HGEN 48600/STAT 35450: Fundamentals of Computational Biology

Lecture 11 — February 9

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Note: These lecture notes are still rough, and have only have been mildly proofread.

11.1 Continuous Time Markov Chains

11.1.1 Differential equations that lead to the poisson distribution

We can describe the probability that the number of events that have occured by time t as N_t, and can write the probability as: $P(N_t = i) = P_i(t)$
With the rate parameter λ, the probability that $N_t = i$ at $t + h$ is given by:
$P_i(t+h) = P_{\mathrm{i}-1}(t)(\lambda h + o(h)) + P_i(t)(1 - \lambda h + o(h))$
Here we are summing over the probability of two scenarios. The first represents that $N_t = i - 1$ and that there was another event in time h. The second is that $N_t = i$ and that there was no event in time h. For small vaues of h we can ignore the probabilty of two steps in time h.
The limit as h goes to 0 is: $\frac{P_i(t+h)-P_i(t)}{h} = \frac{d}{dt}P_i(t) = P_{i-1}(t)(\lambda h + o(h)) + P_i(t)(1 - \lambda h + o(h)) - P_i(t)$
Cancel the one and divide by h to get:
$(\lambda)P_{i-1}(t) - P_i(t)P_0(t+h) = P_0(t)(1 - \lambda h + o(h))$
$\frac{dP_0(t)}{dt} = -\lambda P_0(t)$
The solution to this differential equation is: $P_0(t) = e^{-\lambda \mathrm{t}}$ plus some constant
$\frac{P_i(t)}{dt} = \lambda P_0(t) - \lambda P_i(t) = \lambda e^{-\lambda t} - \lambda P_1(t)$
To get the solution for P_1 we use an integrating factor
$\frac{dP_1(t)}{dt} + \lambda P_1(t) = \lambda e^{-\lambda t}$
$\int_0^T e^{-\lambda t}\frac{dP_1(t)}{dt} + \lambda e^{-\lambda t}P_1(t) = \int_0^T \lambda$
Remembering the product rule: $(fg)' = f'g + g'f$

$$\int_0^T \frac{d}{dt} = \int_0^T \frac{d}{dt}(e^{\lambda t}P_1(t)) = \int_0^T \lambda dt = P_1(t) = \lambda t e^{-\lambda t}$$

We can keep iterating: $P_2(t) = \frac{(\lambda t)^2}{2}e^{-\lambda t}$ And eventually we have $P_n(t) = \frac{(\lambda t)^n}{n!}e^{-\lambda t}$
This is the poisson process

11.1.2 A More General Process, the Pure Birth Process

More general than the poisson process is a "birth process", or "pure birth process"
In a pure birth process there is a state dependent rate of arrival:
$\frac{d}{dt}P_i(t) = \lambda_{i-1}P_{i-1}(t) - \lambda_i P_i(t)$
The poisson process is a special case where λ_i is constant.
Another example is the **linear birth process**, where the $\lambda_i = i\lambda$ (This is also known as a Yule process)
$P_j(t) = \binom{j-1}{k-1} e^{-\lambda t}(1 - e^{\lambda t})^{k-i}$ where k is the starting size. This is a negative binomial distribution (and is a transient solution)
Another major class is a birth-death process. We have a set of birth rates and a set of death rates. (λ from 0 to infinity, and μ from 1 to infinity)
$\frac{d}{dt}P_i(t) = \lambda_{i-1}P_{i-1}(t) + \mu_{i-1}P_{i+1}(t) - (\lambda_i + \mu_i)P(i)(t)$
There is a linear birth-death process $\lambda_i = i\lambda$ and $\mu_i = i\mu$
There is also linear birth-death with immigration
$\lambda_i = i\lambda + \theta$ $\mu_i = i\mu$

11.1.3 Continuous version of the Markov property

Independence of the past before the immediate past $P(X(t+s) = j|X(s) = i, X_u = x(u), 0 \leq u < s) = P(X(t+s) = j|X(s) = i)$

11.1.4 Rate matrix Q

We have been thinking about going from 0 to 1, but we can think in general about going from i to j Defining the generator matrix or Rate Matrix Q $P_{i,j}(h) = q_{ij}h + o(h)$ $P_{i,i}(h) = 1 - v_i h + o(h)$ Where $v_i = \sum_j q_{ij}$
If we define $q_{ii} = -v_i$ Then $Q = q_{ij}$
Inter-event times depend on i and they are exponential with rate v_i $P_{ij} = \frac{q_{ij}}{v_i}$ This looks like a discrete markov chain. There is an idea that we have a discrete markov chain embedded in a continuous markov chain

Q matrix for poisson

For the poisson process, Q is infinite in both directions. The diagonal has $-\lambda$ along the diagonal. One to the right of the diagonal is λ, the rate at which we arrive at the next state. (There is no return to previous states in the poisson process)

Q matrix for the birth-death process

Matrix goes on infinitely in both directions. Along the diagonal we have $\lambda 0$ for 0,0 followed by $-(\mu_k + \lambda_k)$ at k, k at $k, k-1$ we have μ_k and at $k, k+1$ we have λ_k For P, we have $\frac{\mu_k}{\lambda_k+\mu_k}$, at $k, k-1$. At $k, k+1$ we have $\frac{\lambda_k}{\lambda_k+\mu_k}$, and at the diagonal we have 1 minus the two off diagonals
$\frac{P_{ij}(t)}{dt} = v_j Pij(t) + \sum_{k \neq j} P_{ik}(t) q_{kj}$ This is the probability of going from i to j, plus the probability of going form i to k and then going to j
$\frac{dP_t}{dt} = P_t Q \ P_t = e^{Qt}$
If Q is diagonalizable, then we can write $Qt = UDU^{-1}$ where D is a diagonal matrix, then $e^{Qt} = Ue^D U^{-1}$
There are a branch of methods called Krylov methods for exponentiating matrices.

11.1.5 What about stationary distributions?

The Global Balance Equations

Define P_i as the stationary probability of being in state i which is the limit as t goes to infinity of $P_{ij}(t)$ $v_j P_j = \sum_k q_{kj} P_k$ This equation describes a situation where the rate out of state j (weighted by the probability of being in state j, or the flux) is equal to the flux into state j
If a Continuous Time Markov Chain is time reversible, then $P_i q_{ij} = P_j q_{ji}$ and it satisfies the local balance equations. The flux from i to j is equal to the flux from j to i
What is the flux out for state 0?

State	Flux out	Flux in
0	$\lambda_0 P_0$	$\mu_1 P_1$
1	$(\lambda_1 + \mu_1) P_1$	$\lambda_0 P_0 + \mu_2 P_2$
2	$(\lambda_2 + \mu_2) P_2$	$\lambda_1 P_1 + \mu_3 P_3$
n	$(\lambda_n + \mu_n) P_n$	$\lambda_{n-1} + \mu_{n+1} P_{n+1}$

These all have to be equal
$\lambda_0 P_0 = \mu_1 P_1 \ \lambda_1 P_1 = \mu_2 P_2 \ \lambda_n P_n = \mu_{n+1} P_{n+1}$
We can start solving everything in terms of P_0
$P_1 = \frac{\lambda_0 P_0}{\mu_1} \ P_3 = \frac{\lambda_2}{\mu_3} P_2 \ P_n = \frac{\lambda_{n-1} \ldots \lambda_1}{\mu_n \ldots \mu_1} P_0$
We know that $1 = P_0 + \sum_{n=1}^{\infty} P_n P_0$
in the linear birth-death model $P_n = \frac{\lambda}{\mu}^n \left(\frac{1}{1+\sum_{i=1} \infty \frac{\lambda}{\mu}^n}\right.$
Even though this is an infinte sum, it turns out that: $P_n = \frac{\lambda}{\mu}^n (1 - \frac{\lambda}{\mu})$
We know this because $\sum_{n=1}^{\infty} p(1-p)^{n-1} = 1$