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Positive periodic solutions for a model of gene regulatory system with time-varying coefficients and delays

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Abstract

The paper is concerned with periodic solutions of a model of gene regulatory system with time-varying coefficients and delays. We establish some sufficient conditions for the existence, positivity, and permanence of solutions, which help to derive the global exponential stability of positive periodic solutions for this model. Our method depends on differential inequality technique and Lyapunov functional. At last, we give an example and its numerical simulations to verify theoretical results.

Keywords: gene regulatory system; delay; periodic solution; global exponential stability

1 Introduction

In order to explain the complex dynamic behavior of genetic regulatory systems, the authors of [1] presented a model of ordinary differential system for the transcript factors (*TFs*). Furthermore, taking account of the delay between changes in the transcription rate of either gene and changes in the concentration of the corresponding protein, Smolen *et al.* [2] generalized the ordinary differential system to the following delayed differential system:

$$\begin{cases} \frac{d[TF\text{-}A]}{dt} = \left(\frac{k_{1,f}[TF\text{-}A]^2}{[TF\text{-}A]^2+K_{1,d}(1+[TF\text{-}R]/K_{R,d})}\right)(t-\tau) - k_{1,d}[TF\text{-}A] + r, \\ \frac{d[TF\text{-}R]}{dt} = \left(\frac{k_{2,f}[TF\text{-}A]^2}{[TF\text{-}A]^2+K_{2,d}(1+[TF\text{-}R]/K_{R,d})}\right)(t-\tau) - k_{2,d}[TF\text{-}R], \end{cases} \tag{1.1}$$

where $[TF\text{-}A]$ denotes the level of the transcriptional activators, $[TF\text{-}R]$ denotes the level of the protein that represses transcription by binding to *TA-REs* (the responsive elements of the *TFs*), $k_{1,f}$ is the maximal transcription rate of *TF-A*, $k_{2,f}$ is the maximal synthesis rate, $k_{1,d}$ and $k_{2,d}$ are degradation rates, $K_{1,d}$ and $K_{2,d}$ are the dissociation constants of *TF-A* dimer from *TF-REs*, r is a basal rate of synthesis of activator at negligible dimer concentration, and $K_{R,d}$ is the dissociation constant of *TF-R* monomers from *TF-REs*. For simplicity, letting

$$x_1 = [TF\text{-}A], \qquad x_2 = [TF\text{-}R], \qquad K_{R,d} = q, \quad \text{and}$$

$$k_i = k_{i,f}, \qquad p_i = K_{i,f}, \qquad l_i = k_{i,d} \quad \text{for } i = 1, 2,$$

system (1.1) can be translated to

$$\begin{cases} \frac{dx_1}{dt} = \frac{k_1 x_1^2(t-\tau)}{x_1^2(t-\tau)+p_1(1+x_2(t-\tau)/q)} - l_1 x_1(t) + r, \\ \frac{dx_2}{dt} = \frac{k_2 x_1^2(t-\tau)}{x_1^2(t-\tau)+p_2(1+x_2(t-\tau)/q)} - l_2 x_2(t). \end{cases} \tag{1.2}$$

Recently, the authors of [3] and [4] studied Hopf bifurcation and global attractivity of system (1.2), respectively. Moreover, in the past decade, a great deal of mathematical effort in other gene regulatory network models has been devoted to the study of stability and bifurcations (see references [5–12]). However, limited work has been done on the global exponential stability of positive periodic solutions for genetic regulatory system (1.2) with time-varying coefficients and delays. Thus, considering that parameters periodically vary due to changes of external environment, we modify the genetic regulatory system (1.2) as follows:

$$\begin{cases} \frac{dx_1}{dt} = \frac{k_1(t) x_1^2(t-\tau(t))}{x_1^2(t-\tau(t))+p_1(t)(1+x_2(t-\tau(t))/q(t))} - l_1(t) x_1(t) + r(t), \\ \frac{dx_2}{dt} = \frac{k_2(t) x_1^2(t-\tau(t))}{x_1^2(t-\tau(t))+p_2(t)(1+x_2(t-\tau(t))/q(t))} - l_2(t) x_2(t), \end{cases} \tag{1.3}$$

where q, r, τ, k_1, k_2, l_1, l_2, p_1, p_2 are all nonnegative continuous ω-periodic functions.

In the real-world phenomena, the periodic variation of the environment (*e.g.*, temperature, moisture, pressure, seasonal effects of weather, reproduction, food supplies, mating habits, *etc.*) plays a pivotal role in determining the dynamics, so that some classic models, such as the Nicholson blowflies model [13, 14], hematopoiesis model [15, 16], *etc.*, have been generalized to the nonautonomous nonlinear delay differential equation with time-varying coefficients and delays. Consequently, it is worth studying the model of gene regulatory system with time-varying coefficients and delays.

It is convenient to introduce some notation. Given a bounded continuous function f defined on R, we define f^+ and f^- as

$$f^- = \inf_{t\in R} f(t), \qquad f^+ = \sup_{t\in R} f(t).$$

Let R^n (R^n_+) be the set of all (nonnegative) real vectors; by $x = (x_1, \ldots, x_n)^T \in R^n$ we denote a column vector, in which the symbol (^{T}) denotes the transpose of a vector. We denote by $|x|$ the absolute-value vector $|x| = (|x_1|, \ldots, |x_n|)^T$ and define $\|x\| = \max_{1\le i\le n} |x_i|$. For $\tau^+ > 0$, we denote by $C = C([-\tau^+, 0], R^2)$ the Banach space equipped with the supremum norm, that is, $\|\varphi\| = \sup_{-\tau^+\le t\le 0} \max_{1\le i\le 2} |\varphi_i(t)|$ for all $\varphi(t) = (\varphi_1(t), \varphi_2(t))^T \in C$. Let $C_+ = \{\varphi \in C | \varphi(t) \in R^2_+ \text{ for } t \in [-\tau^+, 0]\}$. If $x_i(t)$ is defined on $[t_0 - \tau^+, \nu)$ with $t_0, \nu \in R$ and $i = 1, 2$, then we define $x_t \in C$ as $x_t = (x_t^1, x_t^2)^T$ where $x_t^i(\theta) = x_i(t+\theta)$ for all $\theta \in [-\tau^+, 0]$ and $i = 1, 2$.

It is biologically reasonable to assume that only positive solutions of system (1.3) are meaningful and therefore admissible. The initial conditions associated with system (1.3) are of the form

$$x_{t_0} = \varphi, \qquad \varphi = (\varphi_1, \varphi_2)^T \in C_+, \quad \text{and} \quad \varphi_i(0) > 0, \quad i = 1, 2. \tag{1.4}$$

We denote by $x_t(t_0, \varphi) = x(t; t_0, \varphi)$ a solution of the initial value problem (1.3) and (1.4). Also, let $[t_0, \eta(\varphi))$ be the maximal right-interval of the existence of $x_t(t_0, \varphi)$.

Definition 1.1 Let $x^*(t)$ be a solution of (1.3). For any given initial value φ that satisfies (1.4), if there are positive constants λ, K_φ, and $T_\varphi > t_0$ such that every solution $x(t; t_0, \varphi)$ to system (1.3) satisfies

$$\left|x_i(t; t_0, \varphi) - x_i^*(t)\right| \le K_\varphi e^{-\lambda(t-t_0)} \quad \text{for } t > T_\varphi, i = 1, 2,$$

then $x^*(t)$ is said to be globally exponentially stable.

The objective of this paper is twofold. The first is getting the attracting set for system (1.3). The other is deriving conditions on the existence, uniqueness, and global exponential stability of positive periodic solutions. Finally, we give an example and its numerical simulations to illustrate our main results.

2 Preliminary results

In this section, we derive the following lemmas, which will be used to prove our main results in Section 3.

Lemma 2.1 *Suppose that* $r^- > 0$ *and* $l_i^- > 0$ $(i = 1, 2)$ *and define the positive constants*

$$B_1 = \frac{r^-}{l_1^+}, \qquad C_1 = \frac{k_1^+ + r^+}{l_1^-}, \qquad B_2 = \frac{k_2^- B_1^2}{l_2^+(B_1^2 + +p_2^+(1 + C_2/q^-))}, \qquad C_2 = \frac{k_2^+}{l_2^-}.$$

Then there exists a unique positive global solution $x(t; t_0, \varphi)$ *to initial value problem* (1.3) *and* (1.4) *on the interval* $[t_0 - \tau^+, +\infty)$. *Moreover, there exist* $t_0(\varphi) > t_0$ *such that for any* $t > t_0(\varphi)$,

$$B_i \le x_i(t; t_0, \varphi) \le C_i, \quad i = 1, 2. \tag{2.1}$$

Proof Set $x(t) = x(t; t_0, \varphi) = (x_1(t), x_2(t))^T$ for all $t \in [t_0, \eta(\varphi))$. From the variation-of-constants formula we have

$$\begin{cases} x_1(t) = \varphi_1(0)e^{-\int_{t_0}^t l_1(s)\,ds} + \int_{t_0}^t e^{-\int_s^t l_1(u)\,du}\left[\frac{k_1(s)x_1^2(s-\tau(s))}{x_1^2(s-\tau(s))+p_1(s)(1+x_2(s-\tau(s))/q(s))} + r(s)\right] ds, \\ x_2(t) = \varphi_2(0)e^{-\int_{t_0}^t l_2(s)\,ds} + \int_{t_0}^t e^{-\int_s^t l_2(u)\,du} \frac{k_2(s)x_1^2(s-\tau(s))}{x_1^2(s-\tau(s))+p_2(s)(1+x_2(s-\tau(s))/q(s))}\, ds \end{cases} \tag{2.2}$$

for $t \in [t_0, t_0 + \tau^+]$.

Since the initial value φ satisfies (1.4), Eq. (2.2) leads to $x_i(t) > 0$ $(i = 1, 2)$ for $t \in [t_0, t_0 + \tau^+]$. Then, by the method of steps we obtain that $x(t; t_0, \varphi)$ is positive and exists on $[t_0 - \tau^+, +\infty)$.

In what follows, we prove that (2.1) holds for $t > t_0(\varphi)$. In view of the first equation of (1.3), we get

$$\frac{dx_1}{dt} = \frac{k_1(t)x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_1(t)(1 + x_2(t-\tau(t))/q(t))} - l_1(t)x_1(t) + r(t) \le k_1^+ + r^+ - l_1^- x_1(t)$$

and

$$\frac{dx_1}{dt} = \frac{k_1(t)x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_1(t)(1 + x_2(t-\tau(t))/q(t))} - l_1(t)x_1(t) + r(t) \ge r^- - l_1^+ x_1(t),$$

which, by the comparison principle, imply that there exists $t_1 > t_0$ such that for any $t > t_1$, $B_1 \leq x_1(t) \leq C_1$. From the second equation of (1.3) we have

$$\frac{dx_2}{dt} = \frac{k_2(t)x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_2(1 + x_2(t-\tau(t))/q(t))} - l_2(t)x_2(t) \leq k_2^+ - l_2^- x_2(t),$$

which yields that there exists $t_2 > t_1$ such that for any $t > t_2$, $x_2(t) \leq C_2$. So for $t > t_2 + \tau^+$, $x_2(t)$ satisfies

$$\frac{dx_2}{dt} = \frac{k_2(t)x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_2(1 + x_2(t-\tau(t))/q(t))} - l_2(t)x_2(t) \geq \frac{k_2^- B_1^2}{B_1^2 + p_2^+(1 + C_2/q^-)} - l_2^+ x_2(t).$$

Consequently, there exists $t_3 > t_2$ such that for any $t > t_3$, $x_2(t) \geq B_2$. The proof is now completed. □

Lemma 2.2 *Suppose that* $q^- > 0$, $r^- > 0$, $l_i^- > 0$ $(i = 1,2)$, *and*

$$-l_i^- + k_i^+(D_i + E_i) < 0, \quad i = 1,2, \tag{2.3}$$

where $D_i = \frac{2C_1^3 + 2C_1(B_1^2 + p_i^-(1+B_2/q^+))}{(B_1^2 + p_i^-(1+B_2/q^+))^2}$, $E_i = \frac{C_1^2 p_i^+/q^-}{(B_1^2 + p_i^-(1+B_2/q^+))^2}$ $(i = 1,2)$. *Moreover, let* $x(t) = x(t; t_0, \varphi)$, $\widetilde{x}(t) = \widetilde{x}(t; t_0, \psi)$. *Then, there exist positive constants* λ, $K_{\varphi,\psi}$, *and* $t_{\varphi,\psi} > t_0$ *such that*

$$\left|x_i(t) - \widetilde{x}_i(t)\right| \leq K_{\varphi,\psi} e^{-\lambda(t-t_0)} \quad \textit{for all } t > t_{\varphi,\psi}, i = 1,2. \tag{2.4}$$

Proof For $i = 1,2$, define the continuous functions $\Gamma_i(u)$ as

$$\Gamma_i(u) = u - l_i^- + k_i^+\left(D_i e^{u\tau^+} + E_i e^{u\tau^+}\right), \quad u \in [0,1].$$

Then, in view of (2.3), we obtain

$$\Gamma_i(0) = -l_i^- + k_i^+(D_i + E_i) < 0, \quad i = 1,2,$$

which implies that there exist two constants $\eta > 0$ and $\lambda \in (0,1]$ such that

$$\Gamma_i(\lambda) = \lambda - l_i^- + k_i^+\left(D_i e^{\lambda\tau^+} + E_i e^{\lambda\tau^+}\right) < -\eta < 0, \quad i = 1,2. \tag{2.5}$$

Set $y(t) = x(t) - \widetilde{x}(t) = (y_1(t), y_2(t))^T$, where $y_i(t) = x_i(t) - \widetilde{x}_i(t)$, $t \in [t_0 - \tau^+, +\infty)$, $i = 1,2$. Then

$$\begin{aligned}\frac{dy_i}{dt} = -l_i(t)y_i(t) + k_i(t)\Bigg[&\frac{x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_i(t)(1 + x_2(t-\tau(t))/q(t))} \\ &- \frac{\widetilde{x}_1^2(t-\tau(t))}{\widetilde{x}_1^2(t-\tau(t)) + p_i(t)(1 + \widetilde{x}_2(t-\tau(t))/q(t))}\Bigg], \quad t > t_0, i = 1,2.\end{aligned} \tag{2.6}$$

It follows from Lemma 2.1 that there exists $t_{\varphi,\psi} > t_0$ such that

$$B_i \leq x_i(t), \widetilde{x}_i(t) \leq C_i \quad \text{for all } t \in \left[t_{\varphi,\psi} - \tau^+, +\infty\right), i = 1,2. \tag{2.7}$$

We consider the Lyapunov functional

$$V_i(t) = |y_i(t)|e^{\lambda(t-t_0)}, \quad i = 1, 2. \tag{2.8}$$

In view of (2.7), for all $t > t_{\varphi,\psi}$ and $i = 1, 2$, calculating the upper left derivative of $V_i(t)$ along the solution $y_i(t)$ of (2.6), we have

$$\begin{aligned}
D^-\big(V_i(t)\big) \le{}& \lambda|y_i(t)|e^{\lambda(t-t_0)} + e^{\lambda(t-t_0)}k_i(t)\bigg|\frac{x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_i(t)(1 + x_2(t-\tau(t))/q(t))} \\
&- \frac{\widetilde{x}_1^2(t-\tau(t))}{\widetilde{x}_1^2(t-\tau(t)) + p_i(t)(1 + \widetilde{x}_2(t-\tau(t))/q(t))}\bigg| - l_i(t)|y_i(t)|e^{\lambda(t-t_0)} \\
\le{}& \big(\lambda - l_i(t)\big)|y_i(t)|e^{\lambda(t-t_0)} + e^{\lambda(t-t_0)}k_i(t) \\
&\times \bigg[\bigg|\frac{x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_i(t)(1 + x_2(t-\tau(t))/q(t))} \\
&- \frac{x_1^2(t-\tau(t))}{\widetilde{x}_1^2(t-\tau(t)) + p_i(t)(1 + \widetilde{x}_2(t-\tau(t))/q(t))}\bigg| \\
&+ \bigg|\frac{x_1^2(t-\tau(t))}{\widetilde{x}_1^2(t-\tau(t)) + p_i(t)(1 + \widetilde{x}_2(t-\tau(t))/q(t))} \\
&- \frac{\widetilde{x}_1^2(t-\tau(t))}{\widetilde{x}_1^2(t-\tau(t)) + p_i(t)(1 + \widetilde{x}_2(t-\tau(t))/q(t))}\bigg|\bigg] \\
\le{}& e^{\lambda(t-t_0)}k_i(t)\bigg[\frac{x_1^2(t-\tau(t))}{x_1^2(t-\tau(t)) + p_i(t)(1 + x_2(t-\tau(t))/q(t))} \\
&\times \frac{(x_1(t-\tau(t) + \widetilde{x}_1(t-\tau(t)))|y_1(t-\tau(t))| + p_i(t)|y_2(t-\tau(t))|/q(t)}{\widetilde{x}_1^2(t-\tau(t)) + p_i(t)(1 + \widetilde{x}_2(t-\tau(t))/q(t))} \\
&+ \frac{(x_1(t-\tau(t)) + \widetilde{x}_1(t-\tau(t)))|y_1(t-\tau(t))|}{\widetilde{x}_1^2(t-\tau(t)) + p_i(t)(1 + \widetilde{x}_2(t-\tau(t))/q(t))}\bigg] + \big(\lambda - l_i(t)\big)|y_i(t)|e^{\lambda(t-t_0)} \\
\le{}& e^{\lambda(t-t_0)}k_i^+\bigg[\frac{C_1^2(2C_1|y_1(t-\tau(t))| + p_i^+|y_2(t-\tau(t))|/q^-)}{(B_1^2 + p_i^-(1 + B_2/q^+))^2} \\
&+ \frac{2C_1|y_1(t-\tau(t))|}{B_1^2 + p_i^-(1 + B_2/q^+)}\bigg] + \big(\lambda - l_i^-\big)|y_i(t)|e^{\lambda(t-t_0)} \\
={}& k_i^+\big(D_iV_1\big(t-\tau(t)\big)e^{\lambda\tau(t)} + E_iV_2\big(t-\tau(t)\big)e^{\lambda\tau(t)}\big) + \big(\lambda - l_i^-\big)V_i(t) \\
\le{}& \big(\lambda - l_i^-\big)V_i(t) + k_i^+\big(D_iV_1\big(t-\tau(t)\big)e^{\lambda\tau^+} + E_iV_2\big(t-\tau(t)\big)e^{\lambda\tau^+}\big).
\end{aligned} \tag{2.9}$$

We now claim that

$$\begin{aligned}
V_i(t) ={}& |y_i(t)|e^{\lambda(t-t_0)} \\
<{}& e^{\lambda t_{\varphi,\psi}}\Big(\max_{1\le i\le 2}\max_{t\in[t_0-\tau^+, t_{\varphi,\psi}]}|x_i(t) - \widetilde{x}_i(t)| + 1\Big) \\
:={}& K_{\phi,\psi} \quad \text{for all } t > t_{\varphi,\psi}, i = 1, 2.
\end{aligned} \tag{2.10}$$

Contrarily, there must exist $t_4 > t_{\varphi,\psi}$ and $i \in \{1, 2\}$ such that

$$V_i(t_4) = K_{\varphi,\psi} \quad \text{and} \quad V_j(t) < K_{\varphi,\psi} \quad \text{for all } t \in [t_0 - \tau^+, t_4), j = 1, 2. \tag{2.11}$$

From (2.9) and (2.11) we get

$$\begin{aligned}0 &\le D^-\big(V_i(t_4)\big)\\ &\le \big(\lambda - l_i^-\big)V_i(t_4) + k_i^+\big(D_i V_1\big(t_4-\tau(t_4)\big)e^{\lambda\tau^+} + E_i V_2\big(t_4-\tau(t_4)\big)e^{\lambda\tau^+}\big)\\ &< \big\{\lambda - l_i^- + k_i^+\big(D_i e^{\lambda\tau^+} + E_i e^{\lambda\tau^+}\big)\big\}K_{\varphi,\psi}.\end{aligned}$$

Thus,

$$0 \le \lambda - l_i^- + k_i^+\big(D_i e^{\lambda\tau^+} + E_i e^{\lambda\tau^+}\big),$$

which contradicts (2.5). Hence, (2.10) holds. It follows that

$$\big|y_i(t)\big| < K_{\varphi,\psi}e^{-\lambda(t-t_0)} \quad \text{for all } t > t_{\varphi,\psi}, i = 1,2. \tag{2.12}$$

The proof is completed. □

3 Main results

In this section, we establish sufficient conditions on the existence, uniqueness, and global exponential stability of positive ω-periodic solutions for system (1.3).

Theorem 3.1 *Suppose that all conditions in Lemma* 2.2 *are satisfied. Then system* (1.3) *has exactly one positive ω-periodic solution $\widetilde{x}(t)$. Moreover, $\widetilde{x}(t)$ is globally exponentially stable.*

Proof Let $x(t) = x(t;t_0,\varphi) = (x_1(t),x_2(t))^T$ be a solution of system (1.3) and (1.4). By Lemma 2.1 we obtain that there exists $s_\varphi > t_0$ such that

$$B_i \le x_i(t) \le C_i \quad \text{for all } t \ge s_\varphi - \tau^+, i = 1,2.$$

By the periodicity of coefficients and delay for system (1.3) we have that, for any natural number h,

$$\begin{aligned}&\big[x_1\big(t+(h+1)\omega\big)\big]'\\ &\quad= \frac{k_1(t+(h+1)\omega)x_1^2(t+(h+1)\omega-\tau(t))}{x_1^2(t+(h+1)\omega-\tau(t)) + p_1(t+(h+1)\omega)(1+x_2(t+(h+1)\omega-\tau(t))/q(t+(h+1)\omega))}\\ &\qquad - l_1\big(t+(h+1)\omega\big)x_1\big(t+(h+1)\omega\big) + r\big(t+(h+1)\omega\big)\\ &\quad= \frac{k_1(t)x_1^2(t+(h+1)\omega-\tau(t))}{x_1^2(t+(h+1)\omega-\tau(t)) + p_1(t)(1+x_2(t+(h+1)\omega-\tau(t))/q(t))}\\ &\qquad - l_1(t)x_1\big(t+(h+1)\omega\big) + r(t)\end{aligned} \tag{3.1}$$

and

$$\begin{aligned}&\big[x_2\big(t+(h+1)\omega\big)\big]'\\ &\quad= \frac{k_2(t+(h+1)\omega)x_1^2(t+(h+1)\omega-\tau(t))}{x_1^2(t+(h+1)\omega-\tau(t)) + p_2(t+(h+1)\omega)(1+x_2(t+(h+1)\omega-\tau(t))/q(t+(h+1)\omega))}\\ &\qquad - l_2\big(t+(h+1)\omega\big)x_2\big(t+(h+1)\omega\big)\end{aligned}$$

$$= \frac{k_2(t)x_1^2(t+(h+1)\omega-\tau(t))}{x_1^2(t+(h+1)\omega-\tau(t))+p_2(t)(1+x_2(t+(h+1)\omega-\tau(t))/q(t))} - l_2(t)x_2\bigl(t+(h+1)\omega\bigr), \tag{3.2}$$

where $t+(h+1)\omega \in [t_0,+\infty)$, $i=1,2$. Thus, for any natural number h, we obtain that $x(t+(h+1)\omega) = (x_1(t+(h+1)\omega), x_2(t+(h+1)\omega))^T$ is a solution of system (1.3) for all $t \geq t_0 - \tau^+ - (h+1)\omega$, $i=1,2$. Hence, $x(t+\omega)$ ($t \in [t_0-\tau^+,+\infty)$, $i=1,2$) is also a solution of system (1.3) with initial values

$$\psi_i(s) = x_i(s+t_0+\omega), \quad s \in \bigl[-\tau^+, 0\bigr], i=1,2.$$

It follows from the proof of Lemma 2.2 that there exists a constant $s_\varphi > t_0$ such that, for any nonnegative integer h and $t+h\omega \geq s_\varphi$,

$$\begin{aligned} \bigl|x_i\bigl(t+(h+1)\omega;t_0,\varphi\bigr) - x_i(t+h\omega;t_0,\varphi)\bigr| &= \bigl|x_i(t+h\omega;t_0,\psi) - x_i(t+h\omega;t_0,\varphi)\bigr| \\ &\leq K_\varphi e^{-\lambda(t+h\omega-t_0)}, \quad i=1,2, \end{aligned}$$

where $K_\varphi = e^{\lambda s_\varphi}(\max_{1\leq i\leq 2}\max_{s\in[t_0-\tau^+,s_\varphi]}|x_i(s;t_0,\psi) - x_i(s;t_0,\varphi)| + 1)$.

Now, we show that $x_i(t+q\omega;t_0,\varphi)$ ($i=1,2$) is convergent on any compact interval as $q \to +\infty$. Let $[a,b] \subset R$ be an arbitrary subset of R. Choose a nonnegative integer q_0 such that $t+q_0\omega \geq s_\varphi$ for $t \in [a,b]$. Then, for $t \in [a,b]$ and $q > q_0$, we have

$$x_i(t+q\omega) = x_i(t+q_0\omega) + \sum_{h=q_0}^{q-1}\bigl[x_i\bigl(t+(h+1)\omega\bigr) - x_i(t+h\omega)\bigr], \quad i=1,2.$$

Then $x_i(t+q\omega)$ converges uniformly to a continuous function, say $\widetilde{x}_i(t)$, on $[a,b]$. Because of arbitrariness of $[a,b]$, we see that $x_i(t+q\omega) \to \widetilde{x}_i(t)$ as $q \to +\infty$ for $t \in R$, $i=1,2$. Moreover,

$$B_i \leq \widetilde{x}_i(t) \leq C_i \quad \text{for all } t \in R, i=1,2. \tag{3.3}$$

It remains to show that $\widetilde{x}(t) = (\widetilde{x}_1(t), \widetilde{x}_2(t))^T$ is an ω-periodic solution of system (1.3). The periodicity is obvious since

$$\widetilde{x}_i(t+\omega) = \lim_{q\to+\infty} x_i(t+\omega+q\omega) = \lim_{q+1\to+\infty} x_i\bigl(t+(q+1)\omega\bigr) = \widetilde{x}_i(t), \quad i=1,2,$$

for all $t \in R$. Now, note that $x(t+q\omega)$ is a solution to system (1.3), that is,

$$\begin{aligned} &x_1(t+q\omega) - x_1(t_0+q\omega) \\ &\quad = \int_{t_0}^t \biggl[\frac{k_1(s)x_1^2(s+q\omega-\tau(s))}{x_1^2(s+q\omega-\tau(s))+p_1(s)(1+x_2(s+q\omega-\tau(s))/q(s))} - l_1(s)x_1(s+q\omega) + r(s)\biggr]\,ds \end{aligned}$$

and

$$\begin{aligned} &x_2(t+q\omega) - x_2(t_0+q\omega) \\ &\quad = \int_{t_0}^t \biggl[\frac{k_2(s)x_1^2(s+q\omega-\tau(s))}{x_1^2(s+q\omega-\tau(s))+p_2(s)(1+x_2(s+q\omega-\tau(s))/q(s))} - l_2(s)x_2(s+q\omega)\biggr]\,ds \end{aligned}$$

for $t \geq t_0$. Letting $q \to +\infty$ gives us

$$\begin{cases} \widetilde{x}_1(t) - \widetilde{x}_1(t_0) = \int_{t_0}^{t} [\frac{k_1(s)\widetilde{x}_1^2(s-\tau(s))}{\widetilde{x}_1^2(s-\tau(s))+p_1(s)(1+\widetilde{x}_2(s-\tau(s))/q(s))} - l_1(s)\widetilde{x}_1(s) + r(s)]\,ds, \\ \widetilde{x}_2(t) - \widetilde{x}_2(t_0) = \int_{t_0}^{t} [\frac{k_2(s)\widetilde{x}_1^2(s-\tau(s))}{\widetilde{x}_1^2(s-\tau(s))+p_2(s)(1+\widetilde{x}_2(s-\tau(s))/q(s))} - l_2(s)\widetilde{x}_2(s)]\,ds \end{cases}$$

for $t \geq t_0$, that is, $\widetilde{x}(t)$ is a solution to system (1.3) on $[t_0 - \tau^+, +\infty)$. Finally, from (2.1) and (3.3), again using a similar argument as in the proof (2.12), we can prove that $\widetilde{x}(t)$ is globally exponentially stable. This completes the proof of the main theorem. □

4 An example

In this section, we give an example and numerical simulations to demonstrate the results obtained in previous sections.

Example 4.1 Consider the following genetic regulatory system with time-varying coefficients and delays:

$$\begin{cases} \frac{dx_1}{dt} = \frac{\frac{1}{10}(2+\sin t)x_1^2(t-2|\sin t|)}{x_1^2(t-2|\sin t|)+(1+\sin t)(1+x_2(t-2|\sin t|))} - (10 + \cos t)x_1(t) + 11, \\ \frac{dx_2}{dt} = \frac{\frac{1}{10}(2+\cos t)x_1^2(t-2|\sin t|)}{x_1^2(t-2|\sin t|)+(1+\cos t)(1+x_2(t-2|\sin t|))} - (10 + \sin t)x_2(t). \end{cases} \tag{4.1}$$

Obviously, $r^- = r^+ = 11$, $q^- = q^+ = 1$, $k_i^- = 0.1$, $k_i^+ = 0.3$, $l_i^- = 9$, $l_i^+ = 11$, $p_i^- = 0$, $p_i^+ = 2$ $(i = 1, 2)$. From (2.1) and (2.3) we obtain $B_1 = 1$, $C_1 = 11.3/9$, $B_2 = 1/264$, $C_2 = 0.1/3$, $D_i \approx 6.46968$, $E_i \approx 3.15284$ $(i = 1, 2)$, and

$$-l_i^- + k_i^+(D_i + E_i) \approx -6.11325 < 0, \quad i = 1, 2, \tag{4.2}$$

which imply that the genetic regulatory system (4.1) satisfies all conditions of Theorem 3.1. Therefore, system (4.1) has a unique positive 2π-periodic solution $\widetilde{x}(t)$, which is globally exponentially stable with the exponential convergent rate $\lambda \approx 0.5$. The numerical simulations in Figure 1 strongly support the conclusion.

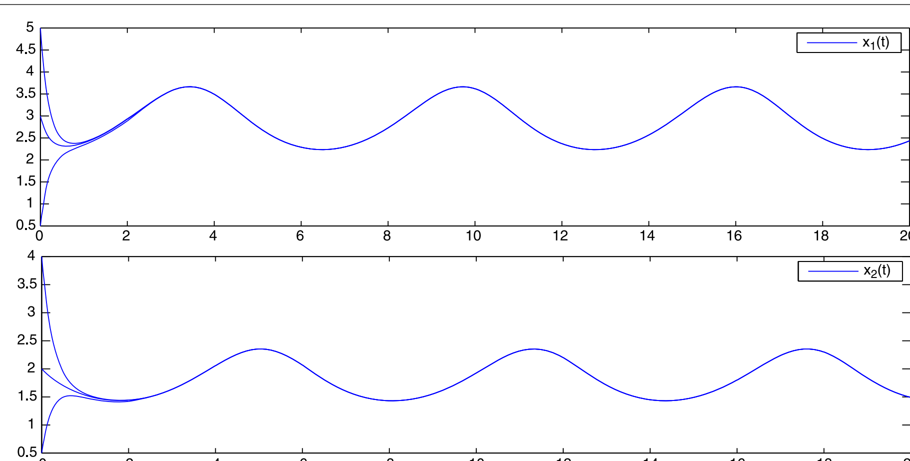

Figure 1 Numerical solutions $x(t) = (x_1(t), x_2(t))^T$ of system (4.1) for initial value $\varphi(s) \equiv (5,4)^T, (3,2)^T, (0.5, 0.5)^T$, $s \in [-2, 0]$.

Remark 4.1 To the best of our knowledge, rare authors studied the problems of the global exponential stability of positive periodic solutions for genetic regulatory system with time-varying coefficients and delays. It is obvious that all results in [3, 4] and the references therein cannot be applicable to prove that all solutions of system (4.1) converge exponentially to a positive periodic solution since the system has time-varying coefficients and delays. This implies that the results of this paper are generalization and complement of previously known results.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
The authors declare that the study was realized in collaboration with the same responsibility. Both authors read and approved the final version.

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References
1. Smolen, P, Baxter, DA, Byrne, JH: Frequency selectivity, multistability, and oscillations emerge from models of genetic regulatory systems. Am. J. Physiol., Cell Physiol. **274**(2), 531-542 (1998)
2. Smolen, P, Baxter, DA, Byrne, JH: Modeling transcriptional control in gene networks-methods, recent results, and future directions. Bull. Math. Biol. **62**(2), 247-292 (2000)
3. Wan, A, Zou, X: Hopf bifurcation analysis for a model of genetic regulatory system with delay. J. Math. Anal. Appl. **356**(2), 464-476 (2009)
4. Chen, S, Wei, J: Global attractivity in a model of genetic regulatory system with delay. Appl. Math. Comput. **232**(1), 411-415 (2014)
5. Cao, J, Jiang, H: Hopf bifurcation analysis for a model of single genetic negative feedback autoregulatory system with delay. Neurocomputing **99**, 381-389 (2013)
6. Wang, K, Wang, L, Teng, Z, Jiang, H: Stability and bifurcation of genetic regulatory networks with delays. Neurocomputing **73**, 2882-2892 (2010)
7. Wang, Z, Liu, Z, Yuan, R: Stability and bifurcation in a gene regulatory network model with delay. Z. Angew. Math. Mech. **92**(4), 290-303 (2012)
8. Zhang, W, Fang, J, Cui, W: Exponential stability of switched genetic regulatory networks with both stable and unstable subsystems. J. Franklin Inst. **350**, 2322-2333 (2013)
9. Liu, P: Robust stability analysis of genetic regulatory network with time delays. ISA Trans. **52**, 326-334 (2013)
10. Xiao, M, Cao, J: Genetic oscillation deduced from Hopf bifurcation in a genetic regulatory network with delays. Math. Biosci. **215**, 55-63 (2008)
11. Zhang, X, Yu, A, Zhang, G: *M*-Matrix-based delay-range-dependent global asymptotical stability criterion for genetic regulatory networks with time-varying delays. Neurocomputing **113**, 8-15 (2013)
12. Hu, J, Liang, J, Cao, J: Stability analysis for genetic regulatory networks with delays: the continuous-time case and the discrete-time case. Appl. Math. Comput. **220**, 507-517 (2013)
13. Chen, W, Liu, B: Positive almost periodic solution for a class of Nicholson's blowflies model with multiple time-varying delays. J. Comput. Appl. Math. **235**, 2090-2097 (2011)
14. Liu, B: Global exponential stability of positive periodic solutions for a delayed Nicholson's blowflies model. J. Math. Anal. Appl. **412**, 212-221 (2014)
15. Wu, X, Li, J, Zhou, H: A necessary and sufficient condition for the existence of positive periodic solutions of a model of hematopoiesis. Comput. Math. Appl. **54**, 840-849 (2007)
16. Liu, B: New results on the positive almost periodic solutions for a model of hematopoiesis. Nonlinear Anal., Real World Appl. **17**, 252-264 (2014)