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Subdiffusive motion of a polymer composed of subdiffusive monomers

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Abstract

We use Brownian dynamics simulations and analytical theory to investigate the physical principles underlying subdiffusive motion of a polymer. Simulations of a single circular polymer reveal that relaxation of the elastic Rouse modes dominates monomer motion, even under strong confinement. Thus, we incorporate two anomalous diffusion models into the theoretical framework of the Rouse model for polymer dynamics. First, a polymer is considered moving within a viscoelastic fluid, in which monomers experience frictional memory described by fractional Brownian motion. Second, we examine a polymer whose monomers are subjected to random pausing events according to the continuous time random walk model. We derive scaling laws for the mean square displacement of a monomer within a polymer, as well as the velocity autocorrelation function. Unlike particles, which exhibit the same ensemble-averaged behavior regardless of subdiffusive mechanism, subdiffusive monomer motion leads to widely varying behavior for a polymer depending on the root cause of the monomer subdiffusion. Our results can be applied directly to experiments as diagnostic tools for determining the dominant physical mechanism underlying anomalous subdiffusive polymer dynamics.

I. INTRODUCTION

Subdiffusive motion of particles has been observed *in vivo* for both prokaryotes [1] and eukaryotes [2], as well as *in vitro* [3, 4]. This anomalous behavior is characterized by a non-linear relationship between mean square displacement (MSD) and time, such that $\langle (R(t) - R(0))^2 \rangle \sim t^\alpha$, where $0 < \alpha < 1$ [5]. Several physical effects have been proposed to explain this phenomenon, including fixed obstacles [6], environment viscoelasticity [7] and random pause events in the particle trajectory [8].

Here, we focus on the latter two mechanisms. The motion of a particle in a viscoelastic environment, as defined by fractional Brownian motion (fBm), includes a frictional memory that couples the current velocity to past velocity, such that a particle jumps to a new position at each time with a direction that is correlated with all previous jumps. These correlations can lead to a subdiffusive MSD if the memory is sufficiently strong. In a continuous time

random walk (CTRW), a diffusing particle experiences random pause events where it waits a time t before re-engaging in its motion. If the waiting-time distribution has long tails, such that the ensemble average waiting time $\langle t \rangle_{\text{pause}}$ diverges, then the overall motion becomes subdiffusive. The fBM and CTRW models generate similar scaling laws for long-time, ensemble-averaged behavior. Recent studies have identified other properties, such as ergodicity and first-passage-time statistics, that can be applied to experimental data to distinguish between these mechanisms [9–12].

Subdiffusive motion has also been observed for monomers in polymers. Specifically, chromosomal loci in several bacterial species [13–14], as well as in budding yeast [15] and human cells [16], exhibit subdiffusive scaling exponents that are approximately half that observed for particles: ~ 0.32 – 0.40 for polymers and ~ 0.70 – 0.77 for particles. This observation raises the question of whether classic polymer dynamics models can explain such scalings, or whether additional physical effects such as environment viscoelasticity and random pausing must be applied to polymers to explain this behavior.

In this manuscript, we address several physical effects as candidate mechanisms underlying the subdiffusive motion recently observed for chromosomal loci in *Escherichia coli* [14]. In Sec. III, we perform Brownian dynamics simulations of a single polymer and find a robust Rouse-like monomer scaling, even under strong confinement and self-interaction. We proceed to address the additional role of environment viscoelasticity and random pausing in the context of the Rouse model for polymer dynamics. In Sec. IV, we study the motion of a single polymer chain in a viscoelastic environment, modeled using fBM. In Sec. V, we analyze the dynamic behavior of a polymer whose monomers experience random pausing events, modeled as a CTRW. Our results provide new diagnostic tools - the monomer MSD scaling and the velocity autocorrelation function - that can be applied to experimental data to determine the underlying mechanism for subdiffusive motion of a polymer.

II. POLYMER MODEL

The physical phenomena of interest occur at length and time scales where the polymer behavior is suitably captured by the Gaussian-chain model [17]. We define a polymer chain with length bN , where b is the Kuhn statistical segment length and N is the number of Kuhn segments within the chain. The chain configuration is defined by the coordinates of $M+1$ discrete effective monomers, where $\vec{R}_m$ is the m th monomer position ($m = 0, 1, 2, \dots, M$). Therefore, each inter-monomer segment is composed of $g = N/M$ Kuhn segments.

The configurational free energy of the polymer chain F_{conf} is defined according to the discrete Gaussian-chain model, such that

$$F_{\text{conf}} = \sum_{m=1}^M \frac{3k_B T}{2gb^2} \left(\vec{R}_m - \vec{R}_{m-1} \right)^2, \quad (1)$$

where $k_B T$ is thermal energy. This purely entropic free energy accounts for the entropic cost associated with the reduction in configurations available to each effective segment upon

stretching the chain. In the absence of other free-energy contributions, this model results in a chain with mean square end-to-end distance $\langle (\vec{R}_M - \vec{R}_0)^2 \rangle = b^2 N$, which is notably independent of the discretization M . This property alludes to the fact that a Gaussian random walk is a continuous fractal, self-similar at all length scales, and invariant to discretization. This model is easily adapted to a circular polymer (as in plasmid DNA) by including a term in the configurational free energy joining bead 0 with bead M . We model both linear and circular polymers in this manuscript.

III. CONFINED POLYMER IN A NEWTONIAN FLUID

The *E. coli* chromosome is a single circular polymer with a contour length 1.6×10^6 nm. Each *E. coli* cell, with diameter $\sim 1 \mu\text{m}$, contains 2 to 4 copies of this circular chromosome. At this level of confinement, these polymers have considerable self-interaction that could potentially impact their dynamic behavior. However, the physical constraints on a confined polymer differ significantly from the assumptions made in existing polymer-dynamics theories. In this section, we adopt a simple approach to address the dynamics of the *E. coli* chromosome by considering a single polymer within a confinement that is much smaller than its unconfined radius of gyration.

The Rouse [18], Zimm [19] and reptation [20] models describe the motion of polymers in infinite solutions. These models do not consider how a polymer interacts with a boundary (*i.e.*, the cell membrane). Furthermore, they assume that polymer chains are linear, which is particularly important for reptation, in which free ends must be able to explore space beyond the reptation tube for large-scale relaxations. Finally, de Gennes's reptation tube is defined by many polymer chains whose motions are uncorrelated with the entangled tracer chain. However, within a single polymer chain, the motion of one segment is correlated with all others, and the reptation tube will relax in concert with the tracer segment. Given these issues of confinement, topology and chain number, it is not clear whether the classic polymer-dynamics models are applicable to our system. Thus, we use Brownian dynamics simulations to explore the scaling of a monomer on a single circular polymer under confinement.

Our simulations include five forces acting on each monomer in the chain. First, the configurational free energy F_{conf} results in an elastic restoring force. Second, the self-interaction force

$$\vec{F}_m^{(E)} = \begin{cases} \frac{3k_B T}{gb^2} (\vec{R}_{m+1} - 2\vec{R}_m + \vec{R}_{m-1}), & m=1, \dots, M-1 \\ \frac{3k_B T}{gb^2} (\vec{R}_2 - 2\vec{R}_0 + \vec{R}_M), & m=0 \\ \frac{3k_B T}{gb^2} (\vec{R}_0 - 2\vec{R}_M + \vec{R}_{M-1}), & m=M. \end{cases} \quad (2)$$

Second, the self-interaction force $\vec{F}_m^{(I)}$ accounts for the finite size of monomers and prevents chain crossing. This force is generally written as

$$\vec{F}_m^{(I)} = - \sum_{m' \neq m} \frac{\partial V_I(R_{m,m'})}{\partial R_{m,m'}} \vec{e}_{m,m'}, \quad (3)$$

where $R_{m,m'} = |\vec{R}_m - \vec{R}_{m'}|$ is the distance between beads m and m' , $\vec{e}_{m,m'} = (\vec{R}_m - \vec{R}_{m'}) / |\vec{R}_m - \vec{R}_{m'}|$ is the unit vector between beads m and m' , and $V_I(R_{m,m'})$ is the two-body interaction potential. Since the nature of these interactions inside the cell is unknown, we test several different V_I including the repulsive Gaussian potential, the Lennard-Jones potential, and the repulsive part of a Lennard-Jones potential. Third, the repulsive interaction between a monomer and the confining boundary is captured by the force

$$\vec{F}_m^{(C)} = \begin{cases} -V_{ex} \left(|\vec{R}_m| - r \right)^3 \frac{\vec{R}_m}{|\vec{R}_m|}, & |\vec{R}_m| > r \\ 0, & |\vec{R}_m| \leq r \end{cases} \quad (4)$$

where V_{ex} is the strength of confinement and r is the radius of confinement. Fourth, a viscous drag force represents friction that opposes the motion of a monomer through the solvent. Hydrodynamic interactions are ignored as they are likely screened *in vivo* due to a high degree of macromolecular crowding [17]. This velocity-dependent force, characterized

by the drag coefficient ξ , is given by $-g\xi \frac{d\vec{R}_m}{dt}$. Finally, a random Brownian force $\vec{F}_m^{(B)}$ arises from collisions between a monomer and solvent molecules. The variance of the magnitude of this force is given by the fluctuation-dissipation theorem

$$\langle \vec{F}_m^{(B)}(t) \vec{F}_{m'}^{(B)}(t') \rangle = 2k_B T \xi \delta_{m,m'} \delta(t - t') \mathbf{I}. \quad (5)$$

Inertial forces are ignored, since these are negligible in comparison to viscous drag. For each timestep in the simulation, the Langevin equation of motion,

$$g\xi \frac{d\vec{R}_m}{dt} = \vec{F}_m^{(E)}(t) + \vec{F}_m^{(I)}(t) + \vec{F}_m^{(C)}(t) + \vec{F}_m^{(B)}(t), \quad (6)$$

is solved using a Runge-Kutta algorithm.

Figure 1 shows the results of a series of simulations with a spherical confinement of decreasing radius r . In these simulations, we choose the model parameters to be $k_B T = 1$, $\xi = 1$, $b = 0.5477$, $g = 1$, and $M = 99$. When $r \rightarrow \infty$ (the free, unconfined case), the polymer behaves according to the Rouse model. The center-of-mass moves diffusively ($\alpha = 1$) across all timescales, while the monomer moves diffusively at short and long times, but subdiffusively for intermediate times, with $\alpha = 0.5$. As the radius of confinement decreases, the scaling exponents do not change until the polymer reaches the boundary and cannot

diffuse further. Interestingly, even under extreme confinement, the subdiffusive scaling of a monomer is Rouse-like ($\alpha = 0.5$) and not reptation-like ($\alpha = 0.25$)

The intermediate-time scaling result found in Fig. 1 ($\alpha = 0.5$) is robust across a broad range of simulation parameters. For example, the scaling of the monomer MSD is insensitive to contour length for $4 \leq M \leq 149$. It also does not depend on polymer topology; linear polymers exhibit the same α as circular polymers. Furthermore, the monomer MSD does not depend on the self-interaction potential. Our results for simulations with no self-interaction and for simulations incorporating three different interaction potentials (repulsive Gaussian, Lennard-Jones, and repulsive Lennard-Jones) give a robust scaling exponent $\alpha = 0.51 \pm 0.03$ for intermediate times. Finally, we performed simulations with five polymers within a single confinement, and with this number of independent chains, we still observe Rouse-like scaling for the monomer MSD. This observation strongly suggests that the elastic Rouse modes dominate polymer behavior. Thus, it appears that the correlated motions of a single confined polymer annihilate the polymer's own reptation tube, leading to a Rouse-like intermediate-time scaling.

IV. POLYMER IN A VISCOELASTIC FLUID

In this section, we analyze the dynamic behavior of a single polymer within a viscoelastic fluid. Our goal is to focus on the Rouse modes of such a polymer in the absence of self-interaction and confinement. With these approximations, we are able to find analytical results for experimentally observable metrics, including the monomer MSD and the velocity autocorrelation function. Our simulation results in the previous section suggest that the dominant scaling behavior for a confined polymer is associated with Rouse-like behavior, so our analyses in this section would adequately predict behavior under conditions of strong confinement and self-interaction.

A particle moving through a viscoelastic environment will undergo subdiffusive motion over a range of time scales due to elastic stresses within the fluid. A further signature of viscoelasticity is the presence of time correlations in the particle's trajectory, also arising from elastic stresses. This viscoelastic behavior can be cast in terms of a fluid memory that propagates past deformation to the future response [17].

We consider a model for viscoelasticity that results in subdiffusive particle motion over all time scales of observation, thus all physical phenomena of interest must be realized within the actual range of subdiffusive behavior. The particle is sufficiently small such that inertial effects are completely negligible. Mathematically, the motion of an isolated particle is governed by the fractional Langevin equation

$$\xi \int_0^t dt' K(t-t') \frac{d\vec{R}(t')}{dt} = \vec{F}^{(B)}(t), \quad (7)$$

where we adopt the memory kernel [10]

$$K(t-t') = \frac{(2-\alpha)(1-\alpha)}{|t-t'|^\alpha}, \quad (8)$$

and the Brownian force $\vec{F}^{(B)}(t)$ satisfies the fluctuation dissipation theorem

$$\left\langle \vec{F}^{(B)}(t) \vec{F}^{(B)}(t') \right\rangle = \xi k_B T K(t-t') \mathbf{I}. \quad (9)$$

The fractional Brownian motion of this model results in a MSD of the particle

$$\left\langle (\vec{R}(t) - \vec{R}(0))^2 \right\rangle = \frac{3k_B T}{\xi} \frac{\sin(\alpha\pi)}{\pi(1-\alpha/2)(1-\alpha)\alpha} t^\alpha. \quad (10)$$

This behavior approaches $\langle (\vec{R}(t) - \vec{R}(0))^2 \rangle = (6k_B T^\xi) t$ as $\alpha \rightarrow 1$, corresponding to diffusion in a Newtonian fluid. Our definition of fractional Brownian motion (fBm) is identical to previous treatments [7, 10] with some minor alterations in the definition of parameters. Specifically, the Hurst parameter $H = 1 - \alpha/2$ typically appears in the definition of fractional Brownian motion; our preference is to define our model by α since this is the physical observable involved in all subsequent discussions.

We now consider a large linear polymer chain that is immersed in a fluid that itself is viscoelastic. Our goal is to derive the behavior for an isolated ideal chain (*i.e.* no self-interaction) in the absence of long-range hydrodynamic interactions. In other words, we address the Rouse modes within a fBm polymer. The model for viscoelasticity defined above results in a governing equation of motion for the m th bead in the chain

$$g\xi \int_0^t dt' K(t-t') \frac{d\vec{R}_m(t')}{dt} = \vec{F}_m^{(E)}(t) + \vec{F}_m^{(B)}(t), \quad (11)$$

where

$$\vec{F}_m^{(E)} = \begin{cases} \frac{3k_B T}{gb^2} (\vec{R}_{m+1} - 2\vec{R}_m + \vec{R}_{m-1}), & m=1, \dots, M-1 \\ \frac{3k_B T}{gb^2} (\vec{R}_{m+1} - \vec{R}_m), & m=0 \\ \frac{3k_B T}{gb^2} (\vec{R}_{m-1} - \vec{R}_m), & m=M. \end{cases} \quad (12)$$

Assuming N is large, we can pass the bead index $m = 0, 1, \dots, M$ to the continuous variable $n \in [0, M]$, resulting in the chain configuration defined by the space curve $\vec{r}(\vec{n}, t)$. With this, we arrive at the governing differential equation

$$\xi \int_0^t dt' K(t-t') \frac{\partial \vec{r}(n, t')}{\partial t} = \frac{3k_B T}{b^2} \frac{\partial^2 \vec{r}(n, t)}{\partial n^2} + \vec{f}_m^{(B)}(n, t), \quad (13)$$

where the Brownian force $\vec{f}_m^{(B)}(n, t)$ satisfies the fluctuation dissipation theorem

$$\left\langle \vec{f}_m^{(B)}(n, t) \vec{f}_m^{(B)}(n', t') \right\rangle = \xi k_B T K(t-t') \delta(n-n') \mathbf{I}. \quad (14)$$

Since the chain ends are free and effectively unstressed, the boundary conditions on the polymer ends are $\vec{r}(\vec{n}=0, t) = 0$ and $\vec{r}(\vec{n}=N, t) = 0$.

As in the Rouse model [17], it is convenient to define a set of normal coordinates that effectively decouple the interactions implicit within the equation of motion (Eq. 13). We define the normal modes

$$\phi_p(n) = \begin{cases} \sqrt{2} \cos\left(\frac{p\pi n}{N}\right), & p=1, 2, \dots \\ 1, & p=0. \end{cases} \quad (15)$$

These modes represent a complete basis set that satisfy the boundary conditions for $\vec{r}(\vec{n}, t)$; orthogonality is demonstrated by

$$\int_0^N dn \phi_p(n) \phi_{p'}(n) = N \delta_{p,p'}. \quad (16)$$

The amplitude of the p th mode $\vec{X}_p(t)$ is given by

$$\vec{X}_p(t) = \frac{1}{N} \int_0^N dn \vec{r}(n, t) \phi_p(n), \quad (17)$$

and the inversion back to chain coordinates is written as

$$\vec{r}(n, t) = \sum_{p=0}^{\infty} \vec{X}_p(t) \phi_p(n). \quad (18)$$

The equation of motion of the p th normal mode is written as

$$N \xi \int_0^t dt' K(t-t') \frac{d\vec{X}_p(t')}{dt} = -k_p \vec{X}_p(t) + \vec{F}_p^{(B)}(t), \quad (19)$$

where $k_p = [3\pi^2 k_B T / (Nb^2)] p^2$, and the Brownian force on the p th mode $\vec{F}_p$ satisfies

$$\left\langle \vec{F}_p^{(B)}(t) \vec{F}_{p'}^{(B)}(t') \right\rangle = N \xi k_B T K(t - t') \delta_{p,p'} \mathbf{I}. \quad (20)$$

The resulting equation of motion (Eq. 19) demonstrates the decoupling of the normal coordinates such that all normal coordinates are dynamically independent. Furthermore, the force on the p th mode $-k_p \vec{X}_p(t)$ corresponds to that of a harmonic spring with spring constant k_p . At equilibrium, the normal-mode amplitude satisfies the equipartition theorem

$$\left\langle \vec{X}_p(t) \vec{X}_{p'}(t) \right\rangle = \frac{k_B T}{k_p} \delta_{p,p'} \mathbf{I}.$$

The chain dynamics are analyzed by defining the correlation function $C_p(t) = \langle \vec{X}_p(t) \cdot \vec{X}_p(0) \rangle$, which is governed by the differential equation

$$N \xi \int_0^t dt' K(t - t') \frac{dC_p(t')}{dt} = -k_p C_p(t) \quad (21)$$

with initial condition $C_p(t=0) = 3k_B T / k_p$ for $p \geq 1$. Performing a Laplace transform of Eq. 21 from t to s , rearranging, and inverting, we arrive at the solution

$$C_p(t) = \frac{3k_B T}{k_p} E_{\alpha,1} \left[-\frac{k_p}{N \xi \Gamma(3 - \alpha)} t^\alpha \right], \quad (22)$$

where $E_{\alpha,\beta}(x)$ is the Mittag-Leffler function

$$E_{\alpha,\beta}(x) = \sum_{j=0}^{\infty} \frac{x^j}{\Gamma(\beta + \alpha j)}. \quad (23)$$

In the limit $\alpha \rightarrow 1$, the correlation function is $C_p(t) = (3k_B T / k_p) \exp[-k_p t / (N \xi)]$, which corresponds to the behavior of the Rouse model in a Newtonian fluid [17]. However, in a viscoelastic fluid, where $0 < \alpha < 1$, the correlation function decays more slowly than an exponential, characteristically as a stretched exponential at short times and as an inverse power law at long times [21].

The $p=0$ solution is found by noting that $\vec{X}_0$ is the polymer center-of-mass. Since the polymer is free draining (no hydrodynamic interactions), the center-of-mass motion is that of an effective particle with total drag coefficient $N \xi$. Thus, the MSD is given by

$$\left\langle (\vec{X}_0(t) - \vec{X}_0(0))^2 \right\rangle = \frac{3k_B T}{N \xi} \frac{\sin(\alpha\pi)}{\pi(1 - \alpha/2)(1 - \alpha)\alpha} t^\alpha. \quad (24)$$

Our analysis facilitates the determination of the MSD of an individual monomer in the chain, which corresponds to the experimentally realizable case of tracking an individual locus on the *E. coli* chromosome. We define the midpoint monomer $\vec{R}_{\text{mid}}(t) = \vec{r}(N/2, t)$, which behaves like all other monomers except the endpoints, $0 \leq n \leq N$. Using our results, we find the MSD to be given by

$$\begin{aligned} \langle (\vec{R}_{\text{mid}}(t) - \vec{R}_{\text{mid}}(0))^2 \rangle &= \langle (\vec{X}_0(t) - \vec{X}_0(0))^2 \rangle + \\ &2 \sum_{p=1}^{\infty} \langle (\vec{X}_{2p}(t) - \vec{X}_{2p}(0))^2 \rangle \\ &= \frac{3k_B T}{N\xi} \frac{\sin(\alpha\pi)}{\pi(1-\alpha/2)(1-\alpha)\alpha} t^\alpha + \\ &\sum_{p=1}^{\infty} \frac{12k_B T}{k_{2p}} \left\{ 1 - E_{\alpha,1} \left[-\frac{k_{2p}}{N\xi\Gamma(3-\alpha)} t^\alpha \right] \right\}, \end{aligned} \quad (25)$$

where $k_{2p} = [3\pi^2 k_B T (Nb^2)](2p)^2$.

Figure 2 plots $\langle (\vec{R}_{\text{mid}}(t) - \vec{R}_{\text{mid}}(0))^2 \rangle / (b^2 N)$ against the dimensionless time $\tau = t/[N^2 b^2 \xi / (k_B T)]^{1/\alpha}$ for three values of the scaling parameter α . Noting that $E_{\alpha,1}(-x) \rightarrow 0$ as $x \rightarrow \infty$, the long-time limiting behavior of Eq. 25 is

$$\langle (\vec{R}_{\text{mid}}(t) - \vec{R}_{\text{mid}}(0))^2 \rangle \rightarrow \frac{3k_B T}{N\xi} \frac{\sin(\alpha\pi)}{\pi(1-\alpha/2)(1-\alpha)\alpha} t^\alpha. \quad (26)$$

This limiting behavior is shown in Fig. 2 as the dotted curves for each α -value. The short-time scaling $\langle (\vec{R}_{\text{mid}}(t) - \vec{R}_{\text{mid}}(0))^2 \rangle / (b^2 N) \sim \tau^{\alpha/2}$ is identified in Fig. 2 by the dashed curves.

The physical justification for the short-time and long-time behaviors is determined by a scaling analysis of Eq. 25. The p th normal mode corresponds to a wavelength $\lambda = bN/p$. Each term within the summation in Eq. 25 represents the contribution of each normal mode to the displacement. The argument of the Mittag-Leffler function (*i.e.* $E_{\alpha,1}$) within the p th term identifies whether the $2p$ th mode remains correlated at time t . Thus, we can identify a time scale t_λ for the relaxation of a wavelength λ by setting the argument to be order unity. This gives

$$t_\lambda \sim \left(\frac{\lambda^2 \xi}{k_B T} \right)^{1/\alpha} \quad \text{or} \quad \lambda \sim \left(\frac{\lambda_B T}{\xi} \right)^{1/2} t_\lambda^{\alpha/2}, \quad (27)$$

which neglects numerical factors from this scaling argument. At the time scale t_λ , sections of chain at lengths shorter than λ move in a coordinated fashion, since the corresponding short wavemodes can respond to deformation at these times. Thus, a monomer feels an effective drag coefficient $\xi_\lambda \sim \xi \lambda / b$ at time t_λ . The resulting MSD at time t_λ scales as

$$\left\langle \left(\vec{R}_{\text{mid}}(t_\lambda) - \vec{R}_{\text{mid}}(0) \right)^2 \right\rangle \sim \frac{k_B T}{\xi \lambda} t_\lambda^\alpha \sim b \left(\frac{k_B T}{\xi} \right)^{1/2} t_\lambda^{\alpha/2}, \quad (28)$$

or in dimensionless form, we write

$$\left\langle \left(\vec{R}_{\text{mid}}(t) - \vec{R}_{\text{mid}}(0) \right)^2 \right\rangle / (b^2 N) \sim \tau^{\alpha/2}. \quad (29)$$

This regime persists until $\lambda \rightarrow bN$, defining the terminal time scale $t_R = [N^2 b^2 \xi / (k_B T)]^{1/\alpha}$. The dimensionless time is therefore identified as $\tau = t/t_R$, and the short-time scaling is valid for $\tau \ll 1$. This limiting form is demonstrated in Fig. 2.

At times $\tau \gg 1$, the entire chain moves in a coordinated fashion, and the monomer displacement scales identically to the displacement of the polymer center-of-mass. Since our model neglects long-range hydrodynamic interactions (*i.e.* free-draining behavior), the total drag on the chain is $\xi_{\text{tot}} = N\xi$. The long-time limit of Eq. 25, given by Eq. 26, is exactly that of a single particle (Eq. 10) with an effective drag coefficient ξ_{tot} .

We now proceed in our analysis to more directly address the impact of memory on the monomer trajectory. Towards this end, we define the velocity autocorrelation function $C_v(t) = \langle \vec{V}(t) \cdot \vec{V}(0) \rangle$, which gives a direct indicator of how previous motion impacts current motion. Thus, it can be calculated from experimental data and used as a diagnostic for fBm. We first consider C_v for a single particle, which is governed by the single-particle equation of motion (Eq. 7). The Laplace transform of Eq. 7 from t to s gives

$$\tilde{\vec{V}}(s) = \frac{1}{\xi \Gamma(3 - \alpha)} s^{1-\alpha} \tilde{\vec{F}}^{(B)}(s), \quad (30)$$

where the tilde is used to indicate Laplace transform of the function, and $\vec{V}(t) = \frac{d\vec{R}(t)}{dt}$ is the particle velocity. This is used to find the average quantity

$$\left\langle \tilde{\vec{V}}(s) \cdot \tilde{\vec{V}}(s') \right\rangle = \frac{1}{[\xi \Gamma(3 - \alpha)]^2} s^{1-\alpha} s'^{1-\alpha} \times \left\langle \tilde{\vec{F}}^{(B)}(s) \cdot \tilde{\vec{F}}^{(B)}(s') \right\rangle. \quad (31)$$

Using the fluctuation dissipation theorem (Eq. 9), we find

$$\left\langle \tilde{\vec{V}}(s) \cdot \tilde{\vec{V}}(s') \right\rangle = \frac{3k_B T}{\xi \Gamma(3 - \alpha)} \frac{s s'^{2-\alpha} + s^{2-\alpha} s'}{s s' (s + s')}. \quad (32)$$

Upon Laplace inversion, we arrive at the solution

$$C_v(t) = -\frac{3k_B T}{\xi} \frac{\sin(\alpha\pi)}{\pi(2-\alpha)} |t|^{\alpha-2}. \quad (33)$$

The negative value of C_v arises from the viscoelastic response captured within the memory kernel. Particle motion incurs an elastic component to the response, leading to subsequent motion being pushed back towards the point of origin, thus a negative-valued C_v . This memory decays in time, as does $C_v(t)$.

The value of $C_v(t)$ diverges in the limit of $t \rightarrow 0$. This arises due to the fact that the instantaneous velocity is an ill-defined quantity for a Brownian random walk as defined by the over-damped Langevin equation (Eq. 7). Ultimately, inertial effects are not negligible at sufficiently small times, and the result must be consistent with that found from the Maxwell-

Boltzmann distribution $C_v(0) = \frac{3k_B T}{m}$, where m is the particle mass. The behavior at $t = 0$ cannot be resolved in our inertia-less treatment; however, the $t \rightarrow 0$ behavior is correctly captured provided inertial effects are sufficiently damped at the time of interest.

Experimental measurement of C_v generally requires an approximation to the instantaneous velocity. To facilitate accurate comparison to experiments, we find the average quantity

$$C_v^{(\delta)}(t) = \frac{1}{\delta^2} \left\langle (\vec{R}(t+\delta) - \vec{R}(t)) \cdot (\vec{R}(\delta) - \vec{R}(0)) \right\rangle = \begin{cases} \frac{C_v(t)}{\eta^2 \alpha (1-\alpha)} [2 - (1-\eta)^\alpha - (1+\eta)^\alpha], & t \geq \delta \\ \frac{C_v(t)}{\eta^2 \alpha (1-\alpha)} [2 + (\eta-1)^\alpha - (\eta+1)^\alpha] + \frac{3k_B T}{\xi} \frac{\sin(\alpha\pi)}{\pi(1-\alpha/2)(1-\alpha)} \frac{1}{\delta^2} (\delta-t)^\alpha, & t < \delta \end{cases} \quad (34)$$

where $\eta = \delta/t$. This quantity approaches $C_v(t)$ in the limit $\delta \rightarrow 0$ for $t \geq \delta$. The behavior for $t < \delta$ is valid for sufficiently large values of δ , such that inertial effects remain negligible for times $t < \delta$.

We now turn to the velocity autocorrelation function for the midpoint monomer of the fBm polymer $C_v^{(\text{mid})}(t) = \langle \vec{V}_{\text{mid}}(t) \cdot \vec{V}_{\text{mid}}(0) \rangle$. To determine this correlation function, we define

the mode velocity $\vec{V}_p(t) = \frac{d\vec{X}_p(t)}{dt}$. In finding $C_v^{(\text{mid})}$, we find $\langle \vec{V}_p(t) \cdot \vec{V}_p(0) \rangle$ directly from our results for $C_p(t)$ found in Eq. 22. With this and similar steps as used to find C_v , we arrive at

$$\begin{aligned}
C_v^{(\text{mid})}(t) &= \langle \vec{V}_0(t) \cdot \vec{V}_0(0) \rangle + 2 \sum_{p=1}^{\infty} \langle \vec{V}_{2p}(t) \cdot \vec{V}_{2p}(0) \rangle \\
&= -\frac{3k_B T}{N\xi} \frac{\sin(\alpha\pi)}{\pi(2-\alpha)} |t|^{\alpha-2} \left\{ 1 + \right. \\
&\quad \left. 2\gamma(\alpha-1) \sum_{p=1}^{\infty} E_{\alpha,\alpha-1} \left[-\frac{k_{2p}}{N\xi\Gamma(3-\alpha)} t^\alpha \right] \right\}. \quad (35)
\end{aligned}$$

Noting that $E_{\alpha,\alpha-1}(-x) \rightarrow 0$ as $x \rightarrow \infty$, we find the long-time asymptotic behavior of Eq. 35 to be

$$C_v^{(\text{mid})}(t) \rightarrow -\frac{3k_B T}{N\xi} \frac{\sin(\alpha\pi)}{\pi(2-\alpha)} |t|^{\alpha-2} \quad (36)$$

for $t \gg t_R$. The short-time scaling of Eq. 35, which will be discussed below, is given by

$$C_v^{(\text{mid})}(t)/(Nb^2/t_R^2) \sim \tau^{\frac{\alpha}{2}-2} \quad (37)$$

for $t \ll t_R$.

As in the MSD, we use scaling analyses to understand the short-time and long-time behaviors. Equation 35 features a summation over p modes, representing the contribution of the Rouse modes within the polymer. The argument of the Mittag-Leffler function $E_{\alpha,\alpha-1}$ identifies the time scale t_λ for relaxation of a Rouse mode of wavelength $\lambda = bN/p$. As previously discussed, beads within the wavelength λ respond dynamically at the timescale t_λ , thus they move coherently. As a result, a monomer feels an effective drag coefficient $\xi_\lambda \sim \xi \lambda / b \sim (\xi k_B T)^{1/2} t_\lambda^{\alpha/2} / b$ at time t_λ . Using the result for C_v for a particle (Eq. 33), the scaling of $C_v^{(\text{mid})}$ at time t_λ scales as

$$C_v^{(\text{mid})}(t_\lambda) \sim -\frac{k_B T}{\xi_\lambda} t_\lambda^{\alpha-2} \sim -b \left(\frac{k_B T}{\xi} \right)^{1/2} t_\lambda^{\frac{\alpha}{2}-2}. \quad (38)$$

In dimensionless form, we have $C_v(t)/(Nb^2/t_R^2) \sim \tau^{\frac{\alpha}{2}-2}$ (i.e. Eq. 37), where $\tau = t/t_R$, and $t_R = [N^2 b^2 \xi / (k_B T)]^{1/\alpha}$ is the terminal relaxation time, where all Rouse modes are relaxed and the entire chain moves coherently. This short-time scaling is valid for $\tau \ll 1$.

For times $\tau \gg 1$, the monomer motion is coherent with the motion of the entire chain. Thus, $C_v^{(\text{mid})}$ tends toward that of a particle with effective drag $\xi_{\text{tot}} = N\xi$. This behavior leads directly to the long-time asymptotic form of $C_v^{(\text{mid})}(t)$ given by Eq. 36.

This section provides the fundamental framework for analyzing the Rouse modes of a fBm polymer. Theoretical predictions for the monomer MSD scaling and the velocity autocorrelation function provide diagnostic tools that can be compared with experimental measurements to determine whether fBm is the dominant physical mechanism for subdiffusion. We show that a negative value of the velocity autocorrelation function is prevalent for both a particle and a polymer undergoing fBm.

V. POLYMER SUBJECT TO RANDOM PAUSES

In this section, we address the dynamics of a CTRW polymer as an alternative model for subdiffusive motion. Though this model is consistent with some aspects of particle motion in a cell [9], it remains to be established whether a polymer that is composed of monomers that undergo transient pauses is a suitable model for the anomalous motion of monomer within a polymer. Our goal in this section is to develop the framework for analyzing the motion of a polymer that is subject to random pauses (*i.e.*, CTRW) in order to interpret the feasibility of this model.

We first consider a single, isolated particle that undergoes Brownian motion in a Newtonian fluid while vascillating between *diffusive* and *paused* states. Our adopted model for the distribution of time spent in the *diffusive* state is governed by

$$S_{\text{diff}}(t)dt = \frac{1}{t_{\text{diff}}} \exp\left(-\frac{t}{t_{\text{diff}}}\right) dt, \quad (39)$$

which gives the probability that if the particle transitions from the *paused* state to the *diffusive* state at time zero that it will transition from the *diffusive* state to the *paused* state between time t and $t + dt$. The parameter t_{diff} is equal to the ensemble average time spent in the *diffusive* state (*i.e.* $\langle t \rangle_{\text{diff}} = t_{\text{diff}}$, where the subscript *diff* is an average w.r.t. Eq. 39). In this section, the angle brackets $\langle \dots \rangle$ imply an ensemble average, which is frequently not equal to the time average.

The analogous distribution that we adopt for the *paused* state is

$$S_{\text{pause}}(t)dt = \begin{cases} \frac{\alpha}{\alpha+1} \frac{1}{t_{\text{pause}}} dt, & t < t_{\text{pause}} \\ \frac{\alpha}{\alpha+1} \frac{1}{t_{\text{pause}}} \left(\frac{t_{\text{pause}}}{t}\right)^{\alpha+1} dt, & t \geq t_{\text{pause}} \end{cases} \quad (40)$$

where the power-law tail in the transition time is governed by the scaling constant α . For $\alpha > 1$, the parameter t_{pause} results in the ensemble average time spent in the *paused* state $\langle t \rangle_{\text{pause}} = t_{\text{pause}} \alpha / [2(\alpha - 1)]$, where the subscript *pause* is an average w.r.t. Eq. 40. For $0 < \alpha < 1$, the ensemble average time spent in the *paused* state is infinity; therefore, $\alpha = 1$ is a critical point in the behavior of this model. We will proceed to show that α is the primary determinant for subdiffusive motion in this model.

The motion of the particle position $\vec{R}(\vec{t})$ is governed by the equation of motion

$$\xi \frac{d\vec{R}(t)}{dt} = \sigma^{(\text{diff})}(t) \vec{F}^{(B)}(t), \quad (41)$$

where $\sigma^{(\text{diff})}(t) = 1$ if the particle is in the *diffusive* state at time t , and $\sigma^{(\text{diff})}(t) = 0$ if the particle is in the *paused* state at time t . The times spent in the *diffusive* and *paused* states are selected from $S_{\text{diff}}(t)$ and $S_{\text{pause}}(t)$, respectively. The Brownian force $\vec{F}^{(B)}(t)$ satisfies the fluctuation dissipation theorem for diffusion in a Newtonian fluid

$$\left\langle \vec{F}^{(B)}(t) \vec{F}^{(B)}(t') \right\rangle = 2\xi k_B T \delta(t - t') \mathbf{I}. \quad (42)$$

The particle motion is analyzed using methods that we develop for the behavior of a two-state reaction-diffusion model; we refer the reader to Ref. [22] for details. Using these methods, the Brownian motion of our model gives a MSD of the particle

$$\left\langle (\vec{R}(t) - \vec{R}(0))^2 \right\rangle = \begin{cases} \frac{6k_B T}{\xi} \frac{1}{1 + \frac{\alpha}{2(\alpha-1)} \frac{t_{\text{pause}}}{t_{\text{diff}}}} t, & \alpha > 1 \\ \frac{6k_B T t_{\text{diff}}}{\xi} \frac{(1+\alpha) \sin(\alpha\pi)}{\alpha\pi} \left(\frac{t}{t_{\text{pause}}} \right)^\alpha, & 0 < \alpha < 1. \end{cases} \quad (43)$$

We note that this functional form approaches zero for $\alpha \rightarrow 1$ from both the negative and positive directions. This notable idiosyncrasy is reconciled by the fact that the time required to achieve this limiting behavior also diverges for $\alpha \rightarrow 1$. The overall observation is that the particle behaves diffusively for $\alpha = 1$ and subdiffusively for $0 < \alpha < 1$ with a MSD that scales as t^α .

The behavior for $\alpha > 1$ is justified by noting that the ensemble-averaged probability of being in the *diffusive* state for $\alpha > 1$ is $\langle \sigma^{(\text{diff})}(t \rightarrow \infty) \rangle = t_{\text{diff}} / \{ t_{\text{diff}} + t_{\text{pause}} \alpha / [2(\alpha - 1)] \}$. Thus, the $\alpha > 1$ behavior is exactly the free diffusion behavior $(6k_B T / \xi) t$ times the fraction of time spent in the *diffusive* state.

The subdiffusive behavior that arises for $0 < \alpha < 1$ occurs due to the ergodicity breaking that arises from the *paused*-time distribution. For large time, the ensemble-averaged probability of being in the *diffusive* state for $0 < \alpha < 1$ approaches

$$\left\langle \sigma^{(\text{diff})}(t) \right\rangle \rightarrow \frac{(1+\alpha) \sin(\alpha\pi)}{\pi} \frac{t_{\text{diff}}}{t_{\text{pause}}^\alpha} \frac{1}{t^{1-\alpha}}. \quad (44)$$

The power-law tail in S_{pause} leads to the ensemble-averaged *diffusive*-state probability approaching zero at large time, thus indicating an inequality between the ensemble average and time average indicative of an ergodicity breaking. While a particle is in the *diffusive* state, the time rate-of-change of the MSD is $d\text{MSD}/dt = (6k_B T / \xi)$, which is the result for a freely diffusing particle without pauses. The time rate-of-change of the MSD for the CTRW

particle with $0 < \alpha < 1$ is given by the *diffusive*-state rate-of-change in the previous sentence times the probability of being in the *diffusive* state; thus,

$$\frac{d\text{MSD}}{dt} = \frac{6k_B T}{\xi} \langle \sigma^{(\text{diff})}(t) \rangle = \frac{6k_B T}{\xi} \frac{(1+\alpha)}{\pi} \frac{\sin(\alpha\pi)}{t_{\text{diff}}^\alpha} \frac{1}{t^{1-\alpha}}, \quad (45)$$

which is in exact agreement with Eq. 43 for $0 < \alpha < 1$.

We now consider the motion of a large linear polymer that is subject to random pauses, moving as a CTRW. In this treatment, we address the Rouse modes within a CTRW polymer, neglecting self-interaction and hydrodynamic interaction. The equation of motion is given by

$$g\xi \frac{d\vec{R}_m(t)}{dt} = \sigma_m^{(\text{diff})}(t) \left[\vec{F}_m^{(E)}(t) + \vec{F}_m^{(B)}(t) \right], \quad (46)$$

where $\sigma_m^{(\text{diff})}(t) = 1$ if the m th bead in the chain is in the *diffusive* state at time t , and $\sigma_m^{(\text{diff})}(t) = 0$ if the m th bead is in the *pause* state at time t ($m = 0, 1, 2, \dots, M$). In this model, there are two contributions to subdiffusive motion. The first contribution is the ergodicity breaking inherent in the CTRW model when $0 < \alpha < 1$, and the second contribution is associated with the relaxation of the internal Rouse modes of the polymer.

In the case $0 < \alpha < 1$, each individual bead within the polymer chain exhibits ergodicity breaking with a long-time probability of being in the *diffusive* state given by Eq. 44. The polymer is capable of moving via two distinct mechanisms. If all of the beads are in the *diffusive* state, the polymer moves according to a *free-diffusion* mechanism, where the motion is diffusive with an effective drag coefficient $g(M+1)\xi$. If at least one bead is in the *paused* state, the polymer must move according to an *pin-and-pivot* mechanism, where the unfrozen segments crawl while frozen segments pin parts of the polymer in space. These two mechanisms contribute to the mid-point monomer MSD, which we define as $\text{MSD}_{\text{mid}} = \langle (\vec{R}_{\text{mid}}(t) - \vec{R}_{\text{mid}}(0))^2 \rangle$.

The probability that all beads are in the *diffusive* state is $\langle \sigma^{(\text{diff})}(t) \rangle^{M+1}$, which tends to zero as $1/t^{(M+1)(1-\alpha)}$. The *free-diffusion* mechanism results in a time rate-of-change for the midpoint-monomer MSD that scales as

$$\frac{d\text{MSD}_{\text{mid}}}{dt} \sim \frac{k_B T}{g(M+1)\xi} \langle \sigma^{(\text{diff})}(t) \rangle^{M+1} \sim \frac{k_B T}{g(M+1)\xi} \frac{t_{\text{diff}}^{M+1}}{t_{\text{pause}}^{(M+1)\alpha}} \frac{1}{t^{(M+1)(1-\alpha)}}. \quad (47)$$

From this analysis, we find the long-time scaling behavior of MSD_{mid} to be

$$\text{MSD}_{\text{mid}} \sim \frac{k_B T}{g(M+1)\xi} \frac{t_{\text{diff}}^{M+1}}{t_{\text{pause}}^{(M+1)\alpha}} t^{\alpha_{\text{FD}}}, \quad (48)$$

where α_{FD} is the *free-diffusion* scaling parameter

$$\alpha_{\text{FD}} = \begin{cases} 1 - (M+1)(1 - \alpha), & M < M_c \\ 0, & M \geq M_c \end{cases} \quad (49)$$

with $M_c = 1 + 1/(1 - \alpha)$ being the critical bead number. This results suggests that the scaling behavior depends on the number of beads (or length of chain). Furthermore, for any appreciable length of chain ($M \gg M_c$), this is not a viable transport mechanism, since ergodicity breaking leads to a cessation in the motion.

The *pin-and-pivot* mechanism permits motion to occur under conditions where multiple beads are frozen in the *paused* state. The net scaling of the MSD for this mechanism is not easily reconciled through a scaling analysis due to the complexity associated with the ergodicity breaking and the coordinated dynamics. For this manuscript, we demonstrate these mechanisms through numerical simulations. In Fig. 3, we show the results for the midpoint monomer MSD from an ensemble average over 1000 simulations for several lengths of chain. Parameters for these simulations are $k_B T = 1$, $g = 1$, $b = 0.5477$, $\xi = 1$, $t_{\text{diff}} = 1$, $t_{\text{pause}} = 1$, and $\alpha = 0.7$, and we perform experiments for 1 bead ($M = 0$), 2 beads ($M = 1$), 3 beads ($M = 2$), 4 beads ($M = 3$), and 100 beads ($M = 99$). Included in Fig. 3 are our predictions for the *free-diffusion* mechanisms, governed by the scaling parameter α_{FD} for 1 bead ($\alpha_{\text{FD}} = 0.7$), 2 beads ($\alpha_{\text{FD}} = 0.4$), and 3 beads ($\alpha_{\text{FD}} = 0.1$). The short-time behavior is diffusive (*i.e.*, $\text{MSD}_{\text{mid}} \sim t$) for all simulations due to the discrete nature of the model setting a short-time cutoff for the Rouse modes.

The results shown in Fig. 3 demonstrate the chain-length dependence of the scaling behavior of MSD_{mid} . Our simple analysis of the *free-diffusion* mechanism is accurate for only 1 and 2 beads; thus, we predict the dominant mechanism of motion for more than 3 beads is the *pin-and-pivot* mechanism.

In the previous section, we identify the velocity autocorrelation function C_v as a suitable metric to determine the impact of memory on the monomer motion. There is no inherent memory for a CTRW particle whose motion is governed by Eq. 41; thus, the resulting velocity autocorrelation function $C_v(t)$ is zero for all $t > 0$.

In the case of the CTRW polymer, the elasticity of the polymer results in Rouse relaxation modes, contributing memory to the motion. However, it is unclear how random pausing will impact the memory (or C_v). As a comparison, we note that the midpoint-monomer velocity autocorrelation function for polymer in the absence of random pausing is given by

$$C_v^{(\text{mid})} = -\frac{6k_B T}{N^2 \xi^2} \sum_{p=1}^{\infty} k_{2p} \exp\left(-\frac{k_{2p}}{N \xi} t\right), \quad (50)$$

where $k_{2p} = [3\pi^2 k_B T / (Nb^2)](2p)^2$. This behavior is found by taking the limit of Eq. 35 as $\alpha \rightarrow 1$. We adapt this to the approximate form

$$C_v^{(\text{mid}, \delta)} = \frac{1}{\delta^2} \left\langle (\vec{R}_{\text{mid}}(t+\delta) - \vec{R}_{\text{mid}}(t)) \cdot (\vec{R}_{\text{mid}}(\delta) - \vec{R}_{\text{mid}}(0)) \right\rangle \text{ using similar steps as used to find Eq. 34.}$$

In Fig. 4, we show ensemble average determination of the approximate velocity autocorrelation function $C_v^{(\text{mid}, \delta)}$ (with $\delta = 20$) from simulations of a free polymer chain (*i.e.*, no random pauses) and a CTRW polymer. In both simulations, we use $k_B T = 1$, $\xi = 1$, $b = 0.5477$ $g = 1$, and $M = 99$, and the CTRW polymer is subjected to random pauses with $t_{\text{diff}} = 1$ and $t_{\text{pause}} = 1$. Figure 4 clearly demonstrates that the introduction of random pause events into the polymer dramatically suppresses the elastic memory within the polymer chain. The free polymer exhibits a large negative $C_v^{(\text{mid}, \delta)}$, whereas, the CTRW polymer has a peak negative value at $t = 20$ that is less than one tenth that of the free polymer.

The physical justification for the suppression of $C_v^{(\text{mid}, \delta)}$ for the CTRW polymer lies in the impact of pausing on the internal relaxation times. The free polymer undergoes Rouse-mode relaxation with longer wavelengths requiring longer time to relax. However, the pausing associated with the CTRW polymer eliminates the long wavemodes from the relaxation dynamics by pinning sections of the chain in space. The distance between pinned beads dictates the local relaxation dynamics rather than the natural Rouse mode at any given timescale. Since this pinned length scale is always much less than the chain length, particularly under conditions of ergodicity breaking ($0 < \alpha < 1$), this relaxation time is effectively instantaneous, and the memory effects within the polymer are almost entirely suppressed.

VI. CONCLUSIONS

This manuscript introduces three candidate theories to address the anomalous motion of monomers in a polymer. First, we address the motion of a single polymer that is strongly confined. Second, we study the impact of a viscoelastic environment on the motion of a single polymer chain. Third, we analyze the role of transient pausing of monomers on the overall motion of a polymer chain.

In Sec. III, we investigate how confinement and self-interaction affect the motion of monomers on a single polymer. The Rouse, Zimm, and reptation models address various aspects of polymer motion under dilute, semi-dilute, and concentrated conditions; it is not immediately obvious what role these dynamic models play in our current problem. Our simulation results suggest the Rouse model adequately captures the monomer MSD for intermediate time scales, up to the terminal time where the monomer MSD reaches the confinement length scale. Although reptation seems to be a likely model for the self-

slithering motion of a single polymer chain, we conclude that the correlated motion of the confined chain eliminates this dynamic mechanism. Therefore, the monomer MSD for a single confined polymer in a Newtonian fluid is expected to scale as $t^{0.5}$ for intermediate time scales.

In Sec. IV, we study the role of environment viscoelasticity on the dynamics of a single polymer by introducing a fBm memory function into the monomer drag force. Given the dominant role that the Rouse model plays in the confined polymer, we focus our analysis on the Rouse modes of a fBm polymer. The model introduces the parameter α as the MSD scaling for an individual fBm particle (*i.e.*, $\text{MSD} \sim t^\alpha$). A polymer chain that is composed of such fBm monomers exhibits a monomer MSD with a short-time scaling of $\alpha/2$ (for times up to the longest relaxation time $t_R = [N^2 b^2 \xi / (k_B T)]^{1/\alpha}$).

As a further test of our predictions, we introduce the velocity autocorrelation function C_v as a metric for the environmental memory. A hallmark feature of memory in a viscoelastic fluid is a negative-valued C_v at intermediate time scales. Our results in Sec. IV conclude that a fBm particle exhibits the scaling $C_v \sim -t^{\alpha-2}$ and the midpoint monomer in a fBm polymer has the scaling $C_v \sim -t^{\alpha/2-2}$.

Our final analysis in Sec. V addresses the role of transient pauses in the motion of a monomer in the polymer chain. We draw two primary conclusions from a polymer subjected to random pausing (CTRW polymer). The first conclusion is that a polymer chain that experiences random pause events exhibits considerable arrest in the motion of an individual monomer. Pause events in a long polymer chain hinder motion due to a need to coordinate motion between multiple beads for a monomer to move. Ergodicity breaking leads to the probability of coordinated motion approaching zero at long times, thus dramatically suppressing the monomer motion. The second conclusion is that random pausing within a polymer chain suppresses the memory effects associated with the elastic relaxation processes of the polymer chain. This is due to the arrest of long wavemode relaxations when multiple points on the chain are pinned.

Our results in this manuscript conclude that subdiffusive monomer motion leads to widely varying behavior for a polymer depending on the root cause of the monomer subdiffusion. Particle motion leads to ensemble-averaged MSD that is the same for fBm and CTRW models, and one needs to turn to other average properties to determine whether an ensemble of trajectories are governed by fBm or CTRW models [9–12]. However, these models are easily distinguishable for a polymer composed of subdiffusive monomers. The connectivity of a polymer results in new dynamic mechanisms that are dramatically influenced by the nature of the monomer motion, leading to different scaling behaviors for monomer MSD and C_v .

Our results can be compared directly to experimental observations. By tracking fluorescently labeled chromosomal loci in live cells, we and others have found an MSD scaling of ~ 0.32 – 0.40 [13–16]. These α values are less than expected from the Rouse-like behavior of a polymer under confinement, as demonstrated by our simulations in Sec. III. Therefore, additional physical effects must be responsible for the observed subdiffusion. Our theoretical

predictions in Secs. IV and V allow us to identify fBm as the dominant physical mechanism underlying the anomalous motion of chromosomal loci in *E. coli* [14]. The MSD scaling of chromosomal loci is approximately one-half that of an RNA-protein particle, which scales as $\sim 0.70\text{--}0.77$ [1, 14], *i.e.* particle scaling of α leads to polymer scaling $\sim \alpha/2$, as predicted for a fBm polymer. Furthermore, $C_v < 0$ at short time lags [14], indicating memory, which is characteristic of a fBm polymer (Eq. 35) but suppressed in a CTRW polymer.

The agreement between our theory and experimental measurements [14] suggests that the Rouse model modified by the viscoelastic environment is the dominant dynamic mechanism for chromosome reorganization within *E. coli*, at least on time scales of the experimental measurements. This observation is critical in guiding the development of theories of the dynamics within a complex cellular environment. In this case, classic polymer models, when properly modified, render results that can clearly distinguish between candidate molecular processes for chromosome reorganization. These results represent an important example where we can leverage existing physical understanding of polymer dynamics to render quantitative predictions of *in vivo* phenomena.

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FIG. 1.

Ensemble-averaged MSD of a single circular polymer under spherical confinement. Series of simulations for decreasing radius of confinement: $r \rightarrow \infty$ (black), $r = 6$ (pink), $r = 5$ (orange), $r = 4$ (green), $r = 3$ (red), and $r = 1$ (blue). The inset shows a typical snapshot from the $r = 3$ simulations.

FIG. 2.

Mean-square displacement of the midpoint monomer $\langle (\vec{R}_{\text{mid}}(t) - \vec{R}_{\text{mid}}(0))^2 \rangle / (b^2 N)$ versus the dimensionless time $\tau = t/[N^2 b^2 \xi / (k_B T)]^{1/\alpha}$ for $\alpha = 1.0$ (red), $\alpha = 0.7$ (purple), and $\alpha = 0.4$ (blue). The dotted curves correspond to the long-time asymptotic behavior for these three α values, and the dashed curves give the short-time scaling of $\tau^{\alpha/2}$.

FIG. 3.

The midpoint monomer MSD versus time t from an ensemble average over 1000 numerical simulations with 1 bead, 2 beads, 3 beads, 4 beads, and 100 beads (see text for parameter values). For the curves from 1-bead, 2-beads, and 3-beads simulations, we include the *free-diffusion* scaling $\text{MSD}_{\text{mid}} \sim t^{\alpha_{\text{FD}}}$. The short-time scaling of $\text{MSD}_{\text{mid}} \sim t^1$ is common to all simulations.

FIG. 4.

The midpoint-monomer velocity autocorrelation function $C_v^{(\text{mid}, \delta)}$ from an ensemble average over 2000 simulations of a free polymer chain (black) and a CTRW polymer (blue). The red dashed curve represents analytical results for a free polymer chain.