The Cytoskeleton

Our cells need support too!

Part I

BIOL366

April 17, 2025

Matthew Ellis, PhD

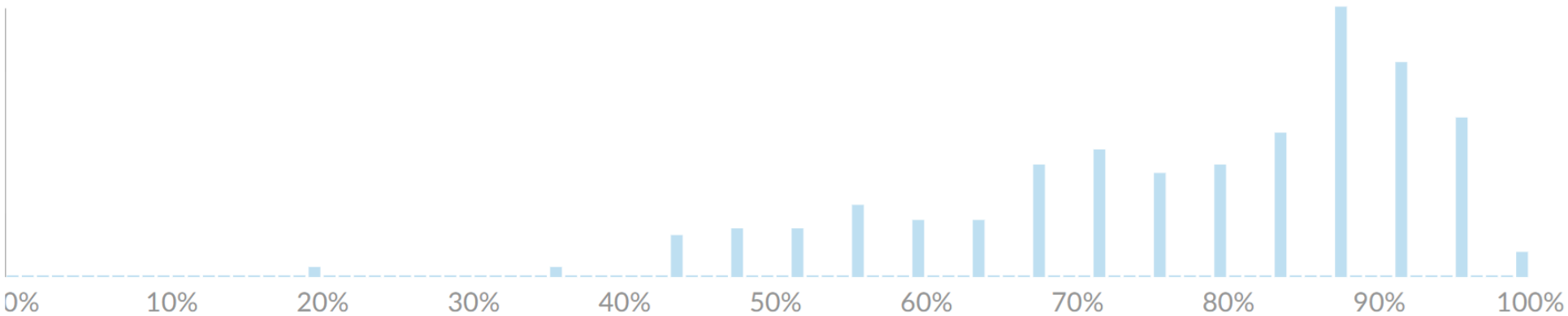
Exam #3

Average Score

78%

High Score

100%



Commonly Missed Exam Question

Question 1 4 pts

A molecule has a higher concentration inside of a cell than outside of a cell.

Which of the following would allow more of this molecule to enter the cell?

- ◯ Using a pump powered by ATP to move the molecule against its concentration gradient
- ◯ Allowing simple diffusion to take its course, which will eventually allow more of the molecule to enter the cell
- ◯ All of the other answers are correct
- ◯ Adding more transporter proteins that have the ability to move the molecule down its concentration gradient

Commonly Missed Exam Question

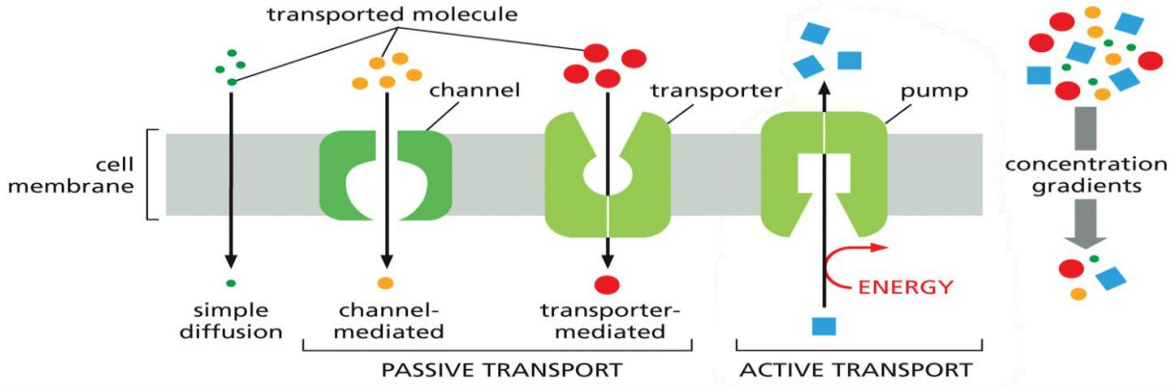
Question 1 4 pts

A molecule has a higher concentration inside of a cell than outside of a cell.

Which of the following would allow more of this molecule to enter the cell?

- ○ Using a pump powered by ATP to move the molecule against its concentration gradient
- ○ Allowing simple diffusion to take its course, which will eventually allow more of the molecule to enter the cell
- ○ All of the other answers are correct
- ○ Adding more transporter proteins that have the ability to move the molecule down its concentration gradient

High concentration



Low concentration

Commonly Missed Exam Question

Question 13 4 pts

Which of the following is NOT a reason $FADH_2$ enters the electron transport chain at a different point that NADH?

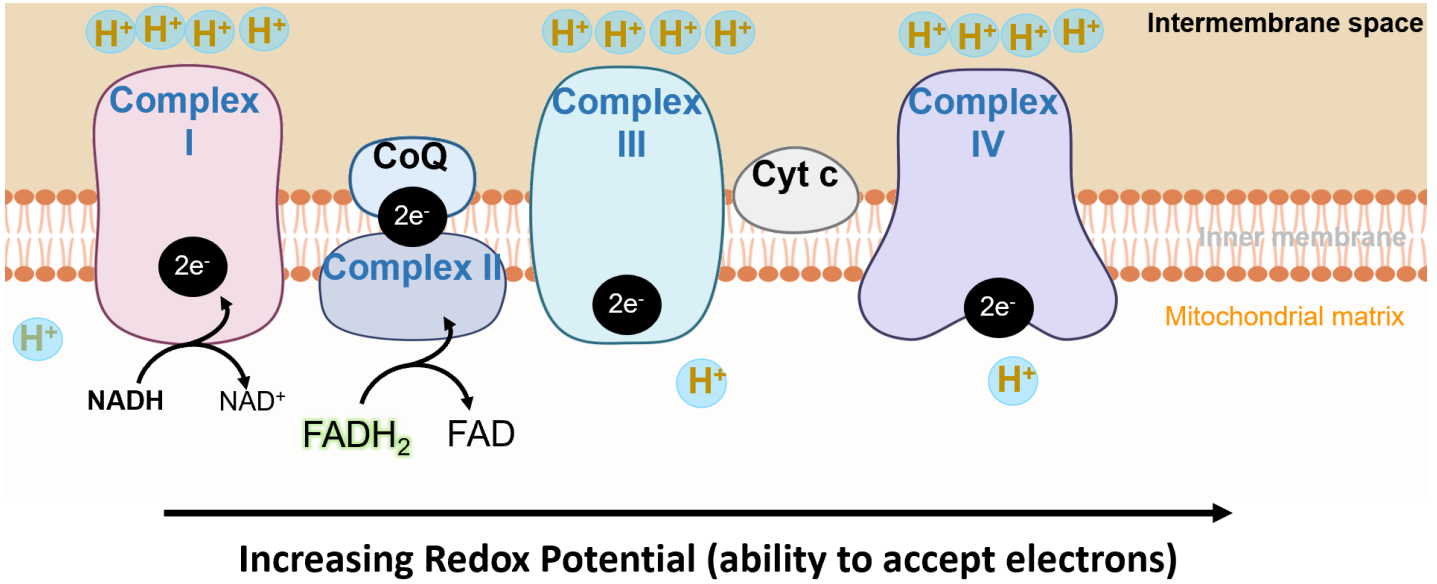
- ◯ The redox potential of $FADH_2$ is greater than that of Complex I and so it would not be able to donate its electrons to Complex I
- ◯ $FADH_2$ utilizes Complex II only to donate its electrons, which is not a proton pump, and so $FADH_2$ does not contribute to the electrochemical proton gradient utilized for oxidative phosphorylation
- ◯ The active site of Complex I is specific to the structure of NADH, and $FADH_2$ would not be acted on by the enzyme
- ◯ These are all reasons why $FADH_2$ enters the electron transport chain at a different point that NADH

Commonly Missed Exam Question

Question 13 4 pts

Which of the following is NOT a reason $FADH_2$ enters the electron transport chain at a different point that NADH?

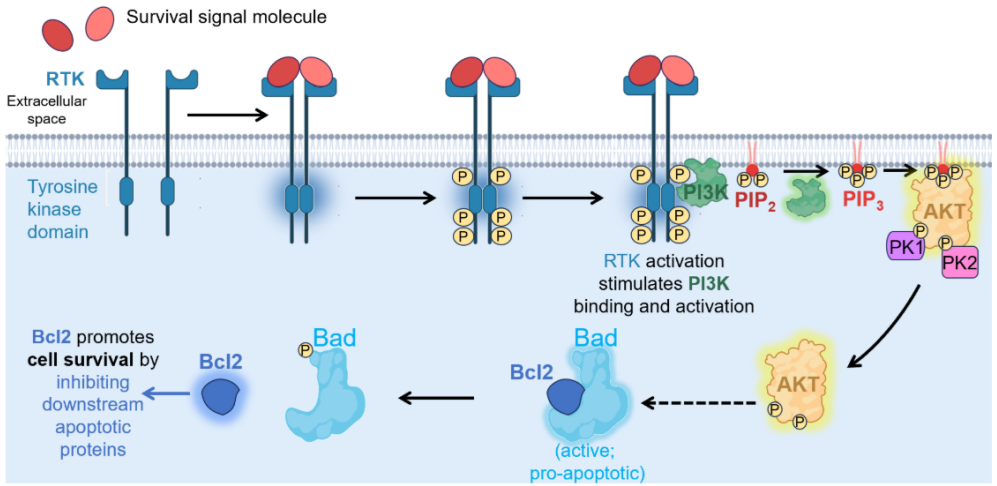
- ○ The redox potential of $FADH_2$ is greater than that of Complex I and so it would not be able to donate its electrons to Complex I
- ○ $FADH_2$ utilizes Complex II only to donate its electrons, which is not a proton pump, and so $FADH_2$ does not contribute to the electrochemical proton gradient utilized for oxidative phosphorylation
- ○ The active site of Complex I is specific to the structure of NADH, and $FADH_2$ would not be acted on by the enzyme
- ○ These are all reasons why $FADH_2$ enters the electron transport chain at a different point that NADH



Commonly Missed Exam Question

Question 23 4 pts

Below is shown the Bcl2 survival signaling cascade. Which of the following scenarios is accurate:

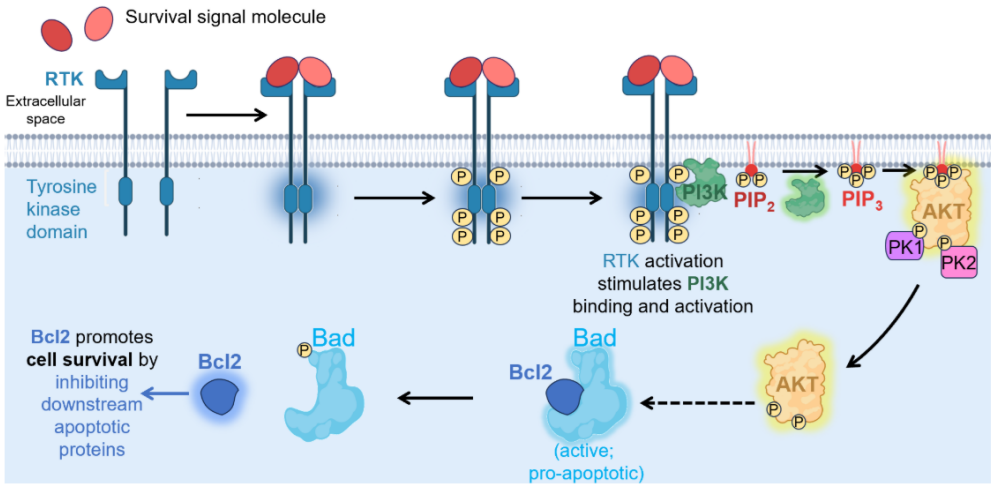


- ○ A mutation in Bad that prevents it from binding to Bcl2 would promote apoptosis
- ○ A mutation in the receptor tyrosine kinase that leads to autophosphorylation in the absence of extracellular ligand binding would promote apoptosis
- ○ A mutation in AKT that makes it catalytically inactive, and therefore unable to phosphorylate Bad, would promote cell survival
- ○ A mutation in PI3K that causes it to phosphorylate PIP_2 in the absence of extracellular ligand binding would promote cell survival

Commonly Missed Exam Question

Question 23 4 pts

Below is shown the Bcl2 survival signaling cascade. Which of the following scenarios is accurate:



- ○ A mutation in Bad that prevents it from binding to Bcl2 would promote apoptosis
- ○ A mutation in the receptor tyrosine kinase that leads to autophosphorylation in the absence of extracellular ligand binding would promote apoptosis
- ○ A mutation in AKT that makes it catalytically inactive, and therefore unable to phosphorylate Bad, would promote cell survival
- ○ A mutation in PI3K that causes it to phosphorylate PIP_2 in the absence of extracellular ligand binding would promote cell survival

Consider signaling pathways to be a binary process, A leads to B, a cause leads to an effect.

Here, extracellular ligand binding (A, the cause) leads to Bcl2 release and cell survival (B, the effect).

Ask yourself: does this mutation cause the cascade to **occur as normal** (i.e., promoting cell survival) or **does it prevent the cascade from happening at some point** (i.e., promoting apoptosis)

← **Outcome:** Bad does not bind Bcl2 → cell survival

← **Outcome:** Signaling cascade occurs uninterrupted→ cell survival

← **Outcome:** Bad remains bound to Bcl2 → apoptosis

← **Outcome:** Signaling cascade occurs uninterrupted→ cell survival

The Cytoskeleton

Our cells need support too!

Part I

BIOL366

April 17, 2025

Matthew Ellis, PhD

Learning Objectives for Today's Lecture:

Upon completing this module, **you should be able to**:

- Describe the functions of the eukaryotic **cytoskeleton**
- Explain the process of dynamic assembly and stability in **microtubules**
- Understand the roles microtubules play in **vesicular trafficking** and **ciliary movement**

Key Terms

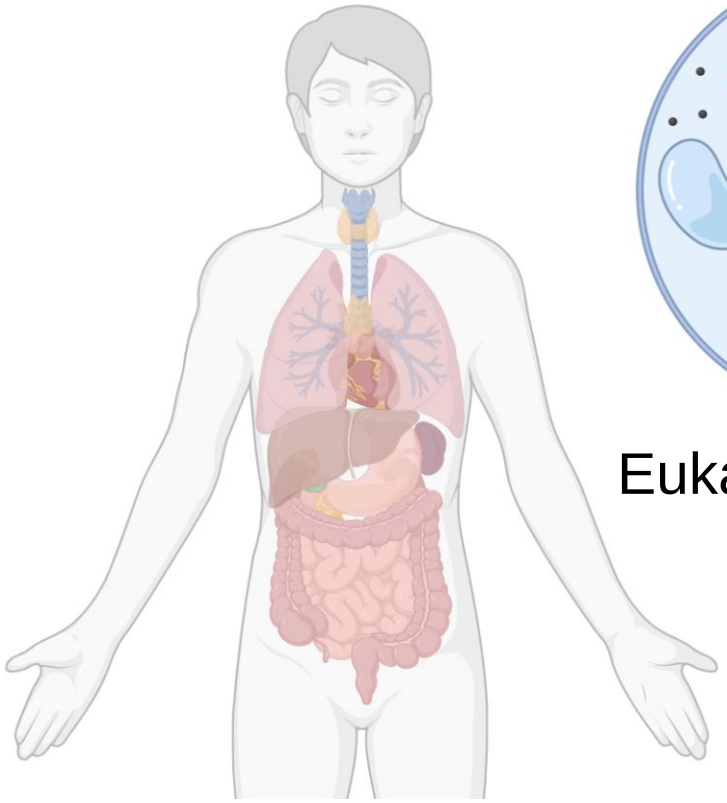
- **Cytoskeleton**: A complex, dynamic network of interlinking protein filaments present in the cytoplasm of all cell
- **Microtubule:** Long rigid tubes extending from the center of cell toward periphery creating a system of tracks to maintain cell shape and facilitate transport within the cell
- **Microtubule Organizing Center (MTOC):** Protect "– end" of the microtubule and allow for initial microtubule formation
- **Protein filament**: Long chains of protein monomers that form the cytoskeleton
- **Dynamic instability**: A property of microtubules that allows them to rapidly reorganize the cytoskeleton. This process involves microtubules alternating between growing and shrinking states
- **Vesicle:** A small, fluid-filled internal cellular compartment
- **Cilia:** Hairlike protrusions from cell surfaces that contribute to particle movement using microtubules
- **Flagella:** Hairlike organelles that provide motility to sperm and protozoans

Learning Objectives for Today's Lecture:

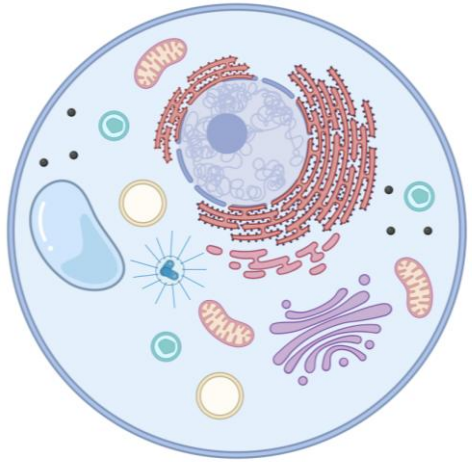
Upon completing this module, **you should be able to**:

- Describe the functions of the eukaryotic **cytoskeleton**
- Explain the process of dynamic assembly and stability in **microtubules**
- Understand the roles microtubules play in **vesicular trafficking** and **ciliary movement**

The Cytoskeleton provides structural support and maintains the shape of cells

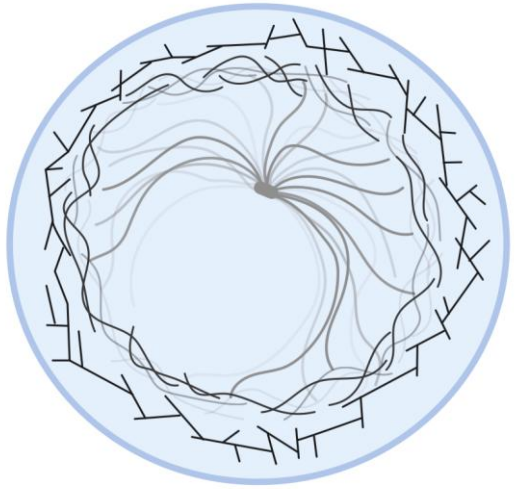


Human body with organs



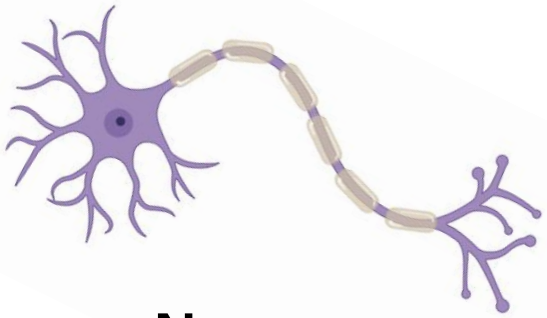
Eukaryotic cell with organelles

Human skeletal system



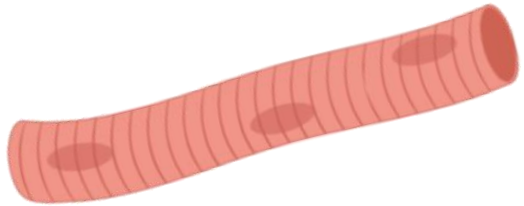
Eukaryotic cytoskeleton

The Cytoskeleton supports cell shape in different tissues

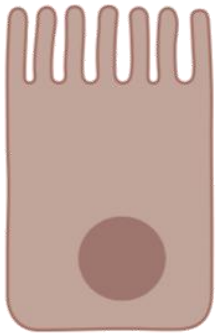


Neuron

Red blood cell

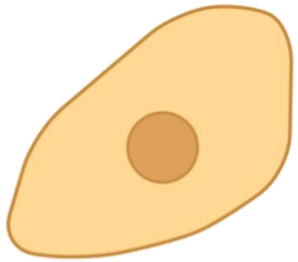


Muscle cell

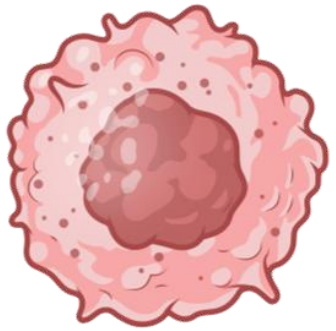


Epithelial cell

White blood cell



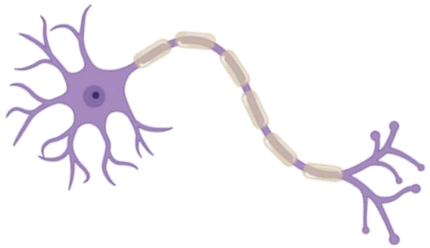
Endocrine cell



Cancer cells rely on the cytoskeleton too

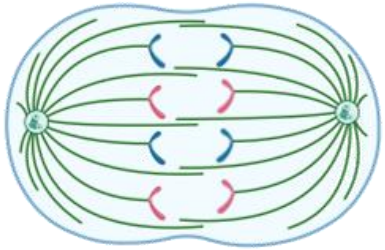
Functions of the Cytoskeleton

Muscle contraction

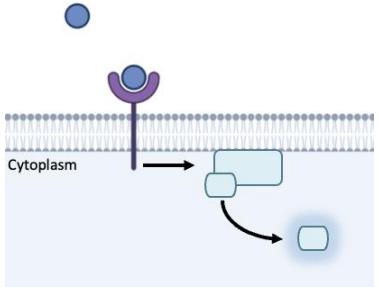


Cell shape maintenance and support

Cell movement



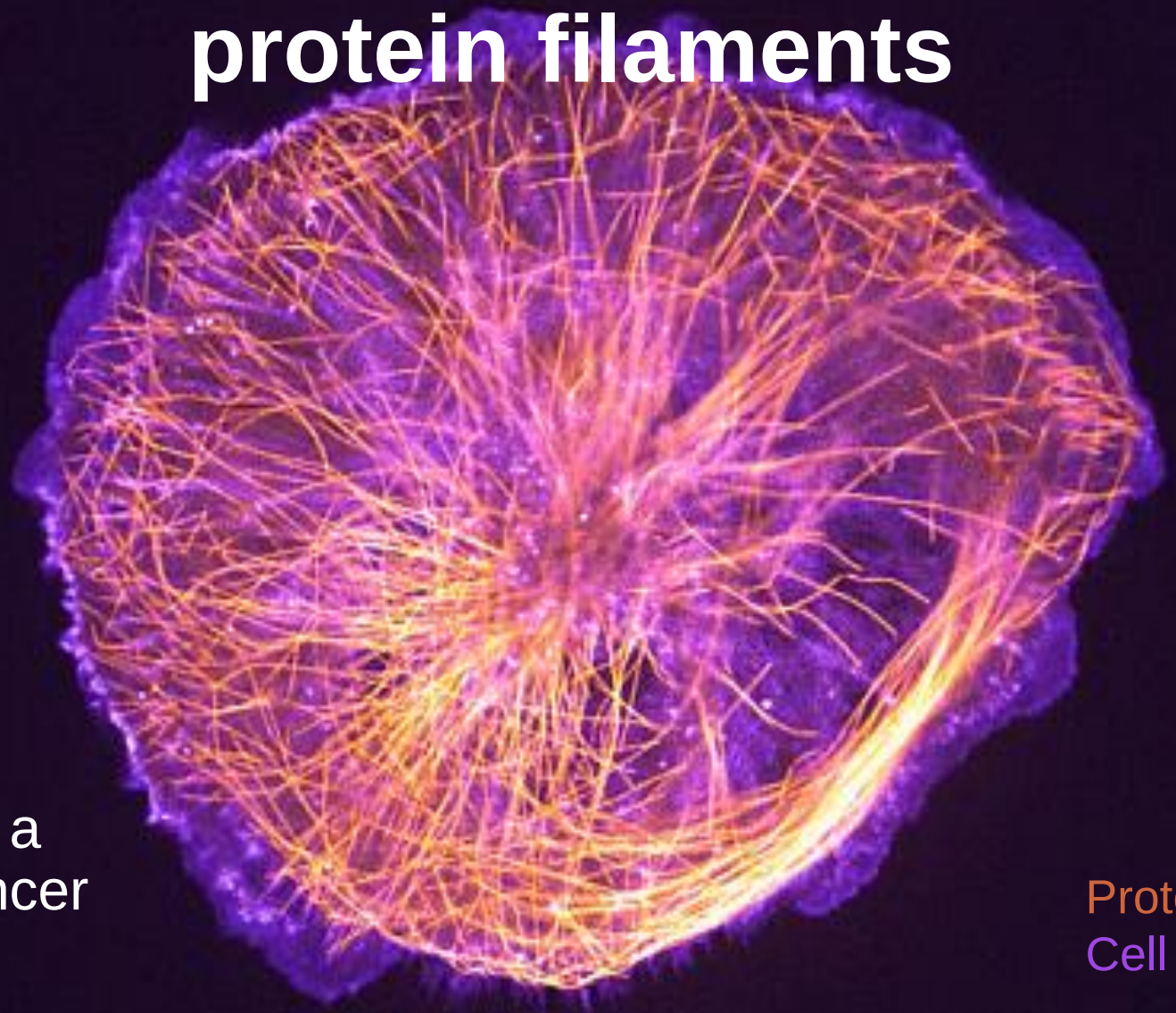
Chromosome segregation during cell division



Aid in signal transduction

Transport of vesicles and organelles

The Cytoskeleton is a dynamic network of protein filaments

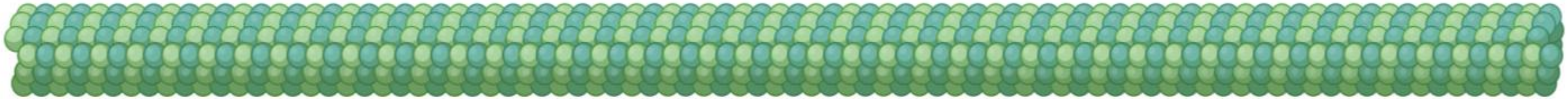


Cytoskeleton of a human breast cancer cell line

Protein filaments
Cell membrane

The 3 essential components of the Cell's skeleton

Microtubules

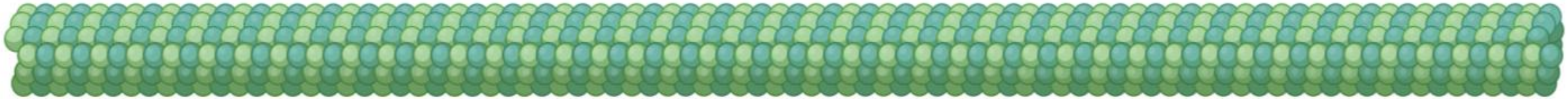


Intermediate filaments

Actin filaments

The 3 essential components of the Cell's skeleton

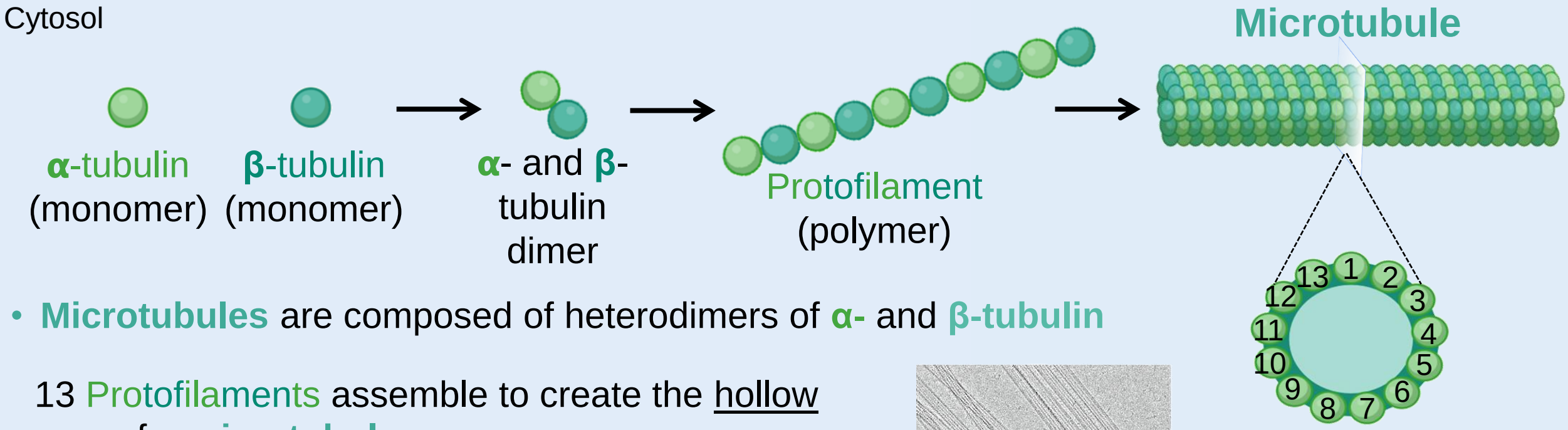
Microtubules



Intermediate filaments

Actin filaments

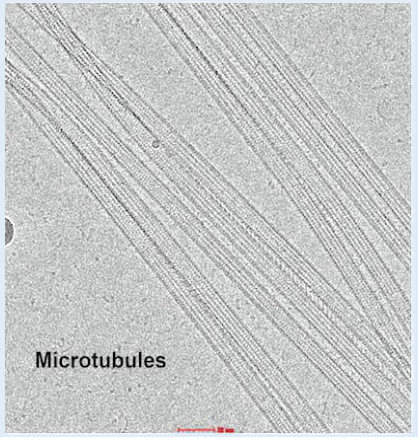
Microtubules are composed of tubulin proteins



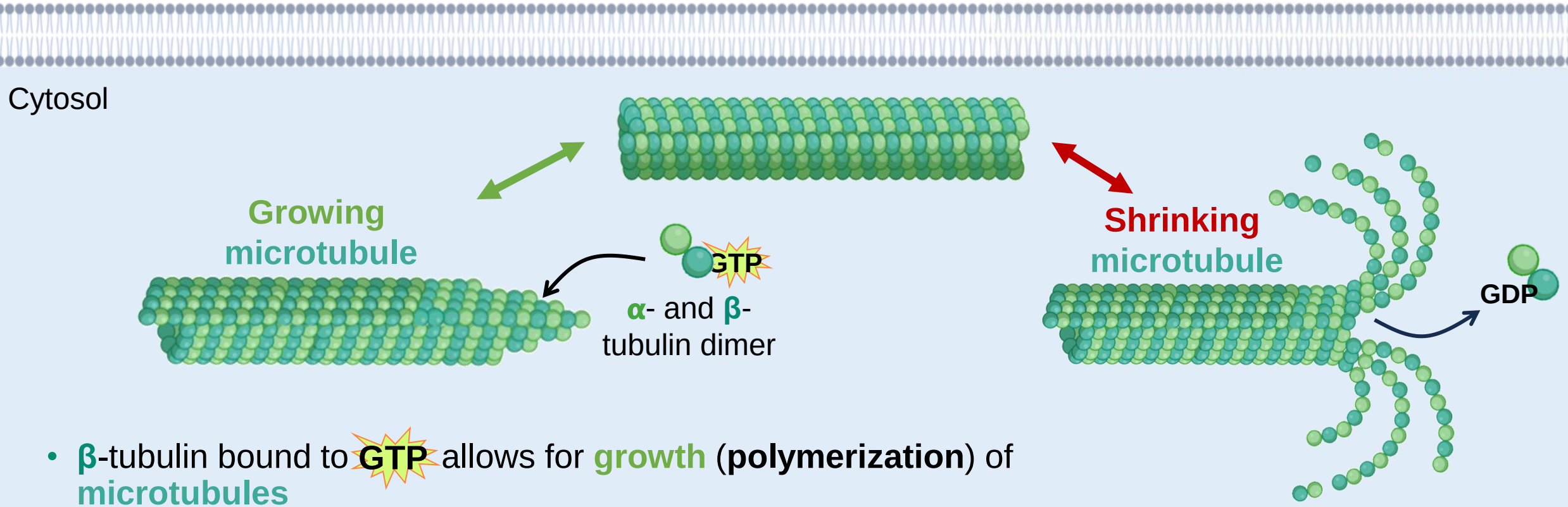
- **Microtubules** are composed of heterodimers of **α-** and **β-tubulin**

13 Protofilaments assemble to create the hollow core of a **microtubule**

- **Microtubules** are the **largest component** of the cytoskeleton, with a diameter of ~25 nm



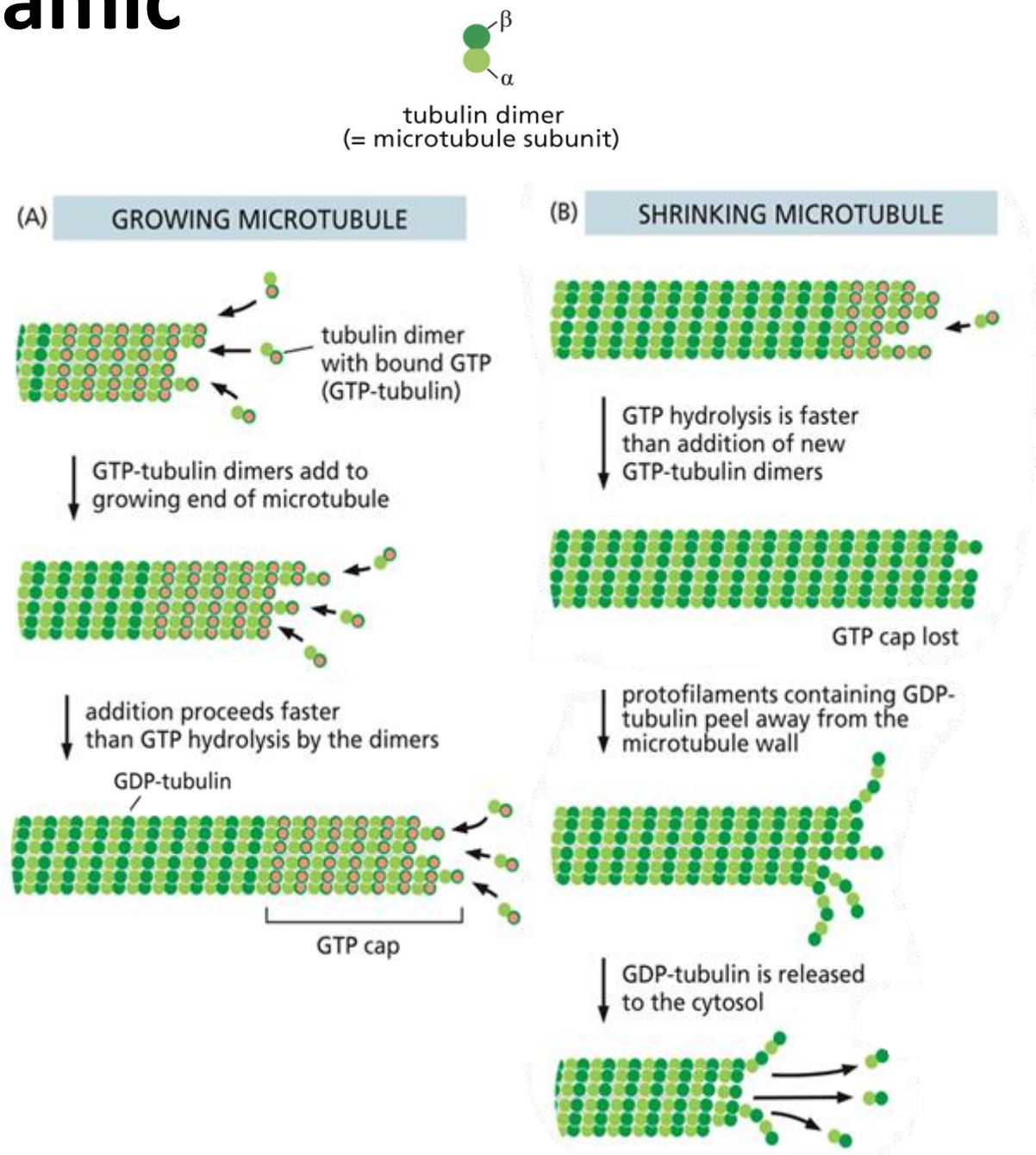
Microtubules are dynamic structures, with their growth regulated by GTP



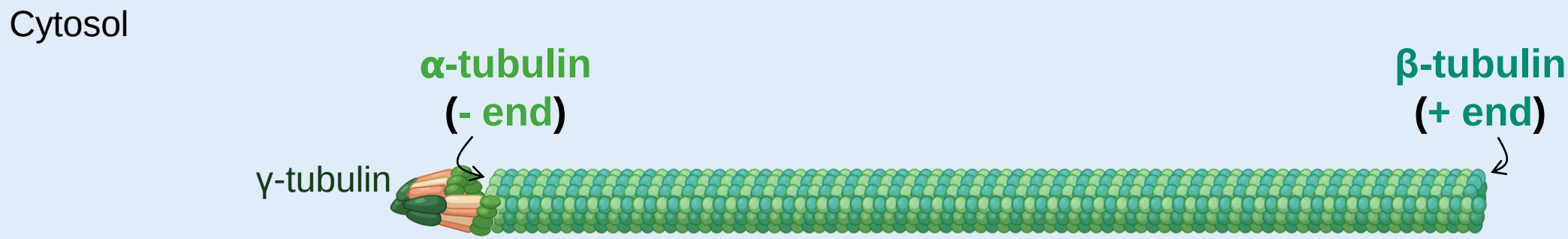
- β-tubulin bound to GTP allows for growth (**polymerization**) of microtubules
- β-tubulin bound to **GDP** leads to **shrinking** (**depolymerization)** of microtubules
- Microtubules grow or shrink depending on the rate of GTP hydrolysis relative to the rate of tubulin addition = **dynamic instability**

Microtubule Assembly is Dynamic

- β-tubulin in the dimer binds GDP or GTP, with the GTP-bound dimer binding *more tightly* than the GDP-bound dimer in the growing microtubule
- Rapidly growing microtubules will thus form a **GTP cap** on the growing end that allows it to keep assembling
- GTP is hydrolyzed to GDP shortly after being added. The rate of GTP hydrolysis *relative* to the rate of assembly determines growth or shrinkage of the microtubule
- Slowly growing microtubules will therefore deplete the GTP cap
- This causes disassembly (catastrophe) due to the lower binding affinity of the GDP-bound tubulin dimers

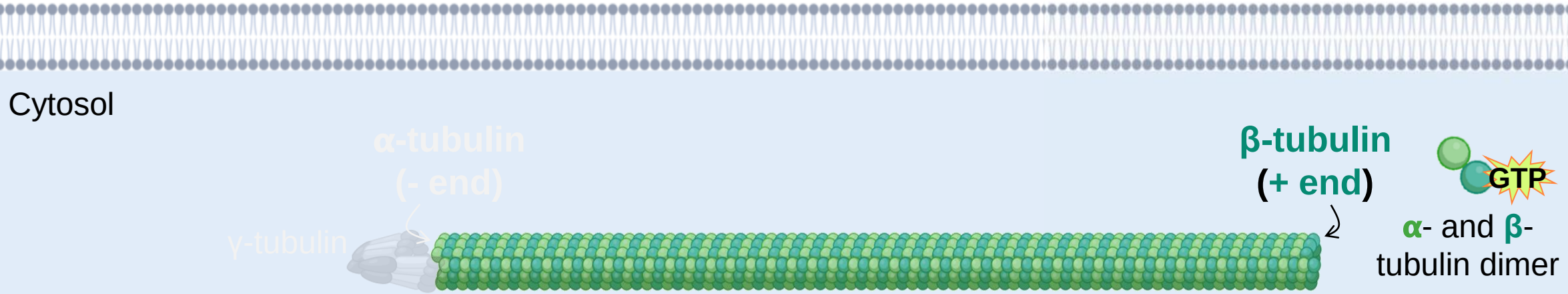


Microtubule polarity determines its growth rate



- The "**-end**" is the **slower growth end** where **α**-tubulin is exposed
- "**- end**" protected by a microtubule organizing center (**MTOC**)
  - e.g., **γ-tubulin**, basal body, centrioles
- **MTOCs** allow for initial microtubule nucleation (creation of microtubules)

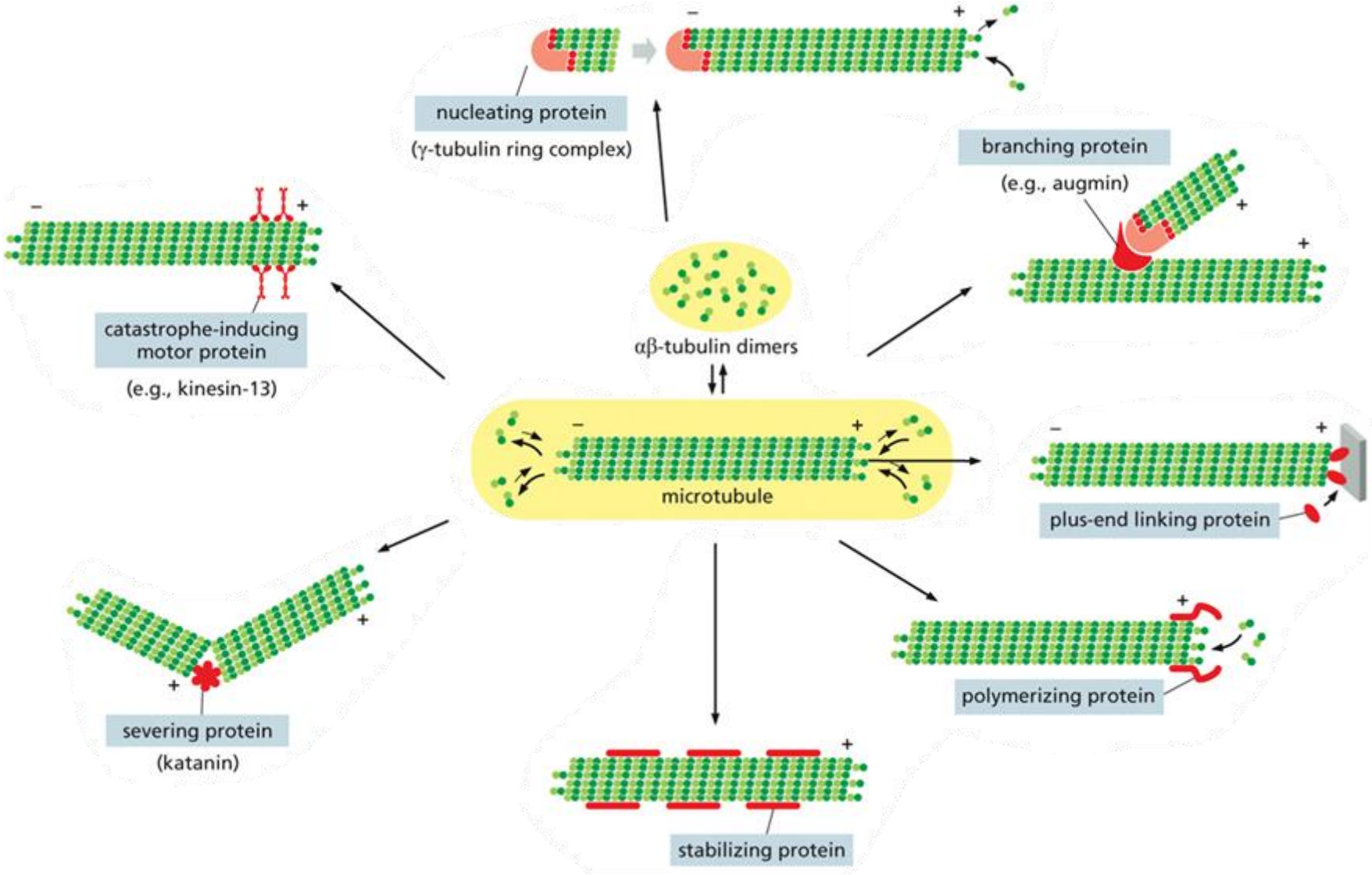
Microtubule polarity determines its growth rate



- The "**-end**" is the **slower growth end** where **α**-tubulin is exposed
- "**- end**" protected by a microtubule organizing center (MTOC)
  - e.g., **γ-tubulin**, basal body, centrioles
- MTOCs allow for initial microtubule nucleation (creation of microtubules)

- The "**+ end**" refers to the **rapid growth end** where **β**-tubulin is exposed
- Microtubule **polymerization and depolymerization** primarily occurs at the "**+ end**"
- "**+ end**" **are protected by microtubule associated proteins (MAPs)**

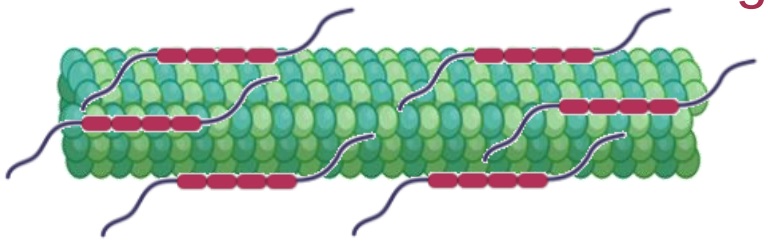
Microtubule–associated proteins (MAPs) regulate dynamics and organization



Dissociation of tau protein from microtubules contributes to Alzheimer's Disease

Healthy brain

Stabilizing tau protein

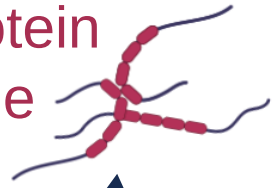


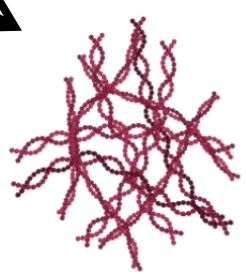
Healthy Microtubule

Healthy neuron

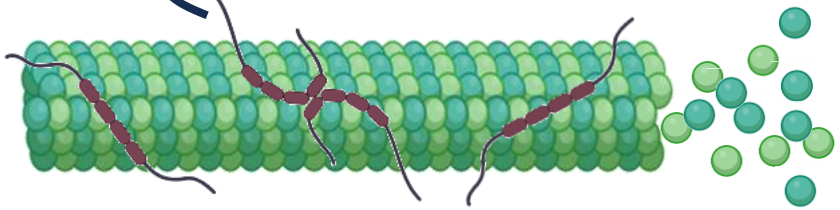
Alzheimer's brain

Tau protein tangle

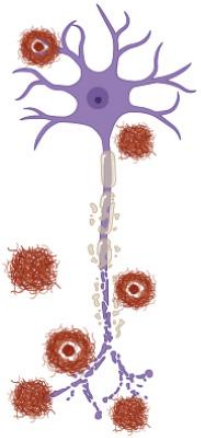




Neurofibrillary tangle

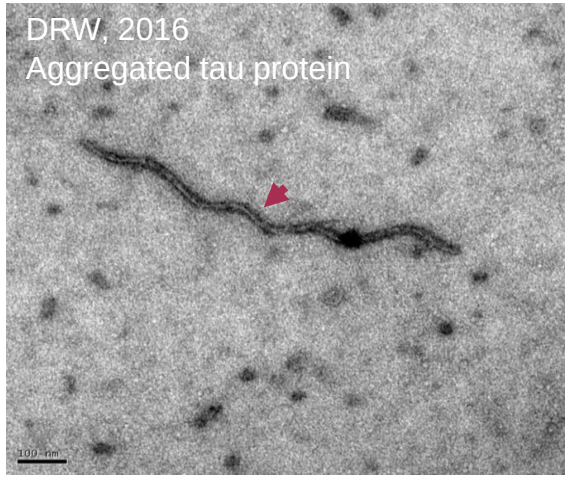


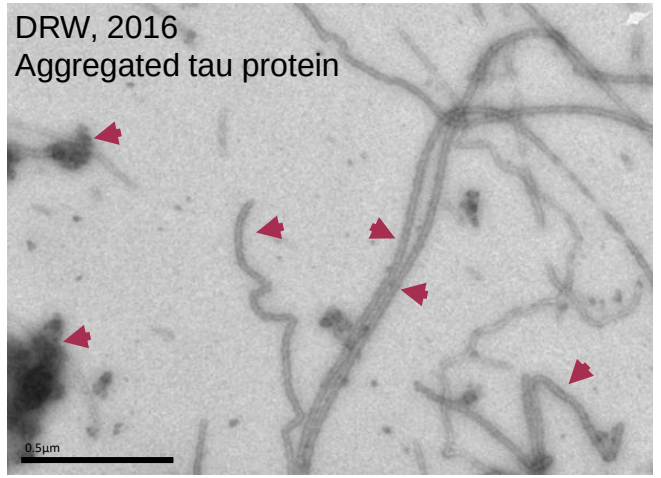
Microtubule depolymerization



Diseased neuron

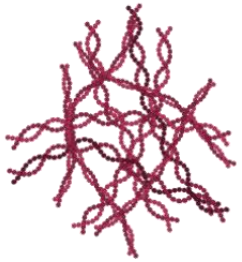
Dissociation of tau protein from microtubules contributes to Alzheimer's Disease



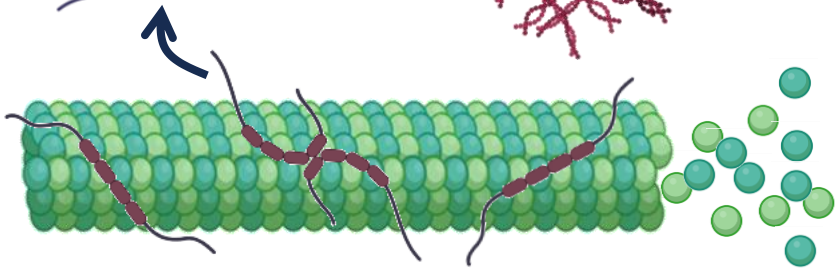


Alzheimer's brain

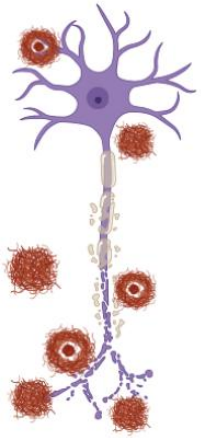
Tau protein tangle



Neurofibrillary tangle



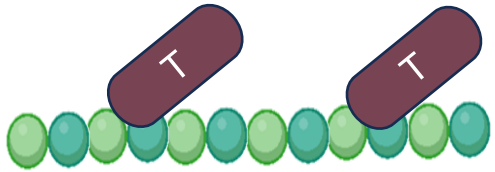
Microtubule depolymerization



Diseased neuron

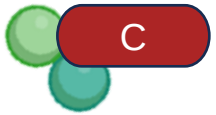
Dynamic instability of microtubules can be modified by microtubule targeting agents

Taxol*



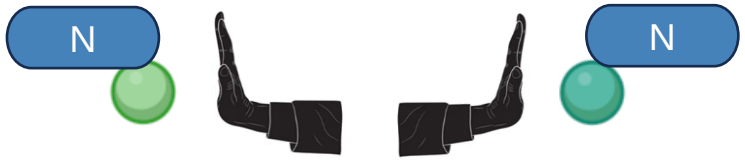
Prevents microtubule depolymerization by binding to protofilaments

Colchicine*



Prevents microtubule polymerization by binding to α- and β-tubulin

Nocodazole*



Prevents α- and β-tubulin from dimerizing

***These drugs are used in cancer treatments to prevent cell division**

Squarecap #1-2

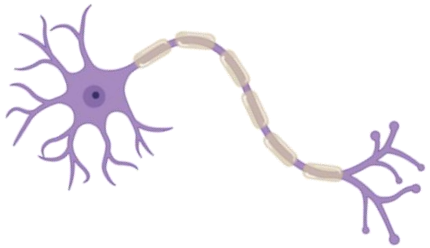
Learning Objectives for Today's Lecture:

Upon completing this module, **you should be able to**:

- Describe the functions of the eukaryotic **cytoskeleton**
- Explain the process of dynamic assembly and stability in **microtubules**
- Understand the roles microtubules play in **vesicular trafficking** and **ciliary movement**

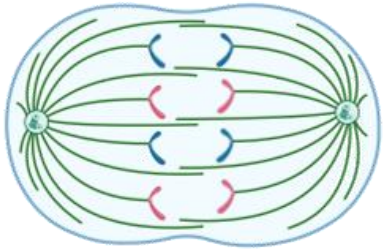
Functions of the Cytoskeleton (Microtubules)

Muscle contraction

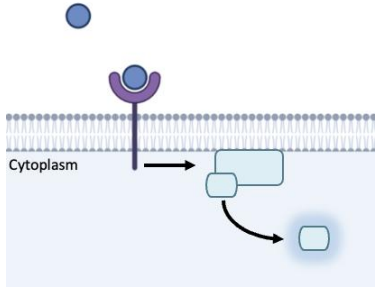


Cell shape maintenance and support

Cell movement



Chromosome segregation during cell division



Aid in signal transduction

Transport of vesicles and organelles

Functions of the Cytoskeleton (Microtubules)

Muscle contraction

Cell shape maintenance and support

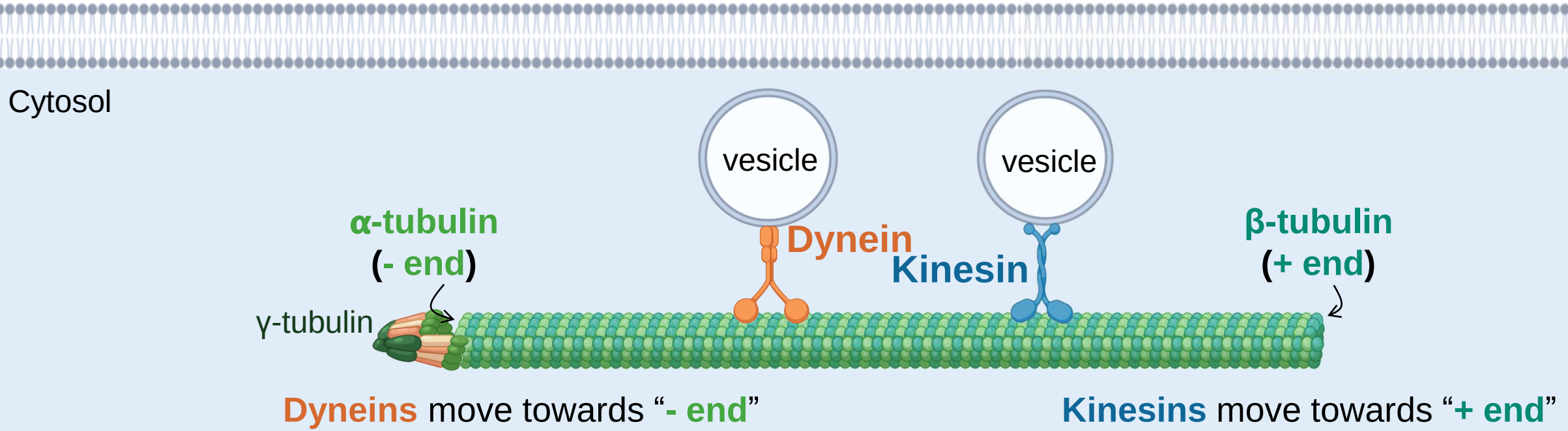
Cell movement

Chromosome segregation during cell division

Aid in signal transduction

Transport of vesicles and organelles

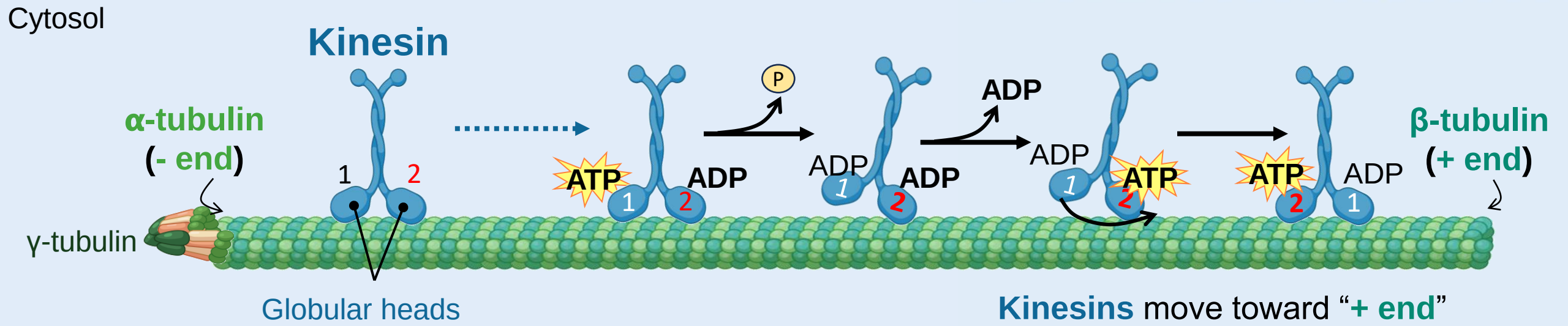
Motor proteins move along microtubules to transport cellular cargo:



- Movement of intracellular cargo (vesicle or organelle) occur over long distances on microtubules

- Dynein and Kinesin can bind cargo directly or use adaptor proteins that help bind cargo

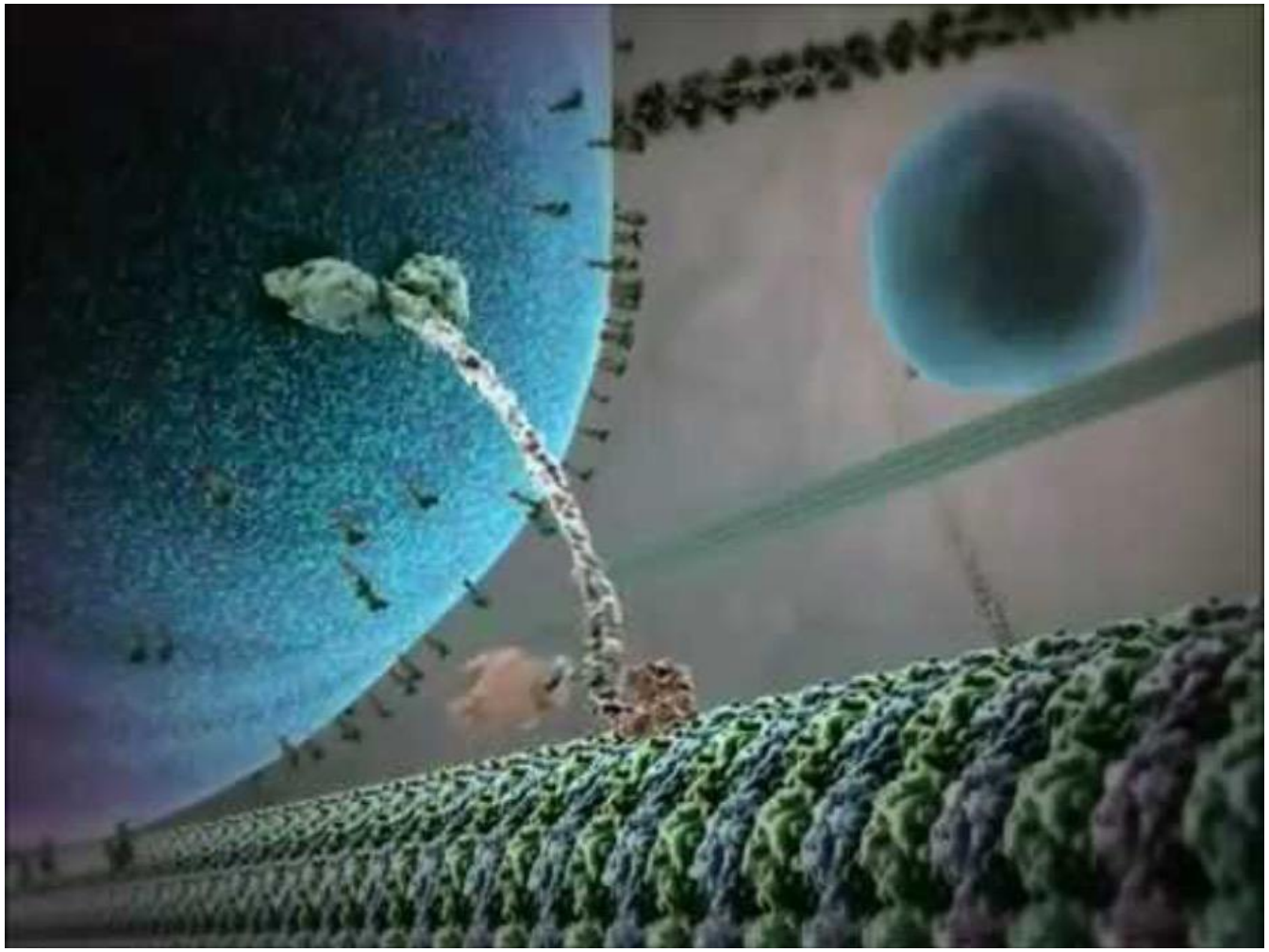
Kinesins utilize ATP to "walk" along microtubules



- Globular heads (1 & 2) of **kinesins** are enzymes with ATP hydrolyzing activity
  - Hydrolysis of ATP on Globular head 1 **loosens grip on microtubule**
  - Globular head **2** **releases ADP, and binds ATP to induce conformational change**
  - Globular head 1 **swings forward** and cycle can repeat for subsequent steps

Note that the conformation of the ADP-bound state is time-dependent, with increased affinity for microtubule binding with time

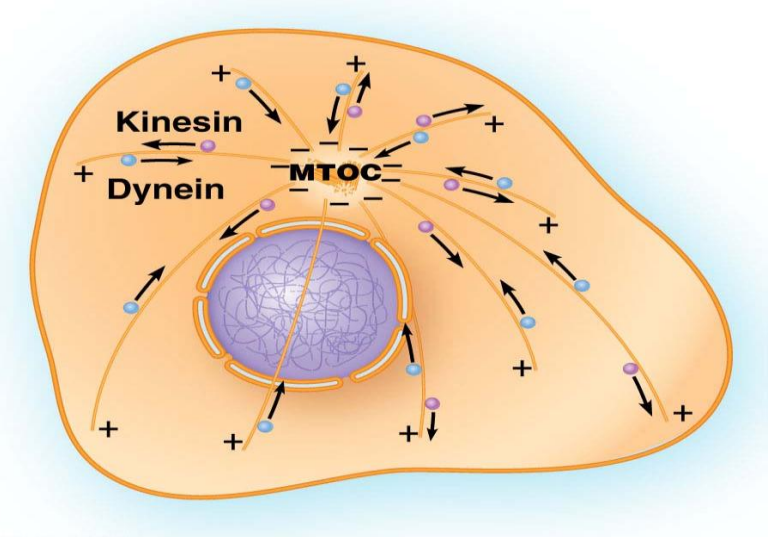
Kinesins mediate Vesicle and Organelle Transport

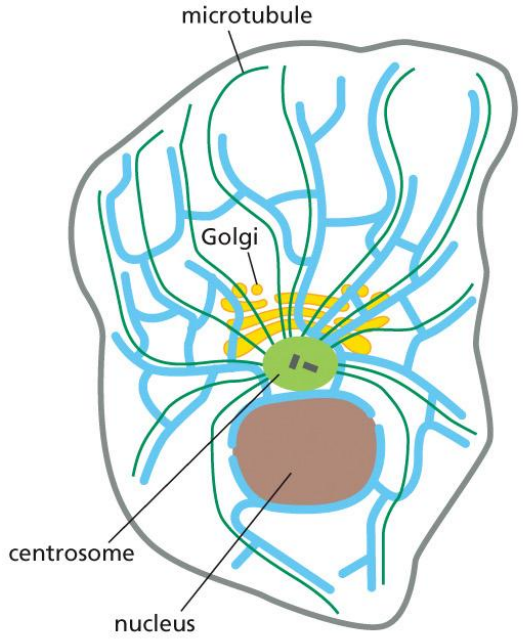


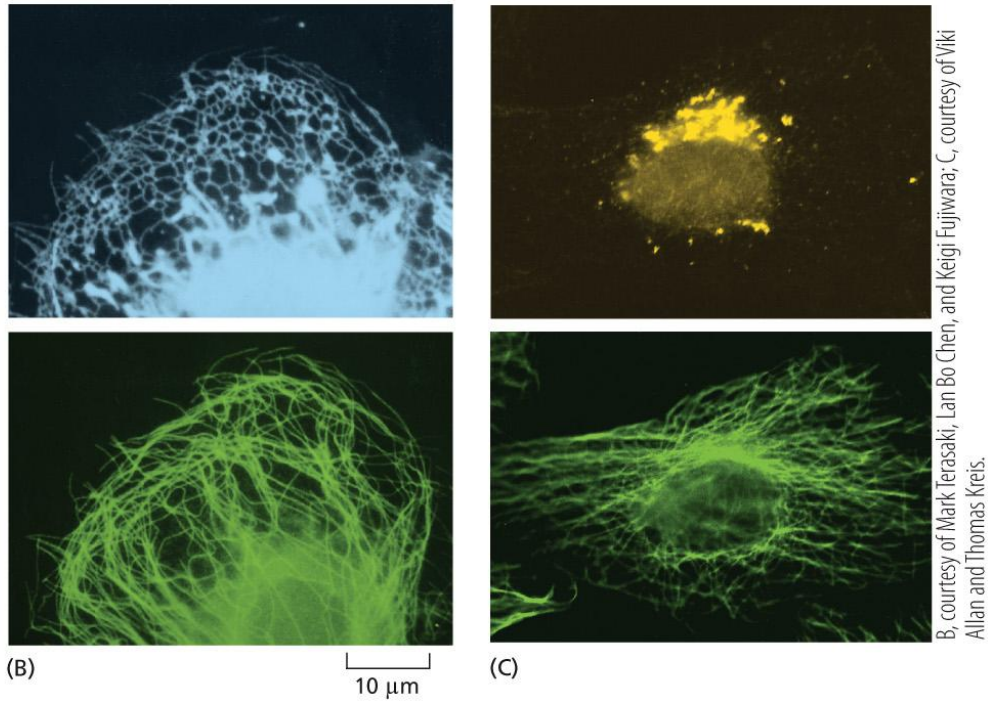
- Kinesins transports:
  - Synaptic vesicles
  - Mitochondria
  - Golgi apparatus
  - Endosomes
  - Multiprotein complexes
  - Viruses!
- Move cargo over long distances: 100 steps, ~1 μm

Microtubule motor proteins shape the endomembrane system

- ER (blue) extends out from nuclear envelope to edge of cell
  - Kinesins attached to outside of ER pull it along length of microtubule toward edge
- Golgi (yellow) is located near centrosome on one side of nucleus
  - Dyneins attached to outside of Golgi pull it along microtubule toward nucleus
- Vesicles to and from Golgi are carried by motor proteins



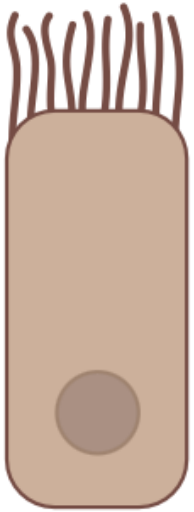




ER (blue); MT (green)

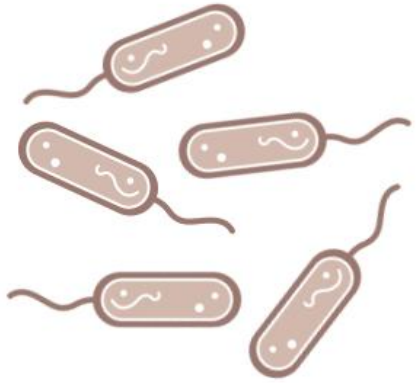
Golgi (yellow); MT (green)

Microtubule-based organelles



Cilia

Flagellum



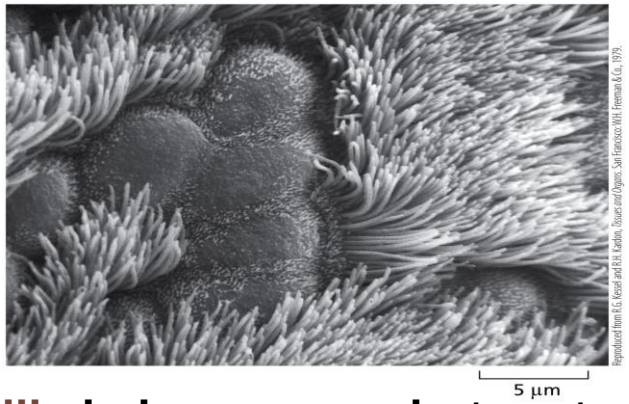
Cilia: hair-like organelles that protrude from cell surfaces

- Cilia are primarily found in epithelial cells
  - Respiratory, reproductive, GI tracts

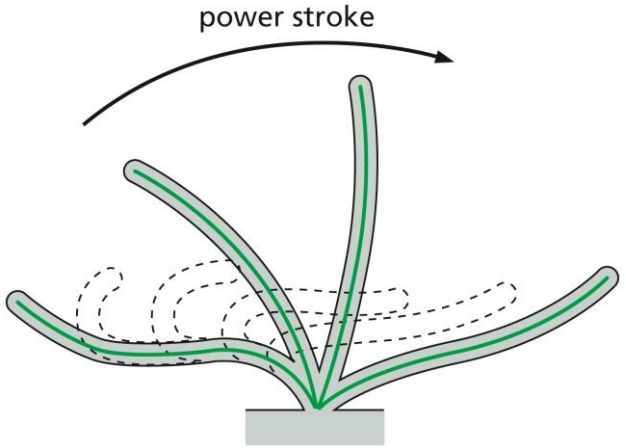
- *Move environment* past the cell (e.g., mucus across epithelial cells of respiratory tract, eggs across oviduct)

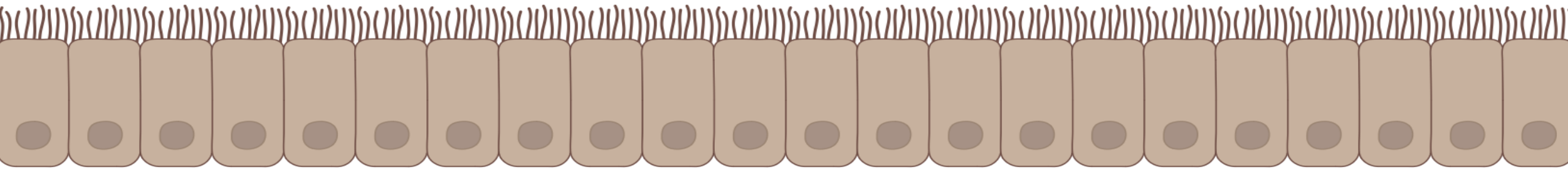
- Present in huge numbers (1 cm^2 of epithelial tissue contains ~1 billion cilia!)

- Power-strokes (whip-like motions) help to move fluid over the cell (dotted lines show slower recovery stroke)



Cilia in human respiratory tract





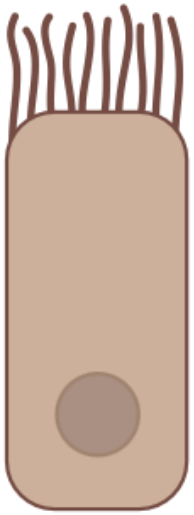
Flagellum: hair-like organelles that propel cells

- Provides motility to sperm and protozoa (e.g., amoeba)
- Designed to *move entire cell through environment* with ‘propagated bending motion’
- Microtubules are essential in **flagellum** for chemotaxis (movement in response to chemical signals)

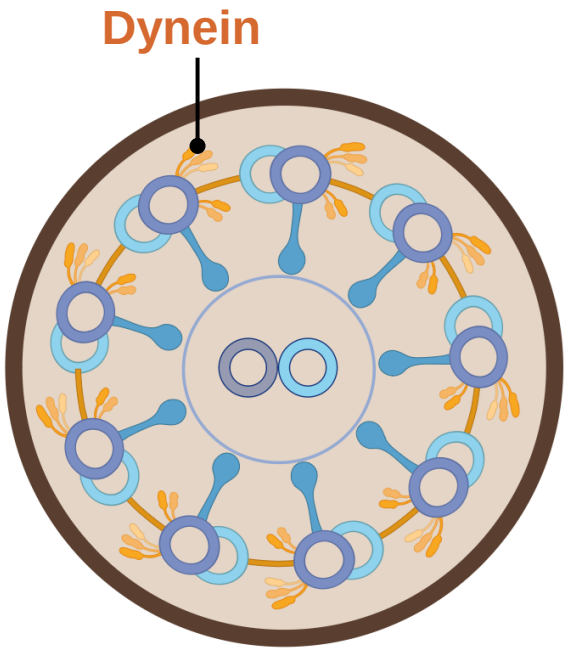
Sperm cell

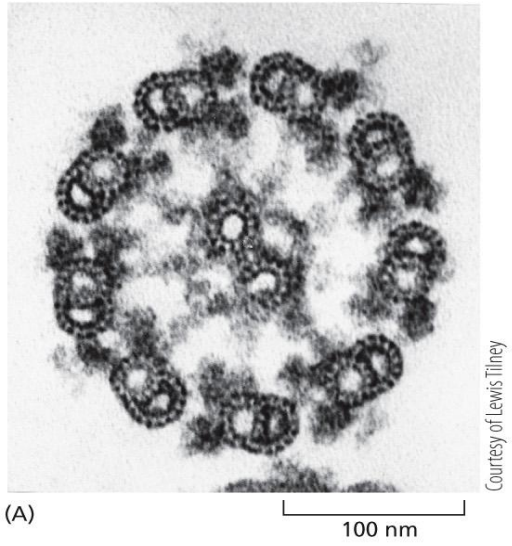
Amoeba

Microtubules are arranged in a “9+2” array in Cilia and Flagella



Cilia

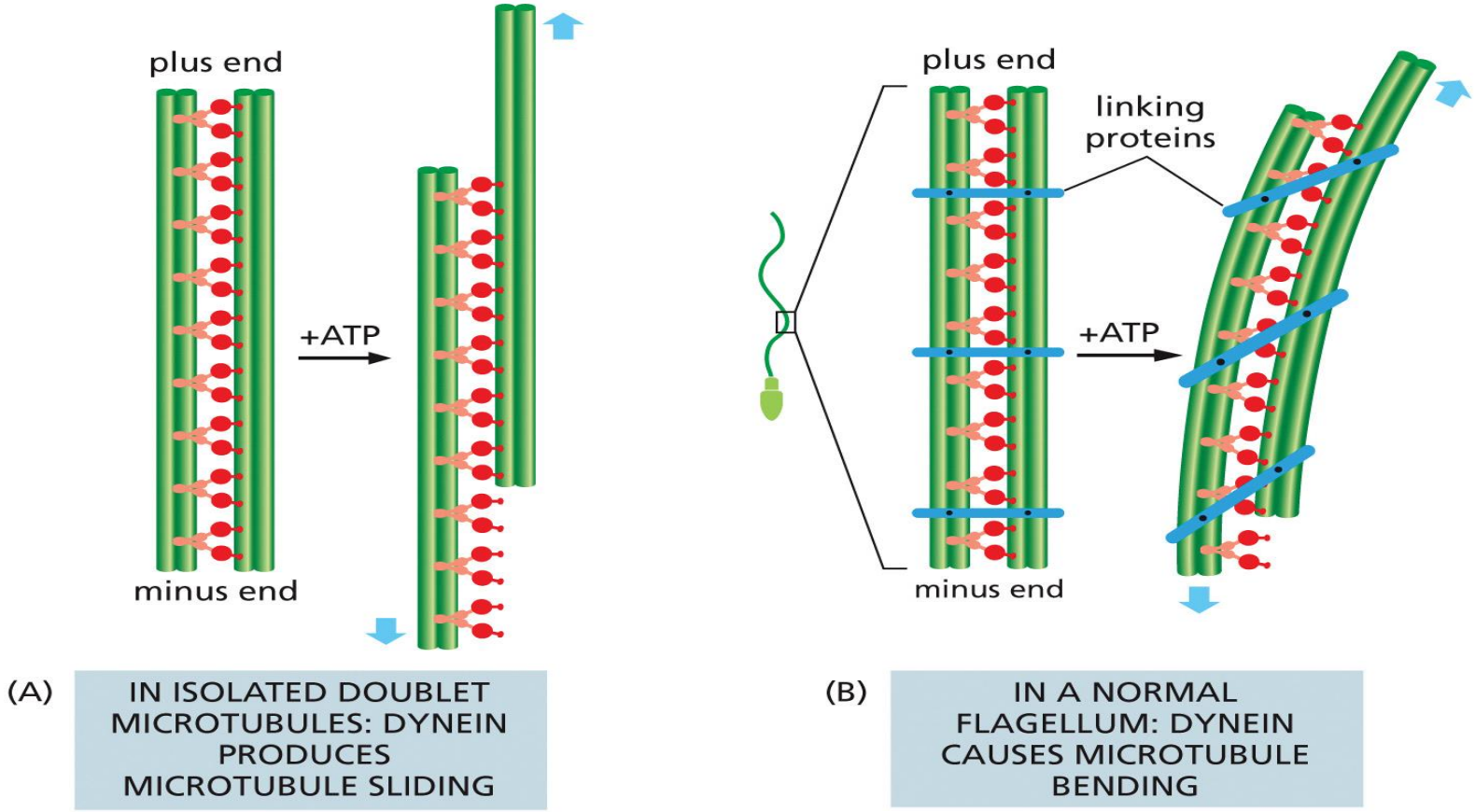


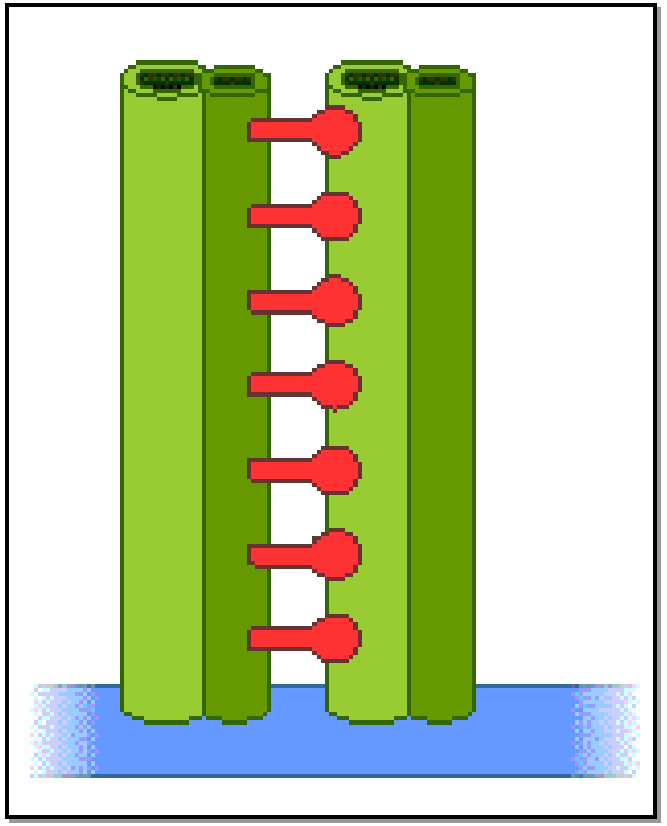


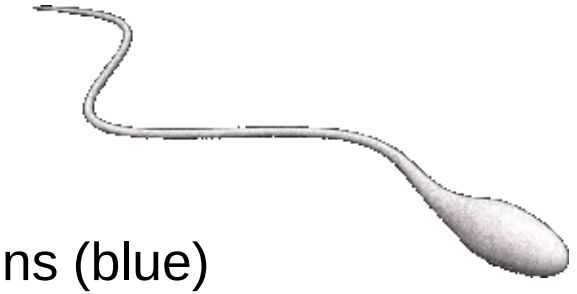
Flagella

- Contain a pair of microtubules surrounded by 9 doublets of microtubules
- Numerous accessory proteins that aid in microtubule stability, including **dyneins**
  - Each microtubule doublet carries two rows of dynein motor proteins (inner and outer arm)
  - Bind to adjacent doublet microtubules to pull itself along and cause sliding of microtubules past each other

Cilia and flagella contain stable microtubules moved by dynein







- **Sliding** of microtubules is mediated by dynein motor proteins
- **Bending** is due to microtubules being tied to each other by linking proteins (blue)

Squarecap #3-4

Learning Objectives for Today's Lecture:

Upon completing this module, **you should be able to**:

- Describe the functions of the eukaryotic **cytoskeleton**
- Explain the process of dynamic assembly and stability in **microtubules**
- Understand the roles microtubules play in **vesicular trafficking** and **ciliary movement**

Metacognitive Reflection Form