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:

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

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

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

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

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

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

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.

5 Solution of Master Equation with Poissonian

$$\begin{aligned}
\dot{\rho}_0 &= -u\rho_0\\
\rho_0 &= Ae^{-ut}\\
A &= 1
\end{aligned}$$

Then solve for ρ_1

$$\begin{aligned}
\dot{\rho}_1 &= u(\rho_0-\rho_1)\\
&= u\left(e^{-ut}-\rho_1\right)\\
\dot{\rho}_1 + u\rho_1 &= ue^{-ut}\\
\frac{d}{dt}\left(e^{ut}\rho\right) &= u\\
\rho_1 &= (ut)e^{-ut}
\end{aligned}$$

Doing a proof by induction and we arrive at the standard Poissonian;

$$\rho_n = \frac{(ut)^n}{n!}e^{-ut}$$

Solution with Fourier

$$\begin{aligned}
\dot{\rho} &= \frac{\tilde{u}\Delta x}{2}\frac{\partial^2}{\partial x^2}\rho - \tilde{u}\frac{\partial}{\partial x}\rho \\
\tilde{u} &= u\Delta x
\end{aligned}$$

$$\begin{aligned}
\tilde{\rho} &= \int_{-\infty}^{\infty} \rho e^{-ikx} dx \\
\tilde{\rho}_x &= \int_{-\infty}^{\infty} \left(\frac{\partial}{\partial x}\rho\right) e^{-ikx} dx \\
\tilde{\rho}_{xx} &= \int_{-\infty}^{\infty} \left(\frac{\partial^2}{\partial x^2}\rho\right) e^{-ikx} dx
\end{aligned}$$

Proof of the differentials Fourier transformed;

$$\begin{aligned}
\tilde{\rho}_x &= \int_{-\infty}^{\infty} \left(\frac{\partial}{\partial x}\rho\right) e^{-ikx} dx \\
&= \left[\rho e^{-ikx}\right]_{-\infty}^{\infty} + ik\tilde{\rho}
\end{aligned}$$

$$\begin{aligned}
\tilde{\rho}_{xx} &= \int_{-\infty}^{\infty} \left(\frac{\partial^2}{\partial x^2}\rho\right) e^{-ikx} dx \\
&= \left[\rho_x e^{-ikx}\right]_{-\infty}^{\infty} + ik\int e^{-ikx}\rho_x dx \\
&= \left[\rho_x e^{-ikx}\right]_{-\infty}^{\infty} + ik\left(\left[\rho e^{-ikx}\right]_{-\infty}^{\infty} + ik\tilde{\rho}\right) \\
&= \left[\rho_x e^{-ikx}\right]_{-\infty}^{\infty} + ik\left[\rho e^{-ikx}\right]_{-\infty}^{\infty} - k^2\tilde{\rho}
\end{aligned}$$

$$\begin{aligned}
\dot{\tilde{\rho}} &= -\frac{\tilde{u}\Delta x k^2}{2}\tilde{\rho} - ik\tilde{u}\tilde{\rho} \\
\tilde{\rho} &= A\exp\left(-\tilde{u}k\left(\frac{k\Delta x}{2} + i\right)t\right) \\
\tilde{\rho}(k,0) &= A \\
\tilde{\rho}(k,0) &= \int_{-\infty}^{\infty} \rho(x,0)e^{-ikx} dx \\
&= \int_{-\infty}^{\infty} \delta(x-x_0)e^{-ikx} dx \\
&= e^{-ikx_0}
\end{aligned}$$

$$\tilde{\rho} = e^{-ikx_0}\exp\left(-\tilde{u}k\left(\frac{k\Delta x}{2} + i\right)t\right) \tag{8}$$

Need to do the inverse Fourier transform to get back to concentration space.

$$\begin{aligned}\rho &= \int_{-\infty}^{\infty} \exp\left(-\tilde{u}k\left(\frac{k\Delta x}{2}+i\right)t - ikx_0\right)e^{ikx}dk \\ &= \sqrt{\frac{2\pi}{\Delta x\tilde{u}t}}\exp\left(-\frac{(\tilde{u}t-x+x_0)^2}{2\Delta x\tilde{u}t}\right)\end{aligned}$$

This is the solution, which gives a Gaussian shape propagating.