Modelling of the motility of Trypanosomes

Proposed by: Centre of Mathematical Biology, Oxford

Instructor: Heike Gramberg

Madrid, 14-21 June 2010

Outline

Introduction

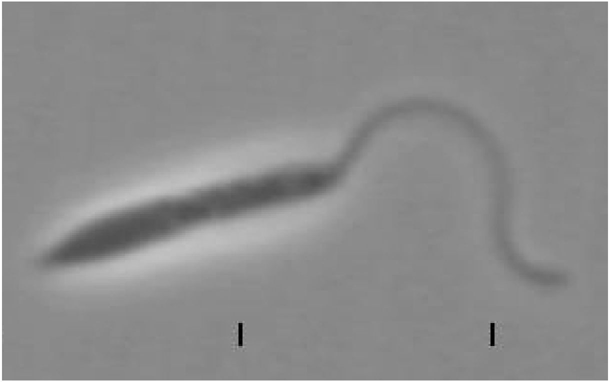
- What are Trypanosomes?
  - Group of kinetoplastid protozoa
  - Charcacterized by having one flagellum
  - Parasitic
- Why do we want to study them?
  - Cause serious diseases such as African sleeping sickness and Chagas disease
  - Not much is known about their dynamics
- How do we study them?
  - Imaging and analyis of beating patterns
  - Measurement of mechanical properties such as bending stiffness
  - Mathematical modelling of flagellar beating

Examples of Trypanosomes

Crithidia

Examples of Trypanosomes

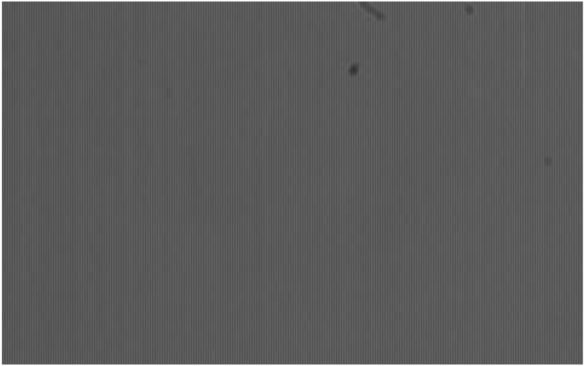
Leishmania



Examples of Trypanosomes

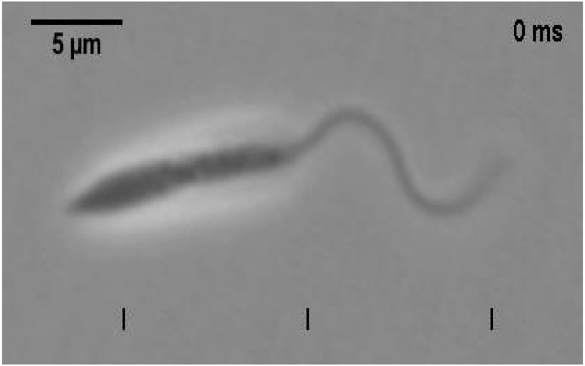
Trypanosoma (bloodstream form)

Flagellar beating patterns: straight ahead



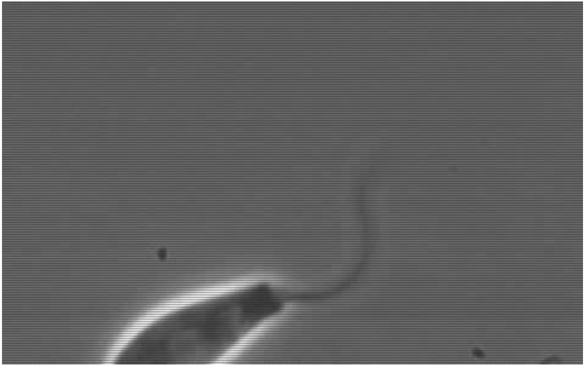
Planar beat pattern
Cell pulls itself through the fluid

Flagellar beating patterns: straight ahead



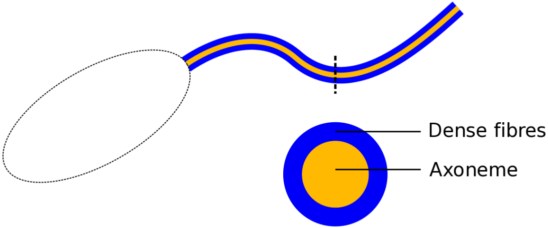
Travelling wave from tip to base of the flagellum

Flagellar beating patterns: turning



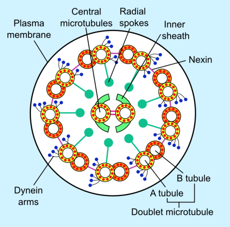
Cilia type beat pattern to turn around

Mechanics of flagellar beating



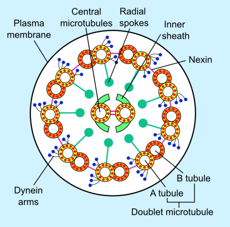
- Flagellum consists of an axoneme surrounded by dense fibres
- Axoneme is responsible for active bending of the flagellum
- Fibres five flagellum stiffness against bending

Mechanics of flagellar beating



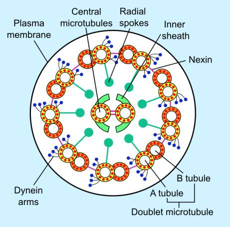
- Main feature of axoneme is a structure of 9+2 inextensible microtubules
- Dynein motors cause a sliding force between two neighbouring outer microtubules
- Relative displacement between fibres in axial direction

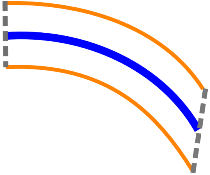
Mechanics of flagellar beating



- Main feature of axoneme is a structure of 9+2 inextensible microtubules
- Dynein motors cause a sliding force between two neighbouring outer microtubules
- Relative displacement between fibres in axial direction

Mechanics of flagellar beating





- Main feature of axoneme is a structure of 9+2 inextensible microtubules
- Dynein motors cause a sliding force between two neighbouring outer microtubules
- Relative displacement between fibres in axial direction

Strategy

- Main assumption: at any time t we have a force balance

$$\mathbf{F}_{\text{drag}} + \mathbf{F}_{\text{bend}} + \mathbf{F}_{\text{sliding}} = 0$$

- The problem is split into three parts
    1. Internal forces in the flagellum
    2. Viscous drag forces on the cell body
    3. Viscous drag forces on the flagellum

Internal forces in the flagellum

- Principle of minimal potential energy

$$\mathbf{F}_{\text{bend}} + \mathbf{F}_{\text{sliding}} = -\frac{\partial}{\partial s}\left(E\mathbf{X}_{sss} - fd\mathbf{n} - T\mathbf{t}\right)$$

- Boundary conditions at $s = 0, L$
  - Force balance: $\mathbf{F}_{\text{ext}} = E\mathbf{X}_{sss} - fd\mathbf{n} - T\mathbf{t}$
  - Balance of angular moment

$$\mathbf{M}_{\text{ext}} \times \mathbf{t} = -E\mathbf{X}_{ss} - d\int_0^L f(s,t)ds\mathbf{n}$$

Viscous drag forces on the flagellum

- Use resistive force theory to approximate viscous drag forces on flagellum

$$\mathbf{F}_{\mathrm{vis}}(s,t) = \left(\xi_{\parallel}\mathbf{tt} + \xi_{\perp}\mathbf{nn}\right)\left(\mathbf{U}_{\mathrm{ext}}(\mathbf{X}(s,t),t) - \dot{\mathbf{X}}(s,t)\right)$$

where

$$\xi_{\perp} = \frac{4\pi\mu}{\log\left(\frac{4\lambda}{d}\right) + \frac{1}{2}} \qquad \xi_{\parallel} = \frac{2\pi\mu}{\log\left(\frac{4\lambda}{d}\right) - \frac{1}{2}}$$

and λ is the wavelength of the undulations

- For $\lambda \gg d$: $\xi_{\perp} \approx 2\xi_{\parallel}$

Objectives during this modelling week

- Study the simplified case where the displacement of the flagellum is small compared to the length of the flagellum
    - Given a beating pattern, what is the velocity of the flagellum?
    - Given a shear force distribution, what is the shape of the flagellum?
    - What is the influence of the various material parameters on the velocity and the shape?