Is the Curvature of the Flagellum Involved in the Apparent Cooperativity of the Dynein Arms along the "9+2" Axoneme?

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IS CURVATURE INVOLVED IN THE APPARENT
COOPERATIVITY OF THE DYNEIN ARMS ALONG THE
“9+2” AXONEME?

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SUMMARY

In a recent study (Cibert, C. (2008). Journal of Theoretical Biology 253: 74-89) assuming that the walls of the microtubules are involved in a cyclic compression/dilation equilibrium because of their cyclic curvature, we showed that the spatial frequencies of the dynein arms and the β-tubulin monomers series — the two facing verniers — change when the axoneme bends. We have proposed that these events create the propagation of joint probability waves that define the spatial coincidence of the two partners. Modeling the occurrence of these interactions along the entire length of an axoneme, without programming by default any cooperative dialog between the molecular complexes within the axoneme and accounting that the movement of the couples “dynein arms – β-tubulin monomers” is limited because of maximum value of the walking distance of the arms (which has been estimated to equal 160 Å), we observe that homogeneous active couples are basically grouped. The numbers of dynein arms included in these groups depend on the probability of interaction between the two partners, the location of the outer doublet pairs around the axonemal cylinder and the local bending of the axoneme. This sheds light on the nature of the apparent cooperativity of the molecular motors and the β-tubulin monomers, being directed (for a part) by the local curvature.

INTRODUCTION

The motile axis of the flagella and cilia of the eukaryotic cells (axoneme) is formed by nine outer doublets of microtubules which form 9 Outer Doublet Pairs (ODPs) surrounding a central apparatus organized around two central microtubules. The relative shear of the ODPs, due to the activity the dynein arms (DAs), is converted into a bend because of the elastic links that interconnect the ODPs (Gibbons, 1981; Lindemann, 1994a), the curvature being or not associated to the twist of the axonemal cylinder around its central axis (Cibert, 2001; Gibbons, 1975).
The nature of the instantaneous regulation of this mechanism that allows the propagation of a coherent wave train along these organelles is, in the main, unknown, in spite of the existence of clever biochemical and topologic models that classify the curvature and the geometrical adjustments of the axonemal machinery as essential in the ensemble of divers mechanisms (Brokaw, 1975; Dynek and Smith, 2007; Gertsberg et al., 2004; Huang et al., 1982; Inaba, 2003; Li et al., 2006; Lindemann, 1994a; Lindemann, 2007; Lindemann and Mitchell, 2007; Mitchell, 2003a; Mitchell, 2003b; Morita et al., 2006; Morita and Shingyoji, 2004; Noguchi et al., 2000; Noguchi et al., 2005; Piperno et al., 1992; Rupp and Porter, 2003; Smith and Yang, 2004; Wilson and Lefebvre, 2004; Woolley, 2007; Woolley, 1997).

In parallel to these biological models, physical ones have been proposed that consider the couples “ODPs – molecular motors” produce on their own alternative fields of internal constraints during the beating movement; one of the most interesting is the pioneering description of these active entities as “auto-driven filaments” (Camalet et al., 1999). These models postulate that the efficient DAs are uniformly distributed along each ODP, while, from a structural point of view, the periodic spatial distributions of both the DAs and the β-tubulin monomers (β-TMs) that must interact to produce a sliding force, are evident. Experimental observations suggest however, that the DAs are active when they are associated in groups of 4 elements (Spungin et al., 1987), making the DAs (and their partners) cooperative systems by essence, when cooperativity is defined as the necessary inter-molecular dialog occurring either inside a given molecular complex or between different molecular complexes at a given time as in the case of allosteric enzymes.

The knowledge of the physical characteristics of the microtubules and the ODPs (Fujime et al., 1972; Schoutens, 1994; Takano et al., 2003) allows to think that in the range of normal they suffer during the beating cycle, they are inextensible and incompressible. Different elements that plead however, in favor of a their deformation during the beating cycle, allowed us to propose that the two opposite sides of the outer doublets included in the bending plane are subjected to dilation/compression equilibrium because of the local balance of forces and torque (Cibert, 2008). Accounting these properties, assuming that they modulate the periodic distributions of the DAs and the β-TM along the two facing verniers they constitute, we demonstrated that, during the beating cycle, the joint probability of interaction (JPI) of two facing partners depends on: (i) the local curvature, (ii) the local rate of sliding and (iii) the location of the ODPs within the axoneme accounting the orientation of the bending plane (Cibert, 2008).

In the present paper, we modeled the distribution of the couples DAs – β-TMs along the nine ODPs during a beating cycle, assuming that the orientation of the bending plane is constant along the entire length of the model. We observe that these distributions are very heterogeneous around and along the axonemal cylinder. The two partners tend to form group series along the 9 ODPs in relation to the sliding speed and the cylindrical location of the ODPs. These results allow us to confirm that geometry is one of the major elements in the definition of the apparent cooperativity that must exist between the DAs and the β-TMs during the axonemal beating.

MATERIAL, CALCULATIONS AND ASSUMPTIONS

Dedicated program was written under ImageJ (1.37v) running on a MacBook Pro (Intel) OS-X platform (rsbweb.nih.gov/ij/download.html).

According to Gray (Gray, 1955; Gray, 1958; Gray and Hancock, 1955), the traces of the flagellum of a sea urchin spermatozoon were calculated as the products of an exponential
envelope and a periodic function (Cibert, 2008), whose equations are \( y_1 = a_0 \cdot (1 - \exp(-a_1 x)) \) and \( y_2 = \sin(w(k - x/v) + \varphi) \), respectively, where: \( a_0 = 100 \), \( a_1 = 2 \), \( w = 0.8 \), \( v = 0.31 \), \( k = r \cdot 8/160 \), \( \varphi = -23\pi/80 + \varphi_0 \), \( x \) is the abscissa of the 200 points of the traces that ranges on the interval \([0, 3]\), \( r \) is the rank of the trace in the beating cycle (Figure 1), and 160 is the number of traces that constitute the complete beating cycle. \( x \) (abscissa) was calculated as \( x = i \cdot 3/200 \), where \( i \) is the rank of the calculated point that ranges in the interval \([0, 200]\). In the periodic function, \( k \) and \( x/v \) allow the displacement of the wave train along the model as a function of time and define the shape of the wave train for a given time, respectively. The values of the other parameters are defined to mimic the beating of sea urchin spermatozoon. The length of each trace equals 40 \( \mu \)m. When the beating frequency of the model equals 50 Hz, the interval between two images of the bending series equals 1/8,000 s. One image in ten is displayed along the series in Figure 1 A and B — the highest its rank, the darkest the trace, where \( \varphi_0 \) equals 0 and \( \pi/2 \), respectively.

The range of the local shear calculated along each of the 160 traces is characterized by a fish-shaped envelope as already proposed (Figure 1 C) (Cibert, 2002). This plot characterizes the P0 points as the curvilinear abscissas where the relative shear of the ODPs tends to a minimum, because of the synchronous (Brokaw, 1996; Brokaw, 1993; Goldstein, 1976) and cumulative (Cibert, 2001; Cibert, 2002; Cibert, 2003) sliding of the ODPs. Then, the wave train that moves along the axoneme delineates a series of P0-P0 modules along the model (Cibert, 2002). Because of the ratio “length of the model” / “wavelength of the wave train”, there is roughly 1.5 P0-P0 module along the flagellum.

Along the modeled axoneme, we have considered five abscissas of interest shown in Figure 1 C, where we have calculated the incidence of the JPI wave trains in the formation of the couples DA–\( \beta \)-TM after the two partners detach when the complete walking distance of the arm has been achieved.

the relative shears of the 9 ODPs and (ii) the JPI between facing DAs and \( \beta \)-TMs taking into consideration the rank of the ODP and the local curvature of the axoneme (Figure 2) (Cibert, 2008).

Figure 3 shows the evolution of the mechano-chemical cycle of the DAs according to the sliding amplitude of the ODPs. The minus end of the ODP is oriented towards the left side of the scheme. The length of the DAs equals 180 A; their interval ranges between 240 A (outer DAs) and 320 A (inner DAs). Under the conformation #1, activated but free DAs are able to grasp a \( \beta \)-TM along the facing vernier, as a function of their JPI. After the couple is formed, the tilt angle of the DA was calculated as a function of the amplitude of the local shear and the maximal length of the walking distance. We postulated first that, whatever the polarity of their movement (Lorch et al., 2008), the walking distances of the DAs are of the same magnitude, and second, that the change in the sliding polarity does not induce the disruption of the link between the two partners.

In Figure 3, the colors of the DAs are defined as a function of their putative potential energy (Figure 4).

The results obtained from constrained dynein c (Gennerich et al., 2007) show that speed of the forward and backward movements of the dynein c (prepared from S. cerevisiae) depend and do not depend on the ATP concentration, respectively, and that in absence of ATP the two polarized constrained movements (walking cycles) occur. In these experiments, because the dynein c are involved in more than one attachment/detachment cycle preserving however, their join basic binding properties, these properties appear as...
independent on ATP hydrolysis. These results agree the already proposed model according to which the attachment/detachment between the DAs and the β-TM is basically ATP-independent but tension-dependent whatever the polarity of their movement (Lindemann and Hunt, 2003).

This contradicts however, the experimental evidences according to which the activity of the DAs is described by a four steps enzymatic cycle, where the detachment of the DAs from the β-TM is strictly ATP dependent (Omoto et al., 1991).

Consequently, in vivo, even if the hydrolysis of ATP has to occur concomitantly with the detachment of the two partners, ATP is mainly the necessary trigger and activator of the DAs when they accomplish their forward movement, being the basic substrate of these enzymes. It improves the capabilities of the arms to achieve their forward cycles when they are under tension, modifying the ratchet mechanism that could exist inside the DA (Lindemann and Hunt, 2003).

Since the molecular mechanisms involved in the attachment and the detachment of the two partners are due to their intrinsic properties, the variation of the potential energy of the molecular system they constitute has to range between E0 (the two partners detach) and E1 (the two partners are just linking) (Figure 4 A). Since, under tension, and in absence of ATP, force that promotes the forward movement of the DAs along a microtubule is lower than that promotes the opposite backward movement (Gennerich et al., 2007), it is legitimate to assume that the energies of activation of these two movements (EaF and EaB) are necessarily different. In presence of ATP, only EaF decreases (being obviously nil) making the DA an engine (Gennerich et al., 2007). Thus, the potential energy of a couple DA – β-TM could be described by a Morse plot during the two opposite polar movements in which it can be involved (Figure 4 B), even if the effective potential energy due to the real conformational changes of a protein remains difficult to be measured or determined (Felcy et al., 2002).

In our model we have considered that: (i) the attachment of the two partners induces the increase in the potential energy of the couples, whatever the nature of the activity of the couple during the active phase. (ii) The grasping of the β-TM monomer by the activated DA depends of the JPI wave train. (iii) The activated couple is controlled by the range in which the tilt has to occur, depending on the rank of the ODP within the axonemal cylinder it links. (iv) As a function of the ratio between the local sliding speed and the ranged capabilities of the couple, the DA (within the coupe) is either a motor, or neutral or a brake. (v) These activities are defined locally as a function of the evolution of the local shear. And finally, (vi) the corollary of our postulate (according to which the couple DA – β-TM is stable during the shear reversion) is that the decrease of the tilt angle induces the increase of its potential energy of the DA because the conformation of the arm goes back to that referred as #1 in Figure 3.

RESULTS AND DISCUSSION

In this study, we model — for the first time in literature — the activity of the DAs along the entire length of the “9+2” axoneme. In this way we calculated one flagellar wave train and the corresponding sliding of the axonemal cylinder as already described (Cibert, 2008), and we model the formation of the couples DA – β-TM under the following six principles. (i) The ODP shear is nil at the basal anchor of the axoneme. (ii) The beating plan is constant and stable, and contains the doublet #1 and the center of the model. (iii) The maximum length of the step taken by the DAs is assumed to equal 160 Å. (iv) The link
between a given DA and a facing β-TM occurs as a function of the propagation of the JPI wave trains along each ODP (Cibert, 2008) — the tables describing the propagation of the JPI wave train are those shown in this paper. (v) The four mecano-chemical steps of the DAs (Omoto et al., 1991) are converted into a turn-off (stand-by activated position), a turn-on (linked to a β-TM) conformation, and a continuous series of tilted conformations between these two extrema. (vi) A DA turns-off when it reaches the maximum of its walking capabilities assuming that the maximum tilt angle of a DA is of the same amplitude when it moves in the two directions (Gennerich et al., 2007; Lindemann and Hunt, 2003; Lorch et al., 2008). Because of the ratio that exists between the rate of displacement of the JPI wave train vs. the lifetime of each couple DA – β-TM, each of the spatial coincidences between the two partners does not induce the grasping between them. This link occurs only when the two facing partners are free. This means that when a either DA or a β-TM involved in an active couple, faces exactly a free partner, a new grasping does not occurs, because it works yet. It is noteworthy that because of the synchronous and cumulative sliding (Brokaw, 1996; Brokaw, 1993; Goldstein, 1976), the shear of the ODPs along the entire length of the axoneme occurs irrespectively of the local curvature (Cibert, 2002; Cibert, 2008).

In the calculations we have apparently ignored the direct effects of the forces (whatever their nature) that the active couples produce and that constraint them during the movement. In fact, we have assumed that the shape of the wave train that propagates along the flagellum is mechanically possible because it depends on all the interactions and constraints that must exist within the axoneme when it beats. Consequently, the internal forces as well as the external forces are taken into consideration by default in the calculation of the shape of the wave train that propagates along the model, the only data from which the shears of the ODPs were calculated.

For simplicity, the descriptions of the behavior of the couples DA – β-TM along only one segment of the axoneme (#2 in Figure 1) are shown here; this abscissa is that where the shear amplitude is the highest along the model. The time series that we have calculated at the 5 abscissas of interest (Figure 1 C) are presented as supplementary material. The couples of figures [Figure 5, Figure 6] and [Figure 7, Figure 8] describe the conformations of the couples DA – β-TM when the sliding speed is the lowest or the highest at this abscissa, respectively.

In these figures A and B refer to the calculation of the conformation of the couples DA – β-TM assuming that the spatial frequencies of the β-TMs and DAs are either constant (in absence of JPI wave trains), or depend on the propagation of a JPI wave train, respectively. In C we show the result of the same calculation as done in B, excepted that the stand-by DAs were masked, because we have postulated that a DA grasps a β-TM when the two partners are exactly facing; this induces the formation of larger groups of “inactive” DAs along the ODPs.

Figure 5 A¹, Figure 6 A², Figure 7 A³, and Figure 8 A⁴ show that in absence of variation of the spatial frequencies of the two facing verniers, the couples are clearly synchronized along very long segments, whatever the ranks of the ODPs around the axonemal cylinder.

¹ Movie S-2-A.
² Movie G-2-A.
³ Movie S-2-A.
⁴ Movie G-2-A.
Figure 5 B⁵, Figure 6 B⁶, Figure 7 B⁷, and Figure 8 B⁸ show that the propagation of the JPI wave trains induces the formation of heterogeneous groups of synchronized DAs along the ODPs included in (or close to) the neutral surface (#3-4 and #8-9). In (or close to) the bending plane (e.i. ODP #1-2, #5-6 and #9-1), the couples are synchronized along longer segments. If we consider the ODPs included in the bending plane and specifically the #5-6 ODP, the active couples DA – β-TMs never — rarely — detach. This means that their consumption of chemical energy (ATP), which is assumed to occur synchronously to the disruption of the link between the two partners, is nil — very low —, while their potential energy must vary. This raises the question about their exact function within the axoneme because of the expected consequences of the ATP hydrolysis, which is assumed to adjust the ratchets that drive the activity of the DAs. Are these ODPs only spring? On the other hand, are the ODPs located on both sides of the neutral surface only, which appears as the most active, the only actuators of the axonemal movement?

The addition of a stringent condition according to which the DAs have to be perpendicular to the ODPs when they grasp their facing partners (Figure 5 C⁹, Figure 6 C¹⁰, Figure 7 C¹¹ and Figure 8 C¹²) does not change this observation, even if, as expected, this increases the number of DAs being in a stand-by conformation and which form longer groups along the ODPs.

As a general rule, it could be concluded that: the more active the ODP, the highest its consumption of ATP, the larger their relative shear amplitude, the shorter the groups, the shorter their lifetime. This is not intuitive at all.

The lines that describe the groups constituted by the dynein arms within the groups (Figure 6 and Figure 8), show that the movements of the groups are metachronal, because their slopes do not equal 0, excepted when the change of the shear polarity occurs. This raises the question about the function of the nexin links. In effect, when the couples included in long segments are disrupted, according to a metachronal manner, the nexin links are, at this instant, the only elements that insure the axonemal cohesion (Gibbons, 1981). If the links are not strong enough to insure this function, because of the intensity of the transverse-forces (Lindemann, 1994b), the transient disruption of the axoneme may occur (Brokaw, 1997) and modify the local sliding to bending conversion (Lindemann, 1994a; Lindemann, 1994b).

Our results demonstrate that the arrangement of the DAs — active couples DA – β-TM — into groups along and around the axonemal cylinder is the direct consequence of the geometry of the axoneme in absence of dedicated molecular dialog between the molecular complexes that build the axoneme. The JPI wave trains that propagate along each of the ODPs make the movement of the DAs analogous to that of cilia (Gueron and Levit-Gurevich, 1998; Gueron and Levit-Gurevich, 1999) even if the dimensions of the molecular complexes (DAs and/or DA – β-TM complexes) and those of these organelles are of different order of magnitude.

This does not deny however, the role of a molecular dialog of allosteric nature that

⁵ Movie S-2-B.
⁶ Movie G-2-B.
⁷ Movie S-2-B.
⁸ Movie G-2-B.
⁹ Movie S-2-C.
¹⁰ Movie G-2-C.
¹¹ Movie S-2-C.
¹² Movie G-2-C.
must/could exist between the molecular complexes of the axoneme. (Cibert, 2003). In Chlamdomonas it was demonstrated that the series of Outer Dynein Arms along a given doublet interact because of the fitment of their sub-units, and two different models, in which the AAA systems (Roberts et al., 2009) play different functions, were proposed (Ishikawa et al., 2007). Using the same biological model, it was shown that AAA rings constitute the Inner Dynein Arms as well as the Outer Dynein Arms and it was confirmed that the Inner Dynein Arms interact with the Outer Dynein Arms and the radial spokes either directly or via the Dynein Regulatory Complex (Bui et al., 2008). These structural interactions facilitate the exchanges of energy — the dialog — between all these different molecular complexes.

This study complements the previous paper in which the JPI wave trains only was described (Cibert, 2008). and reinforces the regulative function of the sliding itself on its own regulation (Cibert, 2008; Lindemann, 2004) Because the model we propose is funded on geometry, it could be proposed that that the JPI wave trains, as well as their consequences, are generic properties of all the axonemal architectures whatever the forms of the wave trains they generate along the organelle they make motile.

The creation of these groups of very different lengths along the neighboring ODPs as a function of their location around the axonemal cylinder raises the question about the function of the nexin links. In effect, because of their elastic properties, the nexin links are involved in the sliding to bending conversion (Lindemann, 1994a; Lindemann, 1994b) and make (for a part) the axonemal scaffold cohesive (Gibbons, 1981).

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BIBLIOGRAPHY


Figure 1: The modeled flagellar wave train. A and B show the 160 traces we have calculated (see text) when the difference between the phases of the periodic functions equal 0 and $\pi/2$, respectively; one trace in 10 is represented. C: The local extrema of the sum of the local shear along the 160 traces is clearly fish-shaped (Cibert, 2002). The five abscissas numbered 1, 2, 3, 4 and 5 are the loci where the conformations of the dynein arms were calculated; the abscissas defined as -1, -2, -3, +1, +2 and +3 refer to the abscissa #5 and were used to describe the relation between the local sliding speed and the local sum of the curvature through the fixed P0 point/segment. In A, B and C the ordinates are represented according to an arbitrary unit raging between -1 and +1. It is noteworthy that the in A and B, the plots are those obtained using the product $y_1*y_2$ as described in the MM section. They are not the design of the model of the ODP, and consequently their lengths are not corrected as a function of the length of the model.

Figure 2: Scheme of the used cross-section of the axoneme. The nine ODPs were designed according to Schoutens (Schoutens, 1994) as proposed in our previous study (Cibert, 2008). The DAs are represented as black arrows. The rank of each ODP is included within its tubule A. The bending plane includes the central hub of the axoneme and the center of inertia (Schoutens, 1994) of the first ODP. The green (positive) and the red (negative) values are the dilation and the compression of the spatial frequencies of the DAs and the $\beta$-TMs calculated as described in Cibert 2008, when the bending angle equals $\pi$ along a 10 $\mu$m long segment. These values were calculated using the equation $s=\alpha*h$ (Warner, 1976), where $s$ (Å) is the shear, $\alpha$ (rd) is the local curvature and $h$ is the length (Å) of the projection in the bending plane of the distance that separates the axis of inertia of the ODP and the end of the DA or of the $\beta$-TM; $h_{\text{dynein}} \in (89.10, 302.33, 397.75, 302.33, 79.46, 213.64, 373.39, 373.39, 207.46)$ and $h_{\text{tubulin}} \in (49.06, 167.49, 217.75, 163.30, 0.00, 114.99, 213.53, 192.18, 90.35)$; each value written in parentheses is that relative to each of the ODPs. This model could be used for any bending configuration changing the values of $h_{\text{dynein}}$ and $h_{\text{tubulin}}$ as a function of the local change of the local orientation of the bending plane.

Figure 3: The dynein mechano-chemical cycle. (See text). In this image, the spatial frequencies of the DAs and the $\beta$-TMs equal $1/320$ Å$^{-1}$ (the one of the inner DAs) and $1/80$ Å$^{-1}$, respectively.

Figure 4: Potential energy of a couple DA – $\beta$-TM (see text). A couple DA – $\beta$-TM is constituted because of the intrinsic properties of the two free facing partners whose curvilinear abscissas coincide, and its potential energy equals E1. A: In absence of ATP, the couple is able to move when an external force loads it, and the two partners are capable to reinitiate a new cycle as they do under the normal conditions. We assume that only difference between the forward and the backward movement is relative to their energies of activation, which explain that the forces, which induce the two opposite movements, are different in module (and evidently in direction). In presence of ATP, the
energy of activation of only the forward movement is reduced considerably; this converts the couple to a forward engine. The backward movement is only possible when the arm is loaded. B: The Morse plot shows the potential energy of a couple versus its conformational changes from E1 to E0 whatever the polarity of the movement of the couple. When the potential energy of the couple reaches E0 the two partners detach. The supplied energy that ranges between 0 and 1, is calculated as the cumulative potential energy when the potential energy of the couple decreases from E1 to E0; the arrow indicates the direction in which this curve has to be read. The ATP hydrolysis is written between parentheses, because it is not involved directly in the increase of the potential energy of the couple, but in the change of the ratchets that drive its activity. According to our model, if the polarity of the movement is reverted because of the reversion of the shear direction, the tilt angle of the couple has to decrease and its potential energy increases to its maximum value (E1) — it acts as a brake — before to decrease again after it has crossed the position #1 defined in Figure 3.

Figure 5: Series S-2-25. Arbitrarily, S, 2 and 25 refer to the shear, the abscissa of the segment and the rank of the image in the series, respectively. A refers to the standard calculation, according to which efficient DA – β-TM couples were defined when the spatial frequencies of the two facing verniers are constant (in absence of compression/dilation equilibrium), whatever the local curvature of the model. B, and C refer to the calculation of these couples accounting the incidence of the JPI wave train in the interaction between the two facing verniers. In B, the association between a DA and a facing β-TM is allowed when the relative locations of the two partner is calculated accounting a standard deviation that equals 27 Å. In C, this calculation assumes that the standard deviation is nil; in this case, the stand-by DAs are not represented. The same conventions are used in Figure 6, Figure 7 and Figure 8. The rank #25 is that of the image where the sliding speed is the lowest in the series. The numbers located on the left and right sides of the images are the local sliding speed and the maximum walking distances of the DAs (during the forward (left) and the backward (right) phases of their mechano-chemical cycle), respectively. Arbitrarily, the sliding speed is positive and negative when the DAs are in the forward and the backward phase of their cycle, respectively. The series was calculated considering the 240 Å long interval between the DAs. No differences were observed when this interval was 320 Å long (not shown). The trace of the axoneme is included on the left-hand side of the images; its proximal end is located at the top of the scheme. The segment of interest is represented on the trace by an open circle located as a function of its curvilinear abscissa.

Figure 6: Series G-2-25 (See Figure 5). Arbitrarily, G refers to the building of the groups of the DAs of close potential energies. As shown above, the individual potential energy of each DA is equivalent to its hue shown in Figure 5. When the conformation of the DA is almost vertical, when its potential energy is the highest (Figure 4 B) the open circle is located on the horizontal blue line. Arbitrarily, the potential energy of the arms is positive (upper blue line) and negative (lower blue line), when they are tilted tipward and baseward, respectively. The distance of a point from the blue line equals the quantity of
energy powered by the couple. s. When the DAs are not linked to a $\beta$-TM they are not represented.

Figure 7: Series S-2-64. The rank #64 corresponds to the highest sliding speed in the series. (See Figure 5).

Figure 8: Series G-2-64. The rank #64 corresponds to the highest sliding speed in the series. (See Figure 6).
Figure 1

A

B

C
Figure 2
Figure 3

Rank of the outer doublet that carries the dynein arms (open circles)

Rank of the outer doublet that carries the tubulin monomers (points)
Figure 4

A

Without ATP

“+” BACKWARD displacement

E0

E1

EaB

EaF

With ATP

“−” FORWARD displacement

E0

E1

B

Potential energy of the arm (arbitrary unit)

Supplied work (arbitrary unit)

(ATP hydrolysis) Mechano-chemical Cycle

Motor

Walking step
Figure 5

(S-2-25)
Figure 6

(G-2-25)
Figure 7

(S-2-64)
Figure 8

(G-2-64)