

Forces and Torques on Rotating Spirochete Flagella

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Spirochetes are a unique group of motile bacteria that are distinguished by their helical or flat-wave shapes and the location of their flagella, which reside within the tiny space between the bacterial cell wall and the outer membrane (the periplasm). In *Borrelia burgdorferi*, rotation of the flagella produces cellular undulations that drive swimming. How these shape changes arise due to the forces and torques that act between the flagella and the cell body is unknown. It is possible that resistive forces come from friction or from fluid drag, depending on whether or not the flagella are in contact with the cell wall. Here, we consider both of these cases. By analyzing the motion of an elastic flagellum rotating in the periplasmic space, we show that the flagella are most likely separated from the bacterial cell wall by a lubricating layer of fluid. This analysis then provides drag coefficients for rotation and sliding of a flagellum within the periplasm.

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Spirochetes are long, thin bacteria with lengths of $\sim 10 \mu\text{m}$ and circular cross sections of diameter $\sim 300 \text{ nm}$ [1]. Like many swimming bacteria, spirochetes generate thrust against the surrounding fluid by rotating helical filaments known as flagella; however, unlike other bacteria, spirochete flagella are not immersed in the surrounding fluid but are contained in the periplasm, the space between the cell cylinder (i.e., the cytoplasm, the inner cell membrane, and the cell wall) and the outer membrane of the cell [Figs. 1(a)–1(d)]. The periplasm is extremely narrow, being only 16 nm thick away from the flagella and 42 nm near the flagella [2]. In many spirochetes, rotation of the flagella leads to changes in the shape of the cell. It is these shape undulations that drive the swimming of these bacteria.

The biophysics of spirochete swimming is complex and is relevant for the pathogen-host interactions that accompany disease, as some spirochete species are pathogenic. For example, *Borrelia burgdorferi* and *Treponema pallidum* cause Lyme disease and syphilis, respectively. Both of these bacteria have planar, wavelike shapes, known as flat-wave morphologies [3,4]. In *B. burgdorferi*, 7–11 flagella are attached to motors near each end of the spirochete [Figs. 1(c) and 1(d)] [5,6]. The flagella wind down the length of the cell and are long enough to overlap with flagella originating at the other end of the bacterium. The flat-wave shape has amplitude $\mathcal{A} \sim 1.0 \mu\text{m}$ and wavelength $\lambda \sim 3.0 \mu\text{m}$ [Fig. 1(a)] [3,7]. This shape is a minimum energy configuration if the flagella are helical and the cell cylinder is preferentially straight [7]. When the flagella rotate, the cell shape undulates as a traveling wave with wave speed $2\pi\omega/\lambda$, where ω is the wave frequency. As shown by Taylor, these wave motions lead to a swimming speed proportional to $\mathcal{A}^2\omega/\lambda$ [8]; the method of regularized Stokeslets provides an accurate means for

calculating the constant of proportionality and has been used to compute spirochete swim speeds [9].

A complete biophysical model for the swimming of spirochetes could lead to a better understanding of how these bacteria infiltrate mammalian hosts. But even absent that motivation, these bacteria provide a unique, complex physical system. For example, how does torque applied by

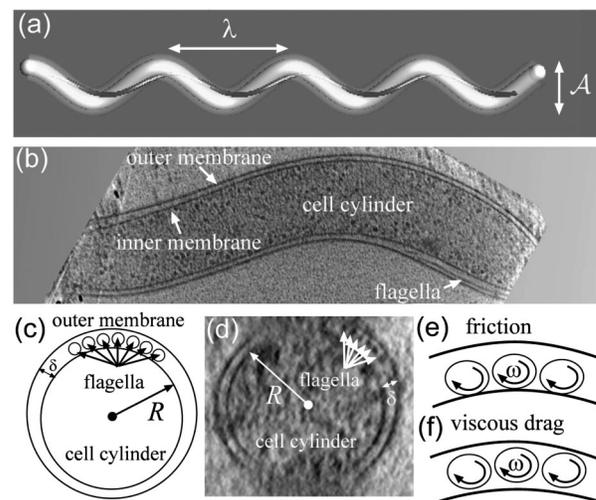


FIG. 1. (a) *B. burgdorferi* has a flat-wave shape, with wavelength λ and amplitude \mathcal{A} , produced by the helical flagella (dark grey) wrapping around the cylindrical cell body (white). (b) A lengthwise slice through *B. burgdorferi* shows the flagella located in the periplasm. (c),(d) Cells have circular cross sections of radius $R \approx 0.15 \mu\text{m}$. There are two possible scenarios for how forces and torques are transmitted between the cell body and the flagella: (1) The flagella are in contact with the cell wall (e) and frictional forces resist rotation of the flagella; (2) there is a thin fluid layer between the flagella and the cell cylinder (f), and resistive drag impedes the motion. (b),(d) Cryo EM images courtesy of S. Goldstein and N. Charon.

the flagellar motor to the flagella lead to traveling wave deformations of the cell body?

In this Letter, we do not address this question completely but begin analyzing the physics of borrelial motility by determining the forces and torques that act on a flagellum when it rotates in the narrow periplasmic space. We consider a filamentary flagellum with centerline position given by the vector $\mathbf{r}(s)$, where s is the arclength. It is expected that rotation of the flagellum is resisted by the environment, and we define a resistive force per length that acts on the flagellum, \mathbf{f}_r . The resistive forces produce deformations of the flagellum. Since the flagellum is elastic [7], deformation of the flagellum leads to an elastic restoring force per length, which is given by the functional derivative of the elastic energy, $-\delta\mathcal{E}/\delta\mathbf{r}$, where the energy comes from linear elasticity [10],

$$\mathcal{E} = \int \left(\frac{A}{2} (\kappa - \kappa_0)^2 + \frac{C}{2} (\Omega - \Omega_0)^2 \right) ds. \quad (1)$$

Here A and C are the bending and twisting moduli, κ and Ω are the curvature and twist density, and κ_0 and Ω_0 are the preferred curvature and twist density. For bacterial motility, the resistive forces are large compared to inertial forces. Therefore, $\mathbf{f}_r - \delta\mathcal{E}/\delta\mathbf{r} = 0$. In addition to these forces, there are also resistive and elastic torques per unit length. Like the elastic force, the elastic restoring torque can be defined from the functional derivative of the elastic energy with respect to Ω [11].

But, what are the resistive forces and torques that act against the flagellum in the periplasmic space? Here we consider two possibilities: (1) the flagella are in contact with the bacterial cell wall and motion is resisted by friction [Fig. 1(e)], or (2) the flagella are separated from the cell wall by a layer of fluid and the resistance comes from fluid drag [Fig. 1(f)]. These two scenarios produce different predictions for the deformation of a rotating flagellum and allow us to determine that there must be a lubricating fluid in between the flagella and the cell wall. Our analysis then provides the drag coefficients for a flagellum as it rotates between the cell cylinder and the outer membrane.

We first consider the case of a flagellum that is rotating and sliding while in contact with a solid wall (Fig. 2). We term this scenario the frictional model. Since the radius of a flagellum is much smaller than the helical radius of curvature, we focus on the simplified, two-dimensional case of a cylinder of radius a rotating against a wall with angular speed ω . We allow the cylinder to slip along the wall at velocity $v = V_f \hat{\mathbf{x}}$. The wall is aligned with the x axis, and we assume that the frictional force between the flagellum and the wall is proportional to the velocity. Therefore, $\mathbf{f}_r = -\zeta(V_f - a\omega)\hat{\mathbf{x}}$. Here, ζ is a drag coefficient that depends on the specific frictional interaction between the wall and the flagellum; it cannot be calculated *a priori*. However, because the resistive force is applied

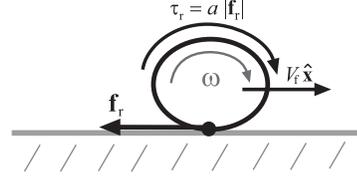


FIG. 2. The resistive forces and torques on a cylinder rotating and translating against a wall. A cylinder of radius a rotates at speed ω and moves with velocity $V_f \hat{\mathbf{x}}$. A resistive force acts on the cylinder at the point of contact. The resistive torque on the cylinder is equal to the radius of the cylinder times the magnitude of the resistive force.

locally to the surface of the flagellum, the resulting resistive torque is simply the radius of the cylinder times the magnitude of the resistive force, $\tau_r = a\zeta(V_f - a\omega)$. It is important to note that the resistive force and torque for this scenario are determined by a single drag coefficient.

Next, we consider the case where the flagellum is not in direct contact with the cell cylinder, and, instead, a layer of fluid mediates the interaction between the flagellum and the cell cylinder and outer membrane. The periplasmic space is treated as the region between two concentric cylinders of radii R and $R + \delta$, where the inner cylinder is the cell cylinder and the outer cylinder represents the outer membrane [Fig. 3(a)]. The periplasm is filled with fluid of viscosity η_p . Rotation of the flagellum in this space is opposed by fluid drag caused by the relative motion of the flagellum with respect to the cell cylinder and the outer membrane. In *Borrelia*, the distance from the flagellum to the cell cylinder, h_- , and the distance from the flagellum to the outer membrane, h_+ , are roughly comparable to the radius of the flagellum. The case of a cylinder rotating and translating near a single wall (e.g., $h_+ \rightarrow \infty$) has been solved analytically [12]. For this case, a rotating (translating) cylinder experiences no force (torque). However, recent computational analysis has shown that

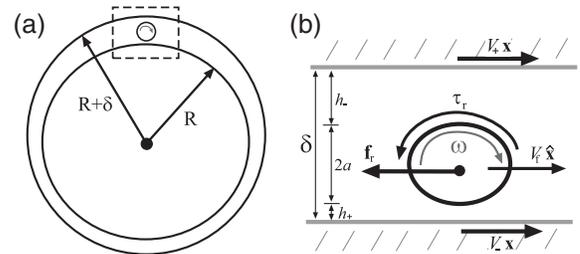


FIG. 3. The resistive force and torque on a cylinder rotating with speed ω and translating with velocity $V_f \hat{\mathbf{x}}$ in a fluid between two concentric cylinders. (a) The cell cylinder and the outer membrane are considered to be concentric cylinders with a fluid in between them. The cell cylinder has radius R , and the outer membrane has radius $R + \delta$. A single cylinder of radius a rotates in the space between these two cylinders. (b) The geometric parameters for the region about the flagellum.

the presence of a second wall leads to a net force on a purely rotating cylinder [13]. We have analyzed this problem using lubrication theory and numerical analysis [14,15] and have found that the force on the rotating cylinder arises from the constraint that the volume flux of fluid in the gap above the cylinder must equal the flux of fluid through the lower gap. This simple constraint can be used to derive approximate relationships between the resistive force, torque, rotational speed, and flagellar velocity [16].

We first note that rotation of the outer membrane with respect to the cell cylinder in Fig. 3(a) will produce a resistive torque on the cell cylinder that is approximately equal to $2\pi\eta_p R^2(V_+ - V_-)/\delta$ [17]. In addition, rotation of the flagellum can produce torques on the cell cylinder and outer membrane. Since δ is comparable in size to a , the magnitudes of these torques scale independently of δ . Therefore, to leading order in δ , the outer membrane and the cell cylinder rotate together, and $V_+ \approx V_-$ [Fig. 3(b)]. We can then set V_f to be the velocity of the flagellum relative to the cell cylinder and outer membrane. For *B. burgdorferi*, the flagellar diameter is roughly half of the width of the periplasmic space. Therefore, in what follows we assume that $\delta = 4a$. It is also useful to define the ratio of the top and bottom gaps, $h = h_+/h_-$. The resistive force and torque on the flagellum are then approximately [14]

$$\mathbf{f}_r = \frac{6\sqrt{2}\eta_p(1+h)^{5/2}}{(1+h^{5/2})} \left[\left(\frac{1-h}{1+h} \right) a\omega - 5V_f \right] \quad (2)$$

$$\tau_r = \frac{2\pi a\eta_p(1+h)^{5/2}}{(1+h^{5/2})} \left(\frac{5(1-h)}{2(1+h)} V_f - (h-1+h^{-1})a\omega \right) \quad (3)$$

where the force is in the positive x direction and a positive torque is clockwise.

In both the frictional model and the fluid drag model, the resistive drag force that we defined represents the resistive force per length in the direction perpendicular to the long axis of the flagellum, $\hat{\mathbf{n}}$, and tangential to the surface cell cylinder. We have shown that this resistive force can be written as $\mathbf{f}_r = -(\zeta_{\perp}V_f - \zeta_{\omega}a\omega)\hat{\mathbf{n}}$, where V_f is the velocity in the direction perpendicular to the long axis of the flagellum, and ζ_{\perp} and ζ_{ω} are drag coefficients. Likewise the resistive torque per length about the centerline of the flagellum can be written as $\tau_r = \xi_v V_f - \xi_{\omega} a\omega$, where ξ_v and ξ_{ω} are rotational drag coefficients. Rotation of the flagellum does not lead to resistive forces in the tangent direction of the flagellum. Therefore, the net resistive force in that direction is proportional to the tangential velocity of the filament, $\mathbf{f}_r \cdot \hat{\mathbf{t}} = \zeta_{\parallel}(\partial\mathbf{r}/\partial t) \cdot \hat{\mathbf{t}}$, where ζ_{\parallel} is the tangential drag coefficient.

A convenient way to compare the frictional model to the lubricating fluid model is by considering the dimensionless ratio of the magnitude of the resistive force to the resistive torque, $a|\mathbf{f}_r|/\tau_r$. For the frictional sliding interaction, this

ratio is always equal to one. For a flagellum that rotates without translating, this ratio is

$$\frac{a\zeta_{\omega}}{\xi_{\omega}} = \frac{3\sqrt{2}}{\pi} \frac{(h^{-1/2} - h^{1/2})}{(h^{-3/2} + h^{3/2})}, \quad (4)$$

which is less than 0.31 for all h [Fig. 4(a)]. This implies that a flagellum rotating in the periplasmic space will be less deformed when it is not in direct contact with the cell cylinder.

It is possible, then, that we can determine which of these scenarios describes the relevant physics for the rotation of the flagella in *B. burgdorferi*. We consider a toy model of a preferentially straight ($\kappa_0 = \Omega_0 = 0$), elastic flagellum of length L rotating with frequency ω in the periplasmic space of a rigid, cylindrical cell aligned with the z axis [Fig. 4(b)]. One end of the flagellum is attached to a motor that exerts a torque τ_m about the tangent vector of the flagellum and clamps that end of the flagellum so that it lies along the axis of the cell cylinder. The other end of the filament is free (i.e., no net force or torque is applied to that end). As before, the diameter of the flagellum is a and the radius of the cell cylinder is R . We can then define the position of points along the centerline of the flagellum with the vector $\mathbf{r}(s) = R\cos\phi(s)\hat{\mathbf{x}} + R\sin\phi(s)\hat{\mathbf{y}} + z\hat{\mathbf{z}}$. For a preferentially straight flagellum, one expects to find a steady-state solution at long times. From the elastic energy defined in Eq. (1), and the force and torque balance equations, the steady-state equations for ϕ and Ω are

$$\begin{aligned} \frac{\zeta_{\omega}a\omega}{AR} \cos\theta &= \frac{\partial}{\partial s} \left[\frac{\partial^3\phi}{\partial s^3} \sec^2\theta + 2\left(\frac{\partial\phi}{\partial s}\right)^3 \right] \\ &+ \frac{C}{2AR^2} \sin\theta \frac{\partial}{\partial s} (\Omega \sin 2\theta), \end{aligned} \quad (5)$$

$$C\Omega = \xi_{\omega}a\omega(L-s), \quad (6)$$

where we have assumed that the flagellum is inextensible and defined the angle between the tangent vector and the z axis, θ , which is given by $\sin\theta = R\partial\phi/\partial s$. Equation (6) gives that the torque that the flagellar motor must supply to rotate the flagellum at frequency ω is $\tau_m = \xi_{\omega}a\omega L$.

It is convenient to work in dimensionless units with $\tilde{s} = s/L$. For small deformations of the flagellum, $\partial^4\phi/\partial\tilde{s}^4 \approx \zeta_{\omega}\tau_m L^3/\xi_{\omega}AR \equiv \alpha$. The clamped boundary conditions at the rotated end of the filament set $\phi(0) = \partial\phi/\partial\tilde{s}|_0 = 0$, and the torque- and force-free conditions at the other end set $\partial^2\phi/\partial\tilde{s}^2|_1 = \partial^3\phi/\partial\tilde{s}^3|_1 = 0$. Therefore,

$$\phi = \frac{\alpha}{2} \left(\frac{1}{12} \tilde{s}^4 - \frac{1}{3} \tilde{s}^3 + \frac{1}{2} \tilde{s}^2 \right). \quad (7)$$

The small-amplitude equation shows that there is one primary dimensionless number, α , which determines the shape of the filament. This parameter depends on the torque from the flagellar motor, the length, radius, and bending modulus of the flagellum, the radius of the cell

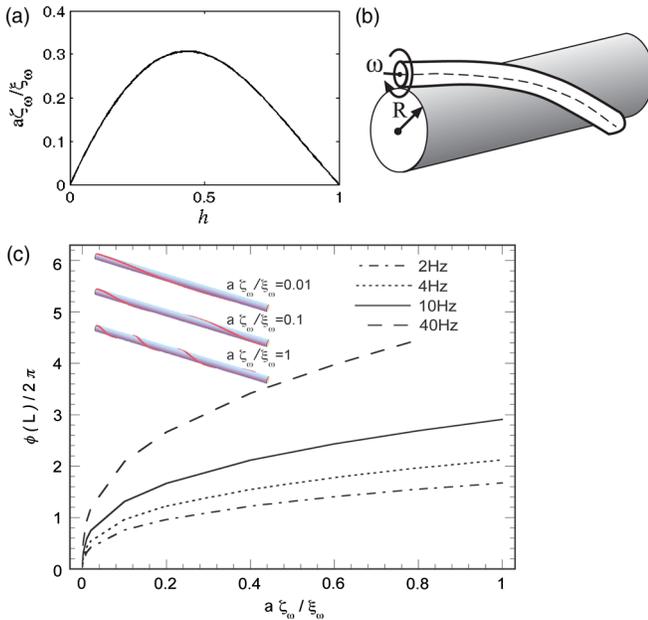


FIG. 4 (color online). (a) The dimensionless drag ratio as a function of the normalized gap width h . (b) Schematic of the toy model. A filament is rotated at one end with frequency ω , while being constrained to slide along the surface of a cylinder of radius R . (c) The angular deformation of the flagellum around the cell cylinder as a function of the drag-coefficient ratio for 4 different rotational speeds. The inset shows the computed shapes for three different values of the drag ratio.

cylinder, and the ratio of the translational to rotational drag coefficient, but is notably independent of the twist modulus. All of these parameters can be estimated from experimental measurements, except for the ratio of the drag coefficients. The torque from the flagellar motor is ~ 300 pN nm [18], the flagella are ~ 20 nm in diameter and $10 \mu\text{m}$ long with a bending modulus of ~ 6 pN μm^2 [7], and the cell cylinder has a radius of around 160 nm [5]. Therefore, $\alpha \sim 3 \times 10^4 (a\zeta_\omega/\xi_\omega)$. For most values of the ratio of the drag coefficients, α is quite large, and we expect large deformations of the flagellum.

To determine the large amplitude deformations of the toy model, we solve Eq. (5) numerically. In Fig. 4(c), we show the shapes of the filament for three different values of the drag-coefficient ratio. We quantify the deformation of the filament by computing the number of turns that the free end of the flagellum makes about the cell cylinder, $\phi(L)/2\pi$ [Fig. 4(c)]. As expected from the linear analysis, the deformation of the filament is large for all cases except when the drag-coefficient ratio is near zero.

In *B. burgdorferi* swimming, the waveform does not change drastically, and since there are 7 to 11 flagella per end, large flagellar deformations are unlikely during rotation, as these would lead to unmanageable tangles in the periplasmic space. On the other hand, our toy model suggests a flagellum that, for most situations, wraps extensively around the cell cylinder. How can these

deformations be avoided? For a nonrigid cell cylinder, bending of the cell could alleviate some of the flagellar deformation; however, it is not likely that this effect would change the order of magnitude of the deformation. Therefore, we predict that there exists a layer of fluid between the flagella and the cell cylinder, such that there is a negligible force on the flagella when they rotate in the periplasmic space. Our calculations then give the torque that the flagella experience when rotating [Eq. (3)], which provides the basis for constructing a full dynamic model of the swimming motility of spirochetes. More broadly, our results also provide a general physical description of the forces and torques that act on filaments rotating in narrow channels.

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