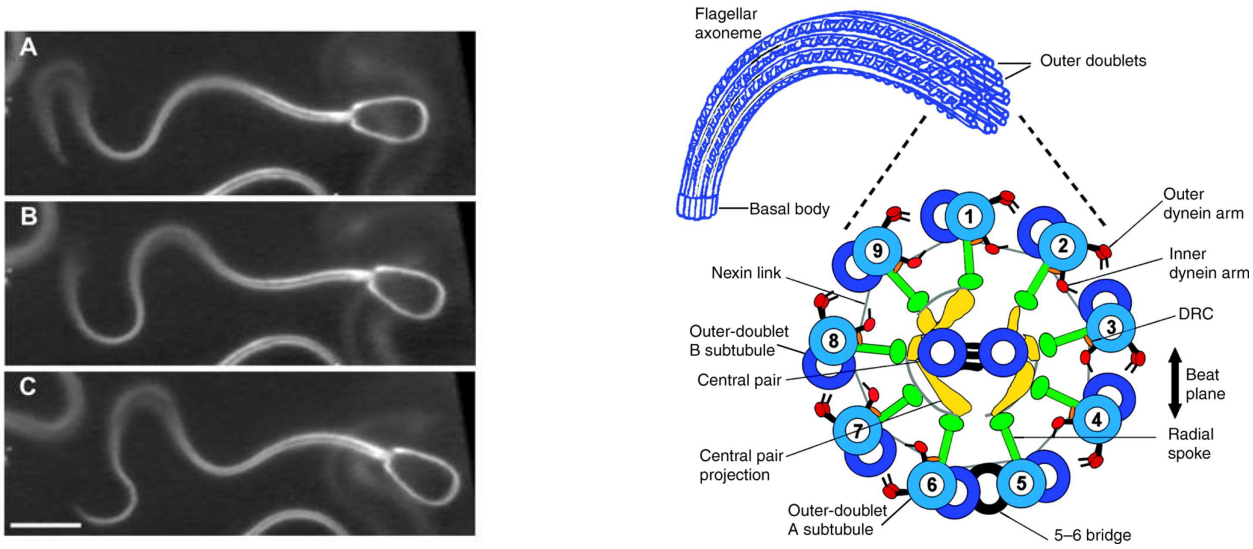
MODELING THE BEATING OF ATP-POWERED NATURAL FLAGELLA

S. Namdeo*,a) & P. R. Onck*
*Zernike Institute for Advanced Materials, University of Groningen, 9747 AG Groningen, The Netherlands

Summary
The working mechanism of dyneins that produces beating of a flagellum is computationally explored using a coupled solid–fluid finite element framework. The axoneme structure is represented by two microtubules that are connected via nexin links and anchored at the base. The ATP-powered dyneins drive the relative sliding of the microtubules, which is eventually converted into flagellar bending, and we show that an overall beating pattern emerges with time due to the coordinated action of the individual dyneins.

INTRODUCTION

A rapidly growing field in biotechnology is the fabrication of micro-fluidic devices for biomedical applications such as biosensors. For a successful future implementation of these micro-fluidic devices, it is important that one is able to accurately move and position micro-objects (cells, organelles) within the device. The primary challenge in designing such a system is that the achieved motion should be non-reciprocal (time-irreversible) in nature to cause any (fluid) propulsion [1-2]. Researchers have mimicked the propulsion strategies of cilia [3-4] and flagellated micro-organisms (e.g., bacteria and spermatozoa) by using externally-applied actuation mechanisms such as magnetic fields [5-6]. However, natural cilia and flagella are actuated by internal forces, generated by ATP-powered motor proteins. How these picoscale forces are translated into an overall beat response is still under debate. The goal of this work is therefore to study the fundamental working mechanisms of natural cilia and flagella in terms of the solid–fluid interaction of the ATP-powered axoneme with the surrounding fluid.



(a) (b)

Figure 1. (*a*) Flagellar oscillation of a typical spermatozoon, the three video-fields (A-C) are successively 200 ms apart. The cell is moving forward by altering the bend curvature and thus propagating the wave. The scale bar is 10 μm [7]. (*b*) Schematic diagram of the flagellar axoneme in cross-section [8]. Structural details are discussed in the text. Figures are reproduced with permission of the copyright owner(s).

Flagella (and cilia) are organelles of eukaryotic cells that produce motility by repetitive episodes of bending and bend propagation as illustrated in Fig. 1a. The internal cytoskeletal arrangement of a flagellum is composed of nine doublet microtubules in a ring surrounding a pair of single microtubules (the central pair); these structures collectively compose the axoneme as illustrated in Fig. 1b. Each of the outer doublets is linked to its neighbors by strands of protein called nexin links, which are elastic and resist the free sliding of the microtubules with respect to each other. The microtubules are filamentous proteins of α- and β-tubulin dimers that contain the possible binding sites for the dyneins, see Fig. 2. The dynein anchors itself at one microtubule and executes a power-stroke (in the presence of ATP) leading to the relative sliding of neighboring microtubules. During the power stroke it utilizes the chemical energy from the ATP hydrolysis. The relative sliding of the microtubule doublets is eventually converted to bending through the restraining influence of the basal anchor and the nexin links.

a) Corresponding author. E-mail: s.k.namdeo@rug.nl

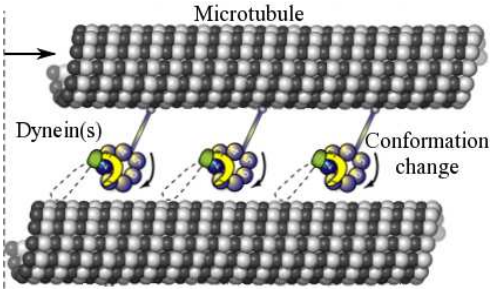


Figure 2. Schematic drawing of working of the dynein. The power stroke (conformation change) of the motor protein, dynein, attached to one microtubule, against a neighboring microtubule causes the microtubules to slide past each other. The relative sliding of the microtubule doublets is eventually converted to bending through the restraining influence of the basal anchor and the nexin links (not illustrated).

MODELING APPROACH AND RESULTS

In this work, we computationally explore how the individual dyneins are able to generate an overall beat response by using a simple model in which the axoneme structure is represented by two representative microtubules that are connected via nexin links and anchored at the base. We analyze such a system using a computational framework in which an integral formulation for Stokes flow is implemented using the boundary element method to represent the fluid environment while the microtubules and nexin links are represented by an assemblage of elastic beam elements. The coupling of the solid mechanics and the fluid dynamics equations is done in an implicit manner and details of the computational approach are given elsewhere [9]. All the nodes on the microtubules are possible binding sites for the dyneins and we model two groups of dyneins responsible for sliding in opposite directions. The dyneins will execute a power-stroke once they are attached to a microtubule, after which they go through a waiting period (given by the duty ratio) to restore the available energy. At the start of the simulations, the dyneins working- (and the waiting-) phase relevant to the duty ratio is randomly allocated. During a power-stroke the dyneins cause relative sliding of the microtubules, which eventually leads to an overall bend generation. We will observe the evolution of local bend regimes in the microtubules and their propagation with time, and relate their beat pattern to the local force-displacement behavior of the ATP-powered dyneins and the viscosity of the surrounding fluid. Furthermore, we will present a new dynein constitutive relation, which is consistent with the experimental observations, and postulate a working mechanism for the dynein motor proteins coordinating their collaborative action to produce overall beating.

References

[1] Lauga E. and Powers T. R.: *Reports on Progress in Physics* **72**:096601, 2009.
[2] Purcell E. M.: *American Journal of Physics* **45**:3, 1977.
[3] Khaderi S. N., Baltussen M. G. H. M., Anderson P. D., Ioan D., den Toonder J. M. J., and Onck P. R.: *Phys. Rev. E* **79**: 046304, 2009.
[4] Khaderi S. N., Craus C. B., Hussong J., Schorr N., Belardi J., Westerweel J., Prucker O., Ruhe J., den Toonder J. M. J., and Onck P. R.: *Lab on a Chip* **11**: 2002, 2011.
[5] Dreyfus R., Baudry J., Roper M. L., Fermigier M., Stone H. A., and Bibette J.: *Nature* **437**:862, 2005.
[6] Garstecki P., Tierno P., Weibel D. B., Sagués F., and Whitesides G. M.: *Journal of Physics: Condensed Matter* **21**: 204110, 2009.
[7] Woolley D. M., Crockett R. F., Groom W. D. I., and Revell S. G.: *J. Exp. Biol.* **212**: 2215–2223, 2009.
[8] Lindemann C. B. and Lesich K. A.: *Journal of Cell Science* **123**: 519–528, 2010.
[9] Namdeo S., Khaderi S. N., den Toonder J. M. J., and Onck P. R.: *Biomicrofluidics* **5**:034108, 2011.