14. Mutation: How do population types change?

We have seen that different types in a population grow and decline in relation to their replication rates x_i, but there is an additional factor in evolution: mutation. Many mutations occur when the genomic material of a cell is being copied during replication, but *mutagens* can also induce changes in the genetic material of a single cell. We shall study here a simple model of mutation that can be applied in both situations.

? What is the difference between *genomic* and *genetic* material?

2-type mutation

Consider first two types 1 and 2 whose fitness is equal: $r_1 = r_2 = 1$. Imagine mutation generates type 1 from type 2 with probability q_{12}, and type 2 from type 1 with probability q_{21}. Now, every type must generate either itself or some other type, so $q_{22} = 1 - q_{12}$ must be the probability that type 2 is generated from type 2, and $q_{11} = 1 - q_{21}$ is the probability that type 1 is generated from type 1. In this case,

$$\left.\begin{array}{l} \dot{x}_1 = (1 - q_{21})x_1 + q_{12}x_2 - Rx_1 \\ \dot{x}_2 = q_{21}x_1 + (1 - q_{12})x_2 - Rx_1 \end{array}\right\}, \text{ or}$$

$$\dot{x} \equiv \begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \end{pmatrix} = \left(\begin{pmatrix} q_{11} & q_{12} \\ q_{21} & q_{22} \end{pmatrix} - R \right) \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = (\boldsymbol{Q} - R\boldsymbol{I}) \cdot \boldsymbol{x},$$

where $\boldsymbol{Q} = (q_{ij})$ is a *stochastic matrix*: it satisfies the conditions $q_{ij} \in [0,1]$ and $\sum_{i=1}^{2} q_{ij} = 1$ (that is, components are probability values, and the sum of all elements in each column is 1).

? Calculate the average fitness $R = x_1 r_1 + x_2 r_2$ of the population, given $x_2 = 1 - x_1$.
? Use these values in the above equations to show that $\dot{x}_1 = q_{12} - x_1(q_{21} + q_{12})$.
? Show that this dynamical equation has a fixed point $x^* = \dfrac{q_{12}}{q_{21} + q_{12}}$.

You have shown here that in the long term, mutation leads to the *stabilisation* of two populations. Their relative frequencies depend on their respective mutation rates: if $q_{21} > q_{12}$, we will end up with a larger type 2 population than type 1; if $q_{21} < q_{12}$, the type 1 population will end up bigger. In both cases, the crucial point is that type 1 and type 2 coexist; it is *not* necessary for one type to drive the other to extinction!

? Often, the mutation rate in one direction is much larger than in the other direction. Imagine that in our 2-type model, $q_{21} \gg q_{12}$: type 1 individuals mutate much more frequently to type 2 individuals. We can approximate this situation by setting $q_{12} = 0$. Substitute this value into the dynamical equations for $\dot{x}_1$ and $\dot{x}_2$, and solve these equations to find the *exact* behaviour of x_1 and x_2 over time.

n-type mutation

We can easily extend this 2-type model of mutation into an n-type model. Again, we define the mutation matrix $\boldsymbol{Q} = (q_{ij})$ as an $(n \times n)$ *stochastic matrix* of probability elements satisfying the conditions $q_{ij} \in [0,1]$ and $\sum_{i=1}^{n} q_{ij} = 1$. Again, since each type generates *some* other type, the sum of all elements in each column is 1. We can write the mutation dynamics:

$$\dot{x} \equiv \begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \end{pmatrix} = \sum_{j=1}^{n} q_{ij}x_j - Rx_i = \boldsymbol{Q} \cdot \boldsymbol{x} - R\boldsymbol{x} = (\boldsymbol{Q} - R\boldsymbol{I}) \cdot \boldsymbol{x}$$

? Again, in n-type mutation dynamics, $R = 1$ (*why?*).

?   The fixed points of mutation dynamics are defined by $\dot{x}(x^*) = 0$. Look back at the previous dynamical equation, and show that this implies that x^* is an eigenvector of Q with eigenvalue R.

The quasi-species equation

Finally, we can combine mutation with constant selection to obtain the *quasi-species equation*. Manfred Eigen and Peter Schuster used the term *quasi-species* to describe what we have here called a *type*: the quasi-species equation describes how types evolve if they possess linear fitness values *and* can mutate into each other:

$$\dot{x} = Q \cdot (x\,r) - (x \cdot r)\,x; \quad \dot{x}_i = \sum_{j=1}^{n} q_{ij}(x_j\,r_j) - R(x)x_i; \quad R(x) = \sum_{j=1}^{n} x_j\,r_j$$

Exercises

1. In julia, create a pure mutation matrix of your choice that mutates three types cyclically into each other: $1 \rightarrow 2 \rightarrow 3 \rightarrow 1$. Use the julia documentation to investigate the function eigen() in the package LinearAlgebra. Use this function to calculate the fixed point of your chosen mutation matrix, and then verify the result of this calculation by visualising the mutation dynamics graphically on S_3.

2. Now use the quasi-species equation to include constant selection into your julia model. Experiment to see what effect different fitness values have on the behaviour of your cyclically mutating S_3 model from the previous exercise.

Summary

- Mutation occurs when replication is not perfectly accurate.
- Pure mutation dynamics are defined by: $\dot{x} = (Q - RI) \cdot x$, where the mutation matrix $Q = (q_{ij})$ satisfies the conditions $q_{ij} \in [0,1]$ and $\sum_{i=1}^{n} q_{ij} = 1$, and $R = \sum_{i=1}^{n} x_i r_i = \sum_{i=1}^{n} x_i = 1$.
- Mutation leads to *stabilisation* – coexistence of alternative types.
- Asymmetric mutation (for example $q_{21} \gg q_{12}$) can lead to selection, even if all individuals have the same replication rate.
- The *quasi-species equation* describes situations where types evolve through mutation combined with constant selection: $\dot{x}_i = \sum_{j=1}^{n} q_{ij}(x_j\,r_j) - Rx_i$, where $R(x) = \sum_{j=1}^{n} x_j\,r_j$.