**The neuronal cytoskeleton**

**Neurons**
- unique architecture with distinct and diverse morphology
  - branching of axon and dendrites
- specialized structure closely related to function
  - electrical signaling
  - synaptic transmission
  - transport
- structural changes with:
  - age, experience, neuronal activity, injury

**Neuronal cytoskeleton**
- essential role in these aspects

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**The cytoskeleton**
- functions as a highway for transport and a framework for the cell.

3 structures
- Actin filaments (microfilament)
- Microtubules
- Intermediate filaments
The neuronal cytoskeleton

**-longitudinal filaments**
1. Microtubules (diameter 25 nm)
2. Neurofilaments (d= 10nm)
   extensive crosslinking

**-cortical network**
Actin microfilaments (d= 8nm)
under the surface membrane
enriched in the growth cone

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**Anchoring proteins to actin filament**
(Fig. 13, page 275)

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**The filaments: polymers of repeating subunits**

<table>
<thead>
<tr>
<th>Filament</th>
<th>Monomer protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microtubules:</td>
<td>α- and β-tubulin (50 kDa)</td>
</tr>
<tr>
<td>Microfilaments:</td>
<td>actin (43 kDa)</td>
</tr>
<tr>
<td>Neurofilaments:</td>
<td>NF-H, NF-M, NF-L</td>
</tr>
<tr>
<td>(Neuronal intermediate filaments)</td>
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</tbody>
</table>
**Microtubules**

- Typically comprise 13 protofilaments
- Dynamic instability
  - GTP hydrolysis and depolymerization, Polarity
- Transport
- Microtubule associated proteins and microtubule motors
  - MAP1a/b - widely spread in axon and dendrites
  - MAP2a/b - Dendrite specific MAPs, major phosphoproteins in adult brain
  - Kinesin - present in microtubule containing cell, axonal transport
  - Dynein - transport of organelles or cytoskeletal elements

**Microtubules (MT) in vivo**

Stable and labile forms present

Multiple genes for α- and β-subunit

Polymerized in MT in a mixed form

Neuron type specific expression

Polarity
  - Axon: Fast growing end (Plus end) toward nerve terminals
  - Dendrite: Random

Posttranslational modification
  - α- subunit: tyrosination-detyrosination
    - C-terminus Glu-Tyr
    - Acetylated tubulin-more stable
  - β-subunit: tubulin kinase
Transport of macromolecules and organelles
Axonal transport and dendritic transport
Anterograde transport and retrograde transport

Fast and slow transport

Slow component A
0.2-1 mm/day
Slow component B
2-8 mm/day

Fast axonal transport
occurs along microtubules
ATP dependent motor protein activation
Kinesin: anterograde motor
Dynein: retrograde motor
**Slow axonal transport**

- Mechanism not clear: Motor proteins considered to be involved
- No apparent retrograde transport
- Slow component A: 0.2-1 mm/day
  - Cytoskeletal proteins: microtubule proteins, neurofilaments
- Slow component B: 2-8 mm/day
  - Actin, soluble enzymes

**Neurofilaments: neuronal intermediate filaments**

- NF-H (180-200kDa), NF-M (130-170kDa), NF-L (60-70kDa)
- N-terminal head domain
- A central α-helical coiled coil rod domain
- Dimerization domain
- C-terminal tail domain