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Mean Exit Time and Escape Probability for a Tumor Growth System under Non-Gaussian Noise^{*}

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Effects of non-Gaussian α -stable Lévy noise on the Gompertz tumor growth model are quantified by considering the mean exit time and escape probability of the cancer cell density from inside a safe or benign domain. The mean exit time and escape probability problems are formulated in a differential-integral equation with a fractional Laplacian operator. Numerical simulations are conducted to evaluate how the mean exit time and escape probability vary or bifurcates when α changes. Some bifurcation phenomena are observed and their impacts are discussed.

Keywords: Fractional Laplacian operator; bifurcation; tumor growth model; non-Gaussian noise; α -stable Lévy motion; quantifying uncertainty

1. Introduction

Mathematical models have been proposed to describe the evolution of numerous biological phenomena such as cancer growth. The deterministic Gompertz growth model for a tumor density growth is given by the

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following differential equation

$$\frac{dx}{dt} = (A - B\ln x)x,\tag{1}$$

where x(t) describes the density of cancer cells at time t, parameters A and B denote growth and decay rates respectively.

This is a deterministic model, nevertheless. As there is a discrepancy between clinical data and basic theory due to subtle environmental fluctuations, we need a stochastic part to describe the fluctuation. A stochastic model proposed as a functional Fokker-Planck equation in consideration of both fission and mortality has been considered in [Lo, 2007] and a diffusion process with modified infinitesimal mean has been studied in [Gutierrez-jaimez *et al.*, 2007]. In [Lo, 2009] and [Albano & Giorno, 2009] a multiplicative noise of Brownian motion has been considered and in [Albano & Giorno, 2006] a deterministic parameter has been modified by a group of random variables to depict the stochastic fluctuation. [Lo, 2009] compared the effect of different therapies by giving their probability density functions(pdfs) and [Albano & Giorno, 2009], [Albano & Giorno, 2006] both deal with the first exit time problem.

In the present paper we consider the Gompertz growth model driven by the non-Gaussian α -stable noise with jumps and quantify the dynamics in terms of mean exit time and escape probability. Specifically, we consider the evolution of the tumor growth in the density range that cannot be diagnosed, and compute the likelihood and mean time for a tumor to become diagnosable or malignant. We examine how this depends on α values. To this end, we investigate the differential equation driven by symmetric α -stable Lévy process L_t^{α} with characteristics $(0, 1, \nu)$ with jump measure $\nu(dy) = dy/|y|^{1+\alpha}$

$$dX = [(A - B \ln X)X]dt + dL_t^{\alpha}, \qquad X(0) = x.$$
(2)

where x is the initial tumor density.

The paper is arranged as follows. We present a brief introduction about Lévy process in section 2 and then a stochastic tumor growth model in section 3. Numerical experiments are conducted in section 4.

2. Lévy process

A Lévy process $(L_t, t \ge 0)$ is a stochastic process defined on a probability space (Ω, \mathcal{F}, P) with the following properties:

- (i) $L_0 = 0$ (*a.s.*);
- (ii) L_t has independent and stationary increments, i.e. for each n and $0 \le t_1 \le t_2 \le \cdots \le t_{n+1} < \infty$ the random variables $(L_{t_{j+1}} L_{t_j}, 1 \le j \le n)$ are independent and each $L_{t_{j+1}} L_{t_j}$ and $L_{t_{j+1}-t_j}$ are equal in law both satisfy a non-Gaussian distribution.
- (iii) L_t has stochastically continuous, i.e. for all c > 0, s > 0

$$\lim_{t \to s} P(|L_t - L_s| > c) = 0.$$

(iv) The paths of L_t are \mathbb{P} -almost surely right continuous with left limits.

For the characteristic exponent $\Psi_t(\lambda) = \log \mathbb{E}(e^{i\lambda L_t})$, with the fact that L_t has independent and stationary increment we get $\mathbb{E}(e^{i\lambda L_t}) = e^{t\Psi_1(\lambda)} =: e^{t\Psi(\lambda)}$, therefore in the next paragraph we refer to $\Psi(\lambda)$ as a characteristic exponent of the Lévy process.

Lévy-Khintchine formula [Applebaum, 2009; Kyprianou, 2006] for Lévy process: Suppose that $a \in \mathbb{R}, \sigma \geq 0$ and ν is a measure concentrated on $\mathbb{R} \setminus \{0\}$ such that $\int_{\mathbb{R}} (1 \wedge x^2) \mu(dx) < \infty$. From this triple (a, σ, ν) defined for each $\lambda \in \mathbb{R}$,

$$\Psi(\lambda) = ia\lambda - \frac{1}{2}\sigma^2\lambda^2 - \int_{\mathbb{R}} (1 - e^{i\lambda x} + i\lambda x I_{|x|<1})\,\nu(dx).$$

Then there exits a probability space $(\Omega, \mathcal{F}, \mathbb{P})$ on which a Lévy process is defined having characteristic exponent Ψ .

It can be seen that after some reorganization the characteristic exponent of Lévy process can be rewritten as

$$\begin{split} \Psi(\lambda) &= \left\{ ia\lambda - \frac{1}{2}\sigma^2\lambda^2 \right\} \\ &- \left\{ \nu(\mathbb{R} \setminus (-1,1)) \int_{|x| \ge 1} (1 - e^{i\lambda x}) \frac{\nu(dx)}{\nu(\mathbb{R} \setminus (-1,1))} \right\} \\ &- \left\{ \int_{0 < |x| < 1} (1 - e^{i\lambda x} + i\lambda x) \nu(dx) \right\} \\ &=: \Psi^{(1)} - \Psi^{(2)} - \Psi^{(3)} \end{split}$$

where $\Psi^{(1)}$, $\Psi^{(2)}$ are respectively the characteristic exponent of $X_t^{(1)} = -\sigma B_t + at$, $t \ge 0$ and $X_t^{(2)} = \sum_{i=1}^{N_t} \xi_i$, $t \ge 0$, here $\{N_t : t \ge 0\}$ is a Poisson process with rate $\nu(\mathbb{R} \setminus (-1, 1))$ and $\{\xi_i : t \ge 0\}$ are i.i.d with distribution $\nu(dx)/\nu(\mathbb{R} \setminus (-1, 1))$ concentrated on $\{x : |x| \ge 1\}$ (if $\nu(\mathbb{R} \setminus (-1, 1)) = 0$ process $X_t^{(2)}$ is identically zero).

We have a result from [Kyprianou, 2006] to say the composition of a Lévy process.

Lévy-Itô decomposition: Given any $a \in \mathbb{R}$, $\sigma \geq 0$ and measure ν concentrated on $\mathbb{R} \setminus \{0\}$ satisfying $\int_{\mathbb{R} \setminus \{0\}} (|x|^2 \wedge 1) \nu(dx) < \infty$, there exists a probability space on which three independent Lévy processes $X^{(1)}, X^{(2)}, X^{(3)}$ exit, where $X^{(1)}$ is a linear Brownian motion with drift with characteristic exponent $\Psi^{(1)}, X^{(2)}$ is a compound Poisson process with characteristic exponent $\Psi^{(2)}$ and $X^{(3)}$ is a square integrable martingale with an almost surely countable number of jumps on each finite time interval which are of magnitude less than unity and with characteristic exponent $\Psi^{(3)}$. By taking $X = X^{(1)} - X^{(2)} - X^{(3)}$ we have that there exist a probability space on which a Lévy process is defined with characteristic exponent

$$\Psi(\lambda) = ia\lambda - \frac{1}{2}\sigma^2\lambda^2 - \int_{\mathbb{R}} (1 - e^{i\lambda x} + i\lambda x I_{(|x|<1)})\,\mu(dx)$$

for $\lambda \in \mathbb{R}$.

A random variable X is said to be stable if for all n > 0, the distribution of X and $S_n = \frac{X_1 + \dots + X_n - a_n}{\sigma_n}$ are equivalent, where X_1, \dots, X_n are a sequence of i.i.d random variable, $a_n \in \mathbb{R}$ and $\sigma_n > 0$ for $n \in \mathbb{N}$. It is well known from [Applebaum, 2009; Feller, 1971] that the only possible choice is $\sigma_n = n^{1/\alpha}$ for $\alpha \in (0, 2]$ so we refer to α as the index.

For $\alpha \in (0,1) \cup (1,2)$ stable variables have characteristic exponents of the form

$$\Psi(\lambda) = ia\lambda - c^{\alpha}|\lambda|^{\alpha}(1 - i\beta\tan\frac{\pi\alpha}{2}sgn\lambda),$$

where $\beta \in [-1, 1]$, $a \in \mathbb{R}$, c > 0 and the sign function $sgn\lambda = I_{(\lambda > 0)} - I_{(\lambda < 0)}$; for $\alpha = 1$, the characteristic exponents have the form

$$\Psi(\lambda) = ia\lambda - c|\lambda|(1 + i\beta\frac{2}{\pi}sgn\lambda\log|\lambda|),$$

where $\beta \in [-1, 1]$, $a \in \mathbb{R}$ and c > 0; for the special case $\alpha = 2$,

$$\Psi(\lambda) = ia\lambda - \frac{1}{2}\sigma^2\lambda^2;$$

and the measure

$$\nu(dx) = \begin{cases} \frac{c_1}{x^{1+\alpha}} dx & for \quad x \in (0,\infty);\\ \frac{c_2}{(-x)^{1+\alpha}} dx & for \quad x \in (-\infty,0), \end{cases}$$

where $c = c_1 + c_2$, c_1 , $c_2 \ge 0$ and $\beta = \frac{c_1 - c_2}{c_1 + c_2}$ if $\alpha \in (0, 1) \cup (1, 2)$. The case $\beta = 0$, i.e. $c_1 = c_2$, is called symmetric α -stable Lévy process.

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The (infinitesimal) generator A of a Lévy process X(t) is defined as $A\varphi = \lim_{t \downarrow 0} \frac{T_t \varphi - \varphi}{t}$ where $(T_t \varphi)(x) = \mathbb{E}_x(\varphi(X(t)) \text{ for any } \varphi \in D_A(\text{the domain of generator } A)$. It has the expression [Applebaum, 2009]

$$(A\varphi)(x) = a\varphi'(x) + \frac{1}{2}\sigma^2\varphi''(x) + \int_{\mathbb{R}\setminus\{0\}} [\varphi(x+y) - \varphi(x) - y\varphi'(x)I_{|y|<1}]\nu(dy) + \int_{\mathbb{R}\setminus\{0\}} [\varphi(x+y) - \varphi(x) - \varphi(x)]\nu(dy) + \int_{\mathbb{R}\setminus\{0\}} [\varphi(x+y) - \varphi(x)]\nu(dy) + \int_{\mathbb{R}\setminus\{0\}} [\varphi(x+y$$

3. Tumor growth under α -stable Lévy noise

In this section we consider the stochastic model driven by symmetric α -stable Lévy process, i.e. a Lévy process L_t , in which each L_t is a stable random variable and here for simplicity we take $c_1 = c_2 = 1$. We refer to the monoclonal benign parathyroid tumor and take A = 6.46 year⁻¹, B = 0.314 year⁻¹, corresponding to a parathyroid tumor mean age of 19.6 years. Here we investigate in the range of the tumor density that cannot be diagnosed, we take the two boundary points $S_1 = 1$ and $S_2 = 1.074 \times 10^8$ (the tumor cell density $x = 1.074 \times 10^8$ is the smallest diagnoseable mass), how the tumor density progresses. When a tumor's density is bigger than 1.074×10^8 , we say it becomes malignant, while if its density is smaller than 1, it is not diagnosable.

Based on the deterministic Gompertz model, the corresponding stochastic model is given by

$$dX = [(A - B \ln X)X]dt + dL_t^{\alpha}, \qquad X(0) = x,$$
(3)

where L_t^{α} is with the characteristics $(0, 1, \nu)$. Here the jump measure $\nu(dy) = dy/|y|^{1+\alpha}$. It is known [Applebaum, 2009] that the infinitesimal generator A for L_t^{α} is

$$(Af)(x) = \frac{1}{2}f''(x) + \int_{\mathbb{R}\setminus\{0\}} \frac{f(x+y) - f(x) - yf'(x)I_{|y|<1}}{|y|^{1+\alpha}} \, dy. \tag{4}$$

Due to the Lévy-Itô decomposition the generator for the process X(t) in (3) is then

$$Af = (A - B\ln x)xf'(x) + \frac{1}{2}f''(x) + \int_{\mathbb{R}\setminus\{0\}} \frac{f(x+y) - f(x) - yf'(x)I_{|y|<1}}{|y|^{1+\alpha}} \, dy.$$
(5)

In this symmetric α -stable Lévy motion case, the integral operator is related to the fractional Laplacian operator [Albeverrio, Rudiger & Wu, 2000; Guan & Ma, 2005; Chen, Kim & Song, 2010; Caffarelli & Silvestre, 2007]. Namely, for $\alpha \in (0, 2)$

$$\int_{\mathbb{R}\setminus\{0\}} \left[u(x+y) - u(x) \right] \nu_{\alpha}(dy) = c_{\alpha} \left(-\Delta \right)^{\frac{\alpha}{2}} u(x), \tag{6}$$

where

$$c_{\alpha} \triangleq \int_{\mathbb{R}\setminus\{0\}} (\cos y - 1) \ \nu_{\alpha}(dy) < 0.$$

Note that when $\alpha = 2$, $L_2 = \Delta$.

We consider two issues: Mean exit time and escape probability. We quantify the stochastic dynamics using these two tools. Especially, we examine possible bifurcation phenomena when the stability parameter α various in (0, 2).

The mean exit time

$$u(x) = \mathbb{E} \inf\{t \ge 0, X_t(\omega, x) \notin D\},\$$

from a bounded interval D, is the first time that the tumor density X(t), initially at value x in D, gets out of D. The mean exit time u(x), from the diagnoseable range $D = (1, 1.074 \times 10^8)$, satisfies an integraldifferential equation [Brannan, Duan & Ervin, 1999]

$$Au(x) = -1, \quad x \in D = (1, 1.074 \times 10^8), u(x) = 0, \quad x \notin D.$$
(7)

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i.e.

$$(A - B \ln x)xu'(x) + \frac{1}{2}u''(x) + \int_{\mathbb{R}\setminus\{0\}} \frac{u(x+y) - u(x) - yu'(x)I_{|y|<1}}{|y|^{1+\alpha}} \, dy = -1, \quad x \in D,$$
$$u(x) = 0, \quad x \notin D. \tag{8}$$

The mean exit time u(x) is the time when the tumor (initially with density x) becomes not diagnoseable (when x(t) exits from the left boundary point x = 1), or becomes malignant (when x(t) exits from the right boundary point x = b) and thus may need medical intervention.

The escape probability p(x), through the right boundary point, is the likelihood that the tumor density X(t), initially at value x in D, first escapes from D through $x = 1.074 \times 10^8$. The p(x) satisfies the following equation [Brannan, Duan & Ervin, 1999]

$$Ap(x) = 0, \quad x \in D = (1, 1.074 \times 10^8),$$

$$p(1) = 0, \quad p(1.074 \times 10^8) = 1.$$
(9)

In the next section we simulate both the mean exit time u(x) and escape probability p(x), when the stability parameter α varies in (0, 2).

4. Numerical experiments

We now discretize the equation (8) for the mean exit time u(x). The discretization of (9) for the escape probability p(x) is similar.

For the numerical scheme as the right boundary point of D is too huge, we need a transformation to change it to a smaller value. Owing to the fact that u(x) = 0 for $x \notin D$ we can take a transformation $\tilde{x} = \ln x$, relevantly $\tilde{y} = \ln(x+y) - \ln x$, nonetheless the integration for y is on $\mathbb{R} \setminus \{0\}$ (u(x+y) = 0 for $x + y \leq 0 < 1$). Omitting the tilde we get

$$(A - Bx)u'(x) + \frac{1}{2}e^{-2x}(u''(x) - u'(x)) + \frac{1}{e^{\alpha x}}\int_{\mathbb{R}\setminus\{0\}} \frac{u(x+y) - u(x) - (e^y - 1)u'(x)I_{\{|e^y - 1| \le e^{-x}\}}}{|e^y - 1|^{1+\alpha}}e^y \, dy = -1, \quad x \in D_1 = (0, 18.4921), \\ u(x) = 0, \quad x \notin D_1.$$

$$(10)$$

where the third term in the integral is

$$\int_{\mathbb{R}\setminus\{0\}} \frac{(e^y - 1)I_{\{|e^y - 1| < e^{-x}\}}}{|e^y - 1|^{1+\alpha}} e^y \, dy = \int_{\mathbb{R}\setminus\{0\}} \frac{(e^y - 1)I_{\{|e^y - 1| < e^{-x}\}}}{|e^y - 1|^{1+\alpha}} \, d(e^y - 1) = \int_{\mathbb{R}\setminus\{0\}} \frac{yI_{\{|y| < e^{-x}\}}}{|y|^{1+\alpha}} \, dy,$$

as $\int_{\mathbb{R}\setminus\{0\}} \frac{yI_{\{|y| \le \delta\}}}{|y|^{1+\alpha}} dy$ always vanishes for any $\delta > 0$, so does the third term in the integral for any fixed x, therefore the integral-differential equation can be changed into

$$\frac{1}{2}e^{-2x}u''(x) + [(A - Bx) - \frac{1}{2}e^{-2x}]u'(x) + \frac{1}{e^{\alpha x}}\int_{\mathbb{R}\setminus\{0\}} \frac{u(x + y) - u(x) - (e^y - 1)u'(x)I_{\{|e^y - 1| < \delta\}}}{|e^y - 1|^{1+\alpha}}e^y \, dy = -1, \quad x \in D_1, \quad u(x) = 0, \quad x \notin D_1. \tag{11}$$

We then take another transformation $\tilde{x} = \frac{x}{b} - 1$ meanwhile $\tilde{y} = \frac{y}{b}$ where b = 18.4921/2 to change $D_1 = (0, 18.4921)$ into (-1, 1), we obtain

$$\frac{1}{2b^2}e^{-2b(x+1)}u''(x) + \left[A - Bb(x+1) - \frac{1}{2}e^{-2b(x+1)}\right]\frac{1}{b}u'(x) \\
+ \frac{1}{e^{\alpha b(x+1)}}\int_{\mathbb{R}\setminus\{0\}}\frac{bu(x+y) - bu(x) - (e^{by} - 1)u'(x)I_{\{|e^{by} - 1| < \delta\}}}{|e^{by} - 1|^{1+\alpha}}e^{by}\,dy = -1, \quad x \in D_2 = (-1,1), \\
u(x) = 0, \quad x \notin D_2.$$
(12)

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The numerical scheme here follows [Li, Gao & Duan, 2011]. A different scheme was also proposed in [Chen, Duan, Li & Zhang, 2011]. We write $\int_{\mathbb{R}} = \int_{-\infty}^{-1-x} + \int_{-1-x}^{1-x} + \int_{1-x}^{\infty}$ and take $\delta = \min \{e^{b(1-x)} - 1, 1 - e^{-b(1+x)}\}$ to get

$$\frac{1}{2b^2}e^{-2b(x+1)}u''(x) + \left[A - Bb(x+1) - \frac{1}{2}e^{-2b(x+1)}\right]\frac{1}{b}u'(x) \\
+ \frac{u(x)}{\alpha e^{\alpha b(x+1)}}\left[1 - \frac{1}{(e^{b(1-x)} - 1)^{\alpha}} - \frac{1}{(1 - e^{-b(1+x)})^{\alpha}}\right] \\
+ \frac{1}{e^{\alpha b(x+1)}}\int_{-1-x}^{1-x}\frac{bu(x+y) - bu(x) - (e^{by} - 1)u'(x)I_{\{|e^{by} - 1| < \delta\}}}{|e^{by} - 1|^{1+\alpha}}e^{by}\,dy = -1, \quad x \in D_3 = (-1,1)$$
(13)

furthermore, for $x \ge 0$

$$\frac{1}{2b^2}e^{-2b(x+1)}u''(x) + \left[A - Bb(x+1) - \frac{1}{2}e^{-2b(x+1)}\right]\frac{1}{b}u'(x) \\ + \frac{u(x)}{\alpha e^{\alpha b(x+1)}}\left[1 - \frac{1}{(e^{b(1-x)} - 1)^{\alpha}} - \frac{1}{(1 - e^{-b(1+x)})^{\alpha}}\right] + \frac{1}{e^{\alpha b(x+1)}}\int_{-1-x}^{-1+x}\frac{u(x+y) - u(x)}{|e^{by} - 1|^{1+\alpha}}be^{by}\,dy \\ + \frac{1}{e^{\alpha b(x+1)}}\int_{-1+x}^{1-x}\frac{bu(x+y) - bu(x) - (e^{by} - 1)u'(x)}{|e^{by} - 1|^{1+\alpha}}e^{by}\,dy = -1, \quad x \in D_3 = (-1, 1)$$
(14)

and for $x \leq 0$

$$\frac{1}{2b^2}e^{-2b(x+1)}u''(x) + \left[A - Bb(x+1) - \frac{1}{2}e^{-2b(x+1)}\right]\frac{1}{b}u'(x) \\ + \frac{u(x)}{\alpha e^{\alpha b(x+1)}}\left[1 - \frac{1}{(e^{b(1-x)} - 1)^{\alpha}} - \frac{1}{(1 - e^{-b(1+x)})^{\alpha}}\right] + \frac{1}{e^{\alpha b(x+1)}}\int_{1+x}^{1-x}\frac{u(x+y) - u(x)}{|e^{by} - 1|^{1+\alpha}}be^{by}\,dy \\ + \frac{1}{e^{\alpha b(x+1)}}\int_{-1-x}^{1+x}\frac{bu(x+y) - bu(x) - (e^{by} - 1)u'(x)}{|e^{by} - 1|^{1+\alpha}}e^{by}\,dy = -1, \quad x \in D_3 = (-1, 1)$$
(15)

For simplicity denote $f(x) = A - Bb(x+1) - \frac{1}{2}e^{-2b(x+1)}$ and $g(x) = e^{-2b(x+1)}$. For numerical schemes generally we divide the interval [-2, 2] into 4J subintervals and define $x_j = jh$ for $-2J \le j \le 2J$ integer, where h = 1/J. We denote the numerical solution of u at x_j by U_j . We can discretize the two integraldifferential equations above using central difference for derivatives and "punched-hole" trapezoidal rule

$$\frac{1}{2b^2}g(x_j)\frac{U_{j+1}-2U_j+U_{j-1}}{h^2} + \frac{1}{b}f(x_j)\frac{U_{j+1}-U_{j-1}}{2h} + \frac{1}{ae^{\alpha b(x_j+1)}}\left[1 - \frac{1}{(e^{b(1-x_j)}-1)^{\alpha}} - \frac{1}{(1-e^{-b(1+x_j)})^{\alpha}}\right]U_j + \frac{h}{e^{\alpha b(x_j+1)}}\sum_{k=-J-j}^{-J+j} "\frac{be^{by_k}(U_{j+k}-U_j)}{|e^{by_k}-1|^{1+\alpha}} + \frac{h}{e^{\alpha b(x_j+1)}}\sum_{k=-J+j,\ k\neq 0}^{J-j} "\frac{be^{by_k}(U_{j+k}-U_j) - e^{by_k}(e^{by_k}-1)(U_{j+1}-U_{j-1})/2h}{|e^{by_k}-1|^{1+\alpha}} = -1, \quad (16)$$

where $j = 0, 1, 2, \dots, J-1$. Here the summation symbol \sum'' means the two end terms are multiplied by 1/2 corresponding to trapezoidformula.

$$\frac{1}{2b^2}g(x_j)\frac{U_{j+1}-2U_j+U_{j-1}}{h^2} + \frac{1}{b}f(x_j)\frac{U_{j+1}-U_{j-1}}{2h} + \frac{1}{b}f(x_j)\frac{U_{j+1}-U_{j-1}}{2h} + \frac{1}{\alpha e^{\alpha b(x_j+1)}} \left[1 - \frac{1}{(e^{b(1-x_j)}-1)^{\alpha}} - \frac{1}{(1-e^{-b(1+x_j)})^{\alpha}}\right]U_j + \frac{h}{e^{\alpha b(x_j+1)}}\sum_{k=J+j}^{J-j} "\frac{be^{by_k}(U_{j+k}-U_j)}{|e^{by_k}-1|^{1+\alpha}} + \frac{h}{e^{\alpha b(x_j+1)}}\sum_{k=J+j,\ k\neq 0}^{-J-j} "\frac{be^{by_k}(U_{j+k}-U_j) - e^{by_k}(e^{by_k}-1)(U_{j+1}-U_{j-1})/2h}{|e^{by_k}-1|^{1+\alpha}} = -1, \quad (17)$$

where $j = -(J-1), -(J-2), \dots, -2, -1$. The boundary conditions require that the values of U_j vanish if the index $|j| \ge J$. But here for the specific problem for first-order derivative we use forward difference or backward difference.

Similarly, we can discretize the equation (9) for the escape probability p(x).

For the viewing convenience, the following figures for the mean exit time u(x) and escape probability p(x) are both plotted for $x \in (0, 18.4921)$, instead of the original huge range $(1, 1.074 \times 10^8)$.

Figures 1–6 show the mean exit time u(x) for various α values in (0, 2).

We observe that when α is small, the mean exit time u(x) is small and is roughly constant, i.e., tumors at all densities are equally unlikely to become non-diagnosable or malignant. As α becomes bigger the whole height will grow with the right part grows up slowly while the left part increases rapidly meanwhile the width of the left part narrows down. In fact, at about $\alpha = 0.2$ the height of the two part begins to have a separation. When $\alpha \approx 0.44$ the separation becomes quite obvious and the left part (for density between 0 and 10) reaches its highest value, which indicates a bifurcation. This means that for a tumor with density between 0 and 10, it takes longest time to become either non-diagnosable or malignant.

For α between 0.44 and 0.48, u(x) keeps similar shape as for $\alpha = 0.44$ but the peak diminishes. For α between 0.48 and 0.6, u(x) has the similar shape although the peak value decreases. Moreover, for α between 0.6 and 2, u(x) keeps almost the same shape; namely, for the Gaussian Brownian motion case, the mean exit time is similar to the large values of $\alpha \in (0.6, 2)$. The dramatic impact of non-Gaussian Lévy noise occurs for $\alpha \in (0, 0.46)$.

Figure 7 shows a three dimensional plot of the above discussed situations.

In the above simulations, the mean exit time u(x) tells us the time for a tumor to become either nondiagnosable (exit from the left boundary point) or become malignant (exit from the right boundary point). To distinguish these two situations, especially examine the situation for a tumor to become malignant, let us now consider the escape probability, p(x), through the right end point. It indicates the likelihood the the tumor is progressing from benign to malignant. We observe that a bifurcation occurs for $\alpha \approx 0.4$ when a tumor at any benign density will highly likely becomes malignant, while for $\alpha < 0.4$, only tumors with high density (near x = 20) are likely to become malignant; see Figures 8 and 9.

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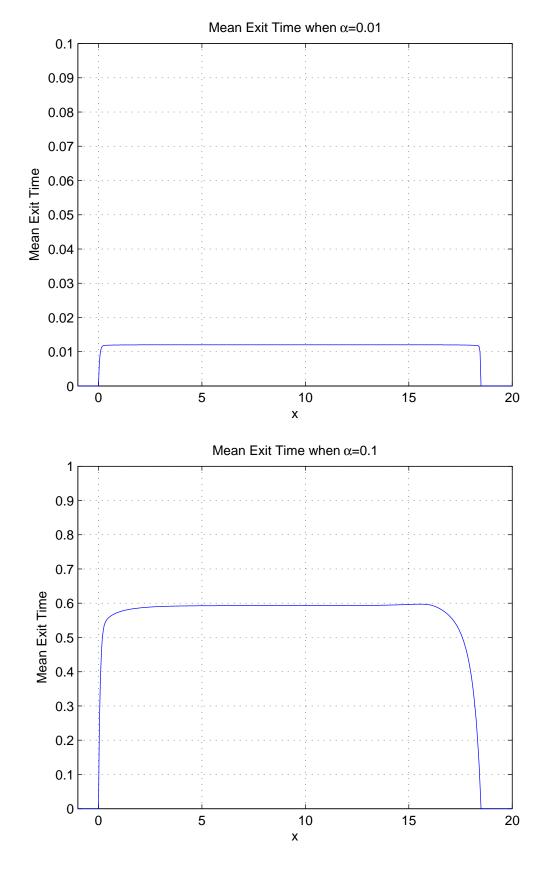


Fig. 1. Plot of u(x) given by (10) with $\alpha = 0.01$ and $\alpha = 0.1$.

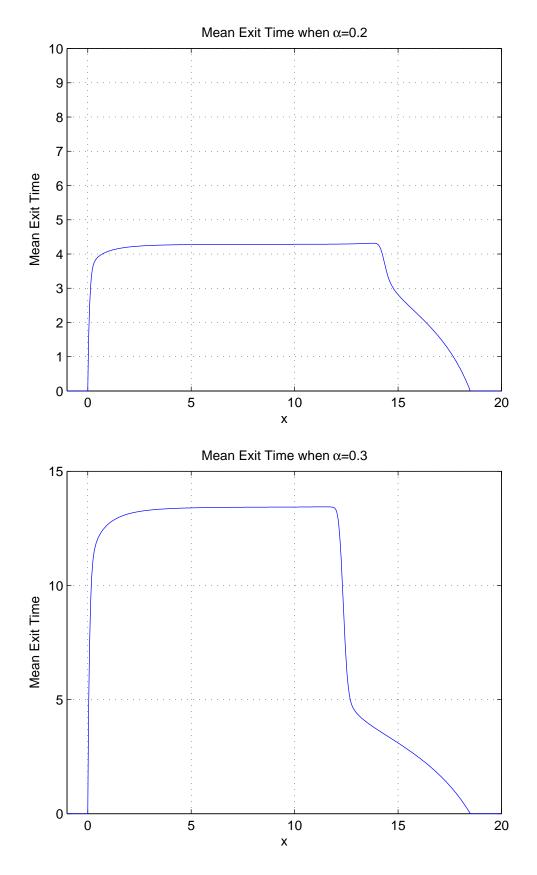


Fig. 2. Plot of u(x) given by (10) with $\alpha = 0.2$ and $\alpha = 0.3$.

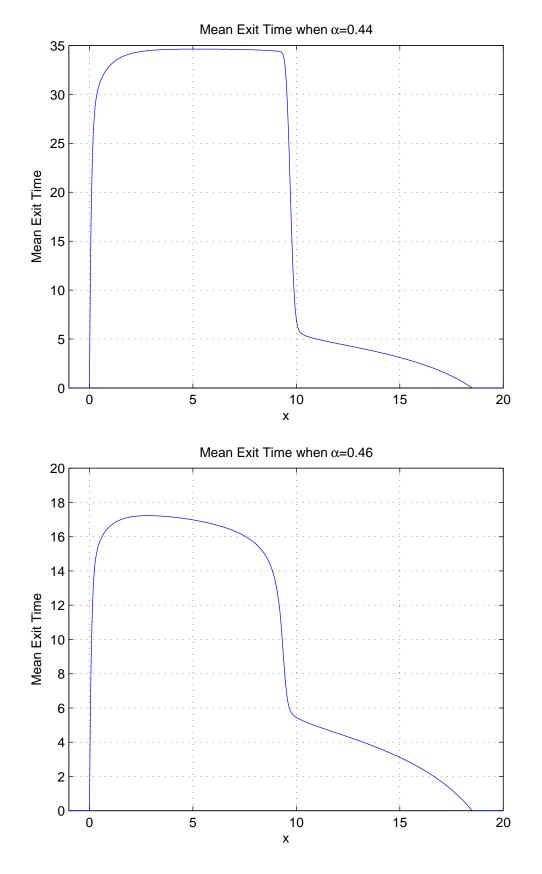


Fig. 3. Plot of u(x) given by (10) with $\alpha = 0.44$ and $\alpha = 0.46$.

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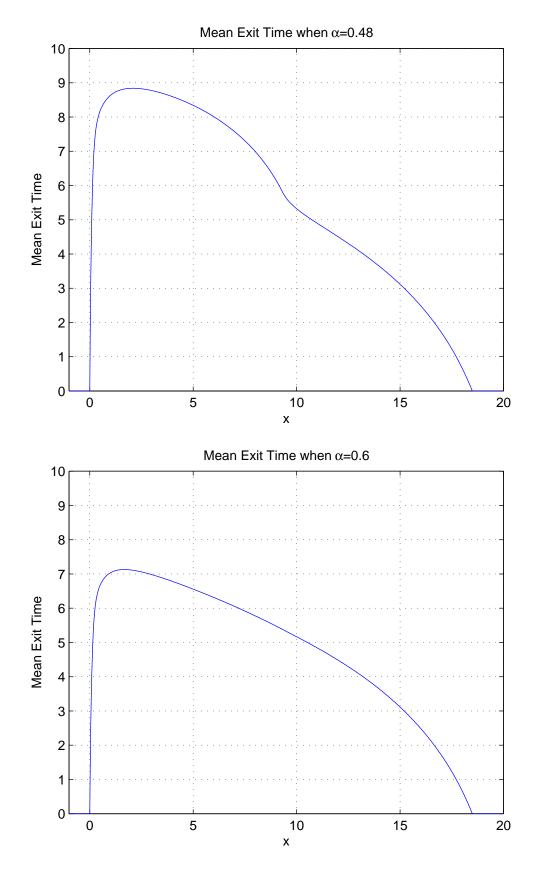


Fig. 4. Plot of u(x) given by (10) with $\alpha = 0.48$ and $\alpha = 0.6$.

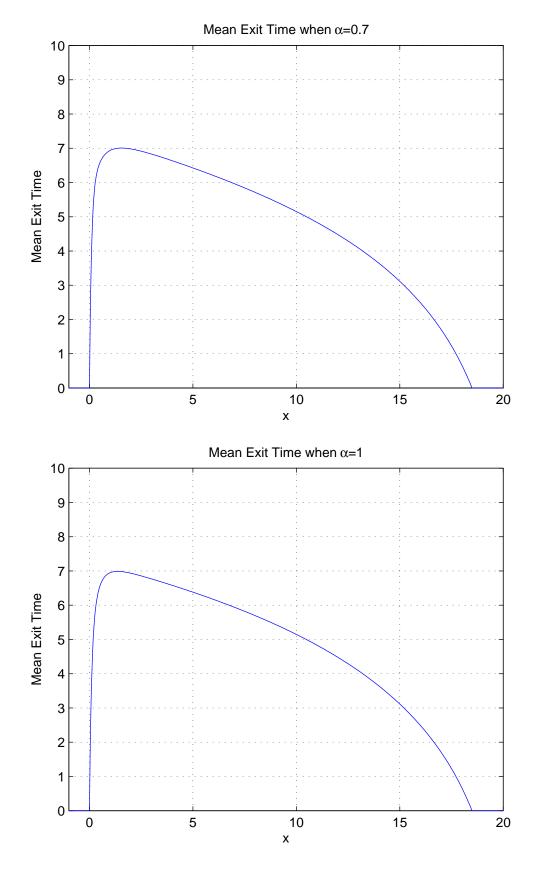


Fig. 5. Plot of u(x,t) given by (10) with $\alpha = 0.7$ and $\alpha = 1$.

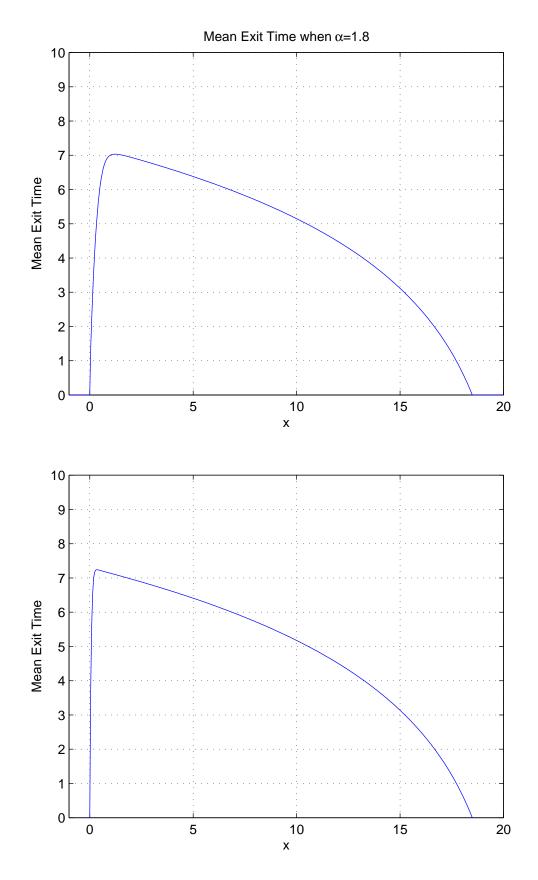
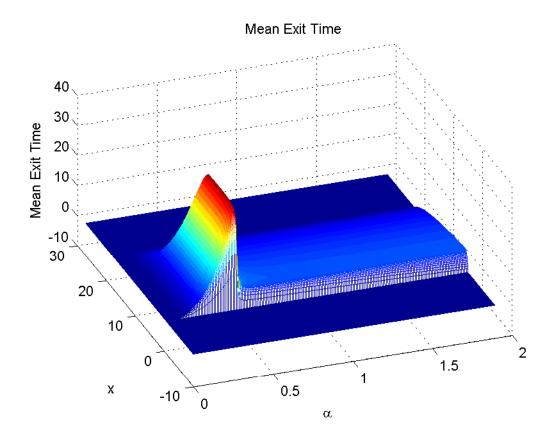


Fig. 6. Plot of u(x,t) given by (10) with $\alpha = 1.8$ and the Brownian motion case.



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Fig. 7. Mean exit time u v.s. α and x.

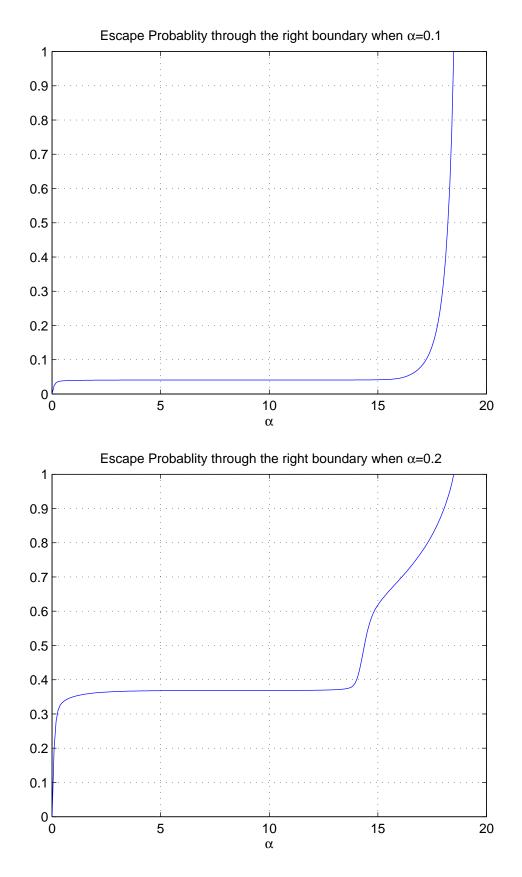


Fig. 8. Escape probability p(x) through the right boundary of (0, 18.4921): $\alpha = 0.1$ and $\alpha = 0.2$.

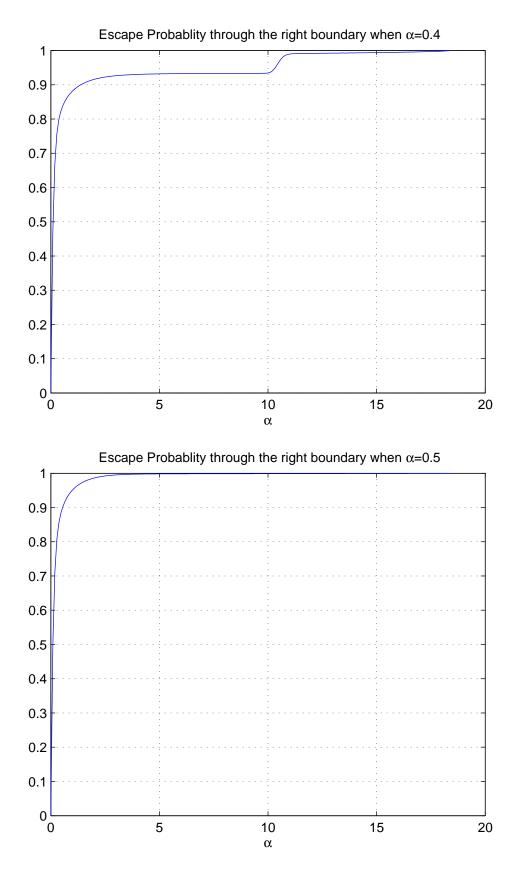


Fig. 9. Escape probability p(x) through the right boundary of (0, 18.4921): $\alpha = 0.4$ and $\alpha = 0.5$.