Diffusion Ratchets and the Modeling of Bio-molecular Motors

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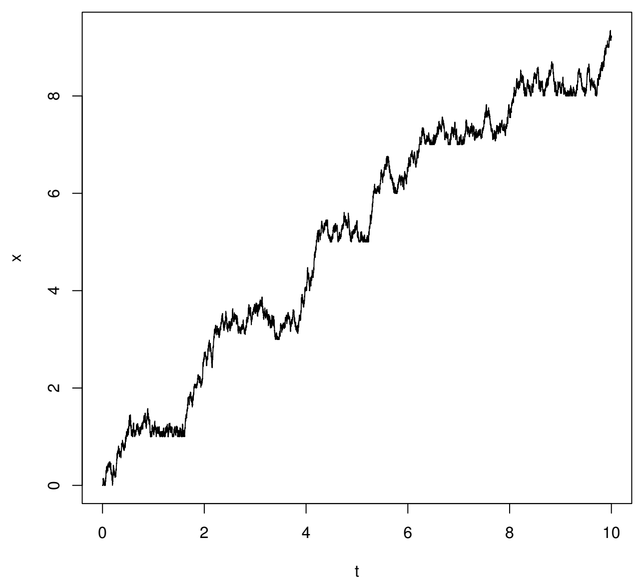
1 Introduction

Bio-molecular motors are proteins, or structures consisting of multiple proteins, that play a central role in accomplishing mechanical work in the interior of a cell. Frequently, the exact nature of the chemical-mechanical energy conversion is not completely understood. However, recent advances in microbiological techniques have enabled *in vitro* observations of molecular motors and/or their cargos which in turn have led to significant research in the mathematical modeling of these motors in the hope of shedding light on the underlying mechanisms involved in intracellular transport. One commonly studied model for the dynamics of a molecular motor is the *Brownian Ratchet* model. In a Brownian ratchet, a particle representing the biological motor diffuses between equally spaced barriers. When the particle encounters the barrier from the left it is free to pass through, however, it is instantaneously reflected back when it encounters the barrier from the right. Hence, the ratchet mechanism has the effect of introducing a positive drift to the dynamics of the particle. In practice, one is interested in gaining information about asymptotic velocity of the motor, first passage times, locations and distances between barrier sites, parameters of the governing diffusion, etc. The goal of this thesis is to address such questions for a motor moving according to a Brownian ratchet mechanism, using the theory of reflected diffusion processes. A sample path of a Brownian ratchet process with a drift coefficient 0 and diffusion coefficient 1, with barriers which are unit distance apart, starting at 0, is given below.



In the general theory that we will develop, the drift and diffusion coefficients may be state dependent, namely between the barriers the process will evolve according to a diffusion process. In order to distinguish from the constant drift and diffusion coefficient case, we will refer to the above mechanism as a *Diffusion Ratchet*.

We will begin by rigorously defining a diffusion ratchet as a $C([0,\infty) : I\!\!R_+)$ (the space of continuous functions from $[0,\infty)$ to $I\!\!R_+$) valued stochastic process. The process is described via a system of stochastic differential equations with reflection (See Definition 2.2). In order to justify the name *Diffusion Ratchet* for the constructed process, denoted hereafter by $X(\cdot)$, we begin by considering the discrete analog of a diffusion ratchet mechanism. Namely, we consider a particle moving on a discrete lattice in $I\!\!R_+$ which is free to move to the left or right when it is on a non-barrier site; however, it cannot move to the left (or does so with a "negligible" probability) when it is on a ratchet site. We will show that, after suitable scaling of time and space, the Markov chain described by the particle dynamics converges weakly in $D([0,\infty) : I\!\!R_+)$ (the space of functions from $[0,\infty)$ to $I\!\!R_+$ which are right continuous and have left limits with the usual Skorokhod topology) to $X(\cdot)$.

A primary focus of this work will be the velocity of the motor, an important biological feature of the system being modeled. Specifically, we will concentrate on asymptotic velocity which is defined to be $\lim_{t\to\infty} \frac{X(t)}{t}$. We will show that such a limit exists almost surely. In the case where the drift and diffusion coefficients are constant we will obtain an explicit expression for the limit. For the general case, we will explore various numerical methods for calculating the asymptotic velocity. We will study fluctuations from the asymptotic velocity for large values of t by establishing a central limit theorem. Future work will focus on a more detailed study of deviations from the nominal velocity via large deviations. In our future work, we will also study the estimation of various parameters of interest.

Motor pulling a cargo. Frequently, biological motors are responsible for intracellular transport of cargos, such as large protein molecules, to places in the cell where they are needed. Unlike the ratchet process which represents the motor, the process representing the cargo has no reflecting barriers since it is floating relatively freely in the cell, attached to the motor via a protein strand. However, there is interaction between the two processes. The more distant the motor and cargo the greater the forward drift for the cargo and the greater the backward drift of the motor. In our future work we will study the dynamics of the pair of stochastic processes : (motor, cargo) $\equiv (X(\cdot), Y(\cdot))$. In this case the study of quantities such as asymptotic velocities is much more challenging; indeed, it is not even clear that $\frac{X(t)}{t}$ converges almost surely as $t \to \infty$. One of the goals of the proposed research is to study the asymptotic velocity of the motor in presence of a cargo. Our first step will be to rigorously obtain the stochastic dynamical system described by the pair. Our approach will be similar to that in the cargo-less case; we will first introduce a natural discrete state Markov process which captures the desired interaction between the cargo and the motor and then take the (weak) limit with an appropriate scaling of time and space. The next step will be to prove the existence of an almost sure limit of $\frac{X(t)}{t}$ as $t \to \infty$. Once more, we will study deviations from the mean value through central limit theorems and large deviations. We will also develop numerical methods for calculating asymptotic velocity and related quantities of interest for this two-dimensional problem.

Motor Observability and Filtering Problems. One major difficulty in the study of intracellular transport mechanisms is that the biological motors frequently are too small to be observed. However, these motors are often pulling cargos which are significantly larger than the motor and technical advances have allowed observations of cargos pulled by the unobservable bio-molecular motors. A natural question that arises which will be explored in our proposed work is the following: Can one gain information on the motor dynamics by observing the cargo dynamics using techniques of nonlinear filtering theory? The quantities of interest include parameters of the diffusion model, location of ratchet sites, current location of the motor, etc. In the proposed work, we will study these parameter estimation and filtering questions and validate the results using simulated and real data.

Fast Motor Limit. Since frequently the biological motors are significantly smaller than their cargos, one can approximate the stochastic dynamical system of the pair by a single averaged equation. The study of asymptotic velocity of the averaged system is comparatively simpler than the original coupled system. In our study, we will establish such a stochastic averaging result and study the asymptotic velocity of the averaged system via analytic and numerical methods.

The proposal is organized as follows. In Section 1.1 we give a short introduction to bio-molecular motors. Section 1.2 contains some mathematical preliminaries, largely focused on reflected diffusion processes. In Section 2 we introduce the diffusion ratchet model. We give a precise definition of the process using the theory of reflected diffusions. We also prove the weak convergence of a suitably scaled Markov chain to the diffusion ratchet. In Section 2.1 we study the asymptotic velocity of a motor moving according to a ratchet mechanism. Section 2.2. develops some numerical methods for computing the asymptotic velocity. Finally, in Section 3 we outline the proposed future work.

1.1 Biomolecular Motors

The interior of a cell is a busy place. "Instructions" from DNA need to be extracted and distributed to the organelles that build proteins. Proteins then need to be transported to where they are needed. Cells must convert chemical energy to mechanical energy to accomplish these and other tasks. Bio-molecular motors are one part of the picture. These bio-molecular motors are proteins and accomplish a great deal of the mechanical work of the cell. Frequently, the exact mechanism of the chemical-mechanical energy conversion is not completely understood. It is hoped that mathematical models may help resolve competing explanations of these mechanisms.

An important aspect of recent research has been the observability of the motors as they function in the cell. This is being done through new methods such as laser traps which allow manipulation and observation of the motors (or objects attached to the motors). Laser traps also allow a constant (or near constant) load to be applied to the motor. Improved light microscopy has also played an important role in being able to observe cell activity. These advances in the observation capabilities have provided an impetus to research in the mathematical modeling for the dynamics of molecular motors.

Kinesin is perhaps the prime example of the type of motor that will be studied in this thesis. Kinesin moves along microtubules that are spread throughout the cell. On one end of the motor, there are twin heads that move step by step on the microtubule. The other end consists of a long amino acid chain which attaches itself to cargo that must be transported. The motion is linked to the presence of a chemical–ATP, but it is not clearly understood how the ATP is involved in motion. Moreover, even the size of each step is difficult to determine, and the way in which the motor interacts with the microtubule is not completely known. Since there is a stepping motion of the heads, point processes have been used to model the behavior of Kinesin [13]. An alternative model views one physical step of the motor as an end result of several chemical steps and transitions between these steps are modeled via a Markov chain [18]. In the present work, we will primarily focus on yet another commonly used model to describe the behavior of Kinesin, namely the Brownian ratchet model [6]. In this model, the physical steps correspond to the location of the barriers of the ratchet.

There are many other types of motors; some of which are modeled by a Brownian ratchet. Many of these are linear motors similar to Kinesin moving along some sort of "track" . An important example is RNA polymerase which moves along a DNA molecule during transcription facilitating the transfer of "information" from the DNA to other parts of the cell [19].

Another example is Myosin, a larger cousin of Kinesin which is found in muscle cells. Myosin slides along actin filaments to perform microscopic tasks similar to Kinesin. By changing the shape of individual cells, Myosin is the muscle's source of contraction and expansion when taken aggregately [3] .

A polymerization ratchet illustrates one of the appeals of a Brownian ratchet model. A cargo, such as a protein, sits on the tip of a polymer chain. Since the protein is being bombarded by smaller particles, such as water molecules, it diffuses, moving slightly away and back to the tip of the chain. When the protein moves far enough from the tip of the chain for another monomer to attach itself, then the protein has been permanently displaced the length of one monomer. The benefit to the cell is obvious. The cell has captured energy that is inherent to its environment while applying a rather small amount of energy itself (only the energy required to bond the monomer). So, the Brownian Ratchet conforms to a guiding principle of Biology which is that evolution has produced highly efficient mechanisms for using energy [14] .

The rotary motor which drives the flagella of the *e. coli* bacteria is still another prominent example [6]. This motor uses an ion stream (produced by the difference in electrical charge from one side of a membrane to another) to produce a rotary action. The Brownian ratchet model for the motor with an elastic linkage to the cargo is one possible explanation for the relatively tiny motors's ability to spin the relatively large flagella.

1.2 Mathematical Preliminaries

The central mathematical element in this project is the theory of reflected diffusion processes. The ratchet process that will be developed behaves as a reflected diffusion after it has passed one barrier but has yet to reach the next. For this reason much of the analysis of the behavior of the ratchet process can be reduced to that of reflected diffusions. The study of reflected processes traces its origin to a paper by Skorokhod in 1961 [15]. The question asked by Skorokhod in this paper is the following: is there a $C([0,\infty) : I\!R_+)$ valued stochastic process which evolves according to a stochastic differential equation (SDE)

$$dX(t) = b(X(t), t)dt + a(X(t), t)dW_t,$$

when $X(t)$ is in $(0, \infty)$ and is instantaneously reflected back when it is about to exit $[0, \infty)$? Here a and b are functions from $I\!R_+ \times I\!R_+ \to I\!R$ satisfying the usual Lipschitz and growth conditions. This work led to the formulation of what is now called the Skorokhod Problem which is defined as follows.

For a Polish space S, denote by $D([0,\infty) : S)$ the space of functions from $[0, \infty)$ to S which are right continuous and have left limits. This space will be endowed with the usual Skorokhod topology. If $S = I\!R$, we will sometime write the above space as $D[0, \infty)$.

Definition 1.1 (The Skorodhod problem in 1-D) *Let $x(\cdot) \in D([0,\infty) : I\!R)$. We say that a pair of trajectories $z(\cdot), l(\cdot) \in D([0,\infty) : I\!R_+)$ solve the Skorokhod Problem for $x(\cdot)$ if*
1. $z(t) = x(t) + l(t)$ for all $t \in [0, \infty)$.
2. $l(0) = 0$.
3. $l(t)$ is increasing, and $l(t)$ increases only when $z(t) = 0$, i.e

$$l(t) = \int_{[0,t]} 1_{\{z(s)=0\}} dl(s).$$

It is easy to see that one solution of the Skorokhod problem posed by $x(\cdot)$ is given by $l(t) \doteq -0 \wedge \inf_{0\le s\le t} x(s) \ = 0 \vee \sup_{0\le s\le t} x(s)^-$ and $z(t) \doteq x(t) + l(t)$. In fact, one can show that the above pair is the unique solution of the Skorokhod problem posed by $x(\cdot)$ [7]. In view of this uniqueness property one can define the Skorokhod map:

$$\Gamma : D([0,\infty) : I\!R) \to D([0,\infty) : I\!R_+)$$

as $\Gamma(x(\cdot)) = z(\cdot)$, where $(z(\cdot), z(\cdot) - x(\cdot))$ is the unique solution of Skorokhod problem posed by $x(\cdot)$. We refer to $z(\cdot)$ as the constrained or relected version of $x(\cdot)$.

The extension of Skorokhod problem to higher dimensions has been studied by various authors (cf. [4], [1], [8], [17], and [20]). In higher dimensions, the shape of the region to which the process is constrained could be quite complicated. Also, the direction of the reflection back into the region is something that must be defined. It is often taken to be the inward normal to the boundary, but it may be defined differently. These differing directions of reflection emerge naturally from applications. There are a number of general results in this area that allow one to say which types of regions and directions of reflections lead to a unique solution to the Skorokhod problem. See [4], [12], [8].

In the next section we will rigorously define a diffusion ratchet using the theory of reflected stochastic differential equations(RSDE) (See Definition 2.2). In doing so, the following existence and uniqueness result will be crucially used. For the rest of this proposal $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}, P)$ will denote a filtered probability space satisfying the usual hypothesis.

Theorem 1.2 (Existence and Uniqueness of the Skorokhod problem in 1-D) *Let $b(\cdot), a(\cdot)$ be Lipschitz continuous, i.e. there exists K such that*

$$|b(x) - b(y)| + |a(x) - a(y)| \le K|x - y| \quad x, y \in \mathbb{R}_+. \tag{1}$$

Let $W(\cdot)$ be a standard Wiener martingale on some filtered probability space $(\Omega, \mathcal{F}, P, \{\mathcal{F}_t\})$. Then for every $x \in \mathbb{R}_+$, there exists a unique, continuous, $\mathcal{F}_t$ adapted process $X(\cdot)$ such that

$$\int_0^T (|b(X(s))| + a^2(X(s)))ds < \infty, \text{ a.e. } \forall\, T > 0$$

and the following integral equation holds.

$$X(t) = \Gamma\Big(x + \int_0^{\cdot} b(X(s))ds + \int_0^{\cdot} a(X(s))dW(s)\Big)(t). \tag{2}$$

Moreover, the following representation for $X(\cdot)$ holds.

$$X(t) = x + \int_0^t b(X(s))ds + \int_0^t a(X(s))dW(s) + l(t) \tag{3}$$

where

$$l(t) = -0 \wedge \inf_{0\le s\le t} \Big(x + \int_0^s b(X(u))du + \int_0^s a(X(u))dW(u)\Big). \tag{4}$$

For the proof of the above result we refer the reader to [4] where a much more general case is treated. The above RSDE will play a central role in our definition of the diffusion ratchet. Roughly speaking, a diffusion ratchet will be obtained by pasting together a sequence $\{X^{(i)}(\cdot)\}$ of reflected diffusion processes, where the i-th process has the reflection barrier at iL instead of 0 and its initial condition is $X^{(i)}(0) = iL$, where L denotes the distance between ratchet sites. As outlined in the introduction, we will justify the name *diffusion ratchet* for the constructed process by showing that this process arises as the weak limit, of a natural discrete time analog of the ratchet mechanism, with a suitable scaling of time and space. One of the key ingredients to the proof of this weak convergence result is the following Aldous-Kurtz criterion for tightness of processes with paths in $D[0,\infty)$. For a proof we refer the reader to Billingsley [2].

Theorem 1.3 (Aldous -Kurtz Tightness Criterion) *Let Λ be an index set. Consider a collection of processes $\{x^\gamma, \gamma \in \Lambda\}$ defined on suitable probability spaces $(\Omega^\gamma, \mathcal{F}^\gamma, P^\gamma)$ and taking values in $D[0,\infty)$. Assume that for each rational $t \in [0,\infty)$ and $\delta > 0$ there exists a compact set $K_{t,\delta} \subset \mathbb{R}$ such that $\sup_{\gamma\in\Gamma} P^\gamma\{x^\gamma(t) \in K_{t,\delta}\} \le \delta$. Define $\mathcal{F}_t^\gamma$ to be the σ-algebra generated by $\{x_s^\gamma, s \le t\}$. Let $\mathcal{T}_T^\gamma$ be the set of $\mathcal{F}_t^\gamma$-stopping times which are less than or equal to T with probability one, and assume for each $T \in [0,\infty)$*

$$\lim_{\delta\to 0} \sup_{\gamma\in\Gamma} \sup_{\tau\in\mathcal{T}_T^\gamma} E^\gamma(1 \wedge |x^\gamma(\tau+\delta) - x^\gamma(\tau)|) = 0. \tag{5}$$

Then $\{x^\gamma, \gamma \in \Gamma\}$ is tight.

Another key step in our proof of the weak convergence result is to split up the rescaled discrete time process into a sum of two processes, one of which will converge to a process which is absolutely continuous to Lebesgue measure and another which converges to an Itô integral. In proving the second convergence we will need the following well known characterization of the Wiener Process [10].

Theorem 1.4 (A Characterization of Wiener Process) *For $f \in C_0^2(\mathbb{R})$ and continuous, $\mathcal{F}_t$-adapted process $W(t)$ define*

$$M_f(t) = f(W(t)) - f(0) - \int_0^t \frac{\partial^2 f}{\partial x^2}(W(s))ds. \tag{6}$$

W(t) is a Wiener process if and only if $M_f(t)$ is a $\mathcal{F}_t$ local martingale.

As stated earlier in the introduction, one of the prime objects of interest is the asymptotic velocity of the motor. Intuitively, asymptotic velocity is closely connected to the amount of time a process takes to travel a given distance. Thus, it becomes important to study the time the process takes to travel from one barrier to the next. In the following theorem, we show that for this random time all moments are finite.

Theorem 1.5 *Let $X^x(t)$ be the process obtained as the unique solution of (2). Further, suppose that the diffusion coefficient is uniformly non-degenerate, i.e. $\inf_{x\in\mathbb{R}_+} |a(x)| \ge m > 0$. Let $L \in (0,\infty)$ and define*

$$\tau^x \doteq \inf\{t : X^x(t) \notin [0, L)\}. \tag{7}$$

Then there exists an $\epsilon > 0$ such that $Ee^{\tau^x u} < \infty$ for all $-\epsilon < u < \epsilon$.

In order to prove the theorem, we begin with the following lemma.

Lemma 1.6

$$\sup_{x\in[0,L]} P[\tau^x > 1] < 1 \tag{8}$$

Proof. We will argue by contradiction. Suppose that

$$\sup_{x\in[0,L]} P[\tau^x > 1] = 1. \tag{9}$$

Then, there is a sequence $\{x_n\} \in [0,L]$ such that $P[\tau^{x_n} > 1] \to 1$. Since $[0,L]$ is in a compact set, there is a convergent subsequence $\{x'_n\}$ which converges to some $x \in [0,L]$. We know that $P[\tau^{x'_n} > 1] \to 1$. Now, if $P[\tau^y > 1]$ is a continuous function in y, then $P[\tau^{x'_n} > 1] \to P[\tau^x > 1]$ which implies that $P[\tau^x > 1] = 1$. This in particular says that $P(X^x(\frac{1}{2}) \in [0,L]) = 1$ which is clearly impossible in view of the uniform non-degeneracy of the diffusion coefficient. Thus we have a contradiction, which proves (8). Therefore it suffices to show that $P[\tau^y > 1]$ is a continuous function of y. Note that $P[\tau^y > 1] = P(Z(y) \geq L)$, where $Z(y) \doteq \sup_{0\leq s\leq 1} X^y(s)$. Note that $Z(y_n) \to Z(y)$ in probability as $y_n \to y$. Finally, observing that the distribution of $Z(y)$ is absolutely continuous with respect to the Lebesgue measure on $[0,\infty)$, we have that $P(Z(y_n) \geq L) \to P(Z(y) \geq L)$ as $y_n \to y$. This proves that $P[\tau^y > 1]$ is a continuous function of y. ■

Proof of Theorem 1.5. Let $\alpha \doteq \sup_{x\in[0,L]} P[\tau^x > 1]$. From Lemma 1.6 we have that $\alpha \in (0,1)$. Now, fix $x \in [0,L]$ and suppress it from the notation.

$$\begin{aligned} P[\tau > n] &= E\Big(I_{[\tau>n]} I_{[\tau>n-1]}\Big) \\ &= E\Big(E[I_{[\tau>n]}|\mathcal{F}_{n-1}] I_{[\tau>n-1]}\Big) \\ &\leq \alpha P[\tau > n-1] \end{aligned}$$

By induction, $P[\tau > n] \leq \alpha^n$. Now we consider the the Laplace transform, $Ee^{\tau u}$. Clearly it is finite for $u \leq 0$. So without loss of generality consider $u \geq 0$. Then

$$\begin{aligned}
\int_0^\infty e^{\tau u} dP &= \int_0^\infty P[e^{\tau u} > s] ds \\
&= \int_0^\infty P[\tau > \frac{ln(s)}{u}] ds \\
&= u \int_0^\infty P[\tau > v] e^{uv} dv \\
&\leq u \sum_{k=0}^\infty P[\tau > k] e^{u(k+1)} \\
&\leq u \sum_{k=0}^\infty \alpha^k e^{u(k+1)} \\
&= ue + ue^u \sum_{k=1}^\infty (\alpha e^u)^k
\end{aligned}$$

The series in the last expression on the right will converge if $\alpha e^u < 1$, i.e. $u < -ln(\alpha)$. Since $\alpha < 1$ this last quantity is greater than zero. Thus the result follows on taking $\epsilon = -ln(\alpha)$. ■

2 Diffusion Ratchet.

In this section, we begin by defining a discrete state space model for the biological motor. Then, we will define the ratchet process using a countable sequence of reflecting diffusion processes, where the i-th process, $X^{(i)}(\cdot)$, in the sequence is a reflected diffusion with the reflecting barrier and initial condition as iL. Denote by $\tau^{(i)}$ the first time the i-th process hits $(i+1)L$. The diffusion ratchet will be a $C([0,\infty):\mathbb{R}_+)$ valued process constructed by patching together the paths of $\{X^{(i)}(t) : 0 \le t \le \tau^{(i)}\}_{n\ge 1}$. Then we will show that on each of the intervals $[iL,(i+1)L)$ the discrete space model converges weakly to the i-th reflected diffusion process. Finally we will show that the mapping from the countable number of processes to the single "patched up" process is continuous, and thus show that the discrete space model converges to the diffusion ratchet.

Discrete space-time model. We consider a particle, representing a biological motor moving on a track positioned along the X-axis. Ratchet sites are located on the track at equally spaced intervals of length L which, without loss of generality, is taken to be a positive integer. When the particle is at a "non-ratchet" site it can either move to the left or to the right. However, when the particle is at a ratchet site, it can move only to the right. First we need to define a lattice on which the discrete space model will be defined. Let $\mathbb{N}' = \{n \in \mathbb{R} : n = \frac{m}{L}, m \in \mathbb{N}\}$. We assume that the particle takes steps of size $1/n$ for $n \in \mathbb{N}'$ and thus the state space of the particle position is $S_n \doteq \{\frac{j}{n}; j \in \mathbb{N}_0\}$. This definition ensures that the ratchet sites are on the lattice.

The precise dynamics of the particle can be described as follows. Let $X_n(t)$ denote the position of the particle at time t. Given that $X_n(t) = x$, the waiting time to the next jump has an exponential distribution with rate $\lambda_n(x)$. If $x = iL$ for some $i \in \mathbb{N}_0$, then the particle moves to the site on the right (i.e. $x + \frac{L}{n}$) with probability $p_n(x)$ and remains on the original site with probability $(1 - p_n(x))$. On the other hand, if $x \in S_n \setminus \{iL; i \in \mathbb{N}_0\}$, the particle moves to the right with probability $p_n(x)$ and to the site on the left with probability $(1 - p_n(x))$. We assume that the rate of jump to the right:

$$\lambda_n(x)p_n(x) = n^2\left(\alpha(x) + \frac{b_1(x)}{n}\right) \tag{10}$$

where as the rate of jump to the left (or at ratchet site: rate of remaining at the original site) is

$$\lambda_n(x)(1 - p_n(x)) = n^2\left(\alpha(x) + \frac{b_2(x)}{n}\right) \tag{11}$$

Thus

$$\lambda_n(x) = n^2\left(2\alpha(x) + \frac{b_1(x) + b_2(x)}{n}\right) \tag{12}$$

and

$$p_n(x) = \frac{n\alpha(x) + b_1(x)}{2n\alpha(x) + b_1(x) + b_2(x)} \tag{13}$$

We next introduce the diffusion ratchet process $X(t)$, which is a stochastic process with continuous sample paths given as follows. Roughly speaking, $X(\cdot)$ behaves like a reflecting diffusion when it lies in the interval $[iL, (i+1)L)$; $i \in I\!N_0$, with iL acting as the reflecting barrier. More precisely, let $\{W^{(i)}(t)\}_{0\le t<\infty}$ be a sequence of independent standard Brownian motions given on some probability space $(\Omega, \mathcal{F}, P)$. Denote by $\mathcal{D}_i$ the subset of $\mathcal{D}([0,\infty) : I\!R)$ defined as

$$\mathcal{D}_i \doteq \{x \in \mathcal{D}([0,\infty) : I\!R) | x(0) = iL\}.$$

Also, let

$$\hat{\mathcal{D}}_i \doteq \{x \in \mathcal{D}\big([0,\infty) : [iL,\infty)\big) | x(0) = iL\}.$$

Let $\Gamma_i : \mathcal{D}_i \to \hat{\mathcal{D}}_i$ be the Skorokhod map defined as:

$$\Gamma_i(x)(t) \doteq x(t) - \inf_{0\le s\le t} \big(x(s) - iL\big). \tag{14}$$

Let $X^{(i)}(\cdot)$ be the unique strong solution of the integral equation:

$$X^{(i)}(t) = \Gamma_i\left(iL + \int_0^{\cdot} b(X^{(i)}(s))ds + \int_0^{\cdot} a(X^{(i)}(s))dW^{(i)}(s)\right)(t),\ t \in (0,\infty), \tag{15}$$

where in addition to the Lipschitz condition (1) on the coefficients, we assume that there exist b^*, a_* and a^* in $I\!R$ such that

$$|b(\cdot)| \le b^* \text{ and } 0 < a_* \le a(\cdot) \le a^*. \tag{16}$$

Next, for $i \in I\!N_0$, define stopping times $\tau^{(i)}$ as

$$\tau^{(i)} \doteq \inf\{t : X^{(i)}(t) \ge (i+1)L\}. \tag{17}$$

Also set $\sigma^{(0)} = 0$ and define

$$\sigma^{(i)} \doteq \tau^{(i-1)} + \sigma^{(i-1)},\ \ i \ge 1. \tag{18}$$

The following lemma will guarantee that the diffusion ratchet we will construct has paths in the space $C([0,\infty) : I\!R_+)$.

Lemma 2.1 *For all $i \in I\!N_0$, $P(0 < \sigma^{(i)} < \infty) = 1$ and $\sigma^{(i)} \to \infty$ almost surely, as $i \to \infty$.*

Proof. In order to show $P(0 < \sigma^{(i)}) = 1$ it suffices to show that $P(0 < \tau^{(0)}) = 1$. Note that $P(X^{(0)}(0) = 0) = 1$, and so $P(X^{(0)}(0) = L) = 0$. The continuity of sample paths of $X^{(0)}(\cdot)$ then implies that and $P(0 < \tau^{(0)}) = 1$.

Next we need to show that $P(\sigma^{(i)} < \infty) = 1$. For this, it suffices to show that $P(\tau^{(j)} < \infty) = 1$ for all j. However, this is an immediate consequence of Theorem 1.5 which in fact says that $E\tau^{(j)} < \infty$. This shows that $P(0 < \sigma^{(i)} < \infty) = 1$ for all i.

For the second part of the lemma, we will first show that there exists $\delta, \epsilon \in (0, \infty)$ such that

$$\inf_{j \in I\!N_0} P(\tau^{(j)} > \delta) \ > \ \epsilon. \tag{19}$$

Let $\epsilon \in (0,1)$ be arbitrary. Define

$$Y^{(i)}(u) = iL + \int_0^u b(X^{(i)}(s))ds + \int_0^u a(X^{(i)}(s))dW^{(i)}(s), \quad u \in [0, \infty). \tag{20}$$

Note that for $\delta > 0$

$$\begin{aligned} P(\tau^{(j)} \leq \delta) &= P(\sup_{0 \leq s \leq \delta} |X^{(j)}(s) - jL| \geq L) \\ &\leq P(\sup_{0 \leq s \leq \delta} |Y^{(j)}(s) - jL| \geq \frac{L}{2}) \\ &\leq 2\frac{E(\sup_{0 \leq s \leq \delta} |Y^{(j)}(s) - jL|)}{L} \\ &\leq \frac{C\delta^{1/2}}{L}, \end{aligned}$$

for a universal constant C, where the last step follows on using (16). Now (19) follows on choosing δ small enough so that $\frac{C\delta^{1/2}}{L} < (1 - \epsilon)$. Finally, using the Borel-Cantelli lemma we have that the $\tau^{(j)} \geq \delta$ for infinitely many j; therefore, the sum is infinite almost surely. ■

We are now ready to define the diffusion ratchet process.

Definition 2.2 (Diffusion Ratchet) *Let, for $i \in I\!N_0$, $X^{(i)}, \tau^{(i)}, \sigma^{(i)}$ be defined via (15), (17) and (18), respectively. Define the stochastic process $X(\cdot)$ with paths in $C([0,\infty) : I\!R_+)$ as follows.*

$$X(t) \doteq X^{(i)}(t - \sigma^{(i)}); \quad t \in [\sigma^{(i)}, \sigma^{(i+1)}), \quad i \in I\!N_0.$$

We will refer to $X(\cdot)$ as the diffusion ratchet process.

Note that the diffusion ratchet has the desired properties, namely, after the process has reached iL and before it hits $(i+1)L$, it behaves like a reflected diffusion with reflecting barrier at iL, drift coefficient $b(\cdot)$ and diffusion coefficient $a(\cdot)$.

The following is the main result of this section. Let α, b_1, b_2 be as in (11) and (10). Set $b(x) = b_1(x) - b_2(x)$ and $\alpha(x) = \frac{a^2(x)}{2}$.

Theorem 2.3 *The sequence $X_n(\cdot)$ converges weakly to $X(\cdot)$, in $\mathcal{D}([0,\infty) : I\!R_+)$, as $n \to \infty$.*

The proof of the above theorem is rather long and, therefore, before proceeding with the proof we outline the key steps involved.

We begin by defining the family of processes $\{\tilde{X}_n^{(i)}(\cdot), \tilde{Y}_n^{(i)}(\cdot)\}_{i \in I\!N_0, n \in I\!N'}$ and stopping times $\{\tau_n^{(i)}\}$ as follows. For fixed $i \in I\!N_0$ and $n \in I\!N'$,

$$
\begin{aligned}
\tilde{X}_n^{(i)}(t) &\doteq \tilde{Y}_n^{(i)}(t) \doteq iL \text{ for } 0 \le t < \beta_n^0 \\
\tilde{Y}_n^{(i)}(t) &\doteq iL + \tilde{X}_n^{(i)}(\beta_n^j -) + \varphi_n^{j-1} \text{ for } \beta_n^j \le t < \beta_n^{j+1} \\
\tilde{X}_n^{(i)}(t) &\doteq iL + (\tilde{Y}_n^{(i)}(t) - iL)^+ \text{ for } \beta_n^j \le t < \beta_n^{j+1} \\
\tau_n^{(i)} &\doteq \inf\{t : \tilde{X}_n^{(i)}(t) = (i+1)L\} \\
\text{where } \beta_n^j &\doteq \sum_{k=0}^{j} \rho_n^k \\
\text{with } (\rho_n^0, \varphi_n^0) &\doteq (0,0) \text{ and } (\rho_n^k, \varphi_n^k) \text{successively defined by} \\
P\left[\rho_n^{k+1} > s, \varphi_n^{k+1} \right. &= \left. \frac{1}{n} \middle| \rho_n^j, \varphi_n^j, j \le k \right] = e^{-\lambda_n(\tilde{X}_n^{(i)}(\beta_n^k -))s} p_n(\tilde{X}_n^{(i)}(\beta_n^k -)) \\
P\left[\rho_n^{k+1} > s, \varphi_n^{k+1} \right. &= \left. -\frac{1}{n} \middle| \rho_n^j, \varphi_n^j, j \le k \right] = e^{-\lambda_n(\tilde{X}_n^{(i)}(\beta_n^k -))s} (1 - p_n(\tilde{X}_n^{(i)}(\beta_n^k -)))
\end{aligned}
$$

Let $\sigma_n^{(i)} \doteq \sum_{j=0}^{i-1} \tau_n^{(i)}$, $i \ge 1$, and $\sigma_n^{(0)} \doteq 0$. Define

$$\hat{X}_n(t) = \tilde{X}_n^{(i)}(t - \sigma_n^{(i)}); \quad t \in [\sigma_n^{(i)}, \sigma_n^{(i+1)}); \quad i \in I\!N_0.$$

Note that, by construction, $\hat{X}_n(\cdot)$ has the same law as $X_n(\cdot)$. So, if we show that $\hat{X}_n(\cdot) \Rightarrow X(\cdot)$, then we have proven the theorem. Next, let

$$\mathcal{X}_0 \doteq \mathcal{D}([0,\infty) : I\!R_+) \times [0,\infty],$$

where $[0,\infty]$ denotes the one point compactification of $I\!R_+$. Let $\mathcal{X} \doteq \mathcal{X}_0^{\otimes\infty}$. We will endow $\mathcal{X}$ with the usual topology and consider the Borel σ-field $\mathcal{B}(\mathcal{X})$. Then for each n,

$$Z_n \doteq \{(\tilde{X}_n^{(i)}, \tau_n^{(i)})\}_{i \in I\!N_0} \quad \text{and} \quad Z \doteq \{(X^{(i)}, \tau^{(i)})\}_{i \in I\!N_0} \tag{21}$$

take values in $\mathcal{X}$. Defining

$$\tilde{\mathcal{X}} \doteq \{(x_i, \beta_i)_{i \in \mathbb{N}_0} \in \mathcal{X} | 0 < \beta_i < \infty \text{ and } x_i \in A \ \ \forall\, i \text{ and } \sum_{i=0}^{j} \beta_i \to \infty \text{ as } j \to \infty\}$$

where

$$\begin{aligned} A \ &= \ \{\phi(\cdot) \in C([0,\infty) : \mathbb{R}_+) : \forall \delta > 0, \exists \text{ some } t' \in [\tau(\phi(\cdot)), \tau(\phi(\cdot)) + \delta] \\ &\quad \text{such that } \phi(t') > L\}, \end{aligned}$$

and

$$\tau(\phi(\cdot)) \doteq \inf\{t : \phi(t) \geq L\}. \tag{22}$$

For each i, $X^{(i)} \in A$, since the diffusion coefficient $a(x)$ is uniformly non-degenerate. We see from this fact and Lemma 2.1 , that

$$P(Z \in \tilde{\mathcal{X}}) = 1. \tag{23}$$

The key step in the proof of Theorem 2.3 is to establish the weak convergence of $\{Z_n\}$ to Z. The first part of the proof will be to show that each component of $\{Z_n\}$ converges to each component of Z. So, for fixed i we will show that

$$(\tilde{X}_n^{(i)}, \tau_n^{(i)}) \Rightarrow (X^{(i)}, \tau^{(i)}). \tag{24}$$

Once more, unless necessary, we will suppress i in the notation to follow. In order to prove (24), we will show that an un-reflected version of $\tilde{X}_n$, i.e. $\tilde{Y}_n$, will converge to an un-reflected version of X i.e. Y. Then using the continuous mapping theorem (since the Skorokhod mapping in one dimension is a continuous map) we will obtain the convergence of $\tilde{X}_n$ to X.

We need to establish some notation for the following calculations and to make clear the above definitions. Define

$$N(t) = \max\{m : \frac{m}{n^3} \leq t\}.$$

Let

$$\Delta_j \tilde{Y}_n = \tilde{Y}_n\left(\frac{j+1}{n^3}\right) - \tilde{Y}_n\left(\frac{j}{n^3}\right),$$

and $\Delta' \tilde{Y}_n = \tilde{Y}_n(t) - \tilde{Y}_n(\frac{N(t)}{n^3})$. Let E_j^n be expectation conditioned on $\mathcal{F}(\tilde{X}_n(\frac{i}{n^3}), \tilde{Y}_n(\frac{i}{n^3}), i \leq j)$ and E_y^n be the expectation conditioned on $\tilde{Y}_n$ having initial state y. Also recalling that $\lambda(\cdot)$ is $O(n^2)$) we have that for $\tilde{Y}_n$ the probability of a jump in a small time interval (of size $\frac{1}{n^3}$) is

$$P\{\Delta_j \tilde{Y}_n = \frac{1}{n} \text{ or } \Delta_j \tilde{Y}_n = -\frac{1}{n}\} = \frac{1}{n^3}(\lambda_n(X_n\left(\frac{j}{n^3}\right))) + o\left(\frac{1}{n}\right) \ \ \to 0, \text{ as } n \to \infty.$$

One of the main steps in the proof is to show that

$$\tilde{Y}_n \Rightarrow Y, \tag{25}$$

where $Y \equiv Y^{(i)}$ is given via (20). Note that $\tilde{X}_n^{(i)}(\cdot) = \Gamma_i(\tilde{Y}_n^{(i)})(\cdot)$. So, (24) is an immediate consequence of (25) in view of the continuous mapping theorem (after we have shown that the hitting times is also a continous function of Y). Before starting, we will first establish that locally–for small time steps–the discrete space model will have approximately the same mean and variance as the continuous process. This will aid in a number of future calculations. Define

$$\tilde{w}_n^{(i)}(t) = \sum_{\ell=0}^{N(t)-1} \frac{[\Delta_\ell \tilde{Y}_n^{(i)} - E_\ell^n \Delta_\ell \tilde{Y}_n^{(i)}]}{a(\tilde{X}_n^{(i)}(\frac{\ell}{n^3}))}.$$

We will next show that $\{(\tilde{X}_n, \tilde{Y}_n, \tilde{w}_n)\}$ is tight, for which it suffices to show that the marginals are tight. The tightness of $\tilde{Y}_n$ and $\tilde{w}_n$ will be shown by using Theorem 1.3 and the tightness of $\tilde{X}_n$ will be an immediate consequence of the continuity of the Skorokhod map.

The next step will be the identification of the weak limits. For this, we will break up the process $\tilde{Y}_n$ into a sum of two terms, one of which will be a Riemann sum that will converge to the absolutely continuous portion of the process in (20) and another which will converge to the Itô integral. To show the convergence to the Itô integral, we will use Theorem 1.4 of the previous section. Using this, we will show that the limit of $\tilde{Y}_n$ solves (20). Finally, we will complete the proof of (24) by proving that the τ_n converge weakly to τ. This will by done by showing that the hitting time is a continuous functional of a diffusion process and appealing to the continuous mapping theorem.

Straightforward calculations can establish the following local consistency conditions which will be used frequently in the sequel and will confirm at least on an intuitive level that the $\tilde{Y}_n(\cdot)$ processes approximate an unreflected version of $\tilde{X}$.

Local Consistency Conditions Let $x' = \tilde{X}_n(\frac{j}{n^3})$.

$$E_j^n \Delta_j \tilde{Y}_n = b(x') \frac{1}{n^3} + o\left(\frac{1}{n^3}\right) \tag{26}$$

and

$$E_j^n (\Delta_j \tilde{Y}_n - E_j^n \Delta_j \tilde{Y}_n)^2 = a^2(x') \frac{1}{n^3} + o\left(\frac{1}{n^3}\right) \tag{27}$$

Lemma 2.4 *$\{(\tilde{X}_n, \tilde{Y}_n, \tilde{w}_n)\}$ is tight.*

Proof. We will first prove the tightness of $\{\tilde{Y}_n\}$ by using Theorem 1.3. The proof of tightness of $\tilde{w}_n$ is very similar and therefore is omitted.

Using (26) and (27), we can establish the following inequality.

$$\begin{aligned}
E_y^n|\tilde{Y}_n(t)-y|^2 &= E_y^n\Big|\sum_{i=0}^{N(t)-1}[E_i^n\Delta_i\tilde{Y}_n+(\Delta_i\tilde{Y}_n-E_i^n\Delta_i\tilde{Y}_n)] \\
&\quad +[E_{N(t)}^n\Delta'\tilde{Y}_n+(\Delta'\tilde{Y}_n-E_{N(t)}^n\Delta'\tilde{Y}_n)]\Big|^2 \\
&\le 2E_y^n\left(\Big|\sum_{i=0}^{N(t)-1}E_i^n\Delta_i\tilde{Y}_n+E_{N(t)}^n\Delta'\tilde{Y}_n\Big|^2\right. \\
&\quad \left.+\Big|\sum_{i=0}^{N(t)-1}(\Delta_i\tilde{Y}_n-E_i^n\Delta_i\tilde{Y}_n)+(\Delta'\tilde{Y}_n-E_{N(t)}^n\Delta'\tilde{Y}_n)\Big|^2\right) \\
&\le 2E_y^n\Big|\sum_{i=0}^{N(t)-1}\left(b(\tilde{X}_n(\frac{i}{n^3}))\frac{1}{n^3}+o(\frac{1}{n^3})\right) \\
&\quad +b(\tilde{X}_n(\frac{N(t)}{n^3}))(t-\frac{N(t)}{n^3})+o(\frac{1}{n^3})\Big|^2 \\
&\quad +2E_y^n\sum_{i=0}^{N(t)-1}\left(a^2(\tilde{X}_n(\frac{i}{n^3}))\frac{1}{n^3}+o(\frac{1}{n^3})\right) \\
&\quad +2E_y^n\left(a^2(\tilde{X}_n(\frac{N(t)}{n^3}))(t-\frac{N(t)}{n^3})+o(\frac{1}{n^3})\right) \\
&\le 2\left|Kt+N(t)o(\frac{1}{n^3})\right|^2+2\left(K^2t+N(t)o(\frac{1}{n^3})\right),
\end{aligned}$$

where K is the bound for the maximum of $|b^*|$, $|b_*|$ and $|a^*|$.

This shows that the first condition in Theorem 1.3 is satisfied.

For the second condition in Theorem 1.3, fix $T>0$ and take an arbitrary stopping time ς s.t. $\varsigma \le T$ $w.p.1$. Note that

$$\begin{aligned}
E_y^n(1\wedge|\tilde{Y}_n(\varsigma+\delta')-\tilde{Y}_n(\varsigma)|) &\le (E_y^n|\tilde{Y}_n(\varsigma+\delta')-\tilde{Y}_n(\varsigma)|^2)^{1/2} \\
&\le \left(2\left|K\delta'+N(\delta')o\left(\frac{1}{n^3}\right)\right|^2\right. \\
&\quad \left.+2\left(K^2\delta'+N(\delta')o\left(\frac{1}{n^3}\right)\right)\right)^{\frac{1}{2}}
\end{aligned}$$

Since the right side above converges to 0 as $\delta'\to 0$, we have that the second condition in Theorem 1.3 holds. So, the sequence of processes $\{\tilde{Y}_n\}$ is tight. The tightness of $\{\tilde{X}_n\}$ is now an immediate consequence of the fact that $\tilde{X}_n = \Gamma(\tilde{Y}_n)$ and that Γ is a continuous map. ■

The next step in the proof is the identification of the weak limits of the sequence $\{(\tilde{X}_n, \tilde{Y}_n, \tilde{w}_n)\}$

Lemma 2.5 *Let $W^{(i)}$ be a Wiener process defined on some probability space $(\Omega, \mathcal{F}, P)$ and let $(X^{(i)}, Y^{(i)})$ be defined via (15) and (20), respectively. Then $(\tilde{X}_n, \tilde{Y}_n, \tilde{w}_n) \equiv (\tilde{X}_n^{(i)}, \tilde{Y}_n^{(i)}, \tilde{w}_n^{(i)})$ converges weakly to $(X^{(i)}, Y^{(i)}, W^{(i)})$, as $n \to \infty$.*

Proof. We know that there exists convergent subsequences for the measures induced by the $\{(\tilde{X}_n, \tilde{Y}_n, \tilde{w}_n)\}$ processes. So we need to establish the following: For any weakly convergent subsequence, the weak limit of $(\tilde{X}_{n'}^{(i)}, \tilde{Y}_{n'}^{(i)}, \tilde{w}_{n'}^{(i)})$, denoted by $(\tilde{X}^{(i)}, \tilde{Y}^{(i)}, \tilde{w}^{(i)})$ has the same law as $(X^{(i)}, Y^{(i)}, W^{(i)})$ We will use n for n' to simplify notation. First we will use Theorem 1.4 to show that the weak limit of $\tilde{w}_{n'}^{(i)}$ is a Wiener process. Fix $t \geq 0, \zeta > 0, q < \infty, t_i \in [0, t]$ with $t_{i+1} > t_i$ for $i \in \{0, ..., q\}$, and let $f \in C_0^2(I\!R)$. Then,

$$
\begin{aligned}
f(\tilde{w}_n(t+\zeta)) \quad - \quad & f(\tilde{w}_n(t)) - \int_t^{t+\zeta} \frac{1}{2} \frac{\partial^2}{\partial x^2} f(\tilde{w}_n(s)) ds \\
= \quad & \sum_{i=N(t)+1}^{N(t+\zeta)-1} [f(\tilde{w}_n(\frac{(i+1)}{n^3})) - f(\tilde{w}_n(\frac{i}{n^3}))] \\
& - \sum_{i=N(t)+1}^{N(t+\zeta)-1} \frac{1}{2} f_{xx}(\tilde{w}_n(\frac{i}{n^3})) \frac{1}{n^3} + \epsilon_n \\
= \quad & \sum_{i=N(t)}^{N(t+\zeta)-1} f_x(\tilde{w}_n(\frac{i}{n^3})) \frac{[\Delta_i \tilde{Y}_n - E_i^n \Delta_i \tilde{Y}_n]}{a(\tilde{X}_n(\frac{i}{n^3}))} \\
& + \frac{1}{2} \sum_{i=N(t)}^{N(t+\zeta)-1} f_{xx}(\tilde{w}_n(\frac{i}{n^3})) \frac{[\Delta_i \tilde{Y}_n - E_i^n \Delta_i \tilde{Y}_n]^2}{a^2(\tilde{X}_n(\frac{i}{n^3}))} \\
& - \frac{1}{2} \sum_{i=N(t)}^{N(t+\zeta)-1} f_{xx}(\tilde{w}_n(\frac{i}{n^3})) \frac{1}{n^3} + \epsilon_n
\end{aligned}
$$

Here, $E^n|\epsilon_n| \to 0$ as $n \to \infty$.

Thus if H is a bounded, continuous function from $I\!R^{3\times q}$ to $I\!R$, then

$$\begin{aligned} & E\Bigg| H(\tilde{X}_n(t_i),\tilde{Y}_n(t_i),\tilde{w}_n(t_i),1\le i\le q) \\ \times \quad & \left[f(\tilde{w}_n(t+\zeta)) - f(\tilde{w}_n(t)) - \int_t^{t+\zeta}\frac{1}{2}\frac{\partial^2}{\partial x^2}f(\tilde{w}_n(s))ds\right]\Bigg| \\ \le \quad & K'(E^n|\epsilon_n|) \quad \to 0 \text{ as } n\to\infty. \end{aligned} \tag{28}$$

Since $(\tilde{X}_n,\tilde{Y}_n,\tilde{w}_n)\Rightarrow(\tilde{X},\tilde{Y},\tilde{w})$, using the Skorokhod representation theorem, we can assume without loss of generality that $(\tilde{X}_n,\tilde{Y}_n,\tilde{w}_n)\to(\tilde{X},\tilde{Y},\tilde{w})$, almost surely. Thus taking limit as $n\to\infty$ on the left side of (28) we have via an application of dominated convergence theorem that

$$E\Bigg|H(\tilde{X}(t_i),\tilde{Y}(t_i),\tilde{w}(t_i),1\le i\le q)\times\left[f(\tilde{w}(t+\zeta))-f(\tilde{w}(t))-\int_t^{t+\zeta}\frac{1}{2}\frac{\partial^2}{\partial x^2}f(\tilde{w}(s))ds\right]\Bigg|=0. \tag{29}$$

Now, let $\mathcal{F}_t=\sigma\{\tilde{X}(s),\tilde{Y}(s),\tilde{w}(s),s\le t\}$ which is generated by functions of the form of $H(\cdot)$. Thus,

$$E\left[\left(f(\tilde{w}(t+\zeta))-f(\tilde{w}(t))-\int_t^{t+\zeta}\frac{1}{2}\frac{\partial^2}{\partial x^2}f(\tilde{w}(s))ds\right)I_F\right]=0 \tag{30}$$

for $F\in\mathcal{F}_t$, and so

$$E\left[f(\tilde{w}(t+\zeta))-f(\tilde{w}(t))-\int_t^{t+\zeta}\frac{1}{2}\frac{\partial^2}{\partial x^2}f(\tilde{w}(s))ds\,\middle|\,\mathcal{F}_t\right]=0 \quad w.p.1 \tag{31}$$

Thus, $f(\tilde{w}(t))-f(\tilde{w}(0))-\int_0^t\frac{1}{2}\frac{\partial^2}{\partial x^2}f(\tilde{w}(s))ds$ is an $\mathcal{F}_t$-martingale for all $f\in C_0^2(I\!R)$. Next, by construction of $\tilde{w}_n(t)$ and $\tilde{Y}_n(t)$

$$|\tilde{w}_n(t)-\tilde{w}_n(t-)|\le\frac{2}{n\times a_*} \tag{32}$$

for every t and therefore the jumps of $\tilde{w}_n(\cdot)$ converge to zero uniformly in t. From Theorem 13.4 of [2], we now have that $\tilde{w}$ has continuous paths almost surely. So, by Theorem 1.4 $w(\cdot)$ is an $\mathcal{F}_t$-Wiener process.

Now, we will identify the limit process $(\tilde{X},\tilde{Y})$. For each $\delta>0$ and $t\in[j\delta,(j+1)\delta)$, define

$$\tilde{Y}_n^\delta(t)\doteq\tilde{Y}_n(j\delta),\quad \tilde{Y}^\delta(t)\doteq\tilde{Y}(j\delta),\quad \tilde{X}_n^\delta(t)\doteq\tilde{X}_n(j\delta),\quad \tilde{X}^\delta(t)\doteq\tilde{X}(j\delta).$$

Using the definition of $w(\cdot)$ and the local consistency properties (26), (27), we have that

$$\tilde{Y}_n^\delta(t) - y = \int_0^t b(\tilde{X}_n^\delta(s))ds + \sum_{j=0}^{N(t)-1} a(\tilde{X}_n^\delta(\delta i))[w_n(\delta(i+1)) - w_n(\delta i)] + \epsilon_n^{\delta,t},$$

where $E|\epsilon_n^{\delta,t}| \to 0$ as $\delta \to 0$, uniformly in n and t in any bounded interval. Since $(\tilde{X}_n, \tilde{Y}_n) \to (\tilde{X}, \tilde{Y})$, we have that $(\tilde{X}_n^\delta(\cdot), \tilde{Y}_n^\delta(\cdot)) \to (\tilde{X}^\delta(\cdot), \tilde{Y}^\delta(\cdot))$ with probability one in $D[0,\infty)$. Thus letting $n \to \infty$ in the above display, we have

$$\tilde{Y}^\delta(t) - y = \int_0^t b(\tilde{X}^\delta(s))ds + \sum_{j=0}^{N(t)-1} a(\tilde{X}^\delta(\delta i))[\tilde{w}(\delta(i+1)) - \tilde{w}(\delta i)] + O(\delta) + \epsilon^{\delta,t} \quad (33)$$

where $E|\epsilon^{\delta,t}| \to 0$ as $\delta \to 0$. Note that for each j, $\tilde{Y}(j\delta)$ and $\tilde{X}(j\delta)$ are independent of all of the random variables $\{\tilde{w}(s) - \tilde{w}(j\delta), s \geq j\delta\}$. So, we have

$$\tilde{Y}^\delta(t) - y = \int_0^t b(\tilde{X}^\delta(s))ds + \int_0^t a(\tilde{X}^\delta(s))d\tilde{w}(s) + \overline{\epsilon_{\delta,t}} \quad (34)$$

where $E|\overline{\epsilon_{\delta,t}}| \to 0$ as $\delta \to 0$. By the continuity of $a(\cdot)$ and $\tilde{X}(\cdot)$, we have that

$$\int_0^t a(X^\delta(s))d\tilde{w}(s) \to \int_0^t a(X(s))d\tilde{w}(s), \quad (35)$$

in probability, as $\delta \to 0$. Similarly, $\int_0^t b(\tilde{X}^\delta(s))ds \to \int_0^t b(\tilde{X}(s))ds$. Furthermore, since $\tilde{X}_n = \Gamma(\tilde{Y}_n)$ for all n, we have that $\tilde{X} = \Gamma(\tilde{Y})$. Therefore, the limit process $(\tilde{X}, \tilde{Y})$ solves

$$\begin{aligned} \tilde{Y}(t) &= y + \int_0^t b(\tilde{X}(s))ds + \int_0^t a(\tilde{X}(s))d\tilde{w}(s) \\ \tilde{X}(t) &= \Gamma(\tilde{Y})(t), \end{aligned}$$

By strong (and weak) uniqueness of the solution to the above equation, we now have that $(\tilde{X}, \tilde{Y}, \tilde{w})$ has the same probability law as $(X^{(i)}, Y^{(i)}, W^{(i)})$. This proves the result. ■

In order to complete the proof of (24) we now need to show the convergence of the stopping times to the corresponding limits. This convergence is an immediate consequence of the following lemma and the continuous mapping theorem.

Lemma 2.6 *Let $\tau(\cdot)$ be defined via (22). Let $\phi \in A$ and $\{\phi_n\}$ be a sequence in $D([0,\infty) : I\!R_+)$ such that $\phi_n \to \phi$. Then $\tau(\phi_n) \to \tau(\phi)$.*

Proof. Note that since ϕ is continuous, ϕ_n converges to ϕ, uniformly on compacts. First we will show

$$\liminf_{n\to\infty} \tau(\phi_n) \geq \tau(\phi). \tag{36}$$

We will argue via contradiction, suppose that (36) is false. Then, $\tau' \doteq \liminf_{n\to\infty} \tau(\phi_n) < \tau(\phi)$. So, there is a subsequence $\{\tau(\phi_{n'})\}$ that converges to τ'. For any $\delta > 0$ and sufficiently large N, $\{\tau(\phi_{n'})\} \in [\tau' - \delta, \tau' + \delta]$ for all $n' \geq N$. Let δ be small enough so that this interval does not include $\tau(\phi(\cdot))$. There exists an $\epsilon > 0$ such that for all t in this interval, $\phi(t) \leq L - \epsilon$ since $t < \tau(\phi(\cdot))$. For some t in this interval $\phi_{n'}(t) = L$. So, $\sup_{t\in[\tau'-\delta,\tau'+\delta]} |\phi_{n'}(t) - \phi(t)| \geq \epsilon$ for all $n' > N$. This is a contradiction to the fact that $\phi_n(\cdot)$ converges to $\phi(\cdot)$, uniformly on compacts.

Next we show that

$$\tau'' \doteq \limsup_{n\to\infty} \tau(\phi_n(\cdot)) \leq \tau(\phi(\cdot)). \tag{37}$$

Once again, we proceed via contradiction. Assume that (37) is false, i.e. $\tau'' > \tau(\phi)$ Again, there is a subsequence $\{\tau(\phi_{n''})\}$ that converges to τ''. Now, if we look at the interval $[\tau(\phi(\cdot)), \tau(\phi(\cdot)) + \frac{\tau(\phi(\cdot))-\tau''}{2}]$, then for sufficiently large N $\tau(\phi_{n''}(\cdot))$ are to the right of this interval for all $n'' > N$. Thus, the corresponding $\phi_{n''}(t)$ are less than L for t in the interval. By our assumption, there is a t' in this interval such that $\phi(t') > L$. This contradicts the fact that $\phi_n(\cdot) \to \phi(\cdot)$. This proves (37). Combining (36) and (37) we have the result. ■

An immediate consequence of the above results is the following corollary.

Corollary 2.7 *Let $\{Z_n\}$ and Z be defined via (21). Then, the sequence $\{Z_n\}$ of $\mathcal{X}$ valued random elements converges weakly to Z.*

Proof. From Lemma 2.5 and Lemma 2.6 we have that

$$(X_n^{(i)}, \tau_n^{(i)}) \equiv (X_n^{(i)}, \tau(X_n^{(i)})) \Rightarrow (X^{(i)}, \tau(X^{(i)})) \equiv (X^{(i)}, \tau^{(i)}).$$

So, every component of Z_n converges to the respective component of Z. This proves the result. ■

The final step in the proof of Theorem 2.3 is the following lemma. We begin with the following notation. For $z = \{x^{(i)}, \tau^{(i)}\}_{i\geq 0} \in \mathcal{X}$, define $J_z : I\!N_0 \to I\!N_0$ as follows. $J_z(0) \doteq 0$ and for $k \geq 1$, $J(k) \doteq \inf\{i > J(k-1) : \tau^{(i)} \neq 0\}$. Also define $x_z \in \mathcal{D}([0,\infty) : I\!R_+)$ as:

$$x_z(t) \doteq \begin{cases} x^{(J(k))}(t - \sigma^{(J(k-1))}) & \text{if } t \in [\sigma^{(J(k-1))}, \sigma^{(J(k))}); \quad k \in I\!N \\ 0 & \text{if } t \geq \sigma^{\infty}, \end{cases} \tag{38}$$

where for $i \geq 1$ $\sigma^{(i)} = \sum_{j=1}^{i} \tau^{(j)}$, $\sigma^{(0)} \doteq 0$ and $\sigma^{\infty} \doteq \lim_{j\to\infty} \sigma^{(j)}$.

Lemma 2.8 *Let $\Psi : \mathcal{X} \to \mathcal{D}([0,\infty) : I\!R_+)$ be defined as $\Psi(z) = x_z$, $z = \{x^{(i)}, \tau^{(i)}\}_{i\geq 0}$, where x_z is given via (38). Then Ψ is continuous at every $z \in \tilde{\mathcal{X}}$.*

Proof: Take a sequence $\{z_n\} \in \mathcal{X}$ which converges to $z \in \tilde{\mathcal{X}}$. We will show that $\Psi(z_n) \to \Psi(z)$. It suffices to show that $\Psi(z_n)(t) \to \Psi(z)(t)$ uniformly on $[\sigma^{(i-1)}, \sigma^{(i)}]$ for all $i \in I\!N$. In order to prove this statement we will show the following two results.
(i)

$$\Psi(z_n)(t) \to \Psi(z)(t), \text{ uniformly for } t \in [\sigma^{(i-1)} + \delta, \sigma^{(i)} - \delta] \tag{39}$$

for any δ s.t. $0 < \delta < \frac{\sigma^i - \sigma^{i-1}}{2}$ and $i \in I\!N$.
(ii)

$$\Psi(z_n)(t) \to \Psi(z)(t), \text{ uniformly for } t \in [\sigma^{(i-1)} - \delta, \sigma^{(i-1)} + \delta] \tag{40}$$

for any δ s.t. $0 < \delta < (\sigma^{i-1} - \sigma^{i-2}) \wedge (\sigma^i - \sigma^{i-1})$ and $i \geq 2$.

Clearly, the result follows once (i) and (ii) are proven.

Now we prove (i). Note that since $\sigma_n^j \to \sigma^j$ for all j as $n \to \infty$, we can find $N \in I\!N$ s.t. for all $n \geq N$, $\sigma_n^{(j)} \in [\sigma^{(j)} - \delta, \sigma^{(j)} + \delta]$ for $j = i, i-1$. So, for t in the fixed interval $[\sigma^{(i-1)} + \delta, \sigma^{(i)} - \delta]$

$$\begin{aligned} \Psi(z_n)(t) &= x_n^{(i)}(t - \sigma_n^{(i-1)}) \\ \Psi(z)(t) &= x^{(i)}(t - \sigma^{(i-1)}) \end{aligned}$$

For simplicity, we will re-parameterize with $s = t - \sigma^{(i-1)}$ and set $\varsigma_n = \sigma^{(i-1)} - \sigma_n^{(i-1)}$. Note that $|\varsigma_n| \leq \delta$.) Thus, for s in $C = [\delta, \tau^{(i)} - \delta]$,

$$\begin{aligned} \Psi(z_n)(s + \sigma^{(i-1)}) &= x_n^{(i)}(s + \varsigma_n) \\ \Psi(z)(s + \sigma^{(i-1)}) &= x^{(i)}(s) \end{aligned}$$

So, we need to show that $x_n(s + \varsigma_n) \to x(s)$ uniformly on C (suppressing the i). We know that $x(s)$ is uniformly continuous on $[0, \tau]$, and that $x_n(s) \to x(s)$ uniformly on compact intervals since $x(s)$ is continuous and $x_n(s)$ converges to $x(s)$ in the Skorokhod space.[2] Now,

$$|x(s) - x_n(s + \varsigma_n)| \leq |x(s) - x(s + \varsigma_n))| + |x(s + \varsigma_n) - x_n(s + \varsigma_n)| \tag{41}$$

for every $s \in C$. Thus,

$$\begin{aligned} \sup_{s \in C} |x(s) - x_n(s + \varsigma_n)| &\leq \sup_{s \in C} |x(s) - x(s + \varsigma_n))| + \sup_{s \in C} |x(s + \varsigma_n) - x_n(s + \varsigma_n)| \\ &\leq \sup_{s \in C} |x(s) - x(s + \varsigma_n))| + \sup_{s \in [0,\tau]} |x(s) - x_n(s)| \end{aligned}$$

Now, the right hand side goes to zero, since x is uniformly continuous, $\varsigma_n \to 0$ and $x_n \to x$ uniformly. This proves (i).

Now we consider (ii). Let us denote the interval $[\sigma^{(i-1)} - \delta, \sigma^{(i-1)} + \delta]$ by K. Let $s = t - \sigma^{(i-1)}$ and $\varsigma_n = \sigma_n^{(i-1)} - \sigma^{(i-1)}$, and again ensure large enough n to guarantee $\sigma_n^{(i)}$ are within δ of the limit.

$$\begin{aligned}
\sup_{s\in K} |\Psi(z_n)(s) - \Psi(z)(s)| &\le \sup_{s\in K} |\Psi(z_n)(s) - \Psi(z)(t - \varsigma_n)| \\
&\quad + \sup_{s\in K} |\Psi(z)(s - \varsigma_n) - \Psi(z)(s)| \\
&\le \sup_{r\in[\sigma^{(i-1)}-2\delta,\sigma^{(i-1)}]} |x_n^{(i-1)}(r) - x(r)| \vee \sup_{r\in[0,2\delta]} |x_n^{(i)}(r) - x(r)| \\
&\quad + \sup_{s\in K} |\Psi(z)(s - \varsigma_n) - \Psi(z)(s)|
\end{aligned}$$

Once more the uniform convergence of $x_n^{(i)}$ to $x^{(i)}$ shows that the right side of the expression above converges to 0 as $n \to \infty$. This proves (ii) and hence the result. ■

Proof of Theorem 2.3 .

The proof is an immediate consequence of Corollary 2.7 and Lemma 2.8 on observing that $X_n = \Psi(Z_n)$ and $X = \Psi(Z)$. ■

2.1 Asymptotic Velocity of a Diffusion Ratchet

An important physical feature of the molecular motors that are being modeled is their velocity which is defined to be

$$V(t) = \frac{X(t)}{t} \tag{42}$$

where $X(t)$ is the diffusion ratchet introduced in the previous section. We are interested in studying the asymptotic velocity of the motor, namely we will like to consider the asymptotics of $V(t)$ as $t \to \infty$. We will begin by considering the case when the drift and diffusion coefficients are periodic with period L. Such an assumption is quite natural in many situations because of the cyclic mechano-chemical steps involved in motor transport. The periodic case includes, as a special case, the commonly studied situation where the drift and diffusion coefficients are constant.

Our work has been motivated by a recent work of Elston and Peskin [6] where the authors study the steady state velocity for an "imperfect ratchet". An imperfect ratchet is defined in terms of a tilted potential, namely, away from a barrier there is a negative linear potential or, in our terminology, a negative constant drift which represents the load F_l. Near the lower barrier, the drift changes in a continuous manner to a positive value $F_0 - F_l$ which represents the "ratchet strength". Thus if F_0 is large enough and the transition from negative drift to positive drift is rapid enough, it has the effect of almost instantaneously reflecting the motor at the lower barrier. However, in an imperfect ratchet model, irrespective of the value of F_0, the motor can, with a positive probability, cross the barrier to the left. This probability, of course, becomes smaller and smaller as F_0 increases. In [6], starting with the Fokker-Planck equation for a diffusion with constant drift and diffusion coefficients, and imposing periodicity conditions consistent with the barrier locations, the authors write a PDE for the transition density of the process. They then investigate the steady-state density of the "imperfect ratchet" by setting the partial derivative of the density with respect to t to zero. Using this new equation, the steady-state velocity is then calculated. The velocity here is defined to be the "net probability flux" of the steady-state distribution times the period (distance between barriers). The "net probability flux" can be thought of as the "asymptotic probability" that a particle moves across a certain area per time period. From these results they take formal limit of the steady state velocity as F_0 goes to infinity. This limit, in [6], is defined to be the steady state velocity of the "perfect ratchet". Intuitively, this last limit should correspond to the asymptotic velocity (i.e. $\lim_{t\to\infty} \frac{X(t)}{t}$) of the diffusion ratchet constructed in Section 2.

In our terminology, the model considered in [6] corresponds to a diffusion ratchet with constant mean (which we will call μ here) and constant diffusion parameter (which we will call σ). For $\mu \neq 0$ they find the steady state velocity of the "perfect ratchet" to be

$$\frac{D}{L}\frac{\omega_l^2}{e^{\omega_l}-1-\omega_l} \tag{43}$$

where $D = \frac{\sigma^2}{2}$ and $\omega_l = -\frac{2\mu}{\sigma^2}L$, and when $\mu = 0$ the steady state velocity is obtained to be

$$\frac{2D}{L}. \tag{44}$$

In this section we will show that for the periodic ratchet case, asymptotic velocity, i.e. $\lim_{t\to\infty}\frac{X(t)}{t}$ exists, almost surely. We will also obtain an explicit expression for the asymptotic velocity in the constant coefficient case and show that it equals the value obtained via steady state analysis undertaken in [6] (See Theorem 2.2). Finally, we will prove a central limit theorem for the asymptotic velocity.

We begin with the following periodicity assumption.

Condition 2.9 *Assume that the coefficients $a, b : I\!R^+ \to I\!R$ satisfy*

$$a(x+L) = a(x), \quad b(x+L) = b(x), \quad \forall x \in I\!R^+.$$

Theorem 2.10 *Suppose that the coefficients a, b satisfy (1), (16) and Condition 2.9. Let $X(\cdot)$ be the diffusion ratchet defined in Definition 2.2. Then $\frac{X(t)}{t}$ converges almost surely to $\frac{L}{E\tau^{(0)}}$, where $\tau^{(0)}$ is defined in (17).*

Proof. Let $X^{(i)}(\cdot)$ be given by (15). Condition 2.9 implies that $\tau^{(i)} \doteq \inf\{t : X^{(i)}(t) \geq (i+1)L\}$ is an i.i.d. sequence. From Theorem 1.5 we have that $E\tau^{(i)} < \infty$. Next, let

$$n_t \doteq \inf\{m : \sum_{i=0}^{m-1}\tau^{(i)} \geq t\}. \tag{45}$$

Then

$$\begin{aligned}\frac{X(t)}{t} &= \frac{\sum_{i=0}^{n_t-1}X^{(i)}(\tau^{(i)})+\epsilon_t}{t}\\ &= \frac{n_t L}{t}+\frac{\epsilon_t}{t}\end{aligned}$$

where $0 \leq \epsilon_t < L$. Next note that $n.$ is a renewal process. Thus by the renewal theorem (Theorem 5.2.1 of [5])

we have that, as $t \to \infty$, $\frac{n_t}{t} \to \frac{1}{E\tau^{(0)}}$, almost surely. Also, the second term above clearly goes to zero. This completes the proof. ■

We will now calculate the asymptotic velocity of a diffusion ratchet with constant coefficients.

Theorem 2.11 *Suppose that $b(x) = \mu$ and $a(x) = \sigma$ for all $x \in \mathbb{R}_+$. Then*

$$\lim_{t\to\infty} \frac{X(t)}{t} = \begin{cases} \frac{D}{L}\frac{\omega_l^2}{e^{\omega_l}-1-\omega_l} & \text{if } \mu \neq 0 \\ \frac{2D}{L}. & \text{if } \mu = 0, \end{cases} \tag{46}$$

where $D = \frac{\sigma^2}{2}$ and $\omega_l = -\frac{2\mu}{\sigma^2}L$.

Proof. In view of Theorem 2.10, in order to calculate the asymptotic velocity , we only need to calculate $E\tau^{(0)}$. To do this we will use the Laplace transform, $\phi(\lambda) \doteq E_0[e^{-\lambda\tau^{(0)}}]$. From Chapter 5 of [7], this Laplace transform is given as

$$\phi(\lambda) = \frac{\alpha+\beta}{\beta e^{-\alpha L} + \alpha e^{\beta L}} \tag{47}$$

where

$$\alpha \equiv \alpha(\lambda) = \frac{\sqrt{\mu^2 + 2\sigma^2\lambda}}{\sigma^2} + \frac{\mu}{\sigma^2}$$
$$\beta \equiv \beta(\lambda) = \frac{\sqrt{\mu^2 + 2\sigma^2\lambda}}{\sigma^2} - \frac{\mu}{\sigma^2}$$

Note that

$$\alpha'(\lambda) = \beta'(\lambda) = \frac{1}{\sqrt{\mu^2 + 2\sigma^2\lambda}} \tag{48}$$

Now,

$$\phi'(\lambda) = \frac{(\alpha'+\beta')(\beta e^{\alpha L} + \alpha e^{-\beta L}) - (\alpha+\beta)(\beta' e^{-\alpha L} - L\alpha'\beta e^{-\alpha L} + \alpha' e^{\beta L} + L\alpha\beta' e^{\beta L})}{(\beta e^{-\alpha L} + \alpha e^{\beta L})^2} \tag{49}$$

Note that,

$$E\tau^{(0)} = -\phi'(0).$$

First, we will evaluate $\phi'(0)$ with $\mu > 0$. We then get

$$\alpha(0) = \frac{2\mu}{\sigma^2}, \;\; \beta(0) = 0, \;\; \alpha'(0) = \beta'(0) = \frac{1}{\mu}.$$

which yields

$$\phi'(0) = \frac{\frac{2}{\mu}\frac{2\mu}{\sigma^2} - \frac{2\mu}{\sigma^2}\left(\frac{1}{\mu}e^{\frac{-2\mu}{\sigma^2}L} + \frac{1}{\mu} + \frac{2\mu}{\sigma^2}\frac{1}{\mu}L\right)}{\left(\frac{2\mu}{\sigma^2}\right)^2} \tag{50}$$

Simplifying gives

$$\phi'(0) = \left(1 - \frac{2\mu}{\sigma^2}L - e^{\frac{-2\mu}{\sigma^2}L}\right)\frac{\sigma^2}{2\mu^2}. \tag{51}$$

When $\mu < 0$, we have that

$$\alpha(0) = 0, \quad \beta(0) = \frac{2|\mu|}{\sigma^2}, \quad \alpha'(0) = \beta'(0) = \frac{1}{|\mu|}$$

which leads to the expression (51) for $\phi'(0)$. So,

$$\begin{aligned} \frac{L}{E\tau^{(0)}} &= \frac{L}{-\phi'(0)} \\ &= \frac{L}{e^{\frac{-2\mu}{\sigma^2}L} - 1 + \frac{2\mu}{\sigma^2}L} \\ &= \frac{L^2\left(\frac{4\mu^2}{\sigma^4}\right)}{L\frac{2}{\sigma^2}\left(e^{\frac{-2\mu}{\sigma^2}L} - 1 + \frac{2\mu}{\sigma^2}L\right)} \end{aligned}$$

Substituting $D = \frac{\sigma^2}{2}$ and $\omega_l = -\frac{2\mu}{\sigma^2}L$, we have the result for the case $\mu \neq 0$.

We now have consider the case when μ is 0. In this case,

$$\phi(\lambda) = \frac{2}{e^{-\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L} + e^{\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L}} \tag{52}$$

and

$$\phi'(\lambda) = \frac{-2\left(e^{\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L} - e^{-\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L}\right)\frac{L}{\sqrt{2\sigma^2\lambda}}}{\left(e^{-\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L} + e^{\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L}\right)^2} \tag{53}$$

which we rewrite (using a Taylor expansion) as

$$\phi'(\lambda) = \frac{-2\left(2\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L + o(\sqrt{\lambda})\right)\frac{L}{\sqrt{2\sigma^2\lambda}}}{\left(e^{-\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L} + e^{\frac{\sqrt{2\sigma^2\lambda}}{\sigma^2}L}\right)^2} + o(\lambda) \quad \text{as } \lambda \to 0 \tag{54}$$

Now, taking a limit, we have

$$\lim_{\lambda \searrow 0} \phi'(\lambda) = \frac{-L^2}{\sigma^2} \tag{55}$$

Using this expression and the fact that $D = \frac{\sigma^2}{2}$, we have that

$$\frac{L}{E\tau^{(0)}} = \frac{L}{\frac{2L^2}{\sigma^2}} = \frac{2D}{L} \tag{56}$$

This completes the proof. ■

The above theorem gives an explicit form for the asymptotic velocity for the relatively simple case of constant drift and diffusion coefficients. In the general situation of a state varying drift and diffusion, explicit calculation of the Laplace transform of $\tau^{(0)}$ becomes untenable. This difficulty also arises when one considers the most basic model of a motor which is pulling a cargo. In the next section we will explore various numerical methods for approximating the asymptotic velocities for situations where exact calculations are not possible.

Theorem (2.10) is a strong law of large numbers for the velocity process $V(t) \doteq \frac{X(t)}{t}$. The next obvious question is whether, with a suitable normalization and centering, we can say something about the asymptotic distribution of the velocity process. This will give us information on fluctuations of $V(t)$ from the asymptotic velocity, for large values of t. The following theorem establishes a central limit theorem for the diffusion ratchet. Recall that from Theorem 1.5 all the moments of $\tau^{(0)}$ are finite.

Theorem 2.12 *Let $X(\cdot)$ be as in Theorem 2.10. Then*

$$\frac{(E\tau^{(0)})^{3/2}\sqrt{t}}{L\varsigma}\left(\frac{X(t)}{t} - \frac{L}{E\tau^{(0)}}\right) \Rightarrow N(0,1) \tag{57}$$

where $\varsigma^2 \doteq Var(\tau^{(0)})$.

Proof. We note that

$$\frac{X(t)}{t} = \frac{\sum_{i=0}^{n_t-1} X^{(i)}(\tau^{(i)}) + \epsilon_t}{S_{n_t} + \delta_t} \tag{58}$$

where $0 \le \epsilon_t < L$, $\delta_t < \tau^{(n_t)}$, n_t is given by (45), and $S_j \doteq \sum_{i=0}^{j-1} \tau^{(i)}$. The right side above can be rewritten as follows.

$$\begin{aligned}
\frac{\sum_{i=0}^{n_t-1} X^{(i)}(\tau^{(i)}) + \epsilon_t}{S_{n_t} + \delta_t} &= \frac{L + \frac{\epsilon_t}{n_t}}{\overline{\tau} + \frac{\delta_t}{n_t}} \\
&= \frac{L}{\overline{\tau} + \frac{\delta_t}{n_t}} + \frac{\frac{\epsilon_t}{n_t}}{\overline{\tau} + \frac{\delta_t}{n_t}} \\
&= \frac{\overline{\tau}}{\overline{\tau} + \frac{\delta_t}{n_t}} \frac{L}{\overline{\tau}} + \frac{\frac{\epsilon_t}{n_t}}{\overline{\tau} + \frac{\delta_t}{n_t}} \\
&= c_t \frac{L}{\overline{\tau}} + d_t
\end{aligned}$$

where $\overline{\tau} \doteq \frac{S_{n_t}}{n_t}$, $c_t \doteq \frac{\overline{\tau}}{\overline{\tau}+\frac{\delta_t}{n_t}}$, and $d_t \doteq \frac{\frac{\epsilon_t}{n_t}}{\overline{\tau}+\frac{\delta_t}{n_t}}$. Define $a_t \doteq \frac{t}{E\tau^{(0)}}$. Note that

$$\sqrt{a_t}(c_t - 1) = \frac{\sqrt{t}}{t\sqrt{E\tau^{(0)}}} \frac{\frac{-t\delta_t}{n_t}}{\overline{\tau} + \frac{\delta_t}{n_t}}$$

and the first quotient goes to zero almost surely. Observing that $E(\delta_t) \leq E(\tau^{(0)}) < \infty$, we have that the denominator of the second quotient converges to a constant almost surely, and the numerator is bounded in probability. So, the term on the right side of the above display converges to zero in probability. A similar argument verifies that $\sqrt{a_t}d_t \to 0$ in probability.

So,

$$\sqrt{a_t}\left(\frac{X(t)}{t} - \frac{L}{E\tau^{(0)}}\right) = \sqrt{a_t}\left(c_t\frac{L}{\overline{\tau}} + d_t - \frac{L}{E\tau^{(0)}}\right) \tag{59}$$

will have the same limit distribution as

$$\sqrt{a_t}\left(\frac{L}{\overline{\tau}} - \frac{L}{E\tau^{(0)}}\right) \tag{60}$$

Now, let $g(z) = \frac{L}{z}$. Using a Taylor expansion, we can see that

$$g(\overline{\tau}) = g(E\tau^{(0)}) + g'(y)(\overline{\tau} - E\tau^{(0)}) \tag{61}$$

where y is a random variable with $|y - E\tau^{(0)}| \leq |\overline{\tau} - E\tau^{(0)}|$. Rearranging terms and multiplying both sides by $\frac{\sqrt{a_t}}{\varsigma}$, we get

$$\frac{\sqrt{a_t}}{\varsigma}\left(g(\overline{\tau}) - g(E\tau^{(0)})\right) = g'(y)\sqrt{a_t}\left(\frac{\overline{\tau} - E\tau^{(0)}}{\varsigma}\right) \tag{62}$$

Now, $g'(y)$ converges in probability to $g'(E\tau^{(0)})$ since g' is continuous on $(0,\infty)$, $E(\tau^{(0)}) > 0$ (See (19)) and $|\overline{\tau} - E\tau^{(0)}|$ converges to zero in probability. Now, we will show that the remainder of the RHS converges weakly to $N(0,1)$. Note that

$$\sqrt{a_t}\left(\frac{\overline{\tau} - E\tau^{(0)}}{\varsigma}\right) \tag{63}$$

will have the same weak limit as

$$\frac{S_{n_t} - n_t E\tau^{(0)}}{\varsigma\sqrt{a_t}} \tag{64}$$

The latter is the former after multiplying by $\frac{n_t}{a_t}$ which converges almost surely to one. Define

$$S'_k \doteq S_k - kE\tau^{(0)} \tag{65}$$

We will now show that

$$\left|\frac{S'_{\lfloor a_t \rfloor}}{\varsigma\sqrt{a_t}} - \frac{S'_{n_t}}{\varsigma\sqrt{a_t}}\right| \to 0 \text{ in probability.} \tag{66}$$

This will imply that the two terms have the same weak limit. Also, notice that since $\tau^{(i)}$ are i.i.d. with finite second moment, the first term converges to $N(0,1)$ by the classical central limit theorem. Fix t and arbitrary $\epsilon > 0$,

$$\begin{aligned} P\left[\left|\frac{S'_{\lfloor a_t \rfloor}}{\varsigma\sqrt{a_t}} - \frac{S'_{n_t}}{\varsigma\sqrt{a_t}}\right| \geq \epsilon\right] &\leq \frac{Var(S'_{\lfloor a_t \rfloor} - S'_{n_t})}{\varsigma^2 a_t \epsilon^2} \\ &\leq \frac{\varsigma^2 E|\lfloor a_t \rfloor - n_t|}{\varsigma^2 a_t \epsilon^2} = \frac{E\left|\frac{\lfloor a_t \rfloor}{a_t} - \frac{n_t}{a_t}\right|}{\epsilon^2} \end{aligned}$$

Wald's equality gives us the second inequality from the first. The renewal theorem [5] implies that, $\frac{n_t}{t} \to \frac{1}{E\tau^{(0)}}$ a.s. Thus, $\frac{n_t}{a_t} \to 1$ with probability one and in L^1, thus the right side above converges to zero as $t \to \infty$ for every ϵ. Combining (66) with the remark regarding the asymptotic equality of laws of terms in (63) and (64) we have that

$$\sqrt{a_t}\left(\frac{\overline{\tau} - E\tau^{(0)}}{\varsigma}\right) \Rightarrow N(0,1). \tag{67}$$

Finally, using (62) and (60)

$$\frac{\sqrt{a_t}}{\varsigma}\left(\frac{X(t)}{t} - \frac{L}{E\tau^{(0)}}\right) \Rightarrow N(0, (g'(E\tau^{(0)}))^2) \tag{68}$$

which immediately yields that

$$\frac{(E\tau^{(0)})^{3/2}\sqrt{t}}{L\varsigma}\left(\frac{X(t)}{t} - \frac{L}{E\tau^{(0)}}\right) \Rightarrow N(0,1) \tag{69}$$

■

2.2 Numerical Methods for the Diffusion Ratchet

As was seen in Theorem 2.2, if the drift and diffusion coefficients are constant, one can do various moment calculations explicitly. However, in the case of state varying coefficients exact calculations are not possible, and thus one needs to resort to numerical approximations. There are three principle numerical methods we will explore for use with the diffusion ratchet. Each method will be briefly discussed, then we will move on to detailed discussions and computational results for each. There will be special attention paid to calculations concerning hitting times of reflected diffusion processes. This is important because of the relationship, proved in Theorem 2.10, between hitting times and asymptotic velocity.

1. **Path Simulation.** The Euler method or some higher order method for the numerical solution of diffusion processes can be adapted to reflected versions. This method is simple to program and is easily adapted to obtain results for hitting times and other functionals of the process. However, it is computationally intensive, since many simulations of the path must be performed and averaged over to get relatively stable results. Moreover, the results would differ if the numerical procedure is repeated (with a new random seed). Error estimates are difficult to obtain.

2. **Markov Chain Approximation.** It is well known that a reflected diffusion process can be approximated in law by a suitably scaled discrete time- discrete state Markov chain [11]. This means that the expected value of a continuous (in $D([0, \infty) : \mathbb{R}_+)$) functional of the linearly interpolated discrete time Markov chain will converge to the expected value of the corresponding functional of the limit diffusion process as the parameters in the time and state discretization approach their limits. So, in practice one can do calculations on an appropriately chosen Markov chain (discrete in time and state) to obtain numerical approximations for the expected value of functionals of the limit diffusion process. In particular, this method can be used for numerical calculations of the expected hitting times for reflected diffusion processes. One drawback is that in this method one needs to calculate the whole probability distribution of the Markov chain, at each time instant, even though one is interested in the expected value of a very specific functional of the Markov chain. In practice, this means that the numerical procedure requires repeated multiplication of large matrices. On the plus side, this is a method well-suited for a bounded state space, which is the situation that we have in the computation of the expected hitting time. Another benefit is that it is often possible to obtain a rigorous evaluation of the procedure such as rates of convergence and error bounds. Furthermore, since one computes exactly the expected values for the approximating Markov chain, unlike path simulation, there is no random number generation and thus repeated calculations will yield identical results.

3. **Linear Programming.** The third method is a rather novel approach to the calculation of moments of hitting times for Markov processes[9]. In this approach one considers

the occupation measure (until the hitting time) of the Markov process and formulates various linear conditions that are satisfied by its moments as constraints in a linear program. The conditions satisfied by the moments are obtained using the martingale characterization of a Markov process via its generater. Furthermore, one can introduce the Hausdorff moment conditions, which are satisfied by moments of any probability measure, as additional constraints in the linear program. The key observation is that, under suitable conditions, the moments of the hitting time can be expressed in terms of the moments of the occupation measure. Thus, in particular, one can use the expected hitting time as the objective function and a subset of the linear moment conditions as constraints to formulate a linear programming problem. By maximizing and minimizing the objective function, under the constraints, one obtains upper and lower bounds for the expected hitting times. If one uses only a few moment conditions as constraints, the interval determined by the lower and upper bound is rather large and thus not very informative about the true value of the expected hitting time. However, in many applications, the interval is seen to shrink dramatically as additional moment conditions are introduced as constraints in the linear program.

We now discuss each of the methods in a greater detail.

1. The Path Simulation technique is appealing on intuitive grounds. We want to simulate

$$X(t) = x_0 + \int_0^t b(X(s))ds + \int_0^t a(X(s))dW_s + l(t) \tag{70}$$

We will use an Euler type method where we simply start at x_0, choose a small $\delta > 0$ and simulate an approximation for the value of X at δ. Then using this estimate for $X(\delta)$, we approximate the value of X at 2δ and so on. We will denote the simulated sequence by $\{Z_i\}_{i\geq 1}$, where Z_i is the simulated approximation of $X(i\delta)$. The equations used to generate $\{Z_i\}_{i\geq 1}$ are as follows.

$$\begin{aligned} Z_0 &= x_0 \\ Z_{i+1} &= (Z_i + b(Z_i)\delta + a(Z_i)N(0,\delta))^+ \end{aligned}$$

where $N(0,\delta)$ is a simulated normal random variable, independent of previous variables, with mean 0 and variance δ. We will simulate until $Z_i \geq L$. This yields a simulated approximate value for τ as $\delta \times i$, where i is the time step at which Z exits $[0, L)$. Path simulation can be improved by adapting many of the other classical methods for solving ODEs. Clearly, one must perform many calculations to get a single simulation from the approximate hitting time distribution. By repeating these steps a large number of times one can obtain an approximation for the mean of τ.

2. In the Markov Chain approximation method, one first writes down a discrete time-discrete state Markov chain which well approximates the probability law of $X(\cdot \wedge \tau)$, where $\tau \doteq \inf\{t : X(t) = L\}$ and $X(\cdot)$ is given by (70). This approximating chain, denoted by $\{Z_i^n\}_{i\geq 1}$, where n is the discretization parameter, will have the state space: $\{\frac{j}{n} : j \in I\!N_0, j \leq nL\}$. The transition probabilities of the approximating chain are given as follows. For $z = \frac{j}{n}$, $j \in \{1, 2, \cdots, L(n-1)\}$,

$$
\begin{aligned}
p_n(z, z+\frac{1}{n}) &= \frac{\frac{a^2(z)}{2} + \frac{b^+(z)}{n}}{S} \\
p_n(z, z-\frac{1}{n}) &= \frac{\frac{a^2(z)}{2} + \frac{b^-(z)}{n}}{S} \\
p_n(z, z) &= 1 - p_n(z, z+\frac{1}{n}) - p_n(z, z-\frac{1}{n}), \qquad (71)
\end{aligned}
$$

where $S \doteq \sup_{x\in[0,L)}(\frac{a^2(x)}{2} + |b(x)|)$. For the lowest state the transition probabilities are given as

$$
\begin{aligned}
p_n(0, 0+\frac{1}{n}) &= \frac{\frac{a^2(z)}{2} + \frac{b^+(z)}{n}}{S} \\
p_n(0, 0) &= 1 - p_n(0, 0+\frac{1}{n}) \qquad (72)
\end{aligned}
$$

The highest state is absorbing and so returns to itself with probability one, namely

$$p_n(L, L) = 1. \qquad (73)$$

Adapting techniques from chapter 5 of [11], one can show that if one linearly interpolates the above Markov chain with time intervals of length $\Delta t_n \doteq \frac{1}{n^2 S}$ then the resulting continuous time process converges weakly to $X(\cdot \wedge \tau)$. From this it follows that if $\tau_n \doteq \inf\{j : Z_j^n = L\}$ then

$$\frac{1}{n^2 S} E(\tau_n) \to E(\tau).$$

Thus one can approximate $E(\tau)$ by computing $E(\tau_n)$. Next note that

$$
\begin{aligned}
E(\tau_n) &= \sum_{i=1}^{\infty} P(\tau_n > i) \\
&= \sum_{i=1}^{\infty} (1 - P(\tau_n \leq i)) \\
&= \sum_{i=1}^{\infty} (1 - P(Z_i^n = L)),
\end{aligned}
$$

where the last step follows on recalling that L is an absorbing state for the Markov chain. Thus one can find $E(\tau_n)$ by computing $P(Z_i^n = L)$ for $i \geq 1$. In practice, of course, one will truncate the above infinite sum to finitely many terms. Since Z_i^n is a finite state Markov chain, one can compute $P(Z_i^n = L)$ by multiplying the probability law vector of Z_{i-1}^n by the transition probability matrix defined by (71), (72), (73).

3. Finally, we describe the linear programming method. We begin by observing that (70) can be rewritten as

$$X(t) = x_0 + \int_0^t b(X(s))ds + \int_0^t a(X(s))dW_s + \ell(t), \tag{74}$$

where $\ell(t)$ is an increasing process satisfying

$$\ell(t) = \int_0^t 1_{\{X(s)=0\}} d\ell(s).$$

Let τ be as before, i.e., $\inf\{t : X(t) = L\}$. Let $f \in C^2(\mathbb{R}_+)$. Then an application of Itô's formula gives

$$f(X(t \wedge \tau)) = f(x_0) + \int_0^{t\wedge\tau} Af(X(s))ds + \int_0^{t\wedge\tau} f'(Z(s))dW(s) + f'(0)\ell(t \wedge \tau), \tag{75}$$

where A is the infinitesimal generator of the diffusion given as follows.

$$Af(x) \doteq \frac{1}{2}a^2(x)\frac{\partial^2 f}{\partial x^2} + b(x)\frac{\partial f}{\partial x}.$$

Taking expected value in (75) we have that

$$Ef(X(t \wedge \tau)) = f(x_0) + E\int_0^{t\wedge\tau} Af(X(s))ds + f'(0)E\ell(t \wedge \tau). \tag{76}$$

Recalling that $E(\tau) < \infty$, we have taking limit as $t \to \infty$ that

$$f(L) = Ef(X(\tau)) = f(x_0) + E\int_0^{\tau} Af(X(s))ds + f'(0)E\ell(\tau). \tag{77}$$

Now define a finite measure μ_0 on $(\mathbb{R}_+, \mathcal{B}(\mathbb{R}_+))$ as follows.

$$\mu_0(B) \doteq E\left[\int_0^{\tau} I_B(X(s))ds\right], \quad B \in \mathcal{B}(\mathbb{R}_+).$$

Note that $\mu_0(B)$ is the expected amount of time the process spends in set B before the hitting time τ, and $\int_{E_0} \mu_0(dy) = E\tau$. In terms of μ_0, (77) can be rewritten as

$$\int_{[0,L]} Af(x)\mu_0(dx) + f(x) - f(L) + f'(0)\vartheta, \tag{78}$$

where $\vartheta \doteq E\ell(\tau)$. Suppose now that the coefficients $a(x)$ and $b(x)$ are polynomials of the form $\sum_{j=0}^{p} a_j x^j$, $\sum_{j=0}^{p} b_j x^j$ for $x \in [0, L]$. In practice, one can always approximate general coefficients a and b by such monomials. If we take f in (78) to be a monomial then the above equation can be rewritten in the form

$$\sum_{i=0}^{n} c_i m_i + \vartheta\, d + \kappa = 0 \qquad \mathbf{(M)}$$

where

$$m_k = \int x^k \mu_0(dx)$$

for $k = 0, 1, 2, ...$ and n, c_i, d, κ are constants which depend on f and can be written explicitly. Note that $m_0 = E\tau$.

Equation (**M**) gives a set of linear conditions which the parameters $\{\{m_i\}_{i\geq 1}, \vartheta\}$ must satisfy. One can obtain additional constraints on these parameters on considering the Hausdorff moment conditions for the sequence $\{m_i\}$ which say that

$$\sum_{j=0}^{n} (-1)^j \binom{n}{j} \frac{m_{j+k}}{L^{j+k}} \geq 0. \qquad \mathbf{(H)}$$

One can now formulate the following linear programming problems.

$$\begin{cases} \textbf{maximize} & m_0 \\ \textbf{subject to:} & \mathbf{(M)} \text{ and } \mathbf{(H)}. \end{cases} \tag{79}$$

$$\begin{cases} \textbf{minimize} & m_0 \\ \textbf{subject to:} & \mathbf{(M)} \text{ and } \mathbf{(H)}. \end{cases} \tag{80}$$

Note that (**M**) and (**H**) contain infinitely many linear constraints and in practice one takes a finite sub-collection (say, of cardinality k) of these constraints. The value of the two linear programs, denoted by $\overline{m}_k$ and $\underline{m}_k$, respectively, must satisfy the condition

$$\overline{m}_k \;\geq\; E(\tau) \;\geq\; \underline{m}_k.$$

As k becomes larger and larger, these upper and lower bounds for $E(\tau)$ become tighter and tighter yielding good approximations for $E(\tau)$.

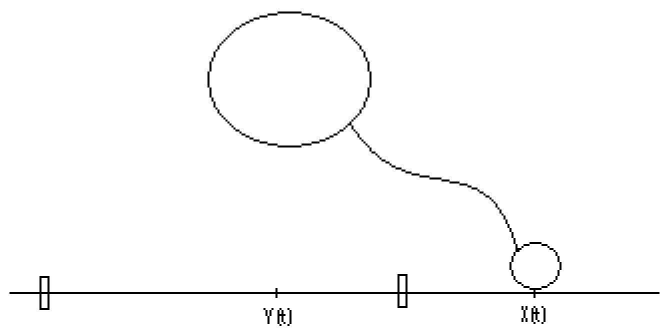
The following are some sample calculation using these methods. They are the estimated expected value for the hitting time for $L = 2$ and a variety of drift and diffusion coefficents. These are compared with the true expected value obtained from theorem .

sigma	mean	true value	simulation	Markov	lp lower	lp upper
1	0	4	4.4302	3.9596	4	4
1	1	1.50916	1.5984	1.4899	1.50916	1.50916
1	2	0.875042	0.9104	0.8647	0.874934	0.875115
1	3	0.611111	0.6404	0.6041	0.610081	0.612025
1	-1	24.7991	29.7683	22.749	24.799	24.7992
1	-2	371.495	-	-	369.484	374.446
1	-3	9041.21	-	-	7231.72	19592.1
1	6	0.319444	29.7683	0.3158	0.305782	0.332666
2	1	0.735759	0.8270	0.7267	0.735759	0.735759
2	-1	1.43656	1.7643	1.4091	1.43656	1.43656

There are a few important things to notice. First, the linear programming approach gives very good results for most of the parameter values. Though performance depreciates for large negative drift with the number of constraints held constant. This can be remedied by increasing the number of constraints. For instance in the case of sigma equal to 1 and drit of -3, the interval changes from (7231.72, 19592.1) to (9037.2, 9058.67) when the number of constraints is increased from 194(the number used for the other cases) to 320. However, this increase rather dramatically increases the computation time. For a diffusion parameter of 1 and drift of -2 and -3, the simulation and Markov chain approaches become unwieldy. The first method is poor because of the length of time on average it takes to reach a level of 2 for these negative drifts. The calculations were done by attempting to take 5,000 paths with a time discretization of 0.005. Even attempting to simulate 500 paths at a discretization of 0.5 took several hours using matlab on a Sun Ultra 10 workstation for the case of sigma equal to 1 and mean of -2. The resulting approximation was more than an order of magnitude away from the true value. For the Markov chain approach one needs to multiply the transition matrix until the chain is mostly absorbed at the level L. The following calculations were done with a space discretization of 21 states (states a distance of 0.2 apart from 0 to 2). Again, this takes a tremendous number of calculations when the drift is negative. For positive drift, 100,000 transitions were sufficient for the chain to be absorbed. For negative drift, a half million transitions were necessary to be "mostly absorbed", i.e. the chain is in the absorption state with a probability greater than 0.95.

3 Proposal for Future Work.

One of the primary functions of biological motors is the intracellular transport of cargos. Frequently, the linkage between the motor and cargo is modeled as a linear spring. Our goal in the proposed work is to study the stochastic dynamical system that describes the evolution of the pair stochastic process: $(X(\cdot), Y(\cdot))$, where $X(t)$ represents the location of the motor and $Y(t)$ represents the projection of the position of the cargo onto the the x-axis, i.e. the linear track along which the motor is moving. The following picture may help illustrate what we have in mind.



Discrete Space Model. We will begin by describing the natural discrete state Markov process $(X_n(t), Y_n(t))$ for the dynamics of the Motor-Cargo pair. The state space for this Markov process will be $\overline{S}_n \doteq S_n \times \tilde{S}_n$, where, $S_n \doteq \{\frac{Lj}{n} : j \in I\!N\}$ and $\tilde{S}_n \doteq \{\frac{Lj}{n} : j \in \mathcal{Z}\}$. Once more, ratchet sites are located on the track at equally spaced intervals of length L; when the motor is at a "non-ratchet" site it can either move to the left or to the right in steps of size L/n, however, when the motor is at a ratchet site, it can only move to the right. The cargo (more precisely, "the projection of its location on the x -axis"), on the other hand, is free to move to the left or to the right, at every site. The fact that the cargo is typically much larger than the motor is modeled by saying that the jump rates for the first component of the Markov process are much higher than that of the second component. The probabilities of jumps to the right (and of jump to the left) take the linear spring action into account. For example, given that the motor jumps at an instant when $(X_n(t), Y_n(t)) \equiv (x, y)$, and $x - y$ is a large positive number, the probability that the jump is to the left is much higher than the probability of jump to the right, the difference in probabilities being propotional to $x - y$. In general the dynamics of the Markov process will be described via jump rates $(\lambda_n^X(x,y), \lambda_n^Y(x,y))$ for the two components of the process and probabilities of jumps to the right: $(p_n^X(x,y), p_n^Y(x,y))$.

The Diffusion Model and Weak Convergence. Our next step will be to study the diffusion limit of the above Markov chain, as $n \to \infty$. In the limit, one would expect to obtain a diffusion ratchet, representing the dynamics of the biological motor, which is coupled with an unconstrained diffusion process representing the cargo. More precisely, we will like to prove that as $n \to \infty$, $(X_n(\cdot), Y_n(\cdot))$ converges weakly, in $D([0,\infty) : I\!R_+ \times I\!R)$ to the process $(X(\cdot), Y(\cdot))$, with paths in $C([0,\infty) : I\!R_+ \times I\!R)$, given as the solution of the following equations. For $t \in [0, \infty)$

$$\begin{cases} Y(t) = & y_0 + \int_0^t b_1(X(s), Y(s))ds + \int_0^t a_1(X(s), Y(s))dB(s), \\ X^{(i)}(t) = & \Gamma_i \left(iL + \int_0^{\cdot} b_2(X^{(i)}(s), Y(s + \sigma^{(i)}))ds + \int_0^{\cdot} a_2(X^{(i)}(s), Y(s + \sigma^{(i)}))dW^{(i)}(s) \right)(t), \\ \tau^{(i)} \doteq & \inf\{t : X^{(i)}(t) = (i+1)L\}, \quad \sigma^{(i)} \doteq \tau^{(i-1)} + \sigma^{(i-1)} \\ X(t) \doteq & X^{(i)}(t - \sigma^{(i)}); \quad t \in [\sigma^{(i)}, \sigma^{(i+1)}), \quad i \in I\!N_0, \end{cases} \tag{81}$$

where $W^{(i)}(\cdot)$ is, as before, a sequence of independent Wiener processes defined on some probability space $(\Omega, \mathcal{F}, P)$, $B(\cdot)$ is another independent Wiener process defined on $(\Omega, \mathcal{F}, P)$, Γ_i is defined via (14) and a_i, b_i; $i = 1, 2$ are suitable coefficients.

In the simplest setting of a linear spring with no external forcing, one would expect, for $(x, y) \in I\!R_+ \times I\!R$,

$$b_1(x,y) = -\beta_1(x - y), \quad b_2(x,y) = -\beta_2(x-y), \quad a_1(x,y) = \alpha_1, \quad a_2(x,y) = \alpha_2. \tag{82}$$

We will refer to the above special case, for obvious reasons, as the "Ornstein-Uhlenbeck model".

Asymptotic Velocity. As stated earlier in the proposal, one of the main quantities of interest is the asymptotic velocity of the motor. In the cargo-less case, with periodic coefficients, the analysis of the asymptotic velocity was facilitated via a "regeneration argument" on observing that every time the motor reaches the ratchet site, the process starts afresh. This enabled us to show that $Z^{(i)}(\cdot) \doteq X^{(i)}((\cdot + \sigma^{(i)}) \wedge \sigma^{(i+1)}) - iL$ are i.i.d. processes where $\sigma^{(i)}$ are given by (18). This was the key step in the study of the asymptotic velocity.

In the current setting of motor with cargo the situation is much more complex. The main difficulty is that each time the motor travels from one ratchet site to next, i.e. moves to the right by L units, the cargo may move by a different amount, thus destroying the periodicity structure. However, at least in the Ornstein-Uhlenbeck model one expects that the distance between the motor and cargo stabilizes rather rapidly around a stationary distribution thus giving some hope for the asymptotic analysis of the velocity of the motor. More precisely, consider the Markov chain

$$Z_i \doteq (\tau^{(i-1)}, Y(\sigma^{(i)}) - iL)$$

representing the time taken by the motor to move from the $(i-1)L$ to iL and the distance between the cargo and motor when the motor reaches the i-th ratchet site. We expect that for the Ornstein-Uhlenbeck model this Markov chain is ergodic and thus admits a unique invariant measure. One of our goals is to prove this statement. Once proved, this will in particular show that,

$$\frac{1}{n}\sum_{i=1}^{n} \tau_i \to \int_{[0,\infty)\times I\!R} t\eta(dt\ dx) \quad \equiv E_\eta(\tau), \tag{83}$$

where η is the unique invariant measure of the Markov chain $\{Z_i\}$. From (83) one can readily show, as in Theorem 2.10, that asymptotic velocity of the motor exists (in the sense of Section 2.1) and equals $\frac{L}{E_\eta(\tau)}$.

Numerical approximation for asymptotic velocity. Since it is not possible to write down the invariant measure of $\{Z_i\}$ explicitly, one needs to use numerical methods for approximating the asymptotic velocity. We begin by noticing that one can decompose $\eta(dt\ dx)$ as $\eta_1(dt,\ x)\eta_2(dx)$, where η_2 is the unique invariant measure of the Markov chain $\{U_i\} \doteq \{Y(\sigma^{(i)}) - iL\}$. This enables us to write

$$E_\eta(\tau) = \int_{I\!R}\left(\int_{[0,\infty)} t\eta_1(dt,\ x)\right)\eta_2(dx). \tag{84}$$

Note that for a fixed $x \in I\!R$, $\int_{[0,\infty)} t\eta_1(dt\ x)$ is the expected hitting time, of the first ratchet site, i.e. L, by the motor which starts at origin with the cargo initially at x. This expected hitting time can be approximated by using one of the numerical schemes discussed in Section 2.2. Next, one needs to approximate $\int_{I\!R} g(x)\eta_2(dx)$, where $g(x) \doteq \int_{[0,\infty)} t\eta_1(dt\ x)$. For this, one needs to approximate the invariant measure $\eta_2(dx)$. A natural way for approximating this invariant measure is via "particle methods". One of the simplest form of such a method is the following.

(i) Choose some convenient initial distribution for the chain $\{U_i\}$.

(ii) Generate N independent observations from the chosen initial distribution, say $\{y_1, \cdots, y_n\}$.

(iii) Evolve the N observations $\{y_1, \cdots, y_n\}$ according to the stochastic dynamical system:

$$\begin{cases} Y^i(t) = & y_i - \beta_1 \int_0^t (Y^i(s) - X^i(s))ds + \alpha_1 B(t), \\ X^i(t) = & \Gamma\left(-\beta_2 \int_0^{\cdot} (X^i(s) - Y^i(s))ds + \alpha_2 W(\cdot)\right)(t), \\ \eta_i = & \inf\{t : X^i(t) = L\} \end{cases} \tag{85}$$

In practice, one will have to discretize the above system, using for example an Euler scheme, in order to approximate the solution of the SDEs.

(iv) Define $y_i \doteq Y_i(\eta_i)$, $i = 1, 2, \cdots N$.

(v) Repeat Step (iii) with the new values of $\{y_1, \cdots, y_n\}$.

After, repeating the above steps a large number of times one can approximate the invariant measure of $\{U_i\}$ via the empirical measure $\frac{1}{N}\sum_{i=1}^N \delta_{y_i}$. One can also consider various refinements of the above particle method. A natural and convenient initial distribution for step (i) above will be the invariant measure of an Ornstein-Uhlenbeck process:

$$d\theta_t = -(\beta_1 + \beta_2)\theta_t dt + \sqrt{(\alpha_1^2 + \alpha_2^2)}dW(t),$$

where $W(\cdot)$ is a standard Wiener process.

The Fast Motor Limit. As stated earlier, frequently the biological motors are much smaller than the cargos that they are transporting. Thus it becomes reasonable to approximate the above coupled system by a single "averaged" equation, describing the dynamics of the cargo, which arises in the limit as the dynamics of the motor become faster and faster in comparison to the cargo. More precisely, consider the system (81) and suppose that the coefficients b_2, a_2 are given as follows.

$$b_2(x,y) \equiv \frac{1}{\epsilon}\tilde{b}_2(x,y), \quad a_2(x,y) \equiv \frac{1}{\sqrt{\epsilon}}\tilde{a}_2(x,y).$$

Denote the corresponding solution of the system (81) by $(X_\epsilon(\cdot), Y_\epsilon(\cdot))$. Note that as ϵ becomes smaller and smaller the dynamics of the motor become faster and faster. We are interested in examining the limit of the process $Y_\epsilon(\cdot)$ as $\epsilon \to 0$. One expects, in analogy with the classical averaging results [16] that, as $\epsilon \to 0$, $Y_\epsilon(\cdot)$ converges weakly in $C([0,\infty) : I\!R)$ to a diffusion process given by a SDE of the form.

$$\hat{Y}(t) = y_0 + \int_0^t \hat{b}_1(\hat{Y}(s))ds + \int_0^t \hat{a}_1(\hat{Y}(s))dB(s),$$

for a suitable choice of coefficients $\hat{a}_1, \hat{b}_1$. The key advantage of the above limit equation is that unlike the cargo dynamics in (81), it is not coupled with any other stochastic dynamical system. Thus the study of asymptotic velocity of the process given by this averaged equation is comparatively simpler. We will like to study the asymptotic velocity of this process, i.e. $\lim_{t\to\infty} \frac{Y(t)}{t}$, which should be a good approximation for the asymptotic velocity of the cargo/motor system when the motor is much smaller in comparison to the cargo. We will study the above asymptotic velocity by both analytical and numerical methods.

Parameter Estimation and Filtering Problems. One of the main difficulties in the study of biological motors is that usually they are too small to be observed directly. However, recent advances in microbiological techniques have enabled the observations of the cargos that are being pulled by such motors. Thus a natural question one will like to address is whether one can infer properties of the dynamics of the motors from the observed dynamics of the cargos. In practice, one would be interested in obtaining parameter estimates of various coefficients in the model, distance between ratchet sites, location of ratchet sites etc. Furthermore, one may want to infer about the current location of the motor from past and current observations. We will address these state and parameter estimation questions by using the classical Bayesian formulation of nonlinear filtering.

More precisely, consider the model described in (81) with the coefficients given via (82). Let $\theta \doteq (L, \beta_1, \beta_2, \alpha_1, \alpha_2)$. Assume that θ takes values in some parameter space Θ. The goal of the filtering problem is to estimate $(X(t), \theta)$ based on the observations $\{Y(s) : 0 \le s \le t\}$. We will begin by putting a suitable prior distribution on the parameter space Θ and consider the augmented Markov process $(X(t), \theta(t), Y(t))$, where $\theta(t) \equiv \theta$. Denote the conditional distribution of $(X(t), \theta(t))$ given $\sigma\{Y(s) : 0 \le s \le t\}$ by $\Pi_t(dy,\ d\vartheta)$. The best estimator of $(X(t), \theta)$ (in the least square sense) based on the observations : $\{Y(s) : 0 \le s \le t\}$ is given as

$$\left(\int_{I\!R_+\times\Theta} x\Pi_t(dx,\ d\vartheta),\ \int_{I\!R_+\times\Theta} \vartheta\Pi_t(dx,\ d\vartheta)\right). \tag{86}$$

In order to numerically approximate these conditional moments we will begin by (time) discretizing the model in (81). This leads us to a Markov chain: $(X_n^\epsilon, \theta_n^\epsilon, Y_n^\epsilon)_{n\ge 1}$ which when suitably interpolated converges weakly to $(X(\cdot), \theta(\cdot), Y(\cdot))$ as $\epsilon \to 0$. Denote by $\Pi_n^\epsilon(dx,\ d\vartheta)$ the conditional distribution of $(X_n^\epsilon, \theta_n^\epsilon)$ given $\mathcal{Y}_n \doteq \sigma\{Y_m^\epsilon : 0 \le m \le n\}$. Then the conditional moments in (86) can be approximated by

$$\left(\int_{I\!R_+\times\Theta} x\Pi_n^\epsilon(dx,\ d\vartheta),\ \int_{I\!R_+\times\Theta} \vartheta\Pi_n^\epsilon(dx,\ d\vartheta)\right) \tag{87}$$

for a suitable choice of n. In order to compute Π_n^ϵ the following recursion formula will be useful. We will suppress ϵ from the notation. Let $p(x_1, \vartheta_1, y_1 | dx_2, d\vartheta_2, dy_2)$ denote the transition probability function of the Markov chain (X_n, θ_n, Y_n). Then for suitable test functions h

$$\begin{aligned} \int h(x, \vartheta) \Pi_n(dx, d\vartheta) &= c \cdot \int h(x, \vartheta) p(x_1, \vartheta_1, Y_{n-1} | dx, d\vartheta, dy) \\ &\quad f_{Y_n | \mathcal{Y}_{n-1}, (X_n, \theta_n) = (x, \vartheta)}(Y_n) \Pi_{n-1}(dx_1, d\vartheta_1), \end{aligned}$$

where c is the normalizing constant, $f_{Y_n | \mathcal{Y}_{n-1}, (X_n, \theta_n) = (x, \vartheta)}$ is the conditional density of Y_n given $\mathcal{Y}_{n-1}$ and $(X_n, \theta_n) = (x, \vartheta)$. The integration on the right side of the above display will be done numerically, once more, using particle methods.

The above filtering techniques will first be tested using simulated data. We then hope to analyze laboratory collected data. By comparing simulated data to collected data, we also hope to make some judgment about the plausibility of the ratchet model that has been presented.

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