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On the Dynamics of Healthy Individuals in an ACL Model

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Abstract

In this research we deal with the dynamics, both analytical and numerical, of a model of American Cutaneous Leishmaniasis (ACL) involving population of humans, donkeys and vectors for different values of parameters considering healthy individuals. Some results on stability, periodic orbits and bifurcations are shown.

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1 Introduction

Leishmaniasis is a parasitic disease caused by some 20 different species of protozoa of the genus, *Leishmania Ross*, (1903). It is transmitted to humans by the bite of insects of the genus Phlebotomus family Psychodidae (Europe, Middle East, Asia and Africa) and of the genus Lutzomyia (America). In nature this condition is maintained for at least a hundred species of mammals that act as potential parasite reservoirs.
American cutaneous leishmaniasis (ACL) is a disease caused by Leishmania

parasites and transmitted by female sandflies (vector) reservoirs. This is the reason why a reservoir host is considered to be the main factor in changing the dynamics of the disease. Mathematical models of general dynamical systems have proven to be essential for the local and global study of numerous phenomena not only in biology but also in other areas. The ACL model has not been thoroughly studied from the mathematical point of view, compared to other diseases such as malaria ([1]).
Study of ACL model as a discrete four-dimensional dynamic system has been performed in [2]. In [3] threshold conditions for the establishment of the disease is calculated as part of a continuous system in three dimensions that includes stability study of the equilibria. In [4] ACL continuous models three and four dimensional were studied, it was also explored the existence of periodic solutions, the connection by orbits between equilibria, and other special solutions. They also allowed to some parameters vary and new solutions were calculated. The stability of such solutions are studied as well.
We have taken as a reference system the model studied in [4] and consider that the total population is the sum of the healthy population and the infected population, we obtain a new system, which represents the dynamics of the healthy population. Our research is concerned with this new system. Conditions for the stability of the system are established and show that no periodic orbits exist. Finally, we implement some numerical simulations in order to show the behavior of the system.

2 The Model and Equilibria

We denote the populations of infected humans, donkeys and vectors as $H = H(t)$, $R = R(t)$, $V = V(t)$ respectively and the populations of healthy humans, donkeys and vectors as $H_n = H_n(t)$, $R_n = R_n(t)$, $V_n = V_n(t)$ respectively. The parameters of the model (all positive) are β_H and β_R represent the rate of infection per individual in vector-human and vector-donkey encounters respectively; γ_H, γ_R represent the rate of mortality of vectors per unit time of infected humans, and donkeys respectively and μ represent the rate of mortality of vectors per unit time. $R(t)$ selected as the only reservoir. The initial model given in [4] is,

$$\begin{cases} \dot{H} = \beta_H V(A - H) - \gamma_H H \\ \dot{R} = \beta_R V(B - R) - \gamma_R R \\ \dot{V} = \beta_R R(C - V) - \mu V. \end{cases} \tag{1}$$

From (1), and taking into account that

$$H + H_n = A \quad \Rightarrow \quad H = A - H_n \quad \Rightarrow \quad \dot{H} = -\dot{H}_n$$

$$R + R_n = B \quad \Rightarrow \quad R = B - R_n \quad \Rightarrow \quad \dot{R} = -\dot{R}_n$$
$$V + V_n = C \quad \Rightarrow \quad V = C - V_n \quad \Rightarrow \quad \dot{V} = -\dot{V}_n.$$

We get that the system for the healthy individuals is given as

$$\begin{cases} \dot{H}_n = [\beta_H(V_n - C) - \gamma_H]H_n + \gamma_H A \\ \dot{R}_n = [\beta_R(V_n - C) - \gamma_R]R_n + \gamma_R B \\ \dot{V}_n = [\beta_R(R_n - B) - \mu]V_n + \mu C, \end{cases} \tag{2}$$

which is the one under our scrutiny in this research. Notice that system (2) does not have a critical point at the origin. Even more, no critical point are located on the axes either and because H_n, R_n and V_n represent populations must be considered all positive.
In the study of critical points, we set

$$V_n - C = \frac{\gamma_H}{\beta_H}\left(1 - \frac{A}{H_n}\right), \quad V_n - C = \frac{\gamma_R}{\beta_R}\left(1 - \frac{B}{R_n}\right), \quad R_n - B = \frac{\mu}{\beta_R}\left(1 - \frac{C}{V_n}\right)$$

from where

$$R_n = \frac{(2B\beta_R\gamma_R + \mu\gamma_R + BC\beta_R^2) \pm \sqrt{(\gamma_R\mu - BC\beta_R^2)^2}}{2\beta_R(\gamma_R + C\beta_R)}.$$

Note that, the discriminant of R_n allows us to find conditions that guarantee the existence of one or two critical points. We look at both cases,

(a) If $\gamma_R\mu - BC\beta_R^2 = 0$, there is a unique critical point if and only if,

$$\beta_R = \sqrt{\frac{\gamma_R\mu}{BC}}. \tag{3}$$

This value is a bifurcation value as we shall see in shortly. The only critical point is $P_c^u = (H_n^u, R_n^u, V_n^u) = (A, B, C)$, which is a trivial case since it represents the absence of disease and with no disease we have no dynamics to study at all.

(b) If $\gamma_R\mu - BC\beta_R^2 \neq 0$, there are two critical points if and only if,

$$\beta_R \neq \sqrt{\frac{\gamma_R\mu}{BC}}, \tag{4}$$

They are given by, $P_{c1} = \left(H_n^{(1)}, R_n^{(1)}, V_n^{(1)}\right) = \left(\frac{A\beta_R\gamma_H(\mu+B\beta_R)}{\mu(\beta_R\gamma_H - \beta_H\gamma_R) + \beta_R^2 B(\gamma_H + \beta_H C)}, \frac{\gamma_R(B\beta_R+\mu)}{\beta_R(\gamma_R+C\beta_R)}, \frac{\mu(\gamma_R+C\beta_R)}{\beta_R(B\beta_R+\mu)}\right)$ and $P_{c_2} = \left(H_n^{(2)}, R_n^{(2)}, V_n^{(2)}\right) = (A, B, C)$. Obviously P_{c_2} corresponds to item (a).

In order to assure that all coordinates of P_{c_1} are positive, we must have,

$$B(\gamma_H + \beta_H C)\beta_R^2 + \mu\gamma_H\beta_R - \mu\beta_H\gamma_R > 0. \tag{5}$$

But the left hand side of (5) is a concave upward parabola, whose cut with the y-axis is,

$$y = -\mu\beta_H\gamma_R$$

and cut with the x-axis given as

$$\beta_R^{(1)} = -\frac{[\mu\gamma_H + \sqrt{(\mu\gamma_H)^2 + 4B\mu\beta_H\gamma_R(\gamma_H + \beta_H C)}]}{2B(\gamma_H + \beta_H C)}$$

$$\beta_R^{(2)} = \frac{\sqrt{(\mu\gamma_H)^2 + 4B\mu\beta_H\gamma_R(\gamma_H + \beta_H C)} - \mu\gamma_H}{2B(\gamma_H + \beta_H C)}.$$

We become aware that $\beta_R > 0$ is equivalent to $\beta_R \in \left(\beta_R^{(2)}, \infty\right)$.

3 Dynamics

This section is started off by giving a formula for the characteristic polynomial associated to (2); the corresponding jacobian matrix at any point is

$$J(H_n, R_n, V_n) = \begin{bmatrix} \beta_H(V_n - C) - \gamma_H & 0 & \beta_H H_n \\ 0 & \beta_R(V_n - C) - \gamma_R & \beta_R R_n \\ 0 & \beta_R V_n & \beta_R(R_n - B) - \mu \end{bmatrix}$$

and at a general critical point (H_n^*, R_n^*, V_n^*)

$$\begin{aligned} P(\lambda) \;=\; & \lambda^3 - [(V_n^* - C)(\beta_H + \beta_R) + \beta_R R_n^* - \beta_R B - \mu - \gamma_H - \gamma_R]\lambda^2 - \{(\mu + \beta_R B - \beta_R R_n^*) \\ & \times[(V_n^* - C)(\beta_R + \beta_H) - (\gamma_H + \gamma_R)] + \beta_R^2 R_n V_n^* + (V_n^* - C)(\gamma_R\beta_H + \beta_R\gamma_H) - \beta_R\beta_H \\ & \times(V_n^* + C)^2 - \gamma_R\gamma_H\}\lambda + (\mu + \beta_R B - \beta_R R_n^*)[\beta_R\beta_H(V_n^* + C)^2 - (V_n^* - C)(\gamma_R\beta_H \\ & + \beta_R\gamma_H) + \gamma_R\gamma_H] + \beta_R R_n^* V_n^*[\beta_R\beta_H(V_n^* - C) - \beta_R\gamma_H]. \end{aligned}$$

It is easy to see that $\lambda_1 = -[\beta_H(C - V_n^*) + \gamma_H]$ is a (negative) eigenvalue of this characteristic polynomial, hence

$$P(\lambda) = (\lambda - \lambda_1)P_2(\lambda)$$

where,

$$\begin{aligned} P_2(\lambda) = \lambda^2 + [\beta_R(C - R_n^*) + \beta_R(B - V_n^*) + \gamma_R + \mu]\lambda + \beta_R^2[B(C - V_n^*) - R_n^* C] \\ + \beta_R[\gamma_R(B - R_n^*) + \mu(C - V_n^*)] + \gamma_R\mu \end{aligned}$$

To determine the sign of the roots of P_2 we use the Routh-Hurwitz's criteria ([5],[6]),

$$\begin{aligned}
a_1 &= \beta_R(C - R_n^*) + \beta_R(B - V_n^*) + \gamma_R + \mu \\
a_2 &= \beta_R^2[B(C - V_n^*) - R_n^* C] + \beta_R[\gamma_R(B - R_n^*) + \mu(C - V_n^*)] + \gamma_R\mu \\
\Delta_1 &= a_1 \\
\Delta_2 &= a_2\Delta_1.
\end{aligned}$$

Now $a_1 > 0$ and $a_2 > 0$, by means of Routh-Hurwitz criterium, if

$$B(C - V_n^*) - R_n^* C \geq 0 \tag{6}$$

stability of (2) is guaranteed.
When (3) is satisfied we can guarantee the existence of $P_c^u = (H_n^u, R_n^u, V_n^u)$ only critical point, which is not stable. If the condition (3) is not satisfied, two critical points $P_{c_1} = \left(H_n^{(1)}, R_n^{(1)}, V_n^{(1)}\right)$ and $P_{c_2} = \left(H_n^{(2)}, R_n^{(2)}, V_n^{(2)}\right)$ are obtained. The critical point P_{c_2} is not stable while the critical point P_{c_1} will be stable if it satisfies the following condition,

$$B^2C^2\beta_R^3 + C^2\mu(B-1)\beta_R^2 - [BC\mu\gamma_R + 2C\mu\gamma_R]\beta_R - \mu\gamma_R(\gamma_R + C\mu) \geq 0. \tag{7}$$

The inequality given in (7) is the condition that guarantees the stability of the second critical point. In order to perform the study of periodic orbits of the system (2), we consider the following subsystem,

$$\begin{cases} \dot{R}_n = [\beta_R(V_n - C) - \gamma_R]R_n + \gamma_R B \\ \dot{V}_n = [\beta_R(R_n - B) - \mu]V_n + \mu C. \end{cases} \tag{8}$$

Define the functions $f(R_n, V_n)$ and $g(R_n, V_n)$ as

$$\begin{aligned}
f(R_n, V_n) &= ([\beta_R(V_n - C) - \gamma_R]R_n + \gamma_R B, [\beta_R(R_n - B) - \mu]V_n + \mu C) \\
g(R_n, V_n) &\equiv 1.
\end{aligned}$$

So,

$$\nabla(gf) = -[\beta_R(C - V_n) + \gamma_R + \beta_R(B - R_n) + \mu].$$

Hence $\nabla(gf) < 0$ and, by Dulac's criteria ([7]), the subsystem (8) does not have periodic orbits.

Proposition 3.1 *The system (2) does not have periodic orbits.*

Proof. Suppose that system (2) has a periodic orbit given by $r(t) = (H_n(t), R_n(t), V_n(t))$ with $t \in [0, T]$, where T is the period, that is, $r(0) = r(T)$.
Consider $b(t) = (R_n(t), V_n(t))$, so $b(0) = b(T)$. This implies that the subsystem (8) has periodic orbits which is contradictory, therefore (2) does not have periodic orbits.

4 Bifurcations

In this section, we are going to study the possible bifurcations of system (2) by means of Sotomayor's theorem ([7]). In order to do so we give a definition and the mentioned theorem.

Definition 4.1 *([7]). For E an open subset of R^n, the second order derivatives of a function $f : E \to R^n$ and $x_0 \in R^n$, is defined as the function $D^2 f(x_0) : E \times E \to R^n$ and for $(x, y) \in E \times E$ we have*

$$D^2 f(x_0)(x,y) = \sum_{j_1,j_2=1}^{n} \frac{\partial^2 f(x_0)}{\partial x_{j_1} \partial x_{j_2}}$$

where $x = (x_1, \cdots, x_n)^T$ and $y = (y_1, \cdots, y_n)^T$.

Theorem 4.2 *([7]). Let $f : E \times J \to R^n$, E is an open set in R^n and $J \subset R$ is an interval. Suppose that $f(x_0, \nu_0) = 0$ and that the $n \times n$ matrix $A \equiv Df(x_0, \nu_0)$ has a simple eigenvalue $\lambda = 0$ with eigenvector v and that A^T has an eigenvector w corresponding to the eigenvalue $\lambda = 0$. Furthermore, suppose that A has k eigenvalues with negative real part and $(n - k - 1)$ eigenvalues with positive real part and that the following conditions satisfied*

$$w^T f_\nu(x_0, \nu_0) = 0, \quad w^T[Df_\nu(x_0, \nu_0)v] \neq 0 \quad \text{and} \\ w^T[D^2 f(x_0, \nu_0)(v, v)] \neq 0, \tag{9}$$

then the system $\dot{x} = f(x, \nu)$ experiences a transcritical bifurcation at the equilibrium point x_0 as the parameter ν varies through the bifurcation value $\nu = \nu_0$.

System (2) can rewritten as

$$\dot{x} = f(x, \nu), \quad x = (H_n, R_n, V_n)^T,$$

ν may be any of the parameters β_H, β_R, γ_H, γ_R or μ, and

$$f(x,\nu) = \begin{pmatrix} [\beta_H(V_n - C) - \gamma_H]H_n + \gamma_H A \\ [\beta_R(V_n - C) - \gamma_R]\, R_n + \gamma_R B \\ [\beta_R(R_n - B) - \mu]\, V_n + \mu C \end{pmatrix}.$$

We denote $Df(x, \nu)$ as the matrix of partial derivatives of the components of f with respect to the components of x and f_ν the vector of partial derivatives of f with respect to ν. If $x = P_{c_1}$ then,

$$Df(P_{c_1}, \nu) = \begin{pmatrix} \frac{\mu(\beta_H\gamma_R - \beta_R\gamma_H) - B\beta_R^2(C\beta_H + \gamma_H)}{\beta_R(B\beta_R + \mu)} & 0 & \frac{A\beta_H\beta_R\gamma_H(\mu + B\beta_R)}{\mu(\beta_R\gamma_H - \beta_H\gamma_R) + \beta_R^2 B(\gamma_H + \beta_H C)} \\ 0 & -\frac{\beta_R B(C\beta_R + \gamma_R)}{B\beta_R + \mu} & \frac{\gamma_R(B\beta_R + \mu)}{\gamma_R + C\beta_R} \\ 0 & \frac{\mu(\gamma_R + C\beta_R)}{B\beta_R + \mu} & -\frac{C\beta_R(\beta_R B + \mu)}{\gamma_R + C\beta_R} \end{pmatrix}.$$

Theorem 4.3 *If* $\beta_R^2 BC - \gamma_R\mu = 0$ *is satisfied then system (2) goes under a transcritical bifurcation when the parameter* γ_R *is varied according to this equality.*

It is worth to mention that even when we chose γ_R as a bifurcation parameter, either of the other involved in the equality given in the hypothesis could be picked as a bifurcation parameter as well with same results.

Proof. $\beta_R^2 BC - \gamma_R\mu = 0$ is equivalent to the existence a simple eigenvalue according to (3). It is easy to show then,

$$Df(P_{c_1}, \nu) = \begin{pmatrix} -\gamma_H & 0 & A\beta_H \\ 0 & -\gamma_R & B\beta_R \\ 0 & \beta_R C & -\mu \end{pmatrix}$$

and their associated eigenvalues are $\lambda_1 = 0$, $\lambda_2 = -(\gamma_R + \mu)$ and $\lambda_3 = -\gamma_H$. Particularly for λ_1 a corresponding eigenvector is given as

$$v = \begin{pmatrix} \frac{A\beta_H}{\gamma_H} \\ \\ \frac{\mu}{\beta_R C} \\ \\ 1 \end{pmatrix}.$$

On the other hand

$$(Df)^T(x, \nu) = \begin{pmatrix} -\gamma_H & 0 & 0 \\ 0 & -\gamma_R & \beta_R C \\ A\beta_H & B\beta_R & -\mu \end{pmatrix};$$

with corresponding eigenvector of $(Df)^T$ associated to $\lambda_1 = 0$,

$$w = \begin{pmatrix} 0 \\ \\ 1 \\ \\ \frac{\beta_R B}{\mu} \end{pmatrix}.$$

Now we set $\nu = \gamma_R$, $\gamma_R^0 = \frac{\beta_R^2 BC}{\mu}$, $B - R_n^{(1)} = \frac{BC\beta_R^2 - \gamma_R\mu}{\beta_R(\gamma_R + C\beta_R)} = 0$ and,

$$f_{\gamma_R}(x, \gamma_R) = \begin{pmatrix} 0 \\ \\ B - R_n \\ \\ 0 \end{pmatrix} = \begin{pmatrix} f^1_{\gamma_R} \\ \\ f^2_{\gamma_R} \\ \\ f^3_{\gamma_R} \end{pmatrix}$$

so,

$$f_{\gamma_R}(P_{c_1},\gamma_R^0)=\begin{pmatrix}0\\0\\0\end{pmatrix}$$

consequently,

$$w^T f_{\gamma_R}(P_{c_1},\gamma_R^0)=\left(0,1,\frac{\beta_R B}{\mu}\right)\begin{pmatrix}0\\0\\0\end{pmatrix}=0. \tag{10}$$

In the same token

$$Df_{\gamma_R}(x,\gamma_R)=\begin{pmatrix}\frac{\partial f^1_{\gamma_R}}{\partial H_n} & \frac{\partial f^1_{\gamma_R}}{\partial R_n} & \frac{\partial f^1_{\gamma_R}}{\partial V_n}\\ \frac{\partial f^2_{\gamma_R}}{\partial H_n} & \frac{\partial f^2_{\gamma_R}}{\partial R_n} & \frac{\partial f^2_{\gamma_R}}{\partial V_n}\\ \frac{\partial f^3_{\gamma_R}}{\partial H_n} & \frac{\partial f^3_{\gamma_R}}{\partial R_n} & \frac{\partial f^3_{\gamma_R}}{\partial V_n}\end{pmatrix}=\begin{pmatrix}0&0&0\\0&-1&0\\0&0&0\end{pmatrix}$$

hence

$$Df_{\gamma_R}(P_{c_1},\gamma_R^0)v=\begin{pmatrix}0&0&0\\0&-1&0\\0&0&0\end{pmatrix}\begin{pmatrix}\frac{A\beta_H}{\gamma_H}\\ \frac{\mu}{\beta_R C}\\ 1\end{pmatrix}=\begin{pmatrix}0\\ -\frac{\mu}{\beta_R C}\\ 0\end{pmatrix},$$

$$w^T[Df_{\gamma_R}(P_{c_1},\gamma_R^0)v]=\left(0,1,\frac{\beta_R B}{\mu}\right)\begin{pmatrix}0\\ -\frac{\mu}{\beta_R C}\\ 0\end{pmatrix}=-\frac{\mu}{\beta_R C}\neq 0. \tag{11}$$

Finally

$$D^2 f(P_{c_1},\gamma_R^0)(v,v)=2\begin{pmatrix}\beta_H\\0\\0\end{pmatrix}\frac{A\beta_H}{\gamma_H}+2\begin{pmatrix}0\\ \beta_R\\ \beta_R\end{pmatrix}\frac{\mu}{\beta_R C}=\begin{pmatrix}\frac{2A\beta_H^2}{\gamma_H}\\ \frac{2\mu}{C}\\ \frac{2\mu}{C}\end{pmatrix}\neq \mathbf{0}$$

and from here,

$$w^T[D^2 f(P_{c_1},\gamma_R^0)(v,v)]=\left(0,1,\frac{\beta_R B}{\mu}\right)\begin{pmatrix}\frac{2A\beta_H^2}{\gamma_H}\\ \frac{2\mu}{C}\\ \frac{2\mu}{C}\end{pmatrix}=\frac{2}{C}(\mu+\beta_R B)\neq \mathbf{0}. \tag{12}$$

From (10), (11) and (12) and Sotomayor's theorem the system (2) has a transcritical bifurcation at P_{c_1}.

5 Numerical Simulations

In order to implement numerical simulation the following values for parameters are set, $\beta_R = 0.01$, $\beta_H = 0.01$, $\gamma_R = 0.09$, $\gamma_H = 0.01$, $\mu = 0.05$, $A = 400$, $B = 350$ and $C = 250$. With these values the corresponding critical points are $P_{c_1} = (1.62, 12.34, 3.65)$ (stable) and $P_{c_2} = (400, 350, 250)$ (unstable).
In figure (1) the region of stability, projected on plane (R_n, V_n) is represented. In this case the region is the bounded by the positive axes and the straight line. The point inside this region is P_{c_1}.

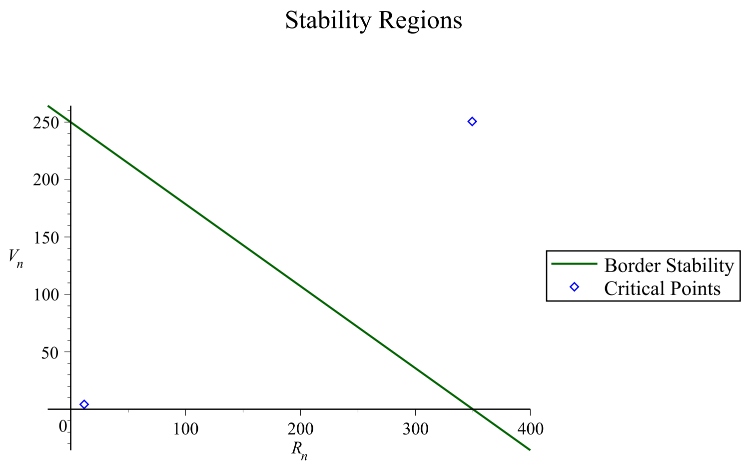

Figure 1: Stability region according to (6) in the plane (R_n, V_n).

Figure (2) represents some orbits of (2) under same values of the given parameters. It shows asymptotic stability of P_{c_1} as predicted by our analytic results.

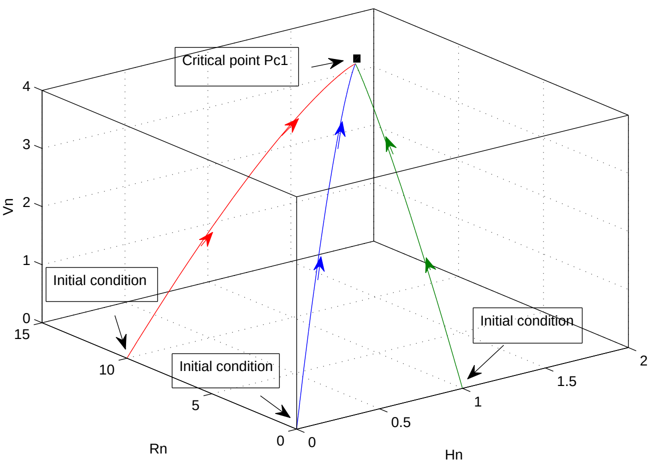

Figure 2: Orbits of system (2).

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