Heterogeneity in epidemic models

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Heterogeneity

- The simplest models we use treat individuals identically.
- But people of course differ in susceptibility, risk, infectivity, and other dimensions. (We've heard from John about how epidemiology is the who, what, why of disease...)
- We think disease—and risk—is not distributed randomly.
- What difference can this make? (Answering this is virtually the whole field!)
- We'll look at one simple case.

Simple model

- Essential idea: Hethcote and Yorke
- Follow Anderson and May 1991; MSM population
- β: transmission coefficient; μ reciprocal residence time in risk group; μ_a mean residence time with the disease
- We have one group of people divided into susceptibles S: $\frac{dS}{dt} = -\beta S \frac{I}{N} + \nu - \mu S$
- and into infectives I: $\frac{dI}{dt} = \beta S \frac{I}{N} - \mu I - \mu_A I$
- where $N = S + I$.

Simple model

- λ, the force of infection, can be written as the coefficient of S, the changing per capita rate of infection of a susceptible. Here, $\lambda = \beta \frac{I}{N}$. probability of infection per partner.
- Susceptibles S: $\frac{dS}{dt} = -\lambda S + \nu - \mu S$
- Infectives I: $\frac{dI}{dt} = \lambda S - \mu I - \mu_A I$
- where $N = S + I$, $\lambda = \beta \frac{I}{N}$.

Simple model

- Also, we can write the transmission coefficient itself as the product of c, number of new partners per unit time, and say π ithe probability of infection per partner.
- Susceptibles S: $\frac{dS}{dt} = -\lambda S + \nu - \mu S$
- Infectives I: $\frac{dI}{dt} = \lambda S - \mu I - \mu_A I$
- where $N = S + I$, $\lambda = \beta \frac{I}{N} = \pi c \frac{I}{N}$

Quick review

Without disease, we just have $\lambda = \beta \frac{0}{N} = 0$.

$$\frac{dS}{dt} = -0S + \nu - \mu S$$

or

$$\frac{dS}{dt} = \nu - \mu S$$

with no-disease equilibrium ν/μ. This is where $\nu = \mu S$.

Quick review

- So what does the no-disease equilibrium ν/μ mean? ν is the inflow rate—new people per time; $1/\mu$ how long they last.
- It is the demographic version of prevalence equals incidence times duration.

Reproduction number

- $R_0 = \frac{\pi c}{\mu + \mu_A}$
- Why?

Reproduction number

- Let's follow the first generation.
- People infected at the beginning.
- Call them $I^{(0)}$.
- $\frac{dI^{(0)}}{dt} = -(\mu + \mu_A)I^{(0)}$.

Reproduction number

So with $\frac{dI^{(0)}}{dt} = -(\mu + \mu_A)I^{(0)}$, we get

$$I^{(0)} = I^{(0)}(0)e^{-(\mu+\mu_A)t}.$$

Waiting time on average is $1/(\mu + \mu_A)$. Each initial infective lasts this long on average.

Reproduction number

Look at the rate of new cases at the beginning:

$$\frac{dI^{(1+)}}{dt} = \pi c S \frac{I}{N} \approx \pi c I$$

So πc is the total rate of making new infections per infective.

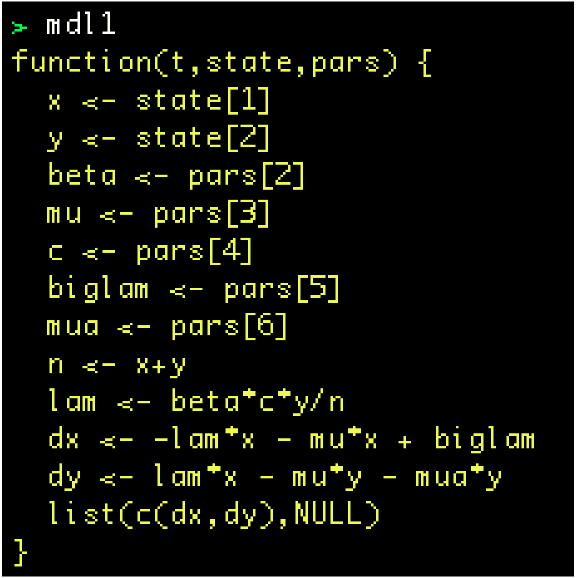
Reproduction number

Therefore, R_0 is how quickly the initial cases make new infectives (πc) times how long they get to do so, $1/(\mu + \mu_A)$.

Equilibrium

Fraction of uninfected people is $1/R_0$.

Model

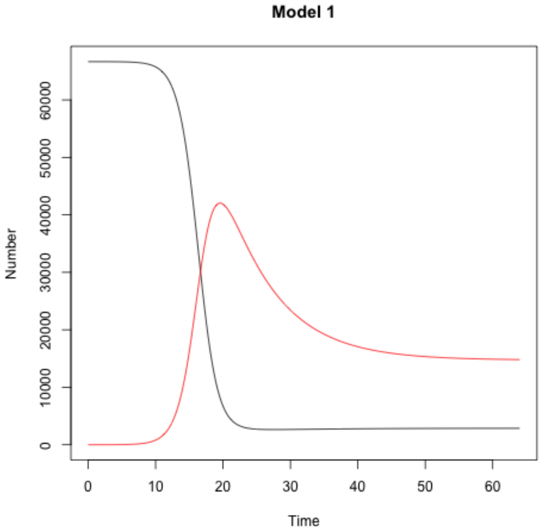


```
> mdl1
function(t,state,pars) {
  x <- state[1]
  y <- state[2]
  beta <- pars[2]
  mu <- pars[3]
  c <- pars[4]
  biglam <- pars[5]
  mua <- pars[6]
  n <- x+y
  lam <- beta*c*y/n
  dx <- -lam*x - mu*x + biglam
  dy <- lam*x - mu*y - mua*y
  list(c(dx,dy),NULL)
}
```

Model

Pick $\mu = 0.03$, $\nu = 2000$, $\pi = 0.1$, $c = 8$. This puts R_0 around 6.2.

Model


Model 1
Number
0
10000
20000
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30
40
50
60
Time

Equilibrium

Does this make sense?

- Take gonorrhea for instance. Usually reported as rates, but a few studies over the years put the prevalence at a few percent. (Ex: Hein, Marks, Cohen, J Peds, 1977).
- If the prevalence were 4%, then what is R_0 if you believe the simple model?
- $1/(1-x) \approx 1 + x$ for tiny x, so around 1.04.
- ... an absurd conclusion.

Extend model

- Let's have a high risk *core group*, with $c_2 > c_1$.
- Lets have each group have a different inflow rate ν_1 and ν_2.
- Same residence times μ.

Equations

- $\frac{dS_1}{dt} = -\lambda_1 S_1 + \nu_1 - \mu S_1$
- $\frac{dS_2}{dt} = -\lambda_2 S_2 + \nu_2 - \mu S_2$

with

- $\lambda_1 = c_1 \pi (p_{11} \frac{I_1}{N_1} + p_{12} \frac{I_2}{N_2})$
- $\lambda_2 = c_2 \pi (p_{21} \frac{I_1}{N_1} + p_{22} \frac{I_2}{N_2})$

where $N_1 = S_1 + I_1$ is the number of people in group 1, and $N_2 = S_2 + I_2$ is the number of people in group 2.

Equations

Let's take a look at the risk more closely. We had this:

$$\lambda_1 = c_1 \pi \left(p_{11} \frac{I_1}{N_1} + p_{12} \frac{I_2}{N_2} \right)$$

Equations

The risk per unit time of a person in group 1 is still the number of new partners per unit time, c_1, times the chance of getting infected per partner.

$$\lambda_1 = c_1 \pi (p_{11} \frac{I_1}{N_1} + p_{12} \frac{I_2}{N_2})$$

Equations

The force of infection:

$$\lambda_1 = c_1 \pi (p_{11} \frac{I_1}{N_1} + p_{12} \frac{I_2}{N_2})$$

Now, what is the chance of getting infected per partner? It is the chance you get the infection if the partner is infected, times the chance the partner is actually infected:

$$\lambda_1 = c_1 \pi (p_{11} \frac{I_1}{N_1} + p_{12} \frac{I_2}{N_2})$$

Equations

Now, what is the the chance the partner is infected?

$$\lambda_1 = c_1\pi(p_{11}\frac{I_1}{N_1} + p_{12}\frac{I_2}{N_2})$$

That is the chance a partner is in group 1 times the chance the partner in group 1 is infected, plus the chance a partner is in group 2 times the chance a partner in group 2 is infected:

$$\lambda_1 = c_1\pi(p_{11}\frac{I_1}{N_1} + p_{12}\frac{I_2}{N_2})$$

Equations

Of course the equations for the infectives are more or less the same as before.

$$\frac{dI_1}{dt} = \lambda_1 S_1 - (\mu + \mu_A) I_1$$

$$\frac{dI_2}{dt} = \lambda_2 S_2 - (\mu + \mu_A) I_2$$

Mixing

These mixing probabilities are related to each other. Let's have p_{ji} be the chance a person in group j has a partner in group i.

$$p_{11} + p_{12} = 1$$

$$p_{21} + p_{22} = 1$$

Mixing

There is one more important equation:

$$c_1 N_1 p_{12} = c_2 N_2 p_{21}$$

This says the total number of ones who have partnerships with group twos at any time has to equal the total number of twos who have partnerships with group ones at any time.

Mixing

- If we just had any one of these mixing probabilities, say p_{11}, we could solve for the others.
- What are the possibilities?
- One idea is $p_{11} = 1$. Then $p_{12} = 0$, and so $p_{21} = 0$, and then $p_{22} = 1$. This is *complete assortative mixing*. Everyone in their own group.

Mixing

- Another is *random mixing*. Each person picks partnerships in proportion to the number of available partnerships.
- So if the number of partnerships per unit time is $c_1 N_1 + c_2 N_2$, and the fraction of partnerships with group one people is $c_1 N_1$, then $p_{11} = p_{21} = \frac{c_1 N_1}{c_1 N_1 + c_2 N_2}$.
- Then you can find that $p_{12} = p_{22} = \frac{c_2 N_2}{c_1 N_1 + c_2 N_2}$.
- This isn't random by people, but by partnership.

Parameterization

You can interpolate between random and completely assortative mixing too, using a parameter $q = 0$ for random, and $q = 1$ for completely assortative:

$$p_{11} = \frac{c_1 N_1 + q c_2 N_2}{c_1 N_1 + c_2 N_2}$$

$$p_{22} = \frac{q c_1 N_1 + c_2 N_2}{c_1 N_1 + c_2 N_2}$$

$$p_{12} = \frac{(1 - q) c_2 N_2}{c_1 N_1 + c_2 N_2}$$

$$p_{21} = \frac{(1 - q) c_1 N_1}{c_1 N_1 + c_2 N_2}$$

Parameterization

Pick $q = 0$:

$$p_{11} = \frac{c_1 N_1}{c_1 N_1 + c_2 N_2}$$

$$p_{22} = \frac{c_2 N_2}{c_1 N_1 + c_2 N_2}$$

$$p_{12} = \frac{c_2 N_2}{c_1 N_1 + c_2 N_2}$$

$$p_{21} = \frac{c_1 N_1}{c_1 N_1 + c_2 N_2}$$

This is *random mixing*.

Parameterization

Pick $q = 1$:

$$p_{11} = \frac{c_1 N_1 + c_2 N_2}{c_1 N_1 + c_2 N_2} = 1$$

$$p_{22} = \frac{c_1 N_1 + c_2 N_2}{c_1 N_1 + c_2 N_2} = 1$$

$$p_{12} = \frac{(1-1) c_2 N_2}{c_1 N_1 + c_2 N_2} = 0$$

$$p_{21} = \frac{(1-1) c_1 N_1}{c_1 N_1 + c_2 N_2} = 0$$

Everybody stays in their own group; complete assortativity. Epidemics completely decoupled.

Initial fractions

$$f_1 = N_1/(N_1 + N_2)$$
$$f_2 = N_1/(N_1 + N_2)$$

Initial fraction

$$p_{11} = \frac{c_1 f_1 + q c_2 f_2}{c_1 f_1 + c_2 f_2}$$

$$p_{22} = \frac{q c_1 f_1 + c_2 f_2}{c_1 f_1 + c_2 f_2}$$

$$p_{12} = \frac{(1 - q) c_2 f_2}{c_1 f_1 + c_2 f_2}$$

$$p_{21} = \frac{(1 - q) c_1 f_1}{c_1 f_1 + c_2 f_2}$$

Reproduction number

- How do we get R_0? It turns out it is similar to what we did before.
- A person in group one still has duration $\frac{1}{\mu+\mu_A}$.
- Per unit time, you have partners at rate c_1.
- The chance a partner is in group one is p_{11}.
- And the chance they get infected is π.
- So the total number of group one infecteds per group one infected starting out, is $\frac{c_1 p_{11} \pi}{\mu+\mu_A}$.

Reproduction number

- We can find the number of infections in group one a group one person can cause.
- Similarly, we can get the number of group two infections a group one person can cause.
- Also: we can get the number of group one infections a group two person can cause.
- And of course, we can get the number of group two infections a group two person can cause.
- The actual R_0 combines all these together.
- It turns out to be the largest eigenvalue of a matrix where you put all four of these numbers (in the right order).

Reproduction number

We won't pursue this in detail, but if we make the matrix r_{ij} and take it's eigenvalues, we will get the right answer:

$$a = \frac{\pi}{(\mu + \mu_A)(c_1 f_1 + c_2 f_2)}$$

$$r_{11} = ac_1(c_1 f_1 + qc_2 f_2)$$

$$r_{12} = ac_1 c_2 (1 - q) f_1$$

$$r_{21} = ac_1 c_2 (1 - q) f_2$$

$$r_{22} = ac_2(qc_1 f_1 + c_2 f_2)$$

Van den Driessche and Watmough, 2002.

Review

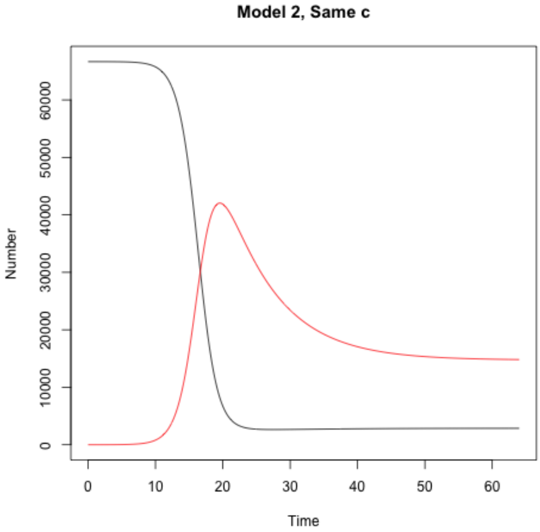
How is heterogeneity incorporated into this model?

- Heterogeneity in risk: different numbers of partners
- Heterogeneity in partner choice: nonrandom mixing

Explore this model

First let's make the groups mix randomly and have the same risk behavior. This should be actually the same model we had before!

Model


Model 2, Same c
Number
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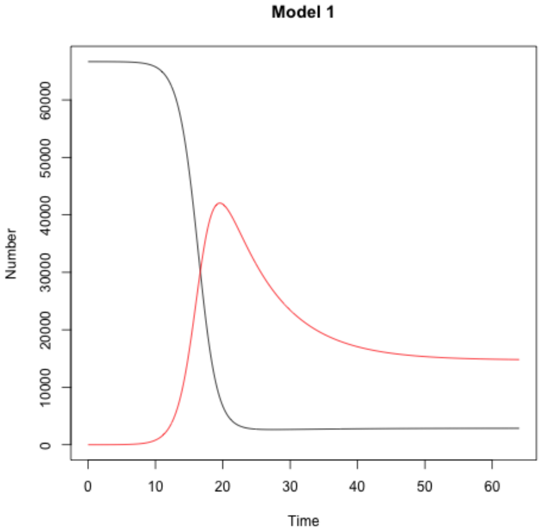
Time

Model


Model 1
Number
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30000
40000
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60000
0
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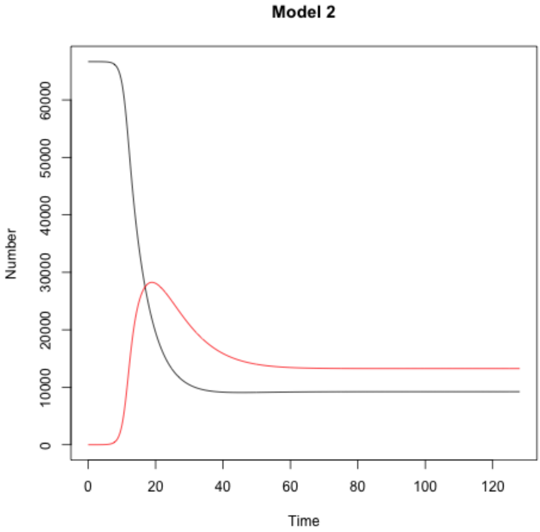
50
60
Time

Model

Now, let's have say a core group of one fifth the population, and let's give them a much higher risk. To start with, how about 2 new partners a year for the large group, but sixteen per year for the core group?

Model


Model 2
Number
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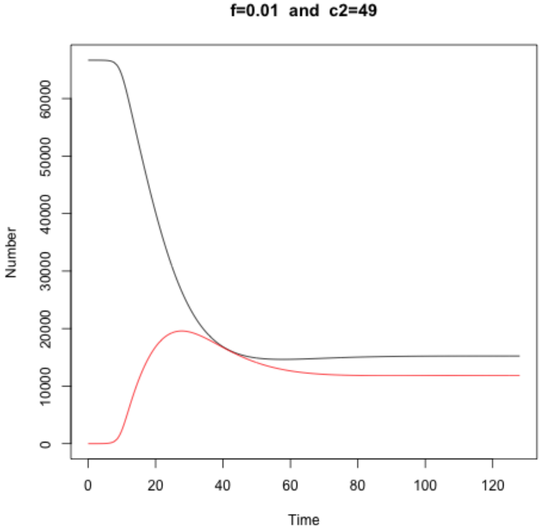
10000
20000
30000
40000
50000
60000
0
20
40
60
80
100
120
Time

Model

Freeze $c_1 = 2$; change size and activity in the core group.



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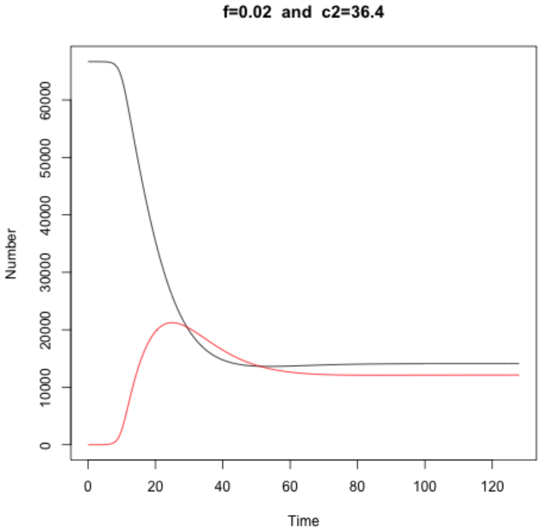

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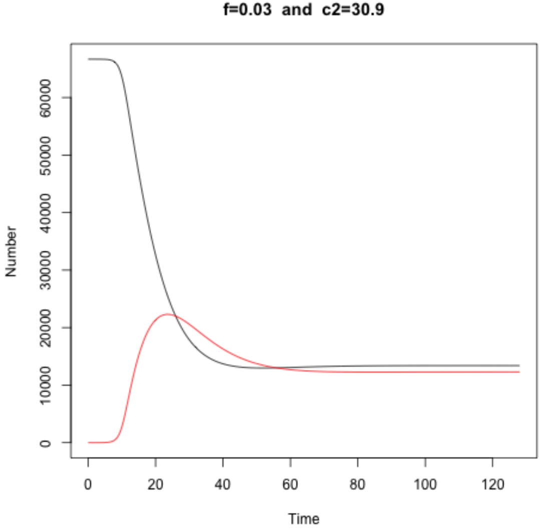

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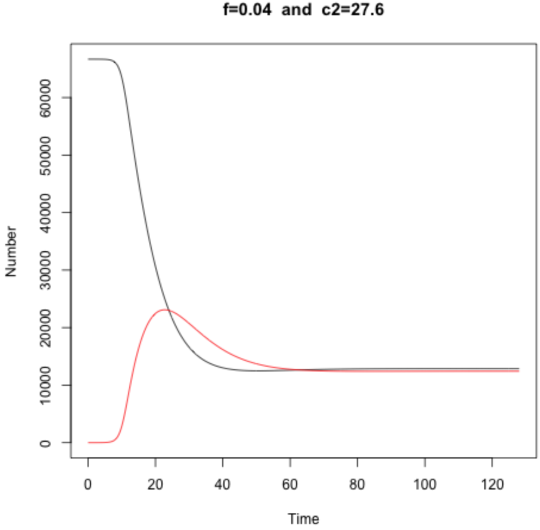

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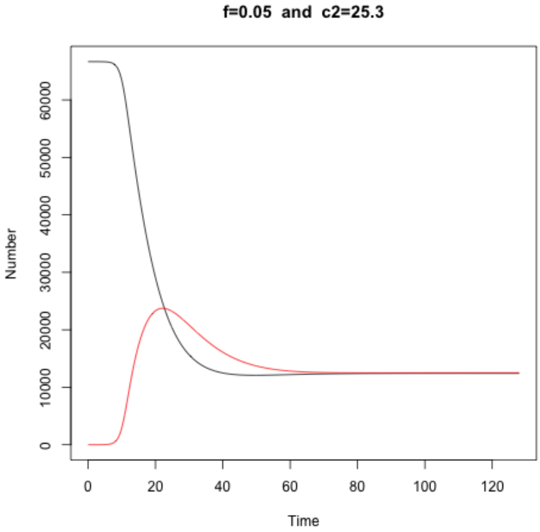

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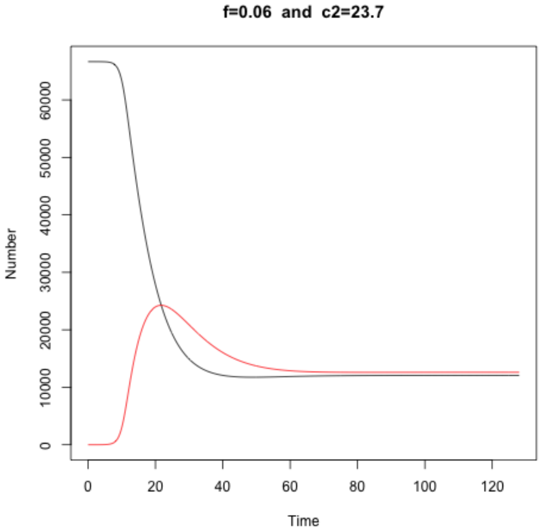

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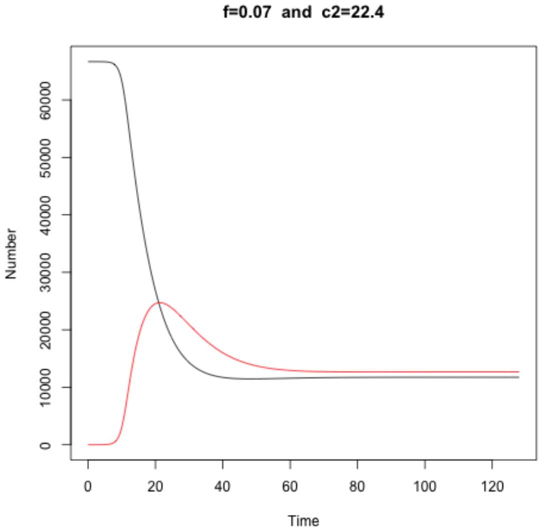

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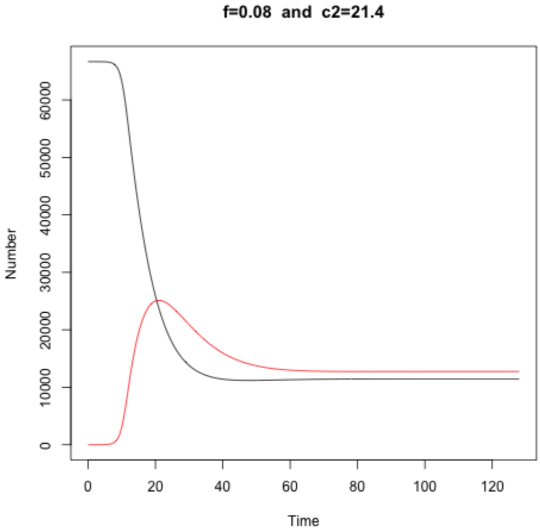

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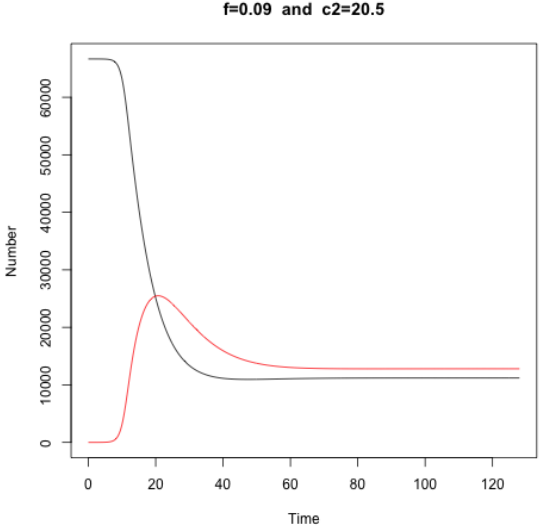

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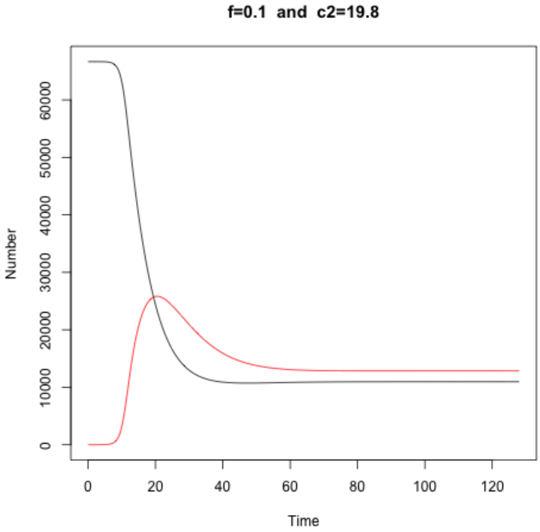

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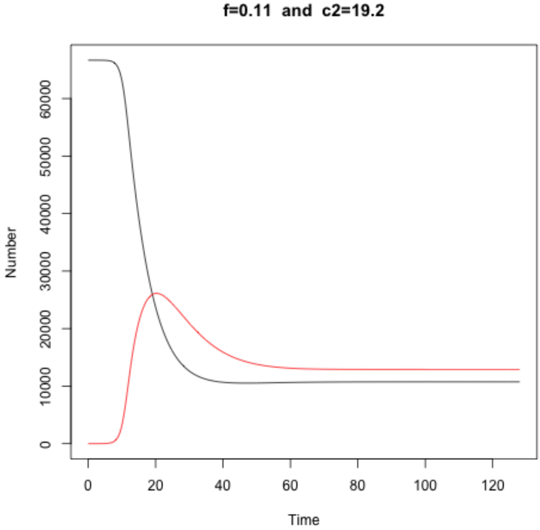

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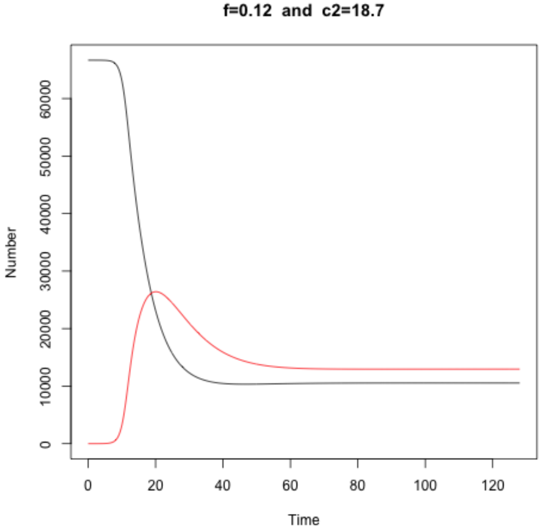

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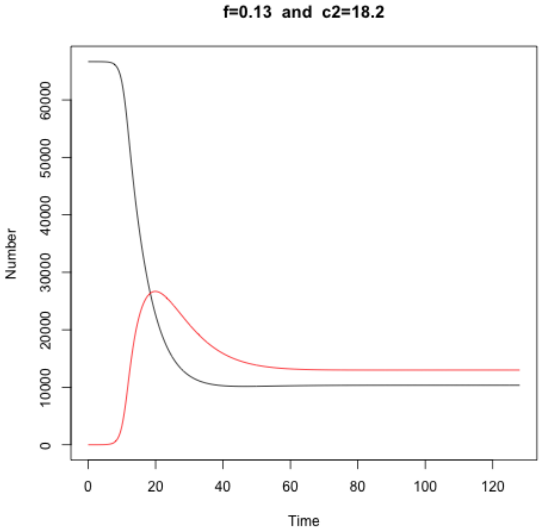

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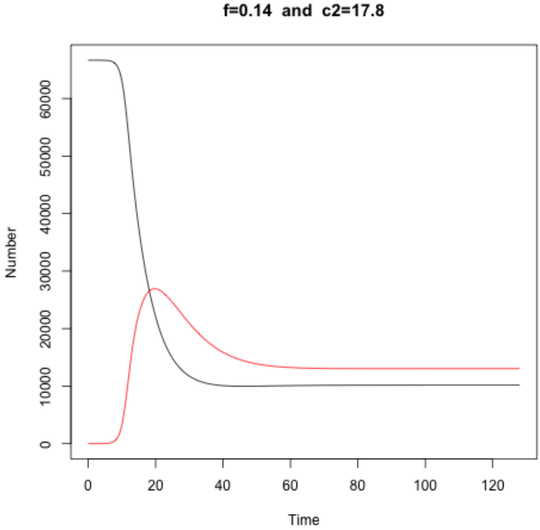

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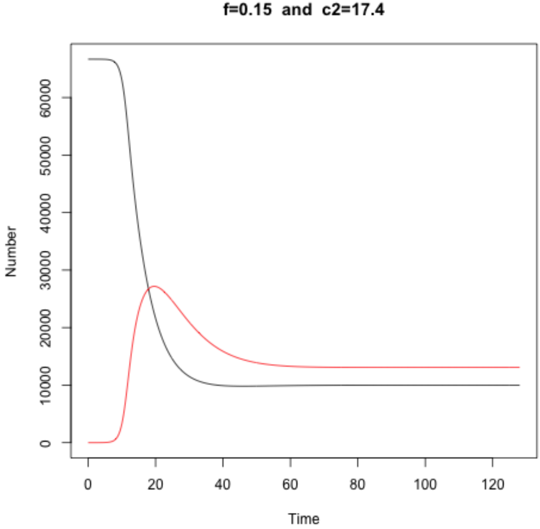

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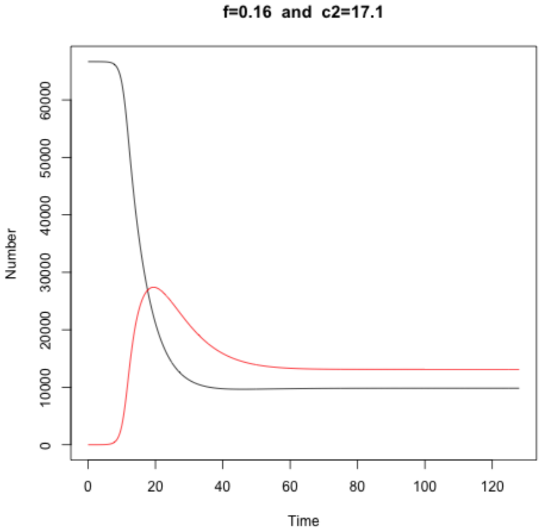

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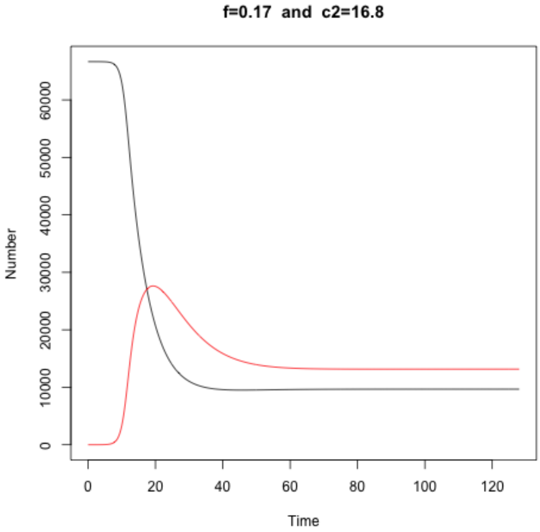

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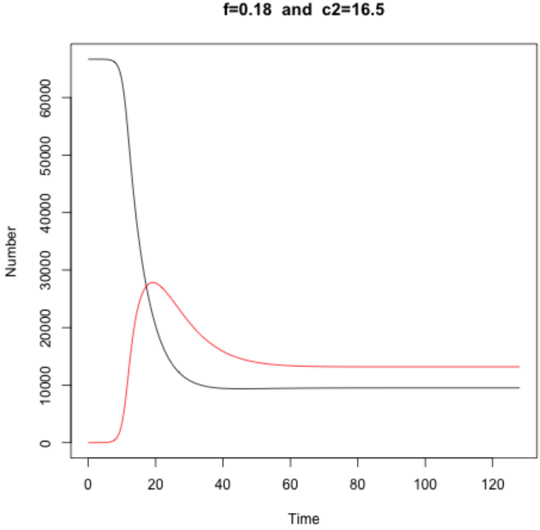

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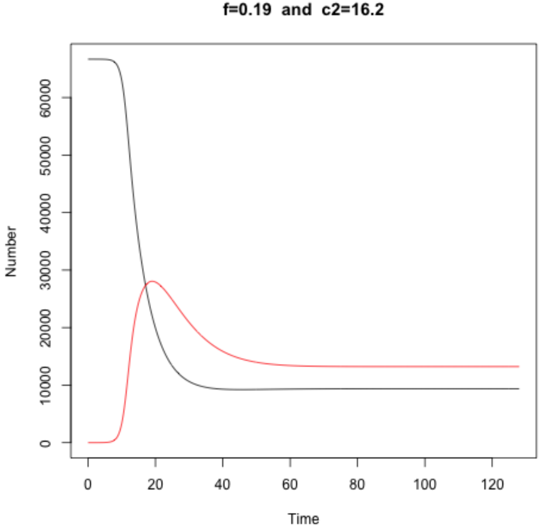

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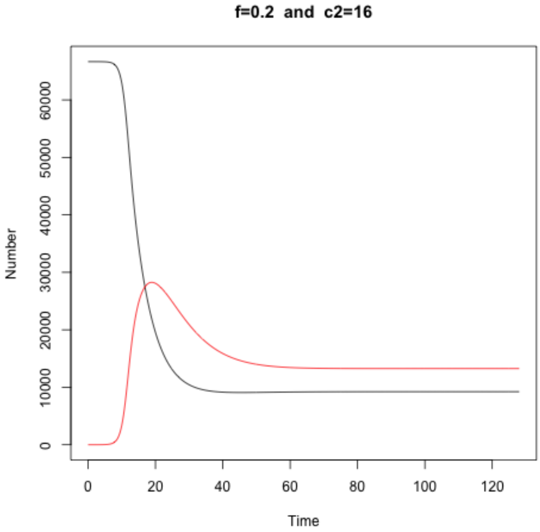
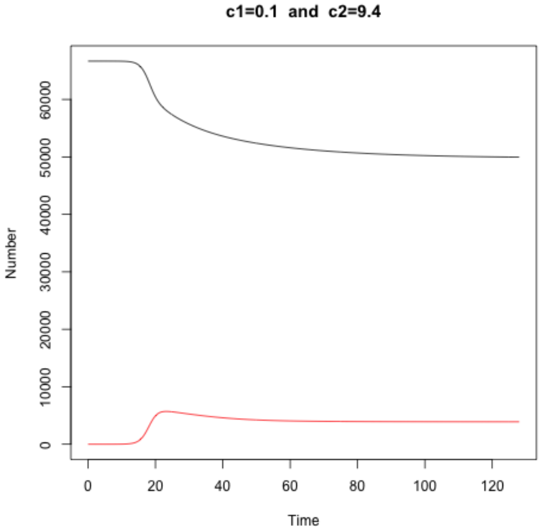


Model

Freeze size of group 2 at 10%.



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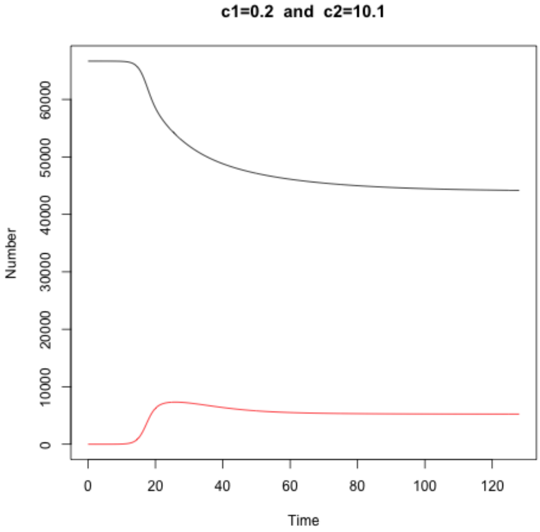

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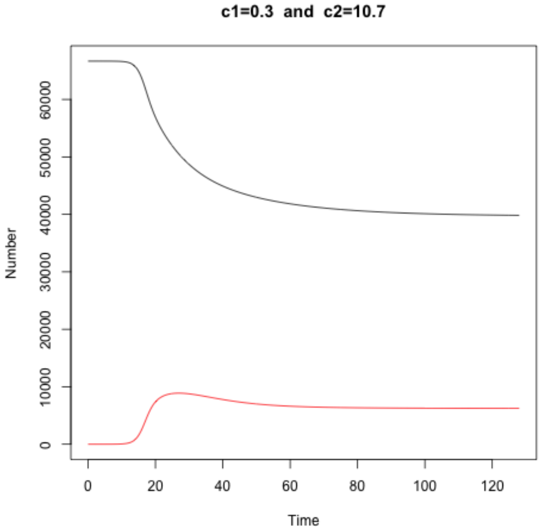

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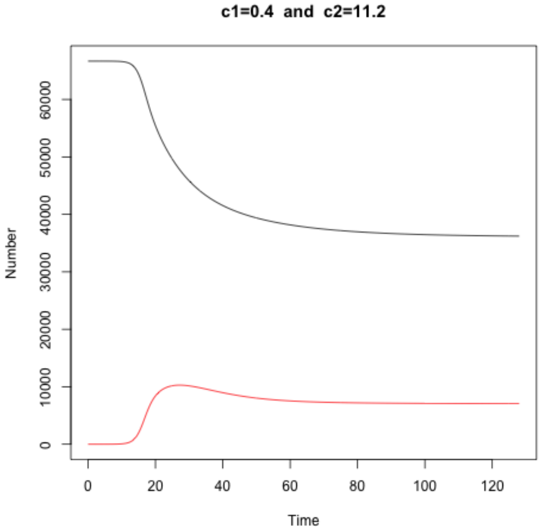

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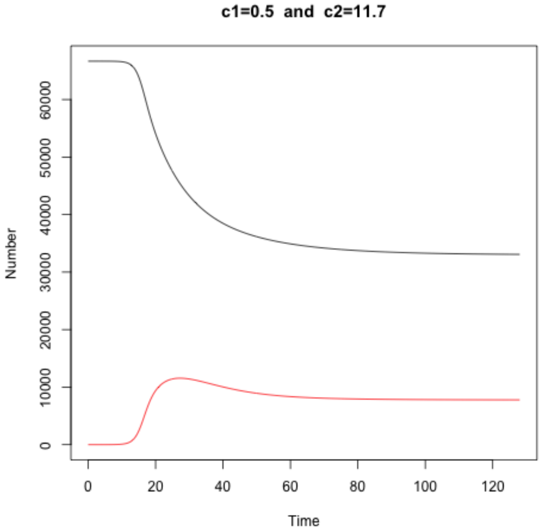

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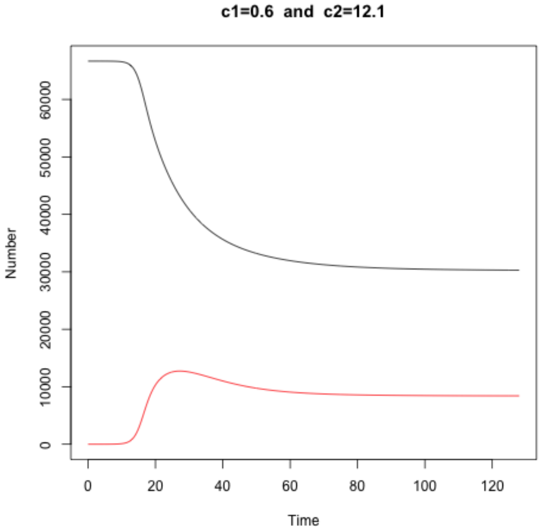

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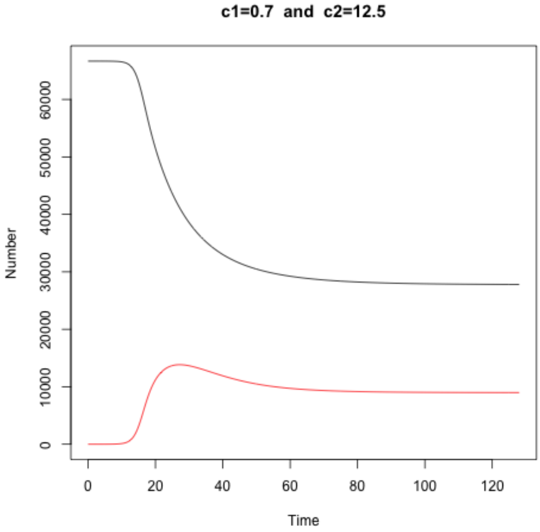

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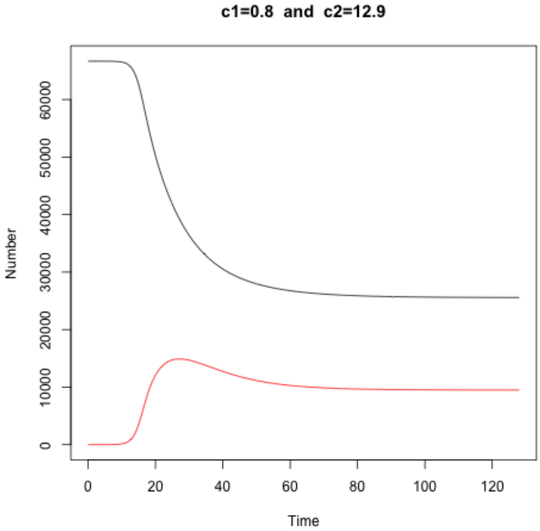
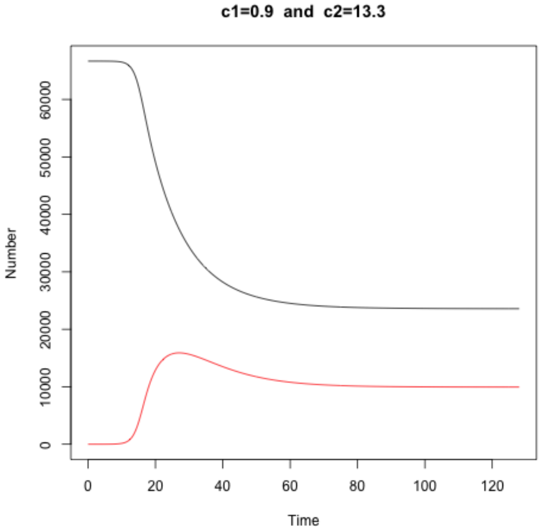


Model

Freeze size of group 2 at 10%.



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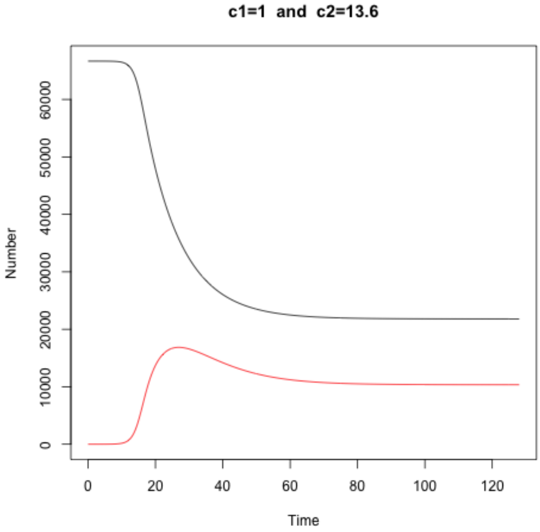

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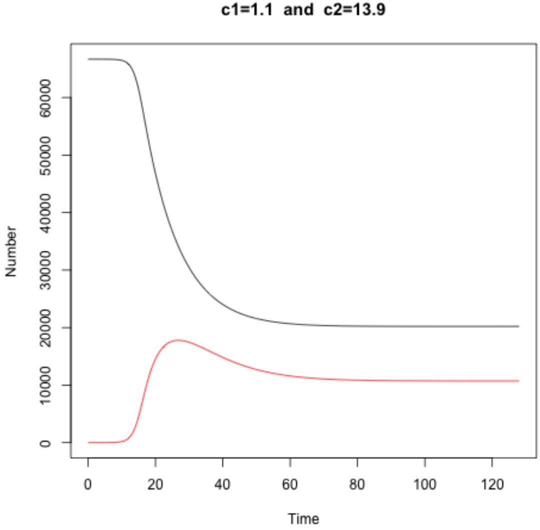

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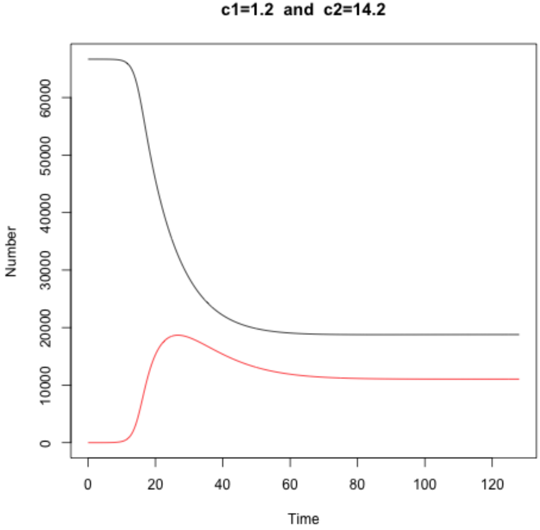

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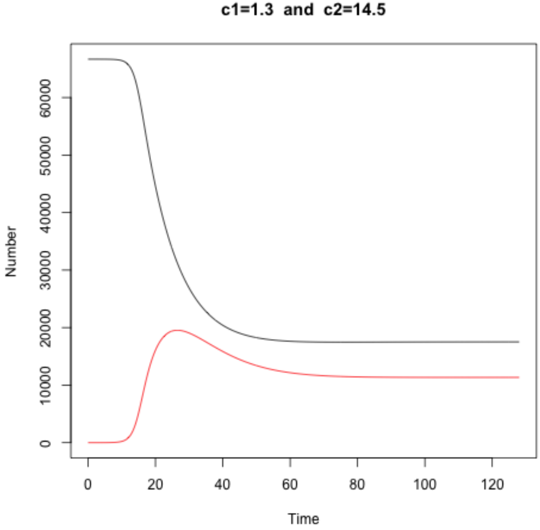

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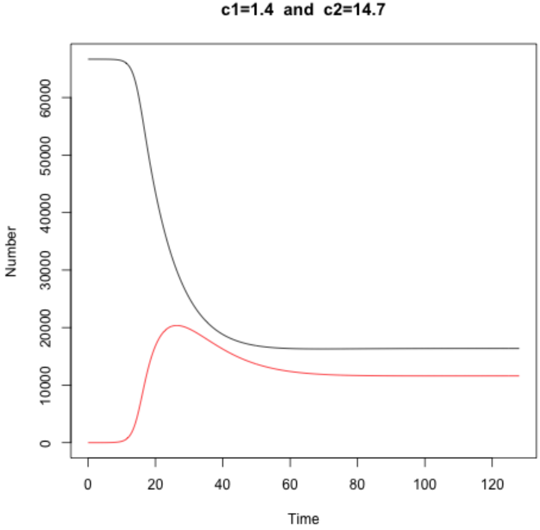

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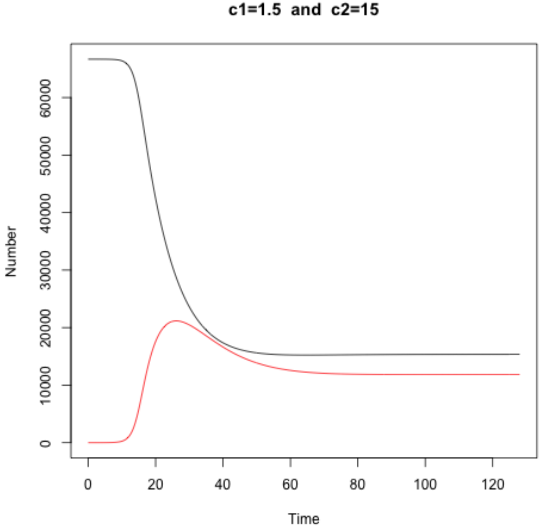

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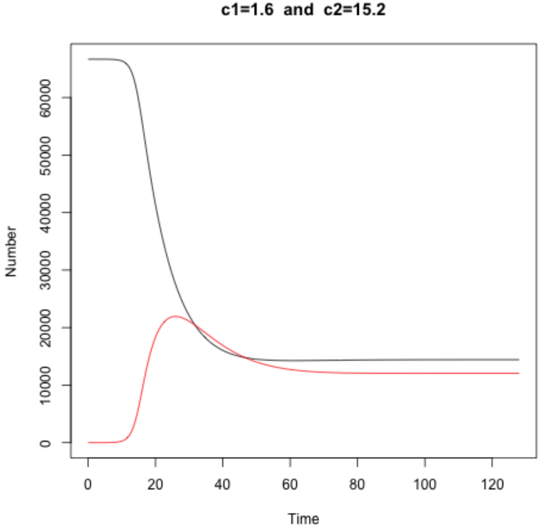

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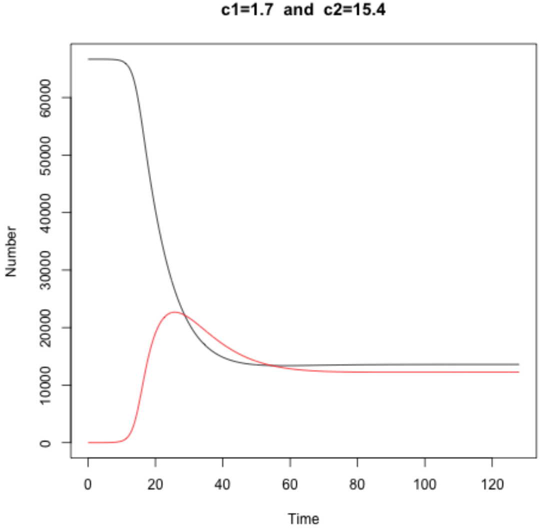

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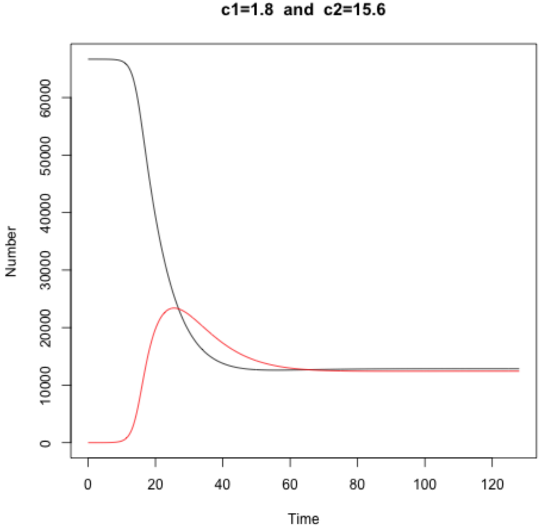

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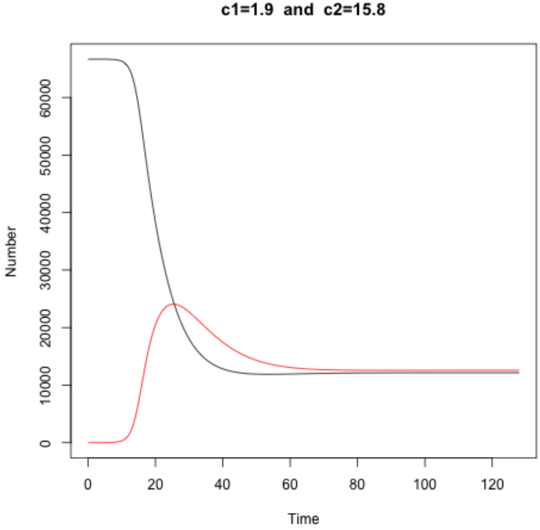

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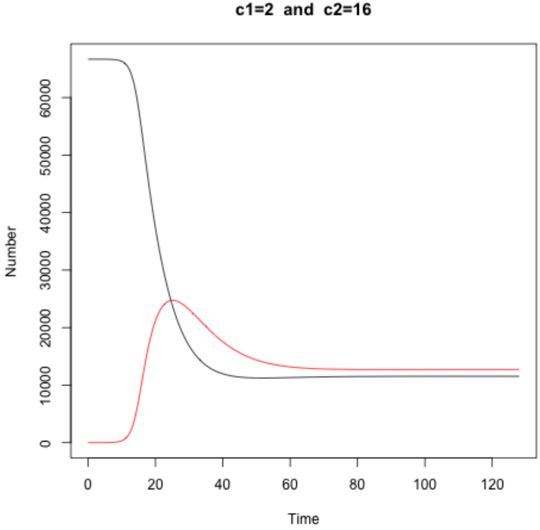

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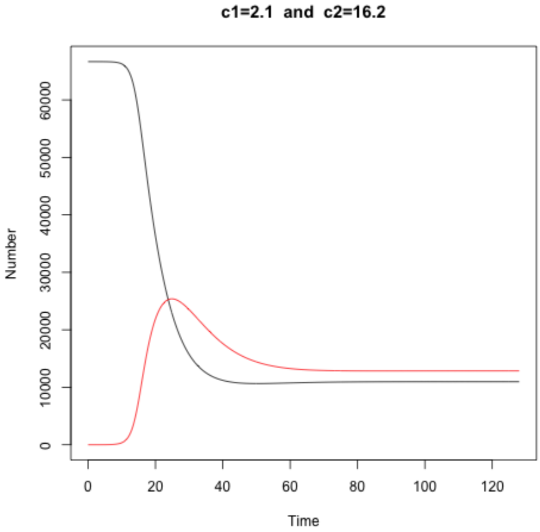

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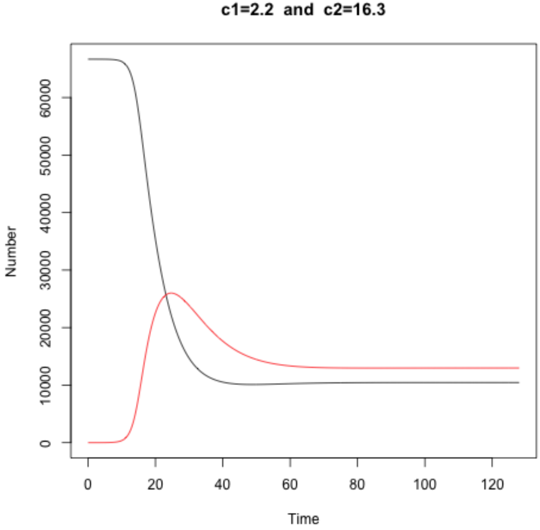

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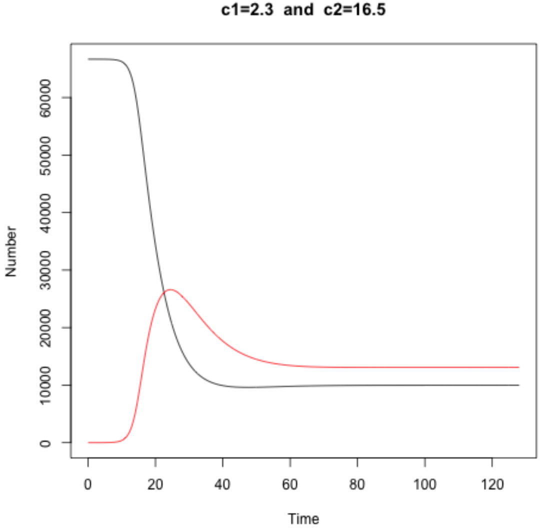

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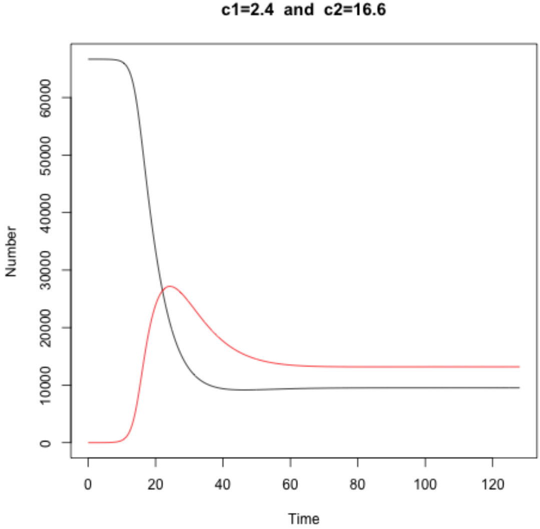

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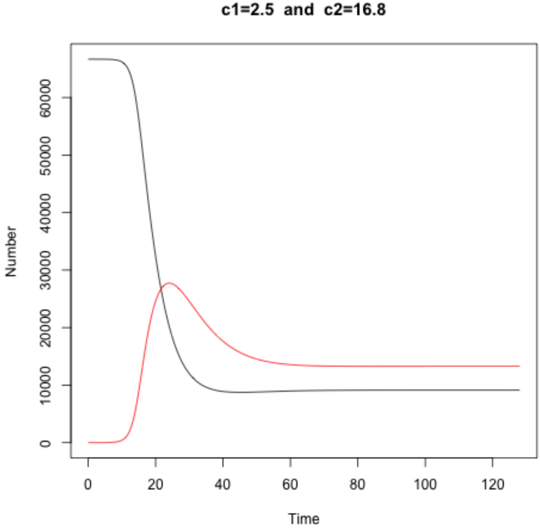

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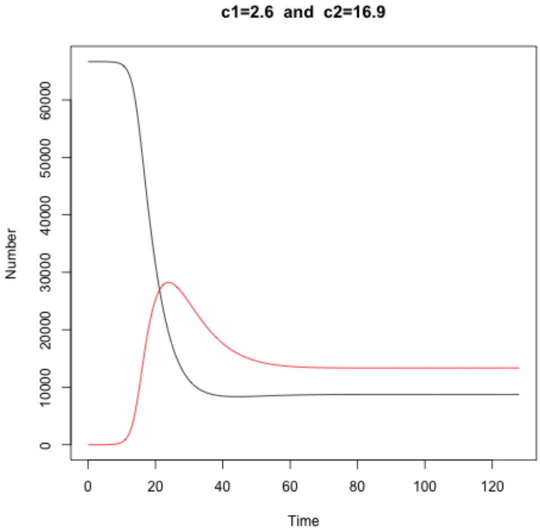

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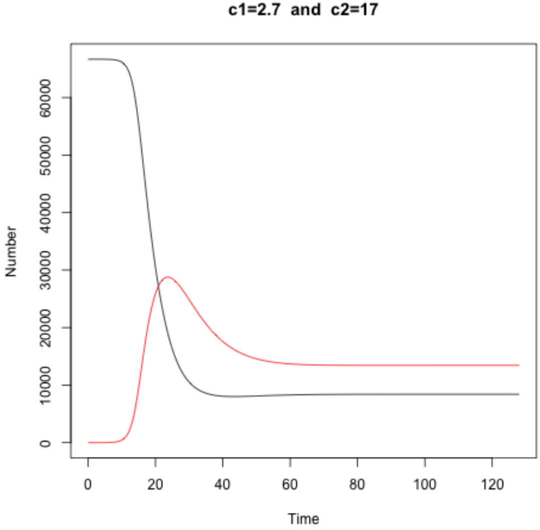

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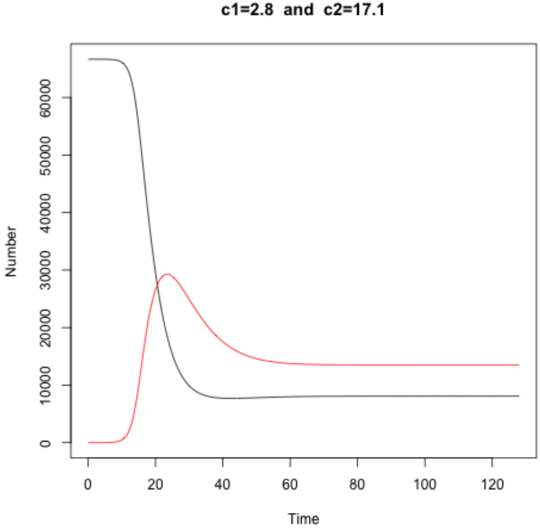

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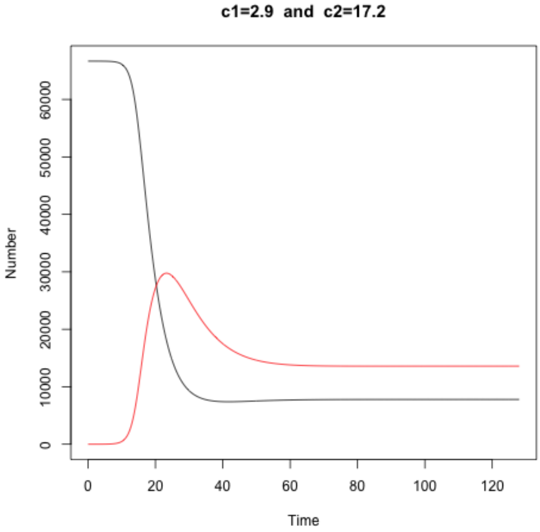

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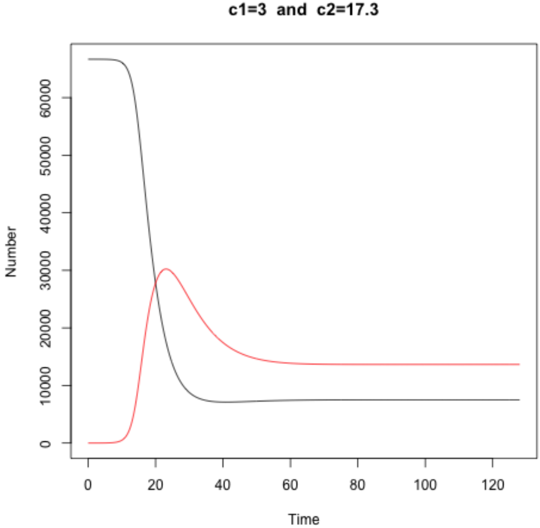

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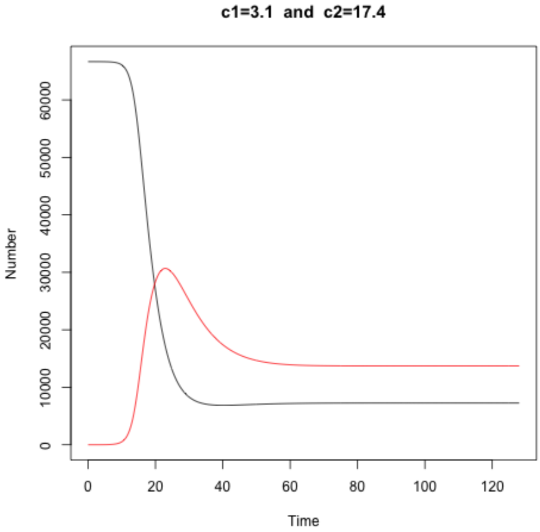

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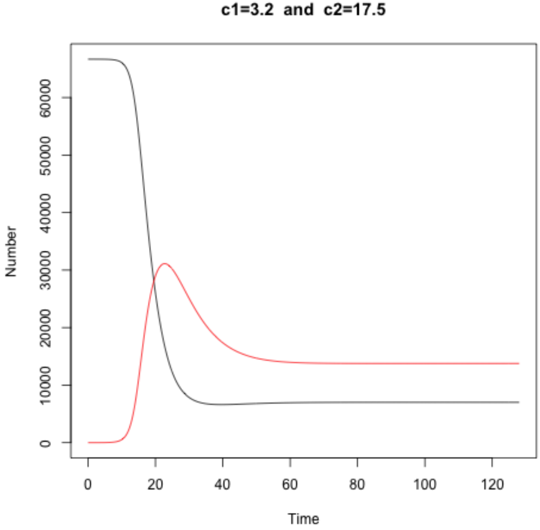

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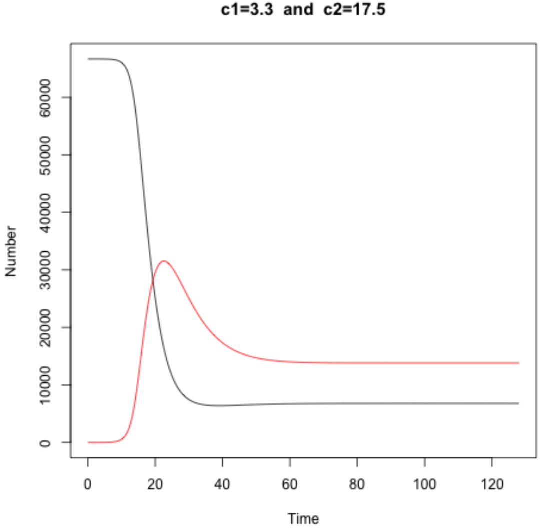

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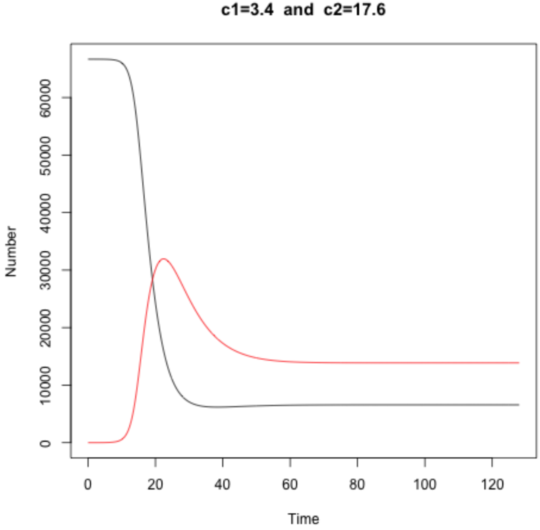

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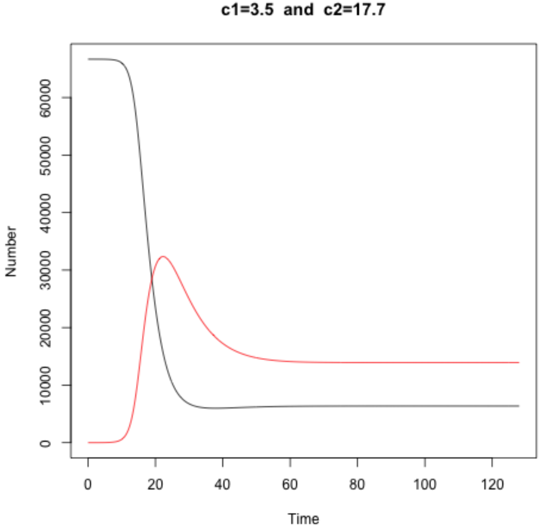

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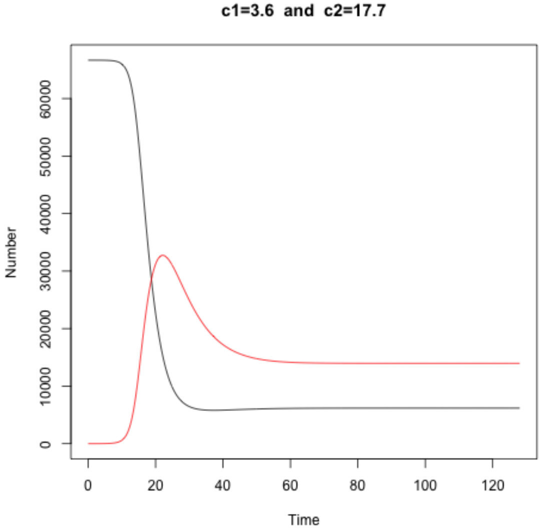

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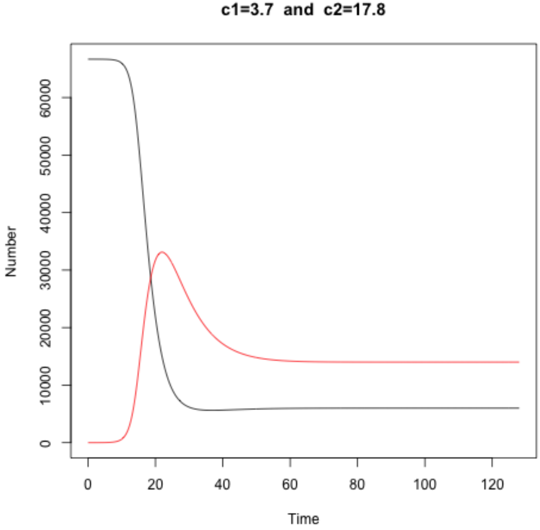

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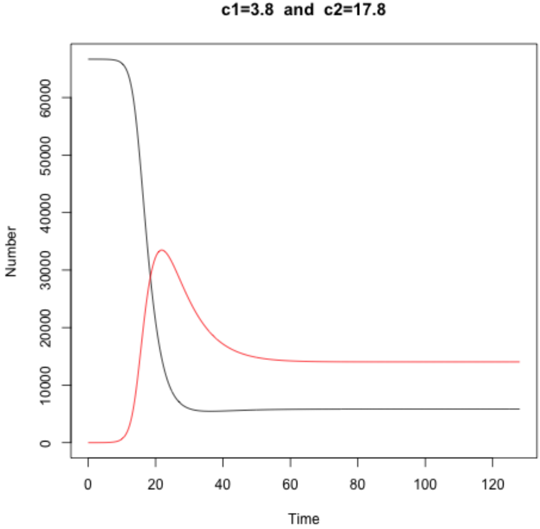

Model

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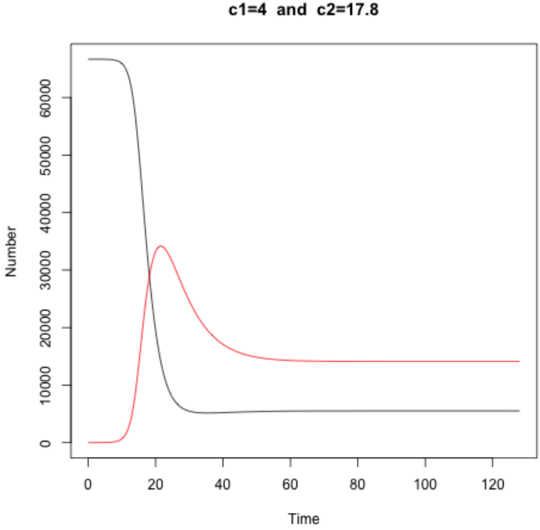

Model

If you wish, code is provided (not for the lab) which will allow you to explore this model further on your own. You may explore the role of q, nonrandom mixing.

Model

The bottom line from this model is that heterogeneity breaks the simple relation between R_0 and equilibrium prevalence. The prevalence can be quite tiny, and yet R_0 high. There can be, seemingly, only a small amount of disease, and yet it can be very hard to get rid of.