Modeling and analysis of hepatitis B and HIV co-infections

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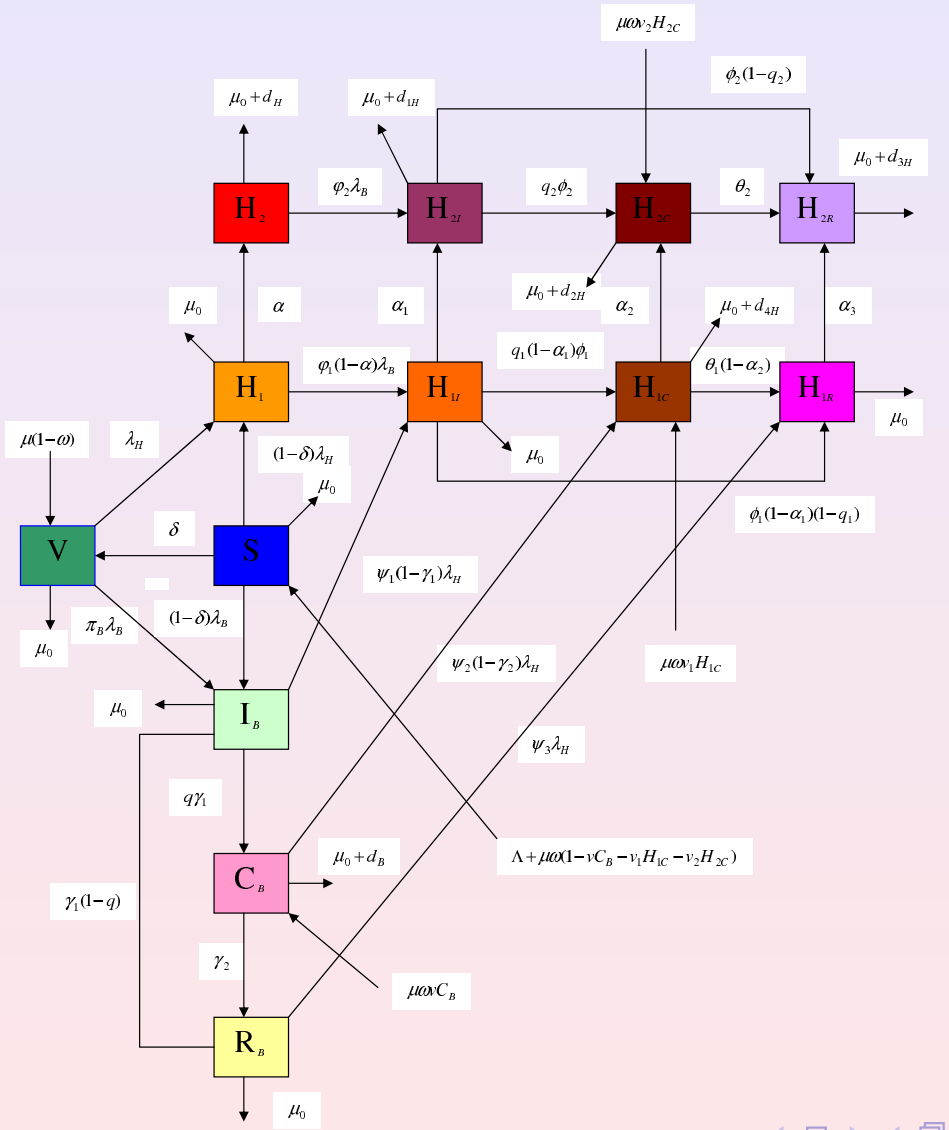

The dynamical system describes by the model is given by :

$$
\begin{cases}
\dot{S} = \Lambda + \mu\,\omega(1 - \nu\, C_B - \nu_1\, H_{1C} - \nu_2\, H_{2C}) - (1-\delta)(\lambda_H + \lambda_B)S \\
\qquad -(\delta + \mu_0)S, \\
\dot{V} = \mu(1-\omega) + \delta\, S - (\lambda_H + \pi_B\lambda_B)V - \mu_0\, V, \\
\dot{H}_1 = [V + (1-\delta)S]\lambda_H - \varphi_1(1-\alpha)\lambda_B\, H_1 - (\mu_0 + \alpha)H_1, \\
\dot{H}_2 = \alpha H_1 - \varphi_2\lambda_B H_2 - (\mu_0 + d_H)H_2, \\
\dot{H}_{1I} = \varphi_1(1-\alpha)\lambda_B H_1 + \psi_1(1-\gamma_1)\lambda_H I_B - [\mu_0 + \phi_1(1-\alpha_1)]H_{1I}, \\
\dot{H}_{2I} = \varphi_2\lambda_B H_2 + \alpha_1 H_{1I} - (\mu_0 + d_{1H} + \phi_2)H_{2I}, \\
\dot{H}_{1C} = \mu\omega\nu_1 H_{1C} + q_1\phi_1(1-\alpha_1)H_{1I} \\
+\psi_2(1-\gamma_2)\lambda_H C_B - [\mu_0 + d_{4H} + \alpha_2 + \theta_1(1-\alpha_2)]H_{1C},
\end{cases}
$$

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$$
\begin{cases}
\dot{H}_{2C} = \mu\,\omega\,\nu_2\,H_{2C} + q_2\,\phi_2\,H_{2I} + \alpha_2\,H_{1C} - (\mu_0 + d_{2H} + \theta_2)H_{2C}, \\
\dot{H}_{1R} = \phi_1(1-\alpha_1)(1-q_1)H_{1I} + \theta_1(1-\alpha_2)H_{1C} + \psi_3\,\lambda_H\,R_B \\
\qquad -(\mu_0 + \alpha_3)H_{1R}, \\
\dot{H}_{2R} = \phi_2(1-q_2)H_{2I} + \theta_2 H_{2C} + \alpha_3 H_{1R} - (\mu_0 + d_{3H})H_{2R}, \\
\dot{I}_B = [\pi_B V + (1-\delta)S]\lambda_B - \psi_1(1-\gamma_1)\lambda_H I_B - (\mu_0 + \gamma_1)I_B, \\
\dot{C}_B = \mu\omega v C_B + q\gamma_1 I_B - \psi_2(1-\gamma_2)\lambda_H C_B - (\mu_0 + d_B + \gamma_2)C_B, \\
\dot{R}_B = \gamma_1(1-q)I_B + \gamma_2\,C_B - \psi_3\,\lambda_H\,R_B - \mu_0\,R_B,
\end{cases}
$$

$$
\lambda_B = \beta_B \frac{I_B + \eta_1(H_{1I} + \eta_{1h}H_{2I}) + \eta(C_B + \eta_{1c}H_{1C} + \eta_{2c}H_{2C})}{N}
$$

$$\begin{aligned}\lambda_H &= \beta_H \frac{H_1 + \varepsilon H_2 + \varepsilon_1 (H_{1I} + \varepsilon_{1h} H_{2I})}{N}, \\ &+ \beta_H \frac{\varepsilon_2 (H_{1C} + \varepsilon_{2h} H_{2C}) + \varepsilon_3 (H_{1R} + \varepsilon_{3h} H_{2R})}{N}\end{aligned}$$

where β_H is the effective contact rate for HIV infection (contact sufficient to result in HIV infection). Further, the modification parameters ε, ε_1, ε_{1h}, ε_2, ε_{2h}, ε_3 and ε_{3h} account for the relative infectiousness of individuals in the H_2, H_{1I}, H_{2I}, H_{1C}, H_{2C}, H_{1R} and H_{2R} classes.

The variables and parameters of the model

Λ is the recruitment rate of susceptible individuals into the population; π_B is the rate of waning vaccine-induced immunity; φ_1 and φ_2 are the probabilities of acquiring HBV infection of individuals in the H_1 and H_2 classes, respectively; ψ_1, ψ_2 and ψ_3 are respectively, the probabilities of acquiring HIV of individuals in the I_B, C_B and R_B classes; μ is the birth rate in the population; ω is the proportion of births without successful vaccination; ν, ν_1 and ν_2 are proportions of perinatally infected born by carriers mothers in the C_B, H_{1C} and H_{2C} classes, respectively;

The variables and parameters of the model

δ is the vaccination rate; γ_1, ϕ_1 and ϕ_2 are respectively, the rates moving from I_B, H_{1I} and H_{2I} classes to C_B, H_{1C} and H_{2C} classes; q, q_1, and q_2 are respectively, the average probability that an individual in the I_B, H_{1I} and H_{2I} classes fail to clear an acute state and develops a carrier state (C_B, H_{1C} and H_{2C}), respectively; γ_2, θ_1 and θ_2 are respectively, rates moving from C_B, H_{1C} and H_{2C} classes to R_B, H_{1R} and H_{2R} classes; d_B is the HBV induced death rate of individuals in the HBV chronic carriers class C_B; d_H, d_{1H}, d_{2H}, d_{3H} and d_{4H} are respectively, the HIV induced death rate of individuals in the H_2, H_{1I}, H_{2I}, H_{1C}, H_{2C} and H_{2R} classes.

We show that all feasible solutions of the system enters the region Ω given by :

$$\left\{ \begin{array}{l} (S, V, H_1, H_2, H_{1I}, H_{2I}, H_{1C}, H_{2C}, H_{1R}, H_{2R}, I_B, C_B, R_B) \in R^{13}_{\geq 0}, \\ \backslash N(t) \leq \dfrac{\Lambda + \mu}{\mu_0} \end{array} \right\}. \tag{1}$$

Theorem : The non-negative orthant $\mathbb{R}^{13}_{+}$ is positively invariant for the system.

The DFE given by

$$Q_0 = \left(\frac{\Lambda + \mu\omega}{\mu_0 + \delta}, \frac{\delta(\mu + \Lambda) + \mu\mu_0(1-\omega)}{\mu_0(\mu_0 + \delta)}, 0, \cdots, 0 \right).$$

The associated reproduction number for the HBV-HIV model denoted by $\mathcal{R}_0$ is given by

$$\mathcal{R}_0 = \max\{\mathcal{R}_0^B, \mathcal{R}_B^H\}, \tag{2}$$

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$$\mathcal{R}_0^B = \frac{\beta_B(A+\eta q\gamma_1)[\pi_B[\delta(\mu+\Lambda)+\mu\mu_0(1-\omega)]+\mu_0(1-\delta)(\Lambda+\mu\omega)]}{A(\mu_0+\delta)(\mu_0+\gamma_1)(\Lambda+\mu)},$$

with $A = \mu_0 + d_B + \gamma_2 - \mu\omega v$.

$$\mathcal{R}_0^H = \frac{\beta_H(\mu_0+d_H+\varepsilon_2\alpha)}{(\mu_0+\alpha)(\mu_0+d_H)} \quad \text{and} \quad \mathcal{R}_B^H = \mathcal{R}_0^H\left(1-\frac{\mu_0\delta(\Lambda+\mu\omega)}{(\Lambda+\mu)(\mu_0+\delta)}\right),$$

Theorem : The DFE Q_0 is LAS if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

The system has four possible nonnegative boundary equilibria in Ω: the disease-free equilibrium (DFE) Q_0, the HBV-only (HIV-free) equilibrium Q_B^*, the HIV-only (HBV-free) equilibrium Q_H^* and the HBV/HIV equilibrium Q_B^H. We have

$$S_H^* = \frac{\alpha\Lambda\lambda_H^*}{(\mu_0+\alpha)(\mu_0+d_H)(\mu_0+\lambda_H^*)},$$

$$\lambda_H^* = \frac{(\mu_0+\alpha)(\mu_0+d_H)(\mathcal{R}_0^H-1)}{\mu_0+\alpha+d_H}.$$

$$I_B^* = \frac{q\gamma_1(\Lambda+\mu)\lambda_B^*}{\beta_B\mu_0(A+\eta q\gamma_1)+d_B q\gamma_1\lambda_B^*}$$

$$S_B^* = \frac{\Lambda+\mu\,\omega\left(1-\dfrac{q\gamma_1\nu(\Lambda+\mu)\lambda_B^*}{\beta_B\mu_0(A+\eta q\gamma_1)+d_B\,q\gamma_1\lambda_B^*}\right)}{(1-\delta)\lambda_B^*+\delta+\mu_0}$$

$$V_B^* = \frac{\mu(1-\omega)}{\pi_B\lambda_B^*+\mu_0}+\frac{\delta\left[\Lambda+\mu\omega\left(1-\dfrac{q\gamma_1 v(\Lambda+\mu)\lambda_B^*}{\beta_B\mu_0(A+\eta q\gamma_1)+d_B q\gamma_1\lambda_B^*}\right)\right]}{[(1-\delta)\lambda_B^*+\delta+\mu_0][\pi_B\lambda_B^*+\mu_0]}$$

where $\lambda_B^* = \dfrac{\beta_B(I_B^* + \eta C_B^*)}{N_B^*}$ (with $N_B^* = S_B^* + V_B^* + I_B^* + C_B^* + R_B^*$) is the force of infection at the steady state Q_B^* which satisfies the following quadratic equation:

$$b_2(\lambda_B^*)^2 + b_1\lambda_B^* + b_0 = 0,$$

with

$$b_2 = (1-\delta)(\Lambda+\mu)[\pi_B[A(\mu_0+\gamma_1) + d_B q\gamma_1] + \mu\,\omega\,\nu\,q\gamma_1(1-\delta)]$$

$$b_0 = A\mu_0(\mu_0+\gamma_1)(\mu_0+\delta)(\Lambda+\mu)(1-\mathcal{R}_0^B)$$

$$
\begin{aligned}
b_1 \quad &= -\pi_B\,\mu(1-\omega)[\beta_B\,\mu_0(1-\delta)(A+\eta\,q\,\gamma_1)+d_B\,q\,\gamma_1(\mu_0+\delta)] \\
&-d_B\,q\,\gamma_1\pi_B\delta(\Lambda+\mu\omega)+\pi_B\,\delta\,\mu\,\nu\,q\gamma_1(\Lambda+\mu) \\
&-\pi_B\beta_B\mu_0(1-\delta)(\Lambda+\mu\omega)(A+\eta q\gamma_1)+\mu_0\,d_B\,q\,\gamma_1(1-\delta)(\Lambda+\mu\omega) \\
&+\mu\,\omega\,\nu\,q\gamma_1(1-\delta)(\mu_0+\delta)(\Lambda+\mu)+A\,\pi_B(\mu_0+\gamma_1)(\Lambda+\mu)(\mu_0+\delta) \\
&+A\,\mu_0(\mu_0+\gamma_1)(\Lambda+\mu)(1-\delta).
\end{aligned}
$$

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$$\mathcal{R}_0^B(Q_H^*) = \frac{\beta_B(1-\delta)S_H^*[A+\psi_2(1-\gamma_2)\lambda_H^*+\eta q\gamma_1]}{N_H^*[\psi_1(1-\gamma_1)\lambda_H^*+\mu_0+\gamma_1][A+\psi_2(1-\gamma_2)\lambda_H^*]}$$

$$\mathcal{R}_B^H(Q_B^*) = \frac{\beta_H[\pi_B V_B+(1-\delta)S_B][\varphi_2\lambda_B^*+\mu_0+d_H+\varepsilon\alpha]}{N_B^*[\varphi_1(1-\alpha)\lambda_B^*+\mu_0+\alpha](\varphi_2\lambda_B^*+\mu_0+d_H)}$$

This formalism permits the derivation of a threshold condition for coexistence, now equivalent to a threshold condition for HBV endemicity in a population where HIV is at equilibrium, $\mathcal{R}_0^B(Q_H^*) = 1$: only HIV persists for $\mathcal{R}_0^B(Q_H^*) < 1$, while for $\mathcal{R}_0^B(Q_H^*) > 1$ HBV can invade a population where HIV state are fixed, that is, to say coexistence is possible.

Simulation datas | GRIMCAPE and UMMISCO

To illustrate the theoretical results contained in this paper, the model is simulated using the following set of parameters:
$\Lambda = 500$,$\pi_B = 0.1$, $\delta = 0.75$, $\eta = 0.16$, $\eta_1 = 1.1$, $\eta_{1h} = 1.2$, $\eta_{1c} = 1.3$, $\eta_{2c} = 1.4$, $\varepsilon = 1.1$, $\varepsilon_1 = 1.2$, $\varepsilon_{1h} = 1.25$, $\varepsilon_2 = 1.5$, $\varepsilon_{2h} = 1.55$, $\varepsilon_3 = 1.3$, $\varepsilon_{3h} = 1.35$, $\varphi_1 = 0.3$, $\varphi_2 = 0.5$, $\psi_1 = 0.4$, $\psi_2 = 0.5$, $\psi_3 = 0.1$, $\mu_0 = 0.019$, $\mu = 0.012$, $\omega = 0.35$, $\gamma_1 = 4$, $\gamma_2 = 0.025$, $v = 0.11$, $v_1 = 0.12$, $v_2 = 0.13$, $\phi_1 = 2$, $\phi_2 = 3$, $q = 0.885$, $q_1 = 0.9$, $q_2 = 0.95$, $\theta_1 = 0.015$, $\theta_2 = 0.01$, $\alpha = 1/33$, $\alpha_1 = 0.04$, $\alpha_2 = 0.05$, $\alpha_3 = 0.06$, $d_H = 0.01$, $d_{1H} = 0.03$, $d_{2H} = 0.05$, $d_{3H} = 0.02$, $d_{4H} = 0.06$ and $d_B = 0.002$.

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The figures 1, 2, 3 and 4 examine changes in infection levels over time. It plots the time series of λ_B/β_B (fraction of acute and chronic HBV infection) and λ_H/β_H (fraction of HIV infection). The top two figures are for the case when $\mathcal{R}_B^H = 1.2908 > 1$ ($\beta_H = 0.03$), $\mathcal{R}_0^B(Q_H^*) = 0.8545 < 1$ ($\beta_B = 0.4$) in (a) and $\mathcal{R}_0^B(Q_H^*) = 2.5634 > 1$ ($\beta_B = 1.2$) in (b). It demonstrates that for $\mathcal{R}_B^H > 1$, the HBV free equilibrium Q_H^* is stable when $\mathcal{R}_0^B(Q_H^*) < 1$ and HIV and HBV coexist when $\mathcal{R}_0^B(Q_H^*) > 1$. The bottom two figures are for the case when $\mathcal{R}_0^B = 1.4596 > 1$ ($\beta_B = 1.2$), $\mathcal{R}_H^B(Q_B^*) = 0.4247 < 1$ ($\beta_H = 0.02$) in (c) and $\mathcal{R}_H^B(Q_B^*) = 1.0619 > 1$ ($\beta_H = 0.1$) in (d). It illustrates that for $\mathcal{R}_0^B > 1$, the HIV free equilibrium Q_B^* only persists when $\mathcal{R}_H^B(Q_B^*) > 1$, while when $\mathcal{R}_H^B(Q_B^*) > 1$, HIV and HBV persist. Also, it clearly appears that the increased of $\mathcal{R}_H^B(Q_B^*)$ generated damped oscillations in the system.

SIMULATIONS | CARI presentation

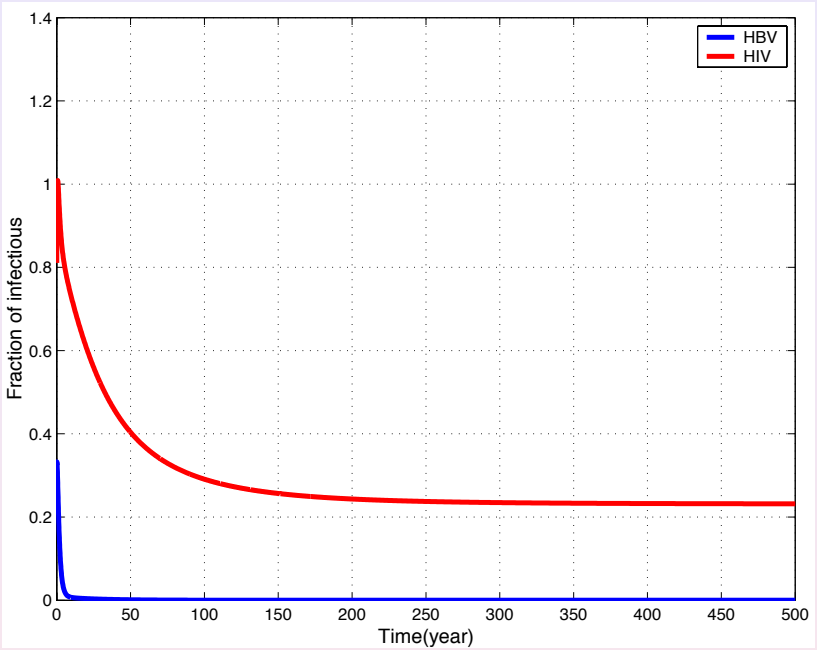

Figure: (a) Time plots of prevalence of HIV and HBV. The curves of HIV infectious (red line) and HBV infectious (bleu line). The top two figures are for the case when $\mathcal{R}_B^H = 1.2908 > 1$ ($\beta_H = 0.03$), $\mathcal{R}_0^B(Q_H^*) = 0.8545 < 1$ ($\beta_B = 0.4$)

SIMULATIONS | CARI presentation

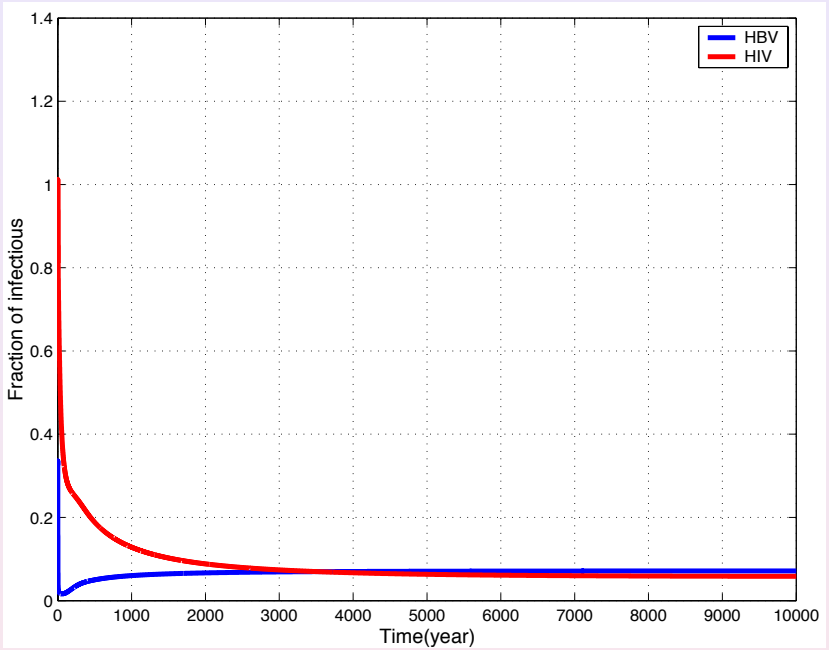

Figure: (b) Time plots of prevalence of HIV and HBV. The curves of HIV infectious (red line) and HBV infectious (bleu line).
$\mathcal{R}_0^B(Q_H^*) = 2.5634 > 1$ ($\beta_B = 1.2$)

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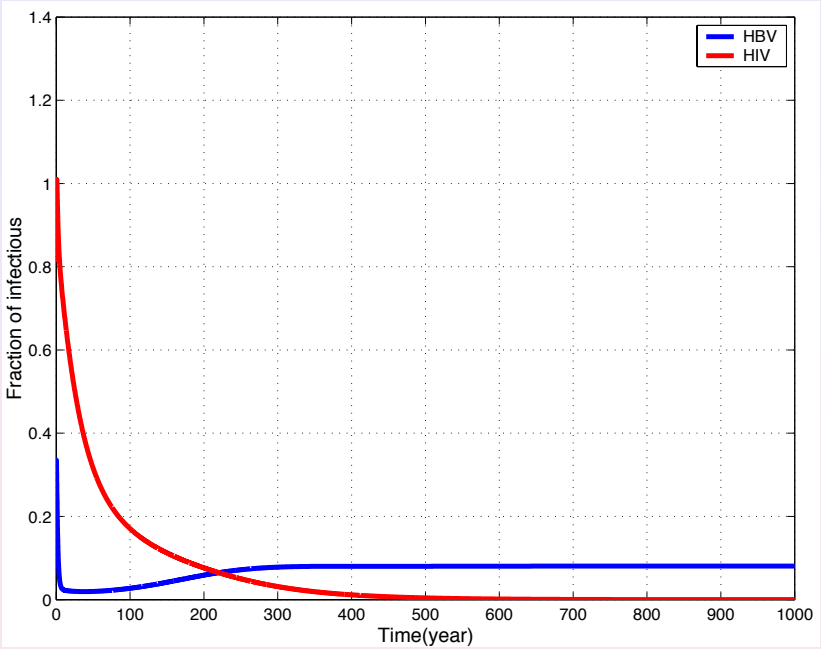

Figure: (c) Time plots of prevalence of HIV and HBV. The curves of HIV infectious (red line) and HBV infectious (bleu line).
$\mathcal{R}_0^B = 1.4596 > 1$ ($\beta_B = 1.2$), $\mathcal{R}_H^B(Q_B^*) = 0.4247 < 1$ ($\beta_H = 0.02$).

SIMULATIONS | CARI presentation

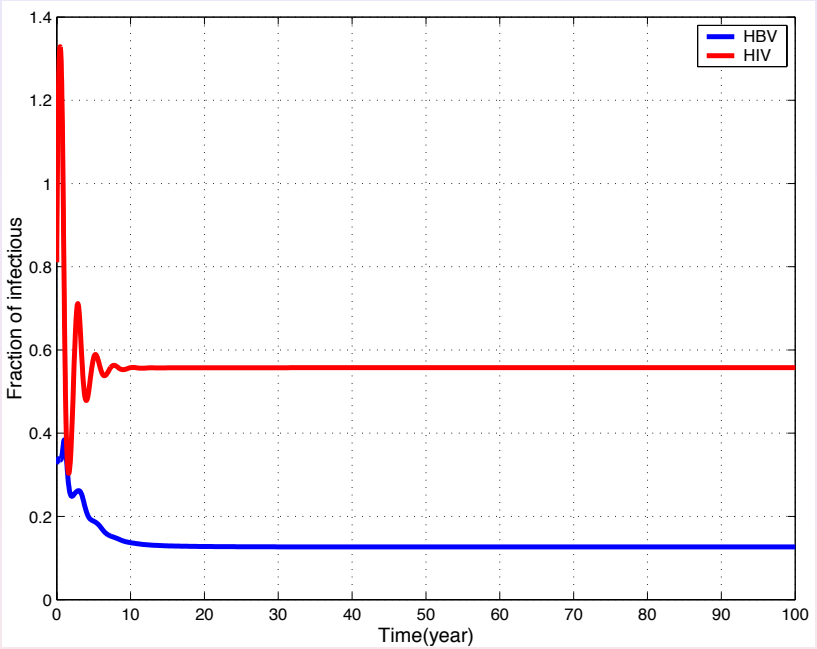

Figure: (d) Time plots of prevalence of HIV and HBV. The curves of HIV infectious (red line) and HBV infectious (bleu line).
$\mathcal{R}_H^B(Q_B^*) = 1.0619 > 1$ ($\beta_H = 0.1$)

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