2z_2 + C_1,$$

其中

$$A_1 = (R + \gamma)P > 0,$$

$$\begin{aligned} B_1 &= (R + \gamma)[QR + (P + \gamma)P\gamma + qBN\alpha + R(P + \gamma)(R + P + \gamma)] + P[Q(P + \gamma) + RP\gamma - \\ &\quad qBN\alpha] + (R + P + \gamma)Q\gamma + (R\gamma + Q)(R + P + \gamma)^2 > PR[A(\delta + A + d + P + \gamma) + \\ &\quad d(A + d + P + \gamma) + \delta(\delta + \eta + q + A + P + \gamma) + (\eta + q)(\delta + \eta + q + P + \gamma)] + \\ &\quad P^2(A + d)\gamma + P(R + \gamma)(P + \gamma)\gamma + (P + \gamma)qBN\alpha > 0, \end{aligned}$$

$$\begin{aligned} C_1 &= \{[Q + (R + \gamma)P + R\gamma](R + P + \gamma) + qBN\alpha - RP\gamma - Q(P + \gamma)\} \times [RP\gamma + Q(P + \gamma) - \\ &\quad qBN\alpha] - (R + P + \gamma)^2(QP\gamma - dqBN\alpha) > [QR + (P + \gamma)P\gamma + qBN\alpha + R(R + P + \gamma)(P + \\ &\quad \gamma)](A + d)P\gamma + Q^2R(P + \gamma) + QR[(R + P + \gamma)P^2 + (R + \gamma)(P + \gamma)\gamma] + [(A + \\ &\quad d)P\gamma + Q(P + \gamma)]qBN\alpha + (R + P + \gamma)^2dqBN\alpha > 0, \end{aligned}$$

所以 $\Delta_3 > 0$.

$$\Delta_4 = \begin{vmatrix} M_1 - N_1 & 1 & 0 & 0 \\ M_3 - N_3 & M_2 - N_2 & M_1 - N_1 & 1 \\ M_5 - N_5 & M_4 - N_4 & M_3 - N_3 & M_2 - N_2 \\ 0 & 0 & M_5 - N_5 & M_4 - N_4 \end{vmatrix} =$$

$$(M_4 - N_4)\Delta_3 - (M_5 - N_5)(M_2 - N_2)[(M_1 - N_1)(M_2 - N_2) - (M_3 - N_3)] + (M_5 - N_5)[(M_1 - N_1)(M_4 - N_4) - (M_5 - N_5)] = A_2(pcy_2z_2)^3 + B_2(pcy_2z_2)^2 + C_2pcy_2z_2 + D_2,$$

其中

$$A_2 = P[(R + \gamma)R\gamma + RQ] > 0,$$

$$\begin{aligned} B_2 &> (Q + R\gamma)B_1 + AP(\eta + q)\gamma A_1 + Q\gamma[(R + P + \gamma)R\gamma + Q(R + P)] - QP\gamma[Q + P(R + \gamma) + R\gamma] - \\ &\quad Q\gamma[RQ + (P + \gamma)P\gamma + R(R + P + \gamma)(P + \gamma) + qBN\alpha] = [A(\delta + A + d + P + \gamma) + d(A + d + P + \\ &\quad \gamma) + \delta(\delta + \eta + q + A) + (\eta + q)(\delta + \eta + q)] \times R^2P\gamma + RP\gamma(P + \gamma)^2 [\delta(\delta + \\ &\quad \eta + q + A) + (\eta + q)(\delta + \eta + q) + (R + \gamma)\gamma] + (R + \gamma)R\gamma qBN\alpha + QP^2\gamma^2 + \\ &\quad QRP[A(\delta + A + d + P) + d(A + d + P) + \delta(\delta + \eta + q + A + P) + (\eta + q) \\ &\quad (\delta + \eta + q + P)] + Q[(A + d)P^2\gamma + RqBN\alpha] + AP^2(\eta + q)(R + \gamma)\gamma > 0. \end{aligned}$$

因为 $\gamma \leq \min\{\alpha, d, \delta + \eta + q\}$, 所以

$$\begin{aligned} C_2 &> A(\eta + q)P\gamma B_1 + (Q + R\gamma)C_1 + (R + P + \gamma)(QP\gamma - dqBN\alpha)Q\gamma - Q\gamma[Q + (R + \gamma)P + \\ &\quad R\gamma][RQ + (R + P + \gamma)(P + \gamma)R + (P + \gamma)P\gamma + qBN\alpha] = A(\eta + q)P\gamma B_1 + [Q\gamma^2 + Q(A + \\ &\quad d)\gamma + Q^2]PqBN\alpha + Q(P + \gamma)P^2\gamma^3 + [(R + P + \gamma)^2R\gamma + Q(R + P + \gamma)(R + P)]dqBN\alpha + \\ &\quad (P + \gamma)[(R + P + \gamma)RPA\delta\gamma^2] + QP^2[A(\eta + q)(R + P)R + (P + \gamma)(A + \\ &\quad d)\gamma^2] + QRP[Q^2 - \gamma^3(\delta + \eta + q)] + RP\gamma^2(P + \gamma)(A + d) \\ &\quad [A(\delta + A + d + P + \gamma) + d(A + d + P + \gamma)] > 0. \end{aligned}$$

因为

$$\Delta_4 = \begin{vmatrix} M_1 - N_1 & 1 & 0 & 0 \\ M_3 - N_3 & M_2 - N_2 & M_1 - N_1 & 1 \\ M_5 - N_5 & M_4 - N_4 & M_3 - N_3 & M_2 - N_2 \\ 0 & 0 & M_5 - N_5 & M_4 - N_4 \end{vmatrix} = (M_4 - N_4)\Delta_3 - (M_5 - N_5) \begin{vmatrix} M_1 - N_1 & 1 & 0 \\ M_3 - N_3 & M_2 - N_2 & 1 \\ M_5 - N_5 & M_4 - N_4 & M_2 - N_2 \end{vmatrix},$$

则 D_2 等于 $(M_4 - N_4)\Delta_3$ 中 pcy_2z_2 的零次幂的系数,又因为 Δ_3 的常数项 $C_1 > 0$ 并且 $(M_4 - N_4)$ 的常数项大于零,所以 $D_2 > 0$.

综上 A_2, B_2, C_2, D_2 均大于零,所以

$$\Delta_4 = A_2(pcy_2z_2)^3 + B_2(pcy_2z_2)^2 + C_1pcy_2z_2 + D_2 > 0.$$

因为 $\Delta_5 = (M_5 - N_5)\Delta_4$,又因为 $M_5 - N_5 = [A(\eta + q) + d(\delta + \eta + q)]\gamma pcy_2z_2 > 0$ 且 $\Delta_4 > 0$,则 $\Delta_5 > 0$,由 Routh-Hurwitz 判别准则得(6)的所有根均具有负实部.证毕.

由定理 4,当 $\tau = 0, R_1 > 1$ 且 $\gamma \leq \min\{\alpha, d, \delta + \eta + q\}$ 时, $G(\lambda) = 0$ 的所有根均具有负实部,由根的连续性可得存在 $\bar{\tau} > 0$ 使得当 $\tau \in [0, \bar{\tau}]$ 时, (5) 所有的根满足 $\text{Re}(\lambda) < 0$,并且当 $\tau = \bar{\tau}$ 时 $\text{Re}(\lambda) = 0$. 下面计算 $\bar{\tau}$ 及相关的纯虚根 $\bar{\epsilon}i$ ($\bar{\epsilon} > 0$).

假设 $\lambda = \omega i$ ($\omega > 0$) 是(5)的一个纯虚根,可得

$$\omega^5 i + M_1 \omega^4 - M_2 \omega^3 i - M_3 \omega^2 + M_4 \omega i + M_5 - (N_1 \omega^4 - N_2 \omega^3 i - N_3 \omega^2 + N_4 \omega i + N_5) e^{-i\omega\tau} = 0$$

分离实部和虚部,可得

$$\begin{aligned} (N_1 \omega^4 - N_3 \omega^2 + N_5) \cos(\omega\tau) + (N_4 \omega - N_2 \omega^3) \sin(\omega\tau) &= M_1 \omega^4 - M_3 \omega^2 + M_5, \\ (N_4 \omega - N_2 \omega^3) \cos(\omega\tau) + (N_3 \omega^2 - N_1 \omega^4 - N_5) \sin(\omega\tau) &= \omega^5 - M_2 \omega^3 + M_4 \omega. \end{aligned} \quad (7)$$

由(7)可得

$$\cos(\omega\tau) = \frac{1}{\Delta} (P_1 \omega^8 + P_2 \omega^6 + P_3 \omega^4 + P_4 \omega^2 + P_5), \quad \sin(\omega\tau) = -\frac{\omega}{\Delta} (Q_1 \omega^8 + Q_2 \omega^6 + Q_3 \omega^4 + Q_4 \omega^2 + Q_5). \quad (8)$$

其中

$$\begin{aligned} P_1 &= N_1 M_1 - N_2, P_2 = N_4 + N_2 M_2 - N_1 M_3 - N_3 M_1, P_4 = N_4 M_4 - N_3 M_5 - N_5 M_3, \\ P_3 &= N_1 M_5 + N_3 M_3 + N_5 M_1 - N_4 M_2 - N_2 M_4, P_5 = N_5 M_5, \\ Q_1 &= N_1, Q_2 = N_2 M_1 - N_1 M_2 - N_3, Q_3 = N_1 M_4 + N_3 M_2 + N_5 - N_4 M_1 - N_2 M_3, \\ Q_4 &= N_4 M_3 + N_2 M_5 - N_3 M_4 - N_5 M_2, Q_5 = N_5 M_4 - N_4 M_5, \\ \Delta &= (N_4 \omega - N_2 \omega^3)^2 + (N_3 \omega^2 - N_1 \omega^4 - N_5)^2 > 0. \end{aligned}$$

由(7)得

$$\omega^{10} + q_1 \omega^8 + q_2 \omega^6 + q_3 \omega^4 + q_4 \omega^2 + q_5 = 0, \quad (9)$$

其中

$$\begin{aligned} q_1 &= M_1^2 - 2M_2 - N_1^2, q_2 = M_2^2 + 2M_4 - 2M_1 M_3 + 2N_1 N_3 - N_2^2, \\ q_3 &= M_3^2 + 2M_1 M_5 - 2M_2 M_4 + 2N_2 N_4 - 2N_1 N_5 - N_3^2, \\ q_4 &= M_4^2 - 2M_3 M_5 + 2N_3 N_5 - N_4^2, q_5 = M_5^2 - N_5^2. \end{aligned}$$

令 $u = \omega^2$, 则(9)变为

$$u^5 + q_1 u^4 + q_2 u^3 + q_3 u^2 + q_4 u + q_5 = 0. \quad (10)$$

定义 $H(u) = u^5 + q_1 u^4 + q_2 u^3 + q_3 u^2 + q_4 u + q_5$, 则 $H'(u) = 5u^4 + 4q_1 u^3 + 3q_2 u^2 + 2q_3 u + q_4$.

若(5)有纯虚根 ωi , 则(10)有正实根 ω^2 . 不失一般性, 设该方程有 n ($1 \leq n \leq 5$) 个正根, 分别定义为 $u_1 < u_2 < \dots < u_n$. 则(9)有 n 个正根 $\omega_1 = \sqrt{u_1}, \omega_2 = \sqrt{u_2}, \dots, \omega_n = \sqrt{u_n}$.

由(8)可得 $\tau_l^{(j)} = \frac{1}{\omega_l} \left(\arccos \frac{P_1 \omega_l^8 + P_2 \omega_l^6 + P_3 \omega_l^4 + P_4 \omega_l^2 + P_5}{(N_4 \omega_l - N_2 \omega_l^3)^2 + (N_3 \omega_l^2 - N_1 \omega_l^4 - N_5)^2} + 2j\pi \right)$, 其中 $l = 1, 2, \dots, n, j = 0, 1, 2, 3, \dots$, 则 $\pm \omega_l$ 是关于 $\tau_l^{(j)}$ 的一对纯虚根.

(5) 关于 τ 求导得

$$\left[\frac{d\lambda}{d\tau} \right]^{-1} = \frac{-(5\lambda^4 + 4M_1\lambda^3 + 3M_2\lambda^2 + 2M_3\lambda + M_4)e^{\lambda\tau}}{\lambda(N_1\lambda^4 + N_2\lambda^3 + N_3\lambda^2 + N_4\lambda + N_5)} + \frac{4N_1\lambda^3 + 3N_2\lambda^2 + 2N_3\lambda + N_4}{\lambda(N_1\lambda^4 + N_2\lambda^3 + N_3\lambda^2 + N_4\lambda + N_5)} - \frac{\tau}{\lambda}.$$

所以,

$$\begin{aligned} \operatorname{Re} \left[\frac{d\lambda}{d\tau} \right]_{\tau=\tau_l^{(j)}}^{-1} &= \frac{1}{\omega_l \Delta_l} \{ (4M_1\omega_l^3 - 2M_3\omega_l) [(N_1\omega_l^4 - N_3\omega_l^2 + N_5) \cos(\omega_l\tau) + (N_4\omega_l - N_2\omega_l^3) \sin(\omega_l\tau)] + \\ &\quad (5\omega_l^4 - 3M_2\omega_l^2 + M_4) [(N_4\omega_l - N_2\omega_l^3) \cos(\omega_l\tau) + (N_3\omega_l^2 - N_1\omega_l^4 - N_5) \sin(\omega_l\tau)] + \\ &\quad (2N_3\omega_l - 4N_1\omega_l^3)(N_1\omega_l^4 - N_3\omega_l^2 + N_5) + (N_2\omega_l^3 - N_4\omega_l)(N_4 - 3N_2\omega_l^2) \}. \end{aligned} \quad (11)$$

将(7)代入(11)可得

$$\begin{aligned} \operatorname{Re} \left[\frac{d\lambda}{d\tau} \right]_{\tau=\tau_l^{(j)}}^{-1} &= \frac{1}{\Delta_l} [5\omega_l^8 + 4(M_1^2 - 2M_2 - N_1^2)\omega_l^6 + 3(M_2^2 - N_2^2 + 2M_4 + 2N_1N_3 - 2M_1M_3)\omega_l^4 + \\ &\quad 2(M_3^2 - N_3^2 + 2N_2N_4 + 2M_1M_5 - 2M_2M_4 - 2N_1N_5)\omega_l^2 + M_4^2 - \\ &\quad N_4^2 + 2N_3N_5 - 2M_3M_5] = \frac{1}{\Delta_l} H'(u_l), \end{aligned}$$

其中 $\Delta_l = (N_4\omega_l - N_2\omega_l^3)^2 + (N_3\omega_l^2 - N_1\omega_l^4 - N_5)^2 > 0$, 假设 $H'(u) \neq 0$, 则

$$\operatorname{sign} \left\{ \operatorname{Re} \left[\frac{d\lambda}{d\tau} \right]_{\tau=\tau_l^{(j)}} \right\} = \operatorname{sign} \left\{ \operatorname{Re} \left[\frac{d\lambda}{d\tau} \right]_{\tau=\tau_l^{(j)}}^{-1} \right\} = \operatorname{sign} \left\{ \frac{H'(u_l)}{\Delta_l} \right\} = \operatorname{sign} \{ H'(u_l) \}, \quad (12)$$

应用定理 4 及 Hopf 分支定理, 可得如下定理,

定理 5 当 $R_1 > 1$ 时, 若 $\gamma \leq \min\{\alpha, d, \delta + \eta + q\}$, 假设(10)至少有一个单正根且 $\bar{\mu} = \bar{\epsilon}^2$ 是(10)的最后一个单正根, 则系统(2)在 $\tau = \bar{\tau}$ 时产生 Hopf 分支, 即从正平衡点 E_2 处分支出周期解, 其中

$$\bar{\tau} = \frac{1}{\bar{\epsilon}} \left(\arccos \frac{P_1 \bar{\epsilon}^8 + P_2 \bar{\epsilon}^6 + P_3 \bar{\epsilon}^4 + P_4 \bar{\epsilon}^2 + P_5}{(N_1 \bar{\epsilon} - N_2 \bar{\epsilon}^3)^2 + (N_3 \bar{\epsilon}^2 - N_1 \bar{\epsilon}^4 - N_5)^2} + 2j\pi \right).$$

注 如果 $\bar{\mu}$ 是(10)的最后一个单正根, 则 $H'(\bar{\mu}) > 0$, 由(12)得 $\operatorname{Re} \left[\frac{d\lambda}{d\tau} \right]_{\tau=\bar{\tau}} > 0$.

3 数值模拟

这一部分, 将利用数值模拟验证本文所给出的理论分析.

首先, 选取参数值 $s = 2, d = 1, \beta = 0.0012, a = 1, b = 1, \delta = 1, q = 1, \alpha = 1, \eta = 1, p = 2, N = 50, \gamma = 1, c = 0.1, r = 3$. 通过简单计算可知 $R_0 = 0.0133 < 1$, 且 $E_0 = (2, 0, 0, 0, 0)$. 因此, 由定理 2, E_0 是全局渐近稳定的. 图 1 验证了这一结论.

另外, 若选取参数 $s = 2, d = 0.01, \beta = 0.0012, a = 0.1, b = 3, \delta = 0.01, q = 0.01, \alpha = 0.1, \eta = 0.01, p = 2, N = 30, \gamma = 1, c = 0.1, r = 3$. 经过计算可 $R_0 = 1.1429 > 1$, 且 $R_0 < 1 + \frac{b\delta s N q + d\gamma(\eta + q)}{\delta\gamma(s\alpha + d)} = 86.8095, R_1 = 0.0011 < 1, E_1 = (199.3363, 0.3319, 0.0332, 0.9956, 0)$, 因此, 由定理 3, E_1 是全局渐近稳定的. 图 2 验证了这一结论.

最后, 若选取参数 $s = 32.5, d = 20, \beta = 0.01, a = 0.1, b = 0.0002, \delta = 1, q = 100, \alpha = 0.2, \eta = 1, p = 2, N = 85, \gamma = 0.1, c = 1, r = 2$. 经过计算可得免疫反应再生数 $R_1 = 52.8317 > 1$, 且正平衡点为 $E_2 = (1.4266, 0.0393, 2.340, 0.882)$. 将以上参数值代入(10)可得

$$u^5 + 1.0918 \times 10^4 u^4 + 5.2914 \times 10^6 u^3 + 2.2199 \times 10^7 u^2 + 8.0145 \times 10^7 u + 4.2128 \times 10^5 = 0.$$

此方程只有一个正根 $u = 0.0052$, 而其他的根均具有负实部, 并且 $\gamma = 0.1 \leq \min\{\alpha, d, \delta + \eta + q\} = 0.2$, 则满足了定理 4 的条件. 另外, 经过计算可得 $\bar{\epsilon} = \sqrt{u} = 0.0721$ 且 $\bar{\tau} = 21.7888$.

若 $\tau = 18 < \bar{\tau}$, 则系统(2)的正平衡点 E_2 是局部渐近稳定的(见图 3). 若 $\tau = 25 > \bar{\tau}$, 则系统(2)的正平

衡点 E_2 是不稳定的,并且在附近出现了周期解(见图4).

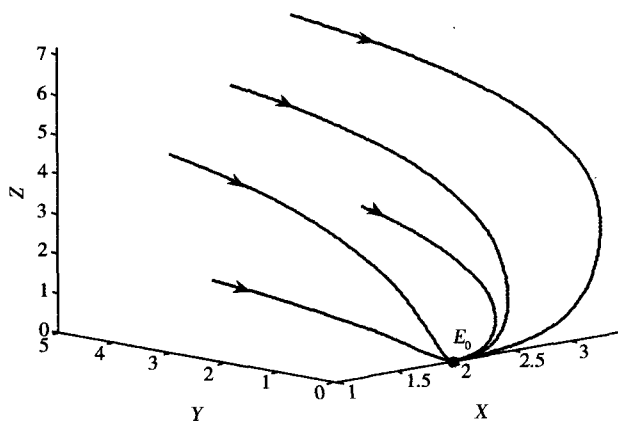


图1 当 $R_0=0.0133 < 1$ 时,无病平衡点 E_0 是全局渐近稳定的

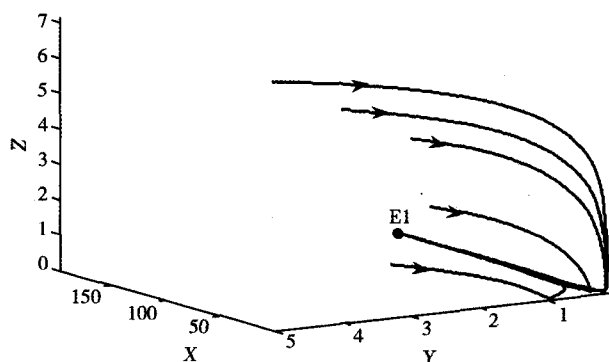


图2 当 $R_0=1.1429 > 1$ 且 $R_0 < 1 + \frac{bsNqd + d\gamma(\eta+q)}{\delta\gamma(sa+d)} = 86.8095$, $R_1=0.0011 < 1$ 时, E_1 是全局渐近稳定的

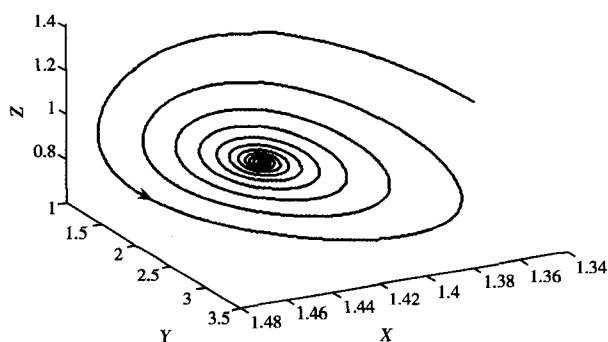


图3 当 $R_1=52.8317 > 1$, $\gamma \leq \min\{a, d, \delta + \eta + q\}$ 且 $\tau=18 < \bar{\tau}$ 时,正平衡点 E_2 局部渐近稳定的

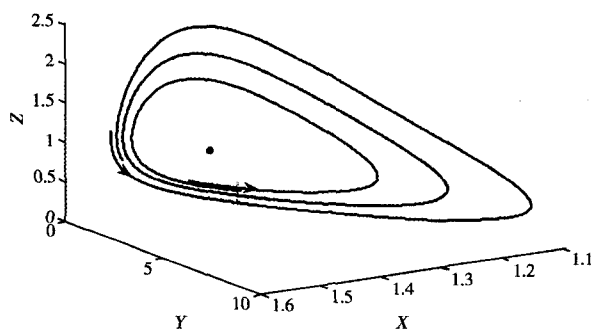


图4 当 $R_1=52.8317 > 1$, $\gamma \leq \min\{a, d, \delta + \eta + q\}$ 且 $\tau=25 > \bar{\tau}$ 时,系统(2)的正平衡点 E_2 是不稳定的,并且在附近出现了周期解

4 结 论

本文研究了一类具有 Beddington-DeAngelis 发生率和免疫反应时滞的艾滋病传染模型,并且此模型还考虑了处于潜伏期的感染细胞,这些细胞会以恒定的速率恢复为正常细胞.通过构造适当的 Lyapunov 泛函并利用 LaSalle 不变原理证明了如下结论:当 $R_0 \leq 1$ 时,则无病平衡点 E_0 是全局渐近稳定的,这表明 HIV 病毒将不会传播;当 $1 < R_0 \leq 1 + \frac{bdsNq + d\gamma(\eta+q)}{\delta\gamma(sa+d)}$ 且 $R_1 \leq 1$ 时,染病无免疫平衡点 E_1 是全局渐近稳定的,这表明若没有免疫反应,则 HIV 病毒将会传播;当 $R_1 > 1$ 时,若 $\tau \in [0, \bar{\tau})$,则感染免疫平衡点 E_2 是局部渐近稳定的,随着 τ 的增大,当 $\tau > \bar{\tau}$ 时, E_2 便不再稳定了并且出现了 Hopf 分支,这表明病毒载量和 CTL 的频率或者稳定在一定水平上,或者出现振荡.显然,与之前的文献[10]相比较,本文引入了免疫反应时滞,其改变了平衡点 E_2 的稳定性,但未改变无病平衡点 E_0 和染病无免疫平衡点 E_1 的稳定性.

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Dynamics Analysis of an HIV Infection Model with Nonlinear Incidence Rate and Delay

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Abstract: An HIV infection model with Beddington-DeAngelis incidence rate and CTL-response delay is investigated. First, with suitable Lyapunov functional and the LaSalle's invariance principle, the global stabilities of the uninfected equilibrium and the infected equilibrium without immunity are proved. Then the sufficient conditions to the local stability of the infected equilibrium with immunity are discussed. The time delay can change the stability of the infected equilibrium with immunity and lead to the existence of Hopf bifurcations. Finally, numerical simulations are carried out to support the main results.

Keywords: Beddington-DeAngelis incidence rate; CTL immune response; delay; stability; Lyapunov functional