THE BASIC REPRODUCTION NUMBER OF AFRICAN TRYPANOSOMIASIS DISEASE WITH A PERIODIC VECTOR POPULATION AND VERTICAL TRANSMISSION

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Abstract. African trypanosomiasis is a vector-borne disease transmitted to humans by tsetse flies. Assuming that the tsetse fly population's growth rate is a periodic function, an African trypanosomiasis epidemic model with seasonality, vertical transmission and latent period is proposed. It is common knowledge that the basic reproduction number plays a vital role in a epidemic model which determines whether the disease is eradicated or not. We derive a basic reproduction number R_0 which is adapted to periodic environments. Parameters are estimated from the province of Kinshasa, Democratic Republic of Congo. This model suggests that the epidemic could be stopped if the vector population were reduced by a factor $R_0^2 = 2.80$.

Keywords: African trypanosomiasis disease; the basic reproduction number; seasonality; vertical transmission.

2010 AMS Subject Classification: 92D25.

1. INTRODUCTION

Vector-borne diseases are infectious diseases caused by viruses, bacteria, protozoa or rickettsia which are primarily transmitted by disease transmitting biological agents (anthropoids), called vectors, who carry the disease without getting it themselves. The oldest mathematical

model of vector-borne disease goes back to the malaria model, which is presented by Ross. He proved the transmission of malaria by biting mosquitoes and demonstrated that the prevalence of malaria tends to a fixed limit depending on the rates of transmission, recovery, and mortality within the host and vector populations [1]. Macdonald [2] placed these rates into an index that we called the basic reproduction number, which was used to develop and evaluate control strategies meant to reduce malaria prevalence. The malaria model has influenced the mathematical analysis of many other vector-borne diseases, including dengue fever [3], rickettsia in cattle [4], Human African trypanosomiasis [5], and West Nile Virus [6].

Human African trypanosomiasis (HAT)–also known as sleeping sickness–is caused by infection with one of two parasites: *Trypanosoma brucei rhodesiense or T. b. gambiense*[7]. These organisms are extra–cellular protozoan parasites that are transmitted by insect vectors in the genus Glossina (tsetse flies). The life cycle of Trypanosoma brucei has been reviewede (see Fig.1). Infection in the human host begins when the infective metacyclic stage is injected by the tsetse fly intradermally. The organisms is immediately transformed into bloodstream from trypomastigotes and are divided by binary fission in the interstitial spaces at the site of the bite. This flagellated stage enters the bloodstream through the lymphatics and repeats further, producing a patent parasitemia. The parasites tend to cause a chronic infection, and a person can be infected for months or years without seeing symptom expression. However, once the disease is expressed, the disease is far advanced, and the nervous system is adversely affected. Later, the tsetse fly becomes infected by ingesting a blood meal from an infected host.

At the end of the 1990s, World Health Organization (WHO) estimated between 300 000 and 500 000 to be the number of sleeping sickness cases per year. Sixty million people are estimated to be at risk, with 4 million people under surveillance. The greatest burden of reported cases is due to *T. b. gambiense*, with $23,832$ in 2002, $19,901$ in 2003, $17,036$ in 2004, $15,651$ in 2005 and $11,382$ in 2006, respectively [8]. Obviously, there is a decline in the number of newly reported cases. However, the situation remains worrying in countries such as Angola, Democratic Republic of Congo, Uganda and Sudan [9]. Approximately two-thirds of reported *T. b. gambiense* cases occur in the Democratic Republic of Congo (DRC) [10]. Kinshasa, the capital of DRC, has been well known as HAT focus since the beginning of the 20th century. The
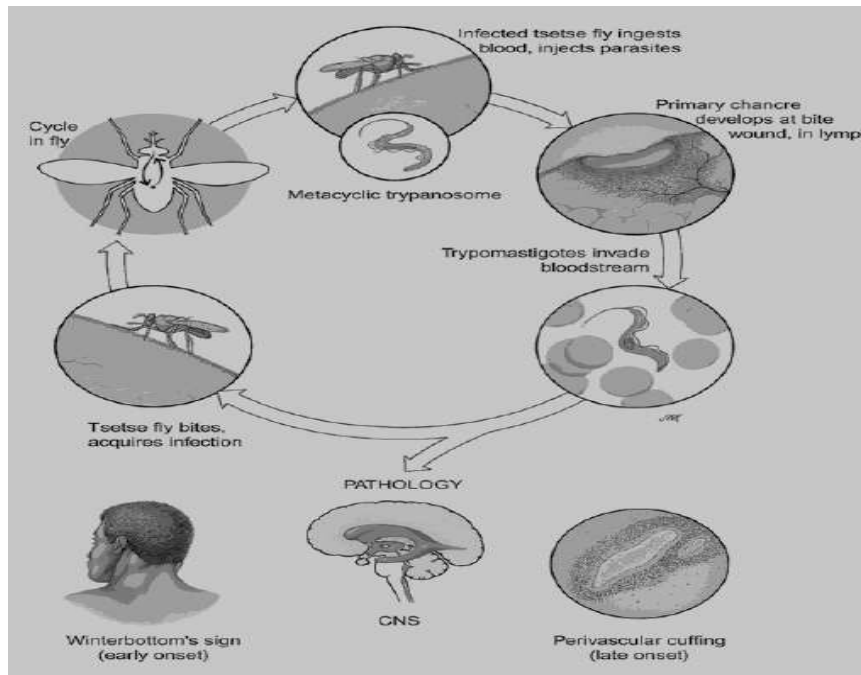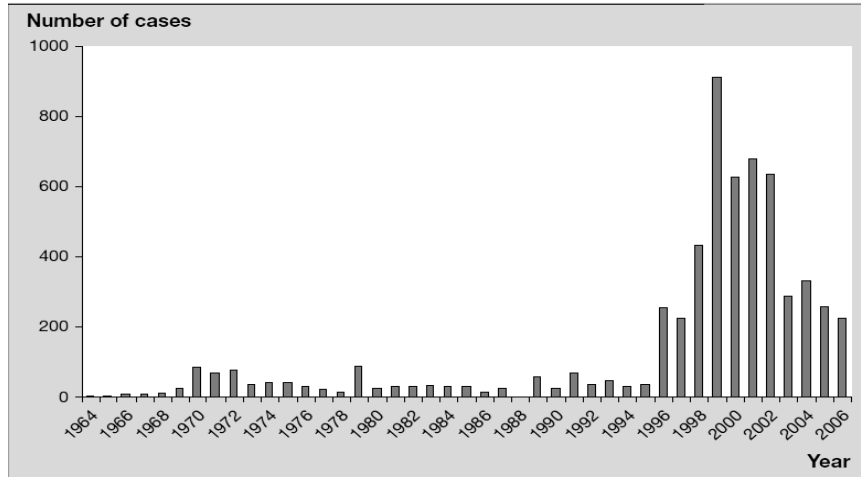
FIGURE 1. Life cycle of Trypanosoma brucei

FIGURE 2. News cases of HAT in the city of Kinshasa/DRC between 1964 and 2007 .

number of new cases is not as well documented between 1960 and 1968. From 1969 to 1995, cases were declared thanks to passive detection, representing an annual mean of less than 50 new cases. The situation suddenly worsened in 1996, as 254 new cases were declared, and 226 in 1997. Two special mobile units were implemented in 1998 and in 2000 respectively; 443 new cases were detected out of 6, 205 examined inhabitants and 912 new cases out of 42, 746 persons

in 1999. Since 2003, the number of new cases detected in Kinshasa has sensibly decreased, but still remains between 200 and 250 patients a year (see Fig. 2) [11].

To understand the epidemiology of HAT, several investigations have been undertaken [12, 13, 14, 15]. In particular, two entomologic surveys were conducted in 2005 (during the rainy season in February and March and the dry season in June and July) at eight sites in Kinshasa [16]. During the two entomologic surveys, the 610 traps captured 897 Glossina fuscipes quanzensis (624 and 273 in the rainy and dry seasons, respectively) [17]. Although tsetse flies habitat may vary considerably, climate and altitude–through their direct effects on vegetation, rainfall, and temperature–are still the primary determinants for proliferation. Adult longevity and puparial duration are related to temperature, and a significant seasonal decline in tsetse populations is normal, particularly in savannah habitats during the dry season [12].

Recently the epidemics of African trypanosomiasis have received much attention of researchers. Vincent and Harry [13] studied the drugs and drug resistance in African trypanosomiasis; Bradford et.al [14] discovered a new Sadenosylmethionine decarboxylase inhibitors for the treatment of Human African Trypanosomiasis (HAT); Courtin et al. [15] derived the association between human African trypanosomiasis and the *IL*6 gene in a Congolese population; Hwang et al.[18] discovered the halo-nitrobenzamides with potential application against Human African Trypanosomiasis. But to our knowledge there have been no mathematical models on African trypanosomiasis taking distributed delay, seasonality and vertical transmission into account.

The section division of the article is as follows. Section 2 presents the system of differential equations used to model the epidemic. Section 3 analyzes the model, in particular the stability of the infection-free state. Furthermore, we presents a simulation with parameters chosen so as to fit the epidemic data from the province of Kinshasa. The epidemic threshold R_0 is then estimated for this particular epidemic. In Section 4, the basic reproduction number (BRN) is discussed for a special cases. Finally, we give a brief conclusion.

2. Model derivation

In this section, we present a mathematical model for the transmission and evolution of African trypanosomiasis in human and tsetse fly population. Following the basic ideas and structure of

mathematical models in epidemiology, the African trypanosomiasis model will be developed under the next basic hypotheses:

(A.1) The total population of human Λ is divided in three subpopulations:

• Susceptible $S_h(t)$: members of human population who may become infected.

• Infected $I_h(t)$: members of human population infected by *T. b. gambiense*.

• Infected $I_h(t, \tau)$: members of human population at time t structured by the time τ since infection. Hence the total number of infectious humans $I_h(t) = \int_0^\infty I_h(t, \tau) d\tau$.

• Recovered $R_h(t)$: members of human population with immunity.

(A.2) The total population of tsetse flies $p(t)$ is divided in two subpopulations:

• Susceptible $S_c(t)$: members of tsetse flies population who may become infected.

• Infected $I_c(t)$: members of tsetse flies population infected by *T. b. gambiense*.

(A.3) The disease is not vertically transmitted from infective tsetse flies to their offspring.

(A.4) Because both adult longevity and puparial duration are related to temperature, and a significant seasonal decline in tsetse fly population is normal during the dry season, we assumed that the growth rate $r(t)$ is a periodic function of period T.

(A.5) The infective tsetse flies neither recover nor reproduce. However, the infective population I_c still contributes with S_c to population growth toward the carrying capacity.

(A.6) The group of "immune" humans contains both people who have acquired some immunity and individuals whose symptoms have recently appeared and have been covered by cloth so that they can not transmit the disease further.

(A.7) The functions $\beta \pi S_h I_c / (\vartheta + S_h)$ and $\beta \hat{\pi} S_c I_h / (\vartheta + S_h)$ are saturated contact rate of the disease. Here β is the biting rate of tsetse fly, π and $\hat{\pi}$ are transmission probability of tsetse fly per bite from tsetse fly to human and from human to tsetse fly, respectively.

(A.8) The parameter μ is mortality of tsetse fly and γ is the rate that recovered individuals lose immunity and return to the susceptible class.

(A.9) The parameter a is the natural mortality rate of human population which is equal to the birth rate. The parameter δ is the proportion of the offspring of infectious mothers uninfected.

(A.10) If $f(\tau)$ is the probability distribution of the time elapsed from infection to symptoms in humans and $g(\tau)$ the probability of not having developed symptoms τ units of time after

infection, then

$$g(\tau) = 1 - \int_0^\tau f(\sigma)d\sigma = e^{-\int_0^\tau (\alpha(\sigma)+\delta a)d\sigma}. \tag{2.1}$$

Therefore, $\alpha(\tau) + \delta a = f(\tau)/[1 - \int_0^\tau f(\sigma)d\sigma]$.

The total population of humans is denoted by

$$\Lambda = S_h(t) + I_h(t) + R_h(t)$$

and the total population of tsetse flies is denoted by

$$p(t) = S_c(t) + I_c(t).$$

On the basis of the above assumptions, we formulate the following plausible epidemic model with seasonality and vertical transmission

$$
\begin{aligned}
&S_c'(t) = r(t) - \mu S_c(t) - \frac{\beta \hat{\pi} S_c(t) I_h(t)}{\vartheta + S_h(t)}, \\
&I_c(t,0) = \frac{\beta \hat{\pi} S_c(t) I_h(t)}{\vartheta + S_h(t)}, \frac{\partial I_c}{\partial t} + \frac{\partial I_c}{\partial \omega} = -\mu I_c(t), \\
&S_h'(t) = a(\Lambda - S_h(t)) - \frac{\beta \pi S_h(t) I_c(t)}{\vartheta + S_h(t)} - a(1-\delta)I_h(t) + \gamma R_h(t), \\
&I_h(t,0) = \frac{\beta \pi S_h(t) I_c(t)}{\vartheta + S_h(t)}, \frac{\partial I_h}{\partial t} + \frac{\partial I_h}{\partial \tau} = -(\alpha(\tau)+\delta a)I_h(t,\tau), \\
&R_h'(t) = \int_0^\infty \alpha(\tau)I_h(t,\tau)d\tau - \gamma R_h(t) - aR_h(t)
\end{aligned}
\tag{2.2}
$$

with some initial conditions $S_c(0), I_c(0), I_h(0,\tau)$ and $R_h(0)$. Furthermore, $p'(t) = S_c'(t) + I_c'(t) = r(t) - \mu p(t)$.

(A.11) The parameter ω is the time since infection in tsetse fly which matches the time τ.

3. MODEL ANALYSIS AND THE ESTIMATION OF R_0

In this section, we introduce a generalization of the definition of the BRN R_0 which is adapted to periodic environments followed by the estimation of the parameters of the model. To prove our main results we first give the following preliminary considerations.

From hypothesis (A.4) it follows that system (2.2) has an infection-free periodic solution given by $S_c = p(t), I_c = 0, S_h = \Lambda, I_h = R_h = 0$, where $p(t)$ is the periodic solution of $p'(t) =$

$r(t) - \mu p(t)$. The corresponding linear system of (2.2) at $(p(t), 0, \Lambda, 0, 0)$ is

$$i'_c(t) = \frac{\beta \hat{\pi} p(t)}{\vartheta + \Lambda} i_h(t) - \mu i_c(t),$$

$$i_h(t, 0) = \frac{\beta \pi \Lambda i_c(t)}{\vartheta + \Lambda}, \frac{\partial i_h}{\partial t} + \frac{\partial i_h}{\partial \tau} = -(\alpha(\tau) + \delta a) i_h(t, \tau)$$

(3.1)

with initial conditions $i_c(0, \tau) = i_{c0}(\tau)$ and $i_h(0, \tau) = i_{h0}(\tau)$. This system involves both linear ordinary differential equations and a linear partial differential equation. Denoted the column vector $J(t, \tau) = (i_c(t, \tau), i_h(t, \tau))$. Then we have

$$\frac{\partial J(t, \tau)}{\partial t} + \frac{\partial J(t, \tau)}{\partial \tau} = -B(\tau) J(t, \tau),$$

(3.2)

where

$$B(\tau) = \begin{pmatrix} \mu & 0 \\ 0 & \alpha(\tau) + \delta a \end{pmatrix}.$$

If this equation is supplemented with

$$J(t, 0) = N(t), \ J(0, \tau) = J_0(\tau) = (i_{c0}(\tau), i_{h0}(\tau)).$$

An immediate consequence of the explicit solution of (3.2) given by

$$J(t, \tau) = \begin{cases} J_0(\tau - t) exp\left(-\int_{\tau - t}^{\tau} B(\sigma) d\sigma\right), & \tau > t, \\ \\ N(t - \tau) exp\left(-\int_0^{\tau} B(\sigma) d\sigma\right), & \tau < t. \end{cases}$$

(3.3)

For $N(t)$ or $J(t, 0)$, we can easily concluded from (3.1) that

$$N(t) = J(t, 0) = \begin{pmatrix} 0 & \frac{\beta \hat{\pi} p(t)}{\vartheta + \Lambda} \\ \frac{\beta \pi \Lambda}{\vartheta + \Lambda} & 0 \end{pmatrix} \int_0^{\infty} J(t, \tau) d\tau.$$

(3.4)

Substituting (3.3) in (3.4) and yielding

$$N(t) = \int_0^t \begin{pmatrix} 0 & \frac{\beta \hat{\pi} p(t)}{\vartheta + \Lambda} e^{-\int_0^{\tau}(\alpha(s) + \delta a) ds} \\ \frac{\beta \pi \Lambda}{\vartheta + \Lambda} e^{-\mu \tau} & 0 \end{pmatrix} N(t - \tau) d\tau$$

$$+ \int_t^{\infty} \begin{pmatrix} 0 & \frac{\beta \hat{\pi} p(t)}{\vartheta + \Lambda} e^{-\int_{\tau - t}^{\tau}(\alpha(s) + \delta a) ds} \\ \frac{\beta \pi \Lambda}{\vartheta + \Lambda} e^{-\mu t} & 0 \end{pmatrix} J_0(\tau - t) d\tau.$$

Then the previous equation is of the form

$$N(t) = \int_0^t A(t, \tau) N(t - \tau) d\tau + \bar{N}(t),$$

(3.5)

where $A(t, \tau)$ is T-periodic in t and $\bar{N}(t)$ is a given function. Notice that the coefficient $A_{ij}(t, \tau)$ in row i and column j of the matrix $A(t, \tau)$ is the expected number of individuals of type i (type 1 stands for vectors, type 2 for humans) that one infected inidividual of type j will infect per unit of time at time t if it was infected at the time $t - \tau$.

Let ξ be the set of T-periodic continuous functions with values in R^2, with the supremum norm, this is a Banach space. The asymptotic behavior of the equation (3.5) has been investigated in some works [19, 20]: $N(t) \sim e^{\lambda^* t} v(t)$, where λ^* is a real number and $v \in \xi$ is a nonnegative, nonzero, and such that

$$v(t) = \int_0^\infty e^{-\lambda^* \tau} A(t, \tau) v(t - \tau) d\tau. \tag{3.6}$$

Now let R_0 be the spectral radius of the linear operator which maps $w \in \xi$ to the function $t \mapsto \int_0^\infty A(t, \tau) w(t - \tau) d\tau$, also in ξ. Recall that since this linear operator is nonnegative, R_0 can also be characterized by the existence of a nonnegative and nonzero $w \in \xi$ such that

$$\int_0^\infty A(t, \tau) w(t - \tau) d\tau = R_0 w(t). \tag{3.7}$$

Then we have the following theorems.

Theorem 3.1. *The R_0 has the properties of an epidemic threshold: $\lambda^* > 0$ if $R_0 > 1$ and $\lambda^* < 0$ if $R_0 < 1$.*

Proof. In fact, for all real number λ, let A_λ be the linear operator which maps $w \in \xi$ to the function $t \mapsto \int_0^\infty e^{-\lambda \tau} A(t, \tau) v(t - \tau) d\tau$ also in ξ. Let R_λ be the spectral radius of A_λ. Notice that this definition is consistent with the definition of R_0. Notice also that for all λ, the linear operator A_λ is nonnegative. Moreover, $\lambda_1 \leq \lambda_2$ implies $A_{\lambda_1} \geq A_{\lambda_2}$. The properties of the spectral radius imply that the function $\lambda \mapsto R_\lambda$ from R to R is decreasing. But according to equation (3.6), $R_{\lambda^*} = 1$. So if $R_0 > 1$, then $\lambda^* > 0$. And if $R_0 < 1$, then $\lambda^* < 0$. The proof is completed.

From now on, we will explicitly use the equations of motion from epidemic system (3.1), to calculate the BRN.

Theorem 3.2. *(i) If $p(t)$ is a constant p, then*

$$R_0 = \sqrt{\frac{\beta^2 \pi \hat{\pi} \Lambda p}{(\vartheta + \Lambda)^2 \mu} \int_0^\infty g(\tau) d\tau} \; ;$$

(ii) If $p(t)$ is T-periodic function, then

$$R_0 = \sqrt{\frac{\beta^2 \pi \hat{\pi} \Lambda r_0}{(\vartheta + \Lambda)^2}},$$

where r_0 is a complex of function $p(t), g(\tau)$ and μ.

Proof. (i) Note that if $p(t)$ is a constant p, then $A(t, \tau)$ is of independent t. In the case, consider a constant function $w(t)$ is equivalent to a nonnegative eigenvector of the nonnegative matrix $\int_0^\infty A(\tau) d\tau$, we conclude that R_0 is the spectral radius of this matrix, which is generally called the next-generation matrix [21]. More precisely, we get

$$R_0 = \sqrt{\frac{\beta^2 \pi \hat{\pi} \Lambda p}{(\vartheta + \Lambda)^2 \mu} \int_0^\infty g(\tau) d\tau},$$

where we see that the product of the mean number of humans infected by one infectious tsetse fly $\beta \pi p / \mu (\vartheta + \Lambda)$ with the mean number of tsetse flies infected by one infectious human $\beta \hat{\pi} \Lambda / (\vartheta + \Lambda) \int_0^\infty g(\tau) d\tau$.

(ii) If $p(t)$ is not constant but T-periodic. Then creating $w = (w_1, w_2)$, (3.7) can be represented in the form

$$\frac{\beta \hat{\pi} p(t)}{\vartheta + \Lambda} \int_0^\infty g(\tau) w_2(t - \tau) d\tau = R_0 w_1(t),$$

$$\frac{\beta \pi \Lambda}{\vartheta + \Lambda} \int_0^\infty e^{-\mu \tau} w_1(t - \tau) d\tau = R_0 w_2(t). \tag{3.8}$$

Inserting the second equation into the first one, we see that if r_0 is such that there exists a nonnegative and nonzero T-periodic function $w_1(t)$ satisfying

$$p(t) \int_0^\infty g(\tau) \int_0^\infty e^{-\mu \tau} w_1(t - \tau - \sigma) d\sigma d\tau = r_0 w_1(t), \tag{3.9}$$

then

$$R_0 = \sqrt{\frac{\beta^2 \pi \hat{\pi} \Lambda r_0}{(\vartheta + \Lambda)^2}}. \tag{3.10}$$

Formula (3.10) generalizes the classical formula of case 1 for the vector-borne disease with a season (periodic) population of vectors. Note that r_0 is a complex function of $p(t), g(x)$ and μ. Obviously, r_0 is a decreasing function of μ. Besides, if $p(t)$ is replaced by $\varepsilon p(t)$, then

r_0 becomes εr_0. So, thanks to the definition of R_0 presented above, for a periodic population of vectors, it is still true that a vector disease can be eradicated if the population of vectors is divided by R_0^2. The proof is completed.

Having established the general framework we now focus on the estimation of the BRN and starting with the estimation of parameters of models.

In Kinshasa, population estimates vary between 5.273 million and 7 million [22]. However, rural populations usually depend on agriculture, fishing, animal husbandry or hunting, and in these pursuits they are often exposed to the bite of the tsetse fly and therefore to the disease. Thus we assume that the population Λ who often exposed to the bite of tsetse fly is 500 per month.

According to current knowledge about tsetse fly, the mean life span $1/\mu$ is from one to three months [23]. So we take $\mu = 0.5$ per month. Denoted by p_{max} the maximum number of tsetse flies during the year satisfies the relation $\bar{p}(t) = p(t)/p_{max}, \bar{r}(t) = r(t)/p_{max}$, $\bar{S}_c(t) = S_c(t)/p_{max}$ and $\bar{I}_c(t) = I_c(t)/p_{max}$. We assume that at $t = 0$, say at the beginning of the year 2005, one human imports the infection into the susceptible population. At that time, the population of vectors is zero. The initial conditions will be $S_c(0) = 0, I_c(0) = 0, S_h(0) = \Lambda - 1, I_h(t,0) = \delta_{\tau=0}$(Dirac's mass at $\tau = 0$) and $R_h(0) = 0$.

Dividing the first two equation of (2.2) by p_{max}, results in the following epidemic model:

$$\bar{S}_c'(t) = \bar{r}(t) - \mu\bar{S}_c(t) - \frac{\beta\hat{\pi}\bar{S}_c(t)I_h(t)}{\vartheta+S_h(t)},$$
$$\bar{I}_c(t,0) = \frac{\beta\hat{\pi}\bar{S}_c(t)I_h(t)}{\vartheta+S_h(t)}, \frac{\partial I_c}{\partial t} + \frac{\partial I_c}{\partial\omega} = -\mu I_c(t),$$
$$S_h'(t) = a(\Lambda - S_h(t)) - \frac{\beta\pi S_h(t)p_{max}\bar{I}_c(t)}{\vartheta+S_h(t)} - a(1-\delta)I_h(t) + \gamma R_h(t), \qquad (3.11)$$
$$I_h(t,0) = \frac{\beta\pi S_h(t)\bar{I}_c(t)p_{max}}{\vartheta+S_h(t)}, \frac{\partial I_h}{\partial t} + \frac{\partial I_h}{\partial\tau} = -(\alpha(\tau)+\delta a)I_h(t,\tau),$$
$$R_h'(t) = \int_0^\infty \alpha(\tau)I_h(t,\tau)d\tau - \gamma R_h(t) - aR_h(t).$$

As for parameters of system (3.11), we use the following values based on some literature data: $\beta\hat{\pi} = 0.58$ per month, $\beta\pi p_{max} = 14352$ per month [20], $\vartheta = 1$.

The remainder of this section is devoted to compute numerically R_0 as defined in the previous section by these parameter values. First, we transform (3.9) by transformation $\theta = \tau + \sigma$. Then

we have

$$p(t) \int_0^\infty g(\tau) e^{\mu\tau} \int_\tau^\infty e^{-\mu\theta} w_1(t-\theta) d\theta d\tau = r_0 w_1(t). \tag{3.12}$$

Integrating by parts and finding

$$p(t) \int_0^\infty h(\tau) w_1(t-\tau) d\tau = r_0 w_1(t), \tag{3.13}$$

where

$$h(\tau) = e^{-\mu\tau} \int_0^\tau e^{\mu\sigma} g(\sigma) d\sigma. \tag{3.14}$$

In view of $w_1(t)$ is T-periodic, we conclude that

$$\int_0^\infty h(\tau) w_1(t-\tau) d\tau = \int_{-\infty}^t h(t-\theta) w_1(\theta) d\theta$$

$$= \int_0^t h(t-\theta) w_1(\theta) d\theta$$

$$+ \sum_{n=0}^\infty \int_0^T h(t+(n+1)T-\theta) w_1(\theta) d\theta$$

$$= \int_0^t H(t-\theta) w_1(\theta) d\theta + \int_t^T H(t-\theta+T) w_1(\theta) d\theta,$$

where we set

$$H(\tau) = \sum_{n=0}^\infty h(\tau + nT). \tag{3.15}$$

It is noted that $H(\tau)$ can be replaced by the sum of the first two terms, that is $H(\tau) = h(\tau) + h(\tau+T)$ which does not affect the estimation of R_0.

We combine (3.13) with (3.15), the eigenvalues problem (3.13) is equivalent to

$$p(t) \left\{ \int_0^t H(t-\theta) w_1(\theta) d\theta + \int_t^T H(t-\theta+T) w_1(\theta) d\theta \right\} = r_0 w_1(t), \tag{3.16}$$

which can be easily estimated since it involves only the values of $w_1(t)$ in the interval $(0, T)$. In fact, let N be a large integer, set $t_i = (i-1)T/N$ for $i = 1 \ldots N$, and let $\bar{\rho}_0$ be the spectral radius of the following matrix eigenvalue problem

$$\bar{p}(t_i) \frac{T}{N} \left\{ \sum_{j=1}^{i-1} H(t_i - t_j) W_j + \sum_{j=i}^N H(t_i - t_j + T) W_j \right\} = \bar{\rho}_0 W_i, \tag{3.17}$$

which is of form $AW = \bar{\rho}_0 W$, where A is a $N \times N$ nonnegative matrix and $W = (W_1, \ldots W_N)$. Considering the relation (3.10) between R_0 and r_0, one can conclude that

$$\sqrt{(\beta\hat{\pi}) \times (\beta\pi p_{max}) \times \bar{\rho}_0 \Lambda / (\vartheta + \Lambda)^2} \longrightarrow_{N \to +\infty} R_0. \tag{3.18}$$

The results are presented in Table 1. In fact, the terms in (3.17) were computed in the following way:

- In order to compute $H(\tau)$, we integrate (3.14) and yield $h(\tau) = [e^{-\mu\tau}\int_0^\tau e^{\mu\sigma}f(\sigma)d\sigma + 1 - e^{-\mu\tau} - \int_0^\tau f(\sigma)d\sigma]/\mu$.

- The sampling in Fig. 3 shows the seasonal fluctuations of the vector population up to a constant multiplicative factor from [24]. We will take as the basis for the periodic population of the model because the number of tsetse flies is not as well documented in Kinshasa in 2005. Of course, the vector population from beginning to end in 2005 was not absolutely the same as from Fig.3 because the mean monthly temperature for example can be slightly different from year to year. Assuming that the tsetse fly emergence rate per month $r(t)$ is a step function, the width of the steps being equal to the time between two observations of tsetse fly population, it is easy to fit the heights of the steps so that $p(t)$ given by $\bar{p}'(t) = \bar{r}(t) - \mu\bar{p}(t)$ coincides with the data (see Fig. 3). For r_k, if $\theta_k < \theta_{k+1}$ are two successive observation times, then

$$\bar{r}(t) = \bar{r}_k = \mu \frac{exp(\mu\theta_{k+1})\bar{p}(\theta_{k+1}) - exp(\mu\theta_k)\bar{p}(\theta_k)}{exp(\mu\theta_{k+1}) - exp(\mu\theta_k)}. \tag{3.19}$$

For the normalized vector population $\bar{p}(t_i)$, the equation $\bar{p}'(t) = \bar{r}(t) - \mu\bar{p}(t)$ and the assumption saying that $\bar{r}(t)$ is a step function given by formal (3.19) imply that $\bar{p}(t_i) = e^{-\mu(t_i-\theta_k)}[\bar{p}(\theta_k) - \frac{\bar{r}_k}{\mu}] + \frac{\bar{r}_k}{\mu}$ if $\theta_k \leq t_i < \theta_{k+1}$.
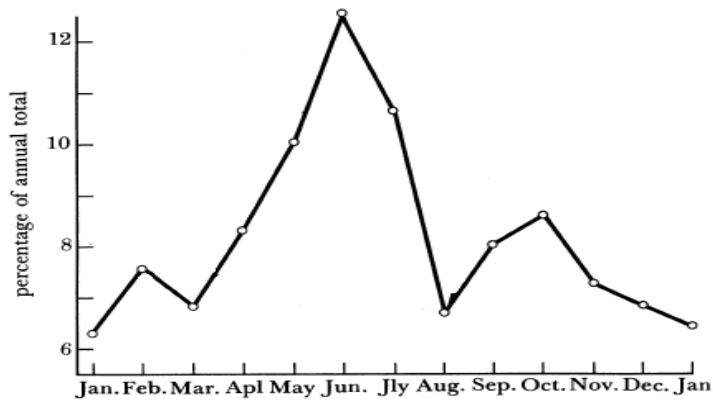

FIGURE 3. Percentage of annual total of tsetse flies.

- The spectral radius $\bar{\rho}_0$ can be computed using numerical mathematics software such as Matlable.

Table 1 Estimation of R_0

N	50	100	200	400
R_0	1.660	1.674	1.675	1.675

Here N is the number of points discretizing the interval (0,T), which represents 1 year.

4. SPECIFIC RESULTS

In this section, as an application, we shall present BRN R_0 for a special case. This case arises for example [25] when considering a single population of infected individuals with a recovery rate and an "effective" contact rate $\phi(a)$, $\beta(t,a)$ (i.e., the product of the contact rate and of the transmission probability per contact) depending on time t and on the time a since infection and subject to a constant immigration inflow $p(t)$. Both $\phi(t,a)$, $\beta(t,a)$ and $p(t)$ are assumed to be T-periodic functions with respect to t. Let $i(t,a)$ be the density of population with age of infection a at time t. In the linear approximation near the disease-free steady state, $i(t,a)$ is the solution of the system

$$\begin{aligned}
(\tfrac{\partial}{\partial t} + \tfrac{\partial}{\partial a})i(t,a) &= -\phi(a)i(a,t) + p(t), \\
i(t,0) &= \int_0^\infty \beta(t,a)i(t,a)da.
\end{aligned} \tag{4.1}$$

Based on the present definition of the basic reproduction number R_0 presented in section 3, it is quite easy to obtain that the matrix $A(t,\tau)$ is of one dimension:

$$A(t,\tau) = p(t)e^{-\int_{t-\tau}^{t}\phi(\sigma)d\sigma}. \tag{4.2}$$

Consequently, the eigenvalue problem can be rewritten as

$$p(t)\int_0^\infty e^{-\int_{t-\tau}^{t}\phi(\sigma)d\sigma}w(t-\tau)d\tau = R_0 w(t). \tag{4.3}$$

Deriving this equation and integrating by parts, we obtain

$$
\begin{aligned}
R_0 w'(t) = {} & p'(t) \int_0^\infty e^{-\int_{t-\tau}^t \phi(\sigma)d\sigma} w(t-\tau)d\tau + p(t)\int_0^\infty e^{-\int_{t-\tau}^t \phi(\sigma)d\sigma} w'(t-\tau)d\tau \\[2mm]
& + p(t)\int_0^\infty e^{-\int_{t-\tau}^t \phi(\sigma)d\sigma}[\phi(t-\tau)-\phi(t)]w(t-\tau)d\tau \\[2mm]
= {} & p'(t)\frac{R_0 w(t)}{p(t)} - p(t)\int_0^\infty \phi(t-\tau)e^{-\int_{t-\tau}^t \phi(\sigma)d\sigma}w(t-\tau)d\tau \\[2mm]
& - p(t)\left[e^{-\int_{t-\tau}^t \phi(\sigma)d\sigma}w(t-\tau)\right]_0^\infty \\[2mm]
& + p(t)\int_0^\infty e^{-\int_{t-\tau}^t \phi(\sigma)d\sigma}[\phi(t-\tau)-\phi(t)]w(t-\tau)d\tau \\[2mm]
= {} & \frac{p'(t)}{p(t)}R_0 w(t) - \phi(t)R_0 w(t) + p(t)w(t).
\end{aligned}
$$

The previous equation can be represented as

$$
\frac{w'(t)}{w(t)} = \frac{p'(t)}{p(t)} - \phi(t) + \frac{p(t)}{R_0},
$$

which can be integrated to get

$$
w(t) = H p(t) e^{-\int_0^t \phi(\tau)d\tau} + \frac{1}{R_0}\int_0^t p(\tau)d\tau,
$$

where H is a positive constant. The function $w(t)$ thus obtained is T-periodic if $w(t+T) = w(t)$ for all t. Using the periodicity of $p(t)$ and $\phi(t)$, we see that this condition holds if and only if

$$
R_0 = \frac{\int_0^T p(\tau)d\tau}{\int_0^T \phi(\tau)d\tau}.
$$

5. CONCLUSIONS

It is well-known that periodic fluctuations are common in the evolution of disease transmissions. Periodic changes in birth rates of populations are evidenced in many biological works. A natural and important problem associated with periodic epidemic models is to define and compute their BRN. The BRN for Vector-Borne diseases are interpreted as the number of secondary infections produced by infected vectors and hosts during the course of their infection. Note that infected hosts produce infected vectors and vise versa. Although BRN for Vector-Borne diseases is independent of the recruit rate, seasonality-through its direct effect on the size of vector population-are still the primary determinants for disease transmissions. We also recall two fundamental properties of BRN in the context of vector-borne diseases: an epidemic can

develop if and only if BRN larger than the unit; an epidemic can be prevented if the vector population is uniformly divided by R_0' all through the year [26].

In this paper we analyze the impact of seasonal variations on the dynamics of African trypanosomiasis. Following the hypothesis (A.4), the corresponding linear system of original model is obtained. It is common knowledge that the basic reproduction number plays a vital role in a epidemic model which determines whether the disease is eradicated or not. We derive the basic reproduction number R_0 which is adapted to periodic environments. Parameters are estimated from the province of Kinshasa, Democratic Republic of Congo. Finally, this R_0 is estimated numerically for the epidemic in Kinshasa: $R_0 = 1.675$. This model suggests that the epidemic could be stopped if the vector population were reduced by a factor $R_0^2 = 2.80$.

Conflict of Interests

The authors declare that there is no conflict of interests.

REFERENCES

[1] R. Ross, The Prevention of Malaria, John Murray, London. (1911).

[2] G. Macdonald, The analysis of equilibrium in malaria, Trop. Dis. Bull. 49 (9) (1952), 813-828.

[3] Z. Feng, J. X. Velasco-Hernandez, Competitive exclusion in a vector-host model for the dengue fever, J. Math. Biol. 35 (1997), 523–544.

[4] T. Yonow, C. C. Brewster, J. C. Allen, M. I. Meltzer, Models for heartwater epidemiology: Practical implications and suggestions for future research, Onderstepoort J. Vet. Res. 65 (4) (1998), 263–273.

[5] J. J. McDermott, P. G. Coleman, Comparing apples and oranges-model-based assessment of different tsetse-transmitted trypanosomosis control strategies, Int. J. Parasitol. 31 (2001), 603–609.

[6] I. M. Foppa, A. Spielman, Does reservoir host mortality enhance transmission of west nile virus? Theor. Biol. Med. Model. 4 (1) (2007), 17.

[7] J. L. Capinera, Sleeping sickness or african trypanosomiasis, Encyclopedia of Entomology. (2008), 3387–3390.

[8] E. M. Févre, B. Von Wissmann, S. C. Welburn, P. Lutumba, The burden of human african trypanosomiasis, PLOS Neglect. Trop. Dis. 2 (12) (2008), 1–7.

[9] D. Courtin, D. Berthier, S. Thevenon, G. Dayo, A. Garcia, B. Bucheton, Host genetics in african trypanosomiasis, Infect. Genet. Evol. 8 (3) (2008), 229–238.

[10] P. P. Simarro, J. Jannin, P. Cattand, Eliminating human african trypanosomiasis: Where do we stand and what comes next? PLOS Med. 5 (2) (2008), e55.

[11] K. Tshimungu, B. B. Kalambayi, M. Kiyombo, L. N. Okenge, P. De Mol, Knowledge, behaviours, practices and beliefs regarding human african trypanosomiasis (hat) among inhabitants of kinshasa (democratic republic of congo), Santé. 18 (3) (2008), 141–147.

[12] H. E. Jahnke, H. E. Jahnke, Livestock production systems and livestock development in tropical Africa, Kieler Wissenschaftsverlag Vauk Kiel. (1982).

[13] V. Delespaux, H. P. de Koning, Drugs and drug resistance in african trypanosomiasis, Drug resistance updates. 10 (2007), 30–50.

[14] B. H. Hirth, H. R. Barker, C. Celatka, J. D. Klinger, H. Liu, B. Nare, A. Nijjar, M. A. Phillips, E. Sybertz, E. K. Willert, et al, Discovery of new s-adenosylmethionine decarboxylase inhibitors for the treatment of human african trypanosomiasis (hat), Bioorg. Med. Chem. Lett. 19 (11) (2009), 2916–2919.

[15] D. Courtin, J. Milet, V. Jamonneau, C. S. Yeminanga, V. K. B. Kumeso, C. M. M. Bilengue, C. Betard, A. Garcia, Association between human african trypanosomiasis and the IL6 gene in a congolese population, Infect. Genet. Evol. 7 (1) (2007), 60–68.

[16] G. Simo, P. M. Diabakana, V. K. B. K. Mesu, E. Z. Manzambi, G. Ollivier, T. Asonganyi, G. Cuny, P. Grebaut, Human african trypanosomiasis transmission, kinshasa, democratic republic of congo, Emerg. Infect. Dis. 12 (12) (2006), 1968–1970.

[17] P. Grebaut, J. Bena, E. Z. Manzambi, P. Mansinsa, V. Khande, G. Ollivier, G. Cuny, G. Simo, Characterization of sleeping sickness transmission sites in rural and periurban areas of kinshasa (republique democratique du congo), Vector-Borne Zoon. Dis. 9 (6) (2009), 631–636.

[18] J. Y. Hwang, D. C. Smithson, M. C. Connelly, J. Maier, F. Zhu, K. R. Guy, Discovery of halo-nitrobenzamides with potential application against human african trypanosomiasis, Bioorg. Med. Chem. Lett. 20 (1) (2010), 149–152.

[19] H. R. Thieme, Renewal theorems for linear periodic volterra integral equations, J. Integral Equ. 7 (1984), 253–277.

[20] O. Diekmann, J. A. P. Heesterbeek, Mathematical epidemiology of infectious diseases: model building, analysis and interpretation, John Wiley & Sons. (2000).

[21] P. Jagers, O. Nerman, Branching processes in periodically varying environment, Ann. Probab. 13 (1985), 254–268.

[22] J. Robays, A. Ebeja Kadima, P. Lutumba, C. Miaka mia Bilenge, V. Kande Betu Ku Mesu, R. De Deken, J. Makabuza, M. Deguerry, P. Van Der Stuyft, M. Boelaert, Human african trypanosomiasis amongst urban residents in kinshasa: a case-control study, Trop. Med. Int. Health. 9 (8) (2004), 869–875.

[23] D. Rogers, Tsetse population dynamics and distribution: a new analytical approach, J. Animal Ecol. 48 (1979), 825–849.

[24] D. Rogers, The dynamics of vector-transmitted diseases in human communities, Phil. Trans. R. Soc. Lond. 321 (1988), 513–539.

[25] N. Bacaër, X. Abdurahman, Resonance of the epidemic threshold in a periodic environment, J. Math. Biol. 57 (5) (2008), 649–673.

[26] N. Bacaër, Approximation of the basic reproduction number R_0 for vector-borne diseases with a periodic vector population, Bull. Math. Biol. 69 (3) (2007), 1067–1091.