

On the zeros of a third degree exponential polynomial with applications to a delayed model for the control of testosterone secretion

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In this paper, we first study the distribution of the zeros of a third degree exponential polynomial. Then we apply the obtained results to a delay model for the control of testosterone secretion. It is shown that under certain assumptions on the coefficients the steady state of the delay model is asymptotically stable for all delay values. Under another set of conditions, there is a critical delay value, the steady state is stable when the delay is less than the critical value and unstable when the delay is greater than the critical value. Thus, oscillations via Hopf bifurcation occur at the steady state when the delay passes through the critical value. Numerical simulations are presented to illustrate the results.

Keywords: exponential polynomial; delay differential equation; control of testosterone secretion; steady state; stability; bifurcation.

1. Introduction

The secretion of testosterone from the gonads is stimulated by a pituitary hormone called *luteinizing hormone* (LH). The secretion of LH from the pituitary gland is stimulated by *luteinizing hormone releasing hormone* (LHRH). This LHRH is normally secreted by the hypothalamus and carried to the pituitary gland by the blood. It is believed that *testosterone* (T) has a feedback effect on the secretion of LH and LHRH. Based on this, Smith (1980) proposed a simple negative feedback compartment model involving the three hormones LHRH, LH and T. Denote the concentrations of LHRH, LH and T by $R(t)$, $L(t)$, and $T(t)$, respectively. Smith considered each of the hormones to be cleared from the bloodstream according to first order kinetics with LH and T produced by their precursors according to first order kinetics. There is a nonlinear negative feedback by T on LHRH. Smith proposed

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the following model of three ordinary differential equations (ODEs):

$$\begin{aligned}\frac{dR}{dt} &= f(T) - b_1(R), \\ \frac{dL}{dt} &= g_1(R) - b_2(L), \\ \frac{dT}{dt} &= g_2(L) - b_3(T),\end{aligned}\tag{1.1}$$

where f is a positive monotonic decreasing function, and b_i ($i = 1, 2, 3$) and g_j ($j = 1, 2$) are positive monotonic increasing functions. We refer to Liu & Deng (1991) and Liu *et al.* (1997) for modifications of system (1.1); see also Keener & Sneyd (1998).

In actual physiological processes, there is a delay between the production of a hormone at one level and its effect on the production of the hormone it stimulates, simply because of the hormones' spatial separation and the fact that they are transported by circulating blood. Smith (1983) incorporated a single delay into system (1.1) in which the production of T is delayed. The model is the following system of three delay differential equations:

$$\begin{aligned}\frac{dR}{dt} &= f(T) - b_1(R), \\ \frac{dL}{dt} &= g_1(R) - b_2(L), \\ \frac{dT}{dt} &= g_2(L(t - \tau)) - b_3(T),\end{aligned}\tag{1.2}$$

where τ is the delay associated with the blood circulation time in the body, i.e. the time that LH requires to travel through the bloodstream to reach its site of action at the gonads. Linear analysis of system (1.2), when b_i ($i = 1, 2, 3$) and g_j ($j = 1, 2$) are all linear functions, was carried out by Murray (1989). The simplified model takes the form

$$\begin{aligned}\frac{dR}{dt} &= f(T) - b_1 R, \\ \frac{dL}{dt} &= g_1 R - b_2 L, \\ \frac{dT}{dt} &= g_2 L(t - \tau) - b_3 T,\end{aligned}\tag{1.3}$$

where the coefficients are all positive constants. Murray (1989) showed that there is a critical delay value τ_c such that the steady state of (1.3) is linearly unstable because of growing oscillations. Thus, limit cycle periodic solutions could be generated by choosing the parameters properly.

Based on some experimental results, Cartwright & Husain (1986) also proposed a delayed model on the control of T secretion which includes delay in the production of each of $R(t)$, $L(t)$ and $T(t)$. They also carried out some analysis to illustrate certain laboratory experiments, and their numerical simulations show stable oscillations in all three components.

In studying a delay model, linearization of the system at its steady state gives us a transcendental characteristic equation or an exponential polynomial equation. It is well

known that the steady state is stable if all eigenvalues of the exponential polynomial equation have negative real parts, and unstable if at least one root has a positive real part. Thus, a Hopf bifurcation occurs when the real part of a certain eigenvalue changes from negative to zero and to positive (i.e. the steady state changes from stability to instability). This is usually caused by the delay.

However, there is a strong possibility that if the coefficients of the exponential polynomial satisfy certain assumptions, the real parts of all eigenvalues remain negative for all values of the delay; that is, independent of the delay. The corresponding delay system is called *absolutely stable* (see, for example, Hale *et al.* (1985)). A general result in Hale *et al.* (1985) says that a delay system is absolutely stable if and only if the corresponding ODE system is asymptotically stable and the characteristic equation has no purely imaginary roots.

In this paper we consider the general delay model (1.2). The linearized system of (1.2) at a positive steady state has the following characteristic equation

$$\lambda^3 + a\lambda^2 + b\lambda + c + de^{-\lambda\tau} = 0, \tag{1.4}$$

which is a third degree exponential polynomial equation. We first study the distribution of the roots of equation (1.3) and find that there are two possibilities.

- (a) Under certain assumptions on the coefficients all roots of (1.3) have negative real parts for all delay value $\tau \geq 0$.
- (b) If the assumptions in (a) are not satisfied, then there is a critical value τ_0 . When the delay $\tau < \tau_0$, the real parts of all roots of (1.3) are still negative; when $\tau = \tau_0$, there is a pair of purely imaginary roots and all other roots have negative real parts; when $\tau > \tau_0$, there is at least one eigenvalue which has a positive real part.

Applying these results to the delay model (1.2), we show that under a set of assumptions on the parameters, the steady state of (1.2) is absolutely stable (i.e. asymptotically stable independent of the delay). Under another set of conditions, the steady state of (1.2) is conditionally stable; that is, there is a critical delay value τ_0 , and the steady state is asymptotically stable when $\tau < \tau_0$, loses its stability when $\tau = \tau_0$, and becomes unstable when $\tau > \tau_0$. Thus, a Hopf bifurcation occurs at the steady state when τ passes through the critical value τ_0 .

To discuss the distribution of the roots of the exponential polynomial equation (1.3), we need the following result which was proved by Ruan & Wei (1999) by using Rouché's theorem (see Dieudonné (1960), Theorem 9.17.4).

LEMMA 1.1 Consider the exponential polynomial

$$\begin{aligned} P(\lambda, e^{-\lambda\tau_1}, \dots, e^{-\lambda\tau_m}) &= \lambda^n + p_1^{(0)}\lambda^{n-1} + \dots + p_{n-1}^{(0)}\lambda + p_n^{(0)} \\ &\quad + [p_1^{(1)}\lambda^{n-1} + \dots + p_{n-1}^{(1)}\lambda + p_n^{(1)}]e^{-\lambda\tau_1} \\ &\quad + \dots + [p_1^{(m-1)}\lambda^{n-1} + \dots + p_{n-1}^{(m-1)}\lambda + p_n^{(m-1)}]e^{-\lambda\tau_m}, \end{aligned} \tag{1.5}$$

where $\tau_i \geq 0 (i = 1, 2, \dots, m)$ and $p_j^{(i)} (i = 0, 1, \dots, m - 1; j = 1, 2, \dots, n)$ are constants. As $(\tau_1, \tau_2, \dots, \tau_m)$ vary, the sum of the orders of the zeros of

$P(\lambda, e^{-\lambda\tau_1}, \dots, e^{-\lambda\tau_m})$ on the open right half plane can change only if a zero appears on or crosses the imaginary axis.

REMARK 1.2 Lemma 1.1 is a generalization of the Lemma in Cooke & Grossman (1982).

2. The third degree transcendental polynomial

In this section, we study the distribution of zeros of a third degree transcendental polynomial.

Consider the following third degree transcendental polynomial

$$\lambda^3 + a\lambda^2 + b\lambda + c + de^{-\lambda\tau} = 0. \quad (2.1)$$

Clearly, $i\omega$ ($\omega > 0$) is a root of equation (2.1) if and only if

$$-i\omega^3 - a\omega^2 + ib\omega + c + d(\cos \omega\tau - i \sin \omega\tau) = 0.$$

Separating the real and imaginary parts, we have

$$\begin{aligned} c - a\omega^2 &= -d \cos \omega\tau, \\ \omega^3 - b\omega &= -d \sin \omega\tau. \end{aligned} \quad (2.2)$$

Adding up the squares of both equations, we obtain

$$\omega^6 + (a^2 - 2b)\omega^4 + (b^2 - 2ac)\omega^2 + (c^2 - d^2) = 0. \quad (2.3)$$

Let $z = \omega^2$ and denote $p = a^2 - 2b$, $q = b^2 - 2ac$, and $r = c^2 - d^2$. Then equation (2.3) becomes

$$z^3 + pz^2 + qz + r = 0. \quad (2.4)$$

CLAIM 1 If $r < 0$, then equation (2.4) has at least one positive root.

Proof. Denote

$$h(z) = z^3 + pz^2 + qz + r. \quad (2.5)$$

Clearly, $h(0) = r < 0$, and $\lim_{z \rightarrow \infty} h(z) = \infty$. Hence, there exists a $z_0 \in (0, \infty)$ so that $h(z_0) = 0$. This completes the proof.

CLAIM 2 If $r \geq 0$, then the necessary condition for equation (2.4) to have positive real roots is

$$\Delta = p^2 - 3q \geq 0. \quad (2.6)$$

Proof. From (2.5) we have

$$\frac{dh(z)}{dz} = 3z^2 + 2pz + q.$$

Set

$$3z^2 + 2pz + q = 0. \quad (2.7)$$

Then the roots of equation (2.7) can be expressed as

$$z_{1,2} = \frac{-2p \pm \sqrt{4p^2 - 12q}}{6} = \frac{-p \pm \sqrt{\Delta}}{3}. \quad (2.8)$$

If $\Delta < 0$, then (2.7) does not have real roots. So the function $h(z)$ is monotone increasing in z . It follows from $h(0) = r \geq 0$ that equation (2.4) has no positive real roots. This completes the proof.

Clearly, if $\Delta \geq 0$, then $z_1 = \frac{-p + \sqrt{\Delta}}{3}$ is the local minimum of $h(z)$. Thus, we have the following claim.

CLAIM 3 If $r \geq 0$, then equation (2.4) has positive roots if and only if $z_1 > 0$ and $h(z_1) \leq 0$.

Proof. The sufficiency is obvious. We only need to prove the necessity. Otherwise, we assume that either $z_1 \leq 0$ or $z_1 > 0$ and $h(z_1) > 0$. If $z_1 \leq 0$, since $h(z)$ is increasing for $z \geq z_1$ and $h(0) = r \geq 0$, it follows that $h(z)$ has no positive real zeros. If $z_1 > 0$ and $h(z_1) > 0$, since $z_2 = \frac{-p - \sqrt{\Delta}}{3}$ is the local maximum value, it follows that $h(z_1) < h(z_2)$. Hence, by $h(0) = r \geq 0$, we know that $h(z)$ does not have positive real zeros. This completes the proof.

Summarizing the above discussion, we have the following lemma.

LEMMA 2.1 Suppose that z_1 is defined by (2.8).

- (i) If $r < 0$, then equation (2.4) has at least one positive root.
- (ii) If $r \geq 0$ and $\Delta = p^2 - 3q < 0$, then equation (2.4) has no positive roots.
- (iii) If $r \geq 0$, then equation (2.4) has positive roots if and only if $z_1 = \frac{1}{3}(-p + \sqrt{\Delta}) > 0$ and $h(z_1) \leq 0$.

Suppose that equation (2.4) has positive roots. Without loss of generality, we assume that it has three positive roots, denoted by z_1, z_2 and z_3 , respectively. Then equation (2.3) has three positive roots, say

$$\omega_1 = \sqrt{z_1}, \quad \omega_2 = \sqrt{z_2}, \quad \omega_3 = \sqrt{z_3}.$$

Let

$$\tau_k^{(j)} = \frac{1}{\omega_k} \left[\sin^{-1} \left(-\frac{\omega_k^3 - b\omega_k}{d} \right) + 2(j-1)\pi \right], \quad k = 1, 2, 3; \quad j = 0, 1, \dots$$

Then $\pm i\omega_k$ is a pair of purely imaginary roots of equation (2.1) with $\tau = \tau_k^{(j)}$, $k = 1, 2, 3; \quad j = 0, 1, \dots$. Clearly,

$$\lim_{j \rightarrow \infty} \tau_k^{(j)} = \infty, \quad k = 1, 2, 3.$$

Thus, we can define

$$\tau_0 = \tau_{k_0}^{(j_0)} = \min_{1 \leq k \leq 3, j \geq 1} \{\tau_k^{(j)}\}, \quad \omega_0 = \omega_{k_0}. \quad (2.9)$$

LEMMA 2.2 Suppose that $a > 0$, $c + d > 0$, $ab - c - d > 0$.

- (a) If $r \geq 0$ and $\Delta = p^2 - 3q < 0$, then all roots of equation (2.1) have negative real parts for all $\tau \geq 0$.
- (b) If $r < 0$ or $r \geq 0$, $z_1 > 0$ and $h(z_1) \leq 0$, then all roots of equation (2.1) have negative real parts when $\tau \in [0, \tau_0)$.

Proof. When $\tau = 0$, equation (2.1) becomes

$$\lambda^3 + a\lambda^2 + b\lambda + c + d = 0. \quad (2.10)$$

By the Routh–Hurwitz criterion, all roots of equation (2.10) have negative real parts if and only if

$$a > 0, \quad c + d > 0, \quad ab - c - d > 0.$$

If $r \geq 0$ and $\Delta = p^2 - 3q < 0$, Lemma 2.1 (ii) shows that equation (2.1) has no roots with zero real part for all $\tau \geq 0$. When $r < 0$ or $r \geq 0$, $z_1 > 0$ and $h(z_1) \leq 0$, Lemma 2.1 (i) and (iii) implies that when $\tau \neq \tau_k^{(j)}$, $k = 1, 2, 3$, $j \geq 1$, equation (2.1) has no roots with zero real part and τ_0 is the minimum value of τ so that equation (2.1) has purely imaginary roots. Applying Lemma 1.1, we obtain the conclusion of the lemma.

Let

$$\lambda(\tau) = \alpha(\tau) + i\omega(\tau) \quad (2.11)$$

be the root of equation (2.1) satisfying

$$\alpha(\tau_0) = 0, \quad \omega(\tau_0) = \omega_0.$$

In order to guarantee that $\pm i\omega_0$ are simple purely imaginary roots of equation (2.1) with $\tau = \tau_0$ and $\lambda(\tau)$ satisfies the transversality condition, we assume that $h'(z_0) \neq 0$. Hence, we have the following lemma.

LEMMA 2.3 Suppose $h'(z_0) \neq 0$. If $\tau = \tau_0$, then $\pm i\omega_0$ is a pair of simple purely imaginary roots of equation (2.1). Moreover, if the conditions of Lemma 2.2 (b) are satisfied, then

$$\frac{d\operatorname{Re}\lambda(\tau_0)}{d\tau} > 0.$$

Proof. If $i\omega_0$ is not simple, then ω_0 must satisfy

$$\frac{d}{d\lambda} [\lambda^3 + a\lambda^2 + b\lambda + c + de^{-\lambda\tau_0}] \Big|_{\lambda=i\omega_0} = 0,$$

that is, ω_0 must satisfy

$$\begin{aligned} 3\omega^2 - b &= -\tau d \cos \omega\tau, \\ 2a\omega &= -\tau d \sin \omega\tau. \end{aligned}$$

Thus, we have

$$\frac{2a\omega}{3\omega^2 - b} = \tan \omega\tau. \quad (2.12)$$

However, from (2.2) we know that ω_0 satisfies

$$\frac{\omega^3 - b\omega}{c - a\omega^2} = \tan \omega\tau. \quad (2.13)$$

From (2.12) and (2.13) we have

$$\frac{\omega^3 - b\omega}{c - a\omega^2} = \frac{2a\omega}{3\omega^2 - b},$$

that is,

$$3\omega^4 + 2(a^2 - 2b)\omega^2 + (b^2 - 2ac) = 0.$$

Recall that $z_0 = \omega_0^2$, which implies that

$$3z_0^2 + 2(a^2 - 2b)z_0 + (b^2 - 2ac) = 0. \quad (2.14)$$

Notice that $p = a^2 - 2b$, $q = b^2 - 2ac$, and $h'(z_0) = 3z_0^2 + 2pz_0 + q$; we obtain a contradiction to the condition $h'(z_0) \neq 0$. This proves the first conclusion.

Differentiating both sides of equation (2.1) with respect to τ gives

$$\frac{d\lambda(\tau)}{d\tau} = \frac{d\lambda e^{-\lambda\tau}}{3\lambda^2 + 2a\lambda + b - d\tau e^{-\lambda\tau}}.$$

It follows from (2.1) that

$$\frac{d\operatorname{Re}\lambda(\tau_0)}{d\tau} = \frac{\omega_0^2}{\Delta} [3\omega_0^4 + 2(a^2 - 2b)\omega_0^2 + (b^2 - 2ac)],$$

where

$$\Delta = (3\omega_0^2 - b + d\tau_0 \cos \omega_0\tau_0)^2 + (2a\omega_0 + d\tau_0 \sin \omega_0\tau_0)^2.$$

As $z_0 = \omega_0^2$ and $h'(z_0) \neq 0$, we have

$$\frac{d\operatorname{Re}\lambda(\tau_0)}{d\tau} = \frac{\omega_0^2}{\Delta} h'(z_0) \neq 0.$$

If $(d/d\tau)\operatorname{Re}\lambda(\tau_0) < 0$ for $\tau < \tau_0$ and close to τ_0 , then equation (2.1) has a root $\lambda(\tau) = \alpha(\lambda) + i\omega(\lambda)$ satisfying $\alpha(\lambda) > 0$, which contradicts Lemma 2.2. This completes the proof.

By Lemmas 2.2 and 2.3, we obtain the following theorem.

THEOREM 2.4 Let ω_0 , τ_0 , and $\lambda(\tau)$ be defined by (2.9) and (2.11), respectively, and $z_0 = \omega_0^2$. Suppose that $a > 0$, $c + d > 0$, $ab - c - d > 0$.

- (i) If $r \geq 0$ and $\Delta = p^2 - 3q < 0$, then all roots of equation (2.1) have negative real parts for all $\tau \geq 0$.
- (ii) If $r < 0$ or $r \geq 0$, $z_1 > 0$ and $h(z_1) < 0$, then all roots of equation (2.1) have negative real parts when $\tau \in [0, \tau_0)$.
- (iii) If the conditions of (ii) are satisfied, $\tau = \tau_0$, and $h'(z_0) \neq 0$, then $\pm i\omega_0$ is a pair of simple purely imaginary roots of equation (2.1) and all other roots have negative real parts. Moreover, $(d/d\tau)\text{Re}\lambda(\tau_0) > 0$.

3. The delayed model for the control of testosterone secretion

In this section we study the stability of the delayed model (1.2) for the control of testosterone secretion.

Let (R_0, L_0, T_0) denote the positive steady state of system (1.2), that is, the solutions of the algebraic equations

$$f(T_0) - b_1(R_0) = 0, \quad g_1(R_0) - b_2(L_0) = 0, \quad g_2(L_0) - b_3(T_0) = 0.$$

Let

$$x = R - R_0, \quad y = L - L_0, \quad z = T - T_0.$$

Then the linearized system of (1.2) at (R_0, L_0, T_0) is

$$\begin{aligned} \frac{dx}{dt} &= f'(T_0)z - b'_1(R_0)x, \\ \frac{dy}{dt} &= g'_1(R_0)x - b'_2(L_0)y, \\ \frac{dz}{dt} &= g'_2(L_0)y(t - \tau) - b'_3(T_0)z. \end{aligned} \tag{3.1}$$

The associated characteristic equation of system (3.1) is

$$\lambda^3 + a\lambda^2 + b\lambda + c + de^{-\lambda\tau} = 0, \tag{3.2}$$

where

$$\begin{aligned} a &= b'_1(R_0) + b'_2(L_0) + b'_3(T_0) > 0, \\ b &= b'_1(R_0)b'_2(L_0) + b'_2(L_0)b'_3(T_0) + b'_1(R_0)b'_3(T_0) > 0, \\ c &= b'_1(R_0)b'_2(L_0)b'_3(T_0) > 0, \\ d &= -f'(T_0)g'_1(R_0)g'_2(L_0) > 0. \end{aligned}$$

We have

$$\begin{aligned} p &= a^2 - 2b = [b'_1(R_0)]^2 + [b'_2(L_0)]^2 + [b'_3(T_0)]^2, \\ q &= b^2 - 2ac = [b'_1(R_0)]^2[b'_2(L_0)]^2 + [b'_1(R_0)]^2[b'_3(T_0)]^2 + [b'_2(L_0)]^2[b'_3(T_0)]^2, \\ r &= c^2 - d^2 = [b'_1(R_0)]^2[b'_2(L_0)]^2[b'_3(T_0)]^2 - [f'(T_0)]^2[g'_1(R_0)]^2[g'_2(L_0)]^2, \\ \Delta &= p^2 - 3q, \\ z_1 &= \frac{1}{3}(-p + \sqrt{\Delta}). \end{aligned}$$

Applying Theorem 2.4 to equation (3.2), we obtain the following theorem.

THEOREM 3.1 Let ω_0 and τ_0 be defined as in (2.9), $z_0 = \omega_0^2$, and

$$h(z) = z^3 + (a^2 - 2b)z^2 + (b^2 - 2ac)z + (c^2 - d^2).$$

Suppose that $ab - c - d > 0$.

- (i) If $r \geq 0$ and $\Delta = p^2 - 3q < 0$, then the steady state (R_0, L_0, T_0) of system (1.2) is absolutely stable (i.e. asymptotically stable for all $\tau \geq 0$).
- (ii) If $r < 0$ or $r \geq 0$, $z_1 > 0$ and $h(z_1) < 0$, then the steady state (R_0, L_0, T_0) of system (1.2) is asymptotically stable for $\tau \in [0, \tau_0)$.
- (iii) If the conditions of (ii) are satisfied, $\tau = \tau_0$, and $h'(z_0) \neq 0$, then system (1.2) exhibits the Hopf bifurcation at (R_0, L_0, T_0) .

Applying Theorem 3.1 to the specific case (1.3), we obtain similar results on the stability and bifurcation of the positive steady state.

4. Discussion

It has been observed in many experiments on intact adult animals that the serum concentrations of both LH and T undergo rapid cyclic fluctuations of roughly the same period. Several models have been proposed to try to account for the pulsatile release of the hormones T, LH and LHRH (for example, Smith, 1980; Liu & Deng, 1991; Liu *et al.*, 1997). Smith (1983) argued that LH requires some time to travel through the bloodstream to reach its site of action at the gonads and proposed a delay model for the control of secretion of T.

In this paper, we first studied the distribution of the zeros of a third degree exponential polynomial and obtained conditions which ensure that the zeros lie on the left, the imaginary axis, and the right of the complex plane, respectively. Then we applied the obtained results to analyse a delay model for the control of secretion of T proposed by Smith (1983). Our analysis indicates that under certain assumptions on the coefficients of the system, the steady state (R_0, L_0, T_0) is asymptotically stable for all delay $\tau \geq 0$. However, if these conditions are not satisfied, then there is a critical value of the time delay τ_0 . When $\tau < \tau_0$, the steady state is asymptotically stable; when $\tau > \tau_0$, it becomes unstable; when $\tau = \tau_0$, there is a Hopf bifurcation at the steady state; that is, a family of periodic solutions bifurcates from the steady state when τ passes through the critical value τ_0 . For the special case when $b_i (i = 1, 2, 3)$ and $g_j (j = 1, 2)$ are linear functions,

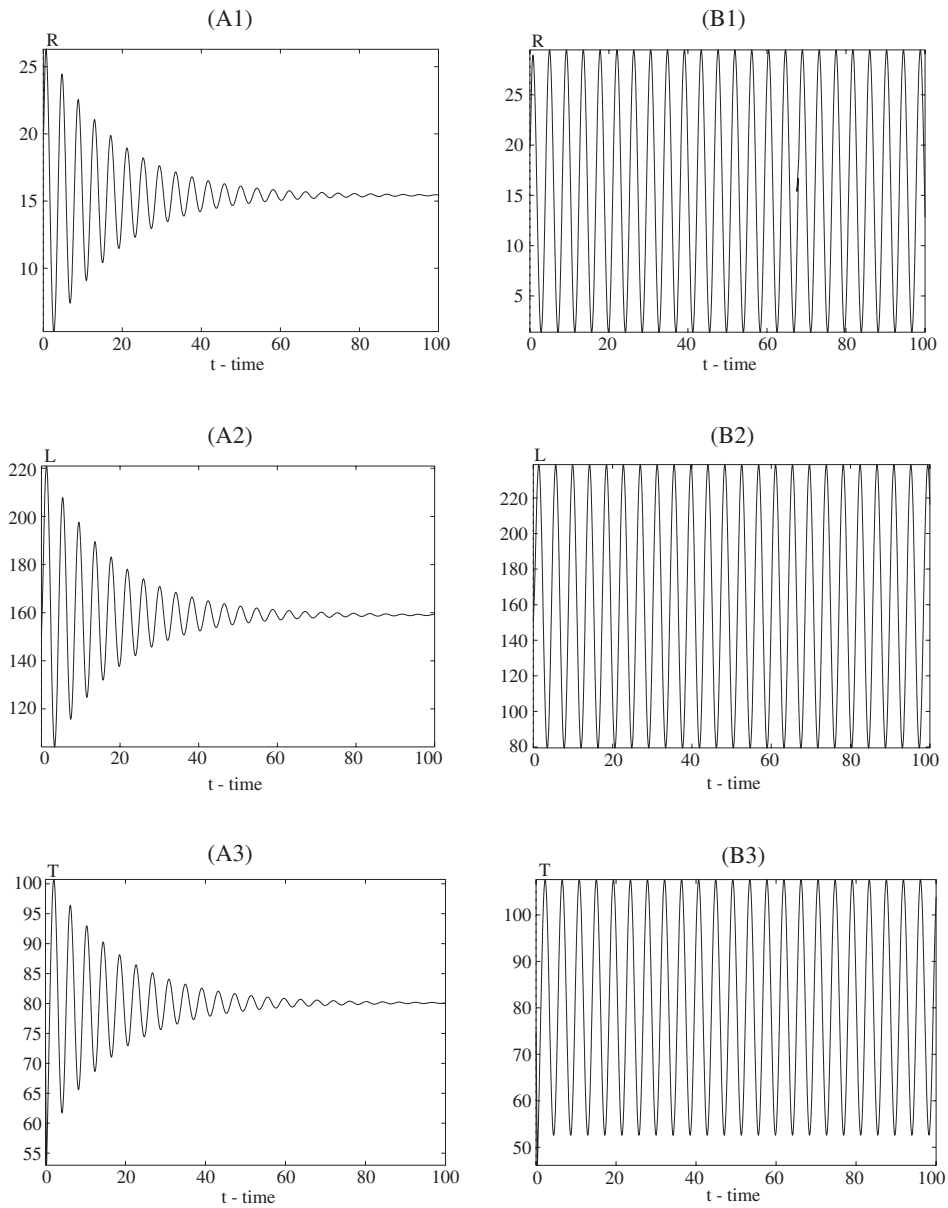


FIG. 1. (A1)–(A3) When $\tau < \tau_0$, the three components converge to the steady state values; here $\tau = 0.2125$. (B1)–(B3) When $\tau > \tau_0$, the three components fluctuate very rapidly; here $\tau = 0.3055$.

the existence of a critical value of the time delay for system (1.3) was obtained by Murray (1989) using a different approach. Thus, our results not only include Murray's but also provide conditions under which the steady state is asymptotically stable independent of

the time delay. The bifurcation result indicates that there are parameter values for which the three hormones undergo cyclic fluctuations.

As an example, we consider system (1.3) with $f(T) = c - hT$, where c and h are positive constants. Using the parameter values of Smith (1980) (except for the value of h), that is, $c = 100$ pg/ml/h, $g_1 = 10$ h⁻¹, $g_2 = 0.7$ h⁻¹, $b_1 = 1.29$ h⁻¹, $b_2 = 0.97$ h⁻¹, $b_3 = 1.39$ h⁻¹. We take $h = 1$ h⁻¹. The steady state is given by $E^* = (R_0, L_0, T_0) = (15.428, 159.05, 80.098)$. Using Theorem 3.1, there is a critical value of the time delay, $\tau_0 = 0.3$. When $\tau < 0.3$, the steady state is asymptotically stable; when $\tau > 0.3$, the steady state becomes unstable and a periodic solution bifurcates from the steady state. With $\tau = 0.2125$, numerical simulation shows that the three components converge to the steady state values. When $\tau = 0.3055$, the three components oscillate very rapidly about the steady state values (see Fig. 1).

We would like to mention that the techniques used in this paper can be applied to other delayed models such as the virus replication model considered by Tam (1999) and the HIV infection model considered by Culshaw & Ruan (2000). Finally, it would be very interesting to study the multiple-delay model proposed by Cartwright & Husain (1986). We leave this for future consideration.

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