Likelihood for transcriptions in a genetic regulatory system under asymmetric stable Lévy noise

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Abstract

We investigate the dynamical effects of non-Gaussian asymmetric stable Lévy fluctuations on the evolution of the transcription factor activator in a genetic regulation system. The noisy fluctuations arise from the synthesis reaction rate. We compute two deterministic quantities, the mean first exit time (MFET) and the first escape probability (FEP), in order to examine the likelihood for transcriptions: The mean time scale for the system exits the low concentration state (the longer the exit time, the less likely for transcription) and the switch probability from low concentration states to high concentration states (corresponding to likelihood for transcription). By focusing on the impact of skewness (i.e., asymmetry) in the probability distributions of noise, we find that the fluctuations in the synthesis reaction rate lead to peculiar transitions to high concentrations and thus to possible transcriptions, such as realizing higher likelihood of transcription for larger positive skewness (i.e., asymmetry) index \( \beta \), causing a bifurcation for the likelihood of transcription at the critical non-Gaussianity index value \( \alpha = 1 \) (i.e., beyond which the likelihood for transcription suddenly increases), and achieving a turning point at the threshold value \( \beta \approx 0.55 \) (i.e., beyond which the likelihood for transcription reversed for \( \alpha \) values). The bifurcation and turning point phenomena do not occur in the symmetric noise case (\( \beta = 0 \)). We conduct a series of numerical experiments about 'regulating' the likelihood of gene transcription by tuning asymmetric stable Lévy noise indexes. These offer insights for possible ways of achieving gene regulation in experimental research.

keywords : Asymmetric stable Lévy motions non-Gaussian noise in gene regulation likelihood for transcription stochastic differential equations bifurcation in transcription

1 Introduction

Gene regulation is a crucial biological process and it is a noisy process [1,2]. The role of noise in genetic networks has been recognized [3,10]. It has been shown recently that noise is a key factor for regime transitions in gene regulatory systems [11,15]. These stochastic fluctuations have been mostly considered under the usual assumption of Gaussian distribution [6,16,19] and are expressed in terms of Brownian motion.

However, when the fluctuations are present in certain events, such as bursty transition events, the Gaussianity assumption is not proper. In this case, it is more appropriate to model the random fluctuations by a non-Gaussian Lévy motion (or Lévy flight) with heavy tails and bursting sample paths [20,22]. Especially,
during the regulation of gene expression, transcriptions of DNA from genes and translations into proteins occur in a bursty, unpredictable, intermittent way [9,10,23–27]. This intermittent manner [28–31] resembles the features of a Lévy motion, which is a non-Gaussian process with jumps. At the microscopic level tiny jumps and short bursts may be regarded as the same phenomenon [32, 33].

Recent studies [34, 35] have recognized that symmetric stable Lévy motion can induce switches between different gene expression states. Note that symmetry (zero skewness) in stable Lévy noise is an idealized, special situation [32, 36].

In this present paper, we examine the likelihood for transitions from low to high concentrations (i.e., likelihood for transcriptions) in a genetic regulatory system under asymmetric (i.e., non-symmetric) stable Lévy noise, highlighting the dynamical differences with the case of symmetric noise. To this end, we compute two deterministic quantities, the mean first exit time (MFET) and the first escape probability (FEP). The MFET is the mean time scale for the system exits the low concentration state (the longer the exit time, the less likely for transcription), while the FEP is the switch probability from low concentration states to high concentration states (corresponding to likelihood for transcription).

Having a better understanding of the genetic regulatory networks, we could shed light on the mechanisms of diseases which are caused by the dysregulation of gene expressions.

This paper is organized as follows. In Section 2, we briefly describe a genetic regulation model with noisy fluctuations in the synthesis reaction rate. In Section 3, we recall basic facts about asymmetric stable Lévy motions and the mean first exit time and the first escape probability. In Section 4, we investigate the transition phenomena by numerically computing both deterministic quantities, highlighting the differences with the symmetric stable Lévy noise case. Finally, we make some concluding remarks in Section 5.

2 A stochastic genetic regulatory system

In order to investigate the capability of genetic regulatory systems for complex dynamic activity, Smolen et al. [37] introduced the following model for the concentration $x$ of the transcription factor activator (TF-A)

$$\dot{x} = \frac{k_f x^2}{x^2 + K_d} - k_d x + R_{bas}. \tag{1}$$

The equation (1) can be written as $\dot{x} = f(x) = -U'(x)$. With the potential

$$U(x) = k_f \sqrt{K_d} \arctan \frac{x}{\sqrt{K_d}} + \frac{k_d}{2} x^2 - (R_{bas} + k_f)x,$$

under the following condition of the parameters:

$$[-\left(\frac{k_d + R_{bas}}{3k_d}\right)^3 + \left(\frac{k_d + R_{bas}}{6k_d}\right) - \left(\frac{K_d R_{bas}}{2k_d}\right)^2 + \left[\frac{K_d}{3} - \left(\frac{k_d + R_{bas}}{3k_d}\right)^2\right]^3 < 0].$$

This is a relatively simple but basic model of positive and negative autoregulation of transcription factors. A single transcription factor activator, which we named (TF-A), is considered as part of a pathway mediating a cellular response to a stimulus. The transcription factor forms a homodimer which can bind to specific responsive elements (TF-REs). The TF-A gene includes a TF-RE, when homodimers bind to this element, TF-A transcription is increased. Only phosphorylated dimers can activate transcription. The regulatory activity of transcription factors is often modulated by phosphorylation. It is assumed that the transcription rate saturates with TF-A dimer concentration to a maximal rate $k_f$, TF-A dimer dissociates from TF-REs with the constant $K_d$, TF-A degrades with first-order kinetics with the rate $k_d$. Meanwhile, the basal rate of the synthesis of the activator is $R_{bas}$.

We choose proper parameters (see the caption of Figure 1) in this genetic regulatory system on the basis of biological significance and convenience. Then, the deterministic dynamical system (1) has two stable states: $x_-$ (the low concentration stable state) and $x_+$ (the high concentration stable state) as well as one unstable state $x_u$, as indicated in Figure 1 (b). However, the basal synthesis rate $R_{bas}$ is unavoidably influenced by
Figure 1: (Color online) Genetic regulatory model with a feedforward (Eq. (1)). (a) The transcription factor activator (TF-A) activates transcription with a maximal rate $k_f$ when phosphorylated (P), and binds to specific responsive-element DNA sequences (TF-REs). The degradation and synthesis rate of the TF-A monomer are $k_d$ and $R_{bas}$, respectively. (b) The bistable potential for the TF-A monomer concentration model: The parameter values are $k_f = 6 \text{min}^{-1}$, $K_d = 10$, $k_d = 1 \text{min}^{-1}$, and $R_{bas} = 0.4 \text{min}^{-1}$.

The stable states are $x_- \approx 0.62685 \text{nM}$ and $x_+ \approx 4.28343 \text{nM}$, and the unstable state is $x_u \approx 1.48971 \text{nM}$.

Many factors [37], such as the biochemical reactions inside the cell, mutations, and the concentration of other proteins. These fluctuations in the genetic regulatory system behave like bursty as we mentioned in the introduction. Therefore, we incorporate a stable Lévy motion as a random perturbation of the synthesis rate $R_{bas}$.

Under the effects of these fluctuations, the concentration of the TF-A monomer may exit from the domain $D = (0, x_u)$, containing the low concentration stable state “$x_-$”. Our goal is to quantify the effects of Lévy noise on the dynamical behaviors of the TF-A monomer concentration in this model. We focus on the likelihood for the TF-A monomer concentration transitions from the low concentration domain $D$ to the high concentration domain $E = [x_u, +\infty)$ (containing the other stable state “$x_+$”), via analyzing two deterministic quantities: the mean residence time (also called mean first exit time) in the domain $D$ before first exit, and the likelihood of first escape from $D$ through the right side (i.e., becoming high concentration).

From the genetic regulation point of view, the biologist focuses primarily on the high TF-A monomer concentration, since that corresponds to the high degree of activity. That is, high concentration indicates effective transcription and translation.

Since the synthesis reaction rate is a highly sensitive parameter [37], subject to uncertainty which we approximately model as asymmetric stable Lévy fluctuations, the model (1) then becomes

$$\dot{X}_t = \frac{k_f X_t^2}{X_t^2 + K_d} - k_d X_t + R_{bas} + \dot{L}_{t}^{\alpha, \beta}, \quad X_0 = x,$$

where $L_{t}^{\alpha, \beta}$ is an asymmetric stable Lévy motion with the jump measure $\nu_{\alpha, \beta}$, which will be recalled in the next section. In stochastic dynamics, it is customary to denote a state variable in a capital letter, with time dependence as subscript. The ‘$x$’ here and hereafter denotes the initial concentration for the transcription activator factor or TF-A monomer in this gene regulatory system.
3 Deterministic quantities capturing stochastic dynamics

3.1 Stable Lévy motions

The aforementioned asymmetric stable Lévy motion $L^\alpha,\beta_t$ is an appropriate model for non-Gaussian fluctuations with bursts or jumps. The parameter $\alpha$ is the non-Gaussianity index ($0 < \alpha \leq 2$) and $\beta$ is the skewness index ($-1 \leq \beta \leq 1$). It is a stochastic process defined on a sample space $\Omega$ equipped with probability $\mathbb{P}$. It has independent and stationary increments, together with stochastically continuous sample paths.

The jump measure, which describes jump intensity and size for sample paths, for the asymmetric Lévy motion $L^\alpha,\beta_t$ is

$$\nu_{\alpha,\beta}(dy) = \frac{C_1 I_{[0<y<\infty]}(y) + C_2 I_{[-\infty<y<0]}(y)}{|y|^{1+\alpha}} dy,$$

with $C_1 = \frac{H_\alpha(1+\beta)}{2}$, $C_2 = \frac{H_\alpha(1-\beta)}{2}$. When $\alpha = 1$, $H_\alpha = \frac{2}{\pi}$; when $\alpha \neq 1$, $H_\alpha = \frac{\alpha(1-\alpha)}{1-(\alpha-\alpha)\cos(\frac{\pi}{2})}$.

Figure 2 shows probability density functions for $L^\alpha,\beta_t$ at $t = 1$ for various $\alpha, \beta$.

Especially for $\beta = 0$, this is the symmetric stable Lévy motion, which is usually denoted by $L^\alpha_t \triangleq L^\alpha,0_t$. The well-known Brownian motion $B_t$ may be regarded as a special case (i.e., Gaussian case) corresponding to $\alpha = 2$ (and $\beta = 0$) [33].

For the stable Lévy motion with the jump measure in [32], the number of larger jumps for small $\alpha$ ($0 < \alpha < 1$) are more than that for large $\alpha$ ($1 < \alpha < 2$), while the number of smaller jumps for $0 < \alpha < 1$ are less than that for $1 < \alpha < 2$, as known in [36].

Figure 2: (Color online) Probability density functions for asymmetric stable Lévy motion $L^\alpha,\beta_t$ at $t = 1$ for various skewness index $\beta$: (a) $\alpha = 0.5$. (b) $\alpha = 1.5$. The asymmetry is clearly seen when $\beta \neq 0$.

To quantify the likelihood for transcription for the genetic regulatory system under asymmetric (i.e., non-symmetric) stable Lévy noise, we examine two deterministic quantities, the mean first exit time (MFET) and the first escape probability (FEP).
3.2 Mean first exit time

We like to quantify how long the system resides in the low concentration domain $D$ before first exit. The first exit time is defined as follows \[33\],

$$\tau(\omega, x) = \inf \{ t \geq 0 : X_t(\omega, x) \notin D \}, \quad \omega \in \Omega,$$

(4)

where $X_t(\omega, x)$ is the solution orbit of the stochastic differential equation (2), starting with the initial TF-A concentration $x$. Then the mean first exit time (MFET) is denoted as $u(x) = \mathbb{E}\tau(\omega, x)$. Here the mean $\mathbb{E}$ is taken with respect to the probability $\mathbb{P}$. The MFET $u(x)$ of the solution orbit $X_t(\omega, x)$, starting with the initial TF-A concentration $x$, is the mean time to stay in the low concentration domain $D$.

Denote the generator of the stochastic differential equation (2) by $A$. It is defined as $Au = \lim_{t \to 0} \frac{P_t u - u}{t}$, where $P_t u(x) = \mathbb{E}u(X_t)$. The generator $A$ for the gene regulatory system (2) will be explicitly given in Section 4.1. Then the mean exit time $u$ satisfies the following equation [33] with an exterior boundary condition

$$Au(x) = -1, \quad x \in D,$$

$$u(x) = 0, \quad x \in D^c.$$  

Here $D^c$ is the complement set of $D$ in $\mathbb{R}^1$.

When we take the domain $D = (0, x_u)$, containing the low concentration stable state “$x_-$”, the MFET is the mean time scale for the system exits the low concentration state. The longer the mean exit time is, the less likely the system is in transcription.

3.3 First escape probability

The first escape probability (FEP), denoted by $p(x)$, is the likelihood that the TF-A monomer, with initial concentration $x$, first escapes from the low concentration domain $D$ and lands in the high concentration domain $E$. That is,

$$p(x) = \mathbb{P}\{X_\tau(x) \in E\},$$

(6)

where $\tau$ is the exit time from $D$, as in \([4]\). This first escape probability $p$ satisfies the following equation [33] with exterior boundary value condition:

$$Ap(x) = 0, \quad x \in D,$$

$$p(x) = 1, \quad x \in E,$$

$$p(x) = 0, \quad x \in D^c \setminus E,$$

(7)

where $A$ is the generator for the stochastic differential equation (2).

We can then compute the first escape probability from the low concentration domain $D = (0, x_u)$ to the high concentration domain $E = [x_u, +\infty)$ (containing the other stable state “$x_+$”). It is the likelihood of escape from $D$ through the right side, i.e., gaining high concentration and corresponding to the likelihood for transcription.

4 Gene regulation with synthesis rate under asymmetric Lévy noise

In this section, we first present the numerical schemes for solving the mean exit time $u$ and escape probability (i.e., solving [5] and (7)), then conduct numerical simulations to gain insights about likelihood for transcription.
4.1 Numerical algorithms

For the stochastic differential equation (2) of genetic regulation system with synthesis rate under asymmetric Lévy noise, we present a numerical scheme to solve deterministic nonlocal partial differential equations (3) and (4) in order to quantify its stochastic dynamics. The generator $A$ for the stochastic differential equation (2) with asymmetric stable Lévy motion is

$$Au(x) = (f(x) + M_{\alpha, \beta})u'(x) + \int_{\mathbb{R}^1 \setminus \{0\}} [u(x + y) - u(x) - I_{\{|y|<1\}}(y)yu'(x)]\nu_{\alpha, \beta}(dy),$$

with $\nu_{\alpha, \beta}(dy) = \frac{C_1I_{(0<y<\infty)}(y) + C_2I_{(-\infty<y<0)}(y)}{|y|^{1+\alpha}}dy$, $C_1 = \frac{H_\alpha(1+\beta)}{2}$ and $C_2 = \frac{H_\alpha(1-\beta)}{2}$. When $\alpha = 1$, $H_\alpha = \frac{1}{2}$; when $\alpha \neq 1$, $H_\alpha = \frac{\alpha(1-\alpha)}{1(2-\alpha)\cos(\pi\alpha)}$. Additionally,

$$M_{\alpha, \beta} = \begin{cases} \frac{C_1-C_2}{1-\alpha}, & \alpha \neq 1, \\ \int_1^\infty \sin(x)\frac{dx}{2^x} + \int_0^1 \sin(x)\frac{dx}{2^x}(C_2-C_1), & \alpha = 1. \end{cases}$$

The MFET $u$ satisfies the following equation:

$$(f(x) + M_{\alpha, \beta})u'(x)$$

$$+ \int_{\mathbb{R}^1 \setminus \{0\}} [u(x + y) - u(x) - I_{\{|y|<1\}}(y)yu'(x)]\frac{C_1I_{(0<y<\infty)}(y) + C_2I_{(-\infty<y<0)}(y)}{|y|^{1+\alpha}}dy$$

$$= -1.$$

(9)

On an open interval $D = (a, b)$, we make a coordinate conversion $x = \frac{b-a}{2}s + \frac{b+a}{2}$ for $s \in [-1, 1]$ and $y = \frac{b-a}{2}r$ to get finite difference discretization for $Au(x) = -1$ as in [38]:

$$(\frac{2}{b-a})f(\frac{b-a}{2}s + \frac{b+a}{2} + M_{\alpha, \beta})u'(s) + (\frac{2}{b-a})\int_{\mathbb{R}^1 \setminus \{0\}} [u(s + r) - u(s) - I_{\{|r|<1\}}(r)ru'(s)]\frac{C_1I_{(0<r<\infty)}(r) + C_2I_{(-\infty<r<0)}(r)}{|r|^{1+\alpha}}dr = -1.$$

(10)

With the numerical simulation via (10), we obtain the MFET $u$ for the stochastic gene regulation model (2).

A similar scheme is applied for numerical simulation for the first escape probability $p$.

4.2 Numerical experiments

As we take domain $D$ to be in the low concentration region, a smaller MFET indicates higher likelihood for gene transcription (and vice versa), and a larger FEP means higher likelihood for gene transcription (and vice versa). Both MFET $u$ and FEP $p$ reflect the interactions between nonlinear vector field $f$ and the noise $L_{t}^{\alpha, \beta}$.

We summarize major numerical simulation results below, and indicate their relevance to the likelihood for gene transcriptions. We highlight the peculiar dynamical differences with the case of symmetric stable Lévy noise ($\beta = 0$) in [35].

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Shorter MFET for larger $\alpha$ and larger $\beta$. Figure 3 shows the impact of the skewness index $\beta$ on MFET, for $\alpha = 0.5$ and $\alpha = 1.5$. When $-1 < \beta < 0$, MFET increases firstly then decreases, but for $0 < \beta < 1$, MFET decreases in the whole interval. This indicates that the asymmetry of the noise (characterized by $\beta$) plays an important role in the dynamical system: Increasing positive asymmetry leads to higher likelihood for gene transcription, while for negative asymmetry there is a minimum likelihood for transcription ($\alpha = 0.5$). But for $\alpha = 1.5$, MFET increases to the maximum and then decreases to 0, i.e., there is a minimum likelihood for transcription for all asymmetry index $\beta$. Meanwhile, we observe that for $\beta < 0$, MFET decreases earlier than that for $\beta > 0$. We also observe a peculiar feature. With $\alpha < 1$, the MFET reaches the maxima value (i.e., the least likelihood for transcription) near the exit boundary $x_u = 1.48971$ for negative $\beta$; while with $\alpha > 1$, the MFET reaches the maxima value near (i.e., the least likelihood for transcription) the exit boundary $x_u = 1.48971$ for positive $\beta$. This indicates that the skewness index $\beta$ may function as a tuning parameter for transcription.

Figure 4 shows that when $\beta$ is fixed, the MFET values decrease with the increasing $\alpha$, i.e., the likelihood for gene transcription increases with increasing $\alpha$. In comparison, Figure 4(b) contains the case with Brownian noise (i.e., corresponding to $\alpha = 2$, $\beta = 0$) and the MFET values break this monotonicity and stay roughly between those for $\alpha = 1.5$ and $\alpha = 1.9$. Figure 3 and Figure 4 indicate that if we start in the gene “off” position, then increasing $\alpha$ and $\beta$ values leads to the higher concentrations, corresponding to the gene “on” position.

Figure 5 plots the dependency of MFET in the low concentration on the asymmetry index $\beta$. Since the transcription behavior is particularly sensitive to initial conditions [37], we investigate the noise effect on different initial concentrations. In the case of $\alpha = 0.5$, MFET increases at first and then decreases. Different initial concentrations $x$ correspond to different maximum MFET values: By tuning the asymmetry index $\beta$ (depending on initial concentration), we can find the least likelihood for transcription. If we fix $x = 0.62685$ (low concentration), MFET increases and then decreases, especially for $\alpha = 0.5$ or 1.5: By increasing non-Gaussian index $\alpha$, we can achieve higher likelihood for transcription.

When skewness $\beta \neq 0$: It makes a great difference on MFET for $\alpha < 1$ and $\alpha > 1$. Figure 6 exhibits that, when $\beta \neq 0$, MFET has a bifurcation or discontinuity point at $\alpha = 1$ when $\beta \neq 0$. We can see that the MFET has a ‘phase transition’ or bifurcation at the critical non-Gaussian index value $\alpha = 1$. This result is consistent with a theoretical analysis in [39]. When the asymmetry index $\beta \neq 0$, in the low concentration region, MFET decreases with the increasing $\alpha$ for $0 < \alpha < 1$, while for $1 < \alpha < 2$, MFET...
Figure 4: (Color online) Mean first exit time (MFET) $u(x)$ as a function of initial concentration $x$ in the low concentration domain $D = (0, 1.48971)$. Effect of non-Gaussianity index $\alpha$ on the MFET: (a) $\beta = -0.5$. (b) $\beta = 0$. (c) $\beta = 0.5$.

increases firstly but then decreases with the increasing $\alpha$. In the symmetric Lévy nose case ($\beta = 0$), MFET is decreasing for all $\alpha$ (no bifurcation). Hence in the asymmetric Lévy noise case ($\beta \neq 0$): We gain higher likelihood for transcription by increasing non-Gaussian index $\alpha \in (0, 1)$, while for $\alpha \in (1, 2)$ there is a specific $\alpha_s$ leading to the minimum likelihood for transcription.

We thus observe that smaller MET for larger non-Gaussianity index $\alpha$ and larger skewness index $\beta$. We can always achieve the minimum MET by tuning non-Gaussianity index $\alpha$ and skewness index $\beta$. The smaller MET means a high level of TF-A, corresponding to a higher likelihood for gene transcription.

**Larger FEP for smaller $\alpha$ and larger $\beta$.** Figure 7 demonstrates that FEP increases with the increasing $\beta$, and FEP for positive $\beta$ is larger than that for negative $\beta$. Comparing (a) with (b), we find that FEP for $\alpha = 1.5$ increases more rapidly than that for $\alpha = 0.5$.

From Figure 8, we observe that when $\beta = -0.5$, FEP corresponding to different $\alpha$ has intersection or crossover points. Before and after the intersection point, there exists an opposite relationship. When $\beta = 0.5$, FEP decreases with the increasing $\alpha$. So in order to get a high likelihood of gene transcription, we can tune asymmetric index $\beta$ larger and $\alpha$ smaller. In comparison, for the Brownian noise case in Figure 8(b), the FEP is approximately linearly increasing in the initial concentration $x$.  

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Figure 5: (Color online) Mean first exit time (MFET) \( u \) as a function of skewness index \( \beta \). (a) Effect of initial concentrations \( x \) and \( \beta \) on the MFET: \( \alpha = 0.5 \). (b) Effect of \( \alpha \) and \( \beta \) on the MFET: \( x \approx 0.62685 \).

Figure 6: (Color online) MFET \( u \) as a function of \( \alpha \). (a) Effect of different initial concentrations \( x \) and \( \alpha \) on the MFET: \( \beta = -0.5 \). (b) Effect of \( \alpha \) and \( \beta \) on the MFET: \( x \approx 0.62685 \).

As shown in Figure 9, we find that, when \( \beta < 0 \), FEP decreases with the increasing \( \alpha \) for initial concentration \( x < x_\text{−} \), then increases with the increasing \( \alpha \) for \( x_\text{−} < x < x_u \). This leads to the conclusion that larger initial concentrations are more likely leading to the transcription. If we consider FEP at the low concentration \( x = 0.62685 \), we see that when \( \beta < 0 \), FEP increases with the increasing \( \alpha \), while when \( \beta \geq 0 \), FEP decreases with the increasing \( \alpha \). A small \( \alpha \) (and \( \beta > 0 \)) or a large \( \alpha \) (and \( \beta < 0 \)) contributes to large FEP (i.e., more likely for transcription).

**FEP has ‘turning points’ with respect to \( \alpha, \beta \).** Figure 10 (a) exhibits that FEP increases with the increasing \( \beta \), i.e., the likelihood for transcription improves with increasing \( \beta \), when the system starts in low concentrations. When starting system at low stable concentration \( x = 0.62685 \), we find that the evolution of FEP has ‘turning points’ for \( \beta = \beta_{\text{turning}} \approx 0.55 \) (this threshold value varies slightly with various \( \alpha \)). As shown in Figure 10 (b), before and after a turning point \( \beta_{\text{turning}} \), FEP presents a reverse relationship: Higher FEP for larger \( \alpha \) suddenly switches to higher FEP for smaller \( \alpha \). That is, the higher likelihood for transcription is attained for larger non-Gaussianity index \( \alpha \) before the turning point \( \beta_{\text{turning}} \).
while the opposite is true after the turning point. This phenomenon does not occur when the system is under symmetric Lévy fluctuations.

On the whole, we can achieve the maximum FEP by tuning the non-Gaussianity index $\alpha$ and skewness index $\beta$. The larger FEP means an increasing in the high concentration of TF-A, which leads to a higher likelihood for gene transcription.

5 Discussion

Random fluctuations to dynamical systems are often assumed to be Gaussian, but this is not proper especially in complex biological networks. The stable Lévy motions, with heavy tails and jumps, are suitable to model various non-Gaussian fluctuations.

We have studied the effects of asymmetric stable Lévy noise on a kinetic concentration model for a genetic regulatory system. We have examined possible switches or transitions from the low concentration states to the high concentration states (i.e., likelihood for transcriptions), excited by the noise. Our results suggest that the asymmetric stable Lévy noise may be used as a possible ‘regulator’ for gene transcriptions. For example, attaining higher likelihood of transcription by selecting a larger positive skewness index (asymmetry index) $\beta$ or by tuning the non-Gaussianity index $\alpha$. We have observed a bifurcation for the likelihood of transcription at the critical value $\alpha = 1$ under asymmetric stable Lévy noise ($\beta \neq 0$), as shown in Figure 6. There is also a turning point in the skewness index $\beta$ for the likelihood of transcription, as seen in Figure 10 (b). The bifurcation and turning point phenomena do not occur in the symmetric noise case ($\beta = 0$).

Our results offer a possible guidance to achieving certain genetic regulatory behaviors by tuning noise index [40], and may also provide helpful insights to further experimental research.

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Conflict of Interest: The authors declare that they have no conflict of interest.
Figure 8: (Color online) FEP $p(x)$ as a function of initial concentration $x$, from $D = (0, 1.48971)$ to $E = [1.48971, \infty)$. Effect of non-Gaussianity index $\alpha$ on the FEP: (a) $\beta = -0.5$. (b) $\beta = 0$. (c) $\beta = 0.5$.

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Figure 9: (Color online) FEP $p$ as a function of $\alpha$, from $D = (0, 1.48971)$ to $[1.48971, \infty)$. (a) Effect of $\alpha$ and different initial concentrations $x$ on the FEP with $\beta = -0.5$. (b) Effect of $\alpha$ and $\beta$ on the FEP at $x \approx 0.62685$.

Figure 10: (Color online) FEP $p$ as a function of $\beta$, from $D = (0, 1.48971)$ to $[1.48971, \infty)$. (a) Effect of $\beta$ and different initial concentrations $x$ on the FEP with $\alpha = 0.5$. (b) Effect of $\alpha$ and $\beta$ on the FEP at the initial concentration $x \approx 0.62685$.

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