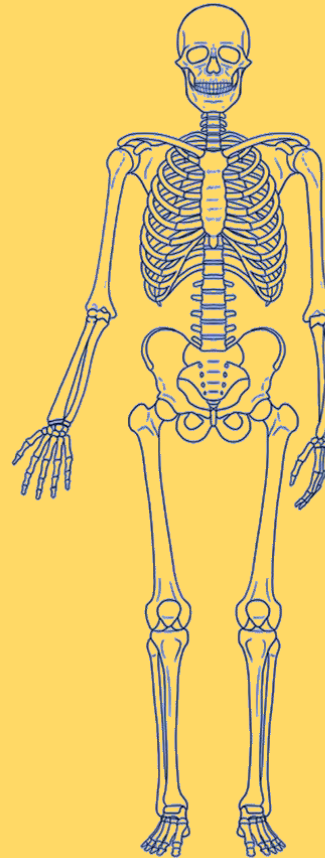
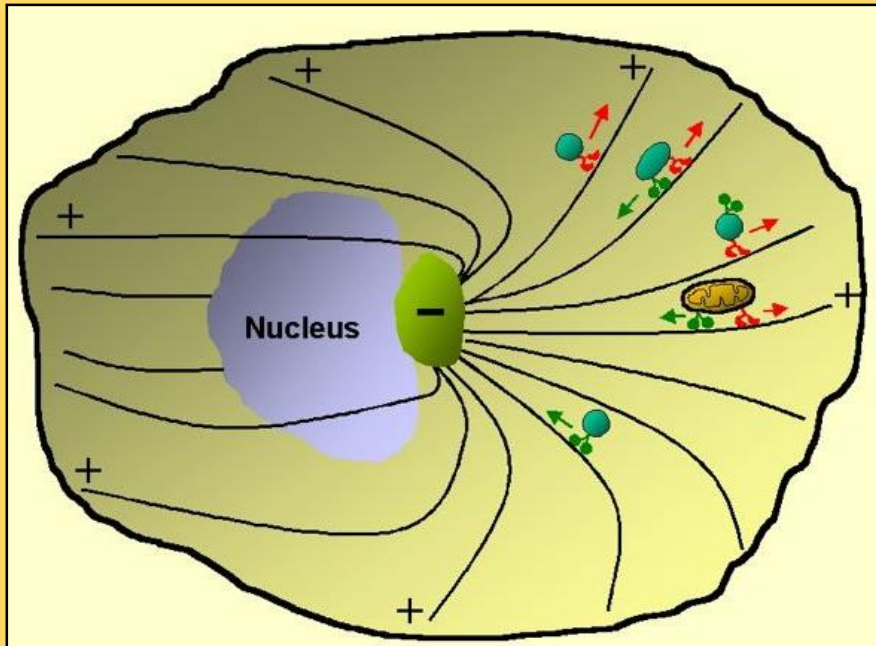


Section 2 : Motion Inside Cells

Lecture 5 : The Cytoskeleton

Microtubule Dynamics



How is the Cellular Skeleton (= Cytoskeleton) different from these Skeletons ?



Resources

- Molecular Biology of the Cell. Alberts, Johnson, Lewis Walter
- Physical Biology of the Cell. Phillips, Kondev, Theriot, Garcia
- Mechanics of Motor Proteins and the Cytoskeleton. Jonathon Howard

[Microtubule Motors in Mitosis \(Scholey et al 2000\)](#)

So, what is the Cytoskeleton useful for ?

A Dynamic Cytoskeleton
makes a Dynamic Cell

White Blood Cell
chasing bacteria

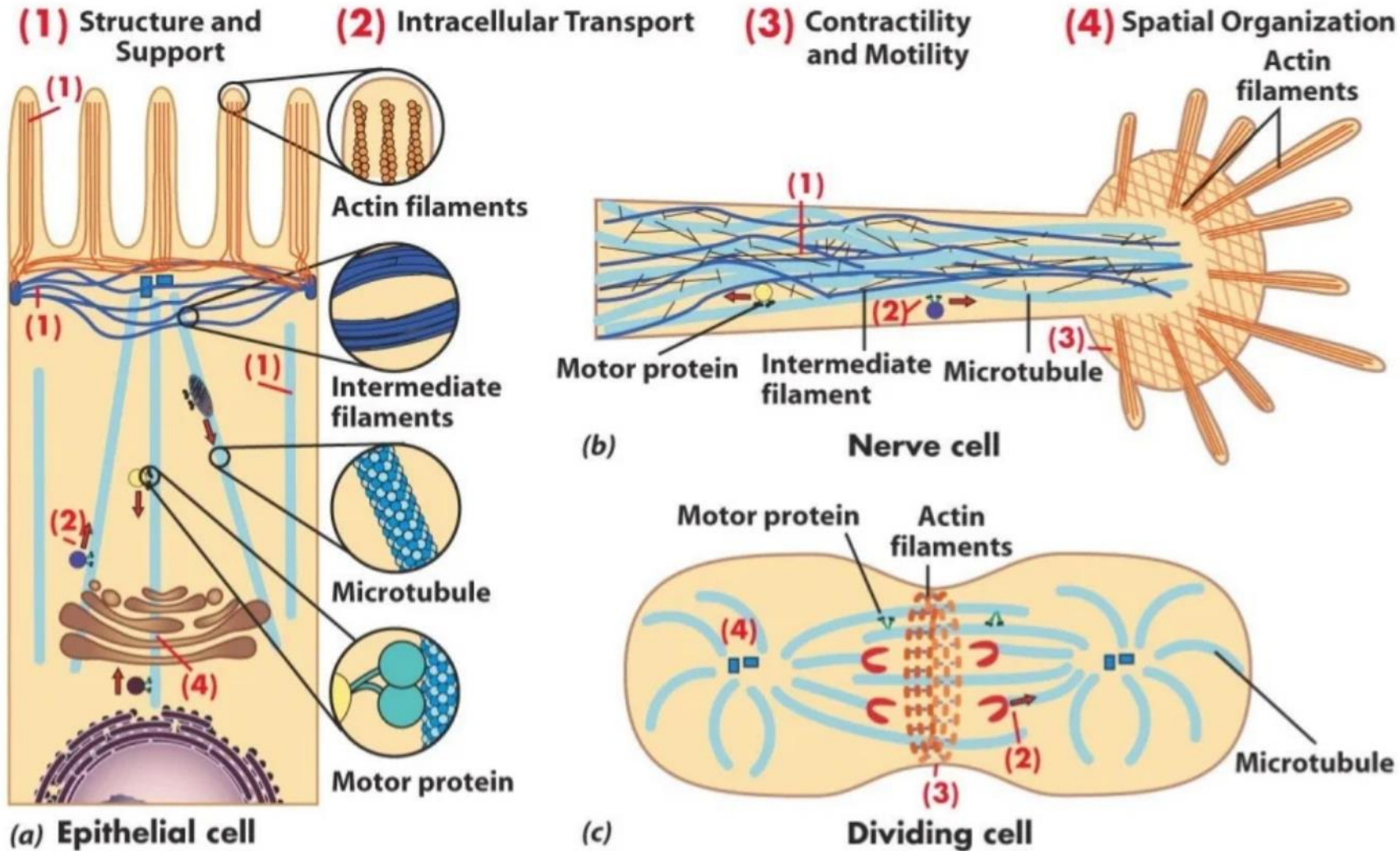
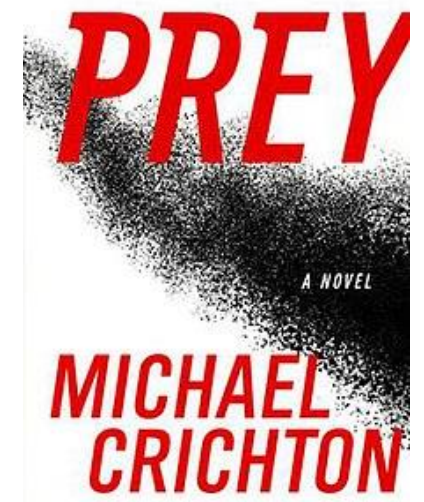
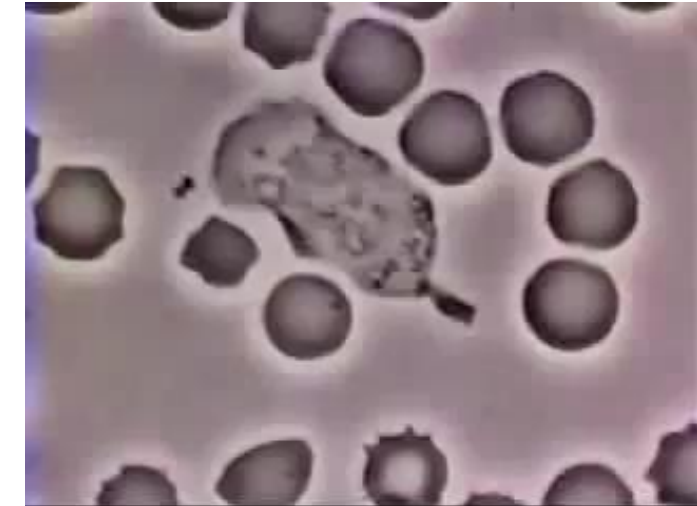


Figure 9-1 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)



The Cytoskeleton – Always Under Construction and destruction



Microtubules

- Transport (Dynein, Kinesin)
- For dividing Cells

Actin

- Transport (Myosins)
- **Motion of the Cell itself**
(Next lecture)

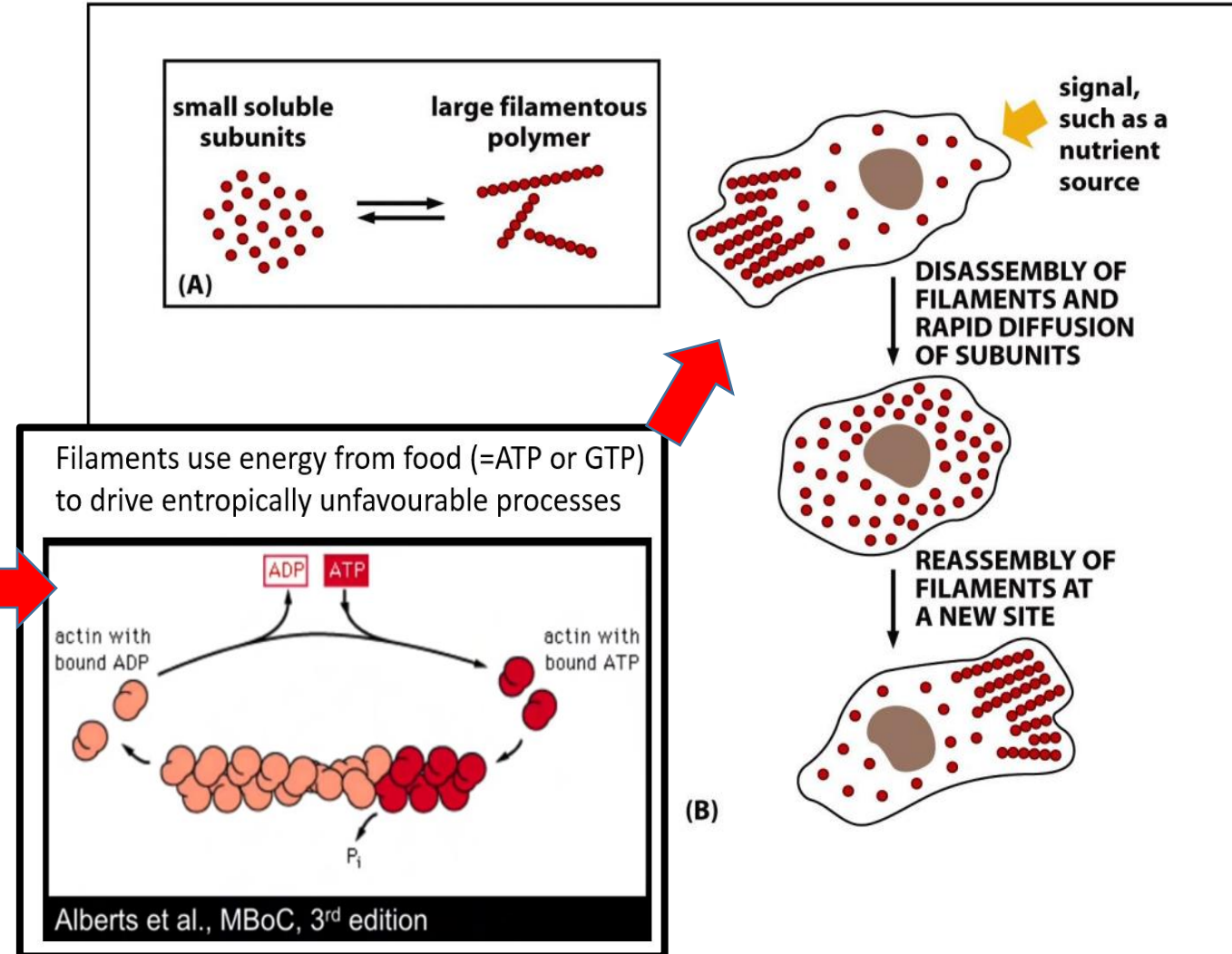
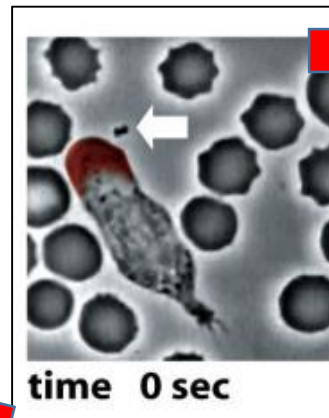
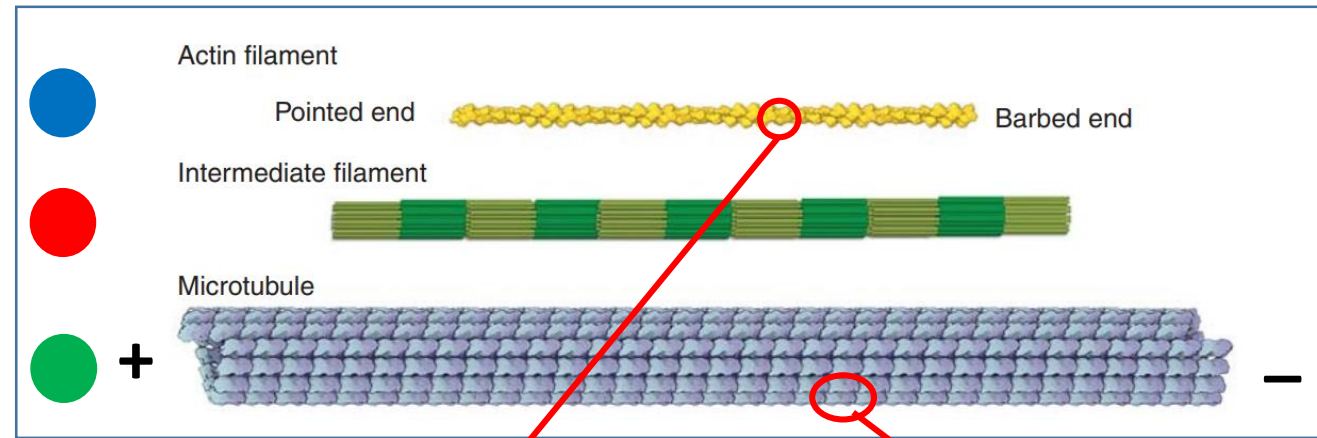
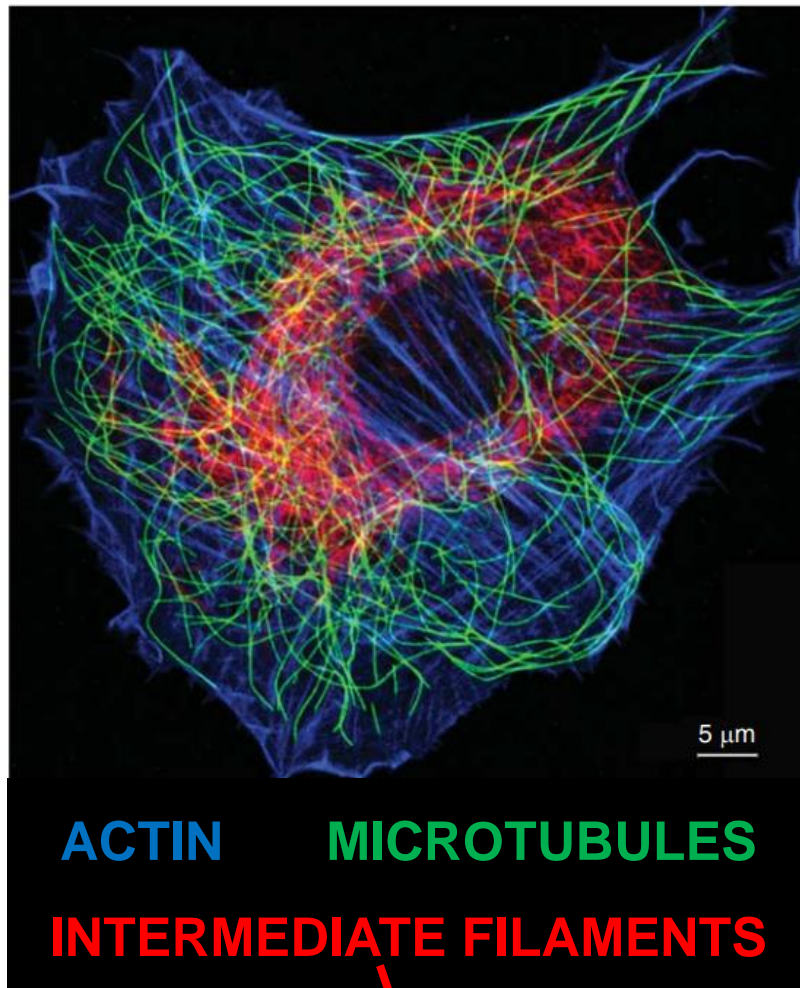


Figure 16-7 *Molecular Biology of the Cell* (© Garland Science 2008)

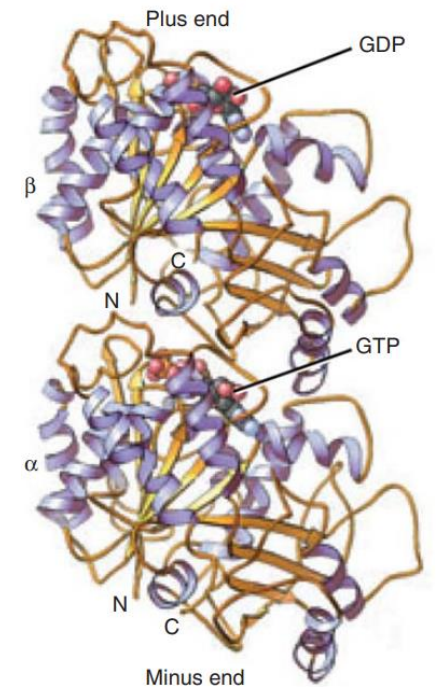
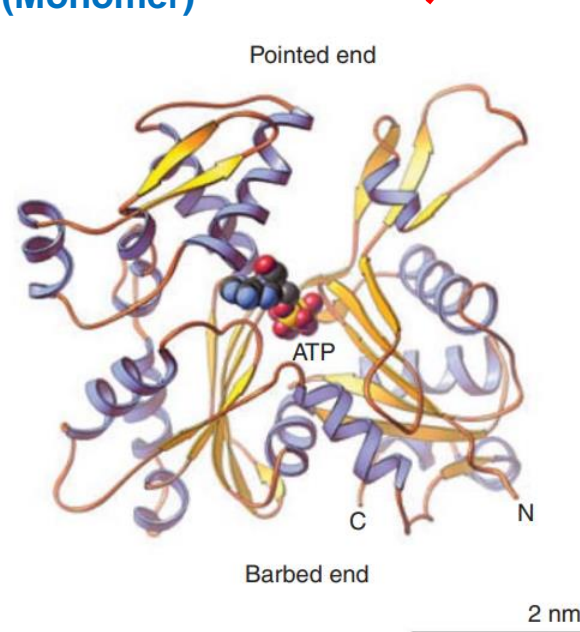
Cultured Cell on a Petridish

Courtesy Harald Herrmann, University of Heidelberg



ACTIN
(Monomer)

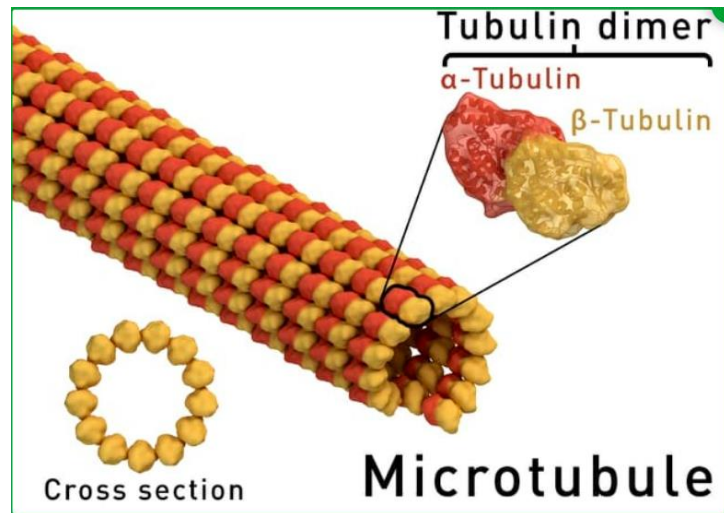
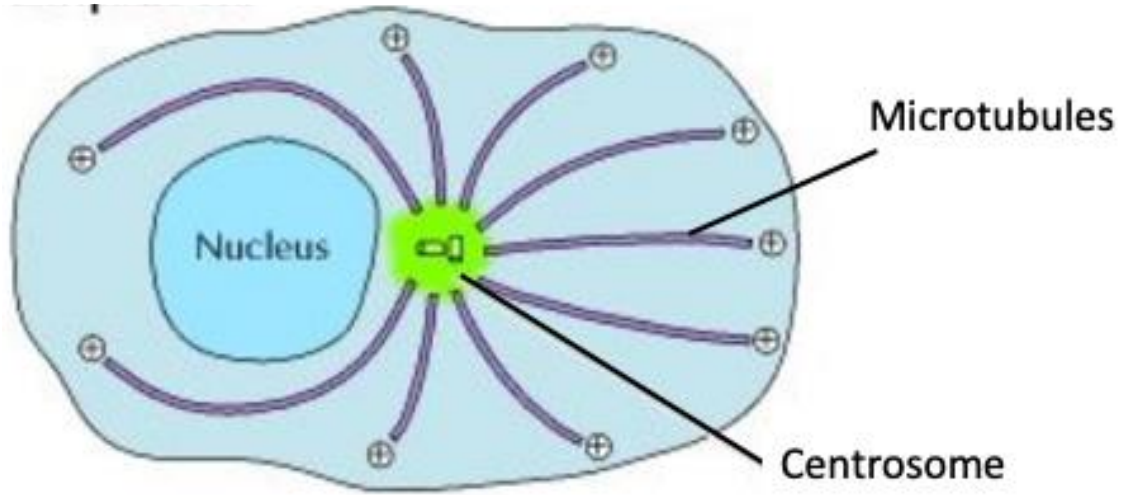
TUBULIN (Dimer)



Interm. Filaments :- Composed of many proteins,
will not discuss further. Example :-
Keratin protein (present in hair)

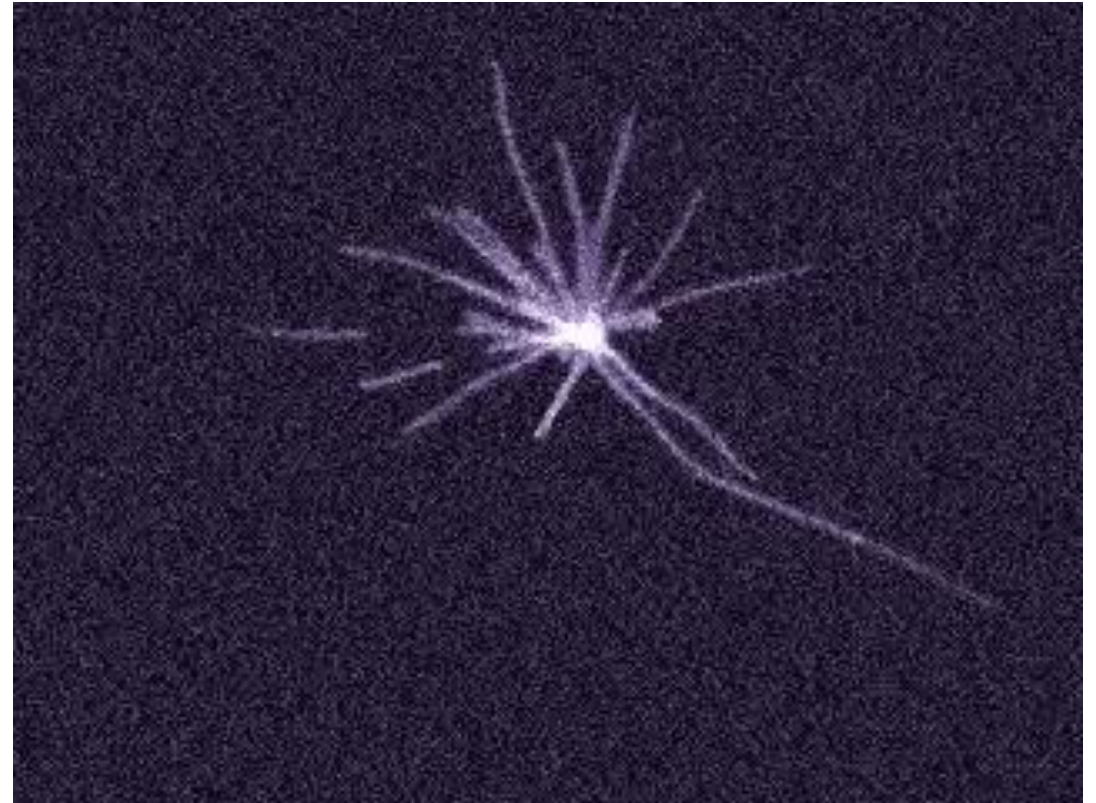
MICROTUBULE DYNAMICS

Interphase Cell

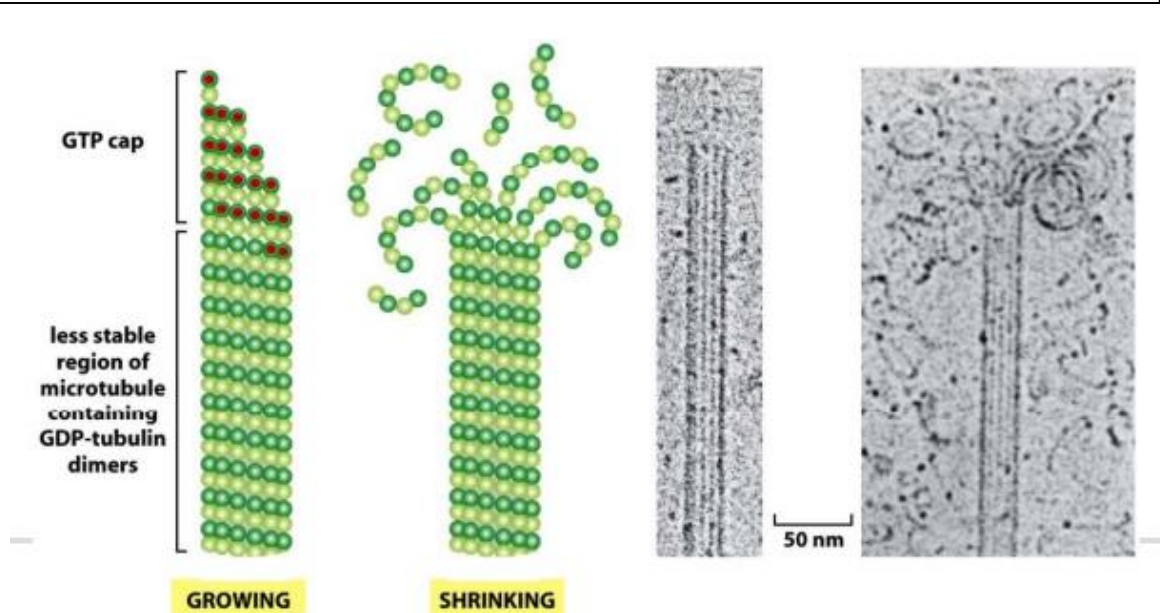
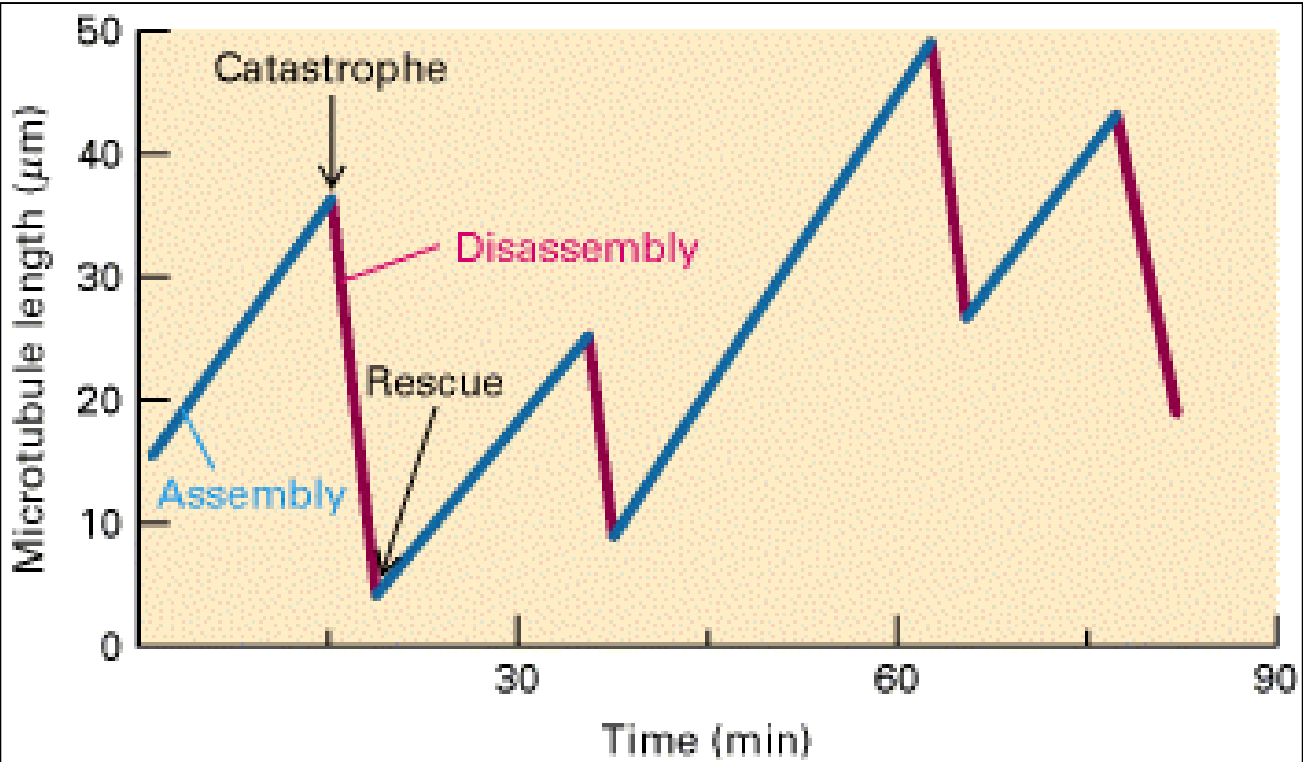
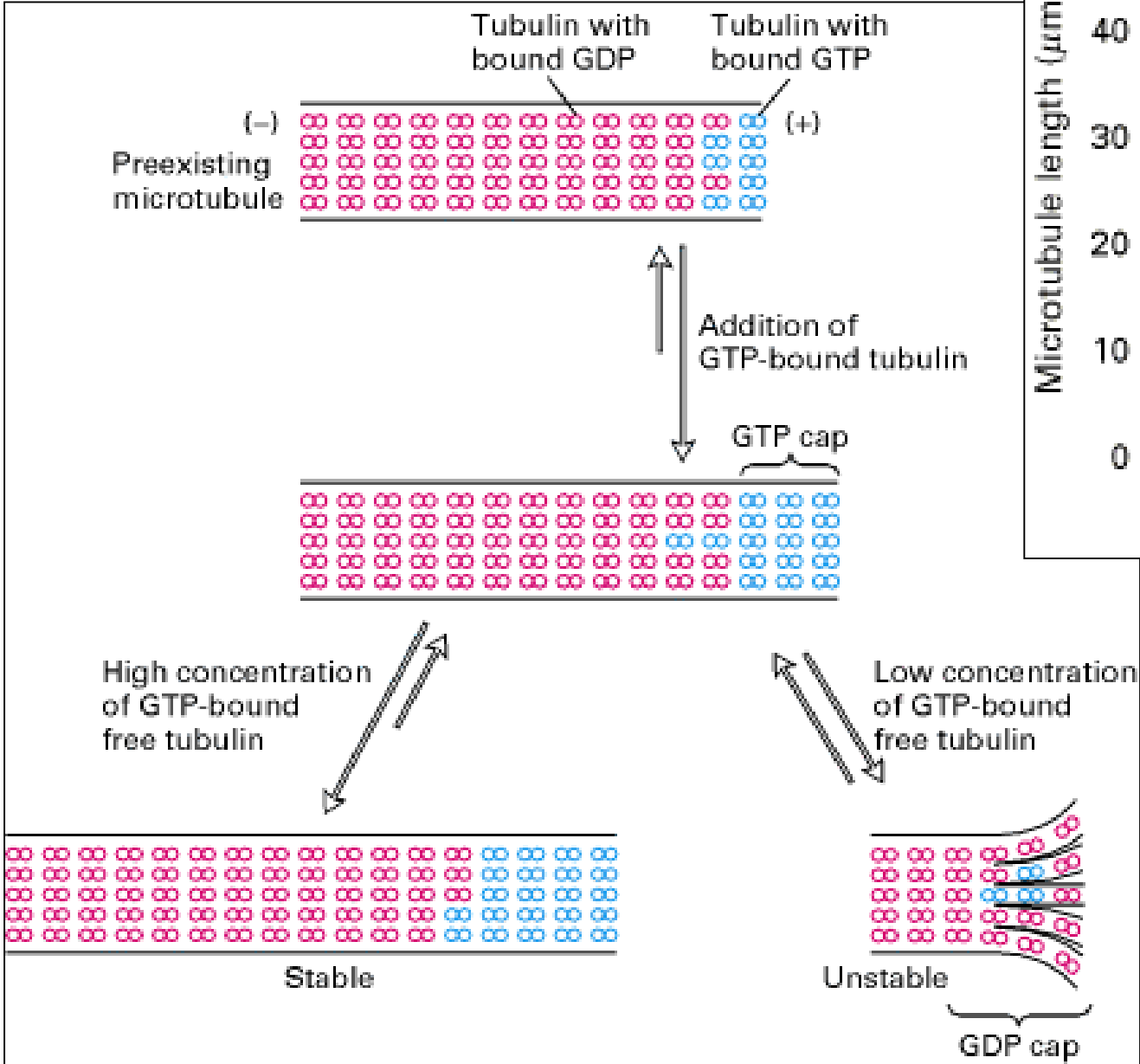


Microtubule dynamics recorded
Live in Interphase Cell

[Movie Link](#)

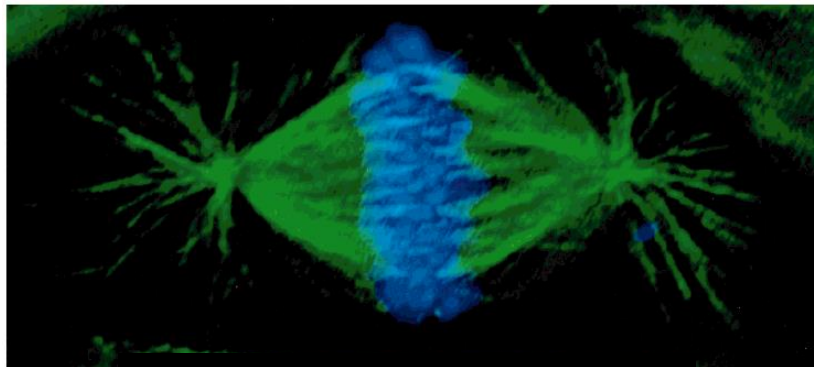


Microtubule dynamics



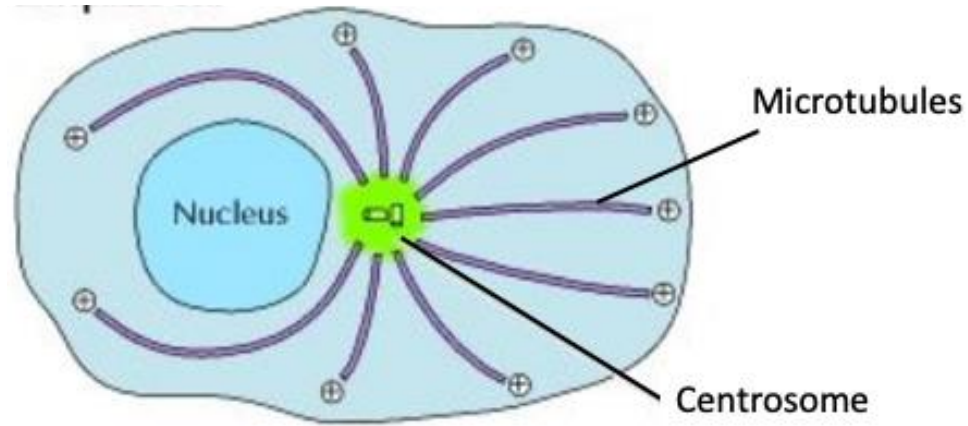
CELL DIVISION (MITOSIS)

- Mitotic Machine that divides One Cell into Two
- Consists of Microtubules and Motors



Microtubules DNA

Interphase Cell



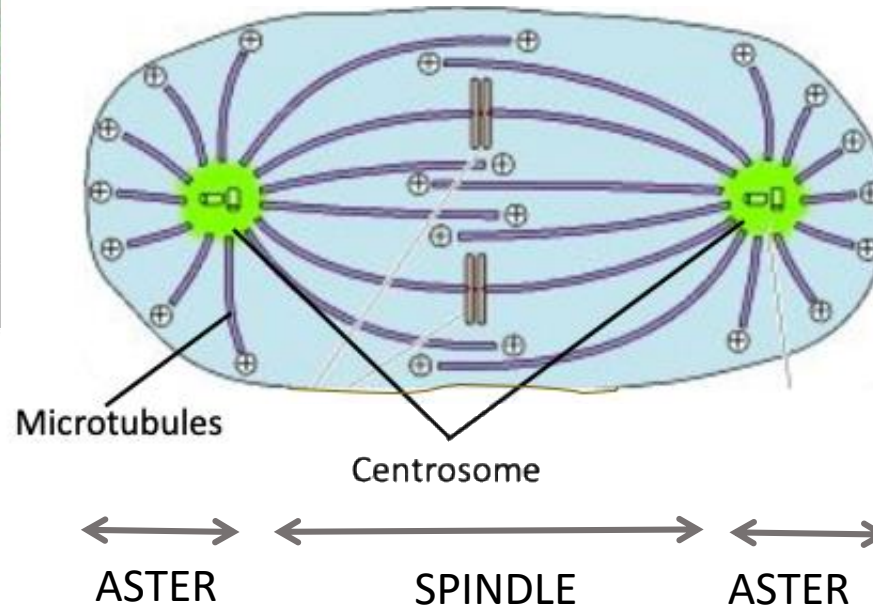
- 1 centrosome
- Microtubules push against plasma membrane to keep centrosome at centre
- Motors transport cargo



Prepare to divide



Mitotic Cell

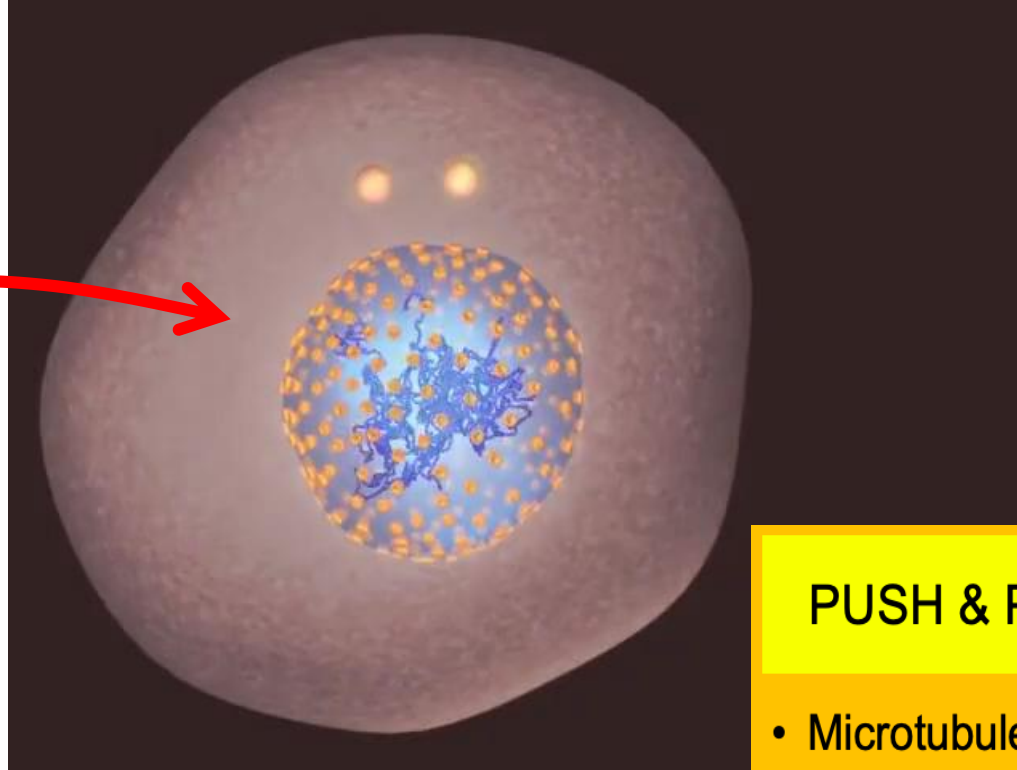


- Centrosomes are duplicated
- DNA is duplicated
- Microtubules push against *Plasma membrane, DNA, Each other ...*
... to position centrosomes
- Cargo transport reduced
- DNA pulled apart & separated
- Cells separated → two new cells



Interphase Cells

The Mitotic Machine must PUSH and PULL



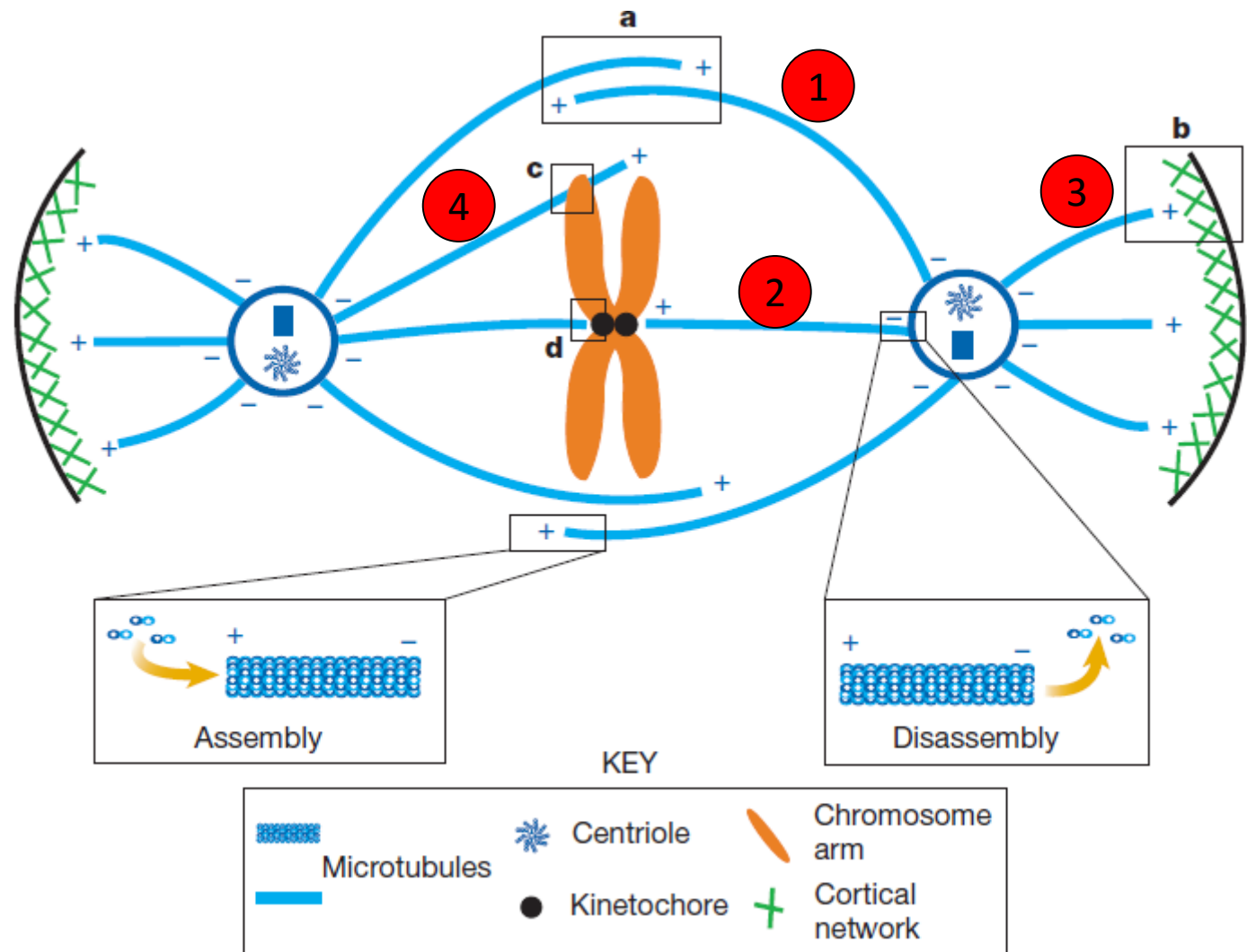
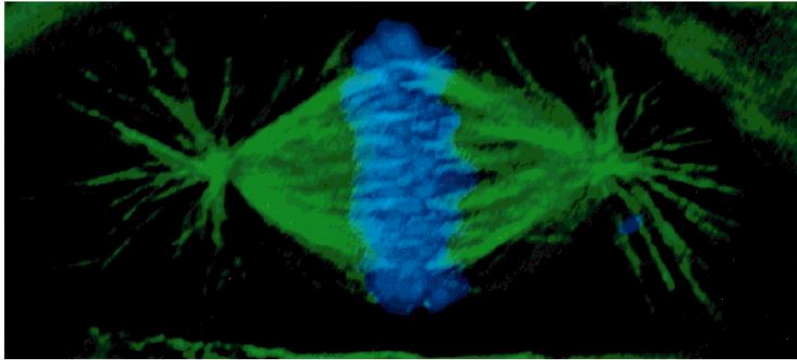
PUSH & PULL : Two main players...

- Microtubule Dynamics (GTP hydrolysis)
 - Polymerization/Depolymerization
 - Search and Find Kinetochores
 - Push/Pull to make symmetric structure
- Mitotic Motor Proteins (ATP hydrolysis)
 - Generate Forces to obtain and maintain the mitotic spindle

[VIDEO LINK](#)

[Video Link](#)

Microtubules in Mitosis



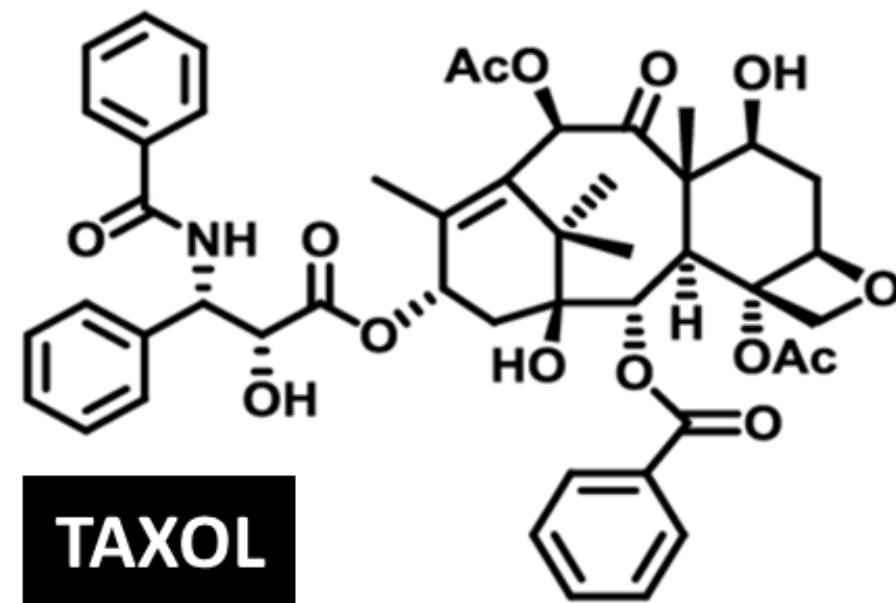
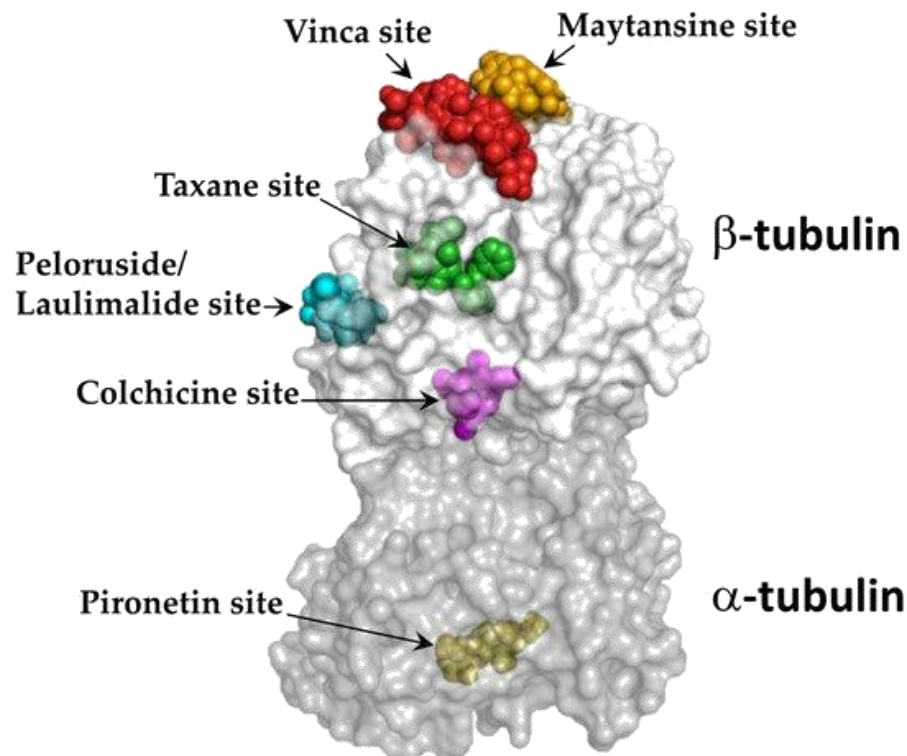
1. POLAR MTs :- Move Spindle poles relative to each other
2. KINETOCHORE MTs:- Move chromosomes relative to spindle poles
3. ASTRAL MTs:- Separation of spindle poles and position w.r.t cell cortex
4. MTs Linking Centrosome to Chromosome arm

Scholey, 2000

Natural compounds that target microtubules are one of the best anti-cancer chemotherapeutic drugs ...

TAXOL – PLANT DERIVED DRUG

Anticancer drug, slows down unchecked cell division (cancer) by binding to microtubule to block GTP hydrolysis.



[Click on Image to read more](#)

Microtubule Assembly Dynamics: An Attractive Target for Anticancer Drugs

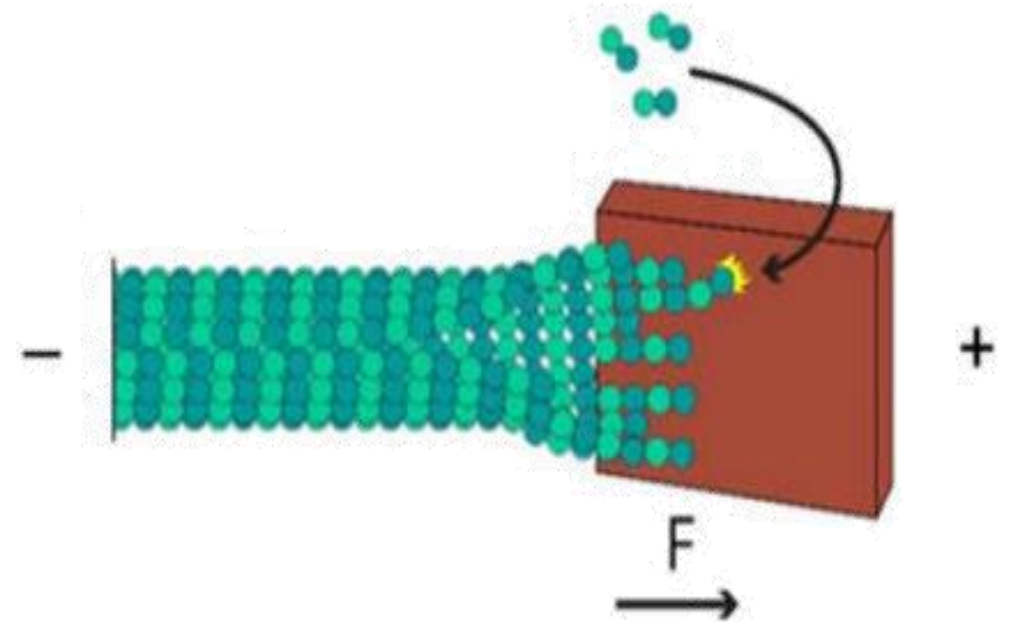
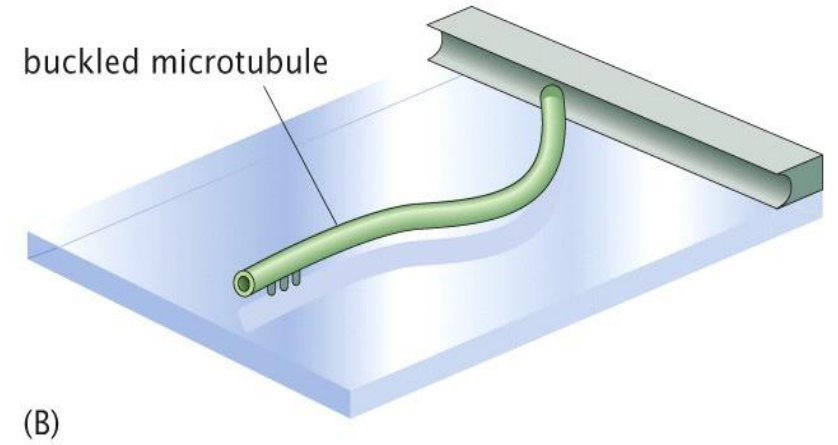
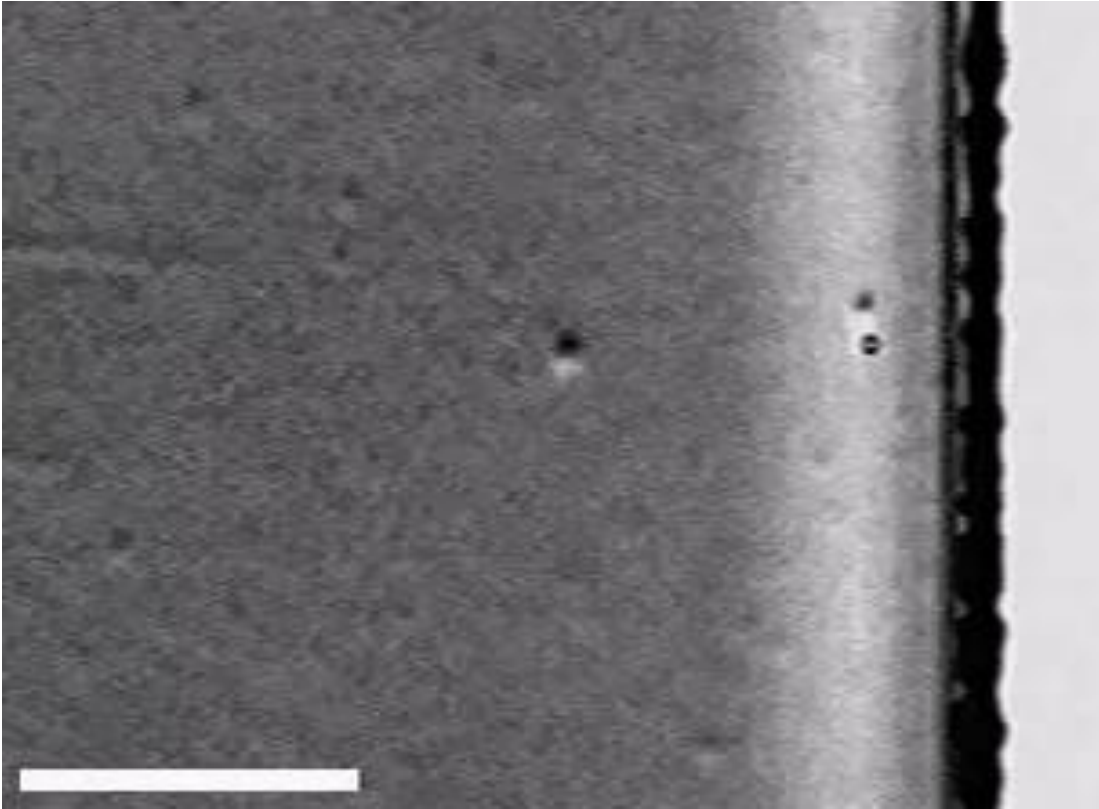
Parminder Singh, Krishnan Rathinasamy, Renu Mohan, and Dulal Panda

School of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Mumbai 400076, India

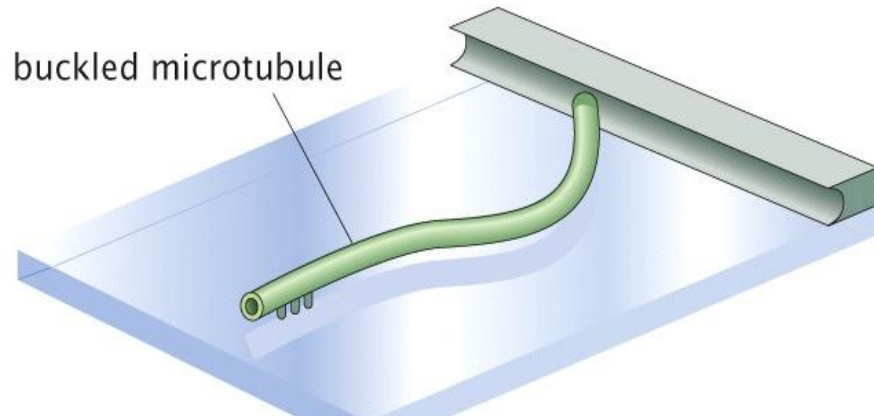


Polymerizing Microtubule filaments can generate a Pushing Force ...

Dynamic instability of microtubules & Force



Single Filaments (*In Vitro*)

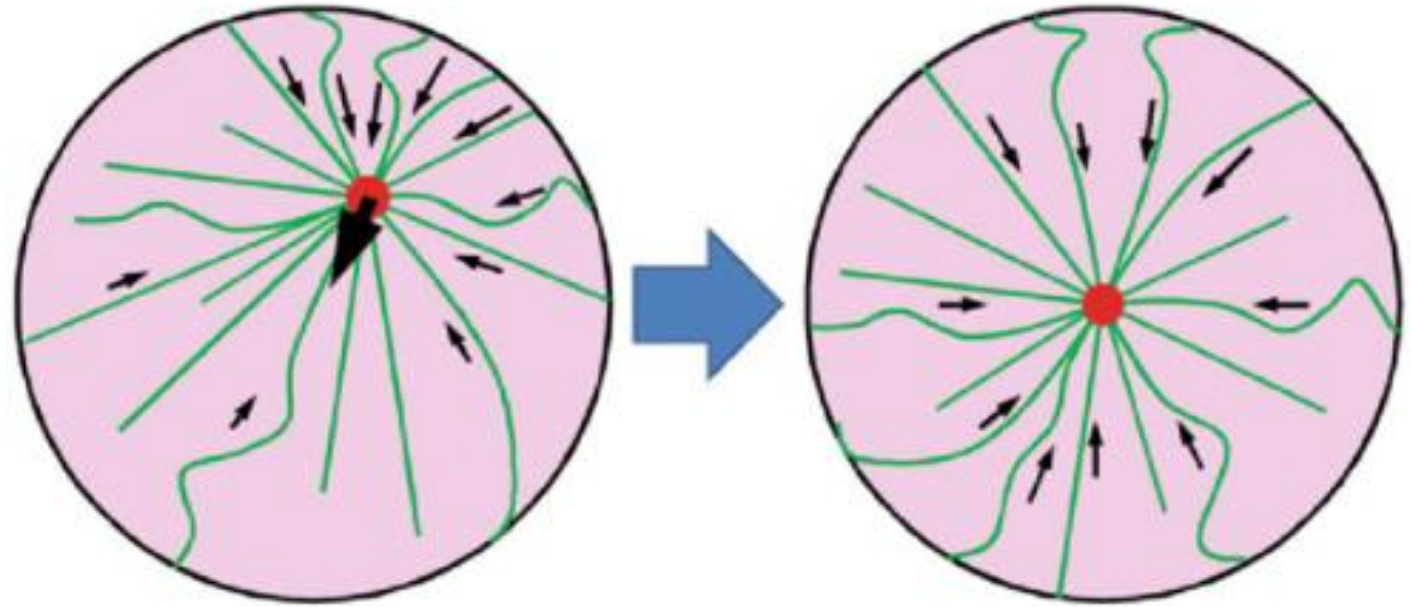


Forced deformation

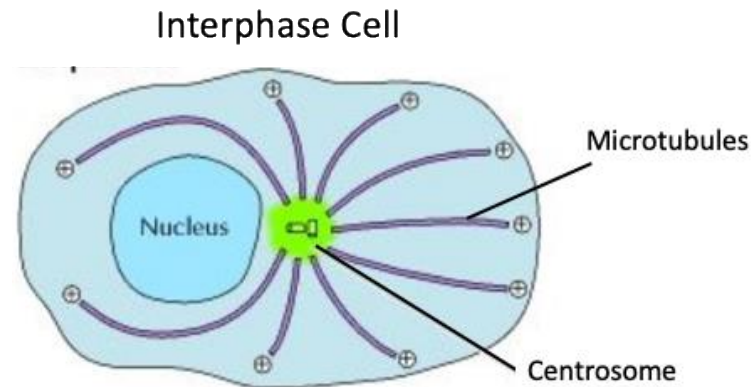
Implication to Cells :-

Centrosome centering by microtubules.

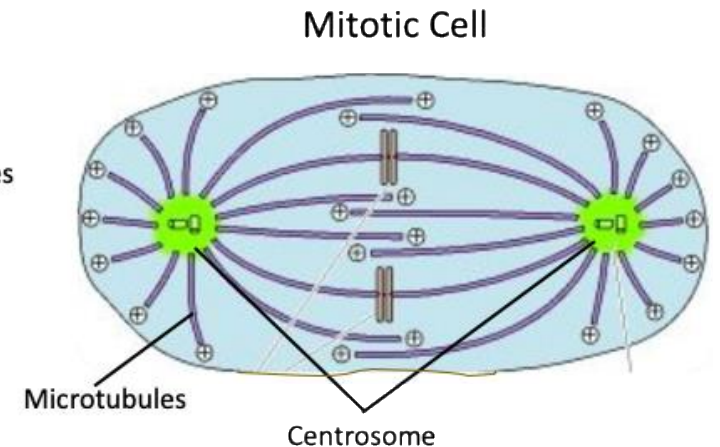
Buckling forces are larger and contacts more frequent leading to a greater pushing force on the side of the centrosome closest to the cell edge.



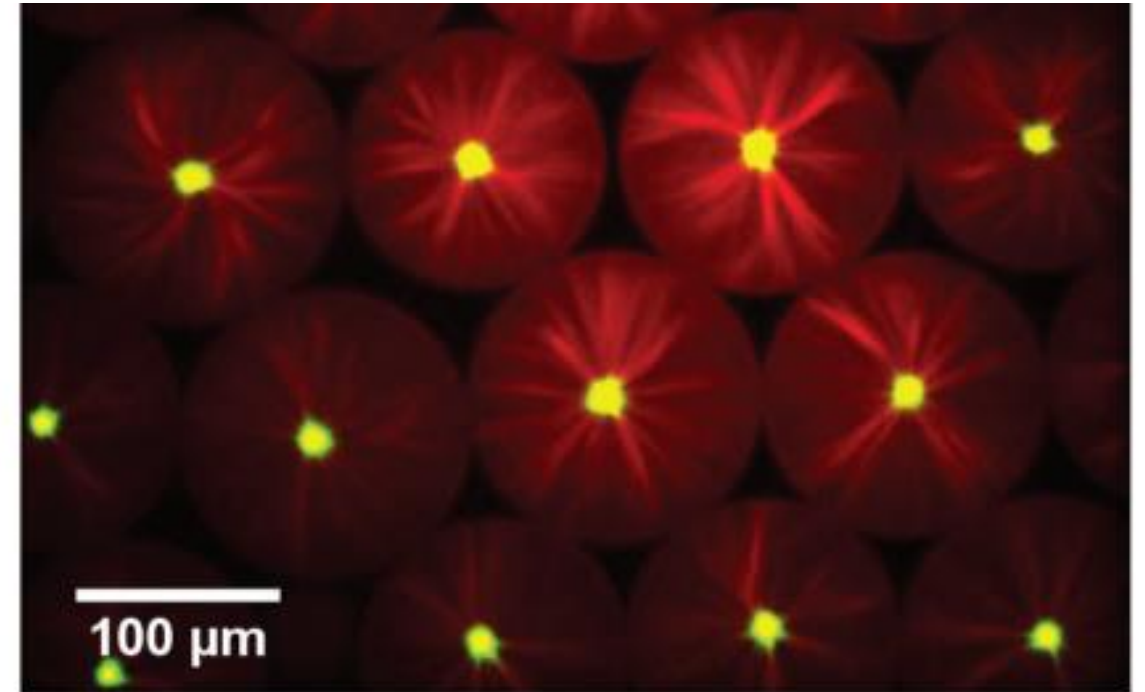
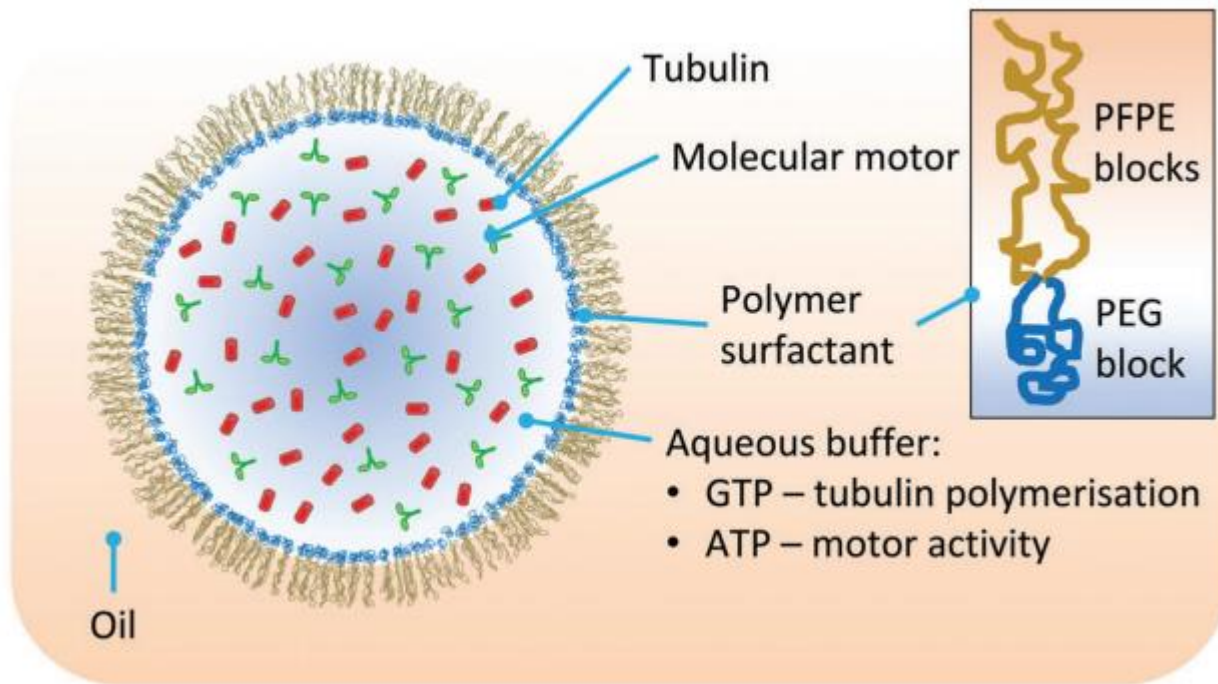
Can help to make this ...

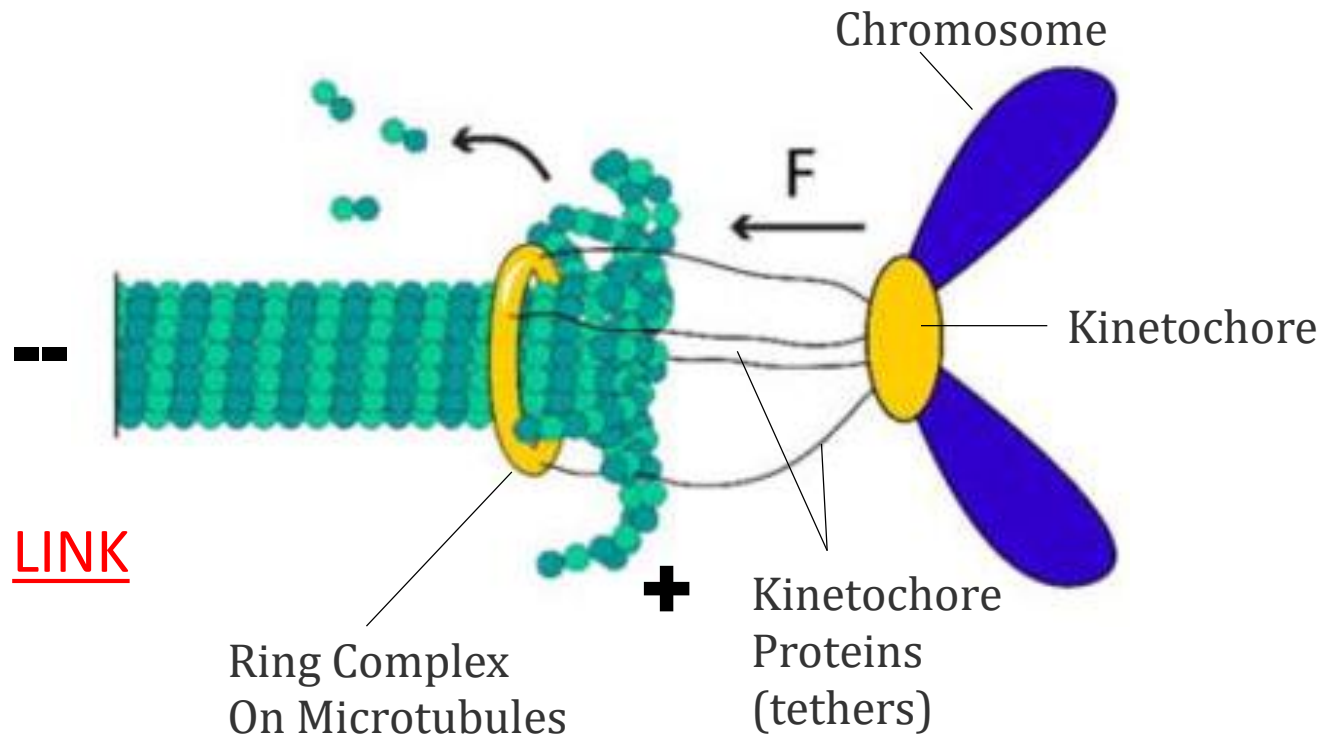


...Or this



You can get it to work in an artificial System ([LINK](#))



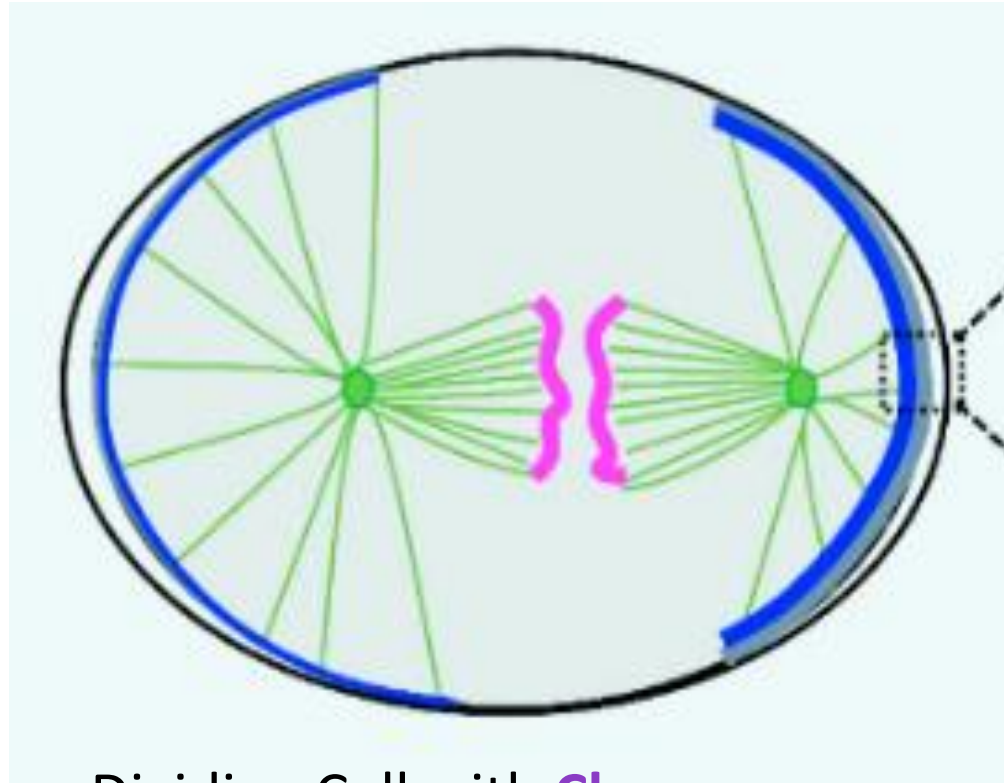


Microtubule Depolymerization can generate Pulling Force

Kinetochore is pulled if she opens her palm

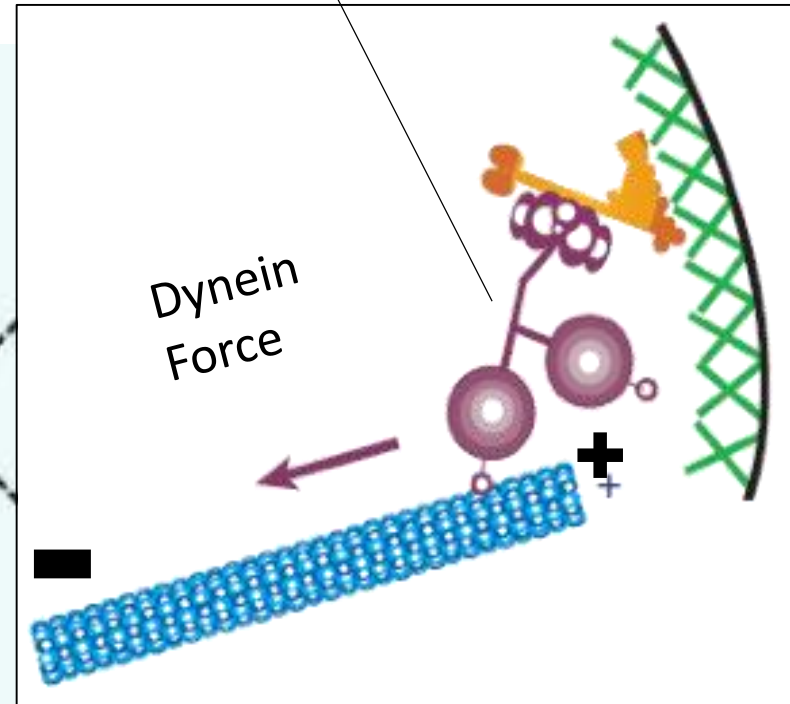


Motor Proteins also generate Pulling force on the DNA (chromosomes)



Dividing Cell with **Chromosomes**
and **Microtubules**

Dynein Motor



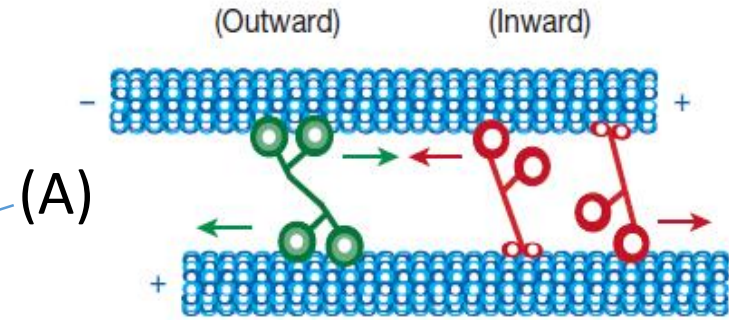
Dynein is Tethered to the Cell membrane and generates force as shown. Which way do chromosomes move? Why ?

What happens if Dynein is replaced by Kinesin?

Number
Type of
Microtubule
(MT)

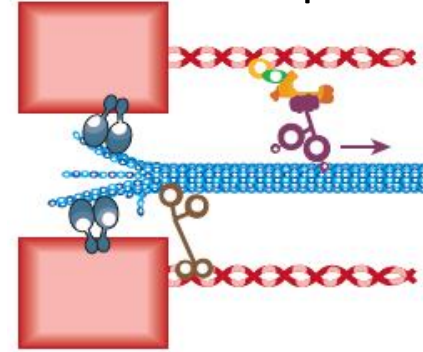
Alphabet
Types of
Motors

1) POLAR MTs move Spindle poles relative to each other



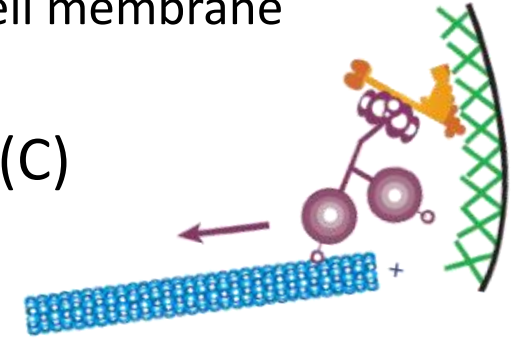
2) KINETOCHORE MTs move kinetochore relative to spindle pole

(B)

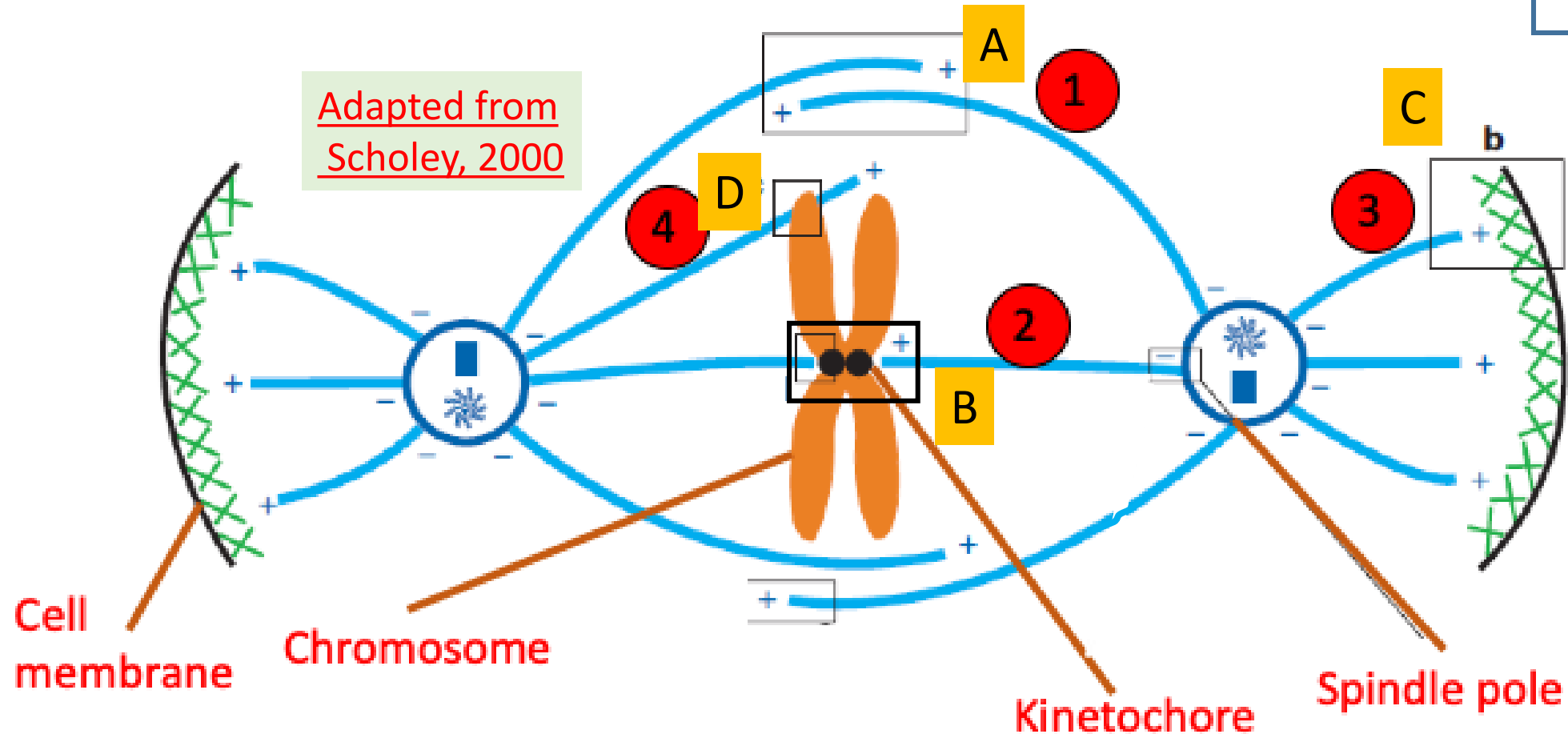


3) ASTRAL MTs:- Separation between spindle poles and Cell membrane

(C)

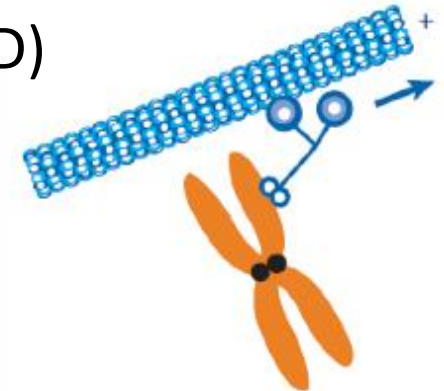


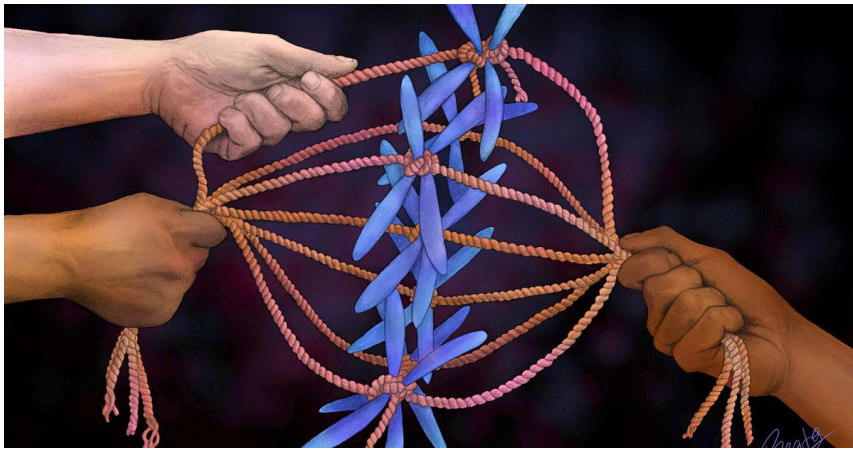
Adapted from
Scholey, 2000



4) CHROMOSOMAL MTs Link Spindle pole to Chromosome arm

(D)

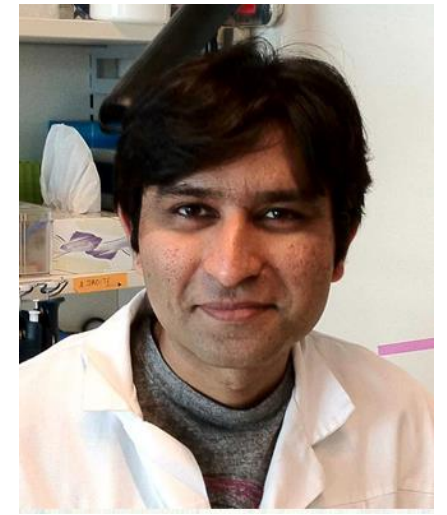




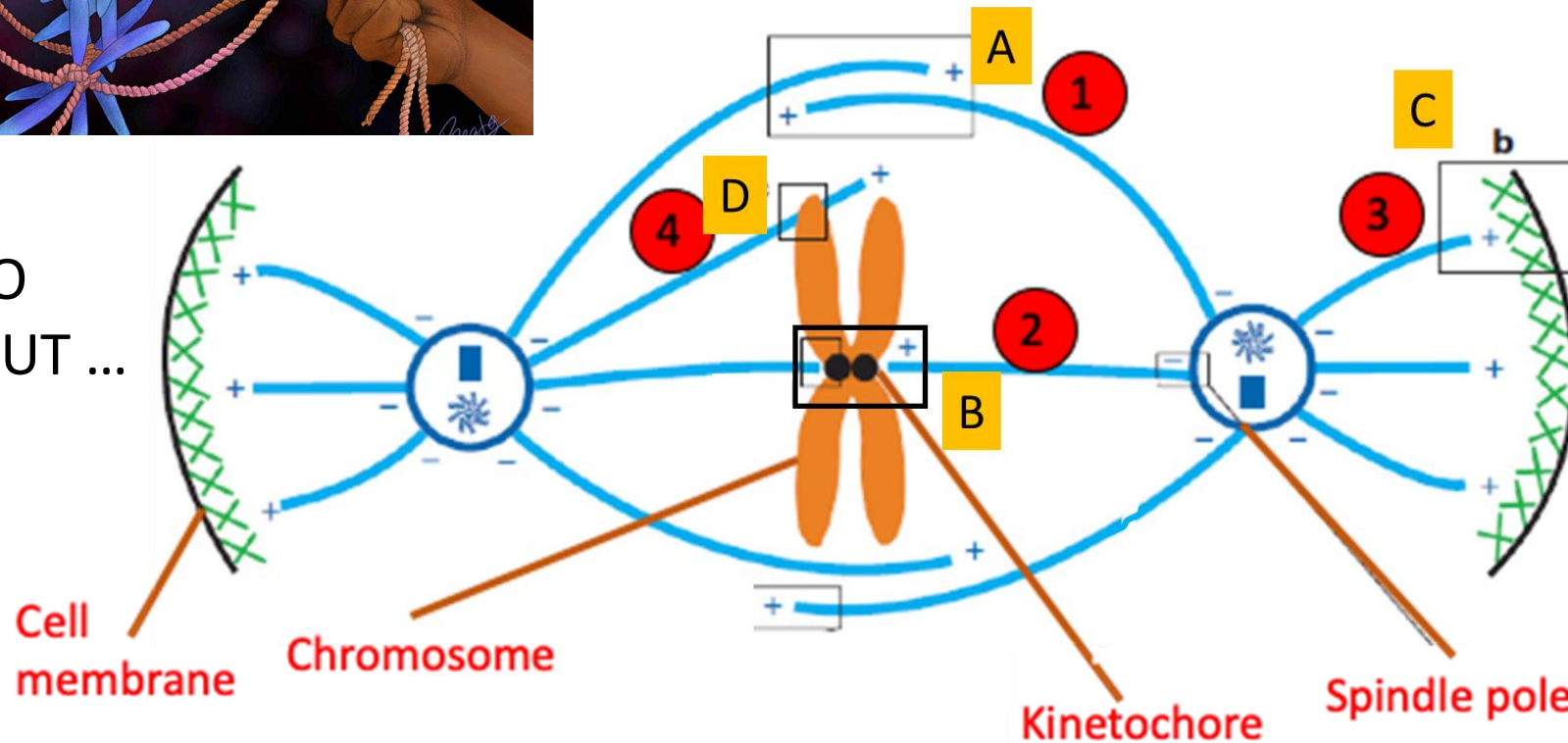
EMBO
Image

Work in India on the
Mitotic spindle

Sachin Kotak, IISc



FOR YOU TO
THINK ABOUT ...



Microtubules generally polymerize or depolymerize at their PLUS end. How can this generate (i) a Pushing force and (ii) a Pulling force to bring the MITOTIC SPINDLE to the center ?

Both Actin and Microtubule can push against a membrane

- They can generate Force, do work
- This means that the filaments must resist bending
- **How stiff are these filaments ?**

Define the Correlation Length (L_p) as :-

$$\langle \cos[\theta(s) - \theta(0)] \rangle = \exp\left(\frac{-s}{2L_p}\right)$$

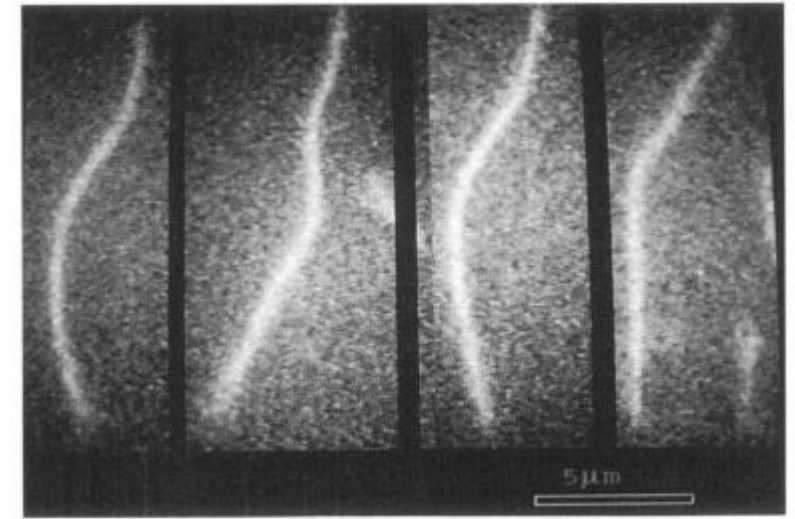
More information

Where S is the distance travelled along the filament

For a straight line, persistence length $L_p = \infty$

How to find L_p ? Take an image of the filament

- Decide an axis
- Find θ with respect to axis at a starting point ($s = 0$)
- Find θ on the filament at a distance s [$= \theta(s)$]
- Find $\cos[\theta(s) - \theta(0)]$
- Repeat along the length of the filament and average



Actin filament undergoing thermal fluctuations observed at 6-sec time intervals

