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Analysis of Mathematical Model of Gene Expression With Effect of Nonlinear Degradation Rate

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Abstract

In this work new scenario for the construction of original models of gene expression has been introduced and then studied theoretically and numerically considering effect of discrete time delay in the process. The dynamical behavior of the model has been studied using stability and bifurcation analysis. New findings have been presented and discussed in more details.

keywords: Gene expression model, Discrete time delay, Hopf bifurcation.

Introduction:

Protein acts as the motor for cellular processes. Gene expression is like a process that includes decoding information from DNA. It starts with synthesis of proteins. Each protein has levels of abundance within a cell and is primarily controlled by the rate of production. Specialized proteins, termed transcription factors, can be governed these production rats. A gene regulatory network is a collection of genes who manage each other's rate of expression [10, 11, 24]. In this study, we will examine into a gene regulatory network that bring about switch- like reactions, uphold memory, generate oscillations, execute logical computations

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and facilitate intercellular connection. Gene expression can be defined as dual phase mechanism. Start with, transcription, transpires when the coding is converted into a corresponding messenger RNA(mRNA). This process is executed by RNA polymerase, protein complex, then latches onto gene's promotor region, then advances into catalyzing the information of the mRNA strand from nucleotide components that is responsible for carrying out this process. Translation, the second stage of gene expression which involves paring the mRNA molecules with a proteinRNA complex that is known as ribosome. Translation involves the transfer of information; a protein which can be made by ribosome advances along the mRNA and catalyses using amino acids as building blocks. While gene regulatory networks share resemblances with metabolic networks and signal transduction pathways in terms of structure and behavior the mechanisms are very dissimilar [7, 15, 25]. Biochemical interactions within metabolic systems are possible to break down into a few fundamental chemical events. Conversely, the complex procedures which are the transcription and translation that include numerous biochemical reactions, many of which remain incompletely understood.

Although at a higher level of abstraction that the earlier topic, in this study we will develop model of gene regulatory networks using a mass action-based formalism. The gene expression descriptions mechanisms more generalized compared to earlier models of biochemical networks. In the Modeling genetic systems, the limited number of molecules included in the expression regulation adds another level of complexity.

The utilization of smoothly varying concentration values which support by continuum hypothesis, holds true only if a significant number of molecules are introduce, which results in negligible changes brought on by individual reaction events. However, proteins that affected gene expression are often found in limited quantities, typically a range of fewer. Additionally, genes are typically presented in a very low copy number [27]. Cells usually only possess a small amount of their inherent genes often just one or two. External genes introduced into bacteria cells, such as though laboratory processes are usually carried on circular DNA molecules that are called Plasmid [5, 6]. Plasmid exist in a higher number of copy's often in the several hundred. The mass-action formalism can be justified in situations with low

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molecular counts by viewing differential equation models as representations of typical behavior across a sizable population of cells [3, 14, 18, 33]. When examining cultures or tissues made up of similar cells behaving similarly, this viewpoint is helpful.

Recent studies in living organisms provide evidence that this stochastic framework can accommodate probabilistic effects that are meaningfully significant at such small scales [8, 16, 30]. studying modules with minimal architectures mediated by sRNAs could aid in the analysis of intricate networks.

Mathematical models have been used to capture pivotal phenomena for the diagnosis of serious conditions like cancer [1, 7, 23, 31]. This study centers on comprehending how interactions between a protein and two mRNAs can lead to oscillations and alter the model's dynamic behavior. Despite the advancement of our understanding of regulatory protein dynamics in biology, a field with a lengthy history dating back centuries, there remains ongoing development. The complex machinery of life is mainly driven by proteins, which arise from the intricate processes of DNA translation and transcription. Considering this we can explore how the interactions of two miRNAs given rise to a protein that possesses more energy compared to a protein resulting from the interaction of just one mRNA. Given the important role of mRNA in diagnosing severe aliments such as cancer, researchers have shown an interest of this study. While earlier research has largely focused on the interaction of a single miRNA leading to a less energetically intense protein, this study explores the potential of two miRNAs interacting. The main goal is to gain understanding the dynamics of the gene expression model, through introducing new scenario with different technique and then after that analysis the constructed model with the effect of discrete transcription time delay. The work that has been done aims to develop an understanding of gene expression processes in order to get prediction of the dynamical behavior that arise from this network. So that could help the ability to provide deep insights into network behavior. In general, the essential goal of the current thesis is to gain understanding keys feature common for many living organisms and that could help in the diagnosed and the treatment of these kind of diseases which effected by genetic factors, such as cancer and genetic disorders. In this research we start with the gene expression model. The model can be represented by Figure

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(1). The biological assumption in Figure (1) can be described as follows: in first gene the information transcribes to mRNA1 and in the second gene the information transcribes to mRNA2 as well. Then, these two mRNA interact together and translated to produce new protein. After that, we consider the effect of transcription time delay in the process; more detail will be provided in next section. Follow that, in final step we analysis the dynamical behavior of the model using stability and bifurcation analysis. Model derivation and formulation

The first step to develop any mathematical model, if it is originally from gene expression or from other back ground, we need to understand the assumption of the model and role of each parameters in it, so that can make the derivation much easier. Second step is to use law of mass action which is subject to the process. For example, in our situation some time the process is regulated and some time is unregulated, more details will be shown in the this section. In our suggestion, we will assume in two gene there is interaction between them mRNA which result in one mRNA and then this new mRNA will translation to produce one protein as shown in Fig. 1

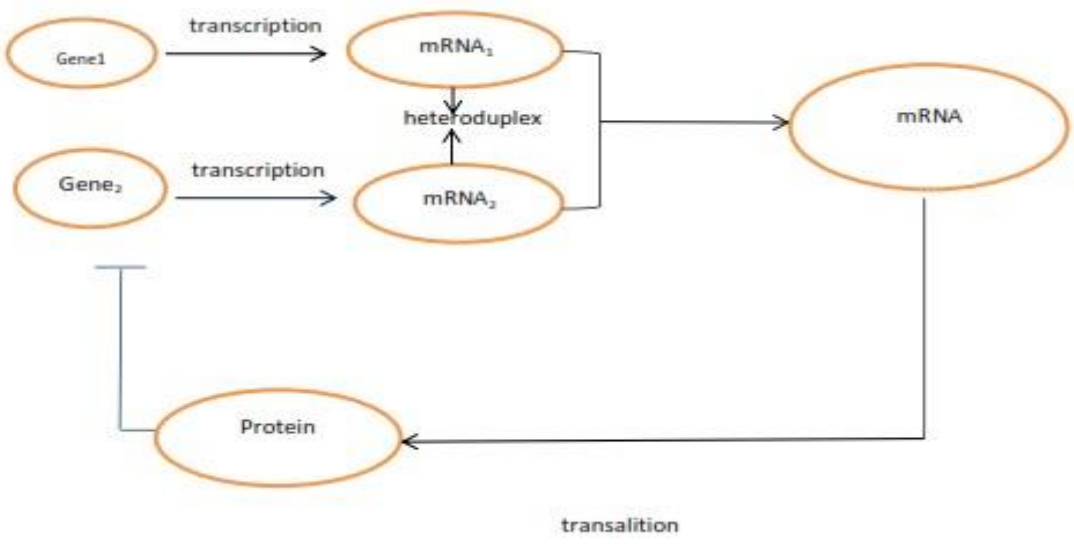

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Figure 1: Gene1 and Gene2 transcribed to mRNA1 and mRNA2 and these mRNAi ,i = 1,2 interacted together to produce new mRNA, then this mRNA translated to produce the protein.

The chemical reaction of the process can be described by

$$\begin{cases} DNA_1 \rightarrow DNA_1 + mRNA_1, \\ DNA_2 \rightarrow DNA_2 + mRNA_2, \\ mRNA_1 + mRNA_1 \rightarrow heteroduplex \\ new\ mRNA \rightarrow protein. \end{cases}$$

if the process of transcription and translation is unregulated, then we have:

$$\overset{k_1}{\rightarrow} m_1 + m_2 \overset{k_2}{\rightarrow} m \overset{k_3}{\rightarrow} P \overset{k_4}{\rightarrow},$$

Let $m_1 = m_2 = m$. The result will be

$$\overset{k_1}{\rightarrow} m + m \overset{k_2}{\rightarrow} m \overset{k_3}{\rightarrow} P \overset{k_4}{\rightarrow},$$

That leads to the following system

$$\begin{cases} \dfrac{dm}{dt} = k_1 - k_3 m - k_2 m^2, \\ \dfrac{dm}{dt} = k_3 m - k_4 p, \end{cases}$$

On the other hand, if the process is controlled, controlling *RNA* polymerase with gene-promoting sections will determine how quickly proteins are produced. Transcription factors are proteins that interact with polymerase by binding *DNA*. If the transcription factor inhibits the rate of *RNA* polymerase binding then it is called a repressor. The reaction scheme for the binding of a molecule *mRNA*, *m* to a protein *p* is given by:

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$$m + p \underset{k_2}{\overset{k_1}{\rightleftharpoons}} mp$$

This reaction can be expressed as differential equations that explain how the concetration of the three component change over time, as shown:

$$\frac{d[m]}{dt} = -k_1[m][p] + k_2[mp],$$
$$\frac{d[p]}{dt} = -k_1[m][p] + k_2[mp],$$
$$\frac{d[mp]}{dt} = -k_2[mp] + k_1[m][p],$$

at the study state

$$\frac{d[mp]}{dt} = 0,$$

we have

$$[mp] = \frac{k_1}{k_2}[m][p] = k[m][p],$$

the fractional saturation of the pool of the proteins can be defined as the fraction of binding sites. The fractional saturation(F) =(occupied binding site's number)/(total binding site's number). Then we get,

$$F = \frac{[mp]}{[m] + [mp]},$$

substitute (4) into (5) we have

$$F = \frac{[p]}{k + [p]}$$

Equation (6) is called promoter occupancy. The rate of transcription factor depends on the promoter occupancy, if the factor of transcription *P* is repressor then rate of gene expression is

$$F = \frac{1}{k + p}$$

In a basic scenario, the transcription factor binding can be represented by a function called the Hill function, which takes the following form for an arbitrary *n*:

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$$H(p) = \frac{1}{1 + kp^n},$$

when factor of the transcription is a repressor, where *n* is Hill's function the coefficient, and

$$k = \frac{k_1}{k_2}$$

Thus, in the event of nonlinear degradation in *mRNA*, the controlled process of transcription and translation of the information can be represented by the following reactions:

$$\xrightarrow{H(p)} m + m \xrightarrow{k_3} p \xrightarrow{k_2}$$

The rule can be represented mathematically as:

$$\begin{cases} \frac{dm}{dt} = H(p) - G(m) - k_3 m(t) \\ \frac{dp}{dt} = k_3 m(t) - k_4 p, \end{cases}$$

where H(p) is the Hill function, $G(m) = k_2 m^2$ is the nonlinear degradation rate, and

k_i (i =1,2,⋯ ,4) symbolize the rate constants of kinetics.

considering the effect of transcription time delay in the model, we get the following:

$$\begin{cases} \frac{dm}{dt} = \frac{1}{1 + Kp^n(t - \tau)} - G(m) - k_3 m(t) \\ \frac{dp}{dt} = k_3 m(t) - k_4 p, \end{cases}$$

Analysis of the model with nonlinear degradation and discrete time delay After constructed the new gene expression model and added discrete delay to the process, the next step is to analysis the dynamical behavior of the model using stability and bifurcation analysis. First if all, we need to find the equilibrium of the model as we can see in the next section.

1. The equilibrium point

In this section, we equating the right hand sides of equation (10) to zero

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$$0 = \frac{1}{1+Kp^n} - k_3 m - k_2 m^2 \ldots\ldots (a)$$

$$0 = k_3 m - k_4 p \ldots\ldots (b)$$

From (b) we get$m^* = \frac{k_4 P^*}{k_3}$, where p^* is the positive root of the equation:

$$f(p) = p^{n+2} + \frac{K_3^2 p^{n+1}}{K_2} + \frac{p^2}{K} + \frac{K_3^2 p}{K_2 K_4 K} - \frac{K_3^2}{K_2 K_4^2 K} = 0, n > 0$$

Since $f(0) = -\frac{K_3^2}{K_2 K_4^2 K} < 0, \bar{f}(p) > 0\ and\ \lim_p \to +\bowtie f(p) = +\bowtie$, this means that the function is an increasing function and has at least one positive root. As a result, the positive equilibrium is unique.

2. The bound of the solution of the model

In this section we will show that the solution of the equation (10) is bonded in positive invariant region.

$$\frac{dm}{dt} = \frac{1}{1+Kp^n} - K_3 m - K_2 m^2$$

$$\frac{dm}{dt} = K_3 m - K_4 p$$

Firstly, we will prove the solution of equation (10) with positive intial values cannot cross the axes,i.e stay positive

Lemma 3.1 *for any solution (m(t),p(t)) at the model* (10)*start with positive initial values* ($m(0)$, $p(0)) \in (R_+)^2$ *It will remains in* $(R_+)^2$.

Proof: *we will use proof by contradiction to prove this result.*

Let $m(t) > 0\ \forall t > 0$, *is not true. Then there is* $t_0 > 0$, *such that* $m(t_0) = 0$ *and*

$\frac{dm(t)}{dt}|_{t=t_0} < 0$. *Furthermore,* $m(t) > 0, \forall t \in [0, t_0]$

Now,

$$\frac{dm(t)}{dt}|_{t=t_0} = \frac{1}{1+kp^n(t_0)} - k_3 m(t_0) - k_2 m^2(t_0) = \frac{dm(t)}{dt}|_{t=t_0} < 0$$

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We have,

$p(t_0) < 0$, *and there exists a* $t_1 \in (0,t_0)$, *such that* $p(t_1) = 0$, *and* $\frac{dp(t)}{dt}|_{t=t_1} < 0$

Furthermore, $p(t) > 0$, *for* $t \in [0,t_1)$.

Then, $\frac{dp}{dt} = k_3 m(t_1) - k_4 p(t_1) = k_3 m(t_1) < 0, i.e. m(t_1) < 0.$

We noticed that $m(t_1) < 0$, *contradicts with* $m(t) > 0$, *for* $t \in [0,t_0)$, *since* $t_1 \in (0,t_0)$.

As a result, this assumption does not hold, namely the trajectories of the solution start with any positive solution values will stay positive for $\forall t > 0$.

Next, we will prove the solution of model (10) starts with positive intial values will be bounded by some positive constants.

Theorem 3.1 *The solution* $(m(t), p(t))$ *on* $[0,\infty)$ *of model* (10) *with initial value* $(m(0), p(0)) \in R_1^2 = [x \in R_1^2 : x_i > 0, i = 1,2]$ *is bounded i.e., there exist some positive constants, such that* $m(t) < D_1$, *and* $p(t) < D_2$ *for* $\forall t > 0$.

Proof: From the previous Lemma we know $(m(t), p(t)) \in R_1^2 = [x \in R_1^2 : x_i > 0, i = 1,2]$. *Then,*

$$\frac{dm}{dt} = \frac{1}{1+Kp^n} - K_3 m - K_2 m^2 < \frac{1}{1+Kp^n} < 1$$

It implies that there exists $D_1 > 0$, *such that* $m(t) \in [0,D_1)$ *for* $\forall t > 0$, *and from*

$$\frac{dm}{dt} = K_3 m - K_4 p < K_3 m < m < D_1$$

We know that, there exists a $D_2 > 0$, *such that* $p(t) \in [0,D_2)$ *for* $\forall t > 0$.

Therefore, we can concluded that $m(t)$ *and* $p(t)$ *are bounded.*

3. Stability analysis

An essential tool for gaining understanding of gene expression mechanisms in general is the stability analysis. Actually, we can analysis the qualitative behavior of the dynamical systems through the stability of the equilibrium points.

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4.1 Linearization and characteristic equation

The first step is to shift the equilibrium point to the origin through adding new variables: $\beta(t) = m(t) - m^*, \Gamma(t) = p(t) - p^*$

$$\frac{d\beta(t)}{dt} = \frac{1}{1 + K(\Gamma(t-\tau) + p^*)^n} - K_3(\beta(t) + m^*) - K_2(\beta(t) + m^*)^2$$

$$\frac{d\Gamma(t)}{dt} = K_3\beta(t) - K_4\Gamma(t)$$

Then, use Taylor expansion to convert the system from nonlinear to linear:

$$f(\Gamma(t-\tau), \beta(t)) = f(0,0) + f_\Gamma(0,0)\Gamma + f_\beta(0,0)\beta$$

where

$$f_\Gamma(0,0) = \frac{-nK(\Gamma(t-\tau) + p^*)^{n-1}}{(1 + K(\Gamma(t-\tau) + p^*)^n)^2} = \frac{-nK(p^*)^{n-1}}{(1 + K(p^*)^n)^2} = f_1$$

$$f_\beta(0,0) = -K_3(\beta + m^*) - K_2(\beta + m^*)^2 = -(K_3 + 2K_2m^*)$$

Therefore, system (11) becomes

$$\frac{d\beta(t)}{dt} = -f_1\Gamma(t-\tau) - (K_3 + 2K_2m^*)\beta(t)$$

$$\frac{d\Gamma(t)}{dt} = K_3\beta(t) - K_4\Gamma(t)$$

Which can written as:

$$\begin{cases} \dfrac{d\beta(t)}{dt} = -f_1\Gamma(t-\tau) - \sigma\beta(t), \\ \dfrac{d\Gamma(t)}{dt} = K_3\beta(t) - K_4\Gamma(t), \end{cases}$$

where

$$\sigma = K_3 + 2K_2m^*,$$

and

$$f_1 = \frac{nkp^{*n} - 1}{(1 + kp^{*2})}$$

The next step is to find the characteristic equation which can be obtained by substitute $\beta(t) = c_1e^{\lambda t}$, and $\Gamma(t) = c_2e^{\lambda t}$ into the equation (12); which can be written as:

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$$\lambda^2 + \lambda a_1 + a_2 = 0$$

where

$$a_1 = \sigma + K_4,$$

and

$$a_2 = \sigma K_4 + K_3 f_1 e^{-\lambda\tau}$$

4.2 Stability analysis without time delay

Firstly, will consider the stability without delay i.e. $\tau = 0$, the characteristic equation will takes the following form:

$$\lambda^2 + (\sigma + K_4)\lambda + \sigma K_4 + K_3 F_1 = 0$$

This lead to the following solution:

$$\lambda_{1,2} = \frac{-(\sigma + K_4) \pm \sqrt{(\sigma + K_4)^2 - 4(\sigma + K_4 + K_4 F_1)}}{2}$$

It can be easily to see without time delay the system has a pair of roots with negative real parts because $(\sigma + K_4) > 0$,$(\sigma K_4 + K_3 F_1) > 0$. Therefore, we conclude that the system is stable without delay.

4.3 Stability analysis with time delay

In case $\tau \neq 0$, i.e if we consider the effect of time delay in the process, the characteristic equation will takes the next form as we mentioned that previously:

$$\lambda^2 + (\sigma + K_4)\lambda + \sigma K_4 + K_3 F_1 e^{-\lambda\tau} = 0$$

Let $\lambda = iw$, is a pair imaginary root of equation (14) and then substituting it in the equation we have the following equation:

$$-w^2 + (\sigma + K_4)iw + \sigma K_4 + K_3 F_1 e^{-iw\tau} = 0$$

$$-w^2 + (\sigma + K_4)iw + \sigma K_4 + K_3 F_1 (\cos w\tau - i \sin w\tau) = 0$$

separating the real and imaginary parts we have:

$$-w^2 + \sigma K_4 + K_3 F_1 \cos w\tau = 0$$

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$$(\sigma + K_4)w - K_3F_1 - i\sin w\tau = 0.$$

Then,

$$\cos w\tau = \frac{w^2 - \sigma K_4}{K_3F_1} \equiv S$$

$$-\sin w\tau = \frac{(\sigma + K_4)w}{K_3F_1} \equiv r$$

square the above equations

$$\cos^2 w\tau = \left(\frac{w^2 - \sigma K_4}{K_3F_1}\right)^2$$

$$\sin^2 w\tau = \left(\frac{(\sigma + K_4)w}{K_3F_1}\right)^2$$

and then add them together we have:

$$G(w) \simeq w^4 + (\sigma^2 + K_4^2)w^2 + \sigma^2K_4^2 - K_3^2F_1^2 = 0$$

let

$$w^2 = u$$

we get

$$u^2 + (\sigma^2 + K_4^2)w^2 + \sigma^2K_4^2 - K_3^2F_1^2 = 0$$

The solution of the equation (16) is

$$u_{1,2} = \frac{-(\sigma^2 + K_4^2) \pm \sqrt{(\sigma^2 + K_4^2)^2 - 4\sigma^2K_4^2 + 4K_3^2F_1^2)}}{2}$$

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$$u_{1,2} = \frac{-(\sigma^2 + K_4^2) \pm \sqrt{(\sigma^2 + K_4^2)^2 + 4K_3^2F_1^2)}}{2}$$

It is clearly $u_1 < 0$ where

$$u_1 = \frac{-(\sigma^2 + K_4^2) \pm \sqrt{(\sigma^2 + K_4^2)^2 + 4K_3^2F_1^2)}}{2}$$

and $u_2 > 0$ if

$$(\sigma^2 + K_4^2) \pm \sqrt{(\sigma^2 + K_4^2)^2 + 4K_3^2F_1^2)}$$

i.e

$$\frac{\sigma K_4}{K_3} < F_1$$

so under this condition we have

$$u_2 > 0$$

Therefore, under the above condition (17) we have one positive root. In other words, the critical frequency will be

$$w^* = \sqrt{u_2}$$

Next step is it find the critical time delay, τ^*

$$\tau_j^* = \begin{cases} 1/w[\cos^{-1}(r) + 2\pi j]\,, & s \geq 0 \\ 1/w[2\pi - \cos^{-1}(r) + 2\pi j], & s < 0 \end{cases} \quad j = 0,1,2, \ldots..$$

Next step is it prove the trance veracity condition: $\frac{dRe\lambda}{d\tau}\ \tau = \tau_j^* \neq 0, j = 0,1,2, \ldots..$ From equation (14), we have:

$$2\lambda\frac{d\lambda}{d\tau} + (\sigma + K_4)\frac{d\lambda}{d\tau} + K_3K_1e^{-\lambda\tau}(-\lambda - \tau)\frac{d\lambda}{d\tau} = 0$$

Then,

$$\left(2\lambda + (\sigma + K_4) - \tau K_3F_1e^{-\lambda\tau}\right)\frac{d\lambda}{d\tau} = K_3\lambda F_1e^{-\lambda\tau}$$

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which leads to:

$$\rightarrow \left(\frac{d\lambda}{d\tau}\right)^{-1} = \frac{\left(2\lambda + (\sigma + K_4)\right)e^{-\lambda\tau} - \tau K_3 F_1}{K_3 \lambda F_1}$$

$$Re\left(\frac{d\lambda}{d\tau}\right)^{-1}_{\lambda=iw^*,\tau=\tau^*} = \frac{2w^* \cos w^*\tau^* + (\sigma + K_4)\sin w^*\tau^*}{K_3 w^* F_1}$$

$$= \frac{2w^*\left((w^*)^2 - \sigma K_4\right) + (\sigma + K_4)(\sigma + K_4)w^*}{{K_3}^2 w^* {F_1}^2}$$

$$= \frac{(2w^*)^3 + \left(\sigma^2 + {K_4}^2\right) w^*}{{K_3}^2 w^* {F_1}^2}$$

$$= \frac{4(2w^*)^3 + 2\left(\sigma^2 + {K_4}^2\right) w^*}{2{K_3}^2 w\, {F_1}^2}$$

$$= \frac{\tilde{G}(w)}{2{K_3}^2 w\, {F_1}^2} > 0$$

Then we have:

$$Re\left(\frac{d\lambda}{d\tau}\right)^{-1}_{\lambda=iw^*,\tau=\tau^*} \neq 0$$

From the previous analysis, we can obtain the following results:

Theorem 4.1 *suppose that condition (17) holds then we have the following results for the characteristic equation of system (10):*

1. *If one of the following hold then all the roots have negative real part*
   - $\tau = 0$,
   - $\tau > 0$,*and* $F_1 \leq \frac{\sigma K_4}{K_3}$,
   - $\tau \in (0, \tau_0^*)$
2. *If* $If\ F_1 > \frac{\sigma K_4}{K_3}$ *and* $\tau = \tau_j^* j = 0,1,2,\ldots$ *then we have purely imaginary roots*

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$\lambda = \pm iw,$

3. *system (1) has one root with positive real part if* $\tau \in (\tau_0, +\infty)$ *and* $F_1 > \frac{\sigma K_4}{K_3}$

Theorem 4.2 *For system (10) we have the following result*

1. *The equilibrium* (m^*, p^*) *is stable if one of the next conditions satisfies*
   - $\tau = 0$
   - $\tau > 0$ *,and* $F_1 > \frac{\sigma K_4}{K_3}$
   - $\tau \in (0, \tau_0^*)$ *and* $F_1 > \frac{\sigma K_4}{K_3}$

2. *If* $F_1 > \frac{\sigma K_4}{K_3}$ *then the equilibrium* (m^*, p^*)
   - *undergoes Hopf bifurcation at* $\tau = \tau_j^*$
   - *Is unstable of* $\tau \in (\tau_0, +\infty)$

4.4 Numerical simulation and discussion

In this section, numerical simulations has been carried out to make comparison with the theoretical analysis that has been done using Matlab code (dde23). Based on that in our simulations we choose the parameters as $k = 0.25, k_2 = 0.1, k_3 = 0.4, k_4 = 0.1$ and the Hill coefficient $n = 3$. In the results which have been discussed in the previous section, the Hopf bifurcation induced by delay happens when $\tau \in (\tau^*, \infty)$. By Theorem 4.2, the positive equilibrium is always stable in the absence of time delay, namely when $\tau = 0$. Please see Fig. 1, where we show the case for $k_2 = 0.1$; and it is also stable when time delay is less than the critical value, namely $\tau \in (0, \tau^*)$ which also shown in Fig. 1. As the delay is going up i.e increase the time delay so that passes through the critical value, a periodic solution arises from the equilibrium due to the stability change of it, see Fig. 2. Furthermore, we have been observed that the amplitude and the period of the periodic solution that has been bifurcated

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from the equilibrium get larger and larger as increasing τ, as shown in Fig. 2. Actually, we noted also the Hill coefficient or the cooperativity controls the periodic solution and the oscillation magnitudes. In other word, the amplitude and period of periodic solutions get larger as the Hill function increase as we can see from Fig. 3. This discovered may point to some method that could help on monitoring changes in the state of gene expression, which may be sign of the onset of genetic illnesses.

5. Conclusion

In this section, we try to give summaries for the work that has been done previously. In more details, new scenario has been introduced to the gene expression model with transcription discrete time delay have been constructed. We have been found that the equilibrium of the system is stable without time delay; however, with time delay the oscillation occurs when the time at it's critical value and the oscillation keep on going as the time keep up. We also noted from our simulation the amplitude and period of periodic solutions increase as increase the Hill function and this can be provided insight into the behavior of gene expression processes. Our work starts with construction of the model, which first started with introduced a nonlinear degradation term for mRNA, and then added transcription time delay to reflect the oscillatory.

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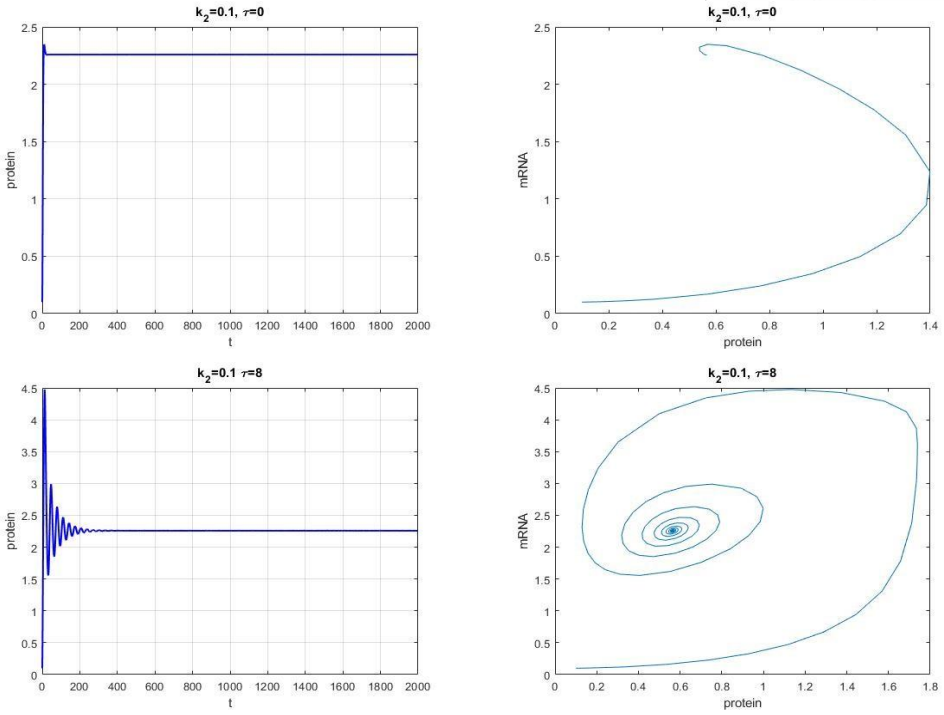

Figure 1: Time series and phase portrait of the model when k_2 = 0.1, showing stable equilibrium when time delay is zero and in case smaller than its critical value.

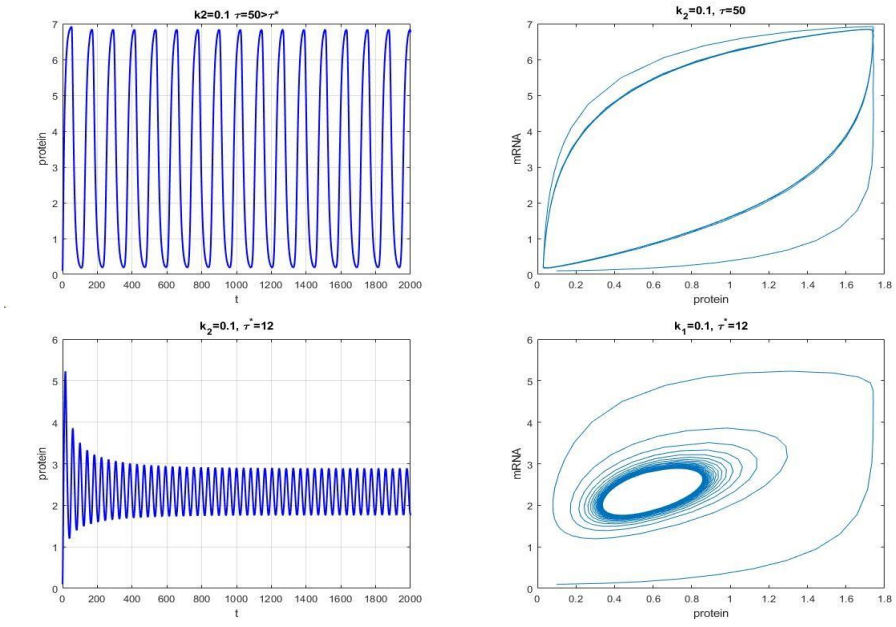

Figure 2: Time series and phase portrait of the model when k_2 = 0.1, showing unstable equilibrium when time delay is greater and at at its critical value.

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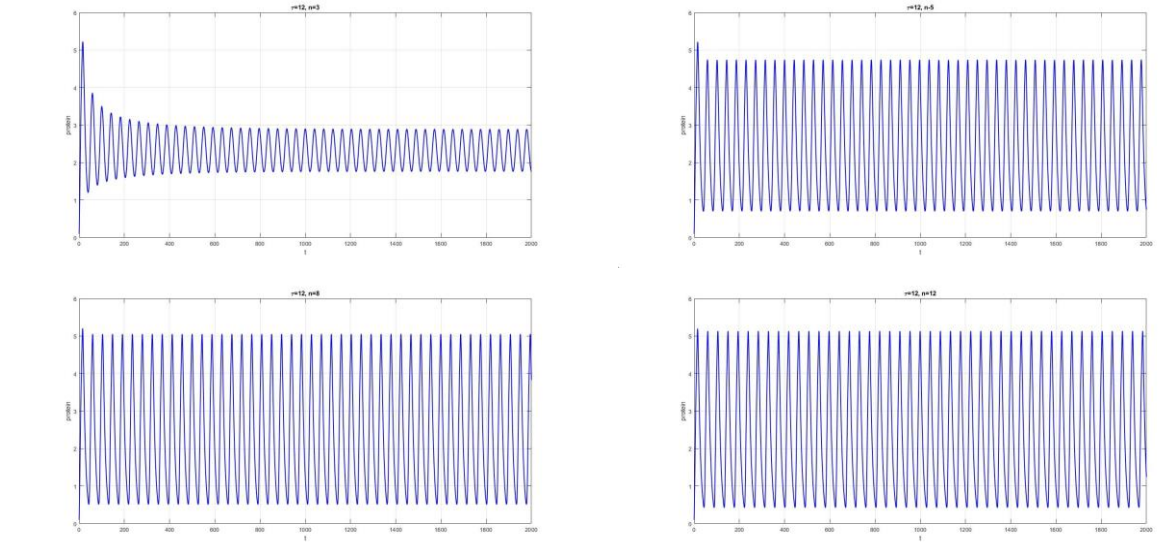

Figure 3: Different values of Hill function at the critical time delay, which shows the amplitude and period of periodic solutions.

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