Stochastic dynamics 5, 11, 2009

Motivation

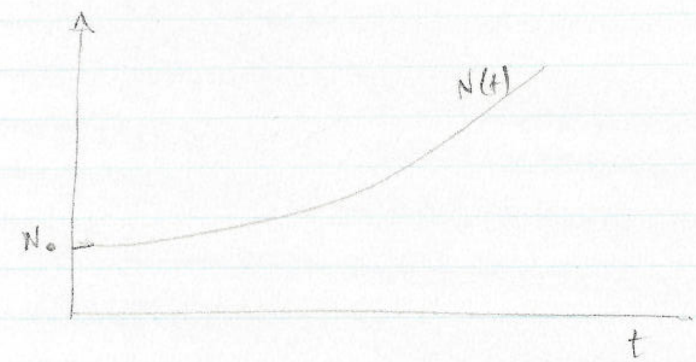
In Malthusian Growth or logistic model.

if we start from a non-zero N we always

get growth in the population,

$$\dot{N} = K N(t) = (b-d-m) N(t)$$

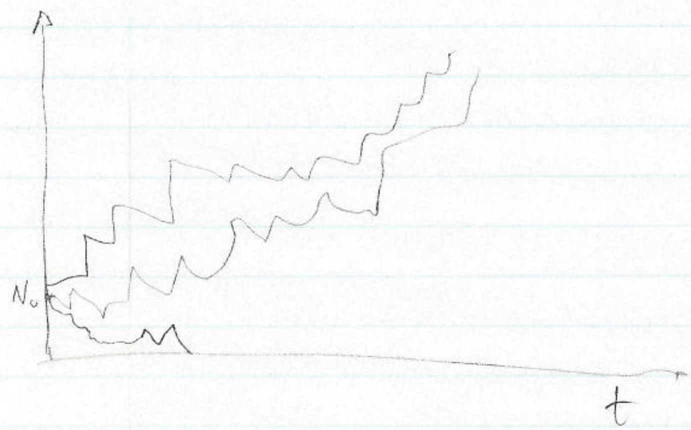
$$N(t) = N_0 e^{Kt}$$



If we N is small (N 1) and the birth and

death events are discrete events, we can have distinction

for non-zero N_0!



Trancription (birth - death process)

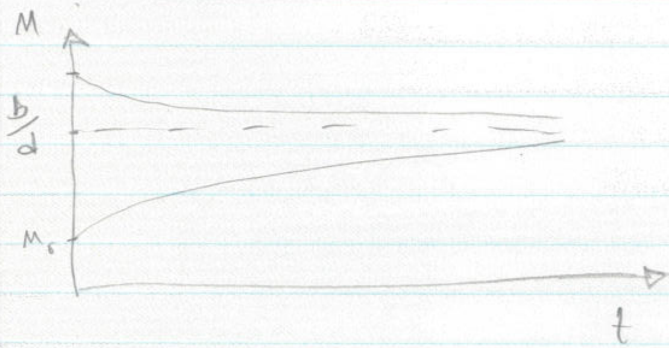
$$DNA \xrightarrow{b} DNA + mRNA$$
$$mRNA \xrightarrow{d} \phi$$

Assume one copy of DNA; $M(t) :=$ levels of mRNA

$$\frac{dM}{dt} = b - d\,M(t)$$

Note: (Birth is not proportional to M; non-malthusian)

$$M(t) = \frac{b}{d}\left(1 - e^{-dt}\right) + M_0 e^{-dt}$$



typical number of mRNAs in bacteria is very low (1 - 10)

We need a stochastic treatment!

<u>Defⁿ</u> $P_m(t) :=$ The probability of having m mRNA at time t.

$$\sum_{m=0}^{\infty} P_m(t) = 1 \quad \forall t \quad ; \quad P_m(t) = 0 \quad \forall m < 0$$

$$P_m(0) = \delta_{m M_0} = \begin{cases} 0 & m \neq M_0 \\ 1 & m = M_0 \end{cases}$$

Master Equation for birth - death process

$$\frac{\partial P_m(t)}{\partial t} = b\left(P_{m-1} - P_m\right) + d\left((m+1)P_{m+1} - m P_m\right)$$

Steady state solution:

$$\frac{\partial P_m}{\partial t} = 0$$

$$(m+1) P_{m+1} = m P_m + \frac{b}{d}(P_m - P_{m-1})$$

$$m=0 \Rightarrow P_1 = \frac{b}{d} P_0 \qquad (P_{-1} = 0)$$

$$m=1 \Rightarrow 2P_2 = P_1 + \frac{b}{d}(P_1 - P_0) = \frac{b}{d}\cancel{P_0} + \frac{b}{d}\left(\frac{b}{d}P_0 - \cancel{P_0}\right) \Rightarrow$$

$$P_2 = \frac{1}{2}\left(\frac{b}{d}\right)^2 P_0$$

$$m = K-1 \Rightarrow P_k = \frac{1}{K!}\left(\frac{b}{d}\right)^K P_0$$

normalization $\sum_{m=0}^{\infty} P_m = 1 \Rightarrow P_0 \overbrace{\sum \frac{1}{m!}\left(\frac{b}{d}\right)^m}^{e^{\frac{b}{d}}} = 1 \Rightarrow$

$$P_0 = e^{-\frac{b}{d}}$$

steady-state: $P_m = \frac{1}{m!}\left(\frac{b}{d}\right)^m e^{-\frac{b}{d}}$. Poisson distribution.

Generating function method:

Def^n The generating function:

$$F(z,t) = \sum_{m=0}^{\infty} z^m P_m(t)$$

properties:

$$F(1,t) = \sum_{m=0}^{\infty} P_m(t) = 1$$

$$\left(\frac{\partial F}{\partial z}\right)_{z=1} = \left(\sum_{m=0}^{\infty} m\, z^{m-1} P_m(t)\right)_{z=1} = \sum_{m=0}^{\infty} m P_m(t) = \langle m(t) \rangle$$

$$\left(\frac{\partial^2 F}{\partial z^2}\right)_{z=1} = \left(\sum_{m=0} m(m-1)\, z^{m-2} P_m(t)\right)_{z=1} = \sum_{m=0}^{\infty} m(m-1) = \langle m(m-1) \rangle$$

$$\sum_{m=0}^{\infty} z^m \frac{\partial P(m,t)}{\partial t} = \sum_{m=0}^{\infty} \left(z^m b (P_{m-1} - P_m) + z^m d(m+1) P_{m+1} - m P_m \right)$$

$$* \quad \frac{\partial F(z,t)}{\partial t} = b(z-1) F(z,t) + d \frac{\partial F(z,t)}{\partial z} (1-z)$$

differentiate with respect to z and put $z=1$

$$\frac{\partial}{\partial t} \frac{\partial F}{\partial z}\Big|_{z=1} = \left[b F(z,t) - d \frac{\partial F(z,t)}{\partial z} + (z-1) \left(b \frac{\partial F}{\partial z} - d \frac{\partial^2 F}{\partial z^2} \right) \right] \Big|_{z=1}$$

$$\frac{\partial \langle m(t) \rangle}{\partial t} = b - d \langle m(t) \rangle \implies \langle m \rangle_{ss} = \frac{b}{d}$$

note that this is similar to the deterministic ode.

differentiate with respecto to z twice!

$$\frac{\partial}{\partial t} \left(\frac{\partial^2 F}{\partial z^2} \right)\Big|_{z=1} = \left[b \frac{\partial F}{\partial z} - d \frac{\partial^2 F}{\partial z^2} + (z-1) \left(b \frac{\partial^2 F}{\partial z^2} - d \frac{\partial^3 F}{\partial z^3} \right) + b \frac{\partial F}{\partial z} - d \frac{\partial^2 F}{\partial z^2} \right]_{z=1}$$

$$\frac{\partial}{\partial t} \left(\langle m^2(t) \rangle - \langle m(t) \rangle \right) = 2b \langle m(t) \rangle - 2d \left(\langle m^2(t) \rangle - \langle m(t) \rangle \right)$$

$$= (2d + 2b) \langle m(t) \rangle - 2d \langle m^2(t) \rangle$$

at steady-state:

$$\sigma_m^2 = \langle m^2 \rangle_{ss} - \langle m \rangle_{ss}^2 = \frac{k}{d} = \langle m \rangle_{ss}$$

note: This is what you expect from a poisson process!

mRNA noise : $\eta_m^2 = \frac{\sigma_m^2}{\langle m \rangle_{ss}^2} = \frac{1}{\langle m \rangle_{ss}}$

Protein noise :

$$\mathrm{DNA} \xrightarrow{k_m} \mathrm{mRNA} \xrightarrow{k_p} \mathrm{Protein}$$

$$\mathrm{mRNA} \xrightarrow{d_m} \phi \qquad \mathrm{Protein} \xrightarrow{d_p} \phi$$

$$\frac{dP_{m,p}}{dt} = k_m P_{m-1,p}(t) - k_m P_{m,p}(t) + k_p m P_{m,p-1}(t) - k_p m P_{m,p}(t)$$
$$+ d_m(m+1) P_{m+1,p}(t) - d_m m P_{m,p}(t) + d_p (p+1) P_{m,p+1} - d_p p P_{m,p}(t)$$

Generating function : $F(z, \omega, t) = \sum_{m,p=0}^{\infty} z^m \omega^p P_{m,p}(t)$

using similar approach we get

Protein noise : $\eta_p^2 = \frac{1}{\langle p \rangle_{ss}} + \frac{d_p}{d_m + d_p} \frac{1}{\langle m \rangle_{ss}}$