

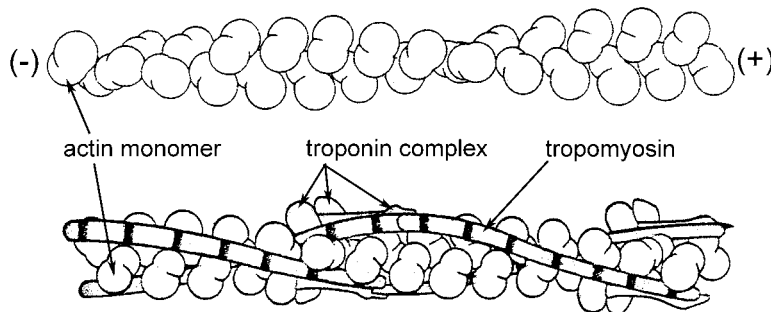
Cytoskeleton Handout

(www.tulane.edu/~wiser/mcbp607/)

- The cell cytoplasm of eukaryotes is a highly organized matrix consisting of 3 distinct filamentous systems.

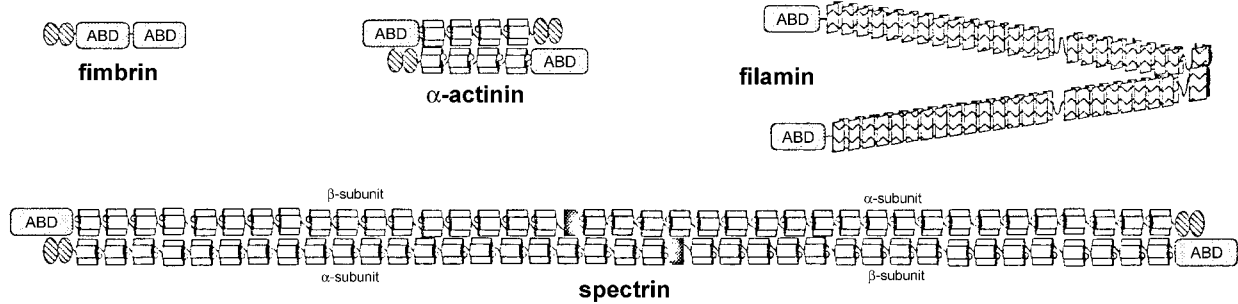
Cytoskeletal Element	Description	Protein Composition
microfilaments	thin filaments 6-7 nm in diameter	actin and associated proteins
microtubules	rigid tubular structures 25 nm in diameter	tubulin and associated proteins
intermediate filaments	rope-like fibers ~10 nm in diameter	intermediate filament proteins

- Actin is a highly conserved globular protein that polymerizes into long filaments. Other proteins regulate microfilament polymerization and assembly as well as stabilize the microfilaments.

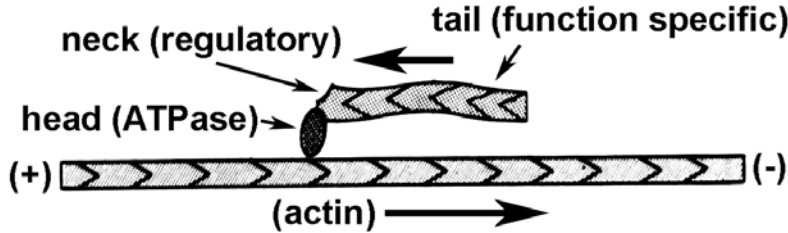


- Actin polymerization is a complex process. In vivo other cellular proteins regulate the process and ATP/ADP are involved. Drugs that affect polymerization can be used to study the role of microfilaments in cellular processes.

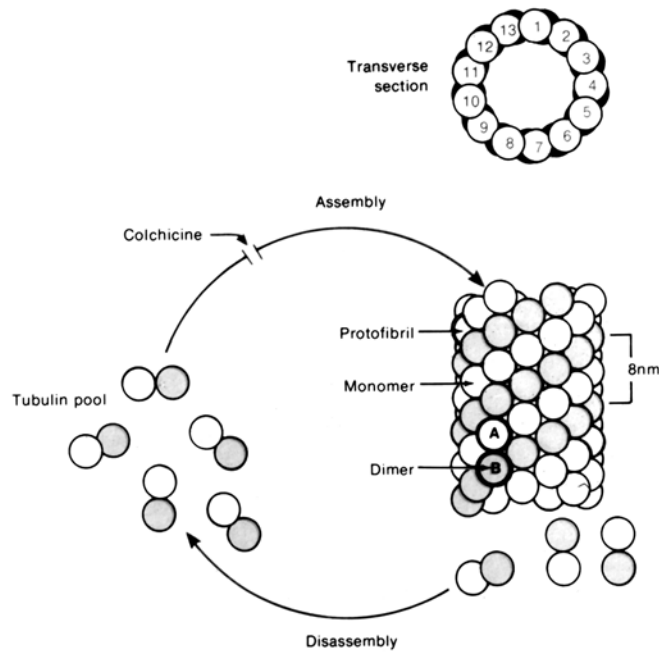
- Actin filaments participate in the formation of many distinct subcellular structures. Various actin-binding proteins determine configuration of microfilaments and their association with other structures. Actin filaments also interact with other cellular structures and organelles such as the plasma membrane via protein-protein interactions.



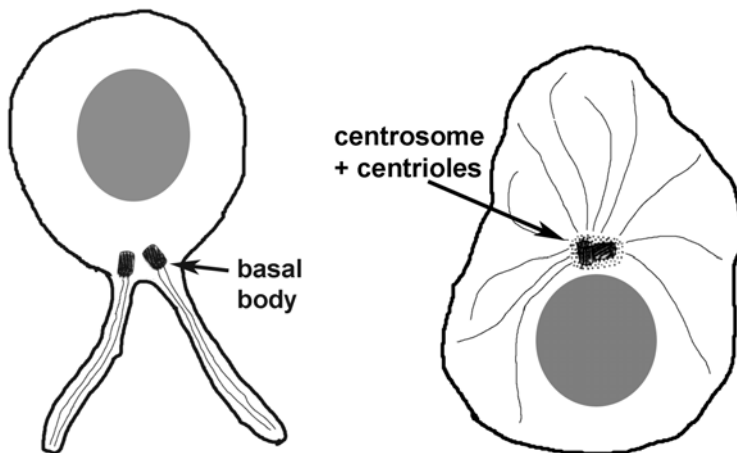
- Actin participates in force generation (eg., cell motility) via interactions with myosin. Myosin is an actin-activated ATPase that converts chemical energy (i.e., ATP) into mechanical energy by moving along microfilaments (or by moving the actin filaments). Cellular motility is a dynamic process involving the assembly and disassembly of actin filaments as well as force generation via myosin.



- Microtubules are long hollow tubes composed of a highly conserved heterodimer (α -tubulin and β -tubulin). Major roles of microtubules include: 1) cell shape and structure, 2) mitotic spindles, and formation of cilia and flagella.

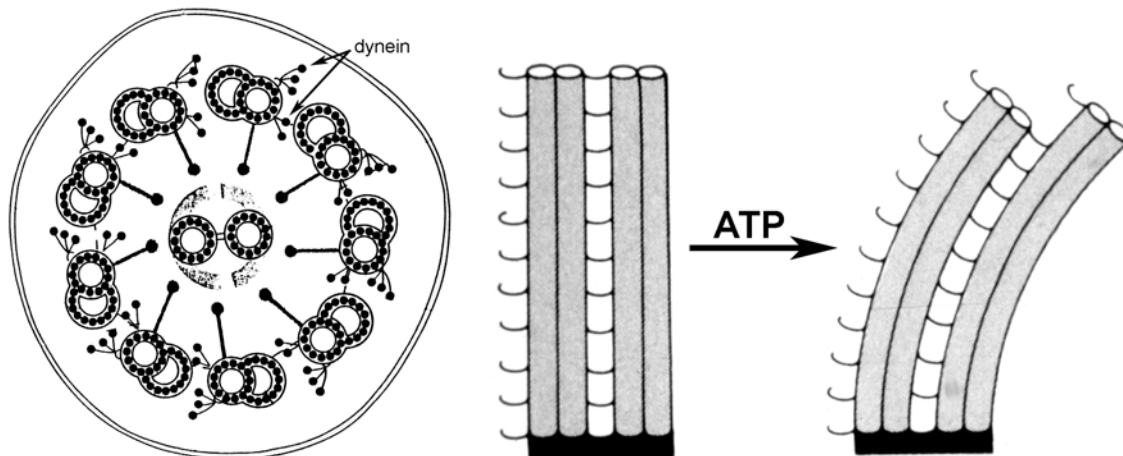


- Microtubule polymerization is initiated from a MTOC (microtubule organizing center). Centrosomes, spindle pole bodies, and basal bodies are examples of MTOC.

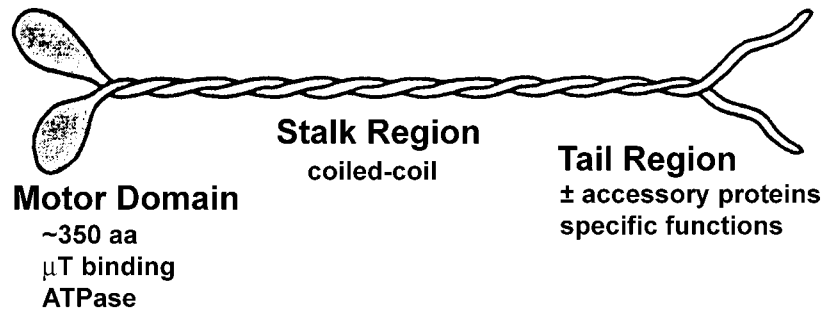


- Microtubules play a mechanical role and contribute to cell shape and structure. Proteins interaction with microtubules will determine the types of structures formed.

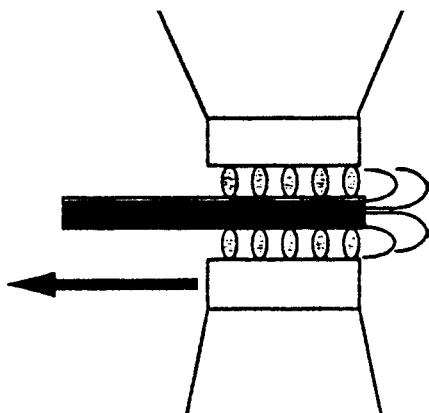
- Microtubules are also the major component of cilia and flagella and thus play a role in cell motility. Force is generated through the action of dynein cross bridges which move along the microtubules and produce a bending. Dynein also plays a role in cellular motility and force generation within the cytoplasm.



- Kinesins are a large family of motor proteins which participate in force generation such as the movement of cytoplasmic organelles and the separation of chromosomes. Force is generated in a chemomechanical cycle analogous to the mechanism of myosin.



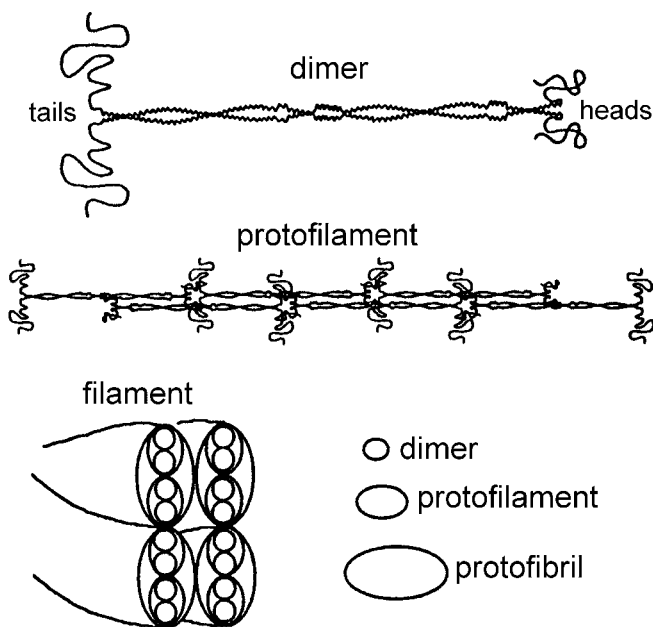
- The mitotic cycle (i.e., cell division) involves the disassembly of the cytoplasmic microtubules and the assembly of the spindle apparatus. At least 4 kinesins are involved in this process. Possible roles include: 1) stabilizing the metaphase plane, 2) sliding the spindle microtubules in opposite directions, 3) pulling aster microtubules towards membrane, and 4) pulling chromosomes along microtubules.



- Intermediate filaments are rope-like fibers that often extend from the nucleus to the cell periphery. Distinct, but related, intermediate filament proteins form filaments that are specific to particular cell types. Intermediate filament proteins are related to the nuclear lamins.

Type	Examples	Cell Type	Size (kDa)
I	acidic keratins	epithelial	40-60
II	basic-neutral keratins	epithelial	50-70
III	vimentin	mesenchymal	53
	desmin	muscle	52
	GFAP	glial cells	51
IV	neurofilament	neurons	57-150
V	lamins (A, B, C)	nuclear lamina	60-70

- Intermediate filament proteins are rod-shaped with a central domain composed of heptad repeats. Heptad repeats promote the association of parallel α -helices into a structure known as a coiled-coil. Intermediate filament proteins assemble into dimers via coiled-coil interactions. The basic unit of intermediate filaments are possibly tetramers formed from dimers in a head-to-tail orientation. Overlapping tetramers form protofilaments. Eight of these protofilaments probably form the intermediate filament.



- A major function of intermediate filaments is stabilize cellular architecture against mechanical stress.