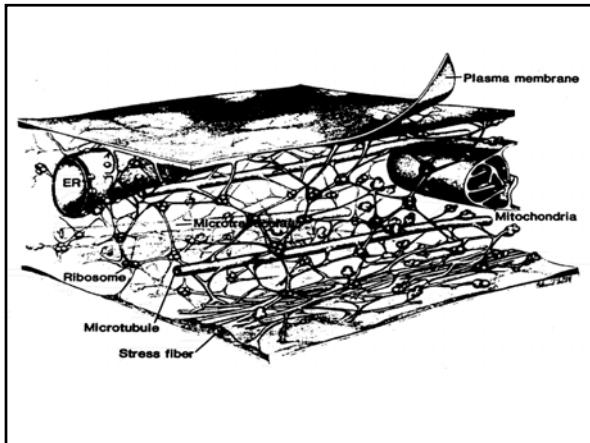
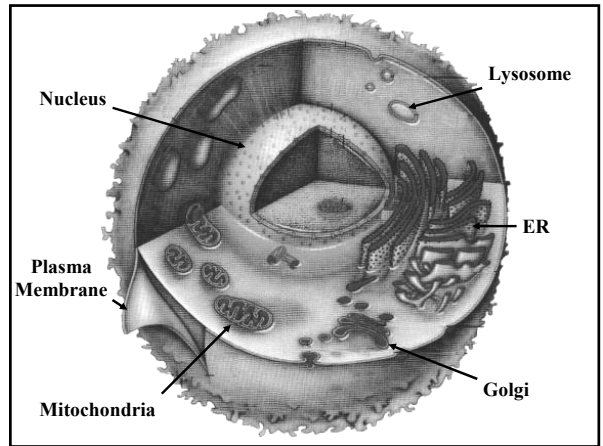


Cytoskeleton

Mark Wiser

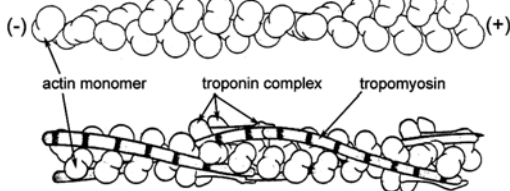


Three Major Filamentous Systems of the Cytoskeleton

| Cytoskeletal Element | Description (diameter) | Protein Composition |
|------------------------|----------------------------|-------------------------------|
| microfilaments | thin filaments (6-7 nm) | actin + associated proteins |
| microtubules | tubular structures (25 nm) | tubulin + associated proteins |
| intermediate filaments | rope-like fibers (~10 nm) | IF proteins |

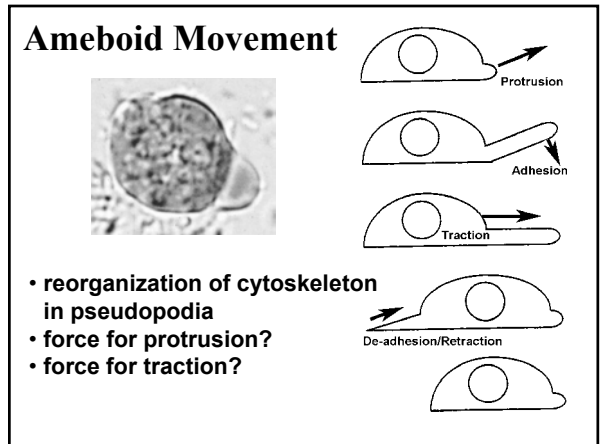
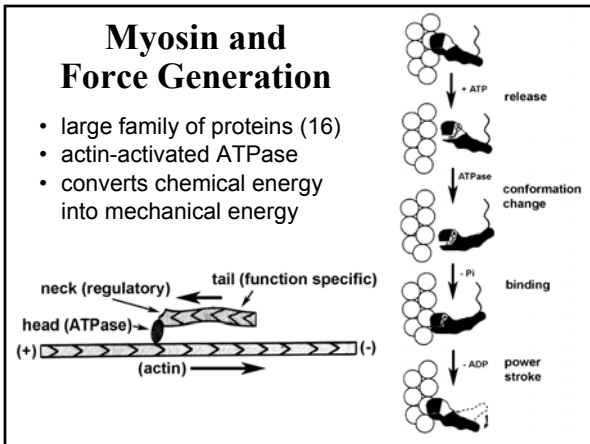
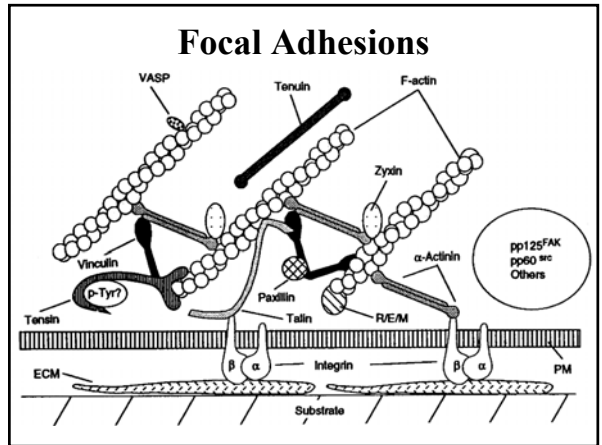
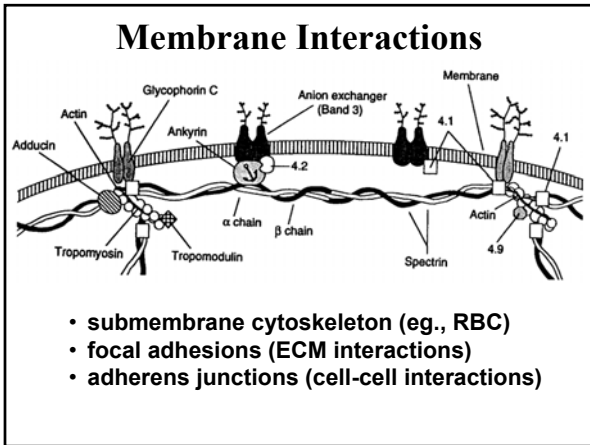
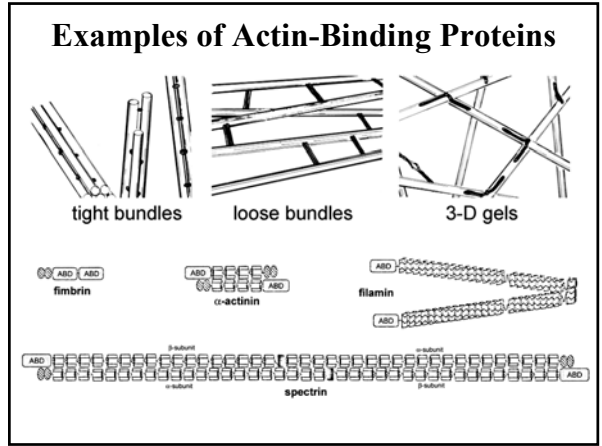
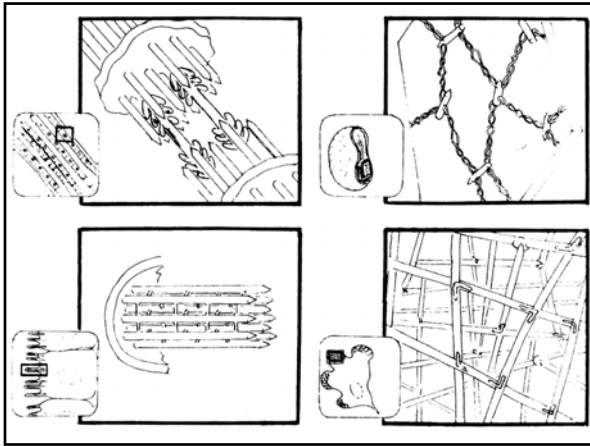
Actin and Microfilaments

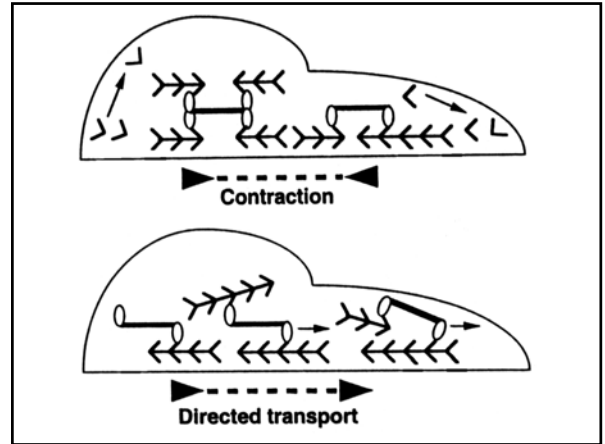
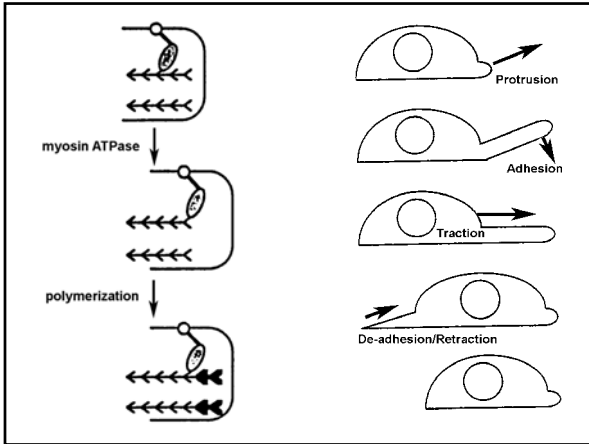
- highly conserved globular protein (G-actin)
- polymerizes into thin filaments (F-actin)
 - exhibits polarity (+ and - ends)
 - (barbed and pointed ends)
- filaments stabilized by other proteins



Actin Polymerization

- requires nucleation (activation)
- elongation primarily at “+” end (= barbed end)
- ATP/ADP
 - G-actin has bound ATP
 - ADP-actin more likely to dissociate
- actin-binding proteins
 - monomer sequestration (eg., profilin)
 - capping proteins (eg., gelsolin)
- cellular regulation
 - rho family (ras-like G-proteins)
 - trimeric G-proteins
- drugs
 - cytochalasins (prevent assembly)
 - phalloidin (prevent disassembly)





Microtubules

Major Roles:

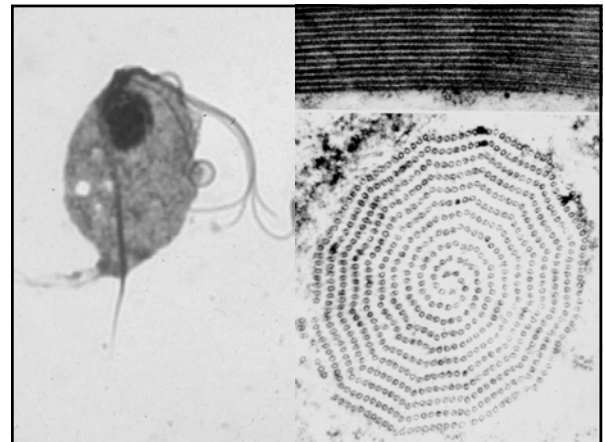
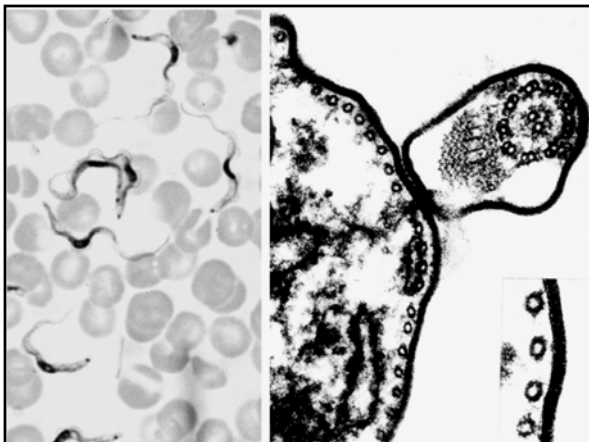
1. Mechanical/Cell Shape
2. Mitotic Spindle
3. Cilia/Flagella

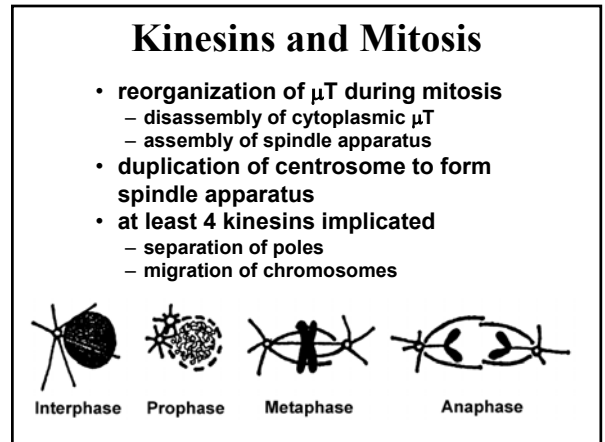
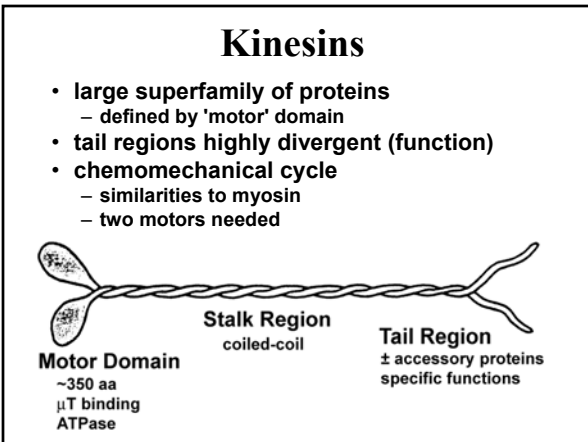
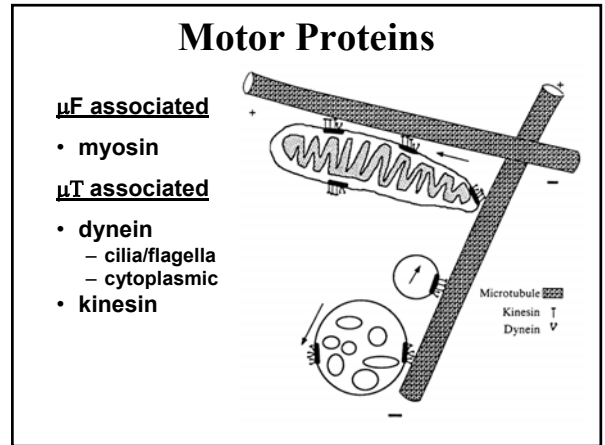
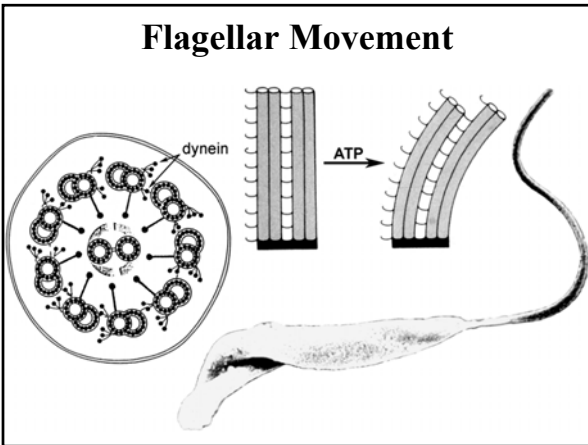
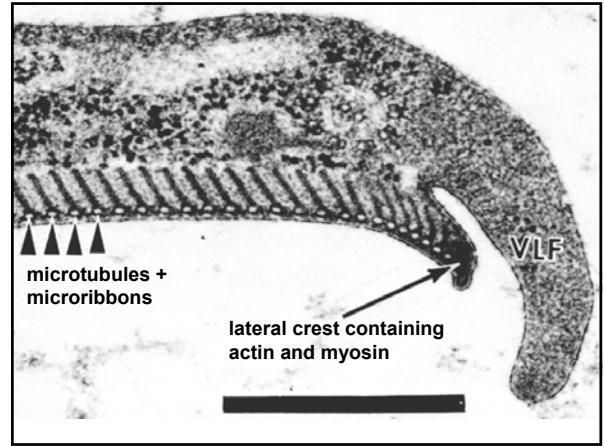
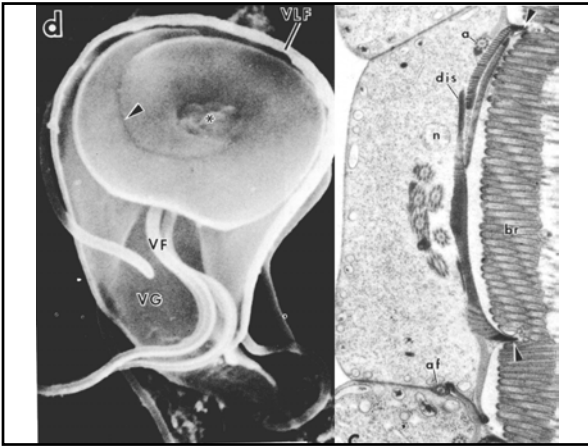
Tubulin:

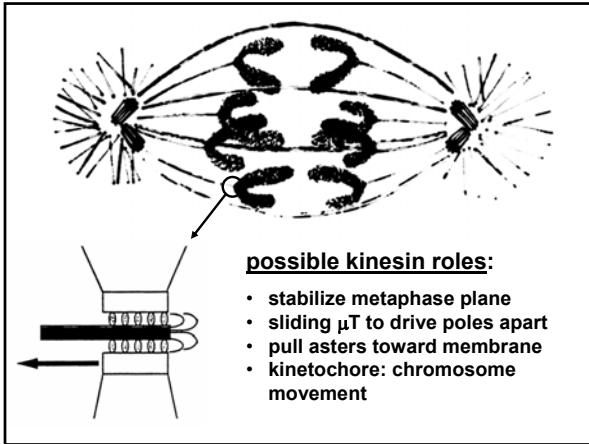
- highly conserved
- heterodimer (α , β)
- in vivo assembly from MTOC

Microtubule Organizing Centers

- **centrioles**
 - aka basal bodies of flagella
 - barrel-shaped (triplets of μ T)
- **centrosomes**
 - amorphous matrix (\pm centrioles)
 - organizes cytoplasmic μ T array
 - forms spindle during cell division
- **spindle pole bodies**
 - located on nuclear membrane
 - forms mitotic spindle in many lower eukaryotes

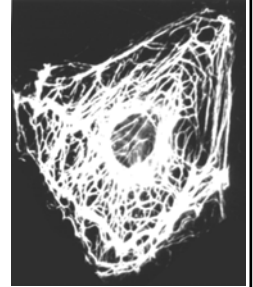






Intermediate Filaments

- rope-like fibers extending from nucleus periphery
- extremely stable
 - resistant to detergent extraction
- only in metazoa
- subunits are part of large multigene family
 - related to nuclear lamins
 - tissue specific expression

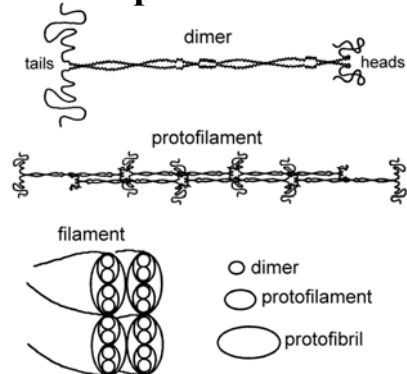


Intermediate Filament Proteins

| 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 |

| | | |
|------|----------------|------|
| head | heptad repeats | tail |
|------|----------------|------|

IF Proposed Structure



IF Function

- mechanical support
 - abundant in cells and structures under mechanical stress (eg, epithelia, hair, nails, muscle, etc)
 - genetic defects linked to keratin: epidermolysis Bullosa simplex, epidermolytic hyperkeratosis
 - links to membranes and other cytoskeletal elements
- specialized function in differentiated cells
 - tissue specific expression
 - markers for tumor diagnosis

