Likelihood for the Branching Process Model for Stem Cell Proliferation

The Author

Suppose the process starts at time $T_0 = 0$ and the number of starting stem cell S_0. The interarrival time of the next event is exponentially distributed

$$\Delta_{T_i} = T_i - T_{i-1} \sim \text{Exp}(r \cdot S_{i-1}), \quad i = 1, \cdots, n,$$

where r is the division rate. At the event time T_i, the pair of random variable (X_i, Y_i) has the following distribution

$$(X_i, Y_i, Z_i) = \begin{cases} (+1, 0, 0), & p_1(T_i) \\ (0, +1, 0), & p_2(T_i) \\ (-1, +2, 0), & p_3(T_i) \\ (0, 0, +1), & p_4(T_i) \end{cases} \tag{1}$$

Assume that there is no dud stem cells (i.e $p_4(t) = 0 \forall t$, and we observe all the events (both the time of the events $T_0, T_1, \cdots, T_n$ and the number of stem cells $S_0, S_1, \cdots, S_n$. Since we observe every events, we can know how the cell changes (X_i, Y_i) at each event time. We define

$$\alpha_{T_i}(S_i) = P(T_1, T_2, \cdots, T_i, S_1, \cdots, S_i).$$

We show that $\alpha_{T_i}(S_i)$ could be computed with dynamic programming.

$$\begin{aligned} \alpha_{T_1}(S_1) &= P(T_1, S_1) \\ &= P(S_1|T_1) \cdot P(T_1) \\ &= P(X_1 = S_1 - S_0|T_1) \cdot P(\Delta_{T_1} = T_1 - T_0) \\ &= [p_1(T_1) \cdot I_{(X_1=1)} + p_2(T_1) \cdot I_{(X_1=0)} + p_3(T_1) \cdot I_{(X_1=-1)}] \cdot [rS_0 e^{-rS_0\Delta_{T_1}}]. \end{aligned} \tag{2}$$

$$\begin{aligned} \alpha_{T_2}(S_2) &= P(T_1, T_2, S_1, S_2) \\ &= P(T_2, S_2|T_1, S_1) \cdot P(T_1, S_1) \\ &= P(S_2|T_2, T_1, S_1) \cdot P(T_2|T_1, S_1) \cdot P(T_1, S_1) \\ &= P(X_2 = S_2 - S_1|T_2, T_1, S_1) \cdot P(\Delta_{T_2} = T_2 - T_1|T_1, S_1) \cdot P(T_1, S_1) \\ &= [p_1(T_2) \cdot I_{(X_2=1)} + p_2(T_2) \cdot I_{(X_2=0)} + p_3(T_2) \cdot I_{(X_2=-1)}] \cdot [rS_1 e^{-rS_1\Delta_{T_2}}] \cdot \alpha_{T_1}(S_1). \end{aligned} \tag{3}$$

$$\begin{aligned} \alpha_{T_i} &= P(T_1, \cdots, T_i, S_1, \cdots S_i) \\ &= P(T_i, S_i|T_1, \cdots T_{i-1}, S_1 \cdots S_{i-1}) \cdot P(T_1, \cdots T_{i-1}, S_1 \cdots S_{i-1}) \\ &= P(S_i|T_1, \cdots T_{i-1}, T_i, S_1 \cdots S_{i-1}) \cdot P(T_i|T_1, \cdots T_{i-1}, S_1 \cdots S_{i-1}) \cdot P(T_1, \cdots T_{i-1}, S_1 \cdots S_{i-1}) \\ &= P(X_i = S_i - S_{i-1}|T_i, S_{i-1}) \cdot P(\Delta_{T_i} = T_i - T_{i-1}|T_{i-1}, S_{i-1}) \cdot P(T_1, \cdots T_{i-1}, S_1 \cdots S_{i-1}) \\ &= [p_1(T_i) \cdot I_{(X_i=1)} + p_2(T_i) \cdot I_{(X_i=0)} + p_3(T_i) \cdot I_{(X_i=-1)}] \cdot [rS_{i-1} e^{-rS_{i-1}\Delta_{T_i}}] \cdot \alpha_{T_{i-1}}(S_{i-1}). \end{aligned} \tag{4}$$