



Available online at <http://scik.org>

Commun. Math. Biol. Neurosci. 2024, 2024:49

<https://doi.org/10.28919/cmbn/8497>

ISSN: 2052-2541

## MODELING THE PROGRESSION OF GENETIC DISORDERS AND INFECTIOUS DISEASES WITH MUTATIONS BY EXTENDED MARKOV PROCESSES ON DYNAMIC STATE-SPACE: A PROBABILISTIC PERSPECTIVE

MOUHAMADOU DJIMA BARANON<sup>1,2,\*</sup>, PATRICK GUGE OLOO WEKE<sup>3</sup>, JUDICAËL ALLADATIN<sup>4,5</sup>,

BONI MAXIME ALE<sup>6,7,8,9</sup>

<sup>1</sup>Department of Mathematics and Statistics, Pan African University Institute for Basic Science, Technology and Innovation (PAUSTI), Nairobi, Kenya

<sup>2</sup>Ecole Nationale de Statistique, de Planification et de Démographie (ENSPD), Université de Parakou, Bénin

<sup>3</sup>School of Mathematics, University of Nairobi, Kenya

<sup>4</sup>Faculté des Sciences de l'Education, Université de Montréal, Canada

<sup>5</sup>Consortium Siabanni pour la Formation, la Recherche et le Développement (Consortium SFR-D), Calavi, Bénin

<sup>6</sup>Institute of Tropical and Infectious Diseases, University of Nairobi, Kenya

<sup>7</sup>Strathmore University Business School, Strathmore University, Nairobi, Kenya

<sup>8</sup>Holo Global Health Research Institute, Nairobi, Kenya

<sup>9</sup>Health Data Acumen, Nairobi, Kenya

Copyright © 2024 the author(s). This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Abstract.** Markov processes have been employed for modeling various diseases. Due to their memoryless property, existing models are predominantly constructed upon static state spaces. However, genetic disorders and infectious diseases involve random events that cause their associated cells and viruses to change over time. This research is motivated by the need to address the shortcomings of current approaches in modeling the mutation behavior of these diseases. Consequently, we propose an expanded version of the discrete Markov model that accounts for the dynamic nature of the state space when modeling mutations in genetic disorders and infectious

---

\*Corresponding author

E-mail address: djima.mouhamadou@students.jkuat.ac.ke

Received February 17, 2024

diseases. Following model development, we investigate a probabilistic framework based on transition probabilities. Simulations have been conducted to compute transition probabilities, probability mass functions, and their statistical properties.

**Keywords:** Markov model; dynamic state space; mutations; genetic disorders; infectious diseases.

**2020 AMS Subject Classification:** 92C60.

## 1. INTRODUCTION

Markov Models, pioneered by the renowned Russian mathematician Andrey Markov (1856-1922), belong to a category of probabilistic models designed to analyze systems that evolve through discrete stages over time. These models leverage the Markov property, where a system's future behavior is determined solely by its current state, independent of its prior history. This inherent feature makes Discrete Markov Models exceptionally useful for scrutinizing processes characterized by memoryless attributes.

A substantial body of preceding research has undertaken a rigorous and thorough investigation into the utilization of the Markovian approach within the domain of disease modeling. These in-depth inquiries have encompassed a wide-ranging spectrum of applications, wherein Markov processes have been employed to simulate and analyze diverse diseases. Notably, these diseases span a multitude of medical conditions, including but not limited to, cancer[1, 2, 3, 4, 5, 6, 7, 8, 9], hepatitis[10], diabetes[11, 12], malaria[13] HIV [14, 15, 16, 17, 18], and cardiovascular diseases[19, 20, 21].

Furthermore, Researchers have utilized molecular biology techniques to study various genetic disorders and infectious diseases with mutations. The investigations have shown promising results in improving clinical outcomes for affected patients[22, 23]. Nevertheless, there exist some patients who do not experience any positive effects from the medications. One of the reasons for this lack of response is the presence of a point mutation in a specific gene[24, 25].

A major limitation of most Markov models is their reliance on a fixed state space, which is inadequate for accurately modeling genetic disorders and infectious diseases with mutations. Moreover, these models often assume a constant rate of disease spread, which may not reflect the true dynamics of these diseases.

Consequently, there is a need for a novel approach that offers greater flexibility and can adapt to changes in the state space over time. In this paper, we aim to address these limitations of fixed state space and constant disease spread assumptions by proposing a novel approach that employs Discrete Markov Models on dynamic state spaces.

## 2. MATERIALS AND METHODS

**2.1. Genetic disorders and Infectious diseases with mutation progression model.** Let's consider a growing disease cell population with two main types of cells: the non-mutant cells and the mutant ones. The non-mutant cells are cells that do not come from a mutation after the most recent event, especially division. Let's assume that the non-mutant cells multiply (divide) at rate  $\lambda$  and die at rate  $\mu$ . When a non-mutant cell divides, the probability of changing its background (mutation) is  $\gamma$  and the probability of being stable (non-mutation) is  $1 - \gamma$ . Concerning the mutant cells, they divide at rate  $\alpha$  and die at rate  $\beta$ . The goal is to get the distribution of the mutant cells until the total size of the cell population reaches  $N$  ( $N$  can be the detection size).

Furthermore, from the state space dynamism perspective, we assume that the mutation over time can lead to different types of mutant cells (type 1, type 2,  $\dots$ , type  $d$ ). But at the beginning, there is just one type and the other types appear over time. Let's then denote by  $n, n_1, n_2 \dots n_d$  the total number of disease cells, the number of mutant cell type 1,  $\dots$ , the number of mutant cell type  $d$ ;  $\alpha_1, \alpha_2, \dots, \alpha_d$  the increasing rate of mutant cell type 1,  $\dots$ , the increasing rate of mutant cell type  $d$ ;  $\beta_1, \beta_2, \dots, \beta_d$ , the decreasing rate of mutant cell type 1,  $\dots$ , the decreasing rate of mutant cell type  $d$ ;  $\gamma_1, \gamma_2, \dots, \gamma_d$  the non-mutant cells background changing to mutant cell type 1, type 2,  $\dots$ , type  $d$  rate respectively, when they divide.

Depending on the number of types of mutant cells, the number of mutant cells and non-mutant cells increases and decreases as follows:

TABLE 1. Non-mutant cells increasing and decreasing rates

$k$	Increasing rate	Decreasing rate
1	$\lambda(1 - \gamma_1)(n - n_1)$	$\mu(n - n_1)$
2	$\lambda(1 - \gamma_1 - \gamma_2)(n - n_1 - n_2)$	$\mu(n - n_1 - n_2)$
$\dots$	$\dots$	$\dots$
$d$	$\lambda(1 - \sum_{s=1}^d \gamma_s)(n - \sum_{s=1}^d n_s)$	$\mu(n - \sum_{s=1}^d n_s)$

That table shows how the non-mutant cells progress as new mutant cells appear.

The increasing and decreasing rates for the mutant cells are presented in the following table:

TABLE 2. Mutant cells increasing and decreasing Rates

$k$	Increasing rate	Decreasing rate
1	$\lambda \gamma_1(n - n_1) + \alpha n_1$	$\beta n_1$
2	$\lambda(\gamma_1 + \gamma_2)(n - n_1 - n_2) + \alpha_1 n_1 + \alpha_2 n_2$	$\beta_1 n_1 + \beta_2 n_2$
...	...	...
$d$	$\lambda(\sum_{s=1}^k \gamma_s)(n - \sum_{s=1}^d n_s) + \sum_{s=1}^d \alpha_s n_s$	$\sum_{s=1}^d \beta_s n_s$

The state space can be  $(n, n_1), (n, n_1, n_2), \dots (n, n_1, n_2 \dots n_d)$ . Then, this space changes over time (dynamic) depending on the appearance of the new types of mutant cells. In virtue of that, the dimension of the Markov process changes (from 2 to  $d + 1$ ).

Let's consider the starting point of the process as state  $(n, n_1) = (1, 0)$ ,  $n \in \{0, 1, 2, \dots, N\}$ .

There are two possibilities of ending the process:  $n = 0$  (extinction) or  $n = N$ .

Let's denote by  $(n_t, n_{1t}, n_{2t} \dots n_{dt})$  the process state after the  $t^{th}$  event (death or division);  $X_t = (n_t, n_{1t})$  (for  $k = 1$ );  $X_t = (n_t, n_{1t}, n_{2t})$  (for  $k = 2$ );  $X_t = (n_t, n_{1t}, n_{2t}; \dots; n_{dt})$  (for  $k = d$ ).

- For  $k = 1$  (One type of mutant cells)

The transition probabilities can be mathematically expressed as follows:

$$(2.1) \quad P_r [X_{t+1} = (i+1, j_1) \mid X_t = (i, j_1)] = \frac{\lambda(1 - \gamma_1)(i - j_1)}{\Psi_{i,j_1}}$$

$$(2.2) \quad P_r [X_{t+1} = (i+1, j_1 + 1) \mid X_t = (i, j_1)] = \frac{\lambda \gamma_1(i - j_1) + \alpha_1 j_1}{\Psi_{i,j_1}}$$

$$(2.3) \quad P_r [X_{t+1} = (i-1, j_1) \mid X_t = (i, j_1)] = \frac{\mu(i - j_1)}{\Psi_{i,j_1}}$$

$$(2.4) \quad P_r [X_{t+1} = (i-1, j_1 - 1) \mid X_t = (i, j_1)] = \frac{\beta_1 j_1}{\Psi_{i,j_1}}$$

with  $\Psi_{i,j_1} = (i - j_1)(\lambda + \mu) + j_1(\alpha_1 + \beta_1)$ , the sum of the rates, ensuring that the overall probability is normalized to 1.

This is the most elementary scenario, where only one type of mutant cell emerges. In this

simplified case, the system involves a single type of mutation event, resulting in a straightforward state space with one additional dimension to track the population of the mutant cells. By focusing on this basic setting, we can establish a foundational understanding of the disease progression dynamics driven by the mutation process. This initial exploration paves the way for more intricate investigations into systems with multiple types of mutant cells and dynamic state space changes, which can better emulate the complexity observed in genetic disorders and infectious diseases with mutations.

- For  $k = 2$  (Two types of mutant cells)

Mathematically, the transition probabilities can be expressed as follows:

$$(2.5) \quad P_r [X_{t+1} = (i+1, j_1, j_2) \mid X_t = (i, j_1, j_2)] = \frac{\lambda(1 - \gamma_1 - \gamma_2)(i - j_1 - j_2)}{\Psi_{i,j_1,j_2}}$$

$$(2.6) \quad P_r [X_{t+1} = (i+1, j_1 + 1, j_2) \mid X_t = (i, j_1, j_2)] = \frac{\lambda\gamma_1(i - j_1 - j_2) + \alpha_1 j_1}{\Psi_{i,j_1,j_2}}$$

$$(2.7) \quad P_r [X_{t+1} = (i+1, j_1, j_2 + 1) \mid X_t = (i, j_1, j_2)] = \frac{\lambda\gamma_2(i - j_1 - j_2) + \alpha_2 j_2}{\Psi_{i,j_1,j_2}}$$

$$(2.8) \quad P_r [X_{t+1} = (i-1, j_1, j_2) \mid X_t = (i, j_1, j_2)] = \frac{\mu(i - j_1 - j_2)}{\Psi_{i,j_1,j_2}}$$

$$(2.9) \quad P_r [X_{t+1} = (i-1, j_1 - 1, j_2) \mid X_t = (i, j_1, j_2)] = \frac{\beta_1 j_1}{\Psi_{i,j_1,j_2}}$$

$$(2.10) \quad P_r [X_{t+1} = (i-1, j_1, j_2 - 1) \mid X_t = (i, j_1, j_2)] = \frac{\beta_2 j_2}{\Psi_{i,j_1,j_2}}$$

with  $\Psi_{i,j_1,j_2} = (\lambda + \mu)(i - j_1 - j_2) + (\alpha_1 + \beta_1)j_1 + (\alpha_2 + \beta_2)j_2$ .

In this more complex scenario, the system involves the appearance of two distinct types of mutant cells. This augmented state space encompasses additional dimensions to account for the numbers of both mutant cell types, allowing comprehensive monitoring of the dynamics of each subtype independently. The consideration of two mutant cell types enriches the model, enabling a more nuanced exploration of disease progression patterns and the interplay between the mutant cell populations. Additionally, this analysis serves as a stepping stone towards addressing more intricate scenarios with multiple mutant cell types and dynamic changes in the state space, reflecting the evolving nature of genetic disorders and infectious diseases with mutations.

- For  $k = d$  ( $d \geq 2$ ) ( $d$  types of mutant cells)

Mathematically, the transition probabilities are expressed as follows:

$$(2.11) \quad P_r [X_{t+1} = (i+1, j_1, \dots, j_d) \mid X_t = (i, j_1, \dots, j_d)] = \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i, j_1, \dots, j_d}}$$

$$(2.12) \quad P_r [X_{t+1} = (i+1, j_1 + 1, \dots, j_d) \mid X_t = (i, j_1, \dots, j_d)] = \frac{\lambda \gamma_1(i - \sum_{s=1}^d j_s) + j_1 \alpha_1}{\Psi_{i, j_1, \dots, j_d}}$$

$$(2.13) \quad P_r [X_{t+1} = (i+1, j_1, j_2 + 1, \dots, j_d) \mid X_t = (i, j_1, \dots, j_d)] = \frac{\lambda \gamma_2(i - \sum_{s=1}^d j_s) + j_2 \alpha_2}{\Psi_{i, j_1, \dots, j_d}}$$

⋮

$$(2.14) \quad P_r [X_{t+1} = (i+1, j_1, \dots, j_d + 1) \mid X_t = (i, j_1, \dots, j_d)] = \frac{\lambda \gamma_d(i - \sum_{s=1}^d j_s) + j_d \alpha_d}{\Psi_{i, j_1, \dots, j_d}}$$

$$(2.15) \quad P_r [X_{t+1} = (i-1, j_1, \dots, j_d) \mid X_t = (i, j_1, \dots, j_d)] = \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i, j_1, \dots, j_d}}$$

$$(2.16) \quad P_r [X_{t+1} = (i-1, j_1 - 1, \dots, j_d) \mid X_t = (i, j_1, \dots, j_d)] = \frac{j_1 \beta_1}{\Psi_{i, j_1, \dots, j_d}}$$

$$(2.17) \quad P_r [X_{t+1} = (i-1, j_1, j_2 - 1, \dots, j_d) \mid X_t = (i, j_1, \dots, j_d)] = \frac{j_2 \beta_2}{\Psi_{i, j_1, \dots, j_d}}$$

⋮

$$(2.18) \quad P_r [X_{t+1} = (i-1, j_1, \dots, j_d - 1) \mid X_t = (i, j_1, \dots, j_d)] = \frac{j_d \beta_d}{\Psi_{i, j_1, \dots, j_d}}$$

with  $\Psi_{i, j_1, \dots, j_d} = (\lambda + \mu)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d (\alpha_s + \beta_s) j_s$ .

In this general scenario, the system encompasses  $d$  distinct types of mutant cells, each contributing to the progression of the disease. As the disease evolves, the state space now expands to  $d + 1$  dimensions, accommodating the numbers of all  $d$  mutant cell types, as well as the non-mutant cell population.

**2.2. Transition matrices.** Let's define by  $A_i$  and  $B_i$  the transition probability sub-matrix from  $i$  to  $i + 1$  and from  $i$  to  $i - 1$  level, respectively.

• **For  $k = 1$**

We start with the simplest case where just one type of mutant cell is known. The state space is  $\{(i, 0), (i, 1), \dots, (i, i)\}$  ( $i$  being the total number of cells).

(2.19)

$$A_i = \begin{pmatrix} \frac{i\lambda(1-\gamma_1)}{\psi_{i0}} & \frac{i\lambda\gamma_1}{\psi_{i0}} & 0 & 0 & \dots & \dots & \dots & 0 \\ 0 & \frac{(i-1)\lambda(1-\gamma_1)}{\psi_{i1}} & \frac{(i-1)\lambda\gamma_1+\alpha_1}{\psi_{i1}} & 0 & \dots & \dots & \dots & 0 \\ 0 & 0 & \frac{(i-2)\lambda(1-\gamma_1)}{\psi_{i2}} & \frac{(i-2)\lambda\gamma_1+2\alpha_1}{\psi_{i2}} & \dots & \dots & \dots & 0 \\ \dots & 0 \\ 0 & 0 & \dots & \dots & \dots & \frac{\lambda(1-\gamma_1)}{\psi_{ii-1}} & \frac{\lambda\gamma_1+(i-1)\alpha_1}{\psi_{ii-1}} & 0 \\ 0 & 0 & \dots & \dots & \dots & \dots & 0 & \frac{i\alpha_1}{\psi_{ii}} \end{pmatrix}$$

where  $A_i$  is a  $(i+1)(i+2)$  matrix.

(2.20)

$$B_i = \begin{pmatrix} \frac{i\mu}{\psi_{i0}} & 0 & 0 & \dots & \dots & 0 \\ \frac{\beta_1}{\psi_{i1}} & \frac{(i-1)\mu}{\psi_{i1}} & 0 & \dots & \dots & 0 \\ 0 & \frac{2\beta_1}{\psi_{i2}} & \frac{(i-2)\mu}{\psi_{i2}} & \dots & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & \dots & \frac{(i-1)\beta_1}{\psi_{ii-1}} & \frac{\mu}{\psi_{ii-1}} \\ 0 & 0 & \dots & \dots & 0 & \frac{i\beta_1}{\psi_{ii}} \end{pmatrix}$$

where  $B_i$  is a  $(i+1)(i)$  matrix.

- For  $k = 2$

(2.21)

$$A_i = \begin{pmatrix} \frac{i\lambda(1-\gamma')}{\psi_{i,0'}} & \frac{i\lambda\gamma'}{\psi_{i,0'}} & 0 & 0 & \dots & \dots & \dots & 0 \\ 0 & \frac{2(i-1)\lambda(1-\gamma')}{\psi_{i,1'}} & \frac{2(i-1)\lambda\gamma'+\alpha'}{\psi_{i,1'}} & 0 & \dots & \dots & \dots & 0 \\ 0 & 0 & \frac{3(i-2)\lambda(1-\gamma')}{\psi_{i,2'}} & \frac{3(i-2)\lambda\gamma'+3\alpha'}{\psi_{i,2'}} & \dots & \dots & \dots & 0 \\ \dots & 0 \\ 0 & 0 & \dots & \dots & \dots & \frac{i\lambda(1-\gamma')}{\psi_{i,(i-1)'}} & \frac{i\lambda\gamma'+\frac{1}{2}i(i-1)\alpha'}{\psi_{i,(i-1)'}} & 0 \\ 0 & 0 & \dots & \dots & \dots & \dots & 0 & \frac{\frac{1}{2}i(i+1)\alpha'}{\psi_{i,i'}} \end{pmatrix}$$

where  $A_i$  is a  $(i+1)(i+2)$  matrix,  $\gamma' = \gamma_1 + \gamma_2$ , and  $\alpha' = \alpha_1 + \alpha_2$ .

$$(2.22) \quad B_i = \begin{pmatrix} \frac{i\mu}{\psi_{i,0'}} & 0 & 0 & \dots & \dots & 0 \\ \frac{\beta'}{\psi_{i,1'}} & \frac{2(i-1)\mu}{\psi_{i,1'}} & 0 & \dots & \dots & 0 \\ 0 & \frac{3\beta'}{\psi_{i,2'}} & \frac{3(i-2)\mu}{\psi_{i,2'}} & \dots & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & \dots & \frac{\frac{1}{2}(i-1)i\beta'}{\psi_{i,(i-1)'}} & \frac{i\mu}{\psi_{i,(i-1)'}} \\ 0 & 0 & \dots & \dots & 0 & \frac{\frac{1}{2}i(i+1)\beta'}{\psi_{i,i'}} \end{pmatrix}$$

where  $B_i$  is a  $(i+1)(i)$  matrix,  $\beta' = \beta_1 + \beta_2$ ,  $\psi_{i,0'} = \psi_{i,0,0}$ ,  $\psi_{i,1'} = \psi_{i,1,0} + \psi_{i,0,1}$ ,  $\psi_{i,2'} = \psi_{i,1,1} + \psi_{i,2,0} + \psi_{i,0,2} \dots$ ,  $\psi_{i,i'} = \psi_{i,i,0} + \psi_{i,i-1,1} + \psi_{i,i-2,2} + \dots + \psi_{i,0,i}$ .

• For  $k \geq 2$

$$(2.23) \quad A_i = \begin{pmatrix} \frac{c_0 i \lambda (1-\gamma')}{\psi_{i,0'}} & \frac{c_0 i \lambda \gamma'}{\psi_{i,0'}} & 0 & 0 & \dots & \dots & \dots & 0 \\ 0 & \frac{c_1 (i-1) \lambda (1-\gamma')}{\psi_{i,1'}} & \frac{c_1 (i-1) \lambda \gamma' + \frac{c_1}{d} \alpha'}{\psi_{i,1'}} & 0 & \dots & \dots & \dots & 0 \\ 0 & 0 & \frac{c_2 (i-2) \lambda (1-\gamma')}{\psi_{i,2'}} & \frac{c_2 (i-2) \lambda \gamma' + \frac{2c_2}{d} \alpha'}{\psi_{i,2'}} & \dots & \dots & \dots & 0 \\ \dots & 0 \\ \dots & 0 \\ \dots & 0 \\ 0 & 0 & \dots & \dots & \dots & \frac{c_{i-1} \lambda (1-\gamma')}{\psi_{i,(i-1)'}} & \frac{c_{i-1} \lambda \gamma' + \frac{(i-1)c_{i-1}}{d} \alpha'}{\psi_{i,(i-1)'}} & 0 \\ 0 & 0 & \dots & \dots & \dots & \dots & 0 & \frac{\frac{ic_i}{d} \alpha'}{\psi_{i,i'}} \end{pmatrix}$$

where  $A_i$  is a  $(i+1)(i+2)$  matrix,  $\gamma' = \sum_{s=1}^d \gamma_s$ , and  $\alpha' = \sum_{s=1}^d \alpha_s$

$$(2.24) \quad B_i = \begin{pmatrix} \frac{c_0 i \mu}{\psi_{i,0'}} & 0 & 0 & \dots & \dots & 0 \\ \frac{\frac{c_1}{d} \beta'}{\psi_{i,1'}} & \frac{c_1 (i-1) \mu}{\psi_{i,1'}} & 0 & \dots & \dots & 0 \\ 0 & \frac{\frac{2c_2}{d} \beta'}{\psi_{i,2'}} & \frac{c_2 (i-2) \mu}{\psi_{i,2'}} & \dots & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & \dots & \frac{\frac{(i-1)c_{i-1}}{d} \beta'}{\psi_{i,(i-1)'}} & \frac{c_{i-1} \mu}{\psi_{i,(i-1)'}} \\ 0 & 0 & \dots & \dots & 0 & \frac{\frac{ic_i}{d} \beta'}{\psi_{i,i'}} \end{pmatrix}$$

where  $B_i$  is a  $(i+1)(i)$  matrix,  $\beta' = \sum_{s=1}^d \beta_s$ ,  $\psi_{i,0'} = \psi_{i,0,0,\dots,0}$ ,  $\psi_{i,1'} = \psi_{i,1,0,\dots,0} + \psi_{i,0,1,0,\dots,0} + \psi_{i,0,0,\dots,1}$ ,  $\psi_{i,2'} = \sum_{(j_1+j_2+\dots+j_k=2)} \psi_{i,j_1,j_2,\dots,j_d}$ , ...,  $\psi_{i,i'} = \sum_{(j_1+j_2+\dots+j_k=i)} \psi_{i,j_1,j_2,\dots,j_d}$ , and  $c_l = \#(\sum_{s=1}^d j_s = l)$ ,  $0 \leq l \leq i$ .

The process transition probability matrix can be expressed using  $A_i$  and  $B_i$  as follows:

$$(2.25) \quad T_m = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & \dots & \dots & \dots & 0 \\ B_1 & 0 & A_1 & 0 & 0 & \dots & \dots & \dots & 0 \\ 0 & B_2 & 0 & A_2 & 0 & \dots & \dots & \dots & 0 \\ 0 & 0 & B_3 & 0 & A_3 & \dots & \dots & \dots & 0 \\ \dots & \dots \\ 0 & \dots & \dots & \dots & \dots & \dots & B_{N-1} & 0 & A_{N-1} \\ 0 & \dots & \dots & \dots & \dots & \dots & \dots & 0 & I_N \end{pmatrix}$$

**2.3. Probability Mass Function (PMF).** Based on the described model, a probability mass function can be established. That will be very useful, especially when it comes to estimating the parameters of the model.

Let's consider  $n_t$ ,  $n_{1(t)}$ ,  $n_{2(t)}$ , ..., and  $n_{d(t)}$  as defined below: the total number of disease cells, the number of mutant cells type 1, the number of mutant cells type 2, ..., the number of mutant cells type  $d$ , respectively.

Then let  $x, x_1, x_2, \dots, x_d$ , and  $z$  be defined as follows:

$$x = n_{t+1} - n_t$$

$$x_1 = n_{1(t+1)} - n_{1(t)}$$

$$x_2 = n_{2(t+1)} - n_{2(t)}$$

$$\vdots$$

$$x_d = n_{d(t+1)} - n_{d(t)}$$

$$z = x + x_1 + \dots + x_d$$

- **Case of one type mutant cell ( $k = 1$ )**

Based on the different scenarios, the variable  $z$  can take the following values as described by Table 3.

TABLE 3. Conceptual table for the random variable  $z$  for one type of mutant cell

$(n_{t+1}, n_{1(t+1)})$	$(x, x_1)$	$z$
$(i+1, j_1)$	$(1, 0)$	1
$(i+1, j_1 + 1)$	$(1, 1)$	2
$(i-1, j_1)$	$(-1, 0)$	-1
$(i-1, j_1 - 1)$	$(-1, -1)$	-2

Therefore, the probability mass function can be written as:

$$(2.26) \quad Pr(Z = z) = \left( \frac{\lambda(1 - \gamma_1)(i - j_1)}{\Psi_{i,j_1}} \right)^{\mathbb{1}_1(z)} \left( \frac{\lambda\gamma_1(i - j_1) + \alpha_1 j_1}{\Psi_{i,j_1}} \right)^{\mathbb{1}_2(z)} \left( \frac{\mu(i - j_1)}{\Psi_{i,j_1}} \right)^{\mathbb{1}_{-1}(z)} \left( \frac{\beta_1 j_1}{\Psi_{i,j_1}} \right)^{\mathbb{1}_{-2}(z)}$$

with  $z \in \{1, 2, -1, -2\}$  and  $\mathbb{1}_l(z)$  ( $l \in \{1, 2, -1, -2\}$ ) an indicator function taking the value 1 when  $z = l$  and 0 else.

- **Case of two types of mutant cell ( $k = 2$ )**

The variable  $z$  can take the following values as described by Table 4 based on the six different scenarios.

TABLE 4. Conceptual table for the random variable  $z$  for two types of mutant cell

$(n_{t+1}, n_{1(t+1)}, n_{2(t+1)})$	$(x, x_1, x_2)$	$z$
$(i+1, j_1, j_2)$	$(1, 0, 0)$	1
$(i+1, j_1 + 1, j_2)$	$(1, 1, 0)$	2
$(i+1, j_1, j_2 + 1)$	$(1, 0, 1)$	2
$(i-1, j_1, j_2)$	$(-1, 0, 0)$	-1
$(i-1, j_1 - 1, j_2)$	$(-1, -1, 0)$	-2
$(i-1, j_1, j_2 - 1)$	$(-1, 0, -1)$	-2

Four possible values can be taken by  $z$  ( $1, 2, -1, -2$ ) with different occurrences.

Therefore, the probability mass function can be written as :

$$\begin{aligned}
 Pr(Z = z) &= \left( \frac{\lambda(1 - \gamma_1 - \gamma_2)(i - j_1 - j_2)}{\Psi_{i,j_1,j_2}} \right)^{\mathbb{M}_1(z)} \left( \frac{\lambda(\gamma_1 + \gamma_2)(i - j_1 - j_2) + \alpha_1 j_1 + \alpha_2 j_2}{\Psi_{i,j_1,j_2}} \right)^{\mathbb{M}_2(z)} \\
 (2.27) \quad &\times \left( \frac{\mu(i - j_1 - j_2)}{\Psi_{i,j_1,j_2}} \right)^{\mathbb{M}_{-1}(z)} \left( \frac{\beta_1 j_1 + \beta_2 j_2}{\Psi_{i,j_1,j_2}} \right)^{\mathbb{M}_{-2}(z)}
 \end{aligned}$$

with  $z \in \{1, 2, -1, -2\}$  and  $\mathbb{M}_l(z)$  defined as previously.

- **General case of  $d$  types of mutant cell ( $d \geq 2$ )**

The variable  $z$  can take the following values as described by Table 5 based on the different scenarios.

TABLE 5. Conceptual table for the random variable  $z$  for the general case of  $d$  types of mutant cell

$(n_{t+1}, n_{1(t+1)}, n_{2(t+1)}, \dots, n_{d(t+1)})$	$(x, x_1, x_2, \dots, x_d)$	$z$
$(i+1, j_1, j_2, \dots, j_d)$	$(1, 0, 0, \dots, 0)$	1
$(i+1, j_1+1, j_2, \dots, j_d)$	$(1, 1, 0, \dots, 0)$	2
$(i+1, j_1, j_2+1, \dots, j_d)$	$(1, 0, 1, \dots, 0)$	2
...	...	...
$(i+1, j_1, j_2, \dots, j_d+1)$	$(1, 0, 0, \dots, 1)$	2
$(i-1, j_1, j_2, \dots, j_d)$	$(-1, 0, 0, \dots, 0)$	-1
$(i-1, j_1-1, j_2, \dots, j_d)$	$(-1, -1, 0, \dots, 0)$	-2
$(i-1, j_1, j_2-1, \dots, j_d)$	$(-1, 0, -1, \dots, 0)$	-2
...	...	...
$(i-1, j_1, j_2, \dots, j_d-1)$	$(-1, 0, 0, \dots, -1)$	-2

**Proposition 2.1** The probability mass function is defined as :

$$\begin{aligned}
 Pr(Z = z) &= \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_1(z)} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_2(z)} \\
 (2.28) \quad &\times \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-1}(z)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-2}(z)}
 \end{aligned}$$

with  $z \in \{1, 2, -1, -2\}$  and  $\mathbb{W}_l(z)$  defined as previously.

### Proof

$(i - \sum_{s=1}^k j_s) \geq 0$  (the total number of disease cells is always greater than the number of mutant cells).

Moreover, the parameters  $\lambda, \mu, \gamma_1, \alpha_1, \beta_1, \gamma_2, \alpha_2, \beta_2, \dots, \gamma_k, \alpha_k, \beta_k$  take their values in  $[0, 1]$  as they are probabilities.

Then

$$(2.29) \quad Pr(Z = z) \geq 0, \forall z \in \{1, 2, -1, -2\}$$

Furthermore,

$$\begin{aligned} \sum_z Pr(Z = z) &= \sum_z \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{W}_1(z)} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{W}_2(z)} \\ &\quad \times \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{W}_{-1}(z)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{W}_{-2}(z)} \\ \sum_z Pr(Z = z) &= \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(1)} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \\ &\quad \times \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} + \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \\ &\quad \times \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(1)} \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \\ &\quad + \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \left( \frac{\lambda(\sum_{s=1}^k \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \\ &\quad \times \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(1)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} + \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \\ &\quad \times \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{(0)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{(1)} \\ &= \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} + \frac{\lambda(\sum_{s=1}^k \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ &\quad + \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} + \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ &= \frac{(\lambda + \mu)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d (\alpha_s + \beta_s) j_s}{\Psi_{i,j_1,\dots,j_d}} = 1 \end{aligned}$$

Therefore,  $P(Z = z)$  is a probability mass function.

**2.4. Statistical properties.** For the statistical properties, we consider the general case of mutant cell types.

**2.4.1. Cumulative distribution function.** To derive the cumulative distribution function (CDF) from the probability mass function (PMF), we need to calculate the cumulative probabilities for each value of  $z$ . The CDF, denoted as  $F(z)$  gives the probability that the random variable Zakes a value less than or equal to  $z$

$$\begin{aligned} F(-2) &= Pr(Z \leq -2) = Pr(Z = -2) = \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ F(-1) &= Pr(Z \leq -1) = \frac{\mu(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ F(1) &= Pr(Z \leq 1) = \frac{(\lambda + \mu - \lambda \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \end{aligned}$$

$$F(2) = Pr(Z \leq 2) = Pr(Z = -2) + Pr(Z = -1) + Pr(Z = 1) + Pr(Z = 2) = 1$$

**2.4.2. 1st and 2nd Moments.** Deriving the moments is crucial when introducing a new distribution. They hold great importance in statistical analysis, especially in practical applications. Moments are utilized to calculate various statistical measures such as measures of central tendency, dispersion, and shape, among others.

$$\begin{aligned} \mathbb{E}(Z) &= \sum_{z \in \{1,2,-1,-2\}} z \cdot Pr(Z = z) \\ &= 1 \cdot \frac{\lambda (1 - \sum_{s=1}^d \gamma_s) (i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} + 2 \cdot \frac{\lambda (\sum_{s=1}^d \gamma_s) (i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ &\quad + (-1) \cdot \frac{\mu (i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} + (-2) \cdot \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ &= \frac{(\lambda - \mu + \lambda \sum_{s=1}^d \gamma_s) (i - \sum_{s=1}^d j_s) + 2 \sum_{s=1}^d (\alpha_s - \beta_s) j_s}{\Psi_{i,j_1,\dots,j_d}} \end{aligned}$$

$$\begin{aligned} \mathbb{E}(Z^2) &= \sum_{z \in \{1,2,-1,-2\}} z^2 \cdot Pr(Z = z) \\ &= 1 \cdot \frac{\lambda (1 - \sum_{s=1}^d \gamma_s) (i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} + 4 \cdot \frac{\lambda (\sum_{s=1}^d \gamma_s) (i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ &\quad + \frac{\mu (i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} + 4 \cdot \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \end{aligned}$$

$$= \frac{(\lambda + \mu + 3\lambda \sum_{s=1}^d \gamma_s) (i - \sum_{s=1}^d j_s) + 4 \sum_{s=1}^d (\alpha_s + \beta_s) j_s}{\Psi_{i,j_1,\dots,j_d}}$$

### 2.4.3. Moment Generating function.

$$\begin{aligned} M_Z(t) &= E[e^{tZ}] = \sum_z e^{tz} Pr(Z=z) \\ &= e^t \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_1(1)} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_2(1)} \\ &\quad \times \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-1}(1)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-2}(1)} + e^{2t} \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_1(2)} \\ &\quad \times \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_2(2)} \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-1}(2)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-2}(2)} \\ &\quad + e^{-t} \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_1(-1)} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_2(-1)} \\ &\quad \times \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-1}(-1)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-2}(-1)} + e^{-2t} \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_1(-2)} \\ &\quad \times \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_2(-2)} \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-1}(-2)} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right)^{\mathbb{M}_{-2}(-2)} \\ M_Z(t) &= e^t \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + e^{2t} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \\ &\quad + e^{-t} \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + e^{-2t} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \end{aligned}$$

### 2.4.4. The $n^{th}$ moment. $\mathbb{E}(Z^n) = \frac{d^n}{dt^n} M_Z(t) \Big|_{t=0}$

$$\begin{aligned} \frac{d^n}{dt^n} M_Z(t) &= \frac{d^n}{dt^n} \left[ e^t \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + e^{2t} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \right. \\ &\quad \left. + e^{-t} \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + e^{-2t} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \right] \\ &= e^t \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + 2^n e^{2t} \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \\ &\quad + (-1)^n e^{-t} \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + (-2)^n e^{-2t} \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \\ \mathbb{E}(Z^n) &= \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + 2^n \lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + 2^n \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \\ &\quad + \frac{(-1)^n \mu(i - \sum_{s=1}^d j_s) + (-2)^n \sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \end{aligned}$$

$$= \frac{\left( \lambda + \lambda(2^n - 1)(\sum_{s=1}^d \gamma_s) + (-1)^n \mu \right) (i - \sum_{s=1}^d j_s) + 2^n \sum_{s=1}^d (\alpha_s + (-1)^n \beta_s) j_s}{\Psi_{i,j_1,\dots,j_d}}$$

#### 2.4.5. Mean deviation.

$$\begin{aligned} \text{Mean Deviation} &= \sum_z |z - E(Z)| \cdot Pr(Z = z) \\ &= |1 - E(Z)| \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + |2 - E(Z)| \\ &\quad \times \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) + |1 + E(Z)| \cdot \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) \\ &\quad + |2 + E(Z)| \cdot \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \end{aligned}$$

#### 2.4.6. Median deviation.

$$\begin{aligned} \text{Median Deviation} &= \sum_z |Z - z_{\text{median}}| \cdot Pr(Z = z) \\ &= |1 - z_{\text{median}}| \cdot \left( \frac{\lambda(1 - \sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) + |2 - z_{\text{median}}| \\ &\quad \times \left( \frac{\lambda(\sum_{s=1}^d \gamma_s)(i - \sum_{s=1}^d j_s) + \sum_{s=1}^d \alpha_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) + |1 + z_{\text{median}}| \cdot \left( \frac{\mu(i - \sum_{s=1}^d j_s)}{\Psi_{i,j_1,\dots,j_d}} \right) \\ &\quad + |2 + z_{\text{median}}| \cdot \left( \frac{\sum_{s=1}^d \beta_s j_s}{\Psi_{i,j_1,\dots,j_d}} \right) \end{aligned}$$

with

$$z_{\text{median}} = \operatorname{argmin}_z \left\{ \sum_{z' \leq z} Pr(Z = z') \geq 0.5 \right\}$$

### 3. SIMULATION STUDY

For the simulations, we examine three main scenarios. The first one investigates two types of mutant cells, while the second one concentrates on five types of mutant cells. Lastly, the third scenario considers ten types of mutant cells. Following the generation of random parameter values and cell sizes for each situation, we determine transition probabilities and transition matrices using our model. For each scenario, we computed the transition probabilities, the probability mass function, the cumulative distribution function, the first and the second moments, and the

moment generating function for different sample sizes: 500, 1000, and 50000. The R software has been used. The results of the simulations show that no matter the dimension (number of mutant cell types), or the number of disease cells, the model is able to give the probability of the next events correctly.

**3.1. Scenarios of two types of mutant cells ( $k = 2$ )**. The table 6 below presents the parameter values randomly generated for two types of mutant cells.

TABLE 6. Parameter values for two types of mutant cells ( $k=2$ )

Parameter	Values
$\lambda$	0.025
$\mu$	0.478
$\gamma$	0.289 0.147
$\alpha$	0.94 0.246
$\beta$	0.046 0.042

**3.1.1. Transition probabilities for 500 disease cells, 42 mutant cells type 1, and 358 mutant cells type 2.** Table 7 shows the transition probabilities for the case of 500 disease cells, 42 mutant cells type 1, and 358 mutant cells type 2.

TABLE 7. Transition probabilities for  $i = 500$  and  $j = (42, 358)$

Probability	Value
Prob[( <b>501</b> , 42 358 )/( 500 , 42 358 )]	0.007122499
Prob[( <b>501</b> , <b>43</b> 358 )/( 500 , 42 358 )]	0.2064125
Prob[( <b>501</b> , 42 <b>359</b> )/( 500 , 42 358 )]	0.4540896
Prob[( <b>499</b> , 42 358 )/( 500 , 42 358 )]	0.2452617
Prob[( <b>499</b> , <b>41</b> 358 )/( 500 , 42 358 )]	0.009821704
Prob[( <b>499</b> , 42 <b>357</b> )/( 500 , 42 358 )]	0.07729203
<b>Total</b>	<b>1</b>

**3.1.2.** *Probability Mass Function (PMF) and statistical properties for  $k = 2$ ,  $i = 500$  and  $j = (42, 358)$ .* The PMF and CDF are presented in table 8.

TABLE 8. PMF and CDF for  $i = 500$  and  $j = (42, 358)$ 

<b>z</b>	-2	-1	1	2	Total
<b>Prob (<math>Z = z</math>)</b>	0.0871	0.2454	0.0072	0.66	1.000
<b>Prob (<math>Z \geq z</math>)</b>	0.0871	0.3325	0.3397	1.000	

$$\mathbb{E}(Z) = 0.9076; \mathbb{E}(Z^2) = 0.7959$$

$$M_Z(t) = 0.0072e^t + 0.66e^{2t} + 0.2454e^{-t} + 0.0871e^{-2t}$$

**3.1.3.** *Transition probabilities for 1,000 disease cells, 142 mutant cells type 1, and 543 mutant cells type 2.* The transition probabilities are computed and presented in Table 9.

TABLE 9. Transition probabilities for  $i = 1000$  and  $j = (142, 543)$ 

<b>Probability</b>	<b>Value</b>
Prob[( <b>1001</b> , 142 543 )/( 1000 , 142 543 )]	0.009611565
Prob[( <b>1001</b> , <b>143</b> 543 )/( 1000 , 142 543 )]	0.2986075
Prob[( <b>1001</b> , 142 <b>544</b> )/( 1000 , 142 543 )]	0.29636
Prob[( <b>999</b> , 142 543 )/( 1000 , 142 543 )]	0.3309721
Prob[( <b>999</b> , <b>141</b> 543 )/( 1000 , 142 543 )]	0.01422581
Prob[( <b>999</b> , 142 <b>542</b> )/( 1000 , 142 543 )]	0.050223
<b>Total</b>	<b>1</b>

**3.1.4.** *Probability Mass Function and statistical properties for  $k = 2$ ,  $i = 1000$  and  $j = (142, 543)$ .* The PMF and CDF are presented in the following table (10).

TABLE 10. PMF and CDF for  $i = 1000$  and  $j = (142, 543)$

<b>z</b>	-2	-1	1	2	Total
<b>Prob (<math>Z = z</math>)</b>	0.0645	0.331	0.0098	0.5947	1.000
<b>Prob (<math>Z \geq z</math>)</b>	0.0645	0.3955	0.4053	1.000	

$$\mathbb{E}(Z) = 0.7392; \mathbb{E}(Z^2) = 0.5896$$

$$M_Z(t) = 0.0098e^t + 0.5947e^{2t} + 0.331e^{-t} + 0.0645e^{-2t}$$

**3.1.5.** *Transition probabilities for 50,000 disease cells, 14182 mutant cells type 1, and 15179 mutant cells type 2.* The transition probabilities are computed and presented as follows (Table 11).

TABLE 11. Transition probabilities for  $i = 50000$  and  $j = (14182, 15179)$

Probability	Value
Prob[( <b>50001</b> , 14182 15179 )/( 50000 , 14182 15179 )]	0.009968881
Prob[( <b>50001</b> , <b>14183</b> 15179 )/( 50000 , 14182 15179 )]	0.4694082
Prob[( <b>50001</b> , 14182 <b>15180</b> )/( 50000 , 14182 15179 )]	0.1326322
Prob[( <b>49999</b> , 14182 15179 )/( 50000 , 14182 15179 )]	0.3432762
Prob[( <b>49999</b> , <b>14181</b> 15179 )/( 50000 , 14182 15179 )]	0.02249057
Prob[( <b>49999</b> , 14182 <b>15178</b> )/( 50000 , 14182 15179 )]	0.0222239
<b>Total</b>	<b>1</b>

**3.1.6.** *Probability Mass Function and statistical properties for  $k = 2$ ,  $i = 50000$  and  $j = (14182, 15179)$ .* The PMF and CDF are presented in the Table 12.

TABLE 12. PMF and CDF for  $i = 50000$  and  $j = (14182, 15179)$ 

<b>z</b>	-2	-1	1	2	Total
<b>Prob (<math>Z = z</math>)</b>	0.0449	0.3433	0.0101	0.6017	1.000
<b>Prob (<math>Z \geq z</math>)</b>	0.0449	0.3882	0.3983	1.000	

$$\mathbb{E}(Z) = 0.7804; \mathbb{E}(Z^2) = 0.6023$$

$$M_Z(t) = 0.0101e^t + 0.6017e^{2t} + 0.3433e^{-t} + 0.0449e^{-2t}$$

**3.2.** *Scenarios of five types of mutant cells ( $k = 5$ .* Now, we consider the scenarios of five types of mutant cells. The parameter values randomly generated are presented in Table 13.

TABLE 13. Parameter values for five types of mutant cells ( $k=5$ )

Parameter	Values				
$\lambda$	0.055				
$\mu$	0.67				
$\gamma$	0.225	0.058	0.396	0.065	0.226
$\alpha$	0.94	0.246	0.289	0.025	0.758
$\beta$	0.046	0.042	0.147	0.478	0.216

**3.2.1.** *Transition probabilities for 500 disease cells, 160 mutant cells type 1, 115 mutant cells type 2, 45 mutant cells type 3, 63 mutant cells type 4, and 18 mutant cells type 5.* The transition probabilities computed are presented in Table 14.

TABLE 14. Transition probabilities for  $i = 500$  and  $j = (160, 115, 45, 63, 18)$ 

Probability	Value
Prob[( <b>501</b> , 160 115 45 63 18 )/( 500 , 160 115 45 63 18 )]	0.000495128
Prob[( <b>501</b> , <b>161</b> 115 45 63 18 )/( 500 , 160 115 45 63 18 )]	0.4575932
Prob[( <b>501</b> , 160 <b>116</b> 45 63 18 )/( 500 , 160 115 45 63 18 )]	0.08631572
Prob[( <b>501</b> , 160 115 <b>46</b> 63 18 )/( 500 , 160 115 45 63 18 )]	0.04571146
Prob[( <b>501</b> , 160 115 45 <b>64</b> 18 )/( 500 , 160 115 45 63 18 )]	0.005737014
Prob[( <b>501</b> , 160 115 45 63 <b>19</b> )/( 500 , 160 115 45 63 18 )]	0.04486874
Prob[( <b>499</b> , 160 115 45 63 18 )/( 500 , 160 115 45 63 18 )]	0.2001755
Prob[( <b>499</b> , <b>159</b> 115 45 63 18 )/( 500 , 160 115 45 63 18 )]	0.02198814
Prob[( <b>499</b> , 160 <b>114</b> 45 63 18 )/( 500 , 160 115 45 63 18 )]	0.01459085
Prob[( <b>499</b> , 160 115 <b>44</b> 63 18 )/( 500 , 160 115 45 63 18 )]	0.01997026
Prob[( <b>499</b> , 160 115 45 <b>62</b> 18 )/( 500 , 160 115 45 63 18 )]	0.09080322
Prob[( <b>499</b> , 160 115 45 63 <b>17</b> )/( 500 , 160 115 45 63 18 )]	0.0117507

Total	1
-------	---

**3.2.2.** *Probability Mass Function and statistical properties for  $k = 5$ ,  $i = 500$  and  $j = (160, 115, 45, 63, 18)$ . The PMF and CDF are presented in the following Table 15.*

TABLE 15. PMF and CDF for  $i = 500$  and  $j = (160, 115, 45, 63, 18)$ 

z	-2	-1	1	2	Total
<b>Prob</b> ( $Z = z$ )	0.1593	0.2001	0.0005	0.6401	1.000
<b>Prob</b> ( $Z \geq z$ )	0.1593	0.3594	0.3599	1.000	

$$\mathbb{E}(Z) = 0.762; \mathbb{E}(Z^2) = 0.7287$$

$$M_Z(t) = 0.0005e^t + 0.6401e^{2t} + 0.2001e^{-t} + 0.1593e^{-2t}$$

**3.2.3.** *Transition probabilities for 1,000 disease cells, 330 mutant cells type 1, 99 mutant cells type 2, 107 mutant cells type 3, 300 mutant cells type 4, and 9 mutant cells type 5. Table 16 presents the computed transition probabilities.*

TABLE 16. Transition probabilities for  $i = 1000$  and  $j = (330, 99, 107, 300, 9)$ 

Probability	Value
Prob[( <b>1001</b> , 330 99 107 300 9 )/( 1000 , 330 99 107 300 9 )]	0.0003821496
Prob[( <b>1001</b> , <b>331</b> 99 107 300 9 )/( 1000 , 330 99 107 300 9 )]	0.4643581
Prob[( <b>1001</b> , 330 <b>100</b> 107 300 9 )/( 1000 , 330 99 107 300 9 )]	0.03695935
Prob[( <b>1001</b> , 330 99 <b>108</b> 300 9 )/( 1000 , 330 99 107 300 9 )]	0.05099581
Prob[( <b>1001</b> , 330 99 107 <b>301</b> 9 )/( 1000 , 330 99 107 300 9 )]	0.01179841
Prob[( <b>1001</b> , 330 99 107 300 <b>10</b> )/( 1000 , 330 99 107 300 9 )]	0.01299544
Prob[( <b>999</b> , 330 99 107 300 9 )/( 1000 , 330 99 107 300 9 )]	0.1544995
Prob[( <b>999</b> , <b>329</b> 99 107 300 9 )/( 1000 , 330 99 107 300 9 )]	0.0223564
Prob[( <b>999</b> , 330 <b>98</b> 107 300 9 )/( 1000 , 330 99 107 300 9 )]	0.006192091
Prob[( <b>999</b> , 330 99 <b>106</b> 300 9 )/( 1000 , 330 99 107 300 9 )]	0.02340854
Prob[( <b>999</b> , 330 99 107 <b>299</b> 9 )/( 1000 , 330 99 107 300 9 )]	0.2131579
Prob[( <b>999</b> , 330 99 107 300 <b>8</b> )/( 1000 , 330 99 107 300 9 )]	0.002896365
<b>Total</b>	<b>1</b>

**3.2.4.** *Probability Mass Function and statistical properties for  $k = 5$ ,  $i = 1000$  and  $j = (330, 99, 107, 300, 9)$ .* The PMF and CDF are presented in Table 17.

TABLE 17. PMF and CDF for  $i = 1000$  and  $j = (330, 99, 107, 300, 9)$ 

<b>z</b>	-2	-1	1	2	Total
<b>Prob</b> ( $Z = z$ )	0.2682	0.1544	0.0004	0.577	1.000
<b>Prob</b> ( $Z \geq z$ )	0.2682	0.4226	0.423	1.000	

$$\mathbb{E}(Z) = 0.4636; \mathbb{E}(Z^2) = 0.4982$$

$$M_Z(t) = 0.0004e^t + 0.577e^{2t} + 0.1544e^{-t} + 0.2682e^{-2t}$$

**3.2.5.** *Transition probabilities for 50,000 disease cells, 14685 mutant cells type 1, 6077 mutant cells type 2, 5524 mutant cells type 3, 9320 mutant cells type 4, and 10609 mutant cells type 5.* The transition probabilities computed are presented in Table 18.

TABLE 18. Transition probabilities for  $i = 50000$  and  $j = (14685, 6077, 5524, 9320, 10609)$ 

Probability	Value
Prob[( <b>50001</b> , 14685 6077 5524 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.0001723519
Prob[( <b>50001</b> , <b>14686</b> 6077 5524 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.3805961
Prob[( <b>50001</b> , 14685 <b>6078</b> 5524 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.041403
Prob[( <b>50001</b> , 14685 6077 <b>5525</b> 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.04611932
Prob[( <b>50001</b> , 14685 6077 5524 <b>9321</b> 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.006669286
Prob[( <b>50001</b> , 14685 6077 5524 9320 <b>10610</b> )/( 50000 , 14685 6077 5524 9320 10609 )]	0.2222832
Prob[( <b>49999</b> , 14685 6077 5524 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.06968025
Prob[( <b>49999</b> , <b>14684</b> 6077 5524 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.01837429
Prob[( <b>49999</b> , 14685 <b>6076</b> 5524 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.007020045
Prob[( <b>49999</b> , 14685 6077 <b>5523</b> 9320 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.02231993
Prob[( <b>49999</b> , 14685 6077 5524 <b>9319</b> 10609 )/( 50000 , 14685 6077 5524 9320 10609 )]	0.1223051
Prob[( <b>49999</b> , 14685 6077 5524 9320 <b>10608</b> )/( 50000 , 14685 6077 5524 9320 10609 )]	0.06305708
<b>Total</b>	<b>1</b>

**3.2.6.** *Probability Mass Function and statistical properties for  $k = 5$ ,  $i = 50000$  and  $j = (14685, 6077, 5524, 9320, 10609)$ .* Table 19 shows the PMF and CDF.

TABLE 19. PMF and CDF for  $i = 50000$  and  $j = (14685, 6077, 5524, 9320, 10609)$ 

z	-2	-1	1	2	Total
<b>Prob</b> ( $Z = z$ )	0.2332	0.0697	0.0002	0.697	1.000
<b>Prob</b> ( $Z \geq z$ )	0.2332	0.3029	0.3031	1.000	

$$\mathbb{E}(Z) = 0.8581; \mathbb{E}(Z^2) = 0.8580$$

$$M_Z(t) = 0.0002e^t + 0.697e^{2t} + 0.0697e^{-t} + 0.2332e^{-2t}$$

**3.3. Scenarios of ten types of mutant cells ( $k = 10$ ).** In the following scenarios, we focus on the case of ten types of mutant cells with various cell numbers. Table 20 shows the parameter values randomly generated.

TABLE 20. Parameter values for ten types of mutant cells (k=10)

Parameter	Values									
$\lambda$	0.409									
$\mu$	0.405									
$\gamma$	0.007	0.198	0.033	0.120	0.258	0.005	0.019	0.098	0.083	0.105
$\alpha$	0.940	0.246	0.289	0.025	0.758	0.318	0.143	0.414	0.152	0.233
$\beta$	0.046	0.042	0.147	0.478	0.216	0.232	0.415	0.369	0.139	0.466

**3.3.1.** *Transition probabilities for 500 disease cells, 33 mutant cells type 1, 68 mutant cells type 2, 100 mutant cells type 3, 10 mutant cells type 4, 9 mutant cells type 5, 5 mutant cells type 6, 2 mutant cells type 7, 60 mutant cells type 8, 158 mutant cells type 9, and 13 mutant cells type 10.* The transition probabilities are as follows (Table 21):

TABLE 21. Transition probabilities for  $i = 500$  and  $j = (33, 68, 100, 10, 9, 5, 2, 60, 158, 13)$ 

Probability	Value
Prob[( 501 , 33 68 100 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.005166555
Prob[( 501 , 34 68 100 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.1248121
Prob[( 501 , 33 69 100 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.08062475
Prob[( 501 , 33 68 101 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.1180709
Prob[( 501 , 33 68 100 11 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.009203987
Prob[( 501 , 33 68 100 10 10 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.04507886
Prob[( 501 , 33 68 100 10 9 6 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.0066954
Prob[( 501 , 33 68 100 10 9 5 3 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.002425458
Prob[( 501 , 33 68 100 10 9 5 2 61 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.1061638
Prob[( 501 , 33 68 100 10 9 5 2 60 159 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.1022036
Prob[( 501 , 33 68 100 10 9 5 2 60 158 14 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.01932053
Prob[( 499 , 33 68 100 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.06819192
Prob[( 499 , 32 68 100 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.006021433
Prob[( 499 , 33 67 100 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.01145537
Prob[( 499 , 33 68 99 10 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.0589235
Prob[( 499 , 33 68 100 9 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.01913718
Prob[( 499 , 33 68 100 10 8 5 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.007801018
Prob[( 499 , 33 68 100 10 9 4 2 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.004638659
Prob[( 499 , 33 68 100 10 9 5 1 60 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.003320769
Prob[( 499 , 33 68 100 10 9 5 2 59 158 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.08864031
Prob[( 499 , 33 68 100 10 9 5 2 60 157 13 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.08784177
Prob[( 499 , 33 68 100 10 9 5 2 60 158 12 )/( 500 , 33 68 100 10 9 5 2 60 158 13 )]	0.02426218
Total	1

**3.3.2.** *Probability Mass Function and statistical properties for  $k = 10$ ,  $i = 500$  and  $j = (33, 68, 100, 10, 9, 5, 2, 60, 158, 13)$ .* The PMF and CDF are presented in the following Table (22).

TABLE 22. PMF and CDF for  $i = 500$  and  $j = (33, 68, 100, 10, 9, 5, 2, 60, 158, 13)$

<b>z</b>	-2	-1	1	2	Total
<b>Prob (<math>Z = z</math>)</b>	0.3123	0.0681	0.005	0.6145	1.000
<b>Prob (<math>Z \geq z</math>)</b>	0.3123	0.3804	0.3854	1.000	

$$\mathbb{E}(Z) = 0.5413; \mathbb{E}(Z^2) = 0.5556$$

$$M_Z(t) = 0.005e^t + 0.6145e^{2t} + 0.0681e^{-t} + 0.3123e^{-2t}$$

**3.3.3.** *Transition probabilities for 1,000 disease cells, 54 mutant cells type 1, 172 mutant cells type 2, 12 mutant cells type 3, 10 mutant cells type 4, 92 mutant cells type 5, 63 mutant cells type 6, 35 mutant cells type 7, 4 mutant cells type 8, 287 mutant cells type 9, and 25 mutant cells type 10.* Table 23 transition probabilities computed are as follows:

TABLE 23. Transition probabilities for  $i = 1000$  and  $j = (54, 172, 12, 10, 92, 63, 35, 4, 287, 25)$

<b>Probability</b>	<b>Values</b>
Prob[( <b>1001</b> , 54 172 12 10 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.01345941
Prob[( <b>1001</b> , <b>55</b> 172 12 10 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.09178924
Prob[( <b>1001</b> , 54 <b>173</b> 12 10 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.1108335
Prob[( <b>1001</b> , 54 172 <b>13</b> 10 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.0120523
Prob[( <b>1001</b> , 54 172 12 <b>11</b> 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.02184757
Prob[( <b>1001</b> , 54 172 12 10 <b>93</b> 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.1705165
Prob[( <b>1001</b> , 54 172 12 10 92 <b>64</b> 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.03655231
Prob[( <b>1001</b> , 54 172 12 10 92 <b>63</b> <b>36</b> 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.01224226
Prob[( <b>1001</b> , 54 172 12 10 92 63 <b>35</b> <b>5</b> 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.02050202
Prob[( <b>1001</b> , 54 172 12 10 92 63 <b>35</b> <b>4</b> <b>288</b> 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.09287073
Prob[( <b>1001</b> , 54 172 12 10 92 63 35 4 287 <b>26</b> )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.02910055
Prob[( <b>999</b> , 54 172 12 10 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.177647
Prob[( <b>999</b> , <b>53</b> 172 12 10 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.004382469
Prob[( <b>999</b> , 54 <b>171</b> 12 10 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.01288747
Prob[( <b>999</b> , 54 172 12 10 92 <b>61</b> 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.003144916
Prob[( <b>999</b> , 54 172 12 <b>9</b> 92 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.008511719
Prob[( <b>999</b> , 54 172 12 10 <b>91</b> 63 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.03546793
Prob[( <b>999</b> , 54 172 12 10 92 <b>62</b> 35 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.02599574
Prob[( <b>999</b> , 54 172 12 10 92 63 <b>34</b> 4 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.02584734
Prob[( <b>999</b> , 54 172 12 10 92 63 35 <b>3</b> 287 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.002628326
Prob[( <b>999</b> , 54 172 12 10 92 63 35 4 <b>286</b> 25 )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.07096842
Prob[( <b>999</b> , 54 172 12 10 92 63 35 4 287 <b>24</b> )/( 1000, 54 172 12 10 92 63 35 4 287 25 )]	0.02075228
<b>Total</b>	<b>1</b>

**3.3.4.** *Probability Mass Function and statistical properties for  $k = 10$ ,  $i = 1000$  and  $j = (54, 172, 12, 10, 92, 63, 35, 4, 287, 25)$ .* The PMF and CDF are presented in Table 24.

TABLE 24. PMF and CDF for  $i = 1000$  and  $j = (54, 172, 12, 10, 92, 63, 35, 4, 287, 25)$ 

<b>z</b>	-2	-1	1	2	Total
<b>Prob (<math>Z = z</math>)</b>	0.2108	0.1775	0.0133	0.5984	1.000
<b>Prob (<math>Z \geq z</math>)</b>	0.2108	0.3883	0.4016	1.000	

$$\mathbb{E}(Z) = 0.611; \mathbb{E}(Z^2) = 0.5960$$

$$M_Z(t) = 0.0133e^t + 0.5984e^{2t} + 0.1775e^{-t} + 0.2108e^{-2t}$$

**3.3.5.** *Transition probabilities for 50,000 disease cells, 9738 mutant cells type 1, 3765 mutant cells type 2, 2406 mutant cells type 3, 340 mutant cells type 4, 4551 mutant cells type 5, 1435 mutant cells type 6, 7041 mutant cells type 7, 6139 mutant cells type 8, 3929 mutant cells type 9, and 7095 mutant cells type 10.* The transition probabilities computed are presented in Table 25.

TABLE 25. Transition probabilities for  $i = 50000$  and  $j = (9738, 3765, 2406, 340, 4551, 1435, 7041, 6139, 3929, 7095)$ 

Probability	Value
Prob[( <b>50001</b> , 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.003136999
Prob[( <b>50001, 9739</b> 3765 2406 340 4551 1435 7041 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.2629948
Prob[( <b>50001, 9738 3766</b> 2406 340 4551 1435 7041 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.03483312
Prob[( <b>50001, 9738 3765 2407</b> 340 4551 1435 7041 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.02132368
Prob[( <b>50001, 9738 3765 2406 341</b> 4551 1435 7041 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.005229878
Prob[( <b>50001, 9738 3765 2406 340 4552</b> 1435 7041 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.109777
Prob[( <b>50001, 9738 3765 2406 340 4551 1436</b> 7041 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.01329274
Prob[( <b>50001, 9738 3765 2406 340 4551 1435 7042</b> 6139 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.0296177
Prob[( <b>50001, 9738 3765 2406 340 4551 1435 7041 6140</b> 3929 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.05178756
Prob[( <b>50001, 9738 3765 2406 340 4551 1435 7041 6139 3930</b> 7095 )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.02065946
Prob[( <b>50001, 9738 3765 2406 340 4551 1435 7041 6139 3929 7096</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.07694221
Prob[( <b>49999, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.04140438
Prob[( <b>49999, 9737 3765 2406 340 4551 1435 7041 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.01272467
Prob[( <b>49999, 9738 3764 2406 340 4551 1435 7041 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.004542089
Prob[( <b>49999, 9738 3765 2405 340 4551 1435 7041 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.01015254
Prob[( <b>49999, 9738 3765 2406 339 4551 1435 7041 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.004659589
Prob[( <b>49999, 9738 3765 2406 340 4550 1435 7041 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.02824921
Prob[( <b>49999, 9738 3765 2406 340 4551 1434 7041 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.009533778
Prob[( <b>49999, 9738 3765 2406 340 4551 1435 7040 6139 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.08372086
Prob[( <b>49999, 9738 3765 2406 340 4551 1435 7041 6138 3929 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.09482647
Prob[( <b>49999, 9738 3765 2406 340 4551 1435 7041 6139 3928 7095</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.06494838
Prob[( <b>49999, 9738 3765 2406 340 4551 1435 7041 6139 3929 7094</b> )/( 50000, 9738 3765 2406 340 4551 1435 7041 6139 3929 7095 )]	0.01564288
<b>Total</b>	<b>1</b>

**3.3.6.** *Probability Mass Function and statistical properties for  $k = 10$ ,  $i = 50000$  and  $j = (9738, 3765, 2406, 340, 4551, 1435, 7041, 6139, 3929, 7095)$ .* The PMF and CDF are presented in the table below (26).

TABLE 26. PMF and CDF for  $i = 50000$  and  $j = (9738, 3765, 2406, 340, 4551, 1435, 7041, 6139, 3929, 7095)$

<b>z</b>	-2	-1	1	2	Total
<b>Prob (<math>Z = z</math>)</b>	0.3292	0.0414	0.0031	0.6263	1.000
<b>Prob (<math>Z \geq z</math>)</b>	0.3292	0.3706	0.3737	1.000	

$$\mathbb{E}(Z) = 0.5559; \mathbb{E}(Z^2) = 0.5661$$

$$M_Z(t) = 0.0031e^t + 0.6263e^{2t} + 0.0414e^{-t} + 0.3292e^{-2t}$$

#### 4. CONCLUSION AND SUGGESTIONS

In conclusion, the development of Dynamic State-Space Markov Modeling represents a significant advancement in the understanding and management of genetic disorders and infectious diseases characterized by mutations. This approach, rooted in a probabilistic perspective, offers a comprehensive framework that goes beyond traditional deterministic models, allowing for a more nuanced analysis of disease dynamics.

By including mutant cell types, a more detailed representation of disease behavior is gained, providing a comprehensive understanding of how different mutation events influence disease progression and treatment responses. This generalized setting allows uncovering essential insights into the relative impacts of each mutant cell type and their combined effect on disease outcomes, applicable to a wide range of genetic disorders and infectious diseases with mutations.

The probabilistic perspective offered by Dynamic State-Space Markov Modeling holds promise for addressing the complex challenges posed by genetic disorders and infectious diseases with mutations. This approach not only deepens the comprehension of these conditions but also empowers to develop more adaptable and effective strategies for prevention, treatment, and mitigation.

Furthermore, enhancing the precision of models through the development of parameter estimation methods and integrating real-time genomic data to enhance predictive capabilities and treatment strategies will be valuable areas for future research.

## FUNDING STATEMENT

This study has been funded by the Pan African University, Institute of Basic Sciences, Technology, and Innovation (PAUSTI).

## ACKNOWLEDGEMENTS

We wish to thank the Pan African University, Institute of Basic Sciences, Technology, and Innovation (PAUSTI), and the African Union for their support that facilitated the successful completion of this study.

## CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

## REFERENCES

- [1] L.A. Liotta, G.M. Saidel, J. Kleinerman, Stochastic model of metastases formation, *Biometrics*. 32 (1976), 535–550. <https://www.jstor.org/stable/2529743>.
- [2] E.L. Kaplan, P. Meier, Nonparametric estimation from incomplete observations, *J. Amer. Stat. Assoc.* 53 (1958), 457–481.
- [3] S. El-Asfouri, B.C. McInnis, A.S. Kapadia, Stochastic compartmental modeling and parameter estimation with application to cancer treatment follow-up studies, *Bull. Math. Biol.* 41 (1979), 203–215. <https://doi.org/10.1007/bf02460879>.
- [4] S.W. Duffy, H. Chen, L. Tabar, et al. Estimation of mean sojourn time in breast cancer screening using a Markov chain model of both entry to and exit from the preclinical detectable phase, *Stat. Med.* 14 (1995), 1531–1543. <https://doi.org/10.1002/sim.4780141404>.
- [5] H.H. Chen, S.W. Duffy, L. Tabar, A Markov chain method to estimate the tumour progression rate from preclinical to clinical phase, sensitivity and positive predictive value for mammography in breast cancer screening, *The Statistician*. 45 (1996), 307–317. <https://doi.org/10.2307/2988469>.
- [6] B. Mohammadi, V. Haghpanah, B. Larijani, A stochastic model of tumor angiogenesis, *Computers Biol. Med.* 38 (2008), 1007–1011. <https://doi.org/10.1016/j.compbiomed.2008.07.003>.

- [7] A. Divoli, E.A. Mendonça, J.A. Evans, et al. Conflicting biomedical assumptions for mathematical modeling: the case of cancer metastasis, *PLoS Comput. Biol.* 7 (2011), e1002132. <https://doi.org/10.1371/journal.pcbi.1002132>.
- [8] P.K. Newton, J. Mason, K. Bethel, et al. A stochastic Markov chain model to describe lung cancer growth and metastasis, *PLoS ONE*. 7 (2012), e34637. <https://doi.org/10.1371/journal.pone.0034637>.
- [9] F. Vermolen, I. Pöölönen, Uncertainty quantification on a spatial Markov-chain model for the progression of skin cancer, *J. Math. Biol.* 80 (2019), 545–573. <https://doi.org/10.1007/s00285-019-01367-y>.
- [10] F. Swarts, Markov characterization of fading channels, Thesis, University of Johannesburg, South Africa, 2014.
- [11] P.K. Andersen, Multistate models in survival analysis: A study of nephropathy and mortality in diabetes, *Stat. Med.* 7 (1988), 661–670. <https://doi.org/10.1002/sim.4780070605>.
- [12] B.A. Craig, D.G. Fryback, R. Klein, et al. A Bayesian approach to modelling the natural history of a chronic condition from observations with intervention, *Stat. Med.* 18 (1999), 1355–1371. [https://doi.org/10.1002/\(sici\)1097-0258\(19990615\)18:11<1355::aid-sim130>3.0.co;2-k](https://doi.org/10.1002/(sici)1097-0258(19990615)18:11<1355::aid-sim130>3.0.co;2-k).
- [13] D.W. Purnell, Discriminative and Bayesian techniques for hidden Markov model speech recognition systems, Ph.D. thesis, University of Pretoria, (2006). <http://hdl.handle.net/2263/29158>.
- [14] H. Frydman, A nonparametric estimation procedure for a periodically observed three-state Markov process, with application to aids, *J. R. Stat. Soc.: Ser. B (Methodol.)* 54 (1992), 853–866. <https://doi.org/10.1111/j.2517-6161.1992.tb01457.x>.
- [15] R.C. Gentleman, J.F. Lawless, J.C. Lindsey, et al. Multi-state Markov models for analysing incomplete disease history data with illustrations for hiv disease, *Stat. Med.* 13 (1994), 805–821. <https://doi.org/10.1002/sim.4780130803>.
- [16] A.D. Sahin, Z. Sen, First-order Markov chain approach to wind speed modelling, *J. Wind Eng. Ind. Aerodyn.* 89 (2001), 263–269. [https://doi.org/10.1016/s0167-6105\(00\)00081-7](https://doi.org/10.1016/s0167-6105(00)00081-7).
- [17] L. Meira-Machado, C. Cadarso-Suárez, J. de Uña-Álvarez, tdc msm: An R library for the analysis of multi-state survival data, *Computer Methods Progr. Biomed.* 86 (2007), 131–140. <https://doi.org/10.1016/j.cmpb.2007.01.010>.
- [18] L. Meira-Machado, J. de Uña-Álvarez, C. Cadarso-Suárez, et al. Multi-state models for the analysis of time-to-event data, *Stat. Methods Med. Res.* 18 (2008), 195–222. <https://doi.org/10.1177/0962280208092301>.
- [19] R. Kay, A Markov model for analysing cancer markers and disease states in survival studies, *Biometrics*. 42 (1986), 855–865. <https://doi.org/10.2307/2530699>.
- [20] L. Schwardt, J. du Preez, Efficient mixed-order hidden Markov model inference, in: Sixth International Conference on Spoken Language Processing, 2000.

- [21] C.H. Jackson, L.D. Sharples, S.G. Thompson, S.W. Duffy, E. Couto, Multistate Markov models for disease progression with classification error, *J. R. Stat. Soc.: Ser. D (The Statistician)*. 52 (2003), 193–209. <https://doi.org/10.1111/1467-9884.00351>.
- [22] J.M. Goldman, J.V. Melo, Chronic Myeloid Leukemia—advances in biology and new approaches to treatment, *N. Engl. J. Med.* 349 (2003), 1451–1464. <https://doi.org/10.1056/nejmra020777>.
- [23] M. Deininger, E. Buchdunger, B.J. Druker, The development of imatinib as a therapeutic agent for chronic myeloid leukemia, *Blood*. 105 (2005), 2640–2653. <https://doi.org/10.1182/blood-2004-08-3097>.
- [24] F. Michor, M. Nowak, Y. Iwasa, Evolution of resistance to cancer therapy, *Curr. Pharm. Design.* 12 (2006), 261–271. <https://doi.org/10.2174/138161206775201956>.
- [25] J. Foo, F. Michor, Evolution of acquired resistance to anti-cancer therapy, *J. Theor. Biol.* 355 (2014), 10–20. <https://doi.org/10.1016/j.jtbi.2014.02.025>.