Introduction to Modeling in Ecology and Evolutionary Biology
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0 Introduction to the course

1. Who is this course for? Grad students in EEB and related fields, ideally students doing research who will use the course term paper as an occasion to connect what they learn in this course with their own research.

2. How it relates to other courses: my other courses are aimed at students who want to focus on modeling. This course can be one of two things: a steppingstone to those course, or a way to learn enough about modeling that you can be more effective at reading papers with models in them, and working with modelers.

3. SPE and NGH Jr as role models: I know about experiments (and have done some), he knows about modeling (and has done some). Now we specialize, but the cross-training has a lot to do with our ability to collaborate successfully.

4. This course isn’t about current research. You will learn some new concepts and skills, in simple contexts. The “current research” part will be what you do for your term project. This is brand new for the course. My current idea is that should be a Nature paper: 10-12 double-spaced pages, 3 or 4 figures, in which you pose a question, develop a model, study the model, and report your results.

5. Why use Otto and Day? To help me forget BMA 567 and stay awake. Therefore, the lectures I give will follow the textbook closely.


7. Collect everyone’s email.

8. Questions?

9. Schedule: we have Rosh Hashanah on coming up soon (Sept. 9), no class then. We will try to get into a regular “groove’ of lecture/discussion after that.

1 Chapter 1: Mathematical Modeling in Biology

This chapter is about the purpose, nature, and value of mathematical models in biology. It is the one chapter in the book I don’t like, because they start with complicated examples instead of simple ones. So I’m going to cover the same ground as Chapter 1, based on my textbook.
The purpose of mathematical models is to connect

\[
\text{Process } \iff \text{Pattern} \\
\text{Function } \iff \text{Structure} \\
\text{Causes } \iff \text{Effects}
\]

That is: mathematical models help us to

- go from observed patterns, to possible underlying causes (could A cause B? try it on the computer!)
- go from known processes to predicting their potential consequences

### 1.1 Descriptive versus dynamic models

Salmon stocks in the Pacific Northwest have been in steady decline for several decades. To reverse this trend, we need to know what’s causing it. Figure 1 shows data on salmon populations on the Thomson River in British Columbia (Bradford and Irvine 2000). Figure 2 presents the results from statistical analyses in which data from individuals streams in the Thomson River basin are used to examine how the rate of decline is affected by variables describing human impacts on the surrounding habitat. Straight lines fitted to the data (a linear regression model) provide a concise summary of the overall trends and quantify how strongly the rate of decline is affected by land use and road density. These are examples of descriptive models – a quantitative summary of the observed relationships among a set of measured variables.

![Graph showing Decline in Coho salmon stocks on the Thomson River, BC](from Bradford and Irvine 2000)

Figure 1: Decline in Coho salmon stocks on the Thomson River, BC (from Bradford and Irvine 2000)

Figure 2 provides very useful information and descriptive models like these are indispensable, but there are some important limitations.
It says nothing about why the variables are related the way they are. Based on the results we might decide that reducing road density would help the salmon. But maybe road density is just an indicator for something else that’s the real problem, such as fertilizer runoff from agriculture.

We can only be confident that the model applies to the river where the data come from. It might apply to other rivers in the same region and even to other regions – or it might not. This is sometimes expressed as the “11th commandment for statisticians”: Thou Shalt Not Extrapolate Beyond the Range of Thy Data. The commandment is necessary because we often want to extrapolate in order to make useful predictions – for example, how salmon stocks might respond if road density were reduced.

The second limitation is related to the first. If we knew why the relationship holds in this particular location, we would have a basis for inferring whether or not it would hold in some other place.

In contrast, a dynamic model is mechanistic, meaning that it explicitly represents the processes that produce our observations. Relationships between variables are a consequence of underlying processes. A dynamic model has two essential components:

- A short list of state variables that are taken to be sufficient for summarizing the properties of interest in the study system, and predicting how those properties will change over time. These are combined into a state vector $X$ (a vector is an ordered list of numbers).
- The dynamic equations: a set of equations or rules specifying how the state variables change with time.
change over time, as a function of the current and past values of the state variables. *These are expressions of your assumptions about the system.* Modeling is the process of taking your biological knowledge, and expressing it as mathematical statements about how state variables change over time.

A model’s dynamic equations may also include a vector $E$ of *exogenous variables* that describe the system’s environment – attributes of the external world that change over time and affect the study system, but are not affected by it.

Modeling means that we use our scientific knowledge to choose the important state variables, and to describe the processes that make them change over time. Then we express it all in mathematics, so we can solve the model on the computer.

Because it is built up from the underlying causal processes, a dynamic model expands the Range of Thy Data to include any circumstances where the same processes can be presumed to operate. This is particularly important for projecting how a system will behave in the future. If there are long term trends, the system may soon exceed the limits of current data. With a dynamic model, we still have a basis for predicting the long-term consequences of the processes currently operating.

Dynamic equations may be deterministic or stochastic. Deterministic means we can say exactly what will happen next, given the current value of all state variables. Stochastic means that we have a list of possibilities, and associated probabilities for each.

*We’ll start with deterministic.* There are two main flavors: difference equations, and differential equations. Difference equations are:

$$x(t + 1) = F(x(t)) \text{ or } x(t + 1) = F(x(t); \theta). \quad (1.1)$$

This means jumping directly from Now to Later, without worrying about In Between. Useful for seasonality, for example.

Differential equations are

$$\frac{dx}{dt} = F(x(t)) \quad (1.2)$$

Here time is continuous (though often we ignore short-term variability, e.g. day vs. night). But these models also come from asking “what happens next?”, because the derivative comes from a *difference quotient.*

$$\frac{dx}{dt} = \frac{x(t + h) - x(t)}{h} \text{ in the limit as } h \to 0 \quad (1.3)$$

So what our model is saying is:

$$x(t + h) = x(t) + h \times F(x(t)) \text{ for small } h. \quad (1.4)$$
1.2 First example: the bathtub

We will start with a simple but very important example: the bathtub, with state variable \( W(t) \) = amount of water in the tub (Figure 3). This is really true, because everything is the same in principle for models \( W(t) \) = amount of mercury in tuna, amount of CO2 in the atmosphere, number of heterozygotes in a population, or number of copies of a transposable element.

Figure 3: Compartment diagram of the bathtub model. The rectangle denotes the state variable – the amount of water in the tub – and the arrows denote flows.

A dynamic equation for this model has to tell us how \( W(t) \) changes over time. Time is continuous in this case, but to derive the model we consider a small interval of time from now (time \( t \)) until a little bit later (time \( t + h \)). We take \( h \) short enough that any changes over the time interval in the process rates \( I(t) \) and \( O(t) \) are small enough to be ignored. Then

\[
W(t + h) = W(t) + \text{Inflow rate} \times \text{time elapsed} - \text{Outflow rate} \times \text{time elapsed}
= W(t) + I(t) \times h - O(t) \times h
\]

(1.5)

We want to let \( h \to 0 \). To do that, we rearrange (1.5) into

\[
\frac{W(t + h) - W(t)}{h} = I(t) - O(t)
\]

(1.6)

The left hand side of (1.6) is a difference quotient for the derivative of \( W \) with respect to time. So we can now let \( h \to 0 \) and we get

\[
\frac{dW}{dt} = I(t) - O(t)
\]

(1.7)
In words: Change in $W = \text{amount coming in} - \text{amount going out}$, with all amounts being \textit{amounts per unit time}.

1.3 Many bathtubs: compartment models

If we connect several bathtubs, so that whatever flows out of one tub can flow into one or more other tubs, we get a \textit{compartment model}. The state variables in a compartment model are the amount of some stuff in a number of distinct locations or categories ("compartments") within the system. Despite their simplicity, or perhaps because of it, compartment models are very widely used in biology.

The "stuff" in the model can be essentially anything. Sometimes it really is the amount of some material in a particular location – the level of lead in blood, liver, brain, etc., or the amount of nitrogen in different layers of soil. It can also be amounts or numbers in a particular state or category: gene copies in active/inactive state; infected versus uninfected T-cells in the immune system; ion channels in open/closed state in a neuron; small, medium, and large sea turtles. The key assumption, as in our simple bathtub, is that items within a compartment are indistinguishable from each other – this is expressed by saying that compartments are "well-mixed". Thus we only need to keep track of the quantity of material in each compartment - how much water is in the bathtub, but not the time when each molecule arrived or which other bathtub it came from.

1.4 Sir Ronald Ross and the epidemic curve

Sir Ronald Ross (1857-1932) received the 1902 Nobel Prize in medicine for determining the life cycle of the malaria parasite, in particular the role of mosquitoes in the parasite life cycle and as vectors for its transmission between humans. From that humble beginning he went on to found the modern application of dynamic models to the study of infectious diseases.

Ross (1916) gave two motivations for modeling epidemic dynamics. First, he noted that infectious diseases could display three different temporal patterns:

1. \textbf{Endemic}: relatively small fluctuations in monthly case counts, and only slow increase or decrease over the course of years (Ross listed leprosy and tuberculosis in this category)

2. \textbf{Outbreak}: constantly present but flaring up in epidemic outbreaks at frequent intervals (measles, malaria, dysentery)

3. \textbf{Epidemic}: Intense epidemic outbreaks followed by disappearance (plague, cholera)

Ross (1916, p. 205) asked “To what are these differences due? Why, indeed, should epidemics occur at all, and why should not all infectious diseases belong to the first group and remain at an almost flat rate?”
Ross’s second motivation was to explain the characteristic shape of the epidemic curve for diseases in the third class. The epidemic curve is the time course of disease incidence, the number of new cases per unit time. Figures 4 and 5 show a few examples. The characteristic features are a symmetric or nearly symmetric rise and fall, with the outbreak terminating before all individuals susceptible to the disease have become infected. Because susceptibles still remain in the population when outbreaks terminate, it was argued by some at the time that outbreaks terminate because the pathogen loses infectivity; others hypothesized that the uninfected individuals must have been less susceptible to the disease.

Ross’s (1916) model was a partial success, allowing him to show that the shape of epidemic curves could be explained without either of these hypotheses. His other goal, to explain different patterns of disease dynamics, was tackled a decade later by Kermack and McKendrick (1927). Current models are largely based on Kermack and McKendrick’s (1927) modified versions of Ross’s models, so we will consider those here. The models are formulated at the level of the

Figure 4: Examples of epidemic curves. (a) Phocine distemper virus in Northern Ireland 1988/89 (data from Figure 4 of Hall et al. 1992, provided by John Harwood). (b) An outbreak of influenza in Fort Benning, Georgia in 1995 (data from Davidson 1995). (c) Recurrent outbreaks of measles in Reykjavik, Iceland (data provided by Andrew Cliff, Department of Geography, University of Cambridge).
available data: the numbers of individuals reported to contract the disease. Individuals are classified as being either Susceptible to the disease, Infected by it, or Recovered or Removed. R-stage individuals are neither infectious nor infectable: either dead, or having immunity (permanent or temporary) against the disease.

The first of Kermack and McKendrick’s basic models described a disease outbreak in a closed population of constant size.

**DRAW COMPARTMENT DIAGRAM**, label arrows, derive equations from that

\[
\begin{align*}
    dS/dt &= -\beta SI \\
    dI/dt &= \beta SI - \gamma I \\
    dR/dt &= \gamma I 
\end{align*}
\] (1.8)

Initial conditions are \( S(0) = S_0 \approx N, \quad I(0) = N - S_0 \approx 0, R(0) = 0 \) where \( N \) is the total population size. Since \( dS/dt + dI/dt + dR/dt = 0 \) the total population size remains constant at \( N \). The population is closed in the sense that no new susceptibles are added by births or immigration, and so long as \( R \) individuals are counted the population size is constant. Thus
the assumption of constant population size is really that the only changes in population size are disease-induced deaths. The fraction of infected individuals, \( I(t)/N \), is called the \textit{prevalence} of the disease.

The first equation in model (1.8) is disease transmission resulting from contact between susceptible and infectives. Ross (1916) justified this transmission rate as follows. Each infected individual transmits the pathogen to \( b \) individuals per unit time, but new cases arise only if the recipient individuals is susceptible. Assuming a constant population of size \( N \), the number of new cases per unit time is therefore \( bI(S/N) = \beta SI \) where \( \beta = b/N \). This form of transmission is called “mass action” (by analogy with the Law of Mass Action in chemical reactions) or “proportional mixing” (Anderson and May 1992). Mass action has been and still remains the most widely used transmission model; McCallum et al. (2002) review alternative models and empirical studies about the validity of the mass action model.

In the second equation, \( \gamma \) is the rate at which infected individuals recover from the disease (or die), at which point they transfer to the \textbf{Re}covered class. The exit-rate \( \gamma \) can be interpreted biologically as the inverse of the mean residence time in the compartment; this interpretation is very important for fitting these models to empirical data.

Whether \textbf{Re}covered individuals are dead versus alive and immune is in one sense irrelevant for the future course of the epidemic, because in either case they have no impact on future infections. However, changes in the number of living individuals invalidates Ross’s (1916) derivation of the disease transmission rate. If the living population is not constant, then to justify the \( \beta SI \) in (1.8) we have to assume that the rate of contacts per individual is proportional to the population size – if you double the number of people on the subway, then the kid with the runny nose infects twice as many people. If so, then the rate of new infections is \( (bN)I(S/N) = \beta SI \) with \( b = \beta \).

1.4.1 Rescaling the model

What is the resulting shape of the epidemic curve? At first sight, it appears that we would need to see how the shape and behavior of solutions depends on 3 parameters: \( \beta, \gamma \) and \( N \). However, by rescaling the model we can reduce to a single parameter.

The benefit of rescaling is that the model becomes simpler just by changing the units of measurement for time and state variables. Usually the most effective rescalings are ones that render all variables in the rescaled model \textit{dimensionless}. For example: \( S, I, R, \) and \( N \) are all “population size”, measured in units like individuals/km\(^2\), or individuals/m\(^2\). The numerical values of these variables depends on the choice of units. However, if we look at the ratios \( X = S/N, Y = I/N, Z = R/N \), their value will be the same regardless of the units used for population size. \( X, Y, Z \) are called \textit{dimensionless} variables because their numerical value does not depend on the units of measurement.
The dynamic equations for our re-scaled variables are easily derived:

\[
\frac{dX}{dt} = \frac{1}{N} \frac{dS}{dt} = -\frac{\beta SI}{N} = -(\beta N)(S/N)(I/N) = -bXY
\]

and similarly

\[
\frac{dY}{dt} = bXY - \gamma Y \\
\frac{dZ}{dt} = \gamma Y
\]

This gets us down to two parameters: \(\gamma\) and the new composite parameter \(b = \beta N\). We can get rid of one more parameter by defining a rescaled time variable \(\tau = \gamma t\). Recall that the mean duration of infection is \(1/\gamma\), so a unit increase in \(\tau\) corresponds to real elapsed time equal to the mean duration of infection. We then have

\[
\frac{dX}{d\tau} = \frac{dX}{(\gamma dt)} = (1/\gamma)\frac{dX}{dt} = -(\beta N/\gamma)X.
\]

The step from \(dX/d\tau\) to \((1/\gamma)dX/dt\) follows from the chain rule, \(\frac{dX}{d\tau} = \frac{dX}{dt}\), but the heuristic calculation in the last equation gets the right answer.

The conclusion is that \(dx/d\tau\) depends on the single parameter combination \(R_0 = \beta N/\gamma\). Doing the same with the other state variables we get the re-scaled model

\[
\begin{align*}
\frac{dX}{d\tau} &= -R_0XY \\
\frac{dY}{d\tau} &= R_0XY - Y \\
\frac{dZ}{d\tau} &= Y
\end{align*}
\]  

(1.9)

with initial conditions \(X(0) = X_0 \approx 1, Y(0) = Y_0 \approx 0, Z(0) = 0\).

An immediate prediction from this model is a threshold condition for an epidemic to occur. At time 0, \(dY/d\tau = Y(R_0X_0 - 1) \approx Y(R_0 - 1)\), for a disease introduced at low incidence into the populations. Consequently, the disease prevalence increases if and only if \(R_0 > 1\). Since \(X(\tau)\) can only decrease over time, if \(Y\) is not increasing at time 0 it can never increase later, so the disease must die out.

The quantity

\[
R_0 = \frac{\beta N}{\gamma}
\]

is called the “basic reproductive rate” of the disease, and can be interpreted as the expected number of new infections produced by a single infected individual introduced into a population of \(N\) susceptibles: \(\beta N\) infections per unit time, multiplied by the expected time \(1/\gamma\) in the infectious stage. It therefore should be (and is) a very general property of epidemic models that a disease can be maintained in a population only if its \(R_0\) (defined appropriately for the model)
is greater than 1. Measures that reduced $R_0$ below 1 would then eradicate the disease, such as quarantine of infectives to reduce $\beta$ or vaccination to reduce the number of susceptibles.

Finally, numerical solution can be used to find the shape of the epidemic curve predicted by the model (1.9), as a function of the single parameter combination $R_0$, for initial conditions $X(0) \approx 1$, $Y(0) \approx 0$, $Z(0) = 0$. The epidemic curve is defined as the rate at which new cases appear, i.e. i.e. $R_0 X(\tau) Y(\tau)$. Figure (1.4.1) shows that the model does indeed produce reasonable-looking epidemic curves. Higher values of $R_0$ naturally lead to a shorter and more intense epidemic, in addition to a higher final infected fraction $Z_\infty$. Recall that $\tau$ measures elapsed time in units of the mean duration of infection, so the solutions show that if $R_0 = 5$ the epidemic only lasts about twice as long as the duration of the infection, while if $R_0 = 1.05$ it last for over 10 times the duration of infection.

![Figure 6: Epidemic curves (number of new cases per unit time) calculated from numerical solution of the Kermack-McKendrick model for a disease without recovery in a closed population of constant size. The plot shows $R_0 X(\tau) Y(\tau)$ as a function of scaled time $\tau$.](image)

1.5 Drug resistance

The effectiveness of antibiotic drugs is being challenged by the emergence of drug-resistant strains. One current concern is anti-retroviral resistant HIV. Combination anti-retroviral (ARV) therapies for HIV, involving simultaneous treatment with 3 or more different drugs, are currently the most effective available treatment. In use since 1996, these have substantially decreased the death rate from AIDS (Blower et al. 2001). However, strains resistant to the 3-drug
“cocktail” have emerged and have been sexually transmitted. Blower et al. (2000, 2001) used a compartment model model to evaluate the magnitude of the threat posed by ARV-resistant HIV strains, and to evaluate possible responses.

The model (Figure 7) describes the transmission dynamics of HIV in the presence of antiretroviral therapy, with resistant and non-resistant strains circulating in the population.

Figure 7: Compartment diagram from Blower et al. (2000) for their model for HIV transmission dynamics in the presence of antiretroviral therapy, with both resistant and non-resistant strains circulating in the population.

The model (Figure 7) describes the transmission dynamics of HIV in the presence of antiretroviral therapy, with resistant and non-resistant strains being transmitted. In structure it is an SIR model with two complications: distinguishing between treated and untreated cases, and between resistant and non-resistant strains of the disease. Dropping the recovered population as usual, the state variables are

- Susceptible individuals $X$
- Infected individuals $Y$, who can have drug-Sensitive, or drug-Resistant strains of the drug, and who can be Treated or Untreated.

The $c$'s are contact rates and $\lambda$'s are the rate of infection per contact, calculated from the number of infected individuals in each category and the infectiousness ($\beta$) of each type of infection.

Parameters $\sigma$ and $g$ represent the rates of individuals entering and leaving treatment. Untreated drug-resistant infections revert to drug-sensitive at rate $q$, while treated drug-sensitive infections acquire drug resistance at rate $r$. 

\[ \begin{align*}
\pi & \rightarrow X \\
\mu & \rightarrow X \\
& \downarrow c\lambda_R \\
& \downarrow q \\
& \downarrow c\lambda_S \\
Y_R^U & \xrightarrow{c\sigma_R} Y_R^T \\
& \xleftarrow{\beta_R} Y_R^U \\
& \xrightarrow{r} Y_S^T \\
& \xrightarrow{\beta_S} Y_S^U \\
& \xrightarrow{c\lambda_S} Y_S^U \\
& \xrightarrow{\sigma_S} Y_S^T \\
& \xrightarrow{\beta_S} Y_S^U \\
& \xrightarrow{v_S^T + \mu} Y_S^T \\
& \xrightarrow{v_R^U - \mu} Y_R^U \\
& \xrightarrow{v_R^T + \mu} Y_R^T \\
& \xrightarrow{v_S^T + \mu} Y_S^T \\
& \xrightarrow{v_S^U + \mu} Y_S^U
\end{align*} \]
Data-based estimates for several model parameters were available for the San Francisco gay community, while others parameters were less certain and probability distributions were used to represent the relative likelihood of different possible values. For example Blower et al. (2001) allowed the rate $r$ at which ARV drug resistance develops in treated cases to range between 10% and 60% per year. Because little is known about ARV resistant strains, and in particular about their transmissibility relative to drug-sensitive strains, they allowed the relative transmissibility to vary between 1% and 100% of the transmissibility of the drug-sensitive strain.

Given this wide range of uncertainty, model predictions were generated for a large number of random draws of parameter values according to the distributions representing parameter uncertainty, and then studied statistically as if they were the results of an experiment – which in a sense they are. Blower et al. (2001) were able to compare model predictions with empirical estimates through 1999; data published later allowed comparison out to 2001 (Blower et al. 2003, Figure 8).

A surprising prediction from the model is that the transmission of resistance is low, and will remain low at least in the short run: for 2005, it was predicted that most new infections will still be by drug-sensitive strains (median 84.4%, interquartile range 72 - 94%). Thus, the main source of drug-resistant cases is conversion of drug-sensitive cases to drug-resistant cases: individuals with a drug-resistant infection are at risk themselves, but do not pose a major threat to the general population. This prediction has some important practical applications. First, it says that combination ARV will remain effective on most new infections, and can continue to be used on newly diagnosed cases. Second, efforts to limit the spread of drug resistant strains should focus on minimizing the rate of conversion from sensitive to resistant cases – by delaying treatment as long as possible, and trying to enforce strict compliance with the treatment program. Finally, the lack of resources to monitor patient compliance in developing countries implies that drug-resistance is likely to be more of a problem than in developed countries.
Figure 8: Fraction of new HIV infections that are resistant to combination ARV treatment: theoretical predictions versus empirical data for San Francisco (redrawn from Blower et al. 2003 using data provided by S. Blower). Model simulations were run over the time period 1996-2005, with initial conditions corresponding to estimated values for 1996. Boxes enclose the interquartile range (25\textsuperscript{th} to 75\textsuperscript{th} percentiles) of model outcomes and bars show outlier cutoffs; the bars inside the boxes are the median values. Triangles show resistance to non-nucleoside reverse transcriptase inhibitor, and crosses show resistance to protease inhibitor, in a study of 243 newly infected individuals in San Francisco from 1996 to 2001 who had no previous exposure to ARV drugs.
Chapter 2: How to Construct a Model

Sally’s exercises: 2.2, 2.3, and 2.7

Chapter 2 uses three focal examples to illustrate the process of model building:

1. How does the number of branches on a tree change over time?
2. How does the presence of a cat change the number of mice in a yard?
3. How does the number of people with the flu change over the flu season?

We’ve already talked about infectious diseases, so I will focus on the cat model, which is just complicated enough to include everything that we need to talk about.

2.1 Modeling process

On p. 18 Otto and Day list “Seven Steps to Modeling a Biological Problem”. My version is slightly shorter (Figure 9):

1. Formulate your objective
2. Conceptual model
3. Model diagram
2.2 Formulating the objective

The first, essential, and most frequently overlooked step in modeling is to decide exactly what the model is for. We can’t ask models to be literally true, but we can insist that they be useful, and that is measured against your objectives. You need to decide:

- What will the model do for you? What is your scientific question, and how will a model help you answer it?

Your goal will determine (for example) what level of detail you need, and what your criteria will be for either accepting your model, or deciding that it needs to be revised.

2.3 Conceptual model

A model begins with your ideas about the important variables and processes in the system. These may come from hard data and experimental evidence, or they may be hypotheses that are being entertained for the moment, in order to determine their consequences. Issues are:

- What are the key process and state variables?
- What level of detail do I need to achieve my objective? Does it need to be stochastic?
- Discrete or continuous time?
- Discrete or continuous state?

You should always start as simple as you can, and add details only when they prove necessary.

2.4 Diagram

The first step in turning concepts into a dynamic model is to represent the conceptual model as a diagram showing the state variables and processes. You need to come up with names (symbols) for your state variables and parameters, and then draw some kind of box-and-arrow diagram to represent the system.

As you draw boxes and arrows, you are formalizing your conceptual model by choosing which components and processes are included, and which are outside the model.
2 CHAPTER 2: HOW TO CONSTRUCT A MODEL

Drawing the diagram also sets your model’s level of detail. If you leave out important variables or processes, you can’t write a valid set of dynamic equations. Biologists often feel that the solution to this problem is to include everything: every detail that can go in, should go in. But you can also get into trouble by including too much detail. Biologists often feel that adding more and more biological detail will make a model more accurate, but that is only true up to a point if parameters are estimated from data. More detail requires more parameters, so the number of observations going into each parameter goes down, and eventually all parameter estimates are unreliable.

So a good strategy for building your diagram is to start with the phenomena or data that figure explicitly in your objectives, work out from there (adding other state variables and processes that affect the ones of primary interest), and stop as soon as you can.

So let’s take the cat-and-mouse model as an example. The conceptual model is this: each day there are three things that happen:

1. Mice give birth
2. Mice move in from surrounding areas
3. The cat eats some mice

First, we’ll model this in discrete time. We’ve said that the goal is to determine how the presence of the cat affects the mouse population, so one state variable that we need is 

\[ n(t) = \text{number of mice on day } t. \]

Our goal is to come up with the number of mice on day \( t + 1 \).

A life cycle diagram represents the chain of events that takes us from day \( t \) to day \( t + 1 \). In a discrete-time model, we have to decide on the order in which the 3 events take place. Suppose we have predation followed by births followed by emigration. That gives the diagram shown in Figure 10 – draw on the blackboard. Primes, as in \( n', n'', n''' \) are used to indicate changes in a state variable that occur within a time step (between \( t \) and \( t + 1 \)), so \( n' \) is the number of mice after predation, but before births and migration.

Another representation is as a flow diagram, very much like the compartment diagrams we drew for the bathtub and infectious disease models, figure 11. To draw this, we need to start making up some names and making assumptions. Keeping it simple, we’ll suppose that each mouse has probability \( d \) of getting killed by the cat, so the expected number of deaths is \( dn(t) \). Each surviving mouse has \( b \) offspring, on average, before the population is censuses again on day \( t + 1 \), so the number of births is \( bn'(t) \). And we’ll assume that \( m \) mice per day immigrate into the population.

Note: the “self loop” for births is not strictly “legal” for compartment diagrams, because there
isn’t an outflow. But this is a widely-used convention: a self-loop represents internal production, whereas an arrow from one compartment to another represents a flow.

Another convention used by Otto and Day (and others) is to use dashed arrows to indicate when a state variable affects a flow rate. Their use of these is completely idiosyncratic, however, because they assume that all outflows are affected by the compartment of origin. Adding the dashes generally makes for cluttered diagrams that are hard to read, so use them with caution.
2.5 Dynamic equations

A complete diagram should imply the dynamic equations. You should be able to look at the picture, and write down the complete model. For cat-and-mouse in discrete time it goes like this:

\[
\begin{align*}
    n'(t) &= n(t) - dn(t) & \text{the cat kills some mice} \\
    n''(t) &= n'(t) + bn'(t) & \text{surviving mice have offspring} \\
    n'''(t) &= n''(t) + m & \text{some new mice move in} \\
    n(t+1) &= n'''(t) & \text{nothing else happens}
\end{align*}
\]  

The rest is algebra: putting working through, we get

\[n(t + 1) = (1 + b)(1 - d)n(t) + m\]
and that’s the model for our assumed sequence of events.

The continuous-time model doesn’t have $n', n''$, etc. because events are continuously happening, and the population is continuously changing. So we think of $b, d, m$ as instantaneous rates: $b$ is the number of births per mouse per day, and in $h$ days ($h \ll 1$) the average mouse has $b \times h$ offspring. So now the model comes from $dW/dt = I(t) - O(t)$ and it is:

$$\frac{dn}{dt} = bn(t) - dn(t) + m = (b - d)n(t) + m.$$ 

It is important to understand the connection between the discrete and continuous time models, which is this: Suppose that the cycle in the life-cycle diagram happens many times per day, so that every $h$ days (where $h$ is much smaller than 1) the cycle goes around completely. The death rate $d$ is then replaced by $dh$, etc. giving

$$n(t + h) = (1 + bh)(1 - dh)n(t) + mh$$

A bit of algebra then gives

$$\frac{n(t + h) - n(t)}{h} = (b - d)n(t) + m - bdn(t)h$$

so letting $h \to 0$ we get back the differential equation model).

Infectious disease models give us some useful practice at translating a diagram into equations.

**DRAW DIAGRAMS FOR:**

- $S \to I \to R$ without births or deaths
- Add births by Susceptibles only
- Add births by Susceptibles and Recovered
- Add disease-induced mortality of Infectives

Look at Blower et al. model?

### 2.6 Checks and balances

Before doing anything else, you want to check and see if the equations you’ve gotten make sense.

1. Are the equations dimensionally correct?
2. Do the equations obey the biological constraints on the variables (e.g., can the number of mice become negative?)
3. Does the model work in special cases where you know the right answer?
4. Is the level of detail and complexity really appropriate for your objective?
Figure 12: Flow diagram for part of Blower model for HIV and AIDS cases in the gay male community in San Francisco
Chapter 3: Deriving classic models

Everything in this chapter is a population model of one sort or another. The more interesting ones are structured population models, meaning that we keep track of several different types of individuals, possibly in several different species. Some of the most important (i.e. frequently used) structuring variables are age, size, genotype, disease state, location

Figure 13: Flow diagram for BIDE balance law

The starting point for population modeling is the fundamental “BIDE” Balance Law for total population size $n(t)$:

$$n(t+h) = n(t) + \text{Births at } t \text{ to } t+h \quad \text{+ Immigration} \quad \text{− Deaths at } t \text{ to } t+h \quad \text{− Emigration} \quad (3.1)$$

Equation (3.1) is always true, but it is vacuous until we specify the values of B,I,D, and E over the time interval $(t, t+h)$.

3.1 Exponential growth

The simplest possibility is to assume a closed population $(I = E = 0)$, ignore all outside influences (food, competitors, weather, etc.) and all differences between individuals. Then each individual has the same chance of giving birth between $t$ and $t + h$ and the same chance of death. Letting $b$ and $d$ be the chances of these per unit time. Then in a

$$B = b \times h \times n(t), D = d \times h \times n(t) \implies n(t+h) = n(t) + (b-d)hn(t) \implies dn/dt = (b-d)n.$$
We can make the models look a bit simpler. If we let $R = 1 + (b - d)h$ and $r = b - d$, then

$$n(t + h) = Rn(t), \quad \frac{dn}{dt} = rn(t).$$

Both of these are simple enough to solve explicitly.

In discrete time, as usual, you have to worry about the order of events. I’ve assumed that each individual might give birth, and each might die, but not both. Alternatively, we can say that between each census there is a short breeding season when births occur, followed by a longer period when deaths occur. This gives

$$n(t + 1) = (1 - d)(1 + b)n(t) \implies n(t + 1) = Rn(t) \text{ with } R = (1 - d)(1 + b).$$

### 3.2 Logistic growth and Lotka-Volterra

The logistic model adds self-limitation in a non-mechanistic way. Without saying why, we assume that when there are lots of others around, $R$ is smaller, and the decrease is assumed linear (why not)? Then

$$R(n) = (1 + r_d) - \frac{r_d}{K} n \implies n(t + 1) = n(t) + r_d n(t) \left(1 - \frac{n(t)}{K}\right).$$

(here the $d$ seems to stand for “discrete”). In continuous time, we let $r(n)$ decrease linearly with $n$,

$$r(n) = r - \frac{r}{K} N \implies \frac{dn}{dt} = rn(1 - n/K).$$

Lotka-Volterra competition model just means: make the same linearity assumption with respect to the density of a competing species. The result is

$$\frac{dn_1}{dt} = r_1 n_1(t) \left(1 - \frac{n_1}{k_1} - \frac{\alpha_{12} n_2}{k_1}\right)$$

$$\frac{dn_2}{dt} = r_2 n_2(t) \left(1 - \frac{n_2}{k_2} - \frac{\alpha_{21} n_1}{k_2}\right)$$

### 3.3 Consumer-resource models

The logistic/Lotka-Volterra line of modeling has a long history in ecology, but (IMHO) they belong to the past rather than the present and future. You can fit them to data sometimes, as in the book, but it’s hard to say what that means because there’s nothing about process in the models. Even if it’s true that a plot of $dn/dt$ as a function of $n$ is close to a straight line, what does that tell you? What do you learn by knowing the slope of the line?

The first step towards mechanistic, process-based models is consumer-resource models, where the growth of the consumer (at least) is explicitly related to the availability of resources. The generic form of such models is
\[
\frac{dn_1}{dt} = f(n_1) - g(n_1, n_2) \\
\frac{dn_2}{dt} = eg(n_1, n_2) - h(n_2)
\] 

This makes the classical assumption that breeding is proportional to eating, with a constant ratio.

There are lots of different options for \( f \) and \( g \), representing different biological assumptions. The resource might be abiotic, e.g. phosphorus in a lake that is mainly supplied from inflowing water, so \( f(n_1) = \theta \), or we might assume that the resource is another species and model it by logistic growth \( f(n_1) = r_1 n_1(1 - n_1/k_1) \).

\( g(n_1, n_2) \) is the consumer's "functional response", something very well studied. It is usually assumed that

\[
g(n_1, n_2) = n_2 G(n_1)
\]

meaning (biologically) that there is no interference between consumers – each one eats at a rate determined by the abundance of prey. This standard assumption has the problem that a lot of evidence now runs against it, even in situations where it seems highly unlikely. CONTRAST Type-II and Beddington-DeAngelis.

### 3.4 Haploid models of natural selection

Turning to genetic variation, we start with the simplest situation: two types.

Haploid models first: some individuals are type \( A \) and some are type \( a \), and each produces offspring of the same type. My favorite example are asexual green algae (chemostat project). State variables are \( n_a \) and \( n_A \). We census the population immediately after juveniles are born.

The simplest model assumes discrete-time exponential growth for each subpopulation:

\[
n_A(t+1) = W_A n_A(t), \quad n_a(t+1) = W_a n_a(t)
\]

But for evolutionary questions we care about the frequencies of the two types,

\[
p = n_A/(n_a + n_A), \quad q = 1 - p = n_a/(n_a + n_A)
\]

so we want to derive the dynamic equations for \( p \) and \( q \). This is just algebra and a bit of a trick. To save writing I will let \( p' \) denote \( p(t+1) \)

\[
p' = \frac{n_A'}{n_A' + n_a'} = \frac{W_A n_A}{W_A n_A + W_a n_a}
\]

This is fine so far as it goes, but we have \( p \) on the left hand side, and \( n's \) on the right, so we need to go further. The trick is to divide through by total population \( n_A + n_a \), getting

\[
p' = \frac{W_A p}{W_A p + W_a q} = \frac{W_A p}{W_A p + W_a (1 - p)}
\]
and we’re done.

Another simplification is a rescaling: divide through by $W_a$, giving the same equation (effectively) with $W_a = 1$. So we see that the behavior of the genotype frequencies depends only on the relative fitness $V_A = W_A/w_A$. As Otto and Day note (p. 65), this is not an entirely trivial point. Even if absolute fitnesses are highly variable (competition, weather, etc.), a simple model like this one may be reasonably accurate if the relative fitnesses of two genotypes is roughly constant. By simplifying the model, we discover which features are really important – in this case, relative fitness.

To get a continuous-time model, we follow the usual approach of letting $h$ (also known as $\Delta t$ go to 0 (Box 2.6). The one new and non-obvious point is that we need to say what happens to the fitnesses $W_a$ and $W_A$ as $h \to 0$, and we can do that by relating them back to births and deaths over a short period of time. Apart from notation, $W$ is the $R$ in the discrete-time exponential growth model, so we can write (for example)

$$ R = (1 - b)(1 + d) $$

and for going to continuous time

$$ R = (1 + bh)(1 - dh). $$

We now want to apply this to both genotypes:

$$ W_A = (1 + b_A h)(1 - d_A h), W_a = (1 + b_a h)(1 - d_a h) $$

We know by know that any $h^2$ terms are going to go away when we let $h \to 0$ so we might as well set

$$ W_A = 1 + (b_A - d_A)h = 1 + r_A h $$

and similarly for $a$. The rest is algebra: the difference quotient is

$$ \frac{p' - p}{h}, $$

we grind through and let $h \to 0$. The result is

$$ \frac{dp}{dt} = sp(1 - p) \text{ where } s = r_A - r_a $$

Note that, as in discrete time, it’s a relative fitness that matters, here the difference in instantaneous (birth-death) rates.

Another way of getting a continuous time model is to start from continuous-time exponential growth

$$ \frac{dn_A}{dt} = r_A n_A, \frac{dn_a}{dt} = r_a n_a $$

and derive the differential equation for $p = n_A/(n_a + n_A)$. This is done in Box 3.1.
3.5 Diploid models for natural selection

In a sexual population, diploid organisms are formed by the union of haploid gametes. So even with 2 genotypes for the haploid stage of the life cycle, we need to track 3 kinds of diploid individuals, $AA, Aa, aa$.

But, to make things as simple as possible, we will census the population at the haploid stage of the life cycle, $p(t)=$ fraction of type-A gametes. And, we will make the assumption that diploids are formed by gametes uniting at random (a HW exercise examines what happens if instead diploid individuals mate at random). The frequencies of diploids produced by random gamete pairing are the familiar Hardy-Weinberg proportions $p^2, 2pq, q^2$ for $AA, Aa, aa$.

Then selection acts (by assumption! Otto and Day don’t explicitly state this assumption, but there is an assumption here about the order of events). The proportions in the population are now

$$p^2 W_{AA}, 2pq W_{Aa}, q^2 W_{aa}.$$  

These aren’t exactly proportions, though, because they don’t sum to 1. Let $\bar{W}$ denote their sum; the genotype proportions are then

$$p^2 W_{AA}/\bar{W}, 2pq W_{Aa}/\bar{W}, q^2 W_{aa}/\bar{W}.$$  

To get back to the gamete stage, we have to look at the proportions of $A$ versus $a$ gametes produced by these individuals. We can do this by explicitly counting how many gametes are produced, and then figuring out what proportion are type $A$. To do that we need to define $N=$ total population size, $G=$ number of gametes produced per diploid individual. By assumption selection has already acted, so all genotypes have the same $G$.

The number of $A$ gametes produced is the number from $AA$ individuals, plus those from $Aa$ individuals.

From $AA$:

$$p^2 W_{AA}/\bar{W} \times \text{total population size} \times \text{gametes per individual} = p^2 W_{AA}/\bar{W} \times N \times G$$

From $Aa$:

$$(1/2)2pq W_{Aa}/\bar{W} \times \text{total population size} \times \text{gametes per individual} = pq W_{Aa}/\bar{W} \times N \times G$$

The total number of games from everybody is $N \times G$.

Fraction of $A$ gametes out of the total: a bit of algebra. The common factor $NG$ cancels, so that the fraction of $A$ gametes out of the total is

$$\left( p^2 W_{AA} + pq W_{Aa} \right)/\bar{W}$$
This gets us to the next generation, so we have

\[ p' = (p^2 W_{AA} + pq W_{Aa})/\bar{W} = p \frac{\bar{W}_A}{\bar{W}} \]

where \( \bar{W}_A \) is the average fitness of A alleles, \( pW_{AA} + (1-p)W_{Aa} \).

4  Chapter 4: Developing a Feeling For Your Model

The theme of this chapter is the “ubiquitous computing” approach to understanding dynamic models. In the old days, confronted with a set of differential equations you would take out pencil and paper, and start doing math. Now, you start by firing up R (or something like it), writing a script to solve the model and making some graphs. You try to learn as much as you can in “let the computer do the work” mode, and then use math to confirm what you saw on the screen, generalize it, and think about whether you have the whole picture or just part of it.

We’ll focus on a few examples:

1. The discrete-time logistic model

\[ n(t + 1) = rn(t) \left(1 - \frac{n(t)}{K}\right) \quad (4.1) \]

Note: this isn’t how Otto and Day write the model, but it’s how everyone else does. Their version can be put into this form by regrouping terms and defining a ’new’ \( r \) and \( K \).

One thing Otto and Day do not emphasize, is that before you do anything else it’s worthwhile to rescale the model to simplify it as much as possible. In this case we can define \( x(t) = n(t)/K \) and we get

\[ x(t + 1) = rx(t) \left(1 - x(t)\right) \quad (4.2) \]

so there’s only one parameter controlling the dynamics, up to a scaling factor on population size.

2. The continuous-time logistic model

\[ \dot{n} = rn \left(1 - \frac{n}{K}\right) \quad (4.3) \]

Here we can rescale \( n \) and time, \( x = n/K, \tau = rt \) (assuming \( r > 0 \)) to get

\[ \dot{x} = x(1 - x) \quad (4.4) \]

Notice that the number of parameters has been reduced to zero, so we see that neither \( r \) nor \( K \) affects the qualitative dynamics.
3. The continuous-time diploid selection model. In discrete time we found

\[ p' = p \frac{W_A}{W}, \]  

so

\[ p' - p = p \frac{W_A - W}{W}. \]

If \( W_{ij} = 1 + hw_{ij} \), as in the derivation of the continuous-time haploid selection model, then \( W_A - W \) is \( O(h) \) and \( W \) is \( 1 + O(h) \), so to leading order in \( h \) we can take \( W = 1 \) in the denominator and get

\[ \frac{p' - p}{h} = p(\bar{w}_A - \bar{w}) \]

so the continuous time model is

\[ \frac{dp}{dt} = p(\bar{w}_A - \bar{w}). \]

4. A model for competition between pathogenic and beneficial (antibiotic-producing microorganisms) in the mucus layer surrounding a hard coral,

\[
\frac{dP}{dt} = rPe^{-\lambda B PS} - P \\
\frac{dB}{dt} = \frac{rBBS}{K+S} - B
\]

where \( S = 1 - P - \alpha B \)

4.1 What do we want to do with the models?

1. Plot solution trajectories using R.
   - Show how to solve logistic differential equation (SolveContinuousLogistic.R)
   - Show how to solve logistic difference equation (SolveDiscreteLogistic.R)
   - Show how to draw bifurcation diagram for logistic difference equation: nested loops, no nested loops

2. Draw phase-line diagrams
   - Logistic differential equation (LogisticPhaseLine.R)
   - Diploid selection differential equation (Fig. 4.13, page 134) (DiploidPhaseLine.R)
   - Note that for discrete-time models, you plot \( x(t+1) - x(t) \), not \( dx/dt \). Otherwise just the same. However, the plots mean a lot less because a discrete-time model can ‘jump over’ an equilibrium.

3. Phase-plane analysis
Vector field plots ⇔ generalization of phase-line diagrams
Nullclines
Where the nullclines cross, you have an equilibrium
Try it out on the coral mucus model
Talk about stability analysis: locally stable vs. unstable, local vs. global stability

Nullcline example: a (simplified) model for interactions between Beneficial and Pathogenic microbes in the mucus layer surrounding a coral, competing for limited Substrate.

\[
\frac{dB}{dt} = r_B BS - \delta B \\
\frac{dP}{dt} = r_P e^{-\lambda P} PS - \delta P \\
\frac{dS}{dt} = S_0 - r_P e^{-\lambda P} PS - r_B BS - \delta S
\]  \hspace{1cm} (4.6)

First simplifications: we can rescale the model so $\delta = 1$ and $S_0 = 1$ (we’ll remember that we did this, but not rename any of the parameters). Still, the model is three-dimensional, so what do we do? Define $\Sigma = B + P + S$. Then $d\Sigma/dt = 1 - \Sigma$. Drawing a phase-line diagram for this equation, we see that $\Sigma \to 1$. So in the long run

$$B + P + S = 1 \Rightarrow S = 1 - B - P.$$  

So we’ll analyze the $B, P$ system with this in place. We then have

\[
\frac{dB}{dt} = r_B B(1 - B - P) - B \\
\frac{dP}{dt} = r_P e^{-\lambda B} P(1 - B - P) - P
\]  \hspace{1cm} (4.7)

So now we need the nullclines. The $B$ nullcline is $B = 0$ or

$$r_B(1 - B - P) = 1 \iff P = \frac{r_B - 1}{r_B} - B,$$

a line with $y$-intercept $(r_B - 1)/r_B$ and slope -1. Similarly the $P$ nullcline is $P = 0$ or

$$P = \frac{r_P - e^{\lambda B}}{r_B} - B,$$

a curve with slope $< -1$ and $y$-intercept $(r_P - 1)/r_P$.

Consider the case where the nullclines cross: $r_P > r_B$ but $\lambda$ is big so the $P$ nullcline decreases fast.

The nullclines let us sketch the phase arrows. Each population is

- Increasing below its interior nullcline
- Decreasing above its interior nullcline
- Constant ($d/dt = 0$) when exactly on the nullcline: phase arrows are either vertical or horizontal
Figure 14: Nullclines (schematically) for the coral mucus model.
5 Ch.5 Equilibria and Stability, 1-Variable Models

5.1 Introduction

The theme for the next block of ideas is using local information to figure out the global dynamics of a model. We will do one-variable models, then multi-variable models with an emphasis on two-variable models ("phase plane analysis"). Things get much harder with more than two variables, so people like me spend a lot of time asking the question: what is the two-variable model that includes all the essentials?

5.2 Finding an equilibrium

Equilibria and their stability are very useful local information.

- Equilibrium \( \hat{n} \) is a value of the state variable such that if \( n(o) = \hat{n} \), then \( n(t) \equiv \hat{n} \).

- For discrete-time model \( n(t+1) = f(n(t)) \), equilibrium if \( \hat{n} = f(\hat{n}) \).

- For ODE \( \frac{dn}{dt} = f(n) \), equilibrium if \( f(\hat{n}) = 0 \). Discrete- and continuous-time models are both similar and different, and you have to remember the differences.

- Equilibrium is locally stable if solutions starting near \( \hat{n} \) converge to \( \hat{n} \) as \( t \to \infty \). Globally stable if all solutions converge to \( \hat{n} \) regardless of where they start. Unstable if some solutions that start near the equilibrium move away from it.

Although a phase-line analysis shows us everything, we’re going to now do some paper-and-pencil work so that we learn to use these ideas in the simplest possible setting.

**Example:** Exponential growth in discrete time, \( n(t+1) = Rn(t) \)

To find possible equilibria, we set \( n(t+1) = n(t) = \hat{n} \), so

\[ \hat{n} = R\hat{n}. \]

Then we divide through by \( \hat{n} \) and get

\[ R = 1. \]

This is not what we were looking for - it’s a value of \( R \), not a value of \( n \). What went wrong?

You can only divide by \( \hat{n} \) if \( \hat{n} \neq 0 \). Our models often have “nobody’s home” equilibria, either zero organisms in a closed population, or some genotype with zero frequency without mutation or immigration. The first thing you need to do is look for those, then divide through by \( \hat{n} \) if possible to find others.

So the only equilibrium in this model is \( \hat{n} = 0 \).
**Example:** Exponential growth in continuous time \( \frac{dn}{dt} = rn \)

Same: set \( r \hat{n} = 0 \) and find the only equilibrium is \( \hat{n} = 0 \).

**Example:** cat-and-mouse model in continuous time, \( \frac{dn}{dt} = (b-d)n + m \) with \( m < 0 \).

Set \( (b-d)n + m = 0 \) and find \( n = m/(d-b) \). So we get a meaningful equilibrium if \( d > b, m > 0 \) (a “sink” population” where \( r = b - d < 0 \)) or \( b > 0, m < 0 \) (a “source population”). But these cases have very different dynamics!

**Haploid genetic model in discrete time** The model is

\[
p(t+1) = \frac{p(t)W_A}{\bar{W}}, \quad \text{where} \quad \bar{W} = p(t)W_A + (1-p(t))W_a.
\]

Substitute in \( p(t+1) = p(t) = \hat{p} \) and get

\[
\hat{p} = \frac{W_A}{\bar{W}}.
\]

There’s \( \hat{p} \) on both sides, so one equilibrium is \( \hat{p} = 0 \). To look for others we divide through by \( \hat{p} \), getting \( W_A = \bar{W} \), i.e.

\[
W_A = W_A\hat{p} + W_a(1 - \hat{p})
\]

Even without algebra we can see that only way for this to happen is if \( \hat{p} = 1 \), unless \( W_A = W_a \) (in which case every value of \( p \) is an equilibrium, because there is no selection).

So in general the only two equilibria are \( \hat{p} = 0 \) and \( \hat{p} = 1 \) : one allele is more fit, and it goes to fixation.

**Diploid genetic model in discrete time** The model is

\[
p(t+1) = \frac{p(t)\bar{W}_A}{W}, \quad \text{where} \quad \bar{W}_A = pW_{AA} + (1-p)W_{aa}, \quad \bar{W} = p^2W_{AA} + 2p(1-p)W_{Aa} + (1-p)^2W_{aa}.
\]

In working through this model, Otto and Day say, “For variety’s sake, however, we proceed without canceling terms.” I say that when pain is unavoidable, do what you can to minimize it. So I will do this example in a different way from the book.

First, simplify by rescaling. We know that everything depends on relative fitnesses (e.g., if we divide all fitnesses by 10, then \( \bar{W}_A \rightarrow W_A/10, \bar{W} \rightarrow W/10 \) and \( p(t+1) \) stays the same). So we can set

\[
W_{AA} = 1 + s_A, W_{Aa} = 1, W_{aa} = 1 + s_a \quad (5.1)
\]
(and remember that all fitnesses are relative to that of the heterozygote, and the $s$’s may be positive or negative). As in the haploid model, one equilibrium is $\hat{p} = 0$; the other way to get equilibria is when $\bar{W}_A = \bar{W}$. Using (5.1) we get

$$\bar{W} = p^2(1 + s_A) + 2p(1 - p) + (1 - p)^2(1 + s_a) = 1 + p^2 s_A + (1 - p)^2 s_a$$

$$\bar{W}_A = p(1 + s_A) + (1 - p) = 1 + ps_A$$

(5.2)

We now need to solve $\bar{W}_A = \bar{W}$ for $p$, which is

$$ps_A = p^2 s_A + (1 - p)^2 s_a.$$

Some good advice given by Otto and Day is that solving equations is often helped by writing them in the form

$$\text{something} = 0.$$

In this case we get

$$0 = ps_A - p^2 s_A - (1 - p)^2 s_a = p(1 - p)s_A - (1 - p)^2 s_a = (1 - p)(ps_A - (1 - p)s_a).$$

So one solution is when $1 - p = 0$, i.e. $\hat{p} = 1$, and the other possibility is when

$$ps_A - (1 - p)s_a = 0 \iff p(s_A + s_a) = s_a \iff p = \frac{s_a}{s_A + s_a}.$$

So we want to know: when is this a valid new equilibrium, i.e. a number between 0 and 1? We need to consider two cases, $s_a > 0$ and $s_a < 0$.

- If $s_a > 0$ we need the denominator to be positive so that $p$ is positive, so $s_A + s_a > 0$. We also need the denominator to be bigger than $s_a$ so that $p < 1$, i.e. we need $s_A > 0$. So we get a third equilibrium if both homozygotes are fitter than the heterozygote.

- If $s_a < 0$ we need the denominator to be negative, and bigger in absolute value than $s_a$, so that’s $s_A < 0$. Thus, we get a third equilibrium if both homozygotes are less fit than the heterozygote.

Again, these two cases are very different dynamically.

Another way to simplify calculations like this is to use Maxima.

```maxima
Wbar:p^2*(WAA)+2*p*(1-p)*WAa+(1-p)^2*Waa;
WbarA:p*WAA+(1-p)*WAa;
eqn1:p*WbarA/Wbar=p;
out:solve(eqn1,p);
```
The result is
\[ p = \frac{Waa - WAa}{WAA + Waa - 2 WAA}, \quad p = 0, p = 1 \]
and we’re happy except that we have to figure out when the first solution is between 0 and 1. But we can apply our rescaling
\[ \text{subst([WAA=1+sA,WAa=1,Waa=1+sa],out);} \]
\[ p = \frac{sa}{sA + sa}, \quad p = 0, p = 1 \]

5.2.1 When we can’t solve for equilibria

Sometimes you can’t solve for equilibria because the model involves functions like \( e^x \). A simple example is
\[ n(t + 1) = r n(t) e^{-\alpha n(t)} + m. \]
The equilibrium condition is
\[ r n e^{-\alpha n} = n - m \]
so it is easy to see graphically that there is an equilibrium, but we can’t solve for it explicitly as a function of \( r, \alpha \) and \( m \) except for the special case \( m = 0 \).

There are algebraic ways of getting approximate solutions in limiting cases (for example, if \( m \) is very small), but that’s for another class. For this class, we use the computer. We will look at simple cases to get conceptual understanding, and then use the computer to do things numerically when algebra doesn’t get us everything we need.

5.3 Stability analysis

When is an equilibrium of a continuous-time one-variable model \( \frac{dn}{dt} = f(n) \) stable versus unstable? We can see answer from a phase-line diagram. At any equilibrium \( f(\hat{n}) = 0 \).

- If \( f'(\hat{n}) > 0 \), then \( f \) is going from negative to positive at \( \hat{n} \), so unstable.
- If \( f'(\hat{n}) < 0 \), \( f \) is going from positive to negative, so stable.

We can get this result another way, by linear stability analysis. For \( n(t) \) near \( \hat{n} \), we define \( \epsilon(t) = n(t) - \hat{n} \) and write a linear differential equation for \( \epsilon(t) \) that is valid when \( \epsilon(t) \) is small in magnitude. The way we do that is by a Taylor series expansion
\[ f(x + a) = f(x) + f'(x)a + \frac{f''(x)}{2}a^2 + \cdots \]
We now apply this with 
\[ x = \hat{n}, \ a = \epsilon(t), \] 
so that 
\[ x + a = \hat{n} + \epsilon(t) = n(t). \]

The result is 
\[ \frac{d\epsilon}{dt} = re \text{ where } r = f'(\hat{n}). \]

What about a discrete-time model \( n(t + 1) = f(n(t)) \)? Again the answer involves \( f'(\hat{n}) \), but it’s a different condition.

- We can use a Taylor Series expansion of \( f \) to find an approximate equation for the dynamics of \( \epsilon(t) = n(t) - \hat{n} \), when \( n(t) - \hat{n} \) is small. The result is 
\[ \epsilon(t + 1) = \lambda \epsilon(t) \text{ where } \lambda = f'(\hat{n}). \]

- The equilibrium is therefore stable if \( |\lambda| < 1 \), and unstable if \( |\lambda| > 1 \). Local behavior is oscillatory versus monotone depending on whether \( \lambda \) is negative or positive.

**Example: Logistic model in discrete time, \( n(t + 1) = n(t) + rn(t)(1 - n(t)/K) \).**

To save some writing I’ll rescale to \( x = n/K \) so that 
\[ x(t + 1) = x(t) + rx(t)(1 - x(t)). \]

We have an equilibrium when \( x(t + 1) = x(t) \), so when \( rx(t)(1 - x(t)) = 0 \). So there are two equilibria, one at \( x = 0 \), the other at \( x = 1 \).

The right-hand side of the model is is 
\[ f(x) = x + rx(1 - x) = x + rx - rx^2 = (1 + r)x - rx^2. \]

For stability analysis we need to compute \( f'(x) \) at the equilibria. We have \( f'(x) = 1 + r - 2rx \) so 
\[ f'(0) = 1 + r, \ f'(1) = 1 - r. \]

When the population is small each parent leaves \( 1 + r \) offspring. This implies the parameter constraint \( 1 + r > 0 \). Actually we have to be stricter than that. If \( r \) is negative, then the per-capita net (birth-death) rate is an increasing function of \( n \), not a decreasing one: populations decrease if they are below \( K \), and increase if they are above it. So we must assume \( r > 0 \) for the model to represent the situation it’s supposed to represent.

The equilibrium at \( 0 \) is therefore stable if \( 0 < 1 + r < 1 \), and unstable if \( 1 + r > 1 \). We conclude that under the biological parameter constraint \( r > 0 \), the equilibrium \( \hat{x} = 0 \) is always unstable.

The equilibrium \( \hat{x} = 1 \) is more complicated. When \( r \) is small, the slope is just below 1, so the equilibrium is stable. But as \( r \) increases, the slope can drop below -1, and then the equilibrium becomes unstable.
**Example**  Logistic model in continuous time, \( \frac{dn}{dt} = rn(1-n) \) after rescaling relative to \( K \), with \( r > 0 \). Here \( f(n) = rn - rn^2, f'(n) = r - 2rn \). The equilibria are at 0 and 1, and we have
\[
 f'(0) = r > 0, f'(1) = -r < 0
\]
so 0 is always unstable, and 1 is always stable.

**Example: The discrete-time diploid model.**

As before, we will use scaled fitnesses \( W_{AA} = 1 + s_A, W_{Aa} = 1, W_{aa} = 1 + s_a \). The model is
\[
p(t+1) = p(t) \frac{W_A}{W}
\]
where
\[
W_A = pW_{AA} + (1-p)W_{aa}, \quad W = p^2W_{AA} + 2p(1-p)W_{Aa} + (1-p)^2W_{aa}.
\]
We have already found that the equilibria are
\[
\hat{p}_0 = 0, \hat{p}_1 = 1, \hat{p}_2 = \frac{s_a}{s_a + s_A}
\]
with \( \hat{p}_2 \) being biologically meaningful (i.e., between 0 and 1) when \( s_a \) and \( s_A \) have the same sign, so the heterozygote is either least fit or most fit. Now we can analyze the stability, using Maxima to help us out:

```maxima
/*-------- Find the equilibria -----*/
WAA:1+sA; Waa:1; WAa:1+sA;
Wbar:p^2*WAA+2*p*(1-p)*WAa+(1-p)^2*Waa;
WbarA:p*WAA+(1-p)*WAa;
eqn1:p*(WbarA/Wbar)=p;
out:solve(eqn1,p);

/* -------- Stability analysis ---- */
f:p*WbarA/Wbar; /* define f in p(t+1)=f(p(t)) */
dfdp:diff(f,p); /* compute f'(p) */
df0:factor(subst(p=0,dfdp)); /* stability of "all aa" */
df1:factor(subst(p=1,dfdp)); /* stability of "all AA" */
df2:factor(subst(out[1],dfdp)); /* stability of polymorphism */
```

The results are
\[
 f'(0) = \frac{1}{1 + s_a}, \quad f'(1) = \frac{1}{1 + s_A}, \quad f'\left(\hat{p}_2\right) = 1 + \frac{s_a s_A}{s_a + s_A + s_a s_A}.
\] (5.3)

So what do these mean? The condition for stability is \(-1 < f' < 1\).

The selection coefficients can be positive or negative, but the fitnesses must be positive, so they are both \( \geq -1 \). That means that \( f'(0) \) and \( f'(1) \) can’t be negative. So in each case, there will be stability if the selection coefficient is positive. That is:
• If $s_a$ and $s_A$ are both positive, both 0 and 1 are stable. The interior equilibrium exists, and we should expect it to be unstable (DRAW phase line diagram).

• If $s_a$ and $s_A$ are both negative, both 0 and 1 are unstable. The interior equilibrium exists and we should expect it to be stable.

• If one is positive and the other negative, then there is no interior equilibrium, and the fitter allele goes to fixation.

To really finish this off, we should verify the stability of the interior equilibrium when it exists.

• If $s_a$ and $s_A$ are both positive, $f'(\hat{p}_2) = 1 + (+)$ and so $\hat{p}_2$ is unstable.

• If they are both negative, then $s_as_A$ is positive, but smaller in magnitude than either $s_a$ or $s_A$ because $|s_a| < 1, |s_A| < 1$. So the denominator of the fraction in $f'(\hat{p}_2)$ is negative and larger in magnitude than $s_a s_A$. Hence, the fraction is a negative number that is smaller than 1 in absolute value. Therefore $0 < f'(\hat{p}_2) < 1$ so the equilibrium is stable, and convergence to the equilibrium is monotonic.

As we knew all along: the interior equilibrium is stable (hence, a polymorphism is maintained) if and only if the heterozygote has higher fitness than either of the homozygotes. But that knowledge came, originally, from doing a stability analysis on the the difference equation, as we have just done.

**Example: Constant-rate harvesting in continuous time**

We consider a logistically growing population, with a constant harvest rate of $H$ individuals per unit time,

$$\frac{dx}{dt} = r x (1 - x/K) - H$$

This model ceases to make sense at $x = 0$ because harvest has to shut down when there is nobody to harvest, but the model lets $x$ become negative. So we have to think of it like this: $dx/dt < r x - H$, so if $x(t)$ ever falls below $H/r$, the population is doomed to extinction.

With that convention, we can now do the usual: find positive equilibria, determine their stability, and interpret the results. With Maxima:
\[ f: r x (1 - x / K) - H; \]
\[ \text{out: solve}(f = 0, x); \]
\[ \text{dfdx: diff}(f, x) \$
\[ \text{df1: factor}(\text{subst(out[1], dfdx}) ; \]
\[ \text{df2: factor}(\text{subst(out[2], dfdx}) ; \]

You should be realizing that the pattern is always the same, it’s just the details that differ. For the equilibria, Maxima gives us

\[
\begin{align*}
\hat{x}^- &= \frac{-\sqrt{r^2 K^2 - 4rHK - rK}}{2r}, \\
\hat{x}^+ &= \frac{\sqrt{r^2 K^2 - 4rHK + rK}}{2r}
\end{align*}
\]

which we recognize as the two roots of a quadratic:

\[
\hat{x} \pm = \frac{rK \pm \sqrt{r^2 K^2 - 4rHK}}{2r}
\]

So there will be two equilibria so long as the discriminant is positive,

\[ 4rHK < r^2 K^2 \iff H < rK / 4. \]

In that case, we can check the stability of the equilibria: the criterion is that \( f'(\hat{x}) < 0 \) because this is a continuous time one-variable model. Maxima gives us:

\[
f'(\hat{x}_-) = \frac{\sqrt{rK(rK - 4H)K}}{K} > 0, \quad f'(\hat{x}_+) = -f'(\hat{x}_-) < 0
\]

so the smaller equilibrium is unstable and the larger one is stable. The direction arrows look like this:

\[ |-----<-<-<q--->--->-----<------<--------<--------<------<--------<------| \]

So the population is OK so long as it stays above the lower, unstable equilibrium.

If \( H > rK / 4 \), then there are no equilibria. We know \( dx/dt < 0 \) when \( x \approx 0 \), and it’s never the case that \( dx/dt = 0 \) for \( x \geq 0 \), so \( dx/dt \) must be zero for all \( x \geq 0 \). Hence the population goes extinct.

DRAW saddle-node bifurcation with \( H \) as the x-axis: as \( H \) increases the two equilibria collide and disappear. DRAW the direction arrows vertically.

**Summary: stability analysis of 1-variable models**

So there are five steps to doing a nonlinear stability analysis:

1. Find the equilibria
2. Find the derivative of the function \( f \) in \( \frac{dn}{dt} = f(n) \) or \( n(t+1) = f(n(t)) \).

3. Evaluate the derivative \( \lambda \) at each equilibrium.

4. Figure out what the derivatives imply, using the criterion for stability \( \lambda < 0 \) (continuous time), \(-1 < \lambda < 1 \) (discrete time).

5. Interpret the results biologically, in terms of model parameters and their biological meanings.

One useful aid in the last step is a diagram summarizing the way parameters affect model predictions. When there is a single parameter of interest, you can draw a bifurcation diagram like Figure 5.3, if there’s only one parameter of interest. To look at the joint effects of two parameters, you can draw a stability diagram or phase diagram in which the axes are the parameters, and the plane is divided into regions where different stability outcomes occur. For the diploid model, the axes would be \( s_a \) and \( s_A \), and we have four different outcomes in the four quadrants.
Chapter 7: Equilibrium and stability in linear 2-D systems

As our next step up in generality, we’re going to consider systems with two state variables. The state of the system is now a vector \( \vec{x} = \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} \), and when we write (for example)

\[
\frac{d\vec{x}}{dt} = f(\vec{x})
\]

that’s short for

\[
\begin{align*}
\frac{dx_1}{dt} &= f_1(x_1, x_2) \\
\frac{dx_2}{dt} &= f_2(x_1, x_2)
\end{align*}
\] (6.1)

To work with these we need to know a bit about \( 2 \times 2 \) matrices \( M = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \).

Adding matrices, and multiplying by a number, are done element-by-element:

\[
\begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} + \begin{pmatrix} 5 & 6 \\ 7 & 8 \end{pmatrix} = \begin{pmatrix} 1+5 & 2+6 \\ 3+7 & 4+8 \end{pmatrix} = 2 \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} = \begin{pmatrix} 2 & 4 \\ 6 & 8 \end{pmatrix}
\]

Matrix-vector multiplication goes like this:

\[
\begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} ax + by \\ cx + dy \end{pmatrix}
\]

So for example

\[
\begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \begin{pmatrix} 5 \\ 6 \end{pmatrix} = \begin{pmatrix} 1 \times 5 + 2 \times 6 \\ 3 \times 5 + 4 \times 6 \end{pmatrix}
\]

As in one-variable system, local stability analysis will say that the stability of an equilibrium can be determined by looking at a linear system that involving the derivatives of \( f_1 \) and \( f_2 \). So first we need to answer the question: what is the behavior of

\[
\frac{d\vec{n}}{dt} = M\vec{n}, \quad M = \begin{pmatrix} a & b \\ c & d \end{pmatrix}, \quad \vec{n} = \begin{pmatrix} n_1 \\ n_2 \end{pmatrix}
\] (6.2)

near the equilibrium \( \vec{n} = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \)?

(Unless \( ad = bc \), some algebra (p. 261 of Otto-Day) shows that this is the only equilibrium).

Example: source-sink metapopulation We may also be interested in the behavior of a linear model for its own sake. Suppose that a population occupies two patches, experiencing
exponential growth in one (the source) and exponential decay in the other (the sink), with the two patches coupled by symmetric migration. A diagram for this system is in Figure 6. The dynamic equations are

\[
\begin{align*}
\frac{dn_1}{dt} &= r_1 n_1 - dn_1 + dn_2 \\
\frac{dn_2}{dt} &= dn_1 + r_2 n_2 - dn_2
\end{align*}
\] (6.3)

Notice that on the right-hand side of (6.3), in both the \(dn_1/dt\) and the \(dn_2/dt\) equations \(n_1\) comes first and \(n_2\) comes second. Doing things this way will help you avoid mistakes, for example in writing the system in matrix form. Letting \(\vec{n} = \begin{pmatrix} n_1 \\ n_2 \end{pmatrix}\) we have

\[
\begin{pmatrix}
\frac{d\vec{n}}{dt} = \begin{pmatrix} \frac{dn_1}{dt} \\ \frac{dn_2}{dt} \end{pmatrix} \\
= \begin{pmatrix} (r_1 - d) n_1 + dn_2 \\ dn_1 + (r_2 - d) n_2 \end{pmatrix} = \begin{pmatrix} r_1 - d & d \\ d & r_2 - d \end{pmatrix} \begin{pmatrix} n_1 \\ n_2 \end{pmatrix}
\end{pmatrix}
\] (6.4)

If \(r_1 < 0 < r_2\) then we suspect that the population will persist so long as migration is low, because the source patch will be self-sustaining. If dispersal is high, then the two patches are effectively one, and the population could be in trouble if the sink is strong \((r_1 \ll 0)\) and the patch is weak \((r_2\) just above 0).

### 6.1 Eigenvalues and Eigenvectors

To understand the behavior of a linear system \(\frac{d\vec{n}}{dt} = M\vec{n}\) we look at the eigenvalues of \(M\) and the corresponding eigenvectors.

1. The eigenvalues are the roots of the characteristic polynomial

\[p(\lambda) = \lambda^2 - T\lambda + D\]
where
\[ T = \text{Trace of } M = a + d \]
\[ D = \text{Determinant of } M = ad - bc \]  \hspace{1cm} (6.5)

So by the quadratic formula,
\[ \lambda = \frac{T \pm \sqrt{T^2 - 4D}}{2}. \]  \hspace{1cm} (6.6)

An important special case is: if a matrix is upper or lower triangular, its eigenvalues are the elements on the diagonal:

\[
\begin{pmatrix} 1 & 0 \\ 3 & 4 \end{pmatrix} \quad \text{and} \quad \begin{pmatrix} 1 & 2 \\ 0 & 4 \end{pmatrix}
\]
both have \( \lambda_1 = 1, \lambda_2 = 4 \). \hspace{1cm} (6.7)

For larger square matrices, the characteristic polynomial is higher order (cubic for a \( 3 \times 3 \) matrix, quartic for a \( 4 \times 4 \) matrix, etc.) and we don’t have a formula for the roots.

2. Corresponding to the eigenvalues \( \lambda_1, \lambda_2 \) are two eigenvectors \( \vec{v}_1, \vec{v}_2 \) satisfying
\[ M\vec{v}_1 = \lambda_1 \vec{v}_1, \quad M\vec{v}_2 = \lambda_2 \vec{v}_2. \]  \hspace{1cm} (6.8)

**Example in R:** create a matrix, find its eigenvalues and eigenvectors. The columns of the eigenvector matrix are the eigenvectors.

\[
> A=\text{matrix}(c(1,2,3,4),2,2,\text{byrow}=\text{T}); \ A
\]
\[
\begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix}
\]

\[
> \text{lambda}=\text{eigen}(A)\$values
\]
\[
> v=\text{eigen}(A)\$vectors;
\]
\[
> \text{lambda}
\]
\[
[1] \quad 5.3722813 \quad -0.3722813
\]

\[
> v
\]
\[
\begin{pmatrix} -0.4159736 & -0.8245648 \\ -0.9093767 & 0.5657675 \end{pmatrix}
\]

6.1.1 Two real eigenvalues

Because the eigenvalues are the roots of a quadratic polynomial, either there are two real eigenvalues, or two complex conjugate eigenvalues.

With two real eigenvalues, we can see what’s going on by using the following fact:
• The solutions to \( \frac{d\vec{n}}{dt} = \mathbf{M}\vec{n} \) are all of the form

\[
\vec{n}(t) = c_1 e^{\lambda_1 t} \vec{v}_1 + c_2 e^{\lambda_2 t} \vec{v}_2
\]  

(6.9)

where \( c_1, c_2 \) are constants determined by the initial value \( \vec{n}(0) \). So a solution that starts on an eigenvector stays on it: if \( n(0) \) is some multiple of \( v_1 \), then \( n(t) \) will always be a multiple of \( v_1 \), ditto for \( v_2 \).

So the equilibrium \( \hat{n} = \hat{0} \) is stable if both eigenvalues are negative, and unstable if either one is positive.

Figure (6.1.1) shows the phase-plane pictures for the three possible cases with real eigenvalues.

6.1.2 Complex conjugate eigenvalues

The other possibility is that \( \lambda_1, \lambda_2 \) are complex conjugates,

\[
\lambda = A \pm Bi, \quad i = \sqrt{-1}
\]

\( A \) and \( B \) are called the real and imaginary parts of \( \lambda \); in R you can use the \texttt{Re} and \texttt{Im} functions.

In that case we get oscillatory solutions (spirals), stable if the real part \( A \) is negative, unstable if it is positive.

**Punchline** Stability is determined by the eigenvalues of \( \mathbf{M} \).

(a) If both real parts are negative, the equilibrium is stable. If one or both is positive, it’s unstable.

(b) If the eigenvalues are complex, solutions spiral around the equilibrium. If eigenvalues are real, solutions are non-spiralling curves or lines.

6.2 Stability Criterion for planar differential equations

Using these results and (6.6), there is an even more useful stability criterion in terms of the Trace and Determinant of the matrix:

• The system is stable if \( D > 0, T < 0 \) and unstable if either inequality is reversed.

• The eigenvalues are real if \( T^2 - 4D \geq 0 \), complex conjugates if \( T^2 - 4D < 0 \)

Note if \( T^2 - 4D = 0 \) the two eigenvalues are identical. This is another borderline situation that we are not going to worry about.

Figure 6.2 summarizes how an equilibrium’s stability and type can be deduced from the Trace and Determinant, for two-dimensional systems of differential equations. Analogous criteria exist
Figure 16: Planar linear system with two real eigenvalues. (a) Both positive (unstable node), (b) One positive one negative (saddle), (c) Both negative (stable node). Only in (c) is the equilibrium stable. This is Figure 7.3 in Otto-Day.
Figure 17: Planar linear system with complex conjugate eigenvalues. (a) Real part negative (stable spiral), (b) Real part positive (unstable spiral). This is Figure 7.6 in Otto-Day.
Figure 18: Classification of equilibrium stability for a two-variable linear system $d\vec{n}/dt = \mathbf{M}\vec{n}$ based on the Trace and Determinant of $\mathbf{M}$. Keep in mind that this diagram only applies to the continuous time system, not to a discrete time system.

for higher-dimensional systems (known as the Routh-Hurwitz Criteria); see pp. 309-310 of Otto and Day for a good explanation of these (but skip what they have to say about discrete-time models).

6.3 Applications

The source-sink metapopulation. The matrix here is $\mathbf{M} = \begin{pmatrix} r_1 - d & d \\ d & r_2 - d \end{pmatrix}$, so we have

$$T = r_1 + r_2 - 2d = 2(\bar{r} - d), \quad D = (r_1 - d)(r_2 - d) - d^2 = r_1 r_2 - (r_1 + r_2)d.$$  

The zero equilibrium (population extinction) is stable if $T < 0, D > 0$.

When $d = 0$, we have $D = r_1 r_2 < 0$ implying that the zero equilibrium is unstable. Why? In this case $\mathbf{M}$ is the diagonal matrix $\begin{pmatrix} r_1 & 0 \\ 0 & r_2 \end{pmatrix}$ which has eigenvalues $r_1 < 0$ and $r_2 > 0$, so zero
is a saddle. We can see (by “plug in and verify”) that the eigenvectors are \( \begin{pmatrix} 1 \\ 0 \end{pmatrix} \) and \( \begin{pmatrix} 0 \\ 1 \end{pmatrix} \), the axes. That is: if we start with patch 1 occupied and patch 2 empty, then patch 2 stays empty and the population in patch 1 goes to 0. If we start with 1 empty and 2 occupied, then 1 stays empty and the population in patch 2 grows exponentially.

What happens when \( d > 0 \) depends on the average growth rate \( \bar{r} = (r_1 + r_2)/2 \). If \( \bar{r} > 0 \) then \( D = r_1 r_2 - (r_1 + r_2) d = \text{(negative)} \cdot \text{(positive)} < 0 \) so the zero equilibrium is unstable: the population persists for any value of \( d \).

If \( \bar{r} < 0 \) then the Trace is always negative but the Determinant can become positive. When that happens the zero equilibrium becomes stable and the population is doomed. This occurs when \( d \) hits

\[
d_c = \frac{r_1 r_2}{r_1 + r_2}
\]

- When \( r_1 \) is just below \(-r_2\) (the largest it can be to have \( \bar{r} < 0 \)), the denominator in \( d_c \) is near 0, so \( d_c \) is very large. Thus, a weak sink is only lethal if there is lots and lots of between-patch movement.

- As \( r_1 \to -\infty \), \( \frac{r_1}{r_1 + r_2} \) converges to 1, so \( d_c \to r_2 \). A “black hole” sink is lethal if the rate of migration out of the source population is high enough to offset the within-source population growth. It’s as if the sink didn’t exist, so that \( \frac{dn_1}{dt} = (r_1 - d)n_1 \).

Romeo and Juliet (from Steve Strogatz’s book) Romeo is in love with Juliet, but the more he loves her, the more Juliet wants to run away and hide. When Romeo gets discouraged and backs off, Juliet finds herself becoming attracted to him. Romeo, on the other hand, tends to echo Juliet: the more affection she shows to him, the more he shows to her. What is the outcome of their relationship?

We will let \( R(t), J(t) \) be Romeo and Juliet’s degree of love (positive) or hate (negative) for the other, at time \( t \). Then a model for their romance is

\[
\dot{R} = aJ, \quad \dot{J} = -bR \quad \text{for some } a, b > 0
\]

(6.10)

The matrix for this system is \( \begin{pmatrix} 0 & a \\ -b & 0 \end{pmatrix} \), so the Trace is 0, and the determinant is \( D = ab > 0 \).

The general formula (6.6) then says that the eigenvalues are \( \lambda = \pm \sqrt{D}i \), purely imaginary. So the general solution to the model is equation (6.9) with

\[
e^{At} = \cos(\sqrt{D}t) \pm i \sin(\sqrt{D}t).
\]

That is, the \( e^{At} \) term is missing because \( A = 0 \), giving \( e^{At} = 1 \) for all \( t \). As a result, we get oscillatory solutions that neither grow or shrink in magnitude. The origin is then called a center, an equilibrium surrounded by an infinite set of periodic solutions (see Figure 6.3).
Romeo and Juliet go round and round, alternating between love-love, love-hate (Juliet backs off from an eager suitor), hate-hate (Romeo gets discouraged), and hate-love (Juliet likes a man who’s hard to get).

Now we’ll consider some more general situations in which where Romeo and Juliet may also pay attention to their own feelings.

2. What happens when two identically cautious partners get together? That is,

$$\dot{R} = -aR + bJ, \dot{J} = -aJ + bR$$

(6.11)

Then $a$ is a measure of their cautiousness, and $b$ a measure of their responsiveness. The ratio of $a$ to $b$ should determine the outcome. The matrix is

$$\begin{pmatrix} -a & b \\ b & -a \end{pmatrix},$$

so

$$T = -2a < 0, D = a^2 - b^2, T^2 - 4D = 4b^2 > 0$$

So we have two real eigenvalues, and the trace is negative so stability depends on the sign of the determinant. If $D$ is positive (overly cautious) the zero equilibrium is a stable node: the relationship always fizzles out to mutual indifference.

If $D$ is negative (responsiveness outweighs caution) then we have a saddle. By the “plug in and verify” method, we can see that the two eigenvalues are $b - a > 0$ and $-b - a < 0$, and the
corresponding eigenvectors are (1, 1) and (1, -1) So the result is either explosive attraction or all-out hatred, depending on their initial impressions of each other.

1. \( \dot{R} = J, \dot{J} = -R + J \). Characterize the relationship and discuss its stability.

3. Do opposites attract? What happens if \( \dot{R} = aR + bJ, \dot{J} = -bR - aJ \), where \( a \) and \( b \) can be either positive or negative.

4. What about peas in a pod? \( \dot{R} = aR + bJ, \dot{J} = bR + aJ \), again allowing \( a \) and \( b \) to be either positive or negative.

6.4 Discrete time models.

The analogous model in discrete time is

\[
\mathbf{n}(t+1) = M\mathbf{n}(t)
\]

and the stability of the equilibrium \( \dot{n} = 0 \) depends again on the eigenvalues of \( M \). In this case the general form of solutions is

\[
\dot{n}(t) = c_1\lambda_1^t\mathbf{v}_1 + c_2\lambda_2^t\mathbf{v}_2.
\]

So we have stability if \( |\lambda_1| < 1 \) and \( |\lambda_2| < 1 \), and instability if either inequality is reversed. This is true regardless of whether the eigenvalues are real or complex; for a complex eigenvalue \( \lambda = A + Bi \), its absolute value is the distance from the point \((A, B)\) in the plane to the origin, i.e.

\[
|\lambda| = |A + Bi| = \sqrt{A^2 + B^2}.
\]

As in the continuous time case, there is a stability criterion in terms of the Trace and Determinant of \( M \) that is very helpful. For discrete-time two-variable systems, the condition for stability is

\[
|T| < 1 + D < 2.
\]

Figure 20 shows the classification of equilibria in terms of Trace and Determinant for a two-variable discrete time linear system.
Figure 20: Classification of equilibrium stability for a two-variable linear system \( \tilde{n}(t+1) = M \tilde{n}(t) \) based on the Trace and Determinant of \( M \). Keep in mind that this diagram only applies to the discrete time system, not to a discrete time system.

7 Chapter 8: Linear stability analysis

7.1 Linear stability analysis for nonlinear differential equations

The key result, as in one-variable models, is that the stability of an equilibrium is usually determined by the stability of a linear approximation involving the derivatives of the functions defining the model. The zero equilibrium in a linear model. To introduce this method of local linearization we will again start a two-variable continuous time system

\[
\begin{align*}
\frac{dx}{dt} &= f(x, y) \\
\frac{dy}{dt} &= g(x, y)
\end{align*}
\]  

(7.1)

and suppose that \((\hat{x}, \hat{y})\) is an equilibrium, meaning that

\[ f(\hat{x}, \hat{y}) = g(\hat{x}, \hat{y}) = 0. \]
Then as in the case of a one-variable system, we can use a Taylor expansion to see what happens near the equilibrium. The result is that stability is determined by a linear system with matrix \( J \) called the Jacobian:

\[
J = \begin{pmatrix}
\frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\
\frac{\partial g}{\partial x} & \frac{\partial g}{\partial y}
\end{pmatrix}
\] (7.2)

where all the partial derivatives of \( J \) are evaluated at the equilibrium. For higher-dimensional systems see Definition 8.2 in Otto and Day (p. 306).

So there are four steps to doing a nonlinear stability analysis

1. Find the equilibria
2. Derive the general form of the Jacobian matrix
3. Substitute each equilibrium into the general form of the Jacobian matrix, simplifying as much as possible.
4. Figure out when the eigenvalues of the Jacobian imply that the equilibrium is stable.

A common beginner’s mistake is to try to do step 4. before step 3., i.e. trying to work out the eigenvalues in general, rather than at the equilibria. This is a recipe for doing lots of unnecessary work. Equilibria are special places, and often the Jacobian takes an especially simple form at equilibria.

**Example: an SIS infectious disease model** (from Otto and Day section 8.2)

\[
d\frac{S}{dt} = \theta - dS - \beta SI + \gamma I
\]

\[
d\frac{I}{dt} = \beta SI - (d + \nu + \gamma) I
\] (7.3)

1. Find equilibria: Factoring the second line, we see that \( dI/dt = 0 \) requires either \( I = 0 \) or \( S = (d + \nu + \gamma)/\beta \equiv \hat{S}_1 \).

   • If \( I = 0 \), substituting \( I = 0 \) into the first line gives \( \theta = dS \) so \( \hat{S}_0 = \theta/d \).

   • If \( I \neq 0 \), we substitute \( \hat{S}_1 \) into the first equation and solve for \( \hat{I} \), getting \( \hat{I}_1 = \frac{\theta - d(d + \nu + \gamma)/\beta}{d+\nu} \).

So we have two equilibria, disease free at \((\hat{S}_0, 0)\) and endemic at \((\hat{S}_1, \hat{I}_1)\). The latter may or may not be biologically meaningful \((\hat{I}_1 > 0)\), depending on parameter values.

To get the (1,1) entry in the Jacobian, we take the first line of the model and take its derivative with respect to \( S \). To get the (2,1) entry, we take the second line of the model and take its
derivative with respect to $S$, getting $\beta I$. Continuing on, the Jacobian matrix at an equilibrium $(\hat{S}, \hat{I})$ is

$$J = \begin{pmatrix} -\beta \hat{I} - d & -\beta \hat{S} + \gamma \\ \beta \hat{I} & \beta \hat{S} - (d + \nu + \gamma) \end{pmatrix} \quad (7.4)$$

The main point of this example is why you always do step 3 before step 4. Consider first the equilibrium $(0, \hat{S}_0)$. Substituting $\hat{I} = 0$ into the Jacobian, we get

$$J = \begin{pmatrix} -d & -\beta \hat{S} + \gamma \\ 0 & \beta \hat{S} - (d + \nu + \gamma) \end{pmatrix} \quad (7.5)$$

This is an upper triangular matrix, so the eigenvalues are the diagonal entries. One of these is $-d$, which cannot cause instability. So stability of the disease-free equilibrium depends on whether the bottom right entry in the Jacobian is negative or positive (implying stability versus instability). So we have that

- The equilibrium is stable if $\beta \hat{S}_0 < d + \nu + \gamma \iff \frac{\beta \hat{S}_0}{d + \nu + \gamma} < 1$.
- The equilibrium is unstable if $\frac{\beta \hat{S}_0}{d + \nu + \gamma} < 1$.

Not surprisingly, we can interpret the threshold as saying that the disease will increase if one infective individual gives rise to more than one new case, on average, when the disease is very rare. We also have found that instability of the disease-free equilibrium is equivalent to existence of an equilibrium with the disease present.

What about the other equilibrium? That one turns out to have a zero in the bottom-right entry (which is not a coincidence), and that makes it easy to compute the trace and determinant:

$$Trace \begin{pmatrix} a & b \\ c & 0 \end{pmatrix} = a, \quad Det \begin{pmatrix} a & b \\ c & 0 \end{pmatrix} = -bc$$

For stability we need to have the Trace $< 0$ and the Determinant $> 0$. In this case, the Determinant works out to be $\beta \theta / d > d + \nu + \gamma$, which is positive whenever the equilibrium exists. The Trace is $(-\beta \theta + \gamma d) / (d + \nu)$. This must be negative whenever the equilibrium exists, because $\beta \theta > \gamma d$. So the endemic equilibrium is stable whenever it exists.

### 7.2 Linear stability analysis for difference equations

Here the nonlinear system is

$$x_1(t + 1) = f_1(x_1(t), x_2(t))$$
$$x_2(t + 1) = f_2(x_1(t), x_2(t)) \quad (7.6)$$
Exactly as for differential equations, equilibrium stability is determined by the linear difference equation

\[ \bar{e}(t+1) = J\bar{e}(t) \]  

(7.7)

where \( J \) is the exact same Jacobian matrix as before. So stability depends on the eigenvalues of \( J \) as in a linear system: stable if they are all less than 1 in absolute value, unstable if any of them is greater than 1 in absolute value.

8  Chapter 12: Evolutionary Invasion Analysis

Now we are to use linear stability analysis to analyze deterministic models of adaptive trait evolution. The scenario we consider is invasion of a rare mutant into a steady-state population with a single “resident” genotype. Whether invasion of this type fails or succeeds is equivalent to stability versus instability of the equilibrium where the mutant is at zero frequency.

8.1  Evolutionary Invasion Analysis of Reproductive effort

The idea and the appeal of invasion analysis is that it completely “shortcuts” analysis at the level of allele frequency change, by

- modeling at the level of phenotypes and their effects on fitness
- thinking only about the ultimate evolutionary outcome when a new mutant arises: does it increase and spread through the population, or decrease to extinction?

In the long run (the argument goes) traits that we observe should be ones that confer higher fitness than any feasible mutant. “Feasible” is crucial: the perfect organism would mature instantly, breed continually and live forever. So a key part of any such modeling exercise is to define the constraints and tradeoffs that determine the set of feasible phenotypes. Having done that, we want to ask what happens when a rare mutant comes into a population monomorphic for a “resident” phenotype, in order to figure out what phenotype would resist all possible invaders.

Our first example is an oldie but goodie: reproductive effort (we will not worry here about how to define reproductive effort, or what units to measure it in...). Step 1 is to model the Resident by itself. The model (for this example) posits a plant species that matures in one year, reproduces each year, and has probability \( p \) of survival to the next year. The survival of new offspring to the next year is density dependent, such that the number of new recruits is \( be^{-\alpha N(t)} \). The Resident model is then

\[ N(t+1) = N(t)(be^{-\alpha N(t)} + p) \]  

(8.1)
We now want to introduce a rare mutant with different values of \( p \) and \( b \), resulting from a different level of reproductive effort i.e. \( b_m = b(E_m), p_m = b(E_m) \) versus \( b(E), p(E) \) for the resident. We assume that only the traits of interest differ between Resident and Invader, so each of them has recruitment limited by the total population density:

\[
N_r(t+1) = N_r(t)(be^{-\alpha(N_r(t)+N_m(t))+p}) = N_r(t)\lambda_r(N_r(t), N_m(t)) \\
N_m(t+1) = N_m(t)(b_me^{-\alpha(N_r(t)+N_m(t))+p_m}) = N_m(t)\lambda_m(N_r(t), N_m(t))
\]  

(8.2)

We are interested in the stability of the “resident-only” equilibrium where the invader is absent, \( N_m = 0 \), and the resident is at the equilibrium of (8.1), namely

\[
\hat{N}_r = \frac{1}{\alpha} \log \frac{b}{1-p}
\]

Before going ahead and computing the Jacobian, we will take advantage of the special form of (8.2). Because we’re at an equilibrium where \( N_m = 0 \), “Jacobian trick” 2(a) applies, and gives us the bottom row of the Jacobian. The bottom-left entry is zero, and the bottom-right entry is \( \lambda_m \) evaluated at the resident-only equilibrium. That means the Jacobian is upper triangular, and its eigenvalues will be its diagonal entries.

So all we need for stability analysis is the top-left entry. To get this we have to differentiate the equation for \( N_r(t+1) \) with respect to \( N_r \), and plug in \( \hat{N}_r > 0, \hat{N}_m = 0 \). This is identical to stability analysis of the resident-only equation (8.1), at the equilibrium where \( \hat{N}_r > 0 \). By assumption the resident alone is stable, or this whole invasion analysis collapses. So the top-left entry must be a number between -1 and 1, giving an eigenvalue of the resident-invader Jacobian that does not cause instability.

So it all comes down to value of \( \lambda_m \), per-capita finite growth rate of the invader. This is always \( > 0 \), so the the equilibrium is unstable if the invader has \( \lambda_m(0, \hat{N}_r) > 1 \), and unstable if \( \lambda_m(0, \hat{N}_r) < 1 \).

So we’ve reached a very simple “recipe” for doing the invasion analysis:

- Write down an equation for the resident, with the invader absent. Find its equilibrium
- Write down an equation for the invader (which must include the resident), and substitute into this the resident steady state.
- See whether the invader increases \( (\lambda_m > 1) \) or decreases.

Conveniently, this is not just a recipe for this example. It’s based on the fact (or more accurately, the assumption) that resident types beget resident types, and invaders beget invaders, leading to the multiplicative forms for the right-hand sides in (8.2). Given that structure, it is always the case that the resident’s stability against invasion depends on the mutant’s value of \( \lambda \) when the mutant is rare and the invader at steady-state. So we have a simple “story” that gets us the
right answer: Pretend that the invader is so rare that the resident doesn’t “see” it at all, and ask whether the invader (with the resident sitting at its equilibrium) will increase or decrease.

To finish the job, we need to relate this condition back to the model and its parameters. Doing the algebra, we get that

$$\lambda_m = b_m \frac{1 - p}{b} + p_m$$

so the condition $$\lambda_m > 1$$ is equivalent (with a bit of algebra) to

$$\frac{b_m}{1 - p_m} > \frac{b}{1 - p}$$

What does that mean? $$\frac{b}{1 - p}$$ is the plants expected lifetime reproductive success: total number of offspring, added up without regard to when they are born. We conclude that a population can be invaded by a mutant with a higher lifetime reproductive success, so evolution in the long run should maximize lifetime reproductive success. The level of reproductive effort that maximizes $$b/(1 - p)$$ is then an evolutionarily stable strategy because no alternative type could invade.

### 8.2 Evolutionary invasion analysis: pathogen virulence

Our starting point is the SI model we’ve looked at before, with (for simplicity) the assumption that there is no chance of recovery from the disease:

\[
\begin{align*}
\frac{dS}{dt} &= \theta - dS - \beta SI \\
\frac{dI}{dt} &= \beta SI - (d + v)I
\end{align*}
\] (8.3)

We want to now consider the fate of an invading pathogen phenotype with a different level of virulence, leading to different values of $$\beta$$ and $$\nu$$, coming into a population where the resident strain is endemic. The biological rationale is that faster pathogen replication within the host makes the disease more transmissible while an infected host is alive, but increases the host death rate. We will assume that a host can only be infected with one strain at a time: once the host immune system is mobilized by one strain, it can fend off the closely-related cocirculating strain. So the model becomes

\[
\begin{align*}
\frac{dS}{dt} &= \theta - dS - \beta SI - \beta_m SI_m \\
\frac{dI}{dt} &= \beta SI - (d + v)I \\
\frac{dI_m}{dt} &= \beta_m SI_m - (d + v_m)I_m
\end{align*}
\] (8.4)

Our “recipe” for invasion analysis says that we put the resident at its endemic steady state $$(\hat{S}_1, \hat{I}_1)$$ and see how the invader fares. Doing that, the equation for the invader is

$$\frac{dI_m}{dt} = \beta_m \hat{S}_1 I_m - (d + v_m)I_m.$$ (8.5)
This implies exponential growth or decay depending on the sign of \( \beta_m \hat{S}_1 - (d + v_m) \), where \( \hat{S}_1 = \frac{d + v_m}{\beta} \). The invading strain increases if this is positive, decreases if it is negative. So the invader is successful if
\[
\frac{\beta_m}{d + v_m} > \frac{1}{\hat{S}_1} = \frac{\beta}{d + v_r}.
\] (8.6)
Thus, the invading strain succeeds if it would have a lower steady-state number of susceptibles at equilibrium. This is an example of the classic “\( R^* \) rule” for resource competition: the competitor that can eat the resource down the furthest is the winner.

There’s another intuitive interpretation of the invasion criterion. With \( \gamma = 0 \), the pathogen’s net reproductive rate in this model is \( R_0 = \frac{\beta}{d+v} \hat{S}_0 \) where \( \hat{S}_0 = \theta/d \) is the number of susceptibles at the disease-free equilibrium. So (8.6) says that pathogen virulence evolves to maximize \( R_0 \).

### 8.3 The Fitness Gradient and ESS’s

Invasion analysis tells about a single substitution event: which mutants, if they arise, will be able to increase and spread through the population. The next step is to think about a sequence of such events and the ultimate outcome of the evolutionary process as we have modeled it.

Evolutionary invasion analysis tells us that in general fitness is an eigenvalue, specifically the eigenvalue \( \lambda(z_m, z_r) \) that determines stability of the equilibrium for the resident (with trait value \( z_r \)) facing potential invasion of a rare mutant (with trait value \( z_m \)). If invader and resident are identical, the eigenvalue must be on the border between stability and instability: \( \lambda = 0 \) in a continuous-time model, and \( \lambda = 1 \) in a discrete-time model. This happens because the frequency of the invader doesn’t go up or down: it always behaves just like the resident.

Invasion success or failure can therefore be determined by the fitness gradient, which is
\[
\Gamma(z) = \frac{\partial \lambda(z_m, z_r)}{\partial z_m} \text{ at } z_m = z_r = z.
\] (8.7)
\( \Gamma \) tells us the direction of trait evolution. If \( \Gamma(z_r) > 0 \), then \( \lambda_m(z_m, z_r) \) will be above the threshold for instability for \( z_m \) slightly above \( z_r \), and below the threshold if \( z_m \) is slightly below \( z_r \). So an invader succeeds if it has a higher value of \( z \) than the resident, and fail otherwise, so evolution moves the trait “to the right”. If \( \Gamma(z_r) < 0 \), then invaders with a smaller value of \( z \) than the resident will succeed. So evolution always “climbs up the fitness gradient”. But at the same time evolution modifies the fitness gradient because the fate an invader depends on which resident it’s facing. Each substitution event creates a new biotic environment and a new fitness gradient for future mutant lineages.

Example: for the pathogen virulence model, the trait \( z \) is virulence \( v \) and transmission \( \beta \) is a function of \( v \). From equation (8.5) we see that the eigenvalue determining invasion success is
\[
\lambda(v_m, v_r) = \beta(v_m) \hat{S}_1 - (d + v_m) = \beta(v_m) \frac{d + v_r}{\beta(v_r)} - (d + v_m).
\] (8.8)
Figure 21: Plot of the invasion eigenvalue $\lambda(z_m, z^*)$ when $z^*$ is an ESS in a continuous time model. The graph shows that when the resident has trait value $z^*$, any invader with a trait value $z_m \neq z^*$ has $\lambda < 0$ and so fails to invade.

Note that the expression for invader fitness must include all effects of the evolving trait on model parameters, so that reflects all of the selective forces acting on the trait. In this case, we have to explicitly include the fact that $\beta$ is a function of $v$ for both the resident and the invader.

To get the fitness gradient, we differentiate $\lambda(v_m, v_r)$ with respect to $v_m$, getting

$$\frac{\partial \lambda(v_m, v_r)}{\partial v_m} = \beta'(v_m) \frac{d + v_r}{\beta(v_r)} - 1 \quad (8.9)$$

and then we set $v_m = v_r = v$ to get

$$\Gamma(v) = \beta'(v) \frac{d + v}{\beta(v)} - 1. \quad (8.10)$$

We can do two (at least) two things with $\Gamma$. First, we can look for a trait value $z^*$ that is noninvasible, or an evolutionarily stable strategy (ESS). As noted above, if $\Gamma(z_r)$ is either positive or negative, there is an invader $z_r$ that will succeed, so for $z^*$ to be an ESS we must have $\Gamma(z^*) = 0$. This condition says that if we plot $\lambda(z_m, z^*)$ as a function of $z_m$, it must be maximized at $z_m = z^*$, so the derivative (which is $\Gamma$) must be zero at the maximum (see Figure 21). To be a local maximum of $\lambda(z_m, z^*)$ rather than a local minimum, we need the second derivative to be negative,

$$\frac{\partial^2 \lambda(z_m, z_r)}{\partial z_m^2} < 0 \text{ at } z_m = z_r = z^*. \quad (8.11)$$
Note that this is not the derivative of $\Gamma(z)$ with respect to $z$; you have to take the second derivative of $\lambda$ with respect to $z_m$ before making the substitution $z_m = z_r = z^*$. Example (as in Otto and Day): assume that $\beta(v) = \frac{\tau v}{k + v}$, so that higher virulence implies increasing transmission rate, but with diminishing returns. To find the ESS we need to set (8.10) equal to 0, with $\beta(v)$ given by our assumed formula, and solve for $v$. With a bit of calculus and algebra this works out to

$$\frac{dk - v^2}{v^2 + kv} = 0.$$ 

So the only possible ESS is when $v^2 = dk$, hence $v^* = \sqrt{dk}$.

To see if this is a local fitness maximum or minimum, we have to take the second derivative of $\lambda$ with respect to $v_m$. With (8.9) giving us the first derivative, we find that the second derivative is $\beta''(v_m) \frac{d + vr}{\beta(v_r)}$. Since $\beta''(v) < 0$ for all $v$, we see that our possible ESS is in fact an ESS.

ESS’s are easier to find if the model has a quantity that is maximized by evolution. In the pathogen virulence model we found that evolution maximized

$$F(v) = \frac{\beta(v)}{d + v}.$$ 

(8.12)

So to find an ESS we just have to see where $F$ is maximized. The first step is finding where $F'(v) = 0$. With a bit of calculus and algebra, we get that

$$F'(v) = \frac{\tau (dk - v^2)}{(v + d)^2 (v + k)^2}.$$ 

So we find again that the only possible ESS is again $v^2 = dk$, hence

$$v^* = \sqrt{dk}.$$ 

We can also see that $F'(v)$ goes from positive when $v^2 < dk$ to negative when $v^2 > dk$, so $v^*$ is a maximum of $F$ and therefore an ESS.

8.4 Fitness gradient and adaptive dynamics

More ambitiously, the fitness gradient is used as the basis for modeling the dynamics of trait evolution. In a variety of (theoretical) situations, it is at least a rough approximation that the rate of trait evolution is proportional to the fitness gradient. The constant of proportionality reflects the amount of genetic variability available for evolution to act on, either the standing additive genetic variance for the trait (in some models) or the rate of advantageous mutations
(in other models). This leads to models like

\begin{align*}
\frac{dS}{dt} &= \theta - dS - \beta(v)SI \\
\frac{dI}{dt} &= \beta(v)SI - (d + v)I \\
\frac{dv}{dt} &= V\Gamma(v, S, I) \quad \text{(8.13)}
\end{align*}

In a model like this $v$ represents the trait mean in the population, and the last line of the model describes how the trait mean changes.

Note that in the $dv/dt$ equation, the fitness gradient is computed using the current values of $S$ and $I$ as the resident densities that an invader faces, rather than using equilibrium values of $S$ and $I$. The reason is that model (8.13) views evolution and population dynamics as occurring on similar time scales, rather than evolution occurring only through rare substitution events in populations that are at ecological steady-state.

Specifically, in model (8.13) the equation for a rare invader would be

\begin{align*}
\frac{dI_m}{dt} &= \beta(v_m)SI - (d + v_m)I_m = [\beta(v_m)S - (d + v_m)]I_m \quad \text{(8.14)}
\end{align*}

so

\[ \lambda(v_m, v) = \beta(v_m)S - (d + v_m). \quad \text{(8.15)} \]

So we have \( \frac{\partial\lambda(v_m, v)}{\partial v_m} = \beta'(v_m)S - 1 \), and therefore the fitness gradient is

\[ \Gamma(v, S, I) = \beta'(v)S - 1. \]

So if we use the tradeoff curve \( \beta(v) = \frac{\tau v}{k + v} \), giving \( \beta'(v) = \frac{k\tau}{(k + v)^2} \), then the model written out in full is

\begin{align*}
\frac{dS}{dt} &= \theta - dS - \frac{\tau v}{k + v}SI \\
\frac{dI}{dt} &= \frac{\tau v}{k + v}SI - (d + v)I \\
\frac{dv}{dt} &= V\left[\frac{k\tau}{(v + k)^2}S - 1\right] \quad \text{(8.16)}
\end{align*}

What does model (8.16) predict for the outcome of evolution? Setting $dI/dt = 0$ we can find the equilibrium value for $S$, and plugging that into $dv/dt = 0$ we can find the equilibrium value of $v$. The result of these calculations is \( \hat{v} = \sqrt{dk} \), so the equilibrium of the dynamic model equals the ESS of the evolutionary invasion analysis. This is not a coincidence. If we set $v = v^*$
and $S, I$ at their equilibrium densities for $v = v^*$, then the selection gradient is zero (because $v^*$ is an ESS) so we have an equilibrium of the dynamic model. However the dynamic model and the evolutionary invasion analysis may reach different conclusions about whether the trait evolves to reach the ESS, because of the differing assumptions about the relative time scales of evolutionary and ecological processes.
9 Chapter 13: Stochastic models

We shift now to models where “what happens next” involves an element of chance, which are called stochastic models. For given parameters and initial conditions, we have many possible solution trajectories, some more likely than others. We will focus on computational approaches to stochastic models. The issues are model construction and methods for stochastic simulation.

9.1 Population Growth: Discrete Time

R files: Ch13DiscreteTime.R

Most of the main ideas and issues are encountered when we try to construct and simulate stochastic analogs of the deterministic models for exponential and logistic population growth in discrete and continuous time. We’ll start simple: stochastic analogs of discrete exponential growth

\[ N(t + 1) = RN(t), R > 0 \]  \hspace{1cm} (9.1)

and imagine this representing a population with discrete nonoverlapping generations. So at each time \( t \), all parents have \( R \) offspring and then die.

There are two main kinds of stochasticity that we can add to (9.1), demographic and environmental. Demographic stochasticity is the randomness that comes from the fact that populations are finite, and what each individual does has an element of chance. Here, rather than each parent having \( R \) offspring exactly, we acknowledge that parents vary in their number of offspring, and posit that the average number of offspring per parent is \( R \).

That’s not precise enough: we need to specify the chance of having no offspring, 1 offspring, 2 offspring, 3 offspring, etc. The example in the text (and one commonly used by modelers) is to assume a Poisson distribution: each parent has a Poisson number of offspring with mean \( R \). In R, \texttt{rpois(n,m)} generates \( n \) random numbers having a Poisson distribution with mean \( m \). So here is our first stochastic analog of (9.1)

\[
\begin{align*}
\text{mean.R} &= 1.2; \ N = \text{numeric}(10); \ N[1] = 10; \\
\text{for}(j \in 2:10) \{ \\
\quad \text{kids} = \text{rpois}(N[j-1], \text{mean.R}) \ # \text{everyone’s kids} \\
\quad \text{N}[j] = \text{sum}(\text{kids}) \\
\}\ \\
\text{plot(1:10,N,xlab="Generation",ylab="Population size");}
\end{align*}
\]

This works fine, but only up to a point. The problem is that you have to generate a random number of offspring for each parent, and when the population size gets big, that’s a LOT of work for the computer. That’s where the Poisson distribution comes in handy. The sum of
several Poisson-distributed random variables is Poisson distributed, with mean of the sum equal to the sum of the means. So an exactly equivalent way to generate offspring is

\[
kids = \text{rpois}(\text{mean.R} \times \text{N}[j-1])
\]

and the model can be summarized as

\[
N(t + 1) \sim \text{Poisson}(RN(t)).
\]

Note that demographic stochasticity only models chance differences between individuals. One happening to have more kids than another is just a roll of the dice, and all individuals roll the same dice (i.e., all have the same probability distribution for number of offspring). All of the models in this chapter, and most in the literature, have this property.

*Environmental stochasticity* refers to random variation over time in model parameters. Exponential growth with environmental stochasticity is

\[
N(t + 1) = R(t)N(t), N(0) = N_0
\]  \hspace{1cm} (9.2)

where \( R(t) \) is drawn from some probability distribution. The simplest is “good years” and “bad years”: toss a coin each year, to decide which kind it is. On the computer this is done using uniformly distributed random numbers, \texttt{runif} in \texttt{R}, as in

\[
R = \text{ifelse(runif(1) < p.good, R.good, R.bad)}
\]

A random number distributed uniformly on \((0,1)\) has probability \( p.good \) of falling in \((0, p.good)\), in which as \( R \) is assigned the value \( R.good \); otherwise \( R = R.bad \). Putting a coin toss inside the for-loop over time is all it takes to iterate the model (SHOW EXAMPLE IN SCRIPT). Or for even more fun, you can use a coin-toss to choose the mean.R for a Poisson distribution, and combine demographic and environmental stochasticity – on the computer it’s effortless.

### 9.2 Population growth: continuous time

R files: Ch13BirthDeath.R

The deterministic starting point is now the differential equation for exponential growth,

\[
\frac{dN}{dt} = (b - d)N,
\]

\( N(0) = N_0, b > 0, d > 0 \) \hspace{1cm} (9.3)

Distinguishing births from deaths (writing \((b - d)N\) rather than \(rN\)) because to model demographic stochasticity we need to “toss coins” for both of them.

For demographic stochasticity, we make births and deaths a coin-toss. The deterministic assumption is that each for each individual now in the population there are \( b\Delta t \) new offspring over
a time interval of length $\Delta t$, and $d\Delta t$ deaths. The stochastic description is that each individual has probability $b\Delta t$ of producing an offspring in the next $\Delta t$ units of time, and probability $b\Delta t$ of dying. In both cases, thinking about small time steps is an approximation to continuous time, and really ideally we want the limit as $\Delta t \to 0$. But in practice, we can keep making $\Delta t$ smaller and smaller, until further decreases don’t change any properties of the simulations that we care about.

But as in discrete time, we need to minimize the number of coin tosses by thinking about the net effect of all the individual-level coin tosses. In this case we get binomial distributions. Between times $t$ and $\Delta t$, all $N(t)$ individuals have the same probability of producing an offspring, so it’s like $N(t)$ tosses of a coin with probability $b\Delta t$ of getting Heads, and the total number of Heads is $B(N(t), b\Delta t)$ distributed. Ditto for deaths, with $d$ replacing $b$. So for $\Delta t$ small, the dynamics of the birth-death process are approximated by

$$N(t + \Delta t) \sim N(t) + B(N(t), b\Delta t) - B(N(t), d\Delta t).$$

We see that with demographic stochasticity, it’s not just the difference of $b$ and $d$ that matters. But we don’t worry about the ordering of birth and death because $\Delta t$ is small – we let them happen simultaneously.

In a language that can simulate Binomial random variables efficiently for large $N$ (which R can do), the last equation is a good recipe for simulating the process. This means that it’s easy to add density-dependence, for example making the birth rate decrease as density increases:

$$N(t + \Delta t) \sim N(t) + B(N(t), be^{-N(t)/K\Delta t}) - B(N(t), d\Delta t).$$

It’s hard to say a priori how small $\Delta t$ needs to be for the binomial approximation to be accurate, but it’s easy to know when it’s too big. What the approximations leave out is the chance of one individual doing 2 things in time interval $\Delta t$, for example one individual having two offspring in that time period, or an individual being born and having an offspring. To make sure that these are infrequent, $\Delta t$ must be small enough that each individual is most likely to do nothing in any time interval of length $\Delta t$. So here, we need to have $b\Delta t \ll 1, d\Delta t \ll 1$.

### 9.2.1 Gillespie algorithm

Another option is to simulate the exact continuous-time limit at the population level. The method is fairly simply, though it takes probability theory beyond the level of this course to explain why it works.

When the population size is $N$, the total event rate is defined to be the sum of the per-individual birth and death rates multiplied by the number of individuals. Without density dependence, this is $(b + d)N$. The time until the next event (either a birth or death) has an exponential distribution with mean equal to the inverse of the total event rate, in this case $\frac{1}{(b+d)N}$. When that event happens, it is a birth with probability $b/(b+d)$ and a death with probability $d/(b+d)$.
9 CHAPTER 13: STOCHASTIC MODELS

So the exact continuous-time process can be simulated by alternating between drawing a random time-to-next-event from an exponential distribution, and tossing a coin to decide which kind of event happens. This is called the Gillespie algorithm after the person who first proposed it (in the context of chemical reaction models). It’s very time-consuming for large populations, so more often people use binomial approximations, possibly with the time step $\Delta t$ shrink or growing as necessary (when the total event rate is high $\Delta t$ must be small, etc.).

9.2.2 Other compartment models

R files: Ch13=SI=CoinToss.R

The binomial simulation method can be used to add demographic stochasticity to any continuous time compartment model specified by a system of differential equations. One example is enough to make the idea clear. Consider an SI infectious disease model

$$
\begin{align*}
\frac{dS}{dt} &= -\beta SI + \gamma I \\
\frac{dI}{dt} &= \beta SI - \gamma I
\end{align*}
$$

(9.4)

There are two processes moving individuals between the $S$ and $I$ compartments: Each susceptible becomes infected at rate $\beta I$, and each infective goes back to being susceptible at rate $\gamma$. To add demographic stochasticity in the manner of a birth-death process, we have each individual do a coin toss to see if they change disease state: the number who become infected between $t$ and $t + \Delta t$ is Binomial with parameters $S(t)$ and $\beta I \Delta t$, the number who recover is Binomial with parameters $I(t)$ and $\gamma \Delta t$. Then

$$
\begin{align*}
S(t + \Delta t) &= S(t) - \text{(number infected)} + \text{(number recover)}, \\
I(t + \Delta t) &= I(t) + \text{(number infected)} - \text{(number recover)}.
\end{align*}
$$

(9.5)

Note that all the coin-tossing is done first, to generate the number of infections and recoveries that occur, then you update the state variables based on the number of events of each type.

9.3 Modeling Demographic Stochasticity

R files: Ch13ClutchModels.R

What if you don’t want a Poisson distribution for the number of kids? If you are aiming to do simulations rather than analyzing the model, there are lots of options for getting closer to reality.

1. Zero-inflated Poisson. Imagine that some individuals live to reproductive age, but never produce offspring. You can then toss a coin to decide whether each individual breeds or not, and (if it’s realistic) give those that breed a Poisson distribution of offspring. In R,
Nkids = ifelse(runif(Nparents)<prob.of.breeding,rpois(Nparents,mean.litter.size),0)

2. A mixture of Poisson random variables can be used to give a Poisson-like distribution but with higher variance/mean ratio. For example, a Normal mixture of Poisson random variables could be

Nkids = rpois(Nparents,mean.litter.size+sigma*rnorm(Nparents))

If the variance in parent-specific mean litter sizes isn’t small compared to the mean, you need to take care to avoid negative values.

3. Bootstrap from your data. If you have recorded a large number of clutch sizes, put them all in a vector clutch.sizes and

Nkids = sample(clutch.sizes,Nparents,replace=TRUE)

will generate Nparents clutch sizes drawn at random from your data.

4. Sample from a probability distribution that you think is a good approximation to the truth, that has a finite number of possible outcomes. Let \( p_k \) be the probability of clutch size \( k \) for \( k = 0, 1, 2, \ldots, M \). Make a vector \( p = (p_0, p_1, p_2, \ldots, p_k) \), then

Nkids = sample(0:M,Nparents,replace=TRUE,prob=p)

will be a random draw of Nparents clutch sizes from your probability distribution.

9.4 Wright-Fisher model


Stochastic models can also be used to track the numbers of different types of individuals, such as individuals with different genotypes. To keep things simple, usually the assumptions of population models are inverted. In population models, population size varies but there are no heritable differences between individuals (e.g., if your parent had lots of kids that doesn’t mean you are more likely to have lots of kids). In population genetics models, population size varies but there is heritable variation for traits affecting fitness.

The Wright-Fisher model assumes that population size remains some constant value \( N \), and the gametes that produce the subsequent generation are drawn at random with replacement from the parents, who then die. This is a model for neutral genetic drift resulting from demographic stochasticity – there is no environmental stochasticity (which in this model would be fitness variation from generation to generation).

To see what these assumptions mean, and how to simulate it, consider the simplest case of a haploid population with genotypes \( a \) and \( A \), equal fitnesses, and \( p(t) \) the frequency of \( A \) in
generation \( t \). In the deterministic model, equal fitness gives \( p(t+1) = p(t) \). Here it gives neutral drift.

For population genetics models it’s useful to think backward in time. Instead of looking at each parents and asking “how many kids will she have?” (as we did for population models), it’s more useful to look at each kid and ask “who was her parent?”. In the Wright-Fisher model each kid’s parent was chosen at random from the parental population, so the parent is type-\( A \) with probability \( p(t) \). Hence, the number of type-\( A \) kids has a binomial distribution with parameters \( N \) and \( p(t) \), giving

\[
p(t + 1) \sim B(N, p(t))/N.
\]  

(9.6)

(here \( x \sim y \) means that \( y \) specifies the probability distribution of \( x \)).

Simulating the Wright-Fisher model (9.6) is easy. Analyzing it is more complicated. For small \( N \), some basic Markov Chain theory can be used (section 14.3 in the text). If there are \( N \) individuals in the population, the number of type-\( A \) individuals can be \( 0, 1, 2, \cdots, N \). The state at time \( t + 1 \) depends only on the state at time \( t \), not on what came before time \( t \); this is the defining property of a Markov Chain.

We define the transition matrix \( M \) whose \( (i,j)^{th} \) entry is \( p_{ij} \) the probability of being in state \( i \) in year \( t + 1 \), given that the state in year \( t \) was \( j \). If the population size is \( N \), then there are \( N + 1 \) possible states: \( 0, 1, 2, \cdots, N \) type=\( A \) individuals. State \( j \) of the Markov Chain for the Wright-Fisher process thus corresponds to there being \( j - 1 \) type-\( A \) individuals in the population.

The numbers \( p_{i+1,j+1}, i = 0, 1, 2, 3, \cdots, N \) are therefore given by the binomial distribution with parameters \( N \) and \( j/N \) (see p. 578 in Otto and Day for an example). That is,

\[
p_{i+1,j+1} = \binom{N}{i} \left( \frac{j}{N} \right)^i \left( 1 - \frac{j}{N} \right)^{N-i}, \quad i = 0, 1, \cdots N
\]  

(9.7)

where \( \binom{N}{i} \) is the binomial coefficient “\( N \) choose \( i \)” (the function in R is \( \text{choose}(N,i) \)). For the first and last columns of \( M \) we don’t need to use (9.7). The first column has a 1 at the top and zeros everywhere else, and the last column has a 1 at the bottom and zeros everywhere else, because without mutation a population that gets to \( p = 0 \) or \( p = 1 \) stays there forever.

Properties of \( M \) tell us what happens in the long run.

- The entries of \( M^k \) are the \( k \)-step transition probabilities, i.e. the \( (i,j)^{th} \) entry is the chance of being in state \( i \) at time \( t + k \), if the state at time \( t \) was \( j \). Note that \( M^2 \) means the matrix product of \( M \) with itself, which in R is \( M \times M \); just plain \( M \times M \) gives you element-by-element multiplication.

- If some power of \( M \) has all positive entries, then there is stationary probability distribution
\( \pi \) such that the probability of being in state \( j \) converges to \( \pi_j \), regardless of where you started.

- The stationary probability distribution is given by the dominant right eigenvalue of \( M \), scaled so that the sum of its elements is 1.

In an evolutionary models where the frequencies 0 and 1 are absorbing, there won’t be a power of \( M \) that has all positive entries. The outcome can’t be independent of where you start, because if you start at 0 or 1, then you stay there. For such models, interest focuses on the probability of fixation versus loss of an allele, and on how long it takes.

Again, for small \( N \) we can get answers computationally by computing successive powers of \( M \). The key property is that the \( j^{th} \) column of \( M^k \) gives the probability distribution of the state at time \( t + k \), given that the state at time \( t \) was \( j \). So for example the fixation probability

\[
F_j(t) = \text{Prob}(p(t) = 0 \text{ or } 1 | p(0) = j/N)
\]

can be calculated by using a for-loop to calculate \( M^t \), and taking the sum of the top and bottom entries in the column \( j + 1 \) of \( M^t \).

For large \( N \) it’s necessary to use diffusion approximations. These are partial differential equations for \( f(p, t) \), the probability distribution of \( p(t) \), based on the fact that for large \( N \) the changes from one time to the next in \( p(t) \) are approximately Gaussian distributed. Most classical results on fixation probabilities, absorption times, etc. for population genetics models are based on diffusion approximations.

### 9.5 Moran model

Wright-Fisher is analogous to discrete-time exponential growth with demographic stochasticity. The analog of a birth-and-death process continuous-time population growth model is the Moran model. We again assume constant population size \( N \), and two haploid types \( A \) and \( a \) with no fitness differential. But instead of assuming that everyone dies at times \( t = 1, 2, 3, \cdots \), we have gradual turnover. In each time interval of length \( dt \), each individual has probability \( dt \) of producing an offspring, who then replaces a randomly chosen member of the population (possibly their parent).

The Moran model is also a Markov chain, if we measure time in birth-death events rather than “clock time”. When an event occurs, the number of \( A \) individuals goes up by 1 if an \( a \) died and was replaced by an \( A \); this has probability \( (1 - p)p \). The number of \( A \) individuals goes down by 1 (by the same logic) with probability \( p(1 - p) \). Otherwise the number of \( A \’s \) stays the same. So in the transition matrix for the Moran model, entry \((j + 1, j + 1)\) is

\[
p_{j+1,j+1} = 1 - 2(j/N)(1 - j/N)
\]

(9.8)
(these are the diagonal elements of the matrix); above and below that entry in column $j+1$ are

$$p_{j,j+1} = p_{j+2,j+1} = \left(j/N\right)\left(1 - j/N\right). \quad (9.9)$$

For looking at long-term properties, measuring time in birth-death events is harmless, because the time required for many birth-death events won’t be very different from the expected time (in terms of relative errors). Since one birth-death event occurs (on average) every $1/N$ time units, the number of birth-death events divided by $N$ can be used as a proxy for the amount of elapsed time (i.e. we pretend that the $k^{th}$ birth-death event occurs at time $k/N$).

As with the Wright-Fisher model, the transition matrix can be used to compute fixation probabilities (Otto and Day do this by simulation). Doing this, it turns out that the Moran model goes to fixation much faster than the Wright-Fisher model (using the factor-of-$1/N$ conversion birth-death events and real time). Intuitively, this is because in the Moran model both deaths and births have demographic stochasticity that affect the change in genotype frequency. In Wright-Fisher there are $N$ deaths every time unit, and the fraction of type-$A$’s that die is exactly $p(t)$. In Moran, there are on average $N$ deaths every unit of real time, but the fraction of type-$A$’s that have died may be lower or higher than the initial frequency of type $A$.

The easiest way to simulate the Moran model in real time is with the Gillespie algorithm. Changes in $p(t)$ occur at rate $2Np(t)(1 - p(t))$, and they are either an increase or decrease by amount $1/N$ with equal probability. This gets slow for large population sizes, and a binomial approximation (as in birth-death process models) could be used.

Simulating the Moran model at birth-death event times is also easy. Toss one coin to decide if there is a change in $p$ - this has probability $2p(1-p)$. If there is a change, toss another to decide if it is an increase by $1/N$, or a decrease.

### 9.6 Coalescent models

Coalescent theory is basically a Wright-Fisher model with more than 2 alleles, running backwards in time. Starting from the set of alleles currently present in the population, we ask where they came from. Specifically, picking a group of individuals from the current population, we ask: how many generations back must we trace their ancestry (on average) before we find that they all descend from the same individual? This is called the coalescence time.

The reason for making this odd calculation is that it makes it possible to answer questions that we actually care about (which is not immediately obvious). For example, sequence a stretch of DNA in two individuals in the current population. How many base-pair differences do we expect to find? The answer is the number of mutations per birth (i.e. the mean number of differences between a parent and an offspring) multiplied by twice the number of generations
back to the first common ancestor of the pair. So the expected number of difference is

\[ 2 \times \text{mutation rate} \times \text{average coalescence time}. \]

So if we know average coalescence time, then the average number of base-pair differences between a pair of individuals in the population gives us an estimate of the mutation rate. Conversely, if we know the mutation rate, the number of base-pair differences gives us an estimate of the effective population size.

So let’s calculate the distribution of time to coalescence of a pair of individuals in the current population. The first of them had somebody as their parent. The second of them had that same somebody as their parent with probability \( \frac{1}{N} \), and somebody different as their parent with probability \( 1 - \frac{1}{N} \). In the former event, coalescence occurred in one generation. In the latter event, we’re back where we started: two distinct individuals.

So if \( \bar{T}_2 \) is the mean time to coalescence, we have

\[ \bar{T}_2 = \left( \frac{1}{N} \right) \times 1 + \left( 1 - \frac{1}{N} \right) \times (1 + \bar{T}_2). \]

which solves to \( \bar{T}_2 = N \): the average coalescence time for a pair of individuals is equal to the population size.

We can actually get the whole distribution of \( T_2 \). In order for \( T_2 \) to equal \( t \), there must have been \( t \) generations (going backward in time) without a coalescence, and finally one where coalescence occurred. Thus,

\[ \text{Prob}(T_2 = t) = \frac{1}{N} \left( 1 - \frac{1}{N} \right)^t \]

This is a geometric distribution with parameter \( p = 1/N \). A story for this distribution is this: we repeatedly toss an unfair coin with \( p \)-probability of getting Heads. The number of tosses until we get a Head has a geometric distribution.

The mean of a geometric distribution is \( 1/p \). This gives us (again) that the mean of \( T_2 \) is \( N \). The variance of a geometric distribution is \( (1-p)/p^2 \), which for \( N \) large is approximately \( N^2 \).

So the mean and standard deviation of \( T_2 \) are approximately equal, telling us that coalescent times are highly variable.

Next, let’s find the distribution for the time to coalescence of \( n \) individuals in the current population, denoted \( M_n \). The key step is writing \( M_n \) as the sum of the times required for each step along the path from \( n \) individuals now, to 1 common ancestor at some past time. That is,

\[ M_n = T_n + T_{n-1} + T_{n-2} + \cdots + T_2 \]

where \( T_i \) is the number of generations that it takes (going backward in time) for the number of ancestors of the current population to go down from \( j \) to \( j - 1 \).

So let’s focus on \( T_i \). The starting point is a population in which \( i \) distinct individuals are the ancestors of the \( n \) alleles at \( t = 0 \). A coalescent event does not occur in the previous generation if those \( i \) individuals have \( i \) distinct ancestors. What is the probability of that happening?
The first of those \( i \) individuals had somebody as their parent. The second had a different parent with probability \((1 - 1/N)\). The third had a parent different from the first two with probability \((1 - 2/N)\). Continuing, the probability of no coalescence is

\[
1 - p(i) = \left(1 - \frac{1}{N}\right) \left(1 - \frac{2}{N}\right) \cdots \left(1 - \frac{i-1}{N}\right).
\] (9.13)

If we assume that \( N \) is large and \( n^2 \ll N \), then \( i^2 \ll N \) and we can approximate the product by dropping all terms of order \((1/N^2)\). This gives

\[
1 - p(i) \approx 1 - \frac{1}{N} - \frac{2}{N} - \frac{3}{N} \cdots - \frac{i-1}{N} = 1 - \frac{i(i-1)}{2N}. \] (9.14)

so

\[
p(i) \approx \frac{i(i-1)}{2N}. \] (9.15)

As with coalescence of a pair: if there is no coalescence we’re right back where we started, so our conclusion is: \( T_i \) is a geometric random variable with parameter \( p(i) = i(i-1)/(2N) \), and therefore mean \( \frac{2N}{i(i-1)} \). Note that \( p(i) \) must be small for all \( i \), otherwise the approximation leading to (9.15) is invalid.

To get the mean of \( M_n \), we add up the means of all the the \( T_i \); the result is

\[
E[M_n] = 2N \left(1 - \frac{1}{n}\right).
\]

Remarkably, this is not quite twice the mean time to coalescence of 2 alleles, regardless of how many alleles in the present generation are being considered.

This also gives us a simple recipe for simulating the process of coalescence.

- Starting from \( n \) specific alleles “now” in a population of size \( N \), we draw the waiting time \( T_n \) from a geometric distribution with parameter \( p(n) \) (in R this is the \texttt{rgeom} function).
- At time \( T_n \) generations prior to the present, we pick two of the \( n \) current alleles at random and have them coalesce, leaving \( n-1 \) distinct alleles at \( T_n \) generations before the present.
- The next waiting time \( T_{n-1} \) is from a geometric distribution with parameter \( p(n-1) \).
- At \( T_n + T_{n-1} \) generations before the present, two of the \( n-1 \) alleles present at \( T_n \) are selected at random to coalesce, leaving \( n-2 \) distinct alleles in the population

\ldots and so on until there is complete coalescence. See Figure 13-18 in the text for examples of what this procedure generates.
9.6.1 Mutation and allelic diversity

Coalescent theory becomes interesting when we overlay onto it processes causing genetic variation, such as mutation. The simplest model is that within the allele (segment of DNA) that is being sampled and modeled, there is a constant probability $\mu$ that an offspring differs from their parent due to a mutation event. We assume that the focal DNA segment is small enough that $\mu$ is very small, but large enough that each mutation event creates a new and unique genotype.

Under these assumptions, the number of mutations along a $k$-generation segment of the phylogenetic tree for the sample has a Binomial distribution with parameters $k$ (number of coin tosses) and $\mu$ (probability of a Head). But since $\mu$ is very small, $k$ must be large in order for mutations to have any chance of happening. In the limit $\mu \to 0, k \to \infty$ with $\mu k$ held constant, the Binomial distribution converges to a Poisson with parameter $\mu k$. We can therefore assume that the number of mutation events on a $k$-generation segment of the tree is Poisson with mean $\mu k$.

As an example of what this lets us compute, consider the probability that two of the $n$ alleles sampled “now” are identical in sequence. This happens if they two descended from their most recent common ancestor without any mutation events down both lines of descent. If the two alleles coalesced $T$ generations ago, the two will be identical if two segments of the phylogenetic tree with total length $2T$ contain zero mutations. For the Poisson distribution of mutation events with mean $2\mu T$, that probability is $e^{-2\mu T}$.

The probability that the two alleles are identical is therefore

$$\sum_{t=1}^{\infty} e^{-2\mu t} \Pr(T = t) = \sum_{t=1}^{\infty} e^{-2\mu} \frac{1}{N} \left(1 - \frac{1}{N}\right)^{t-1}. \quad (9.16)$$

To compute the sum, we can write it as

$$\frac{e^{-2\mu}}{N} \sum_{t=1}^{\infty} e^{-2\mu(t-1)} \left(1 - \frac{1}{N}\right)^{t-1} = \frac{e^{-2\mu}}{N} \sum_{t=0}^{\infty} e^{-2\mu t} \left(1 - \frac{1}{N}\right)^{t}$$

$$= \frac{e^{-2\mu}}{N} \sum_{t=0}^{\infty} \left[e^{-2\mu} \left(1 - \frac{1}{N}\right)^{t}\right].$$

The infinite sum in the last equation is a geometric series, which we can sum: $1 + r + r^2 + r^3 + \cdots = 1/(1 - r)$. Using this and simplifying, we get that the probability of allele identity is

$$\frac{1}{(e^{2\mu} - 1) N + 1}$$

For $\mu$ small, $e^{2\mu} \approx 1 + 2\mu$, so our final result is

$$P(\text{alleles identical}) = \frac{1}{1 + 2N\mu}. \quad (9.17)$$
As a second example: in a sample of \( n \) alleles from a population of size \( N \), what is the expected number of nucleotide sites that will exhibit some variation, rather than being the same in all \( n \) sampled individuals? Such sites are called \textit{segregating sites}. Under the small-\( \mu \) assumption, the number of segregating sites \( S \) equals the total number of mutations along the entire phylogenetic tree leading to the MRCA of the \( n \) alleles, so the expected value of \( S \) is \( \mu \) times the expected value of total tree length \( T \).

To compute the mean of \( T \), we break the tree up into the periods when there are \( i \) distinct alleles, for \( i = n, n-1, n-2, \ldots, 2 \). During the period with \( i \) distinct alleles, there are \( i \) branches in the tree, with expected length equal to the expected coalescence time, which is \( \frac{2N}{i(i-1)} \). The expected total length is therefore \( \frac{2N}{i-1} \). So the expected value of \( T \) is \( \sum_{i=2}^{n} \frac{2N}{i-1} = 2N \sum_{i=1}^{n-1} \frac{1}{i} \), so

\[
E[S] = \mu E[T] = 2N\mu \sum_{i=1}^{n-1} \frac{1}{i}.
\]

\[(9.18)\]

10 Diffusion models in population genetics

The best place by far to learn about diffusion models and theory is the book \textit{Mathematical Population Genetics} by Warren J. Ewens (Springer; 1st edition 1979, 2nd edition 2004), on which this section is based.

Diffusion theory can be approached from a formal mathematical perspective, in which care is taken to prove that as population size becomes larger and larger, the model of interest (such as Moran or Wright-Fisher) with appropriate rescalings of time and allele frequency, converges to a diffusion model. The second, adopted by Ewens and here, is to regard diffusions as a convenient set of models because a lot is known about their properties. For a given model, we try to find a way of rescaling time and allele frequencies in such a way that a diffusion model mimics its dynamics on short time scales.

A one-dimensional diffusion model is characterized by a continuous variable \( x(t) \) that changes stochastically, with time \( t \) continuous. The equations of motion are those of a particle moving in a fluid, subject to two forces:

1. Advection: a tendency to move in one direction rather than the other. In fluid mechanics this is due to motion of the fluid (and other things). In population genetics, it’s caused by selection.

2. Diffusion: undirected random motion. In fluid mechanics this is Brownian motion driven by thermal fluctuations of the fluid molecules. In population genetics, diffusion is caused by random sampling in finite populations.
A diffusion model is characterized by the mean and variance of changes in $x(t)$ over a short period of time $\Delta t$, conditional on the value at time $t$:

$$
E[\Delta x|x] = a(x)\Delta t + o(\Delta t)
$$
$$
Var[\Delta x|x] = b(x)\Delta t + o(\Delta t)
$$

(10.1)

where $\Delta x = x(t + \Delta t) - x(t)$, $\frac{o(\Delta t)}{\Delta t} \to 0$ as $\Delta t \to 0$.

If the functions $a(x)$ and $b(x)$ with those properties exist, then the probability distribution $f(x,t)$ for $x(t)$ satisfies the Kolmogorov forward equation

$$
\frac{\partial f(x,t)}{\partial t} = -\frac{\partial}{\partial x} \left(a(x)f(x,t)\right) + \frac{1}{2} \frac{\partial^2}{\partial x^2} \left(b(x)f(x,t)\right).
$$

(10.2)

This does not look like it’s very helpful, but it is, because a lot of clever people (including Fisher, Wright, and Kimura) have studied its properties, and we can use their results without having to know how they were derived.

Given a model of interest, we can find a diffusion approximation for it by computing the mean and variance of changes in a convenient state variable over a convenient time interval, and let those define the functions $a$ and $b$. In population genetics, allele frequency $p(t)$ is usually a good choice of state variable, but that’s not always the case. We then write down the Kolmogorov equation, and try to rescale time in the Kolmogorov equation so that $N$ disappears from the equation, at least in the limit $N \to \infty$.

**Example: haploid Wright-Fisher model without selection or mutation**  The exact model, in discrete time, is

$$
p(t + 1) \sim Binom(N, p(t))/N.
$$

(10.3)

Taking $p$ as our state variable $x$, and $\Delta t = 1$, we have

$$
E[\Delta p|p] = E[p(t + 1)] - p(t) = 0
$$
$$
Var[\Delta p|p] = Var[p(t + 1)|p] = Np(1-p)/N^2 = p(1-p)/N.
$$

(10.4)

Comparing this to equation (10.1) we see that $a(p) = 0, b(p) = p(1-p)/N$. So the Kolmogorov equation for the diffusion approximation is

$$
\frac{\partial f(p,t)}{\partial t} = \frac{1}{2N} \frac{\partial^2}{\partial p^2} \left(p(1-p)f(p,t)\right).
$$

(10.5)

We’re not done, because this equation depends on population size $N$. We can get rid of $N$ by rescaling time to $\tau = t/N$. Then

$$
\frac{\partial f(p,t)}{\partial \tau} = N\frac{\partial f(p,t)}{\partial t} = \frac{1}{2} \frac{\partial^2}{\partial p^2} \left(p(1-p)f(p,t)\right).
$$

(10.6)

A unit increase in $\tau$ corresponds to $t$ increasing by $N$, i.e. $N$ generations. So if we measure time in units of $N$ generations, we get a single diffusion approximation that is independent of population size.
Example: haploid Moran model without selection or mutation In this model time is already continuous, but it is also measured in generations. Birth-death events occur at rate $N$ per unit time, so on average there are $N$ of them per unit time, which we can regard as a generation because the number of deaths equals the total population size.

In a time interval $\Delta t \ll 1$, neglecting events whose probability is order $(\Delta t)^2$ the possible changes in allele frequency are:

$$
\Delta p = \begin{cases} 
+1/N & \text{with probability } Np(1-p)\Delta t \\
-1/N & \text{with probability } Np(1-p)\Delta t \\
0 & \text{with probability } 1 - 2Np(1-p)\Delta t 
\end{cases}
$$

(10.7)

So to leading order in $\Delta t$ we have

$$
E[\Delta p|p] = 0 \\
$$

(10.8)

So for this model we have $a(p) = 0, b(p) = 2p(1-p)$. This is exactly the same as the Wright-Fisher model, except that $b(p)$ is doubled. So following the same steps, we get the time-rescaled Kolmogorov equation

$$
\frac{\partial f(p,t)}{\partial \tau} = \frac{1}{2} \frac{\partial^2}{\partial p^2} (p(1-p)f(p,t)).
$$

(10.9)

This is exactly the same as the diffusion approximation for the Wright-Fisher model, except that the right-hand side is twice as large. So in the diffusion approximation, the Moran model is identical to the Wright-Fisher model except that it moves exactly twice as fast. This explains the observation that the time to allele fixation in the Moran model is half of what it is in the Wright-Fisher model.

Wright-Fisher when one genotype is very rare This example illustrates that $p(t)$ is not the only possible state variable. To study what happens when the $A$ allele is very rare, we can “zoom in” by defining $z(t) = \sqrt{N} p(t)$, the number of $A$ alleles divided by $\sqrt{N}$. Then

$$
E[\Delta z] = \sqrt{N} E[\Delta p] = 0 \\
Var[\Delta z] = N Var[\Delta p] = p(1-p) = z/\sqrt{N} + O(1/N)
$$

(10.10)

The Kolmogorov equation for the diffusion approximation is therefore

$$
\frac{\partial f(z,t)}{\partial t} = \frac{1}{2\sqrt{N}} \frac{\partial^2}{\partial z^2} (zf(z,t)) + O(1/N).
$$

(10.11)

Rescaling time to $\tau = t/\sqrt{N}$ we get

$$
\frac{\partial f(z,t)}{\partial \tau} = \frac{1}{2} \frac{\partial^2}{\partial z^2} (zf(z,t)) + O(1/\sqrt{N}).
$$

(10.12)

As $N \to \infty$ the $O(1/\sqrt{N})$ goes to zero, leaving a diffusion with $a = 0, b = z$ and time measured in units of $\sqrt{N}$ generations.
10.0.2 Applications of diffusion theory

Diffusion approximations are useful because they let us calculate things that interest us, such as: what is the probability that an advantageous mutation will go to fixation? If it does go to fixation, how long will it take? To illustrate this we now consider a more complicated example where exact analysis is difficult: a Wright-Fisher model with selection.

For simplicity we’ll keep it haploid and assume zero mutation. We define \( W_A = 1 + s \), \( W_a = 1 \) with \( s > 0 \) so \( A \) is the favored allele. The exact model is then

\[
p(t+1) \sim \text{Binom}(N, p^*(t))/N.
\]  

(10.13)

where \( p^*(t) \) is the frequency of the \( A \) allele in generation \( t \) after selection,

\[
p^* = \frac{pW_A}{\bar{W}} = \frac{W_A}{pW_A + (1-p)}.
\]  

(10.14)

The moments of changes in \( p \) are then

\[
E[\Delta p|p] = p^* - p = \frac{sp(1-p)}{1+sp}
\]

\[
\]  

(10.15)

This is the first example we’ve seen where the mean change is zero, and this introduces a new wrinkle. When we rescale time to eliminate \( N \), the same scaling has to work for both the advection term and the diffusion term. So both terms need to be order \( 1/N \). To do that, we have to assume that selection is weak, specifically we will assume that \( s = \psi/N \) (this is the notation that Otto and Day use, see p. 678). And knowing that only leading order terms in \( 1/N \) are going to remain after we rescale time and let \( N \to \infty \), we can expand the expressions in (10.15) in powers of \( \epsilon = 1/N \) and keep only the leading term. This gives

\[
E[\Delta p] = \psi p(1-p)/N
\]

\[
V ar[\Delta p] = V ar[p^*] = p(1-p)/N.
\]  

(10.16)

The final result is a diffusion with \( a(p) = \psi p(1-p) \), \( b(p) = p(1-p) \) and time unit equal to \( N \) generations.

We can now study the fixation process using general results about diffusion processes. These involve two functions derived from the advection and diffusion coefficients:

\[
A(x) = 2 \int \frac{a(x)}{b(x)} dx S(x) = \int e^{-A(x)} dx
\]  

(10.17)

The function \( S(x) \) is called the “scale function” in diffusion theory. The notation in (10.17) is confusing but widespread. It is confusing because the limits of integration are not specified, so the definitions are ambiguous because any function has infinitely many antiderivatives (all
differing from each other by a constant). The reason why this is OK is that the useful things that are computed with these functions wind up being the same regardless of which antiderivative you use.

The key result about fixation probabilities this. Suppose that a diffusion process \( x(t) \) on the interval \([A, B]\) has \( A \) and \( B \) as absorbing points and there are no other absorbing points, so that ultimately \( x(t) \) reaches either \( a \) or \( b \) and then stays there. Let \( u(B|x_0) \) be the probability of absorption at \( B \) given that \( x(0) = x_0 \). Then

\[
u(B|x_0) = \frac{S(x_0) - S(A)}{S(B) - S(A)} \tag{10.18}\]

For Wright-Fisher, \( a(x)/b(x) = \psi, A = 0, B = 1 \) so

\[
\begin{align*}
A(x) &= 2 \int \psi dx = 2\psi x, \\
S(x) &= \int e^{-2\psi x} dx = \frac{e^{-2\psi x}}{-2\psi}, \\
u(1|x_0) &= \frac{1 - e^{-2\psi p_0}}{1 - e^{-2\psi}} = \frac{1 - e^{-2Nsp_0}}{1 - e^{-2Ns}}
\end{align*} \tag{10.19}\]

If a mutation arises in a single individual, then \( Np_0 = 1 \), and the fixation probability becomes

\[
u = \frac{1 - e^{-2s}}{1 - e^{-2Ns}}.\]

If we suppose that \( s \) is small but \( Ns \) is large, the denominator is approximately 1, and the numerator is (by Taylor series) approximately \( 2s \). So the probability of fixation for a weakly advantageous allele in a large population, that arises as a mutation in a single individual, is approximately twice the selection coefficient.

Another interesting limit is to hold \( p_0 \) fixed and let \( s \to 0 \). By L’Hopital’s rule, the limiting value of the fixation probability as \( s \to 0 \) is \( p_0 \). This turns out to be exactly true for the Wright-Fisher model, so it’s reassuring to see that the diffusion approximation has the same property.