Hepatitis C Mathematical Model

Syed Ali Raza

May 18, 2012

1 Introduction

Hepatitis C is an infectious disease that really harms the liver. It is caused by the hepatitis C virus. The infection leads to adverse affects like damage of the liver and ultimately to cirrhosis, which is generally apparent after many years. In some cases, those with cirrhosis will go on to develop liver failure, liver cancer or life-threatening esophageal and gastric varices and so Hep C can be very deadly.

HCV is spread primarily by blood-to-blood contact associated with intravenous drug use, poorly sterilized medical equipment and transfusions. An estimated 130170 million people worldwide are infected with hepatitis C. (Wikipedia)

Overall, 5080 percent of people treated are cured. Those who develop cirrhosis or liver cancer may require a liver transplant. Hepatitis C is the leading cause of liver transplantation though the virus usually recurs after transplantation. No vaccine against hepatitis C is currently available.

There are two types of infections, chronic and acute. Acute infection occurs in about 15 percent of the cases, the symptoms are mild and 10-50 percent of the cases recover quickly. The other type is the chronic infection, About 80 percent of those exposed to the virus develop a chronic infection. Most experience minimal or no symptoms during the initial few decades of the infection. Hepatitis C after many years becomes the primary cause of cirrhosis and liver cancer. About 1030 percent of people develop cirrhosis over 30 years.

The hepatitis C virus (HCV) is a small, enveloped, single-stranded, positive-sense RNA virus. The primary methods of transmission in the developed world is intravenous drug use (IDU), while in the developing world the main methods are blood transfusions and unsafe medical procedures. (Wikipedia)

In our model we would be considering two modes of transport which are statistically significant. One is the transmission through intravenous drug use and the other mode is through blood transfusions. We would have separate compartments for both of these transmission modes. So the susceptible compartment can go into either Acute 1 or Acute 2 compartment depending on the mode of transmission. It depends on the infection rate of susceptibles which in turn depends on the contact rate etc.

You can either recover from the acute condition or progress to the chronic infection compartment. From the chronic compartment you can be moved to Quarantine or you could recover. If you recover you can go back to the susceptible compartment. If you are Quarantined then some fraction moves back to susceptibles and some goes to the acute infection compartment. There is a recruitment rate at which people keep getting added to the susceptible population. All compartments have a natural death rate, however Acute, Chronic and Quarantine have also their own corresponding death rates in addition to the natural death rate.

Also there are similar compartments Acute 2, Chronic 2, Quarantined 2 and Recovered 2 for the other mode of transmission too.

2 Model

Vaiables	
S(t)	Population of susceptible individuals
$A_{1,2}(t)$	Population of individuals with Acute HepC
$C_{1,2}(t)$	Population of individuals with Chronic HepC
$Q_{1,2}(t)$	Population of Quarantined individuals
$R_{1,2}(t)$	Population of Recovered individuals

Parameters	
Π	recruitment rate
μ	natural death rate
λ	infection rate of susceptibles
γ	recovery rate of quarantines
f	fraction of quarantined that become susceptible
δ_c	death rate of chronic individuals
δ_q	death rate of quarantined individuals
ε	progression rate from acute to chronic
w	rate of recovered people becoming susceptible
ψ	recovery rate of chronic individuals
α	quarantine rate of chronics
κ	rate of recovered people people becoming acute
δ_a	death rate of acute individuals
N	total population
θ_{11}	contact rate
θ_{21}	contact rate
ζ	effective contact rate with acute
η	effective contact rate with quarantined

Note: The subscripts 1 and 2 represent the two modes of transfer of HepC

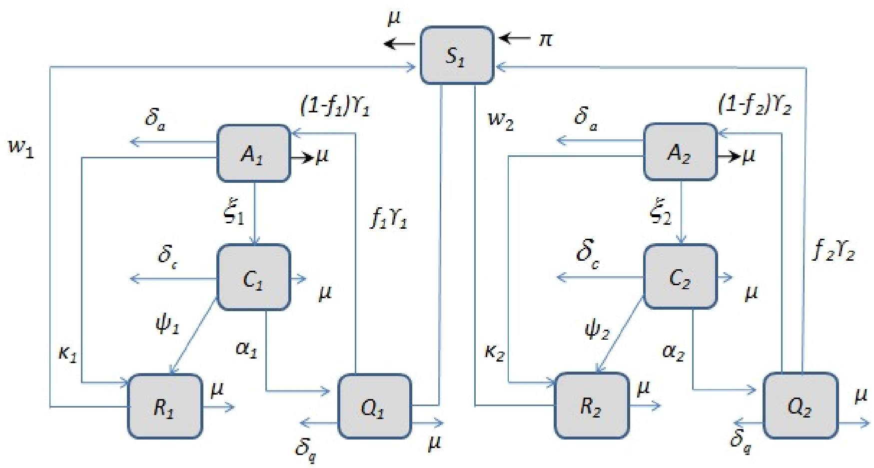


Figure 1: Model

in individuals as discussed in Question 1. The subscripts 1 and 2 also hold for parameters.

3 Positiveness of the system

All variables of our model are non negative integers for all time t¿0. Solution of our data with positive initial values will remain positive for all t¿0. Let $t_1 = sup\{t > 0; S_1 > 0, A_1 > 0, A_2 > 0, C_1 > 0, C_2 > 0, Q_1 > 0, Q_2 > 0, R_1 > 0, R_2 > 0\}$.

$$\frac{dS_1}{dt} = \pi + (\gamma_1 f_1 Q_1 + w_1 R_1 + \gamma_2 f_2 Q_2 + w_2 R_2) - (\lambda_1 + \lambda_2 + \mu)\ S_1 \geq \pi - (\lambda_1 + \lambda_2 + \mu)\ S_1(t) \tag{1}$$

which can be written as

$$\frac{d}{dt}\left\{S_1(t)\ exp\left[\mu t + \int_0^t \lambda_1(\tau) + \lambda_2(\tau) d\tau\right]\right\} \geq \pi\ exp\left[\mu t + \int_0^t \lambda_1(\tau) + \lambda_2(\tau) d\tau\right] \tag{2}$$

Hence

$$S_1(t_1)\ exp\left[\mu t_1 + \int_0^{t_1} \lambda_1(\tau) + \lambda_2(\tau) d\tau\right] - S_1(0) \geq \int_0^{t_1} \pi\ exp\left[\mu y + \int_0^{y} \lambda_1(\tau) + \lambda_2(\tau) d\tau\right] dy \tag{3}$$

so that

$$S_1(t_1) \geq S(0)exp\left[-\mu t_1 - \int_0^{t_1} \lambda_1(\tau) + \lambda_2(\tau) d\tau\right]$$
$$+ exp\left[-\mu t_1 - \int_0^{t_1} \lambda_1(\tau) + \lambda_2(\tau) d\tau\right] \int_0^{t_1} \pi \; exp\left[\mu y + \int_0^{y} \lambda_1(\tau) + \lambda_2(\tau) d\tau\right] dy > 0$$

Similar it can be shown for other variables

4 Boundedness of the system

Closed set $D = \{S_1 + A_1 + A_2 + C_1 + C_2 + Q_1 + Q_2 + R_1 + R_2 \leq \pi/\mu\}$.

Adding all equations gives:

$$\frac{dN}{dt} = \pi - \mu N - \delta_a(A_1 + A_2) - \delta_q(Q_1 + Q_2) - \delta_c(C_1 + C_2) \tag{4}$$

Since $\frac{dN}{dt} \leq \pi - \mu N$, it follows that $\frac{dN}{dt} \leq 0$, if $N \geq \pi/\mu$. So we use the standard comparison theorem (2.8) from the quarantine isolation model paper can be used to show (We have simply integrated it):

$$N(t) \leq N(0)e^{-\mu t} + \frac{\pi}{\mu}(1 - e^{-\mu t}) \tag{5}$$

So if $N(0) \leq \frac{\pi}{\mu}$ then it is always true that $N(t) \leq \frac{\pi}{\mu}$. Hence we have shown that it is bounded.

5 Steady States

5.1 Disease free Steady State

For the disease free steady state we have:

$$(S_1, A_1, A_2, C_1, C_2, Q_1, Q_2, R_1, R_2) = (\frac{\pi}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0) \tag{6}$$

I won't comment on the stability of the disease free steady state here as it wasn't asked in the exam.

5.2 Endemic Steady State

By taking the time derivatives of the variables equal to zero and solving them simultaneously we can find the endemic steady state. We would now indulge in this arduous and painful task.

$$A_1 = \frac{\alpha_1 + \psi_1 + \mu + \delta_c}{\varepsilon_1} C_1 \tag{7}$$

$$A_2 = \frac{\alpha_2 + \psi_2 + \mu + \delta_c}{\varepsilon_2} C_2 \tag{8}$$

$$A_1 = \Omega_0 C_1 \tag{9}$$

$$A_2 = \Delta_0 C_2 \tag{10}$$

$$Q_1 = \frac{\gamma_1 + \mu + \delta_q}{\alpha_1} C_1 \tag{11}$$

$$Q_2 = \frac{\gamma_2 + \mu + \delta_q}{\alpha_2} C_2 \tag{12}$$

$$Q_1 = \Omega_1 C_1 \tag{13}$$

$$Q_2 = \Delta_1 C_2 \tag{14}$$

$$R_1 = \frac{\kappa_1}{w_1 + \mu} A_1 + \frac{\psi_1}{w_1 + \mu} C_1 \tag{15}$$

$$= \frac{\kappa_1 \Omega_0}{w_1 + \mu} C_1 + \frac{\psi_1}{w_1 + \mu} C_1 \tag{16}$$

$$= \frac{\kappa_1 \Omega_0 + \psi_1}{w_1 + \mu} C_1 \tag{17}$$

$$R_1 = \Omega_2 C_1 \tag{18}$$

$$R_2 = \Delta_2 C_2 \tag{19}$$

$$S_1 = \frac{\gamma_1 (f_1 - 1)}{\lambda_1} Q_1 + \frac{\varepsilon_1 + \kappa_1 + \mu + \delta_a}{\lambda_1} A_1 \tag{20}$$

$$= \frac{\gamma_1 (f_1 - 1)\Omega_1}{\lambda_1} C_1 + \frac{\varepsilon_1 + \kappa_1 + \mu + \delta_a}{\lambda_1} \Omega_1 C_1 \tag{21}$$

$$= \frac{\gamma_1 (f_1 - 1)\Omega_1 + (\varepsilon_1 + \kappa_1 + \mu + \delta_a)\Omega_0}{\lambda_1} C_1 \tag{22}$$

$$S_1 = \Omega_3 C_1 S_1 \qquad = \Delta_3 C_2 \tag{23}$$

We already have $A_1, A_2, Q_1, Q_2, R_1, R_2, S_1$ in terms of C_1, we also want C_2, Q_2, R_2 in terms of S_1 and then subsequently in terms of C_1.

$$Q_2 = \frac{\lambda_2}{\gamma_2 (f_2 - 1)} S_1 + \frac{\varepsilon_2 + \kappa_2 - \mu + \delta_a}{\gamma_2 (1 - f_2)} A_2 \tag{24}$$

As $Q_2 = \Delta_1 C_2$ and $C_2 = \frac{A_2}{\Delta_0}$, we get $A_2 = \frac{\Delta_0}{\Delta_1} Q_2$ and we plug it above.

$$\lambda_2 S_1 + \gamma_2(1-f_2)Q_2 - (\varepsilon_2 + \kappa_2 - \mu + \delta_a)\frac{\Delta_0}{\Delta_1}Q_2 = 0 \tag{25}$$

$$Q_2 = \frac{\lambda_2}{(\varepsilon_2 + \kappa_2 - \mu + \delta_a)\frac{\Delta_0}{\Delta_1} + \gamma_2(f_2 - 1)} S_1 Q_2 \qquad = \Omega_4 S_1 \tag{26}$$

As $Q_2 = \Delta_1 C_2$, $R_2 = \Delta_2 C_2$ and $A_2 = \Delta_0 C_2$, we get $Q_2 = \frac{\Delta_1}{\Delta_2} R_2$ and $A_2 = \frac{\Delta_0}{\Delta_2} R_2$. We plug these in and get:

$$\lambda_2 S_1 + \gamma_2(1-f_2)Q_2 - (\varepsilon_2 + \kappa_2 - \mu + \delta_a)A_2 = 0 \tag{27}$$

$$\lambda_2 S_1 + \gamma_2(1-f_2)\frac{\Delta_1}{\Delta_2}R_2 - (\varepsilon_2 + \kappa_2 - \mu + \delta_a)\frac{\Delta_0}{\Delta_2}R_2 = 0 \tag{28}$$

$$R_2 = \frac{\lambda_2}{\gamma_2(f_2 - 1)\frac{\Delta_1}{\Delta_2} + \varepsilon_2 + \kappa_2 - \mu + \delta_a)\frac{\Delta_0}{\Delta_2}} S_1 \tag{29}$$

$$R_2 = \Omega_5 S_1 \tag{30}$$

Now we make R_2, Q_2, C_2, A_2 in terms of C_1 by using $S_1 = \Omega_3 C_1$.

$$R_2 = \Omega_5 S_1 \tag{31}$$

$$R_2 = \Omega_5 \Omega_3 C_1 \tag{32}$$

$$Q_2 = \Omega_4 \Omega_3 C_1 \tag{33}$$

$$C_2 = \frac{\Omega_3}{\Delta_3} C_1 \tag{34}$$

$$A_2 = \Delta_0 \Omega_3 \Delta_3 C_1 \tag{35}$$

Now we have everything in terms of C_1, we would plug them in the first equation and get the endemic steady states.

$$\pi + \gamma_1 f_1 \gamma Q_1 + w_1 R_1 - \lambda_1 S_1 + \gamma_2 f_2 Q_2 + w_2 R_2 - \lambda_2 S_1 - \mu S_1 = 0 \tag{36}$$

$$[(\lambda_1 + \lambda_2 + \mu)\Omega_3 - \gamma_1 f_1 \Omega_1 - \gamma_2 f_2 \Omega_4 \Omega_3 - w_1 \Omega_2 - w_2 \Omega_5 \Omega_3]C_1 = \pi \tag{37}$$

So the steady state is:

$$C_1^* = \frac{\pi}{(\lambda_1 + \lambda_2 + \mu)\Omega_3 - \gamma_1 f_1 \Omega_1 - \gamma_2 f_2 \Omega_4 \Omega_3 - w_1 \Omega_2 - w_2 \Omega_5 \Omega_3} \tag{38}$$

So now we write all endemic steady states in terms of C_1^*:

$$S_1^* = \Omega_3 C_1^* \tag{39}$$
$$A_1^* = \Omega_0 C_1^* \tag{40}$$
$$A_2^* = \Delta_0 \Omega_3 \Delta_3 C_1^* \tag{41}$$
$$Q_1^* = \Omega_1 C_1^* \tag{42}$$
$$Q_2^* = \Omega_4 \Omega_3 C_1^* \tag{43}$$
$$R_1^* = \Omega_2 C_1^* \tag{44}$$
$$R_2^* = \Omega_5 C_1^* \tag{45}$$
$$C_2^* = \frac{\Omega_3}{\Delta_3} C_1^* \tag{46}$$

We would plug these steady states into expressions of λ_1, λ_2 and get steady states for them, we would then solve them simultaneously and get values of λ_1, λ_2. We have taken ζ_1 and ζ_2 equal to zero as discussed with sir.

$$\lambda_1^* = \frac{\beta_1 \theta_{11}}{N} (\eta_1 A_1^* + C_1^*) \tag{47}$$
$$\lambda_2^* = \frac{\beta_2 \theta_{21}}{N} (\eta_2 A_2^* + C_2^*) \tag{48}$$

Simplifying by introducing variables:

$$\lambda_1^* = \Sigma_1 A_1^* + \Sigma_5 C_1^* \tag{49}$$
$$\lambda_2^* = \Sigma_2 A_2^* + \Sigma_6 C_2^* \tag{50}$$

We plug values in and solve simultaneously, I will name new variables in terms of others to simplify. Note that $\Delta_0, \Delta_1, \Delta_2, \Omega_0, \Omega_1, \Omega_2$ are all independent of λ_1, λ_2. However others are not.

So we define them in terms of λ_1, λ_2.

$$\Omega_3 = \frac{\theta_3}{\lambda_1} \tag{51}$$
$$\Omega_4 = \frac{\lambda_2}{\theta_4} \tag{52}$$
$$\Omega_5 = \frac{\lambda_2}{\theta_5} \tag{53}$$
$$\Delta_3 = \frac{\phi_3}{\lambda_2} \tag{54}$$

Plugging in, λ_1, λ_2 in terms of C_1^* become

$$\lambda_1^* = (\Sigma_1\Omega_0 + \Sigma_5)C_1^* \tag{55}$$

$$\lambda_2^* = \left[\Sigma_2 \frac{\lambda_2}{\theta_4}\frac{\lambda_1}{\theta_3} + \Sigma_6 \frac{\theta_3}{\phi_3}\frac{\lambda_2}{\lambda_1}\right] C_1^* \tag{56}$$

As C_1* is also in terms of λ_1, λ_2, so after plugging in all the parameters we can write it in a cleaner way:

$$C_1* = \frac{\pi}{(\lambda_1 + \lambda_2 + \mu)\frac{\theta_3}{\lambda_1} - \gamma_1 f_1 \Omega_1 - \gamma_2 f_2 \frac{\theta_3}{\theta_4}\frac{\lambda_2}{\lambda_1} - w_1\Omega_2 - w_2\frac{\theta_3}{\theta_5}\frac{\lambda_2}{\lambda_1}} \tag{57}$$

$$= \frac{\lambda_1 \pi}{\lambda_1(\theta_3 - \gamma_1 f_1\Omega_1 - w_1\Omega_2) + \lambda_2(\theta_3 - \gamma_2 f_2\frac{\theta_3}{\theta_4} - w_2\frac{\theta_3}{\theta_5}) + \mu\theta_3} \tag{58}$$

$$C_1* = \frac{\pi\lambda_1}{a\lambda_1 + b\lambda_2 + c} \tag{59}$$

We plug C_1^* in λ_1, λ_2 and get :

$$\lambda_1^* = (\Sigma_1\Omega_0 + \Sigma_5)\frac{\pi\ \lambda_1^*}{a\lambda_1^* + b\lambda_2^* + c} \tag{60}$$

$$\lambda_2^* = -\frac{a}{b}\lambda_1^* + (\Sigma_1\Omega_0 + \Sigma_5)\frac{\pi}{b} - \frac{c}{b} \tag{61}$$

and the other equation is :

$$1 = \left[\Sigma_2 \frac{1}{\theta_4}\frac{\lambda_1}{\theta_3} + \Sigma_6 \frac{\theta_3}{\phi_3}\frac{1}{\lambda_1}\right] C_1* = \frac{\pi\ \lambda_1}{a\lambda_1 + b\lambda_2 + c} \tag{62}$$

$$a\lambda_1 + b\lambda_2 + c = \frac{\Sigma_2\Delta_0}{\theta_4}\lambda_1^2 + \frac{\Sigma_6\theta_3}{\phi_3} \tag{63}$$

We plug in the value of λ_2 in terms of λ_1 and get:

$$\lambda_1^{**} = \pm\sqrt{(\Omega_0 + \Sigma_5 + \Sigma_6\frac{\theta_3}{\phi_3})\frac{\theta_4}{\Sigma_2\Delta_0}} \tag{64}$$

We can't have a -ve rate so we only take the positive value and ignore the negative one. We can similarly find λ_2^{**}.

Also note that we can have 4 values of λs. Two we have shown explicitly above. The other two represent semi disease free states. Because when λ_1 is zero, λ_2 is non zero (by equation 61). And same is true for vice versa. What this physically represents is that you could have a stable endemic state for one mode of transfer, and a disease free for other.

$$\lambda_2^{**} = -\frac{a}{b}\lambda_1^{**} + (\Sigma_1\Omega_0 + \Sigma_5)\frac{\pi}{b} - \frac{c}{b} \tag{65}$$

Now that we have $\lambda_1^{**}, \lambda_2^{**}$ in terms of just parameters and are independent of variables we would plug them back in our steady states and get the final endemic steady states:

$$C_1^* * = \frac{\pi}{(\lambda_1^{**} + \lambda_2^{**} + \mu)\Omega_3 - \gamma_1 f_1\Omega_1 - \gamma_2 f_2\Omega_4\Omega_3 - w_1\Omega_2 - w_2\Omega_5\Omega_3} \tag{66}$$

$$S_1^{**} = \Omega_3 C_1^{**} \tag{67}$$

$$A_1^{**} = \Omega_0 C_1^{**} \tag{68}$$

$$A_2^{**} = \Delta_0\Omega_3\Delta_3 C_1^{**} \tag{69}$$

$$Q_1^{**} = \Omega_1 C_1^{**} \tag{70}$$

$$Q_2^{**} = \Omega_4\Omega_3 C_1^{**} \tag{71}$$

$$R_1^{**} = \Omega_2 C_1^{**} \tag{72}$$

$$R_2^{**} = \Omega_5 C_1^{**} \tag{73}$$

$$C_2^{**} = \frac{\Omega_3}{\Delta_3} C_1^{**} \tag{74}$$

Note: Our λ's were not in quadratic form, if they had been then it would have been easier to get the stability as you could use the backward bifurcation criteria and match R_c. In fact I did have quadratic forms of λ before and used the backward bifurcation and critical R R_c method but I was making a mistake in the calculations, when I corrected it then I no longer had the quadratic expressions of λ. So I have not written on latex the whole derivation and working of that method.

6 Stability of the endemic steady state

We tried to evaluate the Jacobian but it gave ridiculously long expressions for determinant. So, we would use the Krasnoselskii sublinearity trick mentioned in the Quarantine/Isolation model chapter.

$$S_1 = N^* - (A_1 + A_2 + C_1 + C_2 + R_1 + R_2 + Q_1 + Q_2)$$

Our system then becomes:

$$dA_1/dt = \lambda_1(N^* - (A_1 + A_2 + C_1 + C_2 + R_1 + R_2 + Q_1 + Q_2)) + \gamma_1(1 - f_1)Q_1 - (\xi_1 + \kappa_1 + \mu + \delta_a)A_1 \quad (75)$$
$$dC_1/dt = \xi_1 A_1 - (\alpha_1 + \psi_1 + \mu + \delta_c)C_1 \quad (76)$$
$$dQ_1/dt = \alpha_1 C_1 - (\gamma_1 + \mu + \delta_q)Q_1 \quad (77)$$
$$dR_1/dt = \kappa_1 A_1 + \psi_1 C_1 - (\omega_1 + \mu)R_1 \quad (78)$$
$$dA_2/dt = \lambda_2(N_1 - (A_1 + A_2 + C_1 + C_2 + R_1 + R_2 + Q_1 + Q_2)) + \gamma_2(1 - f_2)Q_2 - (\xi_2 + \kappa_2 + \mu + \delta_a)A_2 \quad (79)$$
$$dC_2/dt = \xi_2 A_2 - (\alpha_2 + \psi_2 + \mu + \delta_c)C_2 = 0 \quad (80)$$
$$dQ_2/dt = \alpha_2 C_2 - (\gamma_2 + \mu + \delta_q)Q_2 = 0 \quad (81)$$
$$dR_2/dt = \kappa_2 A_2 + \psi_2 C_2 - (\omega_2 + \mu)R_2 \quad (82)$$

Where,
$\lambda_1 = \beta_1\theta_{11}\eta_1\frac{A_1^*}{N_1^*} + \beta_1\theta_{11}\frac{C_1^*}{N_1^*}$
$\lambda_1 = \beta_2\theta_{21}\eta_2\frac{A_2^*}{N_1^*} + \beta_2\theta_{21}\frac{C_2^*}{N_1^*}$

Now we have to linearize this system about the endemic equilibrium $\tilde{\epsilon}_1$.

We define:

$a_1 = \frac{\beta_1\theta_{11}(\eta_1 A_1^* + C_1^*)}{N_1^*}$
$a_2 = \frac{\beta_1\theta_{11}S_1^*}{N_1^*}$
$a_3 = \frac{\beta_2\theta_{12}(\eta_2 A_2^* + C_2^*)}{N_1^*}$
$a_4 = \frac{\beta_2\theta_{12}S_1^*}{N_1^*}$

After linearizing, our equations become (similar to Eq.3.17 in the paper provided by sir):

$$dA_1/dt = [-a_1 - (\xi_1 + \kappa_1 + \mu + \delta_a) + \eta_1 a_1]A_1 + [\gamma_1(1 - f_1) - a_1]Q_1 - [-a_1 + a_2]C_1 - a_1(R_1 + R_2 + C_2 + Q_2 + A_2) \quad (83)$$
$$dA_2/dt = [-a_3 - (\xi_2 + \kappa_2 + \mu + \delta_a) + \eta_2 a_4]A_2 + [\gamma_2(1 - f_2) - a_3]Q_2 - [-a_3 + a_4]C_2 - a_3(R_1 + R_2 + C_1 + Q_1 + A_1) \quad (84)$$

The rest of the equations are the same:

$$dC_1/dt = \xi_1 A_1 - (\alpha_1 + \psi_1 + \mu + \delta_c)C_1 \quad (85)$$
$$dQ_1/dt = \alpha_1 C_1 - (\gamma_1 + \mu + \delta_q)Q_1 \quad (86)$$
$$dR_1/dt = \kappa_1 A_1 + \psi_1 C_1 - (\omega_1 + \mu)R_1 \quad (87)$$
$$dC_2/dt = \xi_2 A_2 - (\alpha_2 + \psi_2 + \mu + \delta_c)C_2 \quad (88)$$
$$dQ_2/dt = \alpha_2 C_2 - (\gamma_2 + \mu + \delta_q)Q_2 \quad (89)$$
$$dR_2/dt = \kappa_2 A_2 + \psi_2 C_2 - (\omega_2 + \mu)R_2 \quad (90)$$

We have essentially reduced to a 8x8 system. This would help alot.

Suppose:

$(\xi_1 + +\kappa_1 + \mu + \delta_a) = \sigma_1$

$(\alpha_1 + \psi_1 + \mu + \delta_c) = \sigma_2$

$(\xi_2 + \kappa_2 + \mu + \delta_a) = \sigma_3$

$(\alpha_2 + \psi_2 + \mu + \delta_c) = \sigma_4$

$J(\tilde{\epsilon}_1) =$

$$\begin{bmatrix} -a_1 - \sigma_1 + \eta_1 a_1 & a_2 - a_1 & \gamma_1(1-f_1) - a_1 & -a_1 & -a_1 & -a_1 & -a_1 & -a_1 \\ \xi_1 & -\sigma_2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha_1 & -(\gamma_1 + \mu + \delta_q) & 0 & 0 & 0 & 0 & 0 \\ \kappa_1 & \psi_1 & 0 & -(\omega_1 + \mu) & 0 & 0 & 0 & 0 \\ -a_3 & -a_3 & -a_3 & -a_3 & -a_3 - \sigma_3 + \eta_2 a_4 & a_4 - a_3 & \gamma_2(1-f_2) - a_3 & -a_3 \\ 0 & 0 & 0 & 0 & \xi_2 & -\sigma_4 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \alpha_2 & -(\gamma_2 + \mu + \delta_q) & 0 \\ 0 & 0 & 0 & 0 & \kappa_2 & \psi_2 & 0 & -(\omega_2 + \mu) \end{bmatrix}$$

You should note that all values in the above matrix are not constant parameters, the a_i are in terms of our steady states that we calculated before.

We will check the stability by the Routh-Herwitz Criteria. We will take $det(J - \lambda I)$ and get an expression in the form of
$\lambda^k + \tilde{a}_1\lambda_{k-1} + \tilde{a}_2\lambda_{k-2} + \tilde{a}_3\lambda_{k-3} + ... + \tilde{a}_k = 0$

The criteria for k = 2 is stability iff $\tilde{a}_1 > 0, \tilde{a}_2 > 0$. In our case, we have k = 8. So, the stability criteria is:

$\tilde{a}_1 > 0, \tilde{a}_2 > 0, \tilde{a}_3 > 0, \tilde{a}_4 > 0, \tilde{a}_5 > 0, \tilde{a}_6 > 0, \tilde{a}_7 > 0, \tilde{a}_8 > 0$ and $\tilde{a}_1\tilde{a}_2\tilde{a}_3\tilde{a}_4\tilde{a}_5\tilde{a}_6\tilde{a}_7 > \tilde{a}_7^7 + \tilde{a}_5^7\tilde{a}_8$ and so on.

Here $\tilde{a}_i's$ are the coefficients of the determinant we calculated. You can plug in the parameters and check from the routh herwitz criteria the stability. The big expression you get for the determinant is attached at the end in the appendix. The change of variables table is given below.

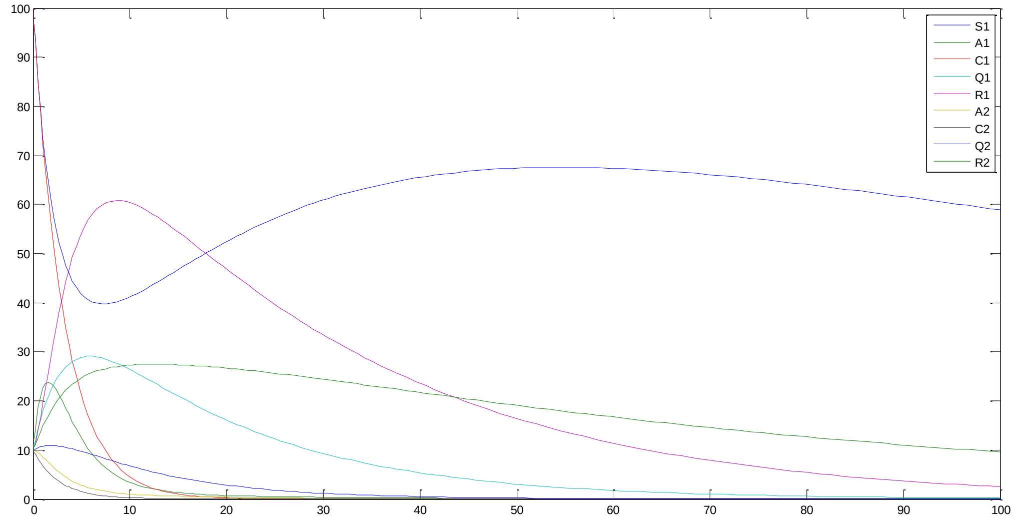
Vaiables	
$X5$	λ
d	λ
$s1$	σ_1
$e1, e2$	$\varepsilon_{1,2}$
$g1, g2$	$\gamma_{1,2}$
dq	δ_q
dq	δ_q
dc	δ_c
da	δ_a
k	δ_q
$ps1, ps2$	$\psi_{1,2}$
$n1, n2$	$\eta_{1,2}$

In the appendix we the polynomial is in the terms of $X5$ which is the eigenvalue variable. Once you plug in the parameters, the roots will give you eigenvalues. Either you can check the stability by the positiveness of the eigenvalues or an alternate way is you use the Routh Herwitz(RH) criteria. You match the coefficients of the polynomials in $X5$ to the criteria and see the stability. A simple algorithm of how we will use RH criteria was discussed above.

The appendix file is attached along the paper.

Simulation Results

Case1: Disease Free Steady State



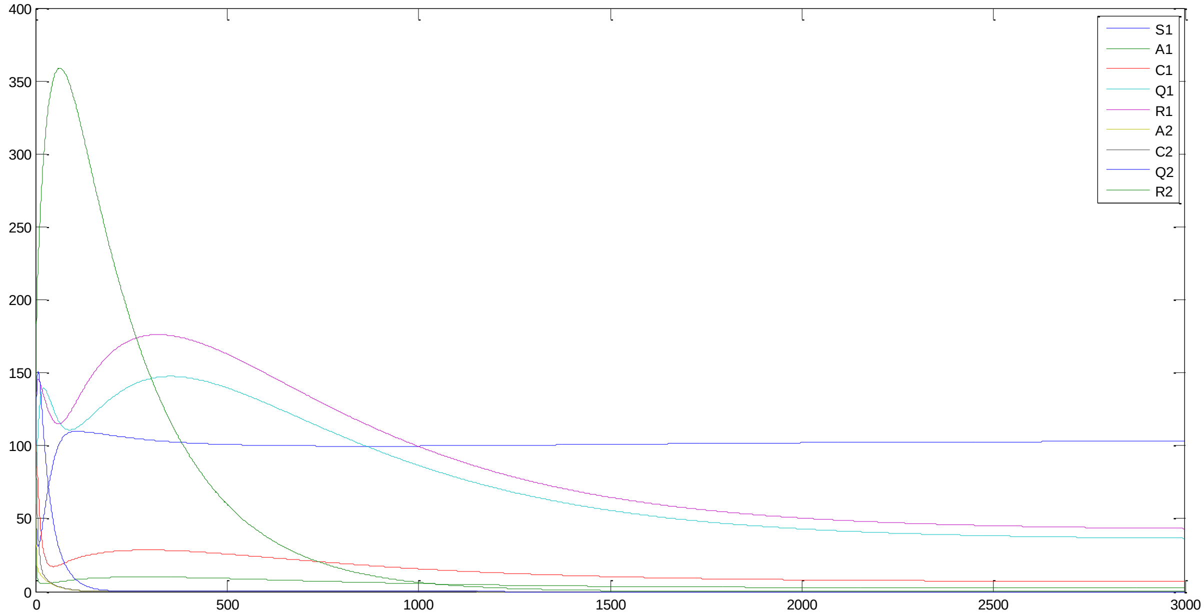

```
[t,y] = ode45(@quarantine1,[0,100],[100,10,100,10,10,10,10,10,10]);
```

```
N=300; pi=0.2; g1=0.0156;g2=0.05; f1=0.05;f2=0.02; w1=0.03;w2=0.004;
b1=0.8;b2=0.8; n1=0.63;n2=0.74; m=0.01; e1=0.02;e2=0.03; k1=.51;k2=0.52;
da=0.02;dq=0.03;dc=0.2; a1=0.1;a2=0.2; p1=0.01;p2=0.01;
```

As Critical1 have a big Initial value, so we see a rise in recovered1 class… and then recovered class gets transferred to susceptibles.

Note: the values highlighted in yellow are the initial conditions, highlighted in grey represent the time boundaries and highlighted in green represent parameters

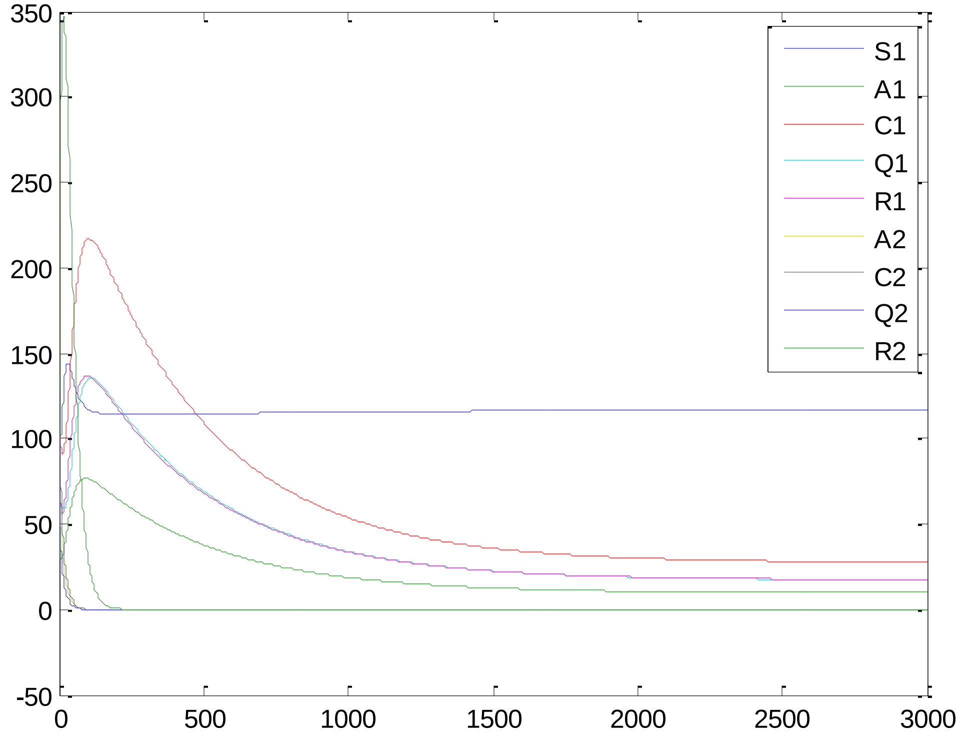
Case2: Endemic Steady State




```
[t,y] = ode45(@quarantine1,[0,3000],[100,50,100,60,100,100,100,100,100]);

N=500; pi=0.22; g1=0.0156;g2=0.05; f1=0.05;f2=0.02; w1=0.03;w2=0.004;
b1=0.8;b2=0.58; n1=0.863;n2=0.974; m=0.0005; e1=0.32;e2=0.203;
k1=.51;k2=0.52; da=0.002;dq=0.003;dc=0.002; a1=0.1;a2=0.2; p1=0.01;p2=0.01;
```

Case 3: Endemic Steady State




```
[t,y] = ode45(@quarantine1,[0,3000],[100,50,100,60,100,100,100,100,100]);

N=500; pi=0.22; g1=0.156;g2=0.5; f1=0.5;f2=0.02; w1=0.3;w2=0.04;
b1=0.8;b2=0.58; n1=0.863;n2=0.974; m=0.0005; e1=0.32;e2=0.203;
k1=.51;k2=0.52; da=0.002;dq=0.003;dc=0.002; a1=0.1;a2=0.2; p1=0.01;p2=0.01;
```

Matlab Code:

File: Quarantine1.m

```
function dydt = quarantine1(t,y)

dydt = zeros(size(y));

%parameters
N=500; pi=0.22; g1=0.156;g2=0.5; f1=0.5;f2=0.02; w1=0.3;w2=0.04;
b1=0.8;b2=0.58; n1=0.863;n2=0.974; m=0.0005; e1=0.32;e2=0.203;
k1=.51;k2=0.52; da=0.002;dq=0.003;dc=0.002; a1=0.1;a2=0.2; p1=0.01;p2=0.01;

S1 = y(1);
A1 = y(2);
C1 = y(3);
Q1 = y(4);
R1 = y(5);
A2 = y(6);
C2 = y(7);
Q2 = y(8);
R2 = y(9);

l1= b1*(n1*A1 + C1)/N;
l2= b2*(n2*A2 + C2)/N;

dydt(1) = pi + g1*f1*Q1 + w1*R1 - l1*S1 + g2*f2*Q2 + w2*R2 - l2*S1 - m*S1;
dydt(2) = l1*S1 + g1*(1-f1)*Q1 - (e1+k1+m+da)*A1;
dydt(3) = e1*A1-(a1+p1+m+dc)*C1;
dydt(4) = a1*C1 - (g1+m+dq)*Q1;
dydt(5) = k1*A1 + p1*C1 - (w1+m)*R1;
dydt(6) = l2*S1 + g2*(1-f2)*Q2 - (e2+k2+m+da)*A2;
dydt(7) = e2*A2-(a2+p2+m+dc)*C2;
dydt(8) = a2*C2 - (g2+m+dq)*Q2;
dydt(9) = k2*A2 + p2*C2 - (w2+m)*R2;
```

File: odesolver1.m

```
%% Ode solver
[t,y] = ode45(@quarantine1,[0,3000],[100,50,100,60,100,100,100,100,100]);

close all;
plot(t,y)

hleg1 = legend('S1','A1','C1','Q1','R1','A2','C2','Q2','R2');
```