Mathematical Methods in Biology

Part 4

Solutions to the homework exercises (spring 2016)

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Exercise 2. Since $I \ll N$, the dynamics of the epidemic is given by

$$\frac{dI}{dt} = \beta(N - I)I - vI \approx \beta NI - vI = (\beta N - v)I$$

so that the number of infected decreases (from an initially small value towards zero) when $\beta N - v < 0$, which is the same as $N < v/\beta$.

Exercise 3. Only unvaccinated hosts can spread the disease, hence in the condition $N < v/\beta$ obtained in exercise 2, we need to replace N with the number of unvaccinated hosts. If a fraction p of hosts is vaccinated, then the number of unvaccinated hosts is $(1 - p)N$, so that the condition for no outbreak is $(1 - p)N < v/\beta$, which can be rearranged into $p > 1 - v/\beta N$.

Exercise 5. At the trivial equilibrium, all individuals are susceptible. At the nontrivial equilibrium $\hat{I} = N - v/\beta$, the number of susceptibles is $\hat{S} = N - \hat{I} = v/\beta$. According to the equation

$$\frac{dI}{dt} = \beta SI - vI = (\beta S - v)I$$

the more susceptibles (S) are, the better the number of infecteds grows. When S is greater than v/β, the number of infecteds increases (and hence the population is not at equilibrium); when S is less than v/β, the number of infecteds declines (and hence the population is again not at equilibrium). Between these two situations, the population is at equilibrium when the number of susceptibles is just reaches, but does not exceed, the critical number of susceptibles that separates the growth and decline of infecteds. And because at the very beginning of the epidemic every host is susceptible, the critical number of susceptibles coincides with the critical population size above which an epidemic outbreak can occur.

Exercise 8. The only equilibrium is $\hat{x} = uk/(c - u)$, which is positive (biologically possible) if $u < c$, i.e., if the intake is less than the maximum speed of removal. $f'(\hat{x}) = -ck/(k + \hat{x})^2$ is always negative, hence the equilibrium is stable.

Exercise 9. (a) The model can have three equilibria, the trivial equilibrium $\hat{x}_1 = 0$ and two nontrivial equilibria

$$\hat{x}_{2,3} = \frac{bc_0 \pm \sqrt{(bc_0)^2 - 4bkd}}{2bk}$$

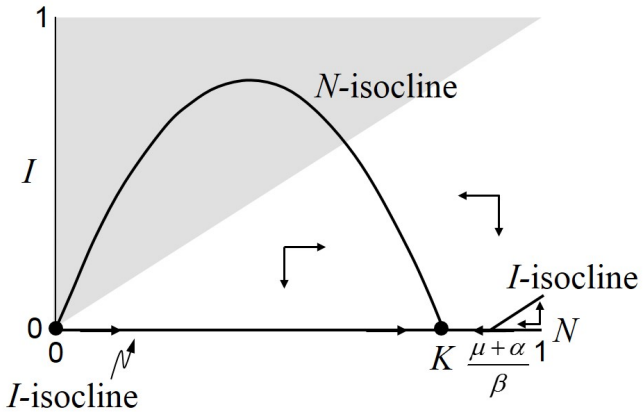
(b) $f'(0) = -d < 0$, the trivial equilibrium is stable for all positive decay rate d. It follows that the smaller of $\hat{x}_{2,3}$ (the "$-$" root) is unstable and the greater (the "$+$" root) is stable.

(c) There is a fold bifurcation where the expression under the square root in $\hat{x}_{2,3}$ becomes zero and thus the two nontrivial equilibria collide and disappear. This happens at

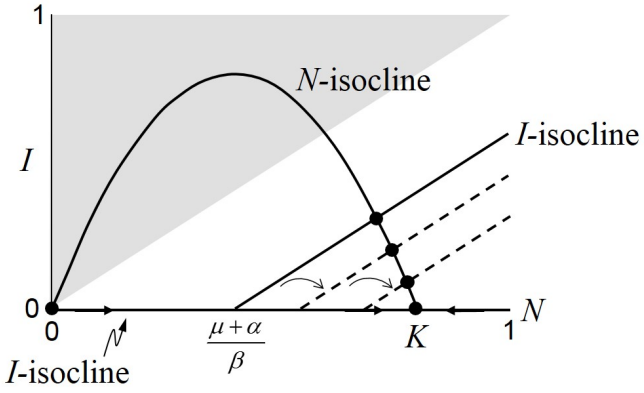
$d = bc_0^2/4k$.

(d) $f'(0) = ac_0 - d$, the trivial equilibrium is unstable for small values of d (where $ac_0 > d$) and there is a transcritical bifurcation at $d = ac_0$.

Exercise 18. The figure below shows the phase plane of the SI-model when $\frac{\mu+\alpha}{\beta} > K$. The N- and I-isoclines do not intersect at positive densities, i.e., the model has no endemic equilibrium. Since the vertical arrow is down in the neighbourhood of the disease-free equilibrium K, the infection cannot invade the disease-free host population. K is also stable with respect to changes of N (the horizontal arrows on the horizontal axis point to K), so that K is a stable equilibrium, and the only stable equilibrium in the case $\frac{\mu+\alpha}{\beta} > K$.



Exercise 19. The N-isocline does not depend on β, hence the parabola remains the same. As β decreases, $\frac{\mu+\alpha}{\beta}$ increases and therefore the I-isocline shifts to the right (dashed lines in the figure below). The endemic equilibrium, at the intersection of the isoclines, slides down on the parabola, and eventually crosses the disease-free equilibrium K when $\frac{\mu+\alpha}{\beta} = K$. When this has happened, the phase plane becomes like the figure obtained in the previous exercise. Before the two equilibria cross (i.e., when $\frac{\mu+\alpha}{\beta} < K$), the endemic equilibrium is stable and the disease-free equilibrium is unstable; when these two equilibria cross each other, they also exchange stability so that for $\frac{\mu+\alpha}{\beta} > K$, the disease-free equilibrium is stable (as in the previous exercise) and the equilibrium that has left the positive part of the phase plane is unstable (this is not shown because non-positive equilibria are biologically not relevant).



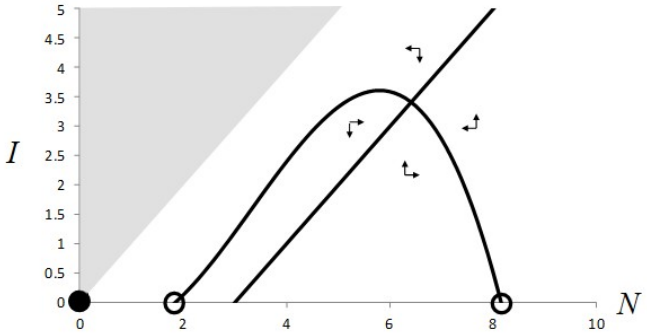
Exercise 21. The N-isocline is the same as in the SI model with mass action (Figure 3 of the lecture notes). The I-isocline is given by the equation $I = [1 - (\mu + \alpha)/\beta]N$, i.e., it is a straight line through the origin. If the slope of the N-isocline at the origin is steeper than the slope of the I-isocline, which is the case when $(b-\mu)/\alpha > 1-(\mu+\alpha)/\beta$, then there is an interior equilibrium. If however the opposite inequality holds, then the only biologically meaningful equilibrium is the origin, and it is stable. In this case, the infection drives the host population extinct.

Exercise 22. (a) One equilibrium or three equilibria depending on whether the quantity under the square root is positive:

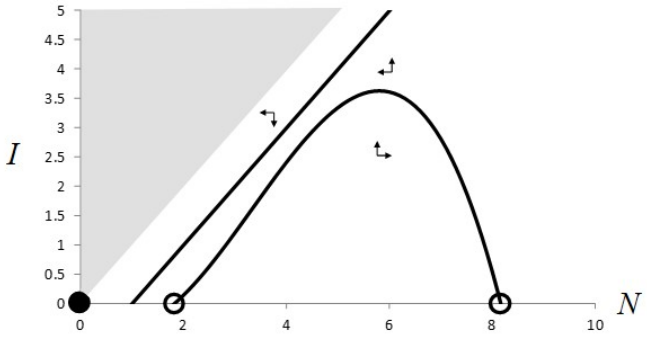
- the trivial equilibrium at $N = 0$ is stable;
- $N = \frac{M}{2} - \frac{\sqrt{M(bM-4\mu)}}{2\sqrt{b}}$ is unstable;
- $N = \frac{M}{2} + \frac{\sqrt{M(bM-4\mu)}}{2\sqrt{b}}$ is stable.

The dots on the horizontal axes of the figures below show the three equilibria above. Note that their stability can be different when the disease is present: an equilibrium that is stable with respect to perturbations of N (horizontally) need not be stable with respect to the introduction of some infected (perturbation vertically). the figures mark stable equilibria with filled dots and unstable equilibria with empty dots.

(b) $\beta = 2$: there is an interior equilibrium at the intersection of the isoclies. Unfortunately its stability cannot be determined from the graphical analysis (and therefore no filled/empty dot is drawn).



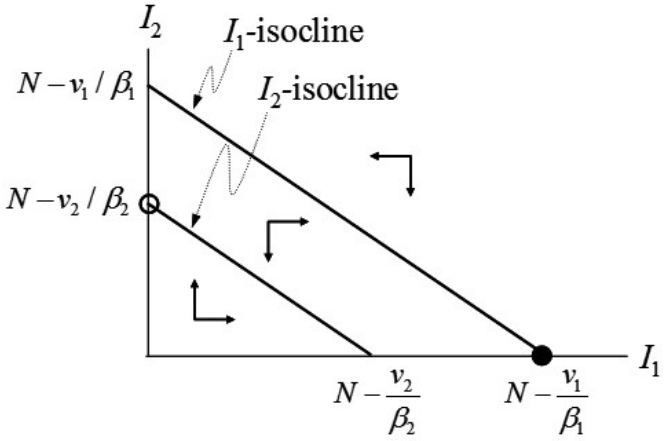
(c) $\beta = 6$: no interior equilibrium, an outbreak of the disease leads to the extinction of the host population.



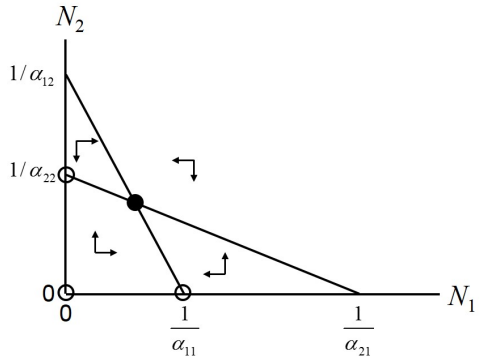
Exercise 23. Using $S = N - I_1 - I_2$ the model can be written as

$$\begin{aligned} \frac{dI_1}{dt} &= [\beta_1(N - I_1 - I_2) - \nu_1]I_1 \\ \frac{dI_2}{dt} &= [\beta_2(N - I_1 - I_2) - \nu_2]I_2 \end{aligned}$$

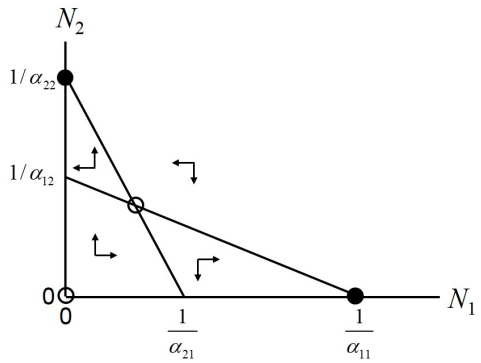
The I_1-isoclines are the straight line $I_2 = N - I_1 - \nu_1/\beta_1$ and the vertical axis $I_1 = 0$; the I_2-isoclines are the straight line $I_2 = N - I_1 - \nu_2/\beta_2$ and the horizontal axis $I_2 = 0$ (see the figure below). The two nontrivial isoclines are parallel to each other. Hence the isoclines do not intersect and the model has no interior equilibrium unless ν_1/β_1 happens to be equal to ν_2/β_2; in this exceptional case $\nu_1/\beta_1 = \nu_2/\beta_2$, the two isoclies coincide and all points on the isocline are equilibria. If $\nu_1/\beta_1 < \nu_2/\beta_2$, then the I_1-isocline is above the I_2-isocline as shown in the figure, and all trajectories go to the equilibrium on the boundary where $I_2 = 0$. Rearranging the inequality we obtain that if $\beta_1/\nu_1 > \beta_2/\nu_2$, then strain 2 of the pathogen goes extinct. In the opposite case, the position of the isoclines is reversed and strain 1 goes extinct.



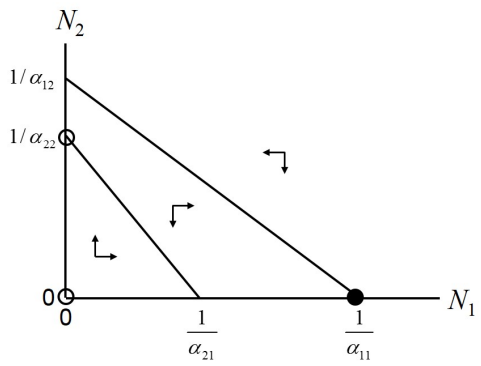
Exercise 24. (i) $\alpha_{11} > \alpha_{21}$ and $\alpha_{22} > \alpha_{12}$: stable interior equilibrium, coexistence (within-species competition is stronger than between-species competition).



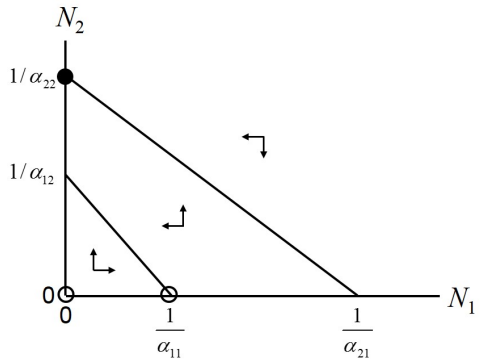
(ii) $\alpha_{11} < \alpha_{21}$ and $\alpha_{22} < \alpha_{12}$: unstable interior equilibrium, the system is bi-stable, i.e., one or the other species goes extinct depending on the initial population densities (between-species competition is stronger than within-species competition)



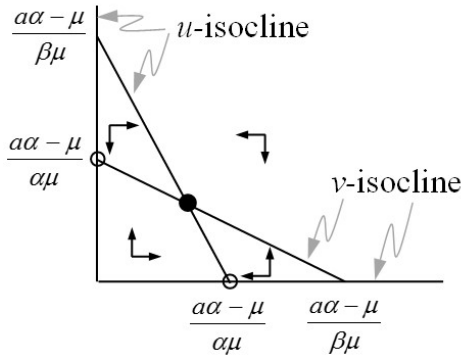
(iii) $\alpha_{11} < \alpha_{21}$ and $\alpha_{22} > \alpha_{12}$: species 1 excludes species 2



(iv) $\alpha_{11} > \alpha_{21}$ and $\alpha_{22} < \alpha_{12}$: species 2 excludes species 1

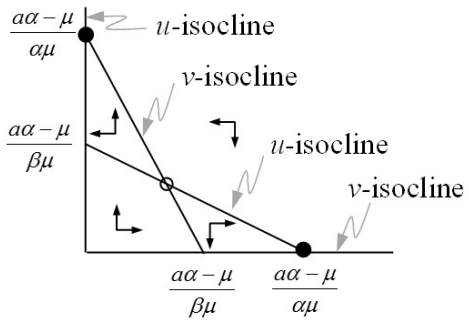


Exercise 25. Assume $a\alpha > \mu$, otherwise all concentrations go to zero.
If $\alpha > \beta$, then the phase plane analysis yields the following figure:



In this case, the system always ends up at the only stable equilibrium (black dot in the middle), hence this is not a genetic switch.

If $\alpha < \beta$, then we obtain



In this case, the interior equilibrium is a saddle point, and there are two stable equilibria on the axes where only one or the other gene is active. This is a genetic switch, which has two stable states.

The system works as a genetic switch if $\alpha < \beta$. Since $\alpha = k_1/k_{-1}$ and $\beta = k_2/k_{-2}$, this condition holds if the regulating sequences bind their inhibitor more strongly than their activator.

Exercise 36. The only equilibrium is at $\hat{x} = a/\mu$, $\hat{y} = ca/\delta\mu$. The Jacobian matrix is

$$\mathbf{J} = \begin{bmatrix} -\mu & 0 \\ c & -\delta \end{bmatrix}$$

which has eigenvalues $\lambda_1 = -\mu$ and $\lambda_2 = -\delta$. Both eigenvalues are negative and therefore the equilibrium is stable.

Exercise 37. The disease-free equilibrium is $\hat{N} = M(b-\mu)/b$, $\hat{I} = 0$. We assume that $b - \mu > 0$ so that the host has a positive disease-free equilibrium. The Jacobian is

$$\mathbf{J} = \begin{bmatrix} b - \mu - 2b\hat{N}/M & -\alpha \\ \beta\hat{I} & \beta\hat{N} - 2\beta\hat{I} - (\mu+\alpha) \end{bmatrix}$$

Substituting $\hat{N}$ and $\hat{I}$ yields

$$\mathbf{J} = \begin{bmatrix} -(b-\mu) & -\alpha \\ 0 & \beta[M(b-\mu)/b] - (\mu+\alpha) \end{bmatrix}$$

The eigenvalues of the Jacobian are $\lambda_1 = -(b-\mu)$ (which is negative since we assumed $b-\mu > 0$) and $\lambda_2 = \beta[M(b-\mu)/b] - (\mu+\alpha)$. The pathogen is viable when the disease-free equilibrium is *not* stable, i.e., when λ_2 is positive. This is likely when the host death rate μ is small; when the density of living sites M is high; and when the host birth rate b is high but the effect of increasing b saturates. Note that the expression in the brackets

$[M(b-\mu)/b]$ is the equilibrium density $\hat{N}$ of the host; M and b affect the outbreak of the disease only through host density, which increases linearly with M but saturates with b because there cannot be more hosts than living sites, however high b is. Of the parameters of the pathogen, high transmission rate β and low virulence α increase λ_2 and therefore make the pathogen viable.

Notice also that $\lambda_2 > 0$ is equivalent to $\beta\hat{N}/(\mu+\alpha) > 1$. An infected hosts dies at a rate $\mu+\alpha$ and therefore the expected time of being infectious is $1/(\mu+\alpha)$ (cf. Part 1, section 2.5). In a population of $\hat{N}$ susceptibles, an infected host makes $\beta\hat{N}$ new infections per unit of time, or on average $\beta\hat{N}/(\mu+\alpha)$ new infections before its own death. If an infected host makes more than one new infections, then the disease spreads.

Exercise 40. If both species are present at equilibrium, then $\hat{N}_1$ and $\hat{N}_2$ are not zero, and the equilibrium densities are determined by the equations

$$\begin{aligned} 1 - \alpha_{11}\hat{N}_1 - \alpha_{12}\hat{N}_2 &= 0 \\ 1 - \alpha_{21}\hat{N}_1 - \alpha_{22}\hat{N}_2 &= 0 \end{aligned}$$

Using these two equalities, the Jacobian becomes

$$\mathbf{J} = \begin{bmatrix} -r_1\alpha_{11}\hat{N}_1 & -r_1\alpha_{12}\hat{N}_2 \\ -r_2\alpha_{21}\hat{N}_1 & -r_2\alpha_{22}\hat{N}_2 \end{bmatrix}$$

(substituting the formulas for $\hat{N}_1$ and $\hat{N}_2$ would not help). The trace of the Jacobian $-r_1\alpha_{11}\hat{N}_1 - r_2\alpha_{22}\hat{N}_2$ is negative when the population densities are positive. The equilibrium is therefore stable if the determinant of the Jacobian is positive, i.e., if

$$r_1 r_2 \hat{N}_1 \hat{N}_2 (\alpha_{11}\alpha_{22} - \alpha_{12}\alpha_{21}) > 0$$

In exercise 24, we found two configurations of the competitive coefficients where both species can be present at equilibrium:
(i) $\alpha_{11} > \alpha_{21}, \alpha_{22} > \alpha_{12}$: in this case the determinant is positive and the equilibrium is stable;
(ii) $\alpha_{11} < \alpha_{21}, \alpha_{22} < \alpha_{12}$: in this case the determinant is negative and the equilibrium is unstable (it is a saddle point, and indeed, the phase plane analysis of exercise 24 shows a saddle point for this case).

Exercise 41. (a) From the second differential equation, we have that $\hat{N} = (\alpha/p)\hat{T}$ must hold at any equilibrium, i.e., either both $\hat{N}$ and $\hat{T}$ are zero or both are positive. This makes perefct sense biologically: the toxin cannot be present without the bacteria, and when bacteria are present, they make some toxin. We consider the nontrivial equilibrium where both $\hat{N}$ and $\hat{T}$ are positive. In this case, dN/dt is zero if $r - cT = 0$ and therefore $\hat{T} = r/c$. Substituting this into $\hat{N} = (\alpha/p)\hat{T}$, we obtain $\hat{N} = \alpha r/pc$.

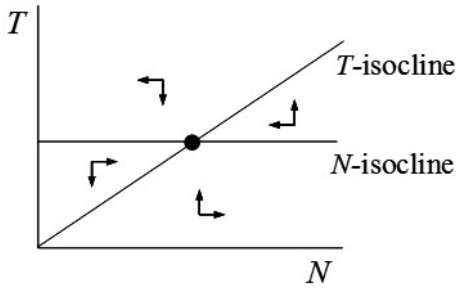
The Jacobian is

$$\mathbf{J} = \begin{bmatrix} r - c\hat{T} & -c\hat{N} \\ p & -\alpha \end{bmatrix} = \begin{bmatrix} 0 & -c\hat{N} \\ p & -\alpha \end{bmatrix}$$

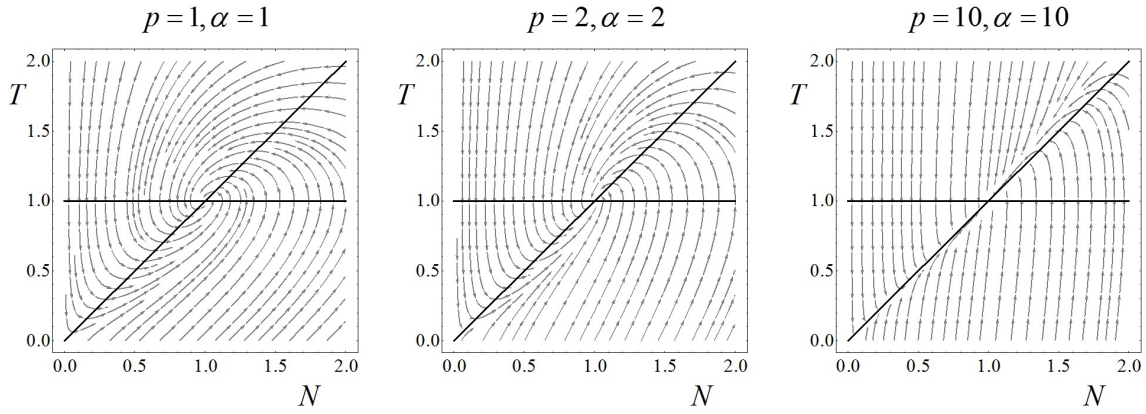
where we could substitute also $\hat{N}$ but it will not make a difference at this step. The trace of this Jacobian $(-\alpha)$ is negative and the determinant $(cp\hat{N})$ is positive, hence the nontrivial equilibrium is stable.

(b) The equilibrium is a focus if the eigenvalues are complex, which happens when $Tr^2 - 4Det = \alpha^2 - 4cp\hat{N} = \alpha^2 - 4\alpha r = \alpha(alpha - 4r)$ is negative (notice that here we had to substitute $\hat{N}$ to get the result in terms of the model parameters). The model exhibits some oscillations before settling at the equilibrium if $\alpha < 4r$, i.e., if the toxin decays only slowly and hence has delayed effect on the bacteria.

(c) The N-isocline is the horizontal line $T = r/c$ and the T-isocline is the straight line $T = (p/\alpha)N$:



The following plots show trajectories for $r = 1, c = 1$ and p, α as shown above the panels. Notice that as the production and decay of the toxin get faster relative to the growth of the bacteria, i.e., the toxin dynamics becomes fast, the trajectories go quickly to the toxin isocline and follow that isocline towards the equilibrium.



(d) The toxin concentration fast converges to the quasi-equilibrium value $T = (p/\alpha)N$. (This happens approximately in the last of the figures above: The vertical movement is very fast, the toxin concentration quickly settles ca on the T-isocline, which corresponds to the quasi-equilibrium.) Substituting the quasi-equilibrium of T into the dynamics of the bacteria, we obtain

$$\frac{dN}{dt} = rN - cTN = rN - c\frac{p}{\alpha}N^2 = rN\left(1 - \frac{cp}{r\alpha}N\right) = rN\left(1 - \frac{N}{r\alpha/cp}\right)$$

which is the logistic model with carrying capacity $r\alpha/cp$.

Exercise 44. The equilibrium concentrations are

$$\hat{a} = \frac{-\mu\delta + \sqrt{(\mu\delta)^2 + 4\mu\delta\gamma ke}}{2\gamma k} \text{ and } \hat{p} = \frac{-\mu\delta + \sqrt{(\mu\delta)^2 + 4\mu\delta\gamma ke}}{2\gamma\mu}$$

(the other solution is negative). The Jacobian is

$$\mathbf{J} = \begin{bmatrix} -\gamma\hat{p} - \delta & -\gamma\hat{a} \\ k - \gamma\hat{p} - \delta & -\mu - \gamma\hat{a} \end{bmatrix}$$

(substituting the complicated formulat for $\hat{a}$ and $\hat{p}$ would not help). The trace of this Jacobian is negative and the determinant

$$(\gamma\hat{p} + \delta)(\mu + \gamma\hat{a}) + \gamma\hat{a}(k - \gamma\hat{p} - \delta) = \gamma\mu\hat{p} + \delta\mu + \gamma k\hat{a}$$

is positive, hence the equilibrium is stable.

Exercise 46. (a) The only equilibrium is at

$$\hat{x}_1 = \frac{m}{k_3 V_1} \text{ and } \hat{x}_2 = \frac{k_1 m}{k_2 k_3 V_2}$$

The Jacobian is

$$\mathbf{J} = \begin{bmatrix} -(k_1 + k_3) & k_2 V_2/V_1 \\ k_1 V_1/V_2 & -k_2 \end{bmatrix}$$

The trace of this Jacobian is negative and the determinant

$$Det = (k_1 + k_3)k_2 - k_1 k_2 = k_2 k_3$$

is positive, hence the equilibrium is stable.

(b) The equilibrium is a focus if the eigenvalues are complex, i.e., if $Tr^2 - 4Det < 0$. Substituting the trace and the determinant we obtain

$$\begin{aligned} Tr^2 - 4Det &= (k_1 + k_2 + k_3)^2 - 4k_2 k_3 = k_1^2 + 2k_1(k_2 + k_3) + (k_2 + k_3)^2 - 4k_2 k_3 \\ &= k_1^2 + 2k_1(k_2 + k_3) + (k_2 - k_3)^2 \end{aligned}$$

which is always positive, i.e., the equilibrium cannot be a focus. (This is good for a medicine, oscillations could complicate the treatment.)

Alternatively, perform a phase plane analysis. The phase plane indicates a stable node, no oscillations: