The Distribution of a Forward Stochastic Disease-Model

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Abstract : In this paper, we derive the distribution of a disease-model which is not possible to have backward transitions. The distribution is the sums of gamma distributions. In special cases, the results reduce to some AIDS models and uniform forward model.

Keywords : forward stochastic disease-model, homogeneous Markov process, first passage probability distribution, random time, generator matrix.

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1 Introduction and main result

This work, we consider the distribution of the disease-model as shown in Figure 1. In this model, $I_1$ corresponds to the exposure state and a patient dies at death-state ($I_{n+1}$) where $n \geq 2$. We assume that it is not possible to have backward transition from $I_i$ to $I_j$ for $j < i$ and call this model forward disease-model.
For every $t \geq 0$, we let $X_t$ be a random variable whose value is the state at time $t$. So the state space of $\{X_t \mid t \geq 0\}$ is $\{I_1, I_2, \ldots, I_{n+1}\}$ where $I_{n+1}$ is the absorbing state and $I_1, I_2, \ldots, I_n$ are transition states. In this work, we assume that $\{X_t \mid t \geq 0\}$ is a homogeneous continuous Markov process. From Chapter 5 of Sidney (2002), we know that the transition matrix $P(t) = [p_{ij}(t)]_{(n+1) \times (n+1)}$ of $\{X_t \mid t \geq 0\}$ is satisfied the followings:

$$
\begin{align*}
p_{ij}(t) &= v_{ij} t + o(t) & \text{where } t \to 0 \text{ and } i \neq j, \\
p_{ii}(t) &= 1 - v_{ii} t + o(t) & \text{where } t \to 0, \\
v_{ij} &\geq 0, \quad v_{ii} = \sum_{j \neq i} v_{ij},
\end{align*}
$$

(1.1)

where $v_{ij}$ is the transition rate at which $X_t$ jumps from $i$ to $j$. From Figure 1,
we know that

\[
v_{ij} = \begin{cases} 
0, & \text{if } i > j, \\
\gamma_i, & \text{if } i = j, \\
\beta_{ij}, & \text{if } i < j, 
\end{cases}
\]  

(1.2)

where \( \gamma_i = \sum_{l=i+1}^{n+1} \beta_{il} \) for \( i = 1, 2, \ldots, n \) and \( \gamma_{n+1} = 0 \). In this paper, we obtain the distribution of the random time which \( I_1 \) is absorbed into \( I_{n+1} \), that is, the random time that a patient will die since he has been infective. Here is our main result.

Theorem 1.1. Let \( W \) be the random time that a patient will die since he has been infective. Assume that \( \gamma_i \)'s are distinct. Then

(i) the probability density function \( f_1 \) of \( W \) can be written as

\[f_1(t) = \sum_{k=1}^{n} \left( \sum_{l=k}^{n} p_{lk} p'_{kl} \beta_{(n+1)} \right) e^{-\gamma_k t},\]

and

(ii) the average time from infective state \( I_1 \) to the death-state \( I_{n+1} \) is

\[
\sum_{k=1}^{n} \sum_{l=k}^{n} \frac{p_{lk} p'_{kl} \beta_{(n+1)}}{\gamma_k}
\]

where

\[
p_{ij} = \begin{cases} 
(-1)^k \sum_{j_0 < j_1 < \cdots < j_k = j} \prod_{q=0}^{k-1} \beta_{j_q j_{q+1}}, & \text{if } i < j, \\
1, & \text{if } i = j, \\
0, & \text{if } i > j,
\end{cases}
\]

and

\[
p'_{ij} = \begin{cases} 
(-1)^k \sum_{j_0 < j_1 < \cdots < j_k = j} \prod_{q=0}^{k-1} p_{j_q j_{q+1}}, & \text{if } i < j, \\
1, & \text{if } i = j, \\
0, & \text{if } i > j.
\end{cases}
\]
Notice that if $\beta_{i(i+2)} = \beta_{i(i+3)} = \cdots = \beta_{i(n+1)} = 0$ for $i = 1, 2, \ldots, n-1$, this model reduces to the AIDS (Acquired Immunodeficiency Syndrome) model considered by Longini et al. (1989a, 1989b, 1991 and 1992). In case of uniform forward model, i.e., the transition rate $\beta_{ij}$’s are equal, it is easy to see that $\gamma_i$’s are distinct. So Theorem 1.1 can be applied to this case. Hence it is reasonable to assume that $\gamma_i$’s are distinct.

2 Proof of the main result

For each $i$, let $W_i$ be the random time that $I_i$ is absorbed into $I_{n+1}$. Then $W_i$ is referred to as the first passage time $I_i$ and $f_i(t)$, the probability density function, the first passage probability density of $I_i$. Let

$$f(t) = [f_1(t), f_2(t), \ldots, f_n(t)]^T,$$

where $X^T$ denotes the transpose of a matrix $X$. Let

$$A = \begin{bmatrix}
\gamma_1 & -\beta_{12} & -\beta_{13} & \cdots & -\beta_{1n} \\
0 & \gamma_2 & -\beta_{23} & \cdots & -\beta_{2n} \\
0 & 0 & \ddots & \ddots & \ddots \\
0 & 0 & \cdots & \gamma_{n-1} & -\beta_{(n-1)n} \\
0 & 0 & \cdots & 0 & \gamma_n
\end{bmatrix}$$

We observe that the generator matrix of $(X_t)$ is

$$\begin{bmatrix}
-A & \mu \\
0_n & 0
\end{bmatrix}$$

where $\mu = [\beta_{1(n+1)}, \beta_{2(n+1)}, \ldots, \beta_{n(n+1)}]^T$ and $0_n = (0, 0, \ldots, 0)$. Since $\det A = \gamma_1 \gamma_2 \cdots \gamma_n > 0$, by Tan and Byers (1993), we obtain that

$$f(t) = \exp(-At)A1_n$$

(2.1)

where $1_n = (1, 1, \ldots, 1)^T$ and

$$e^A = \sum_{j=0}^{\infty} \frac{1}{j!}A^j.$$
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From Curtis (1984) Chapter 7, there are the Jordan canonical form $J$ of $A$ which is of the form

$$
J = \begin{bmatrix}
\gamma_1 & 0 & 0 & \ldots & 0 \\
0 & \gamma_2 & 0 & \ldots & 0 \\
0 & 0 & \gamma_3 & \ldots & 0 \\
\vdots & \vdots & \ddots & \ddots & \vdots \\
0 & 0 & 0 & \ldots & \gamma_n
\end{bmatrix}
$$

and the invertible matrix $P$ such that

$$
A = PJ P^{-1}.
$$

From Appendices 1–2, we know that $P = (p_{ij})$ and $P^{-1} = (p'_{ij})$ where $p_{ij}$ and $p'_{ij}$ are defined as follows:

$$
p_{ij} = \begin{cases}
\sum_{k=1}^{j-i} (-1)^k \sum_{i=j_n<j_1<\ldots<j_k=j} \prod_{q=0}^{k-1} \beta_{j_n,j_{q+1}}, & \text{if } i < j, \\
1, & \text{if } i = j, \\
0, & \text{if } i > j,
\end{cases}
$$

and

$$
p'_{ij} = \begin{cases}
\sum_{k=1}^{j-i} (-1)^k \sum_{i=j_n<j_1<\ldots<j_k=j} \prod_{q=0}^{k-1} p_{j_n,j_{q+1}}, & \text{if } i < j, \\
1, & \text{if } i = j, \\
0, & \text{if } i > j.
\end{cases}
$$

Hence

$$
e^{-At} = e^{-(PJ P^{-1})t} = P e^{-Jt} P^{-1} = \begin{bmatrix}
e^{-\gamma_1 t} & 0 & \ldots & 0 \\
0 & e^{-\gamma_2 t} & \ldots & 0 \\
\vdots & \vdots & \ddots & \vdots \\
0 & \ldots & 0 & e^{-\gamma_n t}
\end{bmatrix} \begin{bmatrix}
a_{ij}
\end{bmatrix} \quad (2.2)
$$
where \( \alpha_{ij} = \sum_{k=1}^{n} p_{ik} p'_{kj} e^{-\gamma_k t} \). From (2.1), (2.2) and the fact that 

\[
A_{1n} = \begin{bmatrix}
\gamma_1 - \sum_{l=1}^{n} \beta_{1l}, 
\gamma_2 - \sum_{l=1}^{n} \beta_{2l}, \ldots, 
\gamma_n - \sum_{l=1}^{n} \beta_{nl},
\end{bmatrix}^T = \begin{bmatrix}
\beta_{1(n+1)}, 
\beta_{2(n+1)}, \ldots, 
\beta_{n(n+1)},
\end{bmatrix}^T,
\]

we have

\[
f_1(t) = (1, 0, \ldots, 0)e^{-At}A_{1n} = 
\left[ \sum_{k=1}^{n} p_{1k} p'_{k1} e^{-\gamma_k t}, \sum_{k=1}^{n} p_{1k} p'_{k2} e^{-\gamma_k t}, \ldots, \sum_{k=1}^{n} p_{1k} p'_{kn} e^{-\gamma_k t} \right] 
\times \begin{bmatrix}
\beta_{1(n+1)}, 
\beta_{2(n+1)}, \ldots, 
\beta_{n(n+1)},
\end{bmatrix}^T
\]

\[
= \sum_{l=1}^{n} \left( \sum_{k=1}^{n} p_{1k} p'_{kl} e^{-\gamma_k t} \right) \beta_{l(n+1)}
\]

\[
= \sum_{l=1}^{n} \sum_{k=1}^{l} p_{1k} p'_{kl} e^{-\gamma_k t} \beta_{l(n+1)}
\]

\[
= \sum_{k=1}^{n} \left( \sum_{l=k}^{n} p_{1k} p'_{kl} \beta_{l(n+1)} \right) e^{-\gamma_k t}.
\]

and the average time \( E(W) = \int_{0}^{\infty} tf_1(t) \, dt = \sum_{k=1}^{n} \sum_{l=k}^{n} \frac{p_{1k} p'_{kl} \beta_{l(n+1)}}{\gamma_k^2} \).

3 Appendices

Appendix 1. Let \( P = (p_{ij}) \) and \( Q = (q_{ij}) \) be \( n \times n \) matrices such that

\[
p_{ij} = \begin{cases} 
1, & \text{if } i = j, \\
0, & \text{if } i > j,
\end{cases}
\]

and

\[
q_{ij} = \begin{cases} 
\sum_{k=1}^{j-1} (-1)^k \sum_{i=j_0<j_1<\cdots<j_k=j} \prod_{q=0}^{k-1} p_{j_qj_{q+1}}, & \text{if } i < j, \\
1, & \text{if } i = j, \\
0, & \text{if } i > j.
\end{cases}
\]

Then \( P = Q^{-1} \).
Proof. Let $PQ = (a_{ij})$.

**Case 1** $i = j$.

We see that

$$a_{ii} = \sum_{r=1}^{n} p_{ir}q_{rj} = p_{ii}q_{ii} = 1.$$  

**Case 2** $i > j$.

We see that

$$a_{ij} = \sum_{r=1}^{n} p_{ir}q_{rj} = 0 + 0 + \cdots + 0 = 0.$$  

**Case 3** $i < j$.

First, notice that

$$a_{ij} = \sum_{r=1}^{n} p_{ir}q_{rj} = \sum_{r=i+1}^{j} p_{ir}q_{rj}.$$  

If $j = i + 1$, then

$$a_{ij} = p_{i(i+1)} + q_{i(i+1)} = p_{i(i+1)} - p_{i(i+1)} = 0.$$  

Now, suppose that $j \geq i + 2$. From (3.1) and (3.2),

$$a_{ij} = p_{ij} + q_{ij} + \sum_{r=i+1}^{j-1} p_{ir}q_{rj}$$

$$= p_{ij} + \sum_{k=1}^{j-i} (-1)^{k} \sum_{i=j_{0}<j_{1}<\cdots<j_{k}=j}^{k-1} \prod_{q=0}^{k-1} p_{j_{0}j_{q+1}} + \sum_{r=i+1}^{j-1} \sum_{r=j_{0}<j_{1}<\cdots<j_{k}=j}^{j-1} \prod_{q=0}^{k-1} p_{j_{0}j_{q+1}}$$

$$= \sum_{k=2}^{j-i} (-1)^{k} \sum_{i=j_{0}<j_{1}<\cdots<j_{k}=j}^{k-1} \prod_{q=0}^{k-1} p_{j_{0}j_{q+1}} + \sum_{k=1}^{j-1} (-1)^{k} \sum_{r=i+1}^{j-1} \sum_{r=j_{0}<j_{1}<\cdots<j_{k}=j}^{k} \prod_{q=0}^{k-1} p_{j_{0}j_{q+1}}$$

$$= \sum_{k=1}^{j-i-1} (-1)^{k+1} \sum_{i=j_{0}<j_{1}<\cdots<j_{k+1}=j}^{k} \prod_{q=0}^{k} p_{j_{0}j_{q+1}} + \sum_{k=1}^{j-1} (-1)^{k} \sum_{i=j_{0}<j_{1}<\cdots<j_{k+1}=j}^{k} \prod_{q=0}^{k} p_{j_{0}j_{q+1}}$$

$$= 0.$$  

From Cases 1–3, we have $PQ = I_{n}$. Hence $P = Q^{-1}$.

**Appendix 2.** Let $A = (a_{ij})$ be an $n \times n$ matrix such that
(i) $a_{ij} = 0$ for all $i > j$,

(ii) $a_{11}, a_{22}, \ldots, a_{nn}$ are all distinct.

Then the Jordan canonical form $J$ of $A$ is

$$J = \begin{bmatrix}
  a_{11} & 0 & 0 & \ldots & 0 \\
  0 & a_{22} & 0 & \ldots & 0 \\
  \vdots & \vdots & \vdots & \ddots & \vdots \\
  0 & 0 & 0 & \ldots & a_{nn}
\end{bmatrix}$$

and $A = PJP^{-1}$ where $P = (p_{ij})$ is defined by

$$p_{ij} = \begin{cases}
  \sum_{k=1}^{j-1} \sum_{i=j_0 < j_1 < \cdots < j_k = j} \prod_{q=0}^{k-1} a_{j_qj_{q+1}}, & \text{if } i < j, \\
  1, & \text{if } i = j, \\
  0, & \text{if } i > j
\end{cases}$$

and $P^{-1} = (p'_{ij})$ where $p'_{ij}$ is defined by (3.1).

Proof. It is obvious from Appendix 1 that the matrix $(p'_{ij})$ is $P^{-1}$. Note that $PJP^{-1} = (b_{ij})$ where

$$b_{ij} = \sum_{r=1}^{n} p_{ir}a_{rr}p'_{rj}.$$  

It is trivial that

$$b_{ii} = \sum_{r=1}^{n} p_{ir}a_{rr}p'_{rj} = p_{ii}a_{ii}p'_{ij} = a_{ii}.$$  

If $i > j$, then $p_{ir}p'_{rj} = 0$ for every $r = 1, 2, \ldots, n$. Hence $b_{ij} = 0$. Suppose that $i < j$. If $j = i + 1$, then

$$b_{i(i+1)} = \sum_{r=1}^{n} p_{ir}a_{rr}p'_{r(i+1)}$$

$$= a_{ii}p'_{i(i+1)} + p_{i(i+1)}a_{i(i+1)(i+1)}$$

$$= -a_{ii}p_{i(i+1)} + p_{i(i+1)}a_{i(i+1)(i+1)}$$

$$= p_{i(i+1)} \left( a_{i(i+1)(i+1)} - a_{ii} \right)$$

$$= a_{i(i+1)}.$$
To prove the rest, we first show that for any \( i, j \) with \( j > i \)

\[
(a_{jj} - a_{ii}) p_{ij} = \sum_{l=i+1}^{j} a_{il} p_{lj}.
\]

Let \( j = i + r \) where \( r \geq 1 \). We see that

\[
p_{i(i+r)} = \sum_{k=1}^{r} \sum_{l=i+1}^{i+r-k+1} \frac{a_{il}}{a_{ii} - a_{ij}} \prod_{q=0}^{k-2} \frac{a_{j_qj_{q+1}}}{a_{(i+r)(i+r)} - a_{j_qj_0}}
\]

Thus,

\[
\left( a_{(i+r)(i+r)} - a_{ii} \right) p_{i(i+r)}
\]

\[
= \sum_{k=1}^{r} \sum_{l=i+1}^{i+r-k+1} \frac{a_{il}}{a_{ii} - a_{ij}} \prod_{q=0}^{k-2} \frac{a_{j_qj_{q+1}}}{a_{(i+r)(i+r)} - a_{j_qj_0}}
\]

\[
= \sum_{l=i+1}^{i+r} \frac{a_{il}}{a_{ii} - a_{ij}} \sum_{k=1}^{i+r-l+1} \prod_{q=0}^{k-2} \frac{a_{j_qj_{q+1}}}{a_{(i+r)(i+r)} - a_{j_qj_0}}
\]

\[
= \sum_{l=i+1}^{i+r} \frac{a_{il}}{a_{ii} - a_{ij}} \sum_{k=1}^{i+r-l} \prod_{q=0}^{k-1} \frac{a_{j_qj_{q+1}}}{a_{(i+r)(i+r)} - a_{j_qj_0}}
\]

\[
= \sum_{l=i+1}^{i+r} \frac{a_{il}}{a_{ii} - a_{ij}} \prod_{q=0}^{i+r-l-1} \frac{a_{j_qj_{q+1}}}{a_{(i+r)(i+r)} - a_{j_qj_0}}
\]

\[
= \sum_{l=i+1}^{i+r} a_{il} p_{l(i+r)}.
\]
Now, let $j \geq i + 2$. Then

\[
b_{ij} = \sum_{r=1}^{n} p_{ir} a_{rr} p'_{rj} = a_{ii} p'_{ij} + \sum_{r=i+1}^{j-1} p_{ir} a_{rr} p'_{rj} + p_{ij} a_{jj}
\]

\[
= \left( a_{ii} \sum_{k=1}^{j-i} (-1)^{k} \sum_{i=0}^{k-1} \prod_{q=0}^{k} p_{a_{q}a_{q+1}} \right)
\]

\[
+ \left( \sum_{r=i+1}^{j-1} \sum_{k=1}^{j-r} (-1)^{k} \sum_{r=\gamma_{1} \ldots \gamma_{k} = j}^{k-1} \prod_{q=0}^{k} p_{\gamma_{q} \gamma_{q+1}} \right) + p_{ij} a_{jj}
\]

\[
= (a_{jj} - a_{ii}) p_{ij} + \left( a_{ii} \sum_{k=2}^{j-i} (-1)^{k} \sum_{i=0}^{k-1} \prod_{q=0}^{k} p_{a_{q}a_{q+1}} \right)
\]

\[
+ \left( \sum_{k=2}^{j-i-1} \sum_{r=i+1}^{j-k} (-1)^{k} a_{rr} p_{ir} \sum_{r=\gamma_{1} \ldots \gamma_{k} = j}^{k-1} \prod_{q=0}^{k} p_{\gamma_{q} \gamma_{q+1}} \right)
\]

\[
= \left( a_{ij} + \sum_{l=i+1}^{j-i} a_{il} p_{lj} \right) + \left( a_{ii} \sum_{k=2}^{j-i} (-1)^{k} \sum_{i=0}^{k-1} \prod_{q=0}^{k} p_{a_{q}a_{q+1}} \right)
\]

\[
+ \left( \sum_{k=2}^{j-i-1} \sum_{r=i+1}^{j-k} (-1)^{k} a_{rr} p_{ir} \sum_{r=\gamma_{1} \ldots \gamma_{k} = j}^{k-1} \prod_{q=0}^{k} p_{\gamma_{q} \gamma_{q+1}} \right)
\]

\[
= a_{ij} + \sum_{l=i+1}^{j-i} a_{il} p_{lj} + \left( \sum_{k=2}^{j-i+1} \sum_{r=i+1}^{j-k} (-1)^{k} a_{ii} p_{ir} \sum_{r=\gamma_{1} \ldots \gamma_{k} = j}^{k-1} \prod_{q=0}^{k} p_{a_{q}a_{q+1}} \right)
\]

\[
+ \left( \sum_{k=2}^{j-i} \sum_{r=i+1}^{j-k} (-1)^{k} a_{rr} p_{ir} \sum_{r=\gamma_{1} \ldots \gamma_{k} = j}^{k-1} \prod_{q=0}^{k} p_{\gamma_{q} \gamma_{q+1}} \right)
\]

\[
= a_{ij} + \sum_{l=i+1}^{j-i} a_{il} p_{lj}
\]

\[
+ \left( \sum_{k=2}^{j-i+1} \sum_{r=i+1}^{j-k} (-1)^{k} (a_{rr} - a_{ii}) p_{ir} \sum_{r=\gamma_{1} \ldots \gamma_{k} = j}^{k-1} \prod_{q=0}^{k} p_{a_{q}a_{q+1}} \right)
\]
where we claim that

\[
\sum_{k=3}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-1} a_{ir} \sum_{r=0}^{r-1} a_{iLPr} \sum_{r=0}^{r-1} a_{iLPr} \prod_{q=0}^{k-2} p_{\alpha_q\alpha_{q+1}} = 0.
\]

To prove the above claim, first, we consider

\[
\sum_{k=3}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-1} a_{ir} \sum_{r=0}^{r-1} a_{iLPr} \prod_{q=0}^{k-2} p_{\alpha_q\alpha_{q+1}}.
\]
We can see that
\[
\sum_{k=3}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-1}a_{ir} \sum_{r=\alpha_0<\alpha_1<\cdots<\alpha_{k-1}=j}^{k-2} \prod_{q=0}^{\alpha_q \alpha_{q+1}} = \\
\sum_{k=3}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-1} a_{ir} p_{\gamma_0 < \cdots < \gamma_{k-2}=j} \prod_{q=0}^{k-3} p_{\gamma_q \gamma_{q+1}}.
\]

Next, we consider
\[
\sum_{k=2}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-1} a_{ir} p_{\gamma_0 < \cdots < \gamma_{k-2}=j} \prod_{q=0}^{k-2} p_{\alpha_q \alpha_{q+1}}.
\]

We obtain that
\[
\sum_{k=2}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-1} a_{ir} p_{L_{i+j+1}} \prod_{q=0}^{k-2} p_{\alpha_q \alpha_{q+1}} = \\
\sum_{k=2}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-1} a_{ir} p_{L_{i+j+1}} \prod_{q=0}^{k-2} p_{\alpha_q \alpha_{q+1}} = \\
\sum_{k=3}^{j-i} \sum_{r=i+1}^{j-k+1} (-1)^{k-2} a_{ir} p_{\gamma_0 < \cdots < \gamma_{k-2}=j} \prod_{q=0}^{k-3} p_{\gamma_q \gamma_{q+1}}.
\]

Hence the claim is proved. \(\square\)

References


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