Mathematical Modeling of Gonorrhea and HIV Transmission

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Abstract

A deterministic gonorrhea transmission model including males and females is proposed. We find the equilibrium points and their stability. Then, simulate the solution and carry out the phase plane and sensitivity analysis. After that, we update the model by splitting the male group into the homosexual and heterosexual male. And show how this model changes if we want to model HIV transmission at both genders and population levels**.**

1 Introduction

Gonorrhea is a sexually transmitted infection caused by the bacterium Neisseria gonorrhoeae. It mainly spreads through sexual contact and can be cured by antibiotics. There is no evidence of a state of immunity. Gonorrhea has been nationally notifiable since 1924 and remains the second most commonly reported bacterial STI in Canada, after Chlamydia.[1]There were 30874 cases of gonorrhea reported in 2018 and 190% increase in gonorrhea rate from 2009-2018.[2] Hence, it is important to construct a mathematical model to simulate the gonorrhea transmission. In 2019, the estimated rates of reported gonorrhea among MSM (male have sex with male) are 42 times the estimated rate among MSW (men who have sex with women only).[3] As a result, we should also include MSM in the model. And there is another virus, HIV, also can be transmitted by sex act and are much more harmful to people' health. We also want to see how those models change for HIV transmission.

2 Gonorrhea Transmission Model Include Male and Female

2.1 Model and Parameters

$$\mathbf{x' = -a\ x + b\ (f\text{-}x)\ y}$$
$$\mathbf{y' = -c\ y + d\ (g\text{-}y)\ x}$$

Parameters	Meaning	unit
x	The fraction of male who are infected	1
y	The fraction of female who are infected	1
a	The Speed of cure for male	t^{-1}
c	The Speed of cure for female	t^{-1}
b	The Speed of infection from female to male	t^{-1}
d	The Speed of infection from male to female	t^{-1}
f	The fraction of male who are promiscuous	1
g	The fraction of female who are promiscuous	1

ax and cy represent recovered male and female. b (f-x)y represents transmission between uninfected male and infected female. d(g-y)x represents transmission between uninfected females and infected male.

2.2 Assumptions

Nature births and deaths are not considered. Mother to fetus transmission is not considered. And we assume that b and d are constant. Any situation that will have significant influence on it will not be considered. For example, using condom, second time infection and covid-19, which could decrease the infection rate significantly.

2.3 Solution

2.3.1 Equilibrium Points and Stability

There two possible equilibrium points are (x_1^*,y_1^*)=(0,0) and (x_2^*,y_2^*)=$\left(\frac{bdfg-ac}{d(a+bg)}, \frac{bdfg-ac}{b(c+df)}\right)$.

We find that bdfg-ac is the critical value, when bdfg-ac<0, the equilibrium point (x_2^*,y_2^*) does not exist since all our parameters should be larger than zero. Based on critical value, we have two cases:

The Jacobian matrix $J(x^*,y^*) = \begin{pmatrix} -a-by & b(f-x) \\ d(g-y) & -c-dx \end{pmatrix}$

Case1: $bdfg-ac<0$, there is only one equilibrium point $(x_1^*, y_1^*)=(0,0)$.

$trJ(0,0) = -(a+c)<0;\ det(0,0)=ac-bdfg<0 \rightarrow (x_1^*, y_1^*)$ is stable.

Case2: $bdfg-ac>0$, there is an coexistence of equilibrium points (x_1^*, y_1^*) and (x_2^*, y_2^*).

$trJ(x_1^*, y_1^*) = -(a+c)<0;\ det(x_1^*, y_1^*)=ac-bdfg>0. \rightarrow (x_1^*, y_1^*)$ is unstable.

$$trJ\left(x_2^*, y_2^*\right) = -\left(a+c\right)-\left(\frac{bdfg-ac}{c+df}\right)-\left(\frac{bdfg-ac}{a+bg}\right)<0.$$

$$det\left(x_2^*, y_2^*\right) = \ldots = \left(a+\frac{bdfg-ac}{a+bg}\right)+\left(c+\frac{bdfg-ac}{c+df}\right)+\left(\frac{bdfg-ac}{c+df}\right)\left(\frac{bdfg-ac}{a+bg}\right)>0 \rightarrow (x_2^*, y_2^*) \text{ is stable.}$$

We can conclude that there will be a gonorrhea epidemic when bdgf-ac>0.

2.3.2 Numerical Value for Parameters

First, I would like to introduce some data for those parameters in this model. The transmission rate from male to female is approximately 50% per sex act and the transmission rate from female to male is approximately 20% per sex act.[4] It may take up to two weeks for people to cure. And recommend attending a follow-up appointment a week or two after treatment to see if you're clear of infection.[5]According to some Ceftriaxone, Azithromycin and Cefixime clinic effectiveness data, the cure rate is approximately 95%.[6] Table 1 comes from the National Survey of Family Growth (NSFG), which surveyed over 13,000 individuals in the U.S aged 15 to 44 between 2006 and 2008.[7] We count having more than six lifetime partners as promiscuous. Then, the fraction of promiscuous for males and females are f=0.427 and g=0.255 respectively.

Number of Partners	Percentage of Men Reporting This Number	Percentage of Women Reporting This Number
0	9.6%	8.6%
1	12.5%	22.5%
2	8.0%	10.8%
3-6	27.2%	32.6%
7-14	19.5%	16.3%
15 or more	23.2%	9.2%

Table 1

Here are some assumptions for numerical simulation: Take one year as the time unit, then t for one day is 1/365. Promiscuous people have one sex act ever two days. The cure time is 21 days, which include two weeks of treatment plus one week of follow-up check.

$$a=c=\frac{\frac{0.95}{21}}{\frac{1}{365}}\approx 16.5,\ b=\frac{\frac{0.2}{2}}{\frac{1}{365}}=36.5,\ d=\frac{\frac{0.5}{2}}{\frac{1}{365}}=91.25$$

2.3.3 Phase Plane Analysis

I used the pplane10.m function in MATLAB to obtain the phase plane, equilibrium, and sample solutions. From Figure1, we can see that all the points move to the stable equilibrium point (0.0384, 0.0447). Figure2 and figure3 are the plots for two sample solutions, we can observe that they converge to the value of stable equilibrium point gradually no matter which value it starts with.

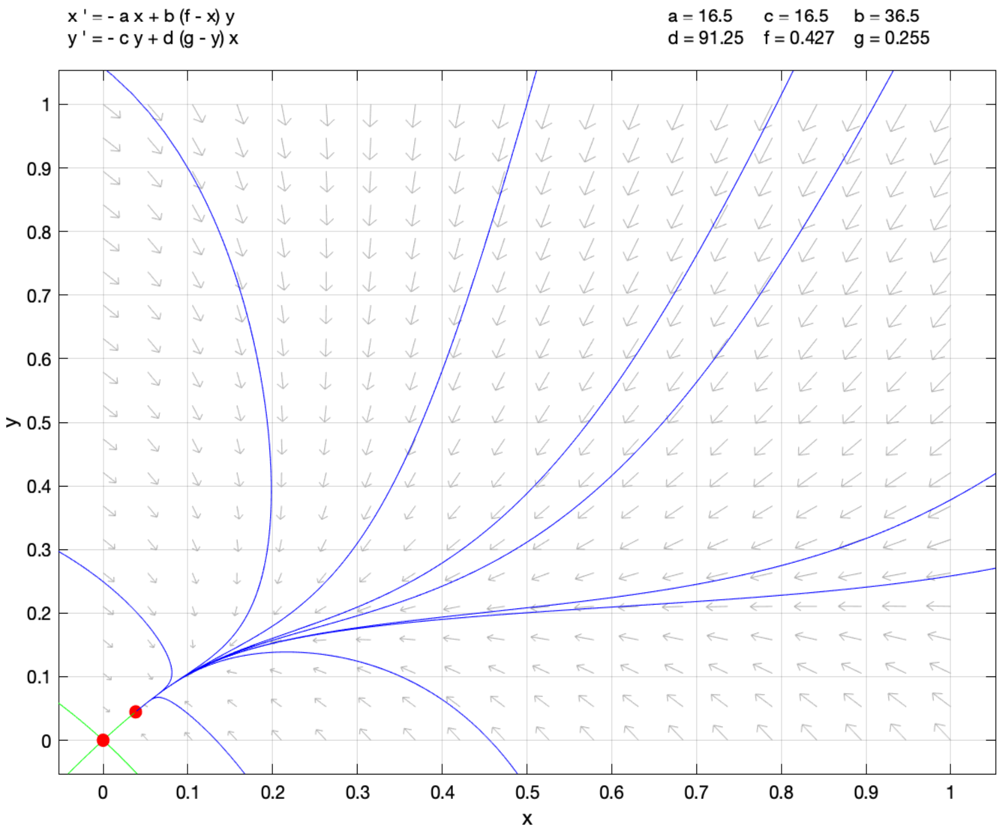


Figure 1

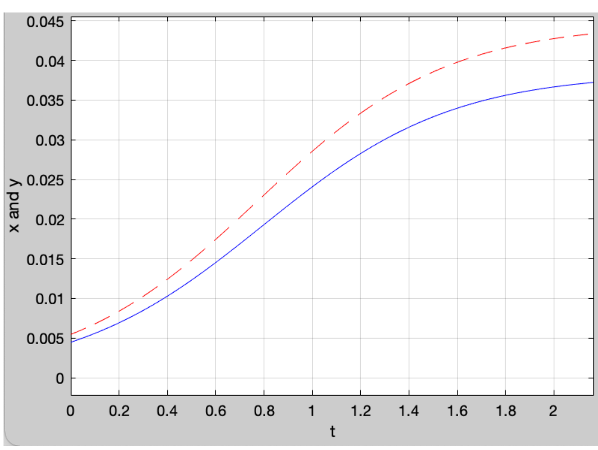


Figure 2

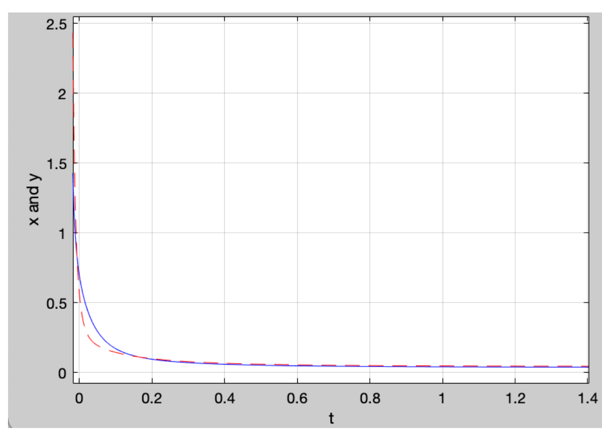


Figure 3

2.3.4 Sensitivity Analysis

For case 2, compute the normalized forward sensitivity indices of fraction of male and female who are infected at the stable equilibrium point (x_2^*,y_2^*)= (0.0384, 0.0447) with respect to their parameters. The results are shown as follows.

$$\gamma_a^{x^*} = \frac{-abg(c+df)}{(a+bg)(bdfg-ac)}, \gamma_b^{x^*} = \frac{abg(c+df)}{(a+bg)(bdfg-ac)}, \gamma_f^{x^*} = \frac{bdfg}{(bdfg-ac)}$$

$$\gamma_c^{y^*} = \frac{-cdf(a+bg)}{(c+df)(bdfg-ac)}, \gamma_d^{y^*} = \frac{cdf(a+bg)}{(c+df)(bdfg-ac)}, \gamma_g^{y^*} = \frac{bdfg}{(bdfg-ac)}$$

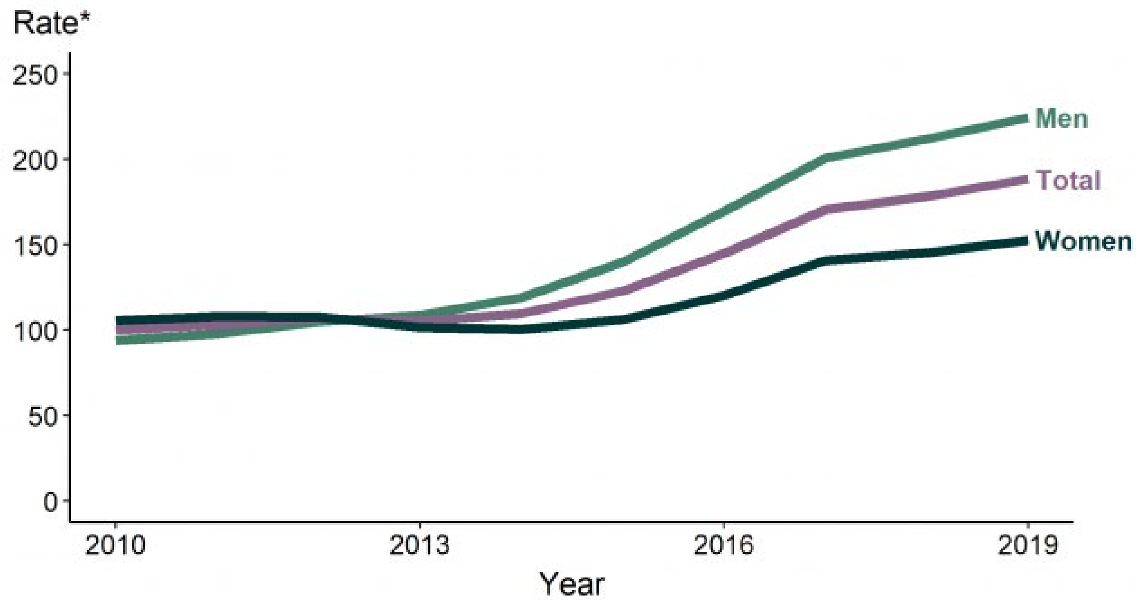
$$\gamma_a^{x^*} = -3.65,\ \gamma_b^{x^*} = 3.65,\ \gamma_f^{x^*} = 4,\ \gamma_c^{y^*} = -3.3,\ \gamma_d^{y^*} = 3.3,\ \gamma_g^{y^*} = 4$$

Therefore, the x is positively related with b and f, and negatively related with a. And y is positively related with d and g, and negatively related with c. The absolute values of all sensitivity indexes are relatively large, which means that x and y are sensitive to all their corresponding parameters. Since the magnitude of the sensitivity index of f and g are the largest, we can deduce that the fraction of promiscuous has larger effects on the fraction of infection.

2.4 Results and Discussion

The results of my simulation are 3.84% for males and 4.47% for females. As of 2012, Gonorrhea affects about 0.6% of men and 0.8% of women globally.[8] From figure4 we can observe that there is approximately a 120% increase in men and a 50% increase in women from 2012 to 2019. Hence, the estimation of the fraction of infection for males and females in 2019 would be 1.32% and 1.2%. My simulation results are three to four times the estimation.

Figure 4: Gonorrhea-Rates of Reported Cases by Sex, United States, 2010-2019.[3]



2.5 Advice on Control Gonorrhea Epidemics

In addition to those general advice, i.e., using condom and keep one sex partner, I want to give some advice for female particularly. Up to 80% of females can be symptomatic when they are infected.[9] The main symptoms are vaginal discharge, lower abdominal pain, or pain with sexual intercourse, which is similar to vaginal infection.[10]When symptoms occur, women are more likely to use over-the-counter medications to treat themselves, which can mask the gonorrhea and delay the diagnosis. As a result, I suggest female have periodic physical examination, i.e., do pap test every three years if you have sex act. And let your sex partner also do a gonorrhea test to prevent you from a second time infection.

3 Gonorrhea transmission models including homosexual male

3.1 Model and Parameters

$$y' = -c\,y + d\,(g-y)\,x$$
$$x' = -a\,x + b\,(f-x)\,y+kz$$
$$z' = -a\,z+ h\,(i-z)\,z-kz$$

Parameters	Meaning	unit
x	The fraction of heterosexual male who are infected	1
z	The fraction of homosexual male who are infected	1
h	The Speed of infection from MSM	t^{-1}
i	The fraction of homosexual male who are promiscuous	**1**
k	Net transmission speed from homosexual male to heterosexual male	t^{-1}

We assume there is a transmission between a heterosexual males and homosexual males, which means they change their sexual orientation. Since only a few people change their sexual orientation and the transformation occurs over a relatively long period of time. The k would be a very small number when we talk about the speed.

3.2 Equilibrium points and stability

We have two solutions for z is 0 and $\frac{hi-a-k}{h}$ and two critical values $\frac{hi-a-k}{h}$ and bdfg-ac. Based on that, we have four cases:

Cases1:$\frac{hi-a-k}{h}$ <0 and bdfg-ac<0, There is only one stable equilibrium point (0,0,0)

Case 2:$\frac{hi-a-k}{h}$ <0 and bdfg-ac>0, There is two coexistence equilibrium points:(0,0,0) is unstable and $(\frac{bdfg-ac}{b(c+df)}, \frac{bdfg-ac}{d(a+bg)}, 0)$ is stable.

Case 3:$\frac{hi-a-k}{h}$ >0 and bdfg-ac<0 and let $e = \frac{k(hi-a-k)}{h}$.

There is two coexistence equilibrium points: unstable (0,0,0) and stable

$$(\frac{(bdfg-ac-de)+\sqrt{(bdfg-ac-de)^2+4bdeg(c+df)}}{2b(c+df)},\frac{c(bdfg-ac-de)+c\sqrt{(bdfg-ac-de)^2+4bdeg(c+df)}}{d(bdfg+ac+de+2bcg)-d\sqrt{(bdfg-ac-de)^2+4bdeg(c+df)}},\frac{e}{k})$$

Case 4:$\frac{hi-a-k}{h}$ >0 and bdfg-ac>0. There is three coexistence equilibrium points: points (0,0,0) and $(\frac{bdfg-ac}{b(c+df)},\frac{bdfg-ac}{d(a+bg)},0)$ are unstable, and the point below is stable

$$\left(\frac{(bdfg-ac-de)+\sqrt{(bdfg-ac-de)^2+4bdeg(c+df)}}{2b(c+df)},\frac{c(bdfg-ac-de)+c\sqrt{(bdfg-ac-de)^2+4bdeg(c+df)}}{d(bdfg+ac+de+2bcg)-d\sqrt{(bdfg-ac-de)^2+4bdeg(c+df)}},\frac{e}{k}\right)$$

3.3 Numerical Simulation

The most relevant data I found are listed below. There are 8% of males were exclusively homosexual for at least three years.[11] The probability of a homosexual man contracting gonorrhea by having a single sex act is estimated up to 25%.[12] Hence, we assume h=0.25*365/2=45.625 and k=0.08/3=0.027. And we assume the fraction of promiscuous are the same for a heterosexual and homosexual male. The simulation results for female, heterosexual male and homosexual male are 4.5%, 6% and 3.9%.

4.HIV Transmission Models Including Homosexual Male

4.1 Model at Gender Level

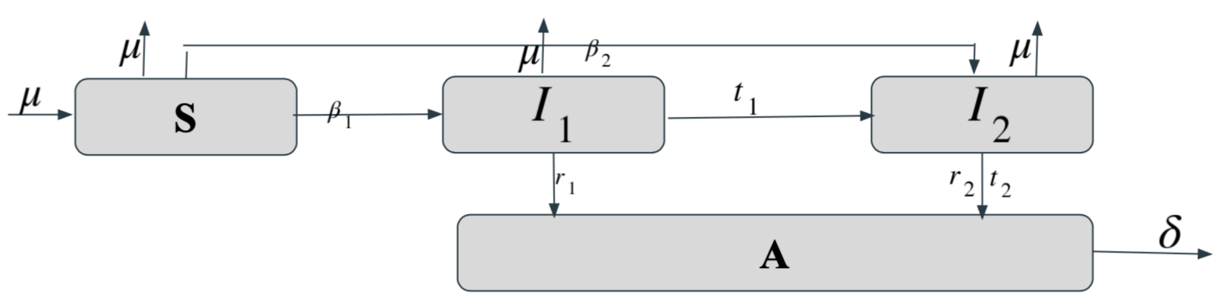
There is no effective cure for HIV. However, as of 2018, nearly 13,000 people with AIDS (stage 3 of HIV) in the United States die each year.[13] Hence, we replace the recovery term with AIDS-related death. HIV has three stages. In stage 1, some people have flu-like symptoms.[14] In stage 2, people may not have any symptoms; Without taking HIV medicine, this period may last a decade or longer.[14] For people in stages 1 and 2, they may not realize they carry the HIV virus. Then, they have the possibility to infect other people. If they have already been diagnosed or entered stage 3, most of them would use strict protective measures or not have sex act. In this case, the probability of infecting other people become extremely low, and we need to remove them from the infectious group.

$$y' = -c\,y + d\,(g-y)(x-lx)$$
$$x' = -a\,x + b\,(f-x)(y-ly) + kz$$
$$z' = -a\,z + h\,(i-z)(z-lz) - kz$$

Parameter	Meaning	unit
a	The speed of death for male	t^{-1}
c	The speed of death for female	t^{-1}
l	The Speed of people were diagnosed or have entered the stage 3 of HIV	t^{-1}

In addition to those assumptions we already have for gonorrhea, we add one more assumption: transmission through injecting drugs is not considered. The equilibrium points and their stability should have the same form as the gonorrhea transmission model with the homosexual male. We only need to replace d with d(1-l), b with b(1-l) and h with h(1-l) for its expression.

4.2 Model at Population Level



$$S' = \mu S_0 - \mu S - \beta_1 I_1 S - \beta_2 I_2 S$$
$$I_1{}' = \beta_1 I_1 S - t_1 I_1 - r_1 I_1 - \mu I_1$$
$$I_2{}' = \beta_2 I_2 S + t_1 I_1 - t_2 I_2 - r_2 I_2 - \mu I_2$$
$$A' = r_1 I_1 + r_2 I_2 + t_2 I_2 - \delta A$$

Parameter	Meanings	unit
S	Number of Susceptible people	1
I_1	Number of people in stage 1	1
I_2	Number of people in stage 2	1
A	Number of people in stage 3 and people from stage 1 and 2 who has been diagnosed with HIV	1
μ	Natural birth and death speed	t^{-1}
δ	Sum of natural and AIDs related death speed	t^{-1}
β_1	The speed of infection from stage 1 to susceptible people	t^{-1}
β_2	The speed of infection from stage 2 to susceptible people	t^{-1}
t_1	The speed of people' condition transform from stage 1 to stage 2	t^{-1}
t_2	The speed of people' condition transform from stage 2 to stage 3	t^{-1}
r_1	The speed of people in stage 1 were diagnosed	t^{-1}
r_2	The speed of people in stage 2 were diagnosed	t^{-1}

Since the first three equations do not contain A, we can only solve the system of equations for the first three. Because those people in group A have been assumed to not have the ability to infect other people, we do not count them into the total population. N= S+ $\boldsymbol{I_1}$+$\boldsymbol{I_2}$.

5. Future Works

First, we can transform the deterministic gonorrhea transmission model into a stochastic model. Second, we split the male group into heterosexual and homosexual groups in this paper and build the connection between homosexual males and others through the change of sexual orientation. We can try adding the bisexual group to see if the connection between different groups will be strengthened. Finally, try to solve the equilibrium points and their stability of HIV Transmission at population level.

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Appendices

1.Calculation for 2.3.1

Equilibrium points:

$$-ax+b(f-x)y=0 \Rightarrow y=\frac{ax}{b(f-x)},\ plug\ y\ into\ equation\ -cy+d(g-y)x=0$$

$$\Rightarrow \frac{-acx}{b(f-x)}+d(g-\frac{ax}{b(f-x)})x=\frac{-acx+bdfgx-bdgx^2-adx^2}{b(f-x)}=0$$

$$\Rightarrow -(ad+bdg)x^2+(bdfg-ac)x=0$$

$$\Rightarrow\ x_1=0\ or\ x_2=\frac{bdfg-ac}{d(a+bg)}$$

When x=0, y=0; when $x=\frac{bdfg-ac}{d(a+bg)}, f-x=\frac{adf+bdfg+ac-bdfg}{d(a+bg)}=\frac{a(c+df)}{d(a+bg)}$.

$y=\frac{ax}{b(f-x)}=\frac{a(-ac+bdfg)d(a+bg)}{d(a+bg)ba(c+df)}=\frac{bdfg-ac}{b(c+df)}$.

Stability:

trJ(x,y)=-a-by-c-dx

detJ(x,y)=(a+by)(c+dx)-bd(f-x)(g-y)

For point (0,0): trJ(0,0)=-(a+c); detJ(0,0)=ac-bdfg

For point $(\frac{bdfg-ac}{d(a+bg)},\frac{bdfg-ac}{b(c+df)})$: trJ$(\frac{bdfg-ac}{d(a+bg)},\frac{bdfg-ac}{b(c+df)})$=-a-c-$(\frac{bdfg-ac}{(c+df)})$-$(\frac{bdfg-ac}{(a+bg)})$<0.

detJ$(\frac{bdfg-ac}{d(a+bg)},\frac{bdfg-ac}{b(c+df)})$ = $(a+\frac{bdfg-ac}{(c+df)})(c+\frac{bdfg-ac}{(a+bg)})$ - $\frac{ab(c+df)}{d(a+bg)}\frac{cd(a+bg)}{b(c+df)}$

$$=(a+\frac{bdfg-ac}{(c+df)})(c+\frac{bdfg-ac}{(a+bg)})-ac$$

$$=\frac{a(bdfg-ac)}{a+bg}+\frac{c(bdfg-ac)}{c+df}+\frac{(bdfg-ac)^2}{(c+df)(a+bg)}>0$$

2.Calculation for 2.3.4

$$\boldsymbol{\gamma_a^{x^*}=\frac{dx^*}{da}\times\frac{a}{x^*}=\frac{-cd(a+bg)-d(bdfg-ac)}{d^2(a+bg)^2}\frac{ad(a+bg)}{bdfg-ac}}$$

$$\boldsymbol{=\frac{(-acd-bcdg-bd^2fg+acd)a}{d(a+bg)(bdfg-ac)}=\frac{-abg(c+df)}{(a+bg)(bdfg-ac)}}$$

$$\boldsymbol{\gamma_b^{x^*}=\frac{dx^*}{db}\times\frac{b}{x^*}=\frac{d^2fg(a+bg)-dg(bdfg-ac)}{d^2(a+bg)^2}\frac{ad(a+bg)}{bdfg-ac}}$$

$$\boldsymbol{=\frac{ad^2fg+bd^2fg^2-bd^2fg^2+acdg}{d^2(a+bg)^2}\frac{bd(a+bg)}{bdfg-ac}}$$

$$\boldsymbol{=\frac{abd^2fg+abcdg}{(a+bg)d(bdfg-ac)}=\frac{abg(c+df)}{(a+bg)(bdfg-ac)}}$$

$$\boldsymbol{\gamma_f^{x^*}=\frac{dx^*}{df}\times\frac{f}{x^*}=\frac{bg}{a+bg}\frac{df(a+bg)}{(bdfg-ac)}=\frac{bdfg}{bdfg-ac}}$$

$$\gamma_c^{y^*} = \frac{dy^*}{dc} \times \frac{c}{y^*} = \frac{-ab(c+df) - b(bdfg - ac)}{b^2(c+df)^2} \frac{bc(c+df)}{bdfg - ac}$$
$$= \frac{(-abc - abcf - b^2dfg + abc)c}{b(c+df)(bdfg - ac)} = \frac{-cdf(a+bg)}{(c+df)(bdfg - ac)}$$
$$\gamma_d^{y^*} = \frac{dy^*}{dd} \times \frac{d}{y^*} = \frac{b^2fg(c+df) - bf(bdfg - ac)}{b^2(c+df)^2} \frac{bd(c+df)}{bdfg - ac}$$
$$= \frac{(b^2cfg + b^2df^2g - b^2df^2g + abcf)d}{b(c+df)(bdfg - ac)} = \frac{cdf(a+bg)}{(c+df)(bdfg - ac)}$$
$$\gamma_g^{y^*} = \frac{dy^*}{dg} \times \frac{g}{y^*} = \frac{df}{c+df} \frac{bf(c+df)}{(bdfg - ac)} = \frac{bdfg}{bdfg - ac}$$

3.Calculation for 3.2

Equilibrium points:

$$-az + hiz - hz^2 - kz = 0 \Rightarrow z(-az + hi - hz - k) = 0 \Rightarrow z_1 = 0 \text{ or } z_2 = \frac{hi - a - k}{h}$$
$$\text{when } z = 0, \text{it is the same as calculations for 2.3.1}$$
$$\text{we have two possible Equilibrium points } (y, x, z)$$
$$= (0,0,0) \text{ or } \left(\frac{bdfg - ac}{b(c+df)}, \frac{bdfg - ac}{d(a+bg)}, 0\right)$$

Let $e = k\frac{hi-a-k}{h}$, then we have $-cy + d(g-y)x = 0 \Rightarrow x = \frac{cy}{d(g-y)}$

Plug into the equation:$-ax + b(g-x)y + e = 0$

$$\frac{-acy}{d(g-y)} + \frac{b(dfg - dfg - dfy - cy)y}{d(g-y)} + \frac{de(g-y)}{d(g-y)} = 0$$
$$\Rightarrow -(bdf + bc)y^2 + (bdfg - ac - de)y + deg = 0.$$

$y = \frac{(bdfg-ac-de)+\sqrt{(bdfg-ac-de)^2+4bdeg(df+c)}}{2b(df+c)}$. we only take one root since y should be nonnegative.

$$g - y = \frac{2bdfg + 2bcg - bdfg + ac + de - \sqrt{(bdfg - ac - de)^2 + 4bdeg(df+c)}}{2b(df+c)}$$
$$x = \frac{cy}{d(g-y)}$$
$$= \frac{(bdfg - ac - de) + \sqrt{(bdfg - ac - de)^2 + 4bdeg(df+c)}}{2bdfg + 2bcg - bdfg + ac + de - \sqrt{(bdfg - ac - de)^2 + 4bdeg(df+c)}} \frac{c}{d}$$
$$= \frac{(bdfg-ac-de)+\sqrt{(bdfg-ac-de)^2+4bdeg(df+c)}}{(bdfg+ac+de)+2bcg-\sqrt{(bdfg-ac-de)^2+4bdeg(df+c)}} \frac{c}{d}$$

Stability:

$$J = \begin{pmatrix} -c-dx & d(g-y) & 0 \\ b(f-x) & -a-by & k \\ 0 & 0 & hi-a-k-2hz \end{pmatrix}$$

For point (0,0,0):

$$\det(J-\lambda I) = -c-\lambda\begin{vmatrix} -a-\lambda & k \\ 0 & hi-a-k-\lambda \end{vmatrix} - dg\begin{vmatrix} bf & k \\ 0 & hi-a-k-\lambda \end{vmatrix}$$

$$= (c+\lambda)(a+\lambda)(hi-a-k-\lambda) - bdfg(hi-a-k-\lambda)$$

$$= (hi-a-k-\lambda)\left(\lambda^2+(a+c)\lambda+ac-bdfg\right)=0$$

$$\lambda_1 = hi-a-k,\ \lambda_2 = \frac{-(a+c)+\sqrt{(a+c)^2+4(bdfg-ac)}}{2}, \lambda_3 = \frac{-(a+c)-\sqrt{(a+c)^2+4(bdfg-ac)}}{2}$$

For point $(\frac{bdfg-ac}{b(c+df)}, \frac{bdfg-ac}{d(a+bg)}, 0)$:

$$\det(J-\lambda I) = \left(c+\frac{bdfg-ac}{a+bg}+\lambda\right)\left(a+\frac{bdfg-ac}{c+df}+\lambda\right)(hi-a-k-\lambda) - \frac{cd(a+bg)}{b(c+df)}\frac{bd(c+df)}{d(a+bg)}(hi-a-k-\lambda)$$

$$= (hi-a-k-\lambda)\left(\lambda^2+\left(a+c+\frac{bdfg-ac}{a+bg}+\frac{bdfg-ac}{c+df}\right)\lambda+\left(c+\frac{bdfg-ac}{a+bg}\right)\left(a+\frac{bdfg-ac}{c+df}\right)-cd\right)$$

$$\lambda_1 = hi-a-k, \lambda_2,\lambda_3 = \frac{-\left(a+c+\frac{bdfg-ac}{a+bg}+\frac{bdfg-ac}{c+df}\right) \pm \sqrt{\left(a+c+\frac{bdfg-ac}{a+bg}+\frac{bdfg-ac}{c+df}\right)^2 - 4\left(\left(c+\frac{bdfg-ac}{a+bg}\right)\left(a+\frac{bdfg-ac}{c+df}\right)-cd\right)}}{2}$$

For point $(\frac{(bdfg-ac-de)+\sqrt{(bdfg-ac-de)^2+4bdeg(df+c)}}{2b(df+c)}, \frac{(bdfg-ac-de)+\sqrt{(bdfg-ac-de)^2+4bdeg(df+c)}}{(bdfg+ac+de)+2bcg-\sqrt{(bdfg-ac-de)^2+4bdeg(df+c)}}\frac{c}{d}, \frac{e}{k})$:

$$\det(J-\lambda I) = (c+dx+\lambda)(a+by+\lambda)(hi-a-k-2hz-\lambda) - bd(g-y)(f-x)(hi-a-k-2hz-\lambda)$$

$$= (hi-a-k-2hz-\lambda)\left(\lambda^2+(a+c+by+dx)\lambda+(c+dx)(a+by)-bd(g-y)(f-x)\right)$$

$$= (hi-a-k-2hz-\lambda)\left(\lambda^2+(a+c+by+dx)\lambda+d(a+bg)x+b(c+df)y+(bdfg-ac)\right)$$

$$\lambda_1 = hi-a-k-2hz = -(hi-a-k)$$

$$\lambda_2,\lambda_3 = \frac{-(a+c+by+dx)\pm\sqrt{(a+c+by+dx)^2-4(d(a+bg)x+b(c+df)y+(bdfg-ac))}}{2}$$

4. R code for 3.3

```
point=function(a,b,c,d,f,g,h,i,k){
  e=k*(h*i-a-k)/h
  z=(h*i-a-k)/h
  t1=((b*d*f*g-a*c-d*e)+sqrt((b*d*f*g-a*c-d*e)^2+4*b*d*e*g*(c+d*f)))
  k1=(2*b*(c+d*f))
  t2=c*((b*d*f*g-a*c-d*e)+sqrt((b*d*f*g-a*c-d*e)^2+4*b*d*e*g*(c+d*f)))
  k2=d*(b*d*f*g+a*c+d*e-sqrt((b*d*f*g-a*c-d*e)^2+4*b*d*e*g*(c+d*f)))
  y=t1/k1
  x=t2/k2
  return(c(y,x,z))
  }
point(16.5,36.5,16.5,91.25,0.427,0.255,42.625,0.427,0.027)
```