

Example 1: Single stochastic growth model

We begin with EXAMPLE1. This is a simple simulation of a birth process. Each individual has a birth rate (births/unit time), r . In a short time, dt , we would expect $r \times dt$ new births for each individual. Thus, in a population of size N there will be $rNdt$ births. So the ODE equation for change in population size is

$$\frac{dN}{dt} = rN$$

where r is the growth rate per individual per unit time. The solution of this equation is exponential growth i.e.

$$N(t) = N(0)e^{rt},$$

where $N(0)$ is the initial population at time $t = 0$.



In this model, how long does it take for the population to double?



How long does it take for the population to reach four times its original size?

For a stochastic simulation, the probability that an individual gives birth in a short time, dt , is given by $r dt$. The same probability applies to each of the N individuals. Hence the number of new births will be binomially distributed:

$$\text{births in time } dt \sim \text{Bin}(r dt, N)$$

Exercise

Check the `odin` code in EXAMPLE 1 to see how this is implemented. Note that as the ODE equation deals with mean values, N doesn't have to be a whole number. For the stochastic simulation, N is always a whole number of individuals.

1. Open the Berkeley Madonna model EXAMPLE1.
2. Click **<RUN>** and you will see the model solution. The exact solution lies on the same line as `N_ODE`, which is a numerical solution of the model and the stochastic solution is shown in green. Click **<RUN>** multiple times.



What do you notice?

3. On Page 2 the same graph is plotted on a semi-log scale.



What is the difference between the solutions' behaviour at early, low populations and at later times with larger populations? Explain this behaviour.



In the long term, are the stochastic runs getting closer to the exact solution or further away, on the log scale?

What about on the linear scale?

4. Try some different values of r using the slider.



How does the value of r affect your comparisons between the exact and stochastic simulations?

5. Madonna allows the user to perform multiple simulations using Batch Runs. Try this:

- a. Select *<Parameters><Batch Runs>* then *<OK>*.
- b. Set the number of runs to 10 and choose the "Keep Runs Separate" option.
- c. Press *<OK>*. Now repeat this but enter "100" in the # of Runs box.

6. Finally repeat once more but select the "Compute Mean" option. Madonna will now perform 100 simulations and calculate the mean at each time point. This is plotted instead of the individual simulations.



How does the mean compare with the exact solution?

For linear differential equation models, the exact solution is the mean of the stochastic simulations. The more stochastic simulations are run, the closer the mean gets to the exact solution. However, this conclusion breaks down when there is the possibility of extinction, as examined in Example 3, and also for non-linear models.

Example 2: Stochastic growth model

In this example we extend the code developed in Example 1 to perform multiple runs **simultaneously using arrays in Berkeley Madonna**. This also allows us look at estimates of the mean over many runs and how that depends on the number of runs.

Exercise

1. Open the Madonna model EXAMPLE2.
2. Look at the equations for the stochastic simulations. Notice that there is now a subscript [i] to denote an individual simulation and this ranges from 1 to nsim (written as e.g. $N[1..nsim]$).
3. Click <RUN> and you will see the model solutions as before. Increase the number of simulations slider, nsim, to perform 10, 100 and 1000 simulations. On Page 3 you will see the mean of these simulations.



How do they compare with the exact solution? How does the number of simulations affect agreement?

Example 3: Stochastic growth and death model

We next extend Example 2 by introducing deaths at a per-capita rate s per week. The ODE for N is made up of the difference between the mean growth rate and the mean death rate:

$$\frac{dN}{dt} = rN - sN$$

The difference $(r - s)$ is the net growth rate and the solution is either exponential growth or decline i.e., $N(t) = N(0) \exp((r - s)t)$. If births exceed deaths ($r > s$) the population grows. If deaths exceed births ($s > r$) the population shrinks.

In the stochastic simulation, we have to be more careful as we are dealing with individuals. Each individual has a probability of reproducing and of dying in some short interval, dt . However, it can't die and then give birth! These two dependent events that can happen are known as *competing hazards*. To calculate the number of births and deaths in a short time, we first calculate the number of births or deaths:

$$\text{Births or deaths in } dt, n \sim \text{Bin}(N, (r + s)dt)$$

We then decide which were births and which deaths:

$$\text{Deaths in } dt \sim \text{Bin}(s / (r + s), n)$$

Check the `odin` code to see how this is done.

Another consequence of dealing with individuals is the possibility of extinction. If the population contains a single individual and they die, no more can be generated and the population will be zero from then on. In this system, individuals are created by

individuals. Extinction can also occur in an infectious disease model, since infected individuals are only generated by other infected individuals. In an ODE model, populations are not whole numbers and extinction cannot occur. This is an important shortcoming of deterministic models.

Exercise

1. Open EXAMPLE3.



In this model, $r = 0.5$ and $s = 0.3$. What do you predict will happen to the population?

2. Set `nsim` to 10, and run the simulation a few times.



Roughly how often does the population die out?

For models which exhibit extinction behaviour, extinction is possible whenever the relevant population is small. Hence, it's often possible to define a critical community size, above which extinction is very unlikely (but not impossible).

3. Set `nsim` back to 100 and run the simulation again. (Set `STOPTIME` at about 15.)



Is there a safe threshold initial population (N_0) above which growth looks assured?

How might we estimate the probability of fade-out? Look at the Model equations. The array `fade` takes the value `TRUE` if $N > 0$ and 0 otherwise. The average value of `fade` at a given time is therefore the probability that a population has not faded out by that time.

4. Set N_0 back to 1 and re-run the model.



What is the fade-out fraction after 28 weeks?

5. Try reversing the values of r and s (so $s > r$), to give a negative net growth rate.



What is the new fade-out fraction?

In this model, the fade-out fraction tends to s/r if $r > s$ and 100% if $s > r$.



What happens when births equal deaths?

Example 4: Stochastic SIS model

The models discussed so far have looked at population size: growth, extinction, or simply "wandering about". In the next example we consider a model of infection transmission within a closed population (no births or deaths): the susceptible-infected-susceptible (SIS) model.

In this model we consider two types of event:

- Infection events, which occur in each time step with probability $\beta I dt / N$ per susceptible individual, and
- Recovery events, which occur in each time step with a probability νdt per infected individual.

The ODE representation of the model is:

$$\begin{aligned}\frac{dS}{dt} &= -\beta S \frac{I}{N} + \nu I \\ \frac{dI}{dt} &= \beta S \frac{I}{N} - \nu I\end{aligned}$$

The analytical solution to this ODE can be shown to be:

$$I(t) = I^* \frac{1}{1 + (I^*/I_0 - 1) \exp(-(\beta - \nu) t)}$$

where I_0 is the initial number of infected individuals and

$$I^* = N(1 - \nu/\beta)$$

\label{eqn:sis_eqm}

After sufficient time, the infection and recovery processes balance each other out. This occurs when the number of infectious individuals reaches its equilibrium value I^* . We can write the equilibrium value as

$$I^* = N (1 - 1/R_0)$$

since R_0 is defined as β / ν . At this point, we say that the disease is **endemic** in the population.

The stochastic simulation of this system is constructed in a similar way to the previous examples (see the code). Its behaviour, differs significantly from the deterministic simulation for some parameter values. We'll investigate these in the rest of this section.

Exercise

1. Open the model EXAMPLE4.
2. First, we look at the endemic situation where there is a continuous population of infected individuals (check in the code that the correct initial condition is in place).

Using Equation \ref{eqn:sis_eqm} How do you expect the contact rate (β), recovery rate (ν) and total population (N) to affect the equilibrium number of infected individuals?

empty table here#####

Now try varying these parameters in the model. Does the model behave as you expect?

3. Now look at the accuracy of the deterministic solution. With default parameter values, vary N from around 400 down to about 50. How does deterministic solution compare to the mean value of I from the stochastic simulation?

For large N ,

For small N ,

The differences between the simulations are due to the non-linear infection term, $\beta SI/N$. The number of susceptibles (S) and infected (I) are negatively correlated, since when an individual leaves one class, he enters the other. This correlation term is absent from the ODE model which then overestimates the force of infection, giving a higher population of infecteds.

4. Fade-out can occur when the endemic infected population is small.

Set $\beta = 0.5$, $\nu = 0.3$, and gradually reduce N from the default value of 100.

From what value do fadeouts start happening?

Can you explain what's happening to the difference between mean stochastic behaviour and the deterministic?

Do a parameter plot of the proportion of simulations that have "faded out" by the end of the simulation, against N , from 150 to 10. What do you notice? Estimate a critical community size.

5. Finally, we look at a growing epidemic starting from a single individual. In the code, comment out the initial condition for endemic behaviour and comment in the epidemic one. Set N high (300+) and n_{sim} to 1000. What proportion of fade-outs are you getting?

You should get the same fade-out rate as in example 3. Can you explain why?