**Stochastic stem cell models with mutation: A comparison of asymmetric and symmetric divisions**

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**Abstract**

In order to fulfill cell proliferation and differentiation through cellular hierarchy, stem cells can undergo either asymmetric or symmetric divisions. Recent studies pay special attention to the effect of different modes of stem cell division on the lifetime risk of cancer, and report that symmetric division is more beneficial to delay the onset of cancer. The fate uncertainty of symmetric division is considered to be the reason for the cancer-delaying effect. In this paper we compare asymmetric and symmetric divisions of stem cells via studying stochastic stem cell models with mutations. Specially, by using rigorous mathematical analysis we find that both asymmetric and symmetric models show the same statistical average, but symmetric model shows higher fluctuation than asymmetric model. We further show that the difference between the two models would be more remarkable for lower mutation rates. Our work quantifies the uncertainty of cell division and highlights the significance of stochasticity for distinguishing between different modes of stem cell division.

**1 Introduction**

In multicellular organisms, many fast renewing tissues are organized in a hierarchical architecture, which proposes a directional cascade from tissue specific stem cells to more differentiated cell states \([1,2,3,4]\). Stem cells possess two major properties: self-renewal and differential potential. That is, not only are stem cells capable of maintaining the size of stem cell population by cell proliferation, but they can also generate more specialized cell types by cell differentiation \([5,6]\).

Two mechanisms of stem cells have been found to coordinate its dual role of self-renewal and differentiation \([7]\). The first is asymmetric cell division \([8,9]\), i.e. stem cells divide asymmetrically to give rise to two daughter cells with different fates: one is identical to the mother stem cell, the other differentiates into a non-stem cell state. The second is symmetric cell division \([10]\), namely, stem cells either perform self-renewal by producing two stem cells identical to their mother, or perform differentiation by generating two differentiated daughter cells. In particular, when the chances for self-renewal and
differentiation are fifty-fifty, statistically speaking, symmetric cell division is equivalent
to asymmetric cell division in the sense that the gain and loss of stem cells are balanced.
In this case, tissue homeostasis can still be achieved in population level. Even though both
asymmetric and symmetric division modes are capable of maintaining tissue homeostasis,
it appears that these two mechanisms are not randomly distributed in the biological world.
For example, strong evidence for asymmetric division has been found in invertebrate sys-
tems [11], and symmetric division is more common in mammals than in invertebrates [12].
Therefore, exploring the evolutionary implications of different modes of cell divi-
sion is of great interest and importance [13, 14]. In recent years, the effect of stem cell
division patterns on the risk of cancer has received special attention in theoretical biology
[15, 16, 17, 18, 19, 20, 21, 22]. Cancer is generally acknowledged as an evolutionary
process involving the accumulation of genetic or epigenetic mutations [23]. Note that
mutations mostly result from errors during the process of DNA replication, division mode
of stem cells is supposed to have a significant impact on the process of tumorigenesis.
Despite the complexity of cancer, theoreticians still provide some interesting and insight-
ful researches on this issue. In particular, Dingli et al showed that mutations with higher
probability of asymmetric division could result in rapid expansion of mutant stem cells
[16]. Shahriyari and Komarova compared asymmetric, symmetric, and mixed stem cell
divisions, and showed that symmetric stem cell divisions could help to delay the onset of
cancer [17]. McHale and Lander also reported similar result that symmetric divisions of
stem cell make mutation accumulation slowly [18]. These results indicates that symmet-
ric division mode has a more significant cancer-delaying effect than asymmetric divisions,
and the fate uncertainty of stochastic symmetric division of mutant stem cells could be
the reason for the cancer-delaying effect [17, 21].

To further address this issue, we here present a comparative study of asymmetric and
symmetric divisions via establishing stochastic stem cell models with mutation. By us-
ing rigorous mathematical analysis, we obtain the explicit expressions of expectation and
variance for both wild-type and mutant cells. We find that even though both asymmet-
ric and symmetric division models have the same expectation, their variances are quite
different. Namely, both models show the same statistical average, but symmetric model
shows higher fluctuation than asymmetric model. This is in line with previous observa-
tion that even though both symmetric and asymmetric division are able to maintain tissue
homeostasis, symmetric division result in greater uncertainty than asymmetric division.
The difference of variance between the two models is shown to be more remarkable for
lower mutation rates.
2 Models

In order to model cellular hierarchies driven by different stem cell division patterns, we employ a compartment model framework composed of stem cell (type $A$) and non-stem cell (type $B$) \[24, 25, 26\]. Initially there are $N$ wild-type stem cells in the population. Non-stem cells are produced by stem cell differentiations. When a stem cell divides, mutation happens with probability $P_0$, whereby either one of the daughter cells becomes mutant at random. In this model there are four different cell types: wild-type stem cell $A_0$, mutant stem cell $A_1$, wild-type non-stem cell $B_0$ and mutant non-stem cell $B_1$. We will incorporate asymmetric and symmetric division patterns into the model framework respectively.

2.1 Model for asymmetric division

For asymmetric division mode, the schematic representation of the model is present as follows

\[
\begin{align*}
A_0 \xrightarrow[\lambda(1-P_0)]{} & A_0 + B_0 \\
A_0 \xrightarrow[\lambda P_0/2]{} & A_1 + B_0 \\
A_0 \xrightarrow[\lambda P_0/2]{} & A_0 + B_1 \\
A_1 \xrightarrow[\lambda]{} & A_1 + B_1
\end{align*}
\] (1)

whereby each wild-type cell $A_0$ performs asymmetric cell division with rate $\lambda$, i.e. the waiting time for each asymmetric cell division event follows exponential distribution with parameter $\lambda$. When it happens, $A_0$ can either perform asymmetric division without any mutation (first arrow), or perform asymmetric division with one mutant daughter cell (second and third arrows). Mutant stem cell $A_1$ can also perform asymmetric division giving rise to $A_1$ and $B_1$ (fourth arrow). Here we assume that the division rate of $A_1$ is the same as $A_0$, i.e. neutral selection \[27\]. Let $S_{A_0}(t)$ and $S_{A_1}(t)$ be the cell numbers of $A_0$ and $A_1$ at time $t$ respectively. Note that asymmetric division keeps the population size of stem cell compartment constant, i.e. $\forall t \geq 0, S_{A_0}(t) + S_{A_1}(t) = N$. The stochastic dynamics of asymmetric division model is captured by the probability distribution of $S_{A_0}(t)$ whose Kolmogorov forward equation \[28\] is given by

\[
\frac{d}{dt} \{ P[S_{A_0}(t) = x] \} = -x \cdot P[S_{A_0}(t) = x] \cdot \frac{\lambda P_0}{2} + (x+1)P[S_{A_0}(t) = x+1] \cdot \frac{\lambda P_0}{2} \quad (x = 0, 1, 2, 3 \cdots N)
\] (2)
Let

\[ E[S_{A_0}(t)] = \sum_{x=0}^{N} x \cdot P[S_{A_0}(t) = x] \]  \hspace{1cm} (3)

be the expectation characterizing the statistical average of \( S_{A_0}(t) \), and

\[ Var[S_{A_0}(t)] = E[S_{A_0}^2(t)] - E[S_{A_0}(t)]^2 \]  \hspace{1cm} (4)

be the variance of \( S_{A_0}(t) \) characterizing the stochastic fluctuation of \( S_{A_0}(t) \) around the average. Similarly we can define the expectation and variance for \( S_{A_1}(t) \). We are interested in how the expectation and variance are changed to different models of stem cell division.

### 2.2 Model for symmetric division

For symmetric division, the schematic representation of the model becomes

\[
\begin{align*}
A_0 & \xrightarrow{\frac{1}{2}(1-P_0)} A_0 + A_0 \\
A_0 & \xrightarrow{\frac{1}{2}(1-P_0)} B_0 + B_0 \\
A_0 & \xrightarrow{\frac{1}{2}P_0} A_0 + A_1 \\
A_0 & \xrightarrow{\frac{1}{2}P_0} B_0 + B_1 \\
A_1 & \xrightarrow{\frac{1}{2}} A_1 + A_1 \\
A_1 & \xrightarrow{\frac{1}{2}} B_1 + B_1
\end{align*}
\]  \hspace{1cm} (5)

whereby each wild-type stem cell \( A_0 \) can either do cell proliferation (first arrow) or cell differentiation (second arrow). When mutation happens, one of the daughter cells becomes mutant (third and fourth arrows). By neutrality assumption, mutant stem cell \( A_1 \) performs symmetric divisions with rate \( \lambda \) (fifth and sixth arrows). In contrast to asymmetric model whereby \( S_{A_0}(t) + S_{A_1}(t) = N \) all the time, in symmetric model the sum of \( S_{A_0}(t) \) and \( S_{A_1}(t) \) is not constant anymore. Their joint probability distribution is captured
\[\frac{d \{ P [S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \}}{dt} = P [S_{A_1}(t) = x_1, S_{A_0}(t) = x_0 - 1] \cdot \frac{\lambda (1 - P_0) (x_0 - 1)}{2} + P [S_{A_1}(t) = x_1, S_{A_0}(t) = x_0 + 1] \cdot \frac{\lambda (x_0 + 1)}{2} - P [S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \cdot \frac{\lambda x_0}{2} - P [S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \cdot \frac{\lambda (1 - P_0) x_0}{2} + P [S_{A_1}(t) = x_1 - 1, S_{A_0}(t) = x_0] \cdot \frac{\lambda P_0 x_0}{2} - P [S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \cdot \frac{\lambda P_0 x_0}{2} + P [S_{A_1}(t) = x_1 - 1, S_{A_0}(t) = x_0] \cdot \frac{\lambda (x_1 - 1)}{2} + P [S_{A_1}(t) = x_1 + 1, S_{A_0}(t) = x_0] \cdot \frac{\lambda (x_1 + 1)}{2} - P [S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \cdot \left[ \frac{\lambda x_1}{2} + \frac{\lambda P_0 x_0}{2} \right]. \tag{6}\]

We can also define the expectation and variance for \(S_{A_0}(t)\) and \(S_{A_1}(t)\) respectively. In what follows we will compare asymmetric and symmetric models via calculating their expectations and variances.

### 3 Results

#### 3.1 Comparison of expectation

We first check the expectation of the two models. The main result is present in Theorem 1 (see A for proof)

**Theorem 1.** Both asymmetric model Eq. (2) and symmetric model Eq. (6) have the same expectations as follows:

\[E [S_{A_0}(t)] = \sum_{x=0}^{N} x \cdot P [S_{A_0}(t) = x] = N \cdot e^{-\frac{\lambda P_0 t}{2}}. \tag{7}\]
The result indicates that, even though the two models have different cell-generating mechanisms, in the population level they are equivalent to each other in the sense that on statistical average their loss of wild-type stem cell or gain of mutant stem cells follow the same function relation. In order to explain this result, let us check the cellular processes of the two models in more details. In asymmetric model, the process \( A_0 \xrightarrow{\frac{\lambda P_0}{2}} A_1 + B_0 \) produces one mutant stem cell and losses one wild-type stem cell in a single step (with rate \( \frac{\lambda P_0}{2} \)). In symmetric model, the loss and gain of stem cell is more complicated in the agent-based level. However, on average \( A_0 \xrightarrow{\frac{1}{2}(1-P_0)} A_0 + A_0 \) and \( A_0 \xrightarrow{\frac{1}{2}(1-P_0)} B_0 + B_0 \) are balanced, maintaining the number of wild-type stem cell substantially constant. Besides, \( A_0 \xrightarrow{\frac{P_0}{2}} A_0 + A_1 \) produces one mutant stem cell at rate \( \frac{\lambda P_0}{2} \) and \( A_0 \xrightarrow{\frac{P_0}{2}} B_0 + B_1 \) losses one wild-type stem cell at the same rate. In this way, symmetric model realizes the loss and gain of stem cells in several steps instead of one single step, but statistically speaking is equivalent to one single step asymmetric division.

Another feature revealed by Theorem 1 is that on average wild-type stem cells will die out \( (e^{-\frac{\lambda P_0 t}{2}} \rightarrow 0 \text{ as } t \rightarrow \infty) \) and mutant stem cells will eventually take over the whole population of stem cells. This is actually due to the fact that wild-type stem cell can become mutant but mutant stem cell cannot revert to wild-type state. This prediction is in line with the coarse-grained model by [21] (see Chapter 9). Things might be changed if more complicated selection rules are taken into account (e.g. evolutionary game [29, 30]), but even for the simple case here, the process to mutant fixation would be quite diverse due to stochasticity of different division modes. In next section we will calculate the variance for different models and we will see that asymmetric and symmetric model are quite different.

### 3.2 Comparison of variance

Let \( \text{Var}_a [\cdot] \) and \( \text{Var}_s [\cdot] \) be the variances of asymmetric and symmetric models respectively. The main results are present in Theorems 2 and 3 as follows:

**Theorem 2.** For asymmetric model Eq. (2), the variance of wild-type stem cell number is given by

\[
\text{Var}_a [S_{A_0}(t)] = N \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right).
\]  

(9)
Figure 1: The comparison between \( \text{Var}_a [S_{A_0}(t)] \) and \( \text{Var}_s [S_{A_0}(t)] \). From panel (a) to (d), the mutation probability \( P_0 = 0.05, 0.1, 0.15, 0.2 \). The joint parameters are \( N = 100, \lambda = 1 \).

Note that \( S_{A_1}(t) = N - S_{A_0}(t) \), the variance of mutant stem cell number is also given by

\[
\text{Var}_a [S_{A_1}(t)] = \text{Var}_a [S_{A_0}(t)] = N \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right).
\]  

(10)

The proof is present in [B]

**Theorem 3.** For symmetric model Eq. (6), the variance of wild-type stem cell number is given by

\[
\text{Var}_s [S_{A_0}(t)] = \frac{N (2 - P_0)}{P_0} \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right) + N \lambda t \cdot \left[ 1 - (2 - P_0) \cdot e^{-\frac{\lambda P_0 t}{2}} \right].
\]  

(11)

The variance of mutant stem cell number is given by

\[
\text{Var}_s [S_{A_1}(t)] = \frac{N (2 - P_0)}{P_0} \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right) + N \lambda t \cdot \left[ 1 - (2 - P_0) \cdot e^{-\frac{\lambda P_0 t}{2}} \right].
\]  

(12)

The proof is present in [C]

For wild-type stem cells, it is easy to check that

\[
\frac{\text{Var}_s [S_{A_0}(t)]}{\text{Var}_a [S_{A_0}(t)]} = \frac{(2 - P_0)}{P_0}.
\]  

(13)
Figure 2: The comparison between $Var_a [S_{A_1}(t)]$ and $Var_s [S_{A_1}(t)]$. From panel (a) to (d), the mutation probability $P_0 = 0.05, 0.1, 0.15, 0.2$. The joint parameters are $N = 100, \lambda = 1$.

Note that $P_0$ is mutation probability, i.e. $P_0 \leq 1$, then we have

$$\frac{Var_s [S_{A_0}(t)]}{Var_a [S_{A_0}(t)]} \geq 1.$$  \hfill (14)

The condition for equality is $P_0 = 1$, and the smaller $P_0$, the larger the difference between $Var_s [S_{A_0}(t)]$ and $Var_a [S_{A_0}(t)]$ (Fig [1]). Note that the mutation probability is generally very small ($P_0 \ll 1$), the distinction between $Var_a [S_{A_0}(t)]$ and $Var_s [S_{A_0}(t)]$ would be remarkable. Recall that asymmetric and symmetric models have the same statistical average (Theorem [1]), variance rather than expectation could be more powerful to differentiate between the two cell division mechanisms.

Furthermore, an even more significant disparity between asymmetric and symmetric models is present in mutant stem cells. From Fig [2] we can see that $Var_a [S_{A_1}(t)]$ and $Var_s [S_{A_1}(t)]$ show dramatically different trends. In contrast to $Var_a [S_{A_1}(t)]$ which tends to zero as time $t$ goes to infinity, $Var_s [S_{A_1}(t)] \approx N\lambda t$ for large time $t$. To explain it, recall that the expectation of wild-type stem cell will eventually die out (see Theorem [1]), namely, for large time $t$, there are only mutant stem cells $A_1$ in the model. Note that $S_{A_1}(t)$ either increases by one via $A_1 \to A_1 + A_1$, or decrease by one via $A_1 \to B_1 + B_1$, so $S_{A_1}(t)$ can be regarded as a continuous-time symmetric random walk [28][31]. A standard property of the random walk model is that its variance will increase linearly with time $t$. In this way, for mutant stem cells, very little fluctuation arises from asymmetric model as time goes by, whereas the fluctuation arising from symmetric model is linearly mounting up with time (Fig. [2]). Still, this result quantitatively reveals much higher uncertainty of symmetric division than asymmetric division.
3.3 Comparison between asymmetric model and Moran-type symmetric model

In previous section, we have compared the variances of asymmetric model and symmetric model, showing that for both wild-type and mutant stem cells, symmetric division shows higher variance than asymmetric division. Note that the total number of stem cells in asymmetric model remains unchanged, whereas the total stem cells number in symmetric model is variable, so the extra uncertainties of symmetric model could come from the variability of the whole population size instead of symmetric division pattern per se. To check this issue, we present a Moran-type symmetric model whereby the total number of stem cells remains unchanged. According to the birth and death events of stem cells, the six cellular processes in symmetric model Eq. (5) are classified into two classes:

- Stem cell birth class: $A_0 \xrightarrow{\frac{1}{2}(1-P_0)} A_0 + A_0, A_0 \xrightarrow{\frac{1}{2}P_0} A_0 + A_1, A_1 \xrightarrow{\frac{1}{2}} A_1 + A_1$.

- Stem cell death class: $A_0 \xrightarrow{\frac{1}{2}(1-P_0)} B_0 + B_0, A_0 \xrightarrow{\frac{1}{2}P_0} B_0 + B_1, A_1 \xrightarrow{\frac{1}{2}} B_1 + B_1$.

Enlightened from the classical Moran process [32], we assume that at each update, a stem cell is chosen for death due to one of the three death events happening. For ensuring the population size remains constant, one of the three birth events follows to happen. In this way, a Moran-type symmetric model is captured by the following Kolmogorov forward equation

$$
\frac{d}{dt} \{ P[S_{A_0}(t) = x] \} = -\frac{\lambda (1 - P_0) (N - x) x}{2N} \cdot P[S_{A_0}(t) = x] - \frac{\lambda x [N - x (1 - P_0)]}{2N} \cdot P[S_{A_0}(t) = x] + \frac{\lambda (1 - P_0) (N - x + 1)(x - 1)}{2N} \cdot P[S_{A_0}(t) = x - 1] + \frac{\lambda (x + 1) [N - (x + 1) (1 - P_0)]}{2N} \cdot P[S_{A_0}(t) = x + 1],
$$

based on which we can calculate the expectation and variance. Let $Var_m[\cdot]$ be the variance of the Moran-type symmetric model. The result is present in Theorem 4 (see D for the proof):

**Theorem 4.** For the Moran-type symmetric model Eq. (15), the expectations of wild-type and mutant stem cells are given by

$$
E[S_{A_0}(t)] = N \cdot e^{-\frac{\lambda P_0 t}{2}}, \quad E[S_{A_1}(t)] = N - N \cdot e^{-\frac{\lambda P_0 t}{2}}.
$$
Note that $S_{A_0}(t) + S_{A_1}(t) = N$, their variances are the same and given by

$$Var_m [S_{A_0}(t)] = Var_m [S_{A_1}(t)] = \frac{(2 - P_0) N^2}{NP_0 + 2 (1 - P_0)} \cdot e^{-\lambda P_0 t}$$

$$+ \frac{N^2 P_0 (N - 1)}{NP_0 + 2 (1 - P_0)} \cdot e^{-\left[\frac{N\lambda P_0 + \lambda (1 - P_0)}{N}\right] t} - N^2 \cdot e^{-\lambda P_0 t}.$$  \hspace{2cm} (17)

From Theorem 4, it is easy to see that the expectations of Moran-type symmetric model are the same as those of previous two models, namely, they share the same statistical average.

For variance, compared to the symmetric model Eq. (6), the Moran-type symmetric model removes the effect of the variability of the whole population size. Namely, the fluctuation of the Moran-type symmetric model comes from the fate uncertainty of symmetric cell division per se. Fig 3 shows that $Var_m [S_{A_1}(t)]$ is bounded and tends to zero instead of going to infinity as time goes by. Even so, we can see that the Moran-type symmetric model still shows larger variance than asymmetric model (Fig 3). Mathematically we can prove that (see E)

$$Var_m [S_{A_1}(t)] \geq Var_a [S_{A_1}(t)].$$  \hspace{2cm} (18)

The condition for equality is $P_0 = 1$. The smaller $P_0$, the larger the difference between $Var_m [S_{A_1}(t)]$ and $Var_a [S_{A_1}(t)]$. Hence Moran-type symmetric model generally show larger fluctuation around average than asymmetric model, especially for rare mutation cases ($P_0 \ll 1$).

### 4 Conclusions

In this study, we have explored how different cell division modes affect the statistical average (expectation) and the fluctuation around average (variance) of the stochastic stem cell models with mutation. By using rigorous mathematical analysis, we have shown that asymmetric model, symmetric model and Moran-type symmetric model have the same expectations. However, their variances are quite different. Symmetric divisions (both symmetric model and Moran-type symmetric model) show larger variance than asymmetric division model. The fate uncertainty of symmetric division (either cell proliferation or differentiation) and the variability of the total population size are the major sources of the variance arising from symmetric division models.
Figure 3: The comparison between $\text{Var}_a [S_{A_1}(t)]$ and $\text{Var}_m [S_{A_1}(t)]$. From panel (a) to (d), the mutation probability $P_0 = 0.05, 0.1, 0.15, 0.2$. The joint parameters are $N = 100$, $\lambda = 1$.

Our results reveal the importance of stochasticity for distinguishing between different division patterns. Note that the deterministic dynamics of asymmetric and symmetric divisions are the same, namely, it is quite impossible to identify cell division mode only based on average measurements. More attention should be paid to stochastic model, which is not an alternative to deterministic model but a more complete description [33, 34, 35]. As a supplement to statistical average, the fluctuation around average has been proved to be very important information for model comparison and selection [26]. Besides, since variance is very sensitive to division pattern and mutation rate, it can also be used to develop efficient parameter estimation method combining the stochastic stem cell model and high-resolution experimental data, which would be of great value in future researches.

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A Proof of Theorem 1

For asymmetric model Eq. (2), note that $E [S_{A_1}(t)] = N - E [S_{A_0}(t)]$, it is sufficient to prove $E [S_{A_0}(t)] = N \cdot e^{-\frac{\lambda t}{2}}$. Considering the derivative of $E [S_{A_0}(t)]$
\[
\frac{d[E(S_{A0}(t))]}{dt} = \frac{d}{dt}\left(\sum_{x=0}^{N} x \cdot P[S_{A0}(t) = x]\right) = \sum_{x=0}^{N} x \cdot \frac{d\{P[S_{A0}(t) = x]\}}{dt}
\]

(19)

and plugging Eq. (2) we have

\[
\frac{d[E(S_{A0}(t))]}{dt} = \sum_{x=0}^{N} x \cdot \frac{d\{P[S_{A0}(t) = x]\}}{dt}
\]

\[
= \sum_{x=1}^{N-1} x \cdot \frac{d\{P[S_{A0}(t) = x]\}}{dt} + 0 \cdot \frac{d\{P[S_{A0}(t) = 0]\}}{dt} + N \cdot \frac{d\{P[S_{A0}(t) = N]\}}{dt}
\]

\[
= \sum_{x=1}^{N-1} \{-x^2 \cdot P[S_{A0}(t) = x] + (x + 1 - 1)(x + 1) \cdot P[S_{A0}(t) = x + 1]\} \cdot \frac{\lambda P_0}{2}
\]

\[-N^2 \cdot \{P[S_{A0}(t) = N]\} \cdot \frac{\lambda P_0}{2}
\]

\[
= - \sum_{x=1}^{N-1} x^2 \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = x] + \sum_{x=1}^{N} x^2 \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = x]
\]

\[-N^2 \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = N] - \sum_{x=1}^{N} x \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = x]
\]

\[-N^2 \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = N] + \sum_{x=1}^{N} x \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = x]
\]

\[= - \sum_{x=1}^{N} x \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = x]
\]

\[= - N \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = N] - \sum_{x=1}^{N} x \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = x]
\]

\[-N^2 \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = N] = - \sum_{x=1}^{N} x \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = x]
\]

\[= - N \cdot \frac{\lambda P_0}{2} \cdot P[S_{A0}(t) = N] = - E[S_{A0}(t)] \cdot \frac{\lambda P_0}{2}
\]

(20)

Namely,

\[
\frac{d\{E[S_{A0}(t)]\}}{dt} = - E[S_{A0}(t)] \cdot \frac{\lambda P_0}{2}.
\]

(21)

Given the initial condition \(E[S_{A0}(0)] = N\), we obtain the solution that

\[E[S_{A0}(t)] = N \cdot e^{-\frac{\lambda P_0 t}{2}}.
\]

(22)
For the symmetric model, based on the joint distribution given by Eq. (6), we have

\[
\frac{d \{ P [ S_A(t) = x_0 ] \}}{dt} = \sum_{x_1=0}^{+\infty} \frac{d \{ P [ S_A(t) = x_1, S_A(t) = x_0 ] \}}{dt}
\]

\[
= \sum_{x_1=1}^{+\infty} \frac{d \{ P [ S_A(t) = x_1, S_A(t) = x_0 ] \}}{dt} + \frac{d \{ P [ S_A(t) = 0, S_A(t) = x_0 ] \}}{dt}
\]

\[
= P [ S_A(t) = x_0 - 1 ] \cdot \frac{\lambda (1 - P_0) (x_0 - 1)}{2} + P [ S_A(t) = x_0 + 1 ] \cdot \frac{\lambda (x_0 + 1)}{2} - P [ S_A(t) = x_0 ] \cdot \frac{\lambda (2 - P_0) x_0}{2}
\]

\[
+ P [ S_A(t) = x_0 ] \cdot \frac{\lambda P_0 x_0}{2}
\]

(23)

Then considering the derivative of \( E [ S_A(t) ] \)

\[
\frac{d \{ E [ S_A(t) ] \}}{dt} = \sum_{x=1}^{+\infty} x \cdot P [ S_A(t) = x - 1 ] \cdot \frac{\lambda (1 - P_0) (x - 1)}{2} + \sum_{x=1}^{+\infty} x \cdot P [ S_A(t) = x + 1 ] \cdot \frac{\lambda (x + 1)}{2}
\]

\[
- \sum_{x=1}^{+\infty} x \cdot [ S_A(t) = x ] \cdot \frac{\lambda (2 - P_0) x}{2}
\]

\[
= \sum_{x=1}^{+\infty} x^2 \cdot P [ S_A(t) = x ] \cdot \frac{\lambda (1 - P_0)}{2} + E [ S_A(t) ] \cdot \frac{\lambda (1 - P_0)}{2}
\]

\[
= -E [ S_A(t) ] \cdot \frac{\lambda P_0}{2}
\]

(24)

By solving the above equation we have

\[
E [ S_A(t) ] = N \cdot e^{-\frac{\lambda P_0 t}{2}}.
\]

(25)
We now calculate $E[S_A(t)]$ for symmetric model. Note that in the symmetric model, $S_A(t) + S_A(t)$ is not constant. Based on Eq. (6) we have

$$
\frac{d \{ P[S_A(t) = x_1] \}}{dt} = \sum_{x_0=0}^{\infty} \frac{d \{ P[S_A(t) = x_1, S_A(t) = x_0] \}}{dt}
$$

$$
= -\frac{\lambda P_0}{2} \cdot E[S_A(t) = x_0 \mid S_A(t) = x_1] \cdot P[S_A(t) = x_1]
$$

$$
+ \frac{\lambda P_0}{2} \cdot E[S_A(t) = x_0 \mid S_A(t) = x_1 - 1] \cdot P[S_A(t) = x_1 - 1]
$$

$$
- P[S_A(t) = x_1] \cdot \lambda x_1
$$

$$
+ P[S_A(t) = x_1 - 1] \cdot \frac{\lambda (x_1 - 1)}{2} + P[S_A(t) = x_1 + 1] \cdot \frac{\lambda (x_1 + 1)}{2}.
$$

(26)

Then the derivative of $E[S_A(t)]$ is given by

$$
\frac{d \{ E[S_A(t)] \}}{dt} = \sum_{x_1=1}^{\infty} \lambda x_1 \cdot P[S_A(t) = x_1]
$$

$$
+ \sum_{x_1=1}^{\infty} \frac{\lambda}{2} x_1 \cdot P[S_A(t) = x_1] + \sum_{x_1=1}^{\infty} \frac{\lambda}{2} x_1^2 \cdot P[S_A(t) = x_1]
$$

$$
+ \sum_{x_1=1}^{\infty} \frac{\lambda}{2} x_1^3 \cdot P[S_A(t) = x_1] - \sum_{x_1=1}^{\infty} \frac{\lambda}{2} x_1^2 \cdot P[S_A(t) = x_1]
$$

$$
= \frac{\lambda P_0}{2} \cdot E[S_A(t)].
$$

(27)

Solving the above equation as follows completes the proof

$$
E[S_A(t)] = N \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right)
$$

(28)
B Proof of Theorem \[2\]

In order to calculate \(\text{Var} \left[ S_{A_0}(t) \right]\), it is sufficient to calculate \(E \left[ S_{A_0}^2(t) \right]\). Based on Eq. \((2)\) we have

\[
\frac{d \{ E \left[ S_{A_0}^2(t) \right]\} }{dt} = \sum_{x=1}^{N} - \frac{\lambda P_0}{2} x^3 \cdot P \left[ S_{A_0}(t) = x \right] + \sum_{x=1}^{N} \frac{\lambda P_0}{2} x^3 \cdot P \left[ S_{A_0}(t) = x \right]
- \sum_{x=1}^{N} \lambda P_0 x^2 \cdot P \left[ S_{A_0}(t) = x \right] + \sum_{x=1}^{N} \frac{\lambda P_0}{2} x \cdot P \left[ S_{A_0}(t) = x \right]
= -\lambda P_0 \cdot E \left[ S_{A_0}^2(t) \right] + \frac{\lambda P_0}{2} \cdot E \left[ S_{A_0}(t) \right] \tag{29}
\]

By using the method of variation of constant and the fact that

\[
\text{Var} \left[ S_{A_0}(t) \right] = E \left[ S_{A_0}^2(t) \right] - \{E \left[ S_{A_0}(t) \right]\}^2, \tag{30}
\]

we have

\[
\text{Var} \left[ S_{A_0}(t) \right] = N \cdot e^{-\frac{\lambda P_0 t}{2}} - N \cdot e^{-\lambda P_0 t}
= N \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right) \tag{31}
\]

Note that

\[
S_{A_0}(t) + S_{A_1}(t) = N, \tag{32}
\]

then we have

\[
\text{Var} \left[ S_{A_1}(t) \right] = \text{Var} \left[ S_{A_0}(t) \right] = N \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right) \tag{33}
\]

C Proof of Theorem \[3\]

We first calculate \(\text{Var} \left[ S_{A_0}(t) \right]\). Note that

\[
\text{Var} \left[ S_{A_0}(t) \right] = E \left[ S_{A_0}^2(t) \right] - \{E \left[ S_{A_0}(t) \right]\}^2, \tag{34}
\]
it is sufficient to calculate $E \left[ S_{A_0}^2 (t) \right]$. 

\[
\frac{d \{ E \left[ S_{A_0}^2 (t) \right] \}}{dt} = \sum_{x=0}^{+\infty} x^2 \cdot \frac{P [S_{A_0} (t) = x]}{dt} = \sum_{x=1}^{+\infty} \frac{(x-1+1)^2(x-1)\lambda (1 - P_0)}{2} \cdot P [S_{A_0} (t) = x - 1] + \sum_{x=1}^{+\infty} \frac{(x+1-1)^2\lambda (x+1)}{2} \cdot P [S_{A_0} (t) = x + 1] - \sum_{x=1}^{+\infty} \frac{x^3\lambda (2 - P_0)}{2} \cdot P [S_{A_0} (t) = x] \\
= \sum_{x=1}^{+\infty} \frac{x^3\lambda (1 - P_0)}{2} \cdot P [S_{A_0} (t) = x] + \sum_{x=1}^{+\infty} \frac{2x^2\lambda (1 - P_0)}{2} \cdot P [S_{A_0} (t) = x] + \sum_{x=1}^{+\infty} \frac{x\lambda (1 - P_0)}{2} \cdot P [S_{A_0} (t) = x] + \sum_{x=2}^{+\infty} \frac{\lambda x^3}{2} \cdot P [S_{A_0} (t) = x] \\
- \sum_{x=2}^{+\infty} \frac{2\lambda x^2}{2} \cdot P [S_{A_0} (t) = x] + \sum_{x=2}^{+\infty} \frac{\lambda x}{2} \cdot P [S_{A_0} (t) = x] - \sum_{x=1}^{+\infty} \frac{x^3\lambda (1 - P_0)}{2} \cdot P [S_{A_0} (t) = x] - \sum_{x=1}^{+\infty} \frac{x^3\lambda}{2} \cdot P [S_{A_0} (t) = x] \\
= -\lambda P_0 \cdot E \left[ S_{A_0}^2 (t) \right] + E [S_{A_0}^4 (t))] \cdot \frac{\lambda (2 - P_0)}{2}
\]  

(35)
The above equation is solved using the method of variation of constant, and by using Eq. (34) we have

\[ \text{Var} [S_{A_0}(t)] = N \cdot \frac{(2 - P_0)}{P_0} \cdot e^{-\frac{\lambda P_0 t}{2}} - N \cdot \frac{(2 - P_0)}{P_0} \cdot e^{-\lambda P_0 t} \]

\[ = N \cdot \frac{(2 - P_0)}{P_0} \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left(1 - e^{-\frac{\lambda P_0 t}{2}}\right) \]

\[ = N \cdot \frac{(2 - P_0)}{P_0} \cdot e^{-\frac{\lambda P_0 t}{2}} - N \cdot \frac{(2 - P_0)}{P_0} \cdot e^{-\lambda P_0 t}. \]  

(36)

We next calculate \( \text{Var} [S_{A_1}(t)] \).

\[
\frac{d \{ \text{Var} [S_{A_1}(t)] \}}{dt} = \frac{d \{ E [S_{A_1}^2(t)] - E^2 [S_{A_1}(t)] \}}{dt}
\]

\[ = \frac{d \{ E [S_{A_1}^2(t)] \}}{dt} - 2E [S_{A_1}(t)] \cdot \frac{d \{ E [S_{A_1}(t)] \}}{dt} \]

\[ = \lambda P_0 \cdot \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P [S_{A_0}(t) = x_0, S_{A_1}(t) = x_1] \]

\[ + \frac{\lambda P_0}{2} \cdot E [S_{A_0}(t)] + \lambda \cdot E [S_{A_1}(t)] \]

(37)

\[ = \lambda P_0 \cdot E [S_{A_0}(t) \cdot S_{A_1}(t)] + \frac{\lambda P_0}{2} \cdot E [S_{A_0}(t)] + N \lambda \]

\[ - \lambda \cdot E [S_{A_0}(t)] - N \lambda P_0 \cdot E [S_{A_0}(t)] + \lambda P_0 \cdot E^2 [S_{A_0}(t)] \]

\[ = \lambda P_0 \cdot E [S_{A_0}(t) \cdot S_{A_1}(t)] + \left(\frac{\lambda P_0}{2} - \lambda - N \lambda P_0\right) \cdot E [S_{A_0}(t)] \]

\[ + \lambda P_0 \cdot E^2 [S_{A_0}(t)] + \lambda P_0. \]

Hence it is sufficient to calculate \( E [S_{A_0}(t) \cdot S_{A_1}(t)] \).

\[
\frac{d \{ E [S_{A_0}(t) \cdot S_{A_1}(t)] \}}{dt} = \frac{d \{ \sum_{x_1=0}^{+\infty} \sum_{x_0=0}^{+\infty} x_1 x_0 P [S_{A_0}(t) = x_0, S_{A_1}(t) = x_1] \}}{dt}
\]

\[ = \sum_{x_1=1}^{\infty} \sum_{x_0=1}^{\infty} x_1 x_0 \cdot \frac{d \{ P [S_{A_0}(t) = x_0, S_{A_1}(t) = x_1] \}}{dt} \]  

(38)

17
Note that

\[ \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot \frac{d\{P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0]\}}{dt} \]

\[ = \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0 - 1] \cdot \frac{\lambda (1-P_0) (x_0 - 1)}{2} \]

\[ + \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0 + 1] \cdot \frac{\lambda (x_0 + 1)}{2} \]

\[ - \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \cdot \frac{\lambda x_0}{2} \]

\[ - \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \cdot \frac{\lambda (1-P_0)x_0}{2} \]

\[ + \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1 - 1, S_{A_0}(t) = x_0] \cdot \frac{\lambda P_0 x_0}{2} \]

\[ - \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1 - 1, S_{A_0}(t) = x_0] \cdot \frac{\lambda x_1}{2} \]

\[ + \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1 - 1, S_{A_0}(t) = x_0] \cdot \frac{\lambda (x_1 - 1)}{2} \]

\[ + \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1 + 1, S_{A_0}(t) = x_0] \cdot \frac{\lambda (x_1 + 1)}{2} \]

\[ - \sum_{x_1=1}^{+\infty} \sum_{x_0=1}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0] \cdot \left( \frac{\lambda x_1}{2} + \frac{\lambda P_0 x_0}{2} \right) \]

(39)
we have
\[
\frac{d \{E[S_{A_1}(t) \cdot S_{A_0}(t)]\}}{dt} = \sum_{x_1=0}^{+\infty} \sum_{x_0=0}^{+\infty} x_1 x_0 \cdot \frac{d \{P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0]\}}{dt}
\]

\[
= \lambda P_0 \cdot E[S_{A_0}^2(t)] - \frac{\lambda P_0}{2} \cdot \sum_{x_1=0}^{+\infty} \sum_{x_0=0}^{+\infty} x_1 x_0 \cdot P[S_{A_1}(t) = x_1, S_{A_0}(t) = x_0]
\]

\[
= \frac{\lambda P_0}{2} \cdot E[S_{A_0}^2(t)] - \frac{\lambda P_0}{2} \cdot E[S_{A_1}(t) \cdot S_{A_0}(t)]
\]

Given
\[
Var[S_{A_0}(t)] = N \cdot \frac{2 - P_0}{P_0} \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left(1 - e^{-\frac{\lambda P_0 t}{2}}\right)
\]

and
\[
E[S_{A_0}(t)] = N \cdot e^{-\frac{\lambda P_0 t}{2}},
\]

we have
\[
E[S_{A_0}^2(t)] = E^2[S_{A_0}(t)] + Var[S_{A_0}(t)]
\]

\[
= \left(N^2 - N \cdot \frac{2 - P_0}{P_0}\right) \cdot e^{-\lambda P_0 t} + N \cdot \frac{2 - P_0}{P_0} \cdot e^{-\frac{\lambda P_0 t}{2}}
\]

It turns out that
\[
\frac{d \{E[S_{A_1}(t) \cdot S_{A_0}(t)]\}}{dt} = \frac{\lambda P_0}{2} \cdot \left(N^2 - N \cdot \frac{2 - P_0}{P_0}\right) \cdot e^{-\lambda P_0 t}
\]

\[
+ N \cdot \frac{\lambda (2 - P_0)}{2} \cdot e^{-\frac{\lambda P_0 t}{2}} - \frac{\lambda P_0}{2} \cdot E[S_{A_1}(t) \cdot S_{A_0}(t)].
\]

Its solution is given by
\[
E[S_{A_0}(t) \cdot S_{A_1}(t)] = \left(N^2 - N \cdot \frac{2 - P_0}{P_0}\right) \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left(1 - e^{-\frac{\lambda P_0 t}{2}}\right)
\]

\[
+ N \cdot \frac{\lambda (2 - P_0)}{2} \cdot t \cdot e^{-\frac{\lambda P_0 t}{2}}.
\]
To sum up, we obtain the differential equation for $Var \left[ S_{A_1} (t) \right]$ as follows

$$\frac{d \{ Var \left[ S_{A_1} (t) \right] \}}{dt} = N \lambda \cdot \left( -3 + \frac{3}{2} P_0 \right) \cdot e^{-\frac{\lambda P_0 t}{2}} + N \lambda \cdot (2 - P_0) \cdot e^{-\lambda P_0 t}$$ \hspace{1cm} (46)

$$+ N \cdot \frac{\lambda^2 (2 - P_0) P_0}{2} \cdot t \cdot e^{-\frac{\lambda P_0 t}{2}} + N \lambda$$

Solving the above equation completes the proof

$$Var \left[ S_{A_1} (t) \right] = N \lambda \cdot \left( -3 + \frac{3}{2} P_0 \right) \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right) + \frac{N \lambda \cdot (2 - P_0)}{\lambda P_0} \cdot \left( 1 - e^{-\lambda P_0 t} \right)$$ \hspace{1cm} (47)

$$+ N \cdot \frac{2 (2 - P_0)}{P_0} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right) - N \lambda t \cdot (2 - P_0) \cdot e^{-\frac{\lambda P_0 t}{2}} + N \lambda t$$

$$= \frac{N (2 - P_0)}{P_0} \cdot \frac{\lambda P_0}{2} \cdot \left( 1 - e^{-\frac{\lambda P_0 t}{2}} \right) + N \lambda t \cdot \left[ 1 - (2 - P_0) \cdot e^{-\frac{\lambda P_0 t}{2}} \right].$$

### D Proof of Theorem 4

We first calculate $E \left[ S_{A_0} (t) \right]$. Based on Eq. (15) we have

$$\frac{d \{ E \left[ S_{A_0} (t) \right] \}}{dt} = \sum_{x=0}^{N} x \cdot \frac{d \{ P \left[ S_{A_0} (t) = x \right] \}}{dt} = \sum_{x=1}^{N} x \cdot \frac{d \{ P \left[ S_{A_0} (t) = x \right] \}}{dt}$$

$$= - \sum_{x=1}^{N} x \cdot \frac{\lambda (1 - P_0) (N - x) x}{2N} \cdot P \left[ S_{A_0} (t) = x \right]$$

$$- \sum_{x=1}^{N} x \cdot \frac{\lambda x [N - x (1 - P_0)]}{2N} \cdot P \left[ S_{A_0} (t) = x \right]$$ \hspace{1cm} (48)

$$+ \sum_{x=1}^{N} x \cdot \frac{\lambda (1 - P_0) (N - x + 1) (x - 1)}{2N} \cdot P \left[ S_{A_0} (t) = x - 1 \right]$$

$$+ \sum_{x=1}^{N} x \cdot \frac{\lambda (x + 1) [N - (x + 1) (1 - P_0)]}{2N} \cdot P \left[ S_{A_0} (t) = x + 1 \right]$$

$$= - \frac{\lambda P_0}{2} \cdot E \left[ S_{A_0} (t) \right].$$
Its solution is given by

\[ E[S_{A_0}(t)] = N \cdot e^{-\frac{\lambda P_0}{2}}. \]  

(49)

For \( E[S^2_{A_0}(t)] \),

\[
\frac{d\{ E[S^2_{A_0}(t)] \}}{dt} = \sum_{x=0}^{N} x^2 \cdot d\{ P[S_{A_0}(t) = x] \} = \sum_{x=1}^{N} x^2 \cdot \frac{\lambda (1 - P_0) (N - x)x}{2N} \cdot P[S_{A_0}(t) = x]
\]

(50)

\[
- \sum_{x=1}^{N-1} x^2 \cdot \frac{\lambda x [N - x (1 - P_0)]}{2N} \cdot P[S_{A_0}(t) = x]
\]

\[
+ \sum_{x=1}^{N-1} x^2 \cdot \frac{\lambda (1 - P_0) (N - x + 1)(x - 1)}{2N} \cdot P[S_{A_0}(t) = x - 1]
\]

\[
+ \sum_{x=1}^{N-1} x^2 \cdot \frac{\lambda x (x + 1) [N - (x + 1) (1 - P_0)]}{2N} \cdot P[S_{A_0}(t) = x + 1]
\]

\[
= - \left( \frac{N \lambda P_0 + \lambda (1 - P_0)}{N} \right) \cdot E[S^2_{A_0}(t)] + \frac{\lambda (2 - P_0)}{2} \cdot E[S_{A_0}(t)].
\]

Its solution is given by

\[
E[S^2_{A_0}(t)] = N^2 \cdot e^{-\left[\frac{N \lambda P_0 + 2 \lambda (1 - P_0)}{2N}\right]t} + \frac{2P_0(N - 1)}{NP_0 + 2(1 - P_0)} \cdot e^{-\left[\frac{N \lambda P_0 + 2 \lambda (1 - P_0)}{2N}\right]t}.
\]

(51)

Note that

\[
Var[S_{A_0}(t)] = E[S^2_{A_0}(t)] - (E[S_{A_0}(t)])^2,
\]

we have

\[
Var[S_{A_0}(t)] = \frac{(2 - P_0) N^2}{NP_0 + 2(1 - P_0)} \cdot e^{-\lambda P_0 t} + \frac{N^2 P_0(N - 1)}{NP_0 + 2(1 - P_0)} \cdot e^{-\frac{[N \lambda P_0 + 2 \lambda (1 - P_0)]}{2N}t} - N^2 \cdot e^{-\lambda P_0 t}
\]

21
Taking note of \( S_{A_1}(t) = N - S_{A_0}(t) \), we obtain that

\[
E[S_{A_1}(t)] = N - N \cdot e^{-\frac{\lambda P_0 t}{2}}
\]  

and

\[
Var[S_{A_1}(t)] = \frac{(2 - P_0) N^2}{NP_0 + 2 (1 - P_0)} \cdot e^{-\frac{\lambda P_0 t}{2}} + \frac{N^2 P_0 (N - 1)}{NP_0 + 2 (1 - P_0)} \cdot e^{-\left[\frac{N \lambda P_0 + \lambda (1 - P_0) t}{N}\right]} - N^2 \cdot e^{-\lambda P_0 t}.
\]  

(E) Proof of inequality (18)

In order to prove \( Var_m[S_{A_0}(t)] \geq Var_a[S_{A_0}(t)] \), it is equivalent to show

\[
Var_m[S_{A_0}(t)] - Var_a[S_{A_0}(t)] = \left[ \frac{(2 - P_0) N^2}{NP_0 + 2 (1 - P_0)} - N \right] \cdot e^{-\frac{\lambda P_0 t}{2}} + N(N - 1) \cdot e^{-\lambda P_0 t} \cdot \left( \frac{NP_0}{NP_0 + 2 (1 - P_0)} \cdot e^{-\frac{\lambda (1 - P_0) t}{N}} - 1 \right) \geq 0
\]  

We can rewrite above equation as

\[
Var_m[S_{A_0}(t)] - Var_a[S_{A_0}(t)] = \frac{(N^2 - N)}{NP_0 + 2 (1 - P_0)} \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot g(t),
\]  

where

\[
g(t) = (2 - P_0) + NP_0 \cdot e^{-\frac{\lambda (1 - P_0) t}{N}} \cdot e^{-\frac{\lambda P_0 t}{2}} - (NP_0 + 2 (1 - P_0)) \cdot e^{-\frac{\lambda P_0 t}{2}}.
\]  

Note that \( \frac{(N^2 - N)}{NP_0 + 2 (1 - P_0)} \cdot e^{-\frac{\lambda P_0 t}{2}} \) is always non-negative, it is sufficient to show \( g(t) \geq 0 \).

Consider the derivative of \( g(t) \), we have

\[
g'(t) = \lambda NP_0 \cdot \left( \frac{1 - P_0}{N} - \frac{P_0}{2} \right) \cdot e^{-\frac{\lambda (1 - P_0) t}{N}} \cdot e^{-\frac{\lambda P_0 t}{2}} + \frac{\lambda P_0}{2} \cdot (NP_0 + 2 (1 - P_0)) \cdot e^{-\frac{\lambda P_0 t}{2}}
\]

\[
= \lambda P_0 \cdot e^{-\frac{\lambda P_0 t}{2}} \cdot \left( -1 + P_0 - \frac{NP_0}{2} \right) \cdot \left( e^{-\frac{\lambda (1 - P_0) t}{N}} - 1 \right) \geq 0
\]
Namely, $g(t)$ is monotonic increasing. Note that

$$g(0) = (2 - P_0) + N P_0 - (N P_0 + 2 - 2 P_0) = P_0 \geq 0,$$

we have $g(t) \geq 0$, which completes the proof.

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