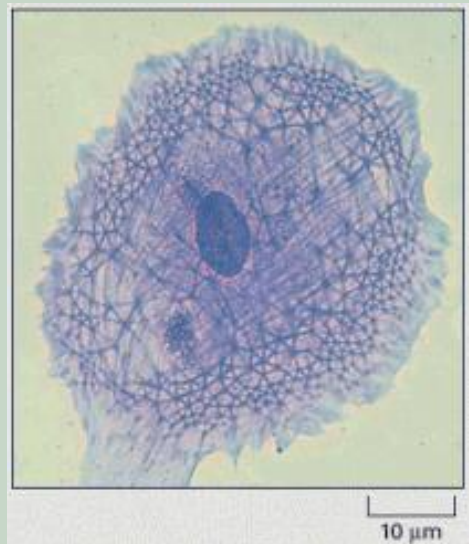
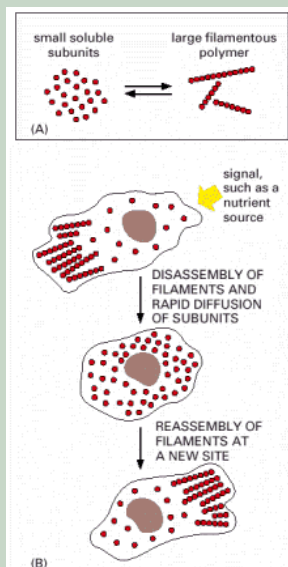


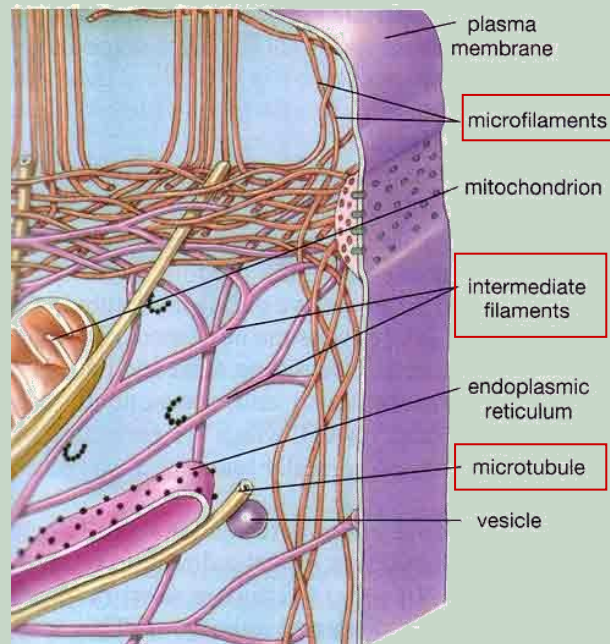
# INTRODUCCION A LA BIOLOGIA CELULAR Y MOLECULAR

## - BIOLOGIA CELULAR - Citoesqueleto

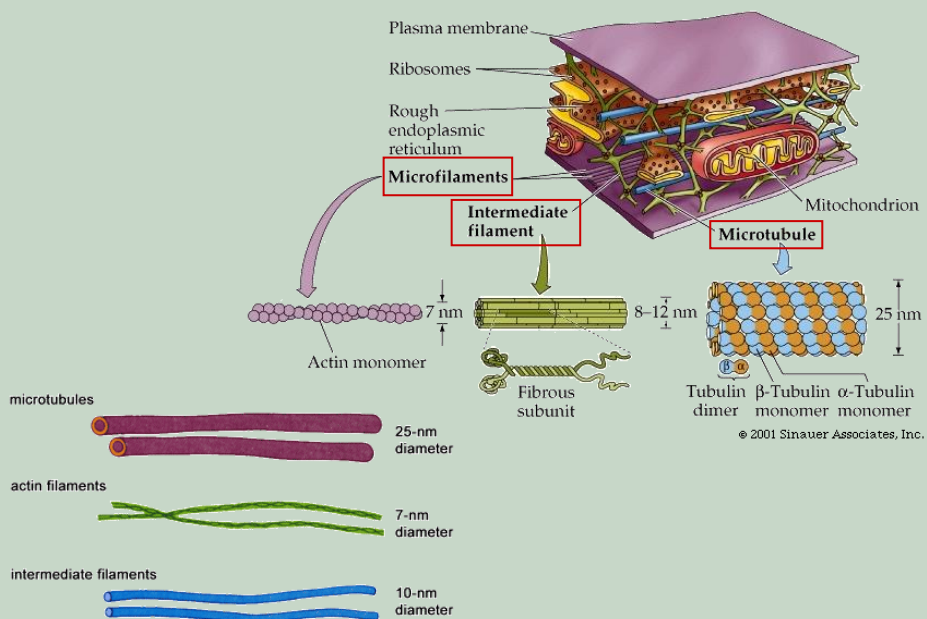
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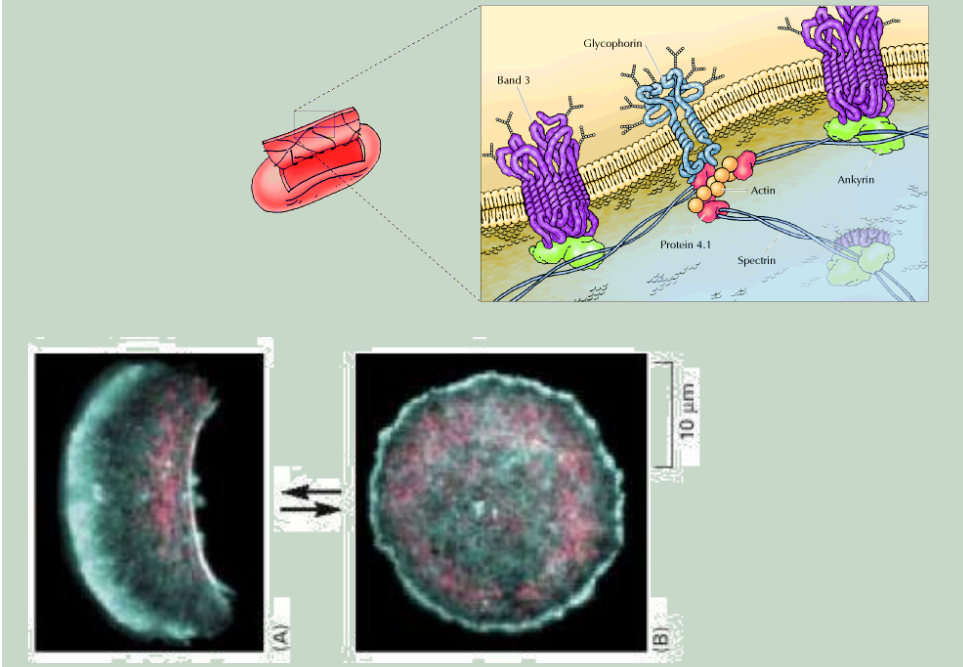
## Citoesqueleto



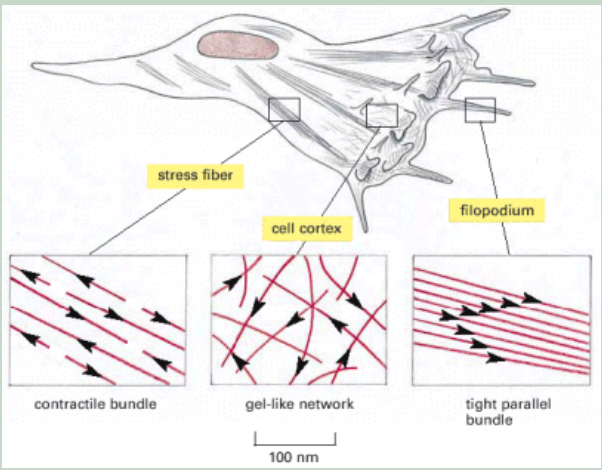
## Filamentos



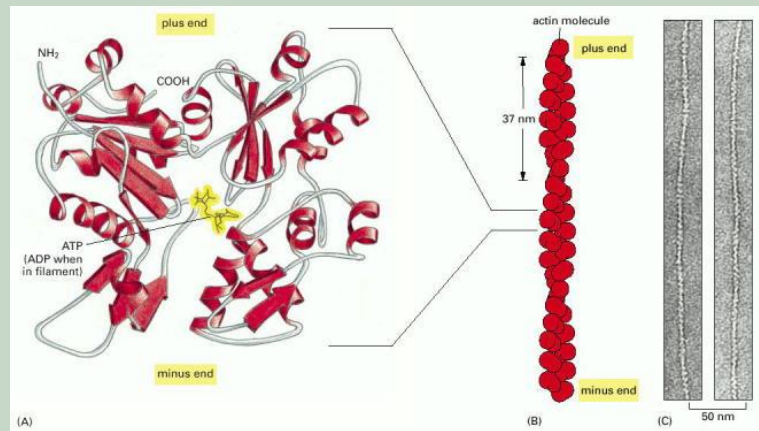
Actina



Actina

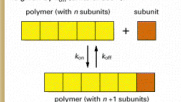


# Actina



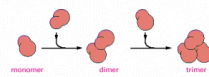
## ON RATES AND OFF RATES

A linear polymer of protein molecules, such as an actin filament or a microtubule, assembles (polymerizes) and disassembles (depolymerizes) by the addition and removal of subunits at the ends of the polymer. The rate of addition of these subunits (called monomers) is given by the rate constant  $k_{on}$ , which has units of  $M^{-1} \text{sec}^{-1}$ . The rate of loss is given by  $k_{off}$  (units of  $\text{sec}^{-1}$ ).



## NUCLEATION

A helical polymer is stabilized by multiple contacts between adjacent subunits. In the case of actin, two actin molecules bind relatively weakly to each other, but addition of a third actin monomer to form a trimer makes the entire group more stable.



Further monomer addition can take place onto this trimer, which therefore acts as a nucleus for polymerization. For tubulin, the nucleus is larger and has a more complicated structure (possibly a ring of 13 or more tubulin molecules)—but the principle is the same. The assembly of a nucleus is relatively slow, which explains the lag phase seen during polymerization. The lag phase can be reduced or abolished entirely if premade nuclei, such as fragments of already polymerized microtubules or actin filaments, are added.

## THE CRITICAL CONCENTRATION

The number of monomers that add to the polymer (actin filament or microtubule) per second will be proportional to the concentration of the free subunit ( $k_{on}C$ ), but the subunits will leave the polymer end at a constant rate ( $k_{off}$ ) that does not depend on  $C$ . As the polymer grows, subunits are used up, and  $C$  is observed to drop until it reaches a constant value, called the **critical concentration** ( $C_c$ ). At this concentration the rate of subunit addition equals the rate of subunit loss. At this equilibrium,

$$k_{on}C_c = k_{off}$$

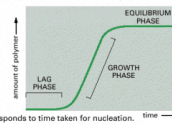
so that

$$C_c = \frac{k_{off}}{k_{on}} = \frac{1}{K}$$

(where  $K$  is the equilibrium constant for subunit addition; see Figure 3-44).

## TIME COURSE OF POLYMERIZATION

The assembly of a protein into a long helical polymer such as a cytoskeletal filament or a bacterial flagellum typically shows the following time course:



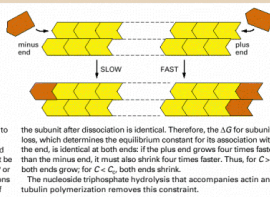
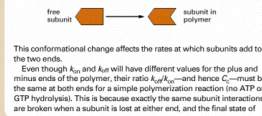
The lag phase corresponds to time taken for nucleation.

The growth phase occurs as monomers add to the exposed ends of the growing filament, causing filament elongation.

The equilibrium phase, or **steady state**, is reached when the growth of the polymer due to monomer addition is precisely balanced by the shrinkage of the polymer due to disassembly back to monomers.

## PLUS AND MINUS ENDS

The two ends of an actin filament or microtubule polymerize at different rates. The fast-growing end is called the **plus end**, whereas the slow-growing end is called the **minus end**. The difference in the rates of growth at the two ends is made possible by changes in the conformation of each subunit as it enters the polymer.



### NUCLEOTIDE HYDROLYSIS

Each actin molecule carries a tightly bound ATP molecule that is hydrolyzed to a tightly bound ADP molecule soon after its assembly into polymer. Similarly, each tubulin molecule carries a tightly bound GTP that is converted to a tightly bound GDP molecule soon after the molecule assembles into the polymer.

Hydrolysis of the bound nucleotide reduces the binding affinity of the subunit for neighboring subunits and makes it more likely to dissociate from each end of the filament (see Figure 16-11 for a possible mechanism). It is usually the (D) form that adds to the filament and the (D) form that leaves.

Considering events at the plus end only:

As before, the polymer will grow until  $C = C_c$ . For illustrative purposes, we can ignore  $K_{on}$  and  $K_{off}$  since they are usually very small, so that polymer growth ceases when  $K_{on}C = K_{off}$  or  $C = \frac{K_{off}}{K_{on}}$ .

This is a steady state and not a true equilibrium, because the ATP or GTP that is hydrolyzed must be replenished by a nucleotide exchange reaction of the free subunit (D)  $\rightarrow$  (T).

### ATP CAPS AND GTP CAPS

The rate of addition of subunits to a growing actin filament or microtubule can be faster than the rate at which their bound nucleotide is hydrolyzed. Under such conditions, the end has a "cap" of subunits containing the nucleotide triphosphate—an ATP cap on an actin filament or a GTP cap on a microtubule.

### TREADMILLING

One consequence of the nucleotide hydrolysis that accompanies polymer formation is to change the critical concentration at the two ends of the polymer. Since  $K_{on}$  and  $K_{off}$  refer to different reactions, their ratio  $\frac{K_{on}}{K_{off}}$  need not be the same at both ends of the polymer, so that:

$$C_c \text{ (minus end)} > C_c \text{ (plus end)}$$

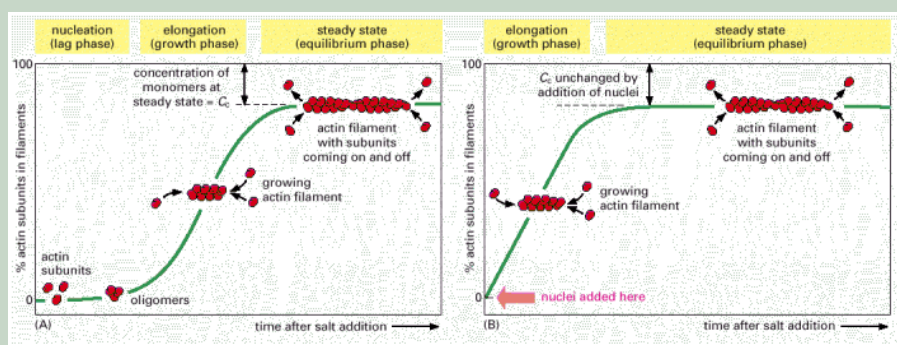
Thus, if both ends of a polymer are exposed, polymerization proceeds until the concentration of free monomer reaches a value that is above  $C_c$  for the plus end but below  $C_c$  for the minus end. At this steady state, subunits undergo a net assembly at the plus end and a net disassembly at the minus end at an identical rate. The polymer maintains a constant length, even though there is a net flux of subunits through the polymer, known as **treadmilling**.

### DYNAMIC INSTABILITY

Microtubules depolymerize about 100 times faster from an end containing GDP tubulin than from one containing GTP tubulin. A GTP cap favors growth, but if it is lost, then depolymerization ensues.

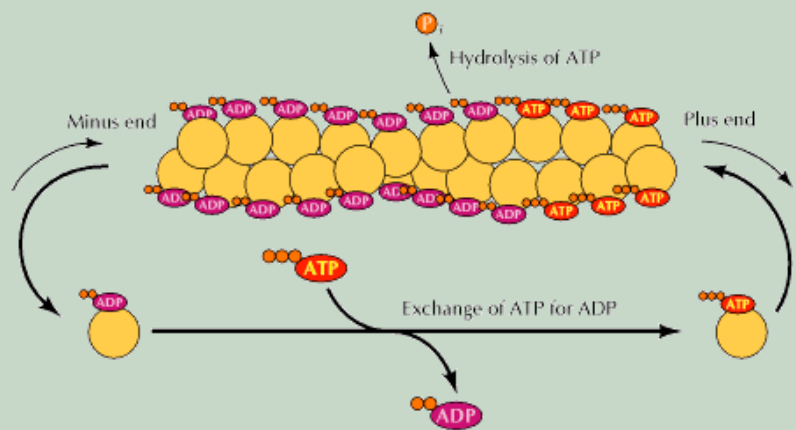
Individual microtubules can therefore alternate between a period of slow growth and a period of rapid disassembly, a phenomenon called **dynamic instability**.

# Inestabilidad Dinámica

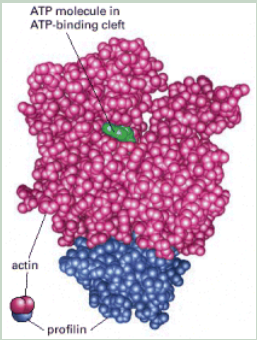
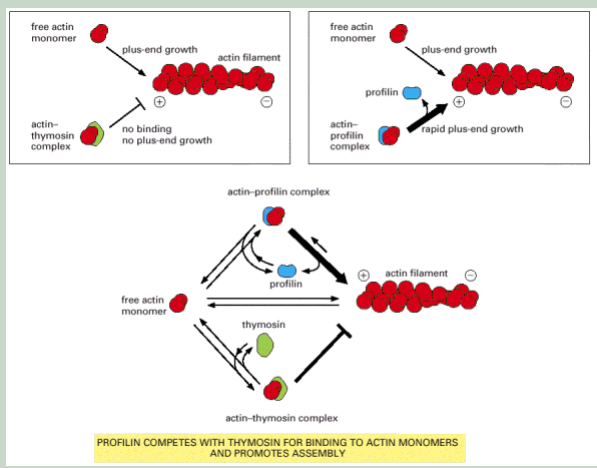




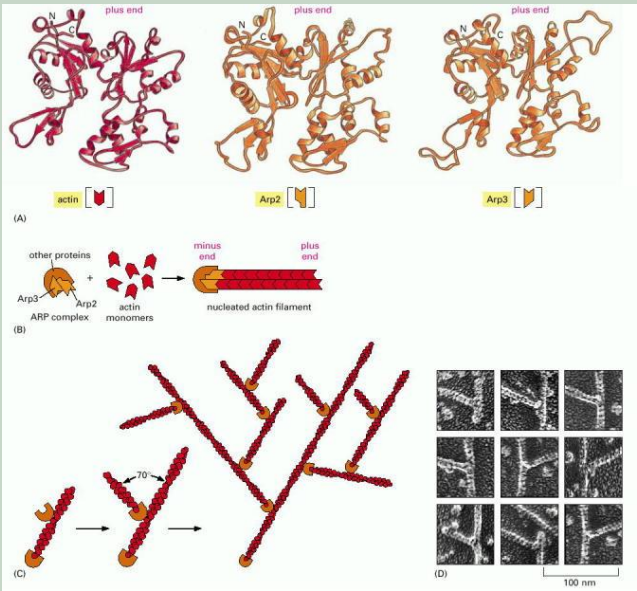
# Inestabilidad Dinámica



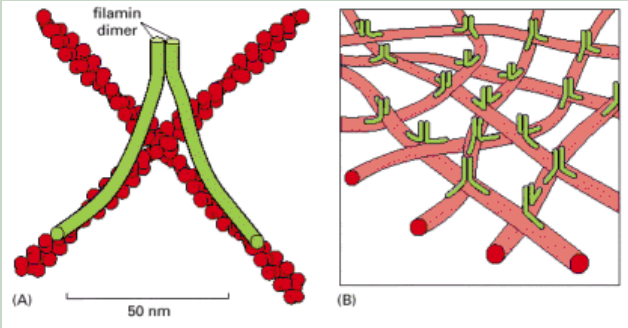
# Regulación de la polimerización



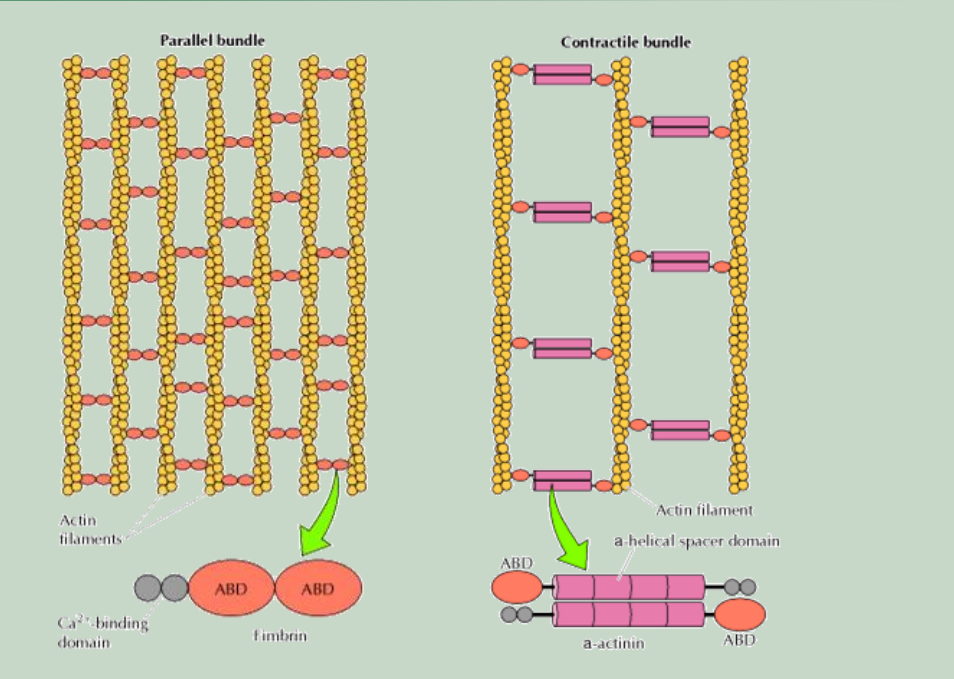
ARP



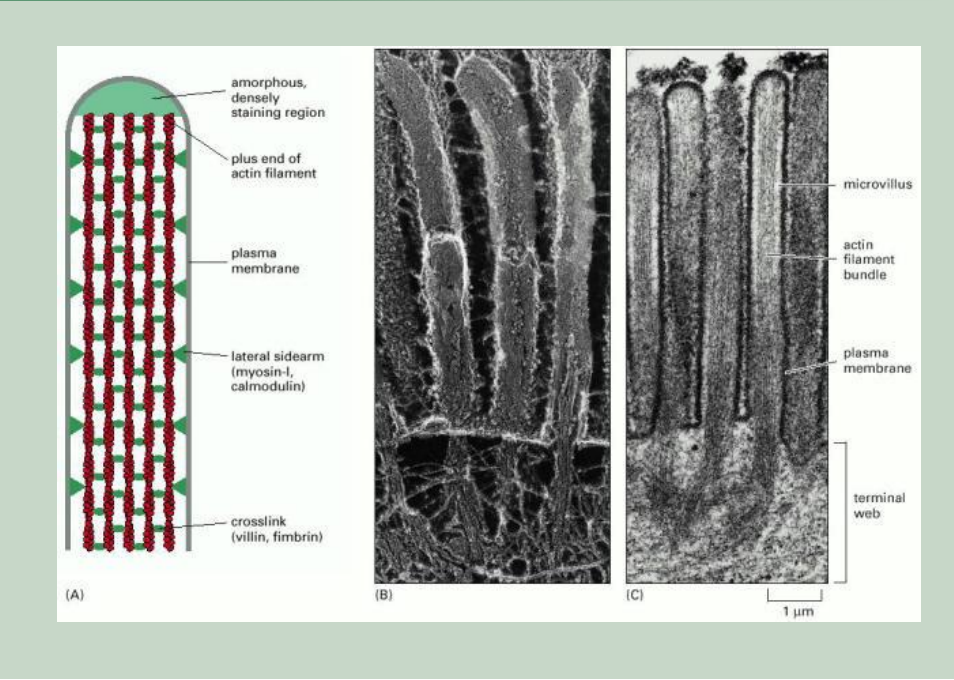
Filamina



Haces de Actina

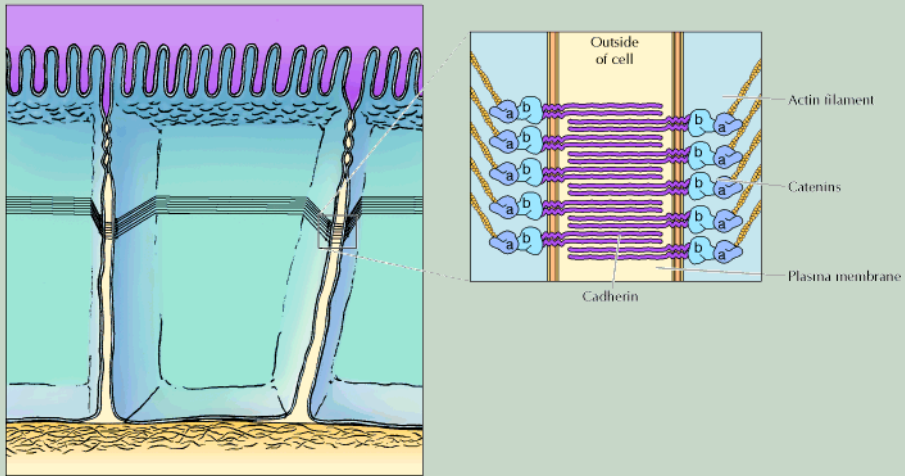


Microvellosidades

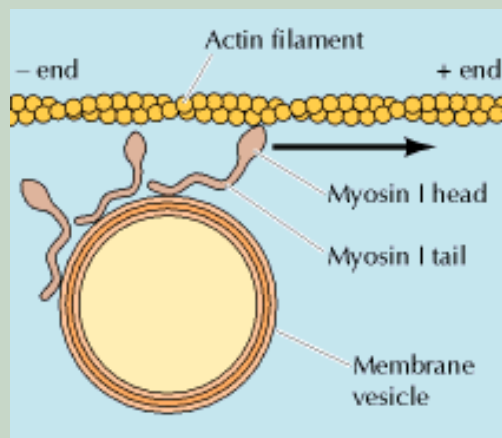




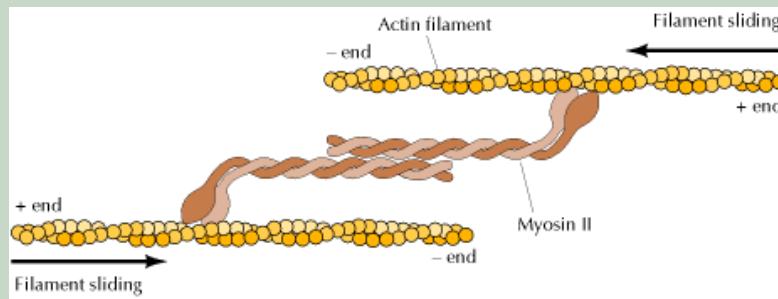
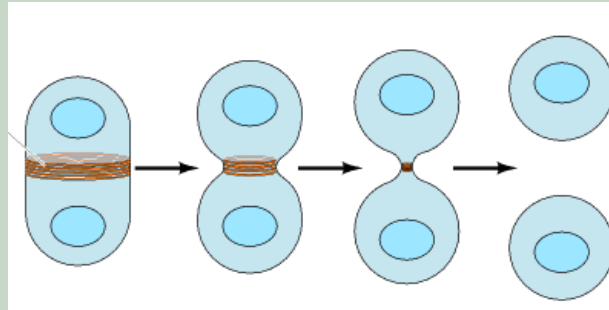
## Uniones adherentes



## Miosina I

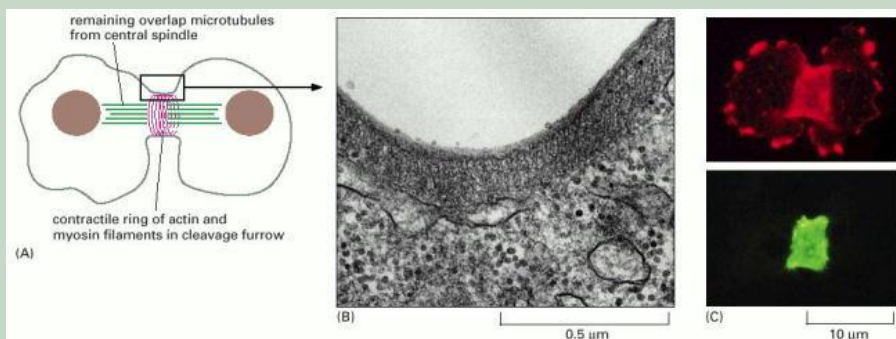


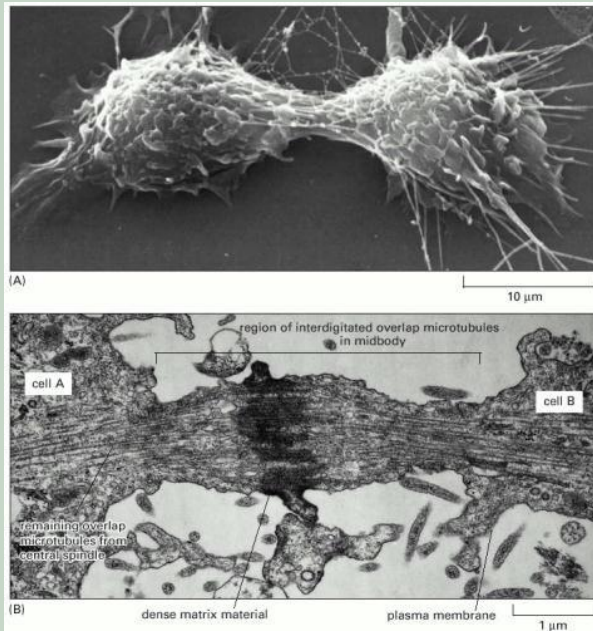
## Miosina II



### La actina y la miosina generan las fuerzas necesarias para la segmentación.

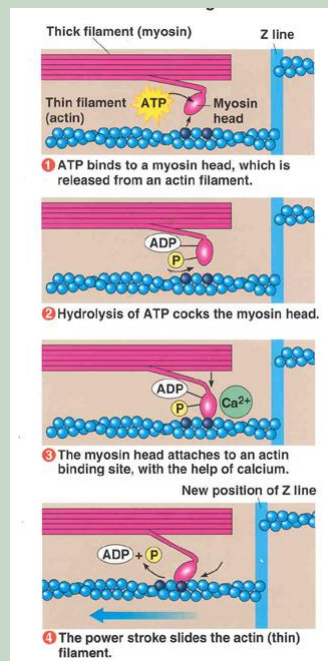
La segmentación se consigue mediante la contracción de un fino anillo compuesto principalmente por una formación superpuesta de filamentos de actina y de filamentos bipolares de miosina II.



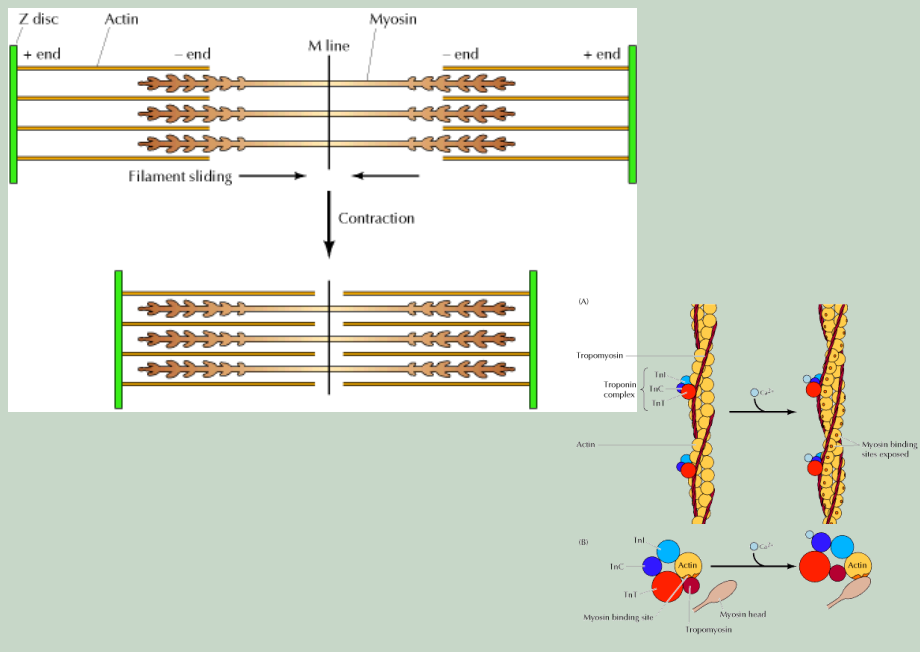


El anillo contráctil se elimina por completo al terminar la segmentación, cuando la membrana plasmática del surco de segmentación se estrecha formando el cuerpo medio, que permanece como un puente entre las dos células hijas.

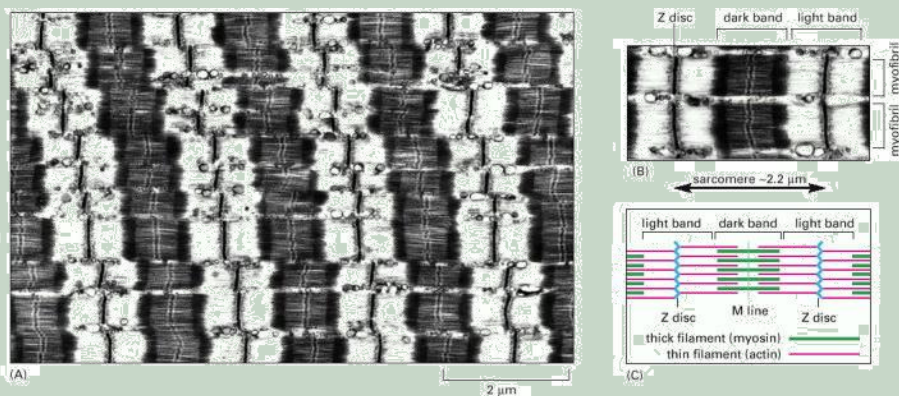
## Contracción Muscular



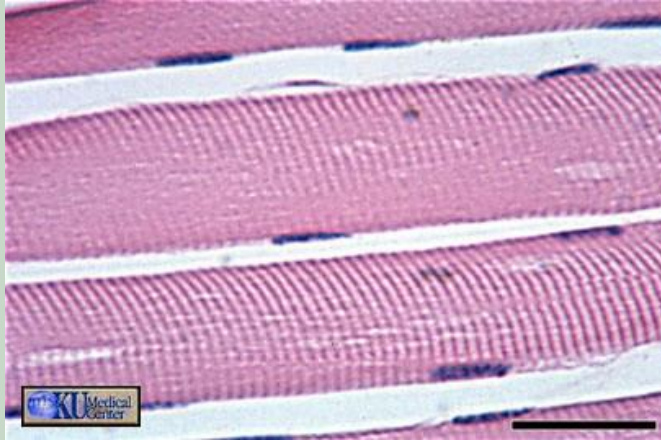
# Contracción Muscular



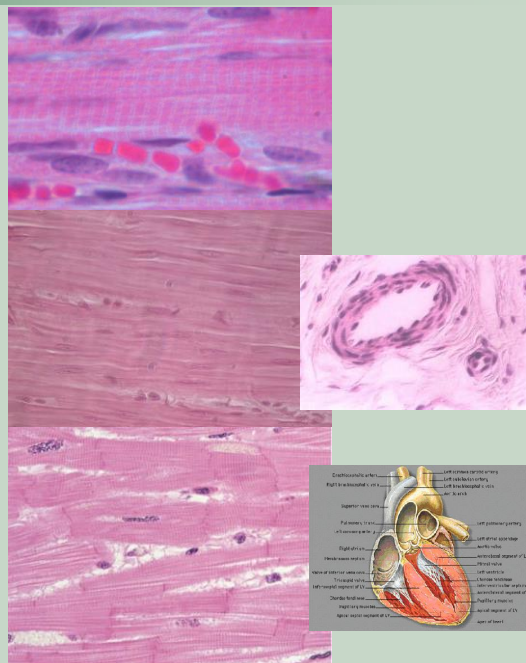
# Sarcómero



## Miositos esqueléticos

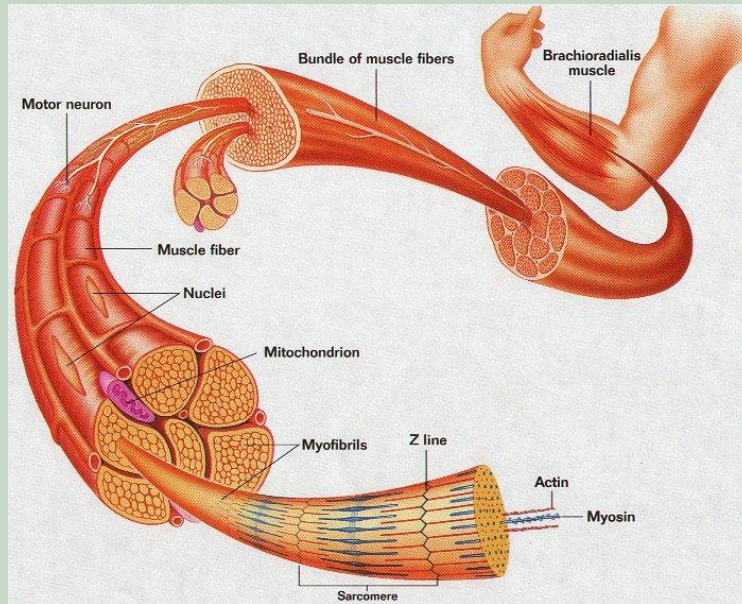


## Músculos

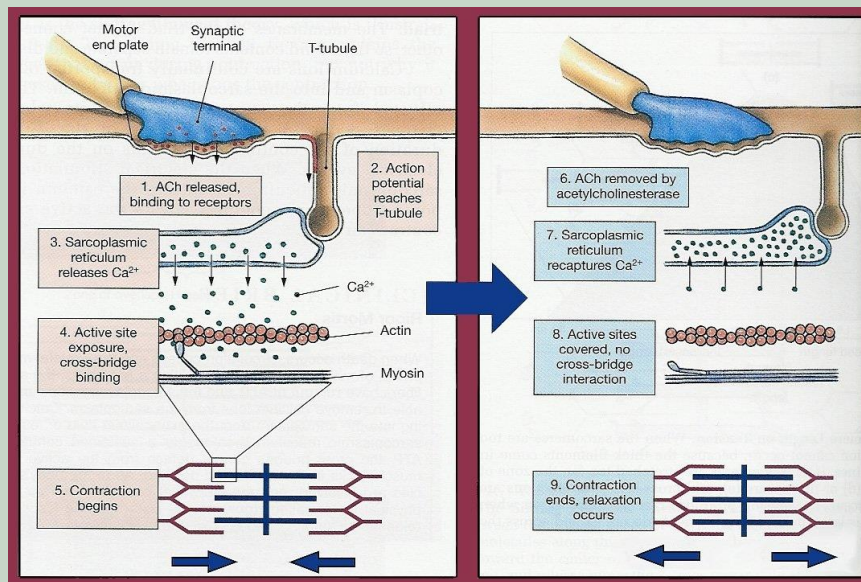




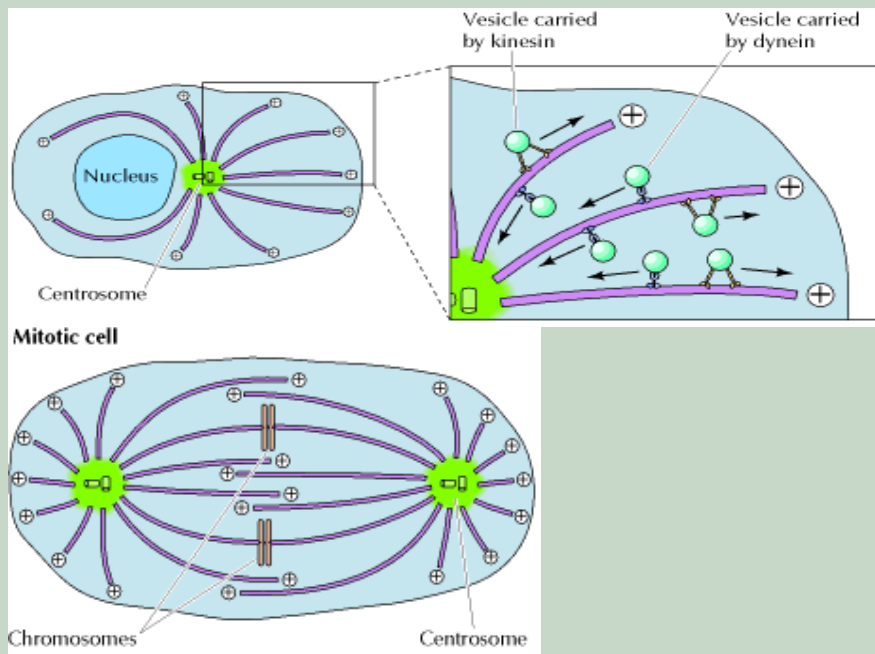
## Músculo esquelético



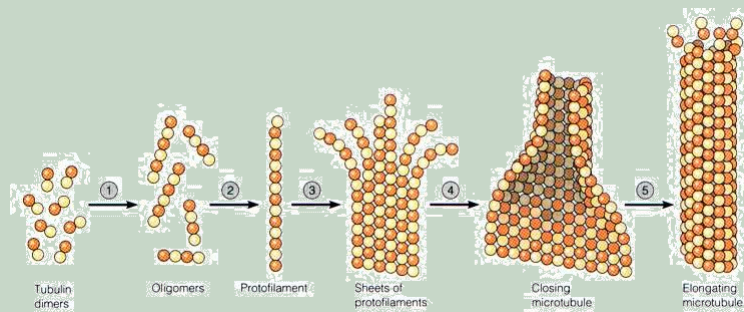
## Placa neuromuscular



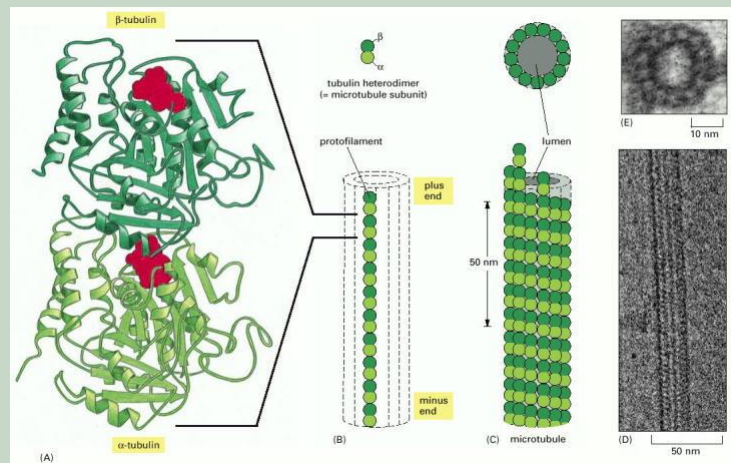
## Microtúbulos



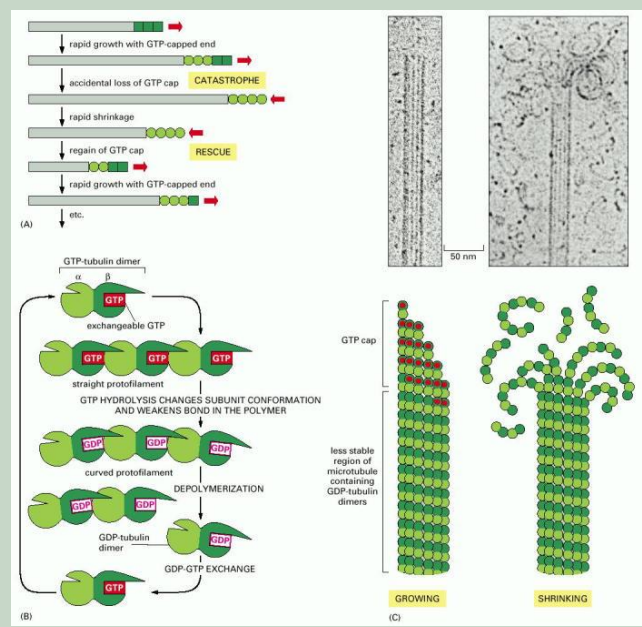
## Microtúbulos



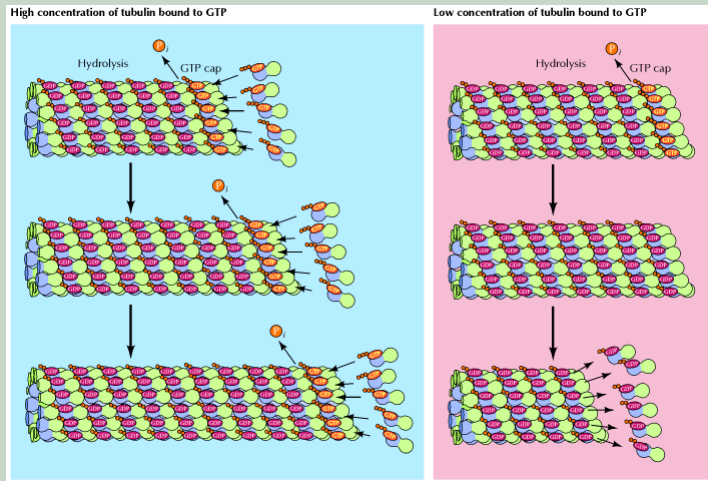
# Microtúbulos



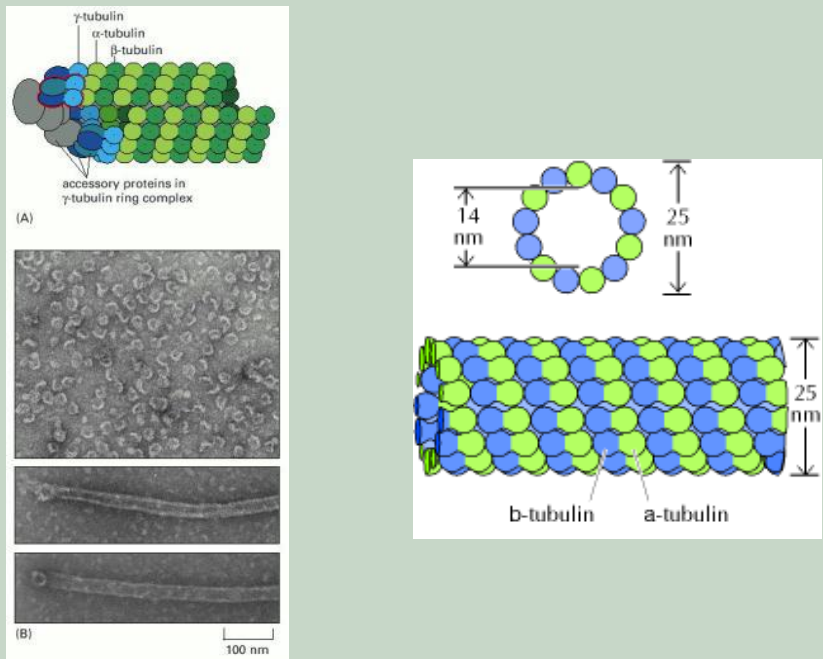
## Inestabilidad dinámica

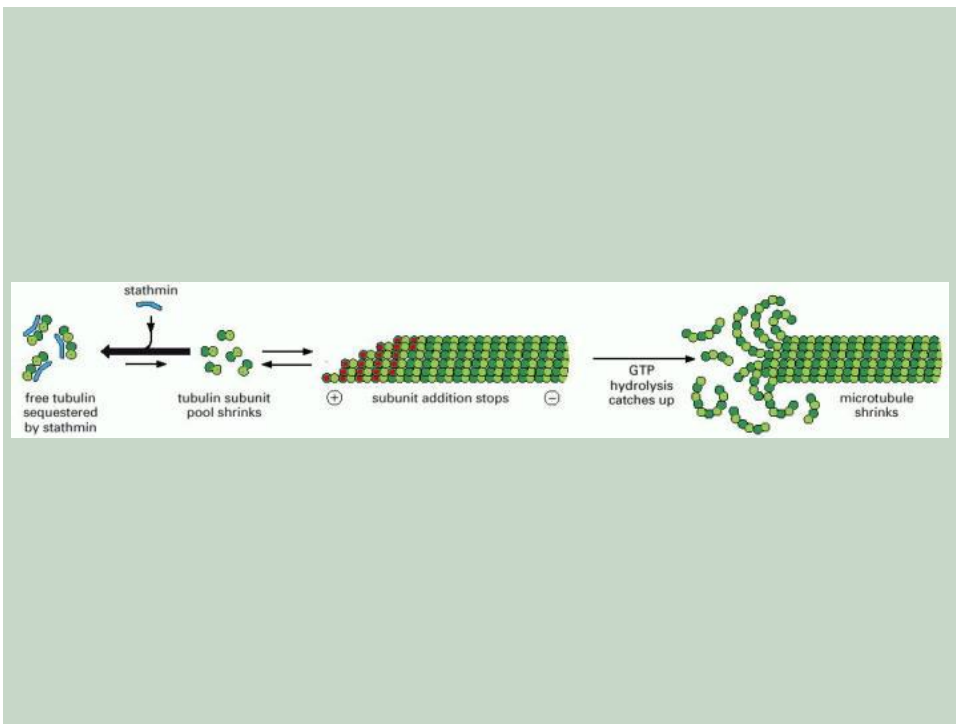


Inestabilidad dinámica

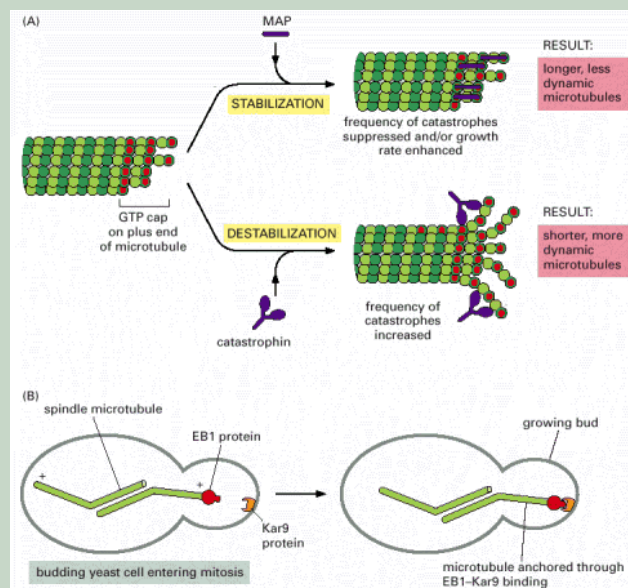


Inestabilidad dinámica



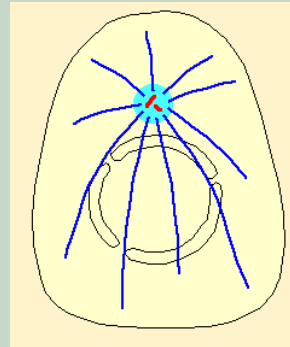
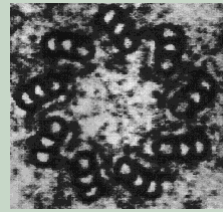


## Inestabilidad dinámica

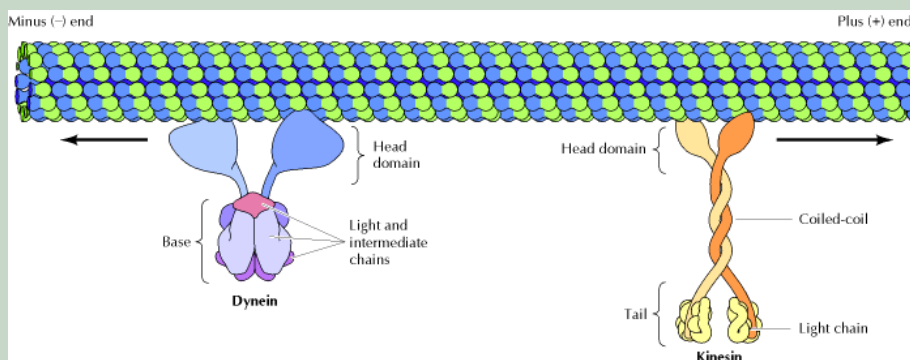




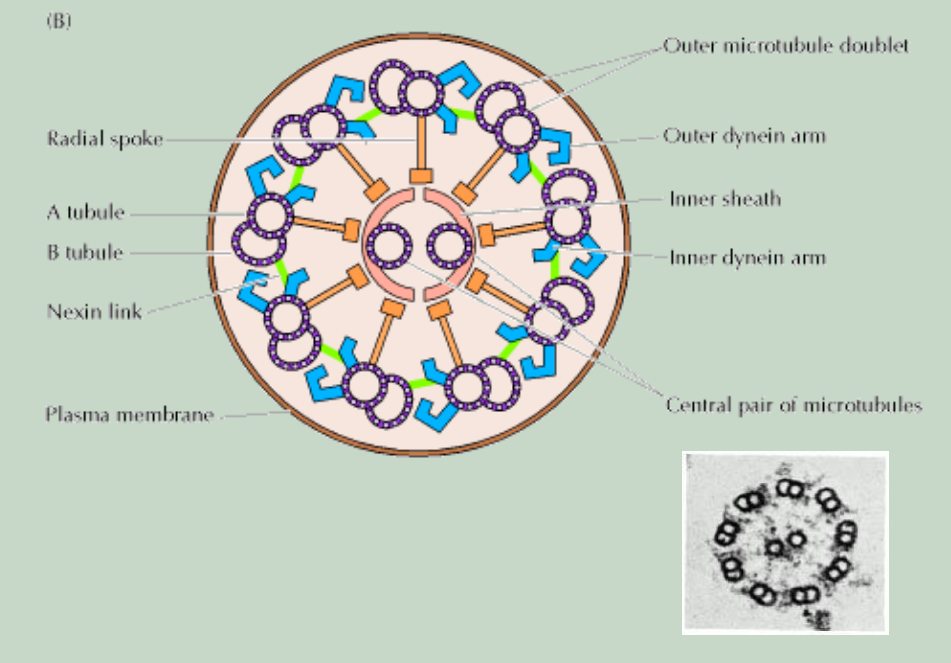
## Centríolos



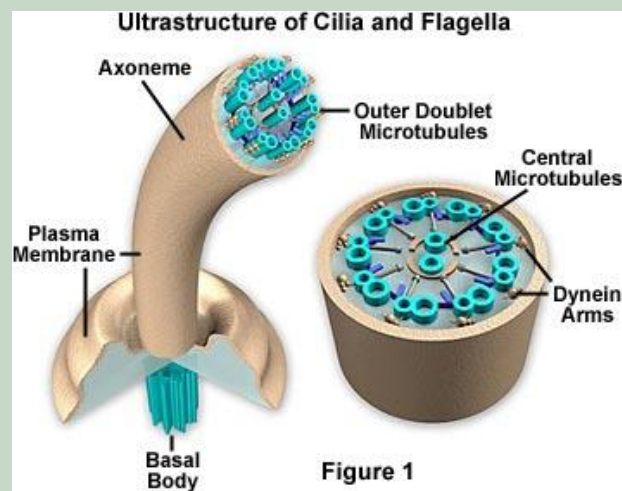
## Dineínas y Quinesinas



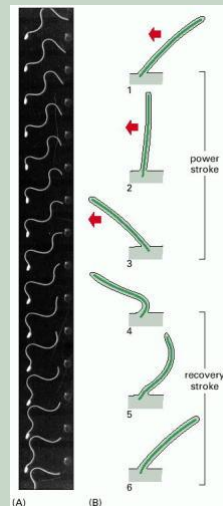
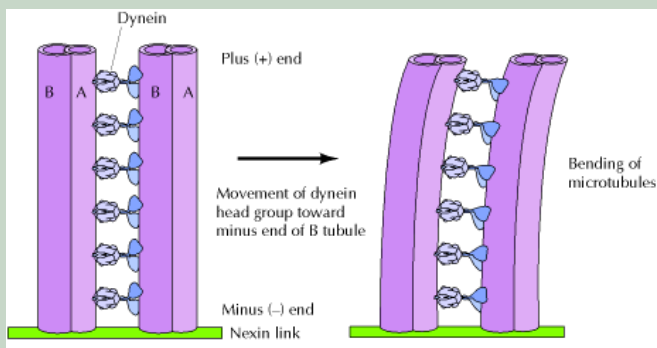
## Cilias y Flagelos



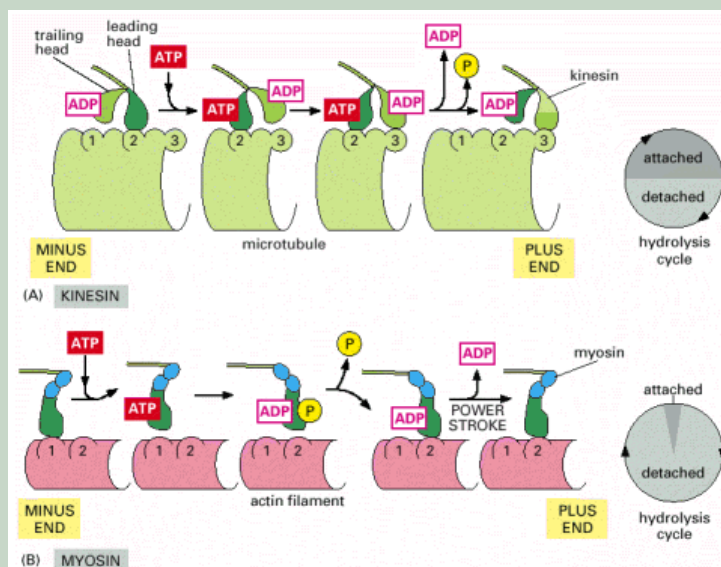
## Cilias y Flagelos



Cilias y Flagelos



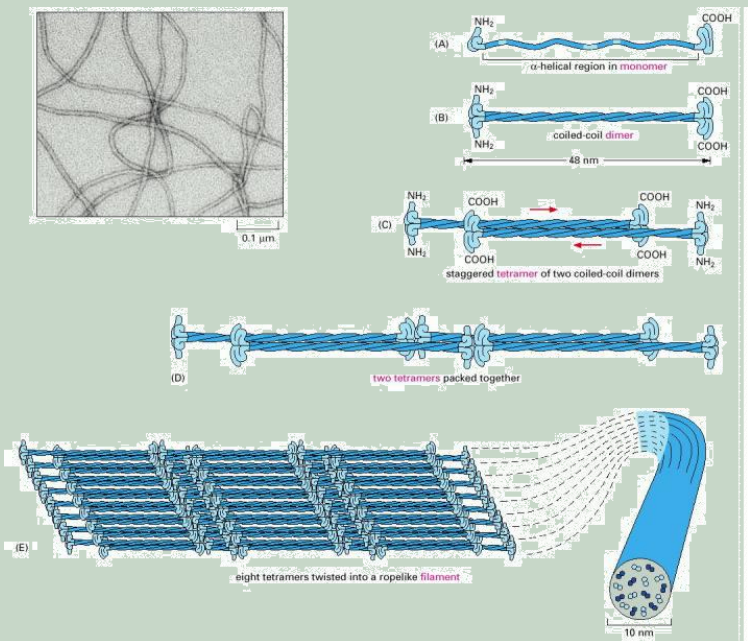
Miosina vs Quinesina



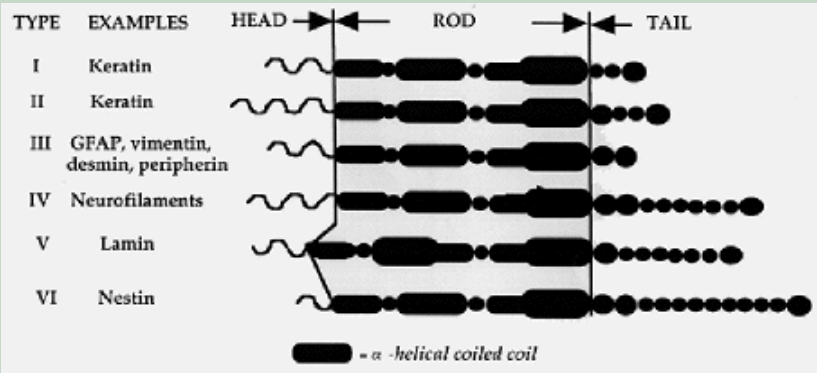
# Filamentos intermedios

TYPES OF IF	COMPONENT POLYPEPTIDES	CELLULAR LOCATION
Nuclear	lamins A, B, and C	nuclear lamina (inner lining of nuclear envelope)
Vimentin-like	vimentin	many cells of mesenchymal origin
	desmin	muscle
	glial fibrillary acidic protein	glial cells (astrocytes and some Schwann cells)
Epithelial	peripherin	some neurons
	type I keratins (acidic) type II keratins (basic)	epithelial cells and their derivatives (e.g., hair and nails)
Axonal	neurofilament proteins (NF-L, NF-M, and NF-H)	

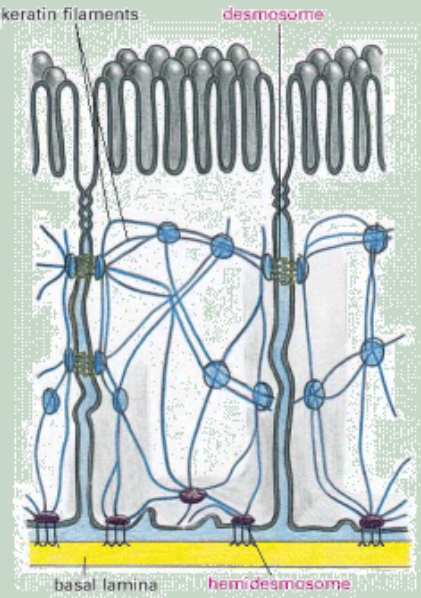
# Filamentos intermedios



# Filamentos intermedios

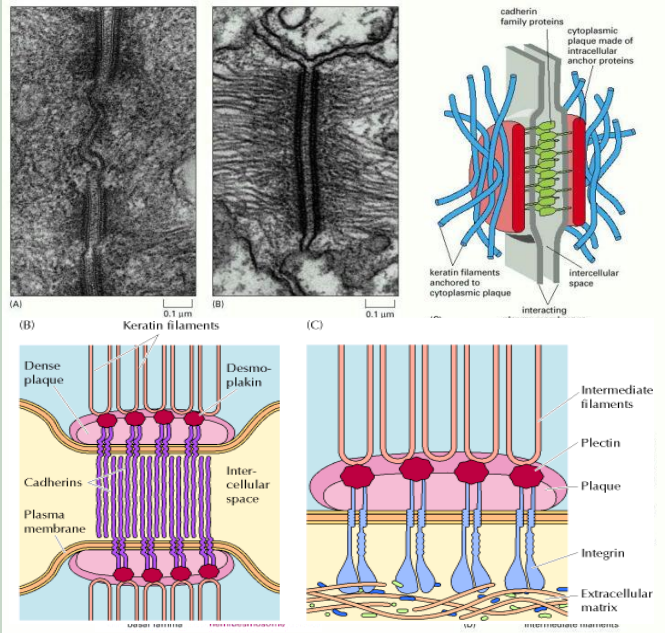


# Desmosomas y Hemidesmosomas





Desmosomas y Hemidesmosomas



Desmosomas

