A Model of the Signal Transduction Process under a Delay

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Abstract. The signal transduction pathway is the important process of communication of the cells. It is the dynamical interaction between the ligand-receptor complexes and an inhibitor protein in second messenger synthesis. The signaling molecules are detected and bounded by receptors, typically G-Protein receptors, across the cell membrane and that in turns alerts intracellular molecules to stimulate a response or a desired consequence in the target cells. In this research, we consider a model of the signal transduction process consisting of a system of three differential equations which involve the dynamic interaction between an inhibitor protein and the ligand-receptor complexes in the second messenger synthesis. We will incorporate a delay $\tau$ in the time needed before the signal amplification process can take effect on the production of the ligand-receptor complex. We investigate persistence and stability of the system. It is shown that the system allows positive solutions and the positive equilibrium is locally asymptotically stable under suitable conditions on the system parameters.

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1. Introduction

Signal transduction process has been a focus of attention of many researchers. As mentioned in \cite{1, 5}, the living organism is composed of cells. To conduct of life, the cells need to interact with each other by releasing a signal molecule of a cell and acts on another cell to produce a change in cell function for example growth, metabolism, catabolism, and so on. All cells are highly responsive to specific chemicals in their external environment. The way of communication of cells is represented by a signaling pathway.

Even though, the functions of cell signaling is to control and maintain normal physiological balance within the body, when the cell senses and responds correctly by signal
transmittance, this can lead to proper development, repairing, and so on, otherwise if it loss the controllable of signaling pathway, this can be a key factor in the generation of disorders such as cancer or many serious diseases, see in [1, 2, 10].

Signal transduction is the mediation of molecular signals from extracellular to intracellular of the cells. The molecular circuits are detection, amplification and diverse integration of external signals to generate responses.

By considering a mechanism for detecting and responding specifically to external signals of cells. One of the more complex strategies for running the signal process concerns a three-stage G protein coupled enzyme cascade, represented in [5, 9]. The process starts from the G protein, which consists of 3 subunits: $\alpha$, $\beta$, and $\gamma$ subunits. It is activated by a specialized membrane receptor's interaction with a particular ligand. After that, the receptor is activated and turns on the heterotrimeric G protein, by causing the G protein to convert GDP (guanosine diphosphate) to GTP (guanosine triphosphate). The GTP-bound $\alpha$—subunit is then separated from $\beta$ and $\gamma$ subunits and either or both regulates the effector unit (the adenylate cyclase or AC), whose activity produces secondary messengers such as cyclic adenosine monophosphate (cAMP). The G protein is transient and is terminated by the GTPase activity of the $\alpha$—subunits. GTPase converts bound GTP to GDP and finally the protein is inactivated.

In the work of C. Rattanakul et al. [8], based on previous research works [3, 4, 6, 7, 9], they obtained a model for the signal transduction pathway consisting of a system of two differential equations which governs the interaction between an inhibitor protein and the ligand-receptor complexes. Their model assumes that cAMP equilibrates very rapidly which reduces their model to a two dimensional one. We do not make such assumptions, making our model more accurate.

Then, as in [8], we will be able to write the following steps for the reference model.

Let $S$ be the amount of $\alpha$—subunits of G protein in the inactive state and $S^*$ be that in the active state. $S$ and $S^*$ can be switched to the other by the activating and inhibiting agents, which are denoted $A$ and $I$, respectively. These agents are stimulated by the external signal, which binds to the cell receptors on the cell membrane. The dynamics of the activator density $A$ and inhibitor density $I$ are shown in the following equations

$$\frac{dA}{dt} = -k_{-a}A + k_aR,$$

$$\frac{dI}{dt} = -k_{-i}I + k_iA,$$

where $R(t)$ is the membrane surface density of the ligand bound receptors. The first terms on the right of equations (1.1) and (1.2) are the corresponding removal rates, and the second terms are the corresponding rates of production.

By using the dynamics of mass action, the equations for $S^*$ is

$$\frac{dS^*}{dt} = -k_{-s}IS^* + k_sAS,$$

where the first term on the right is the removal rate and the second term is the activation rate.
Under the assumption that the total amount of the regulators (AC) remains constant denoted by $S_T$ and that $S_T = S^* + S$, equation (1.3) becomes

$$\frac{dS^*}{dt} = -(k_{-s}I + k_s A)S^* + k_s AS_T. \quad (1.4)$$

Let $C$ be the concentration of the second messenger or cAMP, which is synthesized as a result of the output signal of the transduction process, as seen in [7], yield the following equation

$$\frac{dC}{dt} = -k_{-c}C + k_{c1}[S^*]^2 + k_{c2}, \quad (1.5)$$

where the first term on the right is the removal rate and the last two terms are the synthesis rate, $k_{c2}$ is the zero order rate of production.

The dynamics of $R$ follows the equation

$$\frac{dR}{dt} = -k_{-r}R - \frac{a_1 R}{a_2 + R} + k_r C, \quad (1.6)$$

where the first term on the right is the removal rate, the second term is the rate at which it is transported through the cell membrane and the last term is the signal amplification due to the synthesis of cAMP.

As studied in [3, 4], we may assume that the dynamics of $S^*$ and $A$ are relatively very fast. So their values equilibrate quickly to

$$S^* = \frac{k_s AS_T}{k_{-s}I + k_s A}, \quad (1.7)$$

$$A = \frac{k_c R}{k_{-a}}. \quad (1.8)$$

Substituting equation (1.7) into (1.5) and (1.8) into (1.2), we obtain

$$\frac{dC}{dt} = -k_{-c}C + \frac{k_{c1}}{(k_{-s}I + k_s A)^2}R^2 + k_{c2}, \quad (1.9)$$

and

$$\frac{dI}{dt} = -k_{-i}I + \frac{k_{-a} R}{k_{-a} R}. \quad (1.10)$$

Moreover, if the dynamics of cAMP ($C$) is also relatively fast as argued in [3, 4], this leads to the model system of the work in [8].

According to the model discussed above, the model of this research is consisted of three nonlinear differential equations. In this work we will incorporate a delay $\tau$ in the time needed before the signal amplification process can take effect on the production of the
ligand-receptor complex. Therefore, the system of our model can be written in the following form:

\[
\frac{dR}{dt} = -b_1R - \frac{a_1R}{a_2 + R} + a_3C, \tag{1.11}
\]

\[
\frac{dC}{dt} = -b_2C + \frac{a_4R^2(t - \tau)}{(a_5R(t - \tau) + I)^2} + a_6, \tag{1.12}
\]

\[
\frac{dI}{dt} = -b_3I + a_7R, \tag{1.13}
\]

where the constants \(a_i, i = 1, 2, \cdots, 7\) and \(b_j, j = 1, 2, 3\) are all positive. The first term of equations (1.11)-(1.13) are the removal rates of the corresponding state variables. The second term of equation (1.11) is the rate that \(R\) is internalized through the cell membrane. The third term of equation (1.11) is the signal amplification arising from the synthesis of cAMP. The second term of equation (1.12) is the amplification effect on the production of the ligand-receptor complexes due to the secondary hormone with a delay \(\tau\). The third term of equation (1.12) is the zero order production rate and the second term of equation (1.13) is the production rate of the inhibiting protein in response to the increase in the ligand-receptor complexes.

In this paper, the persistence and stability of the system were investigated. We proved that the system allows positive solutions and finally, we show that the positive equilibrium is locally asymptotically stable under suitable conditions on the system parameters.

2. Physically Meaningful Solution and Persistence System

In this section, we will show the positivity of the solution for the model system and give preliminary results on persistence.

**Theorem 2.1.** Let \(I(t) > 0, C(t) > 0\) and \(R(t) > 0\) be continuous on the interval \([-\tau, 0]\). Then, the model system has a positive solution.

**Proof:** Suppose that \(C(t)\) is not always positive, so \(C(t)\) would become non-positive. By the continuity of the solution, let \(t_0 > 0\) such that \(C(t_0) = 0\) and \(C(t) > 0\) for all \(0 \leq t < t_0\), then we now have \(C'(t_0) \leq 0\). We consider the second equation of the model system

\[
C'(t_0) = -b_2C(t_0) + \frac{a_4R^2(t_0 - \tau)}{(a_5R(t_0 - \tau) + I(t_0)^2) + a_6} > 0.
\]

This is a contradiction. It follows that \(C(t)\) is positive.

Similarly, suppose that \(R(t)\) is not always positive and that \(R(t)\) would become non-positive. Due to the continuity, let \(t_1 > 0\) such that \(R(t_1) = 0\) and \(R(t) > 0\) for all \(0 \leq t < t_1\), then this means \(R'(t_1) \leq 0\). The first equation of the system gives that

\[
R'(t_1) = -b_1R(t_1) - \frac{a_1R(t_1)}{a_2 + R(t_1)} + a_3C(t_1) = a_3C(t_1) \leq 0,
\]
which contradicts with the fact of the previous discussion that \( C(t) \) is positive. Therefore \( R(t) \) must be positive.

Finally, for the third equation, we also assume that \( I(t) \) is not always positive and the same as the continuity reason, we let \( t_2 > 0 \) such that \( I(t_2) = 0 \) and \( I(t) > 0 \) for all \( 0 \leq t < t_2 \), then
\[
I'(t_2) = -b_3 I(t_2) + a_2 R(t_2) = a_2 R(t_2) \leq 0,
\]
which contradicts that \( R(t) \) is positive. Hence \( I(t) \) is also positive.

Next theorem, we show the persistence of the model under certain conditions. This means that the level of the inhibitors, the ligand-receptor complex and the concentration of the second messenger are bounded above and below by positive constants which are defined as the following:

\[
R_m = \lim_{t \to \infty} \inf R(t), \quad R_M = \lim_{t \to \infty} \sup R(t),
\]
\[
C_m = \lim_{t \to \infty} \inf C(t), \quad C_M = \lim_{t \to \infty} \sup C(t),
\]
\[
I_m = \lim_{t \to \infty} \inf I(t), \quad I_M = \lim_{t \to \infty} \sup I(t).
\]

**Theorem 2.2.** If the assumptions of Theorem 2.1 are satisfied, then the system is persistent.

**Proof.** By the property of the persistence, we need to verify that
\[
0 < \lim_{x \to \infty} \inf X(t) \leq \lim_{x \to \infty} \sup X(t) < \infty,
\]
when \( X(t) \) is any positive solution for \( t \geq t^* \). Thus, in this proof we will separate the statement into six parts as below:

i) \( C_M < \infty \); ii) \( R_M < \infty \); iii) \( I_M < \infty \); iv) \( C_m > 0 \); v) \( R_m > 0 \); vi) \( I_m > 0 \).

Part i) We assume that \( C_M = \infty \). By the continuity of solution, there is a time sequence \( \{t_n\} \subset [0, \infty) \) such that
\[
\lim_{n \to \infty} t_n = \infty, \quad \lim_{n \to \infty} C(t_n) = \infty
\]
with \( \frac{dC}{dt} |_{t=t_n} \geq 0 \). Note that
\[
\frac{dC}{dt} |_{t=t_n} = -b_2 C(t_n) + \frac{a_4 R^2 \tau (t_n - \tau)}{(a_5 R (t_n - \tau) + 1)^2} + a_6
\]
tends to \(-\infty\) since \( a_4 R^2 < a_4 (a_5 + 1)^2 / a_5^2 \) for positive \( R \) and \( I \), therefore \( \frac{a_4 R^2 \tau (t_n - \tau)}{(a_5 R (t_n - \tau) + 1)^2} \) is always bounded. This is a contradiction, hence \( C_M < \infty \).

Part ii) We assume that \( R_M = \infty \). By the continuity of the solution, then there exist a time sequence \( \{t_n\} \subset [0, \infty) \) such that
\[
\lim_{n \to \infty} t_n = \infty, \quad \lim_{n \to \infty} R(t_n) = \infty
\]
with $\frac{dR}{dt}\big|_{t=t_n} \geq 0$. Note that

$$\left. \frac{dR}{dt} \right|_{t=t_n} = -b_1 R(t_n) - \frac{a_1 R(t_n)}{a_2 + R(t_n)} + a_3 C(t_n)$$

tends to $-\infty$. This is a contradiction and therefore $R_M < \infty$.

Part iii) Similarly to Part ii, we assume that $I_M = \infty$ and by the continuity of the solution, we obtain a contradiction of the equation $\frac{dI}{dt}\big|_{t=t_n} = -b_3 I(t_n) + a_7 R(t_n)$, which tends to $-\infty$. So we now get $I_M < \infty$.

Part iv) Suppose $C_m = 0$ (otherwise $C_m > 0$ is trivially verified). By the continuity, there is a time sequence $\{t_n\} \subset [0, \infty)$ such that

$$\lim_{n \to \infty} t_n = \infty, \quad \lim_{n \to \infty} C(t_n) = C_m$$

with $\frac{dC}{dt}\big|_{t=t_n} = 0$. We obtain

$$0 = \lim_{n \to \infty} \left( -b_2 C(t_n) + \frac{a_4 R^2(t_n - \tau)}{a_5 R(t_n - \tau) + I(t_n)} + a_6 \right)$$

$$\geq -b_2 C_m + \frac{a_4 R_m^2}{(a_5 R_M + I_M)^2} + a_6.$$

So,

$$a_6 \leq b_2 C_m - \frac{a_4 R_m^2}{(a_5 R_M + I_M)^2} = -\frac{a_4 R_m^2}{(a_5 R_M + I_M)^2} \leq 0,$$

which contradicts the given condition that $a_6$ is a positive constant. Thus, we have $C_m > 0$.

Part v) Similarly to Part iv, we suppose $R_m = 0$. By continuity of the solution, we obtain

$$0 = \lim_{n \to \infty} \left( -b_1 R(t_n) - \frac{a_1 R(t_n)}{a_2 + R(t_n)} + a_3 C(t_n) \right)$$

$$\geq -b_1 R_m - \frac{a_1 R_m}{a_2 + R_m} + a_3 C_m$$

$$\geq a_3 C_m,$$

which contradicts that $C_m > 0$ and $a_3$ is a positive constant. Therefore, $R_m > 0$.

Part vi) Also in this part, we suppose $I_m = 0$. Due to the continuity, we get

$$0 = \lim_{n \to \infty} \left( -b_3 I(t_n) + a_7 R(t_n) \right)$$

$$\geq -b_3 I_m + a_7 R_m$$

$$\geq a_7 R_m,$$

which contradicts the fact that $R_m > 0$ and $a_7$ is a positive constant. We have $I_m > 0$. \qed

Remark 2.1. The combination of the results of Theorems 2.1 and 2.2 give that the model system has positive bounded solutions for any positive conditions.
3. Steady State and Main Results

We now analyze the delay model for the stability of its associated equilibria. We will show that the steady state is positive and we will establish the main theorem as we mentioned before that under certain conditions on parameters the steady state is locally asymptotically stable.

In order to obtain the existence of a positive equilibrium of the system, we denote that

\[ P_0 = \frac{a_4 b_3^2}{(a_5 b_3 + a_7)^2} + a_6. \]  

**(Proposition 3.1)** The system admits a positive steady state solutions \( E^* = (R^*, C^*, I^*) \), according to the following equations

\[ R^* = \frac{1}{2b_1} \left[ \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right) + \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right)^2 + 4b_1 a_3 P_0 a_2 \right]^{\frac{1}{2}}, \]  

\[ C^* = \frac{P_0}{b_2}, \]  

\[ I^* = \frac{a_7}{2b_3 b_1} \left[ \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right) + \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right)^2 + 4b_1 a_3 P_0 a_2 \right]^{\frac{1}{2}}, \]  

which are clearly positive for positive parameter values.

**Proof.** We will find the equilibrium solution \( E^* = (R^*, C^*, I^*) \) by setting \( dR/dt = 0 \), \( dC/dt = 0 \) and \( dI/dt = 0 \) in the model system. We then have

\[ R^* = \frac{1}{2b_1} \left[ \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right) + \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right)^2 + 4b_1 a_3 P_0 a_2 \right]^{\frac{1}{2}}, \]  

\[ C^* = \frac{P_0}{b_2}, \]  

\[ I^* = \frac{a_7}{2b_3 b_1} \left[ \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right) + \left( \frac{a_3 P_0}{b_2} - a_1 - b_1 a_2 \right)^2 + 4b_1 a_3 P_0 a_2 \right]^{\frac{1}{2}}. \]

Obviously, we can see that \( C^* \) is positive. For the positivity of \( R^* \) and \( I^* \), we denote that \( U = a_3 P_0/b_2 - a_1 - b_1 a_2 \) and \( V = 4b_1 a_3 P_0 a_2/b_2 \). It is sufficient to show that the term \( T^* = U + (U^2 + V)^{\frac{1}{2}} \) is positive. Since \( (U^2 + V)^{\frac{1}{2}} > |U| \), so we let \( (U^2 + V)^{\frac{1}{2}} = |U| + \eta \) where \( \eta > 0 \). In case of \( U = 0 \), we have \( T^* > 0 \). If \( U < 0 \), we have \( T^* = \eta > 0 \) and if \( U > 0 \), we have \( T^* = 2U + \eta > 0 \). From each case, we can conclude that \( T^* \) is always positive and the proof is completed. \( \square \)

Next, we consider the coordinate transformation by letting \( x = R - R^* \), \( y = C - C^* \) and \( z = I - I^* \). The corresponding linearized system of the model around the equilibrium \( E^* \) is
of the form
\[
\frac{dx}{dt} = \left(-b_1 - \frac{a_1 a_2}{(a_2 + R^*)^2}\right)x + a_3 y,
\]
\[
\frac{dy}{dt} = \frac{2a_4 R^* I^*}{(a_5 R^* + I^*)^3} x(t - \tau) - b_2 y - \frac{2a_4 R^*}{(a_5 R^* + I^*)^3} z,
\]
\[
\frac{dz}{dt} = a_7 x - b_3 z.
\]

The above linear system can be also written in the form of the Jacobian matrix with \(\lambda\) being an eigenvalue of the matrix \(J\) as the following system
\[
\begin{bmatrix}
\frac{dx}{dt} \\
\frac{dy}{dt} \\
\frac{dz}{dt}
\end{bmatrix}
= J
\begin{bmatrix}
x(t) \\
y(t) \\
z(t)
\end{bmatrix}
\]
where
\[
J =
\begin{bmatrix}
-b_1 - \frac{a_1 a_2}{(a_2 + R^*)^2} & a_3 & 0 \\
\frac{2a_4 R^*}{(a_5 R^* + I^*)^3} e^{-\lambda \tau} & -b_2 & -\frac{2a_4 R^*}{(a_5 R^* + I^*)^3} \\
a_7 & 0 & -b_3
\end{bmatrix}.
\]

In the following proposition, we state the condition under which the model system hold a local asymptotic stability of the equilibrium \(E^*\).

**Theorem 3.1.** The steady state \(E^*\) is locally asymptotically stable for \(\tau = 0\) if and only if
\[
P_1 = \frac{4a_4 a_3 R^* I^*}{b_1 b_3 (a_5 R^* + I^*)^3} < 1. \tag{3.5}
\]

**Proof.** The associated characteristic equation of the Jacobian matrix \(J\) at \(E^*\) is given by \(det(J - \lambda I) = 0\). This becomes
\[
\lambda^3 + B_1 \lambda^2 + B_2 \lambda + B_3 + B_4 - (B_5 + B_6 \lambda) e^{-\lambda \tau} = 0, \tag{3.6}
\]
where
\[
B_1 = b_1 + \frac{a_1 a_2}{(a_2 + R^*)^2} + (b_2 + b_3),
\]
\[
B_2 = \left(b_1 + \frac{a_1 a_2}{(a_2 + R^*)^2}\right)(b_2 + b_3) + b_2 b_3,
\]
\[
B_3 = \left(b_1 + \frac{a_1 a_2}{(a_2 + R^*)^2}\right) b_2 b_3,
\]
\[
B_4 = \frac{2a_3 a_4 R^*}{(a_5 R^* + I^*)^3},
\]
\[
B_5 = \frac{2a_3 b_3 a_4 R^* I^*}{(a_5 R^* + I^*)^3},
\]
\[
B_6 = \frac{2a_3 a_4 R^* I^*}{(a_5 R^* + I^*)^3}.
\]
In the case without delay \((\tau = 0)\), the equation (3.6) becomes
\[
\lambda^3 + B_1 \lambda^2 + (B_2 - B_6)\lambda + B_3 + B_4 - B_5 = 0. \tag{3.7}
\]
It is easy to see that \(B_1 > 0\). If \(P_1 < 1\), we get \(B_2 - B_6 > 0\) and by the fact that \(b_3 l^* = a_7 R^*\), we obtain \(B_3 + B_4 - B_5 = B_3 > 0\). We can see that
\[
B_1(B_2 - B_6) = b_2 b_3(b_2 + b_3) + B_3 + B_4 - B_5
\]
\[
+ \left[ b_1 + \frac{a_1 a_2}{(a_2 + R^*)^2} + (b_2 + b_3) \right] \left[ (b_1 + \frac{a_1 a_2}{(a_2 + R^*)^2})(b_2 + b_3) - \frac{2a_5 a_6 R^* l^*}{(a_2 R^* + I^*)^2} \right],
\]
which is greater than \(B_3 + B_4 - B_5\), if \(P_1 < 1\).

Using the Routh-Hurwitz criteria conditions, we can conclude that the roots of equation (3.7) have negative real parts. Hence, \(E^*\) is locally asymptotically stable for \(\tau = 0\).

We are interested in the case when \(\tau > 0\). We assume \(\lambda(\tau) = \phi(\tau) + i\omega(\tau)\), where \(\phi(\tau), \omega(\tau) \in R\). Plugging this into equation (3.6) and rewriting in the form of real and imaginary parts, we get
\[
\phi^3 - 3\phi \omega^2 + B_1 \phi^2 - B_1 \omega^2 + B_2 \phi + B_3 + B_4 - e^{-\phi \tau} (B_5 + B_6 \phi) \cos \omega \tau - e^{-\phi \tau} B_6 \omega \sin \omega \tau + i \left[ 3\phi^2 \omega - \omega^3 + 2B_1 \phi \omega + B_2 \omega - e^{-\phi \tau} B_6 \omega \cos \omega \tau + e^{-\phi \tau} (B_5 + B_6 \phi) \sin \omega \tau \right] = 0 \tag{3.8}
\]
Since \(\lambda(\tau)\) is a complex number and when \(\tau = 0\) we have that \(Re(\lambda(0)) < 0\). By continuity of \(Re(\lambda(\tau))\), so there exists \(\hat{\tau} > 0\) such that \(Re(\lambda(\tau)) < 0\) for \(0 \leq \tau < \hat{\tau}\). Thus, \(E^*\) remains stable for the value of \(\tau\). This means the equilibrium \(E^*\) may be changed from stable to unstable at \(\tau = \hat{\tau}\) under that assumption of \(Re(\lambda) = 0\) or \(\lambda = i\omega(\hat{\tau})\).

We now suppose that the characteristic equation (3.6) has a purely imaginary root \(i\omega\), with \(\omega\) is real and positive. Then we can rewrite the equation (3.6) in terms of its real and imaginary part and by equating, we have two equations as below
\[
B_7 - B_1 \omega^2 = B_5 \cos(\omega \tau) + B_6 \omega \sin(\omega \tau), \tag{3.9}
\]
\[
B_2 \omega - \omega^3 = B_6 \omega \cos(\omega \tau) - B_5 \sin(\omega \tau), \tag{3.10}
\]
where \(B_7 = B_3 + B_4\).

Squaring and adding the equations (3.9) and (3.10), we get
\[
\omega^6 + (B_1^2 - 2B_2) \omega^4 + (B_2^2 - B_6^2 - 2B_7 B_1) \omega^2 + B_7^2 - B_5^2 = 0. \tag{3.11}
\]
This equation can be reduced to
\[
F(l) = l^3 + g_1 l^2 + g_2 l + g_3 = 0, \tag{3.12}
\]
where \(l = \omega^2\), \(g_1 = B_1^2 - 2B_2\), \(g_2 = B_2^2 - B_6^2 - 2B_7 B_1\) and \(g_3 = B_7^2 - B_5^2\).

We next present the conditions under which the equation (3.12) has no positive solutions.
Lemma 3.1. Assume that $g_1^2 - 3g_2 < 0$, then the equation (3.12) has no positive roots.

Proof. We differentiate $F(l)$ and establish the roots of equation $F'(l) = 0$ are

$$l_1 = \frac{-g_1 + \sqrt{g_1^2 - 3g_2}}{3}$$

and

$$l_2 = \frac{-g_1 - \sqrt{g_1^2 - 3g_2}}{3}.$$ 

Since $g_1^2 - 3g_2 < 0$, so $l_1$ and $l_2$ are complex conjugate numbers. That is $F'(l)$ has no real root. Observe that

$$F'(0) = g_2 > \frac{g_1^2}{3} > 0.$$ 

So, we can conclude that the quadratic polynomial $F'(l)$ is strictly positive on the real numbers. This implies that $F(l)$ is increasing function. It is noticed that $F(l)$ does not vanish for $l > 0$ and hence, the equation (3.12) has no positive solutions.

We now obtain the main theorem.

Theorem 3.2. Assume that the conditions i) $P_1 < 1$ and ii) $g_1^2 - 3g_2 < 0$ are satisfied, then the equilibrium $E^*$ is locally asymptotically stable for $\tau \geq 0$.

Proof. For $\tau = 0$, all real parts of eigenvalues of equation (3.6) are negative, under the condition i) and Theorem 3.1. From the condition ii) and by Lemma 3.1, the equation (3.12) has no positive roots. This implies any real number $\omega$ is not a root of equation (3.11). Hence, for any real number $\omega$, the value $i\omega$ is not a root of equation (3.6). This means there is no $\hat{\tau}$ such that

$$\lambda(\hat{\tau}) = i\omega(\hat{\tau}).$$

Since we have the roots of equation (3.6) are negative real parts for $\tau = 0$. By the continuity of $Re(\lambda(\tau))$, as a function of $\tau$, we conclude that all roots of the characteristic equation (3.6) have negative real part for $\tau > 0$. Therefore, the equilibrium $E^*$ is locally asymptotically stable for $\tau \geq 0$.

4. Conclusion

In this research, we have derived conditions on the system parameters which give a prediction about the dynamical behaviour of a model of the signal transduction pathway under the impact of a delay. It has been shown that the model is uniformly persistent and we have found from Theorem 3.2 that if $P_1 < 1$ and $g_1^2 - 3g_2 < 0$ then for $\tau \geq 0$, the equilibrium $E^*$ is locally asymptotically stable. This would mean that a solution must oscillate about the stationary point level unless it converges to the steady state as time passes.
For further work, we will pay attention to global stability of the equilibrium point and how a delay $\tau$ affects the behavior of the model system when oscillatory solutions may occur. Possibility of periodic behaviour of the delay system is also an attractive aim of our interest in the meantime.

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References