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Multiple bifurcations in an early brain tumor model with piecewise constant arguments

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In this paper, a differential equation with piecewise constant arguments modeling an early brain tumor growth is considered. The discretization process in the interval $t \in [n, n+1)$ leads to two-dimensional discrete dynamical system. By using the Schur–Cohn criterion, stability conditions of the positive equilibrium point of the system are obtained. Choosing appropriate bifurcation parameter, the existence of Neimark–Sacker and flip bifurcations is verified. In addition, the direction and stability of the Neimark–Sacker and flip bifurcations are determined by using the normal form and center manifold theory. Finally, the Lyapunov exponents are numerically computed to characterize the complexity of the dynamical behaviors of the system.

Keywords: Piecewise constant arguments; difference equation; stability; flip and Neimark–Sacker bifurcations; Lyapunov exponents.

Mathematics Subject Classification 2010: 39A28, 39A30, 92B05

1. Introduction

The differential equations with piecewise constant arguments describe hybrid dynamical systems and combine properties both differential and difference equation. In these equations, some of the dependent variables satisfy differential, while others — discrete equations. The qualitative studies on existence and uniqueness of solutions, asymptotic behavior, periodic and oscillating solutions and convergence of solutions of differential equations with piecewise constant arguments have been investigated by many authors [1–6].

Theoretical studies show that differential equations with piecewise constant arguments are equivalent to integral equations and are very close to delay differential equations [1, 2]. In study [7], the authors pointed out that the simplest logistic equation with piecewise constant arguments

$$\frac{dx(t)}{dt} = rx(t)\left(1 - \frac{x([t])}{K}\right), \quad t \geq 0 \tag{1.1}$$

may be viewed as a semi-discretization of the delay logistic equation

$$\frac{dx(t)}{dt} = rx(t)\left(1 - \frac{x(t-1)}{K}\right), \quad t \geq 0. \tag{1.2}$$

Equation (1.1) represents a logistically growing population undergoing a density-dependent harvesting where $[t]$ denotes the integer part of $t \in [0, \infty)$. The parameters r and K are the intrinsic growth rate and environmental carrying capacity, respectively.

The original method of investigation of these equations was based on the reduction to discrete equations. On any interval of the form $t \in [n, n+1)$ for $n = 0, 1, 2, \ldots$, one can integrate (1.1) and obtain

$$x(t) = x(n)e^{r(1-x(n)/K)(t-n)} \tag{1.3}$$

for $n \leq t < n+1$. Taking limits as $t \to n+1$ in Eq. (1.3), we have first-order difference equation

$$x(n+1) = x(n)e^{r(1-x(n)/K)}. \tag{1.4}$$

A further study of the logistic equation with piecewise constant arguments can be found in [7–13]. Gopalsamy and Liu [8] showed that for $0 < a < 1$, the positive equilibrium point of equation

$$\frac{dx(t)}{dt} = rx(t)(1 - ax(t) - bx([t])) \tag{1.5}$$

is globally asymptotically stable. Ozturk and Bozkurt [12] have investigated the stability and oscillatory characteristics of the following differential equation:

$$\frac{dx(t)}{dt} = x(t)(r(1 - \alpha x(t) - \beta_0 x([t]) - \beta_1 x([t-1])) + \gamma_1 x([t]) + \gamma_2 x([t-1])). \tag{1.6}$$

In the study [13], Eq. (1.6) is also used to model population dynamics of an early brain tumor where $[t]$ denotes the integer part of $t \in [0, \infty)$. In this model, the parameters r, α, β_0, β_1, γ_1 and γ_2 are positive numbers and represent the population growth rate of tumor cell, rates for the delayed tumor volume, drug effect on the tumor and negative effect by the immune system on the tumor population, respectively. Having shown that the model is consistency with the biological facts, parameter values were taken in experimental data. Using these parameter values, the author investigated dynamics of the monoclonal tumors under the effects of treatment by using linear stability analysis. However, it is evident that the linear stability analysis is not sufficient to understand the exact stability characteristics of biological model without bifurcation phenomena. Therefore, the present paper deals with the bifurcation analysis of the discrete version of model (1.6).

In discrete time systems, it is very important to study bifurcation analysis for a better understanding mechanism of the biological models. Many interesting research works on bifurcation theory can be found in [14–24]. On the other hand, in the literature, there are limited number of studies which examine bifurcations and chaos phenomena of differential equations with piecewise constant arguments [7, 25–31]. For the parameter values of r, May [25] showed that difference equation (1.4) can be complex and exhibits chaotic dynamics. In Eq. (1.5), Li-Yorke chaos arises for some conditions on certain parameter values of a and b [7]. In the study [26], explicit algorithm for determining the direction of the Hopf bifurcation and the stability of the bifurcating periodic solution was given by using the normal form method and center manifold theorem. Shang and Tian [27] discussed the existence and the stability of both flip and Neimark–Sacker bifurcations in a predator–prey model with the piecewise constant arguments and time delay.

The purpose of this paper is to investigate possible bifurcation type of the discrete version of model (1.6) such as flip and Neimark–Sacker bifurcations using center manifold and bifurcation theory.

2. Local Stability Analysis

The discretization of Eq. (1.6) in the interval $t \in [n, n+1)$ yields the difference equation [12, 13]

$$x(n+1) = \frac{\begin{array}{c} x(n)e^{-(r+(\gamma_1-\beta_0 r)x(n)+(\gamma_2-\beta_1 r)x(n-1))} \\ \times (r + (\gamma_1 - \beta_0 r)x(n) + (\gamma_2 - \beta_1 r)x(n-1)) \end{array}}{\begin{array}{c} r + (\gamma_1 - \beta_0 r - \alpha r)x(n) + (\gamma_2 - \beta_1 r)x(n-1) \\ + \alpha r x(n) e^{r+(\gamma_1-\beta_0 r)x(n)+(\gamma_2-\beta_1 r)x(n-1)} \end{array}}. \tag{2.1}$$

Using the change of variables $u_1(n) = x(n)$ and $u_2(n) = x(n-1)$, we obtain system of difference equations

$$\begin{cases} u_1(n+1) = \dfrac{u_1(n)(r + (\gamma_1 - \beta_0 r)u_1(n) + (\gamma_2 - \beta_1 r)u_2(n))}{\begin{array}{r} (r + (\gamma_1 - \beta_0 r - \alpha r)u_1(n) + (\gamma_2 - \beta_1 r)u_2(n)) \\ \times e^{-(r+(\gamma_1-\beta_0 r)u_1(n)+(\gamma_2-\beta_1 r)u_2(n))} + \alpha r u_1(n) \end{array}}, \\ u_2(n+1) = u_1(n). \end{cases} \tag{2.2}$$

The positive fixed point of system (2.2) is

$$(\overline{u_1}, \overline{u_2}) = \left(\frac{r}{r(\alpha + \beta_0 + \beta_1) - \gamma_1 - \gamma_2}, \frac{r}{r(\alpha + \beta_0 + \beta_1) - \gamma_1 - \gamma_2} \right) \tag{2.3}$$

where

$$r > \frac{\gamma_1 + \gamma_2}{\alpha + \beta_0 + \beta_1}. \tag{2.4}$$

Let $u(n+1) = Ju(n)$ be linearized system of (2.2) about $(\overline{u_1}, \overline{u_2})$. Now, the Jacobian matrix of system (2.2) is

$$\mathbf{J} = \begin{pmatrix} \dfrac{\gamma_1 - r\beta_0 + (r(\alpha+\beta_0) - \gamma_1)e^{-r\alpha\overline{u_1}}}{r\alpha} & \dfrac{(1-e^{-r\alpha\overline{u_1}})(\gamma_2 - r\beta_1)}{r\alpha} \\ 1 & 0 \end{pmatrix}$$

which yields the characteristic equation

$$p(\lambda) = \lambda^2 + \lambda\left(-\left(\frac{\gamma_1 - r\beta_0 + (r(\alpha+\beta_0) - \gamma_1)e^{-r\alpha\overline{u_1}}}{r\alpha}\right)\right) - \frac{(1-e^{-r\alpha\overline{u_1}})(\gamma_2 - r\beta_1)}{r\alpha} = 0. \tag{2.5}$$

Theorem 2.1 ([32]). *The characteristic polynomial* $p(\lambda) = \lambda^2 + p_1\lambda + p_0$ *has all its roots inside the unit open disk if and only if*

(a) $p(1) = 1 + p_1 + p_0 > 0,$

(b) $p(-1) = 1 - p_1 + p_0 > 0,$

(c) $D_1^+ = 1 + p_0 > 0,$

(d) $D_1^- = 1 - p_0 > 0.$

Theorem 2.2. (a) *Let*

$$\frac{\alpha(1+e^{-r\alpha\overline{u_1}})}{1-e^{-r\alpha\overline{u_1}}} < \beta_0 < \frac{2\alpha + \alpha e^{-r\alpha\overline{u_1}}}{1-e^{-r\alpha\overline{u_1}}}, \tag{2.6}$$

$$\beta_1 < \frac{-\alpha(1+e^{-r\alpha\overline{u_1}}) + \beta_0(1-e^{-r\alpha\overline{u_1}})}{1-e^{-r\alpha\overline{u_1}}} \tag{2.7}$$

and

$$\gamma_2 < \frac{\alpha\gamma_1 + \beta_1\gamma_1(1-e^{-r\alpha\overline{u_1}})}{\beta_0(1-e^{-r\alpha\overline{u_1}}) - \alpha e^{-r\alpha\overline{u_1}}}. \tag{2.8}$$

The positive fixed point of system (2.2) *is local asymptotically stable if*

$$\frac{\gamma_1+\gamma_2}{\alpha+\beta_0+\beta_1} < r < \frac{(\gamma_2-\gamma_1)(1-e^{-r\alpha\overline{u_1}})}{\alpha(1+e^{-r\alpha\overline{u_1}}) + (\beta_1-\beta_0)(1-e^{-r\alpha\overline{u_1}})} \tag{2.9}$$

(b) *Let*

$$\beta_0 < \frac{\alpha e^{-r\alpha\overline{u_1}}}{1-e^{-r\alpha\overline{u_1}}}, \tag{2.10}$$

$$\beta_1 > \frac{\alpha}{1-e^{-r\alpha\overline{u_1}}} \tag{2.11}$$

and

$$\gamma_2 > \frac{\gamma_1(\alpha - \beta_1(1-e^{-r\alpha\overline{u_1}}))}{-\alpha(2-e^{-r\alpha\overline{u_1}}) - \beta_0(1-e^{-r\alpha\overline{u_1}})}. \tag{2.12}$$

The positive fixed point of system (2.2) *is local asymptotically stable if*

$$\frac{\gamma_1+\gamma_2}{\alpha+\beta_0+\beta_1} < r < \frac{\gamma_2(1-e^{-r\alpha\overline{u_1}})}{-\alpha+\beta_1(1-e^{-r\alpha\overline{u_1}})} \tag{2.13}$$

Proof. From the characteristic equation (2.5), we obtain

$$p_1 = \frac{r\beta_0-\gamma_1+(\gamma_1-r(\alpha+\beta_0))e^{-r\alpha\overline{u_1}}}{r\alpha}, \tag{2.14}$$

$$p_0 = \frac{(r\beta_1-\gamma_2)(1-e^{-r\alpha\overline{u_1}})}{r\alpha}. \tag{2.15}$$

The condition (2.4) leads to

$$p(1) = (r(\alpha+\beta_0+\beta_1)-\gamma_1-\gamma_2)(1-e^{-r\alpha\overline{u_1}}) > 0. \tag{2.16}$$

From Theorem 2.1(b), we have

$$p(-1) = 1-\left(\frac{r\beta_0-\gamma_1+(\gamma_1-r(\alpha+\beta_0))e^{-r\alpha\overline{u_1}}}{r\alpha}\right) + \frac{(r\beta_1-\gamma_2)(1-e^{-r\alpha\overline{u_1}})}{r\alpha}.$$

Considering the conditions (2.7),

$$\beta_0 > \frac{\alpha(1+e^{-r\alpha\overline{u_1}})}{1-e^{-r\alpha\overline{u_1}}} > \frac{\alpha e^{-r\alpha\overline{u_1}}}{1-e^{-r\alpha\overline{u_1}}}, \tag{2.17}$$

and

$$\gamma_2 < \frac{\alpha\gamma_1+\beta_1\gamma_1(1-e^{-r\alpha\overline{u_1}})}{\beta_0(1-e^{-r\alpha\overline{u_1}})-\alpha e^{-r\alpha\overline{u_1}}} < \gamma_1, \tag{2.18}$$

with the fact that

$$r < \frac{(\gamma_2-\gamma_1)(1-e^{-r\alpha\overline{u_1}})}{\alpha(1+e^{-r\alpha\overline{u_1}})+(\beta_1-\beta_0)(1-e^{-r\alpha\overline{u_1}})} \tag{2.19}$$

we get $p(-1) > 0$. In addition, the condition

$$r > \frac{\gamma_2(1-e^{-r\alpha\overline{u_1}})}{\alpha+\beta_1(1-e^{-r\alpha\overline{u_1}})}, \tag{2.20}$$

guarantees that

$$D_1^+ = 1+\frac{(r\beta_1-\gamma_2)(1-e^{-r\alpha\overline{u_1}})}{r\alpha} > 0. \tag{2.21}$$

Under the condition

$$\beta_1 < \frac{-\alpha(1+e^{-r\alpha\overline{u_1}})+\beta_0(1-e^{-r\alpha\overline{u_1}})}{1-e^{-r\alpha\overline{u_1}}} < \frac{\alpha}{1-e^{-r\alpha\overline{u_1}}} \tag{2.22}$$

we can write

$$D_1^- = 1 - \frac{(r\beta_1 - \gamma_2)(1 - e^{-r\alpha\overline{u_1}})}{r\alpha} > 0. \tag{2.23}$$

Taking in view of (2.4), (2.19), (2.20) with the fact (2.6) and (2.8), we hold

$$\frac{\gamma_2(1 - e^{-r\alpha\overline{u_1}})}{\alpha + \beta_1(1 - e^{-r\alpha\overline{u_1}})} < \frac{\gamma_1 + \gamma_2}{\alpha + \beta_0 + \beta_1} < r$$
$$< \frac{(\gamma_2 - \gamma_1)(1 - e^{-r\alpha\overline{u_1}})}{\alpha(1 + e^{-r\alpha\overline{u_1}}) + (\beta_1 - \beta_0)(1 - e^{-r\alpha\overline{u_1}})}.$$

This completes the proof.

(b) We have already shown that $p(1) > 0$. Under the conditions,

$$\beta_0 < \frac{\alpha e^{-r\alpha\overline{u_1}}}{1 - e^{-r\alpha\overline{u_1}}} < \frac{\alpha(1 + e^{-r\alpha\overline{u_1}})}{1 - e^{-r\alpha\overline{u_1}}}, \tag{2.24}$$

and

$$r > \frac{\gamma_2(1 - e^{-r\alpha\overline{u_1}})}{\alpha + \beta_1(1 - e^{-r\alpha\overline{u_1}})}$$
$$> \frac{(\gamma_2 - \gamma_1)(1 - e^{-r\alpha\overline{u_1}})}{\alpha(1 + e^{-r\alpha\overline{u_1}}) + (\beta_1 - \beta_0)(1 - e^{-r\alpha\overline{u_1}})}, \tag{2.25}$$

we have $p(-1) > 0$ and $D_1^+ > 0$. From (2.11) and

$$r < \frac{\gamma_2(1 - e^{-r\alpha\overline{u_1}})}{-\alpha + \beta_1(1 - e^{-r\alpha\overline{u_1}})}, \tag{2.26}$$

we have $D_1^- > 0$. Considering (2.4) and (2.25) with the fact (2.10), (2.11) and (2.12) we get

$$\frac{(\gamma_2 - \gamma_1)(1 - e^{-r\alpha\overline{u_1}})}{\alpha(1 + e^{-r\alpha\overline{u_1}}) + (\beta_1 - \beta_0)(1 - e^{-r\alpha\overline{u_1}})}$$
$$< \frac{\gamma_2(1 - e^{-r\alpha\overline{u_1}})}{\alpha + \beta_1(1 - e^{-r\alpha\overline{u_1}})} < \frac{\gamma_1 + \gamma_2}{\alpha + \beta_0 + \beta_1}$$
$$< r < \frac{\gamma_2(1 - e^{-r\alpha\overline{u_1}})}{-\alpha + \beta_1(1 - e^{-r\alpha\overline{u_1}})}.$$

This completes the proof. □

3. Bifurcation Analysis

In this section, we will study direction and stability of the both Flip and Neimark–Sacker bifurcations in the system (2.2) using center manifold and bifurcation theorem [16, 23].

3.1. *Flip bifurcation*

To study flip bifurcation, the parameter r is chosen as a bifurcation parameter. Now, we can investigate the conditions and direction of flip bifurcation.

Theorem 3.1 ([32]). *For the system* (2.2), *one of the eigenvalues is* -1 *and the other eigenvalue lies inside the unit circle if and only if*

$$\begin{aligned}&\text{(a)}\ \ p(1) = 1 + p_1 + p_0 > 0,\\ &\text{(b)}\ \ p(-1) = 1 - p_1 + p_0 = 0,\\ &\text{(c)}\ \ D_1^+ = 1 + p_0 > 0,\\ &\text{(d)}\ \ D_1^- = 1 - p_0 > 0.\end{aligned}$$

Lemma 3.2 (Eigenvalue Assignment). *Let the inequalities* (2.6)–(2.8) *hold. If*

$$r = r_1 = \frac{(\gamma_2 - \gamma_1)(1 - e^{-r\alpha\overline{u_1}})}{\alpha(1 + e^{-r\alpha\overline{u_1}}) + (\beta_1 - \beta_0)(1 - e^{-r\alpha\overline{u_1}})}, \tag{3.1}$$

then the eigenvalue assignment condition of flip bifurcation in Theorem 3.1 *holds.*

Proof. The proof is similar as in Theorem 2.2(a) and will be omitted. □

From the conditions of Lemma 3.2, the Jacobian matrix J has the eigenvalues

$$\lambda_1(r_1) = -1,$$

and

$$|\lambda_2(r_1)| = \left|\frac{e^{-r\alpha\overline{u_1}}(\beta_1\gamma_1(1 - e^{-r\alpha\overline{u_1}}) - \gamma_2(\alpha(1 + e^{-r\alpha\overline{u_1}}) + \beta_0(1 - e^{-r\alpha\overline{u_1}})))}{\alpha(\gamma_1 - \gamma_2)}\right| < 1.$$

In order to convert the origin of the coordinates to equilibrium point (2.3), we use

$$\begin{cases} u_1 = \overline{u_1} + x_1, \\ u_2 = \overline{u_2} + x_2, \end{cases} \tag{3.2}$$

which transforms system (2.2) into

$$\begin{cases} x_1(n+1) = \dfrac{(x_1(n) + \overline{u_1})(r + (\gamma_1 - \beta_0 r)(x_1(n) + \overline{u_1}) + (\gamma_2 - \beta_1 r)(x_2(n) + \overline{u_2}))}{(r + (\gamma_1 - \beta_0 r - \alpha r)(x_1(n) + \overline{u_1}) + (\gamma_2 - \beta_1 r)(x_2(n) + \overline{u_2}))}, \\ \qquad\qquad \times e^{-(r + (\gamma_1 - \beta_0 r)(x_1(n) + \overline{u_1}) + (\gamma_2 - \beta_1 r)(x_2(n) + \overline{u_2}))} + \alpha r(x_1(n) + \overline{u_1}) \\ x_2(n+1) = x_1(n) + \overline{u_1}. \end{cases} \tag{3.3}$$

Now system (3.3) can be expressed as

$$X_{n+1} = JX_n + \frac{1}{2}B(X_n, X_n) + \frac{1}{6}C(X_n, X_n, X_n) + O\big(X_n^4\big), \tag{3.4}$$

where

$$J(r_1) = \begin{pmatrix} \dfrac{\gamma_1 - r\beta_0 + (r(\alpha+\beta_0) - \gamma_1)e^{-r\alpha\overline{u_1}}}{r\alpha} & \dfrac{\begin{array}{r} e^{-r\alpha\overline{u_1}}((1+e^{-r\alpha\overline{u_1}})r\alpha \\ +(1-e^{-r\alpha\overline{u_1}})(r\beta_0-\gamma_1)) \end{array}}{r\alpha} \\ 1 & 0 \end{pmatrix}$$

and the multilinear functions B and C are

$$B_i(x,y) = \sum_{j,k=1}^{2} \left.\frac{\partial^2 X_i(\varepsilon,0)}{\partial\varepsilon_j \partial\varepsilon_k}\right|_{\varepsilon=0} x_j y_k, \quad i = 1,2$$

and

$$C_i(x,y,z) = \sum_{j,k,l=1}^{2} \left.\frac{\partial^3 X_i(\varepsilon,0)}{\partial\varepsilon_j \partial\varepsilon_k \partial\varepsilon_l}\right|_{\varepsilon=0} x_j y_k z_l, \quad i = 1,2.$$

For the system (3.3), the values of B and C can be calculated as

$$B(\varepsilon,\eta) = \begin{pmatrix} \delta_1\varepsilon_1\eta_1 + \delta_2\varepsilon_1\eta_2 + \delta_3\varepsilon_2\eta_1 + \delta_4\varepsilon_2\eta_2 \\ 0 \end{pmatrix},$$

and

$$C(\varepsilon,\eta,\zeta) = \begin{pmatrix} \varepsilon_1\eta_1(\varphi_1\zeta_1 + \varphi_2\zeta_2) + \varepsilon_1\eta_2(\varphi_3\zeta_1 + \varphi_4\zeta_2) + \varepsilon_2\eta_1(\varphi_5\zeta_1 + \varphi_6\zeta_2) \\ + \varepsilon_2\eta_2(\varphi_7\zeta_1 + \varphi_8\zeta_2) \\ 0 \end{pmatrix},$$

where

$$\begin{cases} \delta_1 = \dfrac{2(r(\alpha+\beta_0)-\gamma_1)e^{-2r\alpha\overline{u_1}}}{r^3\alpha^2}\big[(r(\alpha+\beta_0)-\gamma_1)(r(\beta_0+\beta_1+\alpha) \\ \quad - \gamma_1 - \gamma_2) + e^{r\alpha\overline{u_1}}\big(-r^2\alpha^2 - r^2\beta_0^2 + r\beta_1(-r\alpha+\beta_1) - \gamma_1((-2+r)r\alpha+\gamma_1), \\ \quad + (r\alpha-\gamma_1)\gamma_2 + r\beta_0((-2+r)r\alpha - r\beta_1 + 2\gamma_1 + \gamma_2)\big)\big], \\ \delta_2 = \delta_3 \\ \quad = \dfrac{(r\beta_1-\gamma_2)e^{-r\alpha\overline{u_1}}}{r^3\alpha^2}\big[-2r^2\alpha^2 + r^3\alpha^2 - 4r^2\alpha\beta_0 + 2r^3\alpha\beta_0 - 2r^2\beta_0^2 \\ \quad - 2r^2\alpha\beta_1 - 2r^2\beta_0\beta_1 + 4r\alpha\gamma_1 - 2r^2\alpha\gamma_1 + 4r\beta_0\gamma_1 + 2r\beta_1\gamma_1 - 2\gamma_1^2, \\ \quad + 2e^{-r\alpha\overline{u_1}}(r(\alpha+\beta_0)-\gamma_1)(r(\alpha+\beta_0+\beta_1)-\gamma_1-\gamma_2) \\ \quad + 2r\alpha\gamma_2 + 2r\beta_0\gamma_2 - 2\gamma_1\gamma_2\big], \\ \delta_4 = \dfrac{1}{r^3\alpha^2}[2e^{-r\alpha\overline{u_1}}(-r\beta_1+\gamma_2)^2(r(\alpha+\beta_0+\beta_1)-\gamma_1-\gamma_2 \\ \quad + e^{r\alpha\overline{u_1}}((-1+r)r\alpha - r(\beta_0+\beta_1)+\gamma_1+\gamma_2))], \end{cases} \tag{3.5}$$

$$
\begin{cases}
\varphi_1 = -\dfrac{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^4}{r^8\alpha^4}\left[-\dfrac{3e^{r\alpha\overline{u_1}}r^7\alpha^3(r\alpha + r\beta_0 - \gamma_1)(-r\beta_0 + \gamma_1)^2}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^4}\right. \\
\qquad + \dfrac{6e^{-2r\alpha\overline{u_1}}(-2 + e^{r\alpha\overline{u_1}})r^5\alpha^2(r\beta_0 - \gamma_1)(r\alpha + r\beta_0 - \gamma_1)^2}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^3} \\
\qquad \left. - \dfrac{6e^{-3r\alpha\overline{u_1}}(-1 + e^{r\alpha\overline{u_1}})r^3\alpha(r\alpha + r\beta_0 - \gamma_1)^2((-1 + e^{r\alpha\overline{u_1}})r\alpha - r\beta_0 + \gamma_1)}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^2}\right] \\
\varphi_2 = \varphi_3 = \varphi_5 \\
\quad = -\dfrac{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^4}{r^8\alpha^4} \\
\qquad \times \left[\dfrac{\begin{array}{l} e^{-r\alpha\overline{u_1}}r^7\alpha^3(r\beta_0 - \gamma_1)(-2(r\alpha + r\beta_0 - \gamma_1)(r\beta_1 - \gamma_2) \\ \quad + (r\beta_0 - \gamma_1)(-r\beta_1 + \gamma_2)) \end{array}}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^4}\right. \\
\qquad + \dfrac{\begin{array}{l} (2e^{-2r\alpha\overline{u_1}}(-2 + e^{r\alpha\overline{u_1}})r^5\alpha^2\big(r^2\alpha^2 + 3r^2\beta_0^2 + 2r\beta_0(2r\alpha - 3\gamma_1) \\ \quad - 4r\alpha\gamma_1 + 3\gamma_1^2\big)(r\beta_1 - \gamma_2)) \end{array}}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^2} \\
\qquad \left. - \dfrac{\begin{array}{l} (2e^{-3r\alpha\overline{u_1}}(-1 + e^{r\alpha\overline{u_1}})r^3\alpha(r\alpha + r\beta_0 - \gamma_1)((-3 + 2e^{r\alpha\overline{u_1}})r\alpha \\ \quad - 3r\beta_0 + 3\gamma_1)(r\beta_1 - \gamma_2)) \end{array}}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^2}\right], \\
\varphi_4 = \varphi_6 = \varphi_7 \\
\quad = \dfrac{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^4 e^{-2r\alpha\overline{u_1}}}{r^8\alpha^4} \\
\qquad \times \left[\dfrac{\begin{array}{l} -(e^{r\alpha\overline{u_1}}r^7\alpha^3(r\beta_1 - \gamma_2)((-r\alpha - r\beta_0 + \gamma_1)(r\beta_1 - \gamma_2) \\ \quad + 2(r\beta_0 - \gamma_1)(-r\beta_1 + \gamma_2))) \end{array}}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^4}\right. \\
\qquad - \dfrac{2(-2 + e^{r\alpha\overline{u_1}})r^5\alpha^2(2r\alpha + 3r\beta_0 - 3\gamma_1)(-r\beta_1 + \gamma_2)^2}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^3} \\
\qquad \left. + \dfrac{(2e^{-r\alpha\overline{u_1}}(-1 + e^{r\alpha\overline{u_1}})r^3\alpha((-3 + e^{r\alpha\overline{u_1}})r\alpha - 3r\beta_0 + 3\gamma_1)(-r\beta_1 + \gamma_2)^2)}{(r\alpha + r\beta_0 + r\beta_1 - \gamma_1 - \gamma_2)^2}\right], \\
\varphi_8 = \dfrac{3e^{-3r\alpha\overline{u_1}}(r\beta_1 - \gamma_2)^3}{r^5\alpha^3}[2(-r\alpha - r(\beta_0 + \beta_1) + \gamma_1 + \gamma_2)^2 \\
\qquad + 2e^{r\alpha\overline{u_1}}(r(\alpha + \beta_0 + \beta_1) - \gamma_1 - \gamma_2)(r(-1 + 2r)\alpha - r(\beta_0 + \beta_1) + \gamma_1 + \gamma_2) \\
\qquad + e^{2r\alpha\overline{u_1}}r^2\alpha((-2 + r)r\alpha - 2r(\beta_0 + \beta_1) + 2\gamma_1 + 2\gamma_2)].
\end{cases} \tag{3.6}
$$

Let $q, p \in R^2$ be an eigenvector such that $J(r_1)q = -q$ and $J^T(r_1)p = -p$, respectively. By direct calculation we obtain

$$q \sim (-1, 1)^T,$$

$$p \sim \left(-\frac{e^{r\alpha\overline{u_1}} r\alpha}{(1 + e^{r\alpha\overline{u_1}})r\alpha - (-1 + e^{r\alpha\overline{u_1}})r\beta_0 + (-1 + e^{r\alpha\overline{u_1}})\gamma_1}, 1\right)^T.$$

To achieve the necessary normalization $\langle p, q\rangle = 1$, we can obtain the normalized vectors as

$$q = (-1, 1)^T,$$

and

$$p = \left(-\frac{e^{r\alpha\overline{u_1}} r\alpha}{(1 + 2e^{r\alpha\overline{u_1}})r\alpha + (1 - e^{r\alpha\overline{u_1}})(r\beta_0 - \gamma_1)},\right.$$
$$\left.\frac{(1 + e^{r\alpha\overline{u_1}})r\alpha + (1 - e^{r\alpha\overline{u_1}})(r\beta_0 - \gamma_1)}{(1 + 2e^{r\alpha\overline{u_1}})r\alpha + (1 - e^{r\alpha\overline{u_1}})(r\beta_0 - \gamma_1)}\right)^T.$$

The critical normal form coefficient $c(0)$ that determines the direction of the flip bifurcation can be calculated by using the following formula:

$$c(0) = \frac{1}{6}\langle p, C(q, q, q)\rangle - \frac{1}{2}\langle p, B(q, (A - I)^{-1}B(q, q))\rangle. \tag{3.7}$$

From the above analysis and theorem in [16, 18, 19], we have following theorem.

Theorem 3.3. *Suppose that* $(\overline{u_1}, \overline{u_2})$ *is the positive equilibrium point of the system* (2.2). *If Lemma* 3.2 *holds and* $c(0) \neq 0$, *then system* (2.2) *undergoes a flip bifurcation at the equilibrium point* $(\overline{u_1}, \overline{u_2})$ *when the parameter* r *varies in a small neighborhood of* r_1. *Moreover if* $c(0) > 0$ (*respectively*, $c(0) < 0$), *then the period*-2 *orbits that bifurcate from* $(\overline{u_1}, \overline{u_2})$ *are stable* (*respectively, unstable*).

Now, we present the bifurcation diagrams, phase portraits and maximum Lyapunov exponents for the system to confirm the above theoretical analysis and show the complex dynamical behaviors by using numerical simulations.

Example 3.4. For the parameters values $\alpha = 0.2$, $\beta_0 = 1.6$, $\beta_1 = 0.1$, $\gamma_1 = 0.4$ and $\gamma_2 = 0.1$ the critical value of flip bifurcation point is obtained as $r_1 = 2.48067$. Now, the Jacobian matrix corresponding to the system (3.3) is

$$J(r_1) = \begin{pmatrix} -1.0756 & -0.0755995 \\ 1 & 0 \end{pmatrix}$$

which has the eigenvalues

$$\lambda_1 = -1, \quad \lambda_2 = -0.0755995 \neq \mp 1.$$

From the (3.5) and (3.6), we have

$$\begin{cases} \delta_1 = 0.535775, \\ \delta_2 = \delta_3 = 0.130074, \\ \delta_4 = 0.00876458. \end{cases}$$

and

$$\begin{cases} \varphi_1 = 8.42926, \\ \varphi_2 = \varphi_3 = \varphi_5 = -0.0541043, \\ \varphi_4 = \varphi_6 = \varphi_7 = -0.0131259, \\ \varphi_8 = -0.000811627. \end{cases}$$

Now the eigenvectors $q, p \in R^2$ corresponding to $\lambda_1(r_1) = -1$ are

$$q \sim (-0.707107, 0.707107)^T$$

and

$$p \sim (-0.997155, -0.0753844)^T.$$

To achieve the necessary normalization $\langle p, q\rangle = 1$, we can obtain

$$q = (-0.707107, 0.707107)^T,$$

$$p = (-1.52987, -0.115658)^T.$$

Finally, using the formula (3.7), the critical normal form coefficient $c(0)$ is computed as $c(0) = 0.894457$ which shows that a unique and stable period-two cycle bifurcates from $(\overline{u_1}, \overline{u_2})$ for $r < r_1 = 2.48067$.

The bifurcation diagram of the system in $(r - u_1)$ space for $\alpha = 0.2, \beta_0 = 1.6, \beta_1 = 0.1, \gamma_1 = 0.4$ and $\gamma_2 = 0.1$ is given in Fig. 1. After calculation, by Lemma 3.2, a flip bifurcation occurs from the fixed point $(0.588775, 0.588775)$ at $r_1 = 2.48067$. From Fig. 1, we can see that the fixed point is stable for $r < r_1$ and loses its stability at the flip bifurcation parameter value $r_1 = 2.48067$. The sign of the critical normal form coefficient is determined as $c(0) = 0.894457$ which determines the direction of the flip bifurcation. For the system (2.2), the maximum Lyapunov exponents corresponding to Fig. 1 are calculated and plotted in Fig. 2 [33]. This figure demonstrates the existence of the chaotic regions and period orbits in the parametric space. From Fig. 2, it is observed that some Lyapunov exponents are bigger than 0, some are smaller than 0, so there exist stable fixed points or stable period windows in the chaotic region.

Now, we study the Neimark–Sacker bifurcation for the system (2.2) in the following section.

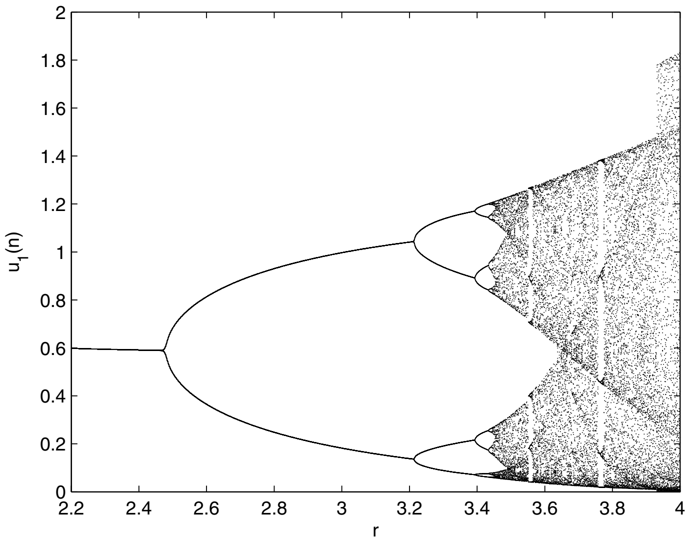

Fig. 1. Flip bifurcation diagram in $(r - u_1)$ plane for the parameters values $\alpha = 0.2$, $\beta_0 = 1.6$, $\beta_1 = 0.1$, $\gamma_1 = 0.4$, $\gamma_2 = 0.1$ and initial value $(1, 1)$.

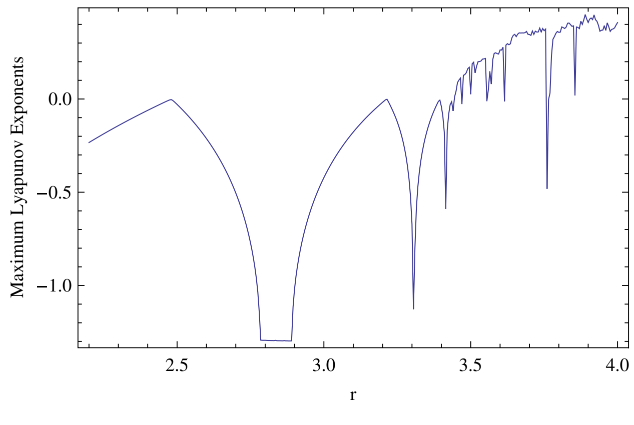

Fig. 2. Maximum Lyapunov exponents corresponding to Fig. 1.

3.2. *Neimark–Sacker bifurcation*

Theorem 3.5 ([32]). *A pair of complex conjugate roots of* (2.2) *lies on the unit circle if and only if*

$$\text{(a)}\ \ p(1) = 1 + p_1 + p_0 > 0,$$

$$\text{(b)}\ \ p(-1) = 1 - p_1 + p_0 > 0,$$

$$\text{(c)}\ \ D_1^+ = 1 + p_0 > 0,$$

$$\text{(d)}\ \ D_1^- = 1 - p_0 = 0.$$

Lemma 3.6 (Eigenvalue Assignment). *Let the inequalities* (2.10)–(2.12) *hold. If*

$$r = r_2 = \frac{\gamma_2(1 - e^{-r\alpha\overline{u_1}})}{-\alpha + \beta_1(1 - e^{-r\alpha\overline{u_1}})},$$

then the eigenvalue assignment condition of Neimark–Sacker bifurcation in Theorem (3.3) *holds.*

Proof. The proof is similar as in Theorem 2.2(b) and will be omitted. □

It is easy to see that the Jacobian matrix J has the eigenvalues

$$\lambda_{1,2}(r) = \frac{e^{-r\alpha\overline{u_1}}\big(r\alpha + (r\beta_0 - \gamma_1)(1 - e^{r\alpha\overline{u_1}})\big)}{2r\alpha} \pm i\frac{e^{-r\alpha\overline{u_1}}\left(\sqrt{\begin{aligned}&4e^{r\alpha\overline{u_1}}r\alpha(1 - e^{-r\alpha\overline{u_1}})(\gamma_2 - r\beta_1)\\ &\quad - ((1 - e^{-r\alpha\overline{u_1}})(\gamma_1 - r\beta_0) - r\alpha)^2\end{aligned}}\right)}{2r\alpha}$$

and for $r = r_2$, these eigenvalues become

$$|\lambda_{1,2}(r_2)| = \left|\frac{e^{-r\alpha\overline{u_1}}(-e^{-r\alpha\overline{u_1}}\alpha\gamma_1 + (\beta_0\gamma_2 - \beta_1\gamma_1)(1 - e^{r\alpha\overline{u_1}}) + \alpha\gamma_2)}{2\alpha\gamma_2} \pm i\frac{e^{-r\alpha\overline{u_1}}\left(\sqrt{\begin{aligned}&4e^{2r\alpha\overline{u_1}}\alpha^2\gamma_2^2 - (e^{r\alpha\overline{u_1}} + \beta_1\gamma_1(1 - e^{-r\alpha\overline{u_1}}) - \alpha\gamma_2\\ &\quad - \beta_0\gamma_2(1 - e^{r\alpha\overline{u_1}}))^2\end{aligned}}\right)}{2\alpha\gamma_2}\right| = 1.$$

On the other hand, the transversality condition leads to

$$\left.\frac{d|\lambda_i(r)|}{dr}\right|_{r=r_2} = \frac{e^{-r\alpha\overline{u_1}}(e^{r\alpha\overline{u_1}}\alpha - (-1 + e^{r\alpha\overline{u_1}})\beta_1)^2}{2(-1 + e^{r\alpha\overline{u_1}})\alpha\gamma_2} \neq 0, \quad i = 1, 2.$$

In addition from the nonresonance condition $\mathrm{tr}J(r_2) = -p_1 \neq 0, -1$, we have

$$r_2 \neq \frac{(1 - e^{r\alpha\overline{u_1}})\gamma_1}{\alpha + \beta_0(1 - e^{r\alpha\overline{u_1}})}, \quad r_2 \neq \frac{(1 - e^{r\alpha\overline{u_1}})\gamma_1}{\alpha(1 - e^{r\alpha\overline{u_1}}) + \beta_0(1 - e^{r\alpha\overline{u_1}})}.$$

Let $q, p \in R^2$ be an eigenvector such that $J(r_2)q = e^{i\theta_0}q$ and $J^T(r_2)p = e^{-i\theta_0}p$, respectively. By direct calculation, we get

$$q \sim (-a + ib, 1)^T$$

and

$$p \sim (a + ib, 1)^T,$$

where

$$a=\frac{e^{-r\alpha\overline{u_1}}(e^{r\alpha\overline{u_1}}\alpha\gamma_1+(\beta_1\gamma_1-\beta_0\gamma_2)(1-e^{r\alpha\overline{u_1}})-\alpha\gamma_2)}{2\alpha\gamma_2}$$

and

$$b=\frac{e^{-r\alpha\overline{u_1}}\sqrt{\begin{array}{c}4e^{2r\alpha\overline{u_1}}\alpha^2\gamma_2^2-((e^{r\alpha\overline{u_1}}\alpha-(-1+e^{r\alpha\overline{u_1}})\beta_1)\gamma_1\\+(\alpha-(-1+e^{r\alpha\overline{u_1}})\beta_0)\gamma_2)^2\end{array}}}{2\alpha\gamma_2}.$$

To obtain the normalization $\langle p,q\rangle=1$, we can take

$$q=(a+ib,1)^T$$

and

$$p=\left(\frac{a+ib}{1-(a+ib)^2},\frac{1}{1-(a+ib)^2}\right)^T.$$

Now we form

$$x=zq+\overline{zq}.$$

In this way, system (3.3) can be transformed for sufficiently small $|r|$ into following form:

$$z\mapsto\lambda_1(r)z+g(z,\overline{z},r).$$

The Taylor expression of g with respect to $(z,\overline{z})=(0,0)$ is

$$g(z,\overline{z},r)=\sum_{k+l\geq 2}\frac{1}{k!l!}g_{kl}(r)z^k\overline{z}^{-l},$$

where

$$\begin{cases}g_{20}(r_2)=\langle p,B(q,q)\rangle,\\ g_{11}(r_2)=\langle p,B(q,\overline{q})\rangle,\\ g_{21}(r_2)=\langle p,C(q,q,\overline{q})\rangle,\\ g_{02}(r_2)=\langle p,B(\overline{q},\overline{q})\rangle.\end{cases}\tag{3.8}$$

Now, the coefficient $a(0)$, which determines the direction of the appearance of the invariant curve in a generic system exhibiting Neimark–Sacker bifurcation, can be computed via

$$a(0)=\mathrm{Re}\left[\frac{e^{-i\theta_0}g_{21}}{2}\right]-\mathrm{Re}\left[\frac{(1-2e^{i\theta_0})e^{-2i\theta_0}}{2(1-e^{i\theta_0})}g_{20}g_{11}\right]-\frac{1}{2}|g_{11}|^2-\frac{1}{4}|g_{02}|^2.\tag{3.9}$$

From the above argument, we have the following theorem.

Theorem 3.7. *Suppose that* $(\overline{u_1},\overline{u_2})$ *is the positive equilibrium point. If the Lemma* 3.6 *holds,* $r_2\neq\frac{(1-e^{r\alpha\overline{u_1}})\gamma_1}{\alpha+\beta_0(1-e^{r\alpha\overline{u_1}})}$, $r_2\neq\frac{(1-e^{r\alpha\overline{u_1}})\gamma_1}{\alpha(1-e^{r\alpha\overline{u_1}})+\beta_0(1-e^{r\alpha\overline{u_1}})}$ *and* $a(0)<0$ (*respectively* $a(0)>0$), *then the Neimark–Sacker bifurcation of system* (2.2) *at* $r=r_2$ *is supercritical* (*respectively, subcritical*) *and there exists a unique closed* *invariant curve bifurcation from* $(\overline{u_1}, \overline{u_2})$ *for* $r = r_2$*, which is asymptotically stable (respectively, unstable).*

Example 3.8. For the parameters values $\alpha = 0.4, \beta_0 = 1.4, \beta_1 = 2.3, \gamma_1 = 0.8, \gamma_2 = 0.95$, we have critical Neimark–Sacker bifurcation point as $r_2 = 1.99485$. In this situation, the Jacobian matrix J at the fixed point is

$$J(r_2) = \begin{pmatrix} 0.232927 & -1 \\ 1 & 0 \end{pmatrix}$$

and has the eigenvalues

$$\lambda_{1,2}(r_2) = 0.116464 \pm 0.993195i = e^{\pm i\theta_0} \quad \text{with } |\lambda_{1,2}(r_2)| = 1, \ \ \theta_0 = 1.45407.$$

In addition it is easy to check that

$$\frac{d|\lambda_i(r)|}{dr}|_{r=r_2} = 0.0654487 \neq 0 \quad \text{and} \quad \lambda_i^k(r_2) \neq 1 \quad \text{for } k = 1, 2, 3, 4.$$

Let $q, p \in C^2$ be complex eigenvectors corresponding to $\lambda_{1,2}$ respectively.

$$q \sim (0.707107, 0.0823522 - 0.7022957i)^T$$

and

$$p \sim (0.707107, -0.0823522 - 0.702295i)^T$$

satisfy $J(r_2)q = e^{1.45407i}q$ and $J^T(r_2)p = e^{-1.45407i}p$. To obtain the normalization $\langle p, q\rangle = 1$, we can take the normalized vectors as

$$q = (0.707107, 0.0823522 - 0.7022957i)^T$$

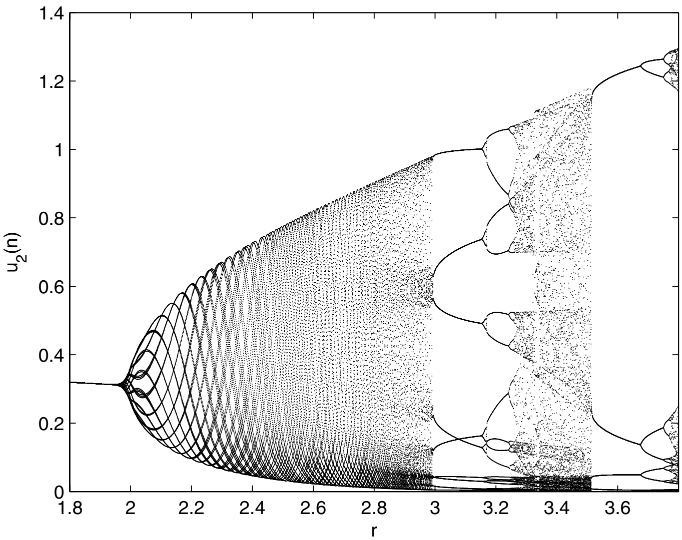

Fig. 3. Neimark–Sacker bifurcation diagram in $(r - u_1)$ plane for the parameters values $\alpha = 0.4$, $\beta_0 = 1.4$, $\beta_1 = 2.3$, $\gamma_1 = 0.8$, $\gamma_2 = 0.95$ and initial value $(1, 1)$.

and

$$p = (0.707107 + 0.0829164i, -2.77556 \times 10^{-17} - 0.711952i)^T.$$

From the formula (3.8) and (3.9) the coefficients of the normal of the system (3.3) are

$$g_{20}(r_2) = -1.9709 + 0.39296i, \quad g_{11}(r_2) = 0.0731496 - 0.00857763i,$$

$$g_{21}(r_2) = 3.97354 - 0.646922i, \quad g_{02}(r_2) = -2.008346 + 0.0736508i$$

and the critical real part is $a(0) = -1.20963$. Therefore, a supercritical Neimark–Sacker bifurcation occurs at $r_2 = 1.99485$ (Fig. 3).

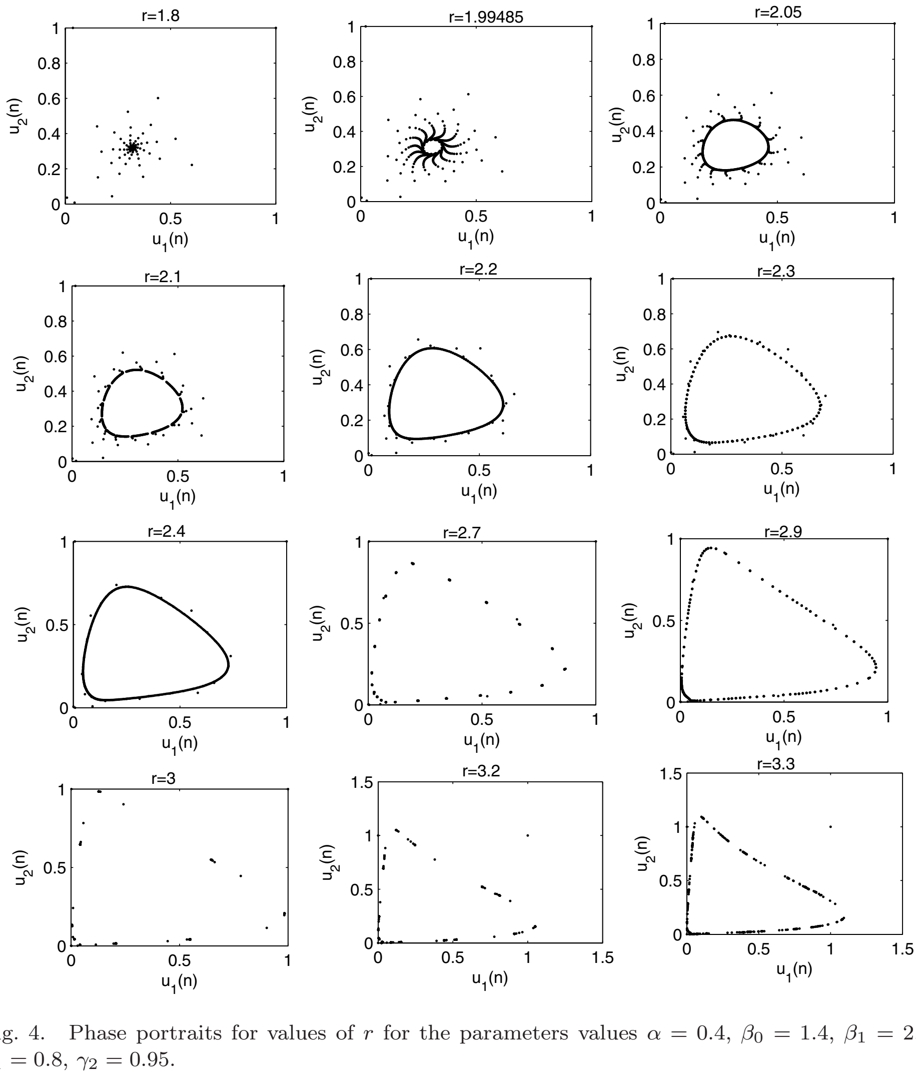

Fig. 4. Phase portraits for values of r for the parameters values $\alpha = 0.4$, $\beta_0 = 1.4$, $\beta_1 = 2.3$, $\gamma_1 = 0.8$, $\gamma_2 = 0.95$.

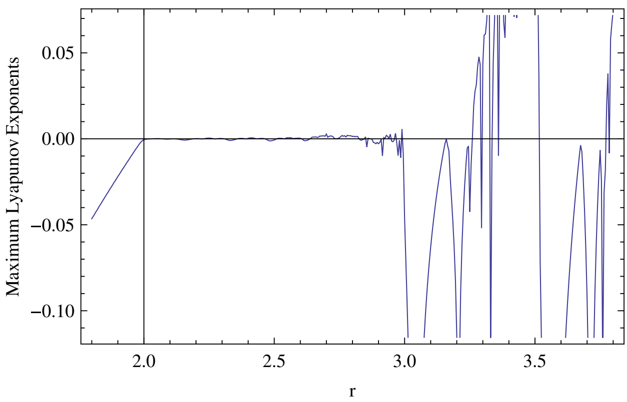

Fig. 5. Maximum Lyapunov exponents corresponding to Fig. 3.

The bifurcation diagram of system (2.2) in the $(r - u_1)$ is given in Fig. 3. From Lemma 3.6, it can be seen that the Neimark–Sacker bifurcation emerges from the fixed point $(\overline{u_1}, \overline{u_2}) = (0.310295, 0.310295)$ at $r_2 = 1.99485$. For this value, the eigenvalues of the positive fixed point of the system are $|\lambda_{1,2}| = |0.1116464 \pm 0.9931295i| = 1$ and $a(0) = -1.20963$. Therefore, the Neimark–Sacker bifurcation is supercritical. In addition, the phase portrait of the system for increasing value of r is obtained in Fig. 4. This figure demonstrates the process of how a smooth invariant circle appears and then disappears from the fixed point. Furthermore, the maximum Lyapunov exponents corresponding to Fig. 3 are given in Fig. 5.

4. Conclusion

In this paper, we investigate the complex behaviors of a discrete system which is based on the discretization of a differential equation with piecewise constant arguments model. In Theorem 2.2, we get two different ranges for the parameter r (population growth rate of tumor cells) along with other system parameters. These ranges play a major role to control tumor population as a tumor dormant state. Hence, it has a significant biological meaning in the context of tumor population model.

The existence of periodic solutions and chaotic behavior is relevant in tumor growth models. In Theorem 3.3, we show that flip bifurcation occurs when the population growth rate reaches a threshold value r_1. That is, there are nearby periodic solutions of approximately double period. As population growth rate of tumor cells increases through r_1, chaotic dynamics occur for the tumor cell leading to uncontrolled tumor growth (Figs. 1 and 2). In Theorem 3.7, we also show the existence of Neimark–Sacker bifurcation around the positive equilibrium point when the population growth rate of tumor cells reaches a threshold value r_2 (Figs. 3 and 4). The importance of Neimark–Sacker bifurcation in the tumor model is that, at the bifurcation point a limit cycle is formed around the equilibrium point, thus resulting in periodic or quasi-periodic solutions (Fig. 4). It means that the tumor population may exhibit damped or undamped oscillation behavior around an equilibrium point even in the absence of any treatment (Figs. 4 and 5). Damped oscillatory solutions may lead to tumor regression, while undamped oscillatory solutions may cause uncontrolled tumor growth. The Lyapunov exponents are numerically computed to confirm further the complexity of the dynamical behaviors.

We note that original model (1.6) and its discretization version (2.2) may have some different dynamic properties. For example the discrete system (2.2) can generate spurious equilibrium points and periodic points which are not present in the continuous time mother version. This is not surprising, because it is well known that difference equations are capable of generating rich dynamics properties according to differential equations. Stability and bifurcation analysis of the system of difference equations obtained according to the above discretization process will be considered in the future works.

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