



Cytoskeleton

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Functions of Cytoskeleton

- Determining and maintaining the cell shape, location and shape of nucleus (elasticity, stability)
- Cell (migration, diapedesis) and organelle movement (saltatory movement)
- Phagocytosis, endocytosis, exocytosis
- Cytokinesis (division of cytoplasm)
- Intracellular transport
- Muscle contraction
- Maintaining the cell-cell and cell-extracellular matrix interrelations

Basic Elements of Cytoskeleton

MICROFILAMENTS (8 nm)

- **Protein subunit:** Actin (42 kD)
- **Pattern:** Fibrillary (F-actin) and globular (G-actin)
- **Isoforms:** alpha, beta, gamma

MICROTUBULES (25 nm)

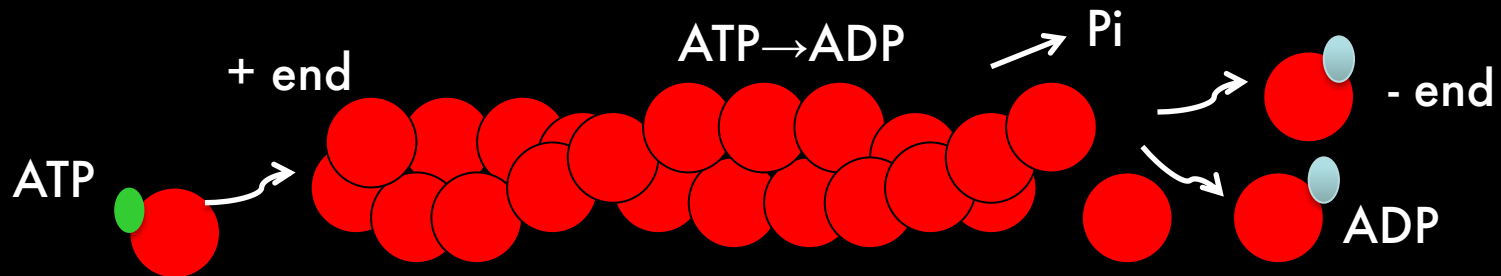
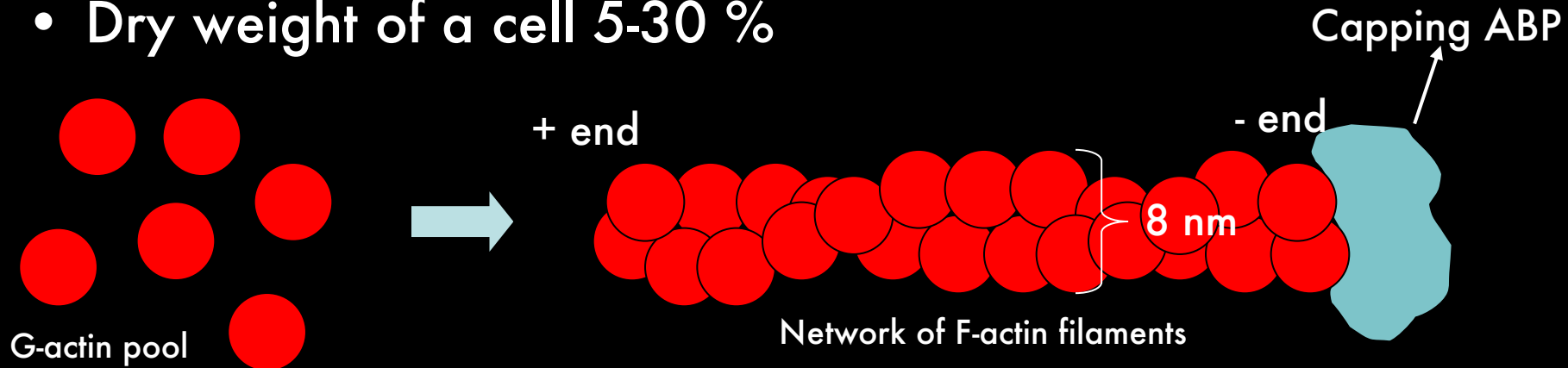
- **Protein subunit:** Tubulin (50 kD)
- **Pattern:** Cylindrical hollow
- **Isoforms:** alpha, beta, gamma, delta, epsilon

INTERMEDIATE FILAMENTS (10 nm)

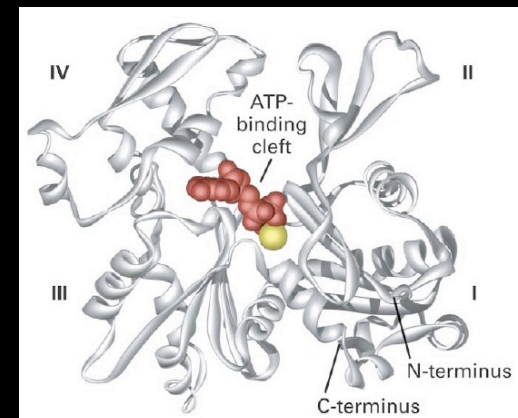
- **Protein subunits:** Keratins, Desmin, GFAP, Vimentin, Peripherin, Neurofilaments, Lamins, Nestin (40-220 kD)
- **Pattern:** Fibrillary filaments

Microfilaments

- G-Actin molecules (42 kD)
- Dry weight of a cell 5-30 %

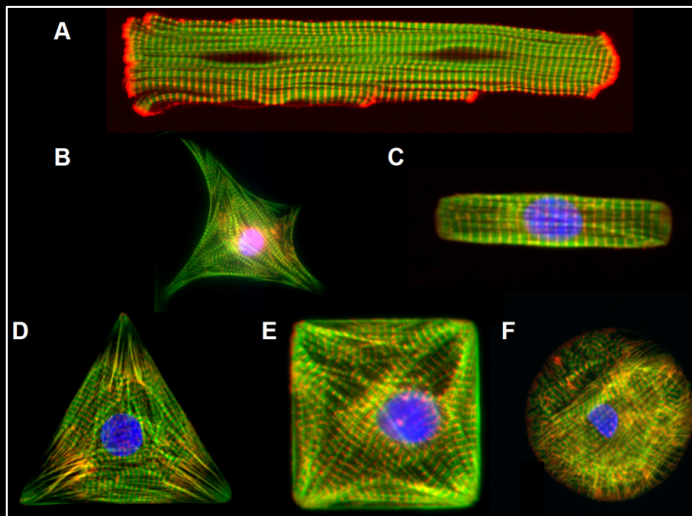


- ATP-dependent polymerization

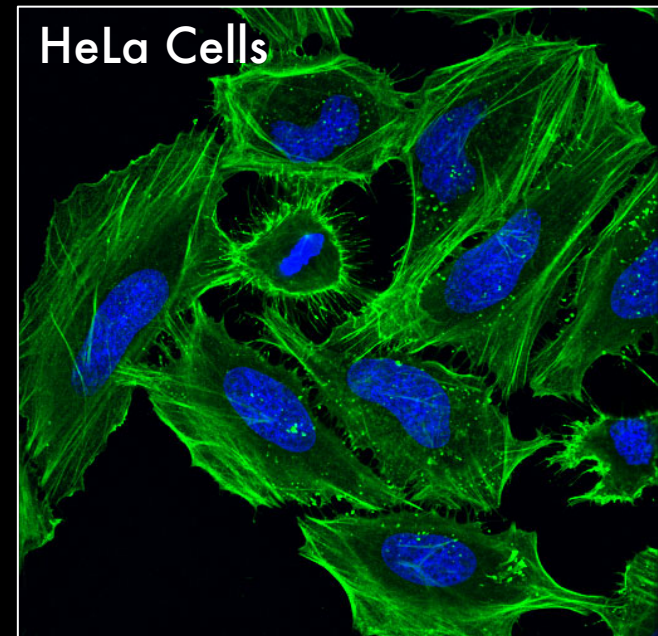


Actin Isoforms

- Alfa (α)
 - Actin filaments in muscle fibers
 - Beta (β)
 - Gamma (γ)
- } Cytoskeletal fibers in many cell types and as regulatory proteins in cell movement

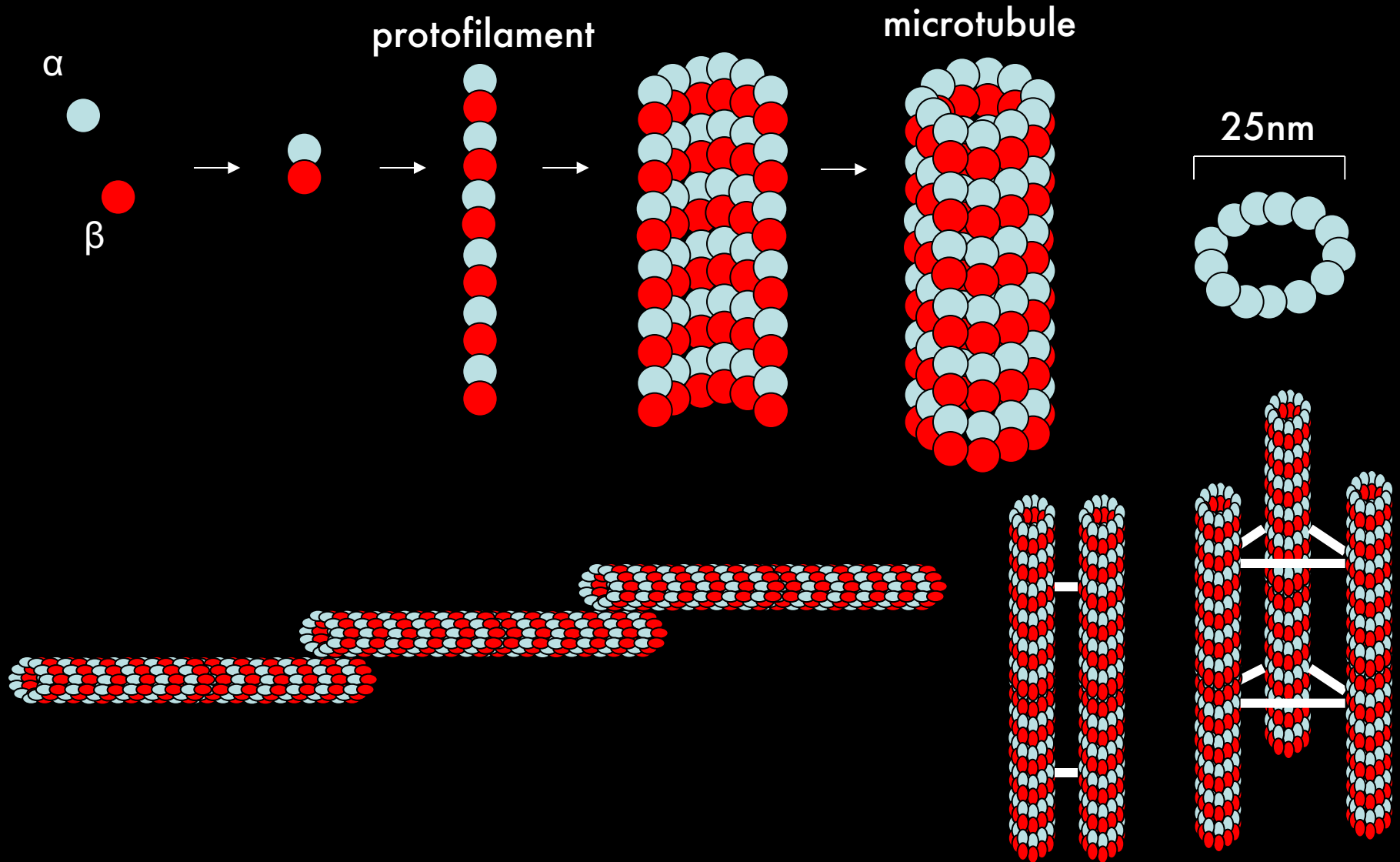


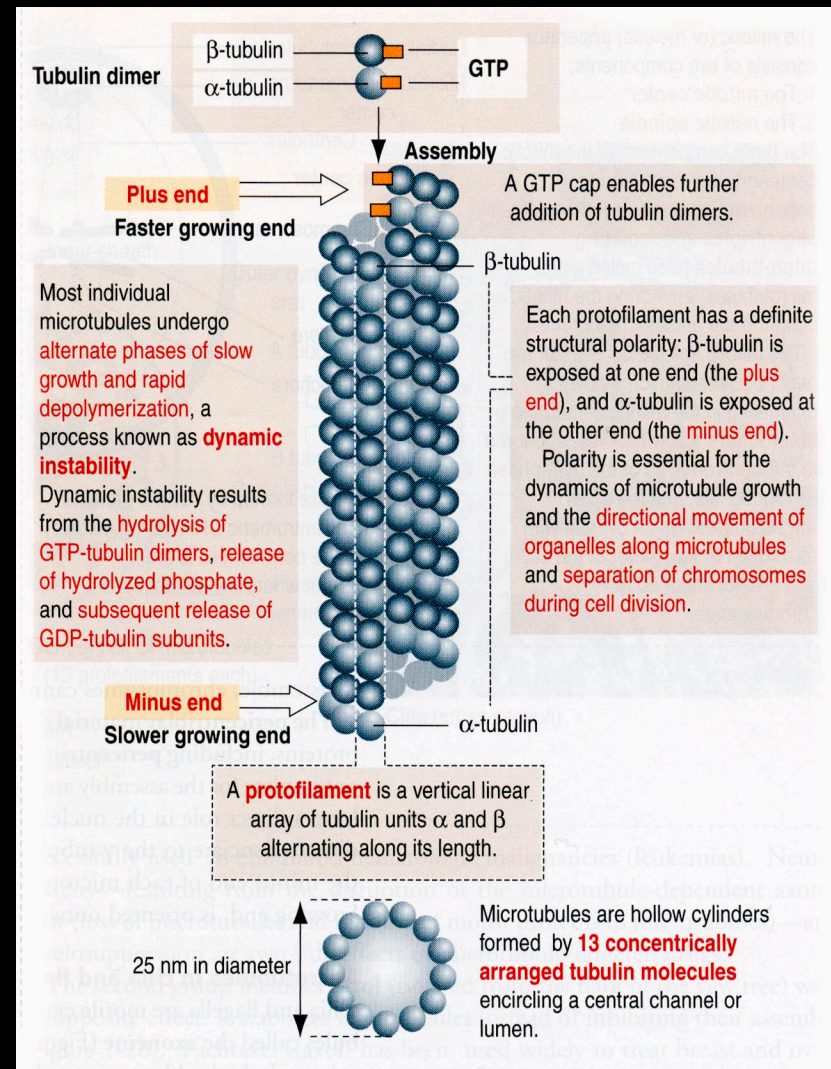
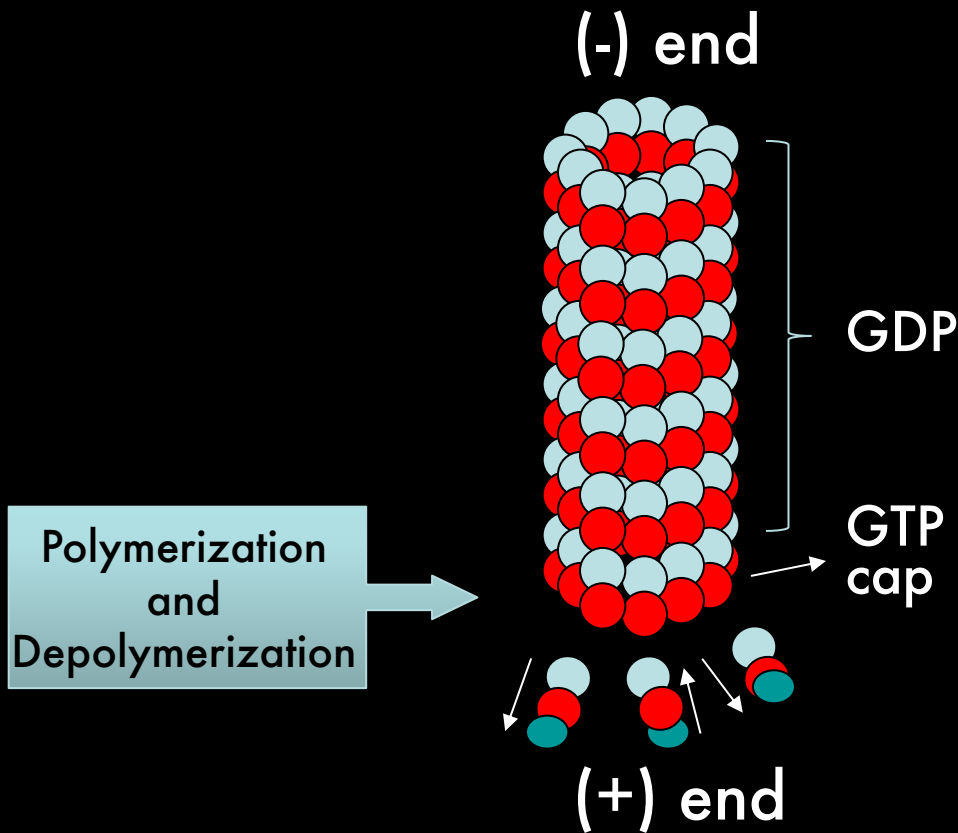
α sarcomeric actin
 α -sarcomeric actinin



β actin

Microtubules (MTs)





Factors regulating the MT polymerization;

- **Tubulin concentration**

Below critical concentration (C_c) of tubulin ($< 10 \mu\text{M}$) = depolymerization

Above critical concentration (C_c) of tubulin ($> 10 \mu\text{M}$) = polymerization

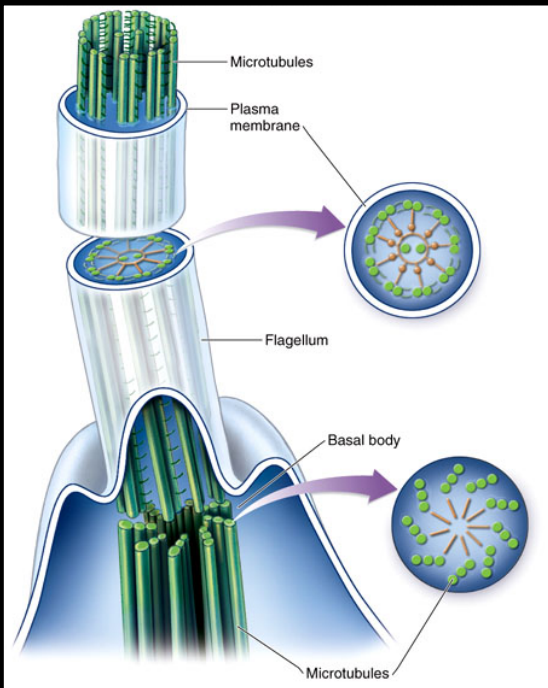
- **Temperature**

Maximum @ 37°C

Total disassembly @ $2-8^\circ\text{C}$ (reversible)

Axoneme

- Serves as a skeleton for a cilium or a flagellum



Major Constituents of Axoneme

Microtubules

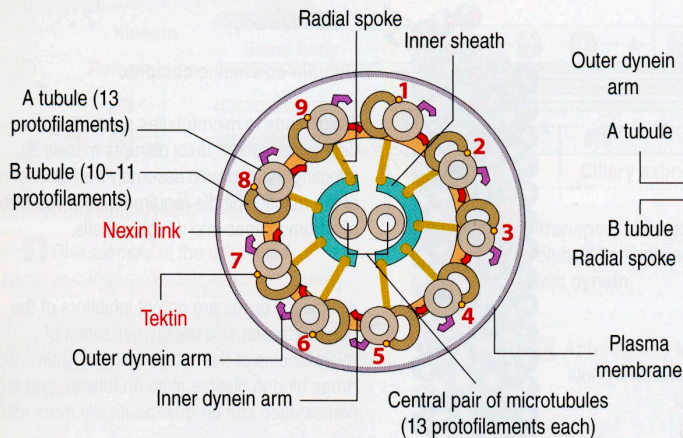
Tectins

Dynein Arms

Nexin links

Radial spokes

Inner sheath

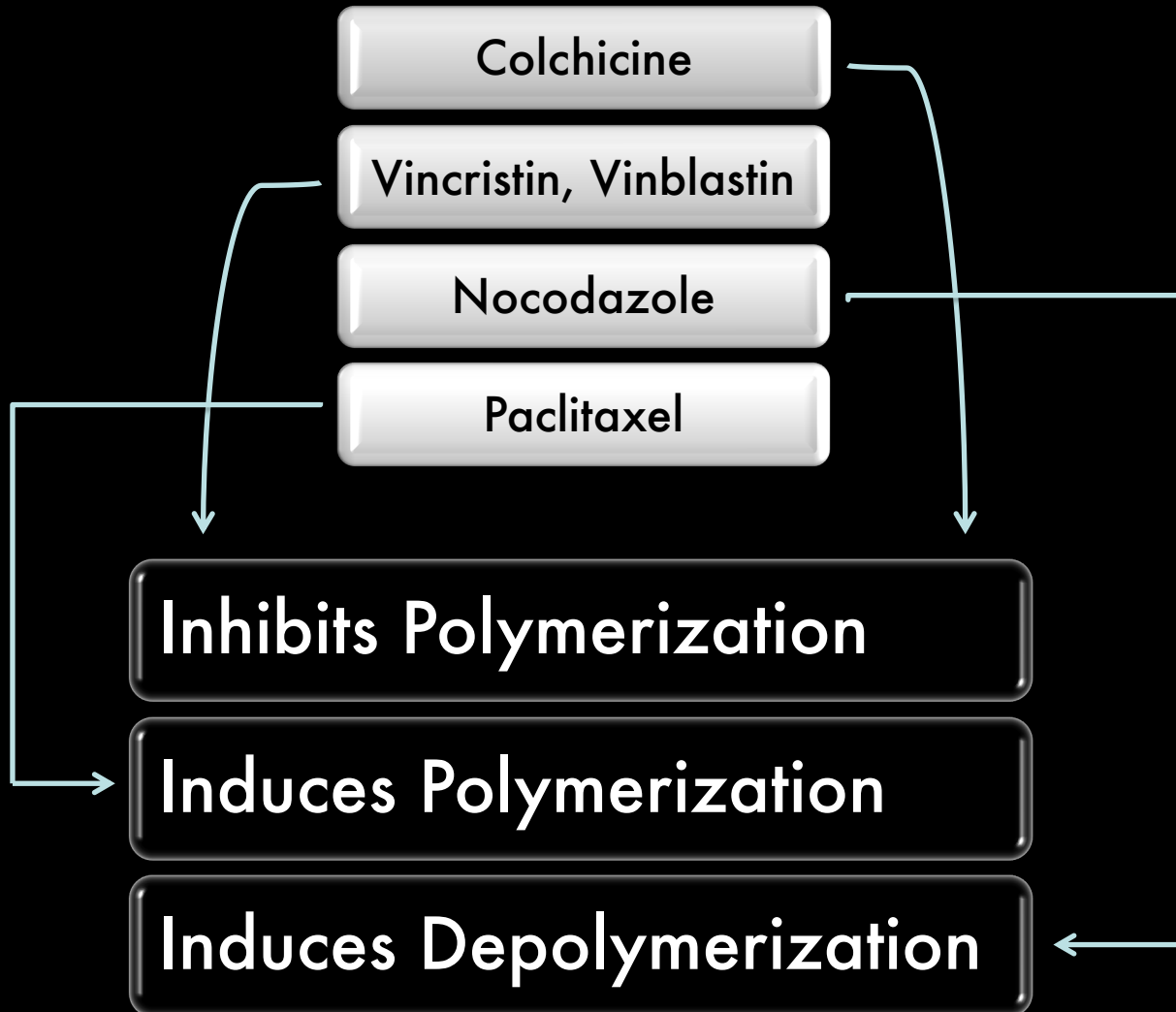


Cilia (cross section)

The relative position of **A and B tubules** and their **dynein side arms** give each cross section of the axoneme a distinct polarity and clockwise orientation (**1-to-9 direction**).

Cilium (plural: cilia) = Hair-like moving appendages on the apical cell surface
Flagellum (plural: flagella) = whip-like structure (tail of spermatozoa)

Drugs Regulating the MT dynamics (cancer chemotherapeutics)

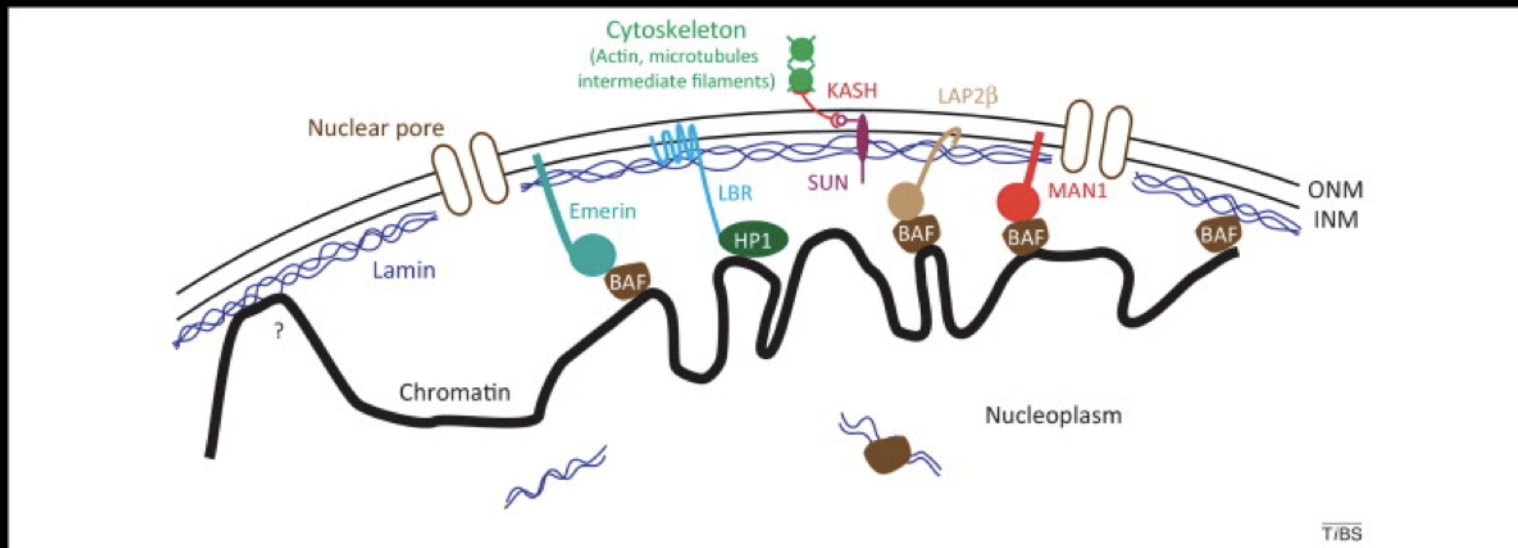
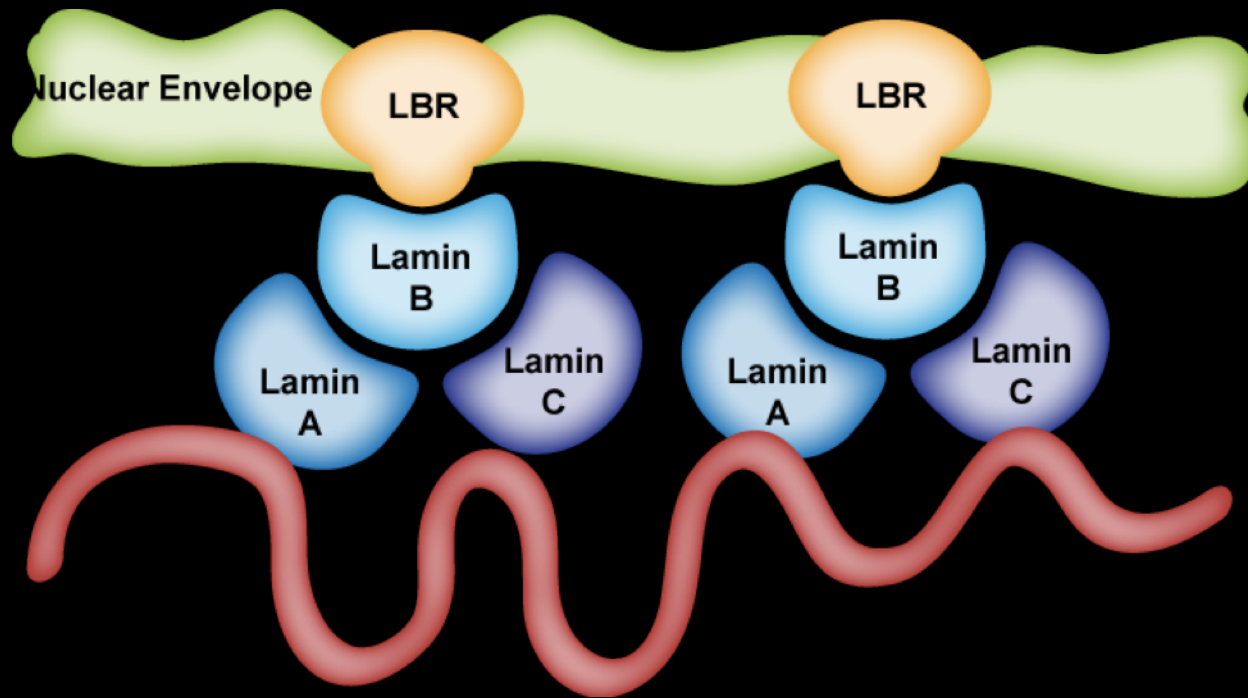


Intermediate Filaments (IFs)

- 9-11 nm in diameter
- Every type has a different molecular mass (40-200 kDa)
- Most stable and durable among other cytoskeletal elements
- Polymerization/depolymerization cycles are based on their phosphorylation states (phosphorylation provides stability)
- Varies due to the cell type; therefore IF type shows the cell type

Intermediate Filaments (IFs)

Type	Name	Cells Found
1	Acidic keratins (40-60kDa)	Epithelial cells and derivatives (hair, nail etc.), Cytoplasmic plaques, Desmosomes and Hemidesmosomes
2	Neutral and basic keratins (50-70kDa)	
3	Vimentin (54 kDa)	Mesenchyme-originated cells
	Desmin (53 kDa)	Muscle cells
	Glial Fibrillary Acidic Protein (51 kDa)	Astrocytes and Schwann cells
	Peripherin (57 kDa)	Some neurons in peripheral nervous system
4	Neurofilaments (68-220 kDa) (NF-L, NF-M, NF-H)	Axons and dendrites
5	Lamins (A, B, C)	Nuclear inner membrane
6	Nestin	Developing neurons



Associated Proteins of Cytoskeleton

Binding/Regulatory (ABP, MAP, IFBP)

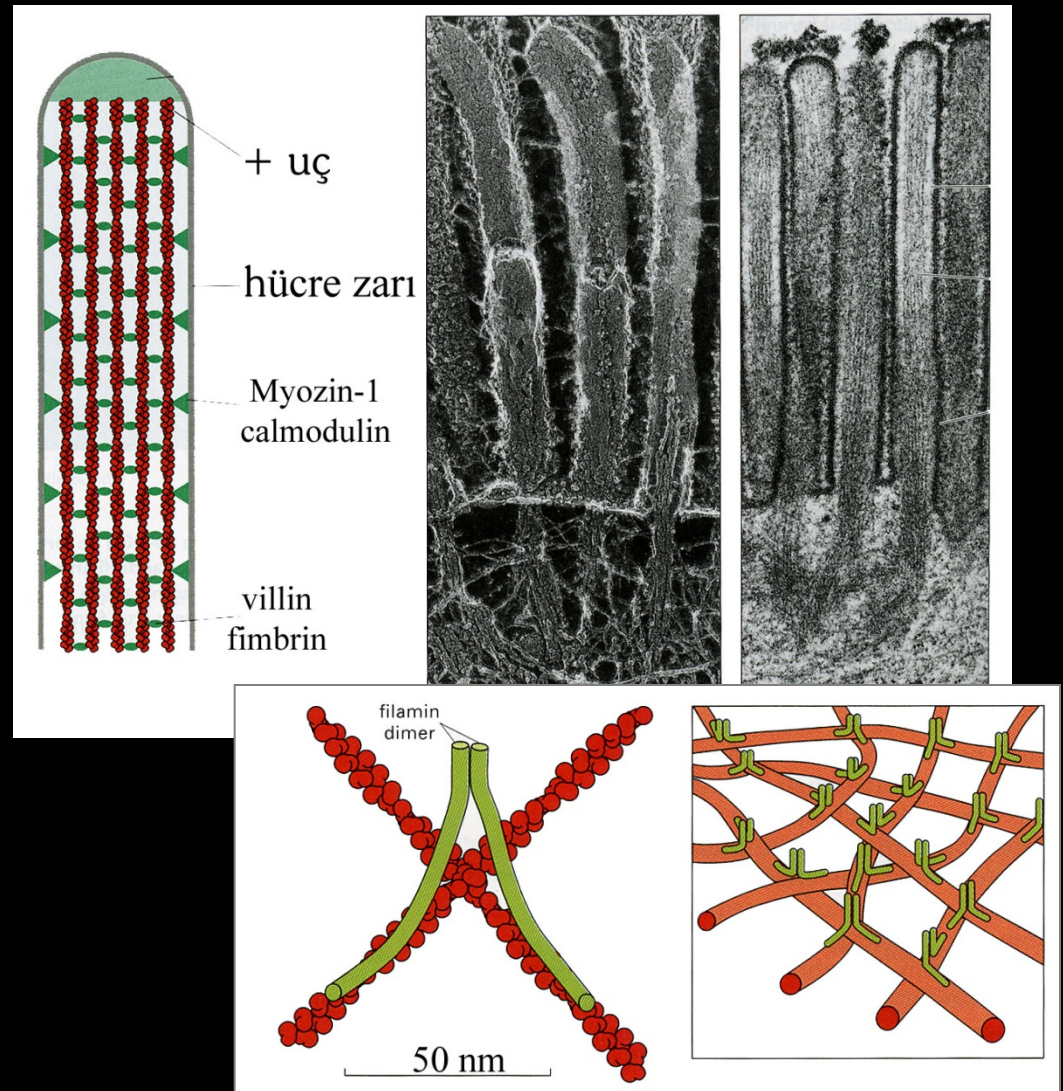
- Attachment to each other
- Determination of length, angle and number

Motor Proteins (kinesin, dynein, myosin)

- Intracellular transport
- Cytokinesis
- Contraction

Actin Binding Proteins

- Villin
- Fimbrin
- Filamin
- Timosin
- Profilin
- Gelsolin (capping)
- Myosin-1
- Calmodulin
- Spectrin (erythrocytes)



Cytoskeletal Diseases

- Cardiovascular syndromes
- Neurodegenerative diseases
- Cancer invasion
- Liver cirrhosis (non alcoholic)
- Pulmonary fibrosis
- Blistered skin diseases

Progeria (Hutchinson-Gilford Progeria syndrome)

- First case in 1886 (Hutchinson)
- 1904 (Gilford)
- 1/4-8 million M/F:1.5/1 spr. OD-OR
- 90% in whites



- ✓ Point mutation in *LMNA* gene result dominant mutant prelamin A (progerin)
- ✓ Characterized by short telomeres
- ✓ Normal at birth, early aging in childhood; live until twenties.
- ✓ Normal motor ve cognitive development
- ✓ Prominent scalp venes, pinched nose characteristic face
- ✓ Scleroderma-like skin and alopecia
- ✓ Generalized atherosclerosis
- ✓ Death due to generalized cardiovascular and cerebrovascular

Cytoskeleton Summary

	Microtubules	Microfilaments	Intermediate Filaments
Structure	13 protofilament hollows	Dual spiral actin chain	Bended thick filaments
Diameter	25 nm	7 nm	8-12 nm
Protein subunits	α ve β tubulin	actin	variable proteins
Basic Function	<ul style="list-style-type: none">• Maintaining the cell shape• Cell movement (cilia, flagella)• Chromosome movement• Organelle movement	<ul style="list-style-type: none">• Maintaining and regulation of cells shape• Muscle contraction• Cytoplasmic flow• Cell movement• Cytokinesis	<ul style="list-style-type: none">• Maintaining the cell shape and nucleus• Determining the location of organelles and nucleus• Nuclear membrane assembly and disassembly