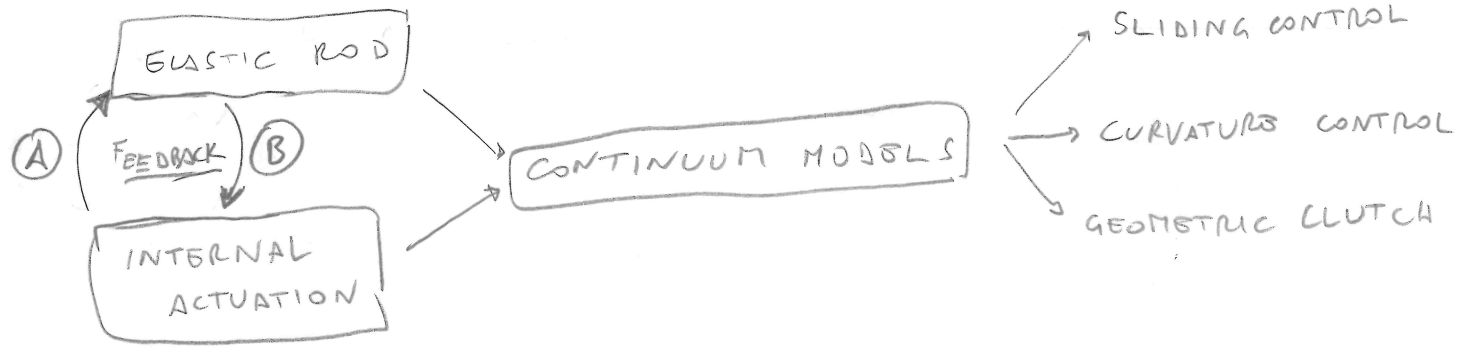
Continuum Models of Eukaryotic flagellar beating

We want to derive/present the three main mechanisms for beating of eukaryotic flagella.



(A) : we are reasonably sure about

(B) : here is the problem

REMEMBER : Eukaryotic flagella $L \sim 10\,\mu m$

$a \sim 250\,nm$

~ 5000 molecular motors (mostly dyneins)

Eukaryotic cilia $L \sim 3\text{-}5\,\mu m$

$a \sim 250\,\mu m$

$\sim 1500 - 2500$ molecular motors

In both cases : SLENDER ; COMPLEX : thousands of internal motors need to COORDINATE to generate beating motion

There is direct experimental evidence that beating motion is NOT the result of a central clock w/in the cell but rather it is the result of spontaneous emergence of oscillations. (e.g. see experiments on demembranated sea urchin sperm cells GIBBONS & GIBBONS JCB (1976))

To introduce the models we will look at:

A. EQUATIONS FOR A BENT ELASTIC ROD
- SMALL SHEAR & SMALL DISPLACEMENT
- SMALL SHEAR & ARBITRARY DISPLACEMENT

B. EQUATIONS OF MOTION FOR A MOVING ELASTIC ROD (LOW RE CASE)

C. MODELS COUPLING FILAMENT MOTION TO INTERNAL MOTOR REGULATION (Linear case)

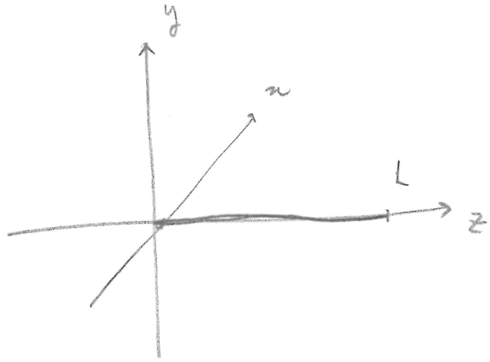
SEE LANDAU: "Theory of Elasticity"

(A) Equations describing a bent slender rod,

(Ai) Small shear & small displacement

Begin with a slender filament of length L straight & along z-axis. Its points are

$\vec{x}(s) = (x(s), y(s), z(s)) \quad s \in [0, L]$



For small deformations, $z(s) \simeq s$ and the rod is described by

POSITION:

$\vec{X}(z) = (X(z), Y(z), z) \qquad z \in [0, L]$] SMALL DEFORMATIONS

TANGENT:

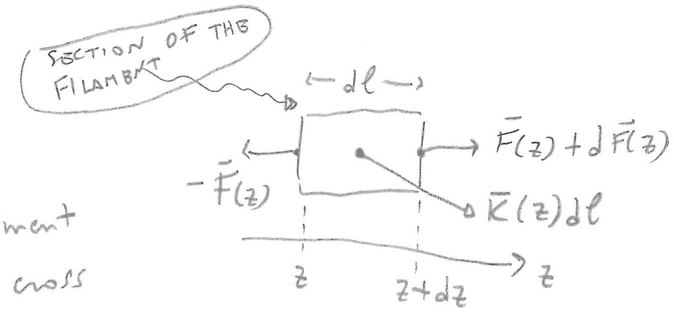
$\hat{t} \simeq \frac{\partial \vec{X}}{\partial z} = (X', Y', 1) \simeq (0, 0, 1) = \hat{e}_z \qquad |Y'|, |X'| \ll 1$] SMALL SHEAR

NORMAL:

$\hat{m} \simeq R \frac{\partial \hat{t}}{\partial z} = R(X'', Y'', 0) \quad \Rightarrow \quad \frac{1}{R} = \sqrt{\left(\frac{\partial^2 X}{\partial z^2}\right)^2 + \left(\frac{\partial^2 Y}{\partial z^2}\right)^2}$ LOCAL CURVATURE

When subjected to externally imposed forces, the filament will bend. The equilibrium configuration is obtained imposing ZERO NET FORCE & MOMENTUM on each section (plus b.c.s)

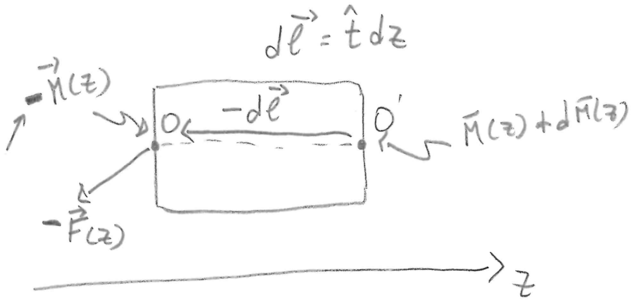
- ZERO NET FORCE



- $\vec{F}(z)$ = net elastic force on filament cross section @ z, when the cross section is oriented along $\hat{z}$
- $\vec{K}(z)$ = external force per unit length

$$-\vec{F}(z) + \vec{F}(z) + d\vec{F}(z) + \vec{K}(z)\,dz = 0 \quad \Rightarrow \quad \boxed{\frac{d\vec{F}(z)}{dz} = -\vec{K}(z)}$$

- ZERO NET MOMENTUM



- O = centre of mass of the cross section at z
- O' = like O but at $z+dz$
- $\vec{M}(z)$ = internal elastic moment on cross section @ z, calculated around O, when the surface is oriented along $\hat{z}$

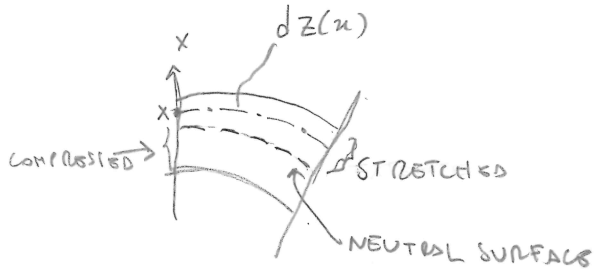
Calculating the net moment around O':

$$-\vec{M}(z) - (dz\,\hat{t}) \times (-\vec{F}(z)) + \vec{M}(z) + d\vec{M}(z) = 0 \quad \Rightarrow \quad \boxed{\frac{d\vec{M}}{dz} = \vec{F} \times \hat{t}} \left(= \vec{F} \times \hat{e}_z \right)$$

$\boxed{\text{NOTICE}}$: $\vec{K}(z)$ does not directly contribute because the momentum contribution is of higher order in dz $(\sim K\,dz^2)$

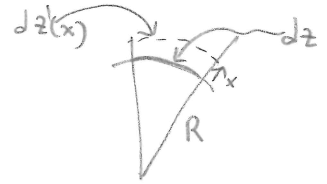
Now we need to connect $\bar{F}(z)$ & $\bar{M}(z)$ to the configuration of the filament.

For pure bending of the filament, some parts will be stretched & others will be compressed (Here bending in the xz-plane)



A small section dz, bending on the xz-plane (i.e. around y-axis), the length of a segment at position x from the neutral surface will be

$$dz'(x) = \frac{dz}{R}(R+x) = \left(1+\frac{x}{R}\right)dz$$



$$\boxed{\frac{dz'-dz}{dz} = \frac{x}{R} = u_{zz}}$$

- $u_{ij} = \frac{1}{2}\left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i}\right)$ STRAIN TENSOR
- displacement of material point due to deformation: $\bar{u} = \bar{x}' - \bar{x}$

For a pure compression along the z-axis, $\boxed{\sigma_{zz} = E\, u_{zz}}$

E = Young's modulus ($[E] = Pa = J/m^3$)

σ_{ij} = stress tensor.

One can show easily that all the other components of $\underline{\sigma}$ except σ_{zz} are negligible wrt σ_{zz} as a consequence of the smallness of the filament thickness compared to its length (see Landau, Elasticity, pg. 65).

HENCE one can use σ_{zz} to calculate the elastic bending moment IF one knows where the neutral surface is. For pure bending, there is NO NET FORCE on the cross section above $\Rightarrow \int_S \underline{\sigma}\cdot d\bar{S} = 0$

Given that $d\vec{S} = \hat{e}_z dx\,dy$, & that $\sigma_{zz} = \frac{EX}{R}$; $\sigma_{ij} = 0$ otherwise,

we get

$$\int_S \frac{EX}{R} dx\,dy = 0 \iff \frac{E}{R} S\, x_{CM} = 0 \iff \underline{\underline{x_{CM} = 0}}$$

$x_{CM} = \frac{1}{S} \int_S x\, dx\,dy$ is the x-coordinate of the centre of mass of the cross section

$\downarrow$

> The <u>NEUTRAL SURFACE</u> runs through the local centre of mass of the filament cross section (the point O that we defined before

The elastic moment $\bar{M}(z)$ is therefore

$$\bar{M}(z) = \int_S \vec{x} \times \underline{\underline{\sigma}} \cdot dS = \frac{1}{R} \int (\vec{x} \times \hat{e}_z) \frac{x}{R}\, dS$$

$$= \frac{E}{R} \left[\int x^2 dS \right] \hat{e}_y - \frac{1}{R} \cancel{\int xy\, dS}^{\,0\ (\text{symmetry})}\, \hat{e}_x$$

$$= \frac{E I_y}{R} \underbrace{\hat{t} \times \hat{n}}_{\substack{\shortparallel \\ (\vec{b}\ \text{binormal})}}$$

$$\left(\begin{array}{l} \text{Here} \\ \hat{t} = \hat{e}_x \,;\ \hat{n} = -\hat{e}_x \\ I_y := \int_S x^2 dS \end{array} \right)$$

This generalises to

$$\boxed{\bar{M} = E\, \underline{\underline{I}} \cdot \left(\hat{t} \times \frac{\hat{m}}{R} \right)}$$

$$\underline{\underline{I}} = \int_S \left(r^2 \mathbb{1} - \vec{r} \otimes \vec{r} \right) dS = \underline{\text{INERTIA TENSOR}}$$

For us: $\underline{\underline{I}} = I\,\mathbb{1}$; $\hat{t} = (0,0,1)$; $\frac{\hat{m}}{R} = (x'', y'', 0)$

$$\downarrow$$

$$\boxed{\bar{M} = EI\left(-y'', x'', 0\right)}$$

$$\downarrow$$

$$\boxed{\vec{F} = \begin{pmatrix} -EI\,x''' \\ -EI\,y''' \\ 0 \end{pmatrix}}$$

- Using $\frac{d\bar{M}}{dz} = \bar{F} \times \hat{t}$
- AND assumption of negligible tension

$$\downarrow$$

- From $\frac{d\bar{F}}{dz} = -\bar{K}$
- $\bar{K} = (K_x, K_y, 0)$
- Derivatives are wrt z.

BEAM EQUATIONS (small deformations)

$$\begin{cases} EI\,x^{(IV)} + K_x = 0 \\ EI\,y^{(IV)} + K_y = 0 \end{cases}$$

These will be accompanied by a suitable set of b.c.s. Remember that fixing second derivatives @ boundary is a requirement on momenta; while fixing third derivatives @ boundary is a requirement on forces

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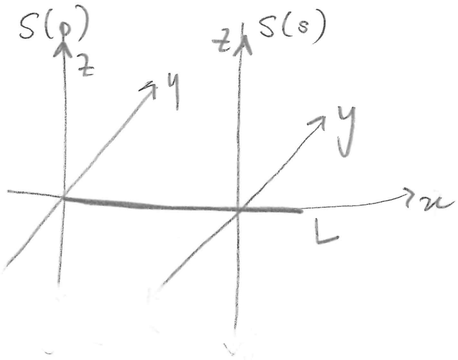
Aii) Small shear but arbitrary displacement

We can have small shear but large displacement if the filament is long (i.e. $L \gtrsim R$). Then, in a sense, the small local shear can "pile up". We cannot use $z \sim s$ anymore; we need another parametrization of the filament shape.



Imagine the filament straight, say on X-axis; and imagine that at every point $s \in [0, L]$ there is a local frame of reference $S(s)$ which is materially attached to the filament @ s.

For my initial straight filament, $S(s)$ is equal to $S(0)$.

For a given configuration, $S(s)$ will have rotated wrt $S(0)$ by an angle $\vec{\phi}(s)$ ($\hat{\phi}(s)$ is the axis of rotation, $\phi(s)$ is the angle). The function $\vec{\phi}(s)$ is what we will use.

If $\hat{t}(0)$ is the tangent @ the origin, then the position $\bar{r}(s)$ of the filament @ a given s will be

$$\bar{r}(s) = \bar{r}(0) + \int_0^s \underbrace{R(\vec{\phi}(s))\,\hat{t}(0)}_{=\,\hat{t}(s)}\, ds$$

$\hat{t}(0)$ will be fixed by b.c.s.

Where $R(\bar{\Phi}(s))$ is the 3D rotation operator corresponding to $\vec{\phi}(s)$.

Remember that $R(\bar{\Phi}(s)) = e^{\vec{L}\cdot\vec{\phi}}$ where $\bar{L} = (L_x, L_y, L_z)$

and

$$L_x = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & -1 \\ 0 & 1 & 0 \end{pmatrix} ; \quad L_y = \begin{pmatrix} 0 & 0 & -1 \\ 0 & 0 & 0 \\ 1 & 0 & 0 \end{pmatrix} ; \quad L_z = \begin{pmatrix} 0 & -1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

are the generators of $SO(3)$.

From these,

$$\boxed{\frac{\partial \hat{t}(s)}{\partial s}} = \frac{\partial}{\partial s}\left[e^{\bar{L}\cdot\bar{\phi}(s)}\,\hat{t}(0)\right] = \left(\bar{L}\cdot\frac{\partial\bar{\phi}}{\partial s}\right)\hat{t}(s) = \boxed{\frac{\partial\bar{\phi}}{\partial s}\times\hat{t} = \frac{\hat{m}}{R}}$$

Ex Show that, for $\vec{a},\vec{b}\in\mathbb{R}^3$, $(\bar{L}\cdot\vec{a})\bar{b} = \bar{a}\times\bar{b}$.

Call $\underline{\vec{\Omega} := \frac{\partial\bar{\phi}}{\partial s}}$ = angular speed, as one travels along the filament @ speed "1".

$$\frac{\hat{m}}{R} = \bar{\Omega}\times\hat{t} \Rightarrow \hat{t}\times\frac{\hat{m}}{R} = \hat{t}\times(\bar{\Omega}\times\hat{t}) = \vec{\Omega} - \hat{t}(\bar{\Omega}\cdot\hat{t})$$

Notice: No loss of information because $\hat{m}\perp\hat{t}$

$$\Downarrow$$

$$\bar{\Omega} = \hat{t}\times\frac{\hat{m}}{R} + \underbrace{\hat{t}(\hat{t}\cdot\bar{\Omega})}_{\text{TWIST}}$$

- We will assume NO TWIST

$$\left(\left|\frac{\partial\bar{\phi}}{\partial s}\right| = \frac{1}{R}\right) \Leftarrow \bar{\Omega} = \hat{t}\times\frac{\hat{m}}{R} = \frac{\hat{b}}{R} \quad (\hat{b} = \hat{t}\times\hat{n} \text{ is the BINORMAL})$$

$$\Downarrow$$

$$\boxed{\vec{M}(s) = E\,I\,\vec{\Omega}(s)}$$

(In general $\bar{M} = E\,\underline{\underline{I}}\,\vec{\Omega}$)

USUALLY NOT PARALLEL

Then

$$\frac{d\bar{M}}{ds} = \bar{F}\times\hat{t} \Rightarrow EI\frac{d\bar{\Omega}}{ds} = \bar{F}\times\hat{t} \Rightarrow EI\frac{d^2\bar{\Omega}}{ds^2} = -\bar{K}\times\hat{t} + \underbrace{\vec{F}\times\frac{\hat{m}}{R}}_{\mathcal{O}\left(\frac{L}{R}\right) \text{ wrt first term}}$$

$$\Downarrow$$

$$EI\frac{d^2\bar{\Omega}}{ds^2} \simeq -\bar{K}\times\hat{t}$$

$$\updownarrow$$

$$\boxed{EI\frac{d^3\bar{\phi}}{ds^3} = -\bar{K}\times\hat{t}}$$

For a PLANAR bending, say in the xy-plane, we will have $\bar{\phi}(s) = \phi(s)\,\hat{e}_z$. The vector $\bar{K}$ will also be on the xy-plane $\Rightarrow \bar{K}\times\hat{t} \parallel \hat{e}_z$, so we want to write the eqn. above as

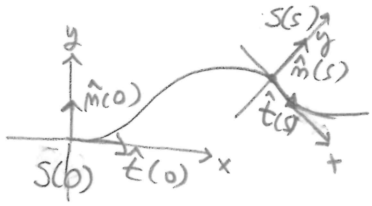
$$EI\frac{\partial^3\phi}{\partial s^3} = \pm K_\perp(s)$$

PROBLEM: In order to decide on the correct sign, we need a local frame of reference $(\hat{t},\hat{m})$ would work well IF it wasn't for the problem that $\hat{m}$ "points" in different directions based on local curvature:

THIS COMPLICATES LIFE

(B) EQUATIONS OF MOTION FOR A MOVING ELASTIC ROD (PLANAR; LOW RE) (SEE HINES & BLUM 1978)

Solution: instead of defining $\hat{m}$ as $\frac{\hat{m}}{R} := \frac{\partial \hat{t}}{\partial s}$, say that $\hat{m}(s)$ is obtained from $\hat{t}(s)$ by rotating on the plane, counterclockwise, by $\pi/2$.



$$\hat{m}(s) := \begin{pmatrix} 0 & -1 \\ 1 & 0 \end{pmatrix} \hat{t}(s)$$

In this description:

- $R(\phi(s)) = \begin{pmatrix} \cos\phi(s) & -\sin\phi(s) \\ \sin\phi(s) & \cos\phi(s) \end{pmatrix}$ (ASSUMES FILAMENT INITIALLY ALONG X-AXIS)

- $\hat{t}(s) = \begin{pmatrix} \cos\phi(s) \\ \sin\phi(s) \end{pmatrix}$

- $\hat{m}(s) = \begin{pmatrix} -\sin\phi(s) \\ \cos\phi(s) \end{pmatrix}$

- $EI \frac{d^3\bar{\phi}}{ds^3} = -\bar{K} \times \hat{t} \Rightarrow \boxed{EI \frac{d^3\phi}{ds^3} = +K_N(s)}$

where $\vec{K}(s) = K_T \hat{t} + K_N \hat{n}$.

We will now use this to derive the eqns of motion for a filament moving in a viscous fluid.

FILAMENT MOVING $\Rightarrow$ $\phi(s,t)$

then, from the definitions above, some useful identities:

$$\frac{\partial \hat{t}(s,t)}{\partial s} = \hat{m}(s,t)\frac{\partial \phi}{\partial s} \quad ; \quad \frac{\partial \hat{m}}{\partial s} = -\hat{t}(s,t)\frac{\partial \phi}{\partial s}$$

$$\frac{\partial \hat{t}}{\partial t} = \hat{m}\frac{\partial \phi}{\partial t} \quad ; \quad \frac{\partial \hat{m}}{\partial t} = -\hat{t}\frac{\partial \phi}{\partial t}$$

When the filament moves @ low Re, the viscous drag balances other forces and moments.

We will treat the viscous forces in the RESISTIVE FORCE approximation (local $\Rightarrow$ much easier)

$\vec{q}(s,t)\,ds$ = viscous force acting on element ds @ position s @ time t

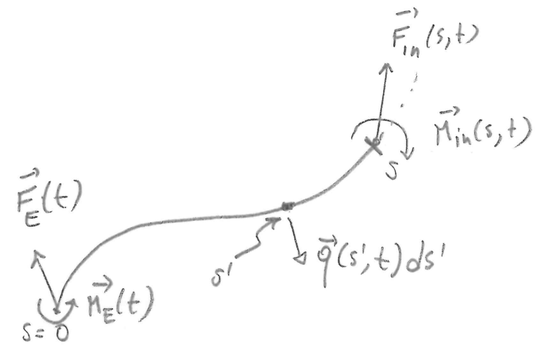
$$= \underbrace{-C_N V_N(s,t)\,\hat{m}(s,t)\,ds}_{\text{NORMAL DRAG}} \; \underbrace{-\,C_T V_t(s,t)\,\hat{t}(s,t)\,ds}_{\text{TANGENTIAL DRAG}}$$

This is based on:

- $\vec{V}(s,t) = V_N\,\hat{m} + V_T\,\hat{t}$ decomposition of local filament speed into normal & tangential components
- C_N, C_T drag coefficients per unit length ($C_N \sim 2C_T$)

Now impose ZERO net force & momentum conditions:

- ASSUME $\underline{\text{External force}}$ (NON-VISCOUS) $\vec{F}_E(t)$ & momentum $\bar{M}_E(t)$ can only be applied @ base $(s=0)$ (this is a condition relevant for our flagella);



- Imagine to focus @ position s & time t. The internal force/momentum $\bar{F}_{in}(s,t)/\bar{M}_{in}(s,t)$ acting on the portion of the filament $[0,s]$ will need to balance the net external force/Momentum:

$$\begin{cases} \bar{F}_{in}(s,t) + \int_0^s ds'\, \vec{q}(s',t) + \bar{F}_E(t) = 0 \\ \bar{M}_{in}(s,t) + \int_0^s ds'\, (\vec{r}(s',t) - \vec{r}(s,t)) \times \vec{q}(s',t) + (\vec{r}(0,t) - \vec{r}(s,t)) \times \vec{F}_E(t) + \bar{M}_E(t) = 0 \end{cases}$$

$\downarrow \frac{\partial}{\partial s}$ INTEGRAL FORM ; DIFFERENTIAL FORM (need b.c.s)

$$\begin{cases} \dfrac{\partial \bar{F}_{in}(s,t)}{\partial s} + \vec{q}(s,t) = 0 \\ \dfrac{\partial \bar{M}_{in}(s,t)}{\partial s} + \hat{t}(s,t) \times \bar{F}_{in}(s,t) = 0 \end{cases}$$

$\longleftarrow$ used the condition above for zero net force.

$\bar{M}_{in} \propto \hat{e}_z$ so the second eqn. above becomes

$$\underline{\frac{\partial M_{in}}{\partial s} + \left(\hat{t}(s,t) \times \bar{F}_{in}(s,t)\right) \cdot \hat{e}_z = 0}$$

Now, let's reexpress using a local decomposition along $(\hat{m}, \hat{t})$:

- $\bar{F}_{in}(s,t) =: T(s,t)\,\hat{t} + N(s,t)\,\hat{m}$

$$\downarrow$$

- $$\frac{\partial \bar{F}_{in}}{\partial s} = \frac{\partial T}{\partial s}\hat{t} + T\frac{\partial \hat{t}}{\partial s} + \frac{\partial N}{\partial s}\hat{m} + N\frac{\partial \hat{m}}{\partial s}$$

$$= \frac{\partial T}{\partial s}\hat{t} + T\frac{\partial \phi}{\partial s}\hat{m} + \frac{\partial N}{\partial s}\hat{m} - N\frac{\partial \phi}{\partial s}\hat{t}$$

- $\vec{q} = -C_N V_N \hat{m} - C_T V_T \hat{t}$

These lead to

$$\begin{cases} \dfrac{\partial T}{\partial s} - N\dfrac{\partial \phi}{\partial s} - C_T V_T = 0 \\[2ex] \dfrac{\partial N}{\partial s} + T\dfrac{\partial \phi}{\partial s} - C_N V_N = 0 \\[2ex] \dfrac{\partial M_{in}}{\partial s} + N = 0 \end{cases}$$

$\boxed{\text{NOTICE}}$ that :

(i) V_T & V_N are currently <u>UNKNOWN</u>

(ii) We have not yet written down the relation b/w filament bending & internal moments (... well, ok, we know it from (A)!)

For a model of a flagellum, we will also need to include internal motor activity : LATER!

Start by looking @ velocities:

$$\vec{V}(s,t) = \frac{\partial \vec{r}(s,t)}{\partial t} = V_T \hat{t} + V_N \hat{m}$$

$$\Big\downarrow \frac{\partial}{\partial s}$$

$$\left(\frac{\partial^2 \vec{r}}{\partial t \partial s} = \frac{\partial \hat{t}}{\partial t} = \right) \frac{\partial \phi}{\partial t} \hat{m} = \frac{\partial V_T}{\partial s} \hat{t} + V_T \frac{\partial \phi}{\partial s} \hat{m} + \frac{\partial V_N}{\partial s} \hat{m} - V_N \frac{\partial \phi}{\partial s} \hat{t}$$

SEPARATE INTO $\hat{t}$ & $\hat{m}$ components

$$\underline{\frac{\partial V_N}{\partial s} = \frac{\partial \phi}{\partial t} - V_T \frac{\partial \phi}{\partial s}} \quad ; \quad \underline{\frac{\partial V_T}{\partial s} = V_N \frac{\partial \phi}{\partial s}}$$

- Use these to eliminate explicit dependence on V_T & V_N from previous eqns:

E.g.

$$\frac{\partial T}{\partial s} - N \frac{\partial \phi}{\partial s} - C_T V_T = 0 \xrightarrow{\frac{\partial}{\partial s}} \frac{\partial^2 T}{\partial s^2} - \frac{\partial N}{\partial s}\frac{\partial \phi}{\partial s} - N \frac{\partial^2 \phi}{\partial s^2} \underbrace{- C_T \frac{\partial V_T}{\partial s}} = 0$$

$$= - C_T V_N \frac{\partial \phi}{\partial s}$$

$$= -\frac{C_T}{C_N} \frac{\partial \phi}{\partial s} C_N V_N$$

$$= -\frac{C_T}{C_N} \frac{\partial \phi}{\partial s} \left[\frac{\partial N}{\partial s} + T \frac{\partial \phi}{\partial s} \right]$$

So, overall,

$$\frac{\partial^2 T}{\partial s^2} - \left(1 + \frac{C_T}{C_N}\right) \frac{\partial N}{\partial s} \frac{\partial \phi}{\partial s} - N \frac{\partial^2 \phi}{\partial s^2} - \frac{C_T}{C_N} T \left(\frac{\partial \phi}{\partial s}\right)^2 = 0$$

$\boxed{\text{EX}}$

Repeat for the other eqn.

- The connection b/w internal moment (torque) & curvature comes from the assumption of elasticity $\rightarrow$ $\boxed{M = EI \frac{\partial \phi}{\partial s}}$

$\downarrow$

- $$EI \frac{\partial^2 \phi}{\partial s^2} + N = 0$$

or, if there is also an ADDITIONAL INTERNAL BENDING MOMENT $\mu(s,t)$

- $$EI \frac{\partial^2 \phi}{\partial s^2} + N = \mu$$

CONVENIENT choice of sign for μ

$\downarrow$

$$\boxed{N = \mu - EI \frac{\partial^2 \phi}{\partial s^2}}$$

Which can be used to remove the dependence on N from the eqns above.

Overall we obtain the following set of equations:

NONLINEAR PART

$$\begin{cases} \dfrac{\partial^2 T}{\partial s^2} - \left(1+\dfrac{C_T}{C_N}\right)\dfrac{\partial \phi}{\partial s}\left[\dfrac{\partial \mu}{\partial s} - EI\dfrac{\partial^3\phi}{\partial s^3}\right] - \left[\mu - EI\dfrac{\partial^2\phi}{\partial s^2}\right]\dfrac{\partial^2\phi}{\partial s^2} - \dfrac{C_T}{C_N}T\left(\dfrac{\partial\phi}{\partial s}\right)^2 = 0 \\ EI\dfrac{\partial^4\phi}{\partial s^4} - \dfrac{\partial^2\mu}{\partial s^2} + C_N\dfrac{\partial\phi}{\partial t} - \left(1+\dfrac{C_N}{C_T}\right)\dfrac{\partial T}{\partial s}\dfrac{\partial\phi}{\partial s} - T\dfrac{\partial^2\phi}{\partial s^2} + \dfrac{C_N}{C_T}EI\dfrac{\partial^2\phi}{\partial s^2}\left(\dfrac{\partial\phi}{\partial s}\right)^2 + \dfrac{C_N}{C_T}\mu\left(\dfrac{\partial\phi}{\partial s}\right)^2 = 0 \\ EI\dfrac{\partial^2\phi}{\partial s^2} + N = \mu \end{cases}$$

NONLINEAR PART

NOTICE: See eg. HINES 1978 for a possible forward stepping method to solve numerically the eqns above. There are problems of numerical stability, though, with that method.

- For small amplitudes, we can reduce to the linear part

$$\begin{cases} \dfrac{\partial^2 T}{\partial s^2} \simeq 0 \\ \boxed{EI\dfrac{\partial^4\phi}{\partial s^4} - \dfrac{\partial^2\mu}{\partial s^2} + C_N\dfrac{\partial\phi}{\partial t} \simeq 0} \\ N = \mu - EI\dfrac{\partial^2\phi}{\partial s^2} \end{cases}$$

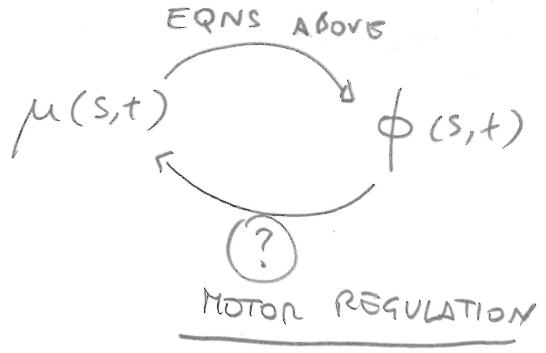
← EQN. FOR THE TENSION.

← THIS IS THE FUNDAMENTAL EQN. WE WERE LOOKING FOR

- Once $\phi(s,t)$ has been solved for, one can use the other eqns to calculate T & N, and then the original eqns to calculate V_T & V_N (or, use $\bar{r}(s,t) = \int \hat{t}\, ds + \bar{r}(0,t)$)
- NOTICE that for $\mu(s,t) = \mu(s)$, the function $\phi(s)$ satisfying $EI\dfrac{\partial^2\phi}{\partial s^2} = \mu$ is a SOLUTION (modulo b.c.s; at LINEAR level) for which $T = \text{const}$; $N = 0$ (again, at linear level).

Now the problem is (besides fixing b.c.s) : WHAT IS $\mu(s,t)$?

$\boxed{\mu(s,t)}$ will describe the motor activity w/in my axoneme.

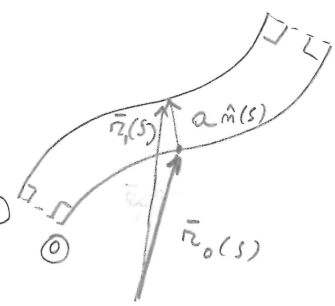


Ⓒ (LINEAR) MODELS OF FLAGELLAR ACTUATION

First, a little excursion that will prove useful

$\boxed{\text{EX}}$

I have a planar curve $\bar{r}_0(s)$, $s \in [0, L_0]$ and from this I construct another curve $\bar{r}_1(s)$ by displacing every point on ⓪ by $a\hat{n}(s)$, a fixed: $\bar{r}_1(s) = \bar{r}_0(s) + a\hat{n}(s)$



$\boxed{Q}$ What is the length of curve ① ? (Assume a is small enough that I avoid pathological cases)

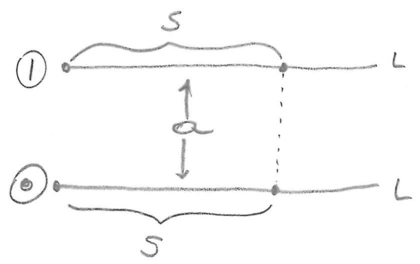
$$\frac{d\bar{r}_1(s)}{ds} = \frac{d\bar{r}_0(s)}{ds} + a\frac{d\hat{n}(s)}{ds}$$

$$= \hat{t}(s) - a\frac{d\phi(s)}{ds}\hat{t} = \left(1 - a\frac{d\phi}{ds}\right)\hat{t}(s)$$

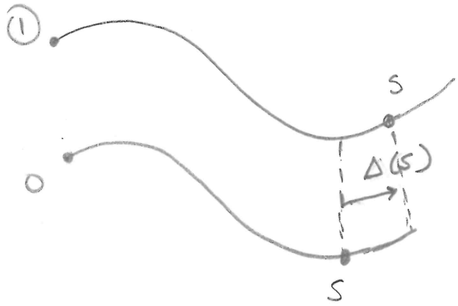
$$\frac{ds_1(s)}{ds} = \left|\frac{d\bar{r}_1(s)}{ds}\right| = \left(1 - a\frac{d\phi}{ds}\right) \Rightarrow L_1 = \int_0^{L_0} \frac{ds_1}{ds}ds = \int_0^{L_0}\left(1 - a\frac{d\phi}{ds}\right)ds$$

$$\boxed{L_1 = L_0 - a\left(\phi(L) - \phi(0)\right)}$$

This implies that, if I start w/ two identical straight filaments



and I bend them



points that were before across from each other will - in general - not be across from each other anymore:

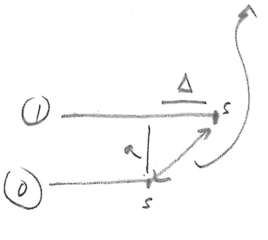
- LOCAL SHEAR: $\Delta(s) = a(\phi(s) - \phi(0))$

(sign as above)

- NEW SEPARATION b/w formerly adjacent points

$$\sqrt{a^2 + a^2(\phi(s)-\phi(0))^2} \simeq a\left(1 + \frac{1}{2}(\phi(s)-\phi(0))^2\right)$$

for small $|(\phi(s)-\phi(0))|$



1 SLIDING CONTROL

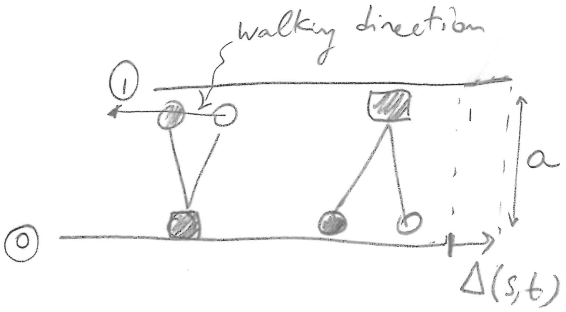
See Prost & Julicher (1997); Camalet & Julicher (2000); Riedel-Kruse (2007)
Hilfinger (2009)

The basic idea is:

- $\dot{\Delta}(s,t)$ is a proxy for local motor velocity
- from the local motor velocity one can infer the motor load
- The motor load will impact on the prob. of motor attachment. (Higher load = smaller # of engaged motor)

Simplified model: two filaments 0 & 1, a distance a apart.

- Motors are attached to either filament & walk on the other one.
- Motors walk always towards base of the opposite filament



Let's look @ the motors on 0:

The force per unit length that they produce @ (s,t) is

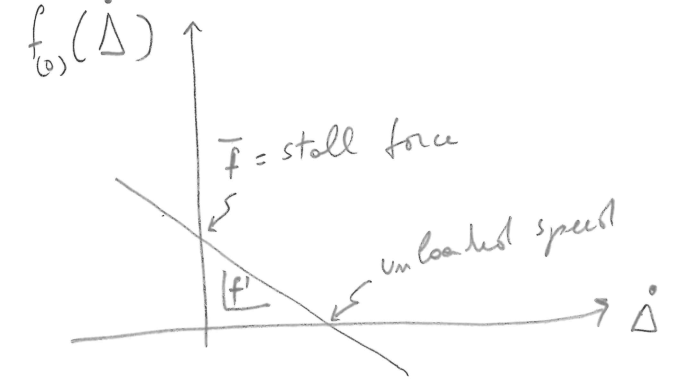
$$F_{0}(s,t) = -\rho P_{(0)} f_{(0)}$$

ρ = # motors per unit length

$P_{(0)}$ = probability that a 0 motor is engaged

$f_{(0)}$ = force generated by 1 0 motor

Assumption: $f_{(0)}$ & $\dot{\Delta}(t)$ are linked by the load-velocity relation of the molecular motor



$f_{(0)} \simeq \bar{f} - f'\dot{\Delta}$ | LINEAR APPROXIMATION... We don't know it in detail anyway!

Probability of motor being engaged will change in time according to

- $\frac{dp_{(0)}}{dt} = -K_{off}\, P_{(0)} + \underline{K_{on}}\,(1 - P_{(0)})$

  ASSUME CONSTANT

- $K_{off} = K_{off}(f_{(0)}) \underset{\text{"Arrhenius"}}{=} k_o\, e^{\frac{f_{(0)}}{f_c}} = k_o\, e^{\frac{\bar{f}}{f_c} - \frac{f'\dot{\Delta}}{f_c}} \simeq \bar{K}_{off}\left(1 - \underbrace{\frac{f'\dot{\Delta}}{f_c}}\right)$

  assumed small

  i.e. $\left|\frac{(K_{off} - \bar{K}_{off})}{\bar{K}_{off}}\right| \ll 1$

- Define $\underline{\bar{P} = \frac{K_{on}}{\bar{K}_{off} + K_{on}}}$; $\underline{\tau = \frac{1}{K_{on} + \bar{K}_{off}}}$

and $\underline{P_{(0)}(s,t) = \bar{p} + \delta p(s,t)}$ to get

$$\frac{d\,\delta p}{dt} = \frac{1}{\tau}\underbrace{\left[\frac{\bar{p}(1-\bar{p})f'}{f_c}\frac{\partial \Delta}{\partial t} - \delta p\right]}$$

δp converges to $\left(\frac{\bar{p}(1-\bar{p})}{f_c}\frac{\partial \Delta}{\partial t}\right)$ w/ timescale τ.

We still need to account for the ① motors!

- A displacement $\Delta(s,t)$ for the ⓪ motors is equivalent to a displacement $-\Delta(s,t)$ for the ① motors;
- the force generated by the ① motors is oriented in the opposite way of that from the ⓪ motors

$$\Downarrow$$

(i) $$-f_{①}(-\dot{\Delta}) = f_{⓪}(\dot{\Delta})$$

$$\Downarrow$$

$$\underline{f_{①}(\dot{\Delta}) = -\bar{f} - f'\dot{\Delta}}$$

(ii) $$P_{①}(-\Delta) = P_{⓪}(\Delta) = \bar{p} - \underline{\underline{\delta p}}$$

same δp as before.

The total force per unit length is then

$$\underline{F = F_{(0)} + F_{(1)}} = -\rho P_{⓪} f_{⓪} - \rho P_{①} f_{①}$$

$$= \underline{-2\rho\bar{f}\,\delta p(t) + 2\rho\,\bar{p}\,f'\dot{\Delta}(t)} \quad \leftarrow \text{to } \mathcal{O}(\dot{\Delta})$$

Using

- $\mu(s,t) = a\,F(s,t)$ ⟵ internal torques (active)

- $\Delta(s,t) = \underbrace{\Delta_0(t)}_{\text{possible basal sliding}} + a\left(\phi(s,t) - \phi(0,t)\right)$ ⟵ we saw this before

possible basal sliding: NOT WELL KNOWN

we get

$$
\begin{cases}
EI\,\dfrac{\partial^4\phi}{\partial s^4} - a\,\dfrac{\partial^2 F}{\partial s^2} + C_N\,\dfrac{\partial\phi}{\partial t} = 0 \\[2ex]
F(s,t) = -2\rho\bar{f}\,\delta p(s,t) + 2\rho\bar{p}\,f'\,\dfrac{\partial\Delta}{\partial t} \\[2ex]
\Delta(s,t) = \Delta_0(t) + a\left(\phi(s,t) - \phi(0,t)\right) \\[2ex]
\dfrac{\partial\,\delta p(s,t)}{\partial t} = \dfrac{1}{\tau}\left[\dfrac{\bar{p}(1-\bar{p})}{f_c}\,f'\,\dfrac{\partial\Delta}{\partial t} - \delta p(s,t)\right]
\end{cases}
$$

⟵ MOMENTUM BALANCE

⟵ MODEL FOR MOTOR REGULATION

(+ b.c.s)

(2) CURVATURE CONTROL

See Hines & Blum (1978) & more recently e.g. Bayly & Wilson (2015)

Based on a GUESS for the relation b/w curvature & active bending moments.

Start w/ the momentum balance eqn:

$$\frac{\partial M_{in}}{\partial s} + N = \mu$$

$\mu = \mu_d + \mu_m$

μ_d = active bending from the dyneins

μ_m = extra bending moment due to nexins & radial spokes

μ_d is ASSUMED to obey:

- $$\frac{\partial \mu_d}{\partial t} = \frac{1}{\tau}\left(m_0 \frac{\partial \phi}{\partial s} - \mu_d(s,t)\right)$$

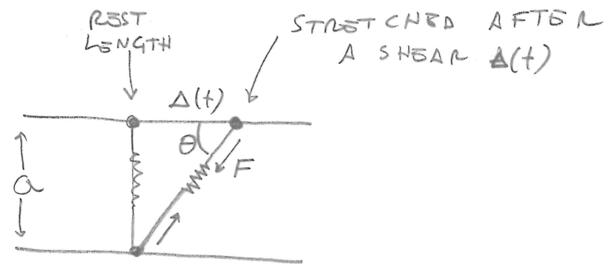
$$\mu_d \xrightarrow[t\to\infty]{} m_0 \frac{\partial \phi}{\partial s}$$ $\Rightarrow$ so active bending converges to something $\propto$ local curvature w/ a timescale τ.

$$\Downarrow$$

$$\boxed{\mu_d \sim \frac{\partial \Delta}{\partial s}}$$

NOTICE DIFFERENCE W/ SLIDING REGULATION!

- $\mu_m \sim -aF\cos\theta$



$$= -a\,K\left(\sqrt{a^2+\Delta^2} - a\right)\frac{\Delta}{\sqrt{a^2+\Delta^2}}$$

$$= -ak\Delta\left(1 - \frac{1}{\sqrt{1+(\Delta/a)^2}}\right) \Longrightarrow \underline{\mu_m \sim \Delta^3}$$

Since $\mu_m \sim \Delta^3$, it will NOT ENTER in our (linear) equations of motion!

Overall

$$\begin{cases} EI \dfrac{\partial^4 \phi}{\partial s^4} - \dfrac{\partial^2 \mu_d(s,t)}{\partial s^2} + C_N \dfrac{\partial \phi}{\partial t} = 0 \\ \dfrac{\partial \mu_d(s,t)}{\partial t} = \dfrac{1}{\tau}\left(m_0 \dfrac{\partial \phi}{\partial s} - \mu_d(s,t) \right) \end{cases}$$

(+ b.c.s)

Often (see e.g. Bayly & Wilson 2015) τ is considered "short" wrt beating period, and $\mu_d(s,t)$ is simply slaved to ϕ : $\mu_d(s,t) = m_0 \dfrac{\partial \phi}{\partial s}$

$$\downarrow$$

$$EI \frac{\partial^4 \phi}{\partial s^4} - m_0 \frac{\partial^3 \phi}{\partial s^3} + C_N \frac{\partial \phi}{\partial t} = 0$$

Notice that w/o the elastic bending component ($EI\, \partial_s^4 \phi$) the eqn can sustain "pure" waves $\phi \sim e^{i(ks-\omega t)}$ but w/ that term then are all decaying (or exploding if $\omega \to -\omega$).

The waves that come out will be more complicated.

(3) GEOMETRIC CLUTCH

See Lindemann 1994 (two papers) & 2002 ; Bayly & Wilson (2014).

We will NOT derive the GC equations (quite long!). If you are interested, look at Bayly & Wilson, Biophys J. 1756:107 (2014).

(The G.C. was originally introduced by Lindemann as a numerical simulation, and only recently recast as a PDE)

BASIC IDEA

- Bending causes slight deformations in the cross section of the axoneme (compression & extension) (Experimental estimates: changes by up to 25%. LINDEMANN & MITCHELL, CELL MOTIL CYTOSKEL. (2007))

These deformations affect the engagement of dyneins across microtubules and therefore the force they can generate

Briefly:

- $\underbrace{\mu(s,t)}_{\text{Local "active" bending}} = a \underbrace{f(s,t)}$ → Force generated by the dyneins, linkers & (potentially) viscous intra-axonemal forces. (anything that is not just elastic µtubule bending)

- $f(s,t) = \underbrace{-\bar{f} A(s,t)}_{\text{MOTOR ACTIVITY}} + \underbrace{2K_T a(\varphi(s,t)-\varphi(0,t)) + 2b_T a \frac{\partial\varphi}{\partial t}}_{\text{POSSIBLE VISCOELASTICITY W/IN AXONEME}}$

(Terms in $\Delta(s,t)$ & $\dot{\Delta}(s,t)$)

$\bar{f}$ = max "effective" force per unit length

it depends on how many dyneins actually engage (max #)

- $A(s,t)$ couples dynein activity to curvature:

$$\frac{\partial A}{\partial t} = -\frac{1}{\tau_N} A(s,t) + \underbrace{C_s (L-s) \frac{\partial \varphi}{\partial s}}_{*}$$

INTRINSIC TIMESCALE OF DYNEIN RECONFIG.

$*$ C_s = control parameter that couples curvature $\left(\frac{\partial \varphi}{\partial s}\right)$ to dynein activity

$(L-s)$ = comes from assumption of ZERO interdoublet tension at the tip.

Altogether

$$\begin{cases} EI \dfrac{\partial^4 \varphi}{\partial s^4} + C_N \dfrac{\partial \varphi}{\partial t} = a \dfrac{\partial^2 f}{\partial s^2} \\[2ex] f(s,t) = -\bar{f} A(s,t) + 2K_T a\big(\varphi(s,t) - \varphi(0,t)\big) + 2b_T a \dfrac{\partial \varphi}{\partial t} \\[2ex] \dfrac{\partial A}{\partial t} = -\dfrac{1}{\tau_N} A(s,t) + C_s (L-s) \dfrac{\partial \varphi}{\partial s} \end{cases}$$

+ b.c.s & initial conditions

For a good (but lengthy) discussion of the eigenvalue problems of these models, see

Bayly & Wilson, Interface (2015).