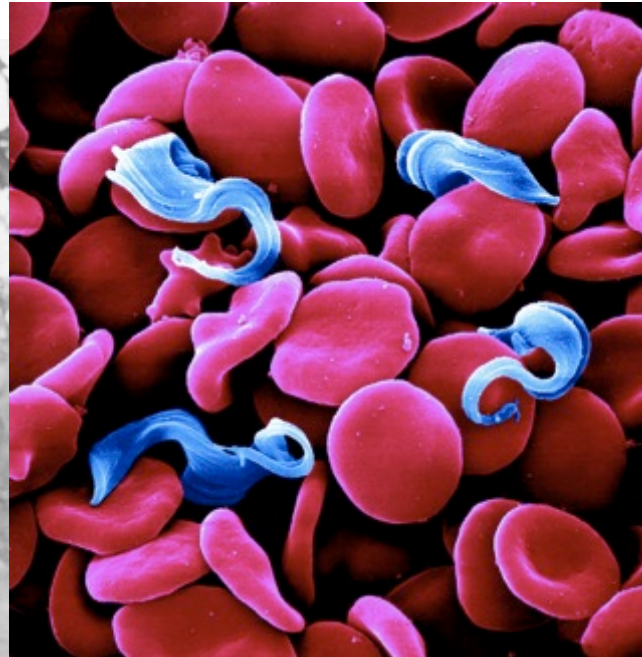
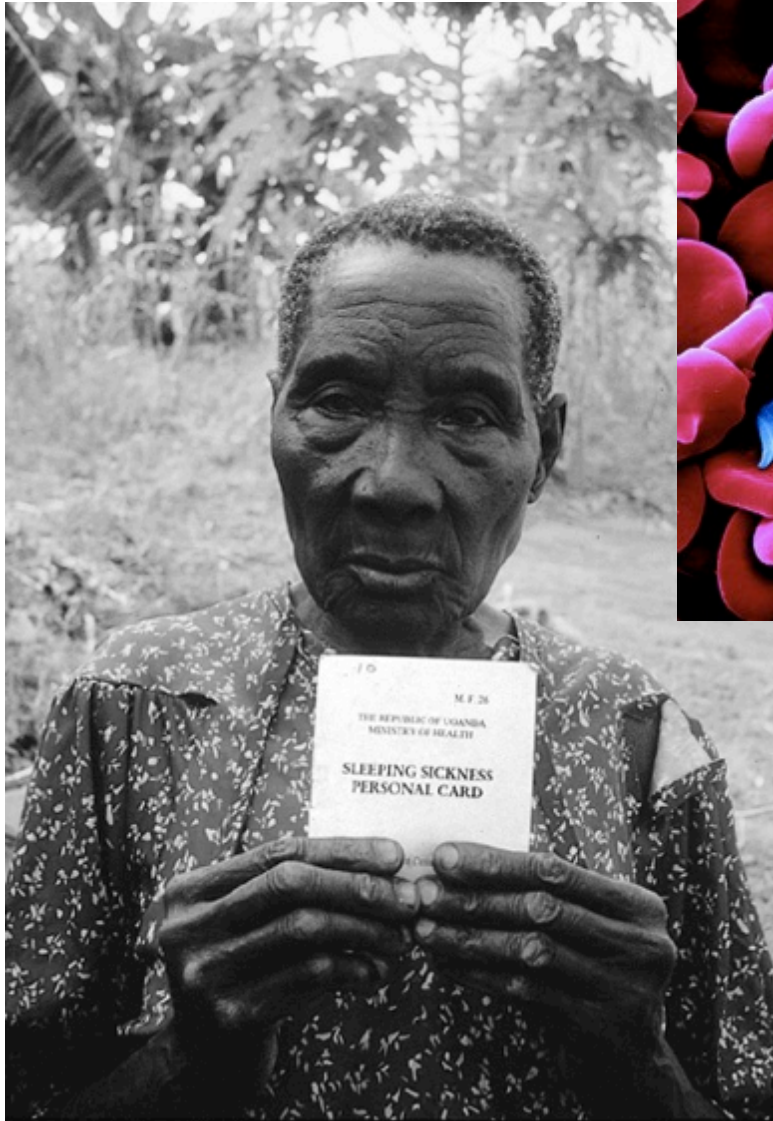


The Cryo-ET Structure of the *Trypanosoma brucei* Flagella Accounts for its Bihelical Motion

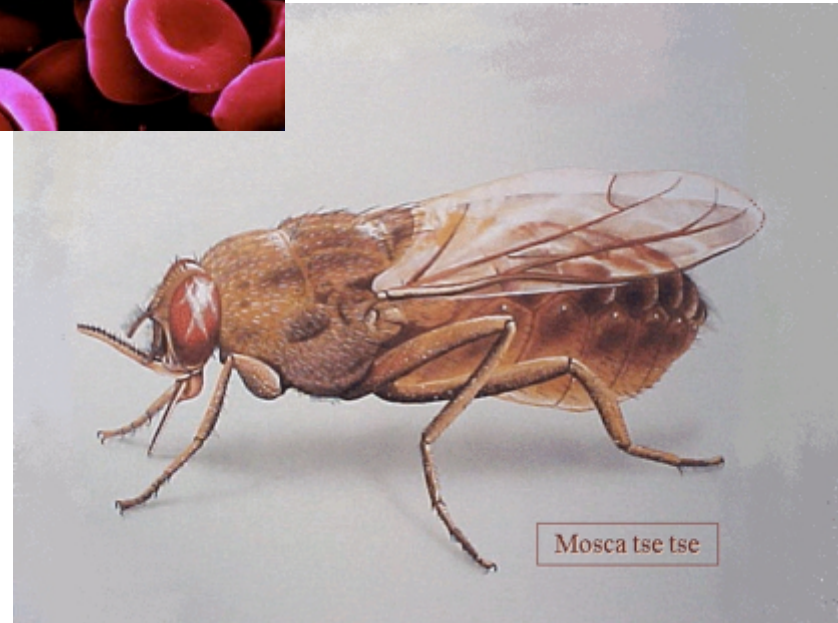
M. F. Schmid, A.Y. Koyfman, C. J. Fu, H. Khant, L. Ghieratmand, D. Huang, C. Y. He, W. Chiu - NCMI, Baylor College of Medicine, & N.U.S., Singapore

Proc Natl Acad Sci U S A. (2011) 108:11105-8
PMID: 21690369

African trypanosomiasis (sleeping sickness)



The tsetse fly transmits
African trypanosomiasis



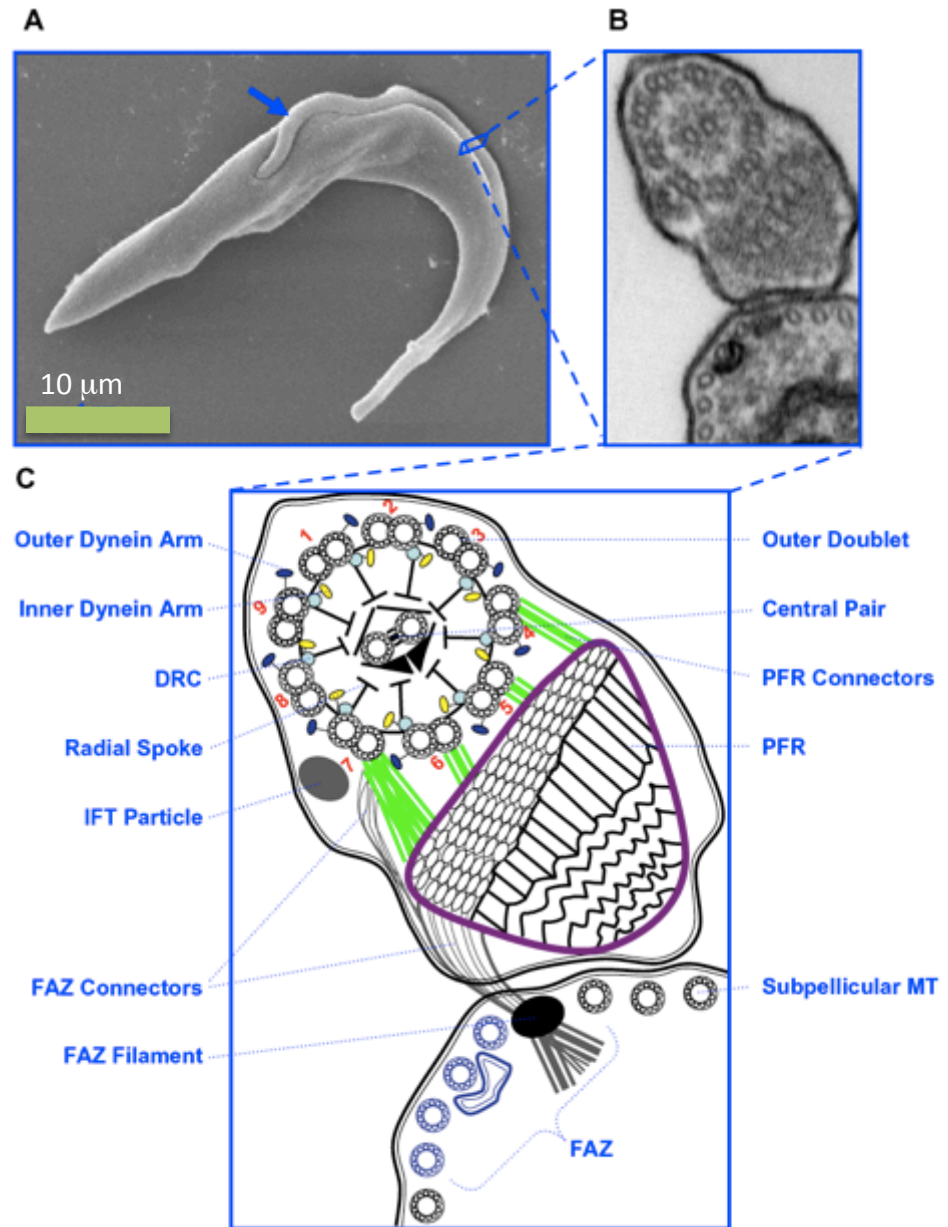
Mosca tse tse

Distribution of the Tse-tse Fly



Trypanosoma brucei

- African Sleeping Sickness
- *Trypanosoma* from the Greek words *trupanon*, meaning 'borer' and *soma*, 'body'
- Flagellum
- 500 nm wide
- 15 μm long
- 3 main components
- **Axoneme**
- **Connectors**
- **Paraflagellar (PFR) Rod**
- ✓ Composed of 2 major proteins:
- ✓ PFR-A of 69 kDa
- ✓ PFR-B of 73 kDa
- ✓ These proteins are predicted to be coiled coil

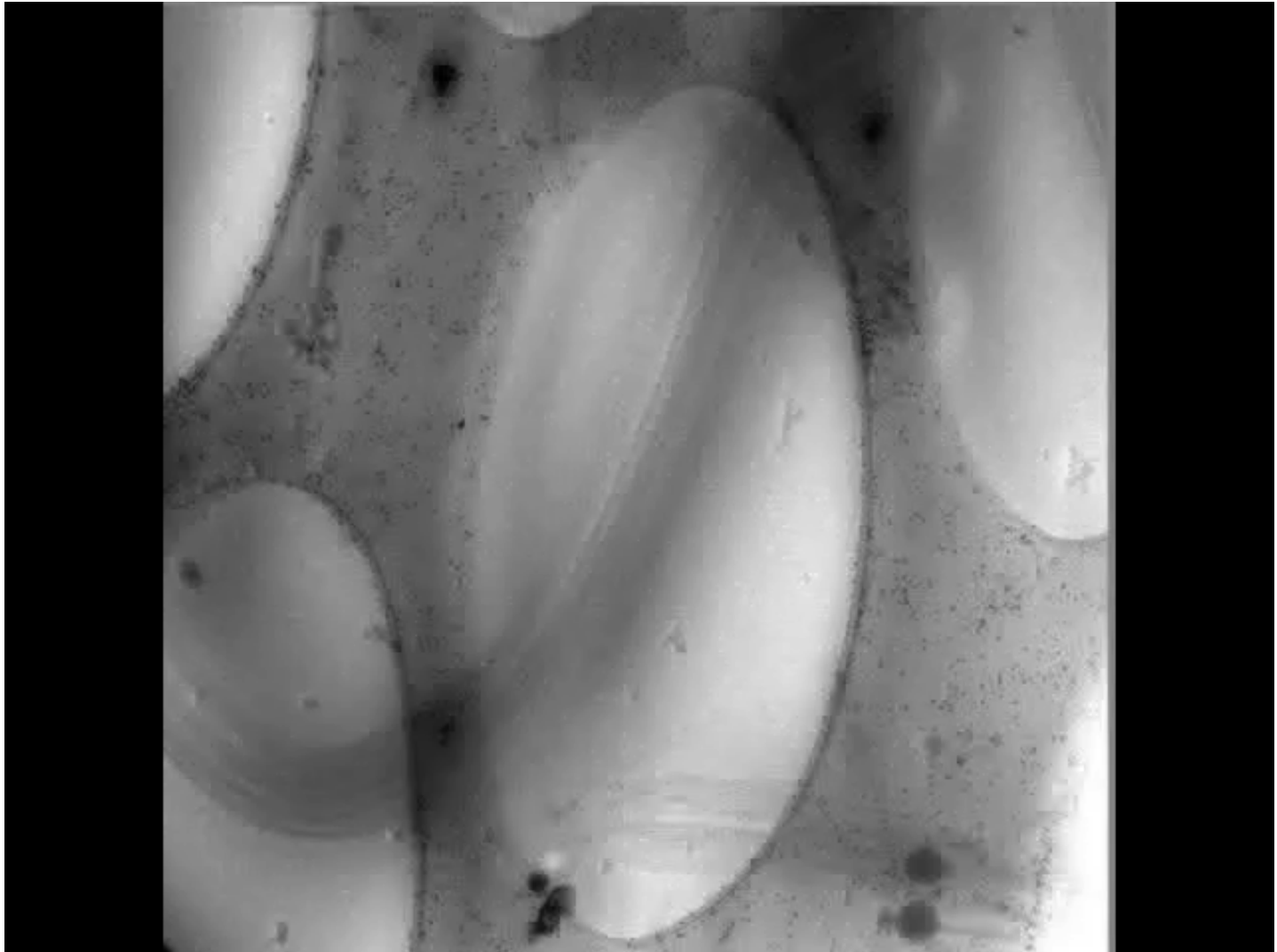


1. How Does it Move?

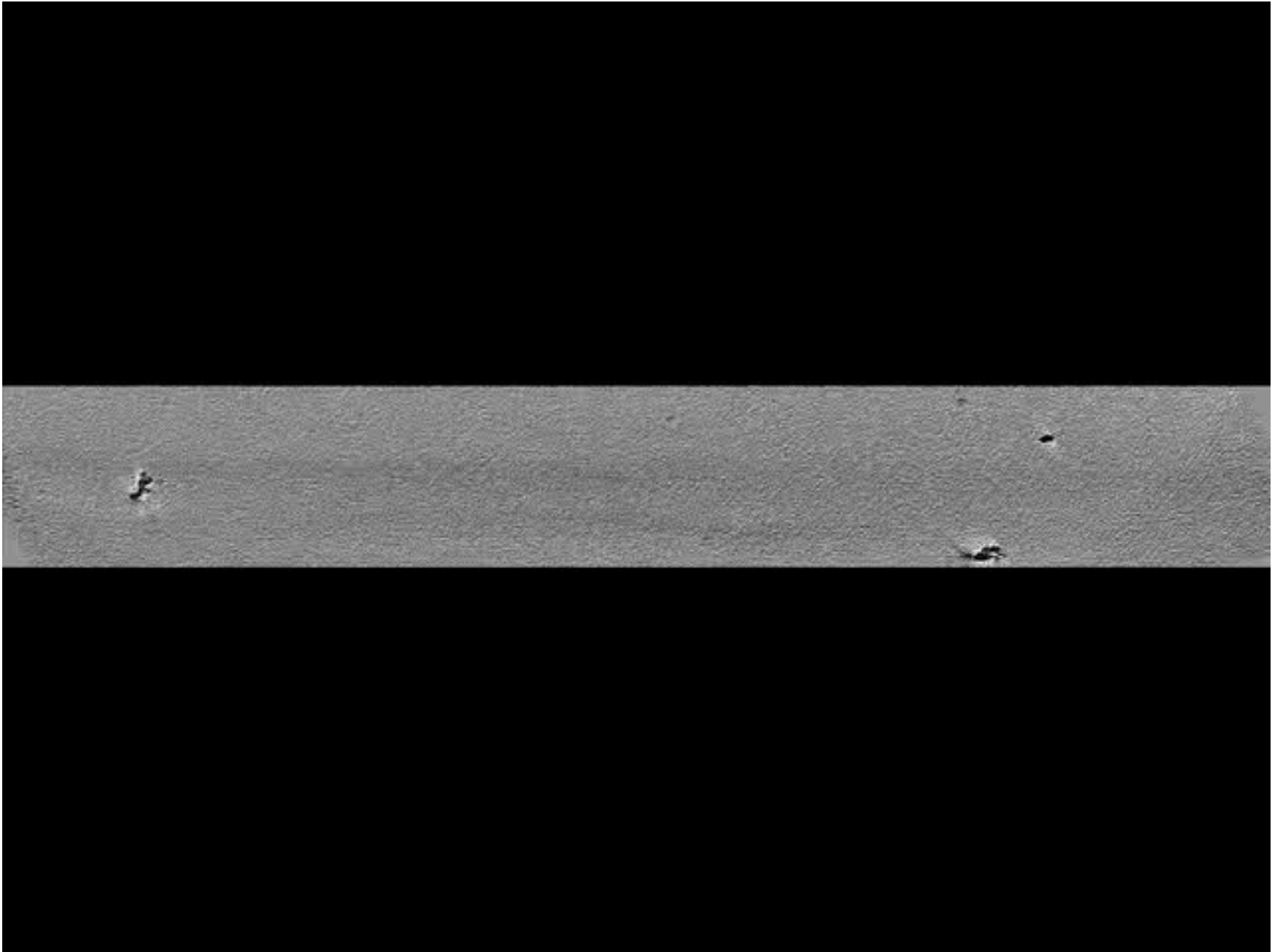


Bihelical Motion

2. What does the flagellum look like?

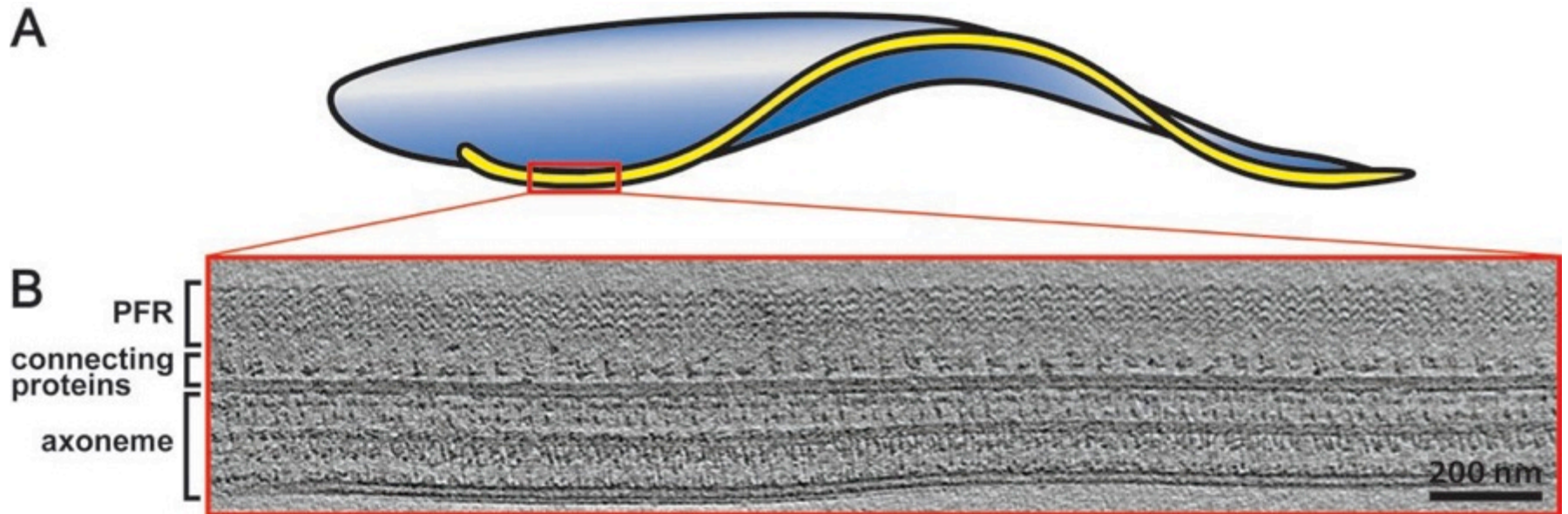


Tilt Series: 2° , $\pm 60^\circ$, $>5\mu\text{m}$ defocus, SerialEM



Tomogram, using IMOD, gold Fiducials

Relationship of the flagellum to the Cell



Averaged structures from 5 tomograms

*The Flagellum of
Trypanosoma brucei*

A66A3D9

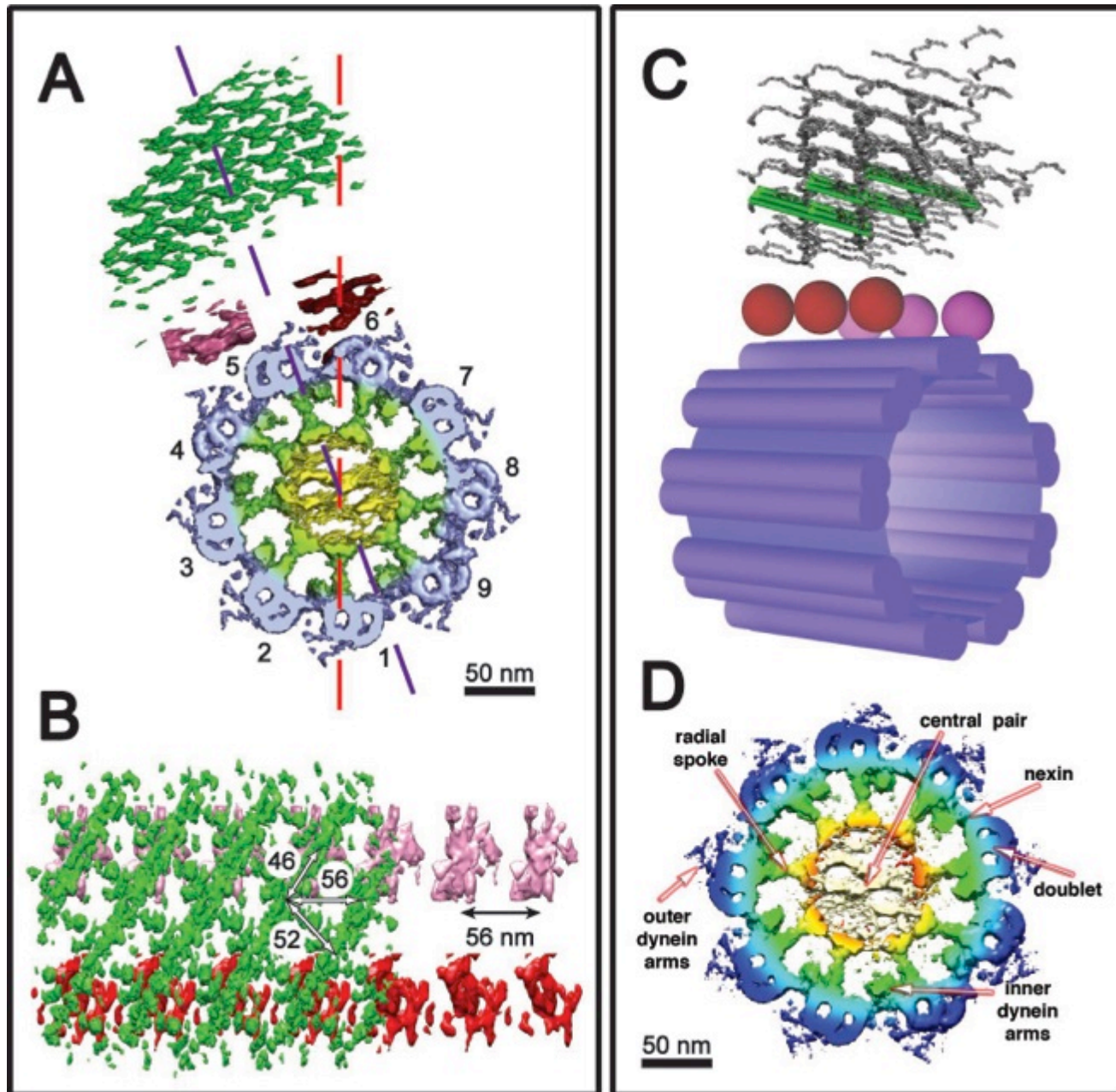
Dynamics: Structures from bent/straight Flagella



P66A1D6

Bent Flagella --> change in unit cell angles

3. Connect structure to dynamics

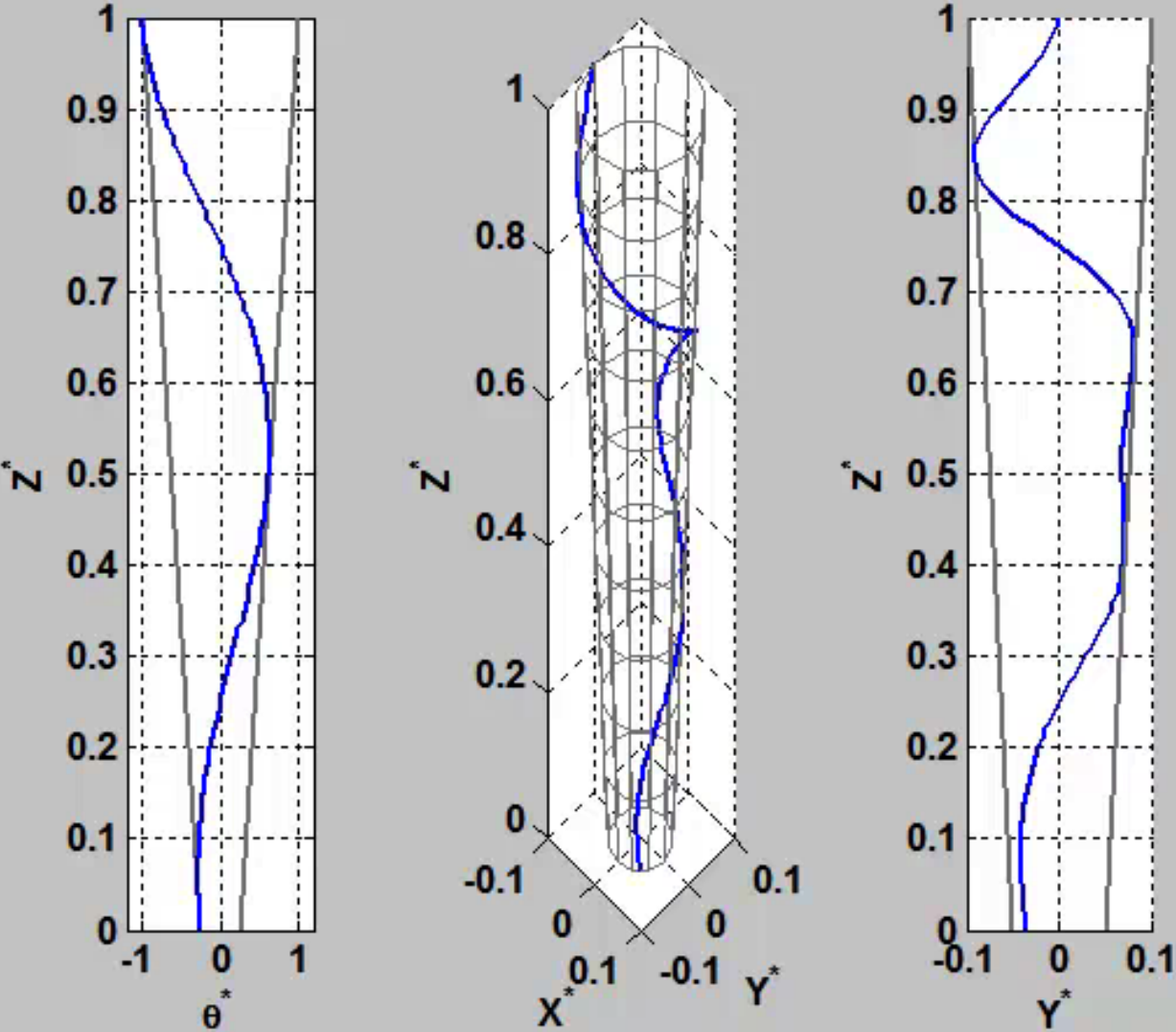


4. A Simple Mechanical Model

Modeling Flagellar Motion

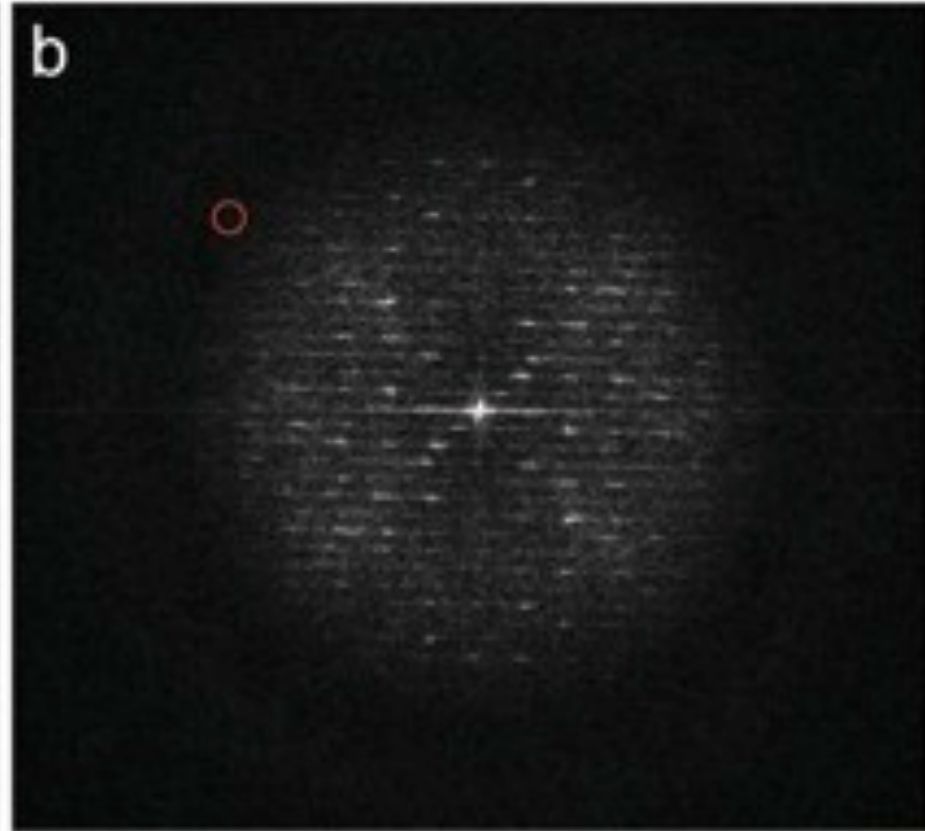
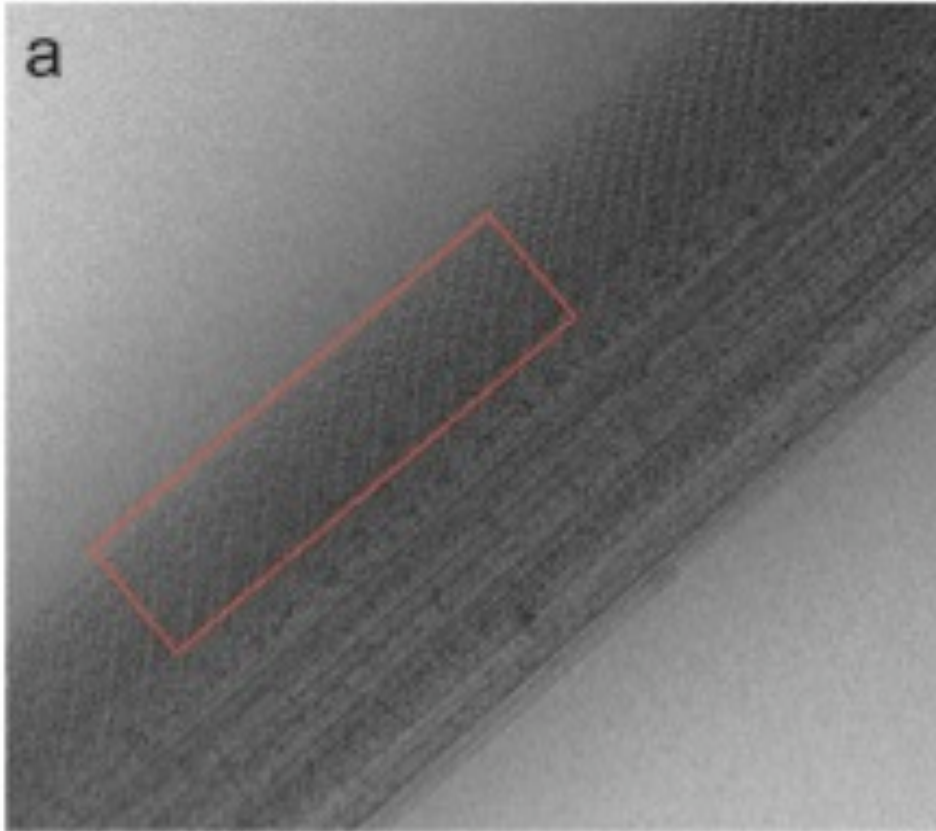
A66A4D3

5. Toward a Mathematical/Mechanical Model



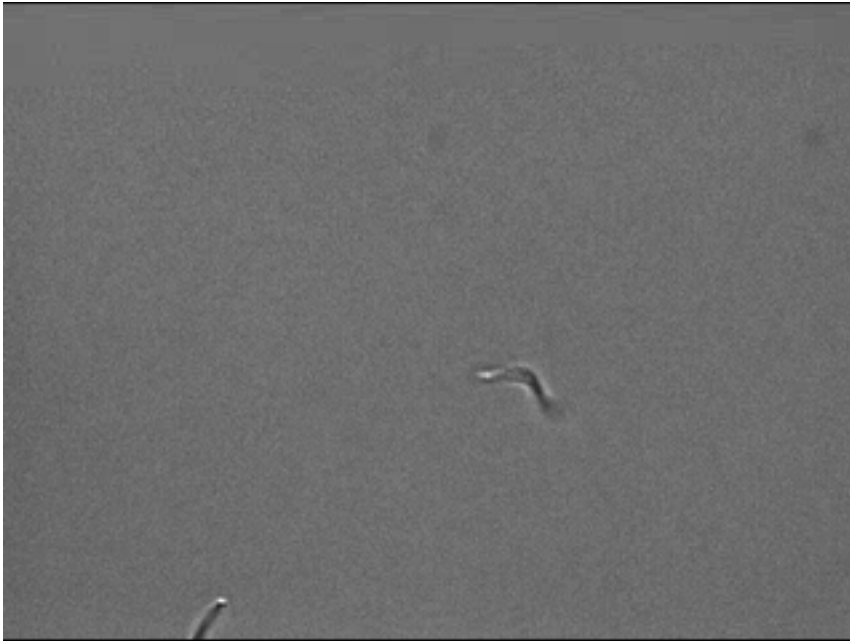
Mark Bathe - MIT

6. Toward Higher Resolution

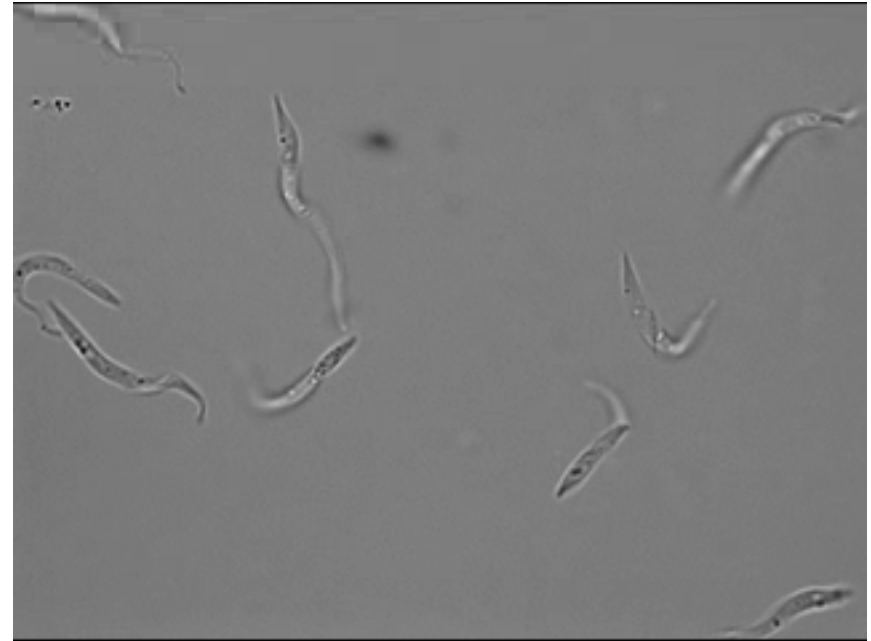


Prospects for Therapeutics

WT *Trypanosoma brucei*
Movement



Mutant *Trypanosoma brucei*
Movement
(PFR-A knockout using RNAi)



Conclusions

- Determined the structure of the *Trypanosoma brucei* Flagellum
- Snapshots of the structure in the process of bending
- PFR is a crystal with flexible properties that can maintain connection to the axoneme
- Simple mechanical model that reproduces the bihelical motion of the flagellum
- Higher resolution – more realistic motion modeling incorporating axoneme and PFR dynamics
- More research necessary to determine therapeutic strategies