

A NOVEL COMPUTATIONAL MODEL OF THE AXONEME FOR MICROSWIMMERS IN STOKES FLOW

Peter M N Hull

MATHS FOR SPERM CELLS

A New Approach to Modelling Microswimmers in Stokes Flow

Peter M N Hull

Overview

Overview

1. What is the problem?

Overview

1. What is the problem?
2. What is my solution?

Overview

1. What is the problem?
2. What is my solution?
3. How can I test it?

Overview

1. What is the problem?
2. What is my solution?
3. How can I test it?
4. Did it work?

Overview

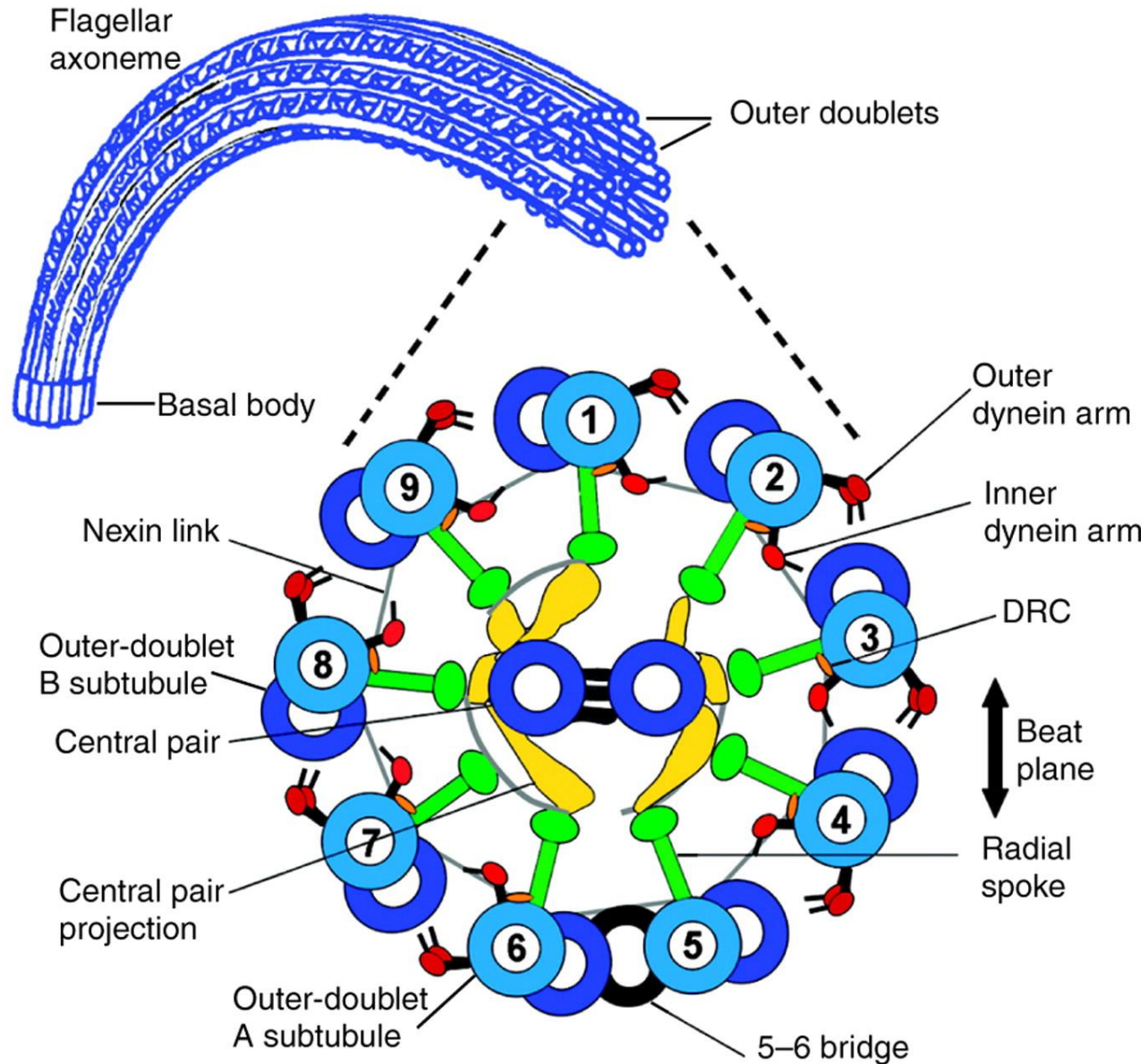
1. What is the problem?
2. What is my solution?
3. How can I test it?
4. Did it work?
5. What's next?

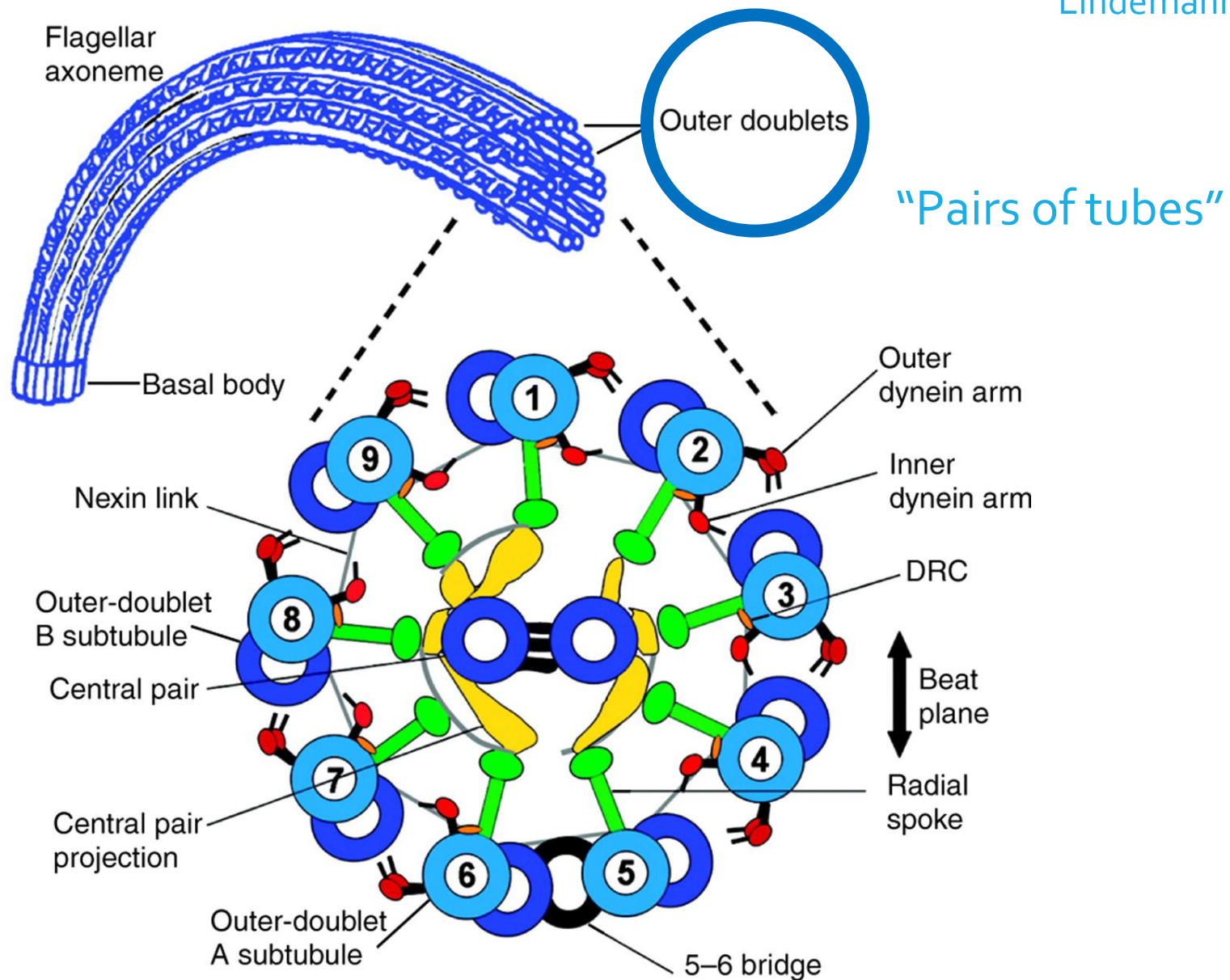
WHAT IS THE PROBLEM?

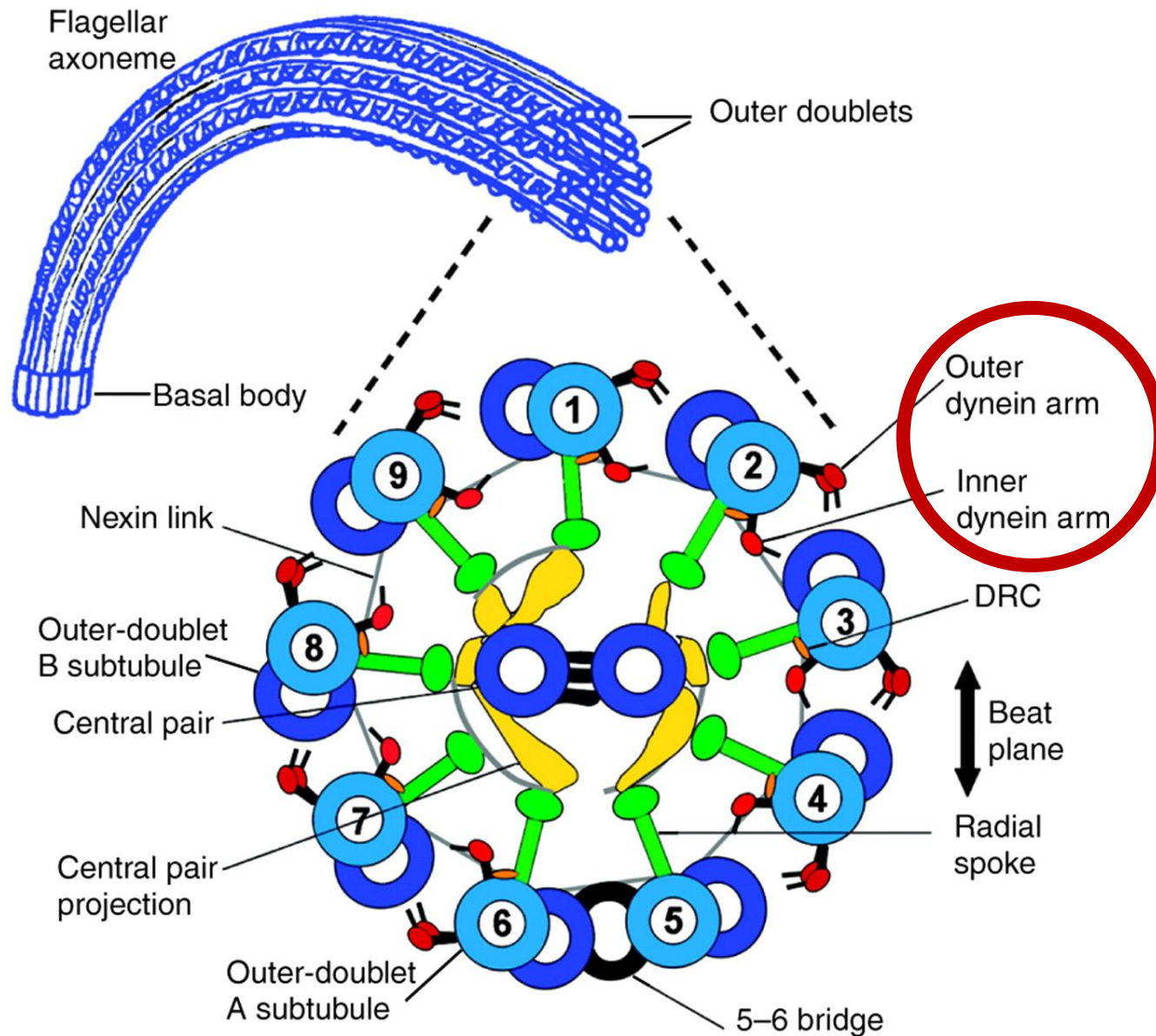
PART I

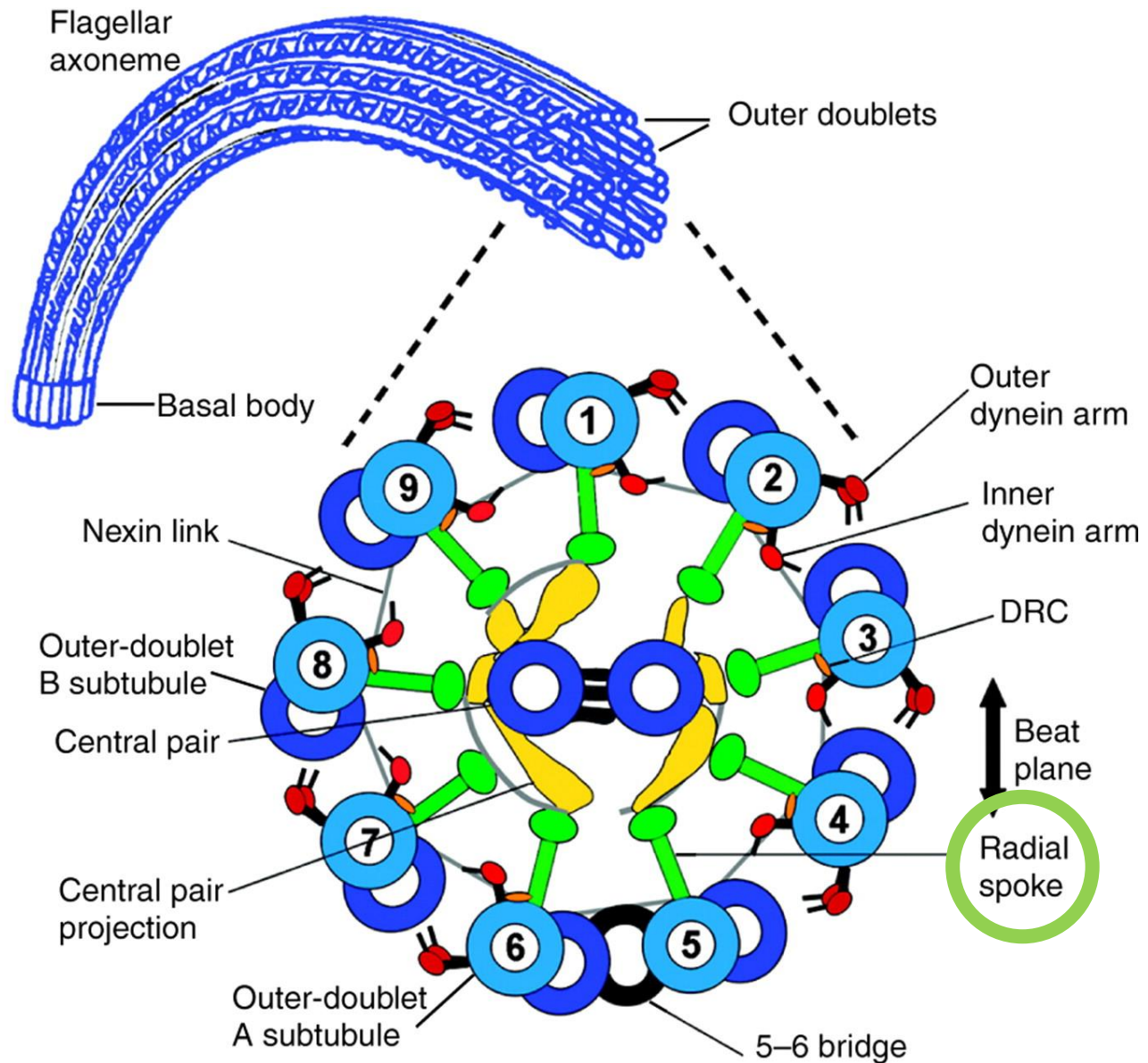
Problem: Sperm cells are hard to understand

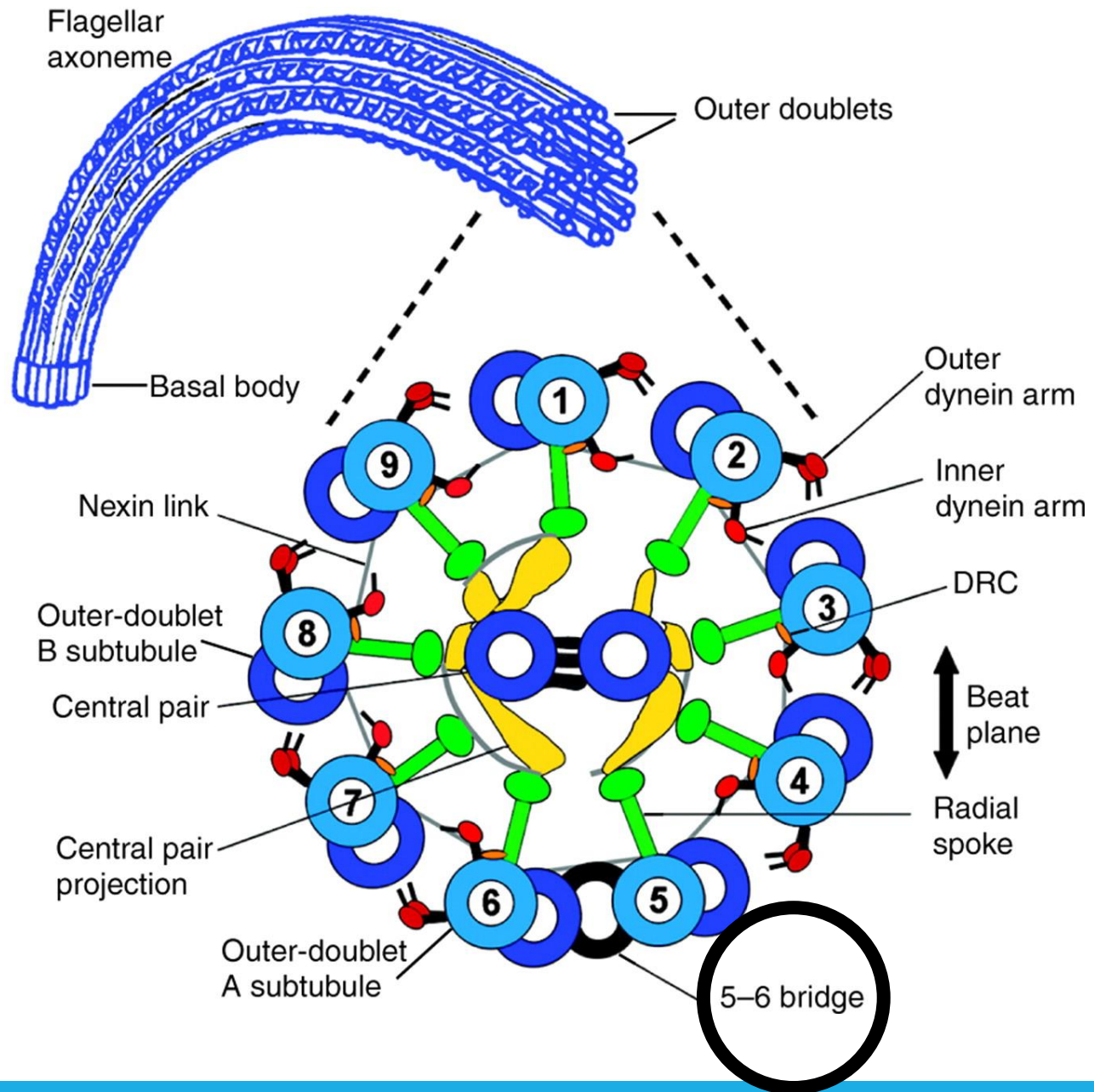


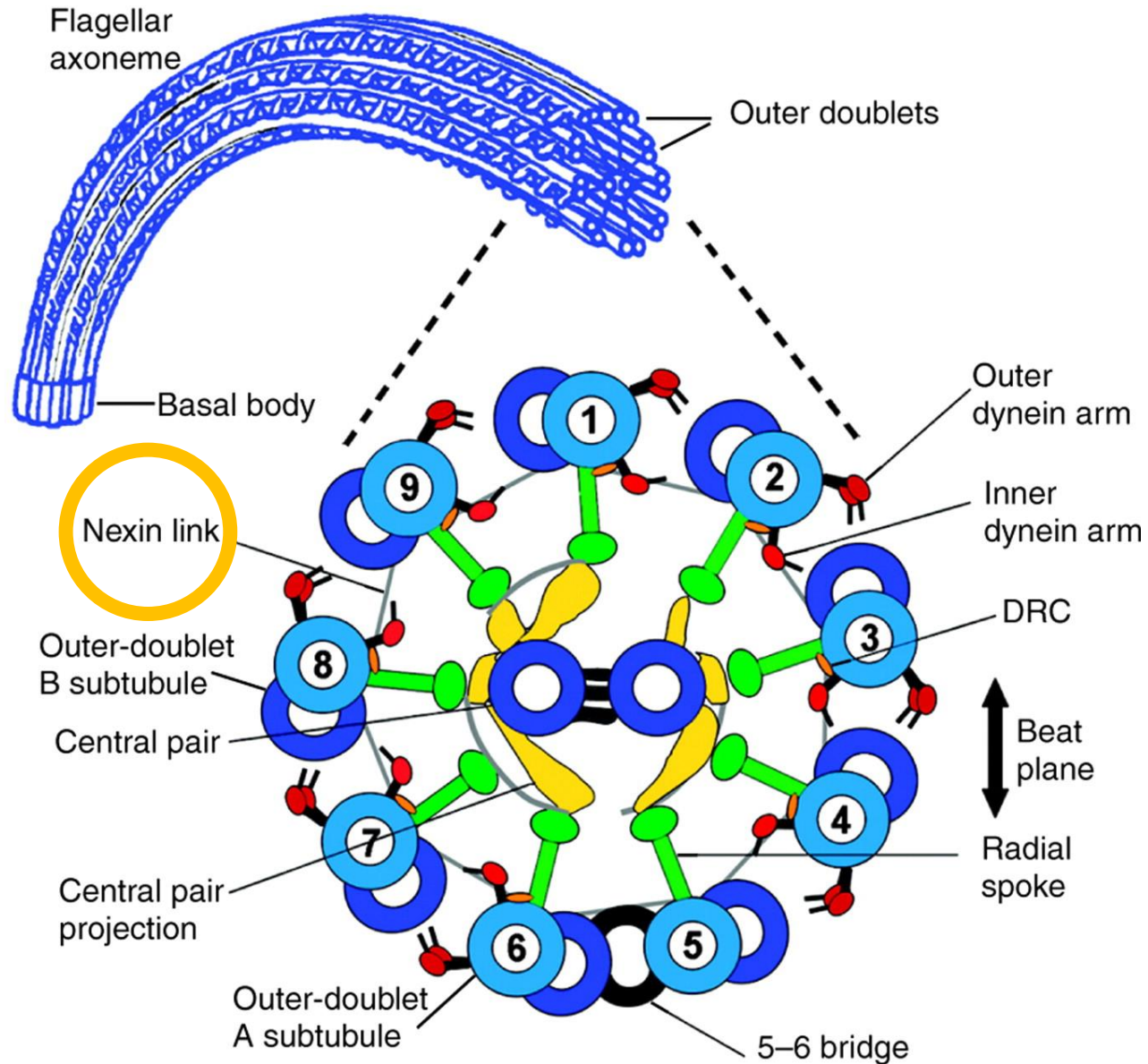


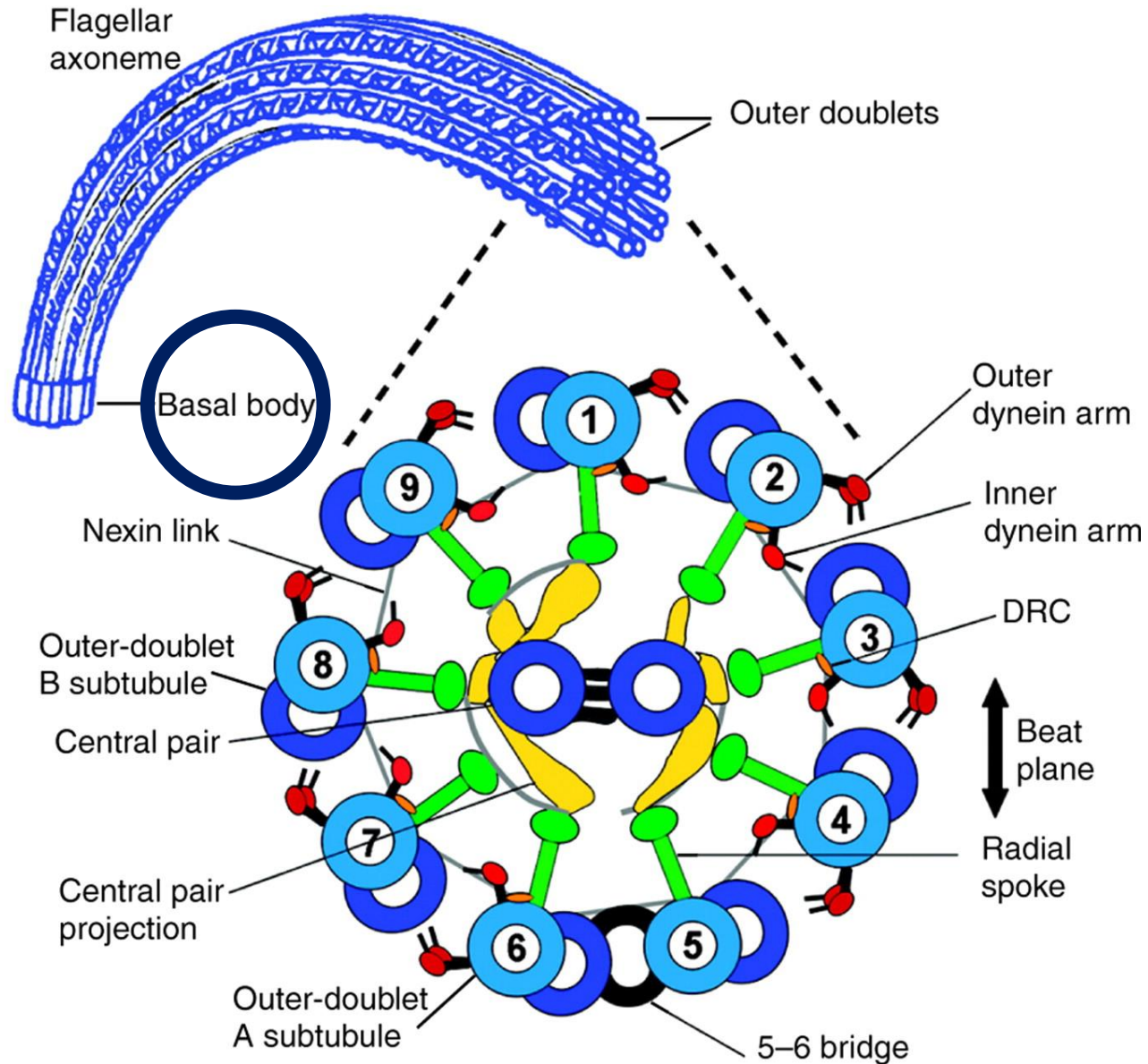












Why should we care?



Why should we care?

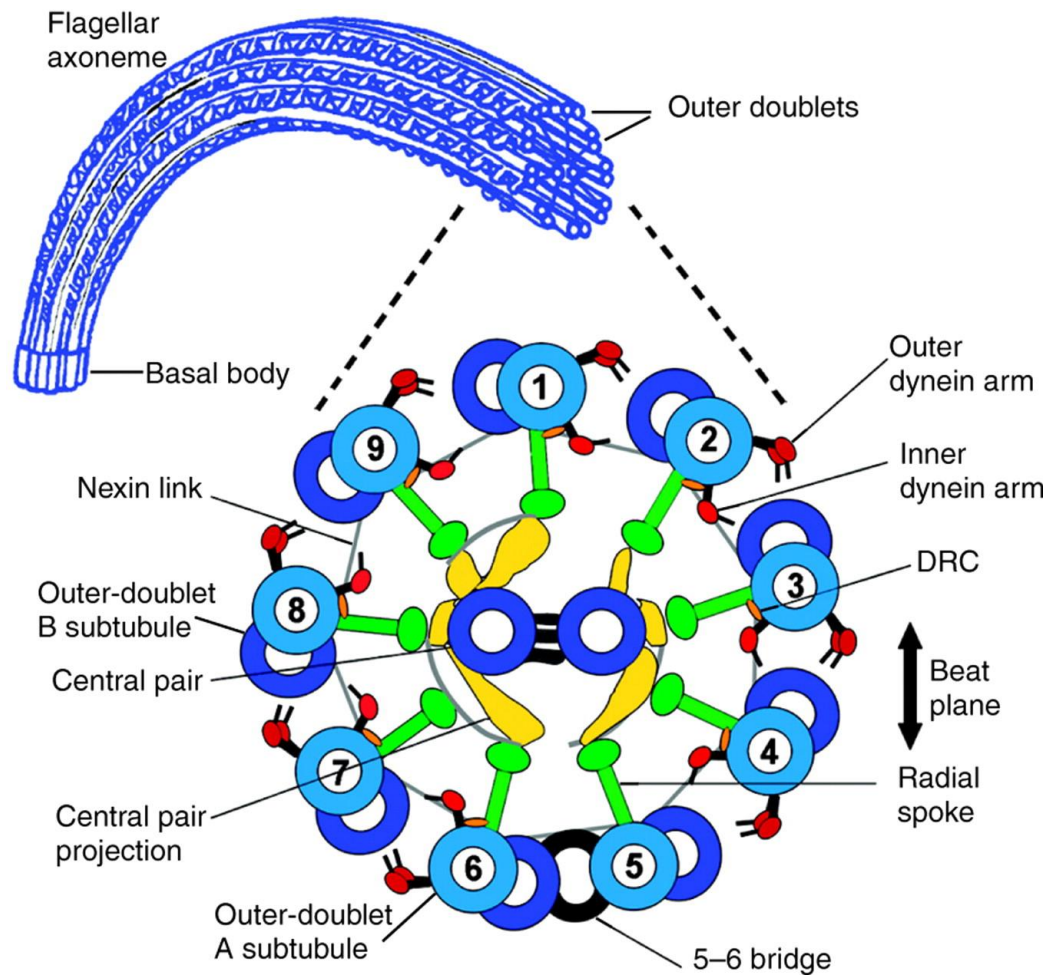


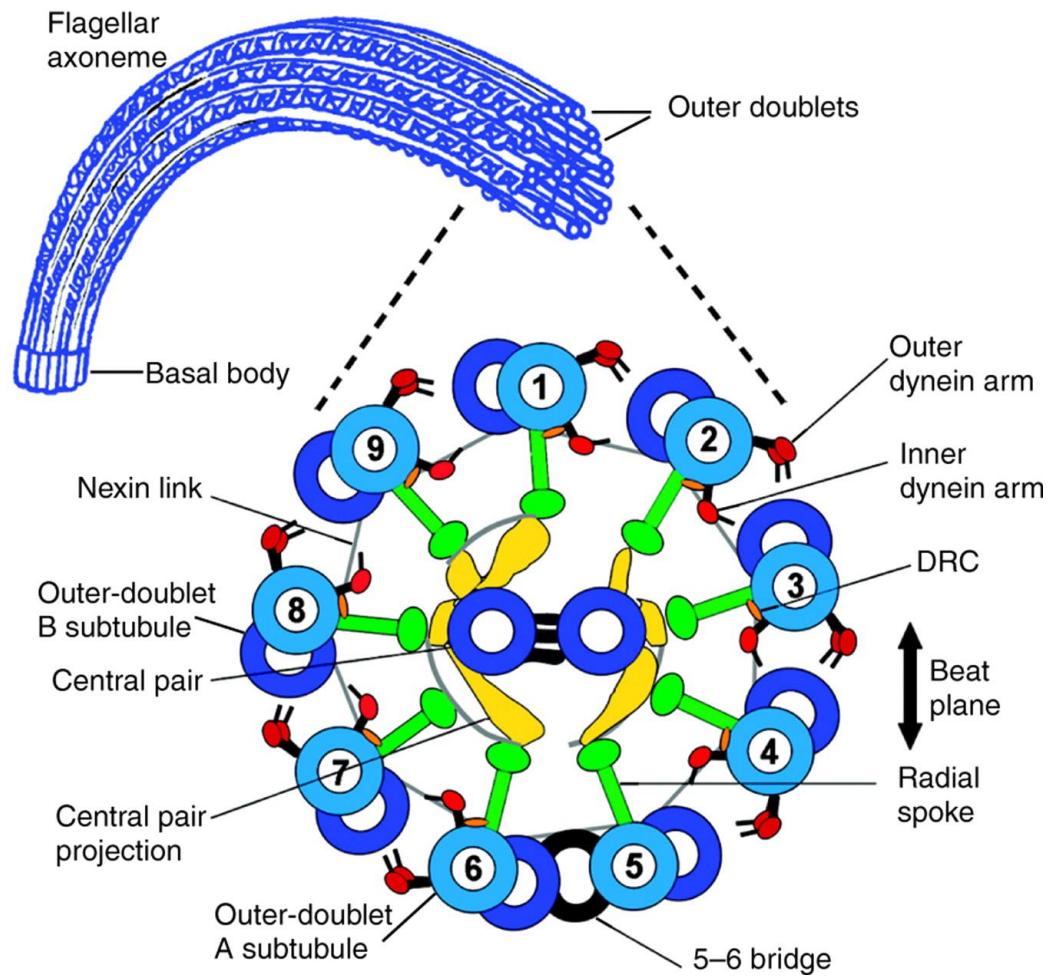
Because sperm are important!

WHAT IS MY SOLUTION?

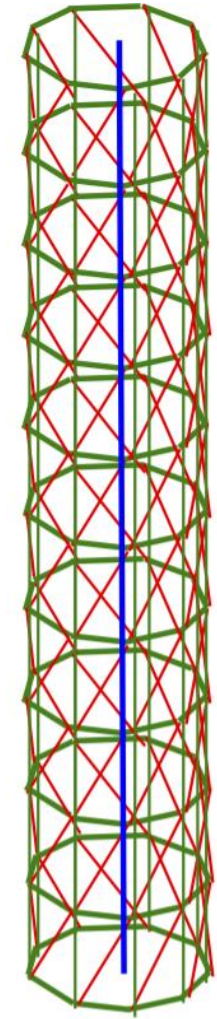
PART II

ANSWER: SIMPLIFY





Han & Peskin (2018)



CAN IT BE SIMPLER?

Can it be simpler?

First Assumption:

Can it be simpler?

First Assumption:

Using a pair of two-dimensional rods is good enough.

Hilfinger, Jülicher & Chattopadhyay (2009)

Can it be simpler?

Second Assumption:

Can it be simpler?

Second Assumption:

Can use internal clocks.

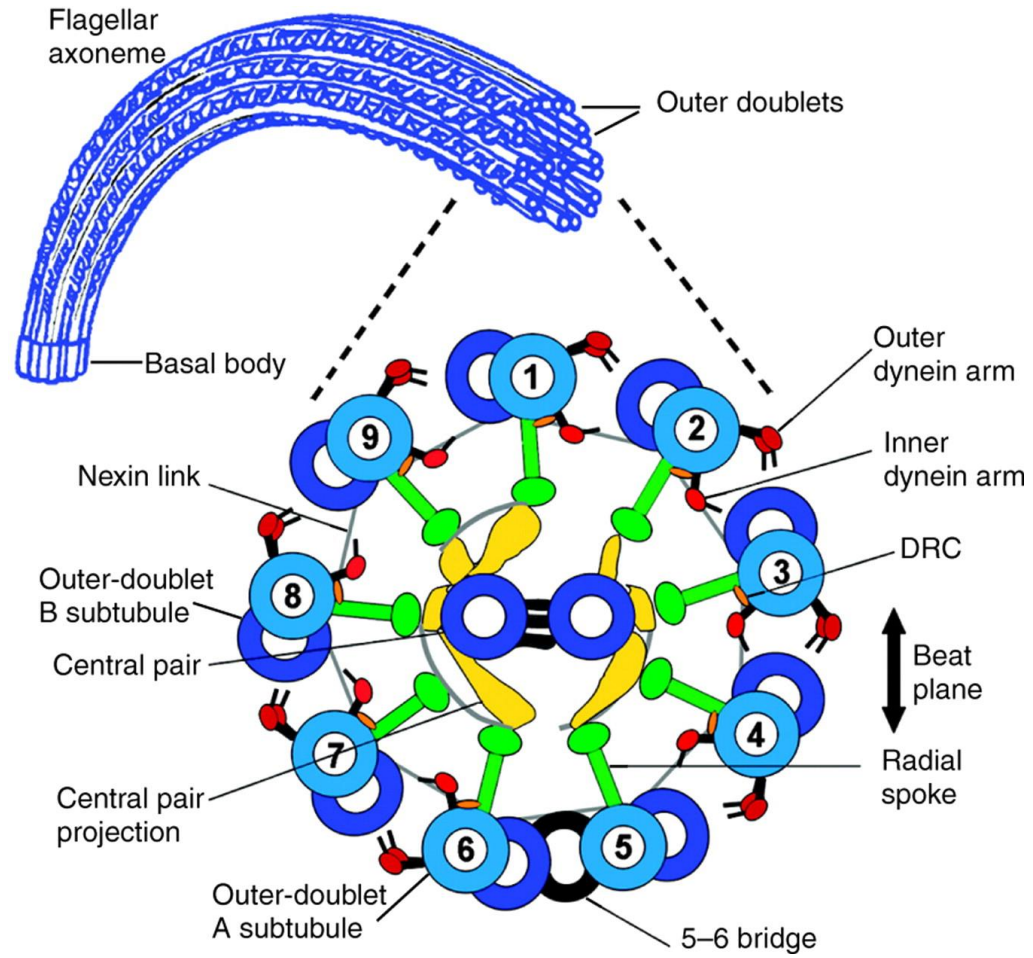
Can it be simpler?

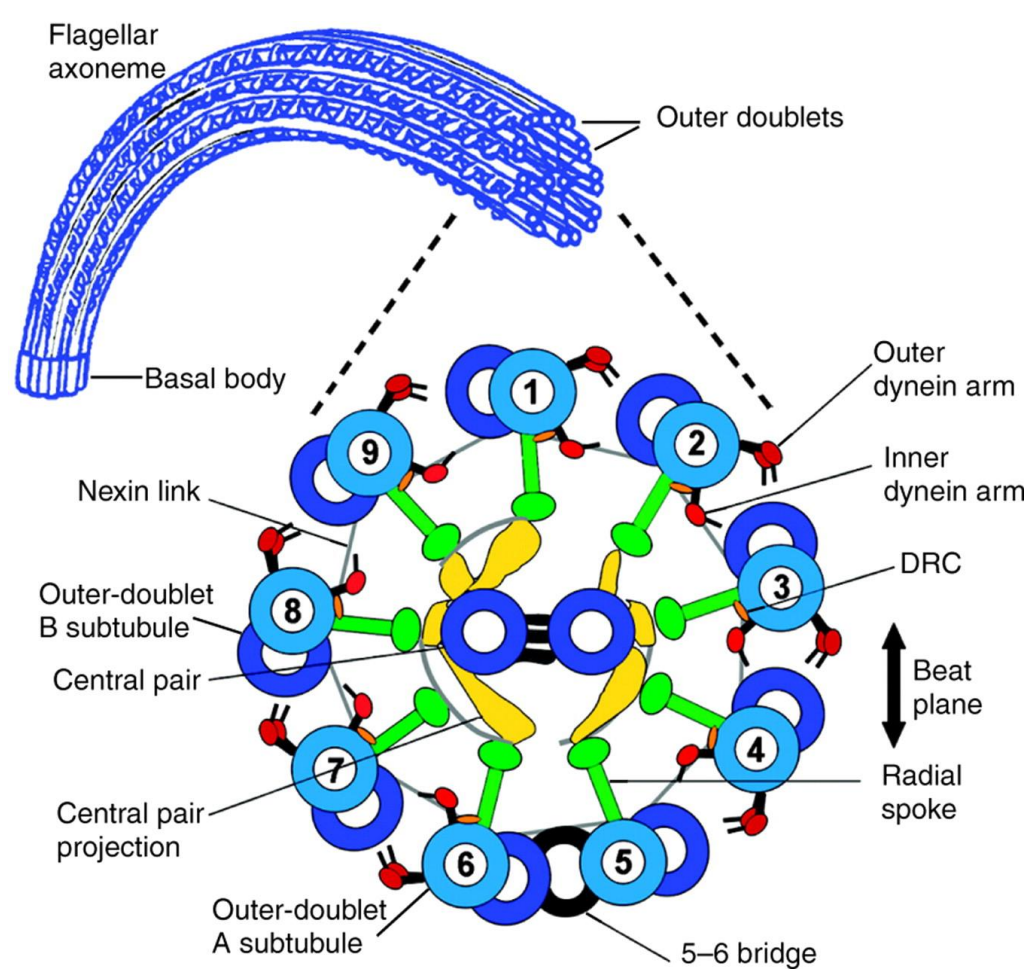
Second Assumption:

Can use internal clocks.

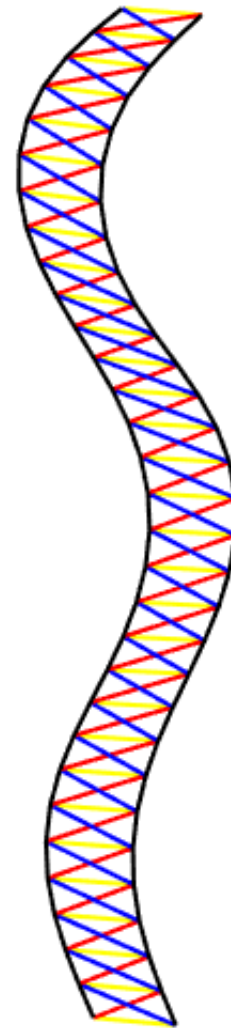
(Spoke-Axis Hypothesis)

Lindemann & Lesich (2010)





Peter Hull (2020)



AXONEME MODEL

Use Springs to Represent Axoneme Driving Forces

Two Components

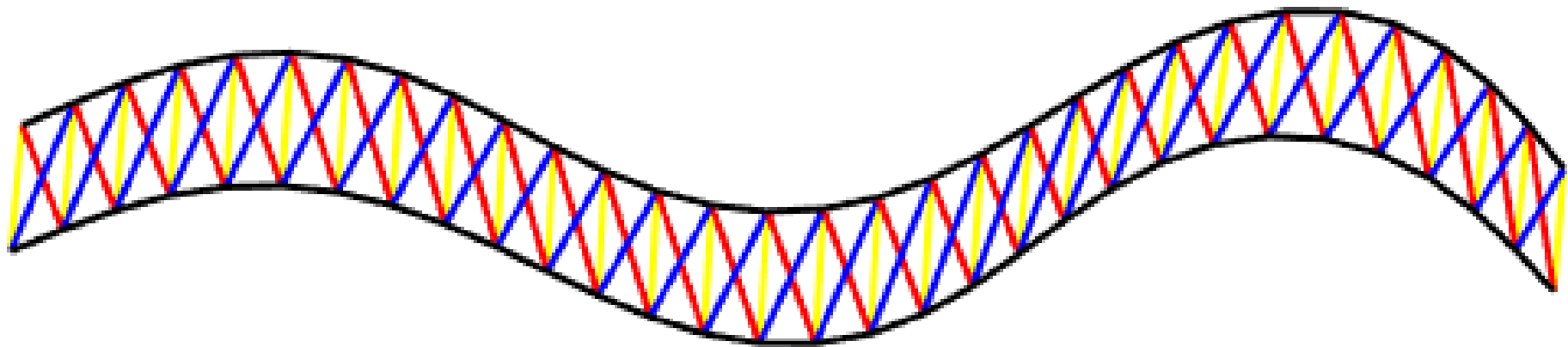
Two Components

1. Maintain body structure

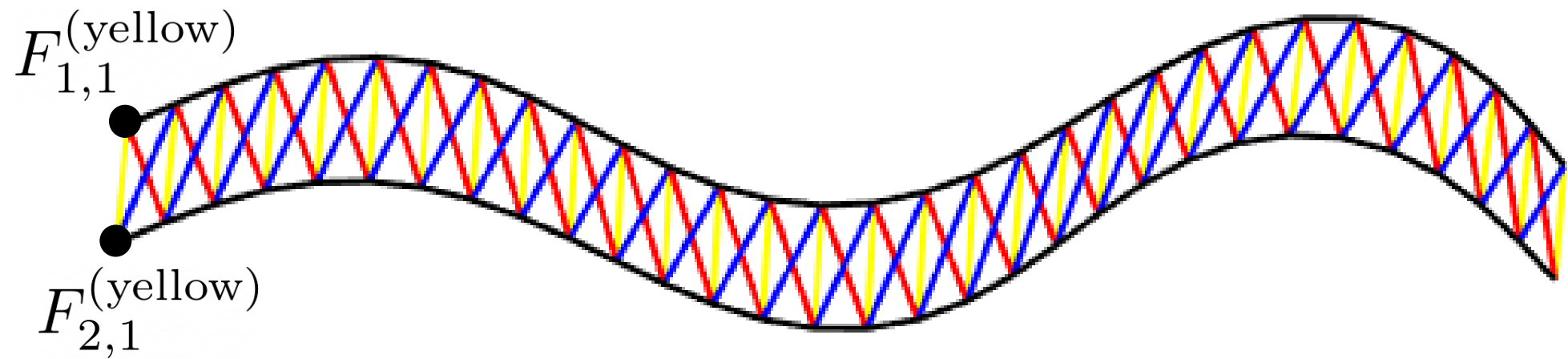
Two Components

1. Maintain body structure
2. Generate motion with active links

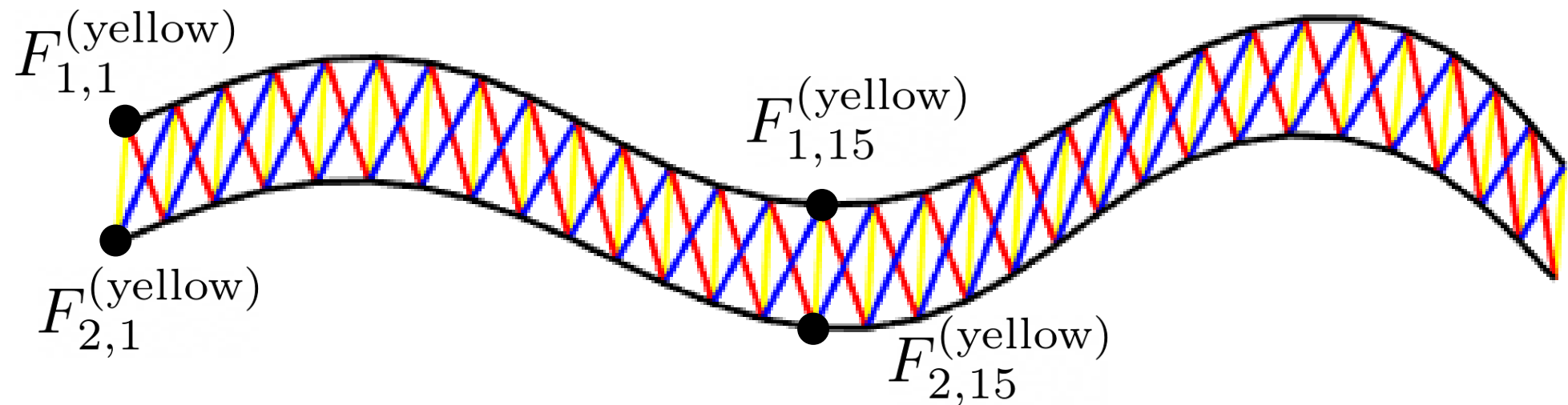
Maintaining Body Structure



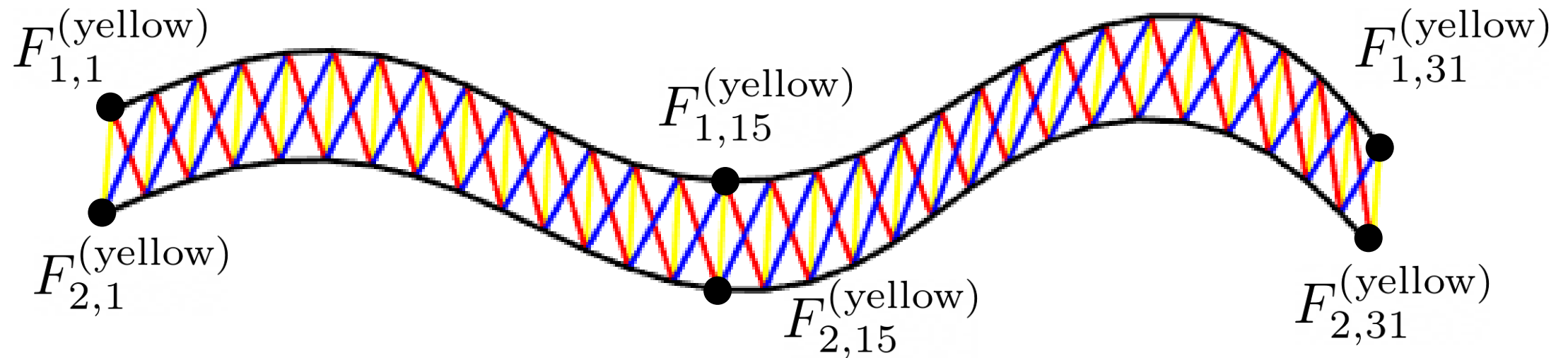
Maintaining Body Structure



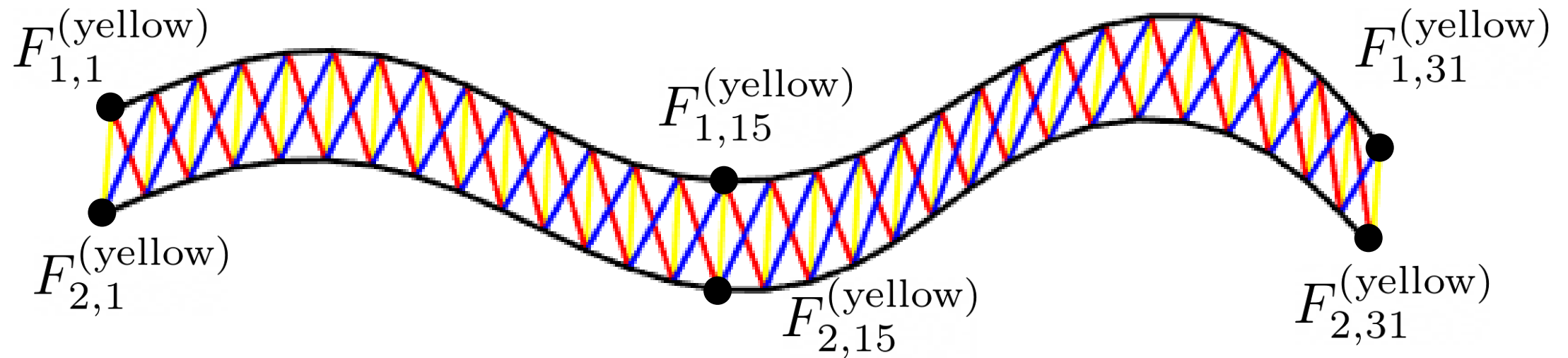
Maintaining Body Structure



Maintaining Body Structure

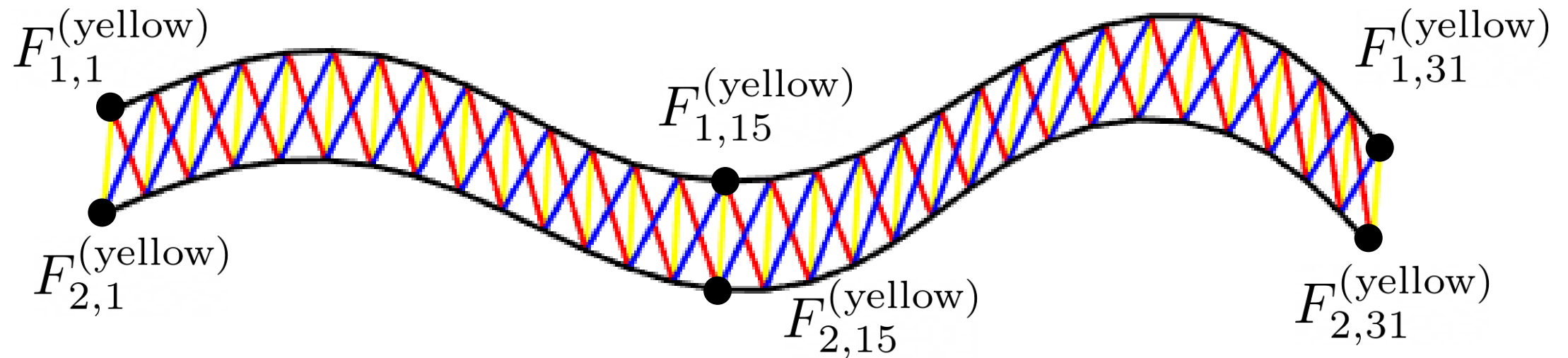


Maintaining Body Structure



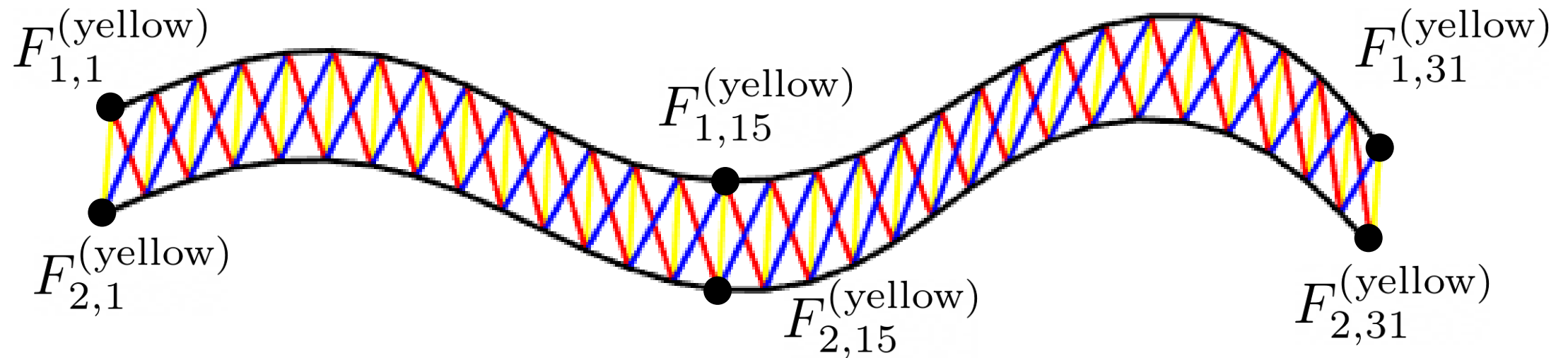
Maintaining Body Structure

$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})}$$



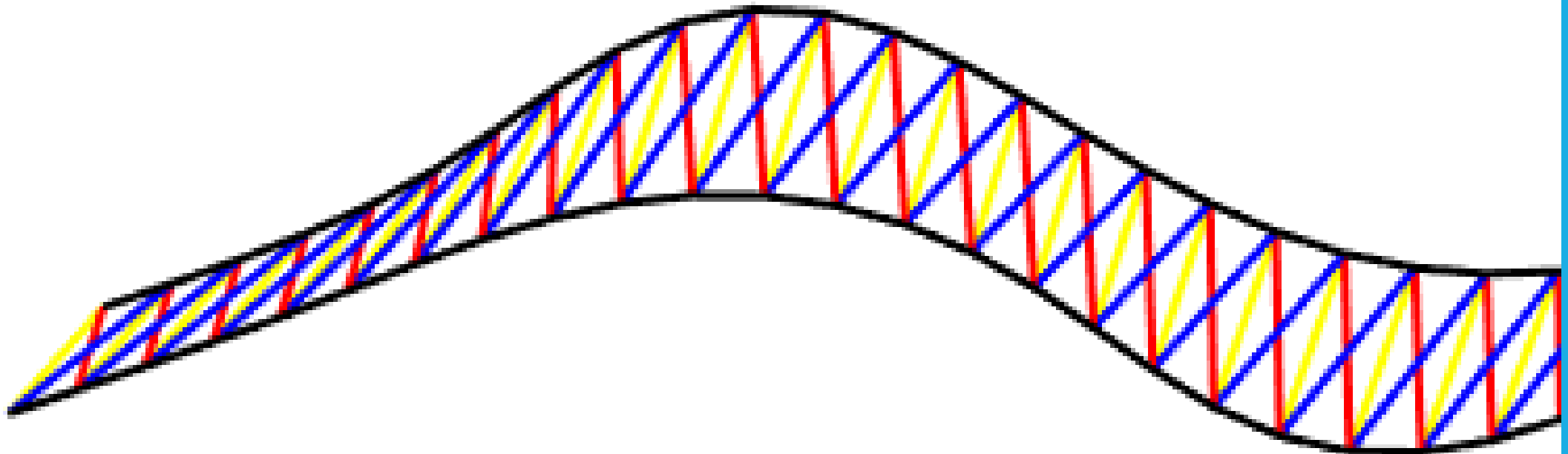
Maintaining Body Structure

$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$



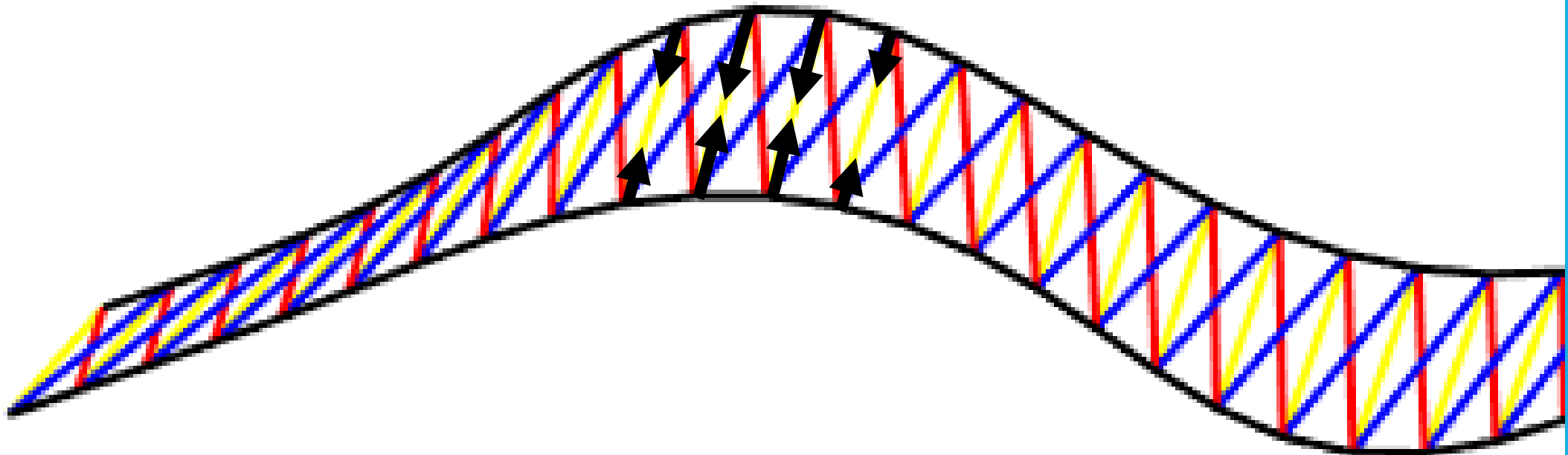
Maintaining Body Structure

$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$



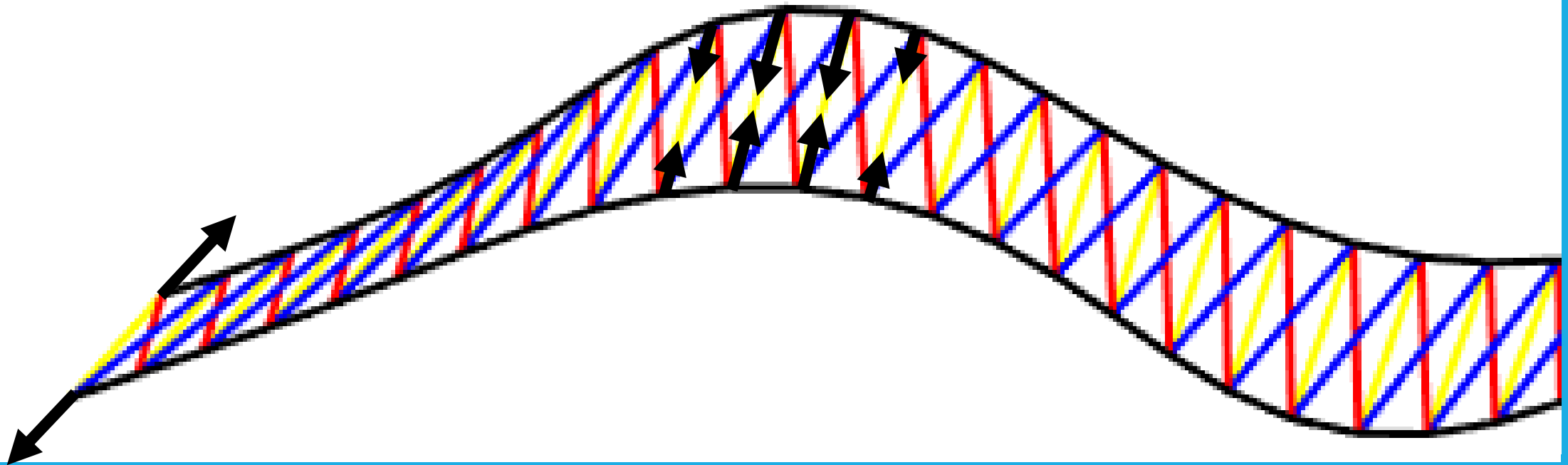
Maintaining Body Structure

$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$

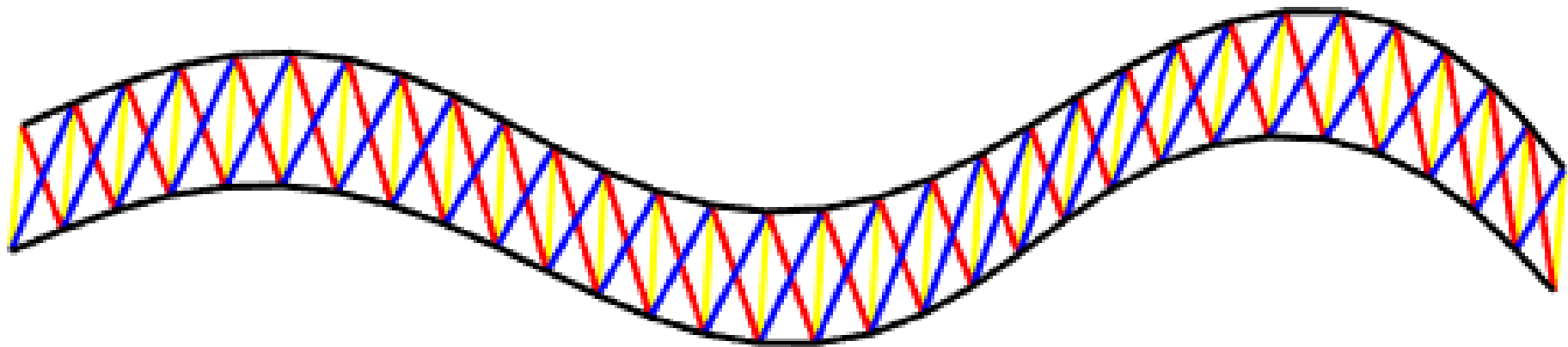


Maintaining Body Structure

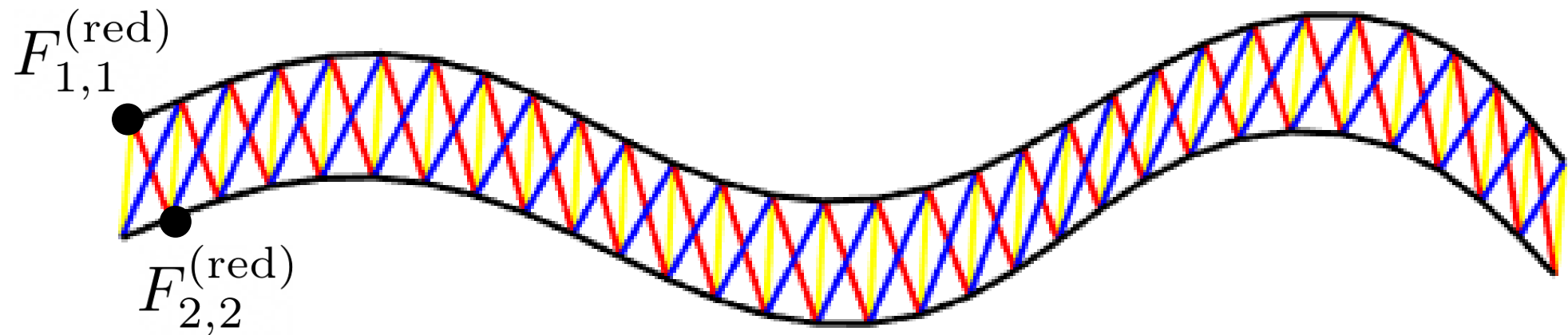
$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$



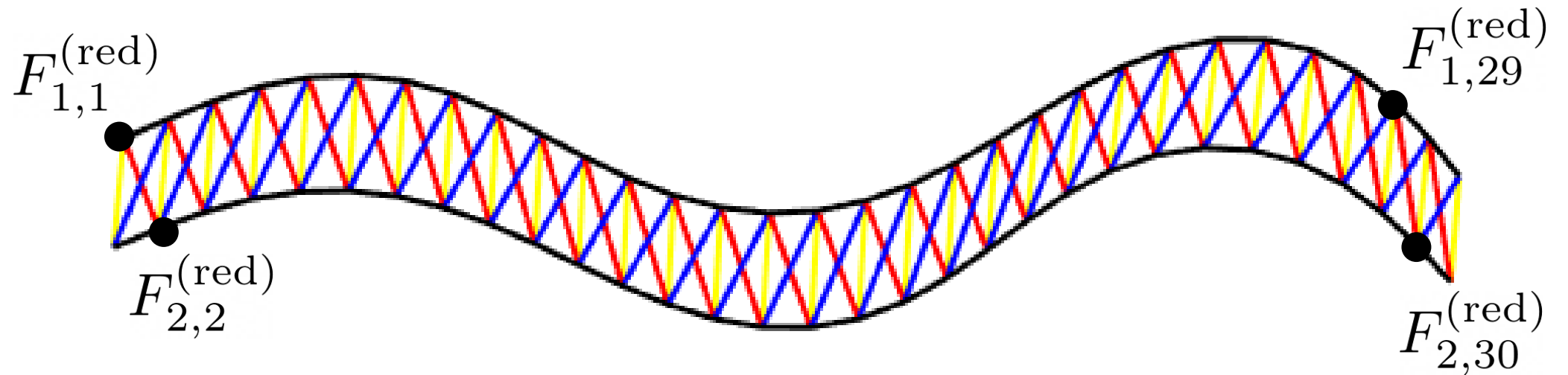
Modelling Active Dynein Motor Proteins



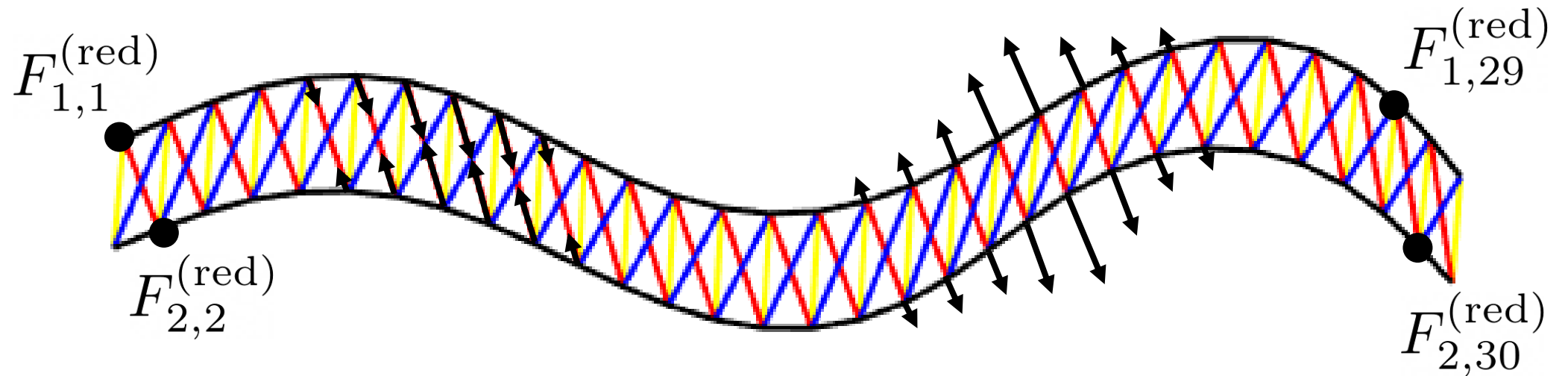
Modelling Active Dynein Motor Proteins



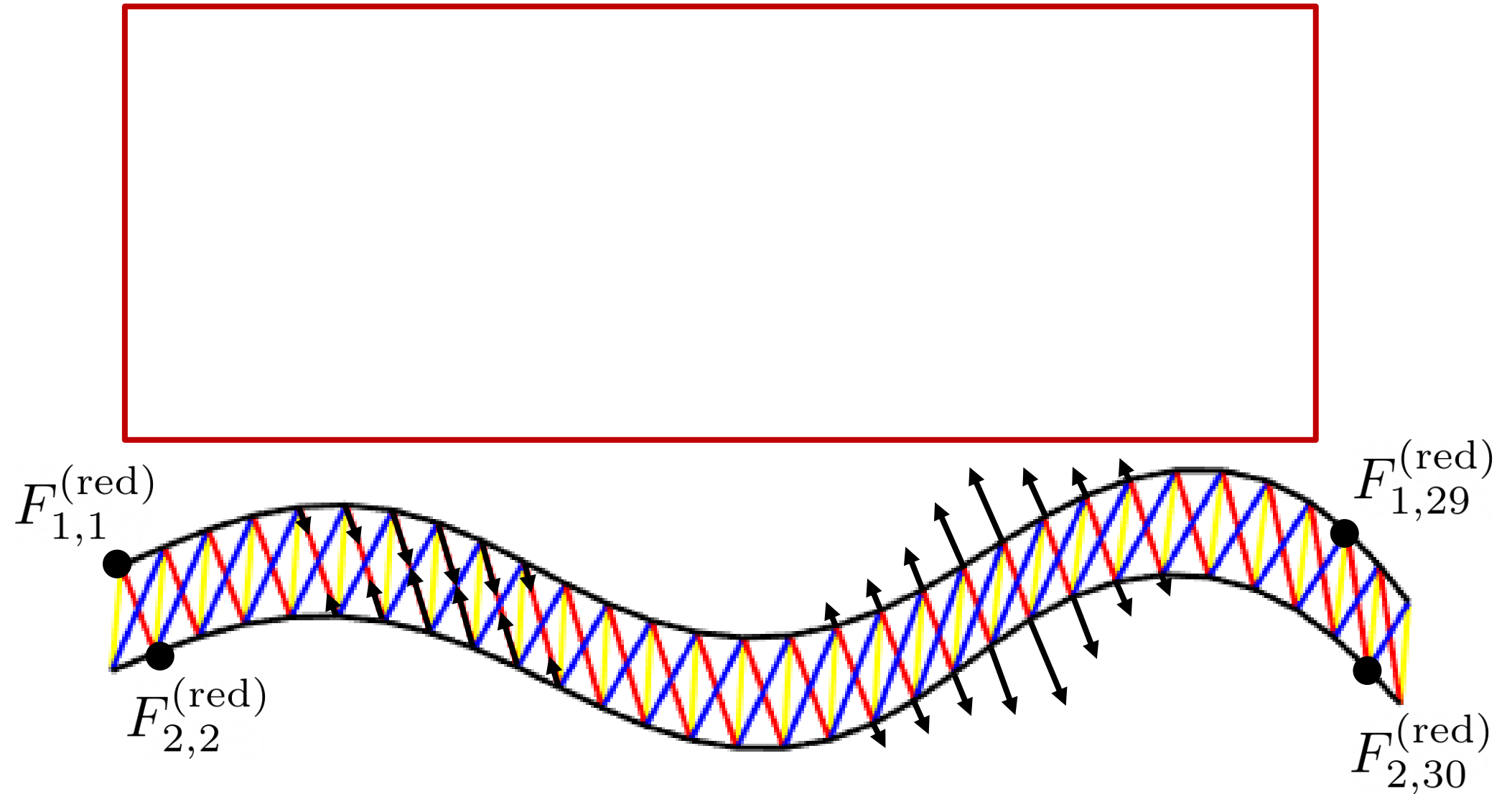
Modelling Active Dynein Motor Proteins



Modelling Active Dynein Motor Proteins

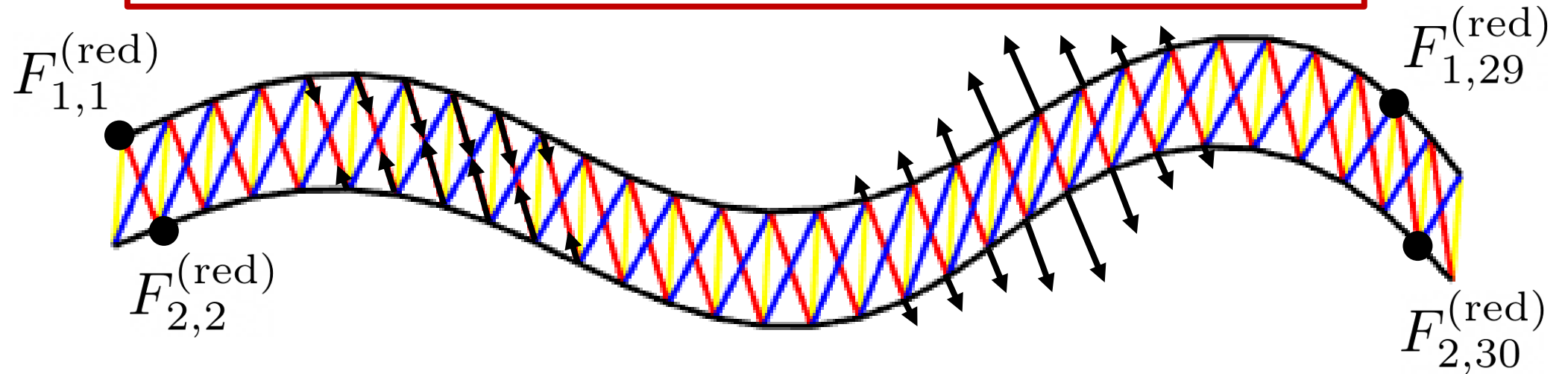


Modelling Active Dynein Motor Proteins



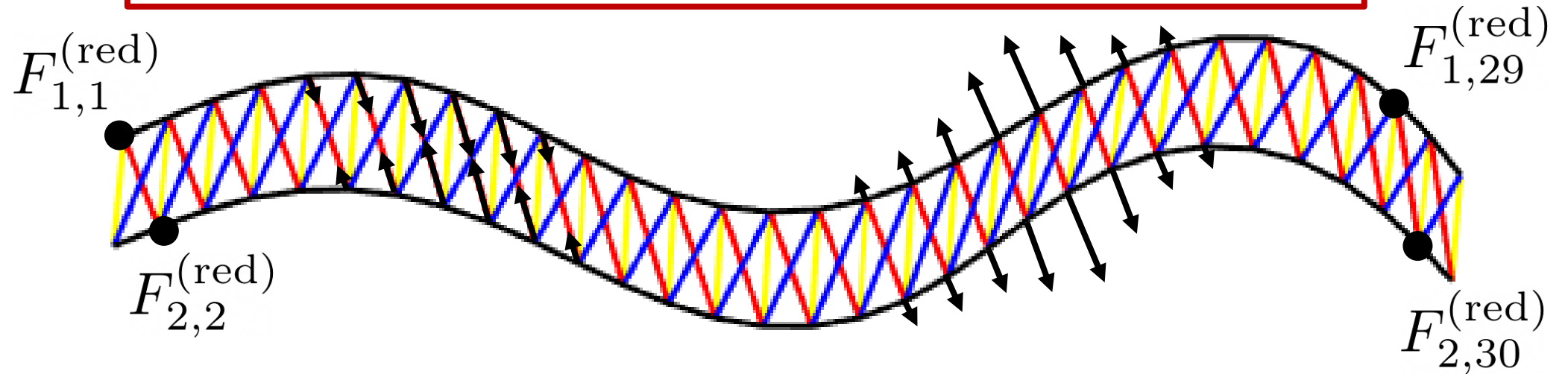
Modelling Active Dynein Motor Proteins

$$F_{1,n}^{(\text{red})} = -F_{2,n+1}^{(\text{red})}$$



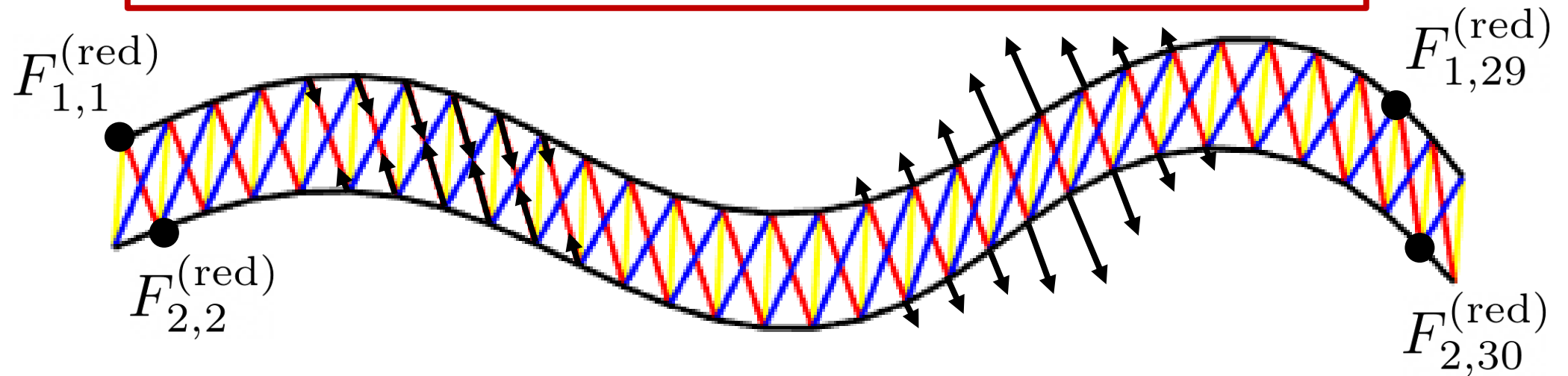
Modelling Active Dynein Motor Proteins

$$F_{1,n}^{(\text{red})} = -F_{2,n+1}^{(\text{red})} \quad := \quad r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t)$$



Modelling Active Dynein Motor Proteins

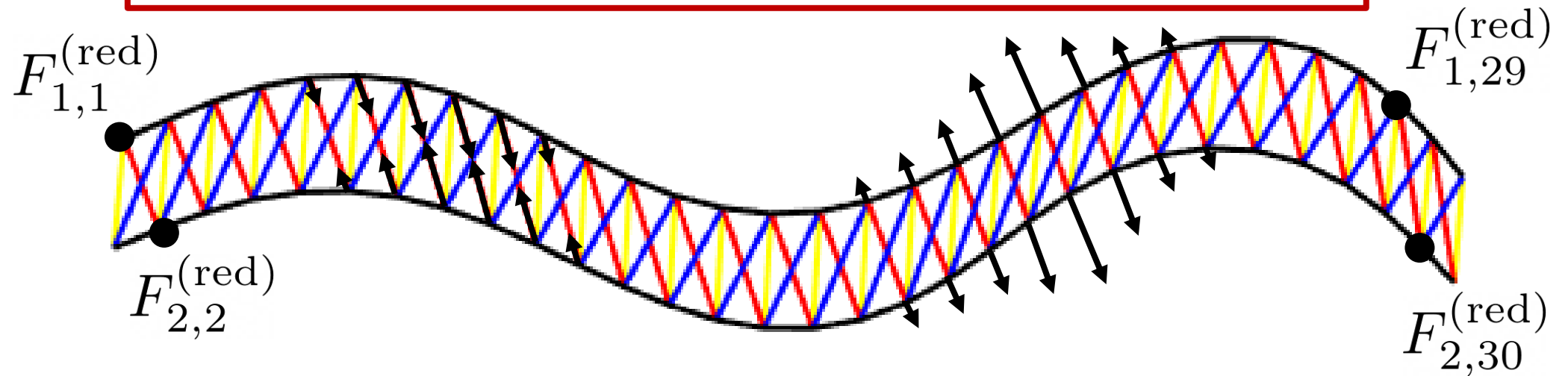
$$F_{1,n}^{(\text{red})} = -F_{2,n+1}^{(\text{red})} \quad := \quad \boxed{r_{n,n+1}^{(\text{red})}(t)} - l_{n,n+1}(t)$$



Modelling Active Dynein Motor Proteins

$$F_{1,n}^{(\text{red})} = -F_{2,n+1}^{(\text{red})} \quad := \quad r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t)$$

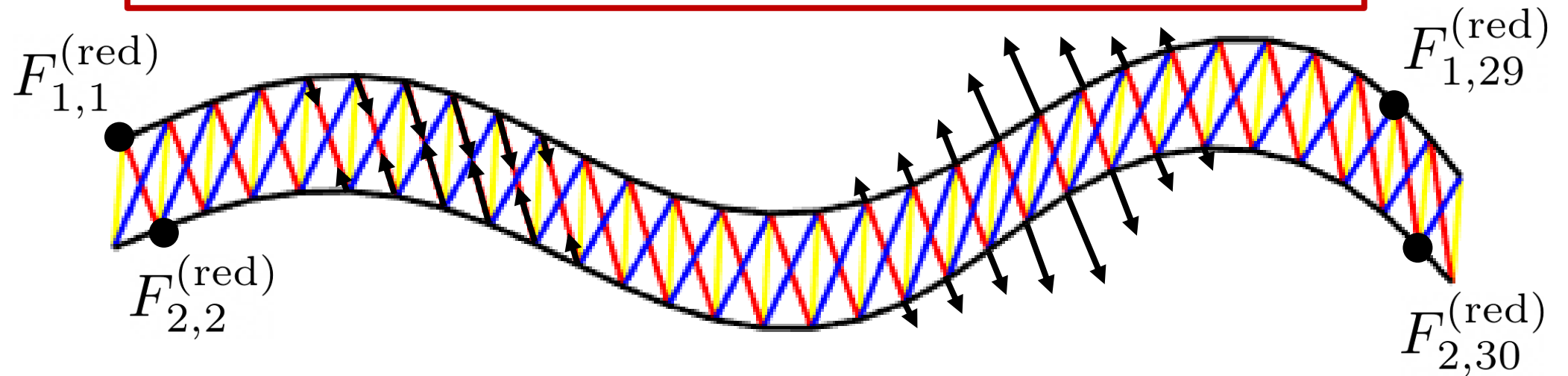
$$\boxed{r_{n,n+1}^{(\text{red})}(t)} = C + f_n^{(\text{red})}(t)$$



Modelling Active Dynein Motor Proteins

$$F_{1,n}^{(\text{red})} = -F_{2,n+1}^{(\text{red})} \quad := \quad r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t)$$

$$r_{n,n+1}^{(\text{red})}(t) = C + \boxed{f_n^{(\text{red})}(t)}$$

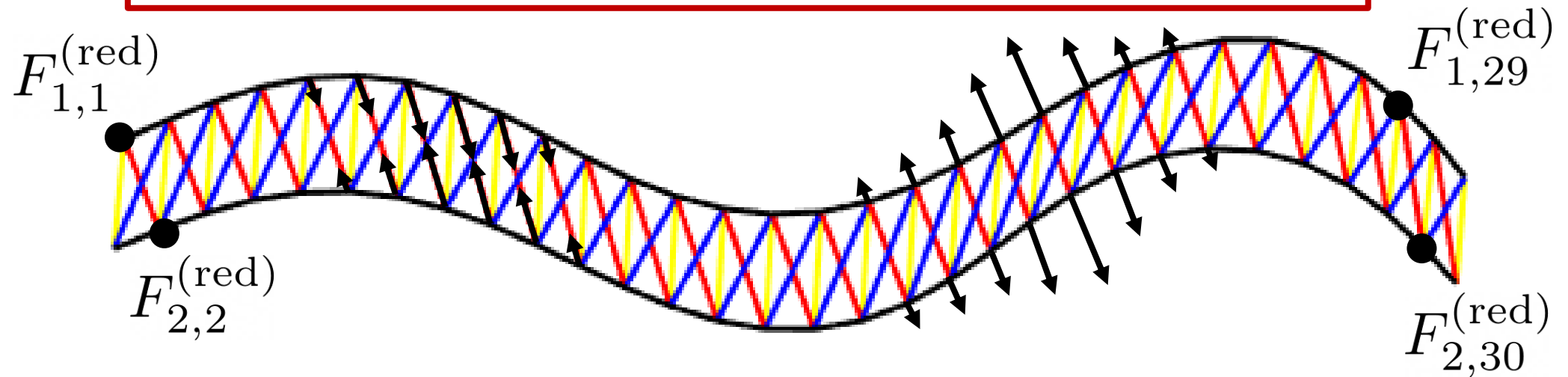


Modelling Active Dynein Motor Proteins

$$F_{1,n}^{(\text{red})} = -F_{2,n+1}^{(\text{red})} \quad := \quad r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t)$$

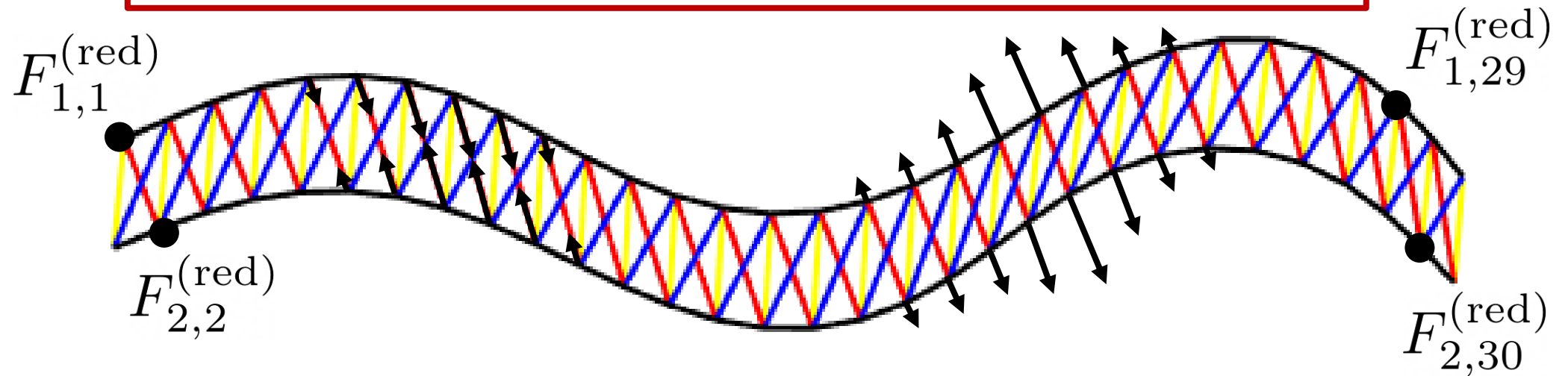
$$r_{n,n+1}^{(\text{red})}(t) = C + f_n^{(\text{red})}(t)$$

$$f_n^{(\text{red})}(t) = \lambda \sin \left(\omega t + \frac{kn}{N} \right)$$



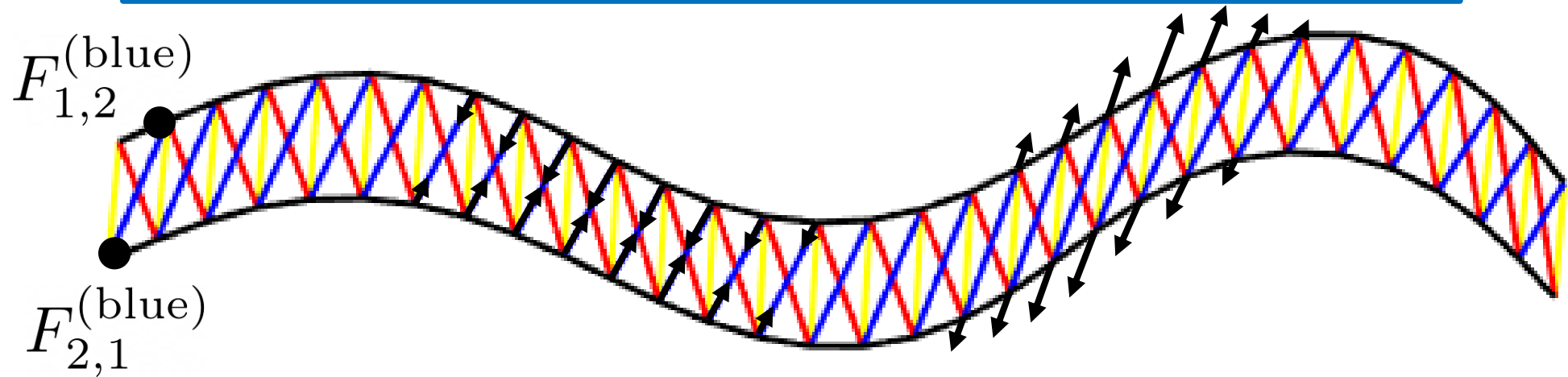
Modelling Active Dynein Motor Proteins

$$\begin{aligned}
 F_{1,n}^{(\text{red})} &= -F_{2,n+1}^{(\text{red})} &:=& \quad r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t) \\
 r_{n,n+1}^{(\text{red})}(t) &= C + f_n^{(\text{red})}(t) \\
 f_n^{(\text{red})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} \right)
 \end{aligned}$$



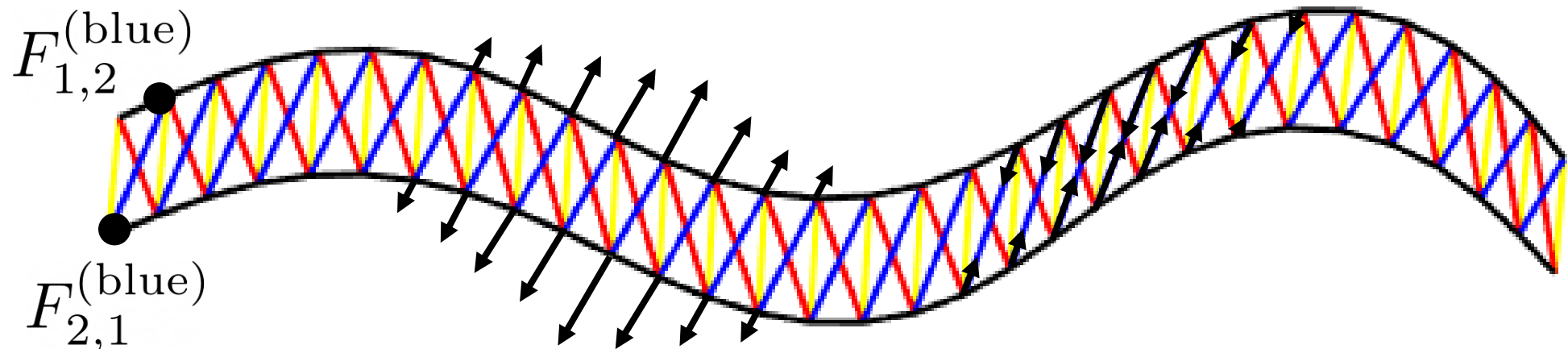
Modelling Active Dynein Motor Proteins

$$\begin{aligned}
 F_{1,n+1}^{(\text{blue})} &= -F_{2,n}^{(\text{blue})} &:=& r_{n+1,n}^{(\text{blue})}(t) - l_{n+1,n}(t) \\
 r_{n+1,n}^{(\text{blue})}(t) &= C + f_n^{(\text{blue})}(t) \\
 f_n^{(\text{blue})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} \right)
 \end{aligned}$$



Modelling Active Dynein Motor Proteins

$$\begin{aligned}
 F_{1,n+1}^{(\text{blue})} &= -F_{2,n}^{(\text{blue})} &:=& r_{n+1,n}^{(\text{blue})}(t) - l_{n+1,n}(t) \\
 r_{n+1,n}^{(\text{blue})}(t) &= C + f_n^{(\text{blue})}(t) \\
 f_n^{(\text{blue})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} \textcircled{+ \pi} \right)
 \end{aligned}$$





$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$

$$\begin{aligned}
F_{1,n}^{(\text{red})} &= -F_{2,n+1}^{(\text{red})} &:=& r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t) \\
r_{n,n+1}^{(\text{red})}(t) &= C + f_n^{(\text{red})}(t) \\
f_n^{(\text{red})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} \right)
\end{aligned}$$

$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$

$$\begin{aligned}
F_{1,n}^{(\text{red})} &= -F_{2,n+1}^{(\text{red})} &:=& r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t) \\
r_{n,n+1}^{(\text{red})}(t) &= C + f_n^{(\text{red})}(t) \\
f_n^{(\text{red})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} \right)
\end{aligned}$$

$$\begin{aligned}
F_{1,n+1}^{(\text{blue})} &= -F_{2,n}^{(\text{blue})} &:=& r_{n+1,n}^{(\text{blue})}(t) - l_{n+1,n}(t) \\
r_{n+1,n}^{(\text{blue})}(t) &= C + f_n^{(\text{blue})}(t) \\
f_n^{(\text{blue})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} + \pi \right)
\end{aligned}$$

$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$

$$\begin{aligned}
F_{1,n}^{(\text{red})} &= -F_{2,n+1}^{(\text{red})} &:=& r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t) \\
r_{n,n+1}^{(\text{red})}(t) &= C + f_n^{(\text{red})}(t) \\
f_n^{(\text{red})}(t) &= \lambda \sin\left(\omega t + \frac{kn}{N}\right)
\end{aligned}$$

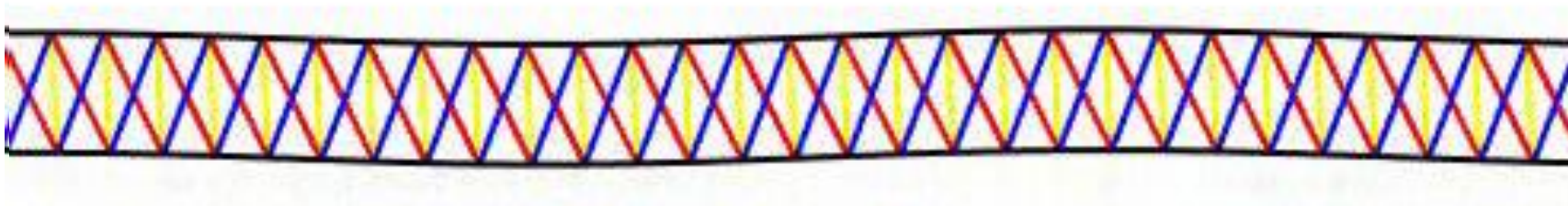
$$\begin{aligned}
F_{1,n+1}^{(\text{blue})} &= -F_{2,n}^{(\text{blue})} &:=& r_{n+1,n}^{(\text{blue})}(t) - l_{n+1,n}(t) \\
r_{n+1,n}^{(\text{blue})}(t) &= C + f_n^{(\text{blue})}(t) \\
f_n^{(\text{blue})}(t) &= \lambda \sin\left(\omega t + \frac{kn}{N} + \pi\right)
\end{aligned}$$

$$\mathbf{F}_{i,n}^A = \mathbf{F}_{i,n}^{(\text{yellow})} + \mathbf{F}_{i,n}^{(\text{red})} + \mathbf{F}_{i,n}^{(\text{blue})}$$

$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$

$$\begin{aligned}
 F_{1,n}^{(\text{red})} &= -F_{2,n+1}^{(\text{red})} &:=& r_{n,n+1}^{(\text{red})}(t) - l_{n,n+1}(t) \\
 r_{n,n+1}^{(\text{red})}(t) &= C + f_n^{(\text{red})}(t) \\
 f_n^{(\text{red})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} \right)
 \end{aligned}$$

$$\begin{aligned}
 F_{1,n+1}^{(\text{blue})} &= -F_{2,n}^{(\text{blue})} &:=& r_{n+1,n}^{(\text{blue})}(t) - l_{n+1,n}(t) \\
 r_{n+1,n}^{(\text{blue})}(t) &= C + f_n^{(\text{blue})}(t) \\
 f_n^{(\text{blue})}(t) &= \lambda \sin \left(\omega t + \frac{kn}{N} + \pi \right)
 \end{aligned}$$



$$F_{1,n}^{(\text{yellow})} = -F_{2,n}^{(\text{yellow})} \quad := \quad D - l_{n,n}(t)$$

HOW CAN I TEST IT?

PART III

HOW CAN I TEST IT?

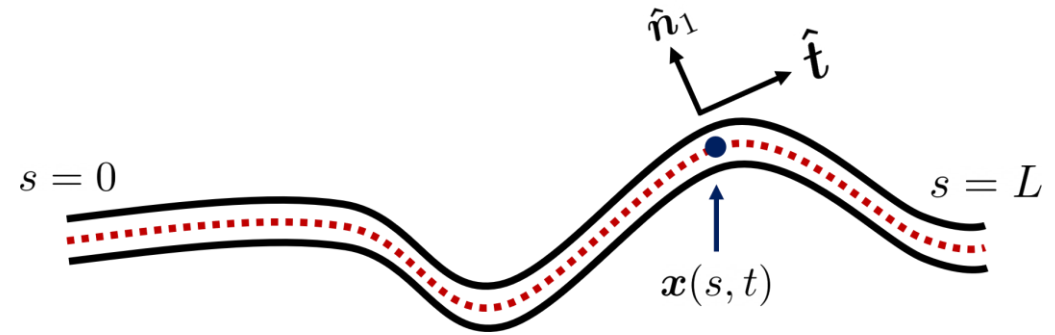
PART III

WARNING : TECHNICAL DETAIL

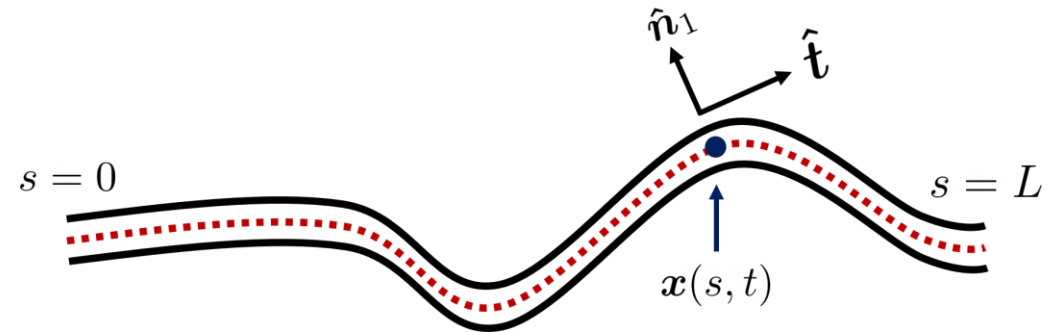
FOUR STEPS TO SUCCESS

Schoeller et. al (2019)

1. Model each of the two walls as a Kirchhoff Rod



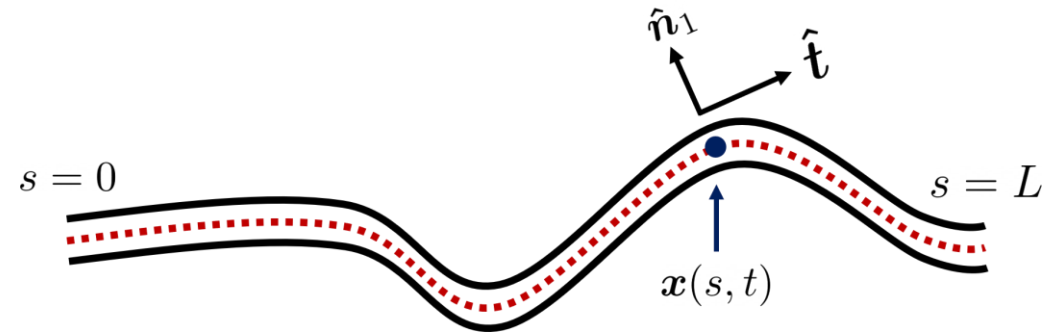
1. Model each of the two walls as a Kirchhoff Rod



$$\mathbf{F}_n^C = \mathbf{\Lambda}_{n+\frac{1}{2}} - \mathbf{\Lambda}_{n-\frac{1}{2}}$$

$$\mathbf{T}_n^C = \frac{\Delta L}{2} \hat{\mathbf{t}}_n \times \left(\mathbf{\Lambda}_{n+\frac{1}{2}} + \mathbf{\Lambda}_{n-\frac{1}{2}} \right) + \left(\mathbf{M}_{n-\frac{1}{2}} - \mathbf{M}_{n+\frac{1}{2}} \right)$$

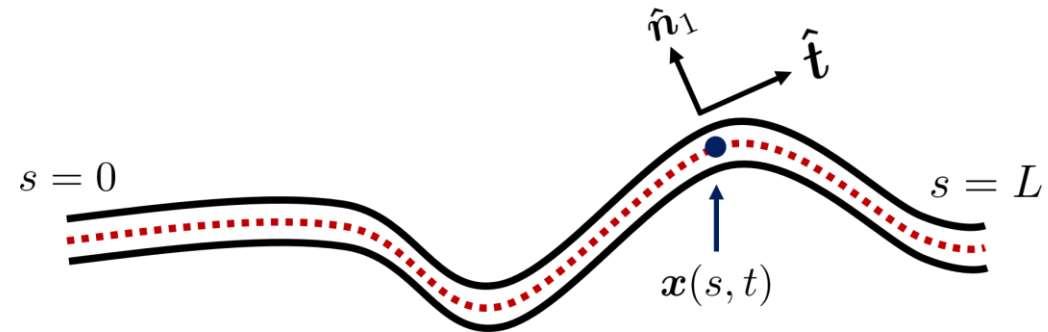
1. Model each of the two walls as a Kirchhoff Rod



$$\mathbf{F}_n^C = \Lambda_{n+\frac{1}{2}} - \Lambda_{n-\frac{1}{2}}$$

$$\mathbf{T}_n^C = \frac{\Delta L}{2} \hat{\mathbf{t}}_n \times \left(\Lambda_{n+\frac{1}{2}} + \Lambda_{n-\frac{1}{2}} \right) + \left(\mathbf{M}_{n-\frac{1}{2}} - \mathbf{M}_{n+\frac{1}{2}} \right)$$

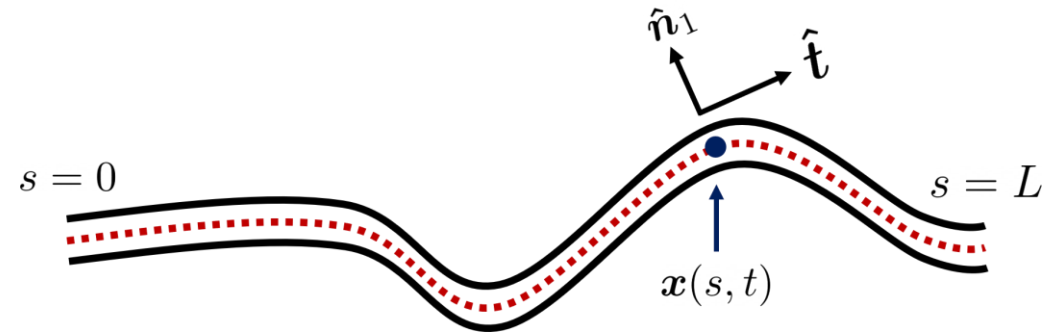
1. Model each of the two walls as a Kirchhoff Rod



$$\mathbf{F}_n^C = \mathbf{\Lambda}_{n+\frac{1}{2}} - \mathbf{\Lambda}_{n-\frac{1}{2}}$$

$$\mathbf{T}_n^C = \frac{\Delta L}{2} \hat{\mathbf{t}}_n \times \left(\mathbf{\Lambda}_{n+\frac{1}{2}} + \mathbf{\Lambda}_{n-\frac{1}{2}} \right) + \left(\mathbf{M}_{n-\frac{1}{2}} - \mathbf{M}_{n+\frac{1}{2}} \right)$$

1. Model each of the two walls as a Kirchhoff Rod



$$\mathbf{F}_n^C = \boldsymbol{\Lambda}_{n+\frac{1}{2}} - \boldsymbol{\Lambda}_{n-\frac{1}{2}}$$

$$\mathbf{T}_n^C = \frac{\Delta L}{2} \hat{\mathbf{t}}_n \times \left(\boldsymbol{\Lambda}_{n+\frac{1}{2}} + \boldsymbol{\Lambda}_{n-\frac{1}{2}} \right) + \left(\mathbf{M}_{n-\frac{1}{2}} - \mathbf{M}_{n+\frac{1}{2}} \right)$$

2. Use rod forces to get hydrodynamics

2. Use rod forces to get hydrodynamics

$$\mathbf{F}_n^H =$$

$$\mathbf{T}_n^H =$$

2. Use rod forces to get hydrodynamics

$$\mathbf{F}_n^H = \mathbf{F}_n^C + \mathbf{F}_n^A + \mathbf{F}_n^S$$

$$\mathbf{T}_n^H = \mathbf{T}_n^C$$

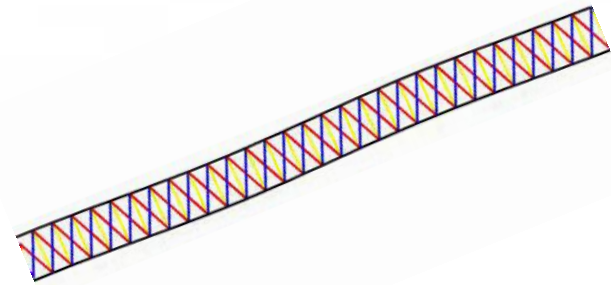
2. Use rod forces to get hydrodynamics

$$\begin{aligned}\mathbf{F}_n^H &= \boxed{\mathbf{F}_n^C} + \mathbf{F}_n^A + \mathbf{F}_n^S \\ \mathbf{T}_n^H &= \boxed{\mathbf{T}_n^C}\end{aligned}$$

2. Use rod forces to get hydrodynamics

$$\mathbf{F}_n^H = \mathbf{F}_n^C + \boxed{\mathbf{F}_n^A} + \mathbf{F}_n^S$$

$$\mathbf{T}_n^H = \mathbf{T}_n^C$$



2. Use rod forces to get hydrodynamics

$$\mathbf{F}_n^H = \mathbf{F}_n^C + \mathbf{F}_n^A + \boxed{\mathbf{F}_n^S}$$

$$\mathbf{T}_n^H = \mathbf{T}_n^C$$



Anything extra we want to add

3. Use hydrodynamics to get velocities

3. Use hydrodynamics to get velocities

$$\begin{pmatrix} \mathbf{u}_n \\ \boldsymbol{\Omega}_n \end{pmatrix} = \sum_{m=1}^N \mathbf{M}_{n,m} \begin{pmatrix} \mathbf{F}_m^H \\ \mathbf{T}_m^H \end{pmatrix}$$

3. Use hydrodynamics to get velocities

$$\begin{pmatrix} \mathbf{u}_n \\ \boldsymbol{\Omega}_n \end{pmatrix} = \sum_{m=1}^N \boxed{\mathbf{M}_{n,m}} \begin{pmatrix} \mathbf{F}_m^H \\ \mathbf{T}_m^H \end{pmatrix}$$

↑
Generalisation of Stokes Law

4. Use velocities to get displacement

4. Use velocities to get displacement

$$\frac{d\mathbf{x}_n}{dt} = \mathbf{u}_n$$

$$\frac{d\theta_n}{dt} = \Omega_n$$

4. Use velocities to get displacement

$$\frac{d\mathbf{x}_n}{dt} = \mathbf{u}_n$$

$$\frac{d\theta_n}{dt} = \Omega_n$$

↑
Restrict movement to a plane

4. Use velocities to get displacement

$$\frac{d\mathbf{x}_n}{dt} = \mathbf{u}_n$$

Shortcut



$$\frac{d\theta_n}{dt} = \Omega_n$$

$$\mathbf{x}_{n+1} = \mathbf{x}_n + \frac{\Delta L}{2} (\hat{\mathbf{t}}_n + \hat{\mathbf{t}}_{n+1})$$

4. Use velocities to get displacement

$$\Delta t \left\{ \begin{array}{l} \frac{d\mathbf{x}_n}{dt} = \mathbf{u}_n \\ \frac{d\theta_n}{dt} = \Omega_n \\ \mathbf{x}_{n+1} = \mathbf{x}_n + \frac{\Delta L}{2} (\hat{\mathbf{t}}_n + \hat{\mathbf{t}}_{n+1}) \end{array} \right.$$

RECAP

Recap: Four steps to success...

1. Use two **Kirchhoff Rods** for the walls.

$$\begin{aligned}\mathbf{F}_n^C &= \boldsymbol{\Lambda}_{n+\frac{1}{2}} - \boldsymbol{\Lambda}_{n-\frac{1}{2}} \\ \mathbf{T}_n^C &= \frac{\Delta L}{2} \hat{\mathbf{t}}_n \times \left(\boldsymbol{\Lambda}_{n+\frac{1}{2}} + \boldsymbol{\Lambda}_{n-\frac{1}{2}} \right) + \left(\mathbf{M}_{n-\frac{1}{2}} - \mathbf{M}_{n+\frac{1}{2}} \right)\end{aligned}$$

Recap: Four steps to success...

1. Use two **Kirchhoff Rods** for the walls.
 2. Use the rods to get **hydrodynamic forces**.
- 


$$\begin{aligned}\mathbf{F}_n^H &= \mathbf{F}_n^C + \mathbf{F}_n^A + \mathbf{F}_n^S \\ \mathbf{T}_n^H &= \mathbf{T}_n^C\end{aligned}$$

Recap: Four steps to success...

1. Use two **Kirchhoff Rods** for the walls.
2. Use the rods to get **hydrodynamic forces**.
3. Use hydrodynamics to get **velocities**.

$$\begin{pmatrix} \mathbf{u}_n \\ \boldsymbol{\Omega}_n \end{pmatrix} = \sum_{m=1}^N \mathbf{M}_{n,m} \begin{pmatrix} \mathbf{F}_m^H \\ \mathbf{T}_m^H \end{pmatrix}$$

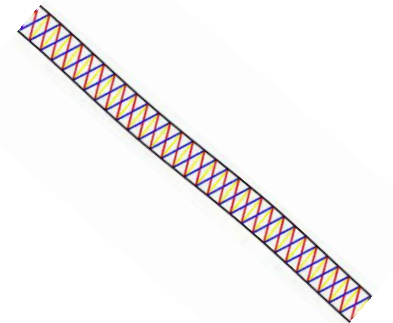
Recap: Four steps to success...

1. Use two **Kirchhoff Rods** for the walls.
 2. Use the rods to get **hydrodynamic forces**.
 3. Use hydrodynamics to get **velocities**.
 4. Use velocities to get **displacement**.
- 

$$\begin{aligned}\frac{d\mathbf{x}_n}{dt} &= \mathbf{u}_n \\ \frac{d\theta_n}{dt} &= \Omega_n\end{aligned}$$

Recap: Five ~~four~~ steps to success...

1. Use two **Kirchhoff Rods** for the walls.
2. Use the rods to get **hydrodynamic forces**.
3. Use hydrodynamics to get **velocities**.
4. Use velocities to get **displacement**.
5. Watch it **swim**...

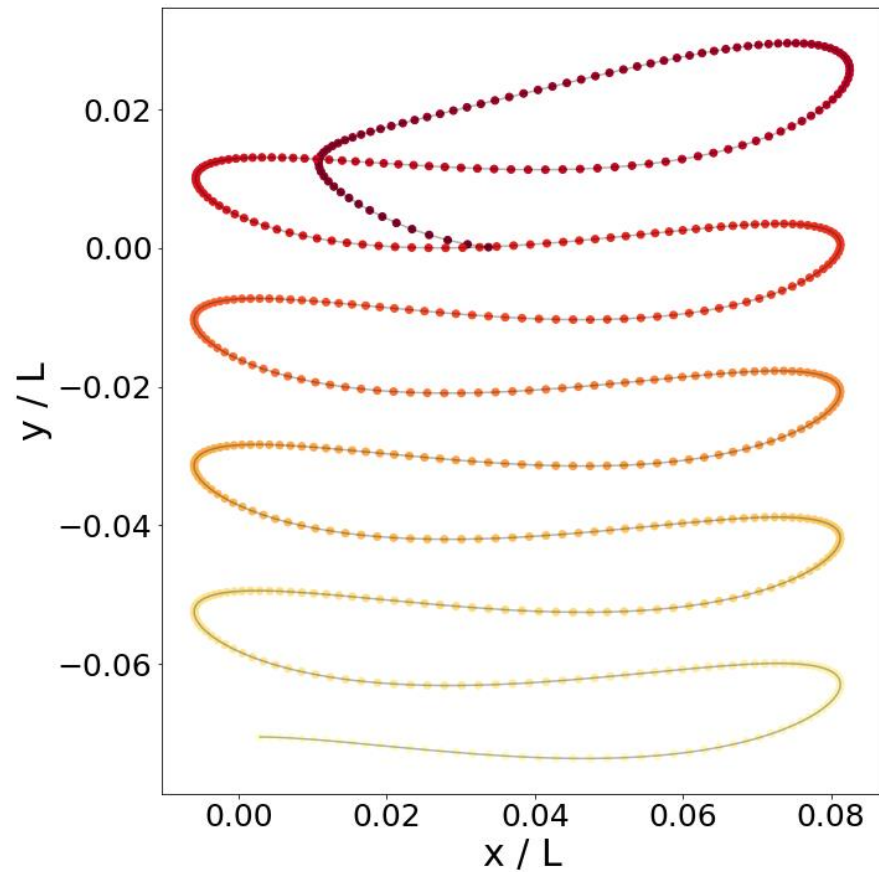


DID IT WORK?

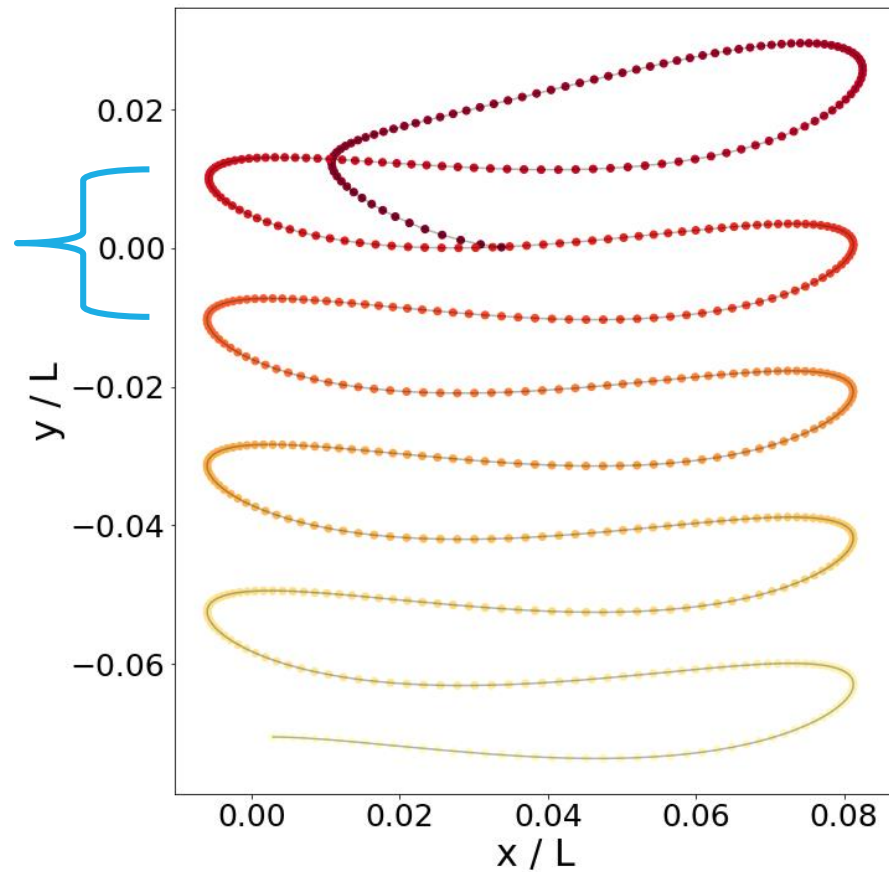
PART IV

THE GOOD

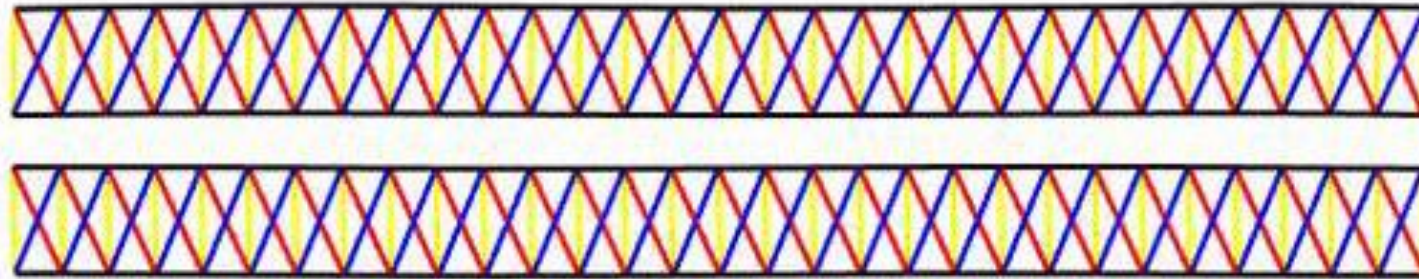
They swim as expected



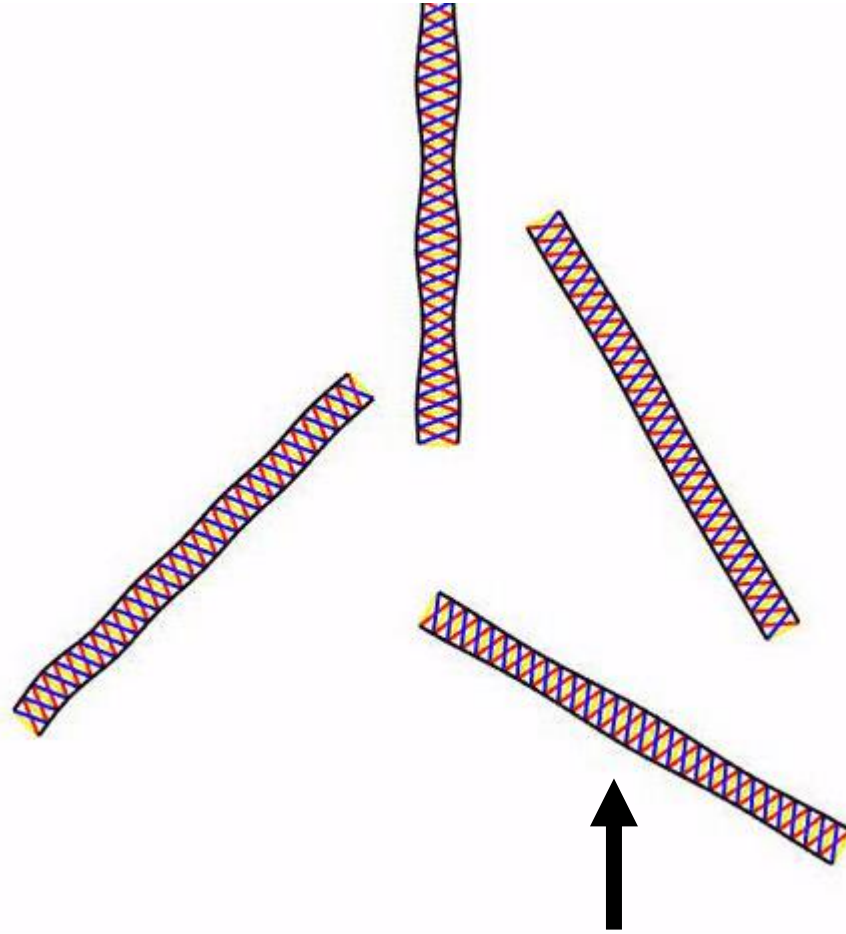
They swim as expected



They coordinate



Variety of swimming styles is possible

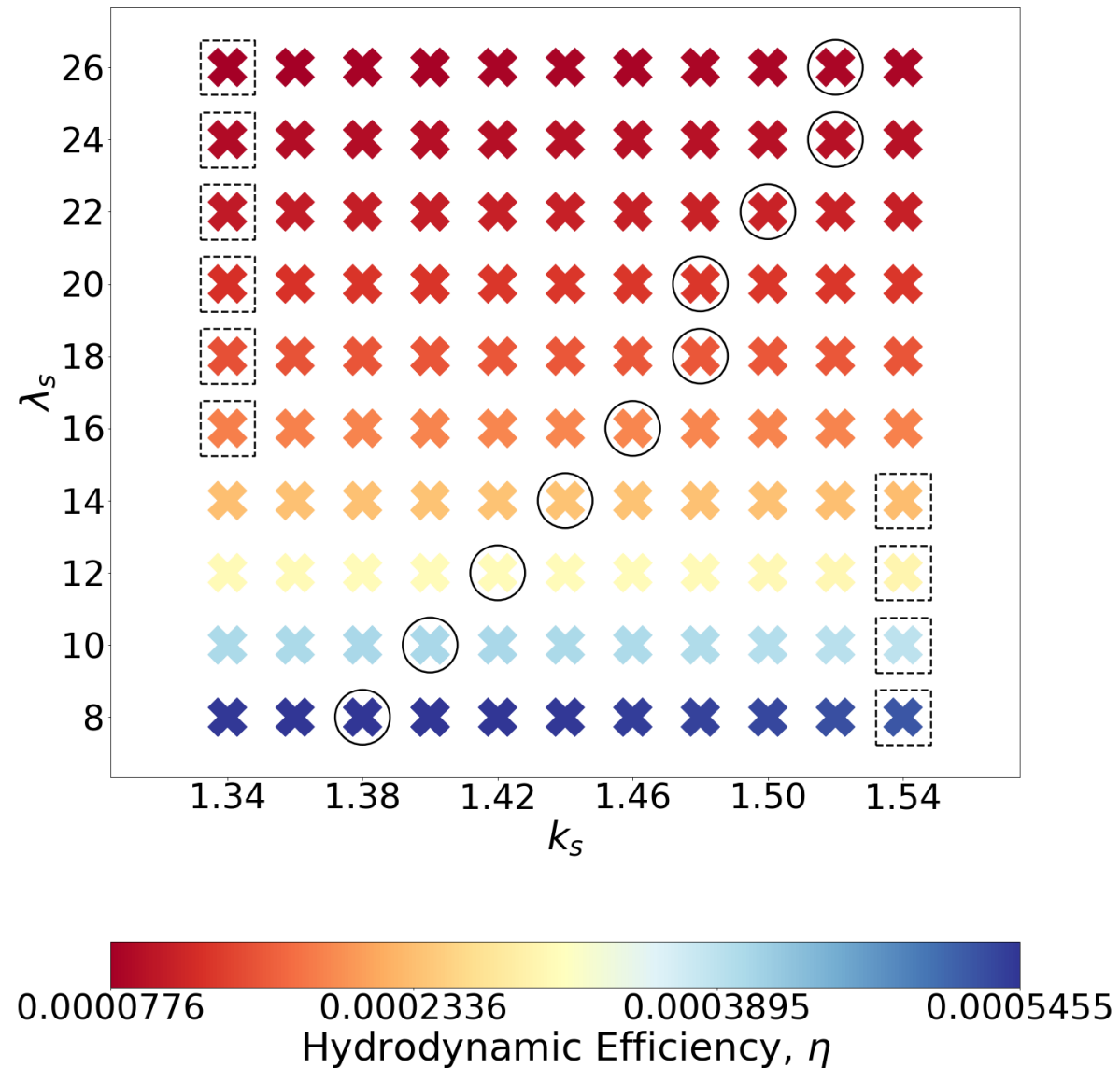


This one not possible in a single filament model.

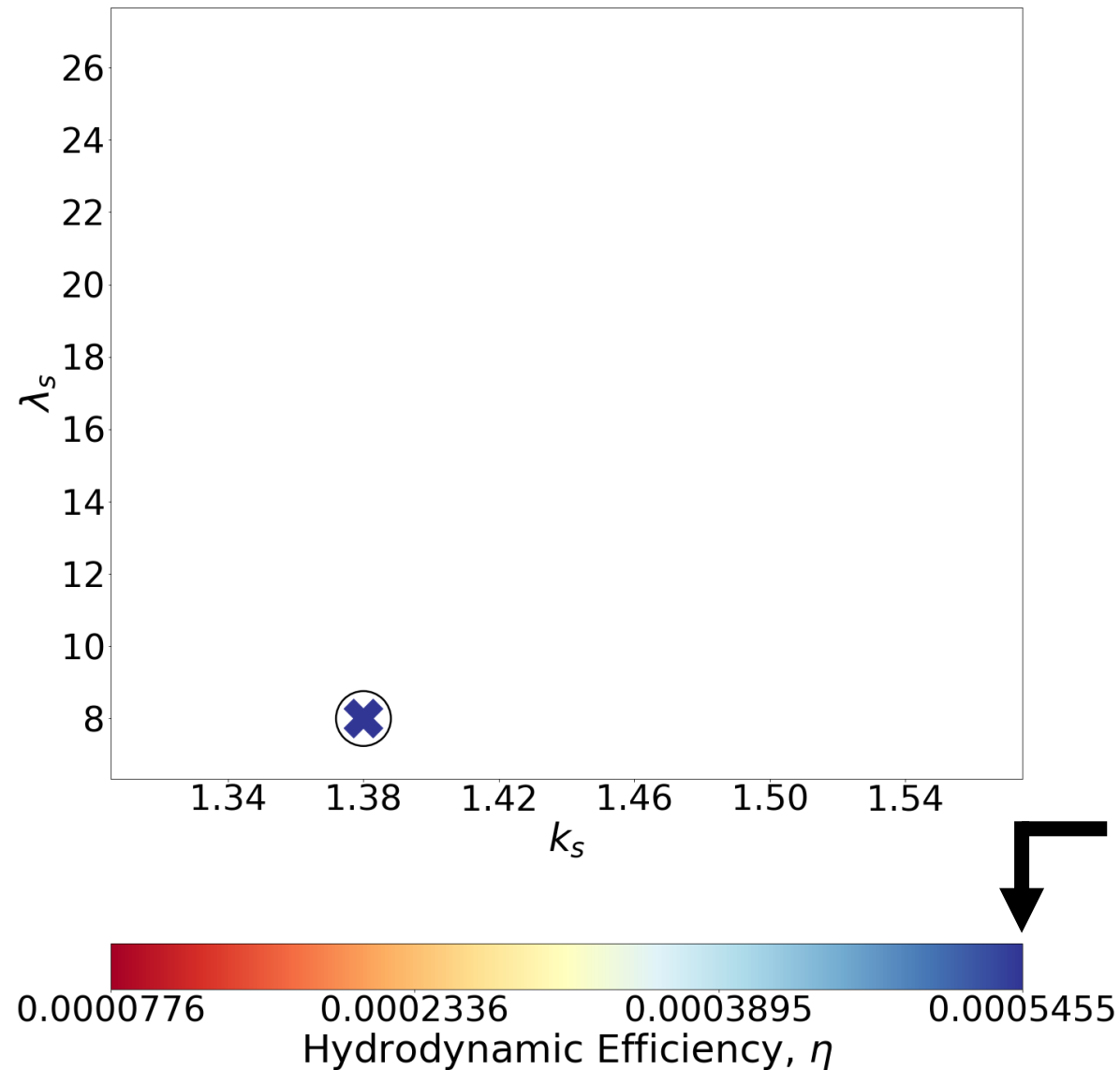
THE BAD

They are **very** inefficient

They are **very** inefficient



They are **very** inefficient



They are **very** inefficient

$$0.002\% < \eta < 0.07\%$$

They are **very** inefficient

$$0.002\% < \eta < 0.07\%$$

$$0.1\% < \eta < 14\%$$



Spagnolie & Lauga (2010), Majmudar et al. (2012)

WHAT'S NEXT?

PART V

What's next?

What's next?

- Improve efficiency.

What's next?

- Improve efficiency.
- Improve biological accuracy.

What's next?

- Improve efficiency.
- Improve biological accuracy.

} Depending on goals.

What's next?

- Improve efficiency.
- Improve biological accuracy.
- Expand to three-dimensions.

What's next?

- Improve efficiency.
- Improve biological accuracy.
- Expand to three-dimensions.
- Dynamically evolving systems instead of internal clocks.

What's next?

- Improve efficiency.
- Improve biological accuracy.
- Expand to three-dimensions.
- Dynamically evolving systems instead of internal clocks.
- Complex environments (mucus, etc.).

What's next?

- Improve efficiency.
- Improve biological accuracy.
- Expand to three-dimensions.
- Dynamically evolving systems instead of internal clocks.
- Complex environments (mucus, etc.).



www.github.com/petermnhull/MastersProject

Bibliography

- Lindemann, C. B. and Lesich K, A. (2010), 'Flagellar and ciliary beating: the proven and the possible', *Journal of Cell Science* **123**, 519-528
- Kumar, N. and Singh, K. A. (2015), 'Trends of male factor infertility, an important cause of infertility: A review of literature', *Journal of Human Reproductive Sciences* **8**, 191-196
- Han, J. and Peskin, C. S. (2018), 'Spontaneous oscillation and fluid-structure interaction of cilia', *Proceedings of the National Academy of Sciences of the United States of America*, **155**, 4417-4422
- Hilgner, A., Jülicher, F. and Chattopadhyay, A. K. (2009), 'Nonlinear dynamics of cilia and flagella', *Physical Review E*. **79**.
- Landau, L. D and Lifshitz, E. M. (1970), *Course of Theoretical Physics, Volume 7: Theory of Elasticity*, Pergamon Press Ltd.
- Wajnryb, E., Mizerski, K. A., Zuk, P. K. and Szymczak (2013), 'Generalization of the Rotne-Yamakawa mobility and shear disturbance tensors', *Journal of Fluid Mechanics*, **731**.
- Schoeller, E., Townsend, A. K., Westwood, T.A. and Keaveny, E. E. (2019), Methods for suspensions of passive and active filaments'. arXiv:1903.12609
- Spagnolie, S. E. and Lauga, E. (2010), 'The optimal elastic flagellum', *Physics of Fluids* **22**
- Majmudar, T. Keaveny, E. E., Zhang, J. and Shelly, M. K. (2012) 'Experiments and theory of undulation in a simple structured medium', *Journal of Royal Society Interface* **9**, 1809-1823