SECTION 1 : THE MOLECULES THAT GENERATE MOTION

LECTURE 3 : LINEAR MOTORS

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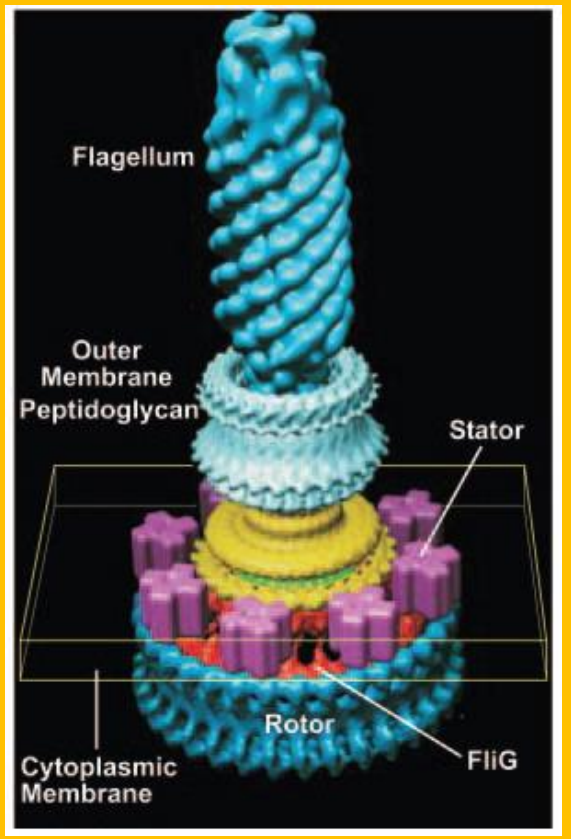
BB101 – Biology. Autumn Semester 2022-2023

RECALL FROM LAST LECTURE

ATP Synthase

Bacterial Flagellar Motor



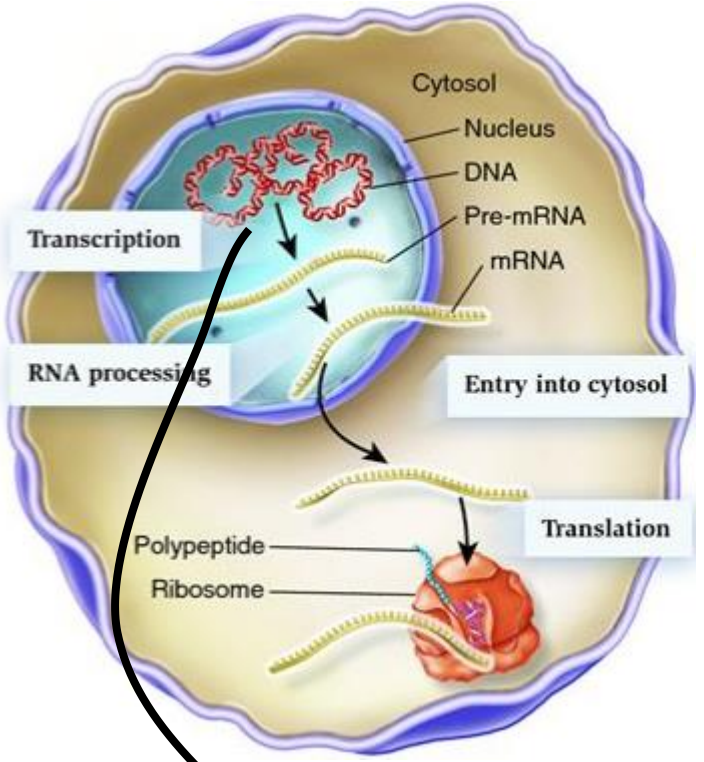
Resources :-

Molecular Biology of the Cell: Alberts
Chapter 4, Single Molecule Biology : Alex Knight
Physical Biology of the Cell by Philips, Kondev, Theriot, Garcia
J. Howard, Mechanics of Motor Proteins and the Cytoskeleton

What kind of motion do Motor Proteins generate ?

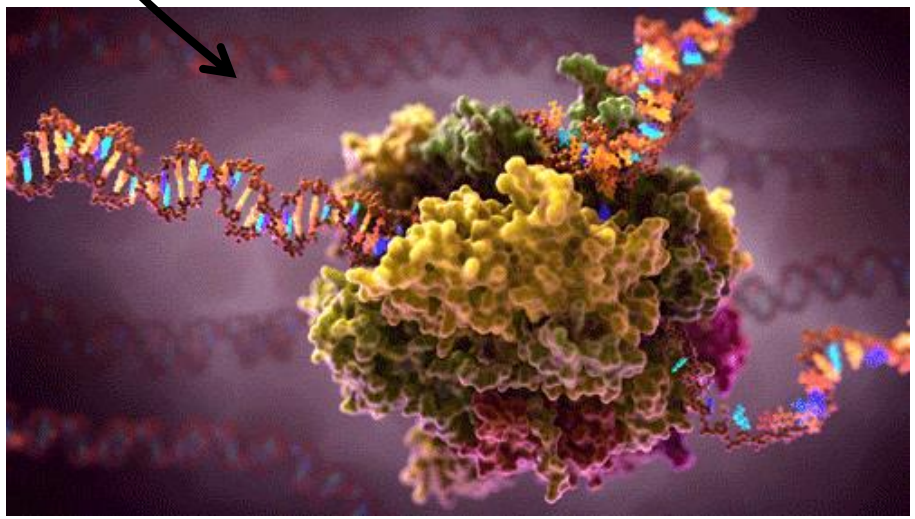
1) Linear Motors

DNA based	Use of Genetic Information (RNA Polymerase) Making Proteins (Ribosome)
Protein based	Moving muscles (Myosin) Moving things in the cell (Myosin, Kinesin, Dynein)



DNA Out

DNA In



RNA Out

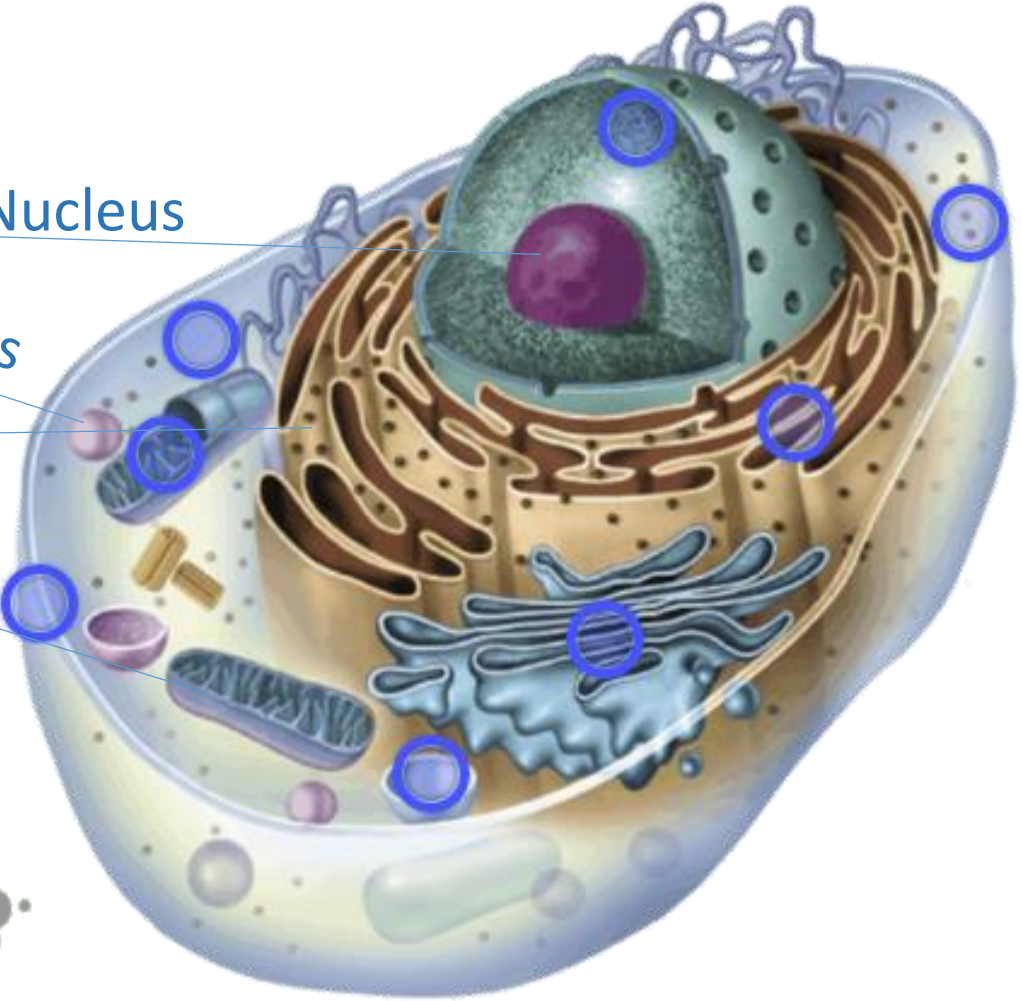
RNA Polymerase

Artofthecell

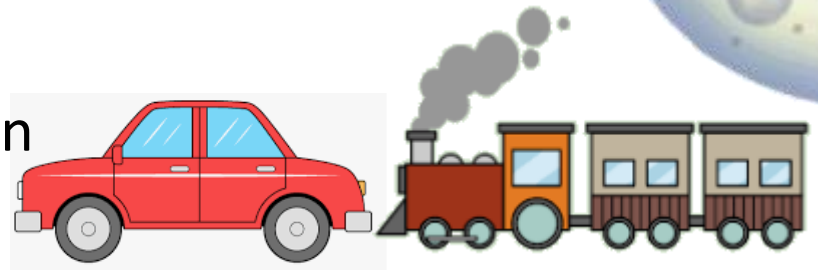
Protein based Motors and Transport Inside Cells

The Living Cell is like a City …

1. Recycling Plant — Lysosomes
2. Information/ Library — Nucleus
3. Power Station — Mitochondria
4. Factories — Ribosome
5. Roads — Microtubules, Actin (not shown)
6. Post Office (??)
7. City Limits (??)



How do you communicate between different parts of the City ?

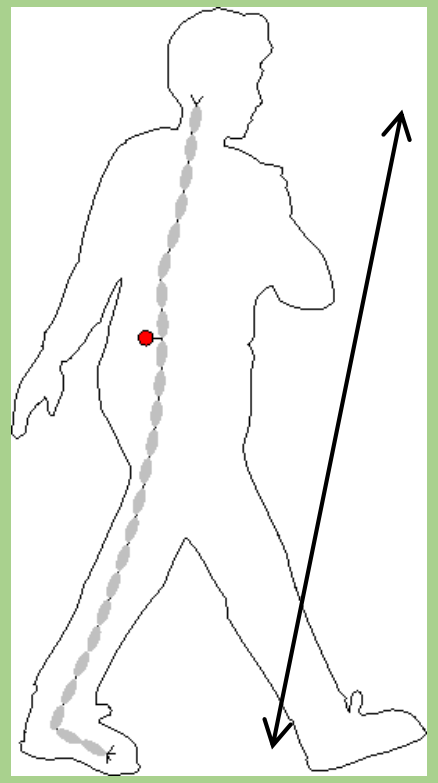


Would diffusion work ??

Time for diffusion ~ $x^2 / 2D$; $D = k_b T / 6\pi\eta R$

D = Diffusion constant; x = Distance moved; k_b = Boltzmann constant;

T = Temp; η = Viscosity; R = Dimension

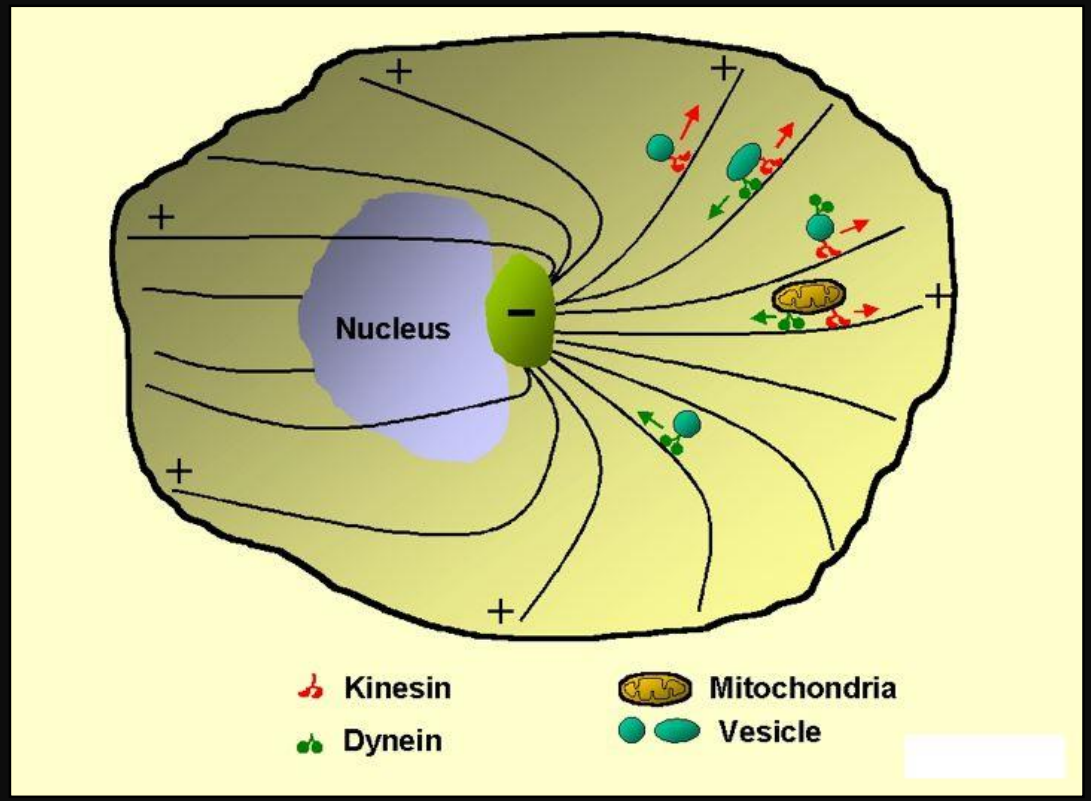


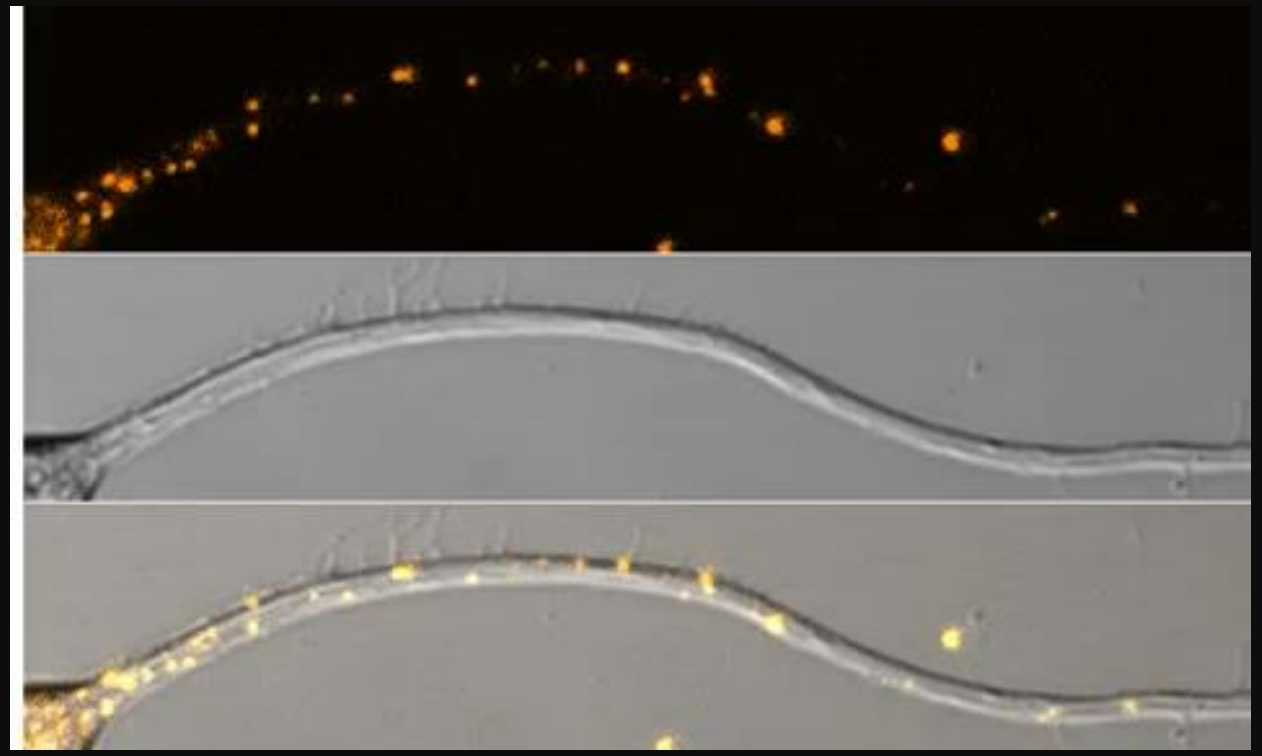
D ~ 1 micron^2/sec for 50 nm diameter synaptic vesicle in Neuron

To travel 1 metre :

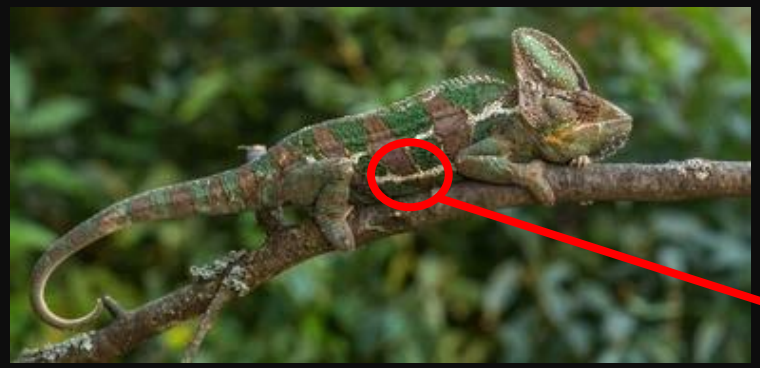
Need ~ 16,000 years

Need active transport

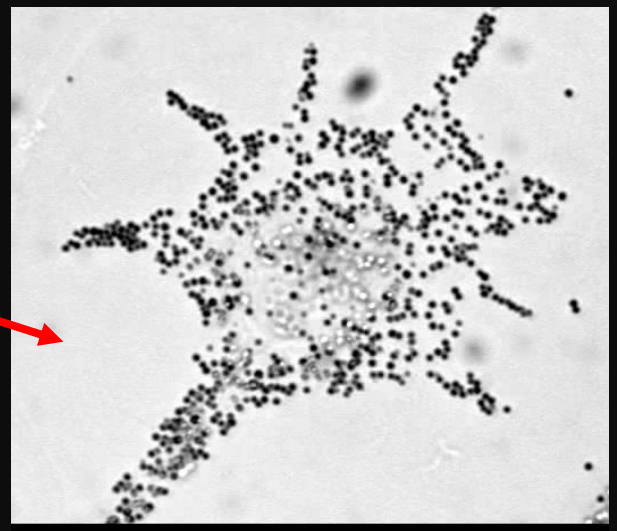


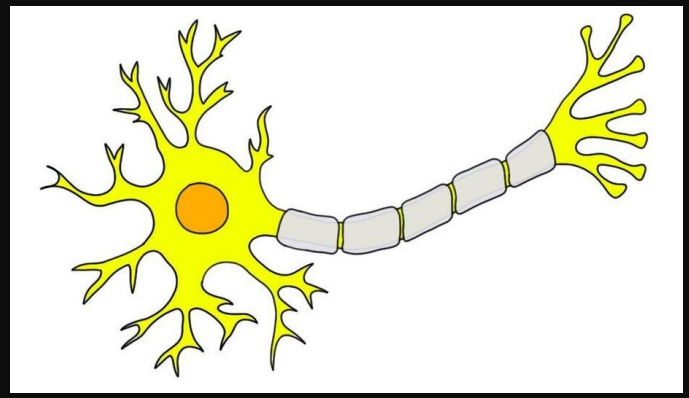


Transport In the axon of a Neuron
Courtesy : G. Goshima

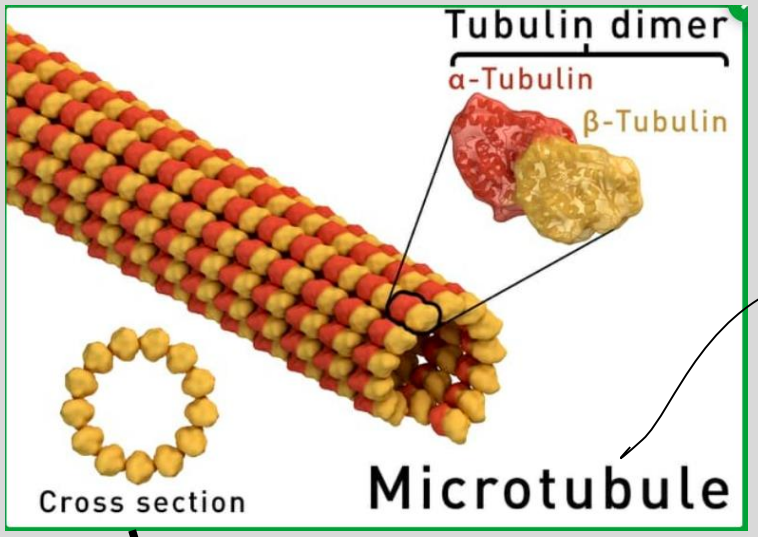


Melanocytes (Pigment cells) under skin
Rodionov et al, 2003, Deacon et al, 2005
For more Information go to ***LINK***

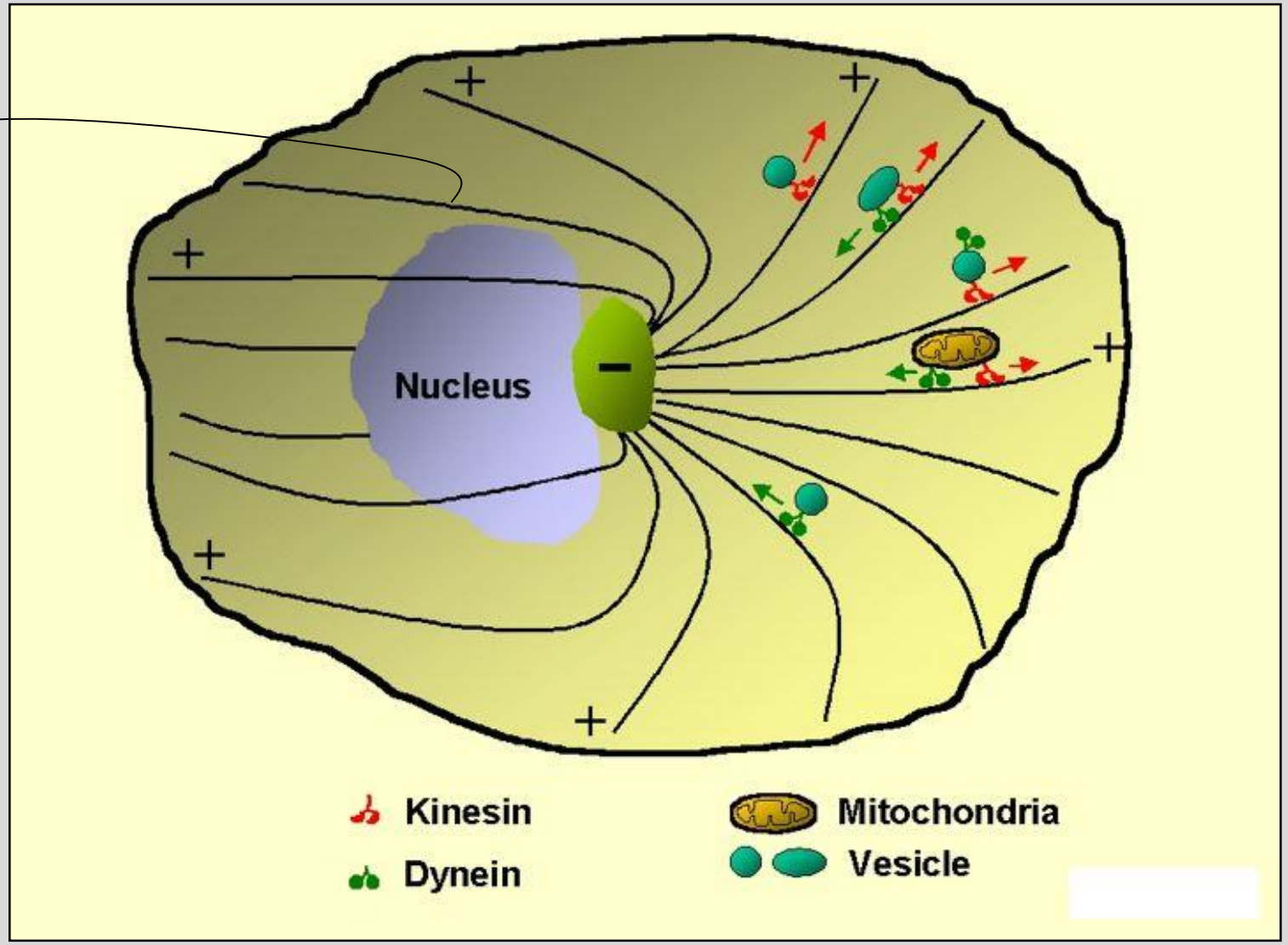




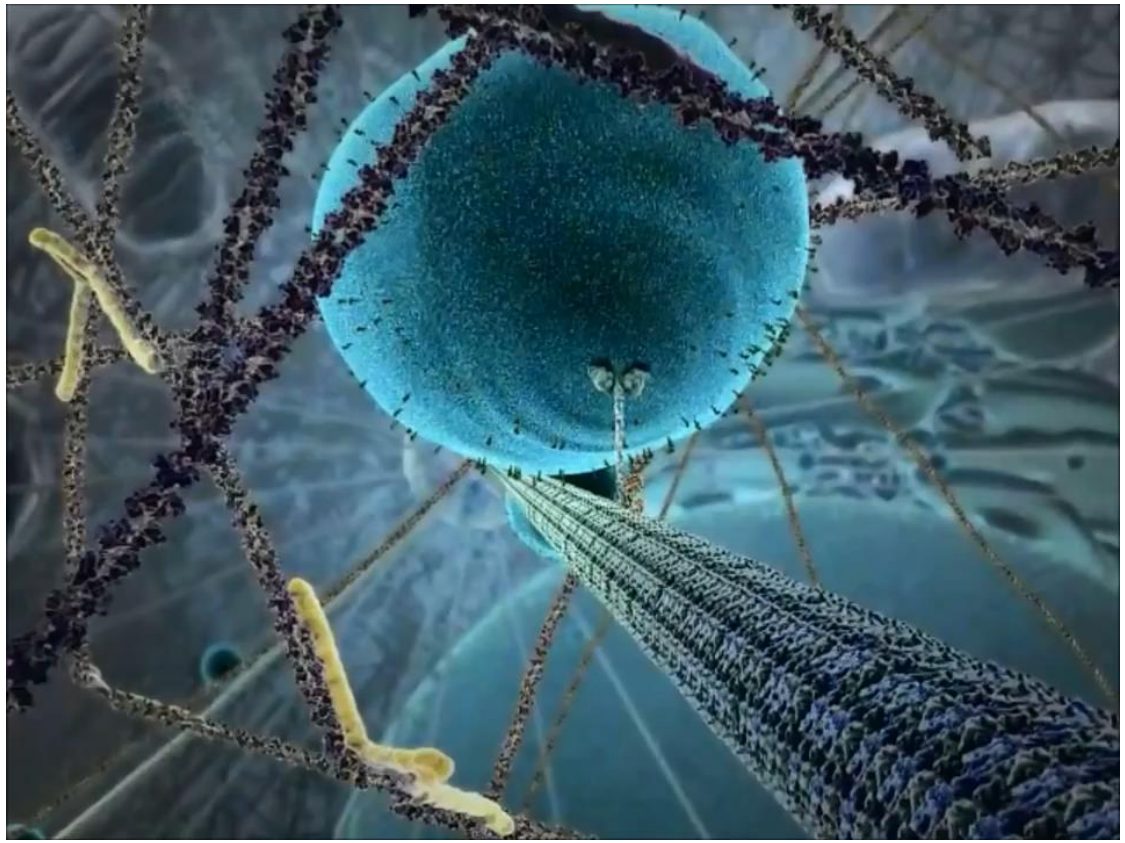
Linear Motors that Transport Products between the Factories of a Cell



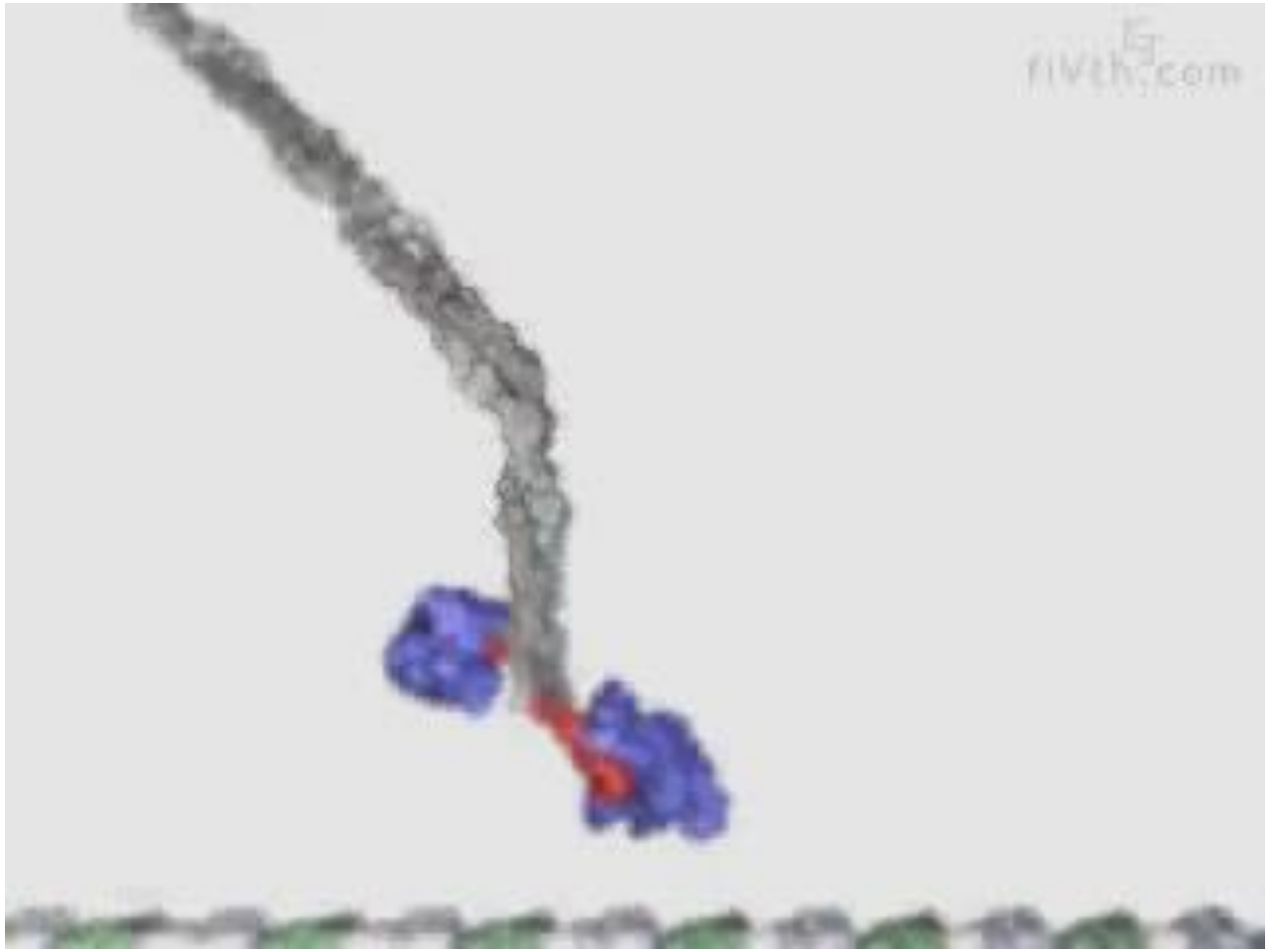
13 Protofilaments make up this microtubule



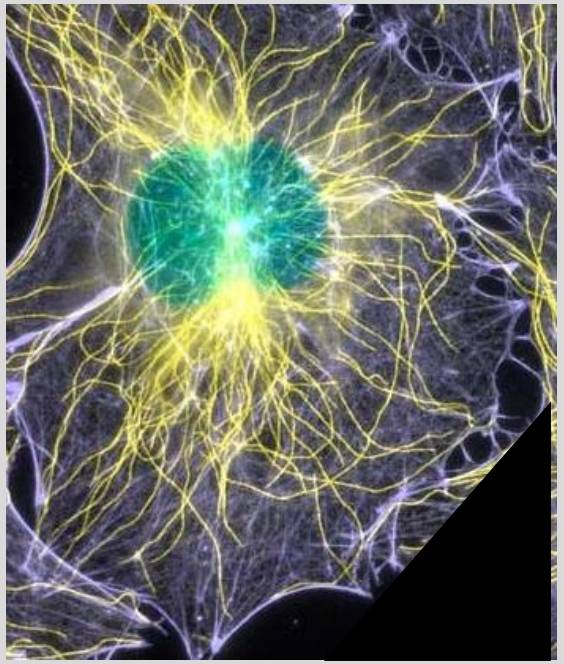
Movie : Inner Life of the Cell



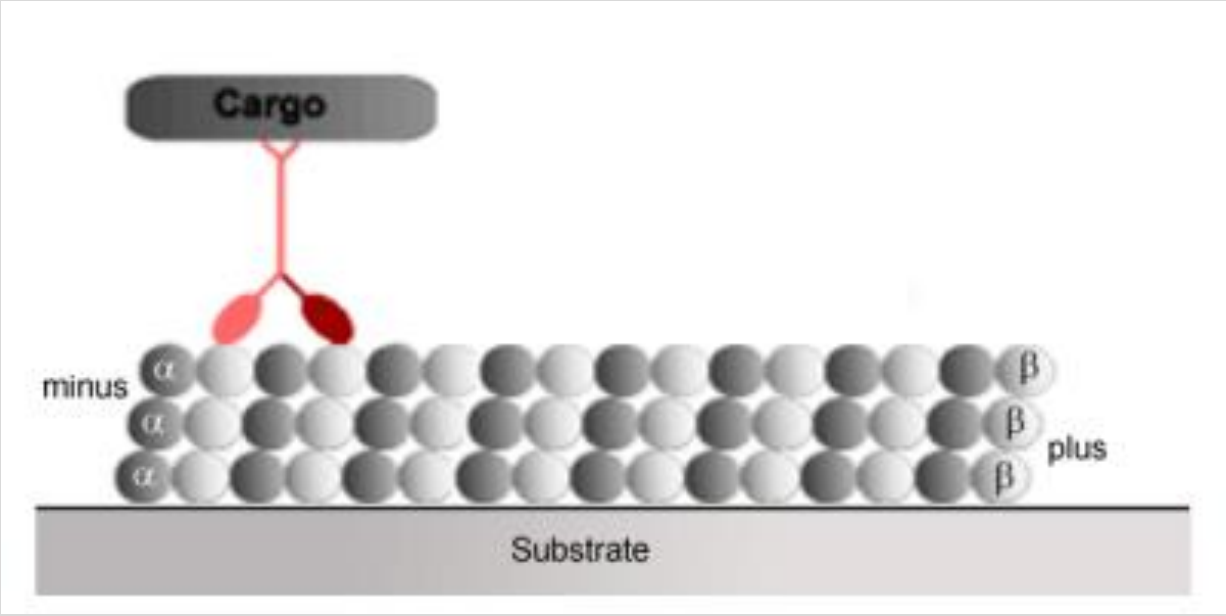
ATPase Cycle of Kinesin



Motors walk on stepping stones



http://www.imb-jena.de/~kboehm



Numbers

Dimension of cells → 10 Microns

Size of a Motor → 50-100 nm

Cargoes carried by Motors → 50nm – Few microns

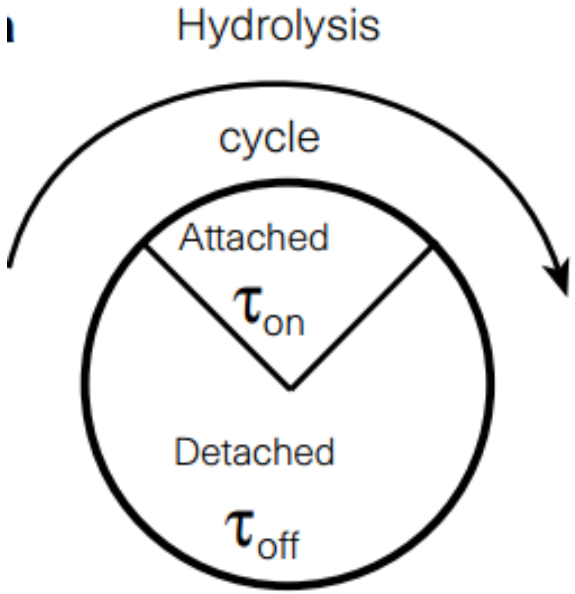
Velocity of motion → 1-2 microns/sec

100 cycles completed in 1 second

Energy available from 1 ATP = 25 K_bT = 100 pN-nm

Work done per cycle ~ 50 pN-nm

Diffusion constant for 50nm object ~ 1 micron^2/sec

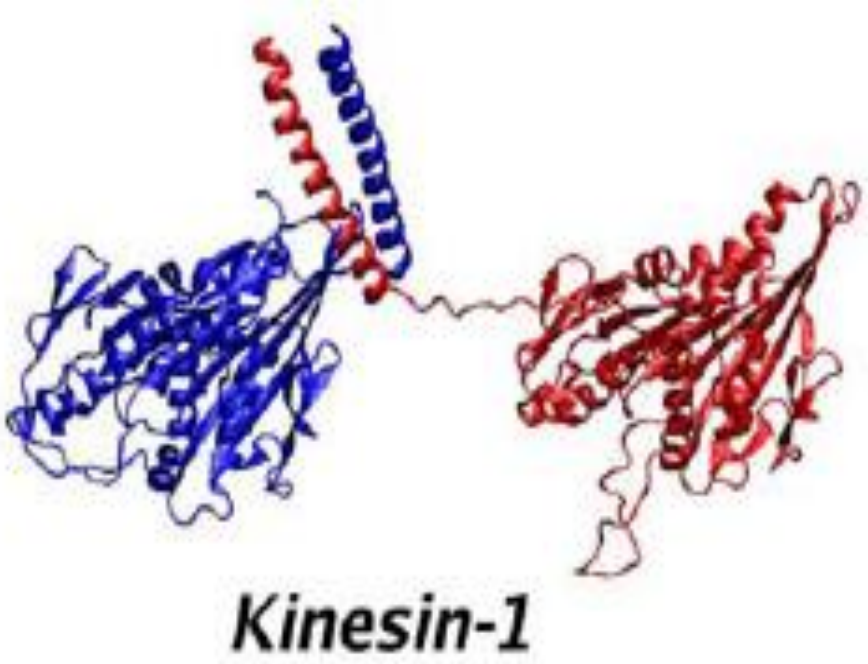


Duty Ratio $r = \dfrac{\tau_{on}}{\tau_{on} + \tau_{off}} = \dfrac{\tau_{on}}{\tau_{total}}$

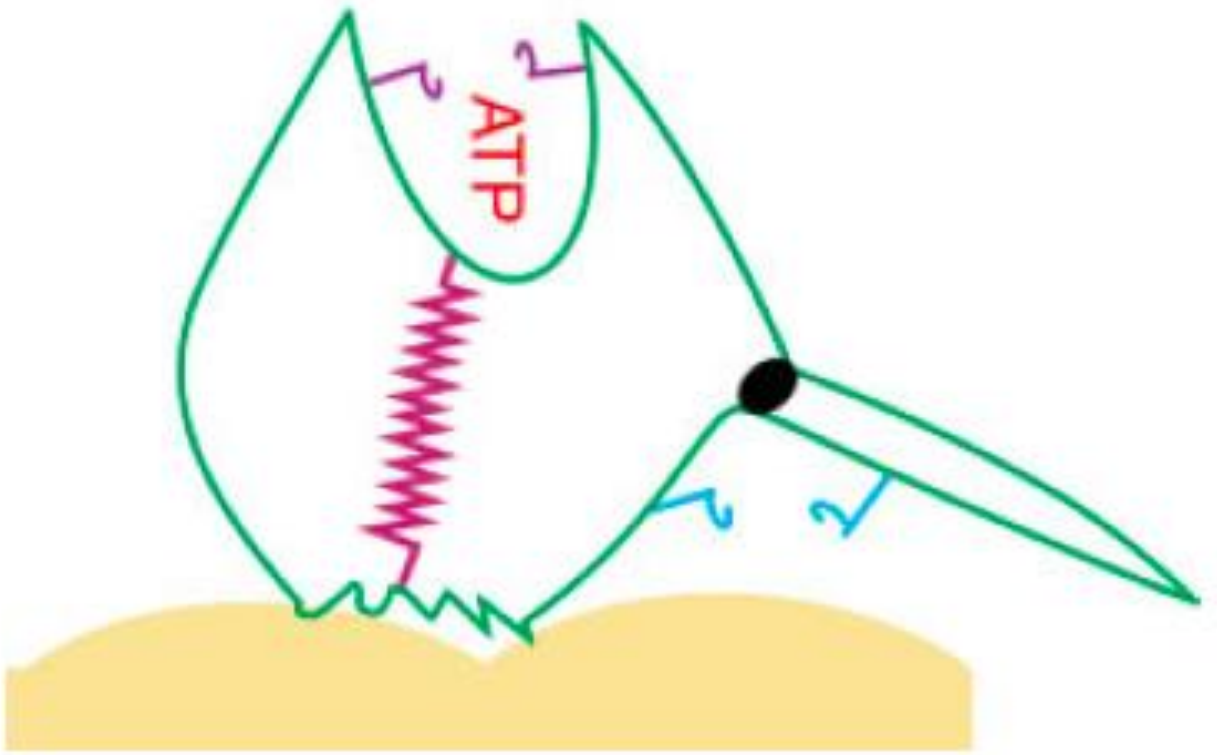
Howard, J. Molecular motors: structural adaptations to cellular functions.
https://doi.org/10.1038/39247

J. Howard, Mechanics of Motor Proteins and the Cytoskeleton

Duty ratio of a leg =
Fraction of the total Cycle time of Motor that the leg spends attached to the filament (e.g. microtubule)

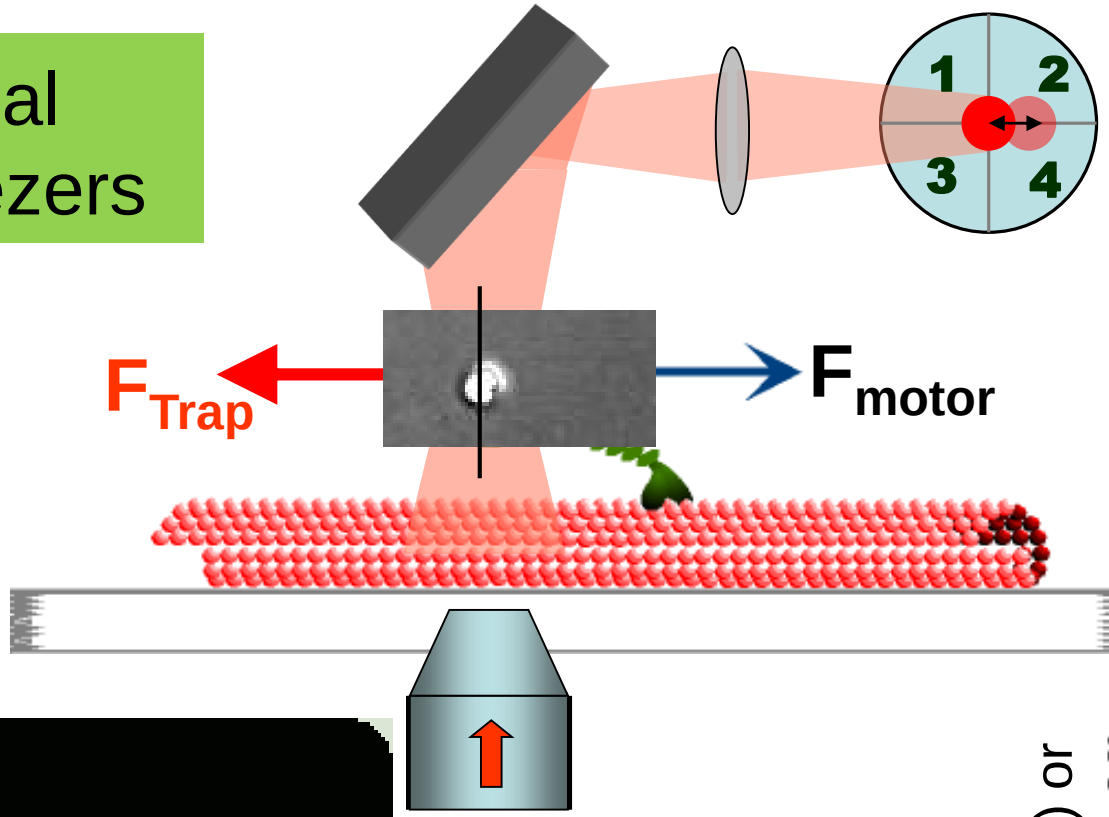


Latches and Springs in the Kinesin Machine

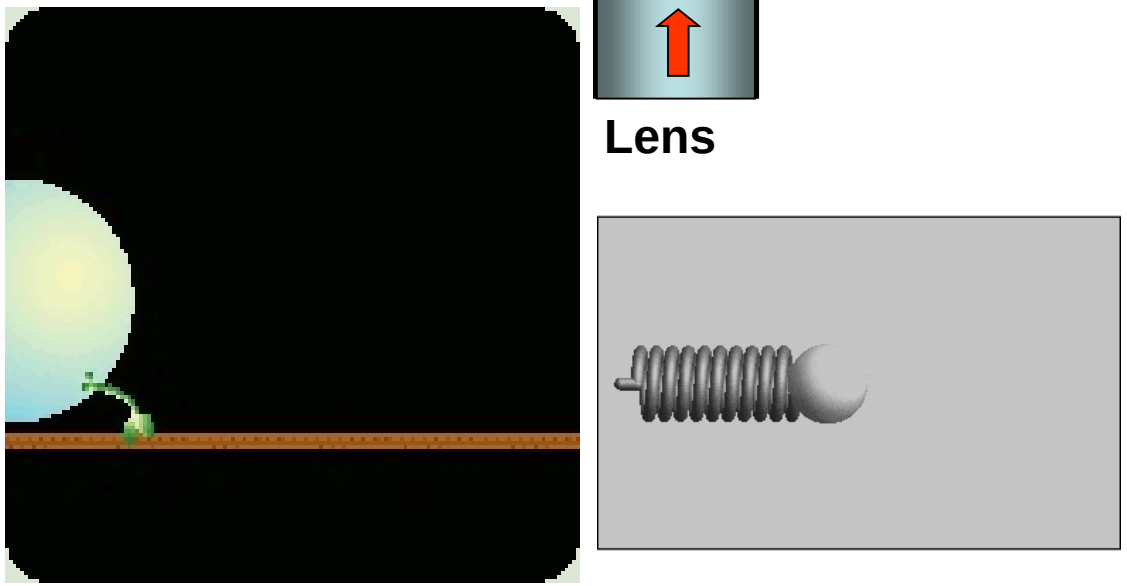


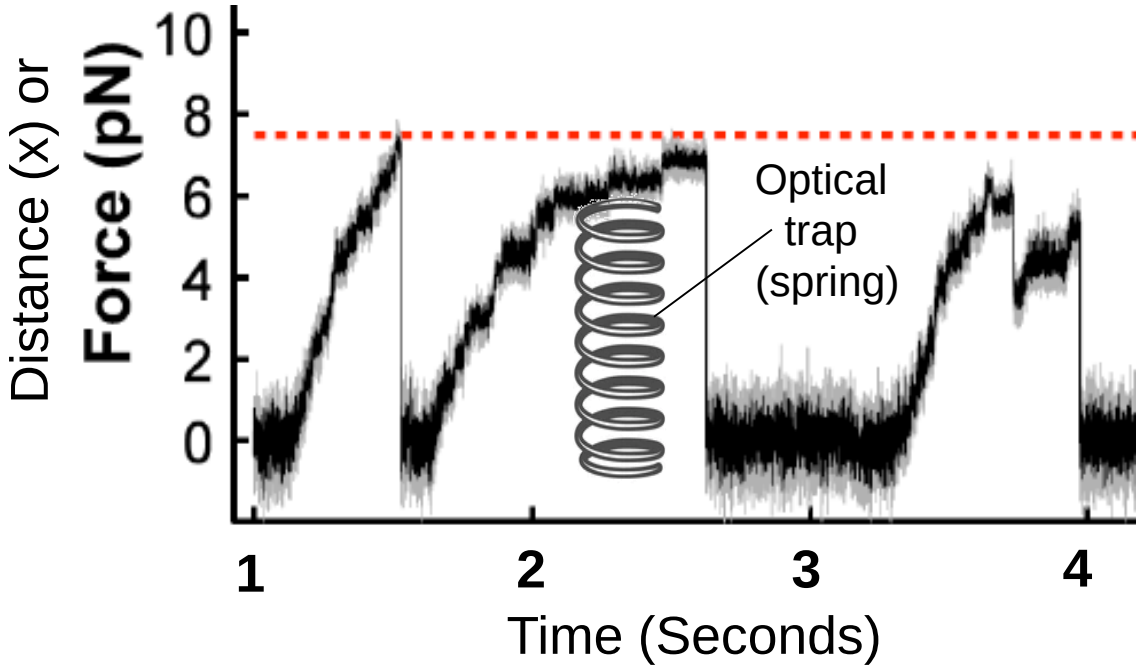
Sharyn Endow 2003

Optical Tweezers



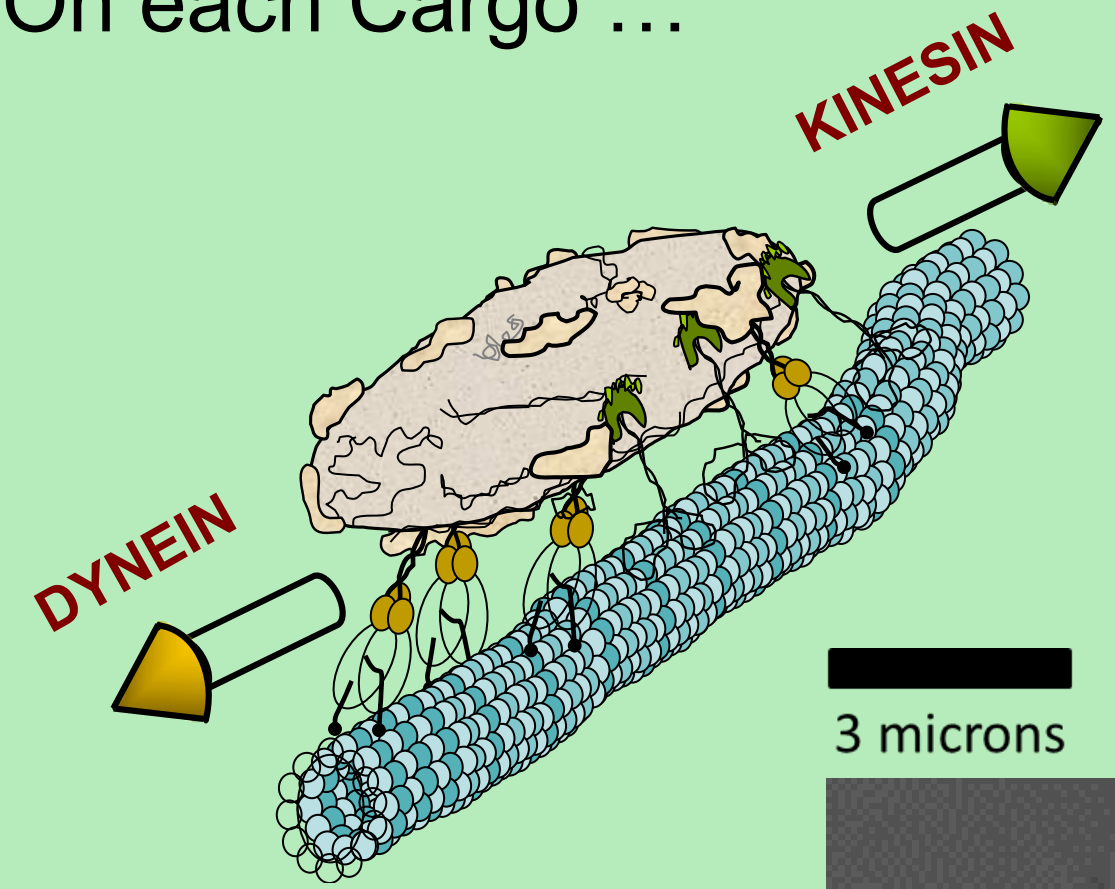
Force = Distance * K_{TRAP}

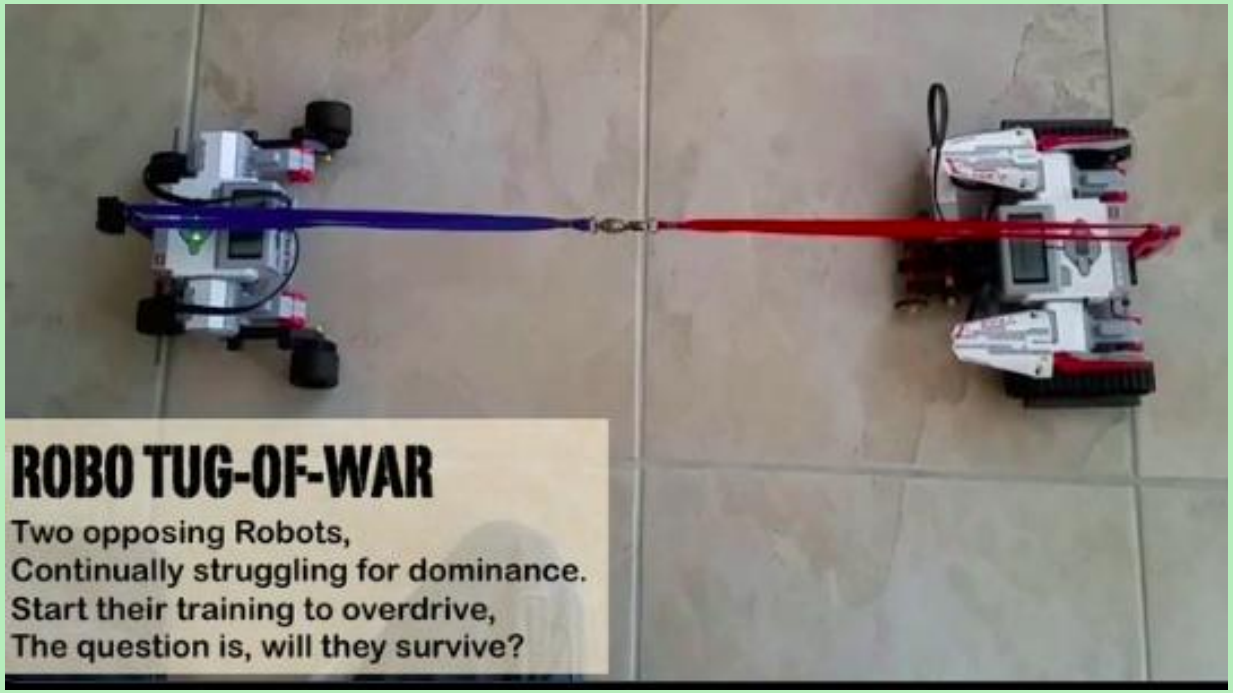




Credit : George Shubeita

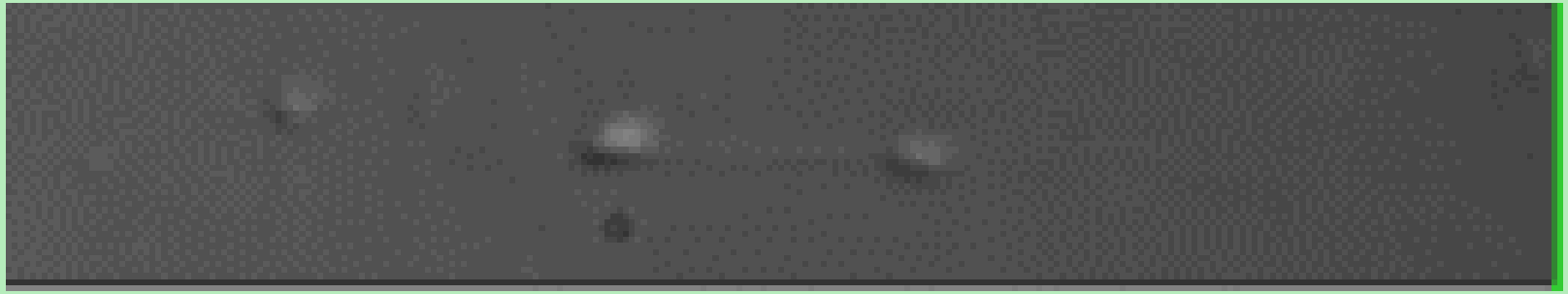
But real Life is complicated !!
On each Cargo …



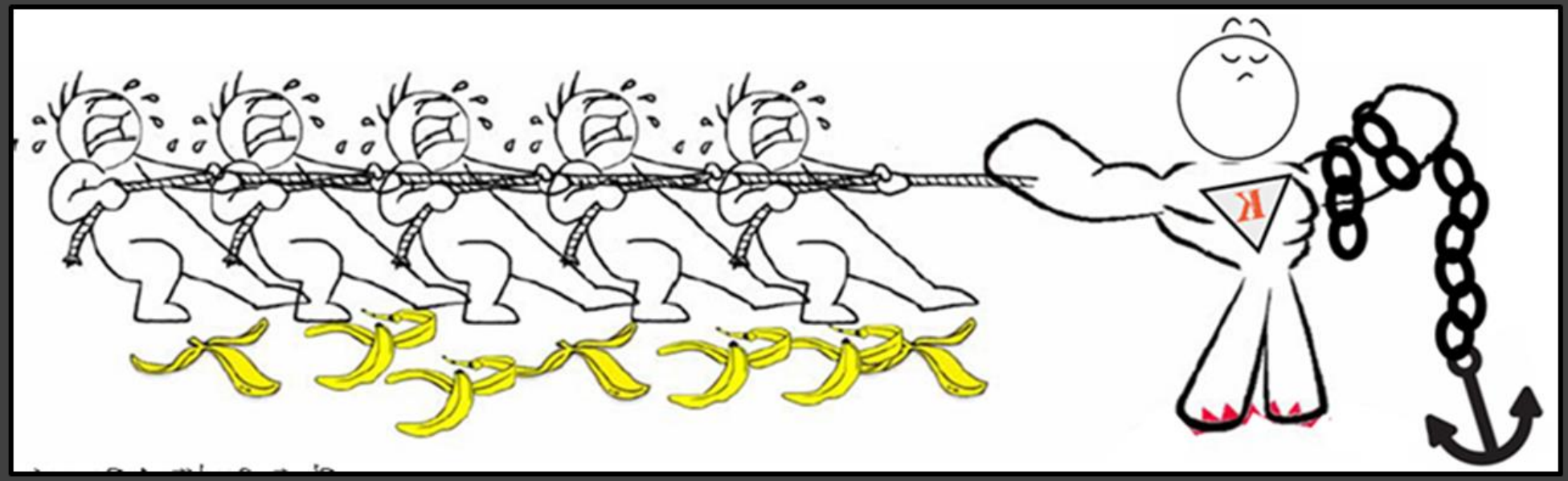


3 microns

A real Tug-of-war at the Nanoscale
Soppina et al, PNAS 2009



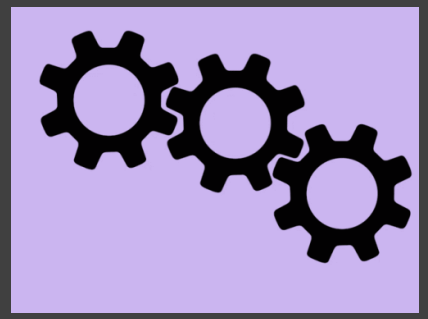
DYNEINS work well in a Team … KINESIN cannot



← 1.1 x 5 = 5.5 picoNewton

6 picoNewton →

The Dynein Nanomachine has an inbuilt Gear



Mallik et al, Nature 2004, *Rai et al Cell (2013)*, *Soppina et al PNAS (2009), Rai et al Cell (2016)*

Some others who work on Motor Proteins in India

Ambarish Kunwar (IITB)
Sunando Dutta (IISER Bhopal)
V. Soppina (IIT Gandhinagar)
Debashish Chowdhury (IIT K)

FOR YOU TO THINK ABOUT …

A Kinesin Motor is walking with a Velocity of 2 microns/second

1. How many molecules of ATP is it using up in a second ?
2. What is the average time between two successive steps ?

You are walking along the road

1. What is the duty ratio for each Leg ?
2. What if you start running instead of walking ?

Observe the Optical Trap data for kinesin in the Figure

1. How is the **Force-Velocity** (***F-V***) response of kinesin determined from such data?
2. Rai et al 2013 found that the ***F-V*** curve of Dynein is fundamentally different from Kinesin.
   What is the implication of this finding ?