Bifurcations and Nonlinear Dynamics of the Follower Force Model

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1. MOTIVATION

Cilia: elastic hairlike filaments, generating **fluid flows** at the **microscale**, e.g.:

- lining the **respiratory system** to move **mucus**,
- used by **cells** to **swim** through fluid.

Cilia in the trachea (https://www.thoughtco.com/cilia-and-flagella-373359)

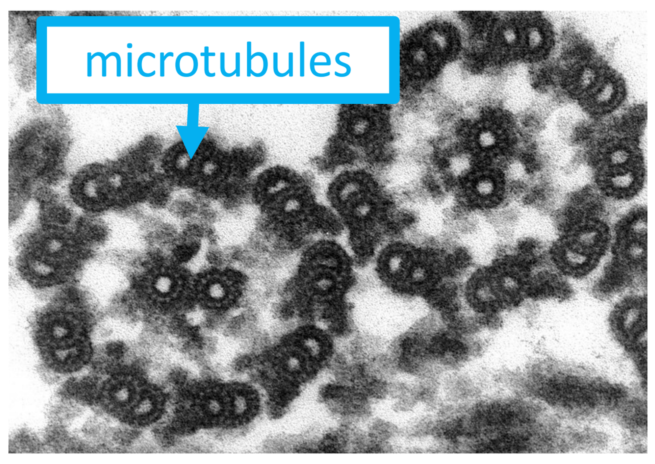
Boar sperm cells [Petkov, Alegre, Biehl, and Sánchez,2007]

Ciliopathies: diseases caused by **defective cilia**.

- Symptoms include **loss of sight**, **hearing loss** and **infertility**.
- Ciliopathies can also lead to issues with vital organs, such as the **liver, heart** and **lungs.**
- Over **1 in 1000** people are estimated to be affected by ciliopathies [1].

Modelling cilia is **vital** to understanding how cilia become **defective**, and how this can lead to **ciliopathies.**

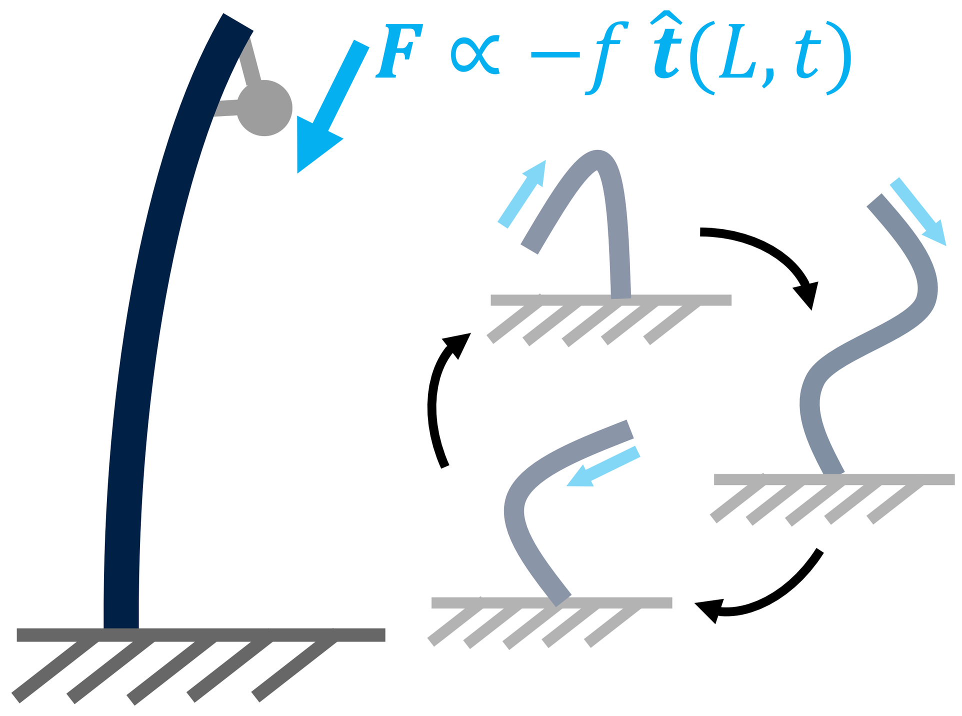
- We don't fully understand how to model cilia, but a surprisingly **simple model** is **motivated** by their internal **structure**:
  - Several slender filaments (called microtubules).
  - Driven by molecular motors (called dynein).



A cross-section of two cilia (https://www.dartmouth.edu/emlab/)

2. FOLLOWER FORCE MODEL

- **Related model** for **cilia**: single **force** at filament **tip** (molecular motor), directed against **tangent**:

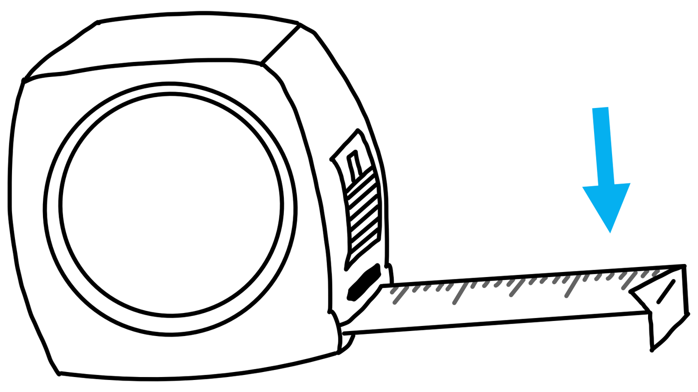


- Filament model [2] accounts for: filament **elasticity, follower force, surrounding fluid.**
- Generates **simulations**, telling us the **stable behaviours**. We want to **find** and **analyse** these states.

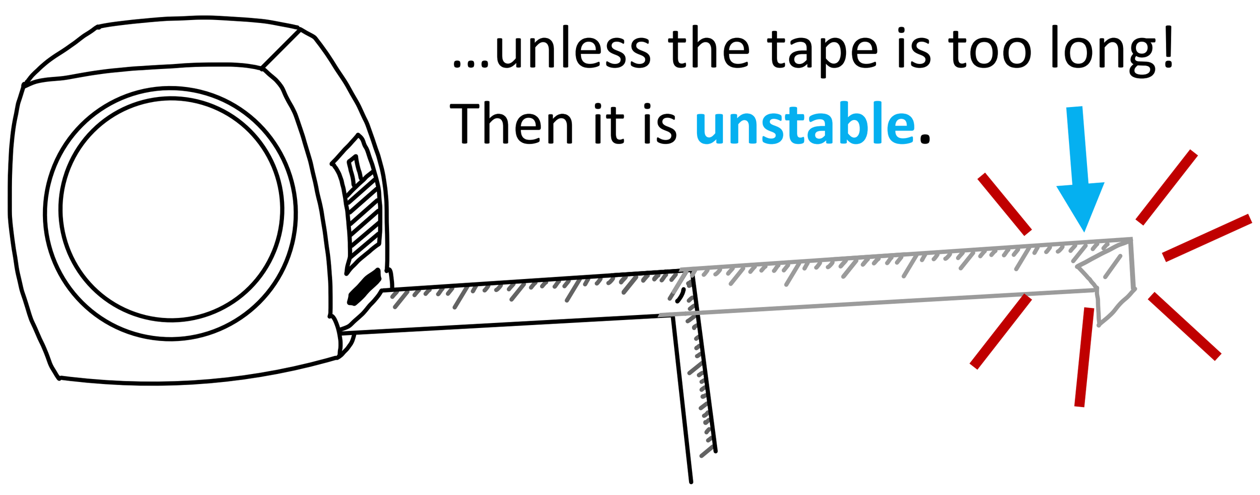
3. WHAT DO WE MEAN BY "STABLE"?

IDEA: "If I give it a kick (*i.e. a small perturbation*), does it come back?"

E.g. a straight tape measure is **stable…**

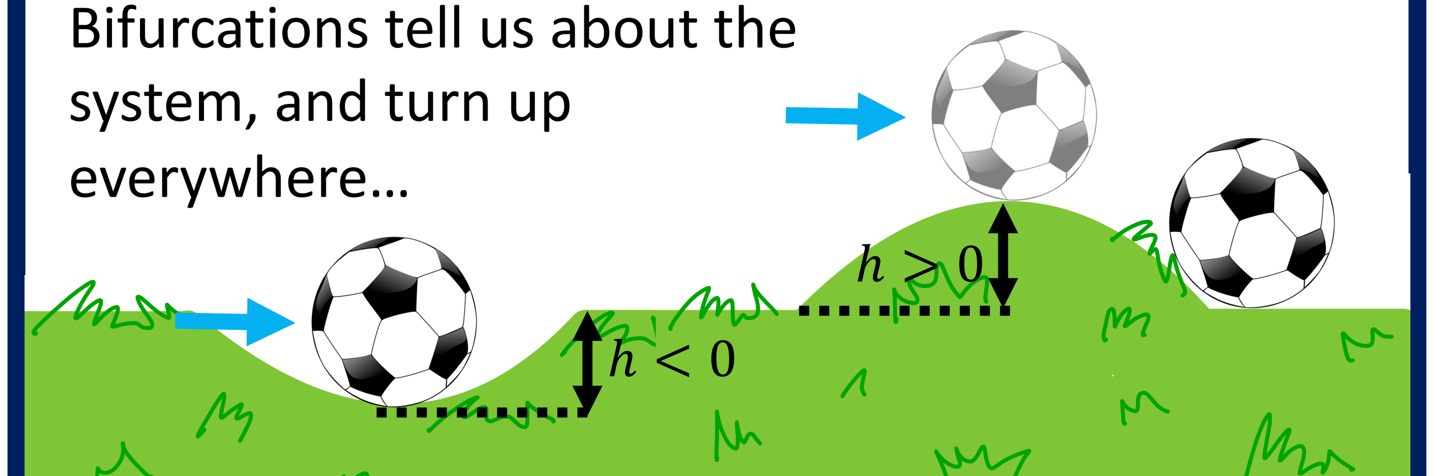


…unless the tape is too long! Then it is **unstable.**



When changing a parameter, e.g. tape measure length**,** we see there is a **change in stability** of the system. This is what we call a **bifurcation.**

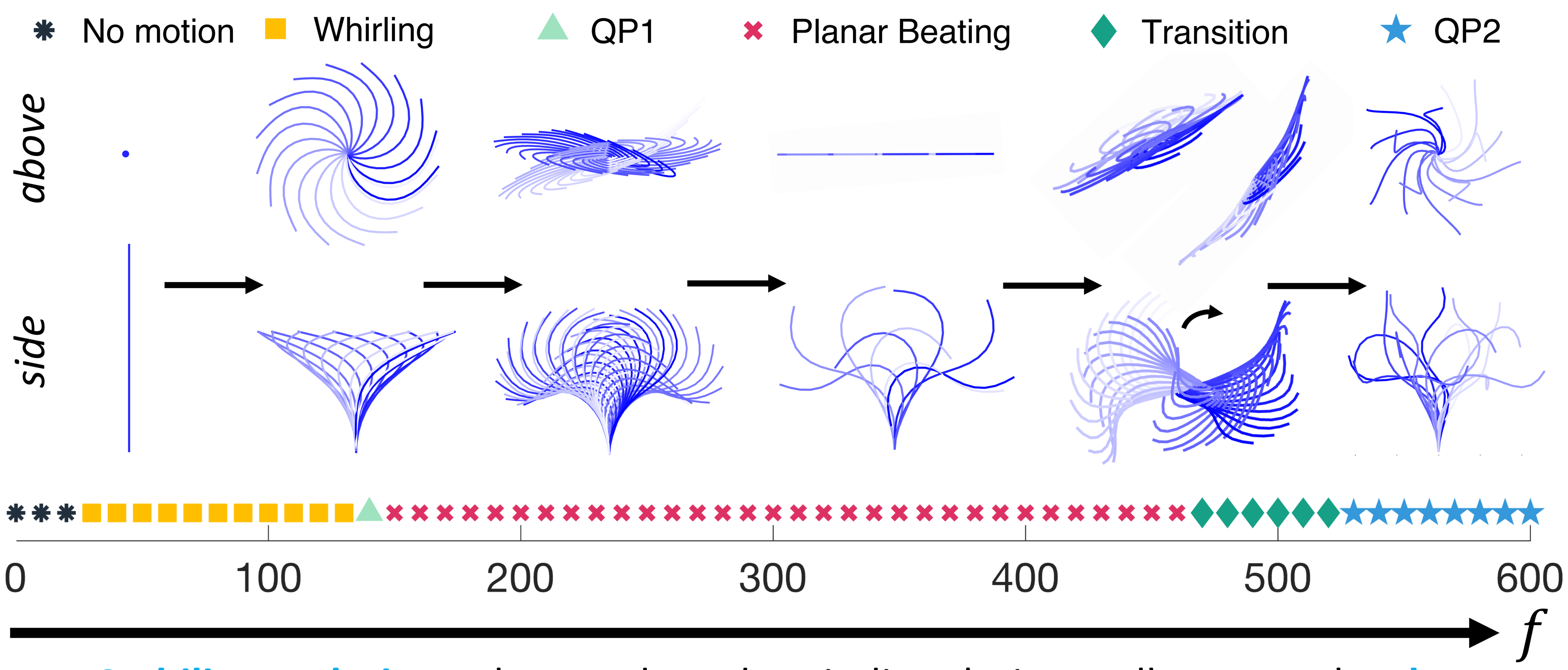
Bifurcations tell us about the system, and turn up everywhere…



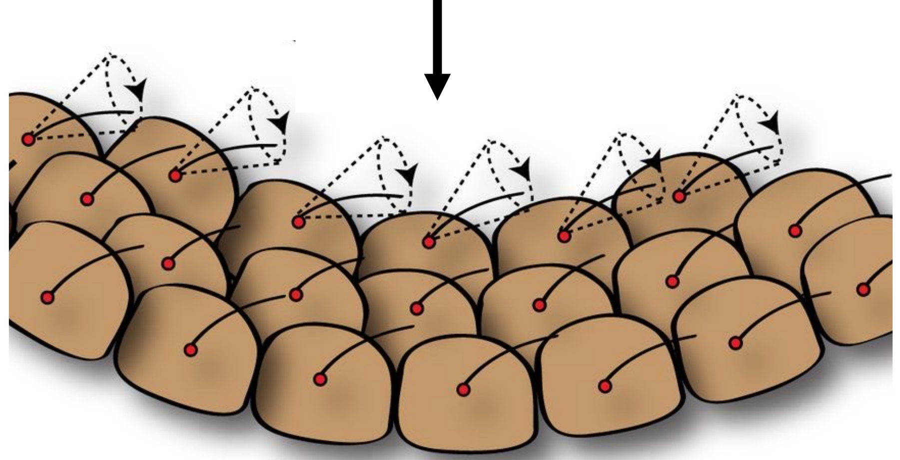
…bifurcations even occur at the microscale!

4. BIFURCATION ANALYSIS

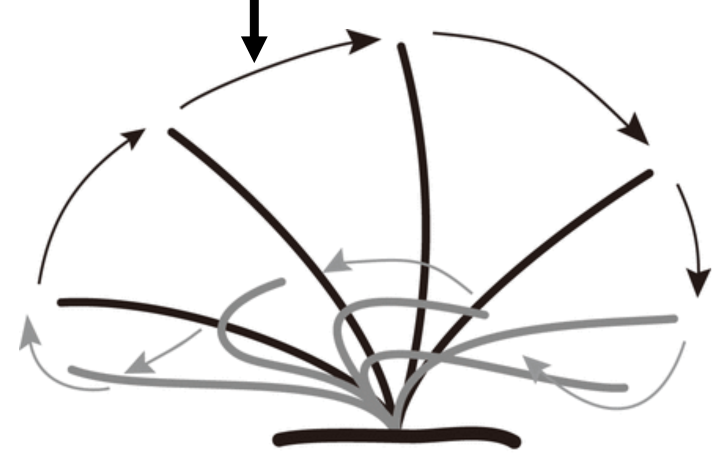
- Using our filament model, we find **different solutions**, whose stability **depends on f** (i.e. the amount of force we apply):



- **Stability analysis** on the steady and periodic solutions tells us exactly **where** (i.e. exactly for *which* f), and **how** (i.e. by what *kind* of bifurcation), these **transitions** happen.
- Some of these behaviours are **similar** to those observed for **real cilia**: e.g. $\underbrace{\text{whirling by nodal cilia in embryos,}}$ or $\underbrace{\text{beating by cilia in our airways}}$.



[D. Babu and S. Roy, Open Biology, 2013]



[J. Raidt et al, European Respiratory Journal 2014]

- Both dynamics found at a **value of f** realistically **achievable** by a **single molecular motor** (which motivated our model).

CONCLUSION: Our **simple model** replicates dynamics of cilia observed in nature, a key step towards **understanding defective cilia**, and in turn, towards **modelling ciliopathies**.

REFERENCES

Preprint: *B Clarke, Y Hwang and E E Keaveny, 2024 (sub judice)*

[1] http://www.alstrom.org.uk/ciliopathy/

[2] S. F. Schoeller, A. K. Townsend, T. A Westwood and E. E. Keaveny, 'Methods for suspensions of passive and active filaments', Journal of Comp. Physics, 2021

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