Mathematical Biology - Coursework

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Part (i)

From the chemical reaction equations we get the following ODE and solution:

$$\frac{dx}{dt} = (\alpha - \beta)x \tag{1}$$
$$\implies x = x(0)e^{(\alpha-\beta)t} \tag{2}$$

Steady-state behaviour, i.e. $\frac{dx}{dt} = 0$, occurs when $\alpha = \beta$, i.e. when birth rate and death rate are equal, or when $x = 0$.

Part (ii)

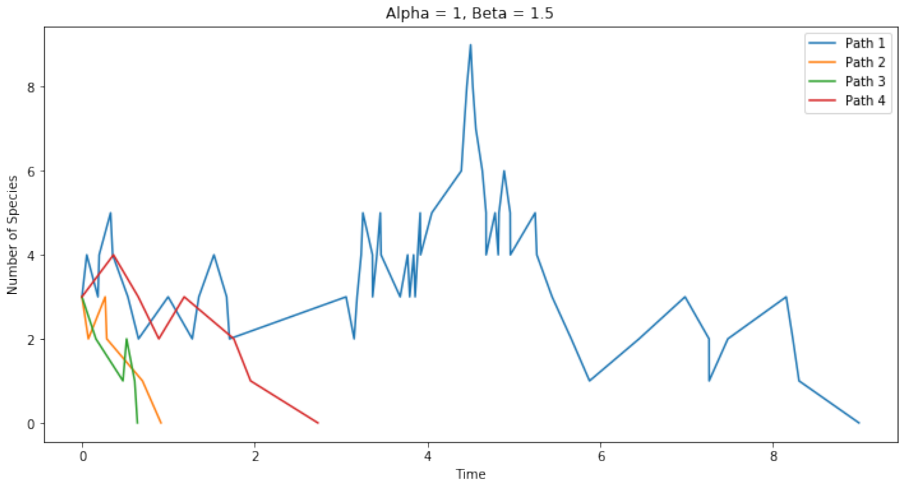
Here we have stochastic simulations of the birth-death process in part (i), using three different combinations for α and β with an initial population of 3 and a maximum time period $T_f = 25$. The plots are on the next page. See Appendix 1 for my code that I used for these plots.

Figure (a) is an example of the sub-critical case $\alpha < \beta$, which signifies that birth rates are lower than death rates. This can be seen above as all simulations lead to extinction well within the maximum time period of 25 seconds.

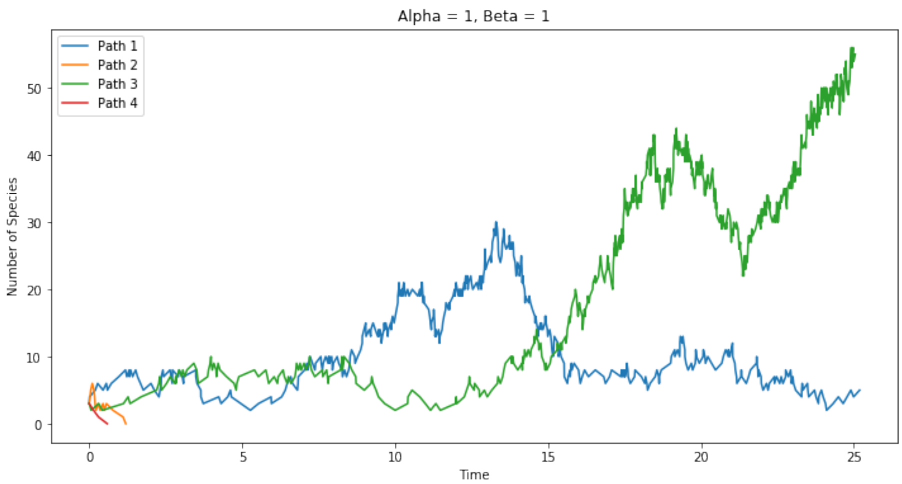
Figure (b) is an example of the critical case $\alpha = \beta$, which signifies that birth rates are equal. This can be seen above as there are both cases that lead to extinction and cases that lead to growth. Both extinction and continuous growth in any given time frame are possible in this scenario. In particular, Paths 2 and 3 lead to extinction within 2.5 seconds, while Paths 1 and 4 lead to growth in population numbers with no extinction within the time period.

Figure (c) is an example of the super-critical case $\alpha > \beta$, which signifies that birth rates are higher than death rates. This can be seen above as all simulations lead to high growth, and over longer time periods we will see this trend.

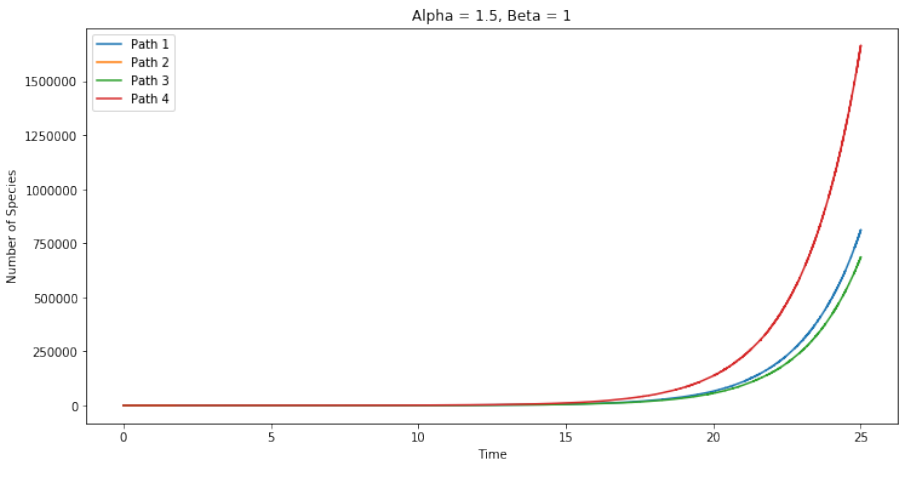
These simulations show a bifurcation, i.e. a change in the overall behaviour in the system, at $\alpha = 1$, $\beta = 1$.



(a) Example of Sub-critical Case



(b) Example of Critical Case



(c) Example of Super-critical Case

Part (iii)

The reaction rates (already used in the code of Part (ii)) are:

$$w_+(x) = \alpha x \quad (3)$$
$$w_-(x) = \beta x \quad (4)$$

So, the Chemical Master Equation for the probability $p(x,t)$ of finding a number x of individuals at time t is:

$$\frac{dp(x,t)}{dt} = w_+(x-1)p(x-1) - w_+(x)p(x) + w_-(x+1)p(x+1) - w_-(x)p(x) \quad (5)$$
$$\implies \frac{dp(x,t)}{dt} = \alpha(x-1)p(x-1) - \alpha x p(x) + \beta(x+1)p(x+1) - \beta x p(x) \quad (6)$$
$$\implies \frac{dp(x,t)}{dt} = \alpha(x-1)p(x-1) + \beta(x+1)p(x+1) - (\alpha+\beta)xp(x) \quad (7)$$

Part (iv)

From Dynkin's formula, setting $f(x) = x$ and recalling that $v_\pm = \pm 1$, we get the following:

$$\frac{dE[f(x(t))]}{dt} = \sum_{r=1}^{R} E\left[\left[f(x(t)+v_r) - f(x(t))\right] w_r(x(t))\right] \quad (8)$$
$$\implies \frac{dE[x]}{dt} = \sum_{r=1}^{R} v_r w_r\left(E[x]\right) \quad (9)$$
$$= v_+ w_+(E[x]) + v_- w_-(E[x]) \quad (10)$$
$$= \alpha E[x] - \beta E[x] \quad (11)$$
$$= (\alpha - \beta)E[x] \quad (12)$$
$$\implies E[x] = Ce^{(\alpha-\beta)t} \quad (13)$$
$$\implies E[x] = x(0)e^{(\alpha-\beta)t} \quad (14)$$

where initially there are a fixed number of individuals, $x(0)$. Similarly, setting $f(x) = x^2$ in Dynkin's formula and following the same process, we get an ODE for $E[x^2]$:

$$\frac{dE[x^2]}{dt} = 2(\alpha-\beta)E[x^2] + (\alpha+\beta)E[x] \quad (15)$$

This is an ODE of the form $\frac{dy}{dz} = yf(z) + g(z)$, which we know has a solution of the form:

$$y(z) = e^{\int f(z)dz}\left(C + \int e^{-\int f(z)dz} g(z)dz\right) \quad (16)$$

Note that this solution comes from multiplying the general form of the ODE by an integrating factor $e^{-\int f(z)dz}$ and integrating/rearranging. We apply this to (15). Set $y = E[x^2]$ and $z = t$ in (16) with $f(z) = f(t) = 2(\alpha-\beta)$ and $g(z) = g(t) = (\alpha+\beta)E[x]$ (which we can do as $x = x(t)$). After some manipulation, the solution to the ODE is as follows:

$$E[x^2] = x(0)\frac{\alpha+\beta}{\alpha-\beta}e^{(\alpha-\beta)t}\left(e^{(\alpha-\beta)t} - 1\right) + (x(0))^2 e^{2(\beta-\alpha)t} \quad (17)$$

The final step to finding the variance is simply taking the square of (14) from (17) to get:

$$Var[x] = E[x^2] - (E[x])^2 \quad (18)$$
$$= x(0)\frac{\alpha+\beta}{\alpha-\beta}e^{(\alpha-\beta)t}\left(e^{(\alpha-\beta)t} - 1\right) \quad (19)$$

Finally, for the coefficient of variation, $CV = \frac{\sqrt{Var[x]}}{E[x]}$, we get that

$$CV = \sqrt{\frac{(\alpha+\beta)\left(e^{(\alpha-\beta)t} - 1\right)}{x(0)(\alpha-\beta)e^{(\alpha-\beta)t}}} \quad (20)$$

For $\alpha > \beta$, $CV \to \sqrt{\frac{\alpha+\beta}{x(0)(\alpha-\beta)}}$ as $t \to \infty$, showing that the dispersion of the probability distribution of x approaches a fixed value. For $\alpha < \beta$, $CV \to \infty$ as $t \to \infty$, showing that dispersion increases to infinity as t increases.

Part (v)

We can use Part (iii) to show that the PDE is satisfied by $G(z,t)$ in the following way, writing $p(x,t) = p(x)$ and $G(z,t) = G$ as shorthand where appropriate

$$\begin{aligned}
\frac{dG}{dt} &= \frac{d}{dt}\sum_{x=0}^{\infty} z^x p(x,t) && (21)\\
&= \sum_{x=0}^{\infty} z^x \frac{dp(x,t)}{dt} && (22)\\
&= \sum_{x=0}^{\infty} z^x \left(\alpha(x-1)p(x-1) + \beta(x+1)p(x+1) - (\alpha+\beta)xp(x)\right) && (23)\\
&= \alpha\sum_{x=0}^{\infty} xz^{x+1}p(x) - \alpha z\sum_{x=0}^{\infty} xz^{x-1}p(x) + \beta\sum_{x=0}^{\infty} xz^{x-1}p(x) - \beta z\sum_{x=0}^{\infty} xz^{x-1}p(x) && (24)\\
&= \alpha z^2\frac{dG}{dt} - \alpha z\frac{dG}{dz} + \beta\frac{dG}{dz} + 0 - \beta z\frac{dG}{dz} && (25)\\
\implies \frac{dG(z,t)}{dt} &= \alpha z(z-1)\frac{dG(z,t)}{dt} + \beta(1-z)\frac{dG(z,t)}{dz} && (26)
\end{aligned}$$

Therefore $G(z,t)$ is a solution to the PDE. The above consisted of careful re-indexing to pull out $\frac{dG}{dz}$ from the summations.

Now we solve $G(z,t)$ using the method of characteristics. Again, I'll write G instead of $G(z,t)$ where it's clear what we mean. Rearranging (26) we get

$$\frac{dG}{dt} + (\alpha z(1-z) + \beta(z-1))\frac{dG}{dz} = 0 \tag{27}$$

From this we get three auxilary equations:

$$\begin{aligned}
\frac{dt}{ds} &= 1, && (28)\\
\frac{dz}{ds} &= \alpha z(1-z) + \beta(z-1), && (29)\\
\frac{dG}{ds} &= 0 && (30)
\end{aligned}$$

Integrating (28) and (29), then eliminating the parameterisation variable s, we get

$$\begin{aligned}
t &= \frac{\ln|\alpha z - \beta| - \ln|z-1|}{\alpha - \beta} + C_1 && (31)\\
\implies C_1 &= t(\alpha-\beta) + \ln|z-1| - \ln|\alpha z - \beta| && (32)
\end{aligned}$$

From (30) we also get $G = C_2$. Now, for any function H, we get a general solution of (26):

$$G(z,t) = H(t(\alpha-\beta) + \ln|z-1| - \ln|\alpha z - \beta|) \tag{33}$$

Now, this is equivalent to saying that $G(z,t) = L(w)$ where L can be any function of $w = e^{(\alpha-\beta)t}\frac{z-1}{\alpha z-\beta}$.

We define the function $F(z) = G(z,0)$. Now we need to choose a particular $L(w)$ such that the above equations are consistent with $F(z) = G(z,0)$. When $t = 0$ we have

$$w = \frac{z-1}{\alpha z - \beta} \implies z = \frac{\beta w - 1}{\alpha w - 1}. \tag{34}$$

We can substitute this into the condition

$$G(z,0) = L(w|_{t=0}) = F(z) \tag{35}$$

to get

$$F\left(\frac{\beta w|_{t=0} - 1}{\alpha w|_{t=0} - 1}\right) = G(z,0). \tag{36}$$

Finally, (34) tells us that $w = 0$ for all $t \geq 0$ at $z = 1$. So, it holds that $G(z,t) = L(w)$ satisfies the additional boundary condition of $G(z = 1, t) = 1$ for all $t \geq 0$ - note that this condition we use here comes from the definition of $G(z,t)$ as a probability generating function.

Now we can use our particular solution derived above to get a specific solution for $G(z,t)$:

$$
\begin{aligned}
G(z,t) &= L(w) && (37)\\
&= F\left(\frac{\beta w - 1}{\alpha w - 1}\right) && (38)\\
&= F\left(\frac{\beta e^{t(\alpha-\beta)}\frac{z-1}{\alpha z-\beta} - 1}{\alpha e^{t(\alpha-\beta)}\frac{z-1}{\alpha z-\beta} - 1}\right) && (39)\\
\implies G(z,t) &= F\left(\frac{\beta + \beta(z-1)e^{t(\alpha-\beta)} - \alpha z}{\beta + \alpha(z-1)e^{t(\alpha-\beta)} - \alpha z}\right) && (40)
\end{aligned}
$$

This concludes the proof.

Part (vi)

Starting from the formula for $G(z,t)$,

$$
\begin{aligned}
G(0,t) &= p(0,t) + \sum_{x=1}^{\infty} z^x p(x,t) && (41)\\
&= p(0,t) && (42)\\
&= \text{probability of finding 0 individuals at time } t. && (43)
\end{aligned}
$$

In order to find no individuals at time t, this means that the population has gone extinct at some time $\hat{t} < t$. In the reverse direction, if the population goes extinct at some time $\hat{t} < t$, this means that at time t there will be 0 individuals present. Therefore from considering these probability events, we conclude that

$$G(0,t) = \text{probability for the population to go extinct before time } t. \tag{44}$$

Naturally,

$$
\begin{aligned}
[1 - G(0,t)] &= 1 - (\text{probability for the population to go extinct before time } t) && (45)\\
&= (\text{probability for the population to go extinct before time } t)^c && (46)
\end{aligned}
$$

If A is the event that the population goes extinct before time t, then we can look at this slightly more formally as

$$[1 - G(0,t)] = Pr(A^c). \tag{47}$$

If the population is *not* extinct before time t, i.e. if A^c, then there exists at least one member of the population, which implies simply that the population has survived up until time t. Reversely, if the population survives up until time t, then this means there are members of the population for all $\hat{t} < t$, and so the population is not extinct before time t, i.e. A^c. Therefore we can conclude that:

$$[1 - G(0,t)] = \text{probability of population to survive up until time } t. \tag{48}$$

We derive the following equation for $G(z,t)$ using (40)

$$
\begin{aligned}
G(z,t) &= F\left(\frac{\beta + \beta(z-1)e^{t(\alpha-\beta)} - \alpha z}{\beta + \alpha(z-1)e^{t(\alpha-\beta)} - \alpha z}\right) && (49)\\
&= G\left(\frac{\beta + \beta(z-1)e^{t(\alpha-\beta)} - \alpha z}{\beta + \alpha(z-1)e^{t(\alpha-\beta)} - \alpha z}, 0\right) && (50)\\
&= \sum_{x=0}^{\infty}\left(\frac{\beta + \beta(z-1)e^{t(\alpha-\beta)} - \alpha z}{\beta + \alpha(z-1)e^{t(\alpha-\beta)} - \alpha z}\right)^x p(x,0) && (51)
\end{aligned}
$$

Setting $z = 0$ we get the following expression

$$G(0,t) = \sum_{x=0}^{\infty} \left(\frac{\beta - \beta e^{t(\alpha-\beta)}}{\beta - \alpha e^{t(\alpha-\beta)}} \right)^x p(x,0) \tag{52}$$

$$= p(0,0) + \sum_{x=1}^{\infty} \left(\frac{\beta - \beta e^{t(\alpha-\beta)}}{\beta - \alpha e^{t(\alpha-\beta)}} \right)^x p(x,0) \tag{53}$$

Now we consider the asymptotic behaviour. First note that in the critical case $\alpha = \beta$, due to the fact that $G(z,t)$ is a probability generating function, we get

$$G(0,t) = \sum_{x=0}^{\infty} p(x,0) = 1 \tag{54}$$

$$\implies \lim_{t\to\infty} G(0,t) = 1 \tag{55}$$

In the case $\alpha < \beta$ we get the same outcome:

$$\lim_{t\to\infty} G(0,t) = \sum_{x=0}^{\infty} \left(\frac{\beta - \beta \cdot 0}{\beta - \alpha \cdot 0} \right)^x p(x,0) \tag{56}$$

$$= \sum_{x=0}^{\infty} p(x,0) \tag{57}$$

$$= 1 \tag{58}$$

Finally for $\alpha > \beta$ we get more complicated behaviour:

$$\lim_{t\to\infty} G(0,t) = \sum_{x=0}^{\infty} \left(\frac{\beta}{\alpha} \right)^x p(x,0) \tag{59}$$

As $\sum_{x=0}^{\infty} p(x,0) = 1$, this is a convergent sum, and we can deduce $\lim_{t\to\infty} G(0,t) > 0$, with the exact value depending on the ratio $\frac{\beta}{\alpha}$.

For the deterministic ODE with a fixed initial population, we know that the probability of extinction as $t \to \infty$ goes to 1 if $\alpha < \beta$, and 0 if $\alpha > \beta$. If $\alpha = \beta$, we have the steady-state solution - so the probability of extinction is 0 if $x(0) > 0$, and, trivially, 1 if $x(0) = 0$.

The cases $\alpha = \beta$ and $\alpha < \beta$ are the same as for the stochastic model as shown above, but we note a difference between the two for $\alpha > \beta$ - the stochastic model shows a non-zero probability of extinction as $t \to \infty$ but the determinstic model shows a 0 probability.

Part (vii)

The distribution of the extinction time is related to the time-derivative of $G(0,t)$ by

$$f(t) = \frac{1}{Z} \frac{dG(0,t)}{dt} \tag{60}$$

$$= \frac{1}{Z} \sum_{x=0}^{\infty} \frac{d}{dt} \left(\frac{\beta - \beta e^{t(\alpha-\beta)}}{\beta - \alpha e^{t(\alpha-\beta)}} \right)^x p(x,0) \tag{61}$$

$$= \frac{1}{Z} \sum_{x=0}^{\infty} \left(\frac{\beta x (\alpha-\beta)^2 e^{t(\alpha-\beta)} \left(\frac{\beta\left(e^{t(\alpha-\beta)} - 1\right)}{\alpha e^{t(\alpha-\beta)} - \beta} \right)^{x-1}}{\left(\beta - \alpha e^{t(\alpha-\beta)}\right)^2} \right) p(x,0) \tag{62}$$

We start with a single individual. So if $x(0) = 1$, then we know that $p(1,0) = 1$, and $p(x,0) = 0 \ \forall x \neq 1$. So the above can be simplified as

$$f(t) = \frac{1}{Z} \left(\frac{\beta(\alpha-\beta)^2 e^{t(\alpha-\beta)}}{\left(\beta - \alpha e^{t(\alpha-\beta)}\right)^2} \right) \tag{63}$$

As $f(t)$ is a probability distribution, we can find Z by rearranging

$$1 = \int_{t=0}^{\infty} f(t)\, dt \tag{64}$$

to get

$$\begin{aligned}
Z &= \int_{t=0}^{\infty} \frac{\beta(\alpha-\beta)^2 e^{t(\alpha-\beta)}}{\left(\beta - \alpha e^{t(\alpha-\beta)}\right)^2}\, dt & (65)\\
&= \beta(\alpha-\beta)^2 \int_{t=0}^{\infty} \frac{e^{t(\alpha-\beta)}}{\left(\beta - \alpha e^{t(\alpha-\beta)}\right)^2}\, dt & (66)\\
&= \beta(\alpha-\beta)^2 \int_{y=1}^{\infty} \frac{y}{(\beta-\alpha y)^2} \frac{1}{(\alpha-\beta)y}\, dy & (67)\\
&= \beta(\alpha-\beta) \int_{y=1}^{\infty} \frac{1}{(\beta-\alpha y)^2}\, dy & (68)\\
&= \beta(\alpha-\beta) \left[\frac{1}{\alpha(\beta-\alpha y)}\right]_{y=1}^{\infty} & (69)\\
&= \frac{\beta}{\alpha}(\alpha-\beta) \left[\frac{1}{\beta-\alpha y}\right]_{y=1}^{\infty} & (70)\\
&= -\frac{\beta}{\alpha}(\alpha-\beta)\left(0 - \frac{1}{\beta-\alpha}\right) & (71)\\
&= \frac{\beta}{\alpha} & (72)
\end{aligned}$$

where at (67) we used the change of variable $y = e^{t(\alpha-\beta)}$. So we get that the normalising constant Z is simply the death-birth rate ratio.

We can now write (63) as

$$f(t) = \frac{\alpha(\alpha-\beta)^2 e^{t(\alpha-\beta)}}{\left(\beta - \alpha e^{t(\alpha-\beta)}\right)^2} \tag{73}$$

Now we can calculate the mean extinction time from this probability distribution.

$$\begin{aligned}
E_{f(t)}[t] &= \int_{t=0}^{\infty} t f(t)\, dt & (74)\\
&= \alpha(\alpha-\beta)^2 \int_{t=0}^{\infty} \frac{t e^{t(\alpha-\beta)}}{\left(\beta - \alpha e^{t(\alpha-\beta)}\right)^2}\, dt & (75)\\
&= \alpha(\alpha-\beta)^2 \left[\frac{\frac{t(\beta-\alpha)}{\alpha e^{t(\alpha-\beta)}-\beta} + \frac{\ln\left(\alpha e^{t(\alpha-\beta)}-\beta\right)}{\beta} + \left(1-\frac{\alpha}{\beta}\right)t}{\alpha(\alpha-\beta)^2}\right]_{t=0}^{\infty} & (76)\\
&= \left[\frac{t(\beta-\alpha)}{\alpha e^{t(\alpha-\beta)}-\beta} + \frac{\ln\left(\alpha e^{t(\alpha-\beta)}-\beta\right)}{\beta} + \left(1-\frac{\alpha}{\beta}\right)t\right]_{t=0}^{\infty} & (77)\\
&= \lim_{t\to\infty}\left(\frac{\ln\left(\alpha e^{t(\alpha-\beta)}-\beta\right)}{\beta} + \left(1-\frac{\alpha}{\beta}\right)t\right) - \frac{\ln(\alpha-\beta)}{\beta} & (78)\\
&= \lim_{t\to\infty}\left(\frac{\ln\left(\frac{\alpha e^{t(\alpha-\beta)}-\beta}{\alpha-\beta}\right)}{\beta} + \left(1-\frac{\alpha}{\beta}\right)t\right) & (79)
\end{aligned}$$

In the critical case $\alpha = \beta$, the mean extinction time is infinite:

$$\begin{aligned}
E_{f(t)}[t] &= \lim_{t\to\infty}\left(\frac{\ln\left(\frac{\alpha e^{t(\alpha-\beta)}-\beta}{\alpha-\beta}\right)}{\beta}\right) & (80)\\
&= \frac{1}{\beta}\lim_{w\to\infty}\ln(w) \to \infty & (81)
\end{aligned}$$

Appendix 1

Below is the code used for part (ii).

```
# Import packages
import math
import random
import matplotlib.pyplot as plt
```

```
# Gillespie algorithm for the birth-death process

def gillespie(
    # Default parameters
    alpha = 1,
    beta = 1.5,
    T = 25.0,
    t_initial = 0.0,
    x_initial = 3
    ):

    # Initialize results list
    time = [t_initial]
    num_x = [x_initial]

    # Initialise variables
    t = t_initial
    x = x_initial

    while t < T:
        # Check for extinction
        if x == 0:
            break

        # Generate two random uniform distributed numbers in (0, 1)
        r1 = random.uniform(0, 1)
        r2 = random.uniform(0, 1)

        # Calculate propensity functions
        w1 = alpha * x
        w2 = beta * x

        # Sum propensity functions
        w_sum = w1 + w2

        if w_sum == 0:
            break

        # Compute next reaction time
        dt = -math.log(r1) / w_sum
        t = t + dt

        if (0 <= r2 and r2 < w1 / w_sum):
            x = x + 1
        else:
            x = x - 1

        time.append(t)
        num_x.append(x)

    return time, num_x
```

```python
def plot_gillespie(
    alpha = 1,
    beta = 1,
    T = 25.0,
    t_initial = 0.0,
    x_initial = 3,
    repeats = 1,
    title = ''
    ):

    fig = plt.gcf()
    fig.set_size_inches(12, 6)
    for i in range(repeats):
        label = 'Path ' + str(i + 1)
        time, number = gillespie(alpha, beta, T, t_initial, x_initial)
        plt.plot(time, number, label = label)

    plt.legend()
    plt.xlabel('Time')
    plt.ylabel('Number of Species')
    plt.title(title)
    fig.show()
```

```python
# Plot example of sub-critical case
plot_gillespie(alpha = 1, beta = 1.5, repeats = 4, title = 'Alpha = 1, Beta = 1.5')

# Plot example of critical case
plot_gillespie(alpha = 1, beta = 1, repeats = 4, title = 'Alpha = 1, Beta = 1')

# Plot example of super-critical case
plot_gillespie(alpha = 1.5, beta = 1, repeats = 4, title = 'Alpha = 1.5, Beta = 1')
```