## 1. Nowak Hepatitis B Model

In a pioneer and effective effort to model chronic HBV infection dynamics and its treatment with the reverse transcriptase inhibitor lamivudine, Nowak et al. employed the following phenomenological model

$\frac{dx}{dt} = -\beta SI - \beta_F SF$
$\frac{dy}{dt} = \beta SI + \beta_F SF - \gamma I$
$\frac{dv}{dt} = \gamma I - \alpha F$

Where x,y,z are number of uninfected (susceptible) hepatocyte, infected hepatocyte, and free virion respectively. Uninfected hepatocytes are assumed to be produced at a constant rate, $\lambda$, to maintain tissue homeostasis in the face of hepatocyte turnover, described by the linear term dx, where d is the per-capita death rate. A healthy liver maintains $\frac{\lambda}{d}$ cells as its homeostatic set-point. However, during infection, healthy (uninfected) hepatocytes are assumed to become infected at rate $\beta vx$, where $\beta$ is the mass action rate constant describing the infection process. Infected hepatocytes are killed by immune cells at rate ay and produce free virions at rate $ky$, where $k$ is the so-called burst constant. Free virions are cleared by lymphatic and other mechanisms at rate $\mu v$, where $\mu$ is constant. Here the amount of virus lost (which is $\beta vx$ if it takes exactly one virus to infect a hepatocyte) due to infection process is assumed as negligible and thus is omitted from the virus equation.

Look at the paper:http://www.pnas.org/content/pnas/93/9/4398.full.pdf

Try to analyze long term dynamics of this model. What does the reproduction number in the paper mean?