

1 Generalised Transition Rate Equation

$$T^{j \rightarrow i} = \left(u_i r_{i-1} \frac{n_{i-1}}{N} + (1 - u_{i+1}) r_i \frac{n_i}{N} \right) \frac{n_j}{\bar{r}} \quad (1)$$

When setting up the system, $u_0 = 0$ and $u_{N+1} = 0$ must be defined in order to stop cells mutating past the maximum number of mutations.

$\frac{n_j}{\bar{r}}$ is selected to die. $u_i r_{i-1} \frac{n_{i-1}}{N}$ is selected to mutate and gain a mutation. I.e. a cell with one less mutation is birthed with a mutation. $(1 - u_{i+1}) r_i \frac{n_i}{N}$ A n_i cell is born and doesn't obtain a mutation.

1.1 Diffusion with Drift Derivation

Taking the large N limit.

$$\dot{x}_i = \frac{1}{N} \left[\sum_j T^{j \rightarrow i} - T^{i \rightarrow j} \right]$$

Using the generalised transition rate equation:

$$\begin{aligned} \bar{r} \dot{x}_i &= \sum_j u_i r_{i-1} x_{i-1} x_j - u_j r_{j-1} x_{j-1} x_i + x_j x_i [(1 - u_{i+1}) r_i - (1 - u_{j+1}) r_j] \\ \alpha &= u_i r_{i-1} \\ \beta &= u_j r_{j-1} \\ \gamma &= (1 - u_{i+1}) r_i - (1 - u_{j+1}) r_j \\ \bar{r} \dot{x}_i &= \sum_j \alpha x_j x_{i-1} - \beta x_{j-1} x_i + \gamma x_j x_i \end{aligned}$$

In a flat fitness and mutation landscape, away from the absorbing state $u_i, r_i = 1 \forall i$. From this $\alpha = 1, \beta = 1, \gamma = 0, \bar{r} = 1$.

$$\dot{\rho}_i = \sum_j \rho_j \rho_{i-1} - \rho_{j-1} \rho_i$$

We now want to expand this sum in order to simplify;

$$\begin{aligned} \dot{\rho}_i &= \rho_0 \rho_{i-1} + (\rho_1 \rho_{i-1} - \rho_0 \rho_i) + (\rho_2 \rho_{i-1} - \rho_1 \rho_i) + \dots + (\rho_{N-1} \rho_{i-1} - \rho_{N-2} \rho_i) + (\rho_N \rho_{i-1} - \rho_{N-1} \rho_i) \\ &= \rho_0 (\rho_{i-1} - \rho_i) + \rho_1 (\rho_{i-1} - \rho_i) + \dots + \rho_N \rho_{i-1} \\ &= \sum_k^{N-1} (\rho_{i-1} - \rho_i) \rho_k + \rho_N \rho_{i-1} \\ &= (\rho_{i-1} - \rho_i) (1 - \rho_N) + \rho_N \rho_{i-1} \\ &= \rho_{i-1} + (\rho_N - 1) \rho_i \\ \dot{\rho}_i &= \rho_{i-1} + (\rho_N - 1) \rho_i \end{aligned}$$

In the large mutation limit $\rho_N \rightarrow 0$.

$$\dot{\rho}_i = \rho_{i-1} - \rho_i \quad (2)$$

We might be breaking our previous assumptions, but for $i = 0$:

$$\begin{aligned} \dot{\rho}_0 &= 0 - \rho_0 \\ \rho_0 &= Ae^{-t} \\ A &= 1 \\ \rho_0 &= e^{-t} \end{aligned}$$

This gives us the first step in solving generally.

$$\begin{aligned} \dot{\rho}_1 &= \rho_0 - \rho_1 \\ &= e^{-t} - \rho_1 \\ \rho_1 &= te^{-t} \\ \dot{\rho}_2 &= \rho_1 - \rho_2 \\ \rho_2 &= \frac{1}{2}e^{-t}t^2 \end{aligned}$$

From this we can see that the general solution for ρ_i ;

$$\rho_i = \frac{t^i}{i!}e^{-t} \quad (3)$$

2 Tobias' Model

Go from state n to $n + 1$ with rate $a + b$. Go from state n to $n - 1$ with rate a .

$$\begin{aligned} \dot{p}_i &= -ap_i - (a + b)p_i + (a + b)p_{i-1} + ap_{i+1} \\ &= -(2a + b)p_i + (a + b)p_{i-1} + ap_{i+1} \end{aligned}$$

Lets start with a generating function:

$$\begin{aligned}
\Phi &= \sum_{n=0}^{\infty} z^n p_n(t) \\
\dot{\Phi} &= \sum_{n=0}^{\infty} z^n \dot{p}_n \\
&= \sum_{n=0}^{\infty} z^n ((a+b)p_{n-1} - (2a+b)p_n + ap_{n+1}) \\
&= -(2a+b)\Phi + a \sum_{n=0}^{\infty} z^n p_{n+1} + (a+b) \sum_{n=0}^{\infty} z^n p_{n-1} \\
&= -(2a+b)\Phi + \frac{a}{z}\Phi + (a+b)z\Phi
\end{aligned}$$

Need to get a differential out of this equation though?

3 Our Cancer Model Version 2

$$\begin{aligned}
\dot{x}_i &= \left(u_i r_{i-1} \frac{n_{i-1}}{N} + (1 - u_{i+1}) r_i \frac{n_i}{N} \right) \frac{n_j}{\bar{r}} - \left(u_j r_{j-1} \frac{n_{j-1}}{N} + (1 - u_{j+1}) r_j \frac{n_j}{N} \right) \frac{n_i}{\bar{r}} \\
\bar{r} \dot{x}_i &= (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) x_j - (u_j r_{j-1} x_{j-1} + (1 - u_{j+1}) r_j x_j) x_i \\
\bar{r} \dot{x}_0 &= ((1 - u_1) r_0 x_0) x_j - (u_j r_{j-1} x_{j-1} + (1 - u_{j+1}) r_j x_j) x_0
\end{aligned}$$

4 Diffusion equation attempt

$$\bar{r} \dot{x}_i = \sum_{j \neq i} (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) x_j - (u_j r_{j-1} x_{j-1} + (1 - u_{j+1}) r_j x_j) x_i$$

Following this explicitly can reproduce the equations in the Ashcroft paper.
Now attempt to simplify it:

$$\begin{aligned}
\bar{r}\dot{x}_i &= \sum_{j \neq i} (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) x_j - (u_j r_{j-1} x_{j-1} + (1 - u_{j+1}) r_j x_j) x_i \\
&= (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) \sum_{j \neq i} x_j - x_i \sum_{j \neq i} (u_j r_{j-1} x_{j-1} + (1 - u_{j+1}) r_j x_j) \\
&= (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) (1 - x_i) - x_i \left(\sum_{j \neq i} u_j r_{j-1} x_{j-1} + \sum_{j \neq i} (1 - u_{j+1}) r_j x_j \right) \\
&= (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) (1 - x_i) - x_i \left(\sum_{j \neq i} u_j r_{j-1} x_{j-1} + \sum_{j \neq i} r_j x_j - \sum_{j \neq i} r_j x_j u_{j+1} \right) \\
&= (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) (1 - x_i) - x_i \left(\sum_{j \neq i} u_j r_{j-1} x_{j-1} + (\bar{r} - r_i x_i) - \sum_{j \neq i} r_j x_j u_{j+1} \right)
\end{aligned}$$

$$\begin{aligned}
\bar{u} &= \sum_{i=1}^N u_i r_{i-1} x_{i-1} \\
\mathbf{u} &= (0, u_1, \dots, u_{N-1}, 0) \\
\sum_{j \neq i} u_j r_{j-1} x_{j-1} - \sum_{j \neq i} u_{j+1} r_j x_j &= (\bar{u} - u_i r_{i-1} x_{i-1}) - \sum_{m \neq i+1} u_m r_{j-1} x_{j-1} \\
&= (\bar{u} - u_i r_{i-1} x_{i-1}) - (\bar{u} - u_{i+1} r_i x_i) \\
&= u_{i+1} r_i x_i - u_i r_{i-1} x_{i-1}
\end{aligned}$$

$$\begin{aligned}
\bar{r}\dot{x}_i &= (u_i r_{i-1} x_{i-1} + (1 - u_{i+1}) r_i x_i) (1 - x_i) - x_i (u_{i+1} r_i x_i - u_i r_{i-1} x_{i-1} + (\bar{r} - r_i x_i)) \\
&= (u_i r_{i-1} x_{i-1} (1 - x_i) + (1 - u_{i+1}) (1 - x_i) r_i x_i) - (u_{i+1} r_i x_i^2 - u_i r_{i-1} x_{i-1} x_i + x_i (\bar{r} - r_i x_i)) \\
&= (u_i r_{i-1} x_{i-1} (1 - x_i) + (1 - u_{i+1}) (1 - x_i) r_i x_i) - u_{i+1} r_i x_i^2 + u_i r_{i-1} x_{i-1} x_i - x_i (\bar{r} - r_i x_i) \\
&= (u_i r_{i-1} x_{i-1} (1 - x_i) + (1 - u_{i+1}) (1 - x_i) r_i x_i) - u_{i+1} r_i x_i^2 + u_i r_{i-1} x_{i-1} x_i - x_i \bar{r} + r_i x_i^2 \\
&= (u_i r_{i-1} x_{i-1} - u_i r_{i-1} x_{i-1} x_i + (1 - u_{i+1}) (1 - x_i) r_i x_i) - u_{i+1} r_i x_i^2 + u_i r_{i-1} x_{i-1} x_i - x_i \bar{r} + r_i x_i^2 \\
&= (u_i r_{i-1} x_{i-1} - u_i r_{i-1} x_{i-1} x_i + (1 - u_{i+1} - x_i + u_{i+1} x_i) r_i x_i) - u_{i+1} r_i x_i^2 + u_i r_{i-1} x_{i-1} x_i - x_i \bar{r} + r_i x_i^2 \\
&= u_i r_{i-1} x_{i-1} - u_i r_{i-1} x_{i-1} x_i + r_i x_i - r_i x_i u_{i+1} - r_i x_i^2 + r_i x_i^2 u_{i+1} - u_{i+1} r_i x_i^2 + u_i r_{i-1} x_{i-1} x_i - x_i \bar{r} + r_i x_i^2 \\
&= u_i r_{i-1} x_{i-1} - u_i r_{i-1} x_{i-1} x_i + r_i x_i - r_i x_i u_{i+1} + u_i r_{i-1} x_{i-1} x_i - x_i \bar{r} + r_i x_i^2 \\
&= u_i r_{i-1} x_{i-1} + r_i x_i - r_i x_i u_{i+1} - x_i \bar{r} \\
&= u_i r_{i-1} x_{i-1} + x_i (r_i (1 - u_{i+1}) - \bar{r})
\end{aligned}$$

$$\bar{r}\dot{x}_i = u_i r_{i-1} x_{i-1} + x_i (r_i (1 - u_{i+1}) - \bar{r}) \quad (4)$$

This reproduces the Ashcroft results as expected. So we can proceed.

$$\bar{r}\dot{x}_0 = x_0 (r_0 (1 - u_1) - \bar{r}) \quad (5)$$

$$\bar{r}\dot{x}_i = u_i r_{i-1} x_{i-1} + x_i (r_i (1 - u_{i+1}) - \bar{r}) \quad (6)$$

$$\bar{r}\dot{x}_N = u_i r_{N-1} x_{N-1} + x_N (r_N - \bar{r}) \quad (7)$$

Assume a constant r and u landscape and just sticking with the middle equation:

$$r\dot{\rho}_i = ur\rho_{i-1} + \rho_i(r(1 - u) - r)$$

$$\dot{\rho}_i = u\rho_{i-1} + \rho_i(1 - u) - \rho_i$$

$$= u(\rho_{i-1} - \rho_i)$$