Stability Analysis of a Novel Mathematical Model of Plasmodium Life Cycle in Mosquito Midgut

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Abstract: ***Present article investigates the complexity and stability analysis of plasmodium life cycle model in mosquito midgut. The existence of equilibrium point of the system are presented. Analysis of global stability are investigated by constructing suitable condition, around the interior equilibrium point. Theoretical results are numerically supported and the diagrams are presented.***

Keywords: ***Plasmodium, Inhost equilibrium point, midgut, stability***.

I. INTRODUCTION

Around the world, 2500 species of mosquitoes are there. Among that 300 species well known disease carriers. One of the most serious infectious diseases in tropical countries is malaria, which comes due to plasmodium parasite. This disease is spread by female Anopheles mosquito. About a half of the world is affected by plasmodium parasite. Five plasmodium species infect human: 'Plasmodium Falciparam', 'Plasmodium Vivax', 'Plasmodium Ovale', 'Plasmodium Malariae', 'Plasmodium Knowles'i. The plasmodium parasite has to complete life cycle in mosquito midgut. There are three stages in plasmodium life cycle . The first two stages parasite development happens in human's vertebrate host. The third stage parasite development starts from mosquito's midgut by taking the gametocytes from human. The gametocytes cantain male and female gametes. This gametocytes are suck up by the mosquito while taking blood meal from infected vertebrate host. Along with the blood meal these male and female gametes travel to the mosquitoes midgut. Here male and female gametes fertilize each other and forming a zygote. The developed 'zygotes' called as ookinete which penetrates the wall of the midgut. In the midgut wall, the ookinete set in the outside membrane of gut associated develops into an oocyst. During this stage, oocyst turn out massive numbers of tiny elongated sporozoan. These sporozoite travel to the salivary glands of the anopheles mosquito. From here they are injected into the blood of the next vertebrate host.

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In the authors knowledge, no one has investigated the mathematical model of plasmodium life cycle in mosquito midgut which we have discussed in this work. A lot of work has been done to describe about the plasmodium life cycle in human and mosquito, but no one has done the control in parasite development. This work is a novel contribution in this area.

The structure of the article presents as follows, In section2, the mathematical model of plasmodium life cycle in mosquito midgut has been presented. The analysis of global stability around the equilibrium point are discussed in section 3 & 4 . Numerical simulation are done for the described system in section 5. Finally the conclusion part with supportive diagrams are presented in section 6.

II. PRELIMINARIES AND PROBLEM DESCRIPTION

The following are assumptions for mathematical modeling of Plasmodium Life Cycle in Mosquito Midgut(PLCMM). The total population of PLCMM consists of seven states, such as Human, Male gametocyte, Female gametocyte, Zygote, Ookinete, Oocyst, Sporozoite.

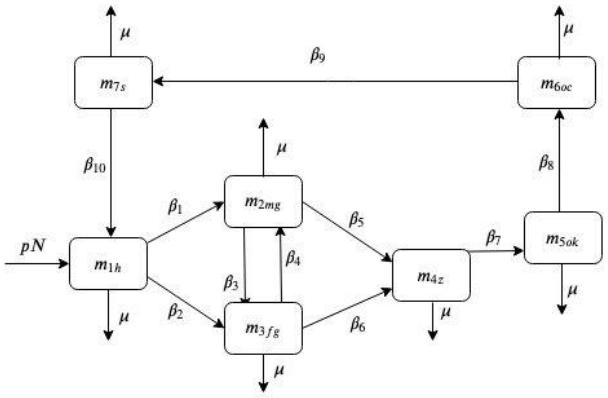

Fig. 1 Flow diagram of PLCMM

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In all states, the natural death rate can be assumed as μ uniformly. Let pN be considered as the existing population, here p is defined as natural birth rate(nbr) in m_{1h} state. Fig.1 depicts the flow diagram of PLCMM.

The Mathematical model of PLCMM is given below with the assumption m_{1h}, m_{2mg}, m_{3fg}, m_{4z}, m_{5ok}, m_{6oc} and m_{7s} are the number of human, male gametocyte, female gametocyte, zygote, Ookinete, Oocyst and sporozoite respectively, at time t. β_1 is the rate of male gametocyte from human, β_2 is the rate of female gametocyte from human, β_3 is the rate of male gametocyte fertilize with female gametocyte forming a zygote, β_4 is the rate of female gametocyte fertilize with male gametocyte forming a zygote, β_5 is the rate of zygote from m_{2mg} fertilize state, β_6 is the rate of zygote from m_{3fg} fertilize state, β_7 is the rate of Ookinete from zygote, β_8 is the rate of Oocyst from Ookinete, β_9 is the rate of sporozoite from Oocyst, β_{10} is the rate of sporozoite penetrate the vertebrate host while the biting of female anopheles mosquito, μ is the normal death at all states and N is the total population. By the assumption the description of the model is given below:

$$\frac{dm_{1h}}{dt} = (pN-\mu)m_{1h} - \beta_1 m_{2mg} - \beta_2 m_{3fg} + \beta_{10} m_{7s}$$
$$\frac{dm_{2mg}}{dt} = \beta_1 m_{1h} - (\beta_3+\beta_5+\mu)m_{2mg} + \beta_4 m_{3fg}$$
$$\frac{dm_{3fg}}{dt} = \beta_2 m_{1h} - (\beta_4+\beta_6+\mu)m_{3fg} + \beta_3 m_{2mg}$$
$$\frac{dm_{4z}}{dt} = \beta_5 m_{2mg} - (\beta_7+\mu)m_{4z} + \beta_6 m_{3fg} \quad (1)$$
(1)
$$\frac{dm_{50k}}{dt} = \beta_7 m_{4z} - (\beta_8+\mu)m_{50k}$$
$$\frac{dm_{60c}}{dt} = \beta_8 m_{50k} - (\beta_9+\mu)m_{60c}$$
$$\frac{dm_{7s}}{dt} = \beta_9 m_{60c} - (\beta_{10}+\mu)m_{7s}$$

III. THE MODIFIED MATHEMATICAL MODEL OF PLCMM

The modified systems are given below:

$$\frac{dm_{1h}}{dt} = Mm_{1h} - \beta_1 m_{2mg} - \beta_2 m_{3fg} + \beta_{10} m_{7s}$$
$$\frac{dm_{2mg}}{dt} = \beta_1 m_{1h} - Im_{2mg} + \beta_4 m_{3fg}$$
$$\frac{dm_{3fg}}{dt} = \beta_2 m_{1h} - Dm_{3fg} + \beta_3 m_{2mg}$$
$$\frac{dm_{4z}}{dt} = \beta_5 m_{2mg} - Gm_{4z} + \beta_6 m_{3fg}$$
$$\frac{dm_{50k}}{dt} = \beta_7 m_{4z} - Um_{5ok}$$
(2)
$$\frac{dm_{60c}}{dt} = \beta_8 m_{50k} - Tm_{6oc}$$
$$\frac{dm_{7s}}{dt} = \beta_9 m_{6oc} - Zm_{7s}$$

where

M = (pN −μ), I = (β_3 +β_5 +μ), D = (β_4 +β_6+μ),
G = (β_7 +μ), U = (β_8 + μ), T = (β_9 + μ), Z = (β_{10} + μ)

IV. EQUILIBRIA ANALYSIS

Let us discuss the equilibrium point and interior equilibrium point(IEP). We obtain, the following equilibrium point by equating the right hand side eqn. (2) to zero. Then we obtain the equilibrium point as,

Emm = ($m_{1h}, m_{2mg}, m_{3fg}, m_{4z}, m_{5ok}, m_{6oc}, m_{7s}$)

Let $m_{7s} = \gamma > 0$ we get,

$$m_{6oc} = \frac{\gamma Z}{\beta_9},\ m_{5ok} = \frac{\gamma ZT}{\beta_8\beta_9},\ m_{4z} = \frac{\gamma ZTU}{\beta_7\beta_8\beta_9},$$
$$m_{3fg} = \frac{\gamma ZTUG(\beta_1\beta_3+\beta_2 I)(\beta_2\beta_4+\beta_1 D)}{(\beta_7\beta_8\beta_9)(\beta_2\beta_4\beta_5+\beta_1\beta_3\beta_6+\beta_1\beta_5 D+\beta_2\beta_6 I)}$$
$$m_{2mg} = \frac{\gamma ZTUG}{(\beta_7\beta_8\beta_9)(\beta_2\beta_4\beta_5+\beta_1\beta_3\beta_6+\beta_1\beta_5 D+\beta_2\beta_6 I)}$$
$$m_{6oc} = \frac{\beta_1\left[\frac{(\beta_2\beta_4+\beta_1 D)}{(\beta_1\beta_3+\beta_2 I)}+\beta_2\right]\left[\frac{\gamma ZTUG(\beta_1\beta_3+\beta_2 I)(\beta_2\beta_4+\beta_1 D)}{(\beta_7\beta_8\beta_9)(\beta_2\beta_4\beta_5+\beta_1\beta_3\beta_6+\beta_1\beta_5 D+\beta_2\beta_6 I)}\right]-\gamma\beta_{10}}{M}$$

And the IEP is

$$E^*_{mm} = (m^*_{1h}, m^*_{2mg}, m^*_{3fg}, m^*_{4z}, m^*_{5ok}, m^*_{6oc}, m^*_{7s})$$

where,

$$m^*_{1h} = \frac{\beta_1 m^*_{2mg}+\beta_2 m^*_{3fg}-\beta_{10} m^*_{7s}}{M},$$
$$m^*_{2mg} = \frac{\beta_1 m^*_{1h}+\beta_4 m^*_{3fg}}{I},\qquad m^*_{3fg} = \frac{\beta_2 m^*_{1h}+\beta_3 m^*_{2mg}}{D},$$
$$m^*_{4z} = \frac{\beta_5 m^*_{2mg}+\beta_6 m^*_{3fg}}{G},\qquad m^*_{5ok} = \frac{\beta_7 m^*_{4z}}{U},$$
$$m^*_{6oc} = \frac{\beta_8 m^*_{5ok}}{T},\quad m^*_{7s} = \frac{\beta_9 m^*_{6oc}}{Z},$$

V. GLOBAL STABILITY ANALYSIS

Theorem 1: The IEP E^*_{mm} is globally asymptotically stable if the following condition holds,

$$\beta_1 = \frac{(-m_{2mg}(m_{2mg}-m^*_{2mg}) + Im_{2mg} - \beta_4 m_{3fg}}{m_{1h}},$$
$$\beta_2 = \frac{(-m_{3fg}(m_{3fg}-m^*_{3fg}) + Dm_{3fg} - \beta_3 m_{2mg}}{m_{1h}},$$
$$\beta_5 = \frac{(-m_{4z}(m_{4z}-m^*_{4z}) + Gm_{4z} - \beta_6 m_{3fg}}{m_{2mg}},$$
$$\beta_7 = \frac{(-m_{5ok}(m_{5ok}-m^*_{5ok}) + Um_{5ok}}{m_{4z}},$$
(3)
$$\beta_8 = \frac{(-m_{6oc}(m_{6oc}-m^*_{6oc}) + Tm_{6oc}}{m_{5ok}},$$
$$\beta_9 = \frac{(-m_{7s}(m_{7s}-m^*_{7s}) + Zm_{7s}}{m_{6oc}},$$
$$\beta_{10} = \frac{(-m_{1h}(m_{1h}-m^*_{1h}) - Mm_{1h} + \beta_1 m_{2mg} + \beta_2 m_{3fg}}{m_{1h}},$$

Proof: Define the Lyapunov function(LF)

$$V(x_i) = \sum_i \aleph[(m_i - m_i^*) - m_i^* \ln(\frac{m_i}{m_i^*})] \quad (4)$$

where i = 1h, 2mg, 3fg, 4z, 5ok, 6oc, 7s are chosen as a positive constants. It is analyzed that V is a pdf (positive definite function) in the defined region except at E^*_{mm}. Then the rate of change of V of eqn. (4) is

$$\dot{V} = \sum_i \aleph \frac{\dot{m}_i}{m_i}(m_i - m_i^*) \quad (5)$$

Where i = 1h, 2mg, 3fg, 4z, 5ok, 6oc, 7s.

$$\dot{V} = \aleph(m_{1h} - m_{1h}^*)\frac{[(pN-\mu)m_{1h} - \beta_1 m_{2mg} - \beta_2 m_{3fg} + \beta_{10} m_{7s}]}{m_{1h}}$$

$$+\aleph(m_{2mg} - m_{2mg}^*)\frac{[\beta_1 m_{1h} - (\beta_3+\beta_5+\mu)m_{2mg} + \beta_4 m_{3fg}]}{m_{2mg}}$$

$$+\aleph(m_{3fg} - m_{3fg}^*)\frac{[\beta_2 m_{1h} - (\beta_4+\beta_6+\mu)m_{3fg} + \beta_8 m_{2mg}]}{m_{3fg}}$$

$$+\aleph(m_{4z} - m_{4z}^*)\frac{[\beta_5 m_{2mg} - (\beta_7+\mu)m_{4z} + \beta_6 m_{3fg}]}{m_{4z}}$$

$$+\aleph(m_{5ok} - m_{5ok}^*)\frac{[\beta_7 m_{4z} - (\beta_8+\mu)m_{5ok}]}{m_{5ok}}$$

$$+\aleph(m_{6oc} - m_{6oc}^*)\frac{[\beta_8 m_{5ok} - (\beta_9+\mu)m_{6oc}]}{m_{6oc}}$$

$$+\aleph(m_{7s} - m_{7s}^*)\frac{[\beta_9 m_{6oc} - (\beta_{10}+\mu)m_{7s}]}{m_{7s}} \quad (6)$$

Now choosing (3) to (6), we get

$$\dot{V} = -\beta_1(m_{1h} - m_{1h}^*)^2 - \beta_2(m_{2mg} - m_{2mg}^*)^2 - \beta_3(m_{3fg} - m_{3fg}^*)^2 - \beta_4(m_{4z} - m_{4z}^*)^2 - \beta_5(m_{5ok} - m_{5ok}^*)^2 - \beta_6(m_{6oc} - m_{6oc}^*)^2 - \beta_7(m_{7s} - m_{7s}^*)^2 \quad (7)$$

and hence $\dot{V}$ is negative definite.

Therefore, E^*_{mm} is globally asymptotically stable, by Laselle's invariance principle.

Numerical Simulation and Discussion

In this paper mathematical model of PLCMM is introduced and it is observed that the IEP E^*_{mm} of the plasmodium life cycle model is feasible. Moreover all the solution converges to the positive equilibrium. It is observed from this analysis that for PLCMM is stabilized. For the numerical simulations, the solution of the system of PLCMM differential equation is obtained by fourth order R.K method. The parameter values are taken as β_1 = 100.999, β_2 = 90.567, β_3 = 20.5, β_4 = 10.741, β_5 = 30.904, β_6 =20.432, β_7 = 15.169, β_8 = 13.228, β_9 = 19.753, β_{10} = 14.896, μ =0.5 and the parameters are taken as $m_{1h}^* = 11.0001$, $m_{2mg}^* = 40.0000090002$, $m_{3fg}^* = 10.000004$, $m_{4z}^* = 20.000001905$, $m_{5ok}^* = 15.0000165$, $m_{6oc}^* = 16.0001909$, m_{7s}^* =19.00032.

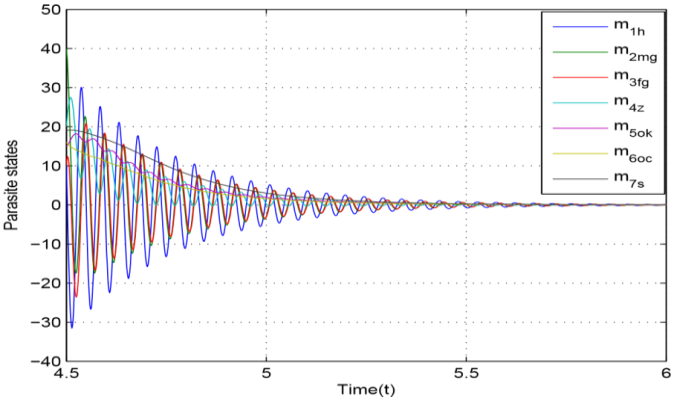

Fig. 2 Stability of deterministic plasmodium life cycle system

The conclusion coming out of this analysis is that for the large value of N, it take a long time to bring the entire populace below short run. Here the birth rate is taken as positive(2) and the total population is taken here as N=10. When the randomness occur in all the states are stabilized at the equilibrium points.

VI. CONCLUSION

In this paper, the complexity of plasmodium life cycle model is investigated. The equilibrium point of the system have been found. By using LF, global stability of the PLCMM are analyzed. By defining suitable LF, it showed that the IEP of the PLCMM is globally stable. The solution converges to the positive equilibrium. The graphical representation are presented which support the numerical simulations part.

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