Chapter 7 Biological Applications of CTMC Models:

Continuous-Time Branching Process: Let $\mathcal{P}(z,t)$ be the p.g.f. for $X(t)$,

$$\mathcal{P}(z,t) = p_0(t) + p_1(t)z + p_2(t)z^2 + \cdots$$

and $f(z)$ be the offspring p.g.f.,

$$f(z) = q_0 + q_1 z + q_2 z^2 + \cdots .$$

Note that $p_i(t)$ and q_i are not the same! $p_i(t) = \text{Prob}\{X(t) = i\}$ and $q_i = \text{Prob}\{Y = i\}$, where Y represents the random variable for the number of offspring produced by one individual. We changed notation to q_i for the probability instead of p_i so there is no confusion with $p_i(t)$. As in discrete-time branching processes, the p.g.f. is a composition of p.g.f.s., $\mathcal{P}(z, t + \Delta t) = \mathcal{P}(\mathcal{P}(z, \Delta t), t)$. We can derive the backward Kolomogorov differential equation satisfied by $\mathcal{P}(z,t)$,

$$\frac{\partial \mathcal{P}(z,t)}{\partial t} = \lambda[f(\mathcal{P}(z,t)) - \mathcal{P}(z,t)],$$

where λ is the parameter in the exponential waiting time between events, $g(t) = \lambda e^{-\lambda t}$. (See Chapter 7 for a derivation, equation (7.3).) At time $t = 0$, $\mathcal{P}(z, 0) = z$ or $X(0) = 1$. We assume that individuals produce offspring independently of others and have the same offspring p.g.f. for all time. Note however, that this assumption is only realistic for small population sizes. A similar theorem applies to continuous-time Markov branching process as it does for discrete-time.

Theorem 1 *Suppose $\{X(t) : t \in [0, \infty)\}$ is a nonexplosive, continuous-time Markov branching process with $X(0) = 1$. Assume f is the p.g.f. of the offspring distribution, where $m = f'(1)$ and $\mathcal{P}(z,t)$ is the p.g.f. of $X(t)$ $[f(0) = q_0 > 0$ and $q_0 + q_1 < 1]$. If $m \leq 1$, then*

$$\lim_{t \to \infty} \text{Prob}\{X(t) = 0\} = \lim_{t \to \infty} p_0(t) = 1$$

and if $m > 1$, then there exists a q satisfying $f(q) = q$ such that

$$\lim_{t \to \infty} \text{Prob}\{X(t) = 0\} = \lim_{t \to \infty} p_0(t) = q < 1.$$

Recall that the branching process is called *subcritical* if $m < 1$, *critical* if $m = 1$ and *supercritical* if $m > 1$. It is the supercritical case that is of interest in our applications.

Simple Birth and Death Process: Let $\lambda > 0$ be the per capita birth rate and $\mu > 0$ be the per capita death rate of an individual, $p_{i+1,i}(\Delta t) = \lambda i \Delta t + o(\Delta t)$ and $p_{i-1,i}(\Delta t) = \mu i \Delta t + o(\Delta t)$. The probability of a birth is $\lambda/(\lambda + \mu)$ and the probability of a death is $\mu/(\lambda + \mu)$. The waiting time distribution for a birth or a death is $g(t) = (\lambda + \mu)e^{-(\lambda+\mu)t}$. Thus, we define the offspring p.g.f. as in a birth and death process as follows:

$$f(z) = \frac{\mu}{\lambda + \mu} + \frac{\lambda}{\lambda + \mu}z^2.$$

An individual either dies with probability $\mu/(\lambda+\mu)$ or survives and gives birth with probability $\lambda/(\lambda+\mu)$. There is an important difference in this offspring p.g.f. and the one for the discrete-time branching process. For this p.g.f., a single offspring does not replace the parent but adds to the population size. Here the waiting time parameter in the exponential distribution is $\mu + \lambda$. Also, $m = f'(1) = 2\lambda/(\mu + \lambda) > 1$ iff $\lambda > \mu$. In this case, the fixed point q of $f(q) = q$ is μ/λ. The probability of ultimate extinction given $X(0) = N$ is $(\mu/\lambda)^N$,

$$\lim_{t \to \infty} p_0(t) = \left(\frac{\mu}{\lambda}\right)^N.$$

Note that the preceding result agrees with p.g.f. of $X(t)$ for the simple birth and death process given in Chapter 6.

SIS Epidemic Model: For the deterministic SIS epidemic model, the differential equations are

$$\frac{dS}{dt} = -\frac{\beta}{N}SI + \gamma I$$

$$\frac{dI}{dt} = \frac{\beta}{N}SI - \gamma I = \left(\beta\frac{S}{N} - \gamma\right)I.$$

The value $\mathcal{R}_0 = \dfrac{\beta}{\gamma}$ is called the *basic reproduction number*. This system has two equilibria, $(\bar{S}, \bar{I}) = (N, 0)$ and $(N/\mathcal{R}_0, N(1 - 1/\mathcal{R}_0)$ if $\mathcal{R}_0 > 1$. If $\mathcal{R}_0 > 1$, then there is an outbreak and solutions approach the endemic equilibrium and if $\mathcal{R}_0 \leq 1$, there is no outbreak. For the CTMC SIS epidemic model, let

$$
\begin{aligned}
\text{Prob}\{\Delta I(t) &= j | I(t) = i\} \\
&= \begin{cases}
\dfrac{\beta}{N}i(N - i)\,\Delta t + o(\Delta t), & j = 1 \\
\gamma i\,\Delta t + o(\Delta t), & j = -1 \\
1 - \left[\dfrac{\beta}{N}i(N - i) + \gamma i\right]\Delta t \\
\quad + o(\Delta t), & j = 0 \\
o(\Delta t), & j \neq -1, 0, 1,
\end{cases}
\end{aligned}
$$

where $i \in \{0, 1, \ldots, N\}$. The SIS epidemic model is a birth and death process with

$$\lambda_i = \frac{\beta}{N}i(N - i) \quad \text{and} \quad \mu_i = \gamma i,$$

for $i = 0, 1, \ldots, N$. There is a single absorbing state at zero, $\lim_{t\to\infty} p_0(t) = 1$. The infectious class always approaches zero (this is true for the deterministic model as well). However, at the initiation of an outbreak, $I(t)$ behaves like a *simple* birth and death process. Consider only the state I when $S \approx N$, then for the deterministic model,

$$\frac{dI}{dt} = \beta I - \gamma I = (\beta - \gamma)I. \tag{1}$$

As noted, the corresponding CTMC model for I behaves like a *simple* birth and death process, where $\beta = \lambda$ and $\gamma = \mu$, provided N is large. Thus, using branching process theory for the simple birth and death process we can *approximate* the dynamics at the beginning of a potential outbreak. What is the probability that I hits zero (no outbreak)? The probability of absorption from branching process theory tells us that the probability of absorption as $t \to \infty$ (no outbreak) given $I(0) = 1$ is $\mu/\lambda = \gamma/\beta = 1/\mathcal{R}_0$ if $\mathcal{R}_0 > 1$. If $I(0) = k$, then the probability of no outbreak is $(1/\mathcal{R}_0)^k$. The process either hits zero rapidly or grows. Even though this is an asymptotic approximation, it is a good prediction for probability of an outbreak:

$$\text{Prob}\{Outbreak | I(0) = k\} \approx 1 - (1/\mathcal{R}_0)^k$$

Although this estimate is for the SIS epidemic model, it also applies to the SIR or SIRS epidemic models, provided the equation for infectives I, equation (1), leads to a simple birth and death approximation with $I(0)$ small and $S(0) \approx N$ large.