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A Model for Analysis of Gene Expression in the Cell Involving Protein Degradation

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Abstract: The gene expression is responsible for the initiation sustenance and termination of various processes taking place in a cell in order to maintain the structure and the function of the cell. In the present paper, a model is proposed to analyze the gene expression in terms of temporal variation of DNA, mRNA and protein concentration along with the stability of molecular processes taking place in the cell. The model incorporates the parameters like replication, transcription, reverse transcription, translation and degradation of the protein. The model is obtained in terms of a system of differential equations along with initial conditions based on the physical and physiological conditions of the problem. The analytical solution is obtained for the model. The results have been obtained for a dataset of E. coli TJK16 strain and E. coli B/r strain, and employed to study the relationships of the parameters involved with the concentration of DNA, mRNA and protein. The asymptotic stability analysis at the equilibrium point has been performed for the molecular processes in the cell. The information generated from the model can be useful for developing the protocols for healthcare.

Keywords: differential equations, DNA, mRNA, protein, gene expression, TJK16, B/r

1. INTRODUCTION

Mathematical modeling is indispensable now-a-days which plays a vital role in better understanding the complexity of any system related to the real world. The real-world problem may arise in different fields as business, agriculture, biology, etc. Many models have been developed to unravel the complexity of the system of real-world problems [5], [16], [19]. A cell is considered as the primordial structural, functional and biological unit in all living organisms that can perform all the functions of life and can be classified as eukaryotic cell and prokaryotic cell. To understand the cell as a system, it is important to understand the molecular mechanisms of the cell. There is a nucleus in the cell which controls the structure and function of the cell. The cell nucleus contains the DNA and mRNA which controls protein synthesis [2]. During the synthesis of functional gene product protein, the genetic information in the cell flows from DNA to mRNA and mRNA to protein. For the growth of the cells, the process has different rates of gene expression in an individual cell due to the different rates of transcription and translation as per the requirements of the cell for a particular protein [1], [9]. In the eukaryotic and prokaryotic cells, the gene expression is stochastic in nature and the stochastic models can be moderated at the transcriptional and translational levels [18]. Also, it is shown experimentally that an increase in the stochasticity in the transcription process leads to an increase in cell variability for protein synthesis [3].

In the view of the central dogma, the needed information for producing protein is

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contained in DNA sequence is then decoded into mRNA and thereafter the information in mRNA molecules is transformed to produce the sequence of amino acids [7][8]. Further, the complexity of the bacterial cell along with the macromolecular composition of Salmonella typhimurium involved in the protein synthesis was unravelled and it was discovered that at a given temperature, the cellular contents of DNA, RNA and protein depends on the growth rate of bacterial cell [12]. The growth of a cell depends on the growth of its cellular contents and a complete study about cell growth and the cellular contents has been reported in the literature [4].

In the gene expression profile of temporal dynamics and spatial patterning, many mathematical models have been reported in the literature which shows how modeling plays an important role to study the molecular mechanism of cells and their function [10] [11]. A differential equation model to study the complexity of gene expression is reported in the literature by using two methods; Minimum Weight Solutions to Linear Equations (MWSLE) and Fourier Transform for Stable System (FTSS) with the set of temporal data [5]. Further, a comprehensive study is elaborated on the time delay model for gene expression. Recently, a system of differential equations on mRNA translocation in the ribosome is developed and employed to test the consistency and inconsistency of the model with different data set [19]. In a probabilistic manner, a Markov chain model of gene expression has been reported in the literature considering DNA, mRNA and protein as the states of the system [17]. A differential equation-based model for gene expression considering Michaelis-Menten's mechanism is reported in the literature to unravel the complexity of gene expression. In this study, the gene expression based on Michaelis-Menten's mechanism involving the processes replication, transcription, reverse transcription and translation has been reported. They assume that there is no degradation of proteins and obtained the analytical solution and performed the stability analysis of the model [13]. In terms of fuzzy, a fuzzy system model is reported considering functional gene products [14]. The gene expression based on Michaelis-Menten's mechanism involving the processes replication, transcription, reverse transcription and translation has been studied. The authors assume that there is no degradation of proteins and obtained the analytical solution and performed the stability analysis of the model. Recently, a delay differential equation-based model on gene expression was reported in the literature which is more realistic to understand the functional gene products [15].

In this paper, an attempt has been made to model gene expression involving protein degradation. Here, the different rates of replication, transcription, reverse transcription, translation and protein degradation of both strains TJK16 and B/r, in a single cell, are incorporated in the model. The E. coli TJK16 is a bacterial strain and due to mutationally altered control of replication initiation, all genes have a lower concentration than their wild type B/r parent. These genes produce the bulk of stable RNA and mRNA which are more active in strain TJK16 in the comparison of strain B/r. Therefore, this strain is useful for studying the variation in the concentrations of DNA, mRNA and protein in the cell. Secondly, the E. coli strain B/r, parent of strain TJK16, is also used for computing the result [6]. Initially, the DNA concentration of strains TJK16 and B/r is 25 micrograms and 10 micrograms, respectively. The exact solution is obtained for the system of differential equations. The model is proposed for both retroviruses and normal cells. The asymptotic stability of the system at the equilibrium point is also analyzed and it is demonstrated by the vector plot.

2. NOMENCLATURE

The abbreviations used in the paper are as follows:
DNA: Deoxyribonucleic acid
RNA: Ribonucleic acid
TJK16: Bacterial strain with genotype thyA deoB
B/r: Bacterial strain
E.coli: Escherichia coli

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$w(t)$: Concentration of DNA in the cell at time t (second)
$x(t)$: Concentration of mRNA in the cell at time t (second)
$p(t)$: Concentration of protein in the cell at time t (second)
k_0: Rate of replication
k_1: Rate of transcription
k_2: Rate of the reverse transcription
k_3: Rate of translation
k_4: Rate of protein degradation

3. MATHEMATICAL MODEL AND METHOD

In the present model, it is assumed that replication, transcription, reverse transcription, translation and degradation of protein are taking place in the cell. The graphical representation of the model is shown in Fig.3.1.

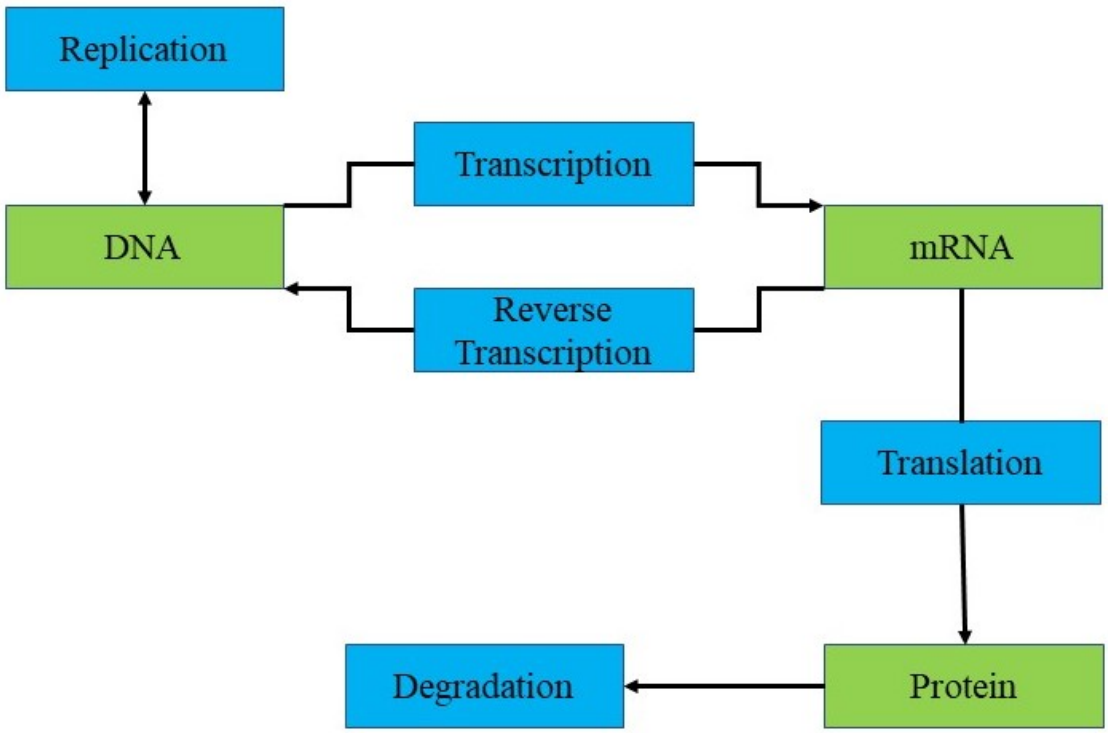

Fig. 3.1. Graphical representation of modelling of gene expressions.

The following assumptions have been made:

1. The time delay in the processes of gene expression is considered to be negligible.
2. The constant temperature is maintained so that there is no effect of temperature on replication, transcription, reverse transcription, translation and protein degradation process in the gene.
3. The constant rates of the processes of gene expression are taken which lie in [0,1].
4. A single cell is considered where replication occurs in the cell.

The Michaelis-Menten's mechanism is used to develop a differential equation-based model of gene expression. The motive to use the proposed mechanism is the applicability

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of enzyme-catalyzed (generally proteins) biochemical reactions and these enzymes (biomolecules: DNA, mRNA and protein) take place in the cell which are synthesized by ribosomes. In 1913, Michaelis-Menten proposed that the binding of the substrate (the molecule acted upon) and the enzyme is reversible and derived a kinetic model to study the kinetic behaviour of the biochemical reaction systems. The advantages of Michaelis-Menten's mechanism are simplicity and broad applicability in the field of biochemistry. The mathematical description of enzyme behaviour is an amazing tool which is useful in the analysis of enzyme activity. The mathematical model for these processes, which is based on Michaelis-Menten's mechanism, is given below [2][19]:

$$w'(t) = k_0 w(t) - k_1 w(t) + k_2 x(t) \tag{3.1}$$

$$x'(t) = k_1 w(t) - k_2 x(t) - k_3 x(t) \tag{3.2}$$

$$p'(t) = k_3 x(t) - k_4 p(t) \tag{3.3}$$

where $w(t), x(t)$ and $p(t)$ represent the concentration of DNA, mRNA and protein respectively. Also, k_0, k_1, k_2, k_3 and k_4 are rates of replication, transcription, reverse transcription, translation and degradation of protein, respectively. A sufficient condition of the stability of zero equilibrium for the system $(3.1) - (3.3)$ is that all its eigenvalues

$$\lambda_1 = -k_4,\ \lambda_2 = \frac{-A + \sqrt{\Delta}}{2},\ \lambda_3 = \frac{-A - \sqrt{\Delta}}{2} \tag{3.4}$$

have negative real parts, where $A = (-k_0 + k_1 + k_2 + k_3)$, the discriminant $\Delta = A^2 - 4(-k_0k_2 - k_0k_3 + k_1k_3)$, and $-(k_0 - k_1)(k_2 + k_3) - k_1k_2 \neq 0$. Further, in view of the stability of the proposed system, three cases are considered as

Case (a): $\Delta > 0$,

Case (b): $\Delta = 0$,

Case (c): $\Delta < 0$. In this case, we have found different positive values of Δ in the form of $0.5756, 0.9995, 0.7122, 1.0237, 2.9502$ and 1.1767 for six different copy numbers of k_0, k_1, k_2 and k_3 where the data has been taken from Table (5.1). Further, we focus on the data of Table (5.2) where the observed value of Δ is 0 for all six different copy numbers of k_0, k_1, k_2 and k_3. Thus, it is evident that the value of Δ is positive and cannot be negative in the closed interval $[0, 1]$ for all values of k_0, k_1, k_2 and k_3. Further, it is also evident that the rates of replication, transcription, reverse transcription and translation can not be negative as per the cell physiology. So, we have discarded this case.

Thus, there are five conditions for stability of the system as

1. If $\lambda_1 < 0 < \lambda_2 < \lambda_3$, then the system is unstable,
2. If $\lambda_1 < \lambda_3 < 0 < \lambda_2$, then the system is unstable,
3. If $\lambda_3 < \lambda_1 < \lambda_2 < 0$, then the system is stable,
4. If $\lambda_1 < \lambda_2 = \lambda_3 < 0$, then the system is stable,
5. If $\lambda_2 = \lambda_3 < \lambda_1 < 0$, then the system is stable.

Further, the stability of the system of linear differential equations is demonstrated. The three-dimensional vector plot of stability of the given system is shown in Fig. 3.2 and Fig. 3.3, respectively.

The points of stability obtained above are for the data set available in the literature for a particular set of conditions. The rate of these processes like replication, transcription, reverse transcription, translation and protein degradation vary in response to environmental factors and the requirement of the organism.

4. SOLUTION

Initially, it is assumed that there is some concentration of DNA in the cell and no concentration of both mRNA and protein is present in the cell. Thus, the initial conditions

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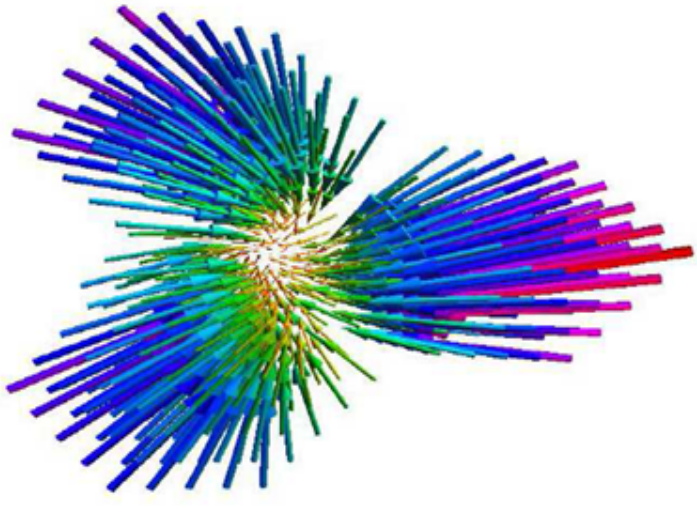

Fig. 3.2. Three-dimensional vector plot of the system of linear differential equations converging to the origin.

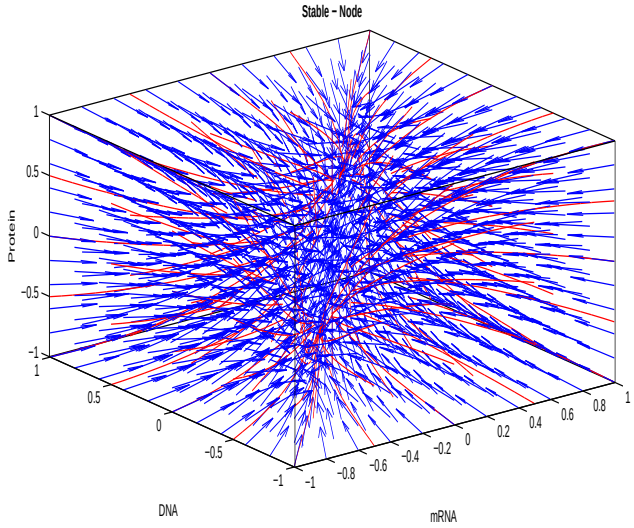

Fig. 3.3. Three-dimensional vector plot of the system of linear differential equations where arrows showing the direction (blue colour) and streamlines (red colour) converging to the equilibrium point $(0, 0, 0)$ which displays the stability of the system as a stable-node. The eigenvalues of the system are $(-0.7655, -0.1016, -0.8603)$.

for differential equations model of DNA, mRNA and protein are given below:

$$w(0) = w_0 > 0, \;\; x(0) = 0, \;\; p(0) = 0.$$

Using these initial conditions, the solution is obtained for both the cases (a) and (b) as follows:

4.1. Case (a):

When $\Delta > 0$, the concentration of DNA, mRNA and protein in the cell is expressed as

$$w(t) = \frac{w_0}{\lambda_3 - \lambda_2} \left[e^{\lambda_3 t}(\lambda_3 + k_2 + k_3) - e^{\lambda_2 t}(\lambda_2 + k_2 + k_3) \right], \tag{4.5}$$

$$x(t) = \frac{w_0 k_1}{\lambda_3 - \lambda_2}(e^{\lambda_3 t} - e^{\lambda_2 t}), \tag{4.6}$$

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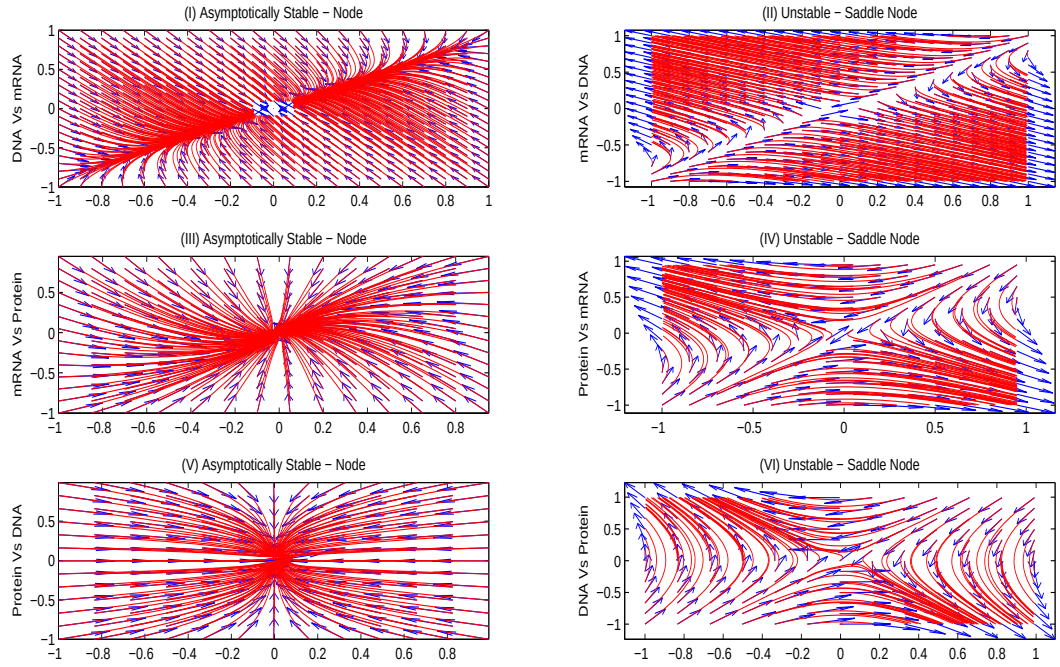

Fig. 3.4. The figures in (I): DNA Vs mRNA, (III): mRNA Vs Protein and (V): Protein Vs DNA are showing the stability behaviour as asymptotically stable-node, where arrows show the direction (blue colour) and streamlines (red colour) are converging towards the equilibrium point $(0, 0, 0)$, and their eigenvalues are $(-0.1016, -0.8603)$, $(-0.7655, -0.6259)$ and $(-0.7655, -0.3360)$ respectively. The figures in (II): mRNA Vs DNA, (IV): Protein Vs mRNA and (VI): DNA Vs Protein are showing stability behaviour as an unstable-saddle node where arrows showing the direction (blue colour) and streamlines (red colour) are diverging from the equilibrium point $(0, 0, 0)$, and the eigenvalues for these figures are $(0.8394, -0.1041)$, $(0.9009, -0.5318)$, and $(0.5072, -0.5072)$ respectively. The initial concentrations of DNA and mRNA, in figures (III), (IV), (V) and (VI), are assumed to be zero.

$$p(t) = \frac{w_0 k_1 k_3}{\lambda_2 \lambda_3 (\lambda_3 - \lambda_2)} e^{\lambda_1 t} \left[\frac{e^{(\lambda_3 - \lambda_1)t} - 1}{\lambda_3 - \lambda_1} - \frac{e^{(\lambda_2 - \lambda_1)t} - 1}{\lambda_2 - \lambda_1} \right]. \tag{4.7}$$

4.2. Case (b):

When $\Delta = 0$, the concentration of DNA, mRNA and protein in the cell is expressed as

$$w(t) = w_0 e^{\lambda_2 t} \left[1 + (\lambda_2 + k_2 + k_3)t \right], \tag{4.8}$$

$$x(t) = w_0 k_1 t e^{\lambda_2 t}, \tag{4.9}$$

$$p(t) = \frac{w_0 k_1 k_3}{\lambda_2 - \lambda_1} e^{\lambda_1 t} \left[e^{(\lambda_2 - \lambda_1)t} \left(t - \frac{1}{\lambda_2 - \lambda_1} \right) + \frac{1}{\lambda_2 - \lambda_1} \right]. \tag{4.10}$$

5. RESULTS

The rate of replication, transcription, reverse transcription, translation and degradation will depend on the circumstances and capacity of the cell depending on different conditions and therefore k_0, k_1, k_2, k_3 and k_4 can be assigned different values. The data of the strains TJK16

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and B/r is used to compute the results [6]. Generally, the values of k_0, k_1, k_2, k_3 and k_4 lie in [0, 1] [1][9]. As a special case, we assign values, given in Table (5.1), to all the above-mentioned rates such that it satisfies the condition of stability.

5.1. Case (a)

Firstly, for case (a), $\Delta > 0$, the nature of the concentration profiles of DNA, mRNA and protein is shown in the form of Fig. 5.5, 5.6, 5.7 and Table (5.1). The Fig. 5.8 (both left and

Table 5.1. Concentration profiles of six copies of DNA ($w(t)$) mRNA ($x(t)$)and protein ($p(t)$) for case (a) $\Delta > 0$ of the strain TJK16 and B/r at time $t = 180$, along with the rates, k_0, k_1, k_2, k_3 and k_4.

		Copy 1	Copy 2	Copy 3	Copy 4	Copy 5	Copy 6
$w(t)$	TJK16	1.96e-07	6.62e-16	7.89e-22	5.95e-06	4.12e-06	9.33e-08
(μg)	B/r	7.86e-08	2.65e-16	3.15e-22	2.38e-06	1.65e-06	3.73e-08
$x(t)$	TJK16	1.79e-07	6.67e-16	1.61e-21	1.10e-05	2.40e-06	1.40e-07
(μg)	B/r	7.17e-08	2.67e-16	6.44e-22	4.39e-06	9.58e-07	5.61e-08
$p(t)$	TJK16	9.97e-08	8.44e-16	2.65e-13	4.52e-06	4.95e-06	8.76e-08
(μg)	B/r	3.99e-08	3.38e-16	1.06e-13	1.81e-06	1.98e-06	3.50e-08
Replication rate	k_0	0.1425	0.3232	0.1084	0.0848	0.2981	0.2477
Transcription rate	k_1	0.4785	0.7696	0.8301	0.7630	0.7722	0.8631
R. transcri. rate	k_2	0.2568	0.2341	0.2142	0.3242	0.6690	0.3397
Translation rate	k_3	0.3691	0.7404	0.4756	0.1689	0.7452	0.3382
protein deg. rate	k_4	0.7655	0.7952	0.1869	0.4898	0.4456	0.6463
Time (sec.)		180	180	180	180	180	180

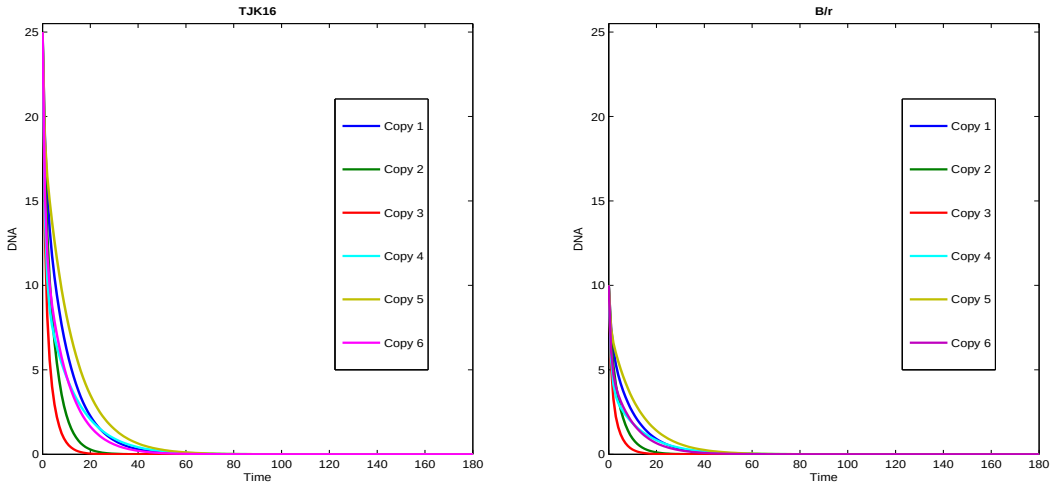

Fig. 5.5. The graph between DNA concentration (μg) and time for the strain TJK16 and B/r of the case (a) $\Delta > 0$.

right figures) shows the protein concentration profiles for the strain TJK16 and B/r of the case (a) with protein degradation and without protein degradation, respectively.

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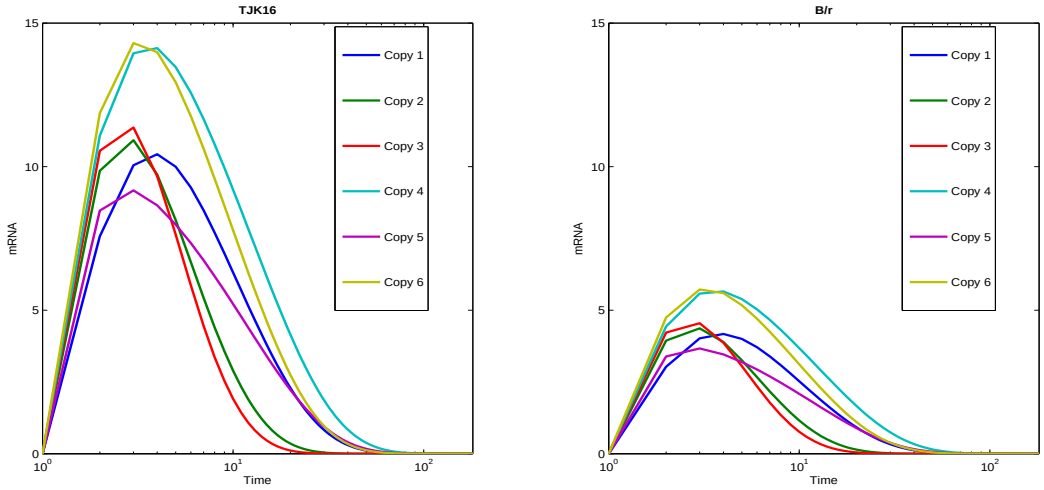

Fig. 5.6. The graph between mRNA concentration (μg) and time for the strain TJK16 and B/r of the case (a) $\Delta > 0$.

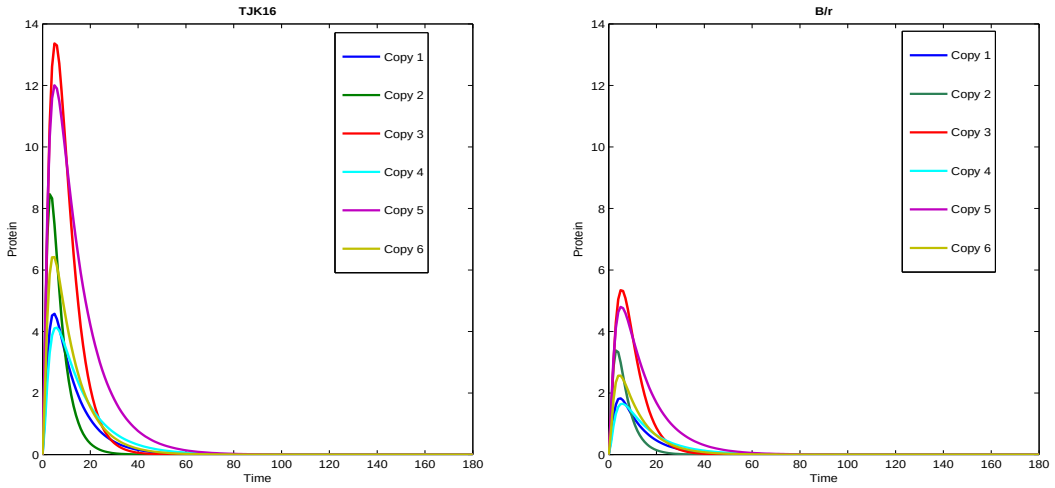

Fig. 5.7. The graph between protein concentration (μg) and time for the strain TJK16 and B/r of the case (a) $\Delta > 0$.

5.2. Case (b)

Secondly, for the case (b), $\Delta = 0$, the parameters justify this condition when the rates of replication and reverse transcription are zero and the rate of transcription and rate of translation are equal to each other. The nature of the concentration profiles of DNA, mRNA and protein are shown in the form of Fig. 5.9, 5.10, 5.11 and in Table 5.2.

The Fig. 5.12 (both left and right figures) shows the protein concentration profiles for the strain TJK16 and B/r of case (b) with protein degradation and without protein degradation, respectively.

Further, the comparison of the general behaviour of concentration profiles of DNA, mRNA and protein for case (a) and copy number 1 respectively, is shown in Fig. 5.13. Also, for case (b) and copy number 1, the comparison of the general behaviour of concentration profiles of DNA, mRNA and protein respectively, can be predicted as we adjust the value of

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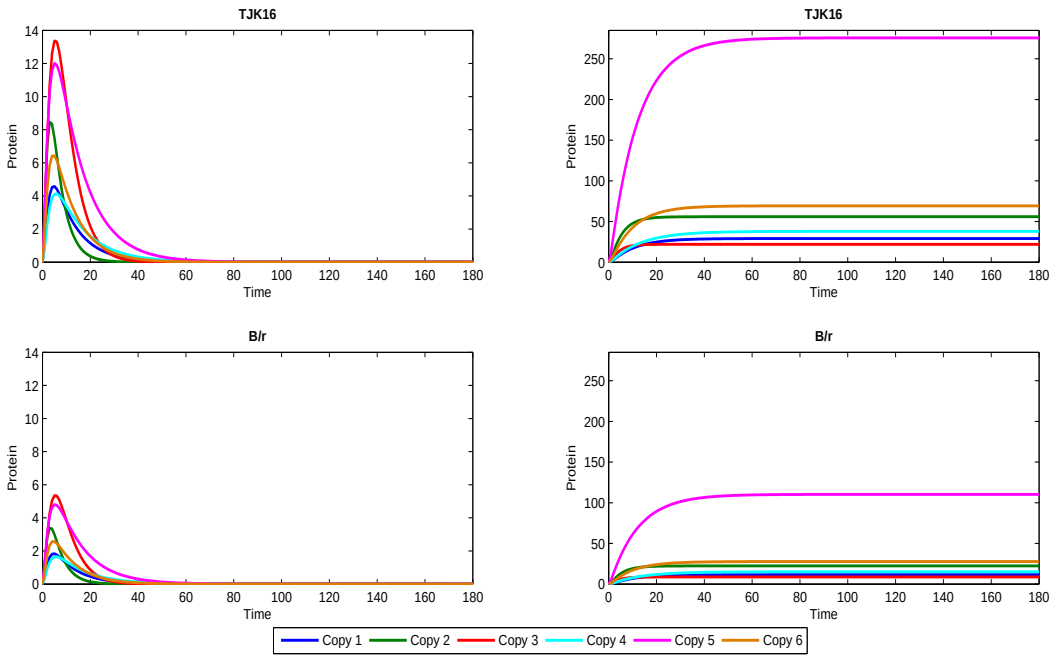

Fig. 5.8. The graph between protein concentration (μg) and time for the case (a) $\Delta > 0$ with protein degradation (both figures left) and without protein degradation (both figures right) of both strains TJK16 and B/r. This shows the comparison of protein concentrations for the strain TJK16 and B/r of the case (a).

Table 5.2. Concentration profiles of six copies of DNA ($w(t)$) mRNA ($x(t)$)and protein ($p(t)$) for the case (a) $\Delta = 0$ of the strain TJK16 and B/r at time $t = 180$, along with the rates $k_0 = k_2 = 0$ and $k_1 = k_3$ respectively, and k_4 is greater than all the rates k_0, k_1, k_2, k_3.

		Copy 1	Copy 2	Copy 3	Copy 4	Copy 5	Copy 6
$w(t)$	TJK16	4.13	0.68	0.11	0.02	3.08e-03	5.10e-04
(μg)	B/r	1.65	0.27	0.05	0.01	1.23e-03	2.04e-04
$x(t)$	TJK16	7.44	2.46	0.61	0.13	2.78e-02	5.51e-03
(μg)	B/r	2.98	0.98	0.24	0.05	1.11e-02	2.20e-03
$p(t)$	TJK16	0.78	0.51	0.19	0.06	1.45e-02	3.45e-03
(μg)	B/r	0.31	0.21	0.08	0.02	5.79e-03	1.38e-03
Replication rate	k_0	0.00	0.00	0.00	0.00	0.00	0.00
Transcription rate	k_1	0.01	0.02	0.03	0.04	0.05	0.06
R. transcri. rate	k_2	0.00	0.00	0.00	0.00	0.00	0.00
Translation rate	k_3	0.01	0.02	0.03	0.04	0.05	0.06
protein deg. rate	k_4	0.10	0.11	0.12	0.13	0.14	0.15
Time (sec.)		180	180	180	180	180	180

parameter k_3 but the change in the parameter k_3 does not follow the condition of the case (b) $\Delta = 0$.

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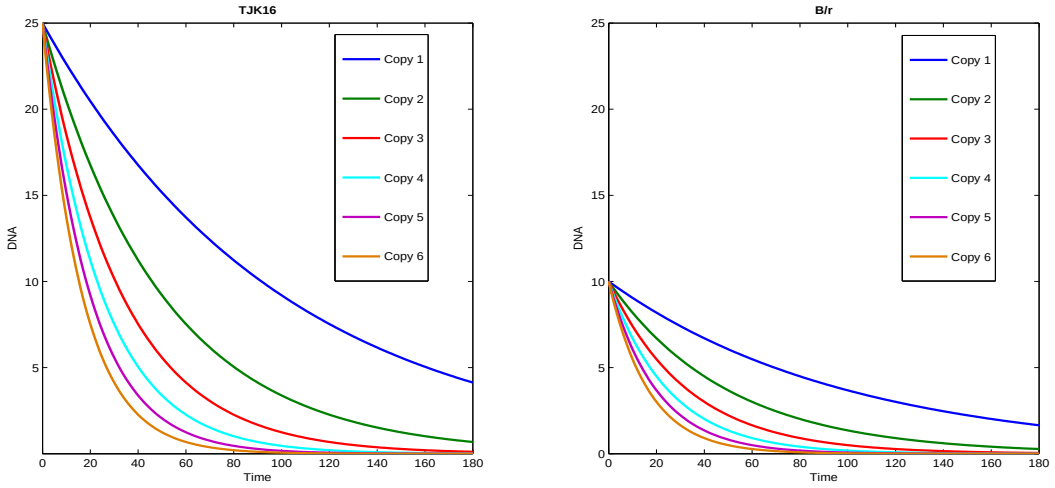

Fig. 5.9. The graph between DNA concentration (μg) and time for the strain TJK16 and B/r of the case (b) $\Delta = 0$.

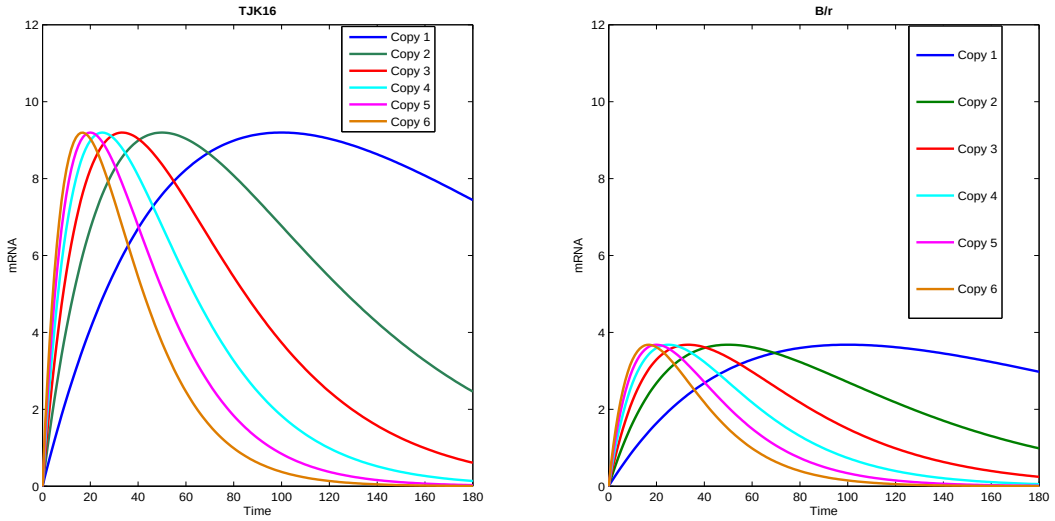

Fig. 5.10. The graph between mRNA concentration (μg) and time for the strain TJK16 and B/r of the case (b) $\Delta = 0$.

6. DISCUSSION

Figs. 5.5, 5.6 and 5.7 show the variation of the concentrations of DNA, mRNA, and protein with degradation for the strains TJK16 and B/r, respectively. In Fig. 5.5, for strain TJK16 (left figure), it is observed that the concentration of all six copy numbers of DNA decreases sharply with respect to time from $t = 0$ up to $t = 29, t = 15, t = 10, t = 30, t = 35$ and $t = 25$, respectively and thereafter, decreases gradually up to $t = 180$. Further, for strain B/r (right figure) the concentration of all six copy numbers of DNA decreases sharply with respect to time from $t = 0$ up to $t = 21, t = 11, t = 7, t = 19, t = 25$ and $t = 17$, respectively and thereafter, decreases gradually up to $t = 180$. In Fig. 5.6, for both strains, TJK16 (left figure) and B/r (right figure), the concentrations of copy number 1 of mRNA increases

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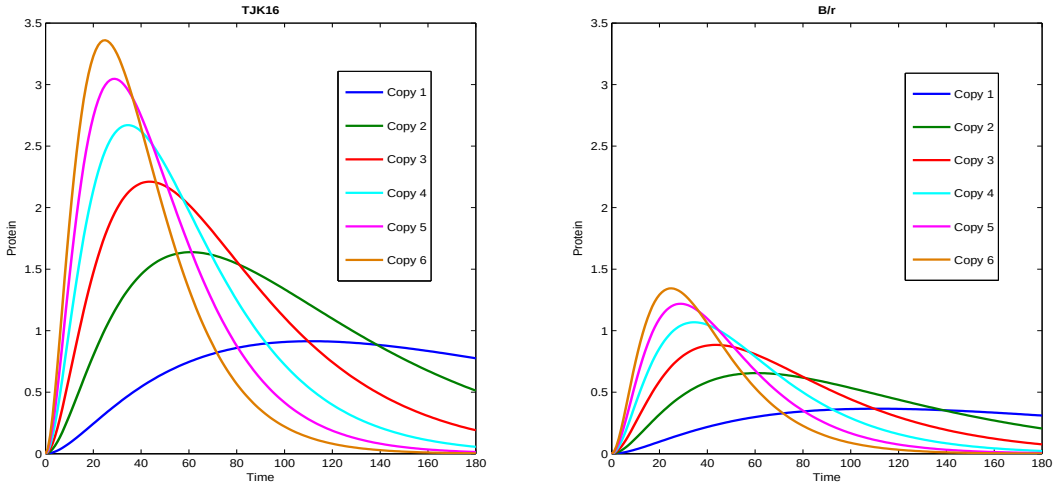

Fig. 5.11. The graph between protein concentration (μg) and time for the strain TJK16 and B/r of the case (b) $\Delta = 0$.

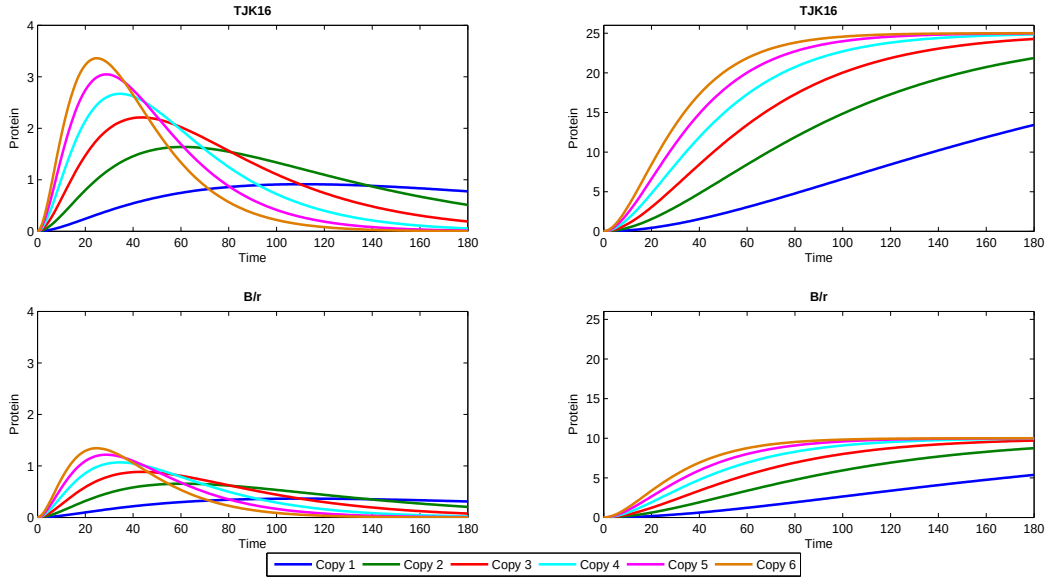

Fig. 5.12. The graph between protein concentration (μg) and time for the case (b) $\Delta = 0$ with protein degradation (both figures left) and without protein degradation (both figures right) of both strains TJK16 and B/r. This shows the comparison of protein concentrations for the strain TJK16 and B/r of case (b).

sharply from $t = 0$ up to $t = 3$, then decreases sharply from $t = 3$ up to $t = 7$ and thereafter decreases gradually up to $t = 180$ for both strains. The concentration of copy number 4 of both strains increases sharply from $t = 0$ up to $t = 3$, decreases sharply from $t = 3$ up to $t = 10$ for TJK16 and up to $t = 6$ for B/r strain, respectively, and thereafter decreases gradually up to $t = 180$ for both strains. The concentration of the remaining copy numbers 2, 3, 5 and 6 of both strains increases sharply from $t = 0$ to $t = 2$ respectively, decrease sharply from $t = 2$ to$t = 9, t = 9, t = 5$ and $t = 11$ for TJK16 (left figure), and for B/r strain (right figure), decreases sharply from $t = 2$ to $t = 9, t = 8, t = 18$ and $t = 20$, respectively and then decreases gradually up to $t = 180$ for both strains. In Fig. 5.7, for both strains TJK16 and

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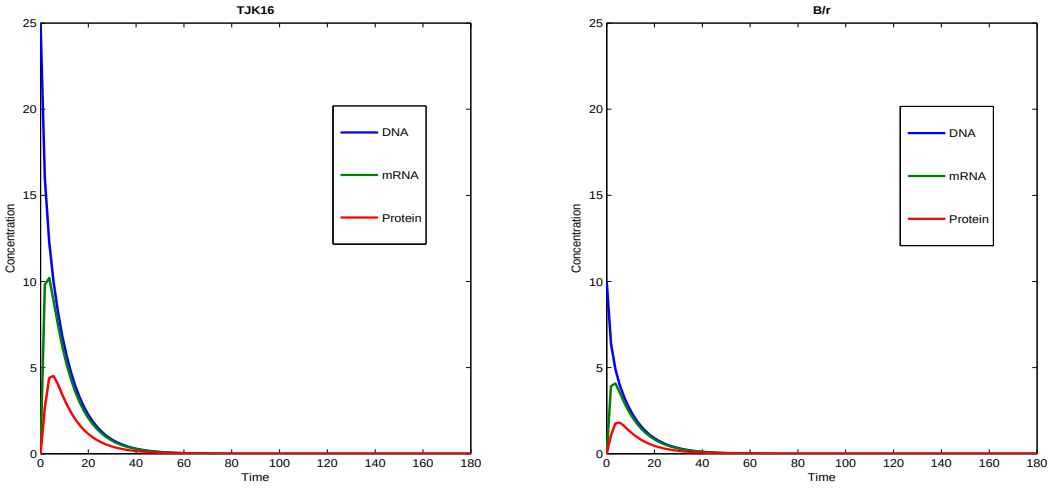

Fig. 5.13. Graphical representation of comparison of the concentrations of DNA, mRNA and protein of copy number 1 for the strain TJK16 (left figure) and B/r (right figure) of the case (a) $\Delta > 0$.

B/r, the protein concentration of copy number 2 increases from $t = 0$ up to $t = 3$, thereafter decreases sharply up to $t = 16$ for TJK16 strain and up to $t = 11$ for B/r strain, respectively and then gradually decreases up to $t = 180$ for both strains. The concentration of protein of copy number 4 increases with time from $t = 0$ to $t = 6$ for both strains, falls sharply up to $t = 26$ seconds for TJK16 strain and up to $t = 15$ for B/r strain, respectively and thereafter gradually decreases up to $t = 180$ for both strains. The concentration of protein in remaining copy numbers 1, 3, 5 and 6 increases from $t = 0$ to $t = 5$ for both strains, respectively, decrease sharply up to $t = 22, t = 25, 37$ and $t = 25$ for TJK16 strain, respectively and up to $t = 13, t = 20, 27$ and $t = 16$ for B/r strain, respectively, and then decreases gradually up to $t = 180$, respectively for both strains.

Also, in Fig. 5.8, the comparison of the concentration profile of protein with degradation and without degradation is shown for both strains TJK16 and B/r. The concentration of protein without degradation (right upper figure) of all copy numbers 1, 2, 3, 4, 5 and 6 increases sharply from $t = 0$ up to $t = 13, t = 13, t = 9, t = 21, t = 45$ and $t = 24$, respectively and thereafter the concentration of protein for all copy numbers becomes constant. In Fig. 5.8 (right upper figure), there is no fall in the protein concentration due to the absence of protein degradation. Further, for strain B/r, the concentration of protein without degradation (right lower figure) of all copy numbers 1, 2, 3, 4, 5 and 6 increases sharply from $t = 0$ up to $t = 6, t = 10, t = 4, t = 6, t = 30$ and $t = 12$, respectively and thereafter the concentration of protein for all copy numbers becomes constant. The concentration profile of protein with degradation for both strains TJK16 and B/r is shown as the left upper figure and left lower figure of Fig. 5.8, respectively and their concentration behaviour has been shown in Fig. 5.7. In this way, the concentration of all six copy numbers first increases sharply and thereafter decreases sharply and then decrease gradually up to $t = 180$, respectively. This is due to the presence of protein degradation which reduces the protein concentration.

Figs. 5.9, 5.10 and 5.11 show the variation of the concentrations of DNA, mRNA, and protein with degradation for the strains TJK16 and B/r, respectively. In Fig. 5.9, the DNA concentration of copy number 1 decreases sharply from $t = 0$ up to $t = 180$ for strain TJK16 (left figure). A similar behaviour in the concentration of the strain B/r (right figure) is found for copy number 1. The DNA concentration of remaining copy numbers decrease sharply from $t = 0$ up to $t = 127, t = 108, t = 82, t = 66$ and $t = 54$, respectively for TJK16 and up to $t = 160, t = 107, t = 80, t = 64$ and $t = 53$ for strain B/r, respectively and thereafter decreases gradually up to $t = 180$, respectively for both strains. In Fig. 5.10, for both

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strains TJK16 (left figure) and B/r (right figure), the mRNA concentration of copy number 1 increases sharply from $t = 0$ up to $t = 100$ and up to $t = 101$, respectively and then decreases gradually up to $t = 180$ for both strains. The mRNA concentration of remaining copy numbers of both strains increases sharply from $t = 0$ up to $t = 50, t = 33, t = 25, t = 20$ and $t = 17$, respectively and up to $t = 51, t = 34, t = 26, t = 21$ and $t = 18$, respectively and thereafter decrease sharply up to $t = 167, t = 160, t = 120, t = 96$ and $t = 80$, respectively and up to $t = 128, t = 120, t = 90, t = 72$ and $t = 60$, respectively and then decreases gradually up to $t = 180$ for both strains. In Fig. 5.11, for both strains TJK16 (left figure) and B/r (right figure), the protein concentration of copy number 1 increases sharply from $t = 0$ up to $t = 45$ and up to $t = 21$, respectively and then increasing gradually up to $t = 112$ and up to $t = 85$, respectively and thereafter decreases gradually up to $t = 180$ for both strains. The concentration of copy number 2 of both strains increases sharply from $t = 0$ up to $t = 61$ and up to $t = 42$, respectively and decreases sharply up to $t = 180$, respectively for both strains. The protein concentration of remaining copy numbers of both strains increase sharply from $t = 0$ up to $t = 44, t = 35, t = 29$ and $t = 25$, respectively and up to $t = 44, t = 35, t = 30$ and $t = 26$, respectively and thereafter decrease sharply up to $t = 106, t = 89, t = 77$ and $t = 68$, respectively and up to $t = 104, t = 100, t = 76$ and $t = 65$, respectively and then gradually decrease up to $t = 180$, respectively for both strains.

Also, in Fig. 5.12, the comparison of the concentration profile of protein with degradation and without degradation is shown for both strains TJK16 and B/r. The concentration of protein in the absence of protein degradation (right upper figure) of copy numbers 1 and 2 increases from $t = 0$ up to $t = 180$, respectively. The concentration of remaining copy numbers increases sharply from $t = 0$ up to $t = 122, t = 105, t = 84$ and $t = 70$, respectively and thereafter increases gradually up to $t = 180$, respectively. There is no decrease in the concentration profiles of all six copy numbers of protein due to the absence of protein degradation. Further, for strain B/r, the concentration of protein without degradation (right lower figure) of copy numbers 1 and 2 increases from $t = 0$ up to $t = 180$, respectively. The concentration of remaining copy numbers increases sharply from $t = 0$ up to $t = 101, t = 76, t = 61$ and $t = 50$, respectively and thereafter increases gradually up to $t = 180$, respectively. The concentration profile of protein with degradation for both strains TJK16 and B/r is shown as the left upper figure and left lower figure of Fig. 5.13, respectively and their concentration behaviour has been discussed in Fig. 5.11. The concentration profiles of protein first increase sharply and thereafter decrease sharply and then decrease gradually. This happens due to the presence of protein degradation. Also, in Fig. 5.12, the variation in the concentration profile of protein of both strains is observed due to the variation in the rates of replication, transcription, reverse transcription and protein degradation.

Further, Fig. 5.13 shows the graphical representation of comparison of the concentrations of DNA, mRNA and protein of both strains and also shows the variation in the concentration profiles of DNA, mRNA and protein with respect to time in presence of protein degradation for case (a). DNA concentration decreases with time, mRNA concentration increases gradually with time and thereafter decreases gradually with time and the protein concentration increases gradually with time and thereafter decreases gradually with time. The same behaviour is obtained for all copy numbers in Figs. 5.5, 5.6 and 5.7 with the same variations in the concentration level of DNA, mRNA and protein for both strains TJK16 and B/r.

The information generated from these cases gives us an idea about the range of rate of processes for which the system or the cell will have normal functions and beyond this range indicate the impairment of the function of the cell due to some abnormal conditions like diseases or due to limited capacity of the cellular processes responding to changes in environmental factors. The results obtained here are in agreement with the biological facts.

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7. CONCLUSION

A model on gene expression, in terms of variations of DNA, mRNA and protein concentration in the cell, is proposed and successfully employed for the strains TJK16 and B/r to analyze the dynamic behavior of DNA, mRNA and protein concentration in the presence and absence of protein degradation. The model has been successfully demonstrated for the normal cell as well as retroviruses. In absence of protein degradation, the protein concentration goes on increasing and the system will become unstable and burst, but the results are contrary to this under certain conditions. Thus, it is concluded from the results that the cell exerts a beautiful control on the process of replication, transcription, reverse transcription and translation in absence of protein degradation in order to meet the condition of stability and avoid the condition of system burst. In the presence of protein degradation, the behaviour of the system will depend on the rates of protein degradation and translation which in turn depends on transcription and availability of DNA by replication. It is concluded that in the cell initially when there is no protein concentration there is no question of degradation and therefore the replication, transcription, reverse transcription and translation will lead to rise in protein concentration in the first few seconds and when the protein becomes available in the cell the degradation starts thereby reducing the protein concentration which has grown in the cell in the initial few seconds. This degradation process decreases the protein concentration sharply and after some time the translation and degradation are in equilibrium thereby making the protein concentration constant in a steady state.

Further, it is observed from the results that the DNA concentration decreases sharply for the initial few seconds due to transcription into mRNA taking place in the cell. This process brings a sharp rise in mRNA concentration for the initial few seconds and then due to translation into protein this mRNA concentration decreases sharply which approaches constant value gradually after some time. The difference in the temporal concentration profiles for different copy numbers is observed due to different rates of replication, transcription, reverse transcription, translation and protein degradation for each copy number. The proposed model gives us better insights of the coordinated mechanism of DNA, mRNA and protein concentration in the cell leading to gene expression. Also, the equilibrium points of the system are carried out and the condition of stability and instability of the system has been identified with the help of this model, which gives us a better insight into the range of rate of processes for which the cell will have normal function and the limit beyond which, the cell will have impaired functions due to any abnormality like diseases or abnormal environmental conditions. Such models can be developed to study the gene expression behavior for different strains under different environmental conditions and for various diseases. The information generated from such models can be useful to biomedical scientists for developing protocols for the diagnosis and treatment of diseases.

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