For unconditioned FPT distribution, $P_{n_0}(T=k)$, consider

$$\sum_{\ell=k+1}^{\infty} P_{n_0}(\ell) = 1 - \sum_{\ell=0}^{k} P_{n_0}(\ell) \equiv \text{Survival } \underbrace{S_{n_0}(k)}$$

probability the system survived up to and including step k

What is equation for "Survival probability"?

Note that
$$\boxed{S_{n_0}(k+1) - S_{n_0}(k) = P_{n_0}(T=k+1)}$$

$=$ probability of ruin (extinction) at step $k+1$

continuous time version

$$-\frac{dS_{n_0}}{dt} = \omega_{n_0}(t)$$

initial conditions $S_{n_0}(0) = 1 \quad \forall \quad 0 \leq n_0 \leq N-1$

Relationships

Recall the recursion for extinction (game ending) time distribution:

$$P_{n_0}(\ell) = p P_{n_0+1}(\ell-1) + q P_{n_0-1}(\ell-1)$$

$$S_{n_0}(k) = 1 - \sum_{\ell=0}^{k} P_{n_0}(\ell) = 1 - \sum_{\ell=0}^{k} \left[p P_{n_0+1}(\ell-1) + q P_{n_0-1}(\ell-1)\right]$$

$$= 1 - p\left(1 - S_{n_0+1}(k-1)\right) - q\left(1 - S_{n_0-1}(k-1)\right)$$

$$= \cancel{1-p-q} + p S_{n_0+1}(k-1) + q S_{n_0-1}(k-1)$$

Same recursion relation:

$$S_{n_0}(k) = p\, S_{n_0+1}(k-1) + q\, S_{n_0-1}(k-1) \qquad k \geq 1 \qquad (1)$$

now take $S_{n_0}(k+1) = p\, S_{n_0+1}(k) + q\, S_{n_0-1}(k)$ $\qquad (2)$

and subtract (1):

$$S_{n_0}(k+1) - S_{n_0}(k) = p\left(S_{n_0+1}(k) - S_{n_0+1}(k-1)\right) + q\left(S_{n_0-1}(k) - S_{n_0-1}(k-1)\right)$$

$$\Rightarrow \boxed{P_{n_0}(T=k+1) = p\, P_{n_0+1}(T=k) + q\, P_{n_0-1}(T=k)}$$

Same recursion eqn

Now, consider $\sum_{k=0}^{\infty} P_{n_0}(k+1)(k+1) =$

$$\sum_{k=0}^{\infty} \left[-S_{n_0}(k+1) + S_{n_0}(k)\right](k+1)$$

$$= \underbrace{-\sum_{\ell=1}^{\infty} \ell\, S_{n_0}(\ell) + \sum_{\ell=0}^{\infty} \ell\, S_{n_0}(\ell)}_{\text{cancels}} + \sum_{\ell=0}^{\infty} S_{n_0}(\ell)$$

$$\boxed{E[T_{n_0}] = \sum_{\ell=0}^{\infty} S_{n_0}(\ell)}$$

Sum over all times of the survival prob. $\Rightarrow E[T_{n_0}]$

Can also write recursion relation for $\mathbb{E}[T_{n_0}]$ directly:

$$\sum_{k=1}^{\infty} \left[S_{n_0}(k) = p\, S_{n_0+1}(k-1) + q\, S_{n_0}(k-1) \right], \quad \text{note that } \sum_{\ell=0}^{\infty} S_{n_0}(\ell) \equiv \mathbb{E}[T_{n_0}]$$

$$\Rightarrow \quad \mathbb{E}[T_{n_0}] - \cancelto{1}{S_{n_0}(0)} = p\,\mathbb{E}[T_{n_0+1}] + q\,\mathbb{E}[T_{n_0-1}]$$

note that for $p = q = 1/2$,

$$\boxed{\frac{1}{2}\mathbb{E}[T_{n_0+1}] - \mathbb{E}[T_{n_0}] + \frac{1}{2}\mathbb{E}[T_{n_0-1}] = -1}$$

$$\text{“} \quad 2\nabla^2_{n_0}\mathbb{E}[T_{n_0}] = -1 \quad \text{”}$$

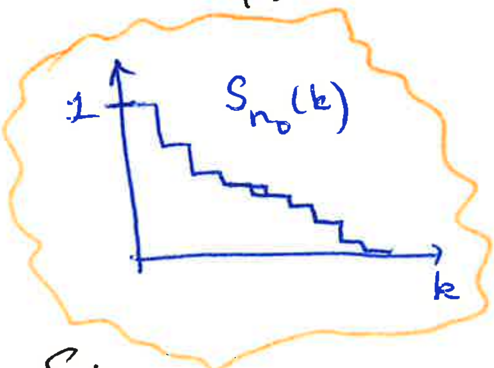
can compute higher moments of the first passage times;

$$\sum_{k=0}^{\infty} P_{n_0}(T = k+1)(k+1)^{\alpha} = \ldots$$

Same 2-term recursion relation (backward eqn)

$$S_{n_0}(k) = p\,S_{n_0+1}(k-1) + q\,S_{n_0-1}(k-1), \quad k \geq 1$$

and $S_{n_0=0}(k) = S_{n_0=N}(k) = 0$ no survival if started dead.



$S_{n_0}(k=0) = 1$ for $1 \leq n_0 \leq N-1$

no ruin or win in zero steps.

Solve using generating functions: $\boxed{G_{n_0}(z) = \sum_{k=0}^{\infty} S_{n_0}(k) z^k}$

$$\sum_{k=1}^{\infty} S_{n_0}(k) z^k = p z \sum_{k=1}^{\infty} S_{n_0+1}(k-1) z^{k-1} + q z \sum_{k=1}^{\infty} S_{n_0-1}(k-1) z^{k-1}$$

$$G_{n_0}(z) - \underbrace{S_{n_0}(0)}_{1} = p z\, G_{n_0+1}(z) + q z\, G_{n_0-1}(z)$$

$$\boxed{p z\, G_{n_0+1}(z) + q z\, G_{n_0-1}(z) - G_{n_0}(z) = -1}$$

homogeneous solution $G^h_{n_0}(z) = A_+(z)\lambda_+^{n_0} + A_-(z)\lambda_-^{n_0}$ as before, plus particular solution: $G^p_{n_0}(z) = \text{const.}$

$$(pz + qz - 1)C = -1 \implies C = \frac{1}{1 - z(p+q)} = \frac{1}{1-z}$$

Now apply boundary conditions

$$G^h_{n_0=0}(z) + G^p_{n_0=0}(z) = A_+(z) + A_-(z) + \frac{1}{1-z} = 0$$

$$\Rightarrow \quad A_+ + A_- = -\frac{1}{1-z}$$

$$G^h_N(z) + G^p_N(z) = A_+\lambda_+^N + A_-\lambda_-^N + \frac{1}{1-z} = 0$$

$$\Rightarrow \quad A_+(z) = \frac{\lambda_-^N - 1}{(1-z)(\lambda_+^N - \lambda_-^N)} \; ; \; A_-(z) = \frac{1-\lambda_+^N}{(1-z)(\lambda_+^N-\lambda_-^N)}$$

$$G_{n_0}(z) = \frac{(\lambda_-^N - 1)\lambda_+^{n_0} + (1-\lambda_+^N)\lambda_-^{n_0}}{(1-z)(\lambda_+^N - \lambda_-^N)} + \frac{1}{1-z} \Bigg|_{z\to 0} = 1 \checkmark$$

$$\lambda_+(z)\Big|_{z\to 0} \sim \frac{1}{pz}, \quad \lambda_-(z) \sim qz$$

$G_{n_0}(1) = \mathbb{E}[T_{n_0}]$ from the definition $\mathbb{E}[T_{n_0}] = \sum_{k=0}^{\infty} S_{n_0}(k)\, 1^k$

$$\lambda_+(z) = 1 - \frac{\varepsilon}{p-q} + O(\varepsilon^2)$$

$$\lambda_-(z) = \frac{q}{p}\left(1 + \frac{\varepsilon}{p-q} + O(\varepsilon^2)\right), \quad \varepsilon \equiv z - 1$$

$$\lambda_-^N = \left(\frac{q}{p}\right)^N \left(1+\frac{\varepsilon}{p-q}\right)^N \simeq \left(\frac{q}{p}\right)^N \left(1+\frac{N\varepsilon}{p-q}\right)$$

$$\lambda_-^N - 1 \simeq \left(\frac{q}{p}\right)^N - 1 + \frac{N\varepsilon}{p-q}\left(\frac{q}{p}\right)^N$$

$$\lambda_+^{n_0} \simeq \left(1-\frac{\varepsilon}{p-q}\right)^{n_0} \simeq 1-\frac{n_0\varepsilon}{p-q}$$

$$\left(1-\lambda_+^N\right) \simeq 1-\left(1-\frac{N\varepsilon}{p-q}\right) = \frac{N\varepsilon}{p-q}$$

$$\lambda_-^{n_0} \simeq \left(\frac{q}{p}\right)^{n_0}\left(1+\frac{n_0\varepsilon}{p-q}\right)$$

Denominator:

$$\lambda_+^N - \lambda_-^N = \left(1-\frac{N\varepsilon}{p-q}\right) - \left(\frac{q}{p}\right)^N\left(1+\frac{N\varepsilon}{p-q}\right)$$

$$= 1-\left(\frac{q}{p}\right)^N - \frac{N\varepsilon}{p-q}\left(1+\left(\frac{q}{p}\right)^N\right)$$

$$= \left(1-\left(\frac{q}{p}\right)^N\right)\left[1-\frac{N\left(1+(q/p)^N\right)}{(p-q)\left(1-\left(\frac{q}{p}\right)^N\right)}\,\varepsilon\right]$$

Numerator

$$\text{Num} = \left[\left(\frac{q}{p}\right)^N - 1 + \left(\frac{q}{p}\right)^N\frac{N\varepsilon}{p-q}\right]\left[1-\frac{n_0\varepsilon}{p-q}\right] + \left(\frac{q}{p}\right)^{n_0}\left(1+\frac{n_0\varepsilon}{p-q}\right)\frac{N\varepsilon}{p-q}$$

$$= \frac{\text{Num}\left[1 + \frac{N(x^N+1)\,\varepsilon}{(p-q)(1-x^N)}\right]}{\varepsilon\,(1-x^N)} \qquad x \equiv q/p$$

$$= \left[(x^N-1) - \frac{n_0\,\varepsilon}{(p-q)}(x^N-1) + x^N\frac{N\varepsilon}{p-q} + x^{n_0}\frac{N\varepsilon}{p-q}\right] \cdot \left(1 + \frac{N(x^N+1)\varepsilon}{(p-q)(1-x^N)}\right)$$

$$\frac{x^N-1 - \frac{n_0\,\varepsilon}{p-q}(x^N-1) + \frac{N x^N \varepsilon}{p-q} + x^{n_0}\frac{N\varepsilon}{p-q} - \frac{N(x^N+1)\,\varepsilon}{(p-q)}}{\varepsilon\,(1-x^N)}$$

$$\Rightarrow -\frac{1}{\varepsilon} - \frac{n_0(x^N-1)}{(p-q)(1-x^N)} + \frac{N\cancel{x^N}}{(p-q)(1-x^N)} + \frac{N x^{n_0}}{(p-q)(1-x^N)} - \frac{N(\cancel{x^N}+1)}{(p-q)(1-x^N)}$$

$$= -\frac{1}{\varepsilon} + \frac{n_0 - N}{(p-q)(1-x^N)} - \frac{n_0 x^N - N x^{n_0}}{(p-q)(1-x^N)}$$

$$+ 1/\varepsilon$$

Singular terms Cancel

$$= \frac{N x^{n_0} - n_0 x^N + n_0 - N}{(p-q)(1-x^N)}$$ as before!

Now lets try to set up the full probability distribution for the Gamblers Ruin problem

$$P_n(k+1) = p\,P_{n-1}(k) + q\,P_{n+1}(k)$$ ("forward" equation)

prob. at site n, after $k+1$ steps

Initial conditions $\quad P_n(0) = \delta_{n,n_0}$

time-generating function

$$G_n(z) = \sum_{k=0}^{\infty} P_n(k) z^k$$

implicit in these functions is the initial condition at n_0

$$\frac{1}{z}\Big(G_n(z) - \underbrace{P_n(0)}_{\delta_{n,n_0}}\Big) = p\,G_{n-1}(z) + q\,G_{n+1}(z)$$

$$\Rightarrow \boxed{zp\,G_{n-1}(z) + zq\,G_{n+1}(z) - G_n(z) = -\delta_{n,n_0}}$$

for $n > n_0 \qquad G_n(z) = A\lambda_+^n + B\lambda_-^n \quad$ where $\lambda_\pm = \frac{1}{2qz} \pm \frac{1}{2qz}\sqrt{1-4pqz^2}$

for $n < n_0 \qquad G_n(z) = C\lambda_+^n + D\lambda_-^n$

Conditions

Continuity: $A\lambda_+^{n_0} + B\lambda_-^{n_0} = C\lambda_+^{n_0} + D\lambda_-^{n_0}$

jump condition:

$$pz\left(C\lambda_+^{n_0-1} + D\lambda_-^{n_0-1}\right) + qz\left(A\lambda_+^{n_0+1} + B\lambda_-^{n_0+1}\right)$$

$$-A\lambda_+^{n_0} - B\lambda_-^{n_0} = -1$$

Boundary conditions

prob. system is in state 0 at time k

$$G_0(z) = \sum_{k=0}^{\infty} P_0(k)\, z^k$$

after the system first reaches 0, it stays there.

how to evaluate

$P_{n_0}(k, \text{ruin})$

For $n_0 \neq 0, N$,

$$G_0(z) = \sum_{k=0}^{\infty} f_{0,n_0}(k)\, z^k \equiv F_0(z)$$

we called this $G_{n_0}(z)$ previously

$$G_N(z) = \sum_{k=0}^{\infty} f_{N,n_0}(k)\, z^k \equiv F_N(z)$$

we called this $H_{n_0}(z)$ previously

$P_{n_0}(k, \text{win})$

we have solved for $f_{0,n_0}(k)$ and $f_{N,n_0}(k)$ already.

at $n=0$ ← solved previously

$$C\lambda_+^0 + D\lambda_-^0 = F_0(z)$$

at $n=N$

$$A\lambda_+^N + B\lambda_-^N = F_N(z)$$

Four conditions, Four coefficients.

$$\begin{bmatrix} \lambda_+^{n_0} & \lambda_-^{n_0} & -\lambda_+^{n_0} & -\lambda_-^{n_0} \\ \left(qz\lambda_+^{n_0+1} - \lambda_+^{n_0}\right) & qz\lambda_-^{n_0+1} - \lambda_-^{n_0} & pz\lambda_+^{n_0-1} & pz\lambda_-^{n_0-1} \\ 0 & 0 & 1 & 1 \\ \lambda_+^N & \lambda_-^N & 0 & 0 \end{bmatrix} \begin{bmatrix} A \\ B \\ C \\ D \end{bmatrix} = \begin{bmatrix} 0 \\ -1 \\ F_0(z) \\ F_N(z) \end{bmatrix}$$

$\Rightarrow$ determines $G_n(z; n_0)$, power series give $P_n(k; n_0)$ explicitly in terms of n_0, N, p, q

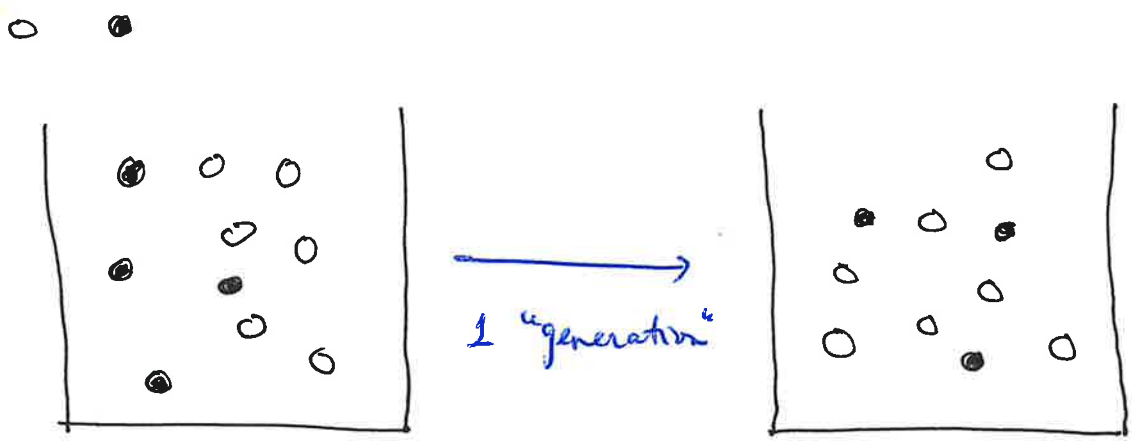
Wright-Fisher Process 1922/1931

describes the number of two types of alleles in a population of N

each allele can have up to 2N copies in the population

* Simpler interpretation: assume a population of N individuals which can be of either of two types, A or B. Such that

$n_A + n_B = N$.



$n_B = 4$ $n_B = 3$

the population replaces itself. Randomly select from the initial population to replicate. Some may be drawn more than once, some not at all.

if the state space is defined as $n \equiv n_A$, we have binomial sampling

Stochastic master equation

$$P_n(k+1) = \sum_m W_{nm} P_m(k)$$

$$\text{so} \quad \boxed{\vec{p}(k) = W^k \vec{p}(0)}$$

transition matrix is not local, (steps greater than ± 1)

zero (fixation of n_B) $\longrightarrow$

$$\begin{pmatrix} 1 & (1-1/N)^N & (1-2/N)^N & \cdots & \\ 0 & N\frac{1}{N}\left(1-\frac{1}{N}\right)^{N-1} & N\left(\frac{2}{N}\right)\left(1-\frac{2}{N}\right)^{N-1} & \cdots & \vdots \\ 0 & & & & 0 \\ 0 & & & & 0 \\ \vdots & & & & 0 \\ & & & & 1 \end{pmatrix}$$

$$\begin{pmatrix} 00 & 01 & \cdots & 0,N \\ 10 = 0 & 11 & 12 & \\ 20 = 0 & 21 & 22 & 23 \\ \vdots & & & \end{pmatrix}$$

Suppose initial number of A is m.

then, in the next-generation population, the probability of having n A individuals is

$$W_{nm} = \binom{N}{n} \underbrace{\left(\frac{m}{N}\right)}_{p}^{n} \underbrace{\left(1-\frac{m}{N}\right)}_{q}^{N-n}, \quad \text{a Binomial}$$

Note that $\mathbb{E}[n_A(k) \mid n_A(k-1) = m]$

is $\displaystyle\sum_{n=0}^{N} \binom{N}{n} n \, p^n (1-p)^{N-n}$

$$= \sum_n \frac{N!\, n}{n!\,(N-n)!} \left(\frac{m}{N}\right)^n \left(1-\frac{m}{N}\right)^{N-n}$$

$$= \sum_n \frac{\cancel{N}(N-1)!}{(n-1)!\,(N-n)!} \left(\frac{m}{N}\right)^{n-1} \cancel{\left(\frac{m}{N}\right)} \left(1-\frac{m}{N}\right)^{(N-1)-(n-1)}$$

$$= m \sum_{n=0}^{N} \binom{N-1}{n-1} \left(\frac{m}{N}\right)^{n-1} \left(1-\frac{m}{N}\right)^{(N-1)-(n-1)}$$

$$= m \quad \therefore \quad \mathbb{E}[n_A(k) \mid n_A(k-1) = m] = m$$

$\boxed{\text{Martingale - expectation is current value}}$

$$\mathbb{E}[n_A] = n_A(0)$$

what about variance?

$$\mathrm{Var}[n_A(k+1) \mid n_A(k) = m] = N \frac{m}{N}\left(1 - \frac{m}{N}\right)$$

define

$$\mathrm{Var}[p(k+1) \mid p(k)] = \frac{p(k)(1-p(k))}{N}$$

Note that $\mathbb{E}[p^2(k+1) \mid p(k)]$

$$= \mathrm{Var}[p(k+1) \mid p(k)] + \left(\mathbb{E}[p(k+1) \mid p(k)]\right)^2$$

$$= \frac{p(k)(1-p(k))}{N} + p^2(k)$$

$$\boxed{\psi(k) \equiv \mathbb{E}[p^2(k)]}$$

$$\psi(k+1) \equiv \mathbb{E}\left[\frac{p(k)(1-p(k))}{N} + p^2(k)\right] = \mathbb{E}\left[\mathbb{E}[p^2(k+1) \mid p(k)]\right]$$

$$= \frac{\underbrace{\mathbb{E}[p(k)]}_{p_0} - \mathbb{E}[p^2(k)]}{N} + \mathbb{E}[p^2(k)]$$

$$\therefore \quad \psi(k+1) = \frac{p_0 - \psi(k)}{N} + \psi(k)$$

$$\psi(k+1) = \psi(k)\left(1 - \frac{1}{N}\right) + \frac{p_0}{N}$$

Iterating $\psi(k) = \left(1 - \frac{1}{N}\right)^k \underbrace{\psi_0}_{p_0^2} + \sum_{l=0}^{k-1}\left(1 - \frac{1}{N}\right)^l \frac{p_0}{N}$

$$\sum_{\ell=0}^{k-1} \left(1-\frac{1}{N}\right)^{\ell} = \frac{1-\left(1-\frac{1}{N}\right)^{k}}{1-\left(1-\frac{1}{N}\right)} = N\left(1-\left(1-\frac{1}{N}\right)^{k}\right)$$

$$\psi(k) = \left(1-\frac{1}{N}\right)^{k} p_0^2 + p_0\left(1-\left(1-\frac{1}{N}\right)^{k}\right)$$

$$\left(1-\frac{1}{N}\right)^{k}(p_0^2-p_0) + p_0$$

$$\mathrm{Var}[p(k)] = \mathbb{E}[p^2(k)] - p_0^2 = \psi(k) - p_0^2$$

$$= \left(1-\frac{1}{N}\right)^{k} p_0(p_0-1) + p_0 - p_0^2$$

$$= \boxed{p_0(1-p_0)\left[1-\left(1-\frac{1}{N}\right)^{k}\right]}$$ increases with k

* <u>Fixation probability</u> π_i prob of fixation starting from $n_A = i$

$$\pi_i = \sum_j P_{ji}\,\pi_j$$ assume form $\boxed{\pi_i = \frac{i}{N}}$

$$\frac{i}{N} \overset{(?)}{=} \sum_j \binom{N}{j}\left(\frac{i}{N}\right)^{j}\left(1-\frac{i}{N}\right)^{N-j}\left(\frac{j}{N}\right)$$

$$= \frac{i}{N} \checkmark$$

Extinction and fixation times

$$\mathbb{E}[T_i] = 1 + \sum_{j=0}^{N} P_{ji}\, \mathbb{E}[T_j] \quad , \quad \mathbb{E}[T_0] = \mathbb{E}[T_N] = 0$$

start from $n_A = i$

Linear system of equations

Conditional fixation time

$$\mathbb{E}[T \mid X_0 = i, \underbrace{X_T = N}]$$

conditioned on fixation

instead of P_{ji}, we need P_{ji}^{fix}

P_{ji} is the unconditional prob of $i \to j$

Fixation prob from $j = \frac{j}{N}$

Fixation prob from $i = \frac{i}{N}$

P_{ji}^{fix} is found by reweighting P_{ji} by the relative likelihood of fixation from j versus from i

$$\Rightarrow \pi_i P_{ji}^{fix} = \pi_j P_{ji}$$

$$\boxed{\mathbb{E}[T_i \mid X_T = N] = 1 + \sum_{j=0}^{N} P_{ji}^{fix}\, \mathbb{E}[T_j \mid X_T = N]}$$

Selection & mutation

Suppose type A is preferentially selected for replication

And that type A can mutate and generate type B as offspring

$p \to p'$ if $p = \frac{m}{N}$, define selection coefficient S and mutation rate γ_A, γ_B

$$p' = \frac{m(S+1)(1-\gamma_A)}{m(S+1) + (N-m)} + \left(1 - \frac{m(S+1)}{m(S+1)+N-m}\right)\gamma_B$$

use p' in Binomial

$$P_{nm} = \binom{N}{n} p'^{\,n} (1-p')^{N-n}$$

m-dependence in p'

$\mathbb{E}[X_{k+1} = n \mid X_k = m] = Np' \neq m$ <u>Not a martingale</u>

Can use P'_{nm} in all calculation for extinction/fixation probabilities and times

$$\boxed{\pi\left(\frac{m}{N}\right) \approx \frac{1 - e^{-2NS\left(\frac{m}{N}\right)}}{1 - e^{-2NS}}}$$

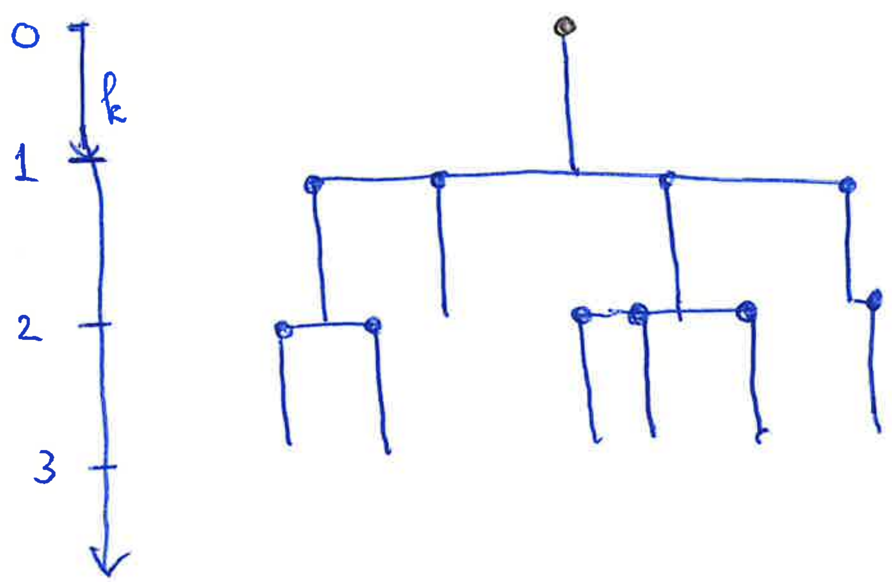
from continuum approx

for small m

Galton-Watson process (1873)

question about last names: starting with unique last names, how many survive after k generations, what are the sizes of each remaining family?

Consider independent births, and no population-dependence.
A single founder begets the tree:



at generation 3
there are 6 individuals

4 individuals at generation 1 gave birth to 2, 0, 3, and 1 individuals for generation 2, respectively

X_k is the total # at generation k, the whole set $\{X_k\}_{k=0}^{\infty}$ is the whole state space

a_n: progeny distribution function; probability that one individual gives rise to n offspring

$H_k(z) \equiv$ prob. gen. function for X_k $\Rightarrow$ $E[z^{X_k}]$

$$= \sum_{l=0}^{\infty} \text{Prob}(X_k = l) z^l$$

for $X_0 = 1$, $H_0(z) = z$, p.g.f of X_1 is

$$H_1(z) = \sum_{n=0}^{\infty} a_n z^n$$

a_n: probability off n offspring

For X_2; each individual at $k=1$ generates a random number (based on a_n) individuals.

$X_2 = Y_1 + Y_2 + \dots Y_{X_1}$ where Y_l is the number of offspring generated by individual l.

$$\text{Prob}\{X_2 = n \mid X_1 = m\} = \text{Prob}\left\{\sum_{l=1}^{m} Y_l = n\right\}$$

in general, 3 random variables

$$\overset{H}{X_{k+1}} = \overset{F}{Y_1} + Y_2 + \dots Y_{\overset{G}{X_k}} = \sum_{l=1}^{X_k} Y_l$$

random variables are Y_l, X_k. and X_{k+1}

$$F(z) = \sum_{j=0}^{\infty} \overbrace{\text{Prob}\{Y_i = j\}}^{a_j} z^j \qquad H(z) \equiv \sum_{j=0}^{\infty} \text{Prob}\{X_{k+1} = j\} z^j$$

$$G(z) = \sum_{j=0}^{\infty} \text{Prob}\{X_k = j\} z^j$$

For a particular $X_\ell = m$, $\quad \text{Prob}\{X_{k+1}=j\} = \sum_{m=0}^{\infty} \text{Prob}\{X_{\ell+1}=j \mid X_\ell=m\} \underbrace{\text{Prob}\{X_\ell=m\}}_{\equiv g_m}$

$$= \underbrace{\sum_{m=0}^{\infty} g_m \, \text{Prob}\{X_{\ell+1}=j \mid X_\ell=m\}}_{\text{Prob}\{X_{k+1}=j\}}$$

for any specific $X_\ell = m$;

$$\mathbb{E}[z^{X_{\ell+1}} \mid X_\ell=m] = \mathbb{E}[z^{Y_1}]\,\mathbb{E}[z^{Y_2}] \cdots \mathbb{E}[z^{m}]$$

$$\equiv \left(\mathbb{E}[z^{Y}]\right)^m \equiv F^m(z)$$

$$\equiv \sum_{j=0}^{\infty} \text{Prob}\{X_{\ell+1}=j \mid X_\ell=m\} \, z^j$$

Then $\quad H(z) = \sum_{j=0}^{\infty} \left(\sum_{m=0}^{\infty} g_m \, \text{Prob}\{X_{\ell+1}=j \mid X_\ell=m\} \right) z^j$

$$= \sum_{m=0}^{\infty} g_m \overbrace{\sum_{j=0}^{\infty} \text{Prob}\{X_{\ell+1}=j \mid X_\ell=m\} \, z^j}^{F^m(z)}$$

$$= \sum_{m=0}^{\infty} g_m \underbrace{F^m(z)}_{\text{like a } z^m \text{ term}}$$

$$\therefore \quad \boxed{H(z) = G(F(z))}$$

Simple example

Suppose $X_0 = 1$ and the offspring generating distribution is $p_0 = \frac{1}{5}$, $p_1 = \frac{4}{5}$, $p_{k \geq 2} = 0$,

that is each individual has $1/5$ chance of dying w/o offspring (creates zero offspring) and a $\frac{4}{5}$ probability of giving birth to one offspring before dying.

$$H_1(z) = \frac{1}{5} + \frac{4}{5} z$$

$$H_2(z) = H_1(H_1(z)) = \frac{1}{5} + \frac{4}{5}\left(\frac{1}{5} + \frac{4}{5} z\right) = \frac{1}{5}\left(1 + \frac{4}{5}\right) + \left(\frac{4}{5}\right)^2 z$$

$$H_3(z) = H_1(H_1(H_1(z))) = \frac{1}{5} + \frac{4}{5}\left(\frac{1}{5}\left(1 + \frac{4}{5}\right) + \left(\frac{4}{5}\right)^3 z\right)$$

$$= \frac{1}{5}\left(1 + \frac{4}{5} + \left(\frac{4}{5}\right)^2\right) + \left(\frac{4}{5}\right)^3 z$$

$$H_k(z) = \frac{1}{5}\left(1 + \frac{4}{5} + \left(\frac{4}{5}\right)^2 + \dots + \left(\frac{4}{5}\right)^{k-1}\right) + \left(\frac{4}{5}\right)^k z$$

$$= \frac{1}{5} \frac{1 - (4/5)^k}{1 - 4/5} + \left(\frac{4}{5}\right)^k z = 1 - \left(\frac{4}{5}\right)^k + \left(\frac{4}{5}\right)^k z$$

$\therefore$ $\mathrm{Prob}\{X_k = 0\} = 1 - \left(\frac{4}{5}\right)^k$, $\mathrm{Prob}\{X_k = 1\} = \left(\frac{4}{5}\right)^k$

$$H_1(z) = \sum_{n=0}^{\infty} q_n z^n = \text{prob gen function for}$$

$$\text{each } Y \equiv F(z) = \sum_{j=0}^{\infty} \underbrace{\text{Prob}\{Y=j\}}_{a_j} z^j$$

Now for $k=1$, $G(z) = \sum_{j=0}^{\infty} \text{Prob}\{X_1 = j\} z^j$

$$= \sum_{j=1}^{\infty} \text{Prob}\{Y=j\} z^j = F(z) = H_1(z)$$

$$\therefore \quad H_2(z) = G(F(z)) = H_1(H_1(z))$$

$$H_{k+1}(z) = H_k(H_1(z)) = H_{k-1}[H_1(H_1(z))]$$

$$= \ldots H_1(H_1(\cdots H_1(z)\ldots)) \quad (k+1 \text{ times})$$

$\boxed{k\text{-fold composition}}$

if we started with $X_0 = N$ instead of $X_0 = 1$, then

$$H_k(z) = [H_1(H_1(H_1(\ldots)\ldots))]^N \quad \text{since}$$

each founder is independent of the others

Extinction

$$H_k(z) = \sum_{n=0}^{\infty} p_n(k)\, z^n$$

$\rightarrow \text{Prob}\{X_k = n\}$

If $a_0 = 0$, then there is at least one offspring in every generation and no extinction occurs.

If $a_0 > 0$, then in our example, $P_0(k) = 1 - \left(\frac{4}{5}\right)^k$ and $P_1(k) = \left(\frac{4}{5}\right)^k$

* mean number of births $b = \sum_{n=0}^{\infty} n\, a_n = \left.\frac{dF(z)}{dz}\right|_{z\to 1}$

if $b > 1$, on average more than one offspring and overall population typically increases

if $b = 1$, one for one replacement, random functuations lead to extinction, even though typical population does not change

if $b < 1$, population decreases, extinction certain

---

extinction condition

probability of extinction $\underline{\underline{q}} = F(q)$

if founder has no offspring $\rightarrow$ extinction

if founder has l offspring, each one starts a lineage

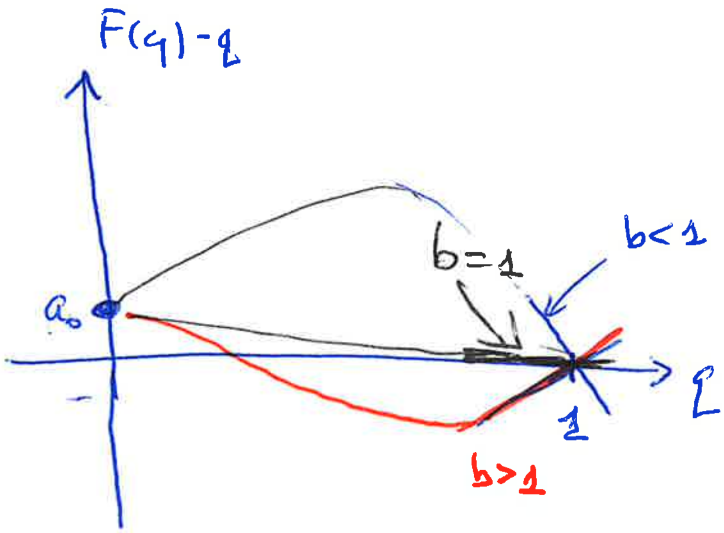
And the probability of ~~extinction~~ extinction requires extinction of each lineage: q^l

$\therefore$ extinction probability should satisfy

$$q = p_0 + p_1 q + p_2 q^2 + \cdots \equiv F(q)$$

Solving for q, the smallest non-negative solution can be identified as the extinction probability.

There is always a root at $q=1$ by definition



$$\frac{d}{dq}\left(F(q)-q\right)\Big|_{q=1} = \underbrace{\frac{dF}{dq}\Big|_{q=1}}_{b} - 1$$

if $b>1$, then slope of $F(q)-q$ at $q=1$ is positive

at $q=0$, $F(0) - 0 = a_0$

$\therefore$ for $b>1$, supercritical dynamics can have finite extinction probability

for $b \leq 1$, extinction probability $= 1$

Mean and variance to total population

$$b_1 = \sum_{n=0}^{\infty} n a_n = \left.\frac{dF(z)}{dz}\right|_{z=1}$$

the mean after k generations $b_k = b_1^k$

variance after 1 generation

$$\sigma_1^2 = \sum_{l=1}^{\infty} l^2 a_l - b_1^2$$

$$\sigma_k^2 = \mathbb{E}[(X_k - b_k)^2] = \begin{cases} \dfrac{b^{k-1}(b^k - 1)\,\sigma_1^2}{b-1} & b \neq 1 \\ k\sigma_1^2 & b = 1 \end{cases}$$

will not derive — look up if interested

Extinction times

$\text{Prob}\{\text{extinction by generation } k\} = \text{Prob}(X_k = 0) \equiv f_k$

$$f_k = F(f_{k-1}), \quad f_0 = 0$$

each lineage in F now needs to go extinct by the step $k-1$

this is a recursion relation for f_n. Suppose $F(z) = \sum_{l=0}^{\infty} a_l z^l$

$$= a_0 + a_2 z^2$$

then, $f_k = a_0 + a_2 f_{k-1}^2, \quad f_0 = 0$

$a_0 + a_2 = 1$

Cond. Extinction time distribution

$$\text{Prob}\{T_{ext}=k \mid \underbrace{T_{ext}<\infty}_{\text{extinction occurs}}\} \cdot \overset{\text{prob. of extinction}}{q} = P(T_{ext}=k)$$

$$P(T_{ext}=k) = P(X_k=0,\ X_{k-1}>0)$$

$$= f_k - f_{k-1}$$

$\therefore$ conditional extinction time distribution

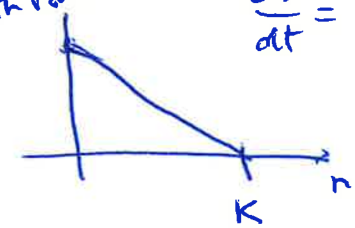
$$\boxed{\frac{f_k - f_{k-1}}{q} = \text{Prob}\{T_{ext}=k \mid T_{ext}<\infty\}}$$

where f_k is found from the recursion

$$f_k = F(f_{k-1}) \quad \text{and } f_0 = 0$$

Birth-death process with interactions

deterministic motivation: $\dfrac{dn}{dt} = \underbrace{r\left(1-\frac{n}{K}\right)}_{\text{growth rate}} n - \mu n$, or



$$\frac{dn}{dt} = rn - \mu\Big(1+\underbrace{\frac{r}{\mu}\frac{n}{K}}\Big)n$$

increase death rate when n increases

$$\frac{dn}{dt} = rn - \frac{rn^2}{K} - \mu n = (r-\mu)n - \frac{rn^2}{K}$$

$$\frac{dn}{dt} = rn - \mu n - \frac{rn^2}{K} = (r-\mu)n - \frac{rn^2}{K}$$

identical models

Stochastic Birth-death w/ carrying capacity

$$\frac{dP_n}{dt} = \underbrace{r_{n-1}}_{r\left(1-\frac{n-1}{K}\right)}(n-1)P_{n-1} - \big(\underbrace{r_n}_{r\left(1-\frac{n}{K}\right)}+\mu_n\big)nP_n + \underbrace{\mu_{n+1}}_{\mu}(n+1)P_{n+1}$$

$$\sum n\dot{P}_n = \frac{d}{dt}E[n] = \sum_n rn\left(1-\frac{n-1}{K}\right)(n-1)P_{n-1} - \sum_n\left(r\left(1-\frac{n}{K}\right)+\mu\right)nP_n + \mu\sum_n n(n+1)P_{n+1}$$

$$rn\left(1-\frac{n-1}{K}\right)(n-1) = r(n-1)\left(1-\frac{n-1}{K}\right)(n-1) + r\left(1-\frac{n-1}{K}\right)(n-1)$$

Consider other simple stochastic process (no spatial dependence — "well-mixed")

* regulated birth $\quad X \xrightarrow{r_0(1-n/K)} 2X, \quad X \xrightarrow{\mu_0} \phi$

* regulated death $\quad X \xrightarrow{r_0} 2X, \quad X \xrightarrow{\mu_0(1+\frac{r_0 n}{\mu_0 K})} \phi$

* annihilation $\quad X \xrightarrow[r_0-\mu_0-\frac{r_0}{K}]{} 2X, \quad X+X \xrightarrow[\frac{r_0}{K}]{} \phi$

---

* regulated birth, birth rate depends on current population (consumption of resources)

$K \equiv$ carrying capacity

$$\dot{P}_n(t) = r_0\left(1-\frac{n-1}{K}\right)(n-1)P_{n-1} - \left(r_0\left(1-\frac{n}{K}\right)+\mu_0\right)n P_n$$
$$+ \mu_0 (n+1) P_{n+1}$$

$$\times \sum_{n=0}^{\infty} n \dot{P}_n(t) \Rightarrow \boxed{\langle \dot{n} \rangle = (r_0-\mu_0)\langle n \rangle - \frac{r_0}{K}\langle n^2 \rangle}$$

$$r_0 \sum_{n=0}^{\infty} n(n-1) P_{n-1} = r_0 \sum_{m=0}^{\infty} (m+1) m P_m$$
$$= r_0 \langle n(n+1) \rangle$$

$$\sum_{n=0}^{\infty} n^2 \dot{P}_n(t) = \boxed{\frac{d\langle n^2 \rangle}{dt} = 2 r_0 \langle n^2 \rangle + r_0 \langle n \rangle - 2\mu_0 \langle n^2 \rangle + \mu_0 \langle n \rangle - \frac{2r_0}{K}\langle n^3 \rangle - \frac{r_0}{K}\langle n^2 \rangle}$$

* Regulated death

$$\dot{P}_n(t) = r_0(n-1)P_{n-1} - \left(r_0 + \mu_0\left(1 + \frac{r_0 n}{\mu_0 K}\right)\right) n P_n + \mu_0\left(1 + \frac{r_0}{\mu_0}\frac{n+1}{K}\right)(n+1)P_{n+1}$$

$$\boxed{\langle \dot{n} \rangle = (r_0 - \mu_0)\langle n \rangle - \frac{r_0}{K}\langle n^2 \rangle}$$

$$\boxed{\frac{d\langle n^2 \rangle}{dt} = 2(r_0 - \mu_0)\langle n^2 \rangle + (r_0 + \mu_0)\langle n \rangle - \frac{2r_0}{K}\langle n^3 \rangle + \frac{r_0}{K}\langle n^2 \rangle}$$

* Annihilation

$$X \xrightarrow{r_0 - \mu_0 - \frac{r_0}{K}} 2X \qquad \underbrace{X + X}_{2 \text{ particles}} \xrightarrow{\frac{r_0}{K}} \phi$$

2 particles $\longrightarrow$ 0 particles

$$\dot{P}_n(t) = \underbrace{\frac{r_0}{2K}}\left[(n+1)(n+2)P_{n+2} - n(n-1)P_n\right]$$

$\frac{1}{2}$ from Indistinguishability

$$+ \left(r_0 - \mu_0 - \frac{r_0}{K}\right)\left[(n-1)P_{n-1} - nP_n\right]$$

$$\sum_{n=0}^{\infty} n\dot{P}_n(t) = \frac{r_0}{2K}\sum_{n=0}^{\infty} n(n+1)(n+2)P_{n+2} + \ldots$$

$$= \frac{r_0}{2K}\sum_{m=0}^{\infty} m(m-1)(m-2)P_m + \ldots$$

$$= \frac{r_0}{2K}\langle n(n-1)(n-2)\rangle + \ldots$$

$$\boxed{\langle \dot{n} \rangle = (r_0 - \mu_0)\langle n \rangle - \frac{r_0}{K}\langle n^2 \rangle}$$

$$\frac{d\langle n^2\rangle}{dt} = 2(r_0-\mu_0)\langle n^2\rangle + (r_0-\mu_0)\langle n\rangle - \frac{3r_0}{K}\langle n\rangle + \frac{2r_0}{K}\langle n^3\rangle + \frac{2r_0}{K}\langle n^2\rangle$$

	mean	correlation
* Regulated birth:	$\langle \dot{n}\rangle = (r_0-\mu_0)\langle n\rangle - \frac{r_0}{K}\langle n^2\rangle$	$\langle \dot{n^2}\rangle = 2(r_0-\mu_0 - \frac{r_0}{2K})\langle n^2\rangle + (r_0+\mu_0)\langle n\rangle - \frac{2r_0}{K}\langle n^3\rangle$
* Regulated death:	$\langle \dot{n}\rangle = (r_0-\mu_0)\langle n\rangle - \frac{r_0}{K}\langle n^2\rangle$	$\langle \dot{n^2}\rangle = 2(r_0-\mu_0 + \frac{r_0}{2K})\langle n^2\rangle + (r_0+\mu_0)\langle n\rangle - \frac{2r_0}{K}\langle n^3\rangle$
* Annihilation:	$\langle \dot{n}\rangle = (r_0-\mu_0)\langle n\rangle - \frac{r_0}{K}\langle n^2\rangle$	$\langle \dot{n^2}\rangle = 2(r_0-\mu_0 + \frac{r_0}{K})\langle n^2\rangle + (r_0-\mu_0)\langle n\rangle \boxed{-\frac{3r_0}{K}\langle n\rangle} + \frac{2r_0}{K}\langle n^3\rangle$

All models yield the same mean, but yield different higher moments

All models are well-mixed, birth & death models require fast equilibration of resource,
annihilation models require fast spatial equilibration of population, i.e. not diffusion-limited

Mass-action approximation $\langle n^2\rangle = \langle n\rangle\langle n\rangle$: $\boxed{\frac{dn}{dt} \simeq (r_0-\mu_0)\, n - \frac{r_0}{K} n^2}$

$$+ \cancel{\mu \mathbb{E}[n^2]} + \frac{r}{k}\cancel{\mathbb{E}[n^3]} - \mu \mathbb{E}[n] - \frac{r}{k}\mathbb{E}[n^2]$$

$$\frac{d\mathbb{E}[n]}{dt} = (r-\mu)\mathbb{E}[n] - \frac{r}{k}\mathbb{E}[n^2]$$ Same mean equation

What about $\mathbb{E}[n^2]$ for these two models?

$$(n-1)^2 = n^2 - 2n + 1 \; ; \quad n^2 = (n-1)^2 + 2(n-1) + 1$$

$$(n+1)^2 = n^2 + 2n + 1 \,) \quad n^2 = (n+1)^2 - 2(n+1) + 1$$

$$\frac{d\mathbb{E}[n^2]}{dt} = \sum_n \left\{ \begin{array}{l} r\,(n-1)^2 \left(1-\frac{n-1}{k}\right)(n-1) \\ + r\,2(n-1)\left(1-\frac{n-1}{k}\right)(n-1) \\ + r\left(1-\frac{n-1}{k}\right)(n-1) \end{array} \right\} \times P_{n-1} \quad - \sum (\underset{\substack{\uparrow \\ (1-\frac{n}{k})}}{r} + \mu)\, n^3 P_n$$

$$\sum \left\{ + \mu(n+1)^3 - 2\mu(n+1)^2 + \mu(n+1) \right\} \times P_{n+1}$$

$$= \cancel{r\mathbb{E}[n^3]} - \cancel{\frac{r}{k}\mathbb{E}[n^4]} + 2r\mathbb{E}[n^2] - \frac{2r}{k}\mathbb{E}[n^3] + \cancel{\frac{r}{k}\mathbb{E}[n^4]}$$

$$+ r\mathbb{E}[n] - \frac{r}{k}\mathbb{E}[n^2] - \cancel{(r+\mu)\mathbb{E}[n^3]}$$

$$+ \cancel{\mu\mathbb{E}[n^3]} - 2\mu\mathbb{E}[n^2] + \mu\mathbb{E}[n]$$

$$= 2(r-\mu)\mathbb{E}[n^2] + (r+\mu)\mathbb{E}[n] - \frac{2r}{k}\mathbb{E}[n^3]$$
$$- \frac{r}{k}\mathbb{E}[n^2]$$

$$r\,\cancel{\mathbb{E}[n^2]} - \cancel{\frac{r}{k}\mathbb{E}[n^3]} \qquad -\left(r\left(1-\frac{n}{k}\right)n^2 + \mu n^2\right)$$

$$+ r\,\mathbb{E}[n] - \frac{r}{K}\mathbb{E}[n^2] \qquad = -r\,\cancel{\mathbb{E}[n^2]} - \cancel{\mu\mathbb{E}[n^2]}$$

$$+ \cancel{\frac{r}{k}\mathbb{E}[n^3]}$$

$$\mu n(n+1) = \mu(n+1)^2 - \mu(n+1)$$

$$= \cancel{\mu\mathbb{E}[n^2]} - \mu\,\mathbb{E}[n] + r\,\mathbb{E}[n] - r\,\mathbb{E}[n^2]$$

$$\frac{d\,\mathbb{E}[n]}{dt} = (r-\mu)\,\mathbb{E}[n] - \frac{r}{K}\mathbb{E}[n^2]$$

$\mathbb{E}[n]$ depends on higher moment

$$\frac{d\,\mathbb{E}[n^2]}{dt} = \cdots \quad \mathbb{E}[n^3]$$

moments do not close — sign of an "interaction"

Now, consider $\mu \to \mu\left(1 + \frac{r}{\mu}\frac{n}{k}\right)$

$$\frac{dP_n}{dt} = r(n-1)P_{n-1} - \left(r + \mu\left(1+\frac{r}{\mu}\frac{n}{k}\right)\right)n P_n + \mu\left(1+\frac{r}{\mu}\frac{n+1}{k}\right)(n+1)P_{n+1}$$

$$\sum_n n\dot{P}_n = \frac{d\,\mathbb{E}[n]}{dt} = \sum r\left[(n-1)^2 + (n-1)\right]P_{n-1} - \sum r n^2 P_n$$

$$- \mu\,\mathbb{E}[n^2] - \frac{r}{K}\mathbb{E}[n^3]$$

$$+ \sum \mu(n+1)^2\left(1 + \frac{r}{\mu}\frac{n+1}{k}\right)P_{n+1}$$

$$- \sum \mu\left(1 + \frac{r}{\mu}\frac{n+1}{k}\right)(n+1)P_{n+1}$$

$$= \cancel{r\,\mathbb{E}[n^2]} + r\,\mathbb{E}[n] - \cancel{r\,\mathbb{E}[n^2]} - \cancel{\mu\mathbb{E}[n^2]} - \cancel{\frac{r}{k}\mathbb{E}[n^3]}$$

Now consider $\mu \to \mu\left(1+\frac{rn}{\mu K}\right)$

$$\frac{d\,\mathbb{E}[n^2]}{dt} = \sum r(n-1)\left[(n-1)^2+2(n-1)+1\right] p_{n-1}$$

$$\sum\left(-rn^3 p_n - \mu\left(1+\frac{rn}{\mu K}\right) n^3 p_n\right)$$

$$+\ \mu \sum \left(1+\frac{r(n+1)}{\mu K}\right) \underbrace{(n+1)\left[(n+1)^2-2(n+1)+1\right]}_{(n+1)^3-2(n+1)^2+(n+1)} p_{n+1}$$

$$= \cancel{r\,\mathbb{E}[n^3]} + 2r\,\mathbb{E}[n^2] + \cancel{r\,\mathbb{E}[n]}$$

$$-\cancel{r\,\mathbb{E}[n^3]} - \cancel{\mu\,\mathbb{E}[n^3]} - \frac{r}{K}\cancel{\mathbb{E}[n^4]}$$

$$+\cancel{\mu\,\mathbb{E}[n^3]} - 2\mu\,\mathbb{E}[n^2] + \cancel{\mu\,\mathbb{E}[n]}$$

$$+\frac{r}{K}\cancel{\mathbb{E}[n^4]} - \frac{2r}{K}\mathbb{E}[n^3] + \frac{r}{K}\mathbb{E}[n^2]$$

$$= (r+\mu)\,\mathbb{E}[n] + 2(r-\mu)\,\mathbb{E}[n^2] + \frac{r}{K}\mathbb{E}[n^2]$$

$$-\cancel{r\,\mathbb{E}[n^3]} - \frac{2r}{K}\mathbb{E}[n^3]$$

$$\frac{d\,\mathbb{E}[n^2]}{dt} = (r+\mu)\,\mathbb{E}[n] + 2(r-\mu)\,\mathbb{E}[n^2] - \frac{r}{K}\mathbb{E}[n^2] - \frac{2r}{K}\mathbb{E}[n^3] \qquad r\left(1-\frac{n}{K}\right)$$

$$\frac{d\,\mathbb{E}[n^2]}{dt} = (r+\mu)\,\mathbb{E}[n] + 2(r-\mu)\,\mathbb{E}[n^2] + \frac{r}{K}\mathbb{E}[n^2] - \frac{2r}{K}\mathbb{E}[n^3] \qquad \mu\left(1+\frac{r}{\mu}\frac{n}{K}\right)$$

different

Master equation with increasing death rate

$$\frac{\partial P(n,t)}{\partial t} = r(n-1)P(n-1,t) - \left[r + \mu\left(1+\frac{r}{\mu}\frac{n}{K}\right)n\right]P(n,t)$$

$$+ \mu\left(1+\frac{r}{\mu}\frac{n+1}{K}\right)(n+1)P(n+1,t)$$

as with other models, try generating functions:

$$\sum_{n=0}^{\infty}\frac{d}{dt}P(n,t)z^n = \frac{\partial G(z,t)}{\partial t}$$

$$+ r\sum(n-1)P(n-1,t)z^n = rz^2\frac{\partial}{\partial z}G(z,t)$$

$$\frac{\partial G(z,t)}{\partial t} = \left[rz^2 - (\mu+r)z + \mu\right]\frac{\partial G}{\partial z} - \frac{r}{K}\sum_{n=0}^{\infty}n^2P(n,t)z^n$$

$$+ \frac{r}{K}\sum_{n=0}^{\infty}(n+1)^2P(n+1,t)z^n$$

$$= \left[rz^2-(\mu+r)z+\mu\right]\frac{\partial G}{\partial z} - \frac{r}{K}z\frac{\partial}{\partial z}\left(z\frac{\partial}{\partial z}G(z,t)\right)$$

$$+ \frac{r}{K}\frac{\partial}{\partial z}\left(z\frac{\partial}{\partial z}G\right)$$

$$= \left[rz^2-(\mu+r)z+\mu\right]\frac{\partial G}{\partial z} - \frac{r}{K}z\left(\frac{\partial G}{\partial z} + z\frac{\partial^2 G}{\partial z^2}\right) + \frac{r}{K}\frac{\partial G}{\partial z} + \frac{r}{K}z\frac{\partial^2 G}{\partial z^2}$$

$$\frac{\partial G}{\partial t} = \left[r z^2 - (r+\mu) z + \mu + \frac{r}{K}(1-z) \right] \frac{\partial G}{\partial z} + \underbrace{\frac{r}{K} z(1-z) \frac{\partial^2 G}{\partial z^2}}_{\text{“singular” term if } K\to\infty}$$

$$G(1,t) = 1 \quad , \quad G(z,0) = z^N$$

Backward equation

$$\frac{\partial P(n,t|n_0)}{\partial t} = p_{n_0} P(n,t|n_0+1) - (p_{n_0}+q_{n_0}) P(n,t|n_0) + q_{n_0} P(n,t|n_0-1)$$

$$= r n_0 P(n,t|n_0+1) - \left(r n_0 + \mu\left(1+\frac{r}{\mu}\frac{n_0}{K}\right) n_0\right) P(n,t|n_0) + \mu\left(1+\frac{r}{\mu}\frac{n_0}{K}\right) n_0 P(n,t|n_0-1)$$

Sum over “surviving” states

$$\frac{\partial S(t|n_0)}{\partial t} = r n_0 S(t|n_0+1) - \left(r n_0 + \mu\left(1+\frac{r}{\mu}\frac{n_0}{K}\right) n_0\right) S(t|n_0) + \mu\left(1+\frac{r}{\mu}\frac{n_0}{K}\right) n_0 S(t|n_0-1)$$

mean time:

$$-1 = r n_0 \tau_{n_0+1} - \left(r n_0 + \mu\left(1+\frac{r}{\mu}\frac{n_0}{K}\right) n_0\right) \tau_{n_0} + \mu\left(1+\frac{r}{\mu}\frac{n_0}{K}\right) n_0 \tau_{n_0-1}$$

"$n_0 \to n$"

$$p_n(\underbrace{\tau_{n+1}-\tau_n}_{=\Delta_n}) - q_n(\tau_n-\tau_{n-1}) = -1$$

$p_0 = 0$, because 0 is absorbing

$$p_n\Delta_n = -1 + q_n\Delta_{n-1}\ , \quad \Delta_0 = \tau_1 - \underbrace{\tau_0}_{=0 \text{ from B.C.}}$$

$$p_1\Delta_1 = -1 + q_1\Delta_0 \Rightarrow \Delta_1 = -\frac{1}{p_1} + \frac{q_1}{p_1}\Delta_0$$

$$p_2\Delta_2 = -1 + q_2\left(-\frac{1}{p_1} + \frac{q_1}{p_1}\Delta_0\right) \Rightarrow \Delta_2 = -\frac{1}{p_2} - \frac{q_2}{p_1p_2} + \frac{q_1q_2}{p_1p_2}\Delta_0$$

$$p_3\Delta_3 = -1 + q_3\left(-\frac{1}{p_2} - \frac{q_2}{p_1p_2} + \frac{q_1q_2}{p_1p_2}\Delta_0\right) \Rightarrow \Delta_3 = -\frac{1}{p_3} - \frac{q_3}{p_2p_3} - \frac{q_2q_3}{p_1p_2p_3} + \frac{q_1q_2q_3\Delta_0}{p_1p_2p_3}$$

$$\Delta_n = -\frac{1}{p_n} - \sum_{\ell=1}^{n-1}\frac{1}{p_\ell}\prod_{j=\ell+1}^{n}\left(\frac{q_j}{p_j}\right) + \prod_{j=1}^{n}\left(\frac{q_j}{p_j}\right)\Delta_0 \qquad (n \geq 1)$$

$\searrow \tau_1$

assume reflecting B.C. at a very large L

$$\Delta_L \simeq 0 \Rightarrow +\frac{1}{p_L} + \sum_{\ell=1}^{L-1}\frac{1}{p_\ell}\prod_{j=\ell+1}^{L}\left(\frac{q_j}{p_j}\right) \simeq \underbrace{\prod_{j=1}^{L}\left(\frac{q_j}{p_j}\right)}\Delta_0$$

solve for $\Delta_0 = \tau_1$, then use

$$\tau_n = \sum_{k=0}^{n-1}\Delta_k$$

$$e^{\sum_{j=1}^{L}\ln\left(\frac{\mu(1+\frac{rj}{\mu K})}{r}\right)}$$

<u>work out carefully</u>

$$\approx e^{\int_1^L \ln\left(\frac{\mu}{r}(1+\frac{rx}{\mu K})\right)}$$

"noninteracting"

Multispecies models — multiple species $n_1, n_2, n_3 \ldots$

how does

$P(n_1, n_2, n_3 \ldots t)$ evolve ?

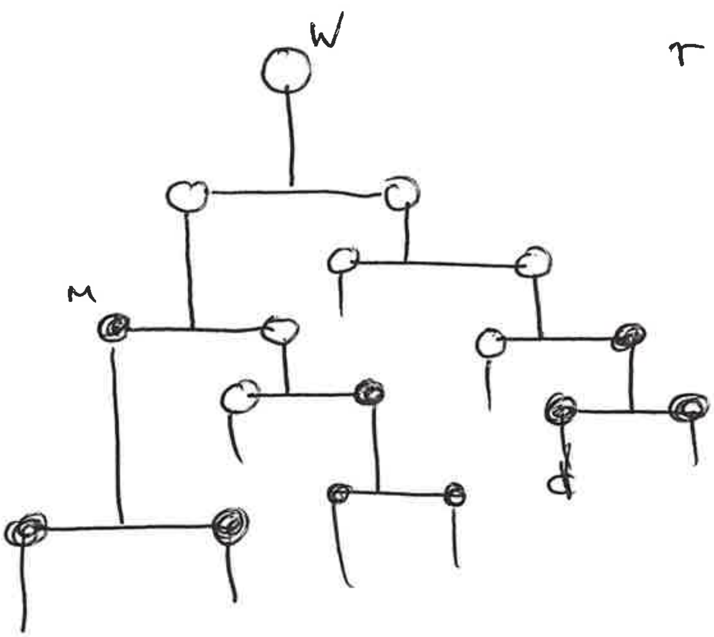
Luria–Delbruck expt/model (1961), fluctuations in mutant population → selection

* Consider two types of cells (bacteria), wild-type and mutant.

* Start with one wild type; each proliferation of wild type can lead to two wild daughters or one wild and one mutant daughter

* mutant proliferation leads to two mutant daughters

* equal proliferation rates r, $\delta \equiv$ prob of mutation



$r(1-\delta)$ = rate of no mutation

$$(W, m) \to (W+1, m)$$

$r\delta$ = rate of mutation

$$(W, m) \longrightarrow (W, m+1)$$

$$r : (W, m) \longrightarrow (W, m+1)$$

$$\frac{dP_{w,m}}{dt} = r(1-\delta)(w-1)P_{w-1,m} + r\delta w P_{w,m-1} + r(m-1)P_{w,m-1}$$
$$- r(m+w)P_{w,m}$$

Can take double generating function

See next page

$$\sum_{m,w} P_{w,m}(t)\, y^w z^m \equiv G(y,z,t),$$ or, use some

intuitive approximations:

for large w, assume $P_{w,m}$ factors

$$\sum_w P_{w,m} \equiv Q_m$$

$$\frac{dQ_m}{dt} = r(1-\delta)\,\mathbb{E}[w|m]\,Q_m + r\delta\,\mathbb{E}[w|m-1]\,Q_{m-1} - r\,\mathbb{E}[w|m]\,Q_m$$
$$+ r(m-1)Q_{m-1} - rmQ_m$$

assume all $\mathbb{E}[w|m] = e^{rt}$

$$\frac{dQ_m}{dt} = r\delta e^{\lambda t}(Q_{m-1} - Q_m) + r(m-1)Q_{m-1} - rmQ_m$$

Solve using generating function $G(z,t) = \sum_{m=0}^{\infty} Q_m z^m$

$$\frac{\partial G(y,z)}{\partial t} = r(1-\delta)y^2\frac{\partial G}{\partial y} + r\delta yz\frac{\partial G}{\partial y} - ry\frac{\partial G}{\partial y}$$

$$+ rz(z-1)\frac{\partial G}{\partial z}$$

$$= \left(r(1-\delta)y^2 + r\delta yz - ry\right)\frac{\partial G}{\partial y} + rz(z-1)\frac{\partial G}{\partial z}$$

$$\frac{dG}{dt} = 0 \quad \text{if} \quad \frac{dy}{dt} = -\left(r(1-\delta)y^2 + r\delta yz - ry\right)$$

$$\text{and} \quad \frac{dz}{dt} = -rz(z-1)$$

$$\frac{\partial G(z,t)}{\partial t} = r\delta e^{\lambda t}(z-1)\,G(z,t) + r\,z(z-1)\frac{\partial G(z,t)}{\partial z}$$

$$\frac{dG}{dt} = \frac{\partial G}{\partial t} + \frac{dz}{dt}\frac{\partial G}{\partial z} = r\delta e^{\lambda t}(z-1)\,G(z,t)$$

$$\frac{dz}{dt} = -rz(z-1) \Rightarrow -rt = \int_{z_0}^{z(t)} \frac{dz'}{z'(z'-1)} = \int\left(\frac{1}{z'-1} - \frac{1}{z'}\right)dz'$$

$$= \ln\left(\frac{z-1}{z_0-1}\right) - \ln\left(\frac{z}{z_0}\right)$$

$$\frac{z-1}{z_0-1}\cdot\frac{z_0}{z} = e^{-rt} \Rightarrow z e^{-rt} = \frac{(z-1)}{(z_0-1)}z_0$$

along these trajectories $\frac{dG}{dt} = r\delta e^{rt}(z(t)-1)\,G$

$$\int\frac{dG}{G} = \int_0^t r\delta e^{rt'}(z(t')-1)\,dt' = \ln(G/G_0)$$

$G_0 \to 1$ because $n=0$ at $t=0$

$$z e^{-rt} - \frac{z z_0}{z_0-1} = -\frac{z_0}{z_0-1} \Rightarrow z\left(e^{-rt} - \frac{z_0}{z_0-1}\right) = -\frac{z_0}{z_0-1}$$

$$z\left((z_0-1)e^{-rt} - z_0\right) = -z_0 \Rightarrow z = \frac{z_0}{z_0-(z_0-1)e^{-rt}}$$

$$z-1 = \frac{(z_0-1)e^{-rt}}{z_0-(z_0-1)e^{-rt}}$$

$$\int_0^t r\delta e^{rt'}(z(t')-1)\,dt' = \int_0^t \frac{r\delta(z_0-1)}{z_0-(z_0-1)e^{-rt'}}\,dt' = \frac{\delta(z_0-1)}{z_0}\ln\left(1+(e^{rt}-1)z_0\right)$$

$$\therefore \quad G(z,t) = \exp\left[\frac{\delta(z_0-1)}{z_0}\ln\left((e^{rt}-1)z_0+1\right)\right] \quad \text{where}$$

$$z_0 = z_0(z,t) \Leftarrow \quad (z_0-1)e^{-rt} = \left(\frac{z-1}{z}\right)z_0$$

$$z_0\left(e^{-rt} - \frac{z-1}{z}\right) = e^{-rt},$$

$$z_0 = \frac{z e^{-rt}}{z e^{-rt} - (z-1)}$$

$$(e^{rt}-1)z_0 = \frac{z e^{-rt}(e^{rt}-1)}{z e^{-rt} - (z-1)} = \frac{z(1-e^{-rt})}{1 - z(1-e^{-rt})}$$

$$(e^{rt}-1)z_0 + 1 = \frac{1}{1 - z(1-e^{-rt})} \; ; \qquad \frac{z_0-1}{z_0} = \frac{e^{rt}(z-1)}{z}$$

$$G(z,t) = \exp\left[-\frac{\delta(1-z)e^{rt}}{z}\ln\left(1 - z(1-e^{-rt})\right)\right]$$

Luria-Delbruck via

2-type branching process:

$$G(z_1, z_2, t) = \sum_{w,m} P(w, m, t)\, z_1^w z_2^m$$

$$G_j(z_1, z_2, t) = z_j \int_t^\infty w_k(z)\, dz + \int_0^t F_k[G(z_1, z_2, t-z)]\, w_k(z)\, dz$$

j is the type of particle which we start with

F is a progeny distribution matrix

$$F_k[z] = \sum_{w=0}^\infty \sum_{m=0}^\infty \underbrace{a^k_{wm}}_{\text{matrix of transition types}} y^w z^m$$

$$G_w(y, z, t) = z \int_t^\infty w(z)\, dz + \int_0^t w(z) \left[(1-\delta) G_w^2(y, z, t-z) + \delta G_w(y, z, t-z) \times G_m(y, z, t-z) \right] dz$$

$$G_m(y, z, t) = z \int_t^\infty w(z)\, dz + \int_0^t w(z)\, G_m^2(y, z, t-z)\, dz$$

(Starts w/ 1 mutant → always mutants → Yule process)

independent of y, only mutants

now, assume $w(z) = re^{-rz}$

$$\frac{dG_m}{dt} = r\,G_m^2(z,t) - r\,G_m(z,t), \qquad G_m(z,0) = z$$

$$\frac{dG_w(y,z,t)}{dt} = r(1-\delta)\,G_w^2 - r\,G_w + r\,\delta\,G_w\,G_m, \qquad G_w(y,z,0) = y$$

Coupled nonlinear equation.

Can solve for $G_m(z,t) = \dfrac{z}{1-(1-z)e^{-rt}}$ first and

plug into $\dfrac{dG_w}{dt}$ equation to find Ricatti.

Notes on Random Sequential Adsorption

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We work out the irreversible binding of k-mers on an infinite discrete lattice.

I. INTRODUCTION

Consider a random sequential adsorption process where particles of length k are irreversibly deposited on a discrete lattice. One way to derive the time evolution of the coverage is to consider the quantity $P(m, k, t)$ defined as the probability that any randomly chosen segment of m contiguous sites is not covered. That is, if one randomly selects m contiguous sites at time t, $P(m, k, t)$ is the probability that none of the m sites are covered by length k particles. For a length L latice, this probability can be measured by scanning a window of m sites across the lattice, one site at a time, and counting the number of times all m sites are uncovered. This number, divided by the numder of sites scanned (the total length) approaches $P(m, k, t)$ as $L \to \infty$.

First, consider the case $m < k$. The effects of deposition of particles of length $k = 4$ on gaps of length $m = 3$ are shown in Fig. 1(a). Within gaps of length k, there is only one way to deposit a length k particle. This deposition destroys $k - m + 1$ gaps of length m. Deposition in larger gaps can also destroy m-gaps by overlapping with them on either end, as shown for gaps of length 5 and 6 in Fig. 1(a).

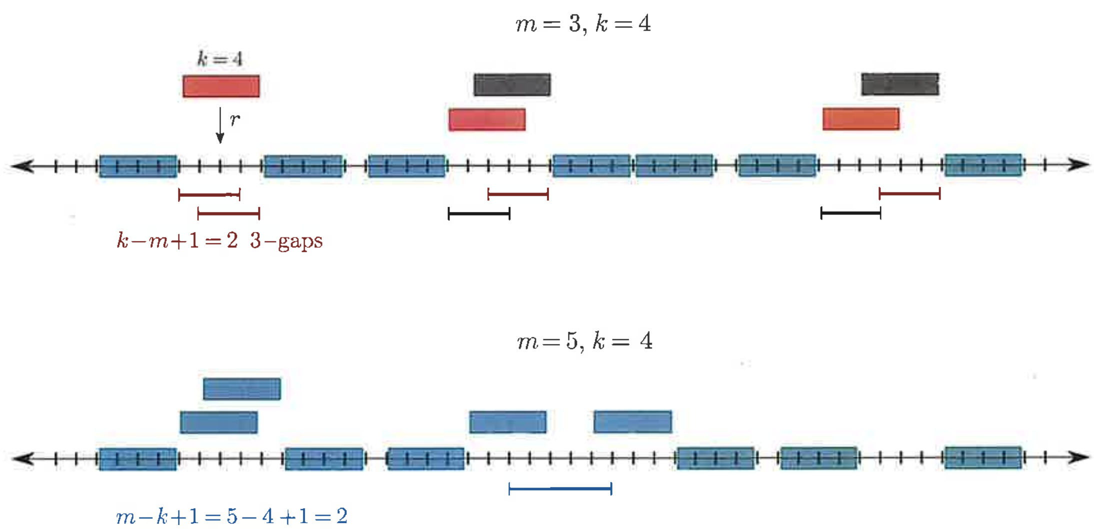

FIG. 1. Gap counts in RSA. (a) For gaps $m < k$, particles that deposite with rate r can destroy gaps in a number of ways. First, for gaps of length k or greater, a depositing particle can destroy $k - m + 1$ m-gaps. For gaps of length $k+1, k+2, ..., k+m-1$, internal gaps of m can be destroyed by partially covering each end of the m-gap. (b) For the case $m \geq k$, there are $m - k + 1$ ways to deposit into an m-gap to destroy it. Larger gaps contains m-gaps within it that can be destroyed by covering either end of the internal m-gaps. How $m = 5$ gaps are destroyed by $k = 4$ particles.

If time is measured in units of $1/r$, the master equation for $P(m < k, k, t)$ is

$$\partial_t P(m, k, t) = -(k - m + 1)P(k, k, t) - 2\sum_{j=1}^{m-1} P(k + j, k, t), \quad m < k. \tag{1}$$

When $m \geq k$, a k-mer can fill it in $m - k + 1$ ways. Within gaps larger than m, internal m-gaps can be destroyed by k-mers overlapping either end of the internal m-gap, as shown in Fig. 1(b) for $m = 5$ and $k = 4$. Therefore,

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$$\partial_t P(m,k,t) = -(m-k+1)P(m,k,t) - 2\sum_{j=1}^{k-1} P(m+j,k,t), \quad m \geq k. \tag{2}$$

The initial condition is an empty lattice $P(m,k,t=0)=1$ for all m,k.

Eq. 2 can be solved by assuming the form

$$P(m,k,t) = e^{-(m-k+1)t}F(k,t), \tag{3}$$

which upon substitution yields

$$\frac{\mathrm{d}F(k,t)}{\mathrm{d}t} = -2\Big(\sum_{j=1}^{k-1} e^{-jt}\Big)F(k,t), \tag{4}$$

which is solved by

$$F(k,t) = \exp\Big[-2\sum_{j=1}^{k-1}\Big(\frac{1-e^{-jt}}{j}\Big)\Big]. \tag{5}$$

Since this holds for $m=k$, and $F(k,t)$ is independent of m, Eq. 1 can be expressed as

$$\frac{\mathrm{d}P(m<k,k,t)}{\mathrm{d}t} = -(k-m-1)e^{-t}F(k,t) - 2e^{-t}\Big(\sum_{j=1}^{m-1} e^{-jt}\Big)F(k,t), \tag{6}$$

where the term $P(k+j,k,t)$ is expressed as $e^{-(k+j-k+1)t}F(k,t) = e^{-jt}e^{-t}F(k,t)$ and $F(k,t)$ is given by Eq. 5. Thus, Eq.!6 can be directly integrated to yield

$$P(m,k,t) = 1 - \int_0^t \Big[(k-m+1) + 2\sum_{j=1}^{m-1} e^{-ju}\Big]e^{-u}F(k,u)\mathrm{d}u. \tag{7}$$

The coverage is defined as

$$\theta(k,t) = 1 - P(1,k,t). \tag{8}$$

For dimers ($k=2$), $F(k,t) = \exp\big[-2+2e^{-t}\big]$ and

$$P(1,2,t) = 1 - 2e^{-2}\int_0^t e^{-u}\exp\big[2e^{-u}\big]\mathrm{d}u = e^{-2(1-e^{-t})}. \tag{9}$$

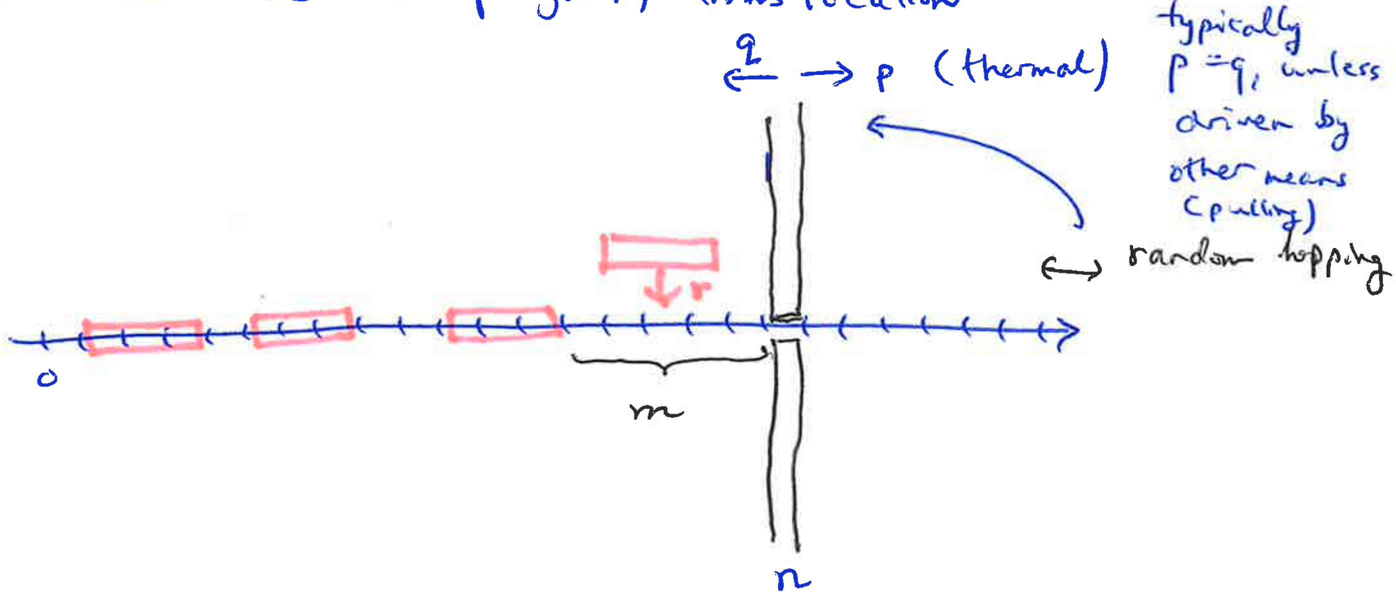
In the $t\to\infty$ limit, we have $P(1,2,\infty) = e^{-2}$ and

$$\theta(k=2,\infty) = 1 - e^{-2} = 0.864665... \tag{10}$$

For the Renyi car parking problem, one can take $k\to\infty$ to find $\theta(k\to\infty, t\to\infty)$.

"Brownian" Ratchet model

protein or nucleic acid (polymer) translocation



Write down master eqn for $P_{m,n}(t)$, the prob. of a first gap of length m when wall is at position n at time t.

$$\frac{d}{dt} P_{m,n} = p\, P_{m-1,n-1} + q\, P_{m+1,n+1} - \left[p + q + r(m-k+1)\,\theta_{m-k}\right] P_{m,n} + r \sum_{j=m+k}^{\infty} P_{j,n}$$

where $\theta_{m-k} = 1$ for $m \geq k$, and zero otherwise

When $m=0$, $$\frac{dP_{0,n}(t)}{dt} = q\, P_{1,n+1} - p\, P_{0,n} + r \sum_{j=k}^{\infty} P_{j,n}$$

Since we are primarily interested in $n(t)$, Marginalize over m:

$$Q_n(t) = \sum_m P_{m,n}(t)$$

Master eqn becomes

$$\frac{dQ_n}{dt} = p\left[Q_{n-1} - Q_n\right] + q\left[Q'_{n+1} - Q'_n\right] \quad \text{because}$$

$$\sum_m r(m-k+1)\, Q_{m-k}\, P_{mn}$$

and $\sum_m r \sum_{j=m+k}^{\infty} P_{j,n}$ cancel precisely

$Q'_n \equiv Q_n - P_{0,n}$ is the probability membrane is at site n and there is there is an empty site before it.

Let's find the mean position

$$\sum_{n=-\infty}^{+\infty} \frac{d}{dt}(n\, Q_n) = p - q \sum_{j=-\infty}^{+\infty} Q'_j \equiv p - q\langle\sigma\rangle$$

$\langle\sigma\rangle = \sum_{j=-\infty}^{+\infty} Q'_j$ = prob site immediately preceding wall is empty

the average velocity is thus $v = p - q\langle\sigma\rangle \leftarrow$ find this?

Sum master eqn $\quad R_m \equiv \sum_{m'=m}^{+\infty} \sum_{n=-\infty}^{+\infty} P_{m',n}(t\to\infty)$

$\boxed{\langle\sigma\rangle \equiv R_1}$ At steady state:

$p + q + r(m-k+1)\, Q.$

for $m \geq k$

$$\frac{dR_m}{dt} = p R_{m-1} + q R_{m+1} - (p+q) R_m$$

$$- r \sum_{j=m}^{\infty} \sum_{n} (j-k+1) P_{j,n} + r \sum_{j=m}^{\infty} \sum_{n=-\infty}^{+\infty}$$

$(m \geq k)$

$$= p R_{m-1} + q R_{m+1} - (p+q) R_m - r \sum_{j=m}^{\infty} (j-k+1) \underbrace{R'_j} + r \sum_{j=m}^{\infty} \sum_{i=j+k} R'_i$$

$$R'_j \equiv \sum_{n=-\infty}^{+\infty} P_{j,n}$$

A B

$$= p R_{m-1} + q R_{m+1} - (p+q) R_m \underbrace{- r(m-k+1) R'_m - r(m-k+2) R'_{m+1} - r(m-k+3) R'_{m+2}} + r \sum_{j=m}^{\infty} (R'_{j+k} + R'_{j+k+1} + \dots)$$

A

$$- r(m-k+1) R'_m - r(m-k+1) R'_{m+1} - r(m-k+1) R'_{m+2} - \dots$$

$$- r R'_{m+1} \qquad - r R'_{m+2} \qquad -$$

$$- r R'_{m+2} \qquad -$$

Since $\sum_{j=m}^{\infty} R'_j \equiv R_m$,

$$- r(m-k+1) R_m - r R'_{m+1} - r R'_{m+2} - r R'_{m+3} - \dots$$

$$- r R'_{m+2} - r R'_{m+2} - \dots$$

A

$$\Rightarrow \boxed{- r(m-k+1) R_m - r R_{m+1} - r R_{m+2} - r R_{m+3} - \dots} \quad - r R'_{m+2} - \dots$$

$$\frac{d}{dt} P_{m,n}(t) = p P_{m-1,n-1} + q P_{m+1,n+1} - (p+q) P_{m,n}$$

$$- r(m-k+1)\underbrace{\theta_{m-k}}\, P_{m,n} + r \sum_{j=m+k}^{\infty} P_{j,n}$$

Enforces minimum gap requirement

$\theta_{m-k} = 1$ if $m \geq k$

$= 0$ if $m < k$

for $m=0$,

$$\boxed{\frac{dP_{0,n}}{dt} = q P_{1,n+1} - p P_{0,n} + r \sum_{j=k}^{\infty} P_{j,n}}$$

Sum equations over $m = [0, \infty)$ and using $Q_n(t) = \sum_{m=0}^{\infty} P_{m,n}(t)$,

$$\Rightarrow \quad \frac{dQ_n}{dt} = p[Q_{n-1} - Q_n] + q[Q'_{n+1} - Q'_n] \quad \text{where } Q'_n \equiv Q_n - P_{0,n}$$

now $\times n$ and sum over n to find the mean,
$(-\infty, \infty)$

$$\frac{d\,\mathbb{E}[N]}{dt} = p - q \underbrace{\sum_{j=-\infty}^{+\infty} Q'_j} \equiv p - q\,\mathbb{E}[M]$$

$\mathbb{E}[M] \equiv$ the probability that site before the wall is empty.

we need to find $\mathbb{E}[M]$ to find how $\mathbb{E}[N]$ behaves.

Now consider the sum $\sum_{j=m}^{\infty} \sum_{n=-\infty}^{+\infty} P_{j,n} \equiv R_m$,

take $\sum_{j=m}^{\infty} \sum_{n=-\infty}^{+\infty} \left[\frac{dP_{j,n}}{dt} = p P_{j-1,n-1} + q P_{j+1,n+1} - (p+q) P_{j,n} \right.$

$$\left. - r(j-k+1)\theta_{j-k} P_{j,n} + r \sum_{i=j+k}^{\infty} P_{i,n} \right]$$

(B) $r\left(R'_{m+k} + R'_{m+k+1} + R'_{m+k+2} + \cdots \right.$

$R'_{m+k+1} + R'_{m+k+2} + \cdots$

$\left. + R'_{m+k+2} + R'_{m+k+3} + \cdots \right)$

$= r R_{m+k} + r R_{m+k+1} + r R_{m+k+2} + \cdots$

(A)+(B): $-r(m-k+1)R_m$

$-rR_{m+1} - rR_{m+2} - rR_{m+3} - \cdots - r\cancel{R_{m+k}} - r\cancel{R_{m+k+1}} - r\cancel{R_{m+k+2}} - \cdots$

$+ r\cancel{R_{m+k}} + r\cancel{R_{m+k+1}} + r\cancel{R_{m+k+2}} + \cdots$

$= -r(m-k+1)R_m - r\sum_{j=m+1}^{m+k-1} R_j$

$\therefore$ for $m \geq k$,

$$\boxed{\frac{dR_m}{dT} = pR_{m-1} + qR_{m+1} - (p+q+r(m-k+1))R_m - r\sum_{j=m+1}^{m+k-1} R_j}$$

for $m < k$, the sum from m to $k-1$ does not include the θ_{m-k} term, thus

$$\frac{dR_m}{dt} = pR_{m-1} + qR_{m+1} - (p+q)R_m - r\sum_{j=k}^{\infty}(j-k+1)R'_j + r\sum_{j=m}^{\infty}\sum_{i=j+k}^{\infty} R'_i$$

$$- r R'_k - 2 R'_{k+1} - 3 R'_{k+2} - \cdots$$

$$+ r \sum_{j=m}^{\infty} \left(R'_{j+k} + R'_{j+k+1} + R'_{j+k+2} + \cdots \right)$$

$$= -r R'_k - r R'_{k+1} - r R'_{k+2} - r R'_{k+3} - \cdots \quad + \quad r R'_{m+k} + r R'_{m+k+1} + \cdots$$

$$- r R'_{k+1} - r R'_{k+2} - r R'_{k+3} - \cdots \quad + r R'_{m+k+1} + r R_{m+k+2} + \cdots$$

$$- r R'_{k+2} - r R'_{k+3} - \cdots$$

$$- r R'_{k+3} - \cdots$$

$$= -r R_k - r R_{k+1} - r R_{k+2} - r R_{k+3} - \cdots \quad \boxed{+ r R_{m+k} + r R_{m+k+1} + r R_{m+k+2} + \cdots}$$

$$= -r R_k - r R_{k+1} - \cdots - \cancel{r R_{k+m}} - \cancel{r R_{k+m+1}} - \cdots$$

$$+ \cancel{r R_{m+k}} + \cancel{r R_{m+k+1}} + \cdots$$

$$= - r \sum_{j=k}^{m+k-1} R_j$$

$$\boxed{\therefore \text{ for } m \le k, \quad \frac{dR_m}{dt} = p R_{m-1} + q R_{m+1} - r \sum_{j=k}^{m+k-1} R_j - (p+q) R_m}$$

We can write all cases in one equation as.

$$\boxed{\frac{dR_m}{dt} = p R_{m-1} - (p+q) R_m + q R_{m+1} - r (m-k+1) \theta_{m-k} R_m - r \sum_{j=\max\{k, m+1\}}^{m-k+1} R_j}$$

Boundary equation $\sum_{n=-\infty}^{+\infty} \left(\frac{d P_{0,n}}{dt} = q P_{1,n+1} - p P_{0,n} + r \sum_{j=k}^{\infty} P_{j,n} \right)$

$$\Rightarrow \frac{d R_0'}{dt} = q R_1' - p R_0' + r \underbrace{\sum_{j=k}^{\infty} R_j'}_{R_k}$$

$$\sum_{j=0}^{\infty} R_j' = R_0' + R_1' + R_2' + \cdots = 1$$

$$R_0' = 1 - \sum_{j=1}^{\infty} R_j' = 1 - R_1$$

$$-\frac{d R_1}{dt} = q R_1' - p(1 - R_1) + r R_k$$

$$1 - R_0' - \sum_{j=2}^{\infty} R_j = 1 - (1 - R_1) - R_2 = R_1 - R_2$$

$$\frac{dR_1}{dt} = q(R_2 - R_1) - p + pR_1 + r R_k$$

$$= (p-q)R_1 - p + r R_k + q R_2$$

Solution for $k=1$

$$R_m = \left(\frac{p}{q}\right)^{m/2} \frac{J_{p/r+q/r+m}\left(\frac{2}{r}\sqrt{pq}\right)}{J_{\frac{p}{r}+\frac{q}{r}}\left(\frac{2}{r}\sqrt{pq}\right)}$$

for $k=2$

$$R_m = \frac{(p/r)^{m/2}}{\left|\frac{q}{r}-1\right|^{m/2}} \frac{Z_{\frac{p}{r}+\frac{q}{r}+m-1}\left(2\sqrt{\frac{p}{r}\left|\frac{q}{r}-1\right|}\right)}{Z_{\frac{p}{r}+\frac{q}{r}-1}\left(2\sqrt{\frac{p}{r}\left|\frac{q}{r}-1\right|}\right)}$$

where $Z_\nu = J_\nu$ for $\frac{q}{r}>1$, and I_ν for $\frac{q}{r}<1$

for $q \to r$, we find $R_m = \dfrac{(p/r)^m\,\Gamma\left(\frac{p}{r}+1\right)}{\Gamma\left(\frac{p}{r}+m+1\right)}$

$\Rightarrow$ (matrix methods for $k \geq 3$)

Note that $E[u] \equiv R_1$

$$\frac{d\,E[u]}{dt} = p - q\,E[u]$$

$$= p - qR_1 \quad \text{(time independent)}$$

$$\therefore \; v = p - qR_1$$

$$= p - q\sqrt{\frac{p}{q}}\, \frac{J_{p/r+q/r+1}\left(\frac{2}{r}\sqrt{pq}\right)}{J_{p/r+q/r}\left(\frac{2}{r}\sqrt{pq}\right)}$$

How does this behave w/ r (depletion rate or chaperone concentration?)

assume $p=q$, we need to evaluate $\dfrac{J_{\nu+1}}{J_\nu}$, $\nu = \frac{2p}{r} \to \infty$ as $r \to 0$

$$J_{\nu+1}(z) = \frac{\nu}{z} J_\nu(z) - \frac{\partial J_\nu(z)}{\partial z}, \quad \text{and} \quad J_\nu(\nu) \xrightarrow[\nu\to\infty]{} \frac{2^{1/3}}{3^{2/3}\Gamma(\frac{2}{3})\nu^{1/3}}$$

$$R_1 = \frac{J_{\frac{2\rho}{r}+1}\left(\frac{2\rho}{r}\right)}{J_{\frac{2\rho}{r}}\left(\frac{2\rho}{r}\right)} = 1 - \left.\frac{\partial \ln J_\nu(z)}{\partial z}\right|_{z=\frac{2\rho}{r}} \sim 1 - \frac{3^{1/3}\Gamma(\frac{2}{3})}{\Gamma(\frac{1}{3})}\left(\frac{r}{\rho}\right)^{1/3}$$

as $\left(\frac{\rho}{r}\right) \to \infty$

$$\therefore \quad \boxed{v = p(1-R_1) \sim 3^{1/3}\frac{\Gamma(\frac{2}{3})}{\Gamma(\frac{1}{3})} p^{2/3} r^{1/3}}$$

but linear in r! (concentration)

very much nonlinear response even though equations are linear.

<u>physical intuition</u>

τ time between successive depositions

$$\tau = \frac{1}{r\,X(\tau)} \; ; \quad X(\tau) \sim \text{distance between proteins.}$$

from diffusion $X(\tau) \simeq \sqrt{p\tau}$
$(p=q)$

$$\therefore \quad \tau \sim \frac{1}{r\sqrt{p\tau}}, \quad \text{then } v \sim \frac{X(\tau)}{\tau} \simeq \frac{\sqrt{p\tau}}{\tau}$$

$$\Downarrow \qquad\qquad \simeq \frac{\sqrt{p}}{\sqrt{\tau}}$$

$$\sqrt{p}\,\tau^{3/2} \simeq \frac{1}{r} \qquad\qquad \simeq \boxed{r^{1/3}p^{2/3}}$$

$$\tau \sim \frac{r^{-2/3}}{p^{1/3}}$$

For $r \gg p, q$

$$v = \frac{p k \left(\frac{q}{p} - 1\right)^2}{\frac{q}{p}\left[\left(\frac{q}{p}\right)^k - 1\right] + k\left[1 - \frac{q}{p}\right]}$$

for $p = q$, $\quad v = \frac{2p}{k+1}$

$$D = \frac{2p}{3}\left(\frac{k^2 + k + 1}{(k+1)^2}\right)$$

2 competing populations n_1, n_2 (we covered this in 201)

Birth-death with interactions:

(n_1, n_2) is the state, and $P(n_1, n_2, t)$ obeys a master equation

$$\frac{d}{dt}P(n_1,n_2,t) = \overset{\times((n-1))}{r_1(n_1-1,n_2)}\,P(n_1-1,n_2) + \overset{\times(n_2-1)}{r_2(n_2-1,n_1)}\,P(n_1,n_2-1)$$

$$- (r_1^{n_1} + r_2^{n_2} + \mu_1^{n_1} + \mu_2^{n_2})\,P(n_1,n_2,t)$$

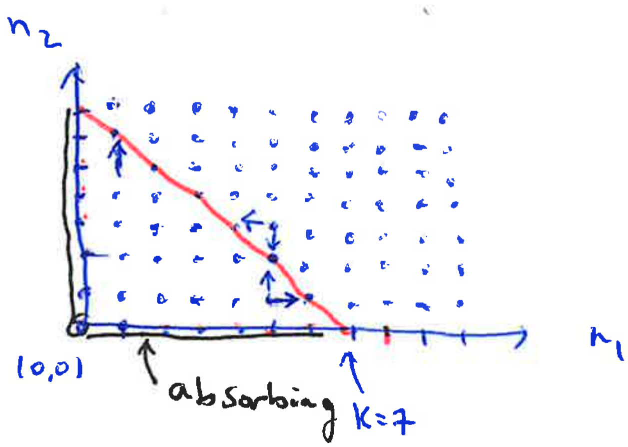
$$+ (n_1+1)\mu_1(n_1+1,n_2)\,P(n_1+1,n_2)$$

$$+ (n_2+1)\mu_2(n_2+1;n_1)\,P(n_1,n_2+1)$$

carrying capacity in birth model

$$r_1(n_1-1,n_2) = r_1\left(1 - \frac{n_1-1}{K_{11}} - \frac{n_2}{K_{12}}\right)$$

$$r_2(n_2-1,n_1) = r_2\left(1 - \frac{n_1}{K_{21}} - \frac{n_2-1}{K_{22}}\right), \quad \mu_1 \text{ and } \mu_2 \text{ constants}$$



$$\frac{dP(0,n_2)}{dt} = r_2(n_2-1)\,P(0,n_2-1)$$

$$+ \mu_1 P(1,n_2)$$

$$+ \mu_2 P(0,n_2+1)$$

$n_1=0$ are absorbing states.

$$\frac{dP(n_1,0)}{dt} = -\mu_2 P(n_1,1) + \mu_1 P(n_1+1,0) + r_1(n_1-1)\,P(n_1-1,0)$$

$n_2=0$ are also absorbing

$$\frac{dP(0,0,t)}{dt} = \mu_1 P(1,0) + \mu_2 P(0,1)$$

---

assume "neutral" limit where $K_{11} = K_{12} = K_{21} = K_{22} \equiv K$,

if $n_1 + n_2 = k$ (on the nullcline line)

$$r_1(n_1 - 1) = r_1\left(1 - \frac{n_1 - 1 + n_2}{k}\right)(n_1 - 1)$$

$$= r_1\left(\frac{1}{k}\right)(n_1 - 1)$$

$$r_2(n_2 - 1) = r_2\left(1 - \frac{n_2 - 1}{k} - \frac{n_1}{k}\right)(n_2 - 1)$$

$$= r_2\left(\frac{1}{k}\right)(n_2 - 1)$$

rates into nullcline "faster" than rates out.

other than absorbing boundaries (signifying extinction of one or both species),

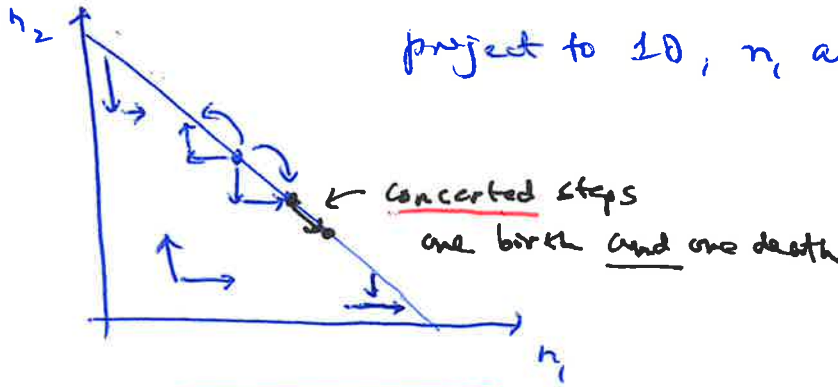
the nullcline $n_1 + n_2 = K$ is most probable.
$\equiv N$

$\therefore$ restrict the dynamics to the states $n_1 + n_2 = N \Rightarrow$ projection to a 1D problem, $n_2 = N - n_1$ always

type 1 birth $n_1 \to n_1 + 1$, but a type 2 birth <u>must</u> decrease n_1 $(n_1 \to n_1 - 1)$

For the $r(1-\frac{n}{K})$ carrying capacity model, $n_1+n_2=N$ is fast,

while n_1/N is slow



project to 1D, n_1 and $\underline{n_2 \simeq N-n_1}$

require small fluctuations in N to move along nullcline.

Moran Model — continuous version of Wright-Fisher

Standard approximation — assume each birth is followed by a death to keep N constant.

at each timestep dt, there is a probability of selecting type i for birth and type j for death.

prob. of selecting type 2 : $\frac{n_2}{N} = \frac{N-n_1}{N}$, prob of selecting type 1 to die $= \frac{n_1}{N}$

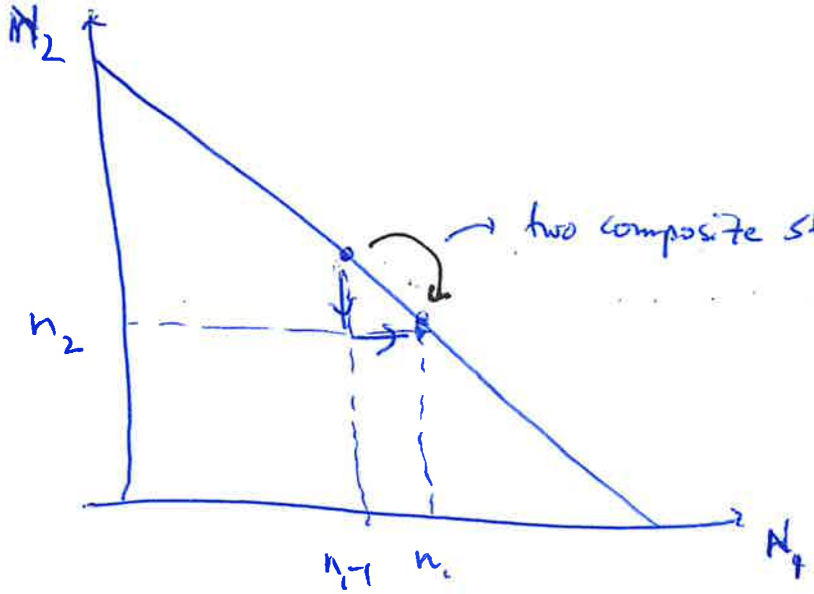
the rate of $n_2 \to n_2+1 = \beta_2 \frac{n_2}{N}\frac{(N-n_1)}{N} \equiv w_2(n) \sim x(1-x)$ if $x=\frac{n_1}{N}$

Similarly rate of $n_1 \to n_1+1 = \beta_1 \frac{n_1}{N}\frac{(N-n_1)}{N} = w_1(n)$

$$\frac{dP(n,t)}{dt} = w_1(n_{-1})\cdot P(n_{-1}) - (w_1(n)+w_2(n))P(n) + w_2(n+1)P(n+1)$$

This derivation is heuristic — how to formally relate β to r, μ?

Another approach/approximation



two composite steps $(n_2+1, n_1-1) \to (n_2, n_1-1)$

$(n_2, n_1-1) \to (n_2, n_1)$

$$(n_2+1, n_1-1) \to (n_2, n_1-1) \; : \quad \mu_2 (n_2+1) = \mu_2 (N-(n_1-1))$$

$$(n_2, n_1-1) \to (n_2, n_1) \; : \quad r_1 \left(1 - \frac{n_1-1}{N} - \frac{n_2}{N}\right)(n_1-1)$$

$$= \frac{r_1}{N}(n_1-1)$$

time to make composite step $\tau \simeq \tau_2 + \tau_1 = \dfrac{1}{\mu_2(N-(n_1-1))} + \dfrac{1}{\frac{r_1}{N}(n_1-1)}$

$\therefore$ typical rate $\omega_1(n-1) \approx \dfrac{1}{\tau}$

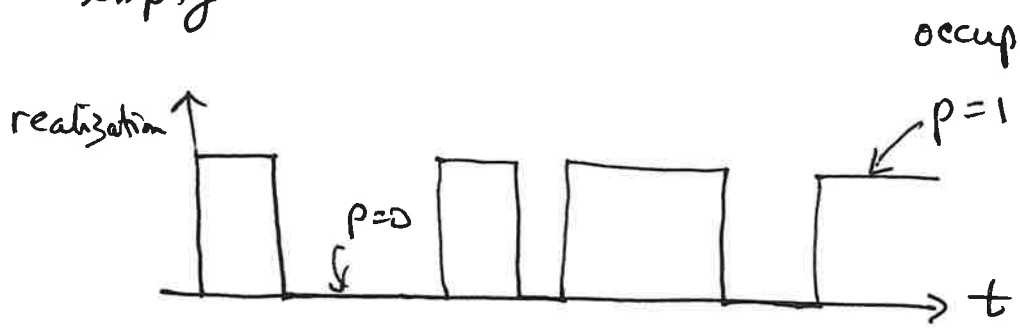
$$= \frac{1}{\dfrac{1}{\mu_2(N-(n_1-1))} + \dfrac{1}{\frac{r_1}{N}(n-1)}} = \frac{r_1 (n-1)}{N r_1 (n-1) + N\mu_2(\quad)}$$

Single receptor statistics

Cell wants to measure outside molecule concentration c

for e.g., chemotaxis

Consider single receptor that can be bound by ligand or empty



define $p(t)$ as the probability of occupancy

$$\dot{p} = k_+ c(1-p) - k_- p$$

binding rate (k_+); dissociation probability / time (rate) (k_-)

at steady-state, $\bar{p} = \dfrac{c}{c+K}$, $K \equiv k_-/k_+$ (mean occupancy is a function of c)

However, a cell can measure occupancy for a finite time T,

$$p_T = \frac{1}{T}\int_{t_1}^{t_1+T} p(t')\,dt' \neq \bar{p}$$

measure p_T, and infer c.

Uncertainty in c: $\left(\frac{\delta c}{c}\right)^2 = \frac{1}{c^2}\left(\frac{dc}{dp}\right)^2 (\delta p)^2$

(coeff. of variation in the inferred c)

relate to uncertainty in p

averaging over many measurements

$$\left\langle \left(\frac{\delta c}{c}\right)^2 \right\rangle = \frac{1}{c^2}\left(\frac{dc}{dp}\right)^2 \langle \delta p^2 \rangle$$

$\langle \delta p^2 \rangle = \langle (p_T - \bar{p})^2 \rangle$ (variation in determining/estimating $\bar{p}$)

$G(\tau) \equiv \langle p(t)\, p(t+\tau) \rangle \equiv$ autocorrelation function

$$\langle p_T^2 \rangle \equiv \left\langle \frac{1}{T^2} \int_{t_1}^{t_1+T} dt' \int_{t_1}^{t_1+T} dt \; p(t')\, p(t) \right\rangle$$

$$= \frac{1}{T^2} \int_0^T dt' \int_0^T dt \; G(t'-t)$$

How to determine G? $p(t)\, p(t+\tau)$ is 1 only if $p(t) = 1$ <u>and</u> $p(t+\tau) = 1$

otherwise $G = 0$

$\therefore$ # of $(1,1)$'s in N measurements $= N G(\tau)$

for $\tau \to \tau + d\tau$, $k_- N G\, d\tau$ is the number of $(1,1) \to (1,0)$

of $(1,0)$s: $\underbrace{N\bar{p}}_{\text{average \# of 1}} - \overbrace{NG}^{\#\text{ of }(1,1)}$, in $d\tau$, $k_+(\bar{p} - G) N\, d\tau$

$\Rightarrow$ # of $(1,0) \xrightarrow[d\tau]{} (1,1)$

We want $\langle p_T^2 \rangle = \left\langle \frac{1}{T^2} \int_{t_1}^{t_1+T} dt' \int_{t_1+T}^{t_1+T} dt \; p(t)\, p(t') \right\rangle$

$$= \frac{1}{T^2} \int_0^T dt' \int_0^T dt \; G(t'-t) \qquad G(\tau) = G(-\tau)$$

How to determine G?

$p(t)\,p(t+\tau)$ is 1 only if $p(t) = 1$ and $p(t+\tau) = 1$

\# of 1,1's in N measurements : $N\,G(\tau)$

for $\tau \to \tau + d\tau$ $\quad k_- N G\, d\tau \quad$ 1, 1's $\longrightarrow$ 1, 0

\# of 1, 0's : $\underbrace{N\bar{p}}_{\text{all } 1,x} - \underbrace{NG}_{\#\text{ of } 1,1}$ in $d\tau$ $\quad N(\bar{p} - G)\, k_+\, d\tau$

1, 0's $\longrightarrow$ 1, 1

$$k_+(1-\bar{p}) = k_- \bar{p}$$

$$\therefore \quad \frac{dG}{d\tau} = -k_- G + k_- (\bar{p} - G) \frac{\bar{p}}{1-\bar{p}}, \quad G(0) = \bar{p}$$

$$\Rightarrow \quad G(\tau) = \bar{p}^2 + \bar{p}(1-\bar{p}) \exp\left[- \frac{k_- |\tau|}{(1-\bar{p})} \right]$$

$$\langle p_T^2 \rangle - \bar{p}^2 = \frac{2}{T} \frac{\bar{p}(1-\bar{p})^2}{k_-}$$

since $\bar{p}$ is determined at steady-state $\quad k_+(1-\bar{p}) = k_-\bar{p}$

$$\therefore \quad \frac{dG}{d\tau} = -k_- G + k_-(\bar{p} - G)\frac{\bar{p}}{1-\bar{p}} \qquad \Rightarrow k_+ = \frac{k_-\bar{p}}{1-\bar{p}}$$

$G(0) = \bar{p}$ (pick any initial time after the system has reached steady state)

$$\therefore \quad G(\tau) = \bar{p}^2 + \bar{p}(1-\bar{p})\exp\left[-\frac{k_-|\tau|}{1-\bar{p}}\right]$$

and $$\langle p_T^2 \rangle - \bar{p}^2 = \frac{2}{T} \cdot \frac{\bar{p}(1-\bar{p})^2}{k_-}$$

$$\left\langle \left(\frac{\delta c}{c}\right)^2 \right\rangle = \frac{1}{c^2}\left(\frac{c^2}{\bar{p}^2(1-\bar{p})^2}\right) \cdot \frac{2\bar{p}(1-\bar{p})^2}{T k_-} = \frac{2}{T\bar{p}k_-}$$

now assume on-rate is to a perfectly absorbing disk of radius s:

$$\left. k_-\bar{p} = \underbrace{k_+}_{4Dsc}(1-\bar{p}) \right\} \Rightarrow k_- = 4Dsc\left(\frac{1-\bar{p}}{\bar{p}}\right)$$

$$\left\langle \left(\frac{\delta c}{c}\right)^2 \right\rangle = \frac{1}{2TDsc(1-\bar{p})}$$

limit of detection of concentration improves for longer T, larger c, and smaller $\bar{p}$.

Extensions: multiple, correlated receptors,
receptor clustering and cooperativity
spatial structure and dynamic $c(\vec{r}, t)$

$$\left(\frac{\delta c}{c}\right)^2 = \frac{1}{c^2}\underbrace{\left(\frac{c^2}{\bar{p}^2(1-\bar{p})^2}\right)}_{\left(\frac{dp}{dc}\right)^{-2}} \cdot \frac{2\bar{p}(1-\bar{p})^2}{T k_-} = \frac{2}{T\bar{p}k_-}$$

Now use $k_-\bar{p}$ = on-rate = perfect absorbing disk

$$\underbrace{4Dsc}_{\sim k_+}(1-\bar{p})$$

$$k_- = 4Ds\,c\left(\frac{1-\bar{p}}{\bar{p}}\right)$$

$$c \to \frac{K\bar{p}}{1-\bar{p}}$$

$$= 4DsK$$

$$\left(\frac{\delta c}{c}\right)^2 \simeq \frac{1}{2TDsc(1-\bar{p})}$$ limit of detection of conc.

<u>Extensions:</u> multiple, correlated receptors

receptor clustering and cooperativity

spatial/diffusion correlations in $c(\vec{r},t)$

Upshot: small bacteria have a hard time measuring small differences in conc. over $1\,\mu m$

nearly same conc. + noise $(\delta c)^2$