A Model Describing Bending in Flagella

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Abstract. In Part I of this paper, we present a model to account for the force generation producing bending, and the formation of a waveform in sperm flagella. The model is based on the observation that dimers, and hence microtubules, possess dipole moments. The electric field these dipoles produce is the source for storing mechanical work in dynein arms. The mechanical work is then released and act on the doublets to produce a distally directed force with the result that bending occurs. The model described is consistent with experimental observations reported in the literature. The flexural rigidity of a dynein arm is also calculated. In Part II of this paper, the consequences of the bending mechanism are discussed. It is shown that the sum of forces from dynein arms acting distally along doublet microtubules in a flagellum is essentially zero when all dyneins are attached thus resulting in the rigor state. The waveform in a flagellum occurs if one of the sets of bending moments is zero, that is, a row of dyneins are detached over some distance along the flagellum. The direction of the bend in the waveform is determined by which set of dynein arms are detached with respect to the vertical median plane of the flagellum. The propagation of a bending wave is the result of a moving region in which alternate sides from the vertical median plane have inactive dynein arms. The processes by which this moving region occurs and the relationship of the above results to the propulsion of the flagellum are not considered.

1. Introduction

Flagella are complex biological structures used by numerous organisms, for example, for propulsion in sperms, removal of particles in bronchia, feeding in certain mollusks and for propulsion in low order organisms [14]. The cross-section of a sperm flagellum is seen to consist of nine doublet microtubules arranged about a circumference centered on the flagellum cross-section. The doublets are equally spaced about the circumference and thus at 40° intervals. A doublet consists of one cylindrical microtubule with 13 protofilaments (in this paper called the A-tubule) and a partially elliptical microtubule with 10 protofilaments (in this paper called the B-tubule). The angle of attachment of the B-tubule to the A-tubule is 10° outward from the local tangent. For the present analysis, all protofilaments are essentially parallel to the microtubule axis. Protofilaments are composed of proteins called dimers, which consist of an α - and a β – quasi-globular protein with nearly identical amino acid sequences. Each dimer possesses dipole moments: a dipole moment p_z pointing in the distal direction, a radial dipole moment p_r directed radially inward, and a tangential dipole moment p_θ [5, 6, 15]. The axial and tangential dipoles lie in a plane that is locally tangential. The resulting dipole electric field outside the

microtubule points in the proximal direction and counterclockwise. Thus, the field is helical, decreasing with increasing distance from the doublet surface. Outer and inner dynein arms arranged along the flagellum circumference and at approximately 90° to the microtubules axes and equally spaced, control the bending of the flagellum. These arms are known to produce forces resulting in bending. The outer dynein arms are rigidly attached to the A-tubule [9] while the other end of the dynein arm possesses a globular protein head that interacts by attachment or detachment with the B-tubule. The dynein arms are essentially straight [9]. Doublets are usually numbered for reference purposes beginning with number 1 located at $x = 0$ and $y = d$, where d is the radial distance of the A-tubule of doublet 1 from the flagellum geometric center. The numbering sequence is from 1 through 9 running clockwise when a cross-section is seen from the basal body looking distally. There is evidence [21] that indicates that doublets 5 and 6 are joined permanently by the outer dynein arms. The function and operation of the outer dynein arms have been fairly well established. On the other hand, while the morphology and some of the functions of the inner dynein arms have been reasonably satisfactorily explained, their operation with regards to flagella bending has not. The outer and inner dynein arms serve distinctly different functions and the inner dynein arms appear to be responsible for the shape of the flagellum waveform [19]. The outer dynein arms appear to be responsible for the beating frequency, relative sliding velocity, and the propulsive power output [19]. In this paper our attention will focus on the outer dynein arms only.

The functional cycle of the outer dynein arms is generally considered to have the following steps [19]: in the absence of adenosine-tri-phosphate (ATP), the head of the outer dynein remains attached to the B-tubule. This attachment appears to be electrostatic in nature. When many are so attached the flagellum is in a state of rigor. The rigor state is observed for any shape: straight, single or multiple bends, or a complete waveform. Such states are attained during a sudden dilution in the ATP concentration of the solution [7]. ATP reacts with the dynein head causing it to detach from the B-tubule and later to re-attach to it, then producing a force along the B-tubule directed towards the distal end of the flagellum. This force has been identified as the cause of bending in flagella. Various theories have been proposed to explain the mechanism of the ATP reaction with the outer dynein arms (see for example Brokaw and Simonick [4]; Omoto [18]) and rate constants for the various steps in the outer dynein arm cycle have been proposed (e.g. Porter and Johnson [20]; Holzbaur and Johnson [10]; Okuno and Brokaw [17]).

In Part I of this paper we will show that the forces causing doublet sliding and bending in a flagellum can be accounted for by considering conditions under which the dipole electric field energy of doublets results in mechanical energy being stored in the arm of the dynein. That stored energy is subsequently released when re-attachment occurs to produce the force necessary to bend a doublet. This model accounts for the correct direction of that force and the observed bending, and does not require curvature control, self-oscillation or a combination of these,

Figure 1. The four stages in the dynein arm doublet interaction proposed in this paper: a) rigor state, b) detached state, c) 'cocking' displacement and re-attachment state, and d) mechanism of bending.

metabolically driven activation switching, or threshold activation. In Part II we discuss the collective behavior of dynein arms resulting in bending moments, and show how waveforms can develop. In the theoretical discussion that follows, the MKS system of units is used throughout.

2. Part I – Mechanism of Bending

We assume that the bending and relative sliding of a set of doublets adjacent to each other involve the dynein arms in four separate stages, each stage independent of the others. We assume further that the initiation mechanism is the result of the interaction of the ATP and reaction with the dynein protein head. Such interaction is generally referred to as 'collision' in the terminology of physics. The dynein arms are assumed to consist of two parts [9]; an arm attached rigidly to the A-tubule at its base, and a head that attaches intermittently to the B-tubule, depending on the function it performs. Figure 1 shows the separate stages in the bending and sliding process.

2.1. RIGOR STATE

It has been well established experimentally [19, 25] that in the absence of ATP an outer dynein arm remains rigidly attached to its neighboring B-tubule. This collective behavior gives rise to the rigor state. The rigor state has been observed in the straight and waveform configurations [25]. Figure 1a shows a partial cross section of a flagellum and a single dynein arm and head attached to the A- and B-tubules. The cross section is viewed from the basal body to the distal end of the flagellum, and indicates the nomenclature in general usage. In this paper it is assumed that the base of the dynein arm is rigidly attached to the A-tubule, in other words, the attachment of the dynein arm to the A-tubule is not a hinged attachment. This point is crucial if the distally directed bending force produced by the dynein arm is to result in bending. A hinged attachment will not result in bending. There is evidence to support this assumption [9], and in the model discussed in this paper, that rigid connection is needed to enable storing and releasing mechanical work by the dynein arm. In Figure 1a, this rigid connection is indicated by the symbol, $\llcorner$. The cross hatching in the dynein head is meant to indicate attachment of the head to the B-tubule and detachment is indicated by a lack of cross-hatching.

2.2. DETACHMENT

The detached state of the dynein head is shown in Figure 1b. This occurs when ATP undergoes a ‘collision’ reaction with the dynein head. This collision reaction may result in exposing charges in the dynein head such that these charges interact with like charges on the dimer (Barlow and Thornton [1]; Stracke et al. [26]) resulting in detachment. Exposing charges may be brought about by a change in conformation of the dynein head as a result of the $\text{ATP} \rightarrow \text{ADP}$ reaction. Stracke et al. [26] measured the number of charges per dimer using a method of microtubule migration in an electric field and determined that there are $0.19 e^-$ charges per dimer, e^- is the charge of the electron. Brown [5] calculated the magnitude and direction of the dipole on the dimer. His results indicate that the axial dipole moment $p_z = 337 \text{ D}$, radial dipole moment $p_r = -1669 \text{ D}$, and the azimuthal and locally tangential dipole moment $p_\theta = 198 \text{ D}$. Therefore, there is a surface dipole moment $p_s^2 = (p_\theta^2 + p_z^2) = 391 \text{ D}$ with a direction clockwise from the microtubule axis of $\theta = \text{atan}(p_\theta/p_z) \cong 30^\circ$. The radial dipole moment results in a force on the dynein head directed outward along the radius of the tubule. Using these data we want to calculate the energy required to detach the dynein head from the B-tubule. From this result we compare the energy required for detachment to the energy available from an ATP collision. In such a collision, the ATP kinetic energy is neglected compared to the energy released by the $\text{ATP} \rightarrow \text{ADP}$ reaction. To detach a dynein head, energy must be supplied to overcome the effects of the radial dipole moment $p_r = -1669 \text{ D}$, and the energy required to overcome the electric field present between the charges of the dynein head and the dimer. The energy required to effect a detachment is given by

$$U_D = N q^2 / (4\pi \epsilon_0 \epsilon_r d) - \mathbf{p}_r \cdot \mathbf{E} \quad (1)$$

where $\mathbf{P}_r$ is the radial polarization vector and $\mathbf{E}$ is the electric field vector. The magnitude of the electric field vector depends on the number charges N on the dimer and the dynein head, then

$$E = N q / \epsilon_0 \epsilon_r A_d \quad (2)$$

And since $p_r = -1669 (3.33 \times 10^{-30}) = -5.56 \times 10^{-27}$ C/m, where the number in parenthesis is a conversion factor from Debye to coulomb/meter. Then equations (1) and (2) yield

$$U_d = N q^2 / (4\pi \epsilon_0 \epsilon_r d) + 5.56 \times 10^{-27} q N / (\epsilon_0 \epsilon_r A_d) \quad (3)$$

where q is the charge on an electron, ϵ_0 and ϵ_r are the permittivity of vacuum and the relative permittivity of the solution surrounding the dimer/dynein head, respectively, d is the separation distance between dimer and dynein head, N is the number of charges of opposite sign required to effect a separation, and A_d is the area over which the electric radial field is acting. The magnitude of A_d is uncertain. Using the following numerical values in equation (3): $q = 1.602 \times 10^{-19}$ C, $\epsilon_0 = 8.85 \times 10^{-12}$ F/m, $\epsilon_r = 80$ (water), $A_d \cong 16 \times 10^{-16}$ m², then

$$U_d = N(2.88 \times 10^{-30}/d + 7.86 \times 10^{-20}) \quad (4)$$

Using a value for $d = 0.2$ nm and $U_d = 5 \times 10^{-20}$ J/ATP [16] as the energy available per ATP molecule during a collision, we find from equation (4) that the number of unbalanced charges required for separation is $N \cong 0.54$. In subsequent calculations we will use $N = 1$ when we determine the magnitude of the force acting on the detached dimer, this force being the result of the electric field produced by the dimer dipoles along and around the B-tubule.

Now we proceed to calculate the dipole electric field strength produced by the surface dipole p_z .

2.3. DIPOLE ELECTRIC FIELD

The external electric field due to the dimer dipoles very close to the microtubule surface is periodic because of the irregular surface that dimers present along the microtubule surface, with a periodicity rapidly decreasing with distance away from the microtubule surface. In this paper we are only interested in the field near and outside the microtubule and assume it to be axially and circumferentially smooth near the surface. This greatly simplifies the field calculations. This field exerts an interaction force on the detached dynein head, which is given by Lorentz's equation

$$\mathbf{F}_D = Q(\mathbf{E} + \mathbf{v} \times \mathbf{B}). \quad (5)$$

where $\mathbf{E}$ is the electric field vector, $\mathbf{v}$ is a velocity vector and $\mathbf{B}$ is a magnetic field vector. However, in the present case there appears to be no external magnetic field, other than that produced by the motion of ATP molecules, so that equation (5) reduces to

$$\mathbf{F}_D = N q \mathbf{E}_D \quad (6)$$

where N out is the total charge on the dynein head that can interact with the field and q is its charge. The force $\mathbf{F}_D$ is directed toward the basal body and thus causes the dynein head to move back towards the basal body as shown in Figure 1c when detached from the B-tubule. The motion of the dynein head in the direction of the basal body bends the dynein arm in the same direction. Because it is rigidly attached to the A-tubule, the electric field energy is converted to mechanical energy stored in the bent dynein arm. Thus, the electric field acting on the dynein as a whole is converted to mechanical work. However, a certain amount of this mechanical work is lost in overcoming ‘friction’ between the dynein head and the dimers. This ‘friction’ force is due to charge-charge interaction [27]. When bending back has reached a maximum displacement $x_{\max}$ (Figure 1c), local deformation of the dynein head and bending of the arm may result in the release of the reaction products or undergo a conformation change, thereby returning the dynein head to its former conformation, and reattachment occurs. This fact is conjecture as dynein heads may be fairly rigid proteins. However, small local stresses on the structure may cause shifting of surface charges, making this mechanism possible. This may result in the charges previously exposed become again shielded. The dynein head then re-attaches to the B-tubule.

2.3.1. *Magnitude of the Dipole Electric Field*

We will now calculate the magnitude of the dipole electric field. To do this, consider a coordinate system (Figure 2) with a single dimer whose dipole field p_z is shown pointing in the positive z -direction, that is, distally. We will ignore the radial field produced by $-p_r$ since its only contribution seems to be to cause dynein head attachment among other as yet unknown effects. We also neglect the fact that the dipole moment p_s is tilted with respect to the B-tubule axis and only consider its axial component p_z . Although the resulting electric field will be helical, the net effect of interest here is the field on the dynein head, which is along the B-tubule axis, with a magnitude $p_z = p_s \cos(30^\circ) = 337$ D. We wish to calculate the magnitude and orientation of the electric field at a point in space labeled $P(R, z, \varphi)$ due to the dipole moment p_z . Furthermore, we are interested only in the electric field component parallel to the z -axis and its radial dependence. Simple geometry (Figure 2) shows that the distance r_{ij} from a dipole to the field point $P(R, z, \varphi)$ is given by

$$r_{ij}^2 = a^2 + R^2 + z^2 - 2aR \cos(\varphi_i). \quad (7)$$

Figure 2. Geometry used in deriving the dipole electric field.

But the distribution of dipoles around the circumference C is discrete. For a B-tubule, which is elliptical with an eccentricity $e = 0.4627$, the angle between filament is given by Schoutens [23]

$$\varphi_i = 2 (\pi - \alpha_0) / (m - 1) = 25.67^\circ \quad (8)$$

where $m = 10$ is the number of protofilaments making up the B-tubule. Consequently, r_{ij} must reflect the discrete distribution of dipoles around the circumference separated by an angle $\varphi_i = 25.67^\circ$. The constant α_0 is the angle the B-tubule is open at its contact with the A-tubule of the doublet [23]. The potential at $P(R, z, \varphi)$ from one protofilament with one dipole in the xy -plane and perpendicular to it is

$$V_{ij}(R, z, \varphi_i) = P_{ij} / 4\pi \varepsilon_0 \varepsilon_r r_{ij}^2 \quad (9)$$

where P_{ij} is the dipole moment, ε_r is the relative permittivity of the solution in which the doublets are immersed, assumed to be water. The index i counts the dipoles around the circumference C and the index j counts dipoles along a protofilament (z -axis), from $-L/2$ to $L/2$, where L is the total length of the straight flagellum. Summing over all dipoles about φ and along z gives

$$V(R) = \sum V_{ij}(R, z, \varphi_i) = (4\pi \varepsilon_0 \varepsilon_r)^{-1} \sum_i^n \sum_j^m P_{ij} / r_{ij}^2 \quad (10)$$

where n represents the total number of protofilaments in the B-tubule around the circumference and m the total number of dimers from $-L/2$ to $L/2$, given by $L/2r_0$, where r_0 is the separation distance along z between dimers. We note that $L/2r_0$ is considerably greater than unity because the spacing between consecutive dimers is small ($\cong 8$ nm) compared to the length of a typical flagellum (several microns). This means that we can replace the sum over j by an integral over z , or

$$V(R) = (2\pi \varepsilon_0 \varepsilon_r L)^{-1} \sum_{i=-n}^n \int_0^{L/2} [a^2 + R^2 + z^2 - 2a \cos(n\varphi_i)]^{-1} \mathbf{P}_{ij} dz \quad (11)$$

In equation (11) the sum over j is twice the sum from $j = -L/2r_0$ to $j = L/2r_0$, consequently, a factor of 2 was removed. We can replace $\mathbf{P}_{ij}$ by $\mathbf{P}_0 = \text{constant}$ (or 337 D), since all dipole moments have essentially of the same magnitude and the same direction, and there are $n = L/2r_0$ of them, so that when integrating equation (11), we find that the potential at $P(R, z, \varphi)$ is

$$V(R) = (nP_0/2\pi \varepsilon_0 \varepsilon_r r_0) \sum_{i=-n}^n [a^2 + R^2 - 2aR \cos(n\varphi_i)]^{-1/2} \text{atan}(L/[a^2 + R^2 - 2aR \cos(n\varphi_i)]^{1/2}) \quad (12)$$

The electric field along z as a function of the radial distance R is then given by

$$E_D(R) = -\partial V/\partial R = (nP_0/2\pi \varepsilon_0 \varepsilon_r r_0) \sum_{i=-n}^n \left[\left[\text{atan}(L/[a^2 + R^2 - 2aR \cos(n\varphi_i)]^{1/2}) \right. \right. \\ \left. \left. (R - a \cos(n\varphi_i)) * [a^2 + R^2 - 2aR \cos(n\varphi_i)]^{-3/2} \right] + \left[L (R - a \cos(n\varphi_i)) \right. \right. \\ \left. \left. [[a^2 + R^2 - 2aR \cos(n\varphi_i)] * [a^2 + R^2 + L^2 - 2aR \cos(n\varphi_i)]]^{-1} \right] \right] \quad (13)$$

and this field produces a force on the dynein arm that is given by

$$F_D = N q E_D(R) \quad (14)$$

where N is the number of charges on the dynein head that the dipole electric field is acting upon, and q is the magnitude of a single charge (1.602×10^{-19} C). The numerical values used in equation (13) for the purpose of calculating the force are: $\varphi_i = 25.67^\circ$; $L = 30 \times 10^{-6}$ m, a typical flagellum length; $R \cong (15.6 + d) \times 10^{-9}$ m, where d is the separation distance from the dimer surface at detachment, and the factor 15.6×10^{-9} m is the mean radial distance of the dynein head center to the B-tubule center, and the mean B-tubule diameter is assumed to be $a = (a_m + b_m)/2 = 13.3 \times 10^{-9}$ m [23]; $P_0 = 1.122 \times 10^{-27}$ C/m; the center-to-center distance between dimers is $r_0 = 8 \times 10^{-9}$ m; and we assume $\varepsilon_r = 80$ (water) for the relative permittivity of the fluid surrounding the flagellum. Using these numerical values in equation (13) and (14) we obtained the following results: with one charge interacting and considering that the field from 5–7 protofilaments of the B-tubule in the immediate neighborhood of the dynein head and which are acting on the dynein head, the

force of interaction pulling the dynein head toward the basal body ranges from 4–12 pN. These results assume that there are no counterions to reduce the magnitude of the field strength. This is patently not the case. However, a calculation that would take account of the counterions is considerably more complicated and the type of model presented here did not warrant such a complexity at the present time. The magnitude of the electric field, and consequently, the magnitude of the force, does not change significantly as the separation distance between the dynein head and the B-tubule varies in the ranges 0.1–0.2 nm. Kamimura and Takahashi [11] devised experiments to measure the force developed by a dynein arm in moving one doublet alongside another. They found the magnitude of this force to be on the order of about 2 pN per dynein arm, with this magnitude depending weakly upon the concentration of ATP. Therefore, the present results are well within the observed order of magnitude. In view of the computed results in this paper and the results of these authors, we will use $F_d = 5$ pN for the remainder of the calculations in this paper.

2.4. THE DYNEIN ARM

Upon reattachment after $\text{ATP} \rightarrow \text{ADP}$ reaction, the dynein arm, being an elastic material, will have stored in it mechanical energy capable of doing work. The mechanical energy stored corresponds to the energy taken from the dipole electric field minus a fraction of that energy used to overcome local ‘friction’ [27]. The term ‘friction’ used here is meant to imply a macroscopic term to account for the interaction among charges on the dimers and the dynein head while it is detached and moving basally under the action of the electric field.

The key to the cause of bending of doublets in the present model lies in the fact that the dynein arm is assumed to form a rigid attachment to the A-tubule (See Goodenough and Heuser [9] for a likely configuration). The mechanism that produces bending is shown schematically in Figure 1d. The first diagram shows how the stored mechanical energy produces a force F pulling on the B-tubule that is anchored in the basal body. The next diagram in Figure 1d shows how the magnitude of F acts on the A-tubule. Without altering anything a force $-F_1$ and F_1 can be attached at the anchor point of the dynein arm. These forces do not change the balance of existing forces. Next, the force $-F_1$ can be slid along the A-tubule until it is anchored in the basal body and replaced by the reaction force $R = F_1$. Now, F can be replaced by a moment as shown or $M = Fd$, and remove F from the B-tubule. Therefore, the A-tubule is locally in compression, the B-tubule locally in tension, while both are acted upon by a moment M . This mechanism then causes bending of the A- and the B-tubules as shown in Figure 3. If the dynein arm were not rigidly attached to the A-tubule no such bending would be possible. What would happen instead is a convergence of the tubules.

When bending the doublets through an angle φ , both doublets remain the same lengths from the basal body, but slide relative to each other to accommodate differ-

Figure 3. Geometry for the connection of maximum bend angle $\varphi_{\max}$.

ent bending radii [22] (Figure 3, inset). This occurs in such a way that the doublet having radius R_2 exceeds the angle φ by an amount $\Delta\varphi$ since the inner doublet *appears* to slide in the distal direction as observed by Satir [22]. We can show (Figure 3, inset) that $l_1 = R_1\varphi$ and $l_2 = R_2(\varphi + \Delta\varphi)$ so that $\Delta l = R_2\Delta\varphi$. Also, $l_1 = R_1\varphi$ and $l_2 + \Delta l = l_1 = R_1\varphi = R_2(\varphi + \Delta\varphi)$, and from $\Delta l = R_2\Delta\varphi$, we conclude as did Satir [22] that

$$\Delta l = R_2\Delta\varphi = (R_1 - R_2)\varphi = \varphi\Delta R \quad (15)$$

Equation (15) implies that as φ increases so does Δl and if the bend is reversed it becomes equal to $-\Delta l$, and so on for bend reversal.

2.4.1. Force Balance

How far is the bending of the dynein arm proceeding when a segment of two adjacent doublets, anchored in the basal body, are acted on by one dynein arm? In other words, what is the maximum value of φ for a bend produced by one dynein arm? The value of φ becomes $\varphi_{\max}$ when the energy *remaining* in the dynein arm corresponds to the energy stored in bending the doublets. We calculate the force required to bent the dynein arm to its maximum deflection so that the energy

Figure 4. Force produced by a dynein head on a doublet as a function of φ : qualitative curve.

balance between the doublets and the remaining energy in the dynein arm occurs when $\varphi = \varphi_{\max}$. Schematically, this appears as the function $F(\varphi)$ in Figure 4, where $F(0) = F_D$, and when the dynein arm is bent back to $x_{\max}$ we have that $F(\varphi_{\max}) = F_B$ when energy balance is achieved. Given these conditions we wish to calculate $\varphi_{\max}$. To begin, we solve the problem of a cantilevered beam representing the dynein arm, deformed to its maximum deflection $x_{\max}$. Figure 5 shows the nomenclature used. The dynein head moves under the action of the electric field outside the B-tubule, and is opposed by a force F_R resulting from the resistance to bending of the dynein arm. The position of the head remains on the axis of the B-tubule. This means that L_0 increases to L when φ increases. Therefore, energy is also stored in extension of the dynein arm. Thus, there is a tangential resisting tensile force F_t acting on the dynein arm. Consequently, we must have that $F_D = F_R/(1 - \sin \theta)$.

The moment equation from elasticity theory for a cantilevered beam is given by

$$d\theta/ds = -(F_D/EI)(L_0 - y) \quad (16)$$

where s is the arc length, or $s = L$ (Figure 5) which is the distance between successive dynein arms. Differentiating both sides with respect to s gives

$$d^2\theta/ds^2 = p^2 dy/ds = p^2 \cos \theta \quad (17)$$

Figure 5. Nomenclature and geometry of cantilevered beam.

where $p^2 = F_D/EI$. The parameter E is the elastic modulus of the dynein arm material and I its moment of inertia with respect to the neutral plane of bending, and EI is the flexural rigidity of the dynein arm, therefore combining material and geometric properties. Multiplying both sides of equation (17) by $d\theta/ds$ and recognizing that $(d\theta/ds)[d^2\theta/ds^2] = d[(d\theta/ds)^2/2]/ds$ and that $\cos \theta \, d\theta/ds = d(\sin \theta)/ds$, we find a differential equation which upon integration yields

$$(1/2)(d\theta/ds)^2 = p^2 \sin \theta + C \quad (18)$$

This differential equation is nonlinear in θ . The boundary condition is that at $y = 0$ ($s = 0$), $\theta = 0$, and $d\theta/ds = 0$, therefore $C = 0$. Then equation (18) reduces to

$$d\theta/ds = p (2 \sin \theta)^{1/2} \quad (19)$$

But $d\theta/ds = (d\theta/dx)(dx/ds) = \sin \theta (d\theta/dx)$, and recalling that $p^{-1} = (EI/F_D)^{1/2} = [EI(1 - \sin \theta)/F_R]^{1/2} = [EI(1 - \sin \theta)/F_D]^{1/2}$ we finally obtain from equation (19) that the deflection caused by the forces acting on the beam is given by

$$x = [EI/2F_D]^{1/2} \int_0^\varphi [(1 - \sin \theta) \sin \theta]^{1/2} d\theta \quad (20)$$

Carrying out the integration gives

$$x = [EI/F_D]^{1/2} f_t(\varphi) \quad (21)$$

where

$$f_t(\varphi) = \frac{[-\log[\cos(\varphi/2) + \sin(\varphi/2) + (\sin \varphi)^{1/2}] + [\cos(\varphi/2) + \sin(\varphi/2)] (\sin \varphi)^{1/2} * [(1 - \sin \varphi) \sin \varphi]^{1/2}]}{[\cos(\varphi/2) - \sin(\varphi/2)] (\sin \varphi)^{1/2}} \quad (22)$$

If the beam were allowed to bend without stretching, in lieu of equation (20) we would have the following integral

$$x = (2)^{-1/2} p^{-1} \int_0^\varphi (\sin \theta)^{1/2} d\theta = [2EI/F_D]^{1/2} f(\varphi) \quad (23)$$

where

$$f(\varphi) = E[(\pi/2), 2] - E[(1/2)[\pi/2 - \varphi], 2] \quad (24)$$

where $E(\psi, m)$ is the elliptic integral of the second kind. Equations (23) and (24) can be used to calculate the energy stored in the doublet when the dynein arm has released all its stored energy since no extension forces are acting on the doublet. We can use equations (23) and (24) to calculate the deflection of the doublet. Table I gives the values of $f_t(\varphi)$ and $f(\varphi)$ as a function of φ . Because the precise value of φ is not conveniently calculated as x varies, it is easier to use the transformation $x(\varphi)$ obtained in the following manner. We can relate R to x by

$$R = [L_0 / \sin(\varphi_{\max})] = [(2 x_{\max}^2 + L_0^2) / (4 x_{\max})] \quad (25)$$

from which we find that

$$\varphi = \text{asin}[4\alpha / (1 + \alpha^2)] \quad (26)$$

where $\alpha = x/L_0$, and L_0 is the length of the doublet between dynein arms. In deriving equation (26) we used the fact that $L = L_0 + \Delta L = L_0 + \varphi \Delta R$ which occurs without tensile load. But $\varphi \Delta R \ll L_0$ so that to first order we find $\alpha = x/L_0$.

The analysis developed above is now used to calculate: 1) the deflection of the doublet pair A and B as the dynein arm releases its stored mechanical energy, and 2) the force $F(\varphi_{\max})$ at which the energy remaining in the dynein arm corresponds to the energy stored in the doublet pair. We now calculate the force corresponding to the radius of curvature in the deflection of the flagellum. The data used for this calculation, while it is approximate, nevertheless gives some indication of the magnitudes involved. The shape of the flagellum waveform is that seen in typical sperm flagella photomicrographs (e.g. Brokaw [3]) for a complete bend between

Table I. Values of the function $f_f(\varphi)$ and $f(\varphi)$

φ ($^\circ$)	$f_f(\varphi)$	$f(\varphi)$
1	0.131208	0.000769
2	0.186814	0.00217
4	0.264115	0.00615
6	0.323309	0.01129
8	0.373059	0.01738
10	0.416711	0.02428
15	0.508743	0.04454
20	0.584825	0.06845
25	0.650091	0.09542
30	0.707107	0.12506
35	0.757348	0.15703
40	0.801740	0.19106
45	0.840896	0.22692

two successive bend reversals in the same direction. Careful measurements made on such a photomicrograph yields $\varphi \cong 65^\circ$ and $R \cong 7 \times 10^{-6}$ m [3]. Thus $s = R\varphi = 7.9 \times 10^{-6}$ m. Using these values we calculated the deflection of a segment of doublet between two dynein arms. The distance between dynein arms is approximately $L_s = 26 \times 10^{-9}$ m [22] as reported in the literature, so that the number of sets of dynein arms over the length s is $s/L_s = 7.9 \times 10^{-6} / 26 \times 10^{-9} \cong 300$. The deflection $x_{\max}$ corresponding to φ and R , is $x_{\max} = R(1 - \cos \varphi_{\max}) = 4.04 \times 10^{-6}$ m which corresponds to a doublet deflection per dynein arm interval of 4.04×10^{-6} m/300 = 1.35×10^{-8} m or approximately 1/2 of the dynein arm spacing. The angular separation corresponding to this deflection is $\varphi_{\max}/300 = 65^\circ/300 = 0.216^\circ$. Now we can write equation (23) for the doublet as

$$F = [2(EI)_D/x^2][f(\varphi)]^2 \quad (27)$$

where $(EI)_D$ is the flexural rigidity of a doublet or 7.05×10^{-23} N m² as calculated by Schoutens [23] and $f(\varphi) = f(0.216^\circ) = 7.6 \times 10^{-5}$. The value for the doublet flexural rigidity is well bracketed by numerous experimental measurements presented in the paper by Schoutens [23]. Using the above numerical values we find that $F = 4.5 \times 10^{-15}$ N or 4.5×10^{-3} pN. Since equation (27) applies only to one doublet the force remaining to bend doublet A and B is $F_B = 2 F = 9 \times 10^{-3}$ pN. Thus the remaining energy in the dynein arm is essentially zero.

The results obtained above can be used also to estimate the flexural rigidity of the dynein arm. To do this we must use equations (21) and (22) since the dynein arm is bent and stretched. Moreover, we can use the condition for the maximum deflection of the dynein arm at reattachment. We make the assumption that $x_{\max} \cong$

$L_s/2 = 1.35 \times 10^{-8}$ m, the same value as above. The separation distance between doublets corresponding to 40° angular separation is estimated to be $L_0 = 70 \times 10^{-9}$ m so that $\alpha = x_{\max}/L_0 = 0.185$, and using this value in equation (26) yields 44° . The $f_t(\varphi) = f_t(44^\circ) = 0.84$. Using these values and $F_D = 5$ pN we find that the value for the flexural rigidity of a dynein arm to be approximately 2.4×10^{-27} N m². By comparison, the calculated flexural rigidity of a sperm flagellum is 75×10^{-21} N m² and the calculated flexural rigidity of a doublet is 7.05×10^{-23} N m² [23]. This can be compared with measured values of the flexural rigidity of a single microtubule: $10\text{--}26 \times 10^{-24}$ N m² [8], compared to the calculated flexural rigidity of a microtubule is 24×10^{-24} N m² [23]. More recently, the measured value for the flexural rigidity of a single microtubule has been reported by Kis et al. [13] and appears to be too low by as much as a factor of 80. In view of these results, the flexural rigidity of a dynein arm predicted by equation (27) appears reasonable.

2.5. DYNEIN ARM DYNAMICS

We now consider the dynamics of the dynein arm when it is displaced proximally before reattachment. The velocity, called here the cocking velocity, with which the dynein arm is moved proximally by the dipole electric field when it has become detached from the B-tubule is calculated using a macroscopic model due Suda and Taylor [27]. The magnitude of the steady state velocity should be larger than that necessary to produce time-dependent bending of the flagellum, otherwise cocking sets up a limitation to propulsion. The relevant equation of motion for this cocking velocity is given by

$$m(d^2x/dt^2) = [6\pi\eta R_d + \mu_s F_D(x)] v + F_D(x) \quad (28)$$

where the first term in the square bracket is the drag due to the motion of the dynein head at low Reynolds numbers ($\sim 10^{-8}\text{--}10^{-6}$) in the surrounding fluid, the second term is the weak friction term referred to above for a dynein head interacting electrostatically with the B-tubule dimers, η is the viscosity of the fluid, and μ_s is an equivalent macroscopic friction term. The last term is the resisting force offered by the elastic dynein arm, which is a function its deflection x when it is bent back. The boundary conditions are: $F_D = F_{\max}$ at $x = 0$, and $F_D = 0$ at $x = x_{\max}$. Since the start up transient in the motion is of short duration and of no particular interest here, a steady state solution of equation (28) gives

$$v = (F_D/2)[6\pi\eta R_d + \mu_s F_D/2]^{-1} \quad (29)$$

where R_d is a calculated radius for the dynein head [24]. Using the following numerical values: $F_D = 5$ pN, $\eta = 1.072 \times 10^{-3}$ Pa sec (water), $R_d = 41 \times 10^{-9}$ m (probably not a very reliable value), and $\mu_s = 2.5 \times 10^3$ sec/m [27], we obtain $v \cong 3.5 \times 10^{-4}$ m/sec = 350 μ m/sec. This value compares to 20–30 μ m/sec for the flagellum speed during propulsion. Therefore, the calculated cocking velocity is well above the propulsion value, meaning that the velocity with which the dynein

Figure 6. Schematic of dynein arms and their moments – force and moment diagram.

arms get cocked to produce bending are not impeding propulsion. In equation (26), the Stokes drag is approximately 13% of the weak friction force. If F_D had a value as low as 1 pN, the cocking velocity would still be as high as $240 \mu\text{m/sec}$. The friction term is difficult to estimate. If the friction term were as small as the Stokes drag, or the Stokes and friction terms were equal, then the cocking velocity would be approximately $1500 \mu\text{m/sec}$. Since the Stokes drag is small compared to the frictional term, large inaccuracies in estimating R_d will not affect the above results significantly.

3. Part II – Waveform

In this part we will discuss the collective behavior of the outer dynein arms as they affect the bending process in a flagellum. We first consider the effects of the collective axial forces and then the consequences of bending moments.

3.1. AXIAL FORCES

The question that now arises is: How is the collective bending behavior of dynein arms contributing to the development of a waveform in the flagellum? To answer this question we examine first the forces in a section of a flagellum consisting of a few doublets and many outer dynein arms as shown in Figure 6. In this figure dynein arms are shown with the forces that produces bending: F_1 is the force dir-

ected toward the distal end of the flagellum and F_2 is that force directed toward the proximal end. These are the result of the bending moment $M = F_1 d = -F_2 d$, where the forces F_1 and F_2 are not only equal but oppositely directed. In Figure 6, doublets 1, 9 and 8 are shown as an example, and all forces along any doublet, occur in pairs. It is of interest to estimate the axial compressive and tensile loads acting on a doublet due to these forces. From the theory of elastic stability, the critical buckling load decreases as the loaded column length CB increases (Figure 6). Assuming that the greatest separation distance between points C and B occurs when the load acting is equal to the separation distance between dynein arms, or 26×10^{-9} m, we have that the critical buckling load for a column with fixed ends is given by Timoshenko and Gere [28]

$$P_{cr} \leq 4\pi^2 EI/L^2 \quad (30)$$

where EI is the flexural rigidity of a doublet and L is the column length. The ends being fixed, they exhibit reactive moments preventing end rotation during buckling thus raising the critical buckling load. Using numerical values listed earlier for EI and L , we obtain that $P_{cr} \leq 1.03 \times 10^{-6}$ N, which is five orders of magnitude greater than the axial force (5 pN) applied by the dynein arms during bending. Therefore, local buckling will not occur.

We calculate the tensile stress on the segment BD of doublet 9 (Figure 6). That value is given by $\sigma_t = F/A$, where $F = 5$ pN and A is the cross-sectional area of a protofilament times the number of protofilaments making up the doublet: 13 for the A-tubule and 10 for the B-tubule, so that $A = 23 \pi R^2 = 3.82 \times 10^{-16}$ m² [23]. With these values we find that the tensile stress is $\sigma_t = 1.13 \times 10^4$ N m⁻². Such a stress will result in an extension of the doublet given by $x = \sigma_t A/k$, where k is the spring constant of a doublet estimated to be 1.2 N m⁻¹ [23]. These results give $x = 4.2 \times 10^{-12}$ m which corresponds to a strain of 8.6×10^{-6} m/m, an insignificant amount. The implication of these crude calculations is that: 1) the forces exerted by the dynein arm are far too weak to cause local buckling, and 2) the resulting tensile stresses are negligible. This confirms earlier observations by Satir [22] and by Brokaw [3].

Since all forces at the ends of dynein arms are equal but oppositely directed, they cancel in pairs if all dyneins are attached. Therefore, the load on the entire length of an axoneme is essentially zero if all dyneins are attached. However, this is not the case for regions where the dyneins are detached. From results obtained above, the calculated axial compression that would cause buckling on a doublet free length would include some 200,000 dimers, or a length equal to over 5000 μ m. Therefore, considerable lengths of a flagellum with all dyneins detached along that length can exist without resulting in buckling. When a significant number of dynein arms along one set of A- and B-tubules are detached, as it would be when bending occurs (see below), the structural integrity and rigidity of the remaining part of the flagellum is such as to prevent local buckling, since the other doublets are held by dynein arms.

Figure 7. Schematic cross-section of a typical sperm flagellum showing bending moment vectors.

3.2. BENDING MOMENTS

Now we address the problem of the effects all dynein arms operating together on bending a flagellum. Figure 7 shows a idealized cross-section of a flagellum. The central pair microtubules and the radial spokes have been omitted because the mechanical interaction of these features on the bending of a flagellum is not yet understood. For simplicity doublets are represented by circles and numbered according to the usual convention. The view is from the basal body looking towards the distal end. The dynein arms are shown as straight lines connecting each doublet and a double line to represent the permanent connection between doublets 5 and 6 [21]. For the moment, we neglect the fact that the B-tubules are rotated by approximately 10° in the outward direction from the local tangent. In reality the moments $\mathbf{M}_{ij}$ would not be pointing toward the center of the section. We delay the discussion of this point until later. The moment vectors produced by the dynein arms are shown as directed in the outward radial direction. For example, $\mathbf{M}_{21}$ refers to the moment produced by dynein arm whose 'foot' is attached to the A-tubule of

doublet 1 and exerts a force on the B-tubule of doublet 2. The $\mathbf{M}_{ij}$ vectors represent moments, which may be decomposed into components along the x- and the y-axis. The components parallel to the y-axis, M_{ij}^y will produce horizontal bending called 'twist' in this paper. The horizontal components of the moments, M_{ij}^x , which lie in a horizontal plane produce bending in a vertical plane. This is the plane that contains the flagellum waveform as observed in photomicrographs (See for example Brokaw [3]). Because of symmetry, all moment vectors $\mathbf{M}_{ij}$ pass through the center of the flagellum cross-section (Figure 7). The distribution of moment vectors about that coordinate system is symmetrical. Moreover, the magnitude of all moment vectors is the same so that the tip of each vector ends on a circle of radius R_M centered on the xy-coordinate system. Summing the components of moments along the x- and y-axis we find that

$$\sum \mathbf{M}_{ij}^x = 0 \quad (31)$$

and

$$\sum \mathbf{M}_{ij}^y = 0 \quad (32)$$

The implication of equations (31) and (32) is that if all dynein arms act simultaneously no waveform can develop since the resultant bending moment is zero. This is in agreement with observations of the rigor state, no matter what the flagellum shape may be when ATP in the solution is suddenly diluted, resulting in massive dynein head attachment.

How can a waveform develop given that these moments have zero resultants? A waveform develops only when any one of a set of moments between two doublets along a certain length of the flagellum is zero, that is, the dyneins are detached over that region. Then the resultant of moments over that length is no longer zero and bending and twisting occurs over that length. Expressed mathematically, this results in the condition that, if

$$\sum \mathbf{M}_{ij}^x \neq 0 \quad (33)$$

and if

$$\sum \mathbf{M}_{ij}^y \neq 0 \quad (34)$$

then a waveform develops. It should be emphasized that if equation (33) is obeyed, then equation (34) is automatically obeyed also since these sets are the components of vectors. If some regions of the flagellum have detached dynein heads, then, unless the twisting moment can be made to vanish, the shape of the flagellum will be that of a corkscrew. This has also been observed.

Since by setting a given set of moments to zero (detached dynein arms), which moments should these be such that the bending moment is maximized while minimizing the twist? To answer this question we calculated the magnitude of all moments when one particular set is zero over the flagellum length. The moment equations are

Table II. Values of the horizontal and the vertical moments when one of the moment is zero

$\mathbf{M}_{ij} = 0$	ΣM_{ij}^x	ΣM_{ij}^y
$\mathbf{M}_{21}$	$-0.342 M$	$-0.939 M$
$\mathbf{M}_{23}$	$-0.866 M$	$-0.500 M$
$\mathbf{M}_{34}$	$-0.984 M$	$0.173 M$
$\mathbf{M}_{45}$	$-0.643 M$	$0.766 M$
$\mathbf{M}_{56}$	0.000	$1.000 M$
$\mathbf{M}_{67}$	$0.643 M$	$0.766 M$
$\mathbf{M}_{78}$	$0.984 M$	$0.173 M$
$\mathbf{M}_{89}$	$0.866 M$	$-0.500 M$
$\mathbf{M}_{91}$	$0.342 M$	$-0.939 M$
All Connected	0.000	0.000

$$\Sigma M_{ij}^x = \Sigma M_{ij}^x \sin(\theta_j + 40^\circ) = M \Sigma \sin(\theta_j + 40^\circ) \quad (35)$$

$$\Sigma M_{ij}^y = \Sigma M_{ij}^y \cos(\theta_j + 40^\circ) = M \Sigma \cos(\theta_j + 40^\circ) \quad (36)$$

where M is the magnitude of a single moment having the value

$$M = 0.684 R_M |\mathbf{F}| \quad (37)$$

where $|\mathbf{F}|$ is the absolute magnitude of the force vector from a single outer dynein arm. Numerical values obtained from equation (35) and (36) are shown in Table II. In the leftmost column the moments set to zero are listed and the corresponding values of the bending and the twisting moments are shown in the next two columns. The sign in front of these values indicate the direction of the bend or twist: negative means bent downward and left twist, and *vice versa*. For example, if $\mathbf{M}_{21} = 0$, the resultant net horizontal moment will produce a downward bend in the yz -plane ($-0.342 M$), while at the same time produce a twist ($-0.939 M$) to the left in the xz -plane. Thus, in this case the twist is numerically greater than the bend. Table II also shows that if the permanent connection between doublets 5 and 6 is cut, the resultant moment will produce only a twist in the flagellum. Table II shows that to obtain the maximum bending moment with the least twist, either the moment vectors $\mathbf{M}_{34}$ or $\mathbf{M}_{78}$ must be zero. Then, the smallest twist is $0.173 M$ and the largest bending moment is $-0.984 M$. In this case the bend is directed downward with the twist to the right. When $\mathbf{M}_{78} = 0$ the bend is upward and the twist is the left since the signs are changed.

This analysis suggests the method of coordinating the bends so that a moving waveform can develop. Figure 8 shows a schematic of a number of doublets on either side of a vertical median plane through the flagellum. In this example,

Figure 8. Production of traveling waveform along a flagellum from the proximal to the distal end.

dyneins arms 3-4 and 7-8 are shown either attached or detached, respectively. There is a region of finite length (BA) over which $\bar{M}_{34} = 0$ and another region further to the right (AC) where $\bar{M}_{78} = 0$. Opposite these regions, the moments are $\bar{M}_{78} \neq 0$ and $\bar{M}_{34} \neq 0$, respectively. This condition yields a downward bend ($-0.984 M$) in the yz -plane and a small twist ($0.173 M$) to the left followed by an upward bend with a twist to the right with the same magnitudes. We can suppose the two regions under consideration are separated by a transition region AA (Figure 8) corresponding to $\Sigma \bar{M}_{ij} = 0$, and because the resultant is zero that region can assume any shape: straight or curved, then the region AA is in a rigor state. The region beyond AA has an upward bend ($0.984 M$) and a small right twist ($0.173 M$). The important point to observe from this is that *bend reversal occurs simply by changing the side in which a region of dynein arms is detached*.

To produce a traveling waveform, the entire region between BB and CC must travel from the proximal end to the distal end. Since the region between BB and AA has a downward waveform and between AA and CC has an upward waveform,

Figure 9. Schematic showing bending moments and their relationship to the shape of a waveform in a sperm flagellum.

this waveform can be made to travel along the flagellum. This can be visualized with the aid of Figure 9 for a sperm flagellum. The circles above and below the waveform indicate the regions in which the moment vector $\bar{\mathbf{M}}_{ij}$ are zero. Only the zero moments are shown to simplify the diagram and not shown are the magnitudes of the resultants in those regions. The empty circles represent a zero resultant of moments. If this entire region, from the flagellum head to its tail, can be made to travel distally then there will result a propulsion waveform moving from head to tail, a consequent motion to the left in the figure. The speed with which this wave travels from the basal body to the tail will determine the speed of propulsion. The model just discussed does not account for the details of propulsive force, wave propagation speed, resistance in the fluid, and propulsive energy expenditure. Therefore, we see that a very simple mechanism is associated with the formation of a waveform.

4. Discussion

It has been known for some time that bending of a flagellum is the result of the action of dynein proteins acting on the doublets of the flagellum. The general

mechanism proposed in the literature (see for example Omoto [19]) is that of the reaction of ATP with the dynein protein heads such that a cycle ensues in which forces are generated on the doublets with the direction of these forces directed toward the distal end of the flagellum. The general mechanism suggested is that of an arm rigidly attached in an unspecified manner to the A-tubule of one doublet with the other end consisting of a large spherical or quasi-spherical protein head acting directly on the B-tubule of the neighboring doublet. In this paper we have considered the details of a possible mechanism. The simplest possible mechanism consistent with experimental observations consists of the following elements. In the absence of ATP, dynein heads remain rigidly attached to the adjacent doublet such that a rigor state exists and no time-dependent waveform can develop. This agrees with experimental observations. If a flagellum is in an activating solution, the beating flagellum can be 'frozen' in time by a sudden dilution of the ATP solution. The model described in this paper reproduces such observation. As ATP flows to the flagellum, reactions occur as a result of 'collisions' of ATP molecules with dynein heads, either directly or through 'stalks' [12]. The evidence for this is that one collision of an ATP molecule is sufficient to initiate a reaction [2]. This reaction detaches the dynein head from the doublet. It is then that the dipole electric field present as a result of the dimer dipole moments [5, 15] act on the detached dynein heads causing them to move in the proximal direction because the electric field acts on the charges in the dynein head. The velocity of this motion has been found to be greatly in excess of the propulsion speed and consequently cocking dynein heads does not impede propulsion. During this proximal motion the energy from the field is stored as mechanical energy in the dynein arm. This requires the dynein arm to be rigidly attached to the A-tubule. Motion in the proximal direction continues until a maximum bending occurs in the dynein arm causing the release of the ATP reaction product. Release of the reaction product is also consistent with experimental observation. The details of the release mechanism of ADP from the dynein head are not known. It is assumed that the release of the reaction product alters the arrangement of the charges in the dynein head and re-attachment occurs. The energy stored in the form of elastic energy in the dynein arm is now released to produce bending in the doublet pair to which it is attached. Bending can occur only if the dynein arm is rigidly attached to the A-tubule [9]. Bending is complete when the mechanical energy stored in the dynein arm is released and stored as energy of bending in the doublets. When balance is achieved there remains a small amount of residual energy in the dynein arm. Using a nonlinear beam theory and published data on flagellum waveform [3] we calculated the minimum value of the flexural rigidity of the dynein arm. This has not been reported before.

We calculated the local compressive buckling and tensile loads between two consecutive points of applications of the forces produced by dynein arms and concluded that the loads are considerably below those required to cause local buckling or tensile failure. We have also shown that when all the bending moments from dynein arms are applied to any cross-section of a flagellum, the result is a zero

resultant moment. Thus, when all dynein bending moments apply, the flagellum is in a state of rigor. Only when local dynein arms between a set of doublets are zero (detached dynein heads) along a certain length of flagellum do they generate a bend, and a twist, in the flagellum. It is possible that the inner dynein arms exert the kind of control over bending that inhibits twisting. This has not been studied, nor is it understood how the inner dynein arms are involved in controlling the bending mechanism. The model further suggests that a fully developed waveform can be generated by alternate regions in the flagellum about by the median vertical plane that have detached dynein arms over a certain length. If this entire region (BB to CC in Figure 8) travels distally the waveform will move distally also. The mechanism that produces this traveling wave is very likely not mechanical, but may be entirely chemical in nature. We have not considered this problem in this paper.

One interesting aspect of the presence of a dipole electric field is that it varies in strength with radial distance. However, it does not vary significantly over fractions of nanometer distances from the microtubule surface. The closer to the tubule surface the greater the field strength, thus, the field strength exhibits a radial gradient. This has implications for the motion of ATP molecules. Large molecules such as ATP possess surface charges, some of them at or near the surface [1]. Consequently, these molecules are acted upon by the dipole electric field, and in the present case, move along the field, and radially inward due to the radial gradient in the electric field. Therefore, the presence of the electric field dominates any diffusion mechanism that might exist as a transport mechanism for ATP. Indeed it can be shown [24] that pure diffusion is much too slow to account for the observed reaction rate. The mechanism may be described by a partial differential equation of the type

$$\partial u / \partial t = D_r \partial^2 u / \partial r^2 + D_z \partial^2 u / \partial z^2 - V_r \partial u / \partial r - V_z \partial u / \partial z \quad (38)$$

The first two terms are the diffusion terms with diffusion coefficients in the r - and the z -directions, and the last two terms are the convection term caused by the field acting on the ATP particles. The magnitude of the velocity term, V_r , can be obtained from the Lorentz force. A simple calculation [24] shows that the first two terms in equation (38) is small compared to the last two terms. This is because the velocity term is the result of the dipole field, hence dominates diffusion. Because the dipole vector of a dimer has three components, $p_r < 0$, and $p_\theta > 0$, $p_z > 0$, the resultant electric field is helical outside the microtubule surface with a large inward radial component. Therefore, ATP molecules in the neighborhood of the microtubule are driven towards and along its surface thereby enhancing the ATP collision rate. Since ATP molecules are essentially charged particles, their motion produces local magnetic fields according to Maxwell's equations. The implications of this point have not been investigated.

The model presented in this paper has a number of shortcomings. The most important one is that it cannot give a relationship between the forces produced by dynein arms and the observed beat frequencies and swimming velocities. The

Table III. Values of the horizontal and the vertical moments when one of the moment is zero. Case for all moments offset by 10° except for $\mathbf{M}_{56}$

$\mathbf{M}_{ij} = 0$	ΣM_{ij}^x	ΣM_{ij}^y
$\mathbf{M}_{21}$	0.326 M	-0.985 M
$\mathbf{M}_{23}$	-0.113 M	-0.643 M
$\mathbf{M}_{34}$	-0.174 M	0.000
$\mathbf{M}_{45}$	0.060 M	-1.089 M
$\mathbf{M}_{56}$	0.826 M	0.985 M
$\mathbf{M}_{67}$	1.326 M	0.866 M
$\mathbf{M}_{78}$	1.765 M	0.342 M
$\mathbf{M}_{89}$	1.592 M	-0.342 M
$\mathbf{M}_{91}$	1.000 M	-0.866 M
All connected	0.826 M	0.000

model can explain qualitatively the formation of a waveform. The propagation of a waveform involves determining the motion of fluid regions around the doublets in the flagellum in which there may be sub-regions containing a high concentration of ATP alternating with sub-regions containing very low concentrations of ATP. This is but a conjecture. There may be other mechanisms responsible for alternate dynein head attachment and detachment. The bulk motion of such a periodically varying ATP concentration in the distal direction, if that is the case, has not been explained. An adequate explanation must account for motion with and without flagellum membrane surrounding the doublets.

It has been observed that B-tubules are rotated outwardly from the local tangent by some 10° . The effects on the moment of inertia of rotating the B-tubule about the center of the A-tubule by 10° has been calculated by Schoutens [23] and was found to have a negligible effect on the overall flexural rigidity of a flagellum. We have calculated the effects on the dynein arm induced bending moment of this 10° anomaly and obtained values for the x- and y-axis moments. These results are shown in Table III. In calculating these results we have assumed that the dynein arms permanently connecting doublets 5 and 6 have, unlike other moments, their moments passing through the center of the flagellum cross-section. Under these conditions, with $M_{34} = 0$, there is a resultant bending moment downwards equal to -0.174 M and zero twist. This would mean that the 10° anomaly serves the purpose of eliminating the twist. However, when we calculated the reverse bend ($M_{78} = 0$) resulting in an upward bend there resulted a large twist (0.342 M). This is because the orientation of the 10° anomaly is in opposite directions for $\mathbf{M}_{34}$ and $\mathbf{M}_{78}$. Repeating these calculations with other similar conditions, we found that there did not exit a condition in which the 10° anomaly in combination with other

moment direction resulted in a negation of the twist both in the upward and the downward bend. It may well be that the elimination of twist in some sperm flagella species is controlled by the inner dynein arms.

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