Flagellar Locomotion

Structure of Cilia and Eukaryotic Flagella

Much more is known of the structure and function of cilia and eukaryotic flagella (we use the single word cilia for convenience) than is known for prokaryotic flagella. Since there are extensive books and review articles (Gray 1928; Sleigh 1962, 1971, 1974a; Holwill 1966a, 1974; Brokaw 1975; Brokaw & Gibbons 1975) on this subject, we attempt only the briefest overview aimed at the fluid mechanician. A typical cross-sectional view of a cilium or eukaryotic flagellum is shown in Figure 1. Within a membrane is the

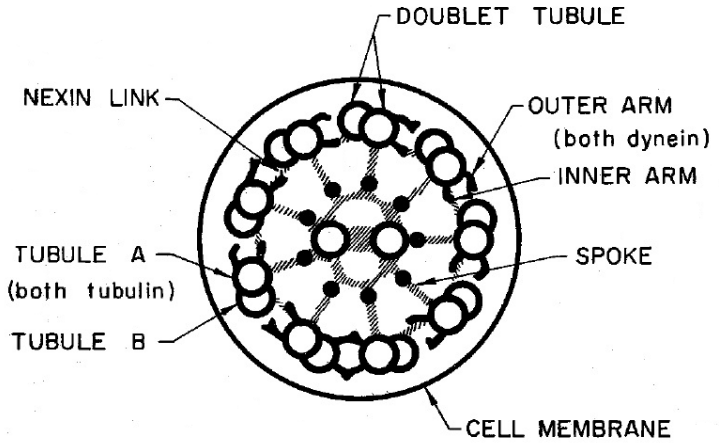

Figure 1: A diagrammatic representation of a cross-section through a cilium (or eukaryotic flagellum). Sliding is generally assumed to be generated longitudinally between the dynein arms and the B tubule across the gap spanned by the nexin link. The active role of the radial spokes in the contraction is not agreed upon. Modified from Brokaw & Gibbons (1975).

"axoneme" which consists of longitudinal fibrils or tubules (one of the structural elements of which is tubulin) arranged as a number of peripheral pairs plus a central pair. The number of outer pairs is often nine (hence the reference to a "$9 + 2$" pattern), although many other numbers and modifications of this basic pattern have been observed. "Arms" consisting of dynein project from the outer pairs of fibrils. The dynein and tubulin are believed to interact in a manner analagous to heavy meromyosin and actin in striated muscle. It has, however, been well established that the energy source, namely ATP, is the same for both systems. The details of the sliding mechanism have not been fully determined as one can gather from the variety of models still being proposed (e.g. Brokaw 1975; Costello 1973a,b; Douglas 1975; Dryl 1975; Harris & Robison 1973; Satir 1974; Summers & Gibbons 1971). Satir (1965, 1968) and Warner & Satir (1974) demonstrated that the microtubules remain constant in length during bending and that the bending is associated with longitudinal switching of the "radial spokes". They concluded that the radial spokes and their attachment to the central fibers are an important component in the generation of the sliding of peripheral subfibers past one another. Summers & Gibbons (1971) demonstrated the sliding phenomenon by inducing spermatozoa whose membranes have been partially digested to extrude subfibers by treating them with ATP. They proposed that the total sliding force is generated between the dynein arms on one pair of peripheral fibrils and subfibril 13 of the adjacent pair. The discovery of motile spermatozoa lacking central fibrils (van Deurs 1974) appears to support the Summers & Gibbons form of the model. A more extensive account of the development of the "sliding filament" model since its proposal by Machin (1958) may be found in Brokaw & Gibbons (1975).

It is evident that the actively generated bending moment in the contracting cilium is balanced by an internal resistance to motion (both elastic and viscous) and by the external viscous resistance. In this review we concentrate on the evaluation of the latter quantity, although it should be borne in mind that in the mechanics of cilia both elastic and viscous internal forces also appear to play significant roles and must be included in any attempt to extract knowledge of the basic activating force from knowledge of the motions of cilia and the fluid flow they create (see for example Brokaw 1970, 1971, 1972). The base of a cilium or eukaryotic flagellum is firmly imbedded in the cell membrane and there is no question of relative motion between that base and the cell membrane as there was for prokaryotic flagella; propulsion is always achieved by propagation of waves along the cilia or flagella. The energy source for the motion, namely ATP, may either diffuse along the length of the flagellum or be diffused in from the surrounding fluid. Therefore, the principal unknown is the control mechanism. Much of the recent work has been directed toward identifying the control and feedback systems evidently associated with eukaryotic flagella and cilia (Sleigh 1966, 1969; Brokaw & Gibbons. 1975).

Eukaryotic Flagellar Motions

In this section we concentrate on some of the characteristics of eukaryotic cell propulsion by single organelles, which we continue to call flagella at the risk of confusion with prokaryotic flagella; later we deal with propulsion by multiple organelles such as cilia.

The first fact to emphasize is the great variety of configurations of flagella and organisms (see Jahn & Votta 1972); here we can do no more than indicate some characteristic forms of flagellar motion and identify in particular those with different hydromechanical implications. Many organisms, including spermatozoa, have long flagella along which they propagate either a planar wave (e.g. *Ceratium*) or a helical wave (e.g. *Trichomonas*) or some combination of the two; typically, one finds about two wavelengths along the flagella as illustrated by the multiple exposure of sea urchin sperm in Figure 2 (Brokaw 1965). Commonly the wave

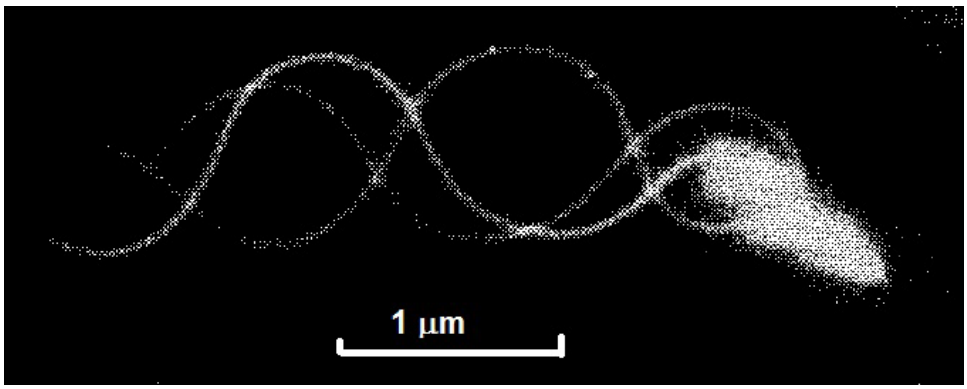

Figure 2: Multiple flash records of swimming tunicate (*Clona intestinalis*) spermatozoa (Brokaw 1965). The flash rate is $50Hz$ ad the scale bar is $10\mu m$. Photograph by C.J.Brokaw.

is propagated from the base to the tip, although the reverse has also been observed in the trypanosomes (Jahn & Votta 1972). Normally the direction of propulsion is opposite to the direction of wave propagation, although there exist counter examples, especially that of *Ochromonas* (Jahn, Landman & Fonseca 1964). This can be explained hydromechanically (Holwill & Sleigh 1967, Brennen 1976) because the flagellum of *Ochromonas* has attached to it a large number of rigid projections known as mastigonemes, which move through the fluid in response to the passage of the flagellar wave as indicated in Figure 4.

Hydromechanics of Flagella with Planar Waves

We begin by considering the propulsion of a simple organism with a spherical body of radius, A, by means of a single flagellum propagating planar waves from base to tip. Suppose the idealized organism in Figure

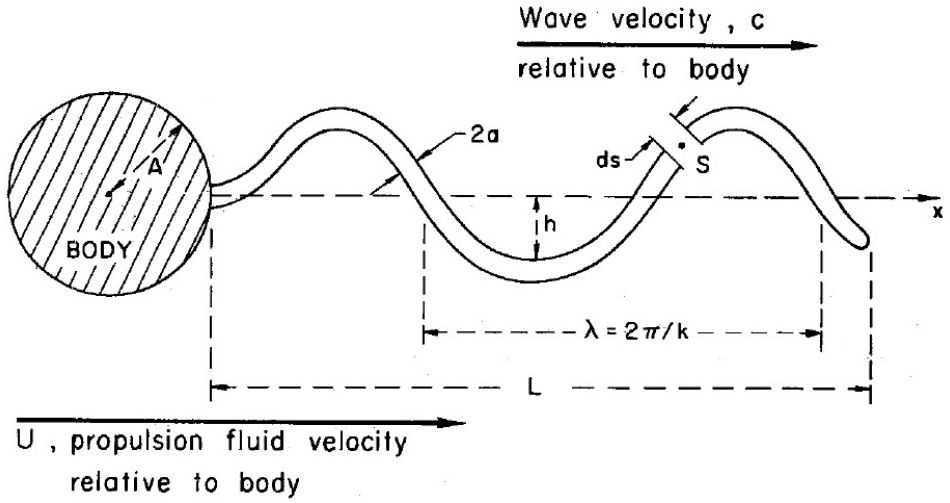

Figure 3: Flagellar propulsion with planar waves.

3 is propelled by means of a flagellum with planar waves of wavelength $\lambda = 2\pi/k$ and wave amplitude, h, traveling at wave velocity, c, relative to the body. We view an element of the flagellum, S, in a frame fixed in the body and assume the motion of S is purely normal to the direction x so that the motion of the element relative to the fluid at infinity (which has a velocity, U, corresponding to the velocity of propulsion) has components normal and tangential to the axis of the slender-body element S given by

$$q_n \;=\; U\sin\phi - kh\;c\cos\theta\cos\phi \qquad \text{and} \qquad q_s \;=\; U\cos\phi + kh\;c\cos\theta\sin\phi \tag{Dfc1}$$

where $\theta = k(x-ct)$ and $\tan\phi = kh\cos\theta$. If we then assume known resistive coefficients C_n and C_s the force on the element of length ds in the x direction is

$$C_n ds\left[U - (1-C_s/C_n)U(\cos\phi)^2 - (1-C_s/C_n)kh\;c\cos\theta\cos\phi\sin\phi\right] \tag{Dfc2}$$

at each instant in time where C_s/C_n is the ratio of the resistive coefficients. From an integration over one cycle in time it, follows that each element is subject to a mean force in the positive x direction which can be integrated over the length L of the flagellum to yield a mean force on the flagellum equal to

$$C_n L\left[U - (1-C_s/C_n)c - \frac{(1-C_s/C_n)(U-c)}{(1+k^2h^2)^{\frac{1}{2}}}\right] \tag{Dfc3}$$

If the organism were self-propelling, this would be equal to the drag $6\pi\mu UA$ on the head. Then the propulsive velocity U is

$$\frac{U}{c} \;=\; \frac{(1-C_s/C_n)\left\{(1+k^2h^2)^{1/2}-1\right\}}{(1+6\pi\mu A/LC_n)(1+k^2h^2)^{1/2}-1+C_s/C_n} \tag{Dfc4}$$

On the other hand, if the organism were restrained from moving, the thrust, T, developed by the flagellum in the positive x direction follows directly from equation Dfc3) with $U=0$ and is

$$T \;=\; \frac{cL(C_n-C_s)\left\{(1+k^2h^2)^{1/2}-1\right\}}{(1+k^2h^2)^{1/2}} \tag{Dfc5}$$

Lighthill (1975, p.55) shows that the results for more general waveforms do not differ from the above provided one uses a more general definition for $(1+k^2h^2)^{-1/2}$ as the mean value of the square of the tangential direction cosine of the waveform. These results show the primary dependence of the performance

of the flagellum on the wave velocity, c, the resistive-force-coefficient ratio C_s/C_n and the dimensionless wave amplitude, kh. The performance is clearly enhanced by decrease in C_s/C_n and increase in kh not only in terms of uniform translational motion as given by U/c but also from the point of view of acceleration from rest and maneuverability, both of which could be characterized by T. Although there has been a tendency for the fluid-mechanical analyses to concentrate on the optimization of the propulsive system in terms of seeking that which would give maximum rectilinear propulsion per unit energy expenditure, it is not at all clear that this is necessarily the most important feature of the system for any particular microorganism. Indeed the ability to accelerate and maneuver could be an asset as important, if not more important, to the organism.

According to the relations (Dfc4) and (Dfc5), U/c and T increase monotonically with increasing dimensionless wave amplitude kh approaching asymptotic values of $(C_n-C_s)/(C_n+6\pi\mu A/L)$ and $L(C_n-C_s)/6\pi\mu A$, respectively, for large kh. But the penalty paid for these enhanced propulsive effects is an increase in the energy required; the mechanical rate of work being done on the fluid can readily be obtained by integrating the increment of rate of work done per unit flagellar length $C_n q_n^2+C_s q_s^2$ over one cycle of time and summing for the entire length of the flagellum. Lighthill (1975) has shown that this leads to a maximum efficiency of rectilinear propulsion by a general planar wave when

$$(1+k^2h^2)^{1/2} \;=\; 1+\left(\frac{C_n}{C_s}\right)^{1/2}\frac{(LC_s+6\pi\mu A)}{(LC_n+6\pi\mu A)} \tag{Dfc6}$$

for which

$$\frac{U}{c} \;=\; \frac{\left\{(1-(C_s/C_n)^{1/2}\right\}}{(1+6\pi\mu A/LC_n)} \tag{Dfc7}$$

Furthermore, this optimum value of $(1+k^2h^2)^{1/2}$ is rather insensitive to the values of either C_s/C_n or $6\pi\mu A/LC_n$ and takes values for $C_s/C_n=1/2$ of 0.586 for very small $6\pi\mu A/LC_n$ (i.e. an organism with a small cell body, A) and 0.471 for vary large $6\pi\mu A/LC_n$ (i.e. an organism with a large cell body). In the case of a sinusoidal waveform, these values correspond to dimensionless wave amplitudes kh of 1.37 and 1.88, respectively. It is of interest to observe that many organisms with planar flagellar waves appear to operate with wave amplitudes of this order. Similarly it is instructive to examine the maximum mean propulsive force in one direction that can be generated by a small element of a slender body, whose position can oscillate sinusoidally in time within one plane and whose angle of inclination in that plane is also allowed to oscillate sinusoidally. One finds that the optimum propulsive force per unit energy expenditure occurs when the position oscillates normal to the direction of the required thrust, the mean inclination to this direction is zero, and the inclination oscillation is $\pi/2$ out of phase with the position oscillation. This corresponds precisely to the form of motion in a traveling wave, and one further finds that the optimum dimensionless amplitude, kh, is 2.

Gray & Hancock (1955) examined the propulsion for sea urchin spermatozoa (*P. milians*), which propagates a particularly sinusoidal waveform (see Figure 2), and observed an average propulsive velocity of $191.4\mu msec^{-1}$, in excellent agreement with a value of $191\mu msec^{-1}$ computed by using the observed wave amplitude, length, and velocity and an expression similar to Equation (Dfc4) with $C_s/C_n=0.5$. Lighthill has since suggested, and Gray & Hancock were probably aware, that such agreement was in some sense fortuitous and misleading. First, the more sophisticated analysis of Hancock (1953) [see also Lighthill (1975)] suggests that a more accurate value of C_s/C_n is significantly higher (about 0.7), which, in view of the factor $(1-C_s/C_n)$ in the expression (Dfc4) would cause significant disagreement. On the other hand, Gray & Hancock (1955) do mention that propulsion was occurring in close proximity to either the glass or the air surface; from section (Ble) we have seen that the value of C_s/C_n can be significantly reduced and propulsion enhanced by the proximity of a boundary and it would seem that the net result is a C_s/C_n of order 0.5.

The last observation serves further to illustrate the difficulty of wall effects upon data obtained in the confined fluid of a microscope slide; it also further exemplifies the beneficial propulsive effect that can be obtained by a flagellated organism moving close to a solid boundary. The detailed analyses of this problem by Katz (1974) yielded further information on these wall effects for flagellated organisms. The results do not differ qualitatively from those expected on the basis of the result (Ble17), although Katz has examined the waveforms on the flagellum that would lead to the maximum benefit in the presence of a boundary.

In concluding this section we must remark that while the simplicity of the resistive-force theory (section (Ble)) is a boon to biologists seeking approximate estimates, many potentially significant hydromechanical effects have been neglected in such an approach. First, there is the uncertainty in the force coefficients, C_n and C_s, which in reality implies the necessity of abandoning such a simplistic approach in order to seek more accurate solutions. Secondly, the effect of the often large cell body on the flow experienced by the flagellum has been entirely neglected. A more accurate analysis would require construction of the entire flow field due to both the cell body and the beating flagellum by means of fundamental singularities (see section (Blc)). Further evidence for the necessity of such an approach is provided by the observations of the flow field near flagellum obtained by Lunec (1975). Lunec compared the actual flow near the flagellum of *Crithidia oncopleti* (as visualized by tracer particles) with a theoretical reconstruction based on a distribution of stokeslets along the flagellar axis, whose strength was obtained from Gray & Hancocks resistive-force coefficients. The resulting fluid velocities were in marked disagreement, and Lunec concluded that this could in part be due to the proximity of the cell body.

Hispid Flagella

Some eukaryotic organisms such as *Ochromonas* (Figure 4) which propagate planar waves have rigid projections known as mastigonemes that protrude from the flagellum. These mastigonemes move through the

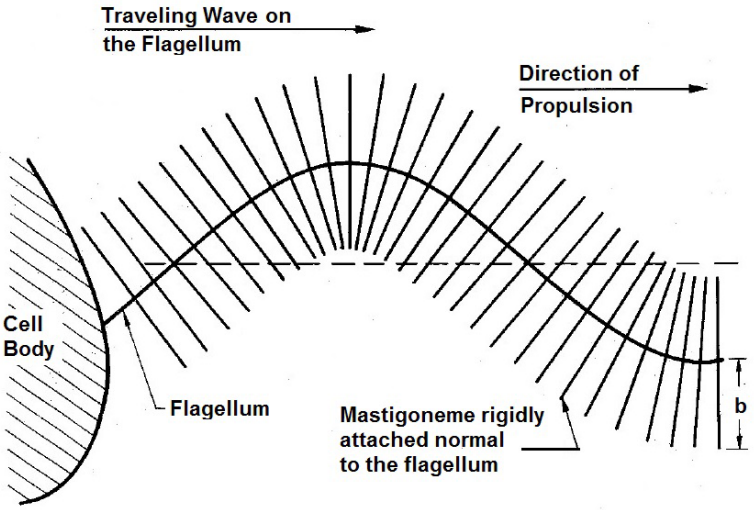

Figure 4: The flagellar/mastigoneme propulsion system. From Brennen (1976).

fluid as the waves pass along the flagellum and their net effect is to propel the organism in the direction opposite to that which would occur in the absence of mastigonemes. Jahn, Landman & Fonseca (1964) suggested that a simple way of viewing the hydromechanical effect of the mastigonemes is that they increase C_s much more than C_n, resulting in values of C_s/C_n greater than unity and thus propelling the organism in the direction opposite to that which occurs when $C_s/C_n < 1$ (see equation (Dfc4)). It is, however, a simple matter to apply resistive theory to the mastigonemes as Holwill & Sleigh (1967) and

Brennen (1976) have done and to show that for rigid mastigonemes the result (Dfc4) is altered

$$\frac{U}{c} = -\frac{\left[(1+k^2h^2)^{1/2}-1\right]\left[1-\frac{LC_n}{bnC_n^m}\right]}{\left[\left(1+\frac{2LC_n}{bnC_n^m}+\frac{12\pi\mu A}{bnC_n^m}\right)(1+k^2h^2)^{1/2}+1-\frac{LC_n}{bnC_n^m}\right]} \tag{Dfc8}$$

where n, b, and C_n^m are respectively the number, length, and normal resistive coefficient of the mastigonemes. Here C_s/C_n has been assumed to be one half for both flagellum and mastigonemes. Clearly if the total length of all the mastigonemes together (bn) is greater than the flagellum length so that $LC_n < bnC_n^m$, then U/c is always negative and an organism with a hispid flagellum moves with its flagellum forward while propagating waves along the flagellum in the same direction. The result (Dfc8) yields a value of $60\mu msec^{-1}$ for *Ochromonas*, which is in good agreement with the observed values of $55-60\mu msec^{-1}$ (Holwill & Sleigh 1967); Brennen (1976) has also examined the case of flexible mastigonemes and concluded that while the mastigonemes of *Ochromonas* are probably thick enough to have sufficient rigidity for hydromechanical purposes, the smaller "hairs" on *Euglena* flagella are probably so flexible that they have little hydromechanical effect.

Helical Flagellar Propulsion

The propagation of a helical wave along any flagellum, as illustrated in Figure 5, gives rise to a net

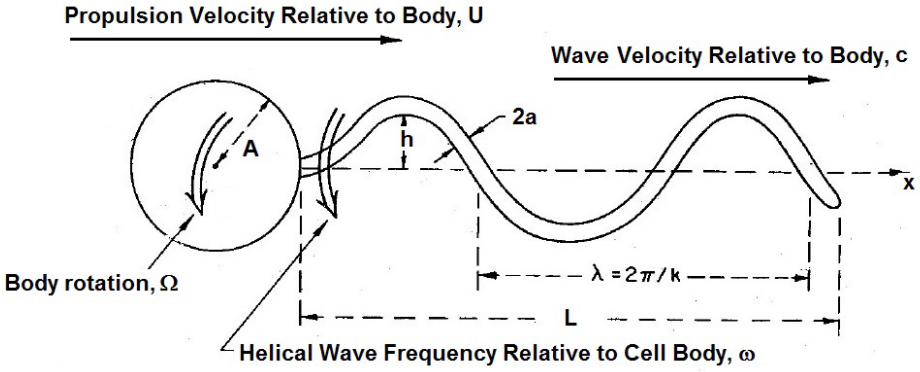

Figure 5: Eukaryotic flagellar propulsion with a helical waveform.

torque on the flagellum about the longitudinal axis; this causes the cell body to rotate (the material of the flagellum must rotate with the same angular velocity) so that an equal and opposite torque on the cell body is generated and the total torque on the organism is zero as it must be from mechanical first principles. Although this point was fully appreciated by Gray (1953), it was left unresolved in some of the early resistive-theory analyses by Holwill & Burge (1963) and Holwill (1966b). Chwang & Wu (1971) (see also Schreiner 1971) first presented a complete solution in which both the condition of zero total longitudinal force and the condition of zero total torque were applied to obtain not only the ratio of the forward speed, U, to the helical wave velocity, c (relative to the cell body), but also the ratio of the angular velocity of spin of the cell body (equal to the material rotation of the flagellum), Ω, to the angular velocity of the helical wave propagation relative to cell body, ω (equal to kc where $k = 2\pi/\lambda$ and λ is the wave length of the helical wave). These interconnected results are

$$\frac{c}{U} = \frac{1+2k^2h^2+A^*}{k^2h^2}\left\{1+\frac{2(1+k^2h^2)^2+(2+k^2h^2)A^*}{(1+2k^2h^2+A^*)B^*}\right\} \tag{Dfc9}$$

$$-\frac{\omega}{\Omega} = 1+\frac{(1+2k^2h^2+A^*)B^*}{2(1+k^2h^2)^2+(2+k^2h^2)A^*} \tag{Dfc10}$$

where we have changed the sign of the second expression by defining values of ω and Ω to be positive in the same rotational sense in order to highlight the fact that, as a result of the torque balance, ω and Ω are naturally of opposite sign. In the above expressions h is the helical wave amplitude and

$$A^* = \frac{3\mu A(1+k^2h^2)^{1/2}}{2\pi LC_s} \qquad \text{and} \qquad B^* = 4\mu\frac{\pi a^2 + A^3(1+k^2h^2)^{1/2}/2\pi L}{h^2C_s} \tag{Dfc11}$$

where A is the radius of the cell body (assumed spherical), L is the distance from the cell body to the end of the flagellum, a is the radius of the circular cross-section of the flagellum, and C_s is the tangential resistive coefficient. It has been assumed that C_s/C_n was equal to 1/2.

These results show interesting asymptotic limits; with a vanishingly small head ($A \to 0$) the forward propulsion given by U/c will become small and the material tends to rotate with a velocity, Ω, almost equal and opposite to the angular wave velocity, ω. This particular limit has relevance to the propulsion of a spirochete, which, lacking a flagellum, propels itself by propagating a helical wave along its long thin body; apparently the torque arising from the helical wave is balanced by an opposite rotation of the surface of the body (Chwang, Winet & Wu 1974; Kaiser & Doetsch 1975; Wang & Jahn 1972). On the other hand, for a large cell body Ω tends to zero, but the propulsive velocity again becomes small due to the large drag on the cell body. Between these limits a maximum value of U/c occurs. For typical values of kh and ka of 1 and 0.1, respectively, this maximum occurs when the "head-to-tail" ratio, A/a, is between 10 and 20, which is apparently typical for many organisms.

As far as the helical flagellar propulsion of eukaryotic cells is concerned, there have been few comprehensive comparisons of the theory with observations; the obvious difficulty is that the material rotation, Ω, is extremely difficult to observe or measure. Some partial analysis for *Euglena* by Holwill (1966b) did, however, appear to yield propulsive velocities of the same order of magnitude as those observed, and the results of Chwang, Wu & Winet (1972) and Winet & Keller (1976) provide a detailed analysis of a more complex form of propulsion, namely that associated with the prokaryote *Spirillum*.