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Prey-predator Model on the Interaction of Pathogenic Bacteria and Bacteriophages in the Presence of Medication

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: <https://doi.org/10.9734/jamcs/2024/v39i91928>

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://www.sdiarticle5.com/review-history/123606>

Original Research Article

Received: 10/07/2024
Accepted: 12/09/2024
Published: 17/09/2024

Abstract

Antimicrobial resistance has become one of the greatest global threats to health, food security and development. This crisis of antimicrobial resistance has led to research on alternative treatment of bacterial infection. Among the possible alternatives is the revival of phage therapy which was widely abandoned after the clinical availability of antibiotics in the mid-20th century in many countries. Based on this information, this study developed a three-species model with two predators (Bacteriophages and medication) and one prey (Pathogenic bacteria). The main aim of the study is to provide an insight on the interaction of the prey and

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Cite as: Kiplang 'at, Ronoh Byrum, Wesley Kirui, Levi Otanga Olwamba, and Bernard Tonui. 2024. "Prey-Predator Model on the Interaction of Pathogenic Bacteria and Bacteriophages in the Presence of Medication". Journal of Advances in Mathematics and Computer Science 39 (9):71-84. <https://doi.org/10.9734/jamcs/2024/v39i91928>.

predators as suitable alternative for the clinical treatment of bacterial infections using combination antibiotics and bacteriophages. The developed model factors in how the two predators function mutually to fight the prey. The local stability analysis of equilibrium points are carryout using Jacobian matrix method from the model. The stability of the model was found at $\frac{\rho-\sigma}{(\frac{2\rho\theta_3}{k}-\mu\theta_1)} < 1$ which is the basic reproduction number of the model and clearly showed how a therapy of both medication and bacteriophages is effective. Numerical simulation was done using MATLAB to visualize the effects of various treatment combinations of the bacterial infection. The results showed that use of both bacteriophages and antibiotics can be effectively be used in the management of bacterial infections.

Keywords: Prey-predator; bacteriophages; pathogenic bacteria; antibiotics.

1 Introduction

Over the years, bacterial infections have continued to pose a threat to human life. The resistance to medication (antibiotics) has become a worldwide challenge [1]. Various studies on clinical efforts to address this challenge are ongoing. This study seeks to understand the dynamics of the interaction between bacterial infection and combination therapy of antibiotics and bacteriophages in the human body.

2 Preliminaries

This section consists of the model flow diagram, formulation and preliminary analysis of the model.

2.1 Model flow diagram

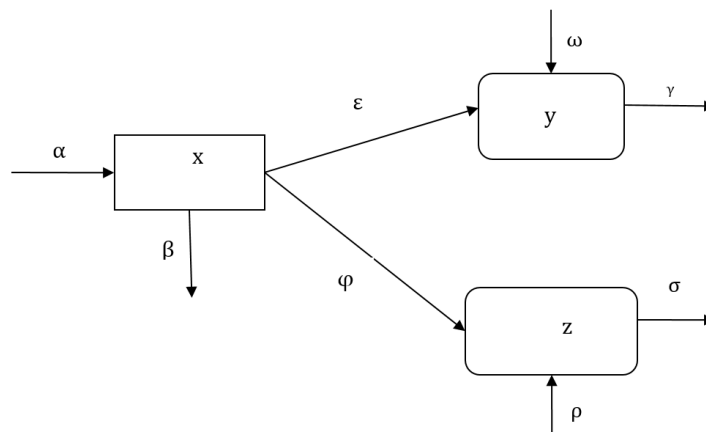


Fig. 1. Model flow diagram

2.2 Model Formulation

The prey-predator model basing on holling type I is formulated with carrying capacity K [2] as follows,

$$\left. \begin{aligned} \frac{dx}{dt} &= \alpha x \left(1 - \frac{x}{k}\right) - \epsilon xy - \phi xz - \beta x \\ \frac{dy}{dt} &= \omega y \left(1 - \frac{y}{k}\right) - \epsilon xy - \gamma y \\ \frac{dz}{dt} &= \rho z \left(1 - \frac{z}{k}\right) + \phi xz - \sigma z \end{aligned} \right\} \quad 2.1$$

Where;

x , y and z are the pathogenic bacteria, primary predator and the secondary predator respectively and
 α is the growth rate of the pathogenic bacteria in the body system
 β is the natural death rate of the pathogenic bacteria
 ω is the rate of introduction of medication into the body system
 γ is the rate of elimination of medication out of the body system.
 ρ is natural growth rate of bacteriophages
 σ is the natural death rate of bacteriophages
 ε is the rate of interaction of the pathogenic bacteria and the primary predator
 μ is the rate of interaction of the pathogenic bacteria and the secondary predator
 t is the time

2.3 Model Preliminary Analysis

Since the model represents the dynamics of cell populations, it is required that the solutions are positive, bounded and feasible. This is confirmed from the following analysis.

2.3.1 Positivity

Properties and boundedness of the model are first done before analysis. The prove that all variables $x(t)$, $y(t)$ and $Z(t)$ are non-negative for all the time t is important in ensuring that the model is well posed and is realistic in representation of population [3].

A well posed problem has a solution, the solution is unique and depends continuously on data and parameters. Having initial conditions $x(0) \geq 0, y(0) \geq 0, z(0) \geq 0$, the basic properties necessary for understanding subsequent results are shown.

Proposition 1

Suppose $\frac{dx}{dt}$, $\frac{dy}{dt}$ and $\frac{dz}{dt}$ are derivatives of the variables x , y and z respectively, then initial conditions of the differential equations (2.1) all positive for any given time t .

Proof

To show Positivity of $x(t)$. Consider the model equation given by;

$$\frac{dx}{dt} = \alpha x \left(1 - \frac{x}{k}\right) - \varepsilon xy - \varphi xz - \beta x.$$

Consider a family of sets where the natural growth rate α of the prey x is monotonically decreasing to a null set. Applying the results in [4 prop 3] on monotonically decreasing sets, we obtain an inequality $\frac{dx}{dt} \geq -(\varepsilon xy + \varphi xz + \beta x)$. Also applying the results in [5, 6] on integral representation of a function and the general properties of integration of a function, we obtain an inequality $x(t) \geq -(\varepsilon xy + \mu xz + \beta x)t$. Consequently $x(t) \geq 0 \geq -(\varepsilon xy + \mu xz + \beta x)t$. Which proves the positivity of $x(t)$.

From the model equation $\frac{dy}{dt} = \omega y \left(1 - \frac{y}{k}\right) - \varepsilon xy - \gamma y$. The positivity of $y(t)$ is shown by taking a family of sets where the rate ω of introduction of the primary predator y is monotonically decreasing to an empty set. Applying the results in [7, 8 prop 5] on monotonically decreasing sets for all values of t , we obtain the inequality $\frac{dy}{dt} \geq -(\varepsilon xy + \gamma y)$. The results in [9, 6] on integrability properties of a function and in [10] on finiteness of a function and known properties of integration are applied to obtain an inequality $y(t) \geq e^{-(\varepsilon xy + \gamma y)t}$. It follows that, $y(t) \geq 0(\varepsilon xy + \gamma y)t$. Therefore $y(t) \geq 0$.

The Positivity of $z(t)$ is shown by taking the equation $\frac{dz}{dt} = \rho z \left(1 - \frac{z}{k}\right) + \varphi xz - \sigma z$ in the model is considered. Given a family of sets where the rate ρ of introduction of secondary predators z Whose number of elements is

diminishing to zero. Applying the results in [4 prop. 11, 12] on monotonically decreasing sets, we obtain the inequality $\frac{dz}{dt} \geq -(-\varphi xz + \sigma z)$. Following the same procedure as in the proof of $x(t) \geq 0$ and $y(t) \geq 0$, we obtain $z(t) \geq 0 \geq (-\mu xz + \sigma z)t$. Which is the required result.

2.3.2 Boundedness

For boundedness we define the total number of pathogenic bacteria in the system at any given time t is given by

$$x = \alpha - \beta x - \varepsilon xy - \varphi xz \tag{2.2}$$

This is where there are changes in the population of the pathogenic bacteria and is known as population dynamics. The feasibility of the developed model is done to describe the region where the system of the equation (2.1) is meaningful biologically.

Proposition 2.

Suppose the equation (2.1) holds, every solution of the model in the system of equation with initial conditions in \mathbb{R}_+^3 approaches and stays in the compact set (Ω) as $t \rightarrow \infty$. Then the feasible solution which is positively invariant set of the model is given by,

$$\Omega = \left\{ (x, y, z) \in \mathbb{R}_+^3 : x(t) \leq \frac{\alpha}{\beta} \right\}$$

Proof

By hypothesis,

$$\frac{dx}{dt} = \alpha - \beta x - \varepsilon xy - \varphi xz \tag{2.3}$$

In the absence of medication and bacteriophages ($y = 0$ and $z = 0$), the equation reduces to

$$\frac{dx}{dt} = -\beta x + \alpha \tag{2.4}$$

$$\frac{dx}{dt} + \beta x(t) = \alpha \tag{2.5}$$

The integrating factor is $e^{\int \beta dt} = e^{\beta t}$

$$\frac{d}{dt} x(t)e^{\beta t} = \alpha e^{\beta t}$$

$$x(t)e^{\beta t} = \int_{t_0}^t \alpha e^{\beta t} dt$$

$$xe^{\beta t} - x(t_0)\alpha e^{\beta t_0} = \frac{\alpha}{\beta} e^{\beta t}$$

$$xe^{\beta t} - x(t_0)\alpha e^{\beta t_0} = \frac{\alpha}{\beta} (e^{\beta t} - e^{\beta t_0})$$

$$x(t) = \frac{\alpha}{\beta} + (x_{t_0} - \frac{\alpha}{\beta}) e^{\beta t_0} \tag{2.6}$$

Therefore

$$x(t) \rightarrow \frac{\alpha}{\beta} \text{ as } t \rightarrow \infty \tag{2.7}$$

Therefore, the solutions of the model equation $\frac{dx}{dt} = \alpha - \beta x - \varepsilon xy - \varphi xz$ are bounded in the compact set (Ω) as illustrated in [5] on compact sets. Therefore, $\Omega = \left\{ (x, y, z) \in \mathbb{R}_+^3 : x(t) \leq \frac{\alpha}{\beta} \right\}$, this implies that Ω is invariant positively for all values of $t > 0$, we therefore conclude that the model is meaningful biologically.

2.4 Stability analysis of the model Equilibria

Let $E = (x, y, z) \in \Omega$ be the equilibrium point of the system given by the system (2.1). The states of equilibrium are obtained by setting the conditions $\frac{dx}{dt} = \frac{dy}{dt} = \frac{dz}{dt} = 0$ [13].

That is;

$$\left. \begin{aligned} \alpha x \left(1 - \frac{x}{k}\right) - \varepsilon xy - \varphi xz - \beta x &= 0 \\ \omega y \left(1 - \frac{y}{k}\right) - \varepsilon xy - \gamma y &= 0 \\ \rho z \left(1 - \frac{z}{k}\right) + \varphi xz - \sigma z &= 0 \end{aligned} \right\} \quad 2.8$$

3 Main Results

3.1 Equilibrium points and their stabilities

The equilibrium points of the system are found at $\frac{dx}{dt}, \frac{dy}{dt}, \frac{dz}{dt} = 0$. This section considers equilibrium points $E_1(x_1, 0, 0), E_2(x_2, 0, z_2), E_3(x_3, y_3, 0)$ and $E^*(x^*, y^*, z^*)$ and the conditions for their stabilities.

3.2 Predator Free Equilibrium Point $E_1(x_1, 0, 0)$

P-Free Equilibrium (PFE) point in the system is the point in the system at which there are no traces of both primary and secondary predators in the body system.

By substituting $(x_1, 0, 0)$ the model (2.1), we obtain;

$$\alpha \left(1 - \frac{x_1}{k}\right) - \beta = 0$$

$$x_1 = k \left(1 - \frac{\beta}{\alpha}\right)$$

Extinction of both predators $\left(k \left(1 - \frac{\beta}{\alpha}\right), 0, 0\right)$

3.2.1 Local Stability for E_1

The local stability of E_1 is computed at $\left(k \left(1 - \frac{\beta}{\alpha}\right), 0, 0\right)$.

Predator-Free Equilibrium (PFE) point in the system is the point in the system at which there are no traces of predators in the body system. Both medication and Bps are not in the body system.

$$\left. \begin{aligned} \frac{dx}{dt} &= \alpha x \left(1 - \frac{x}{k}\right) - \varepsilon xy - \varphi xz - \beta x \\ \frac{dy}{dt} &= \omega y \left(1 - \frac{y}{x}\right) - \varepsilon xy - \gamma y \\ \frac{dz}{dt} &= \rho z \left(1 - \frac{z}{x}\right) + \varphi xz - \sigma z \end{aligned} \right\} \quad (3.1)$$

To establish the equilibrium stability, the Jacobian matrix J of the equation (3.1) is computed and evaluated around the equilibrium state E . To obtain the Jacobian matrix of the system (3.1), the system is linearized at the PFE by partially differentiating the system with respect to the state variables. Therefore, at the Predator-free equilibrium, the Jacobian matrix J is

$$J = \begin{bmatrix} \alpha - \frac{2\alpha x}{k} - \varepsilon y - \varphi z - \beta & -\varepsilon x & -\varphi x \\ -\varepsilon y & \omega - \frac{2\omega y}{k} - \varepsilon x - \gamma & 0 \\ \varphi z & 0 & \rho - \frac{2\rho z}{k} + \varphi x - \sigma \end{bmatrix} \quad (3.2)$$

At $(k(1 - \frac{\beta}{\alpha}), 0, 0)$ we obtain;

$$J_1 = \begin{bmatrix} -\alpha - 3\beta & -\varepsilon k \left(1 - \frac{\beta}{\alpha}\right) & \varphi k \left(1 - \frac{\beta}{\alpha}\right) \\ 0 & \omega - \varepsilon k \left(1 - \frac{\beta}{\alpha}\right) - \gamma & 0 \\ 0 & 0 & \rho + \varphi k \left(1 - \frac{\beta}{\alpha}\right) - \sigma \end{bmatrix}$$

The results in [11] the determinant matrix of the system is given by

$$J_1 - I\lambda = \begin{bmatrix} -\alpha - 3\beta - \lambda & -\varepsilon k \left(1 - \frac{\beta}{\alpha}\right) & \varphi k \left(1 - \frac{\beta}{\alpha}\right) \\ 0 & \omega - \varepsilon k \left(1 - \frac{\beta}{\alpha}\right) - \gamma - \lambda & 0 \\ 0 & 0 & \rho + \varphi k \left(1 - \frac{\beta}{\alpha}\right) - \sigma - \lambda \end{bmatrix} \quad (3.3)$$

The solution of $J_1 - I\lambda = 0$ are the eigen values:

$$\left. \begin{aligned} (-\alpha - 3\beta - \lambda) \left(\omega - \varepsilon k \left(1 - \frac{\beta}{\alpha}\right) - \gamma - \lambda\right) \left(\rho + \varphi k \left(1 - \frac{\beta}{\alpha}\right) - \sigma - \lambda\right) &= 0 \\ \lambda_1 &= -(\alpha + 3\beta) \\ \lambda_2 &= \omega - \varepsilon k - \frac{\varepsilon k \beta}{\alpha} - \gamma \\ \lambda_3 &= \rho + \varphi k - \frac{\varphi k \beta}{\alpha} - \sigma \end{aligned} \right\} \quad (3.4)$$

Clearly λ_1 and $\lambda_2 < 0$ but

For the PFE to be stable we need to show that $\lambda_3 < 0$

Proposition 3

The predator free equilibrium point E_1 in the equation (3.1) is asymptotically stable if Clearly $\lambda_1, \lambda_2, \lambda_3 < 0$ and is unstable if at least one of the $\lambda_1, \lambda_2, \lambda_3$ is positive for all $\alpha, \varepsilon, \varphi, \beta, \omega, \gamma, \rho, \sigma$ and k greater than zero.

Proof

The PFE is asymptotically stable if all the eigen values $\lambda_1, \lambda_2, \lambda_3$ of the $J_1(E_1)$ satisfy the Routh-Hurtwitz criterion [14,15,16]. Applying the Routh-Hurtwitz theorem, λ_1 and λ_2 from equation (3.4) have negative real parts. We move on to establish a necessary and sufficient condition for λ_3 to also have a negative real part. This will ensure that the PFE is stable and asymptotically stable as well.

From λ_3 we obtain

$$\rho + \varphi k - \frac{\varphi k \beta}{\alpha} - \sigma < 0 \tag{3.5}$$

The inequality (3.5) now becomes

$$\varphi k - \frac{\varphi k \beta}{\alpha} < \sigma - \rho \tag{3.6}$$

Dividing (3.6) by φ we obtain

$$k \left(1 - \frac{\beta}{\alpha} \right) < \frac{\sigma - \rho}{\varphi} \tag{3.7}$$

The inequality (3.7) is the necessary and sufficient condition for the PFE state E_1 of the model for it to be asymptotically stable.

Since k is always positive then the death σ rate of bacteriophages must be higher than its growth rate ρ . This is a clear proof that at this equilibrium, there are no predators at all.

Also (3.7) gives the necessary and sufficient condition for the PFE to be in a stable state. The number of bacteriophages $\frac{\rho - \sigma}{\varphi}$ must always be less than the pathogenic bacteria in the body system $k \left(1 - \frac{\beta}{\alpha} \right)$.

3.3 Primary Predator Free Equilibrium Point $E_2(x_2, 0, z_2)$

This is a point where there is no medication in the body system, the Bps are the only ones that are fighting with the pathogenic bacteria.

By substituting $(x_2, 0, z_2)$ in the model (3.1), we obtain;

$$\alpha - \frac{\alpha x}{k} - \varphi z - \beta = 0 \text{ and } \rho - \frac{\rho z}{k} + \varphi x - \sigma = 0.$$

The values of x and z are evaluated and are found to be;

$$x_2 = \frac{k\alpha\rho - k\rho\beta - k^2\varphi\rho + k^2\varphi\sigma}{\alpha\rho - k^2\varphi^2} \tag{3.8}$$

$$z_2 = \frac{k\alpha\rho - k\alpha\sigma + k^2\alpha\varphi - k^2\beta\varphi}{\alpha\rho - k^2\varphi^2} \tag{3.9}$$

$$\text{Let } \frac{k\alpha\rho - k\rho\beta - k^2\varphi\rho + k^2\varphi\sigma}{\alpha\rho - k^2\varphi^2} = A \text{ and } \frac{k\alpha\rho - k\alpha\sigma + k^2\alpha\varphi - k^2\beta\varphi}{\alpha\rho - k^2\varphi^2} = B$$

3.3.1 Local Stability for E_2

The points of computing the local stability of E_2 is at $(A, 0, B)$

The Jacobian matrix of the equilibrium point E_2 is computed by substituting the values of x and z above in (3.2) and is obtained as;

$$J_2 = \begin{bmatrix} \alpha - \frac{2\alpha A}{K} - \varphi B - \beta & -\varepsilon A & -\varphi A \\ 0 & \omega - \varepsilon A - \gamma & 0 \\ \varphi B & 0 & \rho - \frac{2\rho B}{K} + \varphi A - \sigma \end{bmatrix}$$

The determinant matrix $J_2 - I\lambda$ for the matrix is

$$J_{2-I\lambda} = \begin{bmatrix} \alpha - \frac{2\alpha A}{K} - \varphi B - \beta - \lambda & -\varepsilon A & -\varphi A \\ 0 & \omega - \varepsilon A - \gamma - \lambda & 0 \\ \varphi B & 0 & \rho - \frac{2\rho B}{K} + \varphi A - \sigma - \lambda \end{bmatrix} \tag{3.10}$$

The solution of $J_2 - I\lambda = 0$ are the eigen values:

$$\left. \begin{aligned} \lambda_1 &= \alpha - \frac{2\alpha A}{K} - \varphi B - \beta \\ \lambda_2 &= \omega - \varepsilon A - \gamma \\ \lambda_3 &= \rho - \frac{2\rho B}{K} + \varphi A - \sigma \end{aligned} \right\} \tag{3.11}$$

From equation (3.11), λ_1 and λ_3 have negative real parts and for the stability of the equilibrium point, we need to show the sufficient and necessary condition for $\lambda_2 < 0$. This is by applying the Routh-Hurtwitz theorem.

From λ_2 we obtain

$$\omega - \varepsilon A - \gamma < 0 \tag{3.12}$$

From (3.12), the inequality now becomes

$$\frac{\omega - \gamma}{\varepsilon A} < 1 \tag{3.13}$$

The inequality in (3.13) is the necessary and sufficient condition for the PPFE point to be stable. This means that at any given instance, the amount of medication with respect to the pathogenic bacteria is the less than one.

3.4 Secondary Predator Free Equilibrium Point $E_3(x_3, y_3, 0)$

At this equilibrium point, there are no bacteriophages, the pathogenic bacteria are being acted upon by the medication.

We substitute $(x_3, y_3, 0)$ the model (3.1), we obtain;

$$\alpha - \frac{\alpha x}{k} - \varepsilon y - \beta = 0 \text{ and } \omega - \frac{\omega y}{k} - \varepsilon x - \gamma = 0.$$

The evaluation of x and y from the above gives;

$$x_3 = \frac{k\alpha\omega - k\beta\omega - k^2\varepsilon\omega + k^2\varepsilon\gamma}{\alpha\omega - k^2\varepsilon^2} \tag{3.14}$$

$$y_3 = \frac{k\alpha\omega - k\alpha\gamma - k^2\varepsilon\alpha - k^2\varepsilon\beta}{\alpha\omega - k^2\varepsilon^2} \tag{3.15}$$

Let $\frac{k\alpha\omega - k\beta\omega - k^2\varepsilon\omega + k^2\varepsilon\gamma}{\alpha\omega - k^2\varepsilon^2} = C$ and $\frac{k\alpha\omega - k\alpha\gamma - k^2\varepsilon\alpha - k^2\varepsilon\beta}{\alpha\omega - k^2\varepsilon^2} = D$

3.4.1 Local stability for E_3

The local stability of E_3 is computed at $(C, D, 0)$. The Jacobian matrix of the equilibrium point E_3 is computed by substituting the above values of x and z in (3.2) and is obtained as;

$$J_3 = \begin{bmatrix} \alpha - \frac{2\alpha C}{k} - \varepsilon D - \beta & -\varepsilon C & -\varphi C \\ \varepsilon D & \omega - \frac{2\omega D}{K} - \varepsilon C - \gamma & 0 \\ 0 & 0 & \rho + \varphi C - \sigma \end{bmatrix}$$

The determinant matrix $J_3 - I\lambda$ for the matrix is;

$$J_3 = \begin{bmatrix} \alpha - \frac{2\alpha C}{k} - \varepsilon D - \beta - \lambda & -\varepsilon C & -\varphi C \\ \varepsilon D & \omega - \frac{2\omega D}{K} - \varepsilon C - \gamma - \lambda & 0 \\ 0 & 0 & \rho + \varphi C - \sigma - \lambda \end{bmatrix} \tag{3.16}$$

The solution of $J_3 - I\lambda = 0$ are the eigen values:

$$\left. \begin{aligned} \lambda_1 &= \alpha - \frac{2\alpha C}{k} - \varepsilon D - \beta \\ \lambda_2 &= \omega - \frac{2\omega D}{K} - \varepsilon C - \gamma \\ \lambda_3 &= \rho + \varphi C - \sigma \end{aligned} \right\} \tag{3.17}$$

From the eigen values λ_1 and λ_2 have negative real parts and for the stability of the equilibrium point, we need to show the sufficient and necessary condition for $\lambda_3 < 0$. This is by applying the Routh-Hurtwitz theorem.

From λ_3 we obtain

$$\rho + \varphi C - \sigma < 0 \tag{3.18}$$

From (3.18) the inequality becomes

$$\frac{\mu C}{\sigma - \rho} < 1 \tag{3.19}$$

From (3.19) the condition satisfies stability of SPFEP point, this means that the number of pathogenic bacteria with respect to bacteriophages at any given time is less than one.

3.5 Equilibrium Point for the Presence of the Prey and both Predators $E^* (x^*, y^*, z^*)$

At this equilibrium point, the pathogenic bacteria are acted upon mutually by both bacteriophages and antibiotics.

We substitute (x^*, y^*, z^*) the model (3.2), where $x^*, y^*, z^* > 0$ we obtain;

$$\left. \begin{aligned} \alpha - \frac{\alpha x^*}{k} - \varepsilon y^* - \mu z^* - \beta &= 0 \\ \omega - \frac{\omega y^*}{k} - \varepsilon x^* - \gamma &= 0 \\ \rho - \frac{\rho z^*}{k} + \mu x^* - \sigma &= 0 \end{aligned} \right\} \tag{3.20}$$

$$\text{From equation 3.20 } x^* = \frac{k(\alpha - \varepsilon y^* - \mu z^* - \beta)}{\alpha} \tag{3.21}$$

From 3.21 let $\frac{k}{\alpha} = a_1, \alpha - \beta = a_2$

$$\text{Therefore, } x^* = a_1(a_2 - \varepsilon y^* - \mu z^*) \tag{3.22}$$

$$y^* \text{ from 3.20 is obtained as } y^* = \frac{k(\omega - \varepsilon x^* - \gamma)}{\omega} \tag{3.23}$$

$$\text{let } \frac{k}{\omega} = b_1, \omega - \gamma = b_2$$

$$\text{Therefore, } y^* = b_1(b_2 - \varepsilon x^*) \tag{3.24}$$

$$\text{Also } z^* = \frac{k(\rho + \mu x^* - \sigma)}{\rho} \tag{3.25}$$

$$\text{let } \frac{k}{\rho} = c_1, \rho - \sigma = c_2$$

$$\text{Therefore, } z^* = c_1(c_2 + \mu x^*) \tag{3.26}$$

Substituting the value of x^* in (3.22) in (3.24) we get

$$y^* = b_1(b_2 - \varepsilon a_1(a_2 - \varepsilon y^* - \mu z^*))$$

$$\text{Let } b_1 b_2 = d_1, \varepsilon a_1 a_2 b_1 = d_2, \varepsilon^2 a_1 b_1 = d_3 \text{ and } \varepsilon a_1 b_1 \mu = d_4$$

$$y^* = d_1 - d_2 - d_3 y^* - d_4 z^*$$

$$y^* = \frac{d_1 - d_2 - d_4 z^*}{1 + d_3} \tag{3.27}$$

$$z^* = c_1(c_2 + \mu x^*)$$

$$z^* = c_1(c_2 + \mu a_1 \left(a_2 - \varepsilon \left(\frac{d_1 - d_2 - d_4 z^*}{1 + d_3} \right) - \mu z^* \right))$$

$$\text{Let } \frac{\varepsilon}{1 + d_3} = f_1, \text{ then}$$

$$z^* = c_1(c_2 + \mu a_1(a_2 - f_1 d_1 - f_1 d_2 - f_1 d_4 z^* - \mu z^*))$$

$$\text{Let } c_1 c_2 = e_1, c_1 \mu a_1 a_2 = e_2, c_1 \mu f_1 d_1 = e_3, c_1 \mu a_1 f_1 d_2 = e_4, c_1 \mu a_1 f_1 d_4 = e_5, c_1 \mu^2 a_1 = e_6$$

Therefore, the value of z^* is found to be

$$z^* = e_1 + e_2 - e_3 - e_4 - e_5 z^* - e_6 z^*$$

$$z^* = \frac{e_1 + e_2 - e_3 - e_4}{1 + e_5 + e_6} \tag{3.28}$$

From equation (3.27)

$$y^* = \frac{d_1 - d_2 - d_4 \left(\frac{e_1 + e_2 - e_3 - e_4}{1 + e_5 + e_6} \right)}{1 + d_3}$$

$$\text{Let } \frac{d_1}{1+d_3} = g_1, \frac{d_2}{1+d_3} = g_2, \frac{d_4}{1+d_3} = g_4, \frac{g_3}{1+e_5+e_6} = g_4$$

$$y^* = g_1 - g_2 - g_4 e_1 - g_4 e_2 + g_4 e_3 + g_4 e_4$$

$$\text{By letting } \frac{e_1+e_2-e_3-e_4}{1+e_5+e_6} = \theta_3 \text{ and } g_1 - g_2 - g_4 e_1 - g_4 e_2 + g_4 e_3 + g_4 e_4 = \theta_2$$

The value of x^* in equation (3.22) is;

$$x^* = a_1 a_2 - a_1 \varepsilon \theta_2 - a_1 \mu \theta_3$$

We also let $a_1 a_2 - a_1 \varepsilon \theta_2 - a_1 \mu \theta_3 = \theta_1$

From this stability points the values of x^*, y^* and z^* are obtained as

$$\left. \begin{aligned} x^* &= \theta_1 \\ y^* &= \theta_2 \\ z^* &= \theta_3 \end{aligned} \right\} \tag{3.29}$$

3.5.1 Local Stability for the Presence of the Prey and both Predators E^*

The local stability of E^* is computed at $(\theta_1, \theta_2, \theta_3)$. The values of x, y and z are substituted in the Jacobian matrix and computed as follows;

$$J^* = \begin{bmatrix} \alpha - \frac{2\alpha\theta_1}{k} - \varepsilon\theta_2 - \varphi\theta_3 - \beta & -\varepsilon\theta_1 & -\varphi\theta_1 \\ -\varepsilon\theta_2 & \omega - \frac{2\omega\theta_2}{k} - \varepsilon\theta_1 - \gamma & 0 \\ \varphi\theta_3 & 0 & \rho - \frac{2\rho\theta_3}{k} + \varphi\theta_1 - \sigma \end{bmatrix} \tag{3.30}$$

The determinant matrix $J^* - I\lambda$ for the matrix is;

$$J^* = \begin{bmatrix} \alpha - \frac{2\alpha\theta_1}{k} - \varepsilon\theta_2 - \varphi\theta_3 - \beta - \lambda & -\varepsilon\theta_1 & -\varphi\theta_1 \\ -\varepsilon\theta_2 & \omega - \frac{2\omega\theta_2}{k} - \varepsilon\theta_1 - \gamma - \lambda & 0 \\ \varphi\theta_3 & 0 & \rho - \frac{2\rho\theta_3}{k} + \varphi\theta_1 - \sigma - \lambda \end{bmatrix} \tag{3.31}$$

The solution of $J^* - I\lambda = 0$ are the eigen values;

$$\left. \begin{aligned} \lambda_1 &= \alpha - \frac{2\alpha\theta_1}{k} - \varepsilon\theta_2 - \varphi\theta_3 - \beta \\ \lambda_2 &= \omega - \frac{2\omega\theta_2}{k} - \varepsilon\theta_1 - \gamma \\ \lambda_3 &= \rho - \frac{2\rho\theta_3}{k} + \varphi\theta_1 - \sigma \end{aligned} \right\} \tag{3.32}$$

From the above eigen values λ_1 and λ_2 have negative real parts and for the stability of the equilibrium point, we need to show the sufficient and necessary condition for $\lambda_3 < 0$. This is by applying the Routh-Hurtwitz theorem.

From λ_3 we obtain,

$$\rho - \frac{2\rho\theta_3}{k} + \varphi\theta_1 - \sigma < 0 \tag{3.33}$$

From the inequality (3.33), we find the following condition for stability;

$$\frac{\rho - \sigma}{\left(\frac{2\rho\theta_3}{k} - \mu\theta_1\right)} < 1 \tag{3.34}$$

From (3.34) the condition for stability is that the bacteriophages should not grow to the carrying capacity of the system. This gives room for the pathogenic bacteria and antibiotics.

4 Graphical Representation of the Results

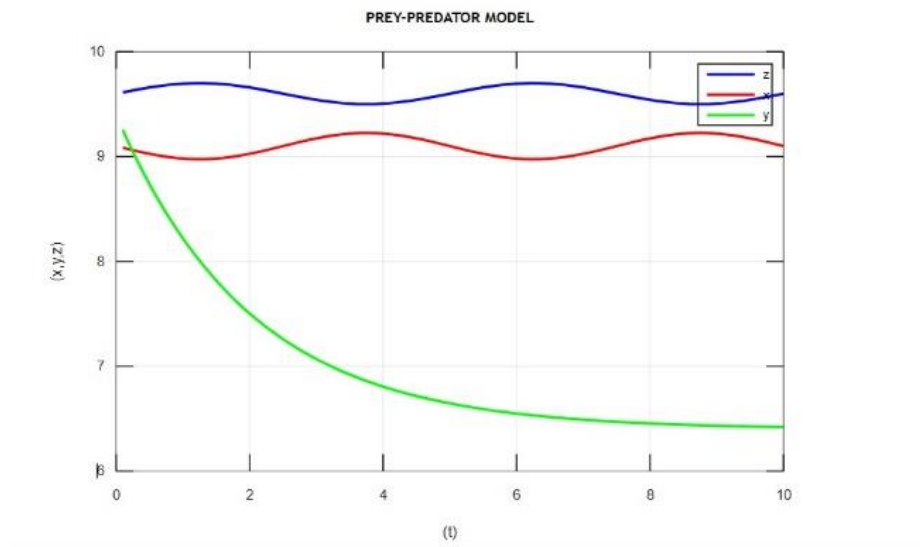


Fig. 2. The graph of (x, y, z) against time t

Fig. 2. Illustrates the best management strategy for the treatment of bacterial infections. In particular, the number of bacteriophages is dominant over the pathogenic bacterial infections. In this case, the biological impact of the pathogenic bacteria is suppressed where the practical utility of medication and bacteriophages is optimally attained.

5 Conclusion and Recommendation

5.1 Conclusion

In this study, a prey-predator model was formulated using differential equations with respect to time. It further established the equilibrium points and determined their stabilities. This study aimed at finding the best management strategy for pathogenic infections, this was achieved in equilibrium point $E^*(x^*, y^*, z^*)$. At this point, it was noted that the bacteriophages were dominant over pathogenic bacteria. Therefore, the biological impact of the pathogenic bacteria is suppressed demonstrating the practical utility of medication and Bps in managing bacterial infections.

5.2 Recommendation

This study achieved the results on the formulation of a prey-predator model. The study can be extended to formulate a model where time delay is considered to establish the required time for recovery at which point treatment can be stopped.

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 the writing or editing of this manuscript.

Acknowledgement

This research was supported by University of Kabianga.

Competing Interests

Authors have declared that no competing interests exist.

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