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Dynamics of Fractional Order Bio-Regulatory System

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Abstract: In this paper a fractional-order bio-regulatory system is proposed. Stability and Hopf bifurcation of the systems have been investigated. Several numerical examples are demonstrated to validate the theoretical results.

Keywords: Goodwin-Griffith system, fractional-order, stability, Hopf bifurcation, numerical solutions.

1 Introduction

In order to understand the internal mechanism of the gene's action, we need to first know what the term operon is [1], which is used to explain the regulatory process of the gene. An operon is defined as a set of structural genes before which there is a small portion of DNA that is known as an operator, and when repression occurs, mRNA polymerse bind in order for transcription to begin.

The regulation process sometimes includes transcription attenuation or inhibition of the feedback and repression enzyme. Operon suppression occurs when an active repressor part binds to the operator and blocks it, in addition to preventing the binding of mRNA polymerse.

There are many important operon systems that are getting a lot of attention, such as lactose operons and operon-tryptophan [1]. In this paper, we will direct our attention to operon-tryptophan for its ability to be suppressed, which is known to be an amino acid containing five genes, in addition to the important role in the process of gene regulation.

Goodwin (1965) and Griffith (1968) developed a mathematical model for the operon based on negative feedback see([1]-[5]).

In this paper stability analysis of the fractional order Goodwin-Griffith systems are studied, where fractional calculus was applied as a powerful tool for mathematical modeling in various fields of science such as engineering, economics, and biological systems [6]. Many applications show a great demand for the most realistic and sufficient mathematical modeling of real phenomena using fractional calculus that provides one possible approach as such.

Definitions and properties of the fractional integrals and derivatives are given in [6].

Definition 1.1 The Caputo fractional derivative of order $q > 0$ of $f(t)$, $t > 0$ is defined by

$$D^q f(t) = \frac{1}{\Gamma(n-q)} \int_0^t (t-s)^{n-q-1} f^{(n)}(s)\, ds,$$

where $\Gamma(\cdot)$ is the Gamma function and $n-1 < q \le n, n \in \mathbb{N}$.

2 The fractional Goodwin-Griffith system

Consider the fractional order model

$$D^q M(t) = \frac{1}{1+T^n} - \alpha M,$$
$$D^q E(t) = M - \beta E,$$
$$D^q T(t) = E - \gamma T,$$

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where α, β, γ are constants, D^q $(0 < q \leq 1)$ is the Caputo fractional derivative of order q, M denotes the operon related mRNA concentration, E be the concentration of the enzyme produced by the operon genes, T is the concentration of the end product of the reaction catalyzed by enzyme E and n is the cooperativity of the end production repression [7].

To evaluate the equilibrium points, let

$$D^q M(t) = 0,$$
$$D^q E(t) = 0,$$
$$D^q T(t) = 0,$$

which yield

$$M = \beta E = \beta \gamma T, \tag{2}$$

and

$$T(1+T^n) = \frac{1}{\alpha\beta\gamma} \tag{3}$$

if T_0 is a root of equation (3), then the equilibrium point is $(M_{eq}, E_{eq}, T_{eq}) = (\beta\gamma T_0, \gamma T_0, T_0)$ where

$$T_0(1+T_0^n) = \frac{1}{\alpha\beta\gamma}$$

with T_0 non-negative as it represents tryptophan concentration.

For the equilibrium point $(\beta\gamma T_0, \gamma T_0, T_0)$, we find that the characteristic polynomial is

$$p(\lambda) = \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0,$$

where

$$a_1 = (\alpha+\beta+\gamma), a_2 = (\alpha\beta+\beta\gamma+\alpha\gamma), a_3 = \alpha\beta\gamma(1+n\alpha\beta\gamma T_0^{n+1})$$

and its discriminant $D(P)$ is given as:

$$D(P) = -\begin{vmatrix} 1 & a_1 & a_2 & a_3 & 0 \\ 0 & 1 & a_1 & a_2 & a_3 \\ 3 & 2a_1 & a_2 & 0 & 0 \\ 0 & 3 & 2a_1 & a_2 & 0 \\ 0 & 0 & 3 & 2a_1 & a_2 \end{vmatrix} = 18a_1a_2a_3 + (a_1a_2)^2 - 4a_3a_1^3 - 4a_2^3 - 27a_3^2. \tag{4}$$

A sufficient condition for $(\beta\gamma T_0, \gamma T_0, T_0)$ to be locally asymptotically stable is ([8]-[11])

$$|\arg(\lambda_i)| > \frac{q\pi}{2}, i = 1, 2, 3. \tag{5}$$

Proposition 2.1 [8]

(i) When $D(P) > 0$, then $(\beta\gamma T_0, \gamma T_0, T_0)$ is locally asymptotically stable if

$$(\alpha+\beta+\gamma)(\frac{1}{\alpha}+\frac{1}{\beta}+\frac{1}{\gamma}) > (1+n\alpha\beta\gamma T_0^{n+1}). \tag{6}$$

(ii) If $D(P) < 0$, then $(\beta\gamma T_0, \gamma T_0, T_0)$ is locally asymptotically stable for $q < 2/3$.

(iii) If $D(P) < 0, (\alpha+\beta+\gamma)(\frac{1}{\alpha}+\frac{1}{\beta}+\frac{1}{\gamma}) = (1+n\alpha\beta\gamma T_0^{n+1})$, then $(\beta\gamma T_0, \gamma T_0, T_0)$ is locally asymptotically stable for all $q \in (0,1)$.

2.1 Hopf bifurcation analysis versus the fractional order q

The fractional order q affects the stability of fractional order model. Therefore we can choose q as a bifurcation parameter in the fractional order model.

Define a function f with respect to q

$$f(q) = q\pi/2 - \min_{1\leq i\leq 3} |\arg(\lambda_i)|.$$

If $f(q) < 0$, then the equilibrium point is locally asymptotically stable; if $f(q) > 0$, then the equilibrium point is unstable.

Theorem 2.1 ([12]; Existence of Hopf bifurcation) When a bifurcation parameter q passes through the critical value $q^* \in (0,1)$, fractional order model (1) undergoes a Hopf bifurcation at (M_{eq}, E_{eq}, T_{eq}), if the following conditions hold:

(i) The Jacobian matrix of model (1) at (M_{eq}, E_{eq}, T_{eq}) has a complex conjugate eigenvalues $\lambda_{1,2} = \theta \pm i\omega$, where $\theta > 0$, and negative real root λ_3,

(ii) $f(q^*) = 0, (q^* = \frac{2}{\pi}|\arg(\lambda_{1,2})|)$

(iii) $\left.\frac{d[f(q)]}{dq}\right|_{q=q^*} \neq 0$ (transversality condition).

So (M_{eq}, E_{eq}, T_{eq}) is locally asymptotically stable for $q \in (0,q^*)$ and is unstable when $q \in (q^*,1)$. Also Hopf bifurcation occurs at $q = q^*$.

3 Control of the Goodwin-Griffith system

If we add the control term, the system (1) becomes

$$\begin{aligned} D^q M(t) &= \frac{1}{1+T^n} - \alpha M, \\ D^q E(t) &= M - \beta E, \\ D^q T(t) &= E - \gamma T + \upsilon, \end{aligned} \tag{7}$$

where $0 < q \leq 1$, $\upsilon = -kM$, and k is an appropriate gain.

To evaluate the equilibrium points, let

$$D^q M(t) = D^q E(t) = D^q T(t) = 0,$$

which yield

$$M = \beta E = \frac{\beta\gamma T}{1-\beta k},$$

and

$$T(1+T^n) = \frac{1-\beta k}{\alpha\beta\gamma},$$

if T_0 is a root of equation (9), then the equilibrium point is $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0)$ where

$$T_0(1+T_0^n) = \frac{1-\beta k}{\alpha\beta\gamma},$$

and the characteristic polynomial is

$$\lambda^3 + (\alpha+\beta+\gamma)\lambda^2 + (\alpha\beta+\beta\gamma+\alpha\gamma-k\tau)\lambda + (\alpha\beta\gamma+\tau(1-\beta k)) = 0,$$

where

$$\tau = \frac{n\alpha^2\beta^2\gamma^2 T_0^{n+1}}{(1-\beta k)^2} > 0.$$

A sufficient condition for the local asymptotic stability of $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0)$ is

$$|\arg(\lambda_i)| > \frac{q\pi}{2}, i = 1,2,3.$$

Proposition 3.1 [8]

(i) When $D(P) > 0$, then $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0)$ is locally asymptotically stable if

$$(\alpha\beta+\beta\gamma+\alpha\gamma-k\tau) > 0, \ \ (\alpha\beta\gamma+\tau(1-\beta k)) > 0, (\alpha+\beta+\gamma)(\alpha\beta+\beta\gamma+\alpha\gamma-k\tau) > (\alpha\beta\gamma+\tau(1-\beta k)). \tag{10}$$

(ii) If $D(P) < 0, (\alpha\beta+\beta\gamma+\alpha\gamma-k\tau) \geq 0, (\alpha\beta\gamma+\tau(1-\beta k)) > 0$, then $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0)$ is locally asymptotically stable for $q < 2/3$.

(iii) If $D(P) < 0, (\alpha\beta+\beta\gamma+\alpha\gamma-k\tau) > 0, (\alpha+\beta+\gamma)(\alpha\beta+\beta\gamma+\alpha\gamma-k\tau) = (\alpha\beta\gamma+\tau(1-\beta k))$, then $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0)$ is locally asymptotically stable for all $q \in (0,1)$.

(iv) The necessary condition for locally asymptotically stable to $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0)$, is $(\alpha\beta\gamma+\tau(1-\beta k)) > 0$.

4 Results and discussion

For solving nonlinear fractional differential equations we used the Adams method ([13]-[15]).

For system (1) approximate solutions are shown in Figs. 1-6 for $\alpha = 0.34, \beta = 0.27, \gamma = 0.38, n = 9$ and $q = 1, 0.95, 0.9$.

$T_0 = 1.3918$ and the equilibrium point $(\beta\gamma T_0, \gamma T_0, T_0) = (0.142799, 0.528884, 1.3918)$ is locally asymptotically stable where,

$$\lambda_1 = -1,$$
$$\lambda_{2,3} = 0.00500125 \pm 0.577562i,$$
$$|\arg(\lambda_1)| = \pi > \frac{q\pi}{2}, |\arg(\lambda_{2,3})| = 1.56214 > \frac{q\pi}{2}, \ 0 < q < q^* < 1,$$

and the bifurcation parameter q^* is $q^* = 0.994487$.

For $q = 1 > q^*$ the equilibrium point $(\beta\gamma T_0, \gamma T_0, T_0) = (0.142799, 0.528884, 1.3918)$ is untable since the condition (6) is not satisfied.

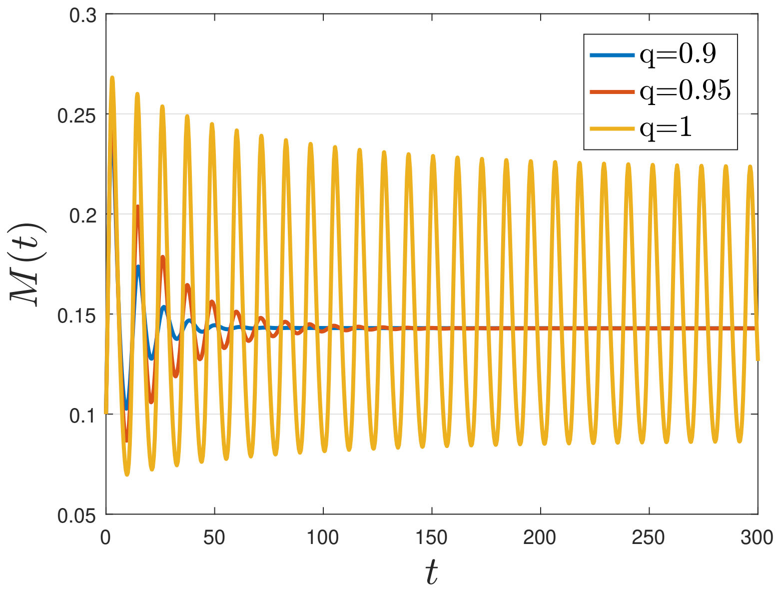

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Fig. 1: Plot of $M(t)$ of system (1) for $q = 0.9, 0.95, 1$.

For the system (7) the approximate solutions are displayed in Figs. 7-12 for $\alpha = 0.34, \beta = 0.27, \gamma = 0.38, n = 9, k = -1.1$.

$T_0 = 1.42997$ and the equilibrium point $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0) = (0.113119, 0.418958, 1.42997)$ is locally asymptotically stable where,

$$\lambda_1 = -0.794114,$$

$$\lambda_{2,3} = -0.0979429 \pm 0.643796i,$$
$$|\arg(\lambda_1)| = \pi > \frac{q\pi}{2}, |\arg(\lambda_{2,3})| = 1.72177 > \frac{q\pi}{2}, \ 0 < q < 1,$$

and for $q = 1$ the equilibrium point $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0) = (0.113113, 0.418938, 1.4299)$ is locally asymptotically stable since the condition (10) is satisfied. But for $0 < q < 1$ the equilibrium point is more stable than for $q = 1$ see Fig. 13 for calculating the time.

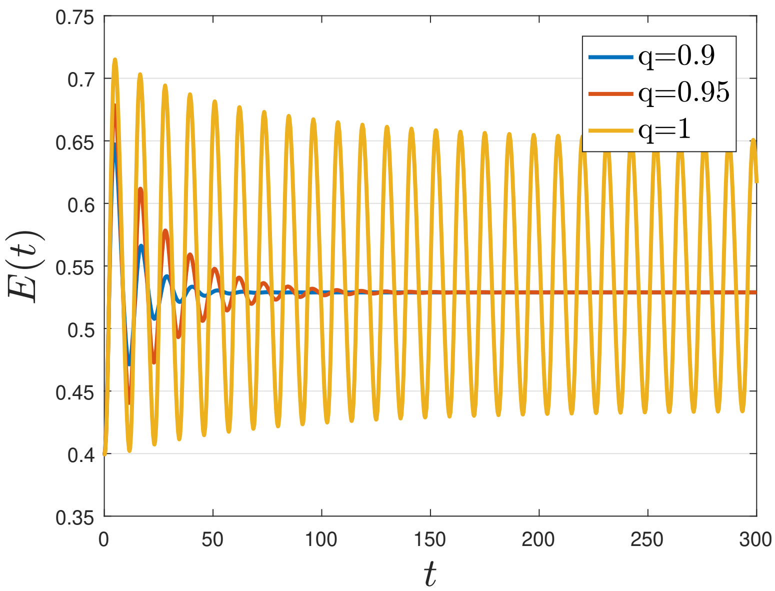

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Fig. 2: Plot of $E(t)$ of system (1) for $q = 0.9, 0.95, 1$.

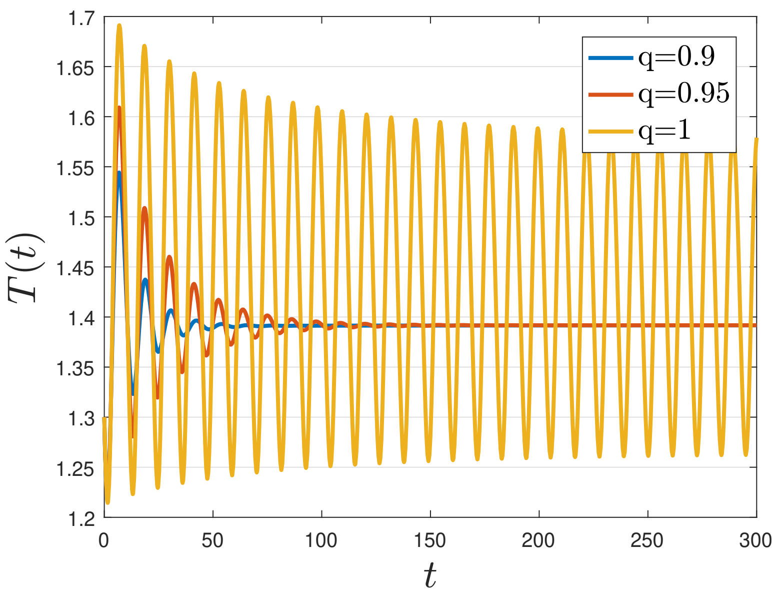

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Fig. 3: Plot of $T(t)$ of system (1) for $q = 0.9, 0.95, 1$.

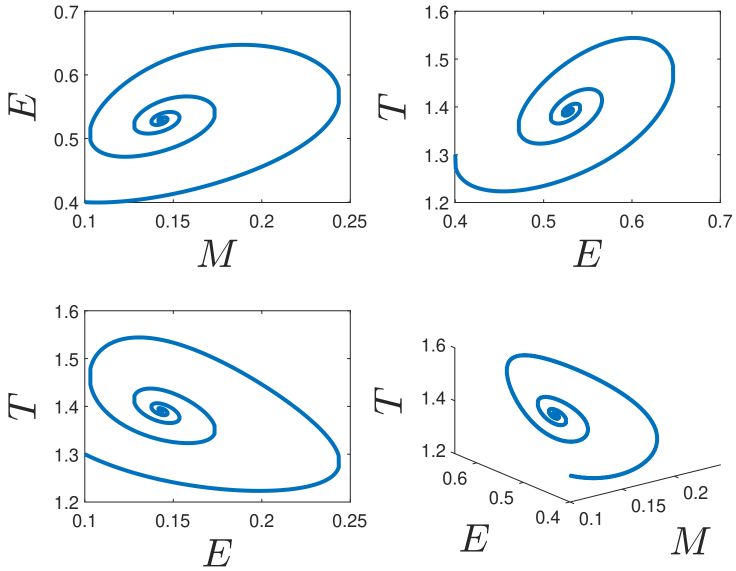

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Fig. 4: Phase portraits of system (1) for $q = 0.9$.

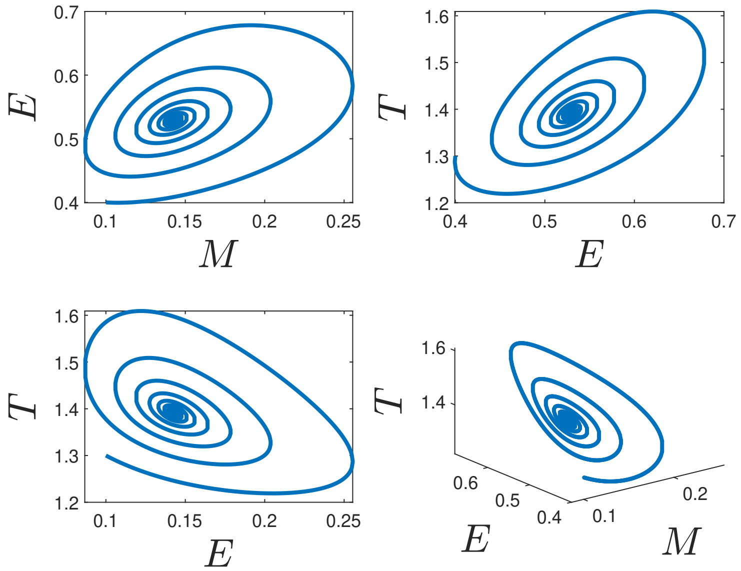

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Fig. 5: Phase portraits of system (1) for $q = 0.95$.

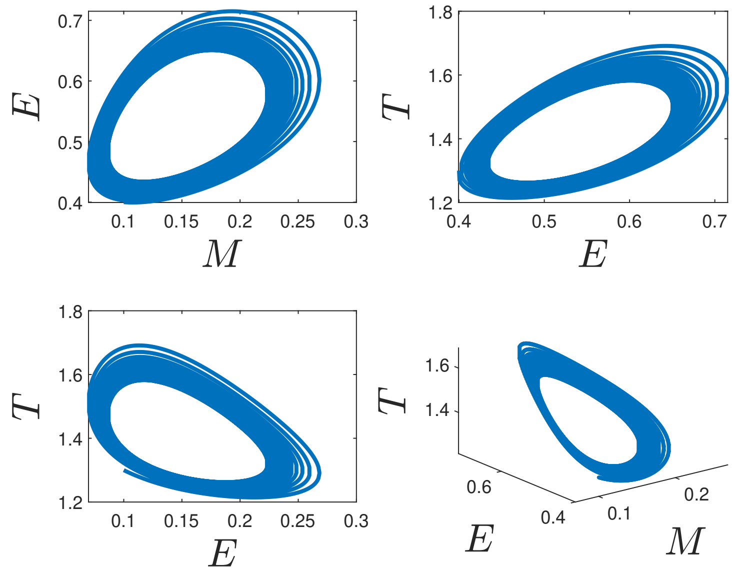

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Fig. 6: Phase portraits of system (1) for $q = 1$.

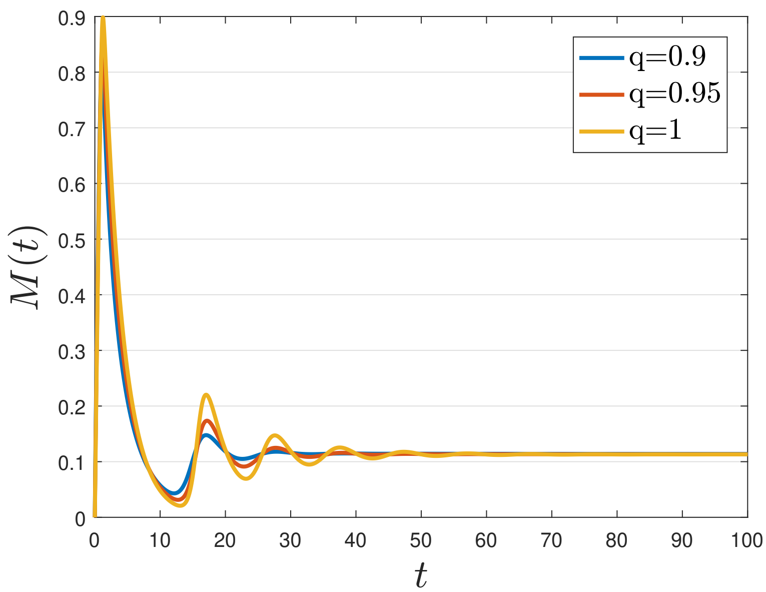

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Fig. 7: Plot of $M(t)$ of system (7) for $q = 0.9, 0.95, 1$.

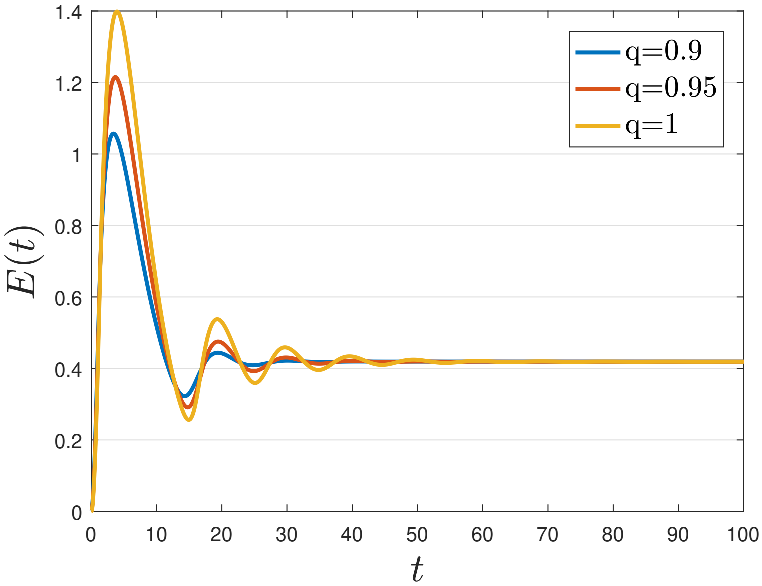

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Fig. 8: Plot of $E(t)$ of system (7) for $q = 0.9, 0.95, 1$.

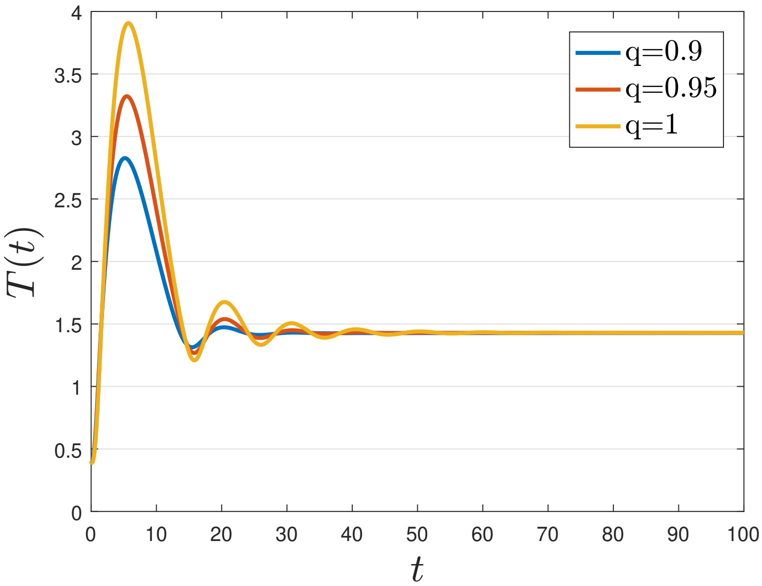

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Fig. 9: Plot of $T(t)$ of system (7) for $q = 0.9, 0.95, 1$.

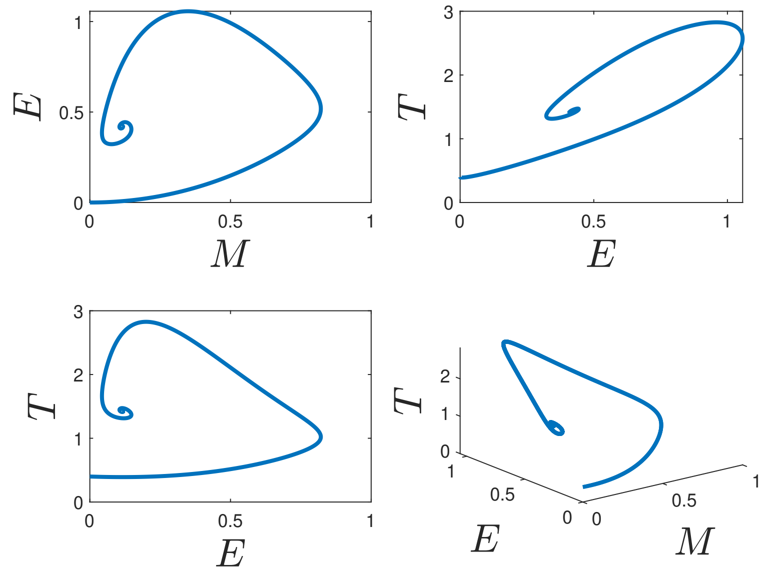

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Fig. 10: Phase portraits of system (7) for $q = 0.9$.

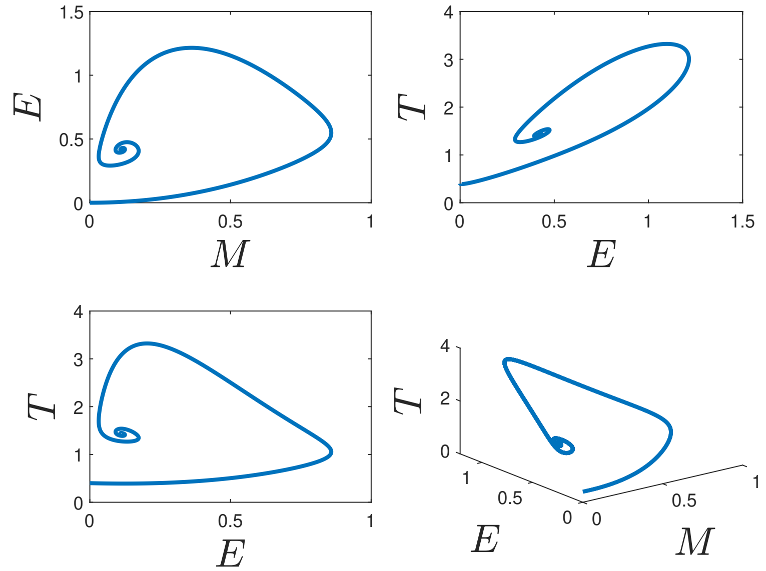

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Fig. 11: Phase portraits of system (7) for $q = 0.95$.

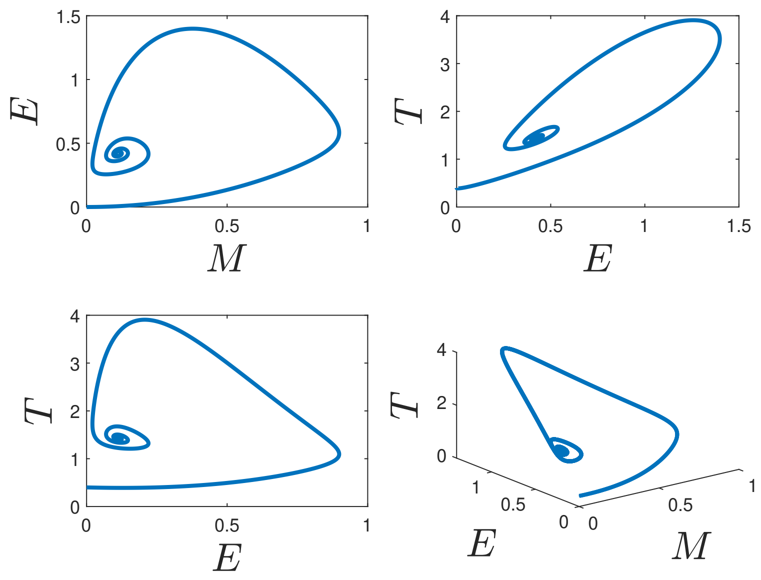

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Fig. 12: Phase portraits of system (7) for $q = 1$.

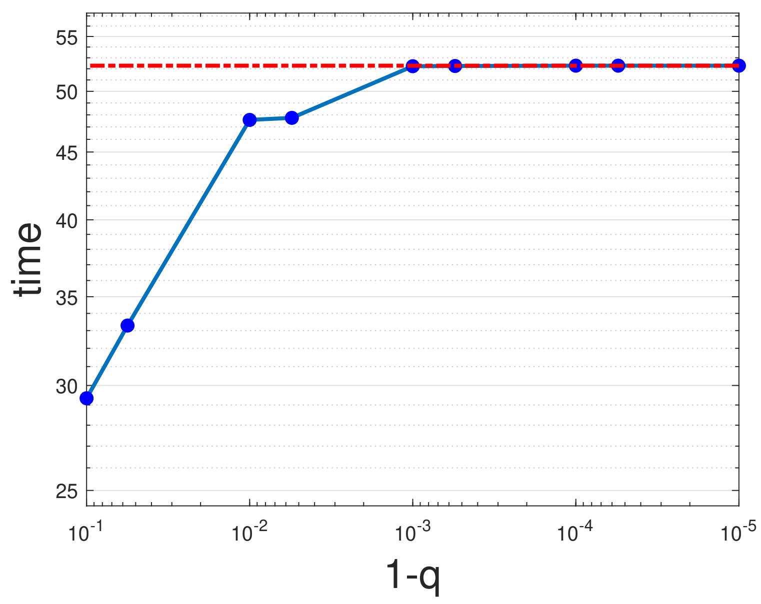

Fig. 13: Time vs. fractional order.

5 Conclusion

We studied the fractional Goodwin-Griffith systems, stability and Hopf bifurcation of the models have been investigated. Also, numerical solutions were presented.

From Figs. 1-6 the equilibrium point $(\beta\gamma T_0, \gamma T_0, T_0)$ is locally asymptotically stable for $0 < q < q^* < 1$ and unstable for $q = 1$. Figs. 1-3 show M, E, T of system (1) for $q = 0.9, 0.95, 1$ and the phase portraits in Figs. 4-6.

From Figs. 7-12 the equilibrium point $(\frac{\beta\gamma T_0}{1-\beta k}, \frac{\gamma T_0}{1-\beta k}, T_0)$ is locally asymptotically stable for $0 < q \leq 1$ but for $0 < q < 1$ the equilibrium point is more stable than $q = 1$ see Fig. 13 for computing the time with different fractional orders.

Figs. 7-9 show M, E, T of system (7) for $q = 0.9, 0.95, 1$ and the phase portraits in Figs. 10-12.

We would argue that fractional order equations are more appropriate than integer order equations in modeling biological, economic, and social systems where memory effects are important.

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