Stochastic analysis of the motion of DNA nanomechanical bipeds

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December 22, 2009; Revised: September 24, 2010

Abstract

In this paper we formulate and analyze a Markov process modeling the motion of DNA nanomechanical walking devices. We consider a molecular biped restricted to a well-defined one-dimensional track and study its asymptotic behavior. Our analysis allows for the biped legs to be of different molecular composition and thus to contribute differently to the dynamics. Our main result is a functional central limit theorem for the biped with an explicit formula for the effective diffusivity coefficient in terms of the parameters of the model. A law of large numbers, a recurrence/transience characterization and large deviations estimates are also obtained. Our approach is applicable to a variety of other biological motors such as myosin and motor proteins on polymer filaments.

Keywords: DNA nanodevices, molecular spiders, controlled random walks, Markov additive processes, law of large numbers, recurrence-transience criteria, large deviations, central limit theorem, regeneration structure.

1 Introduction

Biological molecular motors are of fundamental importance for a variety of cell and tissue level processes. Nanomotors such as polymerases move along one-dimensional DNA templates in assembling messenger RNA macromolecules, while micromotors such as proteins of the myosin family are responsible for actin-based cell motility and the transport of cargo inside cells [10, 19]. Identifying the biochemical control mechanisms regulating such biological motor activities is the subject of current research activity in cellular and molecular biology [25], and different mathematical approaches have been recently employed in elucidating possible mechanisms at work [16, 24].

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Research in biological motors in conjunction with recent advances in DNA nanofabrication technology have spurred a lot of interest in biomimetic nanomotor design and DNA-based devices, such as nanomechanical switches and DNA templates for the growth of semiconductor nanocrystals to name a few [27]. Research activity in this area has been focused on designing and controlling dynamic DNA nanomachines that can be activated by and respond to specific chemical signals in their environment, thus expanding on the biochemical paradigm of eukaryotic and prokaryotic cells [20]. Potential applications of such synthetic molecular machinery include DNA-based computing and engineered DNA motors designed for intelligent drug delivery among other *in vivo* therapeutic applications [3, 18].

Currently, there exist two types of molecular designs implementing DNA-based walking devices. Both designs are based on control mechanisms that rely on nucleic acid hybridization, and the corresponding molecular constructs can be bipedal or multipedal with the latter sometimes referred to as molecular spiders [18]. In the first implementation approach, devised by Sherman & Seeman [22], the walking device consists of two double helical domains (the device legs) connected by flexible linker regions. The construct is held on a self-assembled, one-dimensional path by DNA set strands with nucleic acid domains complementary to molecular imprints on the device legs and the substrate. In this context, the detachment of a leg from the path during a walk cycle is mediated by the removal of the set strand through a hybridization reaction [20, 22].

A more recent molecular design by Pei *et al.* [18] does not require the presence of interface strands in that it allows for each device leg to be directly attached to the substrate through Watson-Crick base pair formation. Leg detachment during the walk cycle is controlled by the cleavase activity of nucleic acid domains imprinted on the leg. This latter attribute of the system leads to a random walk of the device on the substrate, dictated by the stochastic events of leg detachment and relocation. Specific aspects of the long-term dynamics of this random walk have been investigated mathematically by Antal *et al.* [2] and Antal & Krapivsky [1], who have derived explicitly the mean velocity and the diffusion coefficient of the walker under specific conditions on leg relocation rates. Another related work on a molecular spider random walk is the recent paper by Gallesco, Müller and Popov [9].

In this paper we prove a strong law of large numbers and a functional central limit theorem for the location of a molecular biped with explicit expressions for the asymptotic velocity and limiting variance. The existence of a law of large numbers and a functional central limit theorem for the model follows from general theory of regenerative processes. The shortcoming of this purely probabilistic method lies in the quantitative analysis. The expression it provides for the variance in the central limit theorem does not appear to be useful for the actual computation or estimation of the variance, which is crucial for applications. Our work focuses mainly on the computation of the variance in the central limit theorem and generalizes the results of Antal *et al.* [2]. The latter are based on the existence of various symmetries in the definition of the underlying random walk, whereas our analysis relies on a different approach and is not restricted by such assumptions.

We employ an analytic framework presented recently in [4], which is based on the analysis of the generating function of additive functionals associated with an underlying finite Markov chain. In general, the variance in the central limit theorem for dependent sequences differs from the so-called "average variance" experienced by the process, a phenomenon known in the literature as effective diffusivity. The formula for the limiting variance appearing in the CLT for additive functionals of Markov chains contains a "generalized inverse" of the generator (see for instance Theorem 7.6 in Chapter 7 of [8] or representation (17.50) in Section 17.4.3 of [15]). The spectral perturbation approach is a standard technique for establishing CLTs for Markov chains in compact state spaces (see, e.g. [11, 13]). In [4] the authors establish a link between the moment generating function, the generalized inverse and perturbations of the Perron root for matrices. Furthermore, they provide an efficient method for computing these quantities in terms of expectations of hitting times. In our case, these ultimately lead to the desired results.

The remainder of the paper is organized as follows. The random walk formalism of the model is described in Section 2.1. In Section 2.2 we present results obtained through a regenerative approach. The analytic viewpoint is presented in Section 2.3, followed by estimates on the variance and an explicit formula for the variance in Sections 2.4 and 2.5, respectively. In Section 2.6 we present some examples.

2 Random walk analysis of the motion of DNA bipeds

In the following, we formulate the model to be considered in the rest of the paper. In Section 2.2 we employ general results to determine the asymptotic behavior of the model. In Section 2.3 we compute explicitly the asymptotic speed and variance of the molecular biped. The main results of the paper are stated in Corollary 2.3, Corollary 2.6, and Theorem 2.8. The latter establishes a link between the asymptotic speed and variance and perturbations of a Perron root. This, in turn, leads to explicit expressions for the quantities of interest in Theorem 2.11 and Section 2.6.1.

2.1 Random walk formalism

We consider a continuous time random walk modeling the motion of a DNA biped on a one-dimensional walking path (see also [2] and [1, 9]). The legs of the biped are assumed to move on a discrete (integer) lattice representing the nucleic acid binding domains imprinted on the path. The waiting time for each leg follows an exponential distribution, with different legs being in general associated with different exponential clocks. The system is characterized by six parameters: (a) four parameters accounting for the transition rate probabilities corresponding to the relocation of each leg (two legs and two possible movement directions) and (b) the minimum and the maximum possible distance between legs. The latter two parameters represent a mechanical constraint imposed by the design of the molecular construct, whereas the transition rate probabilities for leg movements encode information on the interactions of the legs with the substrate path.

Let α denote the transition rate for the left leg moving to the left and β be the corresponding transition rate for the left leg moving to the right. Similarly, let λ and μ be the transition rate probabilities for the right leg moving to the left/right, respectively. The mechanical constraint is that the right leg is always between 0 and S units to the right of the left leg, where $S \in \mathbb{N}$ is some fixed parameter. Whenever a clock ticks, an attempt to move is made by the corresponding leg in the corresponding direction. The attempt succeeds if

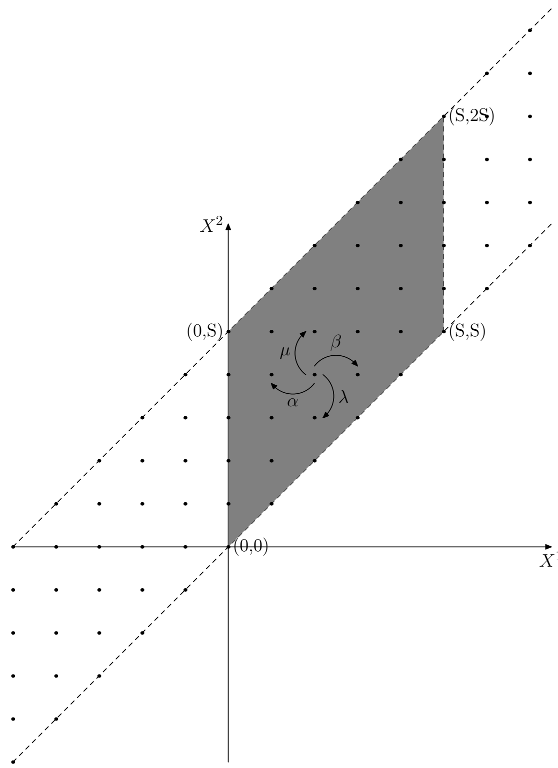

Figure 1: State space for the Markov chain $(X^{(1)}, X^{(2)})$

the new leg configuration satisfies the mechanical constraint. We denote the position of the left and right leg of the spider at time $t \in \mathbb{R}_+$ by $X^{(1)}(t)$ and $X^{(2)}(t)$, respectively. Note that neither $X^{(1)}$ nor $X^{(2)}$ is a Markov chain. However, the pair $(X^{(1)}, X^{(2)})$ is a Markov chain. Figure 1 shows the transition rates and the state space for the Markov chain $(X^{(1)}, X^{(2)})$, consisting of all points in $\mathbb{Z}^2$ between the two dashed diagonal lines. For each state, the horizontal coordinate describes $X^{(1)}$ (left leg) and the vertical coordinate describes $X^{(2)}$ (right leg). Note that the transition rates at each site to each of the allowed directions depend only on the direction.

Remark 2.1. *We remark that the analysis that follows remains valid if we assume that the right leg is always between S_1 and $S_1 + S$ units to the right of the left leg, where $S_1 \in \mathbb{Z}_+$ and $S \in \mathbb{N}$. Indeed, if we denote the locations of the left and right leg of the spider at time $t \in \mathbb{R}_+$ by $\overline{X}^{(1)}(t)$ and $\overline{X}^{(2)}(t)$, respectively, then for any $S_1 \in \mathbb{Z}_+$ the distribution of $(\overline{X}^{(1)}, \overline{X}^{(2)})$ starting from a state (x_1, x_2) coincides with the distribution of $(X^{(1)}, X^{(2)}) + (0, S_1)$ starting from $(x_1, x_2 - S_1)$. Hence, there is no loss of generality in focusing on the case $S_1 = 0$.*

2.2 The regenerative viewpoint

Let $Y(t) = X^{(2)}(t) - X^{(1)}(t)$ denote the process corresponding to the distance between the left and the right leg. Then Y is a pure birth and death Markov chain on $\{0, \dots, S\}$ with rates $x = \alpha + \mu$ to the right and $y = \beta + \lambda$ to the left. A significant amount of information for the asymptotic behavior of $X^{(2)}(t)$ can be derived using a renewal structure induced by Y, defined by successful return times of this chain to a distinguished state, say S. More precisely, let $\tau_0 = 0$ and $\tau_k = \inf\{t > \tau_{k-1} : Y(t) = S\}$ for $k \in \mathbb{N}$. Let $N_t = \sup\{k \in \mathbb{N} : \tau_k < t\}$ be the number of returns to S prior time $t > 0$.

The following lemma is standard and its proof is thus omitted.

Lemma 2.2. *We have:*

(i) The time intervals $(\tau_n - \tau_{n-1})_{n\geq 1}$ are independent random variables. Moreover all of them besides perhaps $\tau_1 - \tau_0$ are identically distributed.

(ii) The path fragments $(X^{(2)}(t) - X^{(2)}(\tau_{n-1}) : \tau_{n-1} \leq t < \tau_n)_{n\geq 1}$ are independent. Moreover, all of them except perhaps the first one are identically distributed.

Let $D(\mathbb{R}_+;\mathbb{R})$ denote the set of real-valued functions on $\mathbb{R}_+$, which are right-continuous and possess left limits. We endow this set with the Skorokhod topology and its Borel σ-field. We refer the reader to Billingsley [6, Chapter 3] for details on the Skorohod topology. The following corollary can be derived from Lemma 2.2 by using appropriate moment conditions (see e.g., [12, 23]).

Corollary 2.3.

(i) (strong law of large numbers)

$$\mathrm{v} = \lim_{t\to\infty} \frac{X_t^{(2)}}{t} = \frac{E(X_{\tau_2}^{(2)} - X_{\tau_1}^{(2)})}{E(\tau_2 - \tau_1)} \in (-\infty, \infty), \ \ a.s.$$

(ii) (recurrence/transience dichotomy)

(a) If $\mathrm{v} > 0$, then $\lim_{t\to\infty} X^{(2)}(t) = \infty$, a.s.

(b) If $\mathrm{v} = 0$, then $\liminf_{t\to\infty} X^{(2)}(t) = -\infty$ and $\limsup_{t\to\infty} X^{(2)}(t) = \infty$, a.s.

(c) If $\mathrm{v} < 0$, then $\lim_{t\to\infty} X^{(2)}(t) = -\infty$, a.s.

(iii) (functional central limit theorem) For $t \geq 0$, define a process $W^{(t)}$ in $D(\mathbb{R}_+, \mathbb{R})$ by setting

$$W^{(t)}(s) = \frac{X_{ts}^{(2)} - ts\mathrm{v}}{\sqrt{t}}, \qquad s \geq 0.$$

Then $W^{(t)}$ converges in law in the space $D(\mathbb{R}_+, \mathbb{R})$, as $t \to \infty$, to a Brownian motion with diffusivity coefficient $\sigma_{eff}^2 \in (0, \infty)$ given by

$$\sigma_{eff}^2 = \frac{E\big([X_{\tau_2}^{(2)} - X_{\tau_1}^{(2)} - \mathrm{v}(\tau_2 - \tau_1)]^2\big)}{E(\tau_2 - \tau_1)}. \tag{1}$$

The subscript eff stands for "effective", which is to be compared with the "average" variance defined in (7). It is clear from (1) (see also Theorem 2.9 below) that $\sigma_{eff} > 0$. The main goal of this paper is to derive explicit expressions for v and σ_{eff}.

The law of large numbers can be complemented by the following large deviation principle (see for instance [14] or Remark (ii) in [17, p. 594]).

Proposition 2.4. *There exists a convex lower semi-continuous rate function $J : \mathbb{R} \to \mathbb{R}$ such that*

(i) $J(\mathrm{v}) = 0$, *and* $J(u) > 0$ *for* $u \neq \mathrm{v}$.

(ii) $\lim_{t\to\infty} \frac{1}{t} \log P\big(X_t^{(2)} \geq tu\big) = -J(u)$ *for all* $u > \mathrm{v}$.

(iii) $\lim_{t\to\infty} \frac{1}{t} \log P\big(X_t^{(2)} \leq tu\big) = -J(u)$ *for all* $u < \mathrm{v}$.

2.3 The analytic viewpoint

Let D be the parallelogram in $\mathbb{Z}^2$ whose vertices are $(0,0)$, (S,S), $(S,2S)$ and $(0,S)$. The shaded region in Figure 1 represents D. Let Z be the Markov chain $(X^{(1)}, X^{(2)})$ modulo D. That is, $Z = (Z^1, Z^2)$ is the nearest neighbor Markov chain on D with rates to the left and right equal to α and β, respectively, and rates for moving downwards and upwards equal to λ and μ, respectively. Additionally, we allow jumps to the "left" from $(0,i)$, $i \leq S-1$ to $(S, i+S+1)$ at rate α, and we allow jumps to the "right" from $(S, i+S+1)$ to $(0,i)$ at rate β. We observe then that the difference process $Z^2(t) - Z^1(t)$ coincides with $Y(t) = X^{(2)}(t) - X^{(1)}(t)$.

We further observe that the displacement $X^{(2)}(t) - X^{(2)}(0)$ has the same distribution as the number of jumps Z upwards minus the number of jumps downwards, until time t. We denote the latter by $I(t)$. For fixed $\eta \in \mathbb{R}$, define the semigroup of linear operators $\mathcal{T}^\eta = \{\mathcal{T}_t^\eta : t \in \mathbb{R}_+\}$ on $\mathbb{R}^{S+1}$ by letting

$$\mathcal{T}_t^\eta f(u) = E_u e^{\eta I(t)} f(Z(t)).$$

By setting $f = \delta_{u'}$ for some $u' \in D$, it follows that $\mathcal{T}^\eta$ has an infinitesimal generator $\mathcal{L}^\eta$, defined by $\mathcal{L}^\eta f(u) = \sum_{u'} \eta(u,u') f(u')$, where the rates $\eta(u,u')$ are non zero only if $u = u'$ or u' is one step away from u, and $\eta(u,u')$ is given by the following table:

u' relative to u	-1	+1
horizontal	α	β
vertical	$\lambda e^{-\eta}$	μe^{η}

We remark that $\mathcal{L}^\eta$ is the h-transform of the generator of Z, $\mathcal{L}^0$, with the positive function $h(a,b) = e^{\eta b}$. That is for any function f, we have $\mathcal{L}^\eta f = \frac{1}{h}\mathcal{L}^\eta(hf)$.

Now $\eta(u,u) = \lim_{t\to 0} \frac{1}{t}\big[E_u[\delta_u(Z(t))] - 1\big] = \frac{d}{dt} P_u(X(t) = u)|_{t=0}$, and is then equal to $-(\alpha+\mu)$ when $u = (i,i)$, to $-(\beta+\lambda)$ when $u = (i, i+S)$ and is equal to $-(\alpha+\beta+\lambda+\mu)$ otherwise. As a result, $\eta((i,j),(i',j')) = \eta(i'-i, j'-j)$, which in turn implies that if $\varphi(i,j) = \varphi(j-i)$ then $(\mathcal{L}^\eta\varphi)(i,j)$ is also a function of $j-i$. In particular, it follows that for all $t \in \mathbb{R}_+$, $\mathcal{T}_t^\eta \mathbf{1}(i,j) = E_{(i,j)} e^{\eta I(t)}$ is a function of $j-i$. Let then $\varphi(t,y) = E_{(i,i+y)} e^{\eta I(t)}$ for some arbitrary i. It follows that $\frac{d}{dt}\varphi(t,y) = A(\eta)\varphi(t,y)$, where $A(\eta)$ is the following matrix, whose rows and columns are indexed from 0 to S:

$$A(\eta)=\begin{pmatrix} -x & x(\eta) & & & & & \\ y(\eta) & -(x+y) & x(\eta) & & & & \\ & \ddots & \ddots & \ddots & & & \\ & & & & & & \\ & & & & \ddots & \ddots & \\ & & & & y(\eta) & -(x+y) & x(\eta) \\ & & & & & y(\eta) & -y \end{pmatrix}.$$

Here $x(\eta)=\alpha+\mu e^{\eta}$ and $y(\eta)=\beta+\lambda e^{-\eta}$. Clearly, $x=x(0),\ y=y(0)$. The solution for the differential equation for $\varphi(t,y)$ with the initial condition $\varphi(0,y)=\mathbf{1}(y)$ is

$$E_{(i,i+y)}e^{\eta I(t)}=e^{A(\eta)t}\mathbf{1}(y). \tag{2}$$

In what follows we write A, A', and A'' for $A(0), A'(0)$, and $A''(0)$, respectively. Note that A is the generator of Y. Since Y is a birth and death process, its invariant distribution π, which satisfies $A^T\pi=0$, also satisfies the detailed balance condition:

$$y\pi_{j+1}=x\pi_j, \quad j=0,\dots,S-1. \tag{3}$$

Let $\Lambda(\eta)$ denote the Perron root of $A(\eta)$, which is an eigenvalue of $A(\eta)$ with maximal real part. Recall that by the Perron-Frobinus Theorem (see for example Seneta [21, Part I, Chapter 1]), $\Lambda(\eta)$ is uniquely determined, it is real and is a simple eigenvalue. Furthermore, it is well known that Λ is analytic in some neighborhood of the origin, and so are the (properly) normalized corresponding left and right eigenvectors (see Wilkinson [26, page 66]). We have the following:

Proposition 2.5. *There exists $\varepsilon>0$ such that for all complex numbers θ with $|\theta|<\varepsilon$,*

$$\lim_{t\to\infty} E\exp\left(\theta\frac{X^{(2)}(t)-\Lambda'(0)t}{\sqrt{t}}\right)=e^{\frac{1}{2}\Lambda''(0)\theta^2}.$$

In view of Corollary 2.3 this implies:

Corollary 2.6.

1. *(Central Limit Theorem)* $\dfrac{X^{(2)}(t)-\Lambda'(0)t}{\sqrt{t}} \underset{t\to\infty}{\to} \mathcal{N}\big(\Lambda''(0)\big)$ *in distribution, where* $\mathcal{N}(\sigma^2)$ *denotes the centered normal distribution with variance* σ^2*.*

2. *(Strong Law of Large Numbers)* $\dfrac{X^{(2)}(t)}{t} \underset{t\to\infty}{\to} \Lambda'(0)$, *$P$-a.s.*

One can derive Proposition 2.5 from [4, Theorem 5]. In the following, we outline the argument.

Proof of Proposition 2.5. Let N denote the matrix-valued process, whose entries are the additive functionals of Y defined as follows. For $i \leq j$, $N_{i,j}(t)$ is the number of jumps Y made from i to j up to time t, and for $i = j$, $N_{i,i}(t)$ is the occupation time at i, the time Y spent at i up to time t. Extend the definitions of $x(\eta)$, $y(\eta)$, and $A(\eta)$ to complex values of η in a neighborhood of 0, and define the additive functional $\tilde{I}$ of Y by letting

$$\tilde{I}(t) = (\ln x(\eta) - \ln x) \sum_{i=0}^{S-1} N_{i,i+1}(t) + (\ln y(\eta) - \ln y) \sum_{i=1}^{S} N_{i,i-1}(t).$$

By the first paragraph of [4, Theorem 4] we have

$$E_j\big(e^{\tilde{I}(t)}\big) = e^{A(\eta)t}\mathbf{1}(j)$$

(here expectation is with respect to Y). However, as shown in (2), the right-hand side is equal to $E_{(0,j)}\big(e^{\eta I(t)}\big)$. That is, $\big(E_{(0,j)}e^{\eta I(t)}\big) = E_j\big(e^{\tilde{I}(t)}\big)$, and so instead of working with I one can work with $\tilde{I}$. It follows (cf. [4, Theorem 4]) that

$$e^{A(\eta)t}\mathbf{1}(j) = \big(e^{\Lambda(\eta)t}P_\eta + J(\eta,t)\big)\,\mathbf{1}(j),$$

where the matrix $J(\eta,t)$ converges to 0 as $t \to \infty$ uniformly in η in some neighborhood of 0, and the matrix P_η converges as $\eta \to 0$ to the matrix whose rows are equal to π^T.

If we let $\eta = \theta/\sqrt{t}$ for some fixed small $\theta \in \mathbb{C}$, then the Taylor expansion for Λ leads to

$$e^{A(\eta)t}\mathbf{1}(j) = \exp\Big(\Big[\Lambda(0) + \Lambda'(0)\frac{\theta}{\sqrt{t}} + \frac{\Lambda''(0)}{2}\frac{\theta^2}{t} + O(t^{-3/2})\Big]t\Big) + o(1).$$

Thus

$$\lim_{t\to\infty} E_{(0,j)}\big(e^{\frac{\theta}{\sqrt{t}}[I(t)-\Lambda'(0)t]}\big) = e^{\frac{1}{2}\Lambda''(0)\theta^2},$$

completing the proof. $\square$

Corollary 2.7. $\Big(\dfrac{X^{(2)} - \Lambda'(0)t}{\sqrt{t}}, X^{(2)}(t) - X^{(1)}(t)\Big) \underset{t\to\infty}{\to} (U,V)$ *in distribution, where U and V are independent, U is $\mathcal{N}(0,\Lambda''(0))$-distributed, and the distribution of V is π.*

Proof. Let

$$\widetilde{X}(t) = \frac{X^{(2)}(t) - \Lambda'(0)t}{\sqrt{t}}.$$

If needed, assume that the probability space is enlarged to include random variables U and V as in the statement of the corollary. Recall the notation $Y(t) = X^{(2)}(t) - X^{(1)}(t)$. By the Cramér-Wold device (see e.g. [8, Section 3.9]), it suffices to show that for any $a, b \in \mathbb{R}$ we have

$$\lim_{t\to\infty} E\big(e^{ia\widetilde{X}(t)} \cdot e^{ibY(t)}\big) = e^{-\frac{a^2\Lambda''(0)}{2}} \cdot E\,e^{ibV}. \tag{4}$$

Since Y is an irreducible continuous time Markov chain on a finite state space, the distribution of $Y(t)$ converges to π exponentially fast in the total variation norm (see e.g. [15, Chapter XVI]). In particular, there exist constants $C, \gamma > 0$ such that for any function $f : \{0, \ldots, S\} \to \mathbb{C}$ with $\max_{0 \leq x \leq S} |f(x)| \leq 1$ we have

$$E\Big(\big|f(Y(t)) - \langle f, \pi\rangle\big|\Big) \leq Ce^{-\gamma t}. \tag{5}$$

Therefore,

$$\begin{aligned}
&\Big|E\big(e^{ia\widetilde{X}(t)} \cdot e^{ibY(t)}\big) - e^{-\frac{a^2\Lambda''(0)}{2}} E\big(e^{ibV}\big)\Big| \\
&\leq \Big|E\big(e^{ia\widetilde{X}(t)} \cdot e^{ibY(t)}\big) - E\big(e^{ia\widetilde{X}(t)} \cdot E(e^{ibV})\big)\Big| + \Big|E\big(e^{ia\widetilde{X}(t)}\big) \cdot E\big(e^{ibV}\big) - e^{-\frac{a^2\Lambda''(0)}{2}} E\big(e^{ibV}\big)\Big| \\
&\leq E\Big(\Big|e^{ibY(t)} - E\big(e^{ibV}\big)\Big|\Big) + \Big|E\Big(e^{ia\widetilde{X}(t)} - e^{-\frac{b^2\Lambda''(0)}{2}}\Big)\Big|.
\end{aligned}$$

As t approaches infinity, the first term in the rightmost expression goes to zero by (5), whereas the second term goes to zero due to the CLT for $X^{(2)}(t)$. This proves (4) and hence the corollary. □

Next we obtain explicit expressions for $\Lambda'(0)$ and $\Lambda''(0)$. We need to recall the notion of the group inverse for the non-invertible matrix A. The Euclidean space $\mathbb{R}^{S+1}$ can be represented as the following direct sum of two A-invariant subspaces: $\mathbb{R}^{S+1} = \text{Span}\{\mathbf{1}\} \oplus V_0$, where $V_0 = \{f : \langle f, \pi\rangle = 0\}$. Since V_0 is A-invariant and the null space of A is $\text{Span}\{\mathbf{1}\}$ (because π is the unique invariant measure for the corresponding birth-and-death process), we have that A is one-to-one on V_0. Let $A^{\#}$ denote the inverse of $-A$ on V_0 and extend it to $\mathbb{R}^{S+1}$ by letting $A^{\#}\mathbf{1} = 0$. Then $A^{\#}$ is the group inverse of $-A$ and for each $f \in \mathbb{R}^{S+1}$, $A^{\#}f$ is the unique solution $u \in V_0$ to $Au = -f_{\perp}$, where $f_{\perp}$ is the projection of f on V_0 along $\text{Span}\{\mathbf{1}\}$. That is:

$$f_{\perp} = f - \langle f, \pi\rangle\mathbf{1}, \;\; f \in \mathbb{R}^{S+1}. \tag{6}$$

For more details on the group inverse, we refer the reader to [5, Chapter 4].

We have:

Theorem 2.8.

1. *$\Lambda'(0) = \mu(1 - \pi_S) - \lambda(1 - \pi_0)$.*
2. *Let $\rho = \frac{y}{x}$ and*

$$Q = \begin{pmatrix} \rho\pi_0 A^{\#}_{0S} & -\frac{1}{2}(\rho\pi_0 A^{\#}_{00} + \rho^{-1}\pi_S A^{\#}_{SS}) \\ -\frac{1}{2}(\rho\pi_0 A^{\#}_{00} + \rho^{-1}\pi_S A^{\#}_{SS}) & \rho^{-1}\pi_S A^{\#}_{S0} \end{pmatrix}.$$

Then

$$\Lambda''(0) = \mu(1 - \pi_S) + \lambda(1 - \pi_0) + 2\Big\langle Q\begin{pmatrix} \mu \\ \lambda \end{pmatrix}, \begin{pmatrix} \mu \\ \lambda \end{pmatrix}\Big\rangle.$$

An interpretation of Theorem 2.8 can be obtained as follows. Recall that π is the invariant distribution for the birth-death process $Y = X^{(2)} - X^{(1)}$. At each state of this process (distance between biped legs), the right leg experiences a local drift. The drift is equal to μ at 0, to $-\lambda$ at S, and to $\mu - \lambda$ at any other state of Y. It follows that the average local drift is

$$\mathrm{v} = (\mu - \lambda)(1 - \pi_0 - \pi_S) + \pi_0\mu - \pi_S\lambda,$$

which coincides with the expression for $\Lambda'(0)$ given in the statement of Theorem 2.8. Similarly, at each site the right-leg experiences a "local variance" or diffusivity, equal to μ at 0, λ at S, and to $\mu + \lambda$ at all other states of Y. Thus, the "average variance" is given by

$$\sigma^2_{ave} := (\mu + \lambda)(1 - \pi_0 - \pi_S) + \mu\pi_0 + \lambda\pi_S = \mu(1 - \pi_S) + \lambda(1 - \pi_0). \tag{7}$$

This is the first term in the expression for $\Lambda''(0)$. We show in Theorem 2.9 that the entries of Q are strictly negative, hence the real, effective variance, $\sigma^2_{eff} = \Lambda''(0)$ is strictly less than σ^2_{ave}. The reason for this inequality is the restrictions imposed on the motion of the biped when the configuration process $Y(t)$ is at one of the two extremal states, 0 or S.

In principle, Theorem 2.8 can be derived from general formulas for the partial derivates of the Perron root (see [7] and the references therein). We provide here a short self-contained proof geared toward the model considered in this paper.

Proof of Theorem 2.8. Let $\varphi(\eta)$ denote the eigenvector for $A(\eta)$ corresponding to the Perron root $\Lambda(\eta)$, normalized to satisfy

$$\langle \varphi(\eta), \pi \rangle = 1. \tag{8}$$

Note that $\varphi(0) = \mathbf{1}$. Then

$$\Lambda(\eta) = \langle A(\eta)\varphi(\eta), \pi \rangle.$$

Differentiating both sides yields

$$\Lambda'(\eta) = \langle A'(\eta)\varphi(\eta), \pi \rangle + \langle A(\eta)\varphi'(\eta), \pi \rangle. \tag{9}$$

Set $\eta = 0$. Then the second term on the left-hand side is equal to $\langle \varphi'(0), A^T\pi \rangle = 0$. Therefore,

$$\Lambda'(0) = \langle A'\mathbf{1}, \pi \rangle.$$

Define the left and right shift operators on $\mathbb{R}^{S+1}$, Θ_l and Θ_r, by letting $\Theta_l\delta_j = \delta_{j-1}$, $\Theta_r\delta_j = \delta_{j+1}$, where $\delta_{-1} = \delta_{S+1} = 0$, and for $j = 0, \ldots, S$, $\delta_j(i) = \mathbf{1}_{\{i=j\}}$ is the indicator function equal to 1 when $i = j$ and to 0 otherwise. Observe then that $A' = \mu\Theta_l - \lambda\Theta_r$. In particular, $A'\mathbf{1} = \mu(\mathbf{1} - \delta_S) - \lambda(\mathbf{1} - \delta_0)$. It follows that

$$\Lambda'(0) = \mu(1 - \pi_S) - \lambda(1 - \pi_0).$$

This proves the first part of the theorem. Next, we differentiate both sides of the equation $A(\eta)\varphi(\eta) = \Lambda(\eta)\varphi(\eta)$ at $\eta = 0$ to obtain $A'\mathbf{1} + A\varphi'(0) = \Lambda'(0)\mathbf{1}$. In what follows, φ' stands for $\varphi'(0)$. Therefore $A\varphi' = -A'\mathbf{1} + \Lambda'(0)\mathbf{1} = -(A'\mathbf{1} - \langle A'\mathbf{1}, \pi\rangle\mathbf{1}) = -(A'\mathbf{1})_\perp$, where the projector operator $\perp$ is defined in (6). Furthermore, it follows from (8) that $\varphi' \in V_0$. Thus,

$$\varphi' = A^{\#}A'\mathbf{1}.$$

Returning to the computation of $\Lambda''(0)$, differentiate (9) to obtain

$$\Lambda''(\eta) = \langle A''(\eta)\varphi(\eta), \pi\rangle + 2\langle A'(\eta)\varphi'(\eta), \pi\rangle + \langle A(\eta)\varphi''(\eta), \pi\rangle.$$

Evaluate this expression at $\eta = 0$. Then the third term on the right-hand side is equal to $\langle\varphi''(0), A^T\pi\rangle = 0$, and so we obtain

$$\Lambda''(0) = \langle A''\mathbf{1}, \pi\rangle + 2\langle A'A^{\#}A'\mathbf{1}, \pi\rangle.$$

Next, observe that $A'' = \mu\Theta_l + \lambda\Theta_r$, therefore $A''\mathbf{1} = \mu(\mathbf{1} - \delta_S) + \lambda(\mathbf{1} - \delta_0)$. This gives

$$\langle A''\mathbf{1}, \pi\rangle = \mu(\mathbf{1} - \pi_S) + \lambda(\mathbf{1} - \pi_0).$$

Using again the equality $A' = \mu\Theta_l - \lambda\Theta_r$, we obtain $A'\mathbf{1} = \mu(\mathbf{1} - \delta_S) - \lambda(\mathbf{1} - \delta_0)$. Thus, we obtain

$$\begin{aligned} A'A^{\#}A'\mathbf{1} &= A'(\lambda A^{\#}\delta_0 - \mu A^{\#}\delta_S) \\ &= \mu\lambda\Theta_l A^{\#}\delta_0 - \mu^2\Theta_l A^{\#}\delta_S - \lambda^2\Theta_r A^{\#}\delta_0 + \mu\lambda\Theta_r A^{\#}\delta_S. \end{aligned} \tag{10}$$

Recall that we have defined $\rho = \frac{y}{x}$. It then follows from the detailed balance condition (3) that $\pi_j = \rho\pi_{j+1}$ for $j = 0, \ldots, S-1$. We then have that for any vector v

$$\langle\Theta_l v, \pi\rangle = \sum_{j=0}^{S-1} v_{j+1}\pi_j = \rho\sum_{j=0}^{S-1} v_{j+1}\pi_{j+1} = \rho(\langle v, \pi\rangle - v_0\pi_0).$$

Similarly,

$$\langle\Theta_r v, \pi\rangle = \sum_{j=1}^{S} v_{j-1}\pi_j = \rho^{-1}\sum_{j=1}^{S} v_{j-1}\pi_{j-1} = \rho^{-1}(\langle v, \pi\rangle - v_S\pi_S).$$

Now since $A^{\#}u \in V_0$ for all u, it follows that

$$\langle\Theta_l A^{\#}u, \pi\rangle = -\rho(A^{\#}u)_0\pi_0, \quad \langle\Theta_r A^{\#}u, \pi\rangle = -\rho^{-1}(A^{\#}u)_S\pi_S.$$

Plugging this into (10) we obtain

$$\langle A'A^{\#}A'\mathbf{1}, \pi\rangle = -\mu\lambda\rho\pi_0 A^{\#}_{00} + \mu^2\rho\pi_0 A^{\#}_{0S} + \lambda^2\rho^{-1}\pi_S A^{\#}_{S0} - \mu\lambda\rho^{-1}\pi_S A^{\#}_{SS}, \tag{11}$$

completing the proof of Theorem 2.8 $\square$

2.4 Bounds on variance in CLT

We next provide specific bounds for the limiting variance in the central limit theorem. We will derive exacts expressions for the limiting variance in Section 2.5. However, the bounds computed here are given by significantly simpler expressions.

Theorem 2.9.

1. *The entries of the matrix Q, defined in Theorem 2.8-(2), are strictly negative. In particular,* $\Lambda''(0) < \mu(1-\pi_S) + \lambda(1-\pi_0)$.
2. $\Lambda''(0) \geq \dfrac{\mu\alpha}{\mu+\alpha}(1-\pi_S) + \dfrac{\lambda\beta}{\lambda+\beta}(1-\pi_0)$.

We note that the lower bound is attained when $\alpha = \beta = \lambda = \mu$, see Section 2.6.1.

Proof of Theorem 2.9. For $j = 1, \ldots, S$, let σ_j denote the first time $Y = X^{(2)} - X^{(1)}$ enters the site j (or re-enters if starts at j). That is

$$\sigma_j = \min\{t > 0 : Y(t) = j\} \tag{12}$$

From [4, Corollary 1] we have

$$A^{\#}_{ij} = \pi_j \cdot \Big[\sum_{k\neq j} \pi_k E_k(\sigma_j) - \mathbf{1}_{\{i\neq j\}} E_i(\sigma_j)\Big],$$

where E_k denotes the expectation conditioned on Y starting from site k, and $\mathbf{1}_{\{i\neq j\}}$ is equal to 0 if $i = j$ and equal to 1 otherwise. In particular,

$$A^{\#}_{SS} = \pi_S \cdot \sum_{k=0}^{S-1} \pi_k E_k(\sigma_S) > 0.$$

Since $E_k(\sigma_S) < E_0(\sigma_S)$ for all $k > 0$, it follows that

$$A^{\#}_{SS} \leq \pi_S(1-\pi_S)E_0(\sigma_S),$$

with equality holding if and only if $S = 1$. This implies

$$A^{\#}_{0S} = A^{\#}_{SS} - \pi_S E_0(\sigma_S) \leq -\pi_S^2 E_0(\sigma_S) < 0.$$

Similarly,

$$A^{\#}_{00} = \pi_0 \sum_{k=1}^{S} \pi_k E_k(\sigma_0) > 0,$$

and then

$$A^{\#}_{00} \leq \pi_0(1-\pi_0)E_S(\sigma_0), \qquad A^{\#}_{S0} < -\pi_0^2 E_S(\sigma_0) < 0.$$

In particular, all entries of Q are strictly negative, and so the inner product in Theorem 2.8 is strictly negative. This provides an upper bound on the variance. We turn to proving a lower bound.

For $e = (i, i+1)$ or $(i, i-1)$ let $\alpha_e(\eta) = \ln A_e(\eta)$. By [4, Theorem 4], Λ is an increasing and convex function of the variables of $\{\alpha_e\}$, and for $i \neq j$,

$$\frac{\partial \Lambda}{\partial \alpha_e} = \pi_i A_{ij}. \tag{13}$$

Next,

$$\Lambda'(\eta) = \sum_e \frac{\partial \Lambda}{\partial \alpha_e} \frac{d\alpha_e}{d\eta}, \tag{14}$$

and so

$$\Lambda''(\eta) = \sum_{e,e'} \frac{\partial^2 \Lambda}{\partial \alpha_e \partial \alpha_{e'}} \frac{d\alpha_e}{d\eta} \frac{d\alpha_{e'}}{d\eta} + \sum_e \frac{\partial \Lambda}{\partial \alpha_e} \frac{d^2 \alpha_e}{d\eta^2} \geq \sum_e \frac{\partial \Lambda}{\partial \alpha_e} \frac{d^2 \alpha_e}{d\eta^2},$$

where the inequality follows from the above mentioned convexity of Λ. We now compute the right-hand side at $\eta = 0$. We have $\alpha_e'(\eta) = \dfrac{A_e'(\eta)}{A_e(\eta)}$. Therefore

$$\alpha_e''(\eta) = \frac{A_e''(\eta) A_e(\eta) - (A_e'(\eta))^2}{A_e(\eta)^2} = \frac{A_e''(\eta)}{A_e(\eta)} - \alpha_e'(\eta)^2.$$

Letting $\eta = 0$, we obtain

$$\alpha_{i,i+1}'(0) = \frac{\mu}{x}, \qquad \alpha_{i,i-1}'(0) = -\frac{\lambda}{y}.$$

The second derivatives are then given by

$$\alpha_{i,i+1}''(0) = \frac{\mu}{x}\Big(1 - \frac{\mu}{x}\Big), \qquad \alpha_{i,i-1}''(0) = \frac{\lambda}{y}\Big(1 - \frac{\lambda}{y}\Big).$$

Equivalently,

$$\alpha_{i,i+1}''(0) = \frac{\mu\alpha}{(\mu+\alpha)^2}, \qquad \alpha_{i,i-1}''(0) = \frac{\lambda\beta}{(\lambda+\beta)^2}.$$

Using this along with (13) and (14), we obtain

$$\begin{aligned} \Lambda''(0) &\geq \frac{\mu\alpha}{(\mu+\alpha)^2} \sum_{i=0}^{S-1} \pi_i(\alpha+\mu) + \frac{\lambda\beta}{(\lambda+\beta)^2} \sum_{i=1}^{S} \pi_i(\beta+\lambda) \\ &= \frac{\mu\alpha}{\mu+\alpha}(1-\pi_S) + \frac{\lambda\beta}{\lambda+\beta}(1-\pi_0), \end{aligned}$$

completing the proof of Theorem 2.9 □

2.5 Explicit formula for σ^2_{eff} in the case $\rho \neq 1$

In this section we assume $\rho \neq 1$. The case $\rho = 1$ will be dealt with in Section 2.6.1. Recall σ_j from (12). We start with the following technical claim.

Proposition 2.10. *Let $H(\rho) = \pi_0 \pi_S E_0(\sigma_S)$, and write $H(\rho^{-1})$ for $\pi_0 \pi_S E_S(\sigma_0)$. Then*

$$H(\rho) = \frac{(1-\rho)(\rho^S - 1) - S(1-\rho)(1-\rho^{-1})}{(y-x)(1-\rho^{-(S+1)})(1-\rho^{S+1})} = \frac{y^{S+1}(y^S - x^S) - Sx^S y^S (y-x)}{(y^{S+1} - x^{S+1})^2},$$

and a similar expression for $H(\rho^{-1})$ is obtained from the one above by replacing ρ with ρ^{-1} and exchanging between x and y.

The proof of the proposition is a standard "gambler's ruin" routine for the birth-and-death Markov chain Y. For the reader's convenience we provide the proof below.

We are now in a position to state a general explicit formula for σ^2_{eff} in the case $\rho \neq 1$. In virtue of Theorem 2.8, it suffices to compute the matrix Q introduced in its statement. Some examples are discussed in details below, in Subsection 2.6.

Theorem 2.11. *Assume $\rho \neq 1$. Let*

$$\begin{aligned}
\Delta &= H(\rho) - H(\rho^{-1}), \\
\Sigma &= H(\rho) + H(\rho^{-1}), \ \text{and} \\
\kappa &= \frac{1}{\rho^{S+1} - 1} - \frac{1}{\rho^{-(S+1)} - 1}.
\end{aligned}$$

1. *Then*

$$Q = \frac{1}{2} \begin{pmatrix} \rho(\kappa\Delta - \Sigma) & -\kappa\Delta \\ -\kappa\Delta & \rho^{-1}(\kappa\Delta - \Sigma) \end{pmatrix}.$$

2. *Furthermore, we have:*

$$\begin{aligned}
\kappa\Delta &= \frac{(\rho^{-(S+1)} - \rho^{S+1})\left((1-\rho)(\rho^S - 1) + (1-\rho^{-1})(\rho^{-S} - 1) - 2S(1-\rho)(1-\rho^{-1})\right)}{(y-x)(1-\rho^{-(S+1)})^2(1-\rho^{S+1})^2} \\
&= \frac{(y^{S+1} + x^{S+1})^2}{(y^{S+1} - x^{S+1})^2}\Sigma - \frac{2Sx^S y^S (y^{S+1} + x^{S+1})(y-x)}{(y^{S+1} - x^{S+1})^3}.
\end{aligned}$$

and

$$\Sigma = \frac{(1-\rho)(\rho^S - 1) - (1-\rho^{-1})(\rho^{-S} - 1)}{(y-x)(1-\rho^{-(S+1)})(1-\rho^{S+1})} = \frac{y^S - x^S}{y^{S+1} - x^{S+1}}.$$

The second term in the right-hand side of the expression for $\kappa\Delta$ can be rewritten as

$$\frac{2Sx^S y^S (y^{S+1} + x^{S+1})(y-x)}{(y^{S+1} - x^{S+1})^3} = \frac{(y^{S+1} + x^{S+1})^2}{(y^{S+1} - x^{S+1})^2} \underbrace{\frac{2Sx^S y^S (y-x)}{(y^{S+1} + x^{S+1})(y^S - x^S)}}_{(*)} \Sigma.$$

Since all entries of Q are strictly negative, $(*) > 1$. This can be diriectly verified by using the identity $y^S - x^S = (y-x)\sum_{k=0}^{S-1} y^k x^{S-1-k}$.

Proof of Proposition 2.10. Let $L_i = E_i(\sigma_S)$. Then $L_i = \sum_{k=i}^{S-1} J_k$, where $J_k = E_k(\sigma_{k+1})$. By conditioning on the time of the first jump from i, we observe that

$$J_i = E_i\big(\min\{\sigma_{i-1}, \sigma_{i+1}\}\big) + P(\sigma_{i-1} < \sigma_{i+1})(J_{i-1} + J_i),$$

where $\min\{\sigma_{i-1}, \sigma_{i+1}\}$ is the jump time from i. The rate to the right is $x = \alpha + \mu$ whereas the rate to the left is $y = \beta + \lambda$. Hence,

$$J_i = \frac{1}{x+y} + \frac{y}{x+y}(J_{i-1} + J_i),$$

which yields $J_i = \frac{1}{x} + \rho J_{i-1}$. Since $J_i < \infty$ with probability one,

$$J_i = x^{-1}(1 + \cdots + \rho^i) = \frac{\rho^{i+1} - 1}{x(\rho - 1)}.$$

Thus,

$$E_0(\sigma_S) = \frac{1}{x(\rho-1)} \sum_{j=0}^{S-1} (\rho^{j+1} - 1) = \frac{1}{x(\rho-1)}\Big(\rho\frac{\rho^S - 1}{\rho - 1} - S\Big) = \frac{1}{y-x}\Big(\frac{\rho^S - 1}{1-\rho^{-1}} - S\Big).$$

In virtue of (3),

$$\pi_0 = \frac{1-\rho^{-1}}{1-\rho^{-(S+1)}}, \qquad \pi_S = \frac{1-\rho}{1-\rho^{S+1}},$$

completing the proof of Proposition 2.10. $\square$

Proof of Theorem 2.11. We have

$$\begin{aligned} A^{\#}_{SS} &= \pi_S \sum_{j=0}^{S-1} \pi_j E_j(\sigma_S) = \pi_0 \pi_S \sum_{j=0}^{S-1} \rho^{-j} \sum_{k=j}^{S-1} J_k = \pi_0\pi_S \sum_{k=0}^{S-1}\sum_{j=0}^{k} \rho^{-j} J_k \\ &= \frac{\pi_0\pi_S}{x(\rho-1)(\rho^{-1}-1)} \sum_{k=0}^{S-1} (\rho^{-(k+1)} - 1)(\rho^{k+1} - 1) = \frac{\Delta}{1-\rho^{-1}}. \end{aligned}$$

Similarly, $A^{\#}_{00} = \frac{-\Delta}{1-\rho} = \frac{\Delta}{\rho - 1}$. Therefore,

$$Q_{01} = Q_{10} = -\frac{1}{2}(\rho\pi_0 A^{\#}_{00} + \rho^{-1}\pi_S A^{\#}_{SS}) = -\frac{1}{2}\kappa\Delta.$$

Finally, by the detailed balance condition (3), $\pi_i A_{ij} = \pi_j A_{ji}$. That is, A is self-adjoint with respect to the reference measure π. By the spectral theorem (or a direct computation), $A^{\#}$ is also self adjoint with respect to π. In particular, $\pi_0 A^{\#}_{0S} = \pi_S A^{\#}_{S0}$. We have

$$\pi_0 A^{\#}_{0S} = \pi_0\big[A^{\#}_{SS} - \pi_S E_0(\sigma_S)\big], \ \pi_S A^{\#}_{S0} = \pi_S\big[A^{\#}_{00} - \pi_0 E_S(\sigma_0)\big].$$

But

$$\pi_0 A^{\#}_{0S} = \frac{\pi_0\Delta}{1-\rho^{-1}} - H(\rho) \qquad \text{and} \qquad \pi_S A^{\#}_{S0} = \frac{\pi_S\Delta}{\rho - 1} - H(\rho^{-1}).$$

Thus,

$$\pi_0 A^{\#}_{0S} = \pi_S A^{\#}_{S0} = \frac{1}{2}(\kappa\Delta - \Sigma),$$

completing the proof of Theorem 2.11. $\square$

2.6 Examples

In this section, we provide three examples showcasing the general computations for variance presented in this paper.

2.6.1 The case $\rho = 1$

Here $\pi_j = \dfrac{1}{S+1}$, and hence

$$\Lambda'(0) = (\mu - \lambda)\frac{S}{S+1}.$$

Let J_k be defined as in the proof of Proposition 2.10. Then similar first-step decomposition arguments show that $J_k = \frac{1}{x}(1+k)$. Therefore,

$$\pi_0 E_S(\sigma_0) = \pi_S E_0(\sigma_S) = \frac{1}{x(S+1)}(1+2+\cdots+S) = \frac{S}{2x}.$$

We also have

$$A^{\#}_{SS} \;=\; \pi_S\pi_0\sum_{k=0}^{S-1}\sum_{j=0}^{k} J_k = \frac{1}{x(S+1)}\sum_{k=0}^{S-1}(1+k)^2 = \frac{S(2S+1)}{6x(S+1)}.$$

Therefore,

$$\pi_0 A^{\#}_{00} = \pi_0 A^{\#}_{SS} = \frac{S(2S+1)}{6x(S+1)^2}$$

and

$$\pi_0 A^{\#}_{0S} \;=\; \frac{1}{x(S+1)}\Big[\frac{S(2S+1)}{6(S+1)} - \frac{S}{2}\Big] = -\frac{S(S+2)}{6x(S+1)^2}.$$

Thus

$$Q = -\frac{S}{6x(S+1)^2}\begin{pmatrix} S+2 & 2S+1 \\ 2S+1 & S+2 \end{pmatrix}.$$

Summarizing the above computation, we obtain

$$\Lambda''(0) = (\lambda+\mu)\frac{S}{S+1}\Big[1 - \frac{1}{3x(S+1)}\Big((S+2)(\lambda+\mu) + 2(S-1)\frac{\mu\lambda}{\mu+\lambda}\Big)\Big]. \qquad (15)$$

To get a lower bound, observe that

$$\begin{aligned}(S+2)(\mu+\lambda) + 2(S-1)\frac{\mu\lambda}{\mu+\lambda} &\le (S+2)2x - (S+2)(\alpha+\beta) + (S-1)(x-\alpha) \\ &= 3(S+1)x - (S+2)(\alpha+\beta) - (S-1)\alpha.\end{aligned}$$

Therefore

$$\Lambda''(0) \geq (\lambda+\mu)\frac{S}{S+1}\frac{(S+2)(\alpha+\beta)+(S-1)\alpha}{3x(S+1)}.$$

The same argument then shows that

$$\Lambda''(0) \geq (\lambda+\mu)\frac{S}{S+1}\frac{(S+2)(\alpha+\beta)+\frac{1}{2}(S-1)(\alpha+\beta)}{3x(S+1)} = \frac{S}{S+1}\frac{(\lambda+\mu)(\alpha+\beta)}{2x}.$$

The equality holds if and only if $\lambda=\mu$, in which case

$$\Lambda''(0) = \frac{S}{S+1}\frac{2\mu\alpha}{\alpha+\mu}.$$

In particular, for the fully symmetric case $\alpha=\beta=\lambda=\mu$, we obtain $\Lambda''(0)=\frac{S}{S+1}\mu$.

2.6.2 The case $S=1$

Here $\pi_1 = \frac{1}{1+\rho} = \frac{x}{x+y}$ and then $\pi_0 = \frac{y}{x+y}$. We have

$$\Lambda'(0) = \frac{\mu y - \lambda x}{x+y}.$$

Now, $E_0(\sigma_1)=\frac{1}{x}$ and hence $A^{\#}_{11} = \frac{\pi_0\pi_1}{x} = \frac{y}{(x+y)^2}$ and $A^{\#}_{00} = \frac{x}{(x+y)^2}$. Since $A^{\#}$ has zero row sum, it follows that

$$A^{\#} = \frac{1}{(x+y)^2}\begin{pmatrix} x & -x \\ -y & y \end{pmatrix}.$$

Hence $\pi_1 A^{\#}_{11} = \frac{xy}{(x+y)^3}$ and $\pi_1 A^{\#}_{10} = -\frac{xy}{(x+y)^3}$.

Similarly, $\pi_0 A^{\#}_{00} = \frac{xy}{(x+y)^3}$ and $\pi_0 A^{\#}_{01} = -\frac{xy}{(x+y)^3}$. Thus, recalling that $\rho=\frac{y}{x}$,

$$Q = -\frac{1}{(x+y)^3}\begin{pmatrix} y^2 & \frac{1}{2}(x^2+y^2) \\ \frac{1}{2}(x^2+y^2) & x^2 \end{pmatrix}.$$

Summarizing, we obtain

$$\Lambda''(0) = \frac{\mu y + \lambda x}{x+y} - \frac{2}{(x+y)^3}\left[(\mu y + x\lambda)^2 + (x-y)^2\lambda\mu\right].$$

The positivity of $\Lambda''(0)$ can be seen directly by writing

$$\lim_{S\to\infty}\Lambda''(0) = \frac{\mu y+\lambda x}{x+y}\Big(1 - 2\Big[\frac{\mu y+\lambda x}{(x+y)^2} + \frac{(x-y)^2\mu\lambda}{(x+y)^2(\mu y+\lambda x)}\Big]\Big),$$

and using the inequalities $\mu < \alpha+\mu = x$, $\lambda < \beta+\lambda = y$.

2.6.3 Limiting behavior as $S \to \infty$ when $\rho \geq 1$

We take $S \to \infty$ while fixing the other parameters of the model. We have $\lim_{S\to\infty} \pi_S = 0$ and $\lim_{S\to\infty} \pi_0 = 1 - \rho^{-1} = \frac{y-x}{y}$. Thus,

$$\lim_{S\to\infty} \Lambda'(0) = \mu - \lambda\rho^{-1} = \mu - \lambda\frac{\alpha+\mu}{\beta+\lambda}.$$

This means that there is no mechanical constraint to move to the right, but moving to the left is possible only a proportion of ρ^{-1} of the time, which is equal to the asymptotic proportion of the time the birth and death process Y is not at 0. To compute $\lim_{S\to\infty} \Lambda''(0)$, we need to separate the case $\rho = 1$ from $\rho > 1$. In the former case, (15) yields

$$\lim_{S\to\infty} \Lambda''(0) = \mu + \lambda - \frac{\mu^2 + \lambda^2 + 4\lambda\mu}{3(\lambda+\beta)}.$$

When $\rho > 1$, we first compute the matrix Q, using the formulas provided by Theorem 2.11. We have

$$\kappa\Delta = \Sigma = \frac{1-\rho^{-1}}{y-x} = \frac{1}{y}.$$

Therefore,

$$Q = -\frac{1}{2y}\begin{pmatrix} 0 & -1 \\ -1 & 0 \end{pmatrix}.$$

It follows that

$$\lim_{S\to\infty} \Lambda''(0) = \mu + \lambda\rho^{-1} - \frac{\lambda\mu}{y} = \mu + \lambda\frac{\alpha}{\lambda+\beta}.$$

Using the fact that for fixed $t > 0$ and $i \in \mathbb{N}$ we have $P_i(\sigma_S > t) \to_{S\to\infty} 0$, one can show that $\left(X^{(1)}(t), X^{(2)}(t)\right)_{t\geq 0}$ converges weakly to the process with $S = \infty$. It is not hard to verify, but is outside the scope of this paper, that the limiting values (as $S \to \infty$) of $\Lambda'(0)$ and $\Lambda''(0)$ represent the asymptotic (as $t \to \infty$) speed and variance of the limiting process.

Acknowledgement

We would like to thank three anonymous referees for their comments and suggestions which allowed us to considerably improve the presentation of the paper.

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