The Brownian Ratchet Revisited: Multiple Filamentous Growth

APPLIED MATHEMATICS
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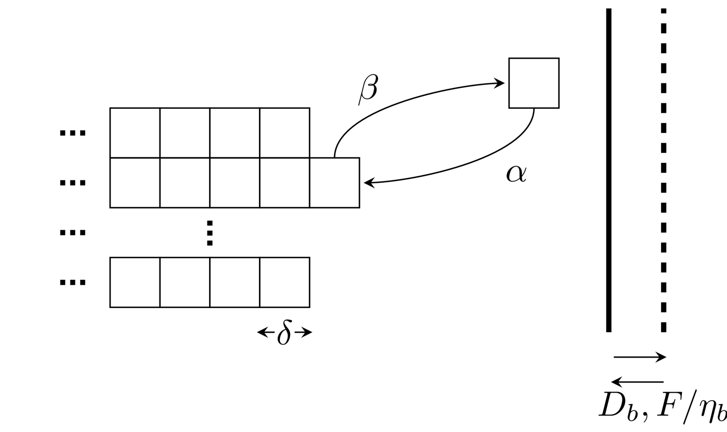

Introduction

The growth of filamentous protein polymers can do work against molecular or intracellular objects that resist movement. The *Brownian ratchet* (**BR**) model was developed to describe such systems [2]. In this work, we use a continuous diffusion formalism for the polymerization of a **BR** instead of the original random-walk approach. For a more details and results, see [1].

Diffusion Formalism: One Filament

- Represent the position of a filament tip, $\mathbf{X}(t)$, as a continuous diffusion process where δ: the length of a monomer,
$$D_a = (\alpha + \beta)\delta^2/2, \qquad V_a = (\alpha - \beta)\delta, \tag{1}$$
and α, β: polymerization & depolymerization rates.
- $f_{\mathbf{X}}(x,t)$: probability density function (*pdf*) for the filament tip
$$\frac{\partial f_{\mathbf{X}}(x,t)}{\partial t} = D_a \frac{\partial^2 f_{\mathbf{X}}(x,t)}{\partial x^2} - V_a \frac{\partial f_{\mathbf{X}}(x,t)}{\partial x}. \tag{2}$$
- Single filament without a barrier: $f_{\mathbf{X}}(x,t) = e^{-\frac{(x-V_a t)^2}{4D_a t}} / \sqrt{4\pi D_a t}$.
- $f_{\mathbf{X}}(x,t)$: traveling peak at $x = V_a t$, with increasing dispersion.

Filamentous Bundle: No Barrier

- Let $\mathbf{X}_i(t)$ $(i = 1, 2, \ldots, N)$ be N independent, identical filaments
- Let $\mathbf{X}^{(k)}(t)$ be the position of the k^{th} longest filament, when the filament positions are ordered from longest to shortest: $\mathbf{X}^{(1)}(t) \geq \ldots \geq \mathbf{X}^{(k-1)}(t) \geq \mathbf{X}^{(k)}(t) \geq \mathbf{X}^{(k+1)}(t) \geq \ldots \geq \mathbf{X}^{(N)}(t)$.
- The formula for the *pdf* of the k^{th} longest filament:
$$f_{\mathbf{X}^{(k)}}(x,t) = \frac{N!}{(k-1)!(N-k)!} F_{\mathbf{X}}(x,t)^{N-k} \left[1 - F_{\mathbf{X}}(x,t)\right]^{k-1} f_{\mathbf{X}}(x,t),$$
where $F_{\mathbf{X}}(x,t)$ is the cumulative distribution function (*cdf*).
- $f_{\mathbf{X}^{(k)}}(x,t)$: single traveling peak with increasing dispersion.
- The location of the peak and the velocity of the peak movement:
$$x^{(k)}(t) = V_a t + \omega_k \sqrt{4 D_a t}, \qquad v^{(k)}(t) = V_a + 2\omega_k \sqrt{D_a/t}, \tag{3}$$
where $\omega_k > \omega_{k+1}$ is a constant that satisfies
$$k = 1 + \frac{1 - \mathrm{erf}(\omega_k)}{2} \left[N - 1 - \sqrt{\pi}\omega_k [1 + \mathrm{erf}(\omega_k)] e^{\omega_k^2}\right].$$
- $v^{(1)}(t)$ is greatest early on, when filaments are even.
- The distance between $\mathbf{X}^{(k)}(t)$ and $\mathbf{X}^{(k+1)}(t)$ grows with $\sqrt{t}$: $x^{(k)}(t) - x^{(k+1)}(t) = 2(\omega_k - \omega_{k+1})\sqrt{D_a t}$.

Bundle Growth: Fluctuating Barrier

- Let $\mathbf{Y}(t)$ represent a fluctuating barrier with resistant force F, frictional coefficient η_b, and diffusion coefficient D_b.
- **BR**: $\mathbf{X}^{(1)}(t)$ and $\mathbf{Y}(t)$ interact subject to $\mathbf{X}^{(1)}(t) \leq \mathbf{Y}(t)$.
- Easier to study $f(\{x_i\}, y, t)$: joint *pdf* for all of the $\mathbf{X}_i(t)$ and $\mathbf{Y}(t)$:
$$\frac{\partial f(\{x_i\}, y, t)}{\partial t} = \sum_{k=1}^{N} \left(D_a \frac{\partial^2 f}{\partial x_k^2} - V_a \frac{\partial f}{\partial x_k} \right) + D_b \frac{\partial^2 f}{\partial^2 y} + \frac{F}{\eta_b} \frac{\partial f}{\partial y}. \tag{4}$$
- ξ_i: gap distance between $\mathbf{X}_i(t)$ and $\mathbf{Y}(t)$; z: center of mass:
$$\xi_i = y - x_i, \ (i = 1, 2, \ldots, N); \qquad z = \frac{D_b \sum_{j=1}^{N} x_j + D_a y}{N D_b + D_a}. \tag{5}$$
- Decouple: $f(\{\xi_i\}, z, t) = \phi(\{\xi_i\}, t) P_{\mathbf{Z}}(z, t)$.
- Gap distances, $\phi(\{\xi_i\}, t)$, approach a stationary distribution:
$$\phi(\{\xi_i\}) = \epsilon^N \exp\left(-\epsilon \sum_{i=1}^{N} \xi_i \right), \quad \epsilon = \frac{V_a + F/\eta_b}{N D_b + D_a}. \tag{6}$$
- Bundle and barrier, together, undergo diffusion with a drift:
$$\frac{\partial P_{\mathbf{Z}}(z,t)}{\partial t} = D_z \frac{\partial^2 P_{\mathbf{Z}}(z,t)}{\partial z^2} - V_z \frac{\partial P_{\mathbf{Z}}(z,t)}{\partial z}, \tag{7}$$
$$D_z = \frac{D_b D_a}{N D_b + D_a}, \qquad V_z = \frac{N D_b V_a - D_a F/\eta_b}{N D_b + D_a}. \tag{8}$$

Force-dependent Polymerization

- α is proportional to: intrinsic polymerization rate, α_0, monomer concentration, c_0, and the probability that the gap is $\geq \delta$:
$$\alpha = \alpha_0 c_0 e^{-\epsilon\delta}. \tag{9}$$
- Recall that D_a and V_a are defined in terms of α, β, and δ in (1):
$$\epsilon(\alpha) = \frac{(\alpha - \beta)\delta + F/\eta_b}{N D_b + (\alpha + \beta)\delta^2/2}. \tag{10}$$
- Consider the case of slow depolymerization, where $\frac{\beta}{\alpha} \approx 0$:
$$\widetilde{V}_z = \widetilde{\alpha} \frac{N - \widetilde{F}/2}{N + \widetilde{\alpha}/2}, \quad \widetilde{D}_z = \frac{\widetilde{\alpha}/2}{N + \widetilde{\alpha}/2}, \quad \widetilde{\alpha} = \widetilde{\alpha}_0 e^{-\left(\frac{\widetilde{\alpha} + \widetilde{F}}{N + \widetilde{\alpha}/2}\right)}, \tag{11}$$
nondimensionalized: $\widetilde{V}_z = V_z \delta / D_b$, $\widetilde{D}_z = D_z / D_b$, $\widetilde{\alpha} = \alpha\delta^2 / D_b$, $\widetilde{\alpha}_0 = \alpha_0 c_0 \delta^2 / D_b$, and $\widetilde{F} = F\delta / (\eta_b D_b)$.
- Implicit force-velocity and force-fluctuation relations (Fig. 1):
$$\widetilde{F} = \frac{2N\widetilde{V}_z}{\widetilde{V}_z + \widetilde{F} - 2N} - \frac{2N^2 - N\widetilde{F}}{2N - \widetilde{V}_z - \widetilde{F}} \ln\left(\frac{2N\widetilde{V}_z / \widetilde{\alpha}_0}{2N - \widetilde{V}_z - \widetilde{F}} \right), \tag{12a}$$
$$\widetilde{F} = \frac{2N\widetilde{D}_z}{\widetilde{D}_z - 1} - \frac{N}{1 - \widetilde{D}_z} \ln\left(\frac{2N\widetilde{D}_z / \widetilde{\alpha}_0}{1 - \widetilde{D}_z} \right). \tag{12b}$$

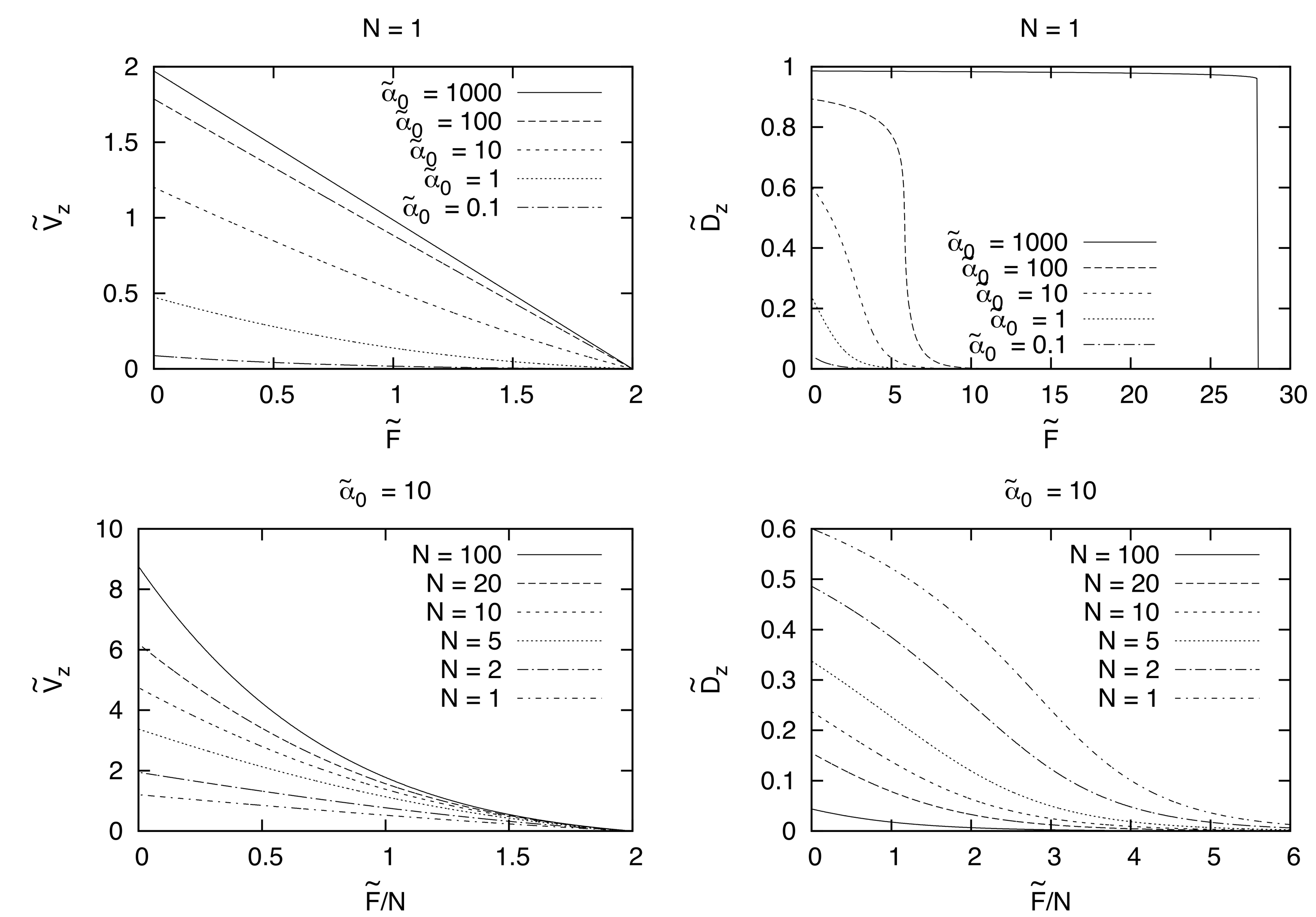

Figure 1: Force-Velocity and Force-Fluctuation Relations. **Top:** Curves are plotted for several values of $\widetilde{\alpha}_0$ all with $N = 1$. Note that as $\alpha_0 c_0 \to \infty$, $\widetilde{V}_z \to 2 - \widetilde{F}$ and $\widetilde{D}_z \to 1$ as expected from [3]. **Bottom:** Curves are plotted for bundles of size N, all with $\widetilde{\alpha}_0 = 10$.

Conclusions

- Without a barrier, the bundle grows as a single filament with all the other filaments lagging behind.
- **BR:** The interactions between the $\mathbf{X}_i(t)$ and $\mathbf{Y}(t)$ allow all N filaments in the bundle to move together.
- V_z and D_z both decrease with an increasing resistant force F.
- V_z and D_z both increase with $\alpha_0 c_0$.
- The critical stalling force F^*, such that $V_z = 0$, is scaled with N.
- The free-load velocity V_z when $F = 0$ is scaled with $\alpha_0 c_0$ and N: $\widetilde{V}_z = \widetilde{\alpha}_0 e^{-\widetilde{V}_z/N}$.
- After being normalized by the critical stalling force F/F^*, $V_z(F/F^*)$ increases with N while $D_z(F/F^*)$ decreases with it.

References

[1] C.L. Cole and H. Qian. The brownian ratchet revisited: Diffusion formalism, polymer-barrier attractions, and multiple filamentous bundle growth. *(Submitted)*, February 2011.

[2] C.S. Peskin, G.M. Odell, and G.F. Oster. Cellular motions and thermal fluctuations: the brownian ratchet. *Biophys. J.*, 65:316–324, 1993.

[3] H. Qian. A stochastic analysis of a brownian ratchet model for actin-based motility and integrate-and-firing neurons. *MCB: Mol. & Cell. Biomech.*, 1:267–278, 2004.