1 Generalised Transition Rate Equation

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

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.

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

Using the generalised transition rate equation:

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

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;

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

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

$$\dot{\rho}_i = \rho_{i-1} - \rho_i \tag{2}$$

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;

$$\rho_i = \frac{t^i}{i!}e^{-t} \tag{3}$$

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:

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

Need to get a differential out of this equation though?

3 Our Cancer Model Version 2

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

$$
\bar{r}\dot{x}_0 = \left((1-u_1)\, r_0 x_0\right) x_j - \left(u_j r_{j-1} x_{j-1} + (1-u_{j+1})\, r_j x_j\right) x_0
$$

4 Diffusion equation attempt

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

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

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

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

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

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

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

$$
\begin{aligned}
\bar{r}\dot{x}_0 &= x_0\left(r_0\left(1-u_1\right)-\bar{r}\right) && (5)\\
\bar{r}\dot{x}_i &= u_i r_{i-1}x_{i-1} + x_i\left(r_i\left(1-u_{i+1}\right)-\bar{r}\right) && (6)\\
\bar{r}\dot{x}_N &= u_i r_{N-1}x_{N-1} + x_N\left(r_N-\bar{r}\right) && (7)
\end{aligned}
$$

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

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

We then make the change of variables $\rho_i \to \rho(t,x)$.

$$
\begin{aligned}
\dot{\rho}(t,x) &= u\left(\rho(t,x-\Delta x) - \rho(t,x)\right)\\
&= u\left(\rho(t,x) - \Delta x\frac{\partial\rho}{\partial x} + \frac{\Delta x^2}{2}\frac{\partial^2\rho}{\partial x^2} - \rho(t,x)\right)\\
&= \frac{u\Delta x^2}{2}\frac{\partial^2\rho}{\partial x^2} - u\Delta x\frac{\partial\rho}{\partial x}
\end{aligned}
$$

This resembles the Fokker Plank Equation.