

# A Model for Hepatitis B with Chronological and Infection Ages

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## Abstract

We construct and study a differential infectivity model with chronological and infection age. The application is done on hepatitis B in Cameroon. We prove the global stability of the disease free equilibrium when the basic reproduction ratio  $R_0$  is less than one and the existence and uniqueness of an endemic equilibrium when  $R_0 > 1$ .

**Keywords:** Nonlinear dynamical systems; Global stability; Lyapunov methods; Differential infectivity models; HBV; Cameroon

## A Simplified Model without Vertical Transmission and With Control Measure

Hepatitis B is endemic in Africa [1-3] (see also the references cited therein) and some models have been constructed in order to understand its dynamic with ODE deterministic (with delay or not) or stochastic processes [2,4-8] or partial differential equations [9,10].

Studies like [9-13] recognized the importance of the age factor in the dynamics of infectious diseases like hepatitis B [10]. Moreover some studies like [4,14] obtained results with ODEs with discrete age(s) that could be generalized with continuous age assumption more realistic and relevant.

We introduce then a model with differential infectivity and chronological or infection ages. We denote by  $s(t, a)$  the density of susceptible at time  $t$  with chronological age  $a$ . We denote by  $i(t, \tau)$  the density of infective that will develop acute disease at time  $t$  contaminated since a time  $\tau$  and  $e(t, \tau)$  the density of infective that will not develop acute disease (asymptomatic carrier) at time  $t$  contaminated since a time  $\tau$ . The model we shall consider reads as follows:

$$\begin{aligned} (\partial_t + \partial_a)s(t, a) &= -\mu s(t, a) - \lambda(t)s(t, a), \quad t > 0, a > 0, \\ s(t, 0) &= \Lambda, \\ (\partial_t + \partial_\tau)i(t, \tau) &= -(\mu + \gamma_i)i(t, \tau), \quad t > 0, \tau > 0, \\ (\partial_t + \partial_\tau)e(t, \tau) &= -(\mu + \gamma_e)e(t, \tau), \quad t > 0, \tau > 0, \end{aligned} \quad (1.1)$$

$$i(t, 0) = \lambda(t) \int_0^\infty p(a)s(t, a)da, \quad e(t, 0) = \lambda(t) \int_0^\infty (1 - p(a))s(t, a)da$$

Here  $\Lambda > 0$  is some constant entering in flux,  $\mu > 0$  is the natural death rate,  $\gamma_i$  is the additional death rate due to the disease,  $a \rightarrow p(a) \in [0, 1]$  is the proportion of individuals going to the acute infective class while  $1 - p(a)$  is the proportion to not develop the acute disease when infection occurs. Finally, it remains to model  $\lambda(t, a)$ , the force of infection, those general form can be written in the form

$$\lambda(t) = \int_0^\infty (\beta_i(\tau)i(t, \tau) + \beta_e(\tau)e(t, \tau))d\tau \quad (1.2)$$

Finally this model is supplemented together with some initial data

$$s(0, \cdot) = s_0(\cdot) \in L^1_+(0, \infty)$$

$$i(0, \cdot) = i_0(\cdot), \quad e(0, \cdot) = e_0(\cdot) \quad \text{with} \quad (i_0, e_0) \in L^1_+(0, \infty)^2$$

The above model takes into account the chronological age of susceptible. This parameter has strong implication in the dynamics of

infection. Indeed, depending on the age at which susceptible enters the infective's classes, the disease will develop indifferent way. For hepatitis B virus (HBV), young infections lead to chronic infection while older infection leads to acute disease.

In the above model, we do not take into account possible vertical transmission and we do not consider any control strategy such vaccination campaign. It seems to be relevant together the assumption of WHO [3] that consider that vertical transmission of the disease does occur in sub-saharian Africa, but its influence of the dynamics of the disease is rather small because the proportion of chronic infections acquired prenatally is low. Under the above assumption, we assume that the chronological age for the infective classes do not play an important role. But the time since infection is a relevant biological variable because of the possibility to have a long latent period (especially for the asymptomatic carrier class, until several years).

The work is organized as follows. In Section 2, we prove the wellposedness of the PDE (1.1-1.2), derive preliminary results useful to study the long term behavior of the model. Sections 3, 4, and 5 is devoted to the uniqueness of endemic equilibrium when the biological basic reproduction rate  $R_0$  is greater than 1 and study the global asymptotically stability of the disease free equilibrium if  $1 > R_0$ . Finally Section 6 presents discussion.

## Abstract Cauchy Problem Reformulation

### Mathematical assumptions

We assume that:

- $\gamma_i(\tau) \equiv \gamma_i > 0, \gamma_e(\tau) \equiv 0$
- The function  $p \in L^\infty(0, \infty)$  with  $p(a) \in [0, 1]$  a.e. and not identically 0 and 1.
- Function  $\beta_i, \beta_e \in L^\infty_+(0, \infty)$ .

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## Abstract Cauchy problem

The aim of this section is to deal with (1.1). To do so, we consider the Banach spaces

$$X = \mathbb{R}^3 \times L^1(0, \infty)^3, \quad X_0 = \{0_{\mathbb{R}^3}\} \times L^1(0, \infty)^3,$$

$$\text{endowed the norm } \left\| \begin{pmatrix} \alpha_1 \\ \alpha_2 \\ \alpha_3 \\ \psi_1 \\ \psi_2 \\ \psi_3 \end{pmatrix} \right\|_X = \sum_{i=1}^3 (|\alpha_i| + \|\psi_i\|_{L^1(0, \infty)}),$$

as well as the non-densely defined linear operator  $A: D(A) \subset X \rightarrow X$  defined by

$$D(A) = \{O_{\mathbb{R}^3}\} \times W^{1,1}(0, \infty)^3$$

together with

$$A \begin{pmatrix} 0 \\ 0 \\ 0 \\ \varphi_1 \\ \varphi_2 \\ \varphi_3 \end{pmatrix} = \begin{pmatrix} -\varphi_1(0) \\ -\varphi_2(0) \\ -\varphi_3(0) \\ -\varphi_1'(a) - \mu\varphi_1(a) \\ -\varphi_2'(\tau) - (\mu + \gamma_i)\varphi_2(\tau) \\ -\varphi_3'(\tau) - (\mu + \gamma_e)\varphi_3(\tau) \end{pmatrix},$$

as well as the nonlinear map  $F: X_0 \rightarrow X$  defined by

$$F \begin{pmatrix} 0 \\ 0 \\ 0 \\ \varphi_1 \\ \varphi_2 \\ \varphi_3 \end{pmatrix} = \begin{pmatrix} \Lambda \\ \int_0^\infty p(a)\varphi_1(a)da \int_0^\infty (\beta_i(\tau)\varphi_2(\tau) + \beta_e(\tau)\varphi_3(\tau))d\tau \\ \int_0^\infty (1-p(a))\varphi_1(a)da \int_0^\infty (\beta_i(\tau)\varphi_2(\tau) + \beta_e(\tau)\varphi_3(\tau))d\tau \\ -\int_0^\infty (\beta_i(\tau)\varphi_2(\tau) + \beta_e(\tau)\varphi_3(\tau))d\tau \end{pmatrix},$$

Let us notice that  $\overline{D(A)} = X_0$

Now by identifying  $(s(t, \cdot), I(t, \cdot), e(t, \cdot))$  in (1.1) together with  $u(t) = (0, 0, 0, s(t, \cdot), i(t, \cdot), e(t, \cdot))^T$ , one obtains that  $u(t)$  satisfies the following abstract Cauchy problem  $\frac{du(t)}{dt} = Au(t) + F(u(t))$ ,  $t > 0$ , (2.3) together with the initial data  $u(0) = x = (0, 0, 0, s_0, i_0, e_0)^T \in X_0$ .

We also consider the positive cones  $X_+ = \mathbb{R}^3 \times L^1_+(0, \infty)^3$ ,  $X_{0+} = X_0 \cap X_+$

**Lemma 2.1:** (Hille-Yosida property) Operator  $A: D(A) \subset X \rightarrow X$  is a Hille-Yosida operator. More precisely we have  $(-\mu, \infty) \subset \rho(A)$  the resolvent set of  $A$  and for each  $\lambda > -\mu$ , each  $(\alpha_1, \alpha_2, \alpha_3, \psi_1, \psi_2, \psi_3)^T \in X$  we have

$$(\lambda - A)^{-1} \begin{pmatrix} 0_{\mathbb{R}^3} \\ \varphi_1 \\ \varphi_2 \\ \varphi_3 \end{pmatrix} = \begin{pmatrix} \alpha_1 \\ \alpha_2 \\ \alpha_3 \\ \psi_1 \\ \psi_2 \\ \psi_3 \end{pmatrix}$$

$\Leftrightarrow$

$$\begin{cases} \varphi_1(a) = e^{-(\lambda+\mu)a} \alpha_1 + \int_0^a e^{-(\lambda+\mu)(a-s)} \psi_1(s) ds \\ \varphi_2(a) = e^{-(\lambda+\mu+\gamma_i)a} \alpha_2 + \int_0^a e^{-(\lambda+\mu+\gamma_i)(a-s)} \psi_2(s) ds \\ \varphi_3(a) = e^{-(\lambda+\mu+\gamma_e)a} \alpha_3 + \int_0^a e^{-(\lambda+\mu+\gamma_e)(a-s)} \psi_3(s) ds \end{cases}$$

Moreover we have for each  $\lambda > -\mu$

$$(\lambda - A)^{-1} X_+ \subset X_{0+} \quad (2.4)$$

**Proof:** Let  $x = (\alpha_1, \alpha_2, \alpha_3, \psi_1, \psi_2, \psi_3)^T \in X$  and  $\lambda > -\mu$  be given. Then the equation

$$(\lambda - A) \begin{pmatrix} 0_{\mathbb{R}^3} \\ \varphi_1 \\ \varphi_2 \\ \varphi_3 \end{pmatrix} = x,$$

rewrites as the following system

$$\begin{cases} \varphi_1(a)' = -(\lambda + \mu) \varphi_1(a) + \psi_1(a) \\ \varphi_2(a)' = -(\lambda + \mu + \gamma_i) \varphi_2(a) + \psi_2(a) \\ \varphi_3(a)' = -(\lambda + \mu + \gamma_e) \varphi_3(a) + \psi_3(a) \quad \forall a \geq 0 \\ \varphi_1(0) = \alpha_1, \varphi_2(0) = \alpha_2, \varphi_3(0) = \alpha_3, \end{cases}$$

that is

$$\begin{cases} \varphi_1(a) = e^{-(\lambda+\mu)a} \alpha_1 + \int_0^a e^{-(\lambda+\mu)(a-s)} \psi_1(s) ds \\ \varphi_2(a) = e^{-(\lambda+\mu+\gamma_i)a} \alpha_2 + \int_0^a e^{-(\lambda+\mu+\gamma_i)(a-s)} \psi_2(s) ds \\ \varphi_3(a) = e^{-(\lambda+\mu+\gamma_e)a} \alpha_3 + \int_0^a e^{-(\lambda+\mu+\gamma_e)(a-s)} \psi_3(s) ds \end{cases}$$

On the other hand one has

$$\begin{cases} \|\varphi_1\|_{L^1(0, \infty)} \leq \frac{|\alpha_1| + \|\varphi_1\|_{L^1(0, \infty)}}{\lambda + \mu}, \\ \|\varphi_2\|_{L^1(0, \infty)} \leq \frac{|\alpha_2| + \|\varphi_2\|_{L^1(0, \infty)}}{\lambda + \mu}, \\ \|\varphi_3\|_{L^1(0, \infty)} \leq \frac{|\alpha_3| + \|\varphi_3\|_{L^1(0, \infty)}}{\lambda + \mu} \end{cases}$$

As a consequence,

$$(-\mu, \infty) \subset \rho(A) \quad \text{and} \quad \|(\lambda - A)^{-1}\|_{L(X)} \leq \frac{1}{\lambda + \mu}, \quad \forall \lambda > -\mu$$

This completes the proof of the Hille-Yosida property. Finally the explicit formula of the resolvent operator implies that (2.4) holds true.

**Theorem 2.2:** There exists a continuous semi flow  $\{U(t)\}_{t \geq 0}$  on  $X_{0+}$  into itself such that for each  $x \in X_{0+}$ , the map  $t \mapsto U(t)x$  is the unique integrated solution of (2.3) with initial data  $x$ , namely  $t \mapsto U(t)x$  satisfies

- (i)  $\int_0^t U(s)x ds \in D(A)$ ,  $\forall t \geq 0$
- (ii)  $U(t)x = x + A \int_0^t U(s)x ds + \int_0^t F(U(s)x) ds$  for each  $t \geq 0$

Moreover we have for each  $x \in X_{0+}$ :

$$\frac{\Lambda}{\mu + \gamma_i + \gamma_e} \leq \liminf_{t \rightarrow \infty} \|U(t)x\| \leq \limsup_{t \rightarrow \infty} \|U(t)x\| \leq \frac{\Lambda}{\mu}$$

**Proof:** Let us first notice that for each  $M > 0$  there exists  $\lambda > 0$  such that

$$F(x) + \lambda x \in X_+, \quad \forall x \in B_x(0, M) \cap X_{0+}$$

With  $B_x(0, M)$  denote the ball of radius  $M$  centered at 0. One obtains the existence of a maximal positive semi flow for (2.3) on  $X_{0+}$  into itself. It remains to prove that this semi flow is globally defined. To do so, let  $x \in X_{0+}$  be given and recall that  $U(t)x = (0, 0, 0, s(t, \cdot), i(t, \cdot), e(t, \cdot))^T$

Consider the quantity

$$P(t) = \|U(t)x\| = \int_0^\infty s(t, a) da + \int_0^\infty i(t, \tau) d\tau + \int_0^\infty e(t, \tau) d\tau,$$

the total population at time  $t$ . Then it satisfies the differential inequality

$$\frac{dP(t)}{dt} \leq -\mu P(t)$$

Thus the map  $t \rightarrow P(t)$  cannot blow up in finite and the global existence result follows.

Let us, in addition, notice that, from this inequality one gets (by density)

$$\limsup_{t \rightarrow \infty} \|U(t)x\| \leq \frac{\Lambda}{\mu}, \quad \forall x \in X_{0+}$$

One the other hand one has

$$\frac{dP(t)}{dt} = \Lambda - \mu P(t) - \left( \gamma_i \int_0^\infty i(t, \tau) d\tau + \gamma_e \int_0^\infty e(t, \tau) d\tau \right) \geq -(\mu + \gamma_i + \gamma_e) P(t),$$

so that  $\liminf_{t \rightarrow \infty} \|U(t)x\| \geq \frac{\Lambda}{\mu + \gamma_i + \gamma_e}$ ,  $\forall x \in X_{0+}$

This completes the proof of the result.

## Stationary States

### The disease free equilibrium

The disease free equilibrium corresponds to a stationary (that is time independent solution)

$$(s_F \equiv s_F(a), i_F \equiv 0, e_F \equiv 0),$$

of (1.1)-(1.2). As a consequence we have the following lemma

**Lemma 3.1:** The dynamical system provided by (1.1)-(1.2) has a unique disease free equilibrium where  $s_F$  is given by  $s_F(a) \equiv \Lambda e^{-\mu a}$

From now one we set

$$S_1 = \int_0^\infty p(a) s_F(a) da, \quad S_2 = \int_0^\infty p(a) s_F(a) da,$$

and we consider the biological basic reproduction rate

$$R_0 = \Lambda \int_0^\infty (P_i \beta_i(\tau) e^{-\gamma_i \tau} + P_e \beta_e(\tau) e^{-\gamma_e \tau}) d\tau \quad (3.5)$$

where we have set

### Endemic equilibrium

We look for stationary solutions  $(s; i; e)$  such that  $(i; e)$  not identically zero satisfying

$$s'(a) = -\mu s(a) - \lambda s(a), \quad a > 0,$$

$$s(0) = \Lambda,$$

$$i'(\tau) = -(\mu + \gamma_i) i(\tau), \quad \tau > 0,$$

$$e'(\tau) = -(\mu + \gamma_e) e(\tau), \quad \tau > 0,$$

$$i(0) = \lambda \int_0^\infty p(a) s(a) da, \quad e(0) = \lambda \int_0^\infty (1 - p(a)) s(a) da$$

$$\lambda \int_0^\infty (\beta_i(\tau) i(\tau) + \beta_e(\tau) e(\tau)) d\tau,$$

**Theorem 3.2:** Recalling definition (3.5), if  $R_0 > 1$ , system (1.1)-(1.2) has a unique endemic equilibrium point denoted by  $(s_E; i_E; e_E)$ .

**Proof:** we have

$$s(a) = \Lambda e^{-(\mu + \lambda)a},$$

$$i(\tau) = e^{-(\mu + \gamma_i)\tau} \lambda \Lambda \int_0^\infty p(a) e^{-(\mu + \lambda)a} da$$

$$e(\tau) = e^{-(\mu + \gamma_e)\tau} \lambda \Lambda \int_0^\infty (1 - p(a)) e^{-(\mu + \lambda)a} da$$

Thus

$$\lambda = \int_0^\infty \beta_i(\tau) e^{-(\mu + \gamma_i)\tau} d\tau \lambda \Lambda \int_0^\infty p(a) e^{-(\mu + \lambda)a} da + \int_0^\infty \beta_e(\tau) e^{-(\mu + \gamma_e)\tau} d\tau \lambda \Lambda \int_0^\infty (1 - p(a)) e^{-(\mu + \lambda)a} da$$

We are looking for endemic stationary state, that is  $\lambda > 0$ , so that

$$1 = \int_0^\infty \beta_i(\tau) e^{-(\mu + \gamma_i)\tau} d\tau \lambda \Lambda \int_0^\infty p(a) e^{-(\mu + \lambda)a} da + \int_0^\infty \beta_e(\tau) e^{-(\mu + \gamma_e)\tau} d\tau \lambda \Lambda \int_0^\infty (1 - p(a)) e^{-(\mu + \lambda)a} da$$

Now the map  $\lambda \rightarrow f(\lambda)$  is non increasing with  $f$  defined by

$$f(\lambda) = \int_0^\infty \beta_i(\tau) e^{-(\mu + \gamma_i)\tau} d\tau \lambda \Lambda \int_0^\infty p(a) e^{-(\mu + \lambda)a} da + \int_0^\infty \beta_e(\tau) e^{-(\mu + \gamma_e)\tau} d\tau \lambda \Lambda \int_0^\infty (1 - p(a)) e^{-(\mu + \lambda)a} da$$

and  $f(\lambda) > 0$  when  $\lambda \rightarrow \infty$ . As a consequence, since  $R_0 = f(0) > 1$ , there exists a unique  $\lambda_E > 0$  such that

$$f(\lambda_E) = 1.$$

Finally, the functions

$$s_E(a) = \Lambda e^{-(\mu + \lambda_E)a},$$

$$i_E(\tau) = e^{-(\mu + \gamma_i)\tau} \lambda_E \Lambda \int_0^\infty p(a) e^{-(\mu + \lambda_E)a} da$$

$$e_E(\tau) = e^{-(\mu + \gamma_e)\tau} \lambda_E \Lambda \int_0^\infty (1 - p(a)) e^{-(\mu + \lambda_E)a} da$$

provides the unique endemic stationary state of system (1.1)-(1.2).

## Dynamical Properties

### Assumption 4.1

Assume that the maps  $a \rightarrow \beta_i(a)$  and  $a \rightarrow \beta_e(a)$  are bounded and uniformly continuous from  $[0, \infty)$  into itself.

### Volterra Integral Formulation:

The solutions of (1.1)-(1.2) can be reformulated as follows

$$\partial_t s + \partial_a s = -\mu s - \lambda(t) s$$

$$s(t, 0) = \Lambda, \quad s(0, \cdot) = s_0,$$

With

$$\lambda(t) = \int_0^t \beta_i(\tau) i(t, \tau) + \beta_e(\tau) e(t, \tau) d\tau,$$

and

$$i(t, \tau) = \begin{cases} e^{(\mu+\gamma_i)\tau} i_0(a-t) & \text{if } a-t \geq 0, \\ e^{(\mu+\gamma_i)a} b_i(t-a) & \text{if } a-t < 0, \end{cases} \quad e(t, \tau) = \begin{cases} e^{(\mu+\gamma_e)\tau} e_0(a-t) & \text{if } a-t \geq 0, \\ e^{(\mu+\gamma_e)a} b_e(t-a) & \text{if } a-t < 0, \end{cases}$$

where  $t \rightarrow b_i(t) = i(t, 0)$  and  $t \rightarrow b_e(t) = e(t, 0)$  are the unique continuous functions satisfying for  $k=i, e$ :

$$b_k(t) = k(t, 0) = p_k[s(t, \cdot)] \int_0^t (\beta_i(\tau) e^{\gamma_i \tau} b_i(t-\tau) + \beta_e(\tau) e^{\gamma_e \tau} b_e(t-\tau)) d\tau \\ + p_k[s(t, \cdot)] \int_t^\infty (e^{\gamma_i \tau} \beta_i(\tau) i_0(\tau-t) + e^{\gamma_e \tau} \beta_e(\tau) e_0(\tau-t)) d\tau$$

where we have set

$$p_i[\varphi] = \int_0^\infty p(a) \varphi(a) da, \quad p_e[\varphi] = \int_0^\infty (1-p(a)) \varphi(a) da.$$

By using results in Sell and You [15], one can find suitable conditions to prove that  $\{U(t)\}_{t \geq 0}$  is asymptotically smooth and derived the following proposition.

**Proposition 4.2:** Let Assumption 4.1 be satisfied. Then there exists a compact set  $A \subset X_{0+}$  such that

- (i) A is invariant under the semi flow  $\{U(t)\}_{t \geq 0}$
- (ii) A attracts the bounded sets of  $X_{0+}$  under  $\{U(t)\}_{t \geq 0}$ . This means that for each bounded set  $B \subset X_{0+}$  we have

$$\lim_{t \rightarrow \infty} \delta(U(t)B, A) = 0,$$

where  $\delta$  is defined as

$$\delta(A, B) = \sup_{x \in A} \inf_{y \in B} \|x - y\|$$

Moreover A is locally asymptotically stable. Next one considers the following quantities  $\tau_k = \sup\{\tau \geq 0 : \beta_k(\tau) > 0\}$ ,  $k \in \{i, e\}$  and the following set:

$$\widehat{M} = \left\{ (\varphi, \psi) \in L_+^1(0, \infty)^2 : \int_0^{\tau_i} \varphi(\tau) d\tau + \int_0^{\tau_e} \psi(\tau) d\tau > 0 \right\}$$

We set also

$$M_0 = \{O_{\mathbb{R}^3}\} \times L_+^1(0, \infty) \times \widehat{M} \subset X_{0+},$$

$$\partial M_0 = X_{0+} \setminus M_0$$

From this Volterra integral formulation one obtains the following lemma:

**Lemma 4.3:** The sets  $M_0$  and  $\partial M_0$  are positively invariant under the semi flow  $\{U(t)\}_{t \geq 0}$ . Moreover if  $x \in \partial M_0$  then

$$\lim_{t \rightarrow \infty} \|U(t)x - x_F\| = 0$$

with  $x_F = (0_{\mathbb{R}^3}, s_F(\cdot) = \Lambda e^{-\mu \cdot}, 0, 0)^T$

## Global Stability of the Disease free Equilibrium when $R_0 < 1$ and Simulations

### Stability with a Lyapunov like function

**Lemma 5.1:** Let  $t \in \mathbb{R}$  and  $a > 0$  be given. For a globally in time solution  $s$ , we get the following inequality:

$$s(t, a) \leq s_F(a)$$

**Proof:** At first we want to prove that:  $s(t, a) \leq s_F(a)$ ,  $\forall a > 0$ . We have on characteristics:

$$s(t, a) = \begin{cases} e^{-\int_0^t \mu + \lambda(s) ds} s_0(a-t) & \text{if } a-t \geq 0 \\ \Lambda e^{-\int_0^t \mu + \lambda(s) ds} & \text{if } a-t < 0 \end{cases} \quad (5.6)$$

As a consequence we obtain for each  $s \in \mathbb{R}$ ,  $t > 0$  and  $a > 0$  that

$$s(t+s, a) = \begin{cases} e^{-\int_0^t \mu + \lambda(s) ds} s(s, a-t) & \text{if } a-t \geq 0 \\ \Lambda e^{-\int_0^t \mu + \lambda(s) ds} & \text{if } a-t < 0 \end{cases}$$

If  $t=a$  then for each  $s \in \mathbb{R}$ :

$$s(s+a, a) = e^{-\int_0^a \mu + \lambda(s) ds} s(s, 0) \leq s_F(a)$$

Let  $t \in \mathbb{R}$  and  $a > 0$  be given. Choose  $s \in \mathbb{R}$  such that  $s=t-a$ . The above equality re-writes as

$$s(t, a) \leq s_F(a),$$

and the result follows.

We will use the lemma above in the proof of the following theorem.

**Theorem 5.2:** For the model (1.1)-(1.2), if  $R_0 < 1$ , then the disease free equilibrium is globally asymptotically stable in  $\partial M_0$ .

**Proof:** Recall that

$$\frac{R_0}{\Lambda} = \int_0^\infty \beta_i(\tau) e^{-(\mu+\gamma_i)\tau} d\tau \int_0^\infty p(a) e^{-\mu a} da \\ + \int_0^\infty \beta_e(\tau) e^{-(\mu+\gamma_e)\tau} d\tau \int_0^\infty (1-p(a)) e^{-\mu a} da,$$

Choose  $\tau$  and  $s$  such that

$$\begin{cases} \Gamma'_i(\tau) = (\mu + \gamma_i) \Gamma_i(\tau) - \beta_i(\tau) \\ \Gamma_i(0) = \int_0^\infty e^{-(\mu+\gamma_i)s} \beta_i(s) ds, \end{cases}$$

And

$$\begin{cases} \Gamma'_e(\tau) = (\mu + \gamma_e) \Gamma_e(\tau) - \beta_e(\tau) \\ \Gamma_e(0) = \int_0^\infty e^{-(\mu+\gamma_e)s} \beta_e(s) ds, \end{cases}$$

Note that

$$R_0 = \Gamma_i(0) \int_0^\infty p(a) s_F(a) da + \Gamma_e(0) \int_0^\infty (1-p(a)) s_F(a) da$$

Then one gets (by density):

$$\frac{d}{dt} \int_0^\infty \Gamma_i(\tau) i(t, \tau) d\tau = - \int_0^\infty \Gamma_i(\tau) i_\tau(t, \tau) d\tau - (\mu + \gamma_i) \int_0^\infty \Gamma_i(\tau) i(t, \tau) d\tau \\ = \lambda(t) \Gamma_i(0) \int_0^\infty p(a) s(t, a) da + \int_0^\infty [\Gamma'_i(\tau) - (\gamma_i) \Gamma_i(\tau)] i(t, \tau) d\tau \\ \frac{d}{dt} \int_0^\infty \Gamma_e(\tau) e(t, \tau) d\tau = - \int_0^\infty \Gamma_e(\tau) e_\tau(t, \tau) d\tau - (\mu + \gamma_e) \int_0^\infty \Gamma_e(\tau) e(t, \tau) d\tau \\ = \lambda(t) \Gamma_e(0) \int_0^\infty (1-p(a)) s(t, a) da + \int_0^\infty [\Gamma'_e(\tau) - (\mu + \gamma_e) \Gamma_e(\tau)] e(t, \tau) d\tau$$

so that

$$\frac{d}{dt} \int_0^\infty [\Gamma_i(\tau) i(t, \tau) + \Gamma_e(\tau) e(t, \tau)] d\tau$$

$$= \left[ \Gamma_i(0) \int_0^\infty p(a)s(t,a)da + \Gamma_e(0) \int_0^\infty (1-p(a))s_F(a)da \right] \times$$

$$\left[ \int_0^\infty \beta_i(\tau)i(t,\tau) + \beta_e(\tau)e(t,\tau)d\tau \right]$$

$$- \left[ \int_0^\infty \beta_i(\tau)i(t,\tau) + \beta_e(\tau)e(t,\tau)d\tau \right]$$

$$\frac{d}{dt} \int_0^\infty [\Gamma_i(\tau)i(t,\tau) + \Gamma_e(\tau)e(t,\tau)]d\tau$$

so that

$$\frac{d}{dt} \int_0^\infty [\Gamma_i(\tau)i(t,\tau) + \Gamma_e(\tau)e(t,\tau)]d\tau$$

$$\leq \left[ \Gamma_i(0) \int_0^\infty p(a)s(t,a)da + \Gamma_e(0) \int_0^\infty (1-p(a))s_F(a)da \right] \times$$

$$\left[ \int_0^\infty \beta_i(\tau)i(t,\tau) + \beta_e(\tau)e(t,\tau)d\tau \right]$$

Since  $R_0 \leq 1$  then,

$$\frac{d}{dt} \int_0^\infty [\Gamma_i(\tau)i(t,\tau) + \Gamma_e(\tau)e(t,\tau)]d\tau$$

$$\leq \left[ \Gamma_i(0) \int_0^\infty p(a)s(t,a)da + \Gamma_e(0) \int_0^\infty (1-p(a))s_F(a)da \right] \times$$

$$\left[ \int_0^\infty \beta_i(\tau)i(t,\tau) + \beta_e(\tau)e(t,\tau)d\tau \right]$$

$$\leq \left[ \Gamma_i(0) \int_0^\infty p(a)s(t,a) - s_F(a)da + \Gamma_e(0) \int_0^\infty (1-p(a))[s(t,a) - s_F(a)]da \right]$$

$$\times \left[ \int_0^\infty \beta_i(\tau)i(t,\tau) + \beta_e(\tau)e(t,\tau)d\tau \right]$$

On the attractor A we check by lemma 5.1 that

$$s(t,a) \leq s_F(a), \forall t \in \mathbb{R}, a > 0,$$

so that the functional

$$V[i,e](t) := \int_0^\infty [\Gamma_i(\tau)i(t,\tau) + \Gamma_e(\tau)e(t,\tau)]d\tau,$$

is non-increasing along the complete orbits.

$V[i,e]$  is a strict Lyapunov function for DFE on  $A \subset \partial M_0$  and global stability of DFE when  $R_0 < 1$  follows.

## Simulations

We first simplify the model by assuming that  $\beta_e$  and  $\beta_i$  are both constant parameters. Then introducing  $I(t) = \int_0^\infty i(t,\tau)d\tau$  and  $E(t) = \int_0^\infty e(t,\tau)d\tau$ .

We will use data in Tables 1-3 for the case of Cameroon.

Age	prevalence $p$	prevalence $q$	Ref.
0 to 1 month (excluded)	0.1 or 10%	0.9 or 90%	[11,5]
1 to 6 months (included)	0.2 or 20%	0.8 or 80%	[5]
7 to 12 months (included)	0.45 or 45%	0.55 or 55%	[5]
1 to 5 years (included)	0.5-0.25 or 50-25%	0.25-0.5 or 25-50%	[11,5]
>5 years	0.94-0.9 or 94-90%	0.06-0.1 or 6-10%	[11,5]

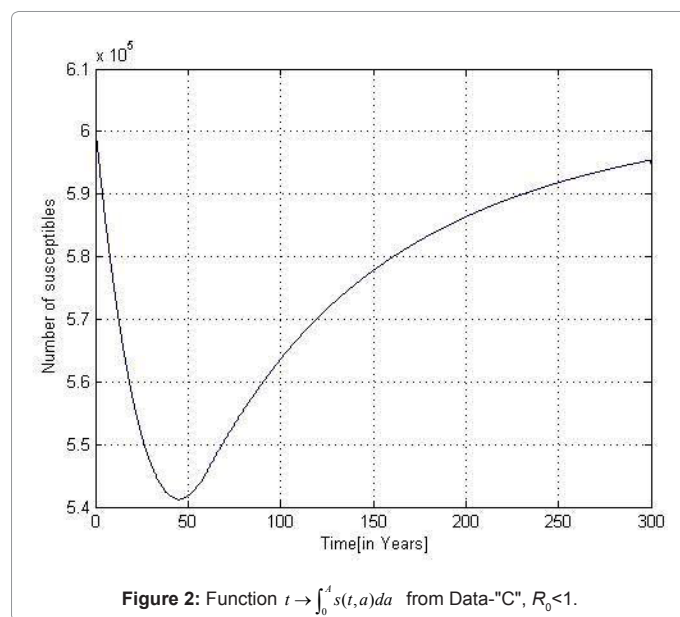
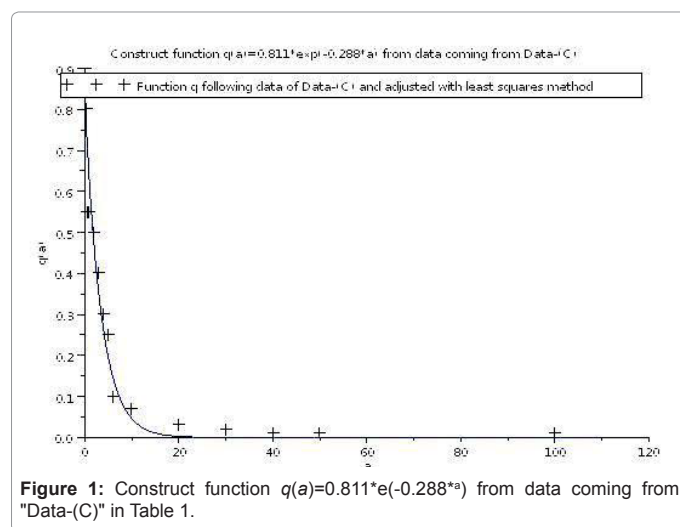
**Table 1:** "Data-(C)", some other data collected on Cameroon.

Age (years)	$p(a)$	$\beta_i$	$B_E$	$V_i$	$V_E$	$\mu$
[0; A=60 yrs]	$0.811 \cdot e^{(-0.288 \cdot a)}$	10-6	10-20	0.036	0.02	$15 \cdot 10^{-5}$

**Table 2:** Values for  $R_0 < 1$ .

Age (years)	$p(a)$	$\beta_i$	$B_E$	$V_i$	$V_E$	$\mu$
[0; A=60 yrs]	$0.811 \cdot e^{(-0.288 \cdot a)}$	0.00006	10-20	0.09	0.05	$15 \cdot 10^{-5}$

**Table 3:** Values for  $R_0 > 1$ .



## Discussion

Simulations illustrate the asymptotic stability of DFE in section 5. The model described by equations (1.1-1.2) exhibit a rich dynamic. We observe that the biological basic reproduction rate  $R_0$  is fundamental for the study of the basic dynamical properties. Applied to hepatitis B, the model suggests that infection rates play a great role in the description of the disease (see expression of  $R_0$ ). Simulations conducted follow our results and suggest the fact that the endemic equilibrium is asymptotically stable if  $R_0 > 1$  (Figures 1-9).



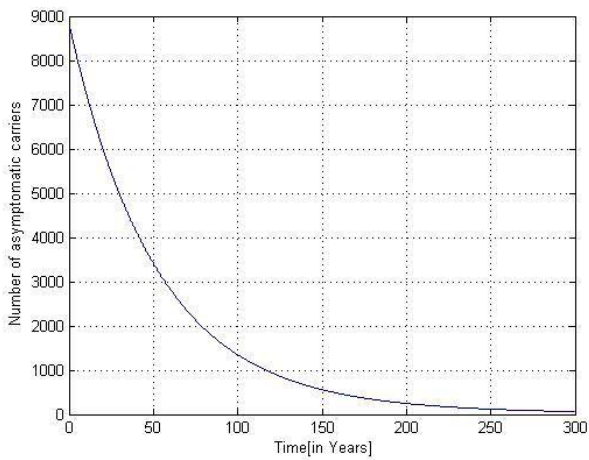


Figure 3: Function  $E(t)$  from Data-"C",  $R_0 < 1$ .

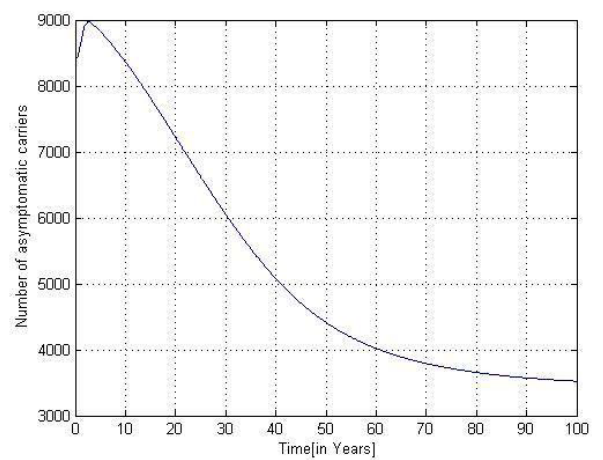


Figure 6: Function  $E(t)$  from Data-"C",  $R_0 > 1$ .

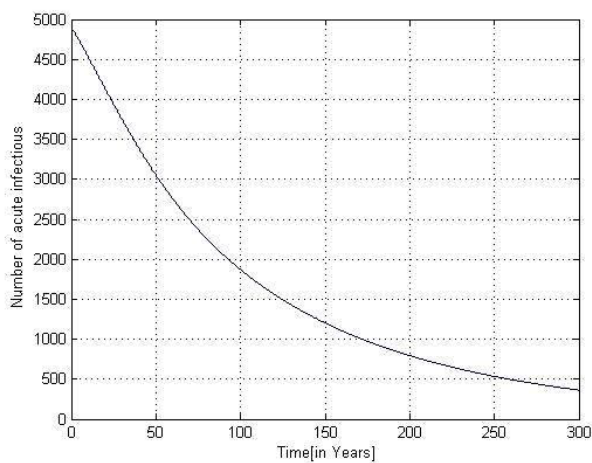


Figure 4: Function  $I(t)$  from data of Data-"C",  $R_0 < 1$ .

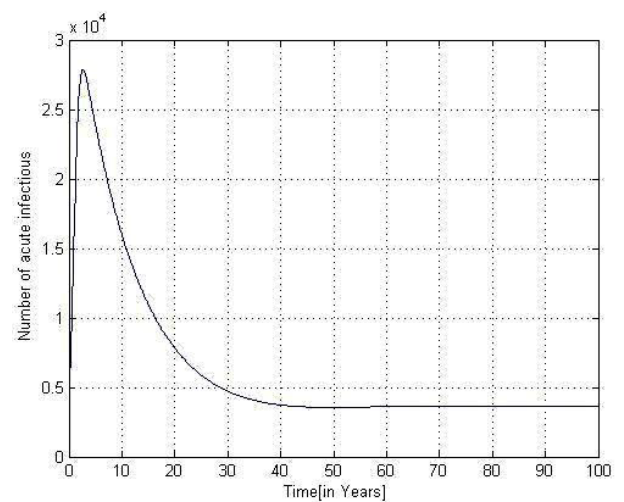


Figure 7: Function  $I(t)$  from data of Data-"C",  $R_0 > 1$ .

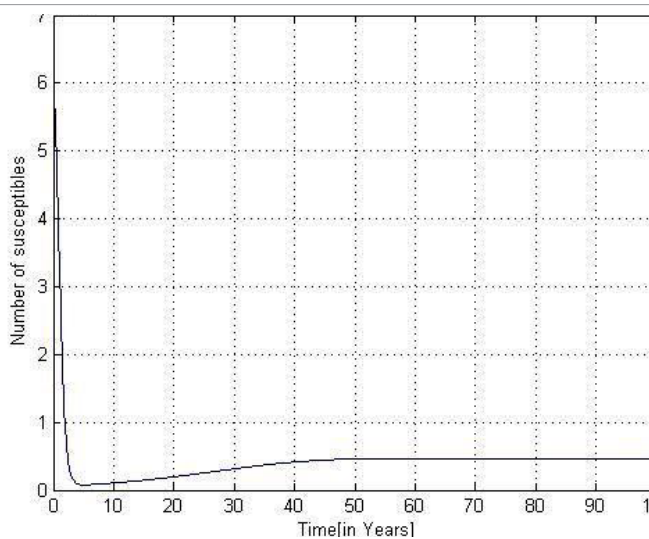


Figure 5: Function  $t \rightarrow \int_0^t s(t,a)da$  from Data-"C",  $R_0 > 1$ .

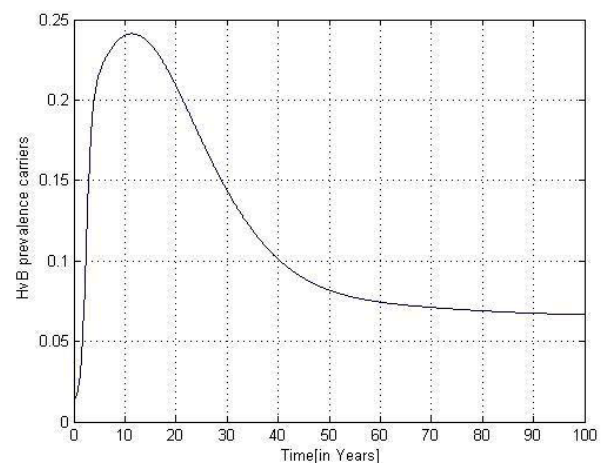
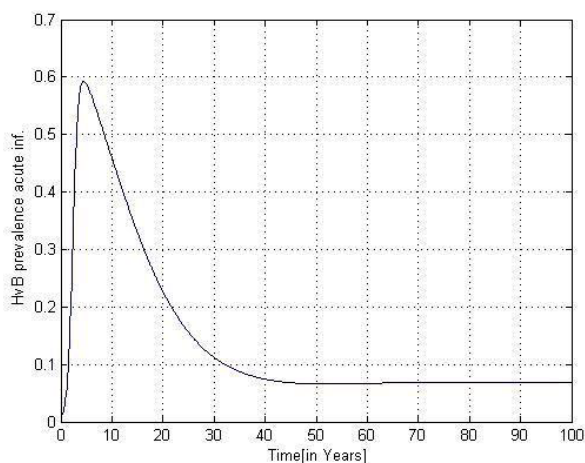


Figure 8: Prevalence of asymptomatic carriers  $E(t)$  from Data-"C",  $R_0 > 1$ .



**Figure 9:** Prevalence of acute infectious  $I(t)$  from data of Data-"C",  $R_0 > 1$ .

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