# Modeling of 3D Cilium Mechanics using Beam Physics with Extrusion Coupling

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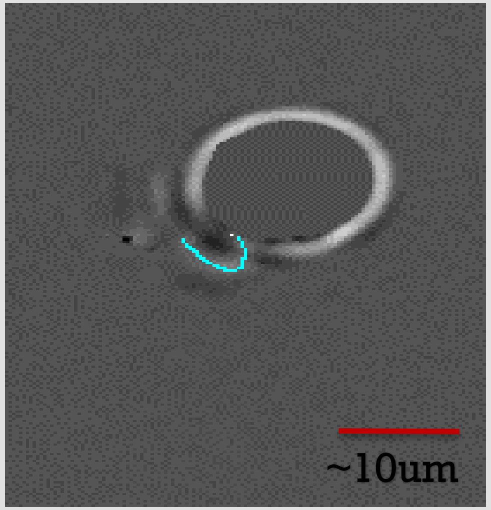
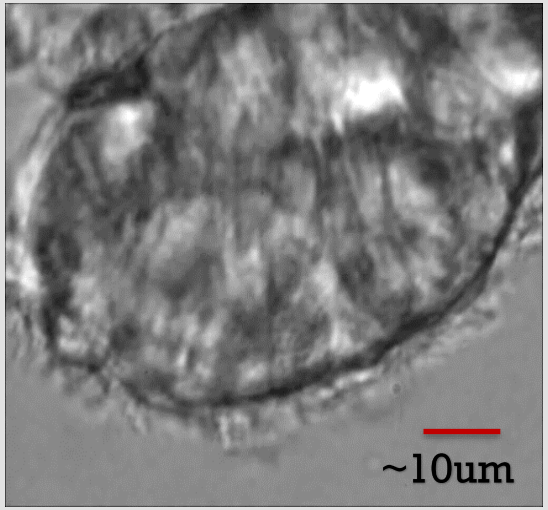
# What is a Cilium?

- Slender organelle on the surface of some cells
- 200 nm diameter, 10 µm length (for *Chlamydomonas* cilia)
- Generates propagating waves to propel fluid or move the cell



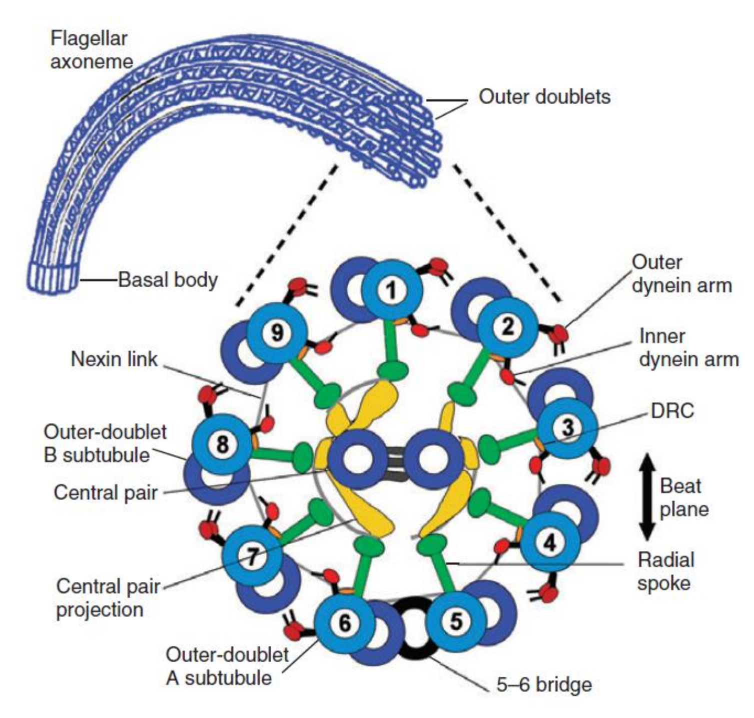

Biciliated *Chlamydomonas reinhardtii*
(Courtesy of Cui, 2020)



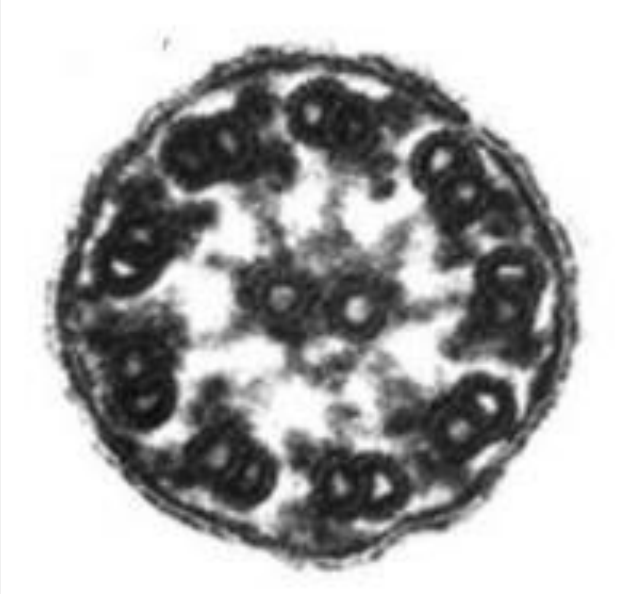

Human nasal epithelial cells
(Bottier et al. 2017)

# Cilium Structure: the Axoneme

- “9+2” structure of *microtubule doublets*
- Connected by circumferential *nexin links* and *radial spokes*
- Activated by *dynein*, a motor protein

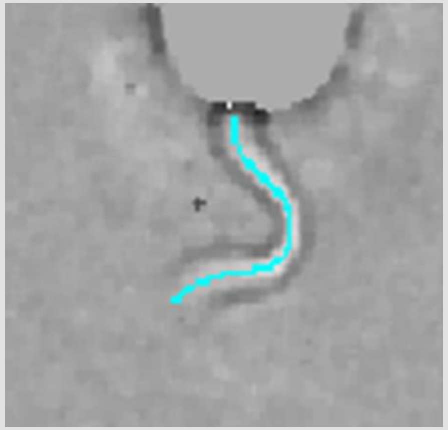


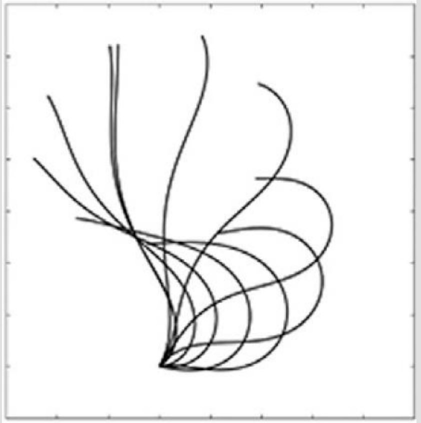

Cilium 3D structure (Lindemann et al. 2010)



Cilium cross-section (electron microscopy) (Hu et al. 2017)

# How do Mechanical Forces Generate Oscillations?





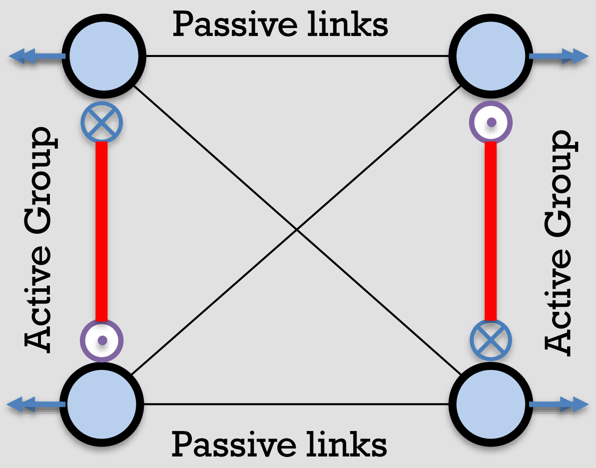
**Does dynein activity need to be dynamically regulated* to produce ciliary beating?** * Open-loop or closed loop (feedback) control

**How do mechanical system parameters such as nexin link stiffness and damping affect beating?**

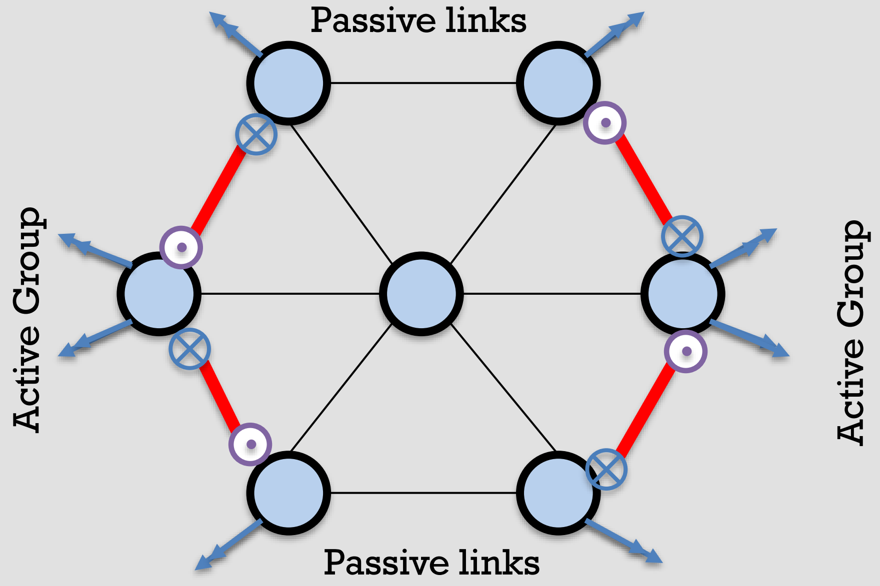
Bayly P. V. and Dutcher S. K., Steady dynein forces induce flutter instability and propagating waves in mathematical models of flagella. 13. J. R. Soc. Interface http://doi.org/10.1098/rsif.2016.0523

# COMSOL Simplified Model

- Aim 1: Verify the results of theoretical stability analysis
- Aim 2: Simulate realistic behavior involving large deformation
- Consider a 4-doublet model and “6+1”-doublet model



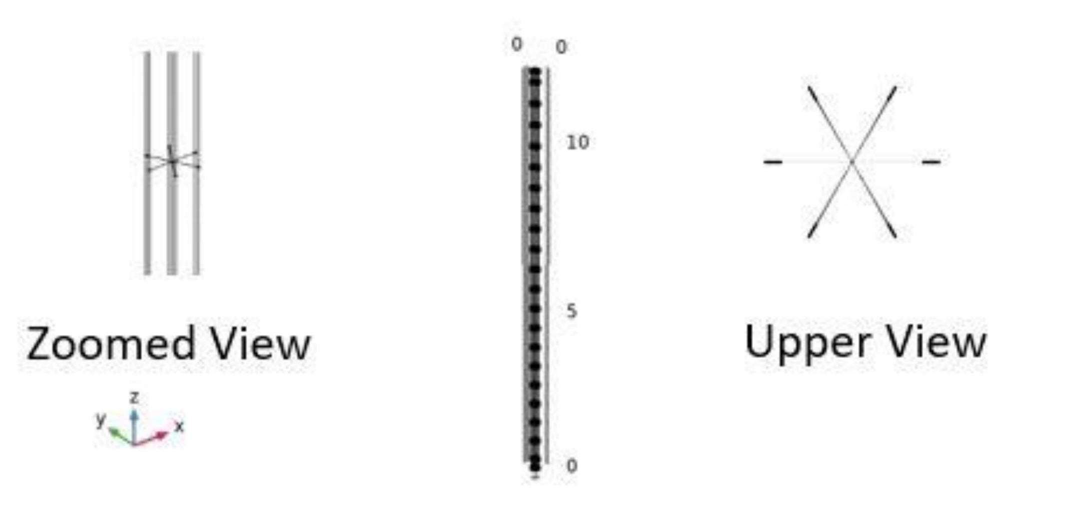

Simplified 4-doublet model




Simplified 6+1-doublet model

# COMSOL Toolboxes

- *Beam physics* is used to build the microtubules and radial spokes
- *Linear extrusion coupling* is used to build the nexin links (connecting outer doublets)



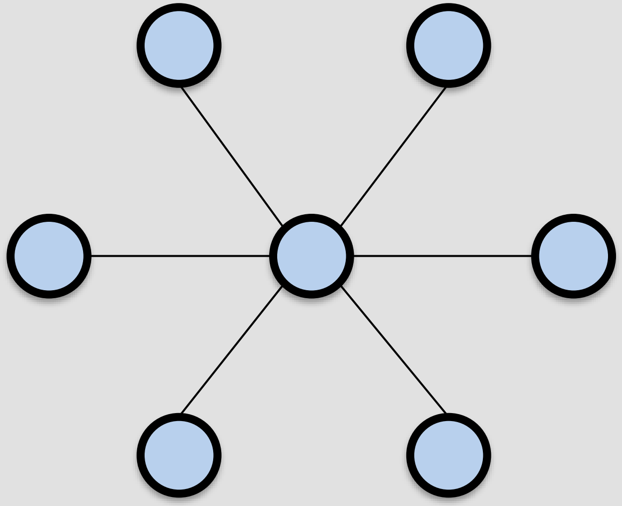

COMSOL 6+1-doublet model geometry
with magnified view and top view

# Beam Physics Governing Equation

- Beams are used to model radial spokes
- Spoke is meshed as 1-element beam
- Choose beam parameters to achieve desired radial (normal) and shear stiffness

$$A = \frac{k_N L a}{E N_{spokes}}$$

$$I = \frac{k_S L a^3}{12 E N_{spokes}}$$

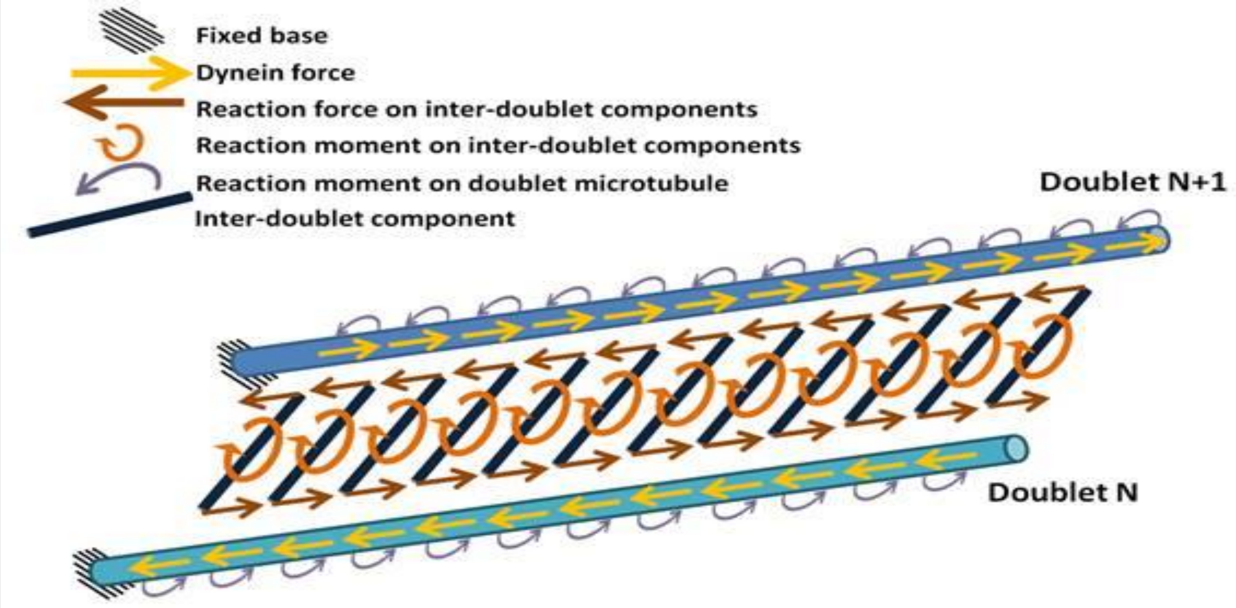


# Extrusion Coupling to Model Nexin Links and Dynein

- Elastic coupling term represents nexin links:

$$\mathrm{F} = kx(1 + \alpha\varepsilon^2) + c\frac{dx}{dt}$$

- Dynein activity is modeled by external loads applied based on the average tangential vectors of active pairs

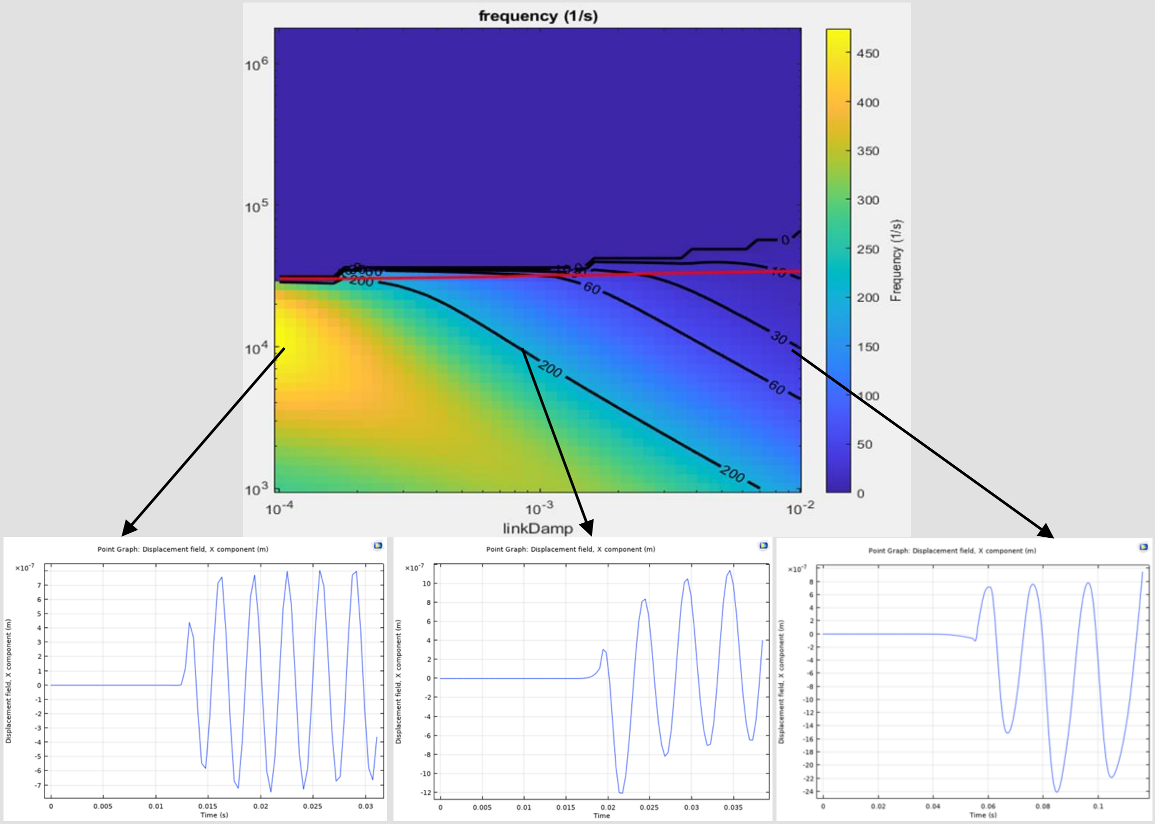



External loading FBD for active pairs (Hu et al. 2017)

# Comparison to the Theoretical Predictions

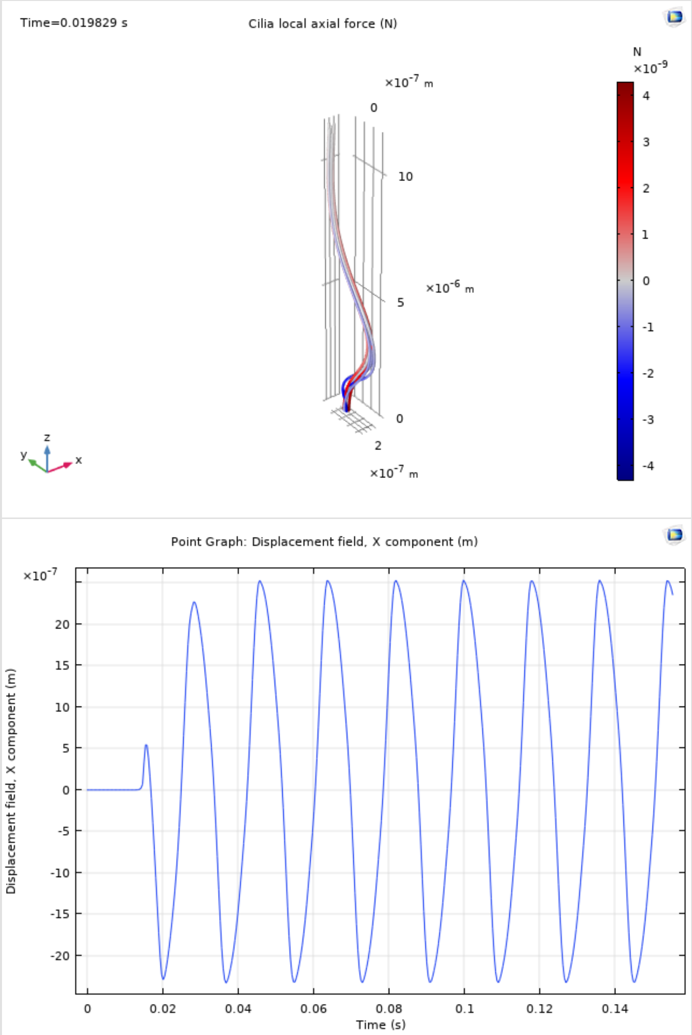
- Theoretical model: Small angle approximation; small deformations
- COMSOL model: Large deformations; more nonlinearities

| Physical Property | Non-dimensionalized Property |
|---|---|
| Time | $\tau = \frac{C_n L^4}{EI}$ |
| **Distributed Stiffness** | $\bar{k} = \frac{kL^4}{EI}$ |
| **Distributed Load** | $\bar{p} = \frac{pL^3}{EI}$ |
| **Viscoelastic Damping** | $\bar{c} = \frac{\tau k}{c_{visco}}$ |



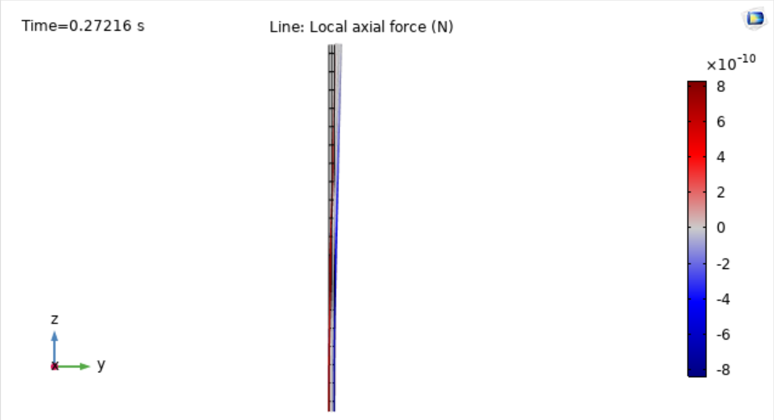
# Dynamic Instability: Flutter

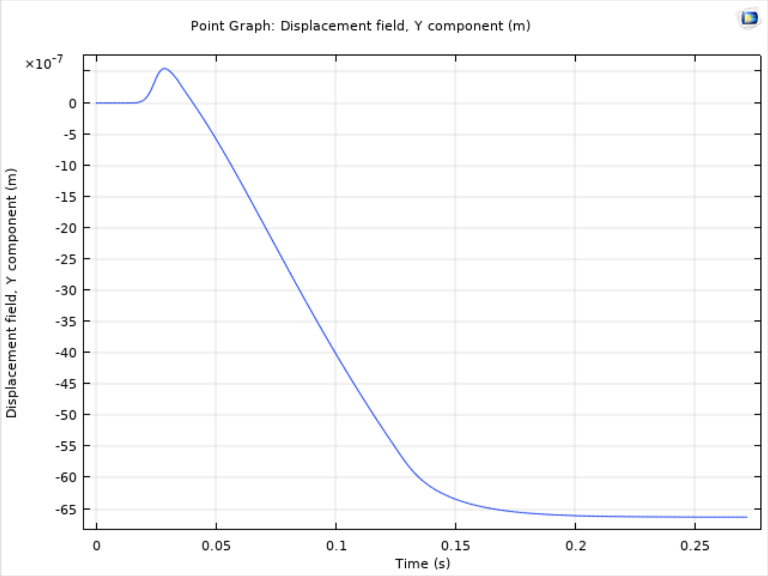
- System oscillates periodically
- Theoretical model: flutter is predicted by complex conjugate pairs of eigenvalues with positive real parts
- COMSOL model: flutter is illustrated by periodic tip displacement
- Constraining the motion to 2D increases susceptibility to flutter



# Dynamic Instability: Divergence

- System does not oscillate
- Theoretical model: divergence predicted when least stable mode has an eigenvalue with only postitive real parts
- COMSOL model: divergence is seen by a tip displacement plot without oscillation
- Allowing increased doublet separation to increase applied moment creates divergence



# Conclusion

- **COMSOL 3D beam physics with extrusion coupling** allows modeling of cilia mechanics, including dynamic instability
- Provides a comparison and extension of theoretical model
- Limitations:
  - Large deformation behavior can create convergence issues.
  - Linear extrusion coupling did not capture torsional stiffness.
- Future work:
  – Improve modeling of dynein (active components)
  – Improve modeling of passive components that provide torsional stiffness

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