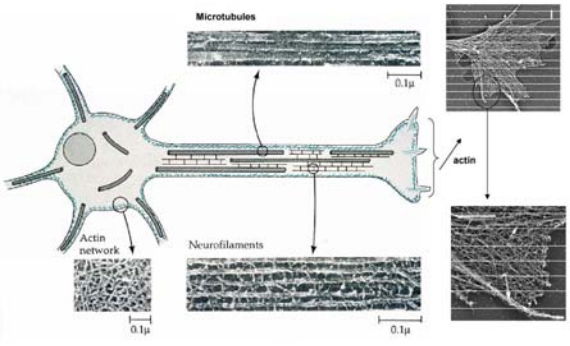
MCB 160L

# Neuron Outgrowth

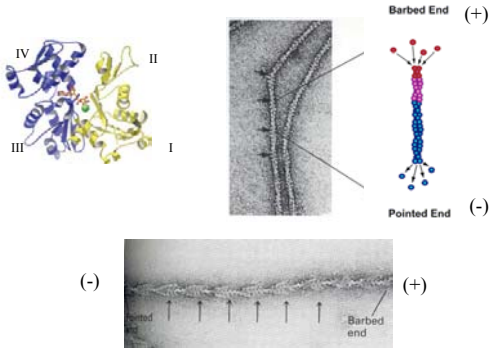
The cytoskeletal components of neurons have characteristic distributions and associations.



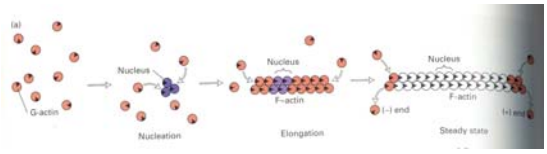

## Function of actin filaments in neurons

- Provides structural integrity to filopodia and spines
- Regulate organization of membrane proteins and associated protein complexes
- Polymerization drives protrusion of filopodia and lamellipodia
- Substrate for intracellular transport
- Involved in targeting of neuronal components
- Transmission of mechanical force

## Structure of G-actin and F-actin

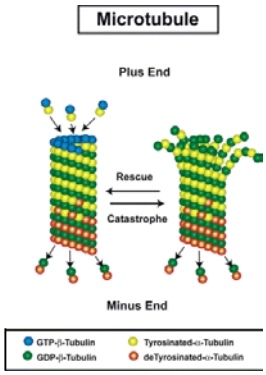



## The three phases of G-actin polymerization in vitro




## Function of microtubules in neurons

- Provide structural rigidity to axons and dendrites
- Major substrate for intracellular transport
- Involved in targeting of neuronal components




## Microtubules

Are polymers of tubulin dimers

Polymerization requires GTP bound to tubulin dimers

Microtubules have intrinsic polarity. This is important in transport.

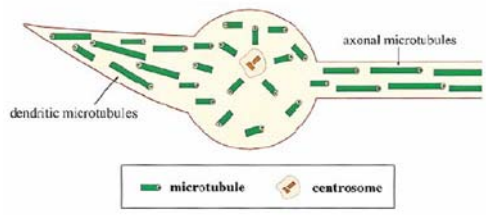
## Microtubule polarity is highly regulated in neurons

Axons

All microtubules have their + end oriented distally (pointing away from soma)

Dendrites

Microtubule polarity is oriented in both directions




## Microtubule Associated Proteins (MAPs) organize microtubules in neurons

Bundle microtubules (assembly MAPs, MAP1A and MAP1B)

Stabilize microtubules (MAP2, MAP4, Tau)

Control rate of tubulin polymerization (phosphorylated MAPs can not bind to MTs, reversible phosphorylation by MAP kinase)

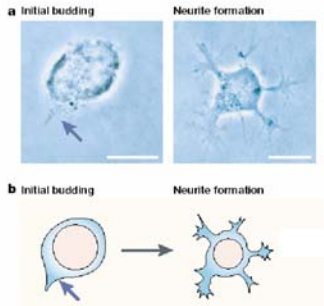
May interconnect microtubules and other cytoskeletal components (NFs and actins)

Use microtubules as substrates for moving cargo (e.g. kinesin and dynein)

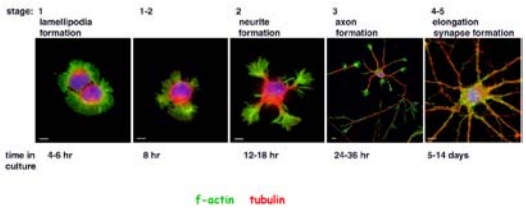
## Motor proteins

1. A motor protein walks in one direction along a polarized filament or track.
2. A mobile head domain at one end attaches to a protein filament and hydrolyzes ATP or GTP to power its walking along the filament.
3. A tail domain at the other end attaches to a cargo.
4. The movement generated by a motor protein depends on the relative resistance or anchorage of the track vs. the cargo.
5. If both the protein filament and the cargo resist movement, tension is generated and maintained while the motor is attached to the cargo and the filament.

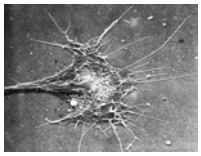

## Neurite formation begins with a bud that sprouts from the cell body. One or several neurites can sprout at a time.

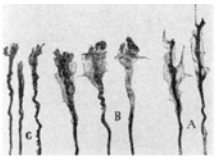



## After an initial period of slow growth, one neurite accelerates its elongation rate and differentiates to become the axon



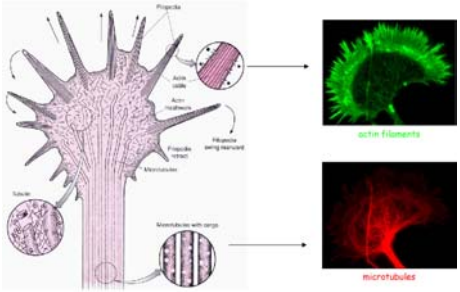
## The Growth Cone



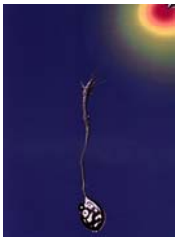


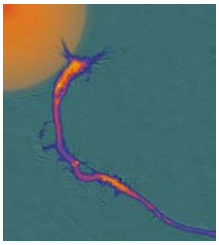
Santiago Ramón y Cajal
1852-1934

## The growth cone is the motile tip of an elongating axon or dendrite




## Axon growth cone is a sensory-motor structure that recognizes and responds to guidance cues





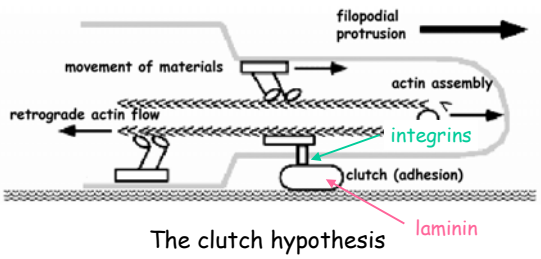
## What gives growth cones motility?

Growth cone motility appears to depend both upon the degree of actin filament polymerization and upon interaction of actin with myosin.

Filopodia (growth cone) extension: driven by the addition of actin monomers to the leading edge of the filament.

Filopodia (growth cone) retraction: translocation of the filament away from the leading edge of the filopodia powered by interaction with molecules of myosin.

## Adhesive contacts and actomysin forces are also important in advancing the leading growth cone margin




The clutch hypothesis