



Research article**A consistent discrete-time counterpart of a gene regulatory network with three time delays****A. M. A. Abo-Bakr^{1,*} and Mohamed Biomy^{2,*}**¹ Department of Mathematics and Computer Science, Faculty of Science, Alexandria University, Alexandria, Egypt² Department of Management Information Systems, College of Business and Economics, Qassim University, Buraydah 51452, Saudi Arabia*** Correspondence:** Email: ali.abobakr@alexu.edu.eg; m.biomy@qu.edu.sa.

Abstract: In this paper, we develop a discrete-time counterpart of a gene regulatory network with three discrete delays which remains fully consistent with its continuous-time counterpart. We begin by showing that standard discretization methods can lead to inconsistencies with the delay parameters $\tau_i \rightarrow 0$, $i = 1, 2, 3$. In order to address this, the proposed construction is based on a suitable transformation combined with a nearly exact discretization scheme, which is specifically designed to construct a consistent discrete-time model. This approach overcomes the limitations inherent in existing discretization methods for systems involving time delays. We investigate fundamental properties of the obtained discrete system, including positivity of solutions, consistency in the zero-delay limit case, and the occurrence of Neimark–Sacker (NS) bifurcation. For comparison, the same model is discretized using the Euler method, demonstrating that it fails to preserve essential dynamical features of the original delayed system. Numerical simulations are presented to support the theoretical findings and to illustrate the advantages of the proposed discretization framework.

Keywords: delay; discretization; nonlinear systems; mathematical model; bifurcation**Mathematics Subject Classification:** 37N25, 37N30, 34D35, 34D05, 39A28

1. Introduction

Genes and proteins interact through highly interconnected biological networks that coordinate cellular activities and ensure the proper functioning of living organisms [1]. Gene expression is the fundamental process through which genetic information is translated into functional gene products, playing a critical role in regulating the growth, development, morphology, and physiological characteristics of plants and animals [2]. Investigating gene expression from a theoretical perspective

not only deepens our understanding of fundamental gene functions but also provides valuable mathematical insights for biomedical research and clinical applications [3].

The activity of a gene is rarely independent. Instead, the expression of one gene can regulate, and be regulated by, other genes and their products, resulting in a complex network of regulatory interactions known as a gene regulatory network (GRN) [4, 5]. Analyzing these regulatory pathways and the underlying principles of gene expression serves as a crucial gateway to uncovering fundamental biological mechanisms [2]. GRNs coordinate numerous cellular processes, including growth, differentiation, and development, by controlling interactions among genes and biomolecules. Consequently, studying GRNs provides a systematic framework for understanding intracellular regulatory mechanisms, predicting cellular behavior, and explaining how groups of genes cooperate to regulate gene expression. Moreover, GRNs have become an important area of systems biology because they provide valuable insights into disease mechanisms and support the diagnosis and treatment of complex disorders, including cancer, inflammation, and immune-related diseases [6–9].

Gene expression primarily consists of two major sequential stages: Transcription and translation. During transcription, DNA-dependent RNA polymerases synthesize messenger RNA (mRNA) from DNA templates under the modulation of various transcription factors. The resulting mRNA serves as the blueprint for protein synthesis during translation, which constitutes the final phase of gene expression. Following translation, the synthesized proteins can translocate back into the nucleus to suppress the transcription of their own coding genes. This forms a negative feedback mechanism known as feedback repression [2], where regulatory proteins bind to the promoter region of their respective genes to homeostatically inhibit further mRNA production.

These feedback inhibition and repression mechanisms provide a robust biological foundation for constructing dynamic mathematical models of cellular regulation. A critical question in these models is whether molecular regulatory processes involve oscillatory behavior. Extensive experimental evidence demonstrates that cellular processes are intrinsically rhythmic or periodic, driven by biological clocks and timing mechanisms [10]. From a theoretical viewpoint, the combination of negative feedback loops coupled with intrinsic time delays within molecular circuits strongly suggests that many molecular species in cells naturally undergo sustained, undamped oscillations [11].

Goodwin [12] pioneered the study of negative feedback in gene expression, simulating the differential equations governing enzyme synthesis via feedback inhibition to demonstrate the emergence of nonlinear oscillations. Later, Mackey [13] connected physiological diseases with bifurcation dynamics, identifying a broad class of dynamical diseases where systems within normal physiological boundaries exhibit pathological behavior due to altered periodic or nonperiodic dynamics. Because biological processes such as transcription, RNA splicing, translation, post-translational modification, and intracellular transport require a finite amount of time, explicit time delays must be incorporated into gene expression models to achieve a realistic description of biological systems [3].

It is well-recognized that many natural processes in biology involve time delays [14–16]. Because biological processes involved in gene expression, including transcription, RNA splicing, translation, post-translational modification, and intracellular transport, require a finite amount of time, incorporating time delays into mathematical models is essential for accurately representing gene regulation [3]. The original Goodwin model assumes instantaneous regulatory processes and adopts a Hill coefficient equal to one. However, Griffith [14] demonstrated that a high Hill coefficient ($n > 8$) is

strictly required to sustain limit-cycle oscillations in this formulation, a requirement widely criticized as biologically unrealistic. To lower the required Hill coefficient to realistic levels and better represent physical reality, researchers introduced explicit time delays into the regulatory processes. A prominent variant of the delayed Goodwin model investigated in [3] is formulated as follows:

$$\begin{aligned}\frac{dx_1(t)}{dt} &= -\alpha x_1(t) + \frac{1}{1 + x_3^n(t - \tau_1)}, \\ \frac{dx_2(t)}{dt} &= -\beta x_2(t) + x_1(t - \tau_2), \\ \frac{dx_3(t)}{dt} &= -\gamma x_3(t) + x_2(t - \tau_3),\end{aligned}\tag{1.1}$$

where $x_1(t)$, $x_2(t)$, and $x_3(t)$ denote the concentrations at time t of a specific gene mRNA, its corresponding protein (Protein 1), and a transcriptional inhibitor (Protein 2, typically the activated form of the protein), respectively. The positive parameters α , β , and γ represent the rate constants for the biological degradation and clearance of mRNA, functional protein, and repressor protein, respectively. The Hill coefficient n characterizes the cooperativity of transcriptional repression at the gene promoter. Furthermore, the system incorporates three distinct non-negative time delays to account for the finite duration of sequential intracellular processes: $\tau_1 > 0$ represents the transcriptional delay required for RNA polymerase movement, transcript elongation, and primary mRNA processing; $\tau_2 > 0$ denotes the translational delay associated with mRNA nuclear export, ribosomal translation, and protein folding; and $\tau_3 > 0$ is the post-translational activation delay, capturing post-translational modifications (e.g., phosphorylation) and the nuclear translocation of the repressor protein back to the gene promoter.

In practice, Model (1.1) is widely applicable to the study of circadian rhythms. In this context, a clock gene mRNA (x_1) is translated into a functional protein (x_2), which subsequently drives the production of a transcriptional inhibitor (x_3). This inhibitor represses further mRNA synthesis, closing the negative feedback loop. Biologically, transcription, translation, and molecular activation operate independently; thus, their associated time delays are not necessarily equal [3].

Continuous-time (CT) formulations of GRNs have been extensively investigated [17–19]. More recently, however, increasing attention has been devoted to discrete-time (DT) models [5, 20–22].

1.1. Motivation and formulation

To the best of our knowledge, the vast majority of existing studies on the discretization of delayed gene expression and GRN models rely on the classical Euler method to derive DT counterparts [5, 20–22]. Although Euler's method is simple and widely used, it suffers from several well-known drawbacks, particularly when applied to delayed systems [23].

Another notable deficiency is that, as the delay parameters tend to zero, the characteristic equation obtained from the resulting DT delayed model does not reduced to that of the discretized nondelay system. This inconsistency undermines the reliability of the discretization procedure and may lead to incorrect dynamical conclusions.

To illustrate this issue, consider the following delayed genetic model studied in [21]:

$$\begin{aligned}\frac{dX(t)}{dt} &= \frac{n_1 n_2}{n_2 + Y(t - \tau)^2} - n_3 X(t), \\ \frac{dY(t)}{dt} &= n_4 X(t) - n_5 \frac{Y(t)}{n_6 + Y(t)}.\end{aligned}\quad (1.2)$$

After imposing several assumptions and transformations, the authors in [21] applied Euler's discretization scheme and obtained the following DT system:

$$\begin{cases} \tilde{x}(n+1) = (1 - \tau h n_3) \tilde{x}(n) + \frac{\tau h n_1 n_2}{n_2 + \tilde{y}(n-d)^2}, \\ \tilde{y}(n+1) = \tau h n_4 \tilde{x}(n) + \tilde{y}(n) - \tau h n_5 \frac{\tilde{y}(n)}{n_6 + \tilde{y}(n)}, \end{cases}\quad (1.3)$$

where $h = 1/d$, and d is a positive integer.

However, when the delay parameter τ approaches zero, System (1.3) does not yield the expected DT representation of the corresponding CT model without delays. This discrepancy already indicates a structural inconsistency in the discretization process.

Furthermore, linearizing System (1.3) at its equilibrium point gives the characteristic equation

$$\lambda^{d+2} + a_1 \lambda^{d+1} + a_2 \lambda^d + a_3 = 0, \quad (1.4)$$

where

$$\begin{aligned}a_1 &= (\tau h b_1 + \tau h n_3) - 2, \quad a_2 = (1 - \tau h b_1)(1 - \tau h n_3), \quad a_3 = 2\tau^2 h^2 b_2, \\ b_1 &= \frac{n_5 n_6}{(n_6 + y^*)^2}, \quad b_2 = \frac{n_1 n_2 n_4 y^*}{(n_2 + y^{*2})^2}.\end{aligned}$$

It is evident that, as $\tau \rightarrow 0$, the characteristic Eq (1.4) does not reduce to that of the discretized nondelay model.

A final observation is that almost all existing studies on the discretization of gene expression and/or GRN models consider systems with at most one discrete delay. However, biological processes often involve multiple time delays arising from different regulatory mechanisms, making models with multiple discrete delays more realistic and biologically relevant.

Motivated by the above observations, we consider in this paper the Goodwin model with three delays given by (1.1). To address the identified inconsistency, we introduce an appropriate variable substitution that enables the construction of a consistent DT analog of System (1.1). Instead of Euler's method, we employ the nearly exact discretization scheme (NEDS) [24], which is specifically designed to preserve the qualitative and spectral properties of the underlying CT system.

In Section 2, we derive a DT model corresponding to System (1.1) using the proposed discretization approach. Section 3 is devoted to the analysis of the dynamical properties of the resulting DT system and to demonstrating its consistency with the original CT model as the delay parameters tend to zero. Finally, numerical simulations are presented to validate the theoretical results and to highlight the failure of classical discretizations in capturing the true dynamics of System (1.1).

2. The discretization processes

In the preceding section, it was shown that standard approximations suffer from structural inconsistencies in the zero-delay limit and frequently introduce spurious numerical artifacts. In this section, we demonstrate that, in contrast to existing discrete-time regulatory models based on such schemes, the proposed discretization scheme—which combines a suitable variable transformation with NEDS—is specifically designed to construct a consistent DT model.

In this work, consistency between CT and DT models is twofold:

1. Structural consistency: In the zero-delay case, the discrete-time system and its characteristic polynomial reduce exactly to the discretized counterpart of the original nondelayed continuous system.
2. Dynamical consistency: The discrete model preserves the qualitative dynamics of the continuous model for any step size $a > 0$.

Here, the proposed variable transformation resolves the structural inconsistency, and the NEDS ensures dynamical consistency.

2.1. The NEDS method

Here, we briefly recall the NEDS proposed by Kwessi et al. [24]. This method extends and refines Mickens' nonstandard finite difference scheme (NSFD) technique [25, 26], offering a more consistent and reliable approach for discretizing differential equations.

To begin, consider a standard ordinary differential equation (ODE):

$$\frac{dy}{dt} = f(y(t)), \quad (2.1)$$

where $f(y)$ is a real-valued function of y .

A function f is said to be of type T_1 if it can be written as $f(y) = \alpha y + g(y)y + c$, and of type T_2 if it takes the form $f(y) = \alpha y - g(y)y + c$, where $g(y)$ is a nonlinear function without linear terms, $\alpha > 0$, and c is any real number.

The following principles are introduced in [24] to apply the NEDS to Eq (2.1):

- P1: dy/dt is discretized as

$$\frac{y_{t+1} - y_t}{\phi(\beta)}, \quad (2.2)$$

where $\phi(\beta) = \beta + O(\beta^2)$ as $\beta \rightarrow 0^+$.

- P2: For f being T_1 or T_2 , define

$$\phi(\beta) = \begin{cases} \frac{e^{\alpha\beta} - 1}{\alpha}, & \text{if } f \text{ is } T_1, \\ \frac{e^{\alpha\beta} - 1}{\alpha}, & \text{if } f \text{ is } T_2. \end{cases} \quad (2.3)$$

This gives the discretized equation

$$y_{t+1} = \begin{cases} e^{\alpha\beta} y_t + \phi(\beta)[g(y_t)y_t + c], & \text{if } f \text{ is } T_1, \\ \frac{e^{\alpha\beta} y_t + \phi(\beta)c}{1 + \phi(\beta)g(y_t)}, & \text{if } f \text{ is } T_2. \end{cases} \quad (2.4)$$

2.2. Discretization of Eq (2.5)

The following delayed Goodwin model with Hill coefficient $n = 2$ was studied in [11] and is given by:

$$\begin{aligned}\frac{dx_1(t)}{dt} &= -\alpha x_1(t) + \frac{1}{1 + x_3^2(t - \tau_1)}, \\ \frac{dx_2(t)}{dt} &= -\beta x_2(t) + x_1(t - \tau_2), \\ \frac{dx_3(t)}{dt} &= -\gamma x_3(t) + x_2(t - \tau_3).\end{aligned}\tag{2.5}$$

In [11], the variables are changed in a manner similar to that in [27]. Sun et al. [11] introduced $u_1(t) = x_1(t - \tau_2 - \tau_3)$, $u_2(t) = x_2(t - \tau_3)$ and $u_3(t) = x_3(t)$, so that Eq (1.1) becomes

$$\left. \begin{aligned}\frac{du_1(t)}{dt} &= -\alpha u_1(t) + \frac{1}{1 + u_3^2(t - \tau)}, \\ \frac{du_2(t)}{dt} &= -\beta u_2(t) + u_1(t), \\ \frac{du_3(t)}{dt} &= -\gamma u_3(t) + u_2(t),\end{aligned}\right\}\tag{2.6}$$

where $\tau = \tau_1 + \tau_2 + \tau_3$.

We now introduce a substitution that enables the construction of a DT analogue of System (2.6) while preserving consistency with its CT formulation. A key advantage of this substitution is that it guarantees exact reduction to the discretized non-delay system when the combined delay $\tau = \tau_1 + \tau_2 + \tau_3$ vanishes. This property is essential for ensuring the reliability of the discretization scheme.

Suppose that $\tau, a \in \mathbb{R}$ and $l \in \mathbb{Z}^+ \cup \{0\}$ satisfy $a > 0$, $\tau = al$. Then, $\tau = 0 \iff l = 0$. Hence, Eq (2.6) becomes

$$\left. \begin{aligned}\frac{du_1(t)}{dt} &= -\alpha u_1(t) + \frac{1}{1 + u_3^2(t - al)}, \\ \frac{du_2(t)}{dt} &= -\beta u_2(t) + u_1(t), \\ \frac{du_3(t)}{dt} &= -\gamma u_3(t) + u_2(t).\end{aligned}\right\}\tag{2.7}$$

Let the step size be a and $t_n = an$, $n = 0, 1, 2, \dots$. Applying the NEDS [24] to the System (2.7), we obtain

$$\left. \begin{aligned}u_1(n+1) &= e^{-a\alpha} u_1(n) + \frac{\phi_1}{1 + u_3^2(n-l)}, \\ u_2(n+1) &= e^{-a\beta} u_2(n) + \phi_2 u_1(n), \\ u_3(n+1) &= e^{-a\gamma} u_3(n) + \phi_3 u_2(n),\end{aligned}\right\}\tag{2.8}$$

where $\phi_1 = (1 - e^{-a\alpha})/\alpha$, $\phi_2 = (1 - e^{-a\beta})/\beta$ and $\phi_3 = (1 - e^{-a\gamma})/\gamma$. $u_1(n)$, $u_2(n)$, and $u_3(n)$ are approximate values of $u_1(an)$, $u_2(an)$, and $u_3(an)$, respectively.

3. Properties of Eq (2.8)

Here, we investigate several fundamental properties of the discretized System (2.8), including positivity of solutions, existence of fixed points, local stability, and bifurcation behavior. Particular attention is devoted to verifying the consistency of the discrete model with the original continuous-time System (1.1) as the delay parameters tend to zero.

The following theorem proves the positivity of the approximate solutions generated by applying the NEDS to System (1.1).

Theorem 1. *Let the initial conditions for System (2.8) satisfy $u_1(0) > 0$, $u_2(0) > 0$, and $u_3(\theta) > 0$ for all $\theta \in \{-l, -l+1, \dots, 0\}$. Then, the approximate solution generated by System (2.8) remains strictly positive for all $n \geq 1$.*

Proof. Because $\alpha, \beta, \gamma, a > 0$, it follows that $e^{-a\alpha}, e^{-a\beta}, e^{-a\gamma} > 0$ with the coefficients $\phi_1, \phi_2, \phi_3 > 0$.

Hence, for the system

$$\left. \begin{aligned} u_1(n+1) &= e^{-a\alpha}u_1(n) + \frac{\phi_1}{1+u_3(n-l)^2}, \\ u_2(n+1) &= e^{-a\beta}u_2(n) + \phi_2u_1(n), \\ u_3(n+1) &= e^{-a\gamma}u_3(n) + \phi_3u_2(n), \end{aligned} \right\} \quad (3.1)$$

the right-hand side of each equation consists entirely of the sum and quotient of strictly positive terms. Consequently, the state variables at the left-hand side of (3.1) remain strictly positive for every positive initial state. $\square$

To discuss the existence of fixed points, the following lemma is introduced.

Lemma 1. [28] *System (1.1) possesses a unique positive equilibrium point $E(u_1^*, u_2^*, u_3^*)$,*

$$\begin{cases} u_1^* = \beta\gamma u_3^*, \\ u_2^* = \gamma u_3^*, \\ u_3^* = \sqrt[3]{\frac{1}{2\alpha\beta\gamma} + \sqrt{\frac{1}{4(\alpha\beta\gamma)^2} + \frac{1}{27}}} + \sqrt[3]{\frac{1}{2\alpha\beta\gamma} - \sqrt{\frac{1}{4(\alpha\beta\gamma)^2} + \frac{1}{27}}}. \end{cases}$$

Theorem 2. *Similar to System (1.1), the DT system (2.8) has the unique positive fixed point $E(u_1^*, u_2^*, u_3^*)$.*

Proof. To find the fixed points of (2.8), we solve the following system of equations:

$$\left. \begin{aligned} u_1 &= e^{-a\alpha}u_1 + \frac{\phi_1}{1+u_3^2}, \\ u_2 &= e^{-a\beta}u_2 + \phi_2u_1, \\ u_3 &= e^{-a\gamma}u_3 + \phi_3u_2, \end{aligned} \right\} \quad (3.2)$$

which can be reduced to the form

$$\left. \begin{aligned} 0 &= -\alpha u_1 + \frac{1}{1+u_3^2}, \\ 0 &= -\beta u_2 + u_1, \\ 0 &= -\gamma u_3 + u_2. \end{aligned} \right\} \quad (3.3)$$

Equation (3.3) is exactly the equation that gives the fixed points of the system (1.1). $\square$

Let $u_1(n) = u_1^* + U_1(n)$, $u_2(n) = u_2^* + U_2(n)$, $u_3(n) = u_3^* + U_3(n)$, where $U_i(n)$ denotes a small perturbation about E , $i = 1, 2, 3$.

Then the linearized system about E is

$$\left. \begin{aligned} U_1(n+1) &= e^{-a\alpha} U_1(n) - \frac{2\phi_1 u_3^*}{(1+u_3^{*2})^2} U_3(n-l), \\ U_2(n+1) &= e^{-a\beta} U_2(n) + \phi_2 U_1(n), \\ U_3(n+1) &= e^{-a\gamma} U_3(n) + \phi_3 U_2(n). \end{aligned} \right\} \quad (3.4)$$

Hence, the characteristic polynomial associated with E^* of System (2.8) is

$$A(\lambda) = \lambda^l (\lambda - e^{-a\alpha})(\lambda - e^{-a\beta})(\lambda - e^{-a\gamma}) + \frac{2\phi_1 \phi_2 \phi_3 u_3^*}{(1+u_3^{*2})^2}. \quad (3.5)$$

The following theorem shows that we have derived a consistent discretized system.

Theorem 3. *The discrete System (2.8) and the DT formulation of the nondelay CT system coincide when $\tau = \tau_1 + \tau_2 + \tau_3$ approaches zero.*

Proof. From Lemma 1, $\tau = 0$ if and only if $l = 0$ for all $a > 0$. Hence, at $\tau = 0$, the System (2.8) becomes

$$\left. \begin{aligned} u_1(n+1) &= e^{-a\alpha} u_1(n) + \frac{\phi_1}{1+u_3^{*2}}, \\ u_2(n+1) &= e^{-a\beta} u_2(n) + \phi_2 u_1(n), \\ u_3(n+1) &= e^{-a\gamma} u_3(n) + \phi_3 u_2(n). \end{aligned} \right\} \quad (3.6)$$

The above system is the resulting DT system by applying NEDS on the nondelay CT system related to (1.1) and given by

$$\left. \begin{aligned} \dot{x}_1(t) &= -\alpha x_1(t) + \frac{1}{1+x_3^2(t)}, \\ \dot{x}_2(t) &= -\beta x_2(t) + x_1(t), \\ \dot{x}_3(t) &= -\gamma x_3(t) + x_2(t). \end{aligned} \right\} \quad (3.7)$$

Furthermore, the characteristic Eq (3.5) as $\tau = \tau_1 + \tau_2 + \tau_3 \rightarrow 0$ becomes

$$(\lambda - e^{-a\alpha})(\lambda - e^{-a\beta})(\lambda - e^{-a\gamma}) + \frac{2\phi_1 \phi_2 \phi_3 u_3^*}{(1+u_3^{*2})^2} = 0, \quad (3.8)$$

which is the same characteristic equation of the system (3.6) at the same fixed point. $\square$

It has been established in [11] that the continuous-time delayed model (1.1) may experience a Hopf bifurcation when parameters vary. Because the Neimark–Sacker (NS) bifurcation serves as the discrete-time analog of the Hopf bifurcation, it is therefore of interest to investigate the occurrence of such bifurcations in the discretized system (2.8). For this purpose, we employ a standard criterion for detecting NS bifurcations in high-dimensional discrete systems.

Lemma 2. [29] *Consider an n -dimensional discrete dynamical system $X_{k+1} = f_\eta(X_k)$, where $\eta \in \mathbb{R}$ is a bifurcation parameter. Let X^* be a fixed point of f , and the characteristic polynomial for the Jacobian matrix $J(X^*) = (d_{ij})_{n \times n}$ of n -dimensional map $f_\eta(X_k)$ is given by:*

$$P_\eta(\lambda) = \lambda^n + d_1 \lambda^{n-1} + \cdots + d_{n-1} \lambda + d_n, \quad (3.9)$$

where $d_i = d_i(\eta, u)$, $i = 1, 2, 3, \dots, n$, and u is a control parameter or another parameter to be determined. Let $\Delta_i^\pm(\eta, u) = \det(M_1 \pm M_2)$, $i = 1, 2, 3, \dots, n$, where

$$M_1 = \begin{bmatrix} 1 & d_1 & d_2 & \dots & d_{i-1} \\ 0 & 1 & d_1 & \dots & d_{i-2} \\ 0 & 0 & 1 & \dots & d_{i-3} \\ \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & \dots & 1 \end{bmatrix}, \quad M_2 = \begin{bmatrix} d_{n-i+1} & d_{n-i+2} & \dots & d_{n-1} & d_n \\ d_{n-1+2} & d_{n-i+3} & \dots & d_n & 0 \\ \dots & \dots & \dots & \dots & \dots \\ d_{n-1} & d_n & \dots & 0 & 0 \\ d_n & 0 & \dots & 0 & 0 \end{bmatrix}.$$

Furthermore, the following conditions are satisfied:

1. $\Delta_{n-1}^-(\eta_o, u) = 0$, $\Delta_{n-1}^+(\eta_o, u) > 0$, $P_{\eta_o}(1) > 0$, $(-1)^n P_{\eta_o}(-1) > 0$, $\Delta_i^\pm(\eta_o, u) > 0$. $i = n-3, n-5, \dots, 1$ (or 2, when n is even or odd, respectively).
2. $\left[\frac{d(\Delta_{n-1}^-(\eta, u))}{d\eta} \right]_{\eta=\eta_o} \neq 0$.
3. Nonresonance condition: $\cos(2\pi/k) \neq \psi$, where $k = 3, 4, 5, \dots$ and $\psi = -1 + 0.5P_{\eta_o}(1)\Delta_{n-3}^-(\eta_o, u)/\Delta_{n-2}^+(\eta_o, u)$.

Then, NS bifurcation occurs at η_o .

Employing Lemma 2, we obtain explicit conditions characterizing the emergence of an NS bifurcation in System (2.8). If $l = 1$, then Eq (2.8) gives the following discrete system:

$$\left. \begin{aligned} u_1(n+1) &= e^{-a\alpha} u_1(n) + \frac{\phi_1}{1+u_3(n-1)^2}, \\ u_2(n+1) &= e^{-a\beta} u_2(n) + \phi_2 u_1(n), \\ u_3(n+1) &= e^{-a\gamma} u_3(n) + \phi_3 u_2(n), \end{aligned} \right\} \quad (3.10)$$

which can be rewritten as

$$\left. \begin{aligned} u_1(n+1) &= e^{-a\alpha} u_1(n) + \frac{\phi_1}{1+v(n)^2}, \\ u_2(n+1) &= e^{-a\beta} u_2(n) + \phi_2 u_1(n), \\ u_3(n+1) &= e^{-a\gamma} u_3(n) + \phi_3 u_2(n), \\ v(n+1) &= u_3(n), \end{aligned} \right\} \quad (3.11)$$

and we have the following result.

Theorem 4. Let $\mu \in \{\tau, \alpha, \beta, \gamma, a\}$ be a bifurcation parameter of System (3.11). Assume that at $\mu = \mu_0$, the following conditions hold:

- (C1) $A(1) > 0$, $(-1)^4 A(-1) > 0$, $B_1^+(\mu_0) > 0$, $B_1^-(\mu_0) > 0$, $B_3^+(\mu_0) > 0$, and $B_3^-(\mu_0) = 0$;
- (C2) $\left. \frac{dB_3^-(\mu)}{d\mu} \right|_{\mu=\mu_0} \neq 0$;
- (C3) $\cos\left(\frac{2\pi}{k}\right) \neq \psi(\mu_0)$, for $k \in \{3, 4, 5, \dots\}$, where $\psi(\mu_0) = -1 + \frac{0.5 A(1) B_1^-(\mu_0)}{B_2^+(\mu_0)}$.

Then, as the parameter μ passes through the critical threshold μ_0 , the fixed point $E(u_1^*, u_2^*, u_3^*, v^*)$ of System (3.11) loses its stability, and a Neimark–Sacker bifurcation occurs at $\mu = \mu_0$.

Proof. At E , the System (3.11) has the following characteristic polynomial:

$$A(\lambda) = \lambda^4 + c_1 \lambda^3 + c_2 \lambda^2 + c_3 \lambda + c_4 = 0, \quad (3.12)$$

where $c_1 = -(e^{-a\alpha} + e^{-a\beta} + e^{-a\gamma})$, $c_2 = e^{-a(\alpha+\beta)} + e^{-a(\alpha+\gamma)} + e^{-a(\beta+\gamma)}$, $c_3 = -e^{-a(\alpha+\beta+\gamma)}$, and $c_4 = 2\phi_1\phi_2\phi_3u_3^*/(1+u_3^{*2})^2$.

From (3.12), we have

$$A(1) = 1 + c_1 + c_2 + c_3 + c_4, \quad (3.13)$$

$$(-1)^4 A(-1) = 1 - c_1 + c_2 - c_3 + c_4. \quad (3.14)$$

Moreover, define the quantities $B_1^\pm$ and $B_3^\pm$ as follows:

$$B_1^+ = 1 + c_4, \quad (3.15)$$

$$B_1^- = 1 - c_4. \quad (3.16)$$

The quantity B_2^+ is defined by

$$B_2^+ = \det \begin{pmatrix} 1 + c_3 & c_1 + c_4 \\ c_4 & 1 \end{pmatrix}, \quad (3.17)$$

which can be expanded as

$$B_2^+ = 1 + c_3 - c_1 c_4 - c_4^2. \quad (3.18)$$

The quantity B_3^+ is defined by

$$B_3^+ = \det \begin{pmatrix} 1 + c_2 & c_1 + c_3 & c_2 + c_4 \\ c_3 & 1 + c_4 & c_1 \\ c_4 & 0 & 1 \end{pmatrix}, \quad (3.19)$$

which yields

$$B_3^+ = 1 + c_2 + c_4 - c_4^2 - c_2 c_4^2 - c_4^3 - c_1 c_3 + c_1^2 c_4 + c_1 c_3 c_4. \quad (3.20)$$

Similarly, B_3^- is defined by

$$B_3^- = \det \begin{pmatrix} 1 - c_2 & c_1 - c_3 & c_2 - c_4 \\ -c_3 & 1 - c_4 & c_1 \\ -c_4 & 0 & 1 \end{pmatrix}, \quad (3.21)$$

which can be expanded as

$$B_3^- = 1 - c_2 - c_4 + 2c_2 c_4 - c_4^2 - c_2 c_4^2 + c_4^3 + c_1 c_3 - c_1^2 c_4 + c_1 c_3 c_4. \quad (3.22)$$

The proof follows immediately from Lemma 2. $\square$

4. Numerical simulations

The numerical simulations reported below are provided to corroborate and validate the findings established in Sections 2 and 3.

The values of $A(1)$, $(-1)^4 A(-1)$, $B_1^\pm$, $B_3^\pm$ at $\alpha = 1$, $\beta = 0.15$, and $\gamma = 0.4$ and different values of $\tau = \tau_1 + \tau_2 + \tau_3$ are shown in Table 1. From the table, we can see that at $\tau = 3$, the values of $A(1)$, $(-1)^4 A(-1)$, $B_1^\pm$, and $B_3^\pm$ are all positive, but at $\tau = 3.1155$, all values remain positive except B_3^- which becomes approximately equal to zero. Then, by Theorem 4, at the critical value $\tau = 3.1155$, the fixed point loses its stability and the System (3.11) undergoes an NS bifurcation.

Table 1. Values of $A(1)$, $(-1)^4 A(-1)$, B_1^+ , B_1^- , B_3^+ , and B_3^- before and at the bifurcation point.

τ	$A(1)$	$(-1)^4 A(-1)$	B_1^+	B_1^-	B_3^+	B_3^-
3	0.6519	2.6482	1.4112	0.5888	0.9634	0.0177
3.1155	0.6885	2.6218	1.4344	0.5656	0.9393	$3.7498 * 10^{-6}$

Let $\alpha = 1$, $\beta = 0.15$, $\gamma = 0.4$. The numerical simulations shown in Figure 1 confirm the above analytical result. The bifurcation diagram in Figure 1(a) illustrates that the fixed point $E = (0.1454, 0.9696, 2.4240, 2.4240)$ remains stable for $\tau < 3.1155$, whereas instability emerges as τ crosses this threshold. Moreover, for the parameter values $\tau = 3$, $\alpha = 1$, $\beta = 0.15$, $\gamma = 0.4$, the phase portrait in Figure 1(b) confirms the stability of the fixed point $E = (0.1454, 0.9696, 2.4240, 2.4240)$. In contrast, when $\tau = 3.1155$, a closed invariant curve begins to form, as depicted in Figure 1(c).

Further increasing the parameter τ to $\tau = 3.2$ and $\tau = 3.3$, as shown in Figure 1(d),(e), respectively, results in a progressive enlargement of the invariant curve. This qualitative change in the system's dynamics is characteristic of an NS bifurcation, marking the transition from a stable equilibrium to oscillatory behavior on a closed invariant set.

To explicitly verify the transversality and spectral conditions for the Neimark–Sacker bifurcation at the critical threshold $\tau = \tau_c = 3.1155$, we have the characteristic polynomial given by

$$A(\lambda) = \lambda^4 + c_1 \lambda^3 + c_2 \lambda^2 + c_3 \lambda + c_4 = 0,$$

where $c_1 \approx -1.229158$, $c_2 \approx 0.354228$, $c_3 \approx -0.007997$, and $c_4 \approx 0.432332$.

Solving $A(\lambda) = 0$ by MATLAB (using the standard QR algorithm with shifts) yields the four characteristic roots:

$$\lambda_{1,2}(\tau_c) = 0.584109 \pm i 0.811675 \implies |\lambda_{1,2}(\tau_c)| = \sqrt{(0.584109)^2 + (0.811675)^2} = 1.000000. \quad (4.1)$$

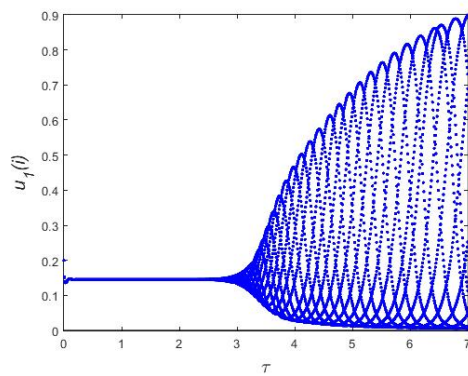
$$\lambda_{3,4}(\tau_c) = 0.030470 \pm i 0.656381 \implies |\lambda_{3,4}(\tau_c)| = \sqrt{(0.030470)^2 + (0.656381)^2} = 0.657088 < 1. \quad (4.2)$$

Furthermore, the numerical evaluation of the transversality derivative gives:

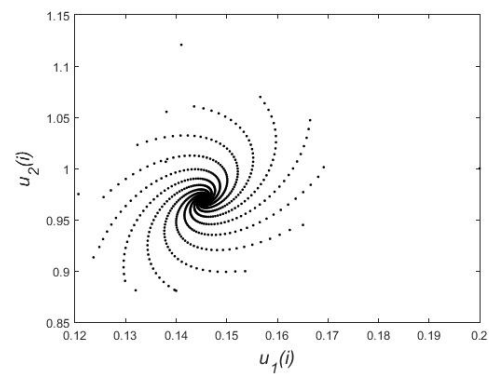
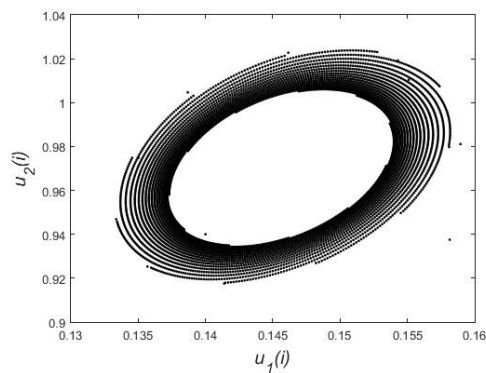
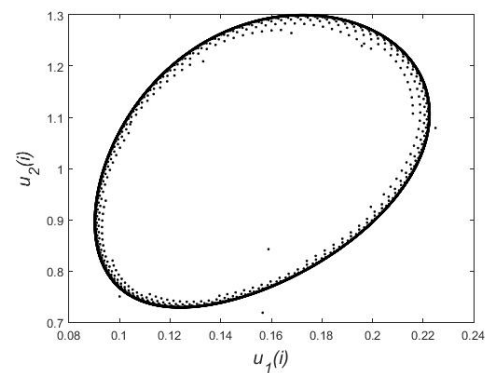
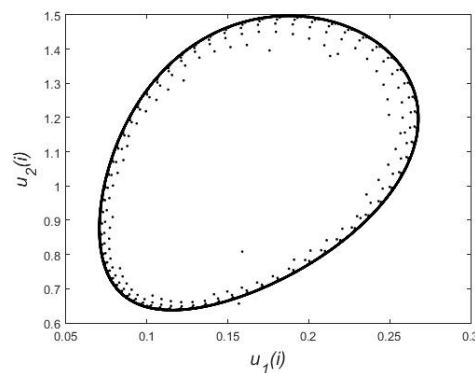
$$\left. \frac{d|\lambda_{1,2}|}{d\tau} \right|_{\tau=\tau_c} \approx 0.148261 > 0. \quad (4.3)$$

Because $\left. \frac{d|\lambda_{1,2}|}{d\tau} \right|_{\tau=\tau_c} \neq 0$, the simple complex-conjugate pair of critical eigenvalues crosses the unit circle transversely with nonzero positive speed as τ increases through τ_c , fully confirming the transversality condition required for the occurrence of an NS bifurcation.

Remark. In the numerical bifurcation analysis, we set $l = 1$, so that the relation $\tau = al$ gives $a = \tau$. Consequently, the reported NS bifurcation corresponds to a one-parameter family of discrete-time systems in which the combined delay and the discretization step size vary simultaneously. Therefore, this result establishes an NS bifurcation of the parameterized DT system and does not, by itself, establish a corresponding Hopf bifurcation of the original CT delayed model.



(a) Bifurcation diagram

(b) $\tau_1 + \tau_2 + \tau_3 = 3$ (c) $\tau_1 + \tau_2 + \tau_3 = 3.1155$ (d) $\tau_1 + \tau_2 + \tau_3 = 3.2$ (e) $\tau_1 + \tau_2 + \tau_3 = 3.3$ **Figure 1.** Simulations of System (3.11) at $\alpha = 1$, $\beta = 0.15$, $\gamma = 0.4$.

4.1. Discretization of System (2.6) by Euler's method

Now, we apply Euler's method to System (2.6) and demonstrate that the resulting DT model may fail to reproduce the qualitative properties of the original CT system. Following standard practice in the literature, we introduce the time-scaling transformation

$$U_i(t) = u_i(\tau t), \quad i = 1, 2, 3$$

under which System (2.6) can be rewritten as

$$\begin{aligned} \frac{dU_1(t)}{dt} &= \tau \left[-\alpha U_1(t) + \frac{1}{1 + U_3^2(t-1)} \right], \\ \frac{dU_2(t)}{dt} &= \tau \left[-\beta U_2(t) + U_1(t) \right], \\ \frac{dU_3(t)}{dt} &= \tau \left[-\gamma U_3(t) + U_2(t) \right], \end{aligned} \quad (4.4)$$

where $\tau = \tau_1 + \tau_2 + \tau_3$.

Applying the forward Euler method to System (4.4) with step size $h = 1/m$, where m is a positive integer, yields the DT system

$$\begin{aligned} U_1(n+1) &= h\tau \left[-\alpha U_1(n) + \frac{1}{1 + U_3^2(n-m)} \right] + U_1(n), \\ U_2(n+1) &= h\tau \left[-\beta U_2(n) + U_1(n) \right] + U_2(n), \\ U_3(n+1) &= h\tau \left[-\gamma U_3(n) + U_2(n) \right] + U_3(n). \end{aligned} \quad (4.5)$$

For $m = 1$, System (4.5) can be rewritten as the following four-dimensional map:

$$\begin{cases} U_1(n+1) = h\tau \left[-\alpha U_1(n) + \frac{1}{1 + U_3^2(n-1)} \right] + U_1(n), \\ U_2(n+1) = h\tau \left[-\beta U_2(n) + U_1(n) \right] + U_2(n), \\ U_3(n+1) = h\tau \left[-\gamma U_3(n) + U_2(n) \right] + U_3(n), \\ V(n+1) = U_3(n). \end{cases} \quad (4.6)$$

If the delay parameters vanish, that is, if $\tau_1 = \tau_2 = \tau_3 = 0$, and consequently, $\tau = 0$, System (4.6) reduces to

$$\begin{cases} U_1(n+1) = U_1(n), \\ U_2(n+1) = U_2(n), \\ U_3(n+1) = U_3(n), \\ V(n+1) = U_3(n). \end{cases} \quad (4.7)$$

It is evident that System (4.7) cannot be regarded as a meaningful DT analog of the corresponding nondelayed CT system (3.7).

To further illustrate this shortcoming, we fix the parameter values $\alpha = 1$, $\beta = 0.15$, $\gamma = 0.4$, for which System (4.6) admits the fixed point $E = (0.1454, 0.9696, 2.4240, 2.4240)$.

Treating τ as a bifurcation parameter, numerical simulations (see Figure 2) show that the solution becomes unbounded for certain parameter ranges. This unreal behavior confirms that the Euler-discretized System (4.6) fails to capture the qualitative dynamics of the original CT model (2.6).

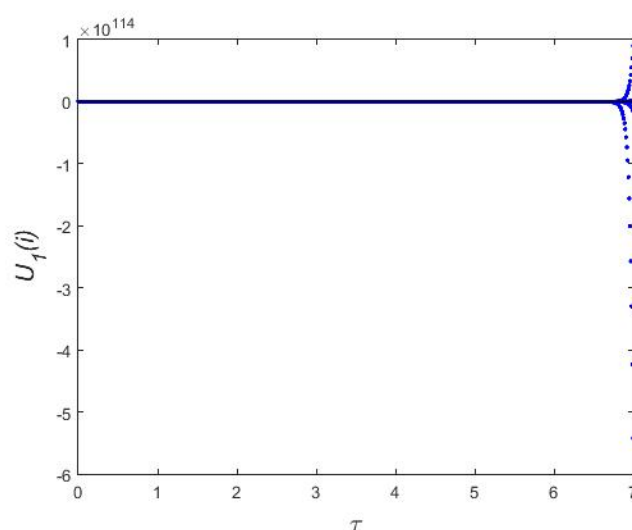


Figure 2. Bifurcation diagram of (4.6) at $\alpha = 1$, $\beta = 0.15$, $\gamma = 0.4$.

Table 2 provides a quantitative single-iteration numerical comparison ($n = 0 \rightarrow n = 1$) between System (2.8) induced by the proposed scheme and the system (4.5) induced by Euler's method at $\alpha = 2.0$, $\beta = 0.15$, $\gamma = 0.4$, and $\tau = a = l = m = 1.0$, where all initial states are set equal to 1. As shown, standard Euler discretization fails to maintain physical reality at the first iteration step ($u_1(1) = -0.5 < 0$), whereas the proposed scheme strictly guarantees positivity.

Table 2. Single-iteration numerical comparison between Systems (2.8) and (4.5).

Iteration / Quantity	Symbol	System (2.8)	System (4.5)
First iteration state 1	$u_1(1)$	0.3515	-0.5000
First iteration state 2	$u_2(1)$	1.7893	1.8500
First iteration state 3	$u_3(1)$	1.4945	1.6000
Positivity status		Preserved ($u_i(1) > 0$)	Failed ($u_1(1) < 0$)

5. Conclusions

In this work, we developed a discrete-time counterpart of a gene regulatory network with three discrete delays that remains consistent with the underlying continuous-time model. The proposed construction is based on a suitable variable transformation combined with a nearly exact discretization scheme. This approach overcomes the well-known limitations associated with the classical discretization approach.

Several fundamental properties of the resulting discrete system were rigorously analyzed, including positivity of solutions, consistency with the discretized nondelayed system in the zero-delay limit, local stability, and the emergence of NS bifurcations. To highlight the necessity of the proposed framework, we also discretized the same model using Euler's method and demonstrated that this classical approach fails to reproduce essential dynamical features of the continuous-time system when delays are present.

Theoretical results were further supported by numerical simulations, which confirm the effectiveness and reliability of the proposed discretization scheme. The methodology presented in

this paper provides a robust foundation for the consistent discretization of delay differential equations with two delays and can be extended to a broad class of delayed dynamical models arising in biological and applied sciences.

Author contributions

A. M. A. Abo-Bakr: Conceptualization, methodology, software, writing—original draft, writing—review and editing, Mohamed Biomy: Software, writing—review and editing. All authors have read and agreed to the published version of the manuscript.

Use of Generative-AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare no conflicts of interest.

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