Research Statement

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Introduction:

My mathematical interests primarily lie in the fields of stochastic processes, stochastic differential equations, operations research, probability theory, and measure theory; in particular, I am concerned with their application to the modeling of physical and biological processes and phenomena. Oftentimes in scientific endeavors, researchers discover systems for which known models cannot explain observable phenomena, particularly when data seem stochastic. I seek to bridge the gap between the scientist's desire to reliably predict information and this new field of noisy data through the construction and careful analysis of qualitative, realistic models. Within my work, I have addressed stochasticity from the macro interaction level to the micro intracellular transport level. My current focus is on describing the behavior of molecular motor proteins through the use of Langevin dynamics and stochastic differential equations.

Completed Work:

Electrostatic Drag and Processive Molecular Motor Transport. One hypothesis for how directionally opposed molecular motors interact to produce intracellular transport is called "microtubule tethering" (see *Intracellular Transport* below). In joint work with Scott McKinley[*], I have investigated the fundamental trade-off of including a tether in processive molecular motor transport. Following [1], we describe the dynamics of a cargo, a weakly bound anchor, and a processing motor complex using stochastic differential equations and a Langevin framework. It remains an open question exactly how a trailing motor or weakly bound anchor interacts with a microtubule; the interaction of charged particles with microtubules, however, can be described as one-dimensional diffusion interspersed with a rapid sequence of transient binding and unbinding events [2]. While transient binding models for diffusive particles are well studied [3, 4], these approaches do not translate to a Newtonian force-balance framework. As such, we account for drag effects in our model by including an electrostatic drag term proportional to the velocity. Additionally, we allow for the possibility that the system does not satisfy the fluctuation-dissipation relationship. We confront this model with available pathwise mean-squared displacement data of cargo and a single weakly bound motor complex [5], and data for a processing motor, cargo, and trailing anchor complex [6], finding evidence for electrostatic drag. Further, we found evidence that the tethering system might not obey fluctuation-dissipation.

[*] *Smith JD and McKinley SA (2018). Assessing the Impact of Electrostatic Drag on Processive Molecular Motor Transport. Bulletin of mathematical biology, 80, 2088–2123.*

Hospital Occupancy Variability. The unpredictable nature of hospital occupancy numbers, often called a census, remains one of the foremost problems of hospital administration. Overcrowding leads to unsafe conditions and low occupancy has severe associated costs. Modeling hospital bed occupancy has been approached through the use of a two stage exponential model [7] and a three stage exponential model [8, 9]. Expanding on these in my master's thesis [10], I create a four-stage model with stochastic admissions and discharges, with rates which depend on the day of the week. I fit my model with data obtained from a university teaching hospital in Adelaide, Australia and determined that surgical admissions contributed the most to the variability of the census.

Work in Progress:

Inferring Motor Parameters through Tensiometer Experiments. Molecular motor parameters, such as the stall force and the unburdened velocity, have a rich history of being estimated through experiments. Many experimenters obtain estimates for these parameters through optical force traps [11, 12, 13]. Due to uncertainties in the number of motors associated with cargo in these experiments, the Hancock lab at the Penn State University have developed a new experimental technique, called a tensiometer (see *Tensiometer Inference* below), in which a single motor steps against a known force-extension profile while the location of a tracking particle is recored by a microscope. In an ongoing work with Scott McKinely[†], we have developed a model approximating the observed process of the recorded tracking particle position. Applying Bayesian techniques, we estimate motor parameters from generated data by calculating the posterior distributions and sampling from

them using various sampling techniques. The major goal of this work is to determine what combinations of motor parameters allow this analysis to work, testing the limitations of the tensiometer experiment.

† *Smith JD and McKinley SA (2018). A Model and Inference for Tensiometer Experiments. Manuscript in progress*.

Transient Binding Events. One of the assumptions made in the microtubule tethering model [14] is that the electrostatic drag term is proportional to the velocity. As previously mentioned, any charged particle can perform one-dimensional diffusion along the microtubule interspersed with a rapid sequence of transient binding and unbinding events [2]. Diffusion models which incorporate transient binding events exist for mucosal interactions [3, 4, 15], as well as for models which have applications to protein diffusion with transient binding to cytoskeleton elements [16]. However, none of these models are concerned with rapid binding and unbinding events applied to one-dimensional diffusion. In this work, I view transient binding sites along the microtubule in two distinct ways. The first of which is to view each binding site as a temporary pulse force which opposes the current direction motion. I take the limit as the magnitude of these pulses goes to zero, while the density of the pulse locations go to infinity and demonstrate that the diffusion process converges to a process with an additional velocity-proportional drag term. The second way to view these transient binding events is to incorporate a staircase potential which switches orientation depending on the direction of travel. Switching potential models have been shown to cause changes in diffusion [17]. In this analysis, I seek to determine if a scaling of the potential's steps in height and frequency will resolve into an additional velocity-proportional drag term.

Molecular Motor Binding and Rebinding. While I have investigated the "cost" of microtuble tethering in the form of electrostatic drag, the microtubule tethering transport model is incomplete without the inclusion of a "benefit" – a increased rebinding rate when a motor is tethered within close proximity of the microtubule. Binding rates of molecular motors to microtubules and individual motor head binding rates have been studied as plain initial binding rates as well as force-dependent initial binding and unbinding rates [18, 19]. Rather than assume a flat rate for binding, I assume a distance dependent binding rate. The primary goal with this research is to determine what type of experiment and data are required in order to recover various types of distance dependent binding rate functions. Rebinding to the microtubule may occur in one of two ways: diffusion-limited and rate-limited. In each scenario, there is a fast process (either the binding or the diffusion) and a slow process (again, either the binding or the diffusion). Each situation requires individual analysis on distance dependent binding rate functions.

Past and Present Work In Greater Detail:

Intracellular Transport.

Intracellular transport refers to the process of active transport of cargoes, such as organelles, mitochondria, melanophores, and others, within cells by molecular motors along cytoskeletal networks. Intracellular transport is typically bidirectional with cargoes exhibiting spurts of anterograde (towards the cell periphery) and retrograde (toward the cell body) movement with non-trivial pauses in between. Microtubules are one type of cytoskeletal track. Microtubules are polarized having both a plus and a minus end; microtubule associated molecular motors typically only travel towards either the plus or the minus end of the microtubule. Anterograde transport is generally accomplished by the plus-end oriented kinesin family of motors, while retrograde transport is driven by minus-end oriented dynein. Dynactin is a helper protein for dynein which mediates travel and allows dynein to attach to cargo [20].

A well known model for the bidirectional movement of cargo along microtubles is the "tug-of-war" model. Under the tug-of-war hypothesis, motor conflict is translated into cargo motion in one of two ways. Either the motors pull each other to stall force, leaving the motor-cargo complex in a stalled, zero-velocity state [21], or the motor-cargo complex has a variable mean velocity dependent on the number of motors attached to the cargo and microtubule simultaneously [22, 23]. While tug-of-war models have enjoyed some success, across multiple in vivo experiments it is a general phenomenon that when one family of directed motors is inhibited, transport by the oppositely directed motors is reduced rather than increased [24].

One possible hypothesis that could explain this phenomenon has been called the *microtubule tethering hypothesis*. This hypothesis originates from the observation that molecular motors can be weakly bound to microtubules while simultaneously not engaged in active stepping and force-generation [24]. Essentially, suppose that there are two motors attached to a cargo; one dynein-dynactin complex, and one kinesin. Further suppose that the dynein-dynactin complex is in this weakly bound state. It is hypothesized that kinesin will drag the weakly bound dynein-dynactin complex towards the plus-end of the microtubule through the motor's connections to the cargo. If the kinesin motor were to detach, the weakly bound dynein-dynactin would tether the cargo and kinesin motor close to the microtubule allowing the kinesin motor to rebind to the microtubule. However, while this tethering effect provides the benefit of rescuing active cargo transport, there is a potential cost. If the kinesin motor is processing with a weakly bound opposing motor in tow, this could introduce an electrostatic drag force and diminish the mean velocity.

We refer to a weakly bound motor which tethers a cargo as an anchor and denote it's one-dimensional position along a microtubule as $Z(t)$. We denote the one-dimensional position of cargo along a microtuble as $X(t)$. Following [1], we begin by developing stochastic differential equations for the cargo and anchor by a balance of forces calculation. We choose to incorporate electrostatic drag in the anchor process by including an additional velocity-proportional drag term, and we also allow for the anchor process to potentially not obey the fluctuation-dissipation relationship. After taking the overdamped limit, the following equations are established:

$$\begin{aligned} \mathrm{d}X(t) &= \frac{\kappa_a}{\gamma_c}\left(Z(t) - X(t)\right)\,\mathrm{d}t + \sqrt{\frac{2k_BT}{\gamma_c}}\,\mathrm{d}W_X(t) \\ \mathrm{d}Z(t) &= \frac{\kappa_a}{q'\gamma_a}\left(X(t) - Z(t)\right)\,\mathrm{d}t + \sqrt{\frac{2k_BTq''}{\left(q'\right)^2\gamma_a}}\,\mathrm{d}W_Z(t). \end{aligned} \tag{1}$$

Here, κ_a is the effective spring constant for the connection between the anchor and the cargo, γ_c is the coefficient of viscous drag, γ_a is the coefficient of viscous drag for the anchor, k_BT is Boltzmann's constant times the absolute temperature, q' is a multiplicative factor which determines how electrostatic drag may modify the velocity-proportional drag term, q'' is a multiplicative factor allowing for the possibility that the anchor process does not obey fluctuation-dissipation, and $W_X(t)$ and $W_Z(t)$ are standard Brownian motion processes for the cargo and anchor respectively. If fluctuation-dissipation were satisfied, then $q'' = q'$.

The existence of a weakly bound state for dynein-dynactin has been observed [5, 25]. Moreover, through a series of experiments on dynein, dynactin, and dynactin sub-components, Culver-Hanlon et al. [5] observed cargo attached to a weakly bound dynactin complex and reported the pathwise mean-square displacement for several paths. In order to begin an estimate for q' and q'' for dynactin using our model, we must calculate the mean-square displacement of System 1. We do so through the following theorem.

Theorem 1. Suppose that a cargo $X(t)$ is bound to $n \geq 1$ identical motors $Z_j(t)$, $j \in \{0, 1, \ldots, n-1\}$ as described by the system

$$\begin{aligned} \mathrm{d}X(t) &= \frac{\kappa_a}{\gamma_c}\sum_{j=0}^{n-1}\left(Z_j(t) - X(t)\right)\,\mathrm{d}t + \sqrt{\frac{2k_BT}{\gamma_c}}\,\mathrm{d}W_X(t) \\ \mathrm{d}Z_j(t) &= \frac{\kappa_a}{q'\gamma_a}\left(X(t) - Z_j(t)\right)\,\mathrm{d}t + \sqrt{\frac{2k_BTq''}{\left(q'\right)^2\gamma_a}}\,\mathrm{d}W_{Z_j}(t). \end{aligned}$$

Then, the asymptotic slope of the mean-square displacement of the cargo $X(t)$ is given by

$$\lim_{t\to\infty}\frac{\mathbb{E}\left[X^2(t)\right]}{t} = 2k_BT\left(\frac{\gamma_c + \gamma_a q'' n^2}{\left(\gamma_c + \gamma_a q' n\right)^2}\right).$$

Notably, this theorem combined with the asymptotic slope of available data is not enough to isolate q' or q'' and we do not have enough information to parametrize the system. However, one can use data from motor processing events to obtain a second assessment of the system. To that end,

we develop a new system incorporating a processing motor $Y(t)$ assumed to attach to the cargo and obey a linear force-velocity curve:

$$\mathrm{d}Y(t) = \nu_m \left(1 - \frac{\kappa_m \left(Y(t) - X(t)\right)}{F_m^*}\right) \mathrm{d}t + \sigma_m \left(X(t), Y(t)\right) \mathrm{d}W_Y(t), \tag{2}$$

where ν_m is the unloaded velocity of the motor, F_m^* is the stall force of the motor, κ_m is the effective spring constant of the connection between the motor and the cargo, $\sigma_m \left(X(t), Y(t)\right)$ is the force-diffusivity curve for the motor, and $W_Y(t)$ is a standard Brownian motion.

Culver-Hanlon et al. [5] further report the asymptotic velocity of cargo pulled by dynein both with and without dynactin. By calculating the asymptotic velocity of a cargo-motor-anchor system and comparing to this experimental value, we can close in on some estimate for q' and q''. We calculate this velocity by way of the following theorem.

Theorem 2. Suppose that a cargo $X(t)$ is attached to n identical anchors, $n \geq 0$, and m identical motors, $m \geq 1$ as described by the system

$$\begin{aligned}
\mathrm{d}X(t) &= \left(\sum_{i=1}^{m} \frac{\kappa_m}{\gamma_c} \left(Y_i(t) - X(t)\right) - \sum_{j=1}^{n} \frac{\kappa_a}{\gamma_c} \left(X(t) - Z_j(t)\right)\right) \mathrm{d}t + \sqrt{\frac{2K_BT}{\gamma_c}}\, \mathrm{d}W_X(t) \\
\mathrm{d}Y_i(t) &= \left(\nu_m - \frac{\nu_m \kappa_m}{F_m^*} \left(Y_i(t) - X(t)\right)\right) \mathrm{d}t + \sigma_m \left(X(t), Y_i(t)\right) \mathrm{d}W_{Y_i}(t) \\
\mathrm{d}Z_j(t) &= \frac{\kappa_a}{q'\gamma_a} \left(X(t) - Z_j(t)\right) \mathrm{d}t + \sqrt{\frac{2k_BTq''}{\left(q'\right)^2 \gamma_a}}\, \mathrm{d}W_{Z_j}(t).
\end{aligned}$$

Then, the asymptotic velocity of the cargo is given by

$$\lim_{t\to\infty} \frac{\mathbb{E}\left[X(t)\right]}{t} = \frac{\nu_m}{1 + \dfrac{\nu_m q' \gamma_a n}{F_m^* m} + \dfrac{\nu_m \gamma_c}{F_m^* m}}.$$

By combining Theorems 1 and 2 along with the pathwise mean-square displacement and asymptotic velocity data in [5], we are able to estimate

$$\frac{q''}{q'} \approx \frac{1}{17}. \tag{3}$$

Provided that this estimate is accurate, then this is strong evidence against the idea that fluctuation-dissipation holds when we include electrostatic drag in our model.

Further in [14], we explore the consequences of assuming both fluctuation-dissipation and an electrostatic drag term and compare predictions of this model with available dynein-dynactin data [5] and available kinesin-myosin data [6].

Resolution of Electrostatic Drag through Transient Binding Events.

As previously mentioned, a large assumption made in the construction of the microtubule tethering model is that electrostatic drag is an additional drag term proportional to the velocity. While this model deals with weakly bound molecular motors, it has been observed that any charged particle can bind loosely to a microtubule and diffuse along its length in a directionally unbiased manner [2]. It is expected that the particles bind to and from the microtubule in a sequence of rapid events with diffusion occurring when the particle receives enough energy to escape the potential well of binding sites, but not enough to escape the microtubule's potential valley.

It is unclear from this alone that the sequence of rapid transient binding events will resolve to an effective drag force proportional to the velocity of the particle. The purpose of this project is to investigate various models for transient binding of particles in order to prove whether or not these models asymptotically yield an effective drag term proportional to the velocity.

Recent laboratory methods have made it possible to monitor several types of transient binding events. Chen et al. [26] encapsulated nanoparticles in a lipid shell and use dark-field microscopy to both increase the number of transient binding events and quantify their interaction. Also, Okada and Hirokawa [27] directly observed transient binding of the K-loop mutation single-headed kinesin

KIF1A motor. They hypothesize that the K-loop mutation functions as a mobile tether, allowing the motor domain to perform a serch for the next binding site. The transient binding of the K-loop was found to be weak, but essential for the processivity of the motor. With the increasing number of experiments considering transient binding events of motors and particles, data are ripe for analysis in discovering a mathematical mechanism for transient binding.

One way to mathematically describe transient binding events is to view each site as a discrete opposing pulse. A natural question arises. If the pulses occur more often, but are less and less intense, do the dynamics of the particle limit to an equation with an additional velocity dependent drag term?

Suppose that a particle $x_N(t)$ with mass m is subject to an external force F and viscous drag with coefficient γ. As the particle is being dragged along with forcing F, we want to subject the particle to opposing pulse forces with some regularity. Assume that at regular intervals with increment $1/N$, an opposing pulse force with intensity β/N hits the particle. Then, assuming the particle starts at zero and has initial velocity v_0, it will satisfy for $t \in [0, T]$

$$\begin{aligned} \ddot{x}_N &= \frac{F}{m} - \frac{\gamma}{m}\dot{x}_N - \frac{\beta}{mN}\sum_{i=1}^{TN} \delta\left(x_N - \frac{i}{N}\right) \\ x_N(0) &= 0 \\ \dot{x}_N(0) &= v_0. \end{aligned} \tag{4}$$

Define $x(t)$ on $[0, T]$ as

$$\begin{aligned} \ddot{X} &= \frac{F}{m} - \frac{\gamma+\beta}{m}\dot{x} \\ x(0) &= 0 \\ \dot{x}(0) &= v_0. \end{aligned} \tag{5}$$

This second system represents the desired limit system with an additional drag term proportional to the velocity.

Theorem 3. Let $x_N(t)$ be defined by System 4 and $x(t)$ be defined by System 5. Then,

$$\lim_{N\to\infty} \sup_{t\in[0,T]} |x_N(t) - x(t)| = 0.$$

This shows that it is possible to scale pulses in such a manner to produce a new drag term.

While the forcing problem is interesting, it does not include any noise or diffusive term. Including a forcing term complicates the calculations as the pulse must be applied as an opposing force. Therefore the sign of the pulse term will change depending on the direction of travel. Finding an appropriate way to include noise is an ongoing project.

A second way to mathematically view the transient binding events is through the use of switching potential fields. For an exploration of multi-scale models involving a potential valley representing a microtubule, see [28]. In this framework, a charged particle weakly binds to and diffuses one-dimensionally along the length of a microtubule. The particle may encounter transient binding sites during its diffusion journey. We view these sites by way of a staircase potential: the potential the particle travels through is flat until it encounters a binding site, then the potential has a step up by a fixed amount. The staircase potential rises to the right if the particle is traveling to the right and rises to the left if the particle is traveling to the left. As the particle is diffusing, it will change its direction many times and hence the potential will switch back and forth many times. The current goal is to determine if a scaling of the potential both in step size and step frequency will asymptotically yield a process with an additional velocity proportional drag term.

Recovery of Distance Dependent Binding Rates.

One final puzzle piece to the microtubule tethering model is the inclusion of increased rebinding rates when an unbound, processive motor is tethered to the microtubule. Consider a motor/cargo complex which diffuses in solution. Denote the position of the complex by $\mathbf{X}(t) = (X(t), Z(t))$ where $X(t)$ represents the horizontal position along the microtubule and $Z(t)$ is the vertical distance above or below the microtubule. The complex is tethered to a fixed, non-mobile location on the microtubule, assumed to be at location zero. Further, the complex is subject to a diffusion potential $\Phi(\mathbf{X}(t))$ that

describes the limitations on how the complex can explore the space. For instance, this potential would describe what type of tether adheres the complex to the microtubule, whether that be Hookean or a non-linear elastic. Allowing γ to be the coefficient of viscous drag for the complex, the dynamics of the pinned complex are described by

$$\gamma \, \mathrm{d}\mathbf{X}(t) = -\nabla \Phi \left(\mathbf{X}(t) \right) \, \mathrm{d}t + \sqrt{2k_B T \gamma} \, \mathrm{d}W_{\mathbf{X}}(t). \tag{6}$$

We assume that the binding rate of the complex is a function of the distance from the microtubule and that the entire surface of the microtubule is reactive. Thus the complex has the ability to bind to any portion of the microtubule and the binding rate will only be a function $Z(t)$. Allow $\lambda\left(Z(t)\right)$ to be the binding rate.

There are two ways to view binding at this point. Either binding is diffusion limited or is rate limited. In the diffusion limited scenario, binding occurs slowly, allowing the complex to explore the whole space. In the rate-limited scenario, binding occurs quickly as soon as the particle diffuses within some fixed distance of the microtubule.

In the diffusion limited scenario, we consider the pseudo-survival function $P(t)$:

$$P(t) = \exp\left(- \int_0^t \lambda\left(Z(s)\right) \, \mathrm{d}s \right). \tag{7}$$

We can think of this in the same manner of a traditional survival function in that it should give us the probability that the true binding time τ is greater than any given time t. However, as written, this is a Cox process in that the random time of binding τ is dependent on the random height $Z(t)$. Here, we use stochastic averaging techniques [29] to approximate this pseudo-survival function with a deterministic survival function by averaging over the stationary distribution of the complex. The benefit of the diffusion limited scenario is that experimentalists can measure the survival probability in lab. Using the averaged survival function, we are currently seeking ways to recover various types of binding rate functions $\lambda\left(Z(t)\right)$ from simulated data.

In the rate limited scenario, we will use Dynkin's formula to calculate the first passage time of the complex to the microtubule (or to within some distance of the microtubule) and assume that binding happens instantaneously. In this situation, binding only occurs within some active zone of the microtubule and the benefit of a tether is clear. Having a tether to restrict the range of motion of the complex to be close to the microtubule will increase the probability of rebinding. To consider this scenario, we must come up with tractable experiments and work closely with laboratories to determine if the rate limited scenario is the true binding situation.

Tensiometer Inference.

At its base level, a tensiometer is a setup in which a motor steps against a known force-extension curve while its position is tracked. In these general terms, an optical trapping experiment could qualify as a tensiometer. As the motor steps against the force, it may slow down as it reaches stall force and it may detach. Sometimes, this can create paths that look rather like a hockey stick – they begin very linear and then slow and approach an asymptote as the motor reaches its stall force. Sometimes, the motor is sensitive to opposing force and detaches while still in the linear regime. Optical trapping experiments by Schroeder et al. [30] demonstrate paths of both natures accomplished by kinesin-2.

From this point forward, we will refer to a tensiometer as a particular type of setup as demonstrated in Figure 1. A DNA origami strand (either single stranded or double stranded) is manufactured so that on one end a fixed number of rigor motors (motors which bind to the microtubule and do not move or step) may attach and on the other end a single stepping motor domain and a tracking particle may attach.

We denote the position of the motor as $Z(t)$ and assume that the motor steps forward with force-dependent stepping rate

$$k_{\text{for}}(f) = \frac{\nu_0}{\delta} \left(1 - \frac{f}{F_*} \right), \tag{8}$$

where ν_0 is the unloaded velocity of the motor, δ is the step size of the motor, f is the opposing force on the motor, and F_* is the stall force of the motor. We further assume that the motor detaches with a force-dependent off rate according to Bell's law for bond rupture as in [31]:

$$k_{\text{off}}(f) = k_0 e^{f/F_c}, \tag{9}$$

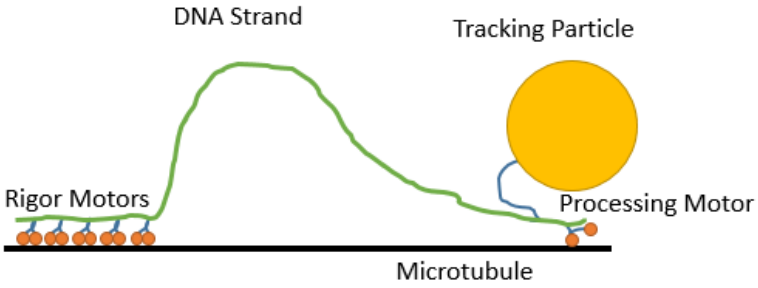

Figure 1: Cartoon depiction of a tensiometer. On the far left, rigor motors hold down one end of a DNA strand. On the far right, a tracking particle and active motor are attached. The motor walks and stretches out the DNA strand while the location of the tracking particle is observed.

where k_0 is the initial off rate and F_c is the critical force.

We denote the position of the tracking particle as $X(t)$ and assume that the dynamics of the tracking particle have no effect on the dynamics of the motor. The tracking particle is assumed to be governed at any given instance t by an Ornstein-Uhlenbeck process centered at $Z(t)$. That is, $X(t)$ obeys the stochastic differential equation

$$\mathrm{d}X(t) = -\frac{\kappa}{\gamma}\left(X(t) - Z(t)\right)\,\mathrm{d}t + \sqrt{\frac{2k_BT}{\gamma}}\,\mathrm{d}W(t). \tag{10}$$

DNA strands are well-modeled by worm-like chains [32]. That is, DNA strands perform as non-linear elastics which stiffen as they extend, and have a maximum possible extension called the contour length L_c. The rate of stiffening is controlled by the persistence length L_p. The force f exerted by the DNA strand on the motor after an extension d is given by

$$f(d) = \frac{k_BT}{L_p}\left[\left(4\left(1 - \frac{d}{L_c}\right)^2\right)^{-1} - \frac{1}{4} + \frac{d}{L_c}\right]. \tag{11}$$

The effective velocity of the motor is given by

$$\lambda\left(Z(t)\right) = \delta k_{\text{off}}\left(f\left(Z(t)\right)\right) \tag{12}$$

In laboratory experiments, microscope cameras are only able to view the tracking particle at discrete points in time, rendering a time series of tracking particle positions $x_1, x_2, \ldots x_N$. Many difficulties arise when attempting to infer motor properties from incomplete tracking particle data. As such, we introduce a stochastic differential equation approximation to the tracking particle process $X(t)$. We assume that the process $\widetilde{X}(t)$ approximates $X(t)$, where $\widetilde{X}(t)$ obeys

$$\begin{aligned} \mathrm{d}\widetilde{X}(t) &= \lambda\left(\widetilde{X}(t)\right)\,\mathrm{d}t + \frac{1}{\sqrt{\eta}}\,\mathrm{d}W(t) \\ \widetilde{X}\left(t_i\right) &= x_i. \end{aligned} \tag{13}$$

Here, η is an unknown parameter which dictates the intensity of the fluctuations of $\widetilde{X}(t)$. Using this approximation and a few other assumptions, it is possible to use Bayesian techniques to recover all motor parameters.

Currently we are determining what types of motors (such as whether or not the motor produces hockey stick like paths) and motor parameters make this type of experimental recovery possible.

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