§8 From discrete to continuum models

8.1 Population growth models

8.1.1 Exponential growth

$P_n(t) = \mathbb{P}($ n individuals in the population at time t, given N_0 individuals at time 0 $)$

Individuals - constant proliferation rate $b > 0$
[units eg. s^{-1}]

For each individual:

$\mathbb{P}($proliferates once in $[t, t+dt)) = b\,dt + o(dt^2)$

$\mathbb{P}($doesn't proliferate in $[t, t+dt)) = 1 - b\,dt + o(dt^2)$

$\mathbb{P}($proliferates more than once in $[t, t+dt)) = o(dt^2)$.

$$P_n(t+dt) = P_n(t)\left[1 - bn\,dt\right] + P_{n-1}(t).(n-1)b\,dt + o(dt^2).$$

↗ discrete conservation equation.

$$\frac{P_n(t+dt) - P_n(t)}{dt} = (n-1)b\,P_{n-1}(t) - nb\,P_n(t)$$

lim $dt \to 0$: $\boxed{\frac{dP_n}{dt} = (n-1)b\,P_{n-1} - nb\,P_n}$

MASTER EQUATION

$$\boxed{\frac{dP_{N_0}}{dt} = -bN_0\,P_{N_0}(t)}$$

Initial conditions $P_n(0) = \begin{cases} 1 & n = N_0 \\ 0 & \text{o/w} \end{cases}$

$$\left(P_n(t) \equiv 0 \quad \text{if } n < N_0 \right)$$

Evolution of the moments

$\hat{n} = n-1$

$$\frac{d}{dt} \sum_{n=0}^{\infty} n P_n(t) = \sum_{n=0}^{\infty} n(n-1) b P_{n-1}(t) - \sum_{n=0}^{\infty} n^2 b P_n(t)$$

$$\frac{d}{dt}\langle n(t) \rangle = \frac{dM}{dt}$$

$$= \sum_{\hat{n}=0}^{\infty} b \hat{n}(\hat{n}+1) P_{\hat{n}}(t) - \sum_{n=0}^{\infty} n^2 b P_n(t)$$

$$= b \sum_{n=0}^{\infty} n P_n(t)$$

$$= bM$$

ie $\frac{dM}{dt} = bM \Rightarrow \boxed{M(t) = N_0 e^{bt}}$

Variance: $V(t) = \langle n^2 \rangle - \langle n \rangle^2$

$\hat{n} = n-1$

$$\frac{d}{dt} \sum_{n=0}^{\infty} n^2 P_n(t) = \sum_{n=0}^{\infty} b n^2 (n-1) P_{n-1} - \sum_{n=0}^{\infty} b n^3 P_n$$

$$= \sum_{\hat{n}=0}^{\infty} b \hat{n}(\hat{n}+1)^2 P_{\hat{n}} - \sum_{n=0}^{\infty} b n^3 P_n$$

$$= \sum_{n=0}^{\infty} b\left(\cancel{n^3} + 2n^2 + n - \cancel{n^3}\right) P_n$$

$$= 2b\langle n^2\rangle + bM$$

$$\frac{dV}{dt} = \frac{d}{dt}\langle n^2\rangle - 2\langle n\rangle \frac{d\langle n\rangle}{dt}$$

$$\frac{dM}{dt} = bM$$

$$= 2b\langle n^2\rangle + bM - 2bM^2$$

$$= 2bV + bM$$

$$= 2bV + bN_0 e^{bt}$$

$$\Rightarrow \boxed{V(t) = N_0 e^{bt}\left(e^{bt} - 1\right)}$$

<u>Generating functions</u> $\quad G: [-1,1] \times [0,\infty) \to \mathbb{R}$

$$G(s,t) = \sum_{n=0}^{\infty} P_n(t)\, s^n$$

$$M(t) = \frac{\partial G}{\partial s}(1,t), \quad V(t) = \frac{\partial^2 G}{\partial s^2}(1,t) + M(t) - M^2(t).$$

multiply the master eqn by s^n and sum:

$$\frac{\partial G}{\partial t} = \sum_{n=0}^{\infty} \frac{dP_n}{dt} s^n = b\left[\sum_{n=0}^{\infty} (n-1) P_{n-1} s^n - \sum_{n=0}^{\infty} n P_n s^n\right]$$

$$= b\left[\sum_{n=0}^{\infty} n P_n s^{n+1} - \sum_{n=0}^{\infty} n P_n s^n\right]$$

$$\frac{\partial G}{\partial t} = b\Big[\underbrace{s^2 \sum_{n=0}^{\infty} n p_n s^{n-1}}_{\frac{\partial G}{\partial s}} - s\underbrace{\sum_{n=0}^{\infty} n p_n s^{n-1}}\Big]$$

$$\therefore \boxed{\frac{\partial G}{\partial t} = bs(s-1)\frac{\partial G}{\partial s}} \qquad G(s,0) = s^{N_0}$$

characteristic eqns : $\frac{dt}{d\tau} = 1$, $\frac{ds}{dt} = -bs(s-1)$,

$$\frac{\partial G}{\partial \tau} = 0$$

data : $t(z,0) = 0$, $s(z,0) = z$, $G(z,0) = z^{N_0}$

$|z| \le 1.$

$t = \tau + \cancel{A(z)}$

$G = c(z) = z^{N_0}$

$$\frac{ds}{d\tau} = -bs(s-1)$$

$$\Rightarrow \int \frac{1}{s(s-1)}\,ds = -b\tau + B(z)$$

$$= -\int \left(\frac{1}{s} - \frac{1}{s-1}\right) ds = \ln\left(\frac{s-1}{s}\right)$$

$\tau = 0 \qquad B(z) = \ln\left(\frac{z-1}{z}\right)$

substitute

$$\Rightarrow \quad z = \frac{se^{-b\tau}}{se^{-b\tau} - (s-1)} = \frac{s}{s-(s-1)e^{b\tau}}$$

$$\therefore \quad G(s,t) = \left(\frac{s}{s-(s-1)e^{bt}} \right)^{N_0} = \left(\frac{se^{-bt}}{1-(1-e^{-bt})s} \right)^{N_0}$$

Generating fn of negative binomial.

ie $\quad P_n(t) \sim NB(N, p)$

$N = N_0 \qquad p = e^{-bt}$

<u>verify</u>

$$m(t) = N_0 e^{bt}$$

$$v(t) = N_0 (e^{bt} - 1) e^{bt}$$

8.1.2 A stochastic model of logistic growth

Assume popⁿ of n individuals

$$\mathbb{P}(\text{a birth in } [t, t+dt)) = \lambda_n dt + O(dt^2)$$

$$\mathbb{P}(\text{a death in } [t, t+dt)) = \mu_n dt + O(dt^2)$$

$$\mathbb{P}(\text{no births or deaths in } [t, t+dt)) = 1 - (\lambda_n + \mu_n) dt + O(dt^2)$$

$$\mathbb{P}(\text{more than one birth or death in } [t, t+dt)) = O(dt^2)$$

Discrete conservation equations

$$P_n(t+dt) = \lambda_{n-1} dt\, P_{n-1}(t) + (1 - \lambda_n dt - \mu_n dt) P_n(t) + \mu_{n+1} dt\, P_{n+1}(t)$$

(MASTER EQN)

$$\Rightarrow \quad \frac{dP_n}{dt} = \lambda_{n-1} P_{n-1}(t) - (\lambda_n + \mu_n) P_n(t) + \mu_{n+1} P_{n+1}(t).$$

specify : $P_{-1}(t) \equiv 0$.

initial conditions

$$P_n(0) = \begin{cases} 1 & n = N_0 \\ 0 & \text{o/w}. \end{cases}$$

Evolution of the mean

$$\frac{d}{dt} \sum_{n=0}^{\infty} n P_n(t) = \sum_{n=0}^{\infty} \lambda_{n-1} n P_{n-1}(t) - \sum_{n=0}^{\infty} (\lambda_n + \mu_n) n P_n(t) + \sum_{n=0}^{\infty} \mu_{n+1} n P_{n+1}(t)$$

$\tilde{n} = n - 1$

$\hat{n} = n + 1$

$$= \sum_{n=0}^{\infty} (n+1)\lambda_n p_n - \sum_{n=0}^{\infty} (\lambda_n + \mu_n) n p_n + \sum_{n=0}^{\infty} (n-1)\mu_n p_n$$

$$\frac{dM}{dt} = \sum_{n=0}^{\infty} \lambda_n p_n - \sum_{n=0}^{\infty} \mu_n p_n$$

Assume: $\lambda_n = \begin{cases} b_1 n + b_2 n^2 & n > 0 \\ 0 & n = 0 \end{cases}$

$$\mu_n = \begin{cases} d_1 n + d_2 n^2 & n > 0 \\ 0 & n = 0 \end{cases}$$

$$\frac{dM}{dt} = (b_1 - d_1) M + (b_2 - d_2) \langle n^2 \rangle$$

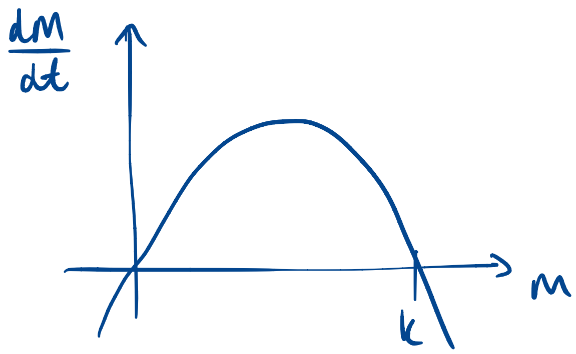
$\uparrow \sum_{n=0}^{\infty} n^2 p_n(t)$.

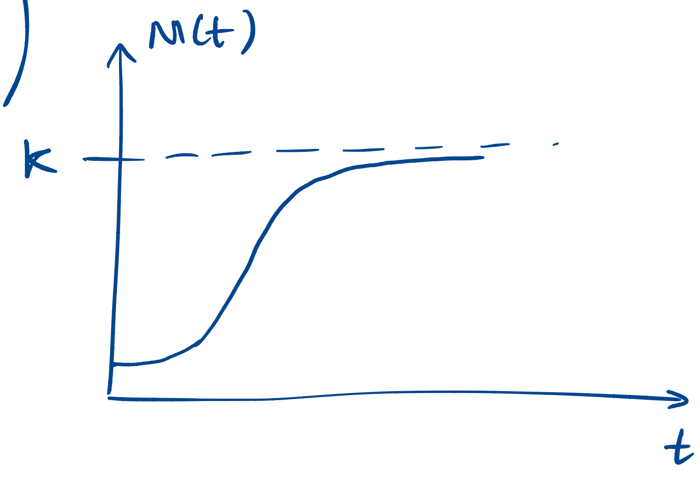
Moment closure approximation : $\langle n^2 \rangle = M^2 \; (= \langle n \rangle^2)$

$$\therefore \frac{dM}{dt} = (b_1 - d_1) M + (b_2 - d_2) M^2$$

$$= \underbrace{(b_1 - d_1)}_{r} M \left(1 - \underbrace{\frac{(d_2 - b_2)}{(b_1 - d_1)}}_{= \frac{1}{K}} M \right)$$

$$= rM \left(1 - \frac{M}{K} \right)$$





$$\frac{d}{dt}\langle n^2\rangle = (b_1+d_1)m + \{2(b_1-d_1) + (b_2+d_2)\}\langle n^2\rangle + 2(b_2-d_2)\langle n^3\rangle .$$

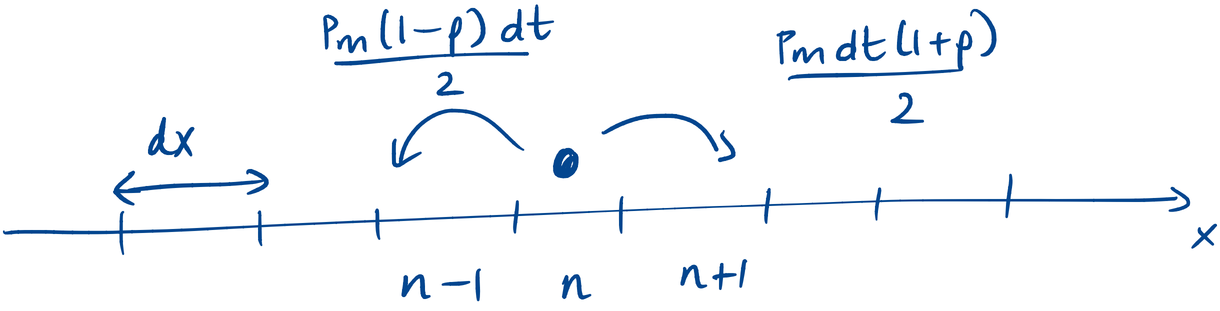
not closed.

Need a moment closure approx. to make progress.

8.2 Individual-based models for cell motility

8.2.1 A simple model of biased cell motility

$[t, t+dt)$



P_m – movement rate

$\Rightarrow \quad P_m\,dt \;=$ probability cell jumps left or right in $[t, t+dt)$

$$\mathbb{P}(\text{right}) = \frac{1+p}{2}, \quad \mathbb{P}(\text{left}) = \frac{1-p}{2}$$

$$p_n(t) = \mathbb{P}(\text{particle at site } n \text{ at time } t)$$

$$p_n(t+dt) = \tfrac{1}{2}(1+p)P_m\,dt\,p_{n-1}(t) - (1-P_m\,dt)\,p_n(t) + \tfrac{1}{2}(1-p)P_m\,dt\,p_{n+1}(t)$$

Want to relate $p_n(t)$ with $p(x,t)$

$$p_n(t) = p(n\,dx, t)$$

$$\frac{p(ndx,t+dt)-p(ndx,t)}{dt} = \frac{1}{2}(1+\rho)P_m\, p((n-1)dx,t)$$
$$- P_m\, p(ndx,t)$$
$$+ \frac{1}{2}(1-\rho)P_m\, p((n+1)dx,t)$$

LHS

$$\frac{\cancel{p(ndx,t)} + \cancel{dt}\frac{\partial p}{\partial t}(ndx,t) + o(dt^{\cancel{2}}) - \cancel{p(ndx,t)}}{dt}$$

$$= \frac{\partial p}{\partial t}(ndx,t) + O(dt).$$

RHS

$$p((n\pm 1)dx,t) = p(ndx,t) \pm dx\frac{\partial p}{\partial x}(ndx,t)$$

substitute

$$+ \frac{1}{2}dx^2\frac{\partial^2 p}{\partial x^2}(ndx,t)$$
$$+ O(dx^3)$$

$$\frac{\partial p}{\partial t} + o(dt) = \underbrace{\left(\frac{1}{2}(1+\rho)P_m - P_m + \frac{1}{2}(1-\rho)P_m\right)}_{=0} p$$
$$+ \left(-\frac{1}{2}(\cancel{1}+\rho)P_m + \frac{1}{2}(\cancel{1}-\rho)P_m\right)dx\frac{\partial p}{\partial x}$$
$$+ \left(\frac{1}{4}(1+\cancel{\rho})P_m + \frac{1}{4}(1-\cancel{\rho})P_m\right)dx^2\frac{\partial^2 p}{\partial x^2}$$
$$+ O(dx^3)$$

Take the limit $dx, dt \to 0$:

$$\frac{\partial p}{\partial t} = D \frac{\partial^2 p}{\partial x^2} - v \frac{\partial p}{\partial x}$$

advection-diffusion PDE

$$D = \lim_{dx \to 0} \frac{P_m dx^2}{2} \qquad P_m \sim \frac{1}{dx^2}$$

$$v = \lim_{dx \to 0} P_m \, p \, dx \qquad p \sim dx$$

$$P(x, 0) = p^0(x)$$

① $p = 0$: $v = 0$ $\quad \frac{\partial p}{\partial t} = D \frac{\partial^2 p}{\partial x^2}$ (diffusion eqn.)

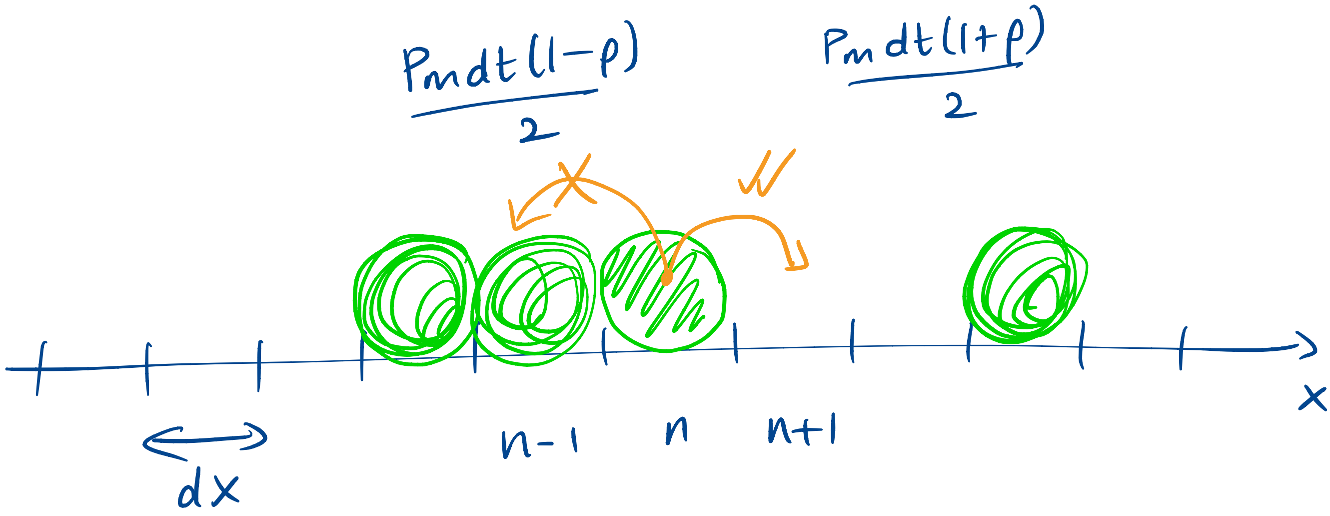
② units of $P_m = s^{-1}$
$dx = m$

} units of D are $m^2 s^{-1}$ ✓✓

p = non-dimensional

$\Rightarrow$ units of v are ms^{-1} ✓✓

8.2.2 A model of biased cell motility with competition for space



$$P(A_n, t) = \mathbb{P}(\text{cell in site } n \text{ at time } t)$$

$$P(O_n, t) = \mathbb{P}(\text{site } n \text{ empty at time } t)$$
$$= 1 - P(A_n, t).$$

$$P(A_n, O_m, t) = \mathbb{P}(\text{site } n \text{ occupied, } + \text{ site } m \text{ empty at time } t)$$

$$\begin{aligned}
P(A_n, t+dt) - P(A_n, t) = & \tfrac{1}{2}(1+\rho) P_m dt\, P(A_{n-1}, O_n, t) \\
& - \tfrac{1}{2}(1-\rho) P_m dt\, P(O_{n-1}, A_n, t) \\
& + \tfrac{1}{2}(1-\rho) P_m dt\, P(O_n, A_{n+1}, t) \\
& - \tfrac{1}{2}(1+\rho) P_m dt\, P(A_n, O_{n+1}, t) \\
= & \frac{P_m}{2} dt \left[P(A_{n-1}, O_n, t) - P(O_{n-1}, A_n, t)\right] \\
& + \frac{P_m}{2} dt \left[P(O_n, A_{n+1}, t) - P(A_n, O_{n+1}, t)\right] \\
& + \frac{P_m}{2} \rho\, dt \left[P(A_{n-1}, O_n, t) - P(O_{n-1}, A_n, t)\right] \\
& - \frac{P_m}{2} \rho\, dt \left[P(O_n, A_{n+1}, t) - P(A_n, O_{n+1}, t)\right]
\end{aligned}$$

For the terms w/o ρ: use conservation statements of the form:

$$p(A_n, A_m, t) + p(A_n, O_m, t) = p(A_n, t)$$

Substitute into {

$$\Rightarrow \quad \frac{P_m}{2} dt \left[p(A_{n-1}, t) - 2p(A_n, t) + p(A_{n+1}, t) \right]$$

For the terms with ρ: need an approximation to close the system:

$$\left\{ \begin{aligned} p(A_n, O_{n\pm 1}, t) &= p(A_n, t)\, p(O_{n\pm 1}, t) \\ &= p(A_n, t)\left[1 - p(A_n, t)\right]. \end{aligned} \right.$$

MEAN-FIELD APPROXIMATION

Substitute back into discrete conservation eqn.

Identify with a continuous probability

$$p(A_n, t) = p(ndx, t)$$

↑ probability of occupancy.

$$\frac{p(ndx, t+dt) - p(ndx, t)}{dt} = \frac{P_m}{2}\Big[p((n-1)dx, t) - 2p(ndx, t) + p((n+1)dx, t)\Big]$$

$$+ \frac{P_m}{2}\rho \Big\{ (1 - p(ndx, t)) \times \big[p((n-1)dx, t) - p((n+1)dx, t)\big] + p(ndx, t)\big[(1 - p((n-1)dx, t))(1 - p((n+1)dx, t))\big] \Big\}$$

Take the limit as $dx, dt \to 0$

$$\frac{\partial p}{\partial t} = D\frac{\partial^2 p}{\partial x^2} - v\frac{\partial}{\partial x}(p(1-p))$$

$$\lim_{dx\to 0} \frac{P_m dx^2}{2} \qquad \lim_{dx\to 0} P_m \rho\, dx$$

cf without competition for space:

$$\frac{\partial p}{\partial t} = D\frac{\partial^2 p}{\partial x^2} - v\frac{\partial p}{\partial x}$$

diff. advection terms.