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Non–trivial solution of a differential equations system for the tuberculosis transmission dynamics

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Abstract

We obtain a non–trivial solution of a system of seven differential equations that describe the transmission dynamics of Tuberculosis (TB). This model considers a susceptible population that can be infected with two types of TB, i.e., those infected with typical TB and others with TB that is resistant to antibiotics. We include the population that can be vaccinated. We obtain the critical point of the system and the five eigenvalues from the evaluation of the Jacobian matrix at this nontrivial critical point.
Keywords: tuberculosis; differential equations; eigenvalues, critical point; transmission dynamics.

Solución no–trivial de un sistema de ecuaciones diferenciales que explica la dinámica de transmisión de la Tuberculosis

Resumen

El trabajo presenta una solución no trivial de un sistema de siete ecuaciones diferenciales que describen la dinámica de transmisión de la tuberculosis (TB). Este modelo considera una población susceptible que puede infectarse con dos tipos de TB diferentes, es decir, aquellas infectadas con la TB tradicional, y otra que es resistente a los antibióticos. El modelo incluye a la población que puede ser vacunada. Gracias a ello, se obtiene un punto crítico del sistema y cinco valores propios de la evaluación de la matriz Jacobiana en este punto crítico no trivial, que nos pueden ayudar a diseñar campañas de vacunación para erradicar esta enfermedad.
Palabras clave: tuberculosis; ecuaciones diferenciales; autovalores; punto crítico; dinámica.

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1 Introduction

Tuberculosis (TB) is one of the ten infectious diseases that affect humans around the world. According to World Health Organization (WHO) data, it has been estimated that 1.3 million people died from TB in 2017. It is estimated that one third of the world's population is infected with this disease [1]. One of the causes of the increase in TB cases is the weakening of the immune system associated with HIV [2], and for this reason the WHO has proposed the eradication of the TB epidemic by the year 2030, and reducing the incidence rate by 90% by 2035 [2].

TB is caused by the bacterium Mycobacterium tuberculosis that is transmitted by air through the inhalation of droplets introduced into the atmosphere by infected individuals when coughing or talking which would affect the lungs. Once a person is infected by the bacteria, a granuloma

forms. This is an aggregate of immune cells that surrounds the mycobacterium and the individual is unable to eliminate it. As a result, the disease becomes latent and the person is at risk for activating the disease. Only 10% of the population is able to activate the disease [3]. However, Davis and Ramakrishnan have suggested that the granulomas probably favor the disease instead of containing it [3].

On the other hand, bacillus Calmette–Guérin (BCG) is a vaccine that has been used against TB. At the present time, this vaccine is infrequently used in the United States. It is given to infants and young children in countries where TB is common although BCG does not always protect adults against this disease.

In the lung, the first line of defense is activated when bacteria are phagocytosed by alveolar macrophages that induce an inflammatory response leading to the formation of the granuloma. However, this process also generates a negative effect in that other types of chemical substances may help in the creation of new cancer cells.

In view of this, several mathematical models have been proposed to explain this behavior. The previous mathematical models only consider a solution where the critical points are almost all zero [4]–[8]. The analysis and the discussion are based upon a calculation of the Basic Reproduction Number (R_0) which is characterized by not obtaining all the critical points of the system of differential equations.

In this work, we obtain a non–trivial solution that has not been previously considered in the scientific literature and include the population that is susceptible to receiving the vaccine.

2 Material and methods

The model that is studied in this paper consists of solving a system of seven ordinary differential equations. This model has been based on the SEIRS model for TB, where the susceptible individuals are exposed to two classes of infections (typical and resistant strains) of TB. This model is based on the published papers [4]–[8].

The model that is considered in this paper assumes that the susceptible population (S) consists

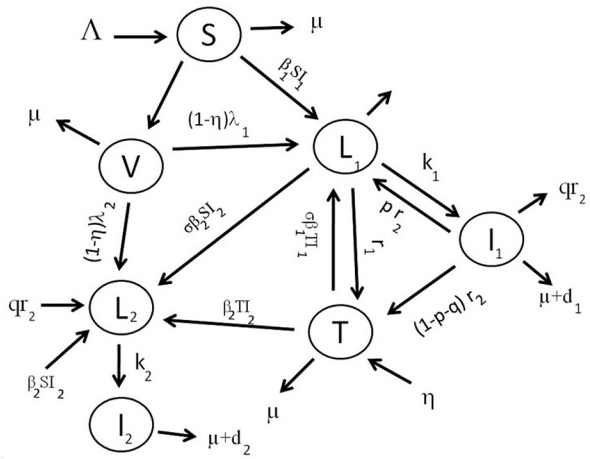

Figure 1: Compartmental model for the transmission dynamics of Tuberculosis.

of two types of latent individuals which can be infected. The group that succumbs to the typical strain of TB (L_1) and the group that succumbs to the resistant strain TB (L_2). The infected individuals are defined as I_1 and I_2. Vaccinated individuals (V) and individuals receiving treatment (T) are considered (see Figure 1).

The proposed mathematical model describing this system is given in the set of Ordinary Differential Equations 1

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - cS\left(\beta_1 I_1 + \beta_2 I_2\right) - (\mu+\varepsilon)\,S,\\
\frac{dV}{dt} &= \varepsilon S - (\mu+\eta)V,\\
\frac{dL_1}{dt} &= \eta V\lambda_1 - (k_1+r_1+\mu)\,L_1 + pr_2 I_1\\
&\quad -\beta_2 c L_1 I_2 + \beta_1 c I_1\left(S+\sigma T\right),\\
\frac{dL_2}{dt} &= \eta V\lambda_2 + \beta_2 c I_2\left(L_1+S+T\right)\\
&\quad +qr_2 I_1 - L_2\left(k_2+\mu\right),\\
\frac{dI_1}{dt} &= k_1 L_1 - (r_2+d_1+\mu)\,I_1,\\
\frac{dI_2}{dt} &= k_2 L_2 - (d_2+\mu)\,I_2,\\
\frac{dT}{dt} &= r_1 L_1 + (1-p-q)\,r_2 I_1\\
&\quad +(1-\lambda_1-\lambda_2)\,V\\
&\quad -cT\left(\beta_2 I_2 + \sigma\beta_1 I_1\right) - \mu T,
\end{aligned} \tag{1}$$

where we have used the definition of the variables

Table 1: Parameter identification in the TB model

Λ	Constant recruitment rate,
β_1	Average proportions of susceptible individuals infected,
β_1	Average proportion of individuals infected by one resistant–TB infectious,
c	Per–capita contact rate,
μ	Per–capita natural death rate,
ε	Average proportions of vaccinated individuals,
η	Proportion of vaccinated individuals who did not complete their treatment,
k_1	Rate at which individuals leave the latent class,
k_2	Rate at which individuals leave the resistant–TB class,
r_1	Per-capita treatment rates for latent individuals,
r_2	Per-capita treatment rates for infectious individuals,
p	Proportion of treated infectious individuals who did not complete their treatment (latent class),
q	Proportion of treated infectious individuals who did not complete their treatment (resistant–TB),
λ_1	Proportion of vaccinated individuals (latent class),
λ_1	Proportion of vaccinated individuals (resistant–TB class),
σ	Proportion of treatment individuals become infected who did not complete their treatment,
d_1	Per–capita disease induced death rate by I_1,
d_2	Per-,capita disease induced death rate by I_2.

and constants that were defined previously [6, 7] as can be seen in Table 1. However, we include two new constant called λ_1 and λ_2 which represent the total proportion of the vaccinated individuals of the two classes L_1 and L_2. These values are positive constants between 0 and 1 which is similar to the constants p and q defined in [6, 7].

3 Results and Discussion

A non–trivial critical point obtained from this differential equation according to the procedure employed previously [9]-[12] is presented in the Equations 2–8

$$S^\star = \frac{\Lambda}{A_2}, \tag{2}$$

$$V^\star = S^\star \frac{\varepsilon}{(\mu+\eta)}, \tag{3}$$

$$L_1^\star = V^\star \frac{\lambda_2 \eta A_0}{A_5}, \tag{4}$$

$$I_1^\star = L_1^\star \frac{k_1}{A_0}, \tag{5}$$

$$L_2^\star = -V^\star \frac{\eta(d_2+\mu)[\lambda_2 A_5 + k_1 r_2 \lambda_1 q]}{[\beta_2 c k_2 (T^\star + S^\star + L_1^\star) - A_4]\, A_5}, \tag{6}$$

$$I_2^\star = L_2^\star \frac{k_2}{d_2+\mu}, \tag{7}$$

$$T^\star = \frac{\varepsilon \Lambda N_0}{den}, \tag{8}$$

where

$$den = k_1 N_3(\sigma T^\star + S^\star) - N_1 A_1 - N_2(T^\star + S^\star + L_1^\star) + N_4.$$

In order to simplify these equations, we have defined the expressions given in the Equations 9–19

$$A_0 \equiv r_2 + \mu + d_1; \tag{9}$$

$$A_1 \equiv \beta_2 c I_2^\star + k_1 + r_1 + \mu; \tag{10}$$

$$A_2 \equiv c\beta_1 I_1^\star + c\beta_2 I_2^\star + \mu + \varepsilon; \tag{11}$$

$$A_3 \equiv \beta_1 c k_1 \sigma T^\star + S^\star + p k_1 r_2; \tag{12}$$

$$A_4 \equiv (k_2+\mu)(d_2+\mu); \tag{13}$$

$$A_5 \equiv A_1 A_0 - A_3; \tag{14}$$

$$N_0 \equiv [\beta_2 c k_2 (T^\star + S^\star + L_1^\star) - A_4] \cdot (1-\lambda_1-\lambda_2)(A_1+A_3) + k_1 \eta r_1 A_0 + \lambda_1 p r_2 (1-p-q), \tag{15}$$

$$N_1 \equiv A_0 A_2 (\mu+\eta)\mu \cdot [A_4(\mu+\varepsilon) - \beta_2 c k_2 (T^\star + S^\star + L_1^\star)] + \beta_2 c \varepsilon \lambda_2 k_2 A_2 \eta \Lambda; \tag{16}$$

$$N_2 \equiv \beta_2 c k_2 \mu(\mu+\eta) A_2 A_3 - \beta_1 \beta_2 c^2 \varepsilon k_1 k_2 \eta \lambda_1 \Lambda; \tag{17}$$

$$N_3 \equiv \beta_1 c \mu A_4 (\mu+\eta) A_2 - \beta_1 \beta_2 c^2 \varepsilon k_2 \eta \lambda_2 \Lambda; \tag{18}$$

$$N_4 \equiv A_4 [\beta_1 c \varepsilon \lambda_1 \eta \sigma \Lambda - \mu(\mu+\eta) p r_2 A_2] + r_2 \beta_2 c \varepsilon k_2 \eta \Lambda (\lambda_1 q - \lambda_2 p). \tag{19}$$

The next step is to evaluate the Jacobian matrix (J) at the critical point derived before and we obtained $(S^\star, V^\star, L_1^\star, L_2^\star, I_1^\star, I_2^\star)$ where we are using the following notation for the terms of the Jacobian matrix defined as

$$J = \begin{pmatrix} J_{11} & \cdots & J_{17} \\ \vdots & \ddots & \vdots \\ J_{71} & \cdots & J_{77} \end{pmatrix}.$$

The terms that are different from zero in Jacobian

Table 2: Eigenvalues $\mathcal{L}_1, \mathcal{L}_2, \mathcal{L}_3, \mathcal{L}_4, \mathcal{L}_5$ obtained from the matrix Jacobian

$$
\begin{aligned}
\mathcal{L}_1 &= -(\mu+\eta), \\
\mathcal{L}_2 &= -\frac{1}{2}\sqrt{3\beta_2 c k_2\left(S^\star+T^\star+L_1^\star\right)+(k_2-d_2)} \\
&\qquad -\frac{2\mu+r_2+k_2}{2}, \\
\mathcal{L}_3 &= -\frac{1}{2}\sqrt{4k_1\left[\beta_1 c\left(S^\star+\sigma T^\star\right)+r_2 p\right]+\left(\beta_2 c I^\star+k_1+r_1-r_2-d_2\right)^2} \\
&\qquad -\frac{\beta_2 c I_2^\star+r_2+r_1+2\mu+d-1+k_1}{2}, \\
\mathcal{L}_4 &= \frac{1}{2}\sqrt{4\beta_2 c k_2\left(S^\star+T^\star+L_1^\star\right)+(k_2-d_2)} \\
&\qquad +\frac{2\mu+r_2+k_2}{2}, \\
\mathcal{L}_5 &= \frac{1}{2}\sqrt{4k_1\left[\beta_1 c\left(S^\star+\sigma T^\star\right)+r_2 p\right]+\left(\beta_2 c I^\star+k_1+r_1-r_2-d_2\right)^2} \\
&\qquad +\frac{\beta_2 c I_2^\star+r_2+r_1+2\mu+d-1+k_1}{2}.
\end{aligned}
$$

matrix are

$$
\begin{aligned}
J_{11} &= -(c\beta_1 I_1+c\beta_2 I_2+\mu+\varepsilon); \\
J_{21} &= \varepsilon; \\
J_{22} &= -(\mu+\eta); \\
J_{32} &= \lambda_1\eta; \\
J_{33} &= -(c\beta_2 I_2+k_1+r_1+\mu); \\
J_{37} &= c\beta_1(\sigma T+S)+pr_2; \\
J_{42} &= \lambda_2\eta; \\
J_{44} &= -(\mu+k_2); \\
J_{45} &= c\beta_2(T+S+L_1); \\
J_{54} &= k_2; \\
J_{55} &= -(\mu+d_2); \\
J_{62} &= (1-\lambda_2-\lambda_1); \\
J_{63} &= r_1; \\
J_{66} &= -(c\beta_1 I_1+c\beta_2 I_2+\mu); \\
J_{73} &= k_1; \\
J_{74} &= qr_2; \\
J_{77} &= -(r_2+\mu+r_1).
\end{aligned}
$$

Finally, we obtain the eigenvalues which help to understand what the conditions are where this system is stable. We can calculate we calculate five eigenvalues given in the Table 2.

The first three eigenvalues are negative independent values of the constant, and therefore we have three stable points.

4 Conclusion

The present paper presents a nontrivial solution of the transmission dynamics of TB model where we consider a solution that has not been previously considered. This solution can help us to design of vaccination strategies in the future, but it is necessary include the results of vaccination campaigns to adjust the parameters of the model in a specific place and time. This point will be resolved in an upcoming work.

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