2008 Lecture No.7[1]
Flagellar Motility
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Next to muscle contraction powered by *myosin–actin* mechano-chemical cycles, the best understood type of cellular motility is flagellar and ciliary beating produced by *dynein–tubulin* mechano-chemical cycles. Although it is well established that flagellar and ciliary movements are based on *active sliding* similar to the well-known mechanism in muscle, the flagellar system seems to be more complicated. This is because the muscle system shows only one-dimensional contraction, due to active sliding occurring homogeneously along the muscle filaments, whereas the flagellar system gives rise to rhythmic initiation and propagation of two- or three-dimensional bends, due to a time- and space-dependent pattern of active sliding within the flagellum. One challenging problem that immediately arises is how bending waves are self-organized in cilia and flagella. Structural and functional considerations of cilia and flagella are necessary in solving this problem.

If many such flagella or cilia are close together, they exhibit on a large scale propagating waves known as *metachronal waves*. In ciliated surfaces of protozoa, for example, where beating cilia occur in large numbers, the activity of adjacent cilia is coordinated via hydrodynamic interactions to produce metachronal waves passing over the surface. Another interesting problem then arising is how metachronal waves are self-organized in the ciliated surface. In attempting to solve this problem, it is important to consider the advantage of these wave phenomena from a functional point of view. Through the metachronal coordination of ciliary activity, ciliated systems seem to achieve higher efficiency for the propulsion of fluids than could be achieved by random movement of the cilia.

Of particular interest is the presence of the two self-organizational phenomena on quite different levels. On one hand, the coordination in time and space of mechano-chemical processes *at the molecular level* produces bending waves *at the level of an individual cilium*. On the other hand, the metachronal coordination of such activity in individual cilia in turn generates wave phenomena *at the level of a ciliated system*. This suggests that

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regardless of the system level, universal principles may apply to the coordination in time and space of the 'active' processes at the lower level leading to self-organization of temporal, spatial and functional orders at the upper level. Cilia and flagella, thus, provide a good example for studying functional and structural hierarchy. In spite of many studies of the structure, biochemistry and motility of individual organelles, few attempts have been made to identify the universal principles.

Like other nonlinear distributed systems, these motile systems exhibit a large repertoire of self-organizational phenomena at each level. At the individual organelle level, flagella and cilia show regular beating patterns such as oscillations and excitability, with or without the *absolute and relative refractory period*. They also show irregular patterns such as reversal of the direction of wave propagation and *intermittent beating* caused by spontaneous *stopping* and *starting transients*. At the ciliated-system level, groups of cilia show at least four types of regular metachronal waves depending on the relationship between the beat direction of individual organelles and the propagating direction of the metachronal waves. They often show irregular patterns due to a weak metachronism, e.g. sometimes two oppositely propagated metachronal waves collide to disappear (*annihilating waves*) or sometimes they collide to evoke a new metachronal wave (*non-annihilating wave* or *soliton*). Irregular patterns of this kind have been studied less intensively than regular patterns. Recently the presence and role of irregularity, or *chaos*, have been pointed out in various biological systems. This suggests that rather than considering them separately, we should consider both regular and irregular patterns as general phenomena characterized by their degree of order (or the degree of disorder).

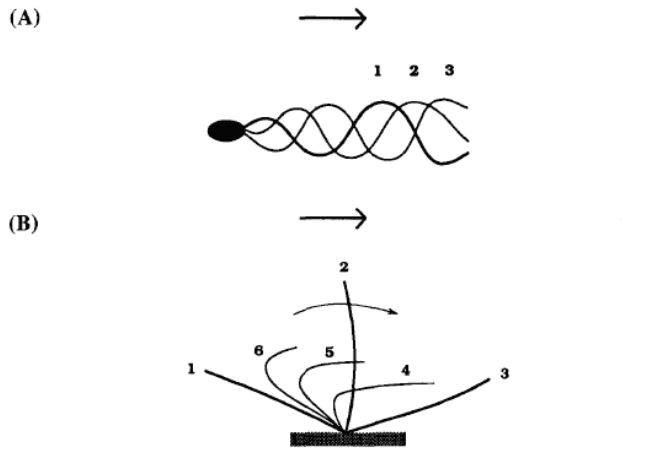

Figure 4.1 Typical beating patterns of flagella and cilia. (A): Successive waves with sustained amplitude (1 – 3) propagated toward the tip of a flagellum move water and thus propel the sperm head forward. (B): The beating cycle of a cilium consists of the effective stroke (1 – 3) in which the extended cilium moves rapidly toward one side by making an 'oar-like' movement, and the recovery stroke (4 – 6) in which the cilium moves more slowly back by propagating a bend from the base to the tip. The effective stroke occurs more or less in one plane. The recovery stroke swings either in the same plane or out of the plane. The arrows indicate the water flow caused by activity of the organelles.

4.1 Introduction

Flagella and cilia are living motile organelles projecting from the surface of eukaryotic cells. They produce bending waves to propel single cells in a medium or to move fluid over the fixed cell surface. Most of them beat at ~10–40 Hz, but the form of the beat is quite variable. Their length ranges from 2 μm to several millimetres and the diameter is about 0.2 μm. Strictly speaking, flagella and cilia have very diverse ultrastructures depending on the species from which they come (Phillips, 1974), but they are generally similar to one another and have a basic structure of *microtubules* in arrangements called *axonemes* (Warner, 1974). So these different names are merely a matter of definition and the experimental results of one system can be assumed to apply to the other. In most cases, therefore, it is not necessary to distinguish between the two systems.

Confusingly, bacterial flagella share the same name as those of eukaryotes. They will not be considered in this book. For even though many attractive problems have arisen from their characteristic properties (cf. Berg, 1983; Murata *et al.*, 1989), they are only 12–20 nm thick and their function is entirely different.

4.2 Internal structure and physiological function

4.2.1 *Typical movements of flagella and cilia*

The names of flagella and cilia are often used interchangeably, though a fundamental distinction can be made between them, as illustrated in Figure 4.1.

Flagella are very long and occur alone or in small numbers per cell. Sperm tails are typical examples of flagella. They show the propagation of undulatory bending waves with sustained amplitude along the length of the flagellum. The resultant effect is to move water along the flagellar axis and thus propel the cell in the opposite direction. As Gray (1955) observed, the movement of many flagella is confined to a single plane.

Cilia are short and occur in large numbers per cell where they generate a flow of fluid parallel to the cell surface. They are found on many self-propelling protozoa (e.g. *Opalina, Paramecium*), where they are used for locomotion, and also within multicellular animals where they perform transport functions such as mucous transport in the lungs.

Cilia generally show asymmetric beating in a cycle that can be separated into two phases: the *effective stroke* and the *recovery stroke*. During the effective stroke the cilium only bends a little, except near its base, and then swings rapidly around the basal region more or less in one plane. This is followed by the recovery stroke in which a bend is initiated at the base and propagates to the tip of the cilium. As a result, the cilium moves more slowly back to the starting point of the effective stroke. The resultant beat cycle is either planar or three-dimensional depending on whether the cilium recovers in the same plane as the effective stroke.

4.2.2 *Typical structure of flagella and cilia*

As pointed out before, many flagella and cilia possess an identical axoneme structure in spite of their various beating patterns. Throughout the length of the cilium, nine microtubules are arranged to form a basic structure of the axoneme though its cross-sectional patterns vary with the distance from the tip. To emphasize this 'structural asymmetry' one of the ciliary axonemes, seen in a longitudinal section, and a series of base-to-tip cross-sections at different levels are illustrated in Figure 4.2.

At level (1), nine *singlet* microtubules and *a central pair* of singlet microtubules are arranged. No other specific structures can be seen. At level (2), instead of singlet microtubules, nine outer *doublet* microtubules are arranged around the central pair. This microtubule arrangement is known as the '9 + 2' axoneme (Summers, 1975). Level (3) is the *transition zone* where the central pair terminates. At level (4), instead of doublet microtubules, nine *triplet* microtubules are arranged to form a basal body.

The intact ciliary or flagellar axoneme is surrounded by an extension of the cell membrane and bathed in cytoplasm. This cytoplasmic communication with the cell body, where ATP is produced by mitochondria, provides the necessary channel for supplying the ATP to the motile system of the axoneme. The transport process of the ATP along the flagellum is simple diffusion. A function of the membrane is thus to maintain the proper concentration of ATP and essential ions (e.g. Mg^{2+}) around the axoneme.

9 + 2 axoneme. As illustrated in detail in Figure 4.3, within the 9 + 2 axoneme the nine doublets are in part connected via *radial spokes* to a *sheath* which surrounds the central pair, and in part interconnected via *nexin links* at

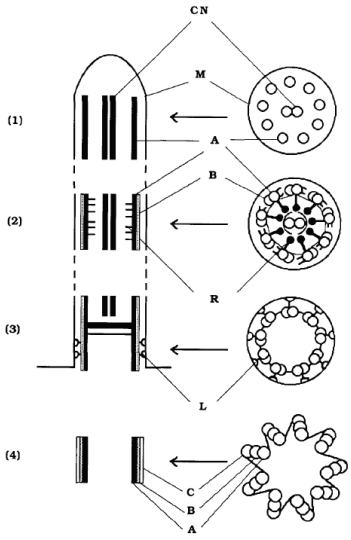

Figure 4.2 Schematic drawing of a median longitudinal section of an axoneme (left), and the cross-section as viewed from base to tip (right) at each level as indicated: A, B and C, are the A-, B- and C-subtubules; CN, the central pair of singlet microtubules; M, the cell membrane; R, radial spokes; L, the ciliary necklace (cf. Gilula and Satir, 1972). (1): At the tip, the B-subtubules disappear, but the A-subtubules remain in the axoneme. (2): The '9 + 2' axonemal structure is retained along most of the length of the flagellum. (3): The transition zone is described as the interval between termination of the central tubules and origin of the C-subtubules. (4): The basal body is composed of nine sets of triplet microtubules, each triplet containing the A-, B- and C-subtubules. Modified from Baba (1974). Reprinted with permission.

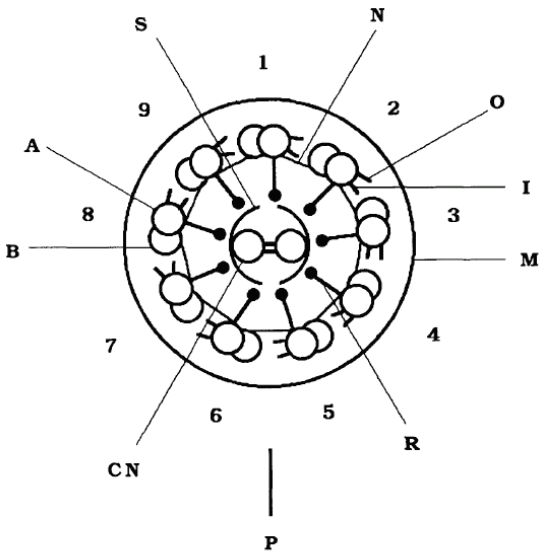

Figure 4.3 Schematic diagram of the 9 + 2 axoneme in cross-section as viewed from base to tip: A and B, the A- and B-subtubules; CN, a central pair of singlet microtubules; O and I, outer and inner arms; M, the cell membrane; N, nexin links; R, radial spokes; S, a sheath. A 'permanent' bridge is often present between doublets 5 and 6, instead of outer and inner arms. A single bend usually occurs in a plane (indicated by P) perpendicular to the plane formed by the central pair of microtubules.

intervals along their length. In addition, the nine doublets possess two rows of arms. The central pair lies in a plane restricting the bend direction of the motile organelle. A single bend prefers to occur in the plane denoted by P in Figure 4.3, which is perpendicular to the central microtubule plane.

Microtubules. The central pair of microtubules are complete, while each of the outer doublets consists of one complete and one partial microtubule – known as the *A-* and *B-subtubules*. Figure 4.4 shows a cross-sectional view and a side view of the doublet microtubule. As indicated in Figure 4.4A, the A-subtubule is formed from 13 *protofilaments*, whereas the B-subtubule comprises 10 (or 11) protofilaments sharing a common wall with 4 (or 5) protofilaments of the A-subtubule (Warner, 1974).

Each protofilament is an assembly of *heterodimers* composed of two monomers, α-*tubulin* and β-*tubulin*, whose diameters are about 4 nm. Many models have been proposed to account for the doublet microtubule structure (cf. Stephens, 1974). One reliable configuration of the doublet microtubule is illustrated in Figure 4.4B (see Amos and Klug, 1974; Linck *et al.*, 1981; Linck and Langevin, 1981; Mandelkow *et al.*, 1986). It should be noted that each subtubule has the same 4 nm 'monomer' lattice arrangement, but a different 8 nm 'dimer' lattice. This indicates that each subtubule has its particular repeat period based on the helical structure, in addition to inherent 4 nm (monomer) and 8 nm (dimer) longitudinal periodicities.

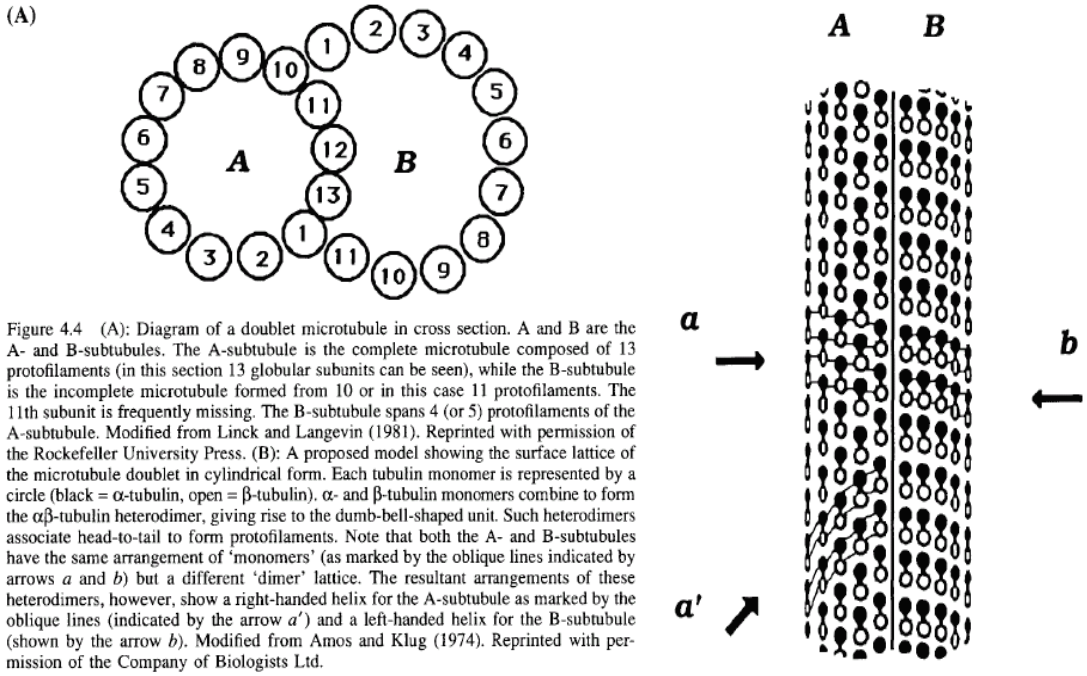

Figure 4.4 (A): Diagram of a doublet microtubule in cross section. A and B are the A- and B-subtubules. The A-subtubule is the complete microtubule composed of 13 protofilaments (in this section 13 globular subunits can be seen), while the B-subtubule is the incomplete microtubule formed from 10 or in this case 11 protofilaments. The 11th subunit is frequently missing. The B-subtubule spans 4 (or 5) protofilaments of the A-subtubule. Modified from Linck and Langevin (1981). Reprinted with permission of the Rockefeller University Press. (B): A proposed model showing the surface lattice of the microtubule doublet in cylindrical form. Each tubulin monomer is represented by a circle (black = α-tubulin, open = β-tubulin). α- and β-tubulin monomers combine to form the αβ-tubulin heterodimer, giving rise to the dumb-bell-shaped unit. Such heterodimers associate head-to-tail to form protofilaments. Note that both the A- and B-subtubules have the same arrangement of 'monomers' (as marked by the oblique lines indicated by arrows *a* and *b*) but a different 'dimer' lattice. The resultant arrangements of these heterodimers, however, show a right-handed helix for the A-subtubule as marked by the oblique lines (indicated by the arrow *a'*) and a left-handed helix for the B-subtubule (shown by the arrow *b*). Modified from Amos and Klug (1974). Reprinted with permission of the Company of Biologists Ltd.

Dynein cross-bridges and permanent bridge. Two rows of *ATPase* or *dynein cross-bridges* (referred to as *inner* and *outer arms*) extend from each A-subtubule toward the B-subtubule of the adjacent doublet in a clockwise manner, when the axoneme is viewed in transverse section from the base of the organelle to its tip (see Fig. 4.3). These arms are spaced along the microtubule at regular 24 nm intervals. *The presence of ATPase along the entire length of the flagellum strongly suggests that the flagellum itself is composed of active elements.* From a morphological point of view, one question arises: what is the role of two rows of arms whose structures differ slightly ? It was found that the outer arms could be selectively removed while the other structures remained intact, and that such axonemes could beat with little change in waveform but at a low frequency (Gibbons and Gibbons, 1973). However, axonemes lacking the entire inner arm were found to be non-motile (Kamiya *et al.*, 1989). This behaviour suggests that inner and outer arms have somewhat different functions in beating axonemes (see Chapter 9).

Some flagella and cilia have a 'permanent' bridge between the two doublets. This bridge is a useful marker for numbering the doublets. The two bridged doublets are numbered 5 and 6 and doublet 1 lies completely opposite, perpendicular to the central microtubule plane (see Satir, 1974). Other outer doublets are then numbered clockwise when the axoneme is viewed from base to tip (see Fig. 4.3). Using this numbering method, each outer doublet can be assigned a specific unchanging number.

Basal plate and basal body. The two central microtubules end at the level of the cell surface, or a little above it, where there is usually a *basal plate*. While the outer doublet microtubules terminate inside the cell in the *basal body* (see Fig. 4.2). The basal body is composed of nine sets of triplet microtubules that form a short cylinder. Each of the outer doublet microtubules of the axoneme extends into the basal body, where the extra *C*-subtubule joins part of the doublet microtubules (i.e. the A- and B-subtubules) to form triplet microtubules.

Interestingly, almost all animal cells have *centrioles* in which the ninefold array of triplet microtubules are the same as those in the basal body and are interchangeable in function. For example, the egg does not usually seem to possess active centrioles, while the sperm contains basal bodies that are donated to the egg during fertilization. These sperm basal bodies act as centrioles to organize the mitotic spindle for the first cleavage divisions. A comparable organizing effect can be seen by artificially injecting purified basal bodies from the ciliated protozoan *Tetrahymena* into frog eggs. Further information on their function may be obtained from the review by Pitelka (1974).

4.3 How do individual flagella and cilia move?

The nature of the basic mechanism producing wave phenomena in a cilium (or a flagellum) has been a subject of interest for many years (see books by Gray (1928) and by Sleigh (1962); and reviews by Brokaw (1972a, 1989), by Blum and Hines (1979), by Gibbons (1981a), and by Satir (1985)). The investigation of this mechanism provides a lot of information, not only about functioning properties of the individual cilium, but also about dynamic properties of groups of cilia leading to metachronal waves on large scales. Before describing the nature of these metachronal waves (see Section 4.6), we shall first try to understand the underlying mechanism by focusing our attention on the bending movements of flagella and cilia.

Active sliding microtubule mechanism. This hypothesis was suggested on the basis of the analogy of the muscle system with the flagellar system after the discovery of 'arms' projecting from the outer doublets (Afzelius, 1959). It is considered that the microtubules do not change their length but *slide actively* relative to one another (Fig. 4.7). When such sliding occurs *inhomogeneously* along the flagellum, bend initiation occurs between points that have different shear (Brokaw, 1971; Shingyoji *et al.*, 1977). This means that *the bending region is not a direct reflection of the active region, but is the result of sliding processes occurring throughout adjacent regions of the flagellum*. Consequently, a propagated bending wave is associated with a propagated wave of active sliding, but they are out of phase.

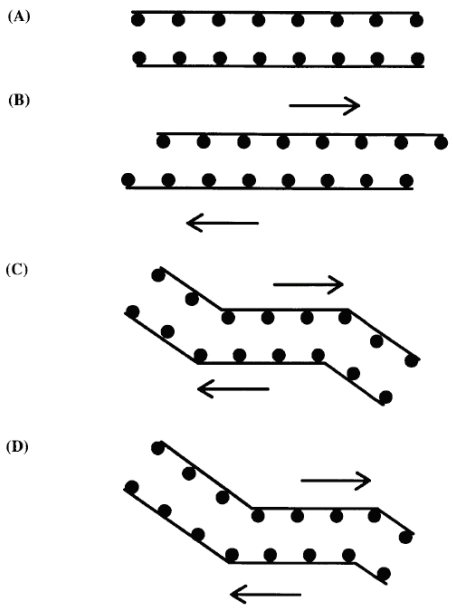

Figure 4.7 Diagrams showing how active sliding causes a bend in a flagellum consisting of two inextensible filaments. (A): The flagellum is straight and no bending occurs without active sliding. (B): No bending is initiated when active sliding occurs *homogeneously* (or *equally*) throughout the length of the flagellum. (C): If there is resistance to sliding at both ends, two bends are formed in opposite directions on either side of the region of active sliding. There is a phase shift between the active region and the bending region. The arrows indicate the active sliding direction of each filament. (D): The resultant bends propagate in accordance with the propagated wave of active sliding with some phase shift. Modified from Shingyoji *et al.* (1977).

4.4 Functional mechanisms

4.4.1 *Force-generating mechanisms*

Although it has been established that ATP-induced force generation by dynein cross-bridges causes active sliding between a pair of doublet microtubules, little information is available on whether or not the active sliding occurs only in one direction. Investigation of this problem provides insight into not only how cilia and flagella beat but also how dynein cross-bridges undergo the mechano-chemical cycle.

Unidirectional active sliding. Sale and Satir (1977) followed the method of Summers and Gibbons (1971) by using electron microscopy to examine a 'polarity' of active sliding between a pair of doublets. In the pair of doublets, the dynein cross-bridges extend from the A-subtubule of one doublet (conventionally referred to as N) and point toward the B-subtubule of the adjacent neighbouring doublet (conventionally referred to as $N + 1$) as illustrated in Figure 4.10.

The active sliding occurs between the two doublets due to the mechano-chemical cycle of the dynein cross-bridges on doublet N. For lack of doublet $N + 2$, the dynein cross-bridges on doublet $N + 1$ would not contribute to the sliding interaction. The relative movement thus depends only on whether the direction of force generation of dynein is toward the tip or toward the base. If the direction of force generation of dynein is from base to tip, doublet $N + 1$ will move toward the tip relative to doublet N (Fig. 4.10B). If, on the other hand, the direction of force generation is from tip to base, doublet $N + 1$ will move toward the base relative to doublet N (Fig. 4.10C).

Sale and Satir found that the case shown in Figure 4.10B always occurs such that *the dynein cross-bridges on doublet N push the doublet N + 1 toward the tip of the axoneme*. This strongly suggests that there is a single polarity for active sliding, and that active sliding cannot reverse along the same pair of doublets. That is, active sliding occurs 'unidirectionally', but not 'bidirectionally'.

Unidirectional mechano-chemical cycle. The polarity of dynein force generation is analogous to that of myosin force generation, which facilitates the sliding of filaments in striated muscle. Figure 4.11 shows major features of the mechano-chemical activity of dynein–tubulin interactions summarized by Satir *et al.* (1981). A cross-bridge on doublet N is attached to doublet $N + 1$ (A). ATP binds to the cross-bridge, causing it to be detached (B). Hydrolysis of ATP to ADP + Pi relaxes the cross-bridge to its original conformation (B $\rightarrow$ C). The cross-bridge re-attaches to doublet $N + 1$ (D). Sliding movement is generated when the attached cross-bridge performs a unidirectional 'power stroke' to return to its equilibrium position accompanied by the release of ADP + Pi (D $\rightarrow$ A).

4.4.2 *Control mechanisms*

It is now clear that the forces in cilia and flagella are produced by a sliding microtubule mechanism, similar to that of striated muscle. However, to produce the observed motion in cilia and flagella, forces have to be developed in the right sequence in time and at the right location in space. This suggests the presence of *temporal* and *spatial control mechanisms*. Without such control mechanisms all dyneins would operate at once – since every dynein arm is potentially identical and every microtubule slides in the same way – and the resultant forces would cancel and no movement would occur (Satir, 1984). Thus one apparent question arises: How is the activity of dyneins coordinated in time and in space?

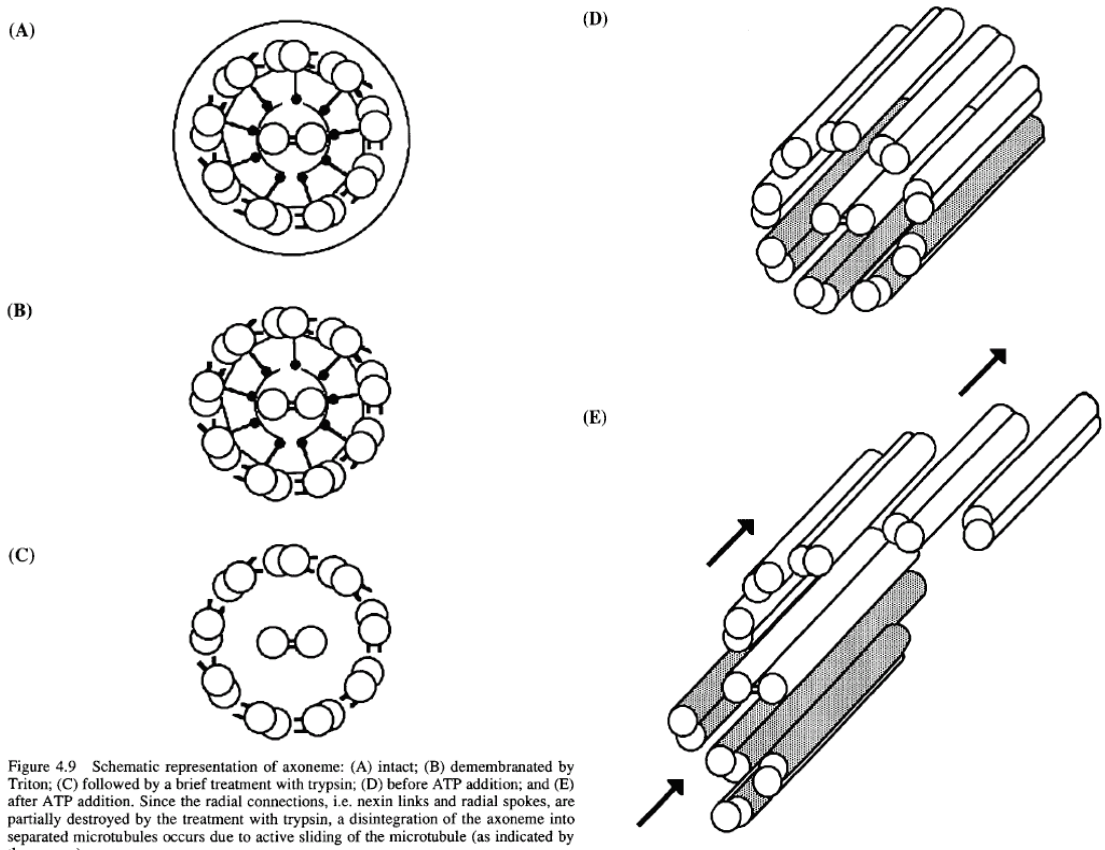

Figure 4.9 Schematic representation of axoneme: (A) intact; (B) demembranated by Triton; (C) followed by a brief treatment with trypsin; (D) before ATP addition; and (E) after ATP addition. Since the radial connections, i.e. nexin links and radial spokes, are partially destroyed by the treatment with trypsin, a disintegration of the axoneme into separated microtubules occurs due to active sliding of the microtubule (as indicated by the arrows).

Temporal control mechanism. Active sliding between each pair of outer doublets only occurs in one direction (Sale and Satir, 1977) due to a unidirectional dynein power stroke (Satir *et al.*, 1981). Because of the closed ring of doublets, backward sliding of the same pair of doublets is passively induced by active sliding of other pairs in the axoneme. Assuming that bending occurs in a single bend plane, the 9 + 2 axoneme would behave as if it were only a two-filament system as illustrated in Figure 4.8.

For convenience, the two sides of the axoneme are identified by the

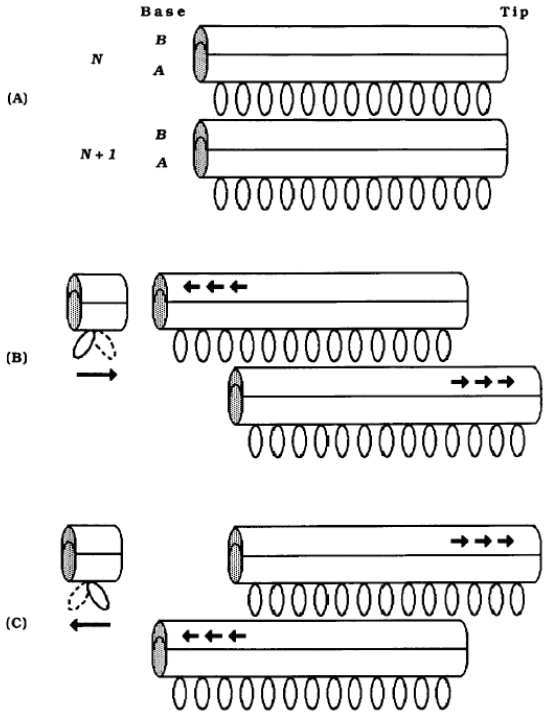

Figure 4.10 Diagram showing a single pair of doublets. (A): Before adding ATP. The upper doublet is conveniently numbered N and the adjacent doublet $N + 1$. The dynein cross-bridges extend from the A-subtubule of doublet N toward the B-subtubule of doublet $N + 1$. Base and tip correspond to left and right. (B): If the direction of force generation of dynein is from base to tip (indicated by the arrow on the left panel), doublet $N + 1$ moves toward the tip relative to doublet N (indicated by the arrow). (C): If the direction of force generation is from tip to base, doublet $N + 1$ moves toward the base relative to doublet $N + 1$. Experimental results always show the case (B).

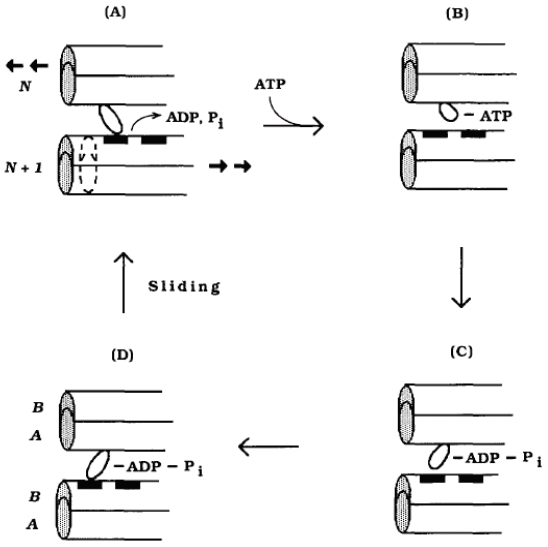

Figure 4.11 Mechano-chemical cycle of dynein cross-bridge. Two successive binding sites on the B-subtubule of doublet $N + 1$ are indicated by filled rectangles. (A): A cross-bridge on the A-subtubule of doublet N attaches to the B-subtubule of doublet $N + 1$. (B): ATP binds to the cross-bridge, which causes the release of the attached dynein. (C): During hydrolysis of ATP to ADP + P_i, the detached dynein changes conformation. (D): Re-attachment of the dynein to the B-subtubule of doublet $N + 1$ occurs. Subsequently, a sliding motion takes place between the two doublets upon the release of ADP + P_i.

orientation of the dyneins projecting into the bend plane: one is the left half (doublets 6–9) of the cross-section of the axoneme at which all dyneins project into the plane incline in the same direction, and the other is the right half (doublets 1–5) of the axoneme at which all dyneins incline in the opposite direction.

As illustrated in Figure 4.12A, if dyneins on the right half of the axoneme (especially dyneins on doublet 3) are active, unidirectional active sliding takes place between doublets 3 and 4. The two-filament model assumes that 9 doublets are divided into two groups with respect to their direction of relative sliding. One is the upper half (doublets 8–3) of the axoneme, which slides toward the base, and the other is the lower half (doublets 4–7), which slides toward the tip.

Of course 'doublet subsets' of the upper and lower halves can be rather arbitrary, i.e. the axoneme can be divided into different subsets of doublets. But such arbitrariness does not matter as long as one assumes the two-filament system to account for planar beating. Although sliding between doublets 3 and 4 is 'active', sliding between doublets 7 and 8 is completely 'passive'. It is passive because the sliding direction is opposed to the 'preferred' direction of the dynein power stroke. The sliding movement of doublets causes the cilium to bend to one side (or downward in this figure).

If dyneins on the left half of the axoneme (especially dyneins on doublet 7) are active, the upper half moves relative to the tip and the lower half relative to the base as illustrated in Figure 4.12B. In this case sliding between doublets 7 and 8 is 'active', whereas sliding between doublets 3 and 4 is 'passive'. Thus the cilium bends toward the opposite side (or upward).

The temporal control mechanism, therefore, seems to be an 'on' and 'off' switch for the activity of dyneins attached to doublets at each side (doublets 1–5 and doublets 6–9) of the axoneme (see Satir, 1984; 1985). Since this control mechanism is allowed to initiate active sliding in the proximal direction and in the distal direction alternately, it may have profound effects on the beat frequency.

Spatial control mechanism. The temporal control mechanism produces alternate active sliding and is probably responsible for the successive changes of bend angle of a cilium between the two opposing stroke positions. However this mechanism cannot produce a typical ciliary cycle which alternates between effective and recovery strokes (see Fig. 4.1).

As illustrated in Figure 4.13, these different beating patterns seem to reflect the strength of microtubule interaction along the length of the cilium – the *spatial control mechanism*. According to the relationship between the geometry of the bent cilium and the sliding displacement of the microtubules, the effective stroke must involve *synchronous sliding*, where simultaneous sliding occurs throughout the length of the axoneme except near its base. The recovery stroke, however, must involve *metachronous sliding*, where sliding occurs in a restricted region along the length of the cilium to form a bend (Sleigh and Barlow, 1982).

One can expect that synchronous sliding occurs when the active processes of most dyneins on the same doublet are strongly coupled by the sliding movement of the doublet itself, and undergo their mechano-chemical cycles almost as a unit. Metachronous sliding, however, takes place when there is weak coupling between dyneins and they perform the mechano-chemical cycles in a limited region. This suggests that activation of dyneins may be triggered in two different ways, one essentially local and one occurring almost simultaneously throughout most of the length of the axoneme (Rikmenspoel and Sleigh, 1970; Sleigh and Barlow, 1982).

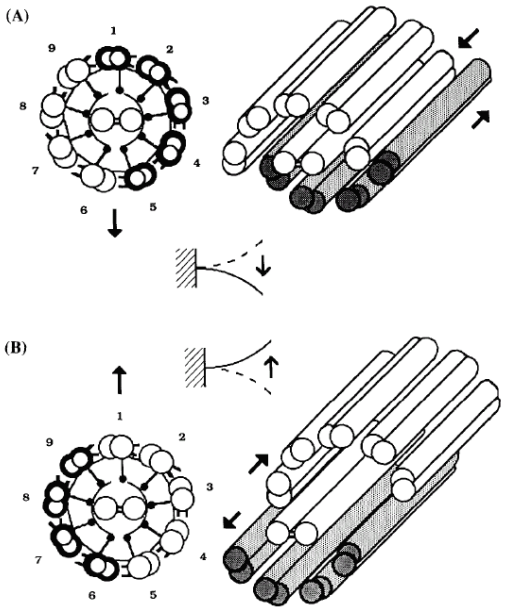

Figure 4.12 Correlations among the activity of dyneins on 9 outer doublets (left), the resultant sliding of doublets (right) and the related configuration of the cilium (middle). (A): If dyneins on the right half (doublets 1–5) of the cross section of the axoneme, especially dyneins on doublet 3, are active (as seen from base to tip, where bending direction is indicated by the arrow), 'active' sliding occurs between doublets 3 and 4 and at the same time 'passive' sliding occurs between doublets 7 and 8. Assuming that beating occurs in a plane, these 9 outer doublets are divided into two subsets according to the direction of sliding: the upper half (doublets 8–3) and the lower half (doublets 4–7) of the axoneme. The resultant planar bending is shown in the middle panel. (B): If dyneins on the left half (doublets 6–9) of the axoneme, especially dyneins on doublet 7, are active, the sliding direction is reversed and the cilium bends toward the opposite side.

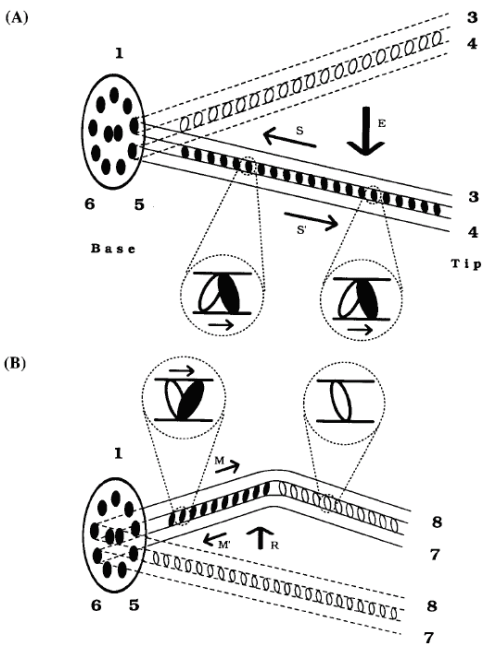

Figure 4.13 Correlations between the strength of 'triggering' interaction and the beating pattern of the cilium. (A): The power stroke of most of the dyneins on doublet 3 is triggered at once (as shown by the dark circles), when there is strong coupling between dyneins along the length of this doublet. Synchronous sliding results (indicated by arrows S and S′) and the effective stroke is produced (indicated by arrow E). (B): When dyneins on doublet 7 are weakly coupled, the power stroke of the dyneins (shown by dark circles) is triggered in the restricted region of the doublet. As a result of this local activation, metachronous sliding occurs (indicated by arrows M and M′) and the recovery stroke is generated (indicated by arrow R). Flagellar beating patterns are ascribed to this type of metachronous sliding alternately occurring on the two halves of the axoneme.

Intermittent swimming of sea-urchin sperm of *Tripneustes gratilla* (a Hawaiian species) was observed in both living cells (Gibbons, 1980; 1981b; Gibbons and Gibbons, 1980b) and demembranated models in a reactivation medium containing Ca^{2+} (Gibbons, 1986). This phenomenon involves the *stopping* and *starting transients* of flagellar movement (Fig. 4.22). The stopping transients are triggered by the abrupt failure of a reverse bend to be developed at the basal end of the flagellum at the expected time in the beat cycle. As a result, the preceding principal bend remains at the base and the flagellum becomes *quiescent*, maintaining a shape that resembles a cane with a sharp bend in the basal region and little curvature in the rest of the flagellum (Gibbons and Gibbons, 1980a). The starting transients begin when a reverse bend is initiated at the base. Comparison of the timing of the peaks and the valleys in θ_{tip} before and after the quiescent episode indicates that the flagellar oscillation does not maintain its phase but shifts by about half a cycle corresponding to the quiescent interval (Fig. 4.22B).

Intermittent oscillations were also observed in the bending pattern of short demembranated sea-urchin sperm flagella (Brokaw, 1982). The sperm head was attached to a microscope slide and no movement of the head was allowed. As illustrated in Figure 4.23, flagella shorter than 4 μm were usually observed to beat with irregular duration of pauses before initiation of new bends (i.e. onset of sliding reversals). It is interesting to note that pauses in bend initiation are also evident in the discontinuous beating cycle of 'excitable' cilia, as mentioned in the preceding sections.

From the above evidence, I suspect that intermittent bending movements are not 'species specific', but are common to all cilia and flagella (see Chapters 7 and 8).