A multi-filament model of the ciliary axoneme with beating driven by dynamic instability

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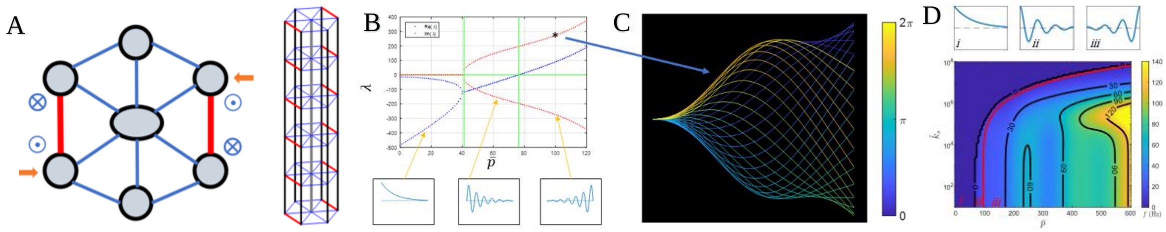
Key Words: *Cilia, Flagella, Stability, Finite-Elements, Beams, Eigenvalues, Oscillation.*

Cilia are slender cellular appendages that clear mucus in our airways, circulate cerebrospinal fluid in our brain ventricles, and propel single-celled organisms and gametes. Inside every cilium is a microtubule-based cytoskeleton known as the axoneme. The axoneme consists of a circular array of nine outer microtubule doublets (MTDs) and a central pair of microtubule singlets, all in parallel. Radial spokes (RSs) and circumferential links interconnect these filaments. Ciliary beating is driven by arrays of the motor protein dynein, which create distributed, unidirectional shear forces and associated bending moments between adjacent MTDs. It is not known how or if dyneins are regulated to create the oscillatory beating observed in cilia. Recent papers have demonstrated that the effects of axial loading (decreased resistance to bending and the resulting reorientation of follower loads) not only strongly affect the shape of ciliary beating [1], but are in fact sufficient to drive oscillation in models of the axoneme where dynein force remains steady [2].

Here, we expand on past work to create a custom multi-filament, finite-element model of the axoneme that exhibits dynamic instability and growing oscillations under steady dynein force. This model allows for efficient estimation of the eigenvalues and eigenvectors of the internally loaded system to reveal how the complex interaction of parameters in this model, such as the elastic and viscous properties of the RSs and links, determine stability, beat frequency, and beat shape. In addition, we introduce a new model of the dynein enzyme which accounts for the kinematics of this nanoscale motor. Variation of the parameters of this model within a biologically plausible range have profound effects on the stability and frequency of the system.



A) Multi-filament model of the axoneme including 6 MTDs, a central filament, RSs, and circumferential links. Dyneins between MTDs are schematically represented by red lines. B) Eigenvalue real parts determine system stability, imaginary parts determine frequency. C) Beating shape is determined from the eigenvectors. D) The current eigenvalue approach allows efficient analysis of parameter space. Here frequency is shown as a function of nondimensional dynein force $\bar{p}$, and RS stiffness $\bar{k}_s$.

REFERENCES

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