Appendix A
Additional Topics in Discrete Dynamical Systems

This appendix contains three topics that are thematically related to Chapter 6. Discrete nonlinear systems (Section A.1) are analogous to the continuous nonlinear systems of Chapter 7, but are more complicated. These models are overused in practice. Discrete models are indicated when life history events are synchronous, such as for many plants and fish that reproduce once per year; continuous models should be used in other cases. Markov chains (Section A.2) are dynamical systems in which the variables are probabilities rather than populations. The development focuses on the problem of measuring the extent to which two different species are genetically related. Boolean algebra models (Section A.3) provide a simplified setting for dynamical systems that is useful for analyzing complicated systems, such as those in gene regulatory networks.

A.1 Discrete Nonlinear Systems

After studying this section, you should be able to:

- Run simulations for discrete nonlinear systems.
- Analyze the stability of fixed points for discrete nonlinear systems.

On conceptual grounds, it would have made sense to present discrete nonlinear systems alongside their linear counterparts in Chapter 6. There are two reasons why this topic appears in a separate appendix instead. First, the analysis of discrete nonlinear systems is easier to understand after studying continuous nonlinear systems.[1] Second, one should only use discrete nonlinear systems when absolutely mandated by the synchrony of life events. There are several reasons for this. As we saw in Chapter 5, discrete models have some mathematical complications that are absent from continuous models. Here again, we will see complications arising in a model with only weak nonlinearities in Example A.1.4. A further problem with discrete models is the weakness of graphical techniques, which are much more complicated and far less general than those for continuous models. In our study of single dynamic models in Chapter 5, we ran simulations and used linearization techniques to determine stability for both discrete and continuous models. These techniques generalize to higher order systems in both cases.[2] The very powerful phase line method for continuous equations[3] generalizes to phase plane methods

[1] See Section 7.5.

[2] See Chapter 7 for continuous systems.

[3] Section 5.4.

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for continuous systems.[4] In contrast, the graphical technique of cobweb analysis for discrete equations,[5] which is less powerful than the phase line method, does not generalize to multi-component discrete systems, with the exception of a limited class of discrete systems that can be recast as single-component models. We begin our study with this limited class for which Chapter 5 methods are applicable.

Suppose a population is divided between two age classes, young (Y) and adults (A), with the additional requirements that all surviving young become adults in the next year and all adults die after reproducing. With these restrictive assumptions, the populations can be modeled by equations of the form

$$\begin{aligned} Y_{n+1} &= f(A_n), \\ A_{n+1} &= g(Y_n). \end{aligned}$$

Because generations do not overlap, we can combine the two equations into a single one that spans a discrete interval of 2 years; for example,

$$Y_{n+2} = f(A_{n+1}) = f(g(Y_n)).$$

We can then define the composite function $h(Y) = f(g(Y))$ and rewrite the system as

$$Y_{n+2} = h(Y_n).$$

This is a single discrete dynamic equation, albeit with a time interval of 2 years rather than 1, and we can apply all of the methods for dealing with such equations from Chapter 5.

Example A.1.1. Suppose the adults of a population occupy an ecological niche that allows for density-independent reproduction, while the young occupy a niche in which resources are limited. If we assume that the survival/recruitment of the young follows the saturation curve used for Holling type II dynamics, we have the model

$$\begin{aligned} Y_{n+1} &= fA_n, \qquad f > 0, \\ A_{n+1} &= \frac{Y_n}{b + Y_n}, \qquad b > 0. \end{aligned}$$

These combine to make a 2-year discrete model

$$Y_{n+2} = \frac{fY_n}{b + Y_n} \equiv h(Y_n).$$

Fixed points satisfy $Y_{n+2} = Y_n = Y$, resulting in the equation

$$Y = h(Y) = \frac{fY}{b + Y}.$$

Thus, $Y = 0$ is a fixed point, and a second fixed point $Y = f - b$ exists if $f > b$. The fixed point $Y^\star$ is stable if and only if $|h'(Y^\star)| < 1$. We have

$$h'(Y) = \frac{fb}{(b + Y)^2};$$

[4] See Section 7.3.

[5] See Section 5.2.

thus,

$$h'(0) = \frac{f}{b}, \qquad h'(f-b) = \frac{b}{f}.$$

The fixed point $Y = 0$ is stable if $f < b$, while the fixed point $Y = f - b$ is stable whenever it exists. Cobweb analysis confirms these conclusions and also demonstrates that the long-term behavior of the population always converges to the stable fixed point.[6] □

A.1.1 Linearization for Discrete Nonlinear Systems

In Chapter 6, we saw that the quantity λ in the discrete model $N_{t+1} = \lambda N_t$ generalizes to the eigenvalues for a discrete linear system. We also saw in Chapter 7 that the stability of an equilibrium solution of a continuous nonlinear system is determined by the eigenvalues of the Jacobian matrix at the corresponding equilibrium point.[7] The same connections hold for discrete nonlinear systems. Near a fixed point, a discrete nonlinear system can be approximated by a linear system represented by the Jacobian matrix.[8] The eigenvalues of the Jacobian determine the behavior near the corresponding fixed point, with $|\lambda| < 1$ for all λ required for stability. It is often more convenient to use the equivalent criterion $|\lambda|^2 < 1$ for all λ; this generalizes to the case of complex eigenvalues, with the magnitude of a complex number defined by $|a+ib|^2 = a^2 + b^2$.

Example A.1.2. The Jacobian for the system of Example A.1.1 is

$$J = \begin{pmatrix} 0 & f \\ \frac{b}{(b+Y)^2} & 0 \end{pmatrix}.$$

Thus, the eigenvalues are given by

$$0 = \det \begin{pmatrix} -\lambda & f \\ \frac{b}{(b+Y)^2} & -\lambda \end{pmatrix} = \lambda^2 - \frac{fb}{(b+Y)^2}.$$

The stability requirement $\lambda^2 < 1$ yields the inequality

$$\frac{fb}{(b+Y)^2} < 1.$$

This is the same requirement that we obtained in Example A.1.1 using the method for single discrete equations. □

Usually it requires significant algebraic calculation to compute eigenvalues for a model with arbitrary parameters. Some of this calculation can be avoided by making use of the Jury conditions for stability, which are a set of inequalities written in terms of quantities calculated directly from the Jacobian matrix.[9]

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[6] See Problem A.1.1.

[7] See Section 7.5.

[8] See Problem A.1.2.

[9] These correspond to the Routh–Hurwitz conditions for continuous systems.

Theorem A.1.1 (Jury Conditions for a System of Two Components). *Let* $\mathbf{J}$ *be the Jacobian matrix that represents a nonlinear system of two components near a fixed point* $\mathbf{x}^\star$*. The fixed point is asymptotically stable if*

$$|tr\mathbf{J}| < 1 + \det\mathbf{J} < 2,$$

where $tr\mathbf{J}$ *is the sum of the main diagonal entries of the Jacobian. The fixed point is unstable if any one of the inequalities*

$$tr\mathbf{J} > 1 + \det\mathbf{J}, \qquad tr\mathbf{J} < -1 - \det\mathbf{J}, \qquad \det\mathbf{J} > 1$$

is true.

Example A.1.3. For the model of Examples A.1.1 and A.1.2, we have

$$\mathrm{tr}\,\mathbf{J} = 0, \qquad \det\mathbf{J} = -\frac{fb}{(b+Y^\star)^2}.$$

The first of these results reduces the Jury conditions to $-1 < \det\mathbf{J} < 1$, and the second of this latter pair is automatically satisfied because the determinant is negative. The remaining condition, $\det\mathbf{J} > -1$, reduces to $(b+Y^\star)^2 > fb$, which is equivalent to the condition $fb/(b+Y^\star)^2 < 1$ that we derived in Example A.1.2. □

As with the Routh–Hurwitz conditions for continuous systems, there are Jury conditions for any size, but they get more complicated as the size increases. Here we present the Jury conditions for 3×3 matrices.

Theorem A.1.2 (Jury Conditions for a System of Three Components). *Let* $\mathbf{A}$ *be the Jacobian matrix for a three-component discrete system at a fixed point. Let* $\mathbf{A_k}$ *be the* 2×2 *matrix obtained from* $\mathbf{A}$ *by deleting row k and column k. Define* c_1*,* c_2*, and* c_3 *by*

$$c_1 = -tr\mathbf{A},\ c_2 = \sum_{k=1}^{3} \det\mathbf{A_k},\ c_3 = -\det\mathbf{A},$$

where $tr\mathbf{A}$ *is the sum of the diagonal elements of* $\mathbf{A}$*. Then the fixed point of the original system is asymptotically stable if*

1. $1 + c_1 + c_2 + c_3 > 0$,
2. $1 - c_1 + c_2 - c_3 > 0$, *and*
3. $|c_2 - c_1 c_3| < 1 - c_3^2$.

The fixed point is unstable if any of the inequalities is reversed.

A.1.2 A Structured Population Model with One Nonlinearity

In Chapter 7, we examined three-component continuous models in which each equation is nonlinear. Here we consider a three-component discrete model with only one nonlinear equation. This is enough to produce some very complicated behavior.

Example A.1.4. Consider a species whose life history encompasses three yearly stages, with the two older stages occupying the same ecological niche, but only the oldest stage reproducing. With linear recruitment for the two older classes and Beverton–Holt[10] recruitment for the youngest class, we have the model

$$L_{t+1} = \frac{fA_n}{b + Y_n + A_n},$$
$$Y_{n+1} = s_1 L_n,$$
$$A_{n+1} = s_2 Y_n,$$

where $f, b > 0$ and $0 < s_1, s_2 < 1$. Figure A.1.1 shows plots of Y and A for three simulations using common values $f = 10{,}000$, $b = 15$, $s_1 = 0.03$, along with different values for s_2. These plots show some of the behaviors that the system can exhibit. □

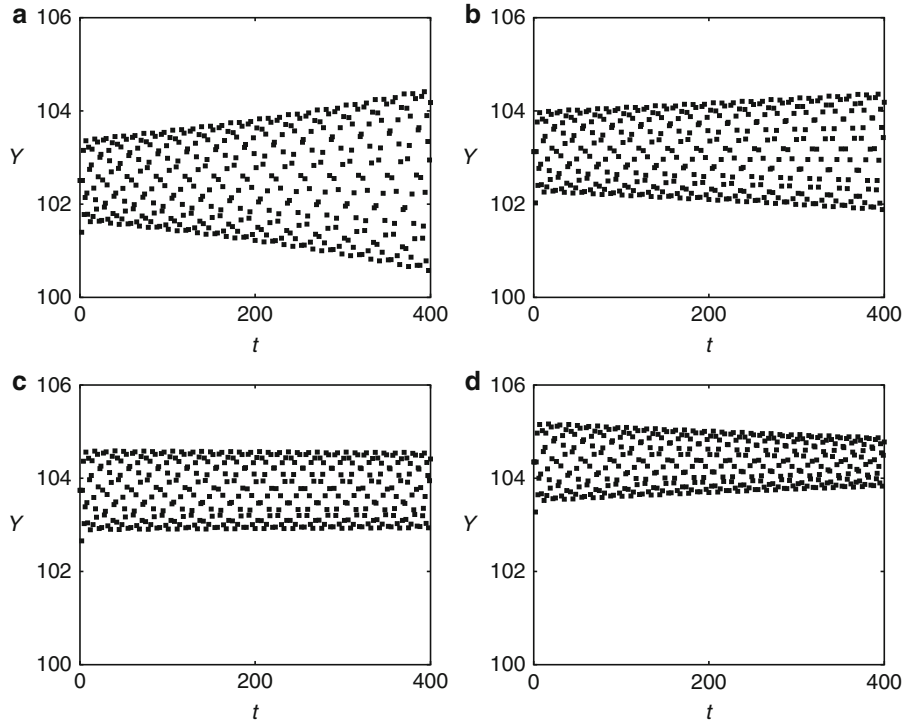

Fig. A.1.1 Y values for the model of Example A.1.4, using $f = 10{,}000$, $b = 15$, $s_1 = 0.03$, with (**a**) $s_2 = 0.595$, (**b**) $s_2 = 0.600$, (**c**) $s_2 = 0.605$, (**d**) $s_2 = 0.610$

How were the parameter sets for the plots of Figure A.1.1 chosen so as to illustrate different behaviors for nearly identical parameter values? Not by trial and error. The only realistic way to identify cases such as these is to do a thorough analysis of the model.[11]

[10] See Section 5.1.

[11] Stumbling across a good set of parameter values by chance is like throwing a dart at a fog-obscured board and managing to hit the bullseye. After the analysis, finding good parameter values is like walking up to the board and stabbing the bullseye with the dart.

Example A.1.5. Consider the model of Example A.1.4. The Jacobian has the form

$$J = \begin{pmatrix} 0 & J_{12} & J_{13} \\ s_1 & 0 & 0 \\ 0 & s_2 & 0 \end{pmatrix},$$

where

$$J_{12} = \frac{-fA}{(b+Y+A)^2}, \qquad J_{13} = \frac{f(b+Y)}{(b+Y+A)^2}.$$

With c_1, c_2, c_3 defined as in Theorem A.1.2, we have

$$c_1 = 0, \quad c_2 = -s_1 J_{12} = \frac{s_1 fA}{(b+Y+A)^2} \geq 0, \quad c_3 = -s_1 s_2 J_{13} = \frac{-s_1 s_2 f(b+Y)}{(b+Y+A)^2} < 0. \quad \text{(A.1.1)}$$

For convenience, we define

$$k_3 = -c_3 = \frac{s_1 s_2 f(b+Y)}{(b+Y+A)^2} > 0, \quad \text{(A.1.2)}$$

whereupon the Jury conditions become

1. $1 + c_2 - k_3 > 0$,
2. $1 + c_2 + k_3 > 0$, and
3. $c_2 < 1 - k_3^2$.

The second of these conditions is automatically satisfied, given $c_2, k_3 > 0$. The third requires $k_3 < 1$, which guarantees that the first condition is satisfied as well. Hence, the stability hinges on the third condition. The subsequent analysis has to be done for each fixed point.

1. There is an obvious fixed point in which all components are 0. For this point,

$$c_2 = 0, \qquad k_3 = \frac{s_1 s_2 f}{b}.$$

   Thus, the extinction point is stable if $s_1 s_2 f < b$. The quantity $s_1 s_2 f/b$ has a clear biological interpretation. If we start with L_0 individuals in year 0, this cohort yields $Y_1 = s_1 L_0$, $A_2 = s_1 s_2 L_0$, and $L_3 = s_1 s_2 f L_0/(b + A_2)$. In the limit of a small population, we have $L_3/L_0 = s_1 s_2 f/b$. Thus, $s_1 s_2 f/b$ represents the maximum possible population growth rate, and of course the population dies out if this quantity is less than 1.

2. Now assume $b < s_1 s_2 f$.

   a. Any non-extinction fixed points must satisfy

$$Y^\star = s_1 L^\star = \frac{s_1 f A^\star}{b + Y^\star + A^\star} = \frac{s_1 s_2 f Y^\star}{b + Y^\star + A^\star}.$$

   With $Y^\star > 0$, this equation reduces to

$$b + Y^\star + A^\star = s_1 s_2 f. \quad \text{(A.1.3)}$$

   Given $A^\star = s_2 Y^\star$, this equation reduces to

$$b + (1 + s_2) Y^\star = s_1 s_2 f,$$

from which we see that there is one fixed point with $Y^\star > 0$, given by

$$Y^\star = \frac{s_1 s_2 f - b}{1 + s_2}, \qquad A^\star = \frac{s_2(s_1 s_2 f - b)}{1 + s_2}. \tag{A.1.4}$$

Note that this fixed point exists under the condition for which the extinction fixed point is unstable.

b. Analysis of this fixed point requires some messy algebra. We can make it a little less messy by defining a new parameter

$$\beta = \frac{b}{s_1 f} < s_2. \tag{A.1.5}$$

In terms of this parameter, we have

$$Y^\star = \frac{s_1 f(s_2 - \beta)}{1 + s_2}. \tag{A.1.6}$$

From here, some careful algebra yields[12]

$$c_2 = \frac{Y^\star}{s_1 s_2 f}, \qquad 1 - k_3 = \frac{Y^\star}{s_1 f}, \qquad 1 + k_3 = 2 - (1 - k_3) = 2 - \frac{Y^\star}{s_1 f}. \tag{A.1.7}$$

By rewriting the stability requirement (the third Jury condition) as

$$c_2 < 1 - k_3^2 = (1 - k_3)(1 + k_3),$$

and substituting from (A.1.7), we get one factor of $Y^\star$ to cancel, leaving the inequality

$$\frac{1}{s_2} < 2 - \frac{Y}{s_1 f}.$$

Substituting the formula for $Y^\star$ and doing more algebra[13] eventually results in the inequality

$$s_2^2 + (1 + \beta)s_2 - 1 > 0. \tag{A.1.8}$$

See Problem A.1.5 for a complete analysis of this condition; here we simply note that the condition is obviously not satisfied if s_2 is too small, given the additional restriction $\beta < s_2$. This is an interesting result. The model is similar to the one-component Beverton–Holt model discussed in the Sections 5.1, 5.2, and 5.5 problem sets; however, there is a wide range of parameter values for which the three-component model has no stable fixed points.[14] As is frequently the case with discrete models, the behavior can be very complicated even when the model is fairly simple. □

[12] See Problem A.1.3a.

[13] See Problem A.1.3b.

[14] See Problem A.1.4 for more simulations of model behavior.

Problems

A.1.1. Plot cobweb diagrams for the cases $f < b$ and $f > b$ for the model

$$Y_{n+2} = \frac{fY_n}{b + Y_n}$$

and use them to confirm the conclusions of Example A.1.1.

A.1.2. Suppose $(X^\star, Y^\star)$ is a fixed point for a system

$$X_{n+1} = f(X_n, Y_n), \qquad Y_{n+1} = g(X_n, Y_n).$$

Near the fixed point, we can replace X and Y by

$$X = X^\star + \varepsilon x, Y = Y^\star + \varepsilon y.$$

Use the method of Section 7.5 to linearize the system near the fixed point. Conclude that the system is approximately

$$\mathbf{z}_{n+1} = \mathbf{J}(X^\star, Y^\star)\mathbf{z}_n,$$

where $\mathbf{z}$ is the vector whose components are x and y and $\mathbf{J}(X^\star, Y^\star)$ is the Jacobian matrix evaluated at the fixed point.

A.1.3. (a) Derive Equation (A.1.7).
(b) Derive Equation (A.1.8).

A.1.4.*

(a) Run numerical simulations for the model

$$L_{t+1} = \frac{fA_n}{b + Y_n + A_n},$$
$$Y_{n+1} = s_1 L_n,$$
$$A_{n+1} = s_2 Y_n,$$

with parameter values $f = 10{,}000$, $b = 15$, $s_1 = 0.03$, and $s_2 = 0.604$ and initial conditions $L_0 = 3{,}482$, $Y_0 = 106$, and $A_0 = 61$. Plot graphs of Y for 1,000 time steps and for 10,000 time steps. [Do not connect the points!] Is there a stable fixed point?
(b) Repeat part (a) with $s_2 = 0.605$.
(c) Repeat part (b) with $b = 210$ and just 100 time steps.
(d) Do the results of these simulations agree with the analysis of Example A.1.5?

A.1.5. This problem completes the general analysis begun in Example A.1.5. Suppose $0 < \beta < s_2$.

(a) Use the case $\beta = 0$ to find a value s_2^+ big enough so that the inequality

$$s_2^2 + (1 + \beta)s_2 - 1 > 0$$

is satisfied for any β values.
(b) Use the case $\beta = s_2$ to find a value s_2^- small enough so that the inequality from part (a) is not satisfied for any β values.

(c) Plot the triangle formed by the lines $\beta = 0$, $\beta = s_2$, and $s_2 = 1$ in the $s_2\beta$ plane. Solve the equation

$$s_2^2 + (1+\beta)s_2 - 1 > 0$$

for β on the interval $s_2^- < s_2 < s_2^+$ and add this curve to the plot.

(d) The region inside the triangle in the graph of part (c) represents the permissible sets of parameter values, and the curve divides this region into two portions. Explain the system behavior that results from points (s_2, β) in each portion of the plot.

Parasitoids[15] are animals whose life history combines a free-living stage and a parasitic stage. Many wasps and flies, for example, lay eggs in a caterpillar or other insect host. When the eggs hatch, the wasp larvae consume the host from the inside. These animals are of significant interest in ecology because they are common in nature and because they can be useful as bio-control agents. In many cases, parasitoids have a synchronized life cycle, with one generation per year; in these cases, a discrete nonlinear model is most appropriate. Models for host-parasitoid systems are explored in Problems A.1.6–A.1.8.

A.1.6. In this problem, we develop a general model for host-parasitoid systems. Assume that the host population dynamics is given by $H_{n+1} = R_0 H_n$ in the absence of parasitoids, where $R_0 > 1$. Let f be the fraction of hosts not parasitized, so that we have $H_{n+1} = R_0 f H_n$.

(a) Assume that each parasitized host results in c parasitoids in the next generation. Write down the equation for the parasitoid population dynamics.

(b) Assume the generic form $f(aP)$ for the fraction of hosts that are parasitized. Nondimensionalize the resulting model by multiplying the H equation by ac and the P equation by a and then using the substitutions $p = aP$, $h = acH$.

(c) Compute the Jacobian matrix for a fixed point $(h, p) = (h^\star, p^\star)$ with both components positive.

(d) The H equation yields a simple equation for the parasitoid population at a fixed point in terms of the function f. Use this equation to eliminate f from the Jacobian. Note that it still contains f'.

(e) Compute $\mathrm{tr}\mathbf{J}$ and $\det\mathbf{J}$. Use the assumption $f' < 0$ to show that $\mathrm{tr}\mathbf{J}$ is positive and that the first of the two conditions in Theorem A.1.1 is always satisfied. Hence, stability is determined by the requirement $\det\mathbf{J} < 1$.

(f) Use the other fixed point equation to eliminate $h^\star$ from the formula for the determinant. Conclude that the fixed point determined by $f(p^\star) = 1/R_0$ is stable if and only if $\det\mathbf{J} < 1$, where

$$\det\mathbf{J} = -p^\star f'(p^\star)\frac{{R_0}^2}{R_0 - 1} > 0.$$

A.1.7.* The dimensionless Nicholson–Bailey host-parasitoid model is

$$h_{n+1} = R_0 h f(p_n), \quad R_0 > 1,$$
$$p_{n+1} = h_n[1 - f(p_n)],$$

with the host survival function $f(p) = e^{-p}$ (see [1]).

(a) Calculate the fixed point $p^\star$ and the corresponding value of $\det\mathbf{J}$.

(b) Show that this fixed point is unstable by putting the stability requirement into the form $g(R_0) > 1$ and using calculus to show $g(R_0) \le 1$.

[15] This is pronounced PAR-uh-si-toid.

(c) Run a simulation using $R_0 = 1.1$, $h_0 = 1$, $p_0 = 0.4$, and a total of 120 years.
(d) Are the results consistent with part (a)? Are they biologically realistic?

A.1.8. The Nicholson–Bailey model corresponds to the assumption of a Poisson distribution for the number of parasitoid attacks in a given amount of time. A different model is obtained from the assumption of a different distribution, called the negative binomial distribution. This model is

$$h_{n+1} = R_0 h f(p_n), \qquad R_0 > 1,$$
$$p_{n+1} = h_n[1 - f(p_n)],$$

with the host survival function

$$f(p) = \left(1 + \frac{p}{k}\right)^{-k}.$$

The parameter $k > 0$ measures the similarity to the Poisson distribution, with the latter achieved in the limit $k \to \infty$.

(a) Calculate the fixed point $p^\star$ for $k = 2$ and determine the stability of the fixed point.
(b) Repeat part (a) for $k = 0.5$.
(c) Run a simulation for the model using $k = 2$, $R_0 = 1.1$, $h_0 = 1$, $p_0 = 0.4$, and a total of 120 years.
(d) Repeat part (c) with $k = 0.5$.
(e) Are the results of the simulations consistent with the theoretical results?

The flour beetle *Tribolium confusum* is often used as a model insect species for both theory and experiment. The best known model for this population is a discrete stage-structured model with a time step of 2 weeks [2, 3]. Flour beetles are larvae for about 2 weeks; then they go through three life stages (nonfeeding larvae, pupae, and callow adults) in approximately 2 weeks before becoming adults that can live for several years.[16] The model assumes that adults lay an average of b eggs, but these numbers lead to far fewer larvae because larvae and adults eat eggs. A fraction s of larvae survive to become "pupae," the pupae are either eaten by adults or survive to become adults, and a fraction m of adults die in each 2-week period. The full model is

$$L_{t+1} = bA_t e^{-\alpha L_t - \beta A_t},$$
$$P_{t+1} = sL_t,$$
$$A_{t+1} = P_t e^{-\gamma A_t} + (1 - m)A_t.$$

Typical parameter values are given in Table A.1.1.[17] The value of γ can be manipulated experimentally by removing additional pupae by hand at each census. The flour beetle model is explored in Problems A.1.9–A.1.11.

[16] It is common in practice to use discrete models for cases such as this, where the stage durations are approximately comparable. My view is that discrete models should only be used when life history events are synchronous, which is not the case for flour beetles. Discrete models impose synchronicity, which adds complexity that is not part of the actual biological setting.

[17] Note that large numbers of measurements allow for relatively small confidence intervals; for example, the 95 % confidence interval for γ for [3] is $(0.004446, 0.004792)$. However, these results are not reproducible, as the value of γ for [2] indicates. One should not put too much faith in reported parameter values, and it does not make sense to use values that appear to indicate a high degree of precision. Two significant digits is as much as is ever warranted for ecological data.

Table A.1.1 Reported parameter values for the *Tribolium* model

Reference	b	s	m	α	β	γ
Cushing et al. [2]	11.6772	0.4871	0.1108	0.0093	0.0110	0.0178
Dennis et al. [3]	10.45	0.8000	0.007629	0.01731	0.01310	0.004619

A.1.9. One of the interesting features of the discrete flour beetle model is that it can exhibit chaotic solutions when there are no stable fixed points. In this problem, we show that cannibalism of eggs by larvae is required for this to occur. To that end, we take $\alpha = 0$ and show that there is always a unique stable fixed point. The result is not quite general, but it can be obtained with the reasonable restrictions $1 < bs < 10$ and $m < 1/8$.

(a) Define additional parameters

$$k = \ln \frac{bs}{m}, \qquad q = mk,$$

which will turn out to be useful in the analysis. Show that q is an increasing function of both bs and m, so that the maximum value of q occurs at $bs = 10$ and $m = 1/8$. Conclude that $q < 0.6$. Note also that $k > 0$.

(b) Write down the system of three equations to determine the fixed points.

(c) Determine the Jacobian matrix for the general case. Simplify the last entry by using one of the equations from part (a) to eliminate P in favor of A. The Jacobian should then include all of the parameters as well as the unknown value $A^\star$ for the fixed point.

(d) Show that the extinction fixed point is unstable with the assumed parameter value restrictions. Conclude that the population persists.

(e) Derive the formula

$$A^\star = \frac{k}{\beta + \gamma}$$

for the unique positive fixed point. We will show that this fixed point is stable.

(f) Use the Jacobian matrix and the result for $A^\star$ to obtain

$$c_1 = \frac{\gamma}{\beta+\gamma} q + m - 1, \quad c_2 = 0, \quad c_3 = \frac{\beta}{\beta+\gamma} q - m,$$

where the c_i are those used in the Jury conditions.

(g) Compute $c_1 + c_3$ and show that the first two Jury conditions are satisfied, using the result of part (a).

(h) Find the maximum values of $|c_1|$ and $|c_3|$ and show that

$$|c_1 c_3| + c_3^2 < 1.$$

Conclude that the third Jury condition is also satisfied.

A.1.10. Consider the discrete flour beetle model for the special case $\gamma = 0$, in which there is no cannibalism of pupae by adults. Use average parameter values of $b = 11$, $s = 0.64$, $m = 0.06$, $\alpha = 0.013$, $\beta = 0.012$.

(a) Determine the Jacobian matrix for the extinction fixed point and use the Jury conditions to show that it is unstable.

(b) Determine the Jacobian matrix for a fixed point with positive values. This matrix can be simplified with some algebraic substitutions. Rewrite the entries in the top row in the form kL, where k is whatever is left over after dividing the entry by L. The values of k do not include any exponential functions if you substitute for L from the first fixed point equation.

(c) Solve the fixed point equations to find the unique fixed point with positive population values.
(d) Determine the stability of the positive fixed point by computing the eigenvalues of the Jacobian or by using the Jury conditions.
(e) Run a simulation showing the behavior of the system starting with a population that consists of 10 adults and running for 2 years (each time step represents 2 weeks). What is the long-term stable behavior of the system? Is this consistent with the stability analysis?

A.1.11. Consider the discrete flour beetle model with average parameter values $b = 11$, $s = 0.64$, $m = 0.06$, $\alpha = 0.013$, $\beta = 0.012$, $\gamma = 0.011$.

(a) Determine the Jacobian matrix for a fixed point with positive values, simplifying it as in part (b) of Problems A.1.9 and A.1.10.
(b) Eliminate the pupae from the three fixed point equations to obtain a pair of fixed point equations for L and A.
(c) Solve one of the remaining fixed point equations for L in terms of A and substitute it into the other to obtain a single nonlinear equation for A. Solve this equation numerically and then determine the corresponding fixed point values for L and P.
(d) Use the Jury conditions or compute eigenvalues to determine the stability of the positive fixed point.
(e) Run a simulation showing the behavior of the system starting with a population that consists of 10 adults. What is the long-term stable behavior of the system? Is this consistent with the stability analysis?

A.2 Markov Chains

After studying this section, you should be able to:

- Construct Markov chain models for stochastic processes in which the state at some future time depends solely on the current state.
- Find steady-state probability distributions for Markov chains.

In Chapter 6, we used equations of the form

$$\mathbf{x}_{t+1} = \mathbf{M}\mathbf{x}_t$$

to model changes in a set of dynamic variables that represent population sizes. The same mathematical structure applies to models that track dynamic changes in probabilities. These mathematical models have become useful tools in molecular biology, leading to important discoveries about the development of species in evolutionary history. The full subject is very complicated, but we can get a general sense of the possibilities by examining the simplest mathematical model for genetic change.

In this section, we consider the problem of estimating the *phylogenetic distance* between species, a concept that refers to the overall amount of genetic difference between genomes. Phylogenetic distance is important because it has caused significant changes in our understanding of the evolutionary relationships of species. For example, scientists had long thought that chimpanzees were more closely related to gorillas than to humans. We now know that the phylogenetic distance between the chimpanzee and human genomes is less than that between the chimpanzee and gorilla genomes, and therefore chimpanzees are more closely related to humans.[18]

[18] We are thinking specifically of the total amount of genetic difference in the genomes. One could still argue that the smaller number of differences between chimpanzee and human are more important than the larger number between chimpanzee and gorilla.

A.2.1 Some Scientific Background

We've seen earlier that DNA carries information in the pattern of four types of nucleotides, labeled A, G, C, and T.[19] DNA containing these nucleotide sequences is arranged in long molecules called chromosomes; taken together, these chromosomes constitute the genome of the individual. We can think of the DNA in a genome as falling broadly into three categories:

1. Essential DNA is in the form of genes that are crucial to species survival, such as the genes that determine the network of blood vessels or the function of organs. These genes are largely resistant to change because such changes from the norm tend to be harmful. The corresponding DNA may be different between species, but will likely be almost the same for individuals in the same species.
2. Some DNA is in the form of genes that play at best a small role in species survival, such as the genes that determine hair color. The corresponding DNA shows significant variation within a population. This DNA is useful for identification of individuals in a species.
3. There is also non-essential DNA, which does not affect the characteristics of the organism but is merely a residue of the evolutionary past. At one time it was thought that most DNA is non-essential, but scientists now estimate that this category encompasses about 20 % of a genome.

The genome of a species can be thought of as being defined by the combination of its essential and non-essential DNA. Although these portions are largely inherited intact from one's parents, there are two important processes that cause them to change over time: natural selection and mutation. Essential DNA is subject to natural selection. If there are individual variations in a portion of this DNA, then some individuals will be more successful at survival and reproduction than others; over time, the population will be dominated by those individuals who have the more successful variation. In contrast, non-essential DNA is not subject to natural selection.

Natural selection must, of course, have individual variation to work with. This variation results from genetic mutations that occur in the production of sperm and egg cells of organisms that reproduce sexually. Mutations are rare events,[20] and those that alter the individual's fitness are either removed by natural selection or replace earlier versions. Successful mutations and mutations in non-essential DNA can accumulate over evolutionary time. This is what allows us to associate the differences in similar regions of DNA between species with their phylogenetic distance. While there is not a simple linear relationship between number of mutations and evolutionary time, it seems reasonable that more evolutionary time should result in more mutations. Thus, a larger difference between species A and B than between species B and C indicates a more recent common ancestor for B and C. The challenge is to use mathematical models to quantify the relationship between genome differences and phylogenetic distance.

The full story is actually much more complicated.

1. Substitutions appear to account for only 35–50 % of mutations [4]. There are a number of other types of mutations, but the most common appear to be insertions and deletions, in which a small bit of DNA is inserted between two formerly adjacent nucleotides, or a small bit is lost from a section of DNA. These mutations are much harder to identify over long

[19] See Section 3.2.

[20] See Problem 3.7.15d.

periods of evolutionary time and harder to quantify.[21] Methods that consider only substitutions can only be used on portions of a chromosome in which any insertions or deletions are known.

2. Non-essential DNA is subject to mutation without natural selection, which raises the question of how mutations in non-essential DNA could be identical for individuals of the same species.
3. Natural selection occurs at the level of genome function, not genome structure. Changes in individual nucleotides do not change the function in cases where both the new and old codons make the same protein. A glance at the genetic code[22] shows that there is a lot of redundancy. For example, the third nucleotide is irrelevant in 8 of the 16 possibilities for the first two codons.
4. Natural selection is based on preferential survival of some mutations over others. The accumulation rate of a mutation depends on how much survival difference that mutation makes. For example, HIV is particularly insidious because one mutation for resistance to a drug can quickly become dominant in a population. We need a new vaccine for influenza every year, but the chicken pox vaccine is the same now as it was when first created. Hence, the molecular clock that connects mutations with time does not tick at a constant rate across species or even within species. The molecular clock is close to constant for species that are closely related and for genome portions that have the same or no function.

A.2.2 A Model for DNA Change

Suppose we leave the details of what portion of a genome to study to the molecular biologists. Assume that there are J nucleotides in a strand that has had no insertions or deletions and let N be the unknown number of generations that have passed between the ancestral strand and the contemporary strand. For any position in the sequence, the nucleotide must be either A, G, C, or T. By comparing the ancestral and contemporary strands, we can measure the fraction of DNA sites that are different between the two. This value, commonly called β, is a measure of the difference between genomes.

Now let α be the probability of a mutation in one site over one generation. Over N generations, we expect the total number of mutations to be αN for each site, yielding a total of αNJ for the strand. The product $d = \alpha N$ is the number of mutations per site. This is the phylogenetic distance, which we tentatively assume to be proportional to evolutionary time. Our goal is to infer d from β.

At first thought, this sounds easy. The total number of differences between the strands is βJ and the total number of mutations is $\alpha NJ = dJ$. These should be equal, so $d = \beta$. However, this reasoning is flawed. If a site starts as A, mutates to G, and then mutates back to A, with no further changes, then both of these mutations are counted toward dJ. However, the two strands are identical because the second mutation reversed the first one, so neither of them contributes to βJ. Thus, $d > \beta$, because some mutations actually *decrease* the number of differences between the strands. We need a nuanced mathematical model to connect the unknown phylogenetic distance with the known fraction of sequence differences.

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[21] One extreme case similar to insertion and deletion can be seen in a comparison of the human and chimpanzee genomes. Humans have 23 pairs of chromosomes, while chimpanzees have 24, which seems to refute the claim that the two species are closely related. However, a careful study of human chromosome 2 shows that it appears to consist of two formerly distinct chromosomes that have been joined together, with the two portions corresponding to two of the chimpanzee chromosomes.

[22] See Table 3.2.1.

Let $p_A(n)$, $p_G(n)$, $p_C(n)$, and $p_T(n)$ be the probabilities of having each given nucleotide at a particular site in the nth generation. Mutations from one generation to the next change these probabilities, and we must quantify these changes. The simplest assumption is that all possible changes are equally likely. Since α is the probability of change, and each nucleotide has three possible changes, the probability of any particular change is $\alpha/3$. Of course the probability of no change is $1-\alpha$. With these assumptions, the probability that a site will contain the nucleotide A at time $n+1$ is the sum of the probabilities of starting with A and not changing plus the probabilities of starting with one of the others and then changing to A:

$$p_A(n+1) = (1-\alpha)p_A(n) + \frac{\alpha}{3}p_G(n) + \frac{\alpha}{3}p_C(n) + \frac{\alpha}{3}p_T(n). \tag{A.2.1}$$

Similar equations can be written for the other probabilities in generation $n+1$, and the four equations can be combined into a single matrix equation of the form

$$\mathbf{x}_{n+1} = \mathbf{M}\mathbf{x}_n.^{23} \tag{A.2.2}$$

Each row in the matrix corresponds to the coefficients in one of the four equations. Since we have arbitrarily chosen the order A, G, C, T, the coefficients of (A.2.1) are the first row of the transition matrix $\mathbf{M}$. The full probability vector $\mathbf{x}$ and the matrix $\mathbf{M}$ are given by

$$\mathbf{x} = \begin{pmatrix} p_A \\ p_G \\ p_C \\ p_T \end{pmatrix}, \quad \mathbf{M} = \begin{pmatrix} 1-\alpha & \alpha/3 & \alpha/3 & \alpha/3 \\ \alpha/3 & 1-\alpha & \alpha/3 & \alpha/3 \\ \alpha/3 & \alpha/3 & 1-\alpha & \alpha/3 \\ \alpha/3 & \alpha/3 & \alpha/3 & 1-\alpha \end{pmatrix}. \tag{A.2.3}$$

Any model consisting of a matrix equation that represents dynamic changes in vectors of probabilities is called a *Markov chain* model. The specific model we are examining, defined by the assumption that the transition probabilities are all the same, is called the *Jukes–Cantor* model.[24]

A.2.3 Equilibrium Analysis of Markov Chain Models

There are some fundamental mathematical differences between the matrices obtained in structured population models and those obtained in Markov chain models. These differences lead to different features for the corresponding dynamical systems.

1. Structured population models have matrices in which the ij entry represents the contribution of population component j at time n to population component i at time $n+1$. Thus, none of the entries can be negative. Nonnegative matrices have three special properties: (1) the eigenvalue of largest magnitude is always positive, (2) there is a one-parameter family

[23] Given that we have always done matrix-vector multiplication with the matrix on the left and the vector on the right, this is the natural way to proceed. Unfortunately, most of the literature on Markov chains makes the opposite choice. In our matrix $\mathbf{M}$, the entry in row i and column j represents the probability of a transition from state j to state i. In the more common representation of Markov chains, the matrix is written so that the entry in row i and column j represents the probability of a transition from state i to state j. This sounds more natural, but it means that the probability vectors must be written as rows rather than columns and the matrix multiplication must have the vector on the left. This necessitates changes in the definition of eigenvectors, which is an unfortunate complication.

[24] Other models make more sophisticated assumptions about the relative probabilities of specific substitutions. The Jukes–Cantor model illustrates the important features of Markov chain models and phylogenetic distance while keeping complications to a minimum.

of eigenvectors corresponding to this dominant eigenvalue, and (3) the eigenvector corresponding to the dominant eigenvalue is positive. These properties guarantee that solutions will approach an asymptotic growth rate that corresponds to a stable distribution of component populations.

2. Markov models have matrices in which the ij entry represents the probability of being in state i at time $n+1$ after having been in state j at time n. Thus, each entry is between 0 and 1. Moreover, there is always exactly one state at the end of each time step, so the total of the probabilities for any time step must be 1. This means that the sum of entries in each column is 1. Most Markov matrices share the same properties as nonnegative matrices, with the dominant eigenvalue $\lambda = 1$.[25] This means that Markov models generally have an equilibrium solution that represents the stable distribution of probabilities.

Example A.2.1. Let $\mathbf{M}$ be the matrix of (A.2.3). Finding eigenvalues of a matrix this size is outside the scope of our presentation; however, we can start with the assumption that $\lambda = 1$ is an eigenvalue. If $\mathbf{x}$ is an eigenvector corresponding to $\lambda = 1$, then it satisfies the equation

$$(\mathbf{M}-\mathbf{I})\mathbf{x} = \mathbf{0}, \quad \mathbf{M}-\mathbf{I} = \begin{pmatrix} -\alpha & \alpha/3 & \alpha/3 & \alpha/3 \\ \alpha/3 & -\alpha & \alpha/3 & \alpha/3 \\ \alpha/3 & \alpha/3 & -\alpha & \alpha/3 \\ \alpha/3 & \alpha/3 & \alpha/3 & -\alpha \end{pmatrix}.$$

The components of $\mathbf{x}$ must satisfy a system of four equations, each corresponding to a row of $\mathbf{M}-\mathbf{I}$. Such a system would normally be difficult to solve, but here we can observe that the entries in each row sum to 0. If all four components of the vector are the same, then the products of coefficients and components will also sum to 0. The stable distribution of probabilities has to be an eigenvector, and as a set of probabilities it also has to sum to 1, which means that each probability is 1/4. This should not be surprising, as the symmetry in the rule that determines the probability of each possible mutation represents a process in which none of the nucleotides is favored over the others. □

A.2.4 Analysis of the DNA Change Model

The initial goal of our analysis is to connect the measured value of β with the phylogenetic distance $d = \alpha N$.[26] The equilibrium distribution discovered in Example A.2.1 is of no help in accomplishing this goal; by definition, this is the distribution we expect to see as $N \to \infty$. Instead, we proceed by a method that follows the strategy of calculating some quantity in two different ways, one involving β and the other involving α and N. The method requires us to use another eigenvector in addition to the one for $\lambda = 1$. This calculation is beyond the scope of our treatment, so we simply present the result.

[25] There are some additional requirements that guarantee these properties; further discussion of this topic is outside the scope of this presentation.

[26] We used the same strategy in Section 6.1 to calculate eigenvalues.

The vectors

$$\mathbf{v_1} = \begin{pmatrix} 1/4 \\ 1/4 \\ 1/4 \\ 1/4 \end{pmatrix}, \qquad \mathbf{v_2} = \begin{pmatrix} 3/4 \\ -1/4 \\ -1/4 \\ -1/4 \end{pmatrix}$$

are eigenvectors of the matrix $\mathbf{M}$ of (A.2.3) corresponding to the eigenvalues $\lambda_1 = 1$ and $\lambda_2 = 1 - \frac{4}{3}\alpha$.

Check Your Understanding A.2.1:
Verify that the vector $\mathbf{v_2}$ is an eigenvector of $\mathbf{M}$ corresponding to the eigenvalue $\lambda_2(\alpha) = 1 - \frac{4}{3}\alpha$.

Define the vector $\mathbf{u}$ by

$$\mathbf{u} = 3\mathbf{M}^N(\mathbf{v_1} + \mathbf{v_2}).^{27} \tag{A.2.4}$$

We now proceed to calculate $\mathbf{u}$ by two different methods, taking advantage of two facts:

1. $\mathbf{v_1}$ and $\mathbf{v_2}$ are eigenvectors, which means that multiplication by $\mathbf{M}$ yields a simple result.
2. The sum $\mathbf{v_1} + \mathbf{v_2}$ is also very simple.

Calculating u in Terms of N and α

The calculation of $\mathbf{u}$ is somewhat tedious, so we leave much of it as a problem. The essential idea is that repeated use of the eigenvector equation $\mathbf{Mv} = \lambda\mathbf{v}$ leads to a more general result,

$$\mathbf{M}^N\mathbf{v} = \lambda^N\mathbf{v}, \tag{A.2.5}$$

with which we eventually obtain the answer

$$\mathbf{u} = \frac{3}{4}\begin{pmatrix} 1 + 3\lambda_2^N \\ 1 - \lambda_2^N \\ 1 - \lambda_2^N \\ 1 - \lambda_2^N \end{pmatrix}, \quad \lambda_2 = 1 - \frac{4}{3}\alpha. \tag{A.2.6}$$

Estimating u in Terms of β

The matrix $\mathbf{M}^N$ represents the overall transition probabilities for N successive generations. We can't calculate this matrix directly, but we can estimate it. Given that β is the measured fraction of sites that have changed nucleotides over N generations, we can approximate $\mathbf{M}^N$ by

[27] There is no obvious reason why this should be helpful. It is always more satisfying when methods have a clear conceptual motivation, but occasionally mathematicians must resort to methods that appear simply as clever tricks.

$$\mathbf{M}^N = \begin{pmatrix} 1-\beta & \beta/3 & \beta/3 & \beta/3 \\ \beta/3 & 1-\beta & \beta/3 & \beta/3 \\ \beta/3 & \beta/3 & 1-\beta & \beta/3 \\ \beta/3 & \beta/3 & \beta/3 & 1-\beta \end{pmatrix}. \tag{A.2.7}$$

This is not entirely correct, as it assumes both that the fraction of changed sites is the same, no matter what the original nucleotide, and that the changed sites are equally distributed among the three possible nucleotides. These assumptions are no worse than the basic Jukes–Cantor assumption about the structure of **M**, however. Combining (A.2.4) and (A.2.7) yields the result

$$\mathbf{u} = \begin{pmatrix} 3(1-\beta) \\ \beta \\ \beta \\ \beta \end{pmatrix}. \tag{A.2.8}$$

The Jukes–Cantor Distance

Equations (A.2.6) and (A.2.8) provide two different results for the same quantity. Comparing them yields the equation

$$\beta = \frac{3}{4} - \frac{3}{4}\lambda_2^N = \frac{3}{4} - \frac{3}{4}\left(1 - \frac{4}{3}\alpha\right)^N, \tag{A.2.9}$$

which predicts the fraction of sites with changes in terms of the mutation rate and the number of generations. We can solve this equation for N, with the elegant result

$$N = \frac{\ln\left(1 - \frac{4}{3}\beta\right)}{\ln\left(1 - \frac{4}{3}\alpha\right)}, \tag{A.2.10}$$

from which we have

$$d = \alpha\frac{\ln\left(1 - \frac{4}{3}\beta\right)}{\ln\left(1 - \frac{4}{3}\alpha\right)} = \frac{\alpha}{\ln\left(1 - \frac{4}{3}\alpha\right)}\ln\left(1 - \frac{4}{3}\beta\right). \tag{A.2.11}$$

This result still appears to depend on α, which is difficult to measure. In practice, this dependence is meaningless. Given the realistic assumption that α is very small, we can approximate[28] the Jukes–Cantor distance as

$$d = -\frac{3}{4}\ln\left(1 - \frac{4}{3}\beta\right). \tag{A.2.12}$$

This simple result is a reasonable approximation of the amount of genetic change corresponding to a particular net substitution probability β. The properties of this function match reasonable expectations.[29] It increases as β increases, with $d \approx \beta$ if β is small and $d \to \infty$ as $\beta \to 3/4$.[30]

[28] See Problem A.2.1b.

[29] See Problem A.2.2.

[30] Note that $\beta = 3/4$ means that the system has reached equilibrium; theoretically this requires infinite time.

Problems

A.2.1. (a) Derive (A.2.6).
(b) Verify that

$$\beta = \frac{3}{4} - \frac{3}{4}\left(1 - \frac{4}{3}\alpha\right)^N$$

satisfies the equation

$$\begin{pmatrix} 3(1-\beta) \\ \beta \\ \beta \\ \beta \end{pmatrix} = \mathbf{u} = \frac{3}{4}\begin{pmatrix} 1+3\lambda_2^N \\ 1-\lambda_2^N \\ 1-\lambda_2^N \\ 1-\lambda_2^N \end{pmatrix},$$

where

$$\lambda_2 = 1 - \frac{4}{3}\alpha.$$

A.2.2. (a) Plot the Jukes–Cantor phylogenetic distance function

$$d = -\frac{3}{4}\ln\left(1 - \frac{4}{3}\beta\right).$$

Be careful to restrict β to values that make sense biologically.
(b) Use linear approximation to show that $d \approx \beta$ for small genome changes. Why does this make sense?
(c) Compute $\lim_{\beta \to 3/4} d$. Explain the meaning of the result.
(d) Use linear approximation to derive (A.2.12) from (A.2.11).

A.2.3. Let $\mathbf{M}$ be a 2×2 Markov chain matrix with entries a and b as shown below.

$$\mathbf{M} = \begin{pmatrix} & a \\ b & \end{pmatrix}.$$

(a)* Fill in the blanks to complete the matrix.
(b) Show that $\begin{pmatrix} 1 \\ 1 \end{pmatrix}$ is an eigenvector for $\lambda = 1$ if and only if the entries in each row of $\mathbf{M}$ sum to 1. What must be true about a and b in this case?

A.2.4. The Kimura model of genetic change assumes that the rates for the AG, GA, CT, and TC substitutions are faster than those for the other substitutions. (There is a biochemical basis for why this should be the case.)

(a) Construct the matrix $\mathbf{M}$ for the Kimura model, using α for the faster rate and β for the slower rate.
(b) Show that $\begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}$ is an eigenvector for the Kimura model for $\lambda = 1$ and conclude that all nucleotides are equally likely.

A.2.5. The Felsenstein model of genetic change assumes that rates of change depend on the nucleotide being changed to, but not the nucleotide being changed from.

(a) Assume that other nucleotides change to A at rate a, G at rate g, and so on. Construct the matrix $\mathbf{M}$.

(b) Show that $\begin{pmatrix} a \\ g \\ c \\ t \end{pmatrix}$ is an eigenvector for the Felsenstein model for $\lambda = 1$.

A.3 Boolean Algebra Models

After studying this section, you should be able to:

- Compute Boolean functions.
- Find fixed points of Boolean networks.

Only a small fraction of an organism's genes are active in any particular cell; genes for the heart muscle, for example, are only expressed in heart cells. Even so, the number of chemical compounds that could be present in a cell, including messenger RNA molecules, proteins, and enzymes, is large. Each of these could be considered as a variable in a dynamical system that represents the cell; at any given time, nearly all are at a concentration of 0. This suggests a modeling strategy of focusing strictly on the distinction between zero and nonzero values, ignoring the specific amounts of those quantities that are not zero. A special type of mathematics, called Boolean algebra,[31] is ideal for this kind of modeling. In this section, we develop the basic principles of Boolean algebra and briefly indicate how Boolean models can be used to study the regulation of gene expression. For a more advanced introduction to gene regulation networks and their Boolean models, the reader should consult the outstanding paper on this topic by Martins et al. [5], from which this section draws heavily.

A.3.1 Boolean Algebra

A *Boolean variable* is a variable that can take on only two values, 0 and 1. These can be combined into dynamical systems, called Boolean networks. As we saw in Chapters 5–7, dynamical systems are defined by a set of formulas that calculate the new state of the system in terms of the old state. For a Boolean network, this means that we need functions that define Boolean dependent variables in terms of Boolean independent variables; in other words, we must first develop the machinery of Boolean algebra.

Algebra with number systems is based on the arithmetic operations of addition and multiplication. Algebra with Boolean variables is instead based on logic. Think of the Boolean variables 1 and 0 as representing the logical constants TRUE and FALSE. Suppose A is a species of animal and B is a group of species that can be divided into mutually exclusive subgroups B1 and B2. Consider the statements

1. A is a species of type B1.
2. A is a species of type B2.
3. A is a species of type B.

Suppose we use the Boolean variables X, Y, and Z to indicate the truth of these statements. Given a particular A, we need assess the values of only two of them; the third can be calculated

[31] Named for its creator, the nineteenth century English mathematician George Boole.

by rules of logic. For example, statement 3 is TRUE when either of statements 1 or 2 is TRUE. In terms of the variables, $Z = 1$ requires either $X = 1$ or $Y = 1$. We can define a Boolean operation X OR Y that is TRUE if either $X = 1$ or $Y = 1$ and FALSE otherwise. Using the notation $\vee$ for this operation,[32] we can write

$$Z = X \vee Y.$$

Note that the definition of Z means $Z = 1$ in the event that $X = 1$ *and* $Y = 1$, although the setting rules out this possibility.

Suppose we want to indicate how to calculate Y from knowledge of X and Z. This is a bit tricky. Certainly $Z = 1$ is necessary for $Y = 1$. In addition, $X = 1$ precludes $Y = 1$. So two separate conditions are necessary for $Y = 1$: we must have $Z = 1$ and $X = 0$. There is an AND operation that is TRUE only when both of its operands are TRUE, but we want Y to be TRUE when one operand is TRUE and the other FALSE. The solution is the negation operation; the symbol $\neg X$ (read "not X") is TRUE when X is FALSE, and vice versa. Thus, we want to require Z and $\neg X$ to be TRUE. Using the symbol $\wedge$ for the AND operation,[33] the correct notation is

$$Y = Z \wedge \neg X.$$

The OR, AND, and negation operations are sufficient to define all necessary logical constructions in Boolean algebra, but there is an additional operation that we define for convenience. Suppose we want to indicate that Z is TRUE whenever one of X and Y is TRUE, but not when both are TRUE. The OR operation does not do this by itself. We can denote this with the EXCLUSIVE OR operation, written as

$$Z = X \oplus Y.$$

Table A.3.1 summarizes the binary operations of Boolean algebra.

Table A.3.1 Binary Boolean operations

AND	$0 \wedge 0 = 0$	$0 \wedge 1 = 1 \wedge 0 = 0$	$1 \wedge 1 = 1$
OR	$0 \vee 0 = 0$	$0 \vee 1 = 1 \vee 0 = 1$	$1 \vee 1 = 1$
EXCLUSIVE OR	$0 \oplus 0 = 0$	$0 \oplus 1 = 1 \oplus 0 = 1$	$1 \oplus 1 = 0$

As in the motivating example, the names of the operations describe how they work. Thus, $a \wedge b$ is TRUE only when both a and b are TRUE, $a \vee b$ is TRUE whenever either a or b is TRUE, and $a \oplus b$ is TRUE when one of a and b is TRUE, but not both. The EXCLUSIVE OR operation could be omitted from the list, as it can be constructed from the other operations in several different ways. However, these constructions are sufficiently complicated to justify thinking of EXCLUSIVE OR as an independent operation.

Example A.3.1. To demonstrate the identity

$$x \oplus y = [x \wedge (\neg y)] \vee [(\neg x) \wedge y],$$

we calculate the complicated expression on the right side for each possible pair of x and y values and check that the answer is the same as $x \oplus y$:

[32] The symbol $\cup$, which represents the union of two sets, is probably more familiar to most readers. Think of the OR operation as similar to a union of sets.

[33] Think of the symbol as being similar to the symbol $\cap$ used for the intersection of sets.

$$[0 \wedge (\neg 0)] \vee [(\neg 0) \wedge 0] = [0 \wedge 1] \vee [1 \wedge 0] = 0 \vee 0 = 0 = 0 \oplus 0;$$
$$[0 \wedge (\neg 1)] \vee [(\neg 0) \wedge 1] = [0 \wedge 0] \vee [1 \wedge 1] = 0 \vee 1 = 1 = 0 \oplus 1;$$
$$[1 \wedge (\neg 0)] \vee [(\neg 1) \wedge 0] = [1 \wedge 1] \vee [0 \wedge 0] = 1 \vee 0 = 1 = 1 \oplus 0;$$
$$[1 \wedge (\neg 1)] \vee [(\neg 1) \wedge 1] = [1 \wedge 0] \vee [0 \wedge 1] = 0 \vee 0 = 0 = 1 \oplus 1.$$

□

Check Your Understanding A.3.1:
Verify the identity $x \oplus y = \neg[(x \wedge y) \vee (\neg x \wedge \neg y)]$.

A.3.2 Boolean Functions and Boolean Networks

A *Boolean function* is a function $f(\mathbf{x})$ that uses the values of the Boolean input vector $\mathbf{x}$ to compute a Boolean variable output. For convenience, we often write the argument $\mathbf{x}$ as a list of the scalar components.

Example A.3.2. Let $\mathbf{x}$ be a Boolean variable with three components, called X, Y, and Z. Define the Boolean function

$$f(\mathbf{x}) = f(X,Y,Z) = X \wedge Y.$$

Then, for example, $f(1,1,0) = 1$, while $f(0,1,1) = 0$. In this particular function, the state of Z does not matter, but it may be convenient to include Z as an independent variable. □

Check Your Understanding A.3.2:
Verify the results $f(1,0,0) = 0$ and $f(1,1,1) = 1$ for the Boolean function of Example A.3.2.

Now suppose $\mathbf{x}$ is a vector of n Boolean variables and $\mathbf{f}$ is a vector of n Boolean functions $f_1, f_2, \ldots, f_n$. Then we can use the function $\mathbf{f}$ to define a **Boolean network** using the dynamic equation

$$\mathbf{x}_{t+1} = \mathbf{f}(\mathbf{x}_t). \tag{A.3.1}$$

Example A.3.3. Suppose the Boolean function $\mathbf{f}$ of three variables has components defined by

$$f_1(X,Y,Z) = \neg Z, \qquad f_2(X,Y,Z) = X \wedge Y, \qquad f_3(X,Y,Z) = X \oplus Y.$$

Suppose further that $\mathbf{x}_0 = (1,1,1)$. Then

$$f_1(1,1,1) = 0, \quad f_2(1,1,1) = 1, \quad f_3(1,1,1) = 0,$$

so $\mathbf{x}_1 = (0,1,0)$. □

Check Your Understanding A.3.3:
Verify that $\mathbf{x}_2 = (1,0,1)$ and $\mathbf{x}_3 = (0,0,1)$ for the Boolean sequence defined in Example A.3.3.

Boolean networks are autonomous, meaning that changes depend only on the state and not on the time. For example, the result $\mathbf{f}(1,1,1) = (0,1,0)$, which we calculated for the Boolean network in Example A.3.3 means that the state $(1,1,1)$ is always followed by the state $(0,1,0)$. We could display this fact as a graph consisting of two nodes for the states $(1,1,1)$ and $(0,1,0)$ along with an arrow that goes from the former to the latter. The network of Example A.3.3 has only eight states, so it is not a difficult matter to construct the complete graph of the Boolean network.

In the discrete models of Chapter 6, the index t had the specific meaning of time. This is not strictly necessary with Boolean networks. The use of dynamical systems notation is often merely an artifice used to identify the long-term behavior of a network from any given starting point. It does not matter what length of time is needed for the system to move from one state to another; all that matters is that states can be classified according to the way they appear in the graph of the network. Many states are *transient*, which means that systems that start in these states never return. Some states are *fixed points*, meaning that the system stops changing once it reaches that state. In some networks, there are *recurrent* states that occur as part of a periodic movement through two or more states.

Example A.3.4. Let $\mathbf{f}$ be the Boolean function defined in Example A.3.3. The dynamics of the Boolean network defined by $\mathbf{f}$ is illustrated in Figure A.3.1. The state $(1,1,0)$ is a fixed point that cannot be attained unless the system is initially at that point. There is a cycle of four states, and there are three transient states, each of which eventually reaches the cycle rather than the fixed point. Note that graphs are defined by the pattern of nodes and arrows. The same graph could be displayed with any number of different layouts. □

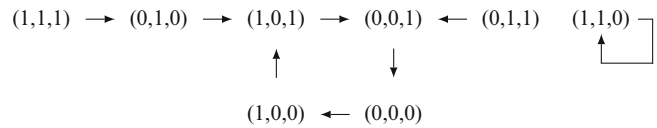

Fig. A.3.1 A graph of the Boolean network of Examples A.3.3 and A.3.4

One important difference between Boolean networks and dynamical systems based on differential equations or difference equations is that the notion of stability does not apply in the same way. In a dynamical system, it makes sense to consider what happens when the initial state is arbitrarily close to a fixed point; in particular, it is possible for the system to evolve away from the fixed point. In a Boolean network, variables can only be 0 or 1, so the system cannot start arbitrarily close to a fixed point. In a sense, fixed points and cycles in a Boolean network are always stable. This limits the kind of questions that can be addressed with Boolean models.

A.3.3 Using a Boolean Network for a Consistency Check

The primary use of Boolean models is to serve as a consistency check on a proposed mechanism. Before we consider using Boolean models for this purpose, it is helpful to consider an alternative notation that streamlines the discovery of fixed points and cycles. The key idea is that each variable in a Boolean network is either present or absent, and the state of the system is determined by the set of variables that are present. We could therefore name states by the list of variables whose value is 1. For example, if the Boolean variables are X, Y, and Z, then the state XZ corresponds to the point $(1,0,1)$, in which X and Z are both present while Y is

absent. Similarly, the state $(0,0,1)$ can be denoted as Z. The null state $(0,0,0)$ can be denoted by the symbol $\emptyset$, which is used in set theory to indicate a set that has no elements. Figure A.3.2 reproduces the graph of the Boolean network of Examples A.3.3 and A.3.4 with this alternative labeling scheme. The advantage of this method is that each of the arrows is easy to check with the definition of the function. One can see at a glance, for example, that X is present at the tip of an arrow precisely when Z is not present at the tail, in keeping with the definition $f_1(X,Y,Z) = \neg Z$.

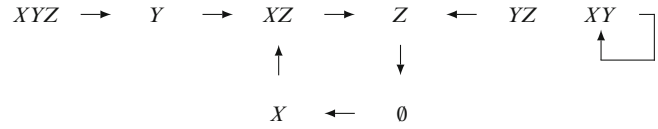

Fig. A.3.2 A graph of the Boolean network of Examples A.3.3 and A.3.4 and defined by the function $\mathbf{f}(X,Y,Z) = (\neg Z, X \wedge Y, X \oplus Y)$

Suppose the quantities X, Y, and Z represent chemicals that could be present in a cell and interact according to the following rules:

1. X forms whenever Z is absent, but never when Z is present.
2. Y cannot be produced in the system, but it can be maintained if X is present.
3. Either X or Y is necessary to produce Z, but the combination of X and Y suppresses formation of Z.

This set of rules corresponds exactly to the Boolean network of Examples A.3.3 and A.3.4. Hence, the network analysis yields predictions about what the physical system will do. Specifically, it predicts that two things can happen. The system could reach a state in which both X and Y are always present and Z is always absent. Alternatively, the system could reach a state in which Y is always absent and X and Z cycle between present and absent in such a way that Z follows X, with some overlap, while X reappears only when Z is absent. These are very specific predictions about what states can be seen in the physical system. If the system exhibits fixed states or cycles that are not in agreement with the network analysis, then the proposed mechanism must be false.

Boolean networks cannot be used to discover mechanisms because for any particular set of fixed points and/or cycles one can find a very large number of possible underlying mechanisms. However, they do find wide employment in biochemistry in cases where some features of the chemical mechanism are known and others are not. Many incorrect mechanisms can be rejected because their Boolean networks do not have the right behavior. For systems with large numbers of components, it is far easier to identify fixed points in Boolean networks than in dynamical systems such as the ones examined in Chapters 6 and 7.

Problems

A.3.1.* Consider the Boolean network $\mathbf{x}_{t+1} = \mathbf{f}(\mathbf{x}_t)$ defined by the functions

$$f_1(X,Y,Z) = Y \vee Z, \qquad f_2(X,Y,Z) = \neg(X \vee Z), \qquad f_3(X,Y,Z) = \neg(X \wedge Z).$$

(a) Determine the action of the function $\mathbf{f}$ on each of the eight possible states.
(b) Arrange the information from part (a) as a graph similar to that in Figure A.3.2.

Problems A.3.2 and A.3.3 consider a situation in which the three components of a Boolean network represent interacting chemical species in a cell.[34]

A.3.2. Suppose we know some elementary facts about the biochemistry:

1. The presence of Y inhibits formation of X, which is naturally present.
2. The presence of X is necessary for the formation of Y.
3. The presence of X promotes the formation of Z.
4. The presence of Y promotes the formation of Z.

(a) Determine the correct Boolean functions for the formations of X and Y at time $t+1$ from the Boolean state at time t. These are unambiguous.
(b) The list of facts is not sufficient to determine the correct function for the formation of Z. In fact, three possibilities are consistent with the data:

   1. It could be that both X and Y must be present together.
   2. It could be that either X or Y is sufficient, regardless of the presence of the other.
   3. It could be that formation of Z requires either X or Y, but not both.

   Determine the correct Boolean function for Z in the first case. Use the complete set of Boolean functions to determine the graph of states. Which states are persistent?
(c) Repeat part (b) for the second case.
(d) Repeat part (b) for the third case.

A.3.3. Repeat problem A.3.2 given the following set of facts.

1. The presence of Y promotes formation of X.
2. The presence of Z inhibits formation of X.
3. The presence of X inhibits the formation of Y.
4. The presence of Y promotes the formation of Z.

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[34] These problems use Boolean networks that the author obtained from Dan Hrozencik of Chicago State University and Timothy Comar of Benedictine Universtiy.

Appendix B
The Definite Integral via Riemann Sums

To estimate the total amount of a quantity V that is produced in an interval $a \le t \le b$, given a production rate $Q(t)$, we can divide the interval $[a,b]$ into n equal subintervals of duration $h = (b-a)/n$. Let $Q_0 = Q(a)$, $Q_1 = Q(a+h)$, $Q_2 = Q(a+2h)$, and so on, with $Q_n = Q(b)$ at the end. For the first subinterval, $a \le t \le a+h$, we can estimate the rate for the entire subinterval using $Q_0 = Q(a)$. Similarly, we can use $Q_1 = Q(t+a)$ for the interval $a+h \le t \le a+2h$. The result is the left-hand sum

$$V_L = Q_0 h + Q_1 h + \cdots + Q_{n-1} h = \sum_{j=0}^{n-1} Q_j h.$$

Similarly, we could use Q_1 for the interval $a \le t \le a+h$, and so on, and generate a right-hand sum

$$V_R = Q_1 h + \cdots + Q_n h = \sum_{j=1}^{n} Q_j h.$$

In general, we cannot say that either V_L or V_R is a maximum estimate or a minimum estimate, since the function Q might not be always increasing or always decreasing. However, we can always say that the difference between the two sums is

$$V_R - V_L = [Q(b) - Q(a)]h = \frac{(b-a)[Q(b) - Q(a)]}{n},$$

so the difference between the two estimates approaches 0 in the limit as $n \to \infty$. This means that the left and right sums converge to the same result, which must be the exact answer. We may summarize the result mathematically as follows:

$$V = \lim_{n\to\infty} \sum_{j=1}^{n} Q(t_j)h, \quad \text{where} \quad a + (j-1)h \le t_j \le a + jh. \tag{B.1}$$

Note that we need not specify a left-hand sum or a right-hand sum. The result is the same if we alternate left endpoints and right endpoints, or if we use the midpoint of each subinterval instead. All that matters is that we use some value of t in each subinterval to represent the rate Q over the entire subinterval.

G. Ledder, *Mathematics for the Life Sciences: Calculus, Modeling, Probability, and Dynamical Systems*, Springer Undergraduate Texts in Mathematics and Technology, DOI 10.1007/978-1-4614-7276-6,

The result of (B.1) motivates the formal definition of the *definite integral*, the second of the two principle concepts of calculus.[35]

Definite integral of a function $Q(t)$ over an interval $a \le t \le b$: *the quantity defined by the formula*

$$\int_a^b Q(t)\,dt = \lim_{n\to\infty} \sum_{j=1}^{n} Q_j h, \tag{B.2}$$

where $Q_j = Q(t_j)$ for any t_j in the interval $a+(j-1)h \le t_j \le a+jh$ and $h = (b-a)/n$.

[35] The other is, of course, the derivative.

Appendix C
A Runge–Kutta Method for Numerical Solution of Differential Equations

It is easy to program simulations for discrete dynamical systems because the equations of the model are all that is needed. For continuous dynamical systems, we need a special numerical method that uses a discrete approximation of the system of differential equations. The simplest of these is Euler's method, which we used in Example 5.3.1. More sophisticated methods work far better. The simplest of these methods is the Runge–Kutta[36] method of order 4.

Like Euler's method, Runge–Kutta methods work by computing approximate values x_j of the dependent variable[37] at a collection of times t_j. Thus, they are based on discrete approximations to a continuous equation. The most obvious way to discretize a differential equation $x' = f(t,x)$ is to evaluate the differential equation at the point (t,x) using a forward difference approximation for the derivative:

$$\frac{x_{j+1} - x_j}{h_j} = f(t_j, x_j),\ h_j = t_{j+1} - t_j,$$

which leads to the Euler approximation

$$x_{j+1} = x_j + h_j f(t_j, x_j).$$

The drawback of Euler's method is the use of the value $f(t_j,x_j)$ to represent dx/dt over the entire interval $[t_j,t_{j+1}]$. As the actual solution curve moves through this interval, its slope changes and the approximation becomes less accurate. A better approximation for the average rate of change over the interval could in theory be obtained by averaging $f(t_j,x_j)$ and $f(t_{j+1},x_{j+1})$, the latter being the slope at the end of the interval. This does not work in practice because the value x_{j+1} is not known. The idea of Runge–Kutta methods is to obtain several approximations for slopes in the interval and average them together to obtain the slope to be used to compute x_{j+1}. The details of how best to do this are beyond the scope of this presentation, so we merely present the algorithm.

[36] This is pronounced Run-ga Kut-ta.

[37] For convenience, we are assuming a single differential equation. Numerical methods for single differential equations also work for systems.

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Algorithm C.1 *Runge–Kutta order 4 for* $x' = f(t,x)$.
Given (t_j,x_j) *and* $h = t_{j+1} - t_j$, x_{j+1} *is given by*

$$\begin{aligned} k_1 &= hf(t_j,x_j)\,, \\ k_2 &= hf(t_j + 0.5h, x_j + 0.5k_1)\,, \\ k_3 &= hf(t_j + 0.5h, x_j + 0.5k_2)\,, \\ k_4 &= hf(t_j + h, x_j + k_3)\,, \\ x_{j+1} &= x_j + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)\,. \end{aligned}$$

Hints and Answers to Selected Problems

Chapter 1

Section 1.1

1.1.1 $t = \dfrac{\ln 3}{0.3}$

1.1.2 $t_z = \dfrac{\ln 650 - \ln z}{0.3}$

1.1.7 (a) $\left(\dfrac{b}{2}, -\dfrac{b^2}{4}\right)$

1.1.12

(a) $y = Ae^{-1.6}$
(b) $y = 650 + Ae^{-1.6}$
(c) $A = \frac{650}{1-e^{-1.6}} \approx 814.4, \quad y_{\min} = Ae^{-1.6} \approx 164.4$

1.1.16

(a) $y(t) = e^{-mt}, \quad s = e^{-m}$
(b) $n = -\dfrac{\ln s}{s - s^2}$. Since $0 < s < 1$, $n > 0$.

Section 1.2

Interval	1960–1970	1970–1980	1980–1990	1990–2000	2000–2010
Average rate of change	0.877	1.300	1.548	1.524	2.038

1.2.1 There is a general increase.

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1.2.5

(a) -156 on $[0.5, 1]$, -134 on $[1, 1.5]$, -145 on $[0.5, 1.5]$
(b) -144.5
(c) The central difference approximation is clearly best.

1.2.8 We get 3.2, 10, 32, and 100. The slope appears to be infinite, and the tangent line is vertical.

1.2.9 0.22, 0.125, and 0.08

Section 1.3

1.3.1 $f'(x) = 2x$

1.3.3 $f'(x) = \cos x$

1.3.7 $f'(x) = -5e^{-5x} + \pi \cos \pi x$

1.3.11 $g'(x) = 2x \ln x + x$

1.3.13 $f'(x) = \sec^2 x = \dfrac{1}{\cos^2 x}$

1.3.16 $g'(t) = \dfrac{e^v(v-1)}{(e^v+v)^2} v'(t)$

1.3.17 $g'(t) = \dfrac{2t - t^4}{(t^3+1)^2}$

1.3.22 $g'(x) = \left(2e^{2x} + \dfrac{1}{x}\right) \cos\left(e^{2x} + \ln x\right)$

1.3.25 $f'(x) = \pi \cos x e^{\pi \sin x}$

1.3.27 $g'(t) = +\dfrac{2\pi t}{(t^2+1)^2} \sin\left(\dfrac{\pi}{t^2+1}\right)$

1.3.33 The answer is 1. To get there, you must simplify the denominator, replace x with $y = -x$, and factor the resulting limit using one factor that matches the appropriate formula in (1.3.3).

Section 1.4

1.4.6 0 is a local minimum.

1.4.8 0 is a local maximum, 2 and -2 are local minima.

1.4.10 -1 is a local minimum and 2 is not a local extremum.

1.4.14

(a) 0 is a local maximum.
(b) $f' = 4x(x^2 - 3x - b)$; the critical points $x = \dfrac{3 \pm \sqrt{9+4b}}{2}$ require $b > -9/4$.

(c) $f''(x^\star) = 4x^\star(2x^\star - 3)$
(d) The value $x^\star$ is a local maximum if it is between 0 and 3/2, and a minimum if it is less than 0 or greater than 3/2.
(e) The larger point is a local minimum, while the smaller is a local maximum.

1.4.16 $\pm 0.01 x_0$

Section 1.5

1.5.1 $r = 1/e$

1.5.2 $r = q$

1.5.3 (d) $v = \dfrac{3}{2}u$

1.5.4

(a) $w = 1$
(b) $F' > 0$ for all p, so the global maximum is at $p = 1$.
(c) $p = 1/(2-w)$
(e) $(1-p)^2 = \left(\dfrac{1-w}{2-w}\right)^2$

1.5.5

(a) $t(x) = X - x + \dfrac{\sqrt{x^2+Y^2}}{s}$
(b) $x^\star = Y\dfrac{s}{\sqrt{1-s^2}}$
(c) $x^\star < X$
(f) $\cos\phi^\star = s$

1.5.9

(a) $x = e^{-kt}$
(b) $f + x$ is constant because resources lost to the patch are gained by the forager. Thus, $f(t) = 1 - D - e^{-kt}$.
(d) $D = 1 - x^\star(1 - \ln x^\star)$

Section 1.6

1.6.1 $30\pi D\,\text{mm}^2/\text{day}$

1.6.6

(a) $\dfrac{dX}{dT} = X - \dfrac{QX}{1+X}$
(b) It will be easier to analyze a model that has one parameter than a model with three parameters.

Section 1.7

1.7.1

(a) $y_L = 5, \quad y_R = 14, \quad \Delta y = 9$
(b) $y_L = 6.875, \quad y_R = 11.375, \quad \Delta y = 4.5$
(c) $\Delta y = 27/n$
(d) 270
(e) $y_L = 8.95006, \quad y_R = 9.05006$
(f) 9.00006
(g) 8.99997
(h) $S_3 = 9.0, \quad S_6 = 9.0$

1.7.6 $\displaystyle\int_0^{100} Lf(x)\,dx$

1.7.9

(a) 2,000
(b) 1.000850
(c) 1.000838
(d) $\approx$1.000834
(e) 0.000016 and 0.000004
(f) The midpoint approximation is generally much better than the left and right approximations; also, the midpoint approximation is more accurate when the function is close to linear.

Section 1.8

1.8.1 $-4/5$

1.8.4 $(e^2+1)/2$

1.8.7 $1/\sqrt{2}+1/2$

Section 1.9

1.9.1 $\dfrac{2}{3}\left(2^{3/2}-1\right)$

1.9.2 1/8

1.9.7 0

Chapter 2

Section 2.2

2.2.3

(a) $q^2, \quad 2pq, \quad p^2$
(b) 0.36, 0.41

2.2.7 (d) $ne^{-ra}\int_0^1 (1-x)\left(e^{5rx}+e^{-5rx}\right)dx = 1$

Section 2.3

2.3.3 The slopes are $m_1 = 1-0.4c$ and $m_2 = 1-0.2c$. Errors at the edges of the graph matter more than errors near the middle.

2.3.5

(a) $C = -15.6 + 4.22t$
(b) There is a lot of scatter in the data, which limits our confidence in the choice of a linear model.

Section 2.4

2.4.1 $N = 6.01e^{0.400t}$

2.4.2 $N = 6.18e^{0.390t}$

2.4.5 $z = 1007e^{-0.0827t}$

Section 2.5

2.5.6

$$\frac{dS}{dT} = -pBSI + QR, \quad \frac{dI}{dT} = pBSI - KI, \quad \frac{dR}{dT} = KI - QR.$$

Section 2.6

2.6.3 $Y = e^{-T}$, where $Y = y/y_0$ and $T = kt$

2.6.8 $\dfrac{dc}{dt} = 1 - c - rc, \quad r = \dfrac{RV}{F}.$

The quantities F/V and R represent the rates for the two processes that eliminate pollutant from the lake. Hence, r is the ratio of the magnitude of the decay process to the magnitude of the flushing process.

Section 2.7

2.7.2

(a) $y = -0.11667x + 0.04x^2 - 0.00083x^3$
(c) The cubic polynomial is too "curvy" for a good fit.

2.7.6

(a) $B = b + m\bar{x} + a\bar{x}^2 - \bar{y}, \quad M = m + 2a\bar{x}$
(b) $m = M - 2a\bar{x}, \quad b = B + \bar{y} - m\bar{x} - a\bar{x}^2$

Chapter 3

Section 3.1

3.1.2 See Figure A.1.

Section 3.2

3.2.1 1/4

3.2.2

(a) 5/36
(b) The experiment is to roll two dice and add the results. The sample space is the set of integers from 2 to 12.

3.2.3 0.15

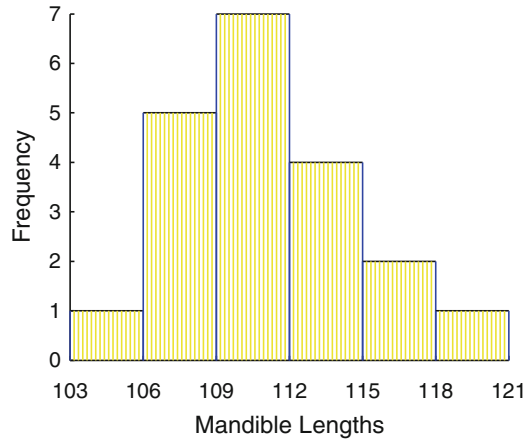

Fig. A.1 Problem 3.1.2

Section 3.3

3.3.1 $\mu = 1.016\,, \quad \sigma = 0.1340$

3.3.3 1/8

3.3.5

(a) $\mathrm{P}[X = 2] = 0.1\,, \quad \mathrm{P}[X = 1] = 0.6\,, \mathrm{P}[X = 0] = 0.3$
(b) $\mu = 0.8\,, \quad \sigma^2 = 0.36\,, \quad \sigma = 0.6$

Section 3.4

3.4.3 Needing at least three tries is equivalent to having two consecutive failures; thus, the probability is $b_{2,\,0.3}(0) = 0.49$.

Section 3.5

3.5.1

(a) $b_{2n,\,0.5}(n) = \dfrac{(2n)!}{(2^n n!)^2}$
(b) 0.176
(c) 0.080

3.5.2

(a) See Table A.1
(b) See Figure A.2
(c) See Figure A.3
(d) See Figure A.4

Table A.1 Problem 3.5.2

Measurement	32	34	36	38	40	42	44	46	48
Frequency	1.5	61	434	1488.5	2080.5	1270	349.5	44.5	2.5

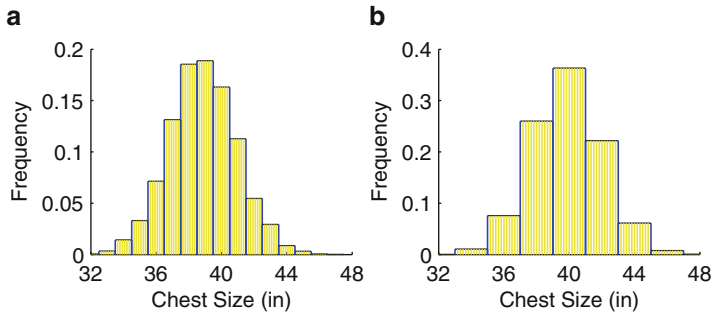

Fig. A.2 Problem 3.5.2b

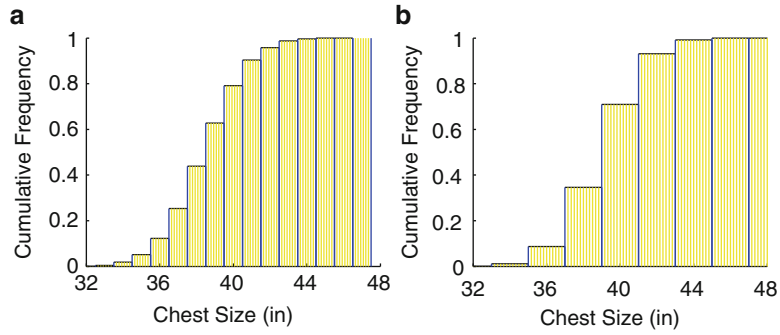

Fig. A.3 Problem 3.5.2c

Section 3.6

3.6.2

(a) 0.0668
(b) 0.3795

3.6.6 See Figure A.5.

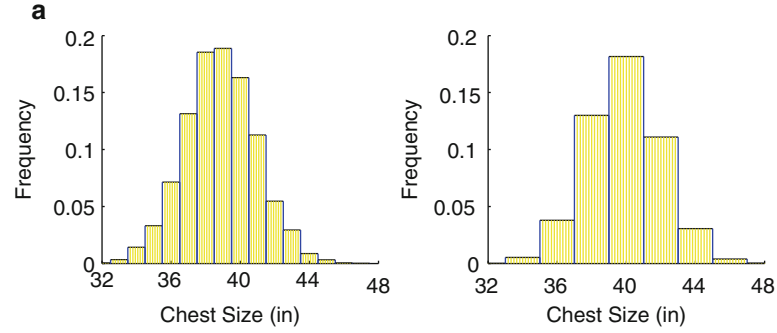

Fig. A.4 Problem 3.5.2d

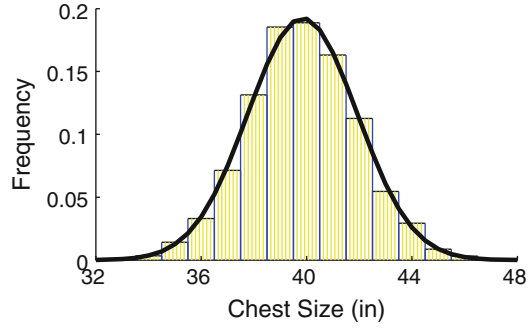

Fig. A.5 Problem 3.6.6

Section 3.7

3.7.2

(a) $f_1(1) = e^{-1} \approx 0.3679$
(b) $f_2(2) = 2e^{-2} \approx 0.2707$
(c) $f_n(n) = \dfrac{n^n}{n!}e^{-n}$, so $f_3(3) = 0.2240$, $f_4(4) = 0.1954$, $f_5(5) = 0.1755$, $f_6(6) = 0.1606$. The probably of hitting the mean goes down as the mean increases.

3.7.3 $E_4(1) = 1 - e^{-4} = 0.9817$

3.7.7 (a) $\mu = 0.425\,, \quad \sigma^2 = 0.453$
(b), (c) See Figure A.6.
(d) $\sigma^2 \approx \mu$ and the shape looks right.

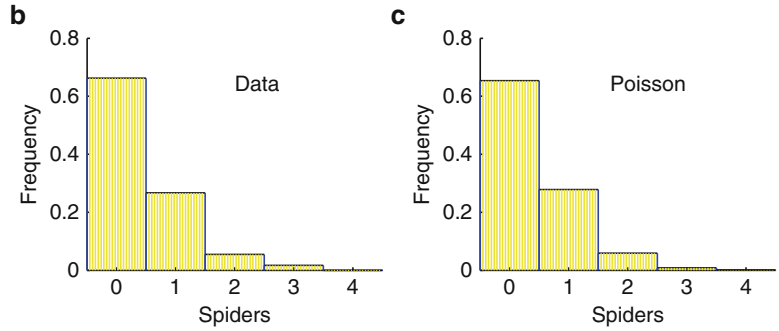

Fig. A.6 Problem 3.7.7

Chapter 4

Section 4.1

4.1.4 $B_{80,0.05}(2) = 0.2306$

4.1.6

(a) 0.0761
(b) $50 \times \dfrac{300}{5651} \times 0.0761 = 0.2020$
(c) 0.2619
(d) 0.2209

Section 4.2

4.2.1

(a) See Figure A.7.
(b) 0.036

(c) 0.028
(d) The fit to a normal distribution is unusually good, but not quite so good as to arouse suspicion.

4.2.9

(a) 0.036
(b) 0.073 and 0.148 respectively. Larger samples score worse. This makes sense. Generally we expect the residual sum of scores to increase with sample size, as it does here. It doesn't increase if the distribution is truly normal because the accuracy improves as the data is sorted into increasing order.
(c) About 0.125 is typical. Note that it is larger than the value for consecutive integers.

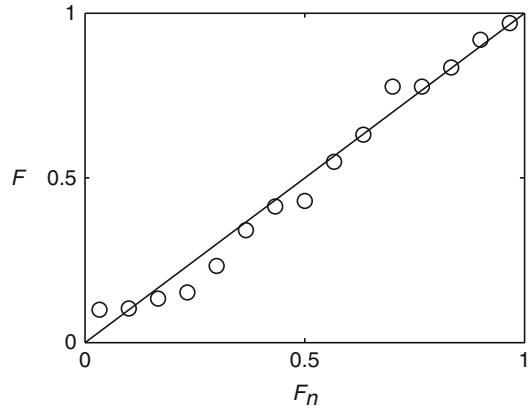

Fig. A.7 Problem 4.2.1

(d) About 0.2 is typical. This is not quite twice that of part (c). Apparently the difference between consecutive and random stays roughly the same (about 0.05) as the sample size increases.
(e) The average residual should be about the same, but there are twice as many points as in part (b).

Section 4.3

4.3.3

(a) Means are all 2; standard deviations are 0.671, 0.335, and 0.168.
(c) 0.183, 0.090, 0.066

Section 4.4

4.4.2

(a) Yes. While we cannot know the distribution from which the data was drawn, the value of the Cramer–von Mises statistic is well within the range of normally distributed data.

(b) The probability of getting the psychotic data from a population of nonpsychotics is 6×10^{-8}, so we can safely conclude that psychotics have higher dopamine levels than nonpsychotics. Given the large difference in the means, we can confidently claim biological significance as well as statistical significance.

4.4.8

(a) 0.0014
(b) 0.0046
(c) The normal distribution is not a good model for such a small number of Bernoulli trials. The binomial distribution probability is correct.
(d) 0.0384 and 0.0500. The handedness of presidents in the period between Roosevelt and Obama, exclusive, is only 5 % likely in the population at large, which (barely) meets the usual requirement for an interpretation of statistical significance. There are two possible explanations. It could be that there is some significant characteristic difference between left-handed and right-handed people that accounts for the difference, or it could merely be an example of the high probability of unrestricted coincidences. Unless more data, such as a high number of left-handed presidents prior to Roosevelt, can strengthen the case for a real difference, the latter explanation seems to be the better tentative conclusion.

Section 4.5

4.5.1 $0.0140 < \mu < 0.0188$ and $0.0133 < \mu < 0.0195$

4.5.6

(a) 0.3377
(b) $L(p) = \left(\dfrac{p}{0.3377}\right)^{106602} \left(\dfrac{1-p}{0.6623}\right)^{209070}$
(c) See Figure A.8
(e) The correct value is $L = 0.146$ rather than $L = 0.15$
(f) $L = 0.036$

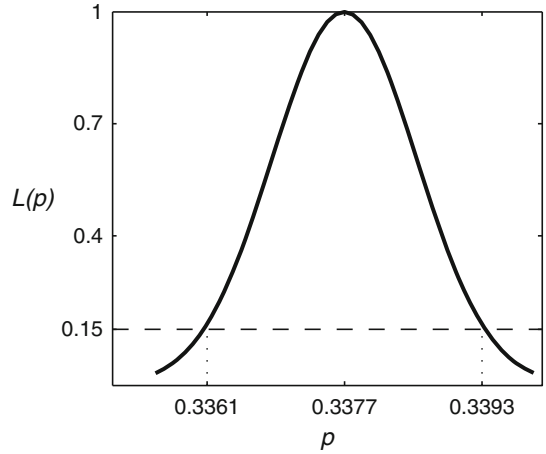

Fig. A.8 Problem 4.5.6

Section 4.6

4.6.1

(a) 0.9670
(b) 0.8523
(c) 0.8242
(d) does not make sense

4.6.3

(a) 13.89 %
(b) 0.33 %

Section 4.7

4.7.2

(a) $\mathrm{P}[B|A] = 0.2, \quad \mathrm{P}[B|A^c] = 0.3$
(b) $\mathrm{P}[A] = 3/7, \quad \mathrm{P}[B] = 9/35$
(c) $\mathrm{P}[A^c|B] = 2/3$

4.7.3

(a) $\mathrm{P}[E] = 0.012$
(b) $\mathrm{P}[E|S] = 0.05$
(c) $\mathrm{P}[E|S^c] = 0.0025$

Chapter 5

Section 5.1

5.1.1

(a) $N^\star = \dfrac{R \pm \sqrt{R^2 - 4}}{2}$. Both roots are positive if $R > 2$.
(b) There are no real roots if $R < 2$. This means $N_t^2 - RN_t + 1 > 0$, which in turn means that $N_{t+1} - N_t < 0$.

5.1.2

(a) $S - 1 + \dfrac{A}{1 + N_t}$
(b) Adults do not survive.
(c) $N^\star = \dfrac{A - (1 - S)}{1 - S}$, provided $A + S > 1$.
(d) The plot viewing window should be $0 \leq S \leq 1$ and $0 \leq A \leq \hat{A}$, where $\hat{A}$ is somewhere around 3–5.
(e) $N \to 0$, consistent with predictions.
(f) $N \to 2$, consistent with predictions.
(g) $N \to 0.6$, consistent with predictions.

Section 5.2

5.2.1 (c) See Figure A.9.

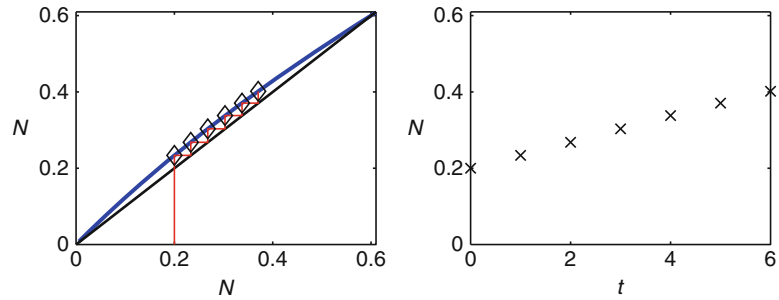

Fig. A.9 Problem 5.2.1

Section 5.3

5.3.4

(a) 0 and 8.9
(b) 0, 0.7, 2.0, and 7.3
(c) 0 and 0.36

5.3.9

(b) The term $\dfrac{cv^2}{1+v^2}$
(c) Use the equilibrium equation to find an alternative that is equivalent to the answer of part (a).
(d) $k/2$
(f) $\dfrac{1}{k}+\dfrac{k}{4}$

Section 5.4

5.4.1 0 and K are stable and T is unstable.

Section 5.5

5.5.1

(a) 0 is stable if $S+A<1$; $\dfrac{A-(1-S)}{1-S}$ is stable if $S+A>1$.
(b) The results of different methods are fully consistent.

5.5.5

(a) $f' = 1 - (2X - B)^2$
(b) $X = 1.64$ and $X = 2.56$, with $f' = 0.154$; asymptotically stable 2-cycle.
(c) For $R = 2.5$: $X = 1.5$ and $X = 3$, with $f' = -1.25$; unstable 2-cycle. For $R = 2.7$: $X = 1.44$ and $X = 3.26$, with $f' = -2.312$; unstable 2-cycle.
(e) Results are in agreement to the extent possible. There is a stable 4-cycle with $R = 2.5$ and no stable cycles for $R = 2.7$; the eigenvalue analysis did not extend to cycles longer than two time steps.

5.5.6 The results of linearized stability analysis match those of the phase line.

Chapter 6

Section 6.1

6.1.1 (b), (c) See Figure A.10.
(d) Steady growth with a fixed population ratio.
(e) Growth rate 1.1, ratio 22:1
(f) The model predicts the population will grow without bound. This is alright in the short term. In the long term, some mechanism must be present to limit population.

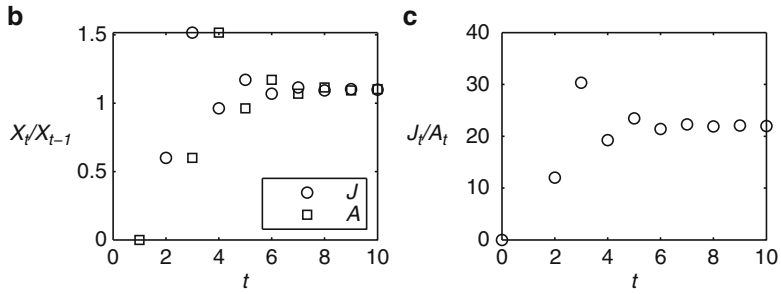

Fig. A.10 Problem 6.1.1

6.1.5 $s + rf = 1$

6.1.8 (b) $\gamma = 1$

Section 6.2

6.2.1 4

6.2.5 $\mathbf{x}_{t+1} = \mathbf{M}\mathbf{x}_t$, where $\mathbf{x} = \begin{pmatrix} J \\ A \end{pmatrix}$ and $\mathbf{M} = \begin{pmatrix} 0 & f \\ r & b \end{pmatrix}$. $\det \mathbf{M} = -rf$

6.2.9

(a) $\lambda = 3, -1$
(b) The ratios of the components of the vectors must be 1:3 and -1:1, respectively.

Section 6.3

6.3.1 $\lambda_1 = 4$. The eigenvector has ratio 3:2.

6.3.5

(a) $\lambda^2 - b\lambda - rf = 0$
(b) $rf + b = 1$

6.3.12 (d) 1.024

Chapter 7

Section 7.1

7.1.4

(a) $\dfrac{dR}{dT} = \gamma I$
(b) They are susceptible.
(c) $\dfrac{ds}{dt} = \varepsilon(1-s) - R_0 si, \quad \dfrac{di}{dt} = R_0 si - i.$
(d) The parameter ε is the ratio of the time scale for the disease to the time scale for births. These are on the order of days and years, respectively.

Section 7.3

7.3.4 (a) $(1,0)$ is always an equilibrium point; $\left(\dfrac{1}{R_0}, \varepsilon\left(1 - \dfrac{1}{R_0}\right)\right)$ is an equilibrium point when $R_0 > 1$.
(b), (c) See Figure A.11.
(d) $(1,0)$ is stable when $R_0 < 1$ and unstable when $R_0 > 1$. The stability of the other equilibrium point cannot be determined from the nullcline plot.

Section 7.4

7.4.1

(a) The origin is stable for $k > 1$ and unstable for $k < 1$.
(b) The nullcline plot is unable to distinguish these cases.

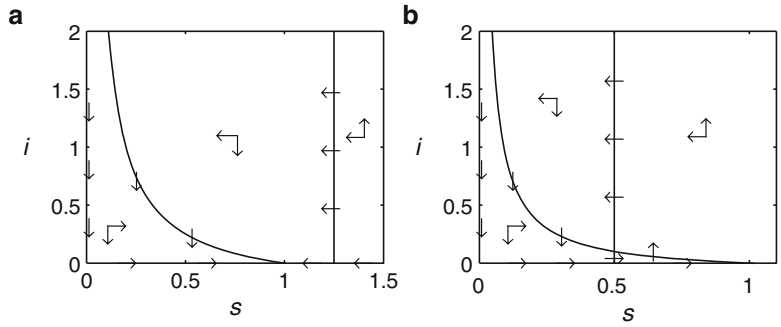

Fig. A.11 Problem 7.3.4

7.4.3

(a) $c_2 \approx (1+a_1+b_1)(a_2+b_2) - a_1a_2 = (1+b_1)a_2 + (1+a_1+b_1)b_2 > 0$
(b) Under the assumption that ε is arbitrarily small, we have $c_3 \to 0$ while $c_1c_2 > 0$. Hence, $c_1c_2 > c_3$ for ε small enough.

Section 7.5

7.5.1

(a) The equilibrium $(1,0)$ is stable when $R_0 < 1$. The equilibrium $(R_0^{-1}, \varepsilon(1-R_0^{-1}))$ is stable when it exists $R-0>1$.
(b) The result for $(1,0)$ is the same as in Problem 7.3.4. The stability of the other point could not be determined from nullcline analysis. All results are consistent with the biological setting. It makes sense that the disease-free state should be stable if R_0 is below some threshold and unstable if it is higher.

7.5.7

(a) $(0,0)$ is unstable; $(1,0)$ is stable if $h < 1$.
(b) Stable when it exists $(h > 1)$.
(c) Results are consistent. Nullcline analysis was unable to determine the stability of the equilibrium with $c > 0$.
(d) Increasing h decreases the vegetation and increases the consumer population. Decreasing h too much drives the consumer to extinction.

Appendix A

Section A.1

A.1.4

(a) There are no stable fixed points.
(b) There is a stable fixed point with positive values.
(c) The origin is stable.
(d) All results are consistent with the analysis.

A.1.7

(a) $p^\star = \ln R_0\,, \quad \det \mathbf{J} = \dfrac{R_0 \ln R_0}{R_0 - 1}$

(b) $g(R_0) = R_0(1 - \ln R_0)$

Section A.2

A.2.3

(a) There is only one way to complete the matrix that is consistent with the requirements for Markov chain matrices.

Section A.3

A.3.1

(a)

$$f(0,0,0) = (0,1,1)\,, \quad f(0,0,1) = (1,0,1)\,, \quad f(0,1,0) = (1,1,1)\,, \quad f(0,1,1) = (1,0,1)\,,$$
$$f(1,0,0) = (0,0,1)\,, \quad f(1,0,1) = (1,0,0)\,, \quad f(1,1,0) = (1,0,1)\,, \quad f(1,1,1) = (1,0,0)\,.$$

(b) See Figure A.12

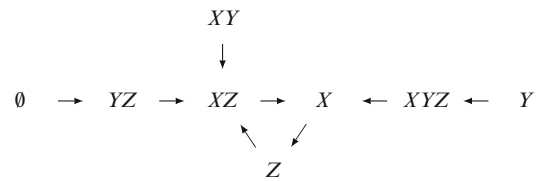

Fig. A.12 Problem A.3.1

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G. Ledder, *Mathematics for the Life Sciences: Calculus, Modeling, Probability, and Dynamical Systems*, Springer Undergraduate Texts in Mathematics and Technology, DOI 10.1007/978-1-4614-7276-6,

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