Applied Mathematical Sciences, Vol. 2, 2008, no. 36, 1749 - 1760

An Avian Influenza Mathematical Model

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Abstract

The present mathematical model deals with the dynamics of human infection by avian influenza both in birds and in humans. Stability analysis is carried out and the behaviour of the disease is illustrated by simulation with different parameters values

Mathematics Subject Classification: 74S05, 74S20, 74S30, 74H15

Keywords: Avian influenza , mathematical model, stability analysis, simulation

1 Introduction

Millions of people are affected each year by seasonal outbreaks of influenza (also known as flu) which kills about 500 000 individuals every year [12]. Human influenza viruses are classified into three serotypes: A, B and C. Only influenza A viruses are known to infect and multiply in avian species. Studies have shown that direct contact with diseased poultry was the source of infection and found no evidence of person-to-person spread of the virus. During the last decade, various mathematical models have been used for infectious diseases in general and for influenza in particular [1,7,8,5,10]. In the case of avian influenza, deterministic models were used for comparing interventions aimed at preventing and controlling influenza pandemics [7,2], and stochastic models were proposed to model and predict the worldwide spread of pandemic influenza [3.4].

In this paper, in order to study the dynamics of human infection by avian influenza, we present a mathematical model that allows for stability analysis and simulation with different parameters values. Parameters such as the average number of adequate contacts of a human susceptible with infected birds in determining the incidence of the disease are seen as important tools for preventive strategies.

2 Formulation of the model and stability analysis

2.1 Parameters of the model

Let N and N_0 denote the human and bird population size. In this model death is proportional to the populations size with rate constant $\mu$and we assume a constant Λ due to births and immigrations. So $\frac{dN}{dt} = \Lambda - \mu N$ whereas for bird population we suppose that N_0 is constant .
The human population (respectively bird population) of size N (resp. N_0) is formed of Susceptibles S, of Infective I and of Removed R (resp. S_0 and I_0).

$\beta S I_0/N_0$ is the human incidence i.e. the rate at which susceptibles become infectious. If the time unit is days, then the incidence is the number of new infection per day. The daily contact rate β is the average number of adequate contacts of a human susceptible with infected birds per day and I_0/N is the infectious fraction of the population. Time units of weeks, months or years could also be used.
Similarly $\beta_0 S_0 I_0/N_0$ is the bird incidence and β_0 is the average number of adequate contacts of a bird susceptible with other birds per day. The man life span is taken equal to 25 000 days (68.5 years), and the one of the bird is about 2500 days. Definitions of the other basis parameters are given in Table 1

Name of the parameter	Notation
births and immigrations rate constant	Λ
Effective contact rate, bird to human	β
Effective contact rate, bird to bird	β_0
Human life span	$\frac{1}{\mu}$
Bird life span	$\frac{1}{\mu_0}$
loss of immunity rate constant	δ
disease-related death rate constant	α
recovery rate constant	γ
Host infection duration	$\frac{1}{\mu+\gamma}$

Table 1: definitions of basis parameters used in simulations

2.2 Equations of the model

A schematic representation of the model is shown in Figure 1. In human we consider SIRS compartmental model that is to say that human susceptible individuals become infectious then removed with temporary immunity after recovery from infection and susceptible when again immunity fades away, in

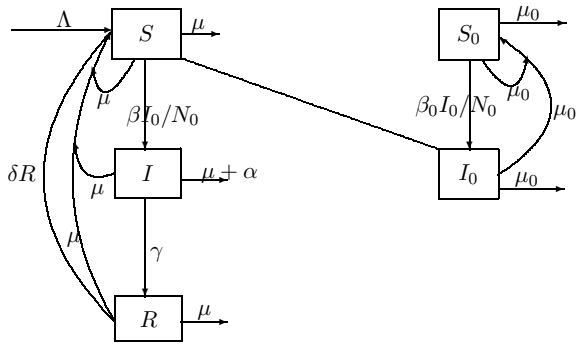

Figure 1: schematic diagram : compartments of human and bird populations

bird population we consider SI compartmental model.

The model is governed by the following equations:
Human population

$$\begin{cases} \frac{dS}{dt} = & \Lambda - (\mu + \beta I_0)/N_0)S + \delta R \\ \frac{dI}{dt} = & \beta I_0/N_0 S - (\mu + \gamma + \alpha)I \\ \frac{dR}{dt} = & \gamma I - (\mu + \delta)R \\ \frac{dN}{dt} = & \Lambda - \mu N - \alpha I \end{cases}$$

Bird population

$$\begin{cases} \frac{dS_0}{dt} = & \mu_0 N_0 - (\mu_0 + \beta_0 I_0/N_0)S_0 \\ \frac{dI_0}{dt} = & (\beta_0 I_0/N_0)S_0 - \mu_0 I_0 \end{cases}$$

For this system the first orthant in the $SIRS_0I_0N$ space is positively invariant. Because $N'(t) < 0$ for $N > \Lambda/\mu$, all paths in the first orthant approach, enter or stay inside the subset Ω given by:

$$\Omega = \{(S, I, R, S_0, I_0, N)/0 \leq S_0; 0 \leq I_0; 0 \leq I; 0 \leq S; S + I + R = N \leq \Lambda/\mu; S_0 + I_0 = N_0\}.$$

The continuity of right side of the previous system and its derivatives implies that unique solutions exit on maximal interval. Since solutions approach, enter or stay in Ω they are eventually bounded and hence exist for $t \geq 0$. Therefore the model is mathematically and epidemiologically well posed.
Introducing the proportions :

$$s = \frac{S}{\Lambda/\mu}, i = \frac{I}{\Lambda/\mu}, r = \frac{R}{\Lambda/\mu}, s_0 = \frac{S_0}{N_0}, i_0 = \frac{I_0}{N_0}$$

and with the conditions $S + I + R = N$ and $S_0 + I_0 = N_0$, we get :
$s + i + r = n$ and $s_0 = 1 - i_0$

the two previous systems become:

$$\begin{cases} \frac{ds}{dt} = & \mu - (\mu + \beta i_0)s + \delta r \\ \frac{di}{dt} = & \beta i_0 s - (\mu + \gamma + \alpha)i \\ \frac{dr}{dt} = & \gamma i - (\mu + \delta)r \\ \frac{di_0}{dt} = & \beta_0 i_0(1 - i_0) - \mu_0 i_0 \end{cases}$$

in the set $\Omega' = \{(s, i, r, i_0)/0 \leq i; 0 \leq s, 0 \leq r, s + i + r \leq n \leq 1; 0 \leq i_0 \leq 1\}$.

2.2.1 Equilibrium points

Theorem 2.1.
Let $\tilde{R} = \frac{\beta_0}{\mu_0}$. The previous system admits two equilibrium points :

- *if $\tilde{R} \leq 1$ the trivial state $E_1(1, 0, 0, 0)$ is the unique equilibrium.*
- *if $\tilde{R} > 1$ then an endemic equilibrium $E_2(\overline{s}, \overline{i}, \overline{r}, \overline{i_0})$ will also be in Ω'. were: $\overline{s} = \frac{M\tilde{R}(\mu+\delta)}{\beta(\tilde{R}-1)\left(M+\frac{\delta}{\mu}(\mu+\alpha)\right)+M\tilde{R}(\mu+\delta)}$ $\overline{i} = \frac{\beta(\mu+\delta)(\tilde{R}-1)}{\beta(\tilde{R}-1)\left(M+\frac{\delta}{\mu}(\mu+\alpha)\right)+M\tilde{R}(\mu+\delta)}$, $\overline{r} = \frac{\beta\gamma(\tilde{R}-1)}{\beta(\tilde{R}-1)\left(M+\frac{\delta}{\mu}(\mu+\alpha)\right)+M\tilde{R}(\mu+\delta)}$ and $\overline{i_0} = \frac{\mu_0}{\beta_0}(\tilde{R} - 1)$,*

Proof :
the equilibrium points satisfy the following relations:

$$\begin{aligned} \mu - (\mu + \beta i_0)s + \delta(n - i - s) &= 0 \quad (1) \\ \beta i_0 s - (\mu + \gamma + \alpha)I &= 0 \quad (2) \\ \gamma i - (\mu + \delta)r &= 0 \quad (3) \\ \beta_0 i_0(1 - i_0) - \mu_0 i_0 &= 0 \quad (4) \end{aligned}$$

From the equation (4) we have: $\beta_0 i_0(1 - i_0) - \mu_0 i_0 = 0$
$\Longrightarrow i_0 = 0$ or $\beta_0 i = \beta_0 - \mu_0)$
$\Longrightarrow i_0 = 0$ or $i_0 = \frac{\mu_0}{\beta_0}(R - 1)$ where $R = \frac{\beta_0}{\mu_0}$
From the equation (3) we have: $r = \frac{\gamma}{\mu + \delta} i$
So from the equation (1) we have: $\mu - \mu s - \beta i_0 s + \delta \frac{\gamma}{\mu + \delta} i = 0$
on the other hand $\beta i_0 s = (\mu + \gamma + \alpha)i$
then $\mu - \mu s - (\mu + \gamma + \alpha)i + \frac{\delta\gamma}{\mu + \delta} i = 0$
$\Longrightarrow \mu s = \mu - (\mu + \gamma + \alpha)i + \frac{\delta\gamma}{\mu + \delta} i$
$\Longrightarrow s = 1 - \frac{1}{\mu}\left((\mu + \gamma + \alpha) - \frac{\delta\gamma}{\mu + \delta}\right) i$
Or from the equation (2) we have: $\beta i_0 s - (\mu + \gamma + \alpha)i = 0$ so

$\beta \times \frac{\mu_0}{\beta_0}(R-1) \times \left[1 - \frac{1}{\mu}\left((\mu+\gamma+\alpha) - \frac{\delta\gamma}{\mu+\delta}\right) i\right] - (\mu+\gamma+\alpha)i = 0$

i.e $\beta \times \frac{\mu_0}{\beta_0}(R-1) \times \left[1 - \frac{1}{\mu}\left(M - \frac{\delta\gamma}{\mu+\delta})\right) i\right] - Mi = 0$

were $M = \mu+\gamma+\alpha$

thus $\beta \times \mu_0(R-1) \times \left[1 - \frac{1}{\mu}\left(M - \frac{\delta\gamma}{\mu+\delta})\right) i\right] - M\beta_0 i = 0$

$\Longrightarrow \beta \times \mu_0(R-1) \times \left[1 - \frac{1}{\mu(\mu+\delta)}\left(\mu M + \delta M - \delta\gamma\right) i\right] - M\beta_0 i = 0$

$\Longrightarrow \beta \times \mu_0(R-1) \times \left[1 - \frac{1}{\mu(\mu+\delta)}\left(\mu M + \delta(\mu+\alpha\gamma) - \delta\gamma\right) i\right] - M\beta_0 i = 0$

$\Longrightarrow \beta \times \mu_0(R-1) \times \left[1 - \frac{1}{\mu(\mu+\delta)}\left(\mu M + \delta(\mu+\alpha)\right) i\right] - M\beta_0 i = 0$

$\Longrightarrow \beta\mu_0(R-1) - \frac{\beta\mu_0(R-1)}{\mu+\delta}\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) i - M\beta_0 i = 0$

$\Longrightarrow \beta\mu_0(R-1) - \left[\frac{\beta\mu_0(R-1)}{\mu+\delta}\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + M\beta_0\right] i = 0$

$\Longrightarrow \beta\mu_0(\mu+\delta)(R-1) - \left[\beta\mu_0(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + M\beta_0(\mu+\delta)\right] i = 0$

$\Longrightarrow \beta\mu_0(\mu+\delta)(R-1) - \left[\beta\mu_0(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + M\mu_0 R(\mu+\delta)\right] i = 0$

(because $\beta_0 = R\mu_o$) So

$$i = \frac{\beta(\mu+\delta)(R-1)}{\beta(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + MR(\mu+\delta)}$$

or we have : $s = 1 - \frac{1}{\mu+\delta}\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) i$

then :$s = 1 - \frac{1}{\mu+\delta}\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) \frac{\beta(\mu+\delta)(R-1)}{\beta(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + MR(\mu+\delta)}$

$$\Longrightarrow s = \frac{\beta(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + MR(\mu+\delta) - \beta(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right)}{\beta(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + MR(\mu+\delta)}$$

So

$$s = \frac{MR(\mu+\delta)}{\beta(R-1)\left(M + \frac{\delta}{\mu}(\mu+\alpha)\right) + MR(\mu+\delta)}$$

Then we obtain two equilibrium points:
i) the first $E_1 = (1, 0, 0, 0)$ is trivial in the sense that all individual are healthy and stay healthy for all time.

ii) The second point is: $E_2(\overline{s}, \overline{i}, \overline{r}, \overline{i_0})$ were

$$\overline{s} = \frac{MR(\mu+\delta)}{\beta(R-1)\left(M+\frac{\delta}{\mu}(\mu+\alpha)\right)+MR(\mu+\delta)}$$

$$\overline{i} = \frac{\beta(\mu+\delta)(R-1)}{\beta(R-1)\left(M+\frac{\delta}{\mu}(\mu+\alpha)\right)+MR(\mu+\delta)},$$

$$\overline{r} = \frac{\beta\gamma(R-1)}{\beta(R-1)\left(M+\frac{\delta}{\mu}(\mu+\alpha)\right)+MR(\mu+\delta)}$$

$$\text{and} \quad \overline{i_0} = \frac{\mu_0}{\beta_0}(R-1),$$

corresponds to the endemic state i.e the case where the disease persists in the two populations.

2.2.2 stability

Theorem 2.2.
i) *For* $\tilde{R} \leq 1$ *the state* E_1 *is globally asymptotically stable (ie* $\lim_{t\to\infty} i(t) = 0$*).*
ii) *For* $\tilde{R} > 1$ *the state* E_2 *is locally asymptotically stable.*

Proof :

$$\begin{array}{llll}
\frac{df_1}{ds} = -\mu - \beta i_0 \ ; & \frac{df_1}{di} = 0 \ ; & \frac{df_1}{dr} = \delta \ ; & \frac{df_1}{di_0} = -\beta s \ . \\
\frac{df_2}{ds} = \beta i_0 \ ; & \frac{df_2}{di} = -M \ ; & \frac{df_2}{dr} = 0 \ ; & \frac{df_2}{di_0} = \beta s \ . \\
\frac{df_3}{ds} = 0 \ ; & \frac{df_3}{di} = \gamma \ ; & \frac{df_3}{dr} = -(\mu_+\delta) \ ; & \frac{df_3}{di_0} = 0 \ . \\
\frac{df_4}{ds} = 0 \ ; & \frac{df_4}{di} = 0 \ ; & \frac{df_4}{dr} = 0 \ ; & \frac{df_4}{di_0} = -2\beta_0 i_0 + \beta_0 - \mu_0 \ .
\end{array}$$

i) For E_1 the matrix of linearization (Jacobian matrix) is giving by :

$$\mathcal{J}_{E_1} = \begin{pmatrix} -\mu & 0 & -\delta & -\beta \\ 0 & -M & 0 & \beta \\ 0 & \gamma & -(\mu+\delta) & 0 \\ 0 & 0 & 0 & \beta_0 - \mu_0 \end{pmatrix}$$

Then the characteristic polynomial of $\mathcal{J}_{E_1}$ is given by :

$$\begin{aligned} P(\lambda) &= (\beta_0 - \mu_0 - \lambda)(-\mu - \lambda)(-M - \lambda)(-(\mu+\gamma) - \lambda) \\ &= \mu_0(R - 1 - \lambda)(-\mu - \lambda)(-M - \lambda)(-(\mu+\gamma) - \lambda) \end{aligned}$$

Thus the eigenvalues of matrix $\mathcal{J}_{E_1}$ are :
$\lambda_1 = R-1$ $\lambda_2 = -\mu$, $\lambda_3 = -M$ and $\lambda_4 = -(\mu+\gamma)$ So E_1 is stable if and only if the eigenvalues of the Jacobian marix have negatif teal part i.e if and only if $R < 1$ then E_1 is stable if and only if $R < 1$.
It remained to show the global stability, So we consider the following Liapunov function:
$V = i_0$ thus

$$\dot{\mathrm{V}} = -\mu_0 i_0(Ri_0 + (1-R))$$

So in Ω and for $R \leq 1$ we have : $\dot{\mathrm{V}} \leq 0$.
$\dot{\mathrm{V}} = 0$
$\Longrightarrow -\mu_0 i_0(Ri_0 + (1-R)) = 0$
$\Longrightarrow$ If $R < 1$ then $i_0 = 0$. And if $R = 1$ then $i_0 = 0$.
Thus the set $\{E_1\}$ is the largest invariant set within the set
$\{(x,y,z)/\dot{\mathrm{V}}(x,y,z) = 0\}$. So according to the invariant set theorem : every trajectory in Ω tends to E_1 as time t increases and as E_1 is locally stable then it is globally asymptotically stable
ii) the point E_2
The local stability of E_2 is governed by the matrix of linearization (Jacobian matrix) of E_2 is given by :

$$\mathcal{J}_{E_2} = \begin{pmatrix} -\mu - \beta\overline{i_0} & 0 & \delta & -\beta\overline{s} \\ \beta\overline{i_0} & -M & 0 & \beta\overline{s} \\ 0 & \gamma & -(\mu+\delta) & 0 \\ 0 & 0 & 0 & -\mu_0(R-1) \end{pmatrix}$$

Then the characteristic polynomial of $\mathcal{J}_{E_2}$ is given by:

$$\begin{aligned} P(\lambda) &= \Big(-\mu_0(R-1) - \lambda \Big)\Big[(-(\beta\overline{i_0}+\mu) - \lambda)(-M-\lambda)(-(\mu+\delta)-\lambda) + \beta\overline{i_0}\gamma\delta\Big] \\ &= \Big(\mu_0(R-1)+\lambda\Big)\Big[((\beta\overline{i_0}+\mu)+\lambda)(M+\lambda)((\mu+\delta)+\lambda) - \beta\overline{i_0}\gamma\delta\Big] \\ &= \Big(\mu_0(R-1)+\lambda\Big)\Big(\lambda^3 + A\lambda^2 + B\lambda + C\Big) \end{aligned}$$

therefore the eigenvalues of the matrix $\mathcal{J}_{E_2}$ are $-\mu_0(R-1)$ and the roots of the polynomial $q(\lambda) = \lambda^3 + A\lambda^2 + B\lambda + C$ where :
$A = M + 2\mu + \delta + \beta\overline{i_0}$,
$B = M(\mu+\delta) + (\beta\overline{i_0}+\mu)(M+\mu+\delta)$ and

$$\begin{aligned} C &= M(\mu+\delta)(\beta\overline{i_0}+\mu)-\gamma\delta\beta\overline{i_0} \\ &= (M\mu+M\delta)(\beta\overline{i_0}+\mu)-\gamma\delta\beta\overline{i_0} \\ &= M\mu(\beta\overline{i_0}+\mu)+M\delta(\beta\overline{i_0}+\mu)-\gamma\delta\beta\overline{i_0} \\ &= M\mu(\beta\overline{i_0}+\mu)+M\delta\beta\overline{i_0}+M\delta\mu-\gamma\delta\beta\overline{i_0} \\ &= M\mu(\beta\overline{i_0}+\mu)+(M-\gamma)\delta\beta\overline{i_0}+M\delta\mu \\ &= M\mu(\beta\overline{i_0}+\mu)+(\mu+\gamma)\delta\beta\overline{i_0}+M\delta\mu(\quad \text{becose}\quad M=\mu+\alpha+\gamma\ ) \end{aligned}$$

Or we have :

$$\begin{aligned} AB&=\left(M+2\mu+\delta+\beta\overline{i_0}\right).B \\ &= (M+\mu+\delta)B+(\beta\overline{i_0}+\mu)B \\ &= (M+\mu+\delta)B+\left(\beta\overline{i_0}+\mu\right)\left(M(\mu+\delta)+(\beta\overline{i_0}+\mu)(M+\mu+\delta)\right) \\ &= (M+\mu+\delta)B+M(\beta\overline{i_0}+\mu)(\mu+\delta)+(\beta\overline{i_0}+\mu)^2(M+\mu+\delta) \\ &= M(\mu+\delta)(\beta\overline{i_0}+\mu)+(M+\mu+\delta)B+\beta\overline{i_0}+\mu)^2(M+\mu+\delta) \\ &> M(\mu+\delta)(\beta\overline{i_0}+\mu)>C \end{aligned}$$

So for $R>1$ we have : $AB>C, A>0, B>0$ and $C>0$ then following **Routh-Hurwitz** conditions for the polynomial P, the state E_2 is locally asymptotically stable for $R>1$

3 Results and Discussion

In this paper, Simulation was carried out with different values of the parameters and stability analysis and values of the threshold were obtained. Illustrations are given by figures 2-5.

Figure 2 shows the endemic equilibrium ($\tilde{R}>1$) and the behaviour of the solutions associated with it.

According to different values of the effective contact rate β (birds to human), a comparison of human infectious is illustrated in Figure 3 and Figure 4.

In Figure 5, the typical behaviour of the solutions indicates that the rate of (human) susceptible, infectious and removed, as well as the avian infectious approaches, asymptotically, the trivial equilibrium ($\tilde{R}\leq 1$). The dynamics of the disease is mainly determined by the average number of adequate contacts of a human susceptible with infected birds . This parameter constitutes an

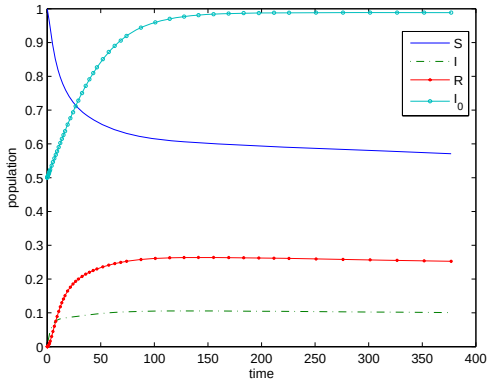

Figure 2: $\mu_0 = 0.0004,\ \beta_0 = 0.035(\tilde{R} > 1), \mu = 0.00004, \gamma = 0.25, \delta = 0.1, \alpha = 0.002$

essential key to preventive strategies against pandemics as indicated by the simulation of different patterns.

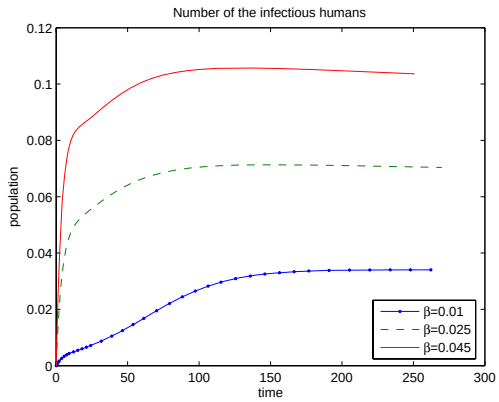

Figure 3: $\mu_0 = 0.0004,\ \beta_0 = 0.035(\tilde{R} > 1), \mu = 0.00004, \gamma = 0.25, \delta = 0.1, \alpha = 0.002$

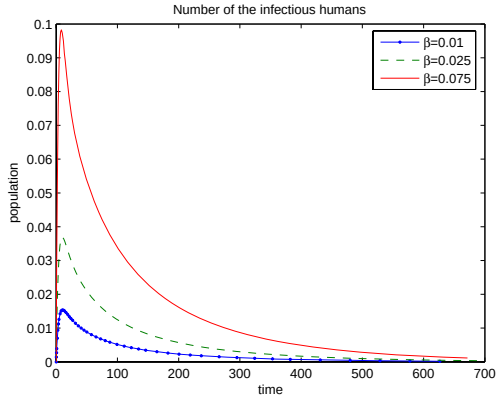

Figure 4: $\mu_0 = 0.04,\ \beta_0 = 0.035(\tilde{R} < 1)$

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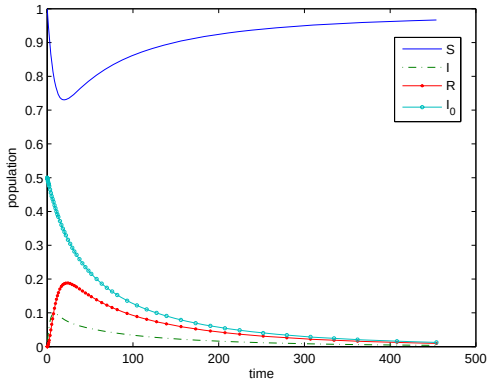

Figure 5: $\mu_0 = 0.04,\ \beta_0 = 0.035(\tilde{R} < 1), \beta = 0.075, \mu = 0.00004, \gamma = 0.25, \delta = 0.1, \alpha = 0.002$

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Received: December 17, 2007