Asian Journal of Mathematics and Computer Research

Volume 31, Issue 3, Page 53-62, 2024; Article no.AJOMCOR.12238

ISSN: 2456-477X

Periodic Solutions for a Modified Disease Mathematical Model

Chunhua Feng [a*]

[a] *Department of Mathematics and Computer Science, Alabama State University, Montgomery, USA.*

Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

Article Information

DOI: https://doi.org/10.56557/ajomcor/2024/v31i38790

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://prh.ikprress.org/review-history/12238

Received: 08/05/2024

Accepted: 13/07/2024

Published: 26/07/2024

Original Research Article

Abstract

The present paper investigates the existence of periodic oscillations for a delayed Parkinson's disease mathematical model. We extend the result in the literature from stability to oscillation. Two sufficient conditions to guarantee the oscillation of the solutions are provided. Some parameter that affects the oscillation is sensitive from our simulation.

Keywords: Modified disease model; delay; periodic solution.

2010 Mathematics Subject Classification: 34K13.

1 Introduction

Many researchers have studied various Parkinson's disease models [1-20]. One can also see the review articles [21-23]. For example, Asai et al. introduced the following model based on the central pattern generator theory:

**Corresponding author: E-mail: cfeng@alasu.edu;*

Cite as: *Feng, Chunhua. 2024. "Periodic Solutions for a Modified Disease Mathematical Model". Asian Journal of Mathematics and Computer Research 31 (3):53-62. https://doi.org/10.56557/ajomcor/2024/v31i38790.*

$$\begin{cases} v_1'(t) = c(v_1(t) - \frac{1}{3}v_1^3(t) - w_1(t) + z_1(t)) + \delta(v_2(t) - v_1(t)), \\ w_1'(t) = \frac{1}{c}(u_1(t) - b_1w_1(t) + a) + \varepsilon v_2(t), \\ v_2'(t) = c(v_2(t) - \frac{1}{3}v_2^3(t) - w_2(t) + z_2(t)) + \delta(v_1(t) - v_2(t)), \\ w_2'(t) = \frac{1}{c}(v_2(t) - b_2w_2(t) + a) + \varepsilon v_1(t), \end{cases} \tag{1}$$

where v_1 and v_2 are outputs to the network system which could be compared to the rotational velocities. All model constants are positive real numbers [1]. Wang et al. have considered the following mathematical model:

$$\begin{cases} \tau_S S'(t) = F_S(-W_{GS}G(t - T_{GS}) + W_{CS}E(t - T_{CS})) - S(t), \\ \tau_G G'(t) = F_G(W_{SG}S(t - T_{SG}) - Str) - G(t), \\ \tau_E E'(t) = F_E(-W_{CC}I(t - T_{CC}) + W_{EE}E(t - T_{EE})) + C - E(t), \\ \tau_I I'(t) = F_I(W_{CC}E(t - T_{CC}) - W_{II}E(t - T_{II})) - I(t), \end{cases} \tag{2}$$

where $S(t), G(t), E(t)$ and $I(t)$ represent the subthalamic nucleus, the globus pallidus, the firing rate of cortical excitatory pyramidal neurons, the firing rate of inhibitory nuclei, respectively. $T(t)$ and $W(t)$ represent the delay and connection weight in different projections. $F_U(x) = \frac{M_U}{1+\frac{(M_U - B_U)e^{(-4x/M_U}}{B_U}}(U = S, G, E, I)$ are activation functions. The Hopf bifurcation critical condition of the system (2) was given in [3]. Recently, Tuwairqi and Badrah provided the following model [5]:

$$\begin{cases} N'(t) = \sigma - \beta N(t)\alpha S(t) - a_1N(t) - a_2N(t) - \mu_1N(t), \\ I'(t) = \beta N(t)\alpha S(t) - d_1I(t) - a_1I(t) - a_2I(t), \\ \alpha S'(t) = ed_1I(t) - a_1\alpha S(t) - a_2\alpha S(t) - \varepsilon_1 ed_1I(t - \tau)e^{-(a_1+a_2)\tau}, \\ M'(t) = a_1I(t) + a_1\alpha S(t) - \varepsilon_2a_1[I(t - \tau) + \alpha S(t - \tau)]e^{-\mu_2\tau} - \mu_2M(t), \\ T'(t) = a_1I(t) + (a_1 + a_2)\alpha S(t) - \varepsilon_3[a_1I(t - \tau) + (a_1 + a_2)\alpha S(t - \tau)]e^{-\mu_3\tau} - \mu_3T(t), \end{cases} \tag{3}$$

where $N(t), I(t)$, and $\alpha S(t)$ represent the density of healthy neurons, the density of infected neurons, and the density of extracellular α-syn in the brain respectively, $M(t)$ represents the density of activated microglia, and $T(t)$ density of activated T cell; $a_i, \varepsilon_i, \mu_i, \sigma$ and β are parameters which belong to (0, 1]. The local stability of the free and endemic equilibrium points was established depending on the basic reproduction number. However, tremor is the most recognizable symptom of Parkinson's disease. Therefore, the existence of periodic solutions of the system (3) is a significant research topic. Considering the effect of time delay, in this paper, we study the existence of periodic solutions for a modified model (3) as follows:

$$\begin{cases} N'(t) = \sigma - \beta N(t)\alpha S(t) - a_{11}N(t) - a_{12}N(t - \tau) - a_{13}I(t - \tau) - \mu_1N(t), \\ I'(t) = \beta N(t)\alpha S(t) - d_1I(t) - a_{21}I(t - \tau) - a_{22}I(t) - a_{23}S(t - \tau), \\ \alpha S'(t) = ed_1I(t) - a_{31}\alpha S(t) - a_{32}\alpha S(t) - \varepsilon_1 ed_1I(t - \tau)e^{-(a_{33}+a_{34})\tau}, \\ M'(t) = a_{41}I(t) + a_{42}\alpha S(t) - \varepsilon_2a_{43}[I(t - \tau) + \alpha S(t - \tau)]e^{-\mu_2\tau} - \mu_2M(t), \\ T'(t) = a_{51}I(t) + (a_{52} + a_{53})\alpha S(t) - \varepsilon_3[a_{51}I(t - \tau) + (a_{52} + a_{53})\alpha S(t - \tau)]e^{-\mu_3\tau} - \mu_3T(t), \end{cases} \tag{4}$$

$a_{ij}, \varepsilon_i, \mu_i, \sigma$ and β are positive parameters. The existence of periodic solution of the system (4) has been studied.

2 Preliminaries

Since $N(t), I(t), S(t), M(t)$, and $T(t)$ represent various densities of neurons. Therefore, we assume that $N(0) \geq 0, I(0) \geq 0, S(0) \geq 0, M(0) \geq 0$ and $T(0) \geq 0$. We first have the following lemma 1.

Lemma 1 Assume that $N(0) \geq 0, I(0) \geq 0, S(0) \geq 0, M(0) \geq 0$, and $T(0) \geq 0$, then all solutions of system (4) are bounded.

Proof Since the initial condition $N(0) \geq 0, I(0) \geq 0, S(0) \geq 0, M(0) \geq 0$, and $T(0) \geq 0$, From system (4), by the variation of the constants method, one can easy to see that $N(t) \geq 0, I(t) \geq 0, S(t) \geq 0, M(t) \geq 0$, and

$T(t) \geq 0$ for arbitrary $t > 0$. Thus, from the first equation of system (4) we have

$$N'(t) \leq \sigma - a_{12}N(t) - a_{12}N(t-\tau) - \mu_1 N(t). \tag{5}$$

Therefore, $N(t) \leq \frac{\sigma}{a_{11}+a_{12}+\mu_1}$. Note that $I(t)$ is always less the healthy neurons $N(t)$. So we have $I(t) \leq \frac{\sigma}{a_{11}+a_{12}+\mu_1}$. Then we have

$$\alpha S'(t) \leq \frac{ed_1\sigma}{a_{11}+a_{12}+\mu_1} - a_{31}\alpha S(t) - a_{32}\alpha S(t). \tag{6}$$

So, $S(t) \leq \frac{ed_1\sigma}{\alpha(a_{11}+a_{12}+\mu_1)(a_{31}+a_{32})}$. Also we get

$$M'(t) \leq \frac{a_{41}\sigma(a_{31}+a_{32}) + a_{42}ed_1\sigma}{(a_{11}+a_{12}+\mu_1)(a_{31}+a_{32})} - \mu_2 M(t). \tag{7}$$

Thus, $M(t) \leq \frac{a_{41}\sigma(a_{31}+a_{32})+a_{42}ed_1\sigma}{\mu_2(a_{11}+a_{12}+\mu_1)(a_{31}+a_{32})}$.Therefore, we have

$$T'(t) \leq \frac{a_{51}(a_{31}+a_{32})\sigma + (a_{52}+a_{53})ed_1\sigma}{(a_{11}+a_{12}+\mu_1)(a_{31}+a_{32})} - \mu_3 T(t). \tag{8}$$

From (8) we have $T(t) \leq \frac{a_{51}(a_{31}+a_{32})\sigma+(a_{52}+a_{53})ed_1\sigma}{\mu_3(a_{11}+a_{12}+\mu_1)(a_{31}+a_{32})}$. This indicates that all solutions of system (4) are bounded. Similar to the result of [5], there exists an endemic equilibrium point $(N^*, I^*.S^*, M^*, T^*)^T$ of the system (4). Then make the change of variables $N(t) \to N(t) - N^*, I(t) \to I(t) - I^*, S(t) \to S(t) - S^*, M(t) \to M(t) - M^*, T(t) \to T(t) - T^*$, we get the following system:

$$\begin{cases} N'(t) = -b_{11}N(t) - b_{13}S(t) - c_{11}N(t-\tau) - c_{12}I(t-\tau) - \beta N(t)\alpha S(t), \\ I'(t) = b_{21}N(t) - b_{22}I(t) + b_{23}S(t) - c_{22}I(t-\tau) - c_{23}S(t-\tau) + \beta N(t)\alpha S(t), \\ S'(t) = b_{32}I(t) - b_{33}S(t) - c_{32}I(t-\tau), \\ M'(t) = b_{42}I(t) + b_{43}S(t) - b_{44}M(t) - c_{42}I(t-\tau) - c_{43}S(t-\tau), \\ T'(t) = b_{52}I(t) + b_{53}S(t) - b_{55}T(t) - c_{52}I(t-\tau) - c_{53}S(t-\tau), \end{cases} \tag{9}$$

where $b_{11} = a_{11} + \mu_1 + \beta\alpha S^*, b_{13} = \beta N^*\alpha, c_{11} = a_{12}, c_{12} = a_{13}, b_{21} = \beta S^*\alpha, b_{22} = d_1 + a_{22}, b_{23} = \beta\alpha N^*, c_{22} = a_{21}, c_{23} = a_{23}, b_{32} = \frac{ed_1}{\alpha}, b_{33} = a_{31} + a_{32}, c_{32} = \frac{\varepsilon_1 ed_1 e^{-(a_{33}+a_{34})\tau}}{\alpha}, b_{42} = a_{41}, b_{43} = a_{42}\alpha, b_{44} = \mu_2, c_{42} = \varepsilon_2 a_{43} e^{-\mu_2\tau}, c_{43} = \varepsilon_2 a_{43}\alpha e^{-\mu_2\tau}, b_{52} = a_{51}, b_{53} = (a_{52} + a_{53})\alpha, b_{55} = \mu_3, c_{52} = \varepsilon_3 a_{51} e^{-\mu_3\tau}, c_{53} = \varepsilon_3(a_{52} + a_{53})e^{-\mu_3\tau}\alpha$.

The system (9) can be expressed as follows:

$$z'(t) = Bz(t) + Cz(t-\tau) + f(z(t)) \tag{10}$$

where $z(t) = [N(t), I(t), S(t), M(t), T(t)]^T$, $z(t-\tau) = [N(t-\tau), I(t-\tau), S(t-\tau), M(t-\tau), T(t-\tau)]^T$, B and C both are 5 by 5 matrices, $f(z(t))$ is a five by one vector:

$$B = (b_{ij})_{5\times5} = \begin{pmatrix} -b_{11} & 0 & -b_{13} & 0 & 0 \\ b_{21} & -b_{22} & b_{23} & 0 & 0 \\ 0 & b_{32} & -b_{33} & 0 & 0 \\ 0 & b_{42} & b_{43} & -b_{44} & 0 \\ 0 & b_{52} & b_{53} & 0 & -b_{55} \end{pmatrix},$$

$$C = (c_{ij})_{2n\times 2n} = \begin{pmatrix} -c_{11} & -c_{12} & 0 & 0 & 0 \\ 0 & -c_{22} & -c_{23} & 0 & 0 \\ 0 & -c_{32} & 0 & 0 & 0 \\ 0 & -c_{42} & -c_{43} & 0 & 0 \\ 0 & -c_{52} & -c_{53} & 0 & 0 \end{pmatrix},$$

$f(z(t)) = [-\beta N(t)\alpha S(t), \beta N(t)\alpha S(t), 0, 0, 0]^T$. The linearized system of (9) is

$$z'(t) = Bz(t) + Cz(t-\tau) \tag{11}$$

Lemma 2 If matrix $S(= B + C)$ is a nonsingular matrix for selected parameters, then there exists a unique equilibrium point $(N^*, I^*.S^*, M^*, T^*)^T$ of the system (3).

Proof Obviously, the trivial solution of the system (10) or ((11)) corresponds to the endemic equilibrium point $(N^*, I^*.S^*, M^*, T^*)^T$ of the system (4). If z^* is an equilibrium point of the system (11), then we have

$$(B + C)z^* = Sz^* = 0 \tag{12}$$

According to the basic linear algebraic knowledge, system (12) has a unique trivial solution since $S = B + C$ is a nonsingular matrix.

3 The Existence of Periodic Solutions

Theorem 1 Assume that zero is the unique equilibrium point of system (11) for selecting parameter values. Let $\beta_1, \beta_2, \cdots, \beta_5$ are characteristic values of matrix B, and $\gamma_1, \gamma_2, \gamma_3, 0, 0$ are characteristic values of matrix C. If there exists one characteristic value, say β_1, such that $Re(\beta_1) > 0$, and $Re(\beta_1) > \max\{|\gamma_1|, |\gamma_2|, |\gamma_3|\}$, then the unique trivial solution of system (11) is unstable, implying that there exists a periodic oscillatory solution in the system (4).

Proof According to the basic differential equation theory, if there exists one characteristic value, say β_1, such that $Re(\beta_1) > 0$, and $Re(\beta_1) > \max\{|\gamma_1|, |\gamma_2|, |\gamma_3|\}$, then the trivial solution $z(t)$ of the system (11) is unstable [24]. Indeed, the characteristic equation associated with the system (11) is the following:

$$\prod_{i=1}^{5}(\lambda - \beta_i - \gamma_i e^{-\lambda\tau}) = 0 \tag{13}$$

Therefore, there is a characteristic equation from the system (13) as follows:

$$\lambda - \beta_1 - \gamma_1 e^{-\lambda\tau} = 0 \tag{14}$$

or

$$\lambda - \beta_1 = 0 \tag{15}$$

If $Re(\beta_1) > 0$, and $Re(\beta_1) > \max\{|\gamma_1|, |\gamma_2|, |\gamma_3|\}$, this means that the equation (14) (or (15)) has a positive real part characteristic value. Thus, the trivial solution of the system (11) is unstable. Meanwhile, the nonlinear term $f(z)$ of the system (10) is a higher order infinitesimal as $N(t) \to 0$ and $S(t) \to 0$. This means that the equilibrium point $(N^*, I^*.S^*, M^*, T^*)^T$ of the system (4) is unstable. The instability of the unique positive equilibrium point together with the boundedness of the solutions will force system(4) to generate a limit cycle, namely, there exists a periodic solution of system (4) [25, 26]. The proof is completed.

For simplify, setting $p = \max\{-b_{11} + b_{21}, -b_{22} + b_{32} + b_{42} + b_{52}, -b_{13} + b_{23} - b_{33} + b_{43} + b_{53}, -b_{44}, -b_{55}\}, q = \max\{-c_{11}, -c_{12} - c_{22} - c_{32} - c_{42} - c_{52}, -c_{23} - c_{43} - c_{53}\}$. Then we have

Theorem 2 Assume that the conditions of Lemma 1 and Lemma 2 hold. If the following inequality is satisfied

$$p + q > 0 \tag{16}$$

Then the system (4) has a periodic oscillatory solution.

Proof To prove the instability of the trivial solution of system (11), let $w(t) = N(t)+I(t)+S(t)+M(t)+T(t)$. Since $N(0) \geq 0, I(0) \geq 0, S(0) \geq 0, M(0) \geq 0$ and $T(0) \geq 0$ Therefore, $w(t) \geq 0$ and

$$w'(t) \leq pw(t) + qw(t-\tau) \tag{17}$$

Specifically, consider the equation

$$v'(t) = pv(t) + qv(t-\tau) \tag{18}$$

Obviously, $w(t) \leq v(t)$. If the trivial solution of equation (18) is unstable, then the trivial solution of (17) is still unstable. The characteristic equation associated with equation (18) is given by

$$\lambda = p + qe^{-\lambda\tau} \tag{19}$$

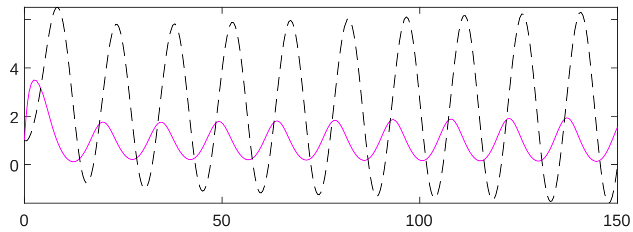
We claim that there exists a positive root of (19) under the condition (16). Let $g(\lambda) = \lambda - p - qe^{-\lambda\tau}$. Thus, $g(\lambda)$ is a continuous function of λ. When $\lambda = 0$, we have $g(0) = -p-q = -(p+q) < 0$. On the other hand, there exists a suitibly large λ, say $\lambda_0 > 0$ such that $g(\lambda_0) = \lambda_0 - p - qe^{-\lambda_0\tau} > 0$ since $e^{-\lambda_0\tau} \to 0$ as $\lambda_0 \to +\infty$. Based on the Intermediate Value Theorem, there exists a $\lambda_* \in (0, \lambda_0)$ such that $g(\lambda_*) = \lambda_* - p - qe^{-\lambda_*\tau} = 0$. In other words, λ_* is a positive characteristic root of equation (19). So the trivial solution of equation (18) is unstable, implying that the unique endemic equilibrium point $(N^*, I^*.S^*, M^*, T^*)^T$ of the system (4) is unstable. Similar to Theorem 1, there exists a periodic solution of the system (4). The proof is completed.

4 Simulation Results

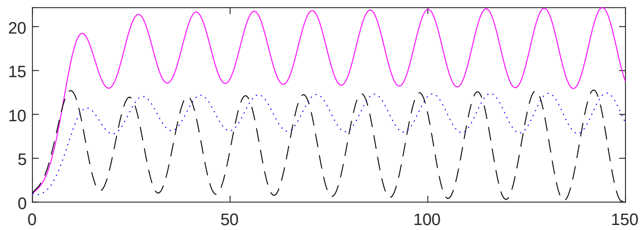
This simulation is based on the system (4). We first select the following parameters: time delay $\tau = 3.8, \sigma = 4.26, \beta = 0.015, \alpha = 0.1, a_{11} = 0.085, a_{12} = 0.025, a_{13} = 0.59, a_{21} = 0.015, a_{22} = 0.0185, a_{23} = 0.095, a_{31} = 0.015, a_{32} = 0.045, a_{33} = 0.085, a_{34} = 0.18, a_{41} = 1.5, a_{42} = 0.0125, a_{51} = 0.025, a_{52} = 0.018, a_{53} = 0.024, e = 0.25, d_1 = 0.18, \varepsilon_1 = 0.015, \varepsilon_2 = 0.025, \varepsilon_3 = 0.075, \mu_1 = 0.62, \mu_2 = 0.85, \mu_3 = 0.75$, Then we get $b_{11} = 0.7267, b_{13} = 0.0013, c_{11} = 0.025, c_{12} = 0.59, b_{21} = 0.0216, b_{22} = 0.1985, b_{23} = 0.0015, c_{22} = 0.015, c_{23} = 0.015, b_{32} = 0.45, b_{33} = 0.06, c_{32} = 0.4116, b_{42} = 1.5, b_{43} = 0.125, b_{44} = 0.85, c_{42} = 0.0029, c_{43} = 0.0003, b_{52} = 0.025, b_{53} = 0.0042, b_{55} = 0.75, c_{52} = 0.0231, c_{53} = 0.0025$. The endemic equilibrium point $(N^*, I^*.S^*, M^*, T^*)^T = (1.0712, 4.3014, 17.4125, 6.4316, 10.1085)^T$.
Then the characteristic values of matrix B are $0.7500, -0.8500, -0.7200, -0.0520, -0.1980$. The characteristic values of matrix C are $-0.0868, -0.0718, -0.0250, 0, 0$. Noting that a characteristic value (0.7500) of matrix B is a positive real number and $0.7500 > 0.0868$. The conditions of Theorem 1 are satisfied. There exists an oscillatory solution for the system (4) (see Fig.1). When we change $\tau = 3.75, \sigma = 3.76, a_{13} = 0.68$, and $\tau = 3.35, \sigma = 3.76, a_{13} = 0.68$, respectively, the other parameters are the same as Fig.1, we see that the oscillatory behavior of the solutions is still maintained (see Fig.2 and Fig.3).

Then we select another set of parameters: time delay $\tau = 3.8, \sigma = 10.76, \beta = 0.012, \alpha = 0.1, a_{11} = 0.025, a_{12} = 0.015, a_{13} = 0.48, a_{21} = 0.015, a_{22} = 0.025, a_{23} = 0.28, a_{31} = 0.035, a_{32} = 0.045, a_{33} = 0.065, a_{34} = 0.12, a_{41} = 0.25, a_{42} = 0.16, a_{51} = 0.27, a_{52} = 0.18, a_{53} = 0.24, e = 0.15, d_1 = 0.18, \varepsilon_1 = 0.15, \varepsilon_2 = 0.12, \varepsilon_3 = 0.28, \mu_1 = 0.82, \mu_2 = 0.75, \mu_3 = 0.95$, Then we get $b_{11} = 0.8625, b_{13} = 0.0061, c_{11} = 0.015, c_{12} = 0.48, b_{21} = 0.0174, b_{22} =$

Fig. 1. Oscillation of the solutions, delay: 3.8, a_{13}=0.59.

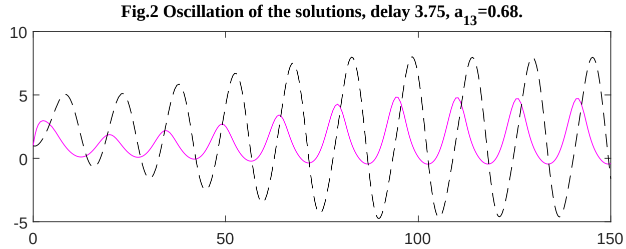


(a) Solid line: N(t), dashed line: I(t).

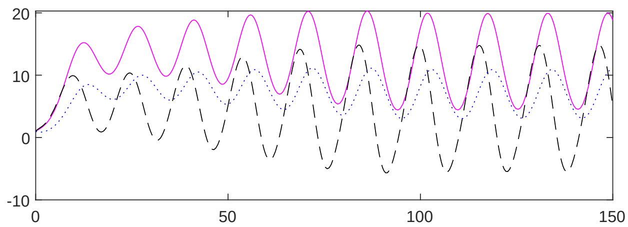


(b) Solid line: S(t), dashed line: M(t), dotted line: T(t).

Fig.2 Oscillation of the solutions, delay 3.75, a_{13}=0.68.



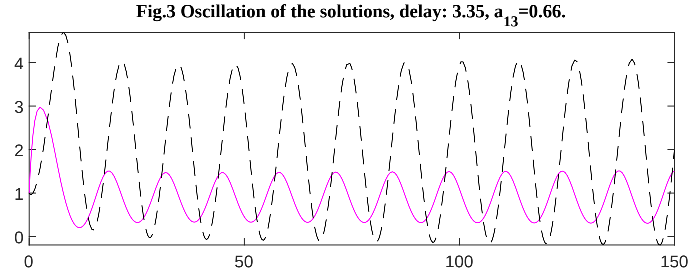
(a) Solid line: N(t), dashed line: I(t).



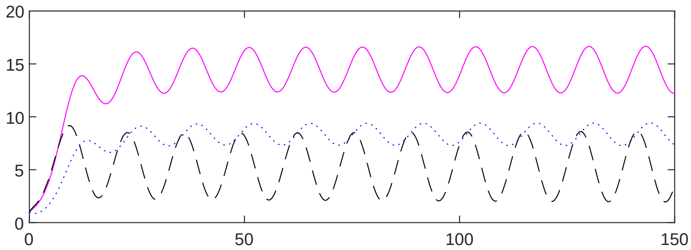
(b) Solid line: S(t), dashed line: M(t), dotted line: T(t).

$0.205, b_{23} = 0.0055, c_{22} = 0.015, c_{23} = 0.28, b_{32} = 0.27, b_{33} = 0.08, c_{32} = 0.382, b_{42} = 0.25, b_{43} = 0.016, b_{44} = 0.75, c_{42} = 0.0017, c_{43} = 0.0002, b_{52} = 0.028, b_{53} = 0.0435, b_{55} = 0.95, c_{52} = 0.0045, c_{53} = 0.0015$. The endemic equilibrium point $(N^*, I^*.S^*, M^*, T^*)^T = (4.5312, 9.9283, 14.6886, 32.5975, 61.9764)^T$. We see that $p = 0.595$, $q = -0.015$, so $p + q > 0$, the conditions of Theorem 2 are satisfied. There exists an oscillatory solution for the system (4) (see Fig.4). When we change $\tau = 3.80, a_{13} = 0.54$, and $\tau = 3.82, a_{13} = 0.52$, respectively, the other parameters are the same as Fig.4, we see that the oscillatory behavior of the solutions is still kept (see Fig.5 and Fig.6).

Fig.3 Oscillation of the solutions, delay: 3.35, a_{13}=0.66.

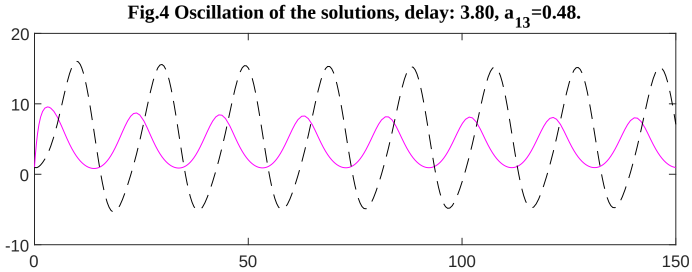


(a) Solid line: N(t), dashed line: I(t).

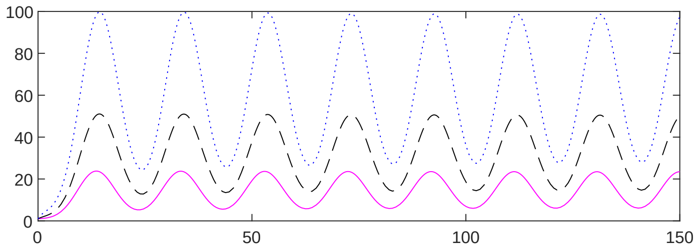


(b) Solid line: S(t), dashed line: M(t), dotted line: T(t).

Fig.4 Oscillation of the solutions, delay: 3.80, a_{13}=0.48.

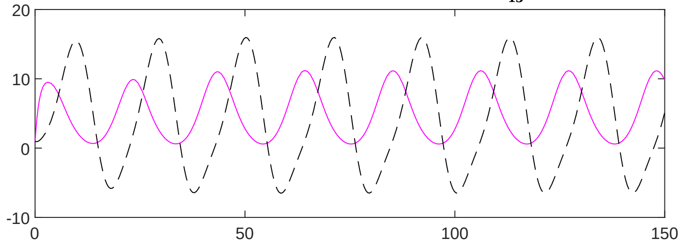


(a) Solid line: N(t), dashed line: I(t).

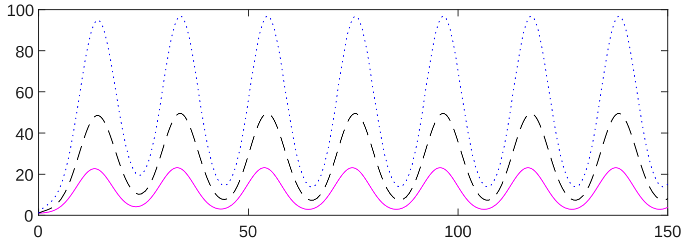


(b) Solid line: S(t), dashed line: M(t), dotted line: T(t).

Fig.5 Oscillation of the solutions, delay: 3.80, a_{13}=0.54.

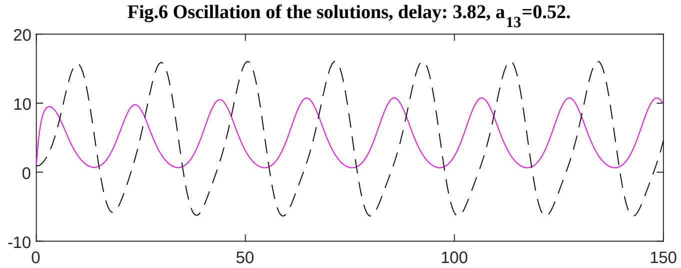


(a) Solid line: N(t), dashed line: I(t).

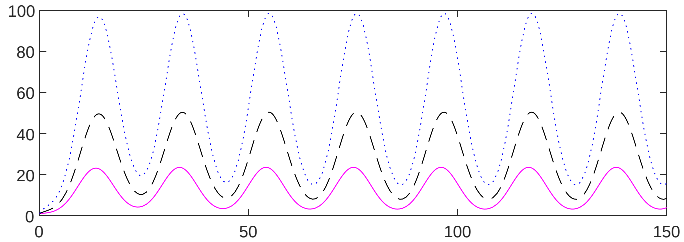


(b) Solid line: S(t), dashed line: M(t), dotted line: T(t).

Fig.6 Oscillation of the solutions, delay: 3.82, a_{13}=0.52.



(a) Solid line: N(t), dashed line: I(t).



(b) Solid line: S(t), dashed line: M(t), dotted line: T(t).

5 Conclusion

This paper discusses the oscillatory behavior of the solutions for a modified delayed Parkinson's disease mathematical model. Based on the method of mathematical analysis, we provided some sufficient conditions to guarantee the oscillation of the solutions. Some simulations are provided to indicate the effectiveness of the criteria. In our simulation, we found that some parameters are sensitive to affect the periodic oscillation. For example, the parameter a_{13} affects the oscillatory behavior too much (see figures). There is a research topic for future study of key parameters in a mathematical model.

Disclaimer (Artificial Intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

Competing Interests

Author has declared that no competing interests exist.

References

[1] Asai Y, Nomura T, Abe K, Matsuo Y, Sato S. Classification of dynamics of a model of motor coordination and comparison with Parkinson's disease data. Biosystems. 2003;71:11-21.
DOI:10.1016/S0303-2647(03)00105-9

[2] Asai Y, Taishin N, Shunsuke S, Akira T, Yoshimi M, Isao M, Kazuo A. A coupled oscillator model of disordered interlimb coordination in patients with Parkinson's disease.Biol. Cybern. 2003;88:152-162.

[3] Wang Z, Hu B, Zhu L, Lin J, Xu M, Wang D. Hopf bifurcation analysis for Parkinson oscillation with heterogeneous delays: A theoretical derivation and simulation analysis. Commun Nonlinear Sci Numer Simulat. 2022;114:106614.

[4] Wang Z, Hu B, Zhou W, Xu M. Wang D. Hopf bifurcation mechanism analysis in an improved cortex-basal ganglia network with distributed delays: An application to Parkinson's disease. Chaos, Solit. Fract. 2023;166:113022.

[5] Tuwairqi SM, Badrah AA. Modeling the dynamics of innate and adaptive immune response to Parkinson's disease with immunotherapy. AIMS Math. 2023;8:1800-1832.

[6] Verheul M, Geuze R. Inter-limb coupling in bimanual rhythmic coordination in Parkinson's disease. Hum. Mov. Sci. 2004;23:503-525.

[7] Ponsen M, Daffertshofer A, Heuve El, Wolters E, Beek P, Berendse H. Bimanual coordination dysfunction in early, untreated Parkinson's disease. Parkinsonism Relat Disord. 2006;12:246-252.

[8] Grado LL, Johnson MD, Netoff TI. Bayesian adaptive dual control of deep brain stimulation in a computational model of Parkinson's disease. Plos. Comput. Biol. 2018;14:1006606.

[9] Mukhtar R, Chang C, Raja MA, Chaudhary NI. Design of intelligent neuro-supervised networks for brain electrical activity rhythms of Parkinson's disease model. Biomimetics. 2023;8:322
Available: https://doi.org/10.3390/biomimetics8030322.

[10] Badrah A, Tuwairqi SA. Modeling the dynamics of innate immune response to Parkinson's disease with a therapeutic approach. Phys. Biol. 2022;19: 056004.

[11] Buatoi S, Retout S, Frey N, Ueckert S. Item response theory as an efficient tool to describe a heterogeneous clinical rating scale in de novo idiopathic Parkinson's disease patients. Pharm. Res. 2017;34:2109–2118.

[12] O'Hara DM, Kalia SK, Kalia LV. Emerging disease-modifying strategies targeting α-synuclein for the treatment of Parkinson's disease. Br. J. Pharmacol. 2018;175:3080–3089.

[13] Lang AE, Espay AJ. Disease modification in Parkinson's disease: current approaches, challenges, and future considerations. Mov. Disord. 2018;33:660–677.

[14] Mukhtar R, Chang CY, Raja MA, Chaudhary NI, Shu CM. Novel nonlinear fractional order Parkinson's disease model for brain electrical activity rhythms: Intelligent adaptive Bayesian networks. Chaos, Soli. Fract. 2024;180:114557.

[15] Kumari S, Rana B, Kumaran SS, Chaudhary S, Jain S, Srivastava AK, Rajan R. Gray matter atrophy in a 6-OHDA-induced model of Parkinson's disease. Neurosci. 2024;551:217-228.

[16] Najjar HA, Rousan NA, Najjar DA. Hybrid grey wolf and whale optimization for enhanced Parkinson's prediction based on machine learning models using biomedical sound. Inf. Med. Unlocked. 2024;48:101524.

[17] Chen L, Sun J, Gao L, Wang J, Ma J, Xu E, Zhang D, Li L, Wu T. Dysconnectivity of the parafascicular nucleus in Parkinson's disease: A dynamic causal modeling analysis. Neurobiol. Disease. 2023;188:106335.

[18] Walker JJ, Meunier E, Garcia S, Messaoudi B, Mouly A, Veyrac A, Buonviso N, Courtiol E. State-dependent alteration of respiration in a rat model of Parkinson's disease. Exper. Neurology. 2024;375:114740.

[19] Gao X, Fu J, Yu DH, Lu E, Liu S. Integrated network pharmacology and phosphoproteomic analyses of Baichanting in Parkinson's disease model mice, Heliyon. 2024;10:e26916.

[20] Fu CL, Dong BC, Jiang X, Li D, Yao J. A cell therapy approach based on iPSC-derived midbrain organoids for the restoration of motor function in a Parkinson's disease mouse model. Heliyon. 2024;10:e24234.

[21] Akyazı O, Korkmaz D, Cevher SC. Experimental Parkinson models and green chemistry approach. Behavio. Brain Res. 2024;471:115092.

[22] Hassani S, Esmaeili A. The neuroprotective effects of ferulic acid in toxin-induced models of Parkinson's disease: A review. Ageing Res. Rev. 2024;97:102299.

[23] Aslam S, Manfredsson F, Stokes A, Shill H. "Advanced" Parkinson's disease: A review.Parkinsonism and Related Disorders. 2024;123:106065.

[24] Kolmanovskii VB, Myshkis AD. Introduction to the theory and applications of functional-differential equations. Math. its Appl. 463, Kluwer Academic Publishers, Dordrecht; 1999.

[25] Chafee N. A bifurcation problem for a functional differential equation of finite retarded type. J. Math. Anal. Appl. 1971;35:312-348.

[26] Feng C, Plamondon R. An oscillatory criterion for a time delayed neural network model. Neural Networks. 2012;29:70-79.

Peer-review history:
The peer review history for this paper can be accessed here (Please copy paste the total link in your browser address bar)
https://prh.ikprress.org/review-history/12238