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,

$$\begin{aligned}\dot{x}_1 &= (1 - q_{21})x_1 + q_{12}x_2 - Rx_1 \\ \dot{x}_2 &= q_{21}x_1 + (1 - q_{12})x_2 - Rx_1\end{aligned}\Bigg\}, \text{ or}$$

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

where $Q = (q_{ij})$ 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 $x^* = \frac{q_{12}}{q_{21}+q_{12}}$.

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 $Q = (q_{ij})$ 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:

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

? Again, in n-type mutation dynamics, $R = 1$ (*why?*).
? The fixed points of mutation dynamics are defined by $\dot{x}(x^*) = 0$. What does this tell us about the mathematical relationship between Q, x^* and 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:

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

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 an appropriate Matlab function to calculate the fixed point of this 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: $\dot{\boldsymbol{x}} = (\boldsymbol{Q} - R\boldsymbol{I}) \cdot \boldsymbol{x}$, where the mutation matrix $\boldsymbol{Q} = (q_{ij})$ 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 $R(\boldsymbol{x}) = \sum_{j=1}^{n} x_j\,r_j$.