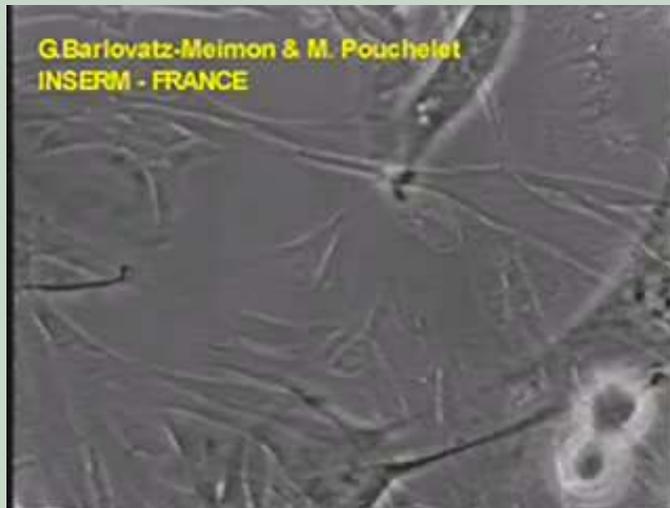


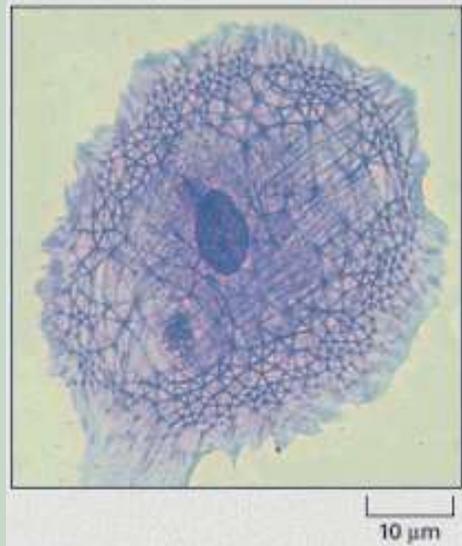
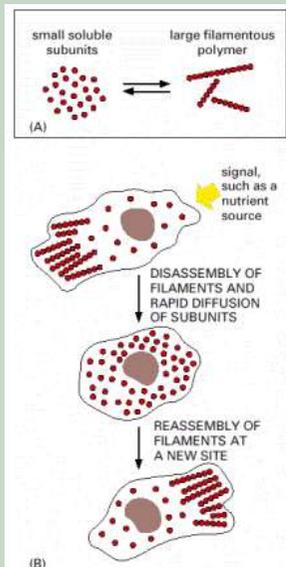
# INTRODUCCION A LA BIOLOGIA CELULAR Y MOLECULAR

- BIOLOGIA CELULAR -  
Citoesqueleto

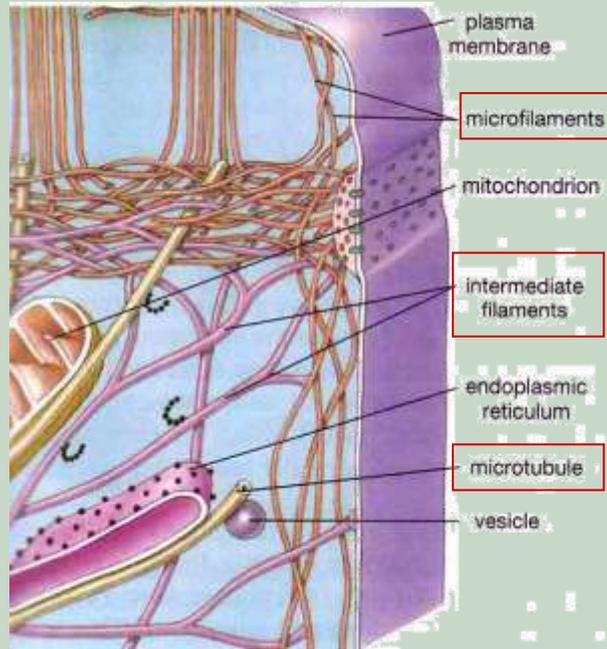




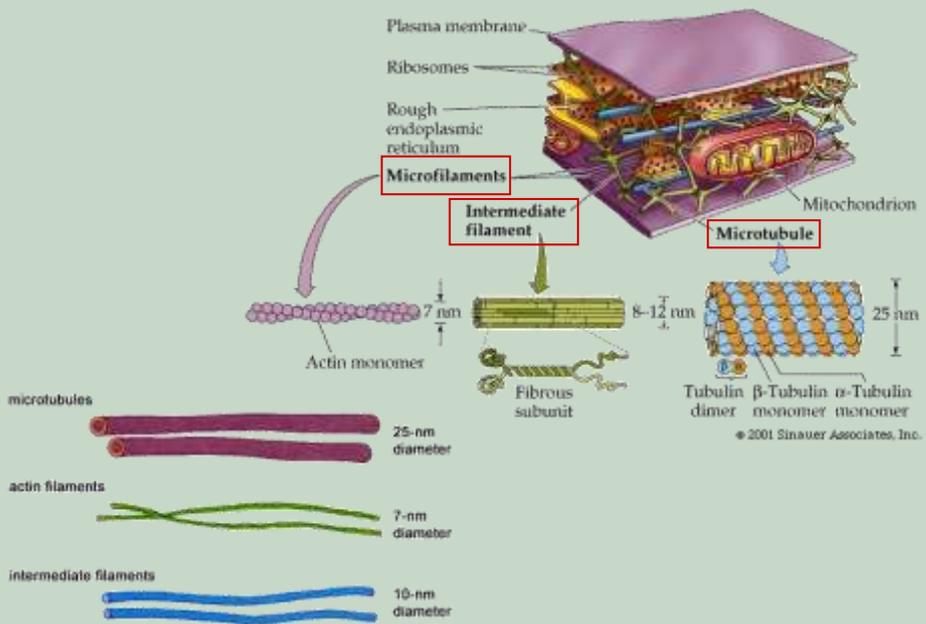
## Citoesqueleto



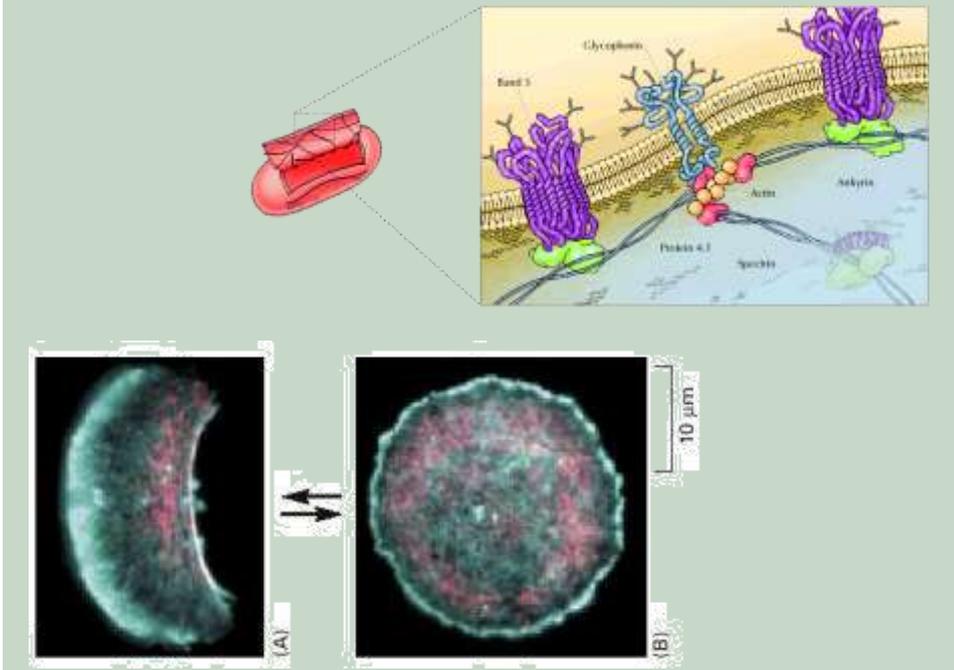
## Citoesqueleto



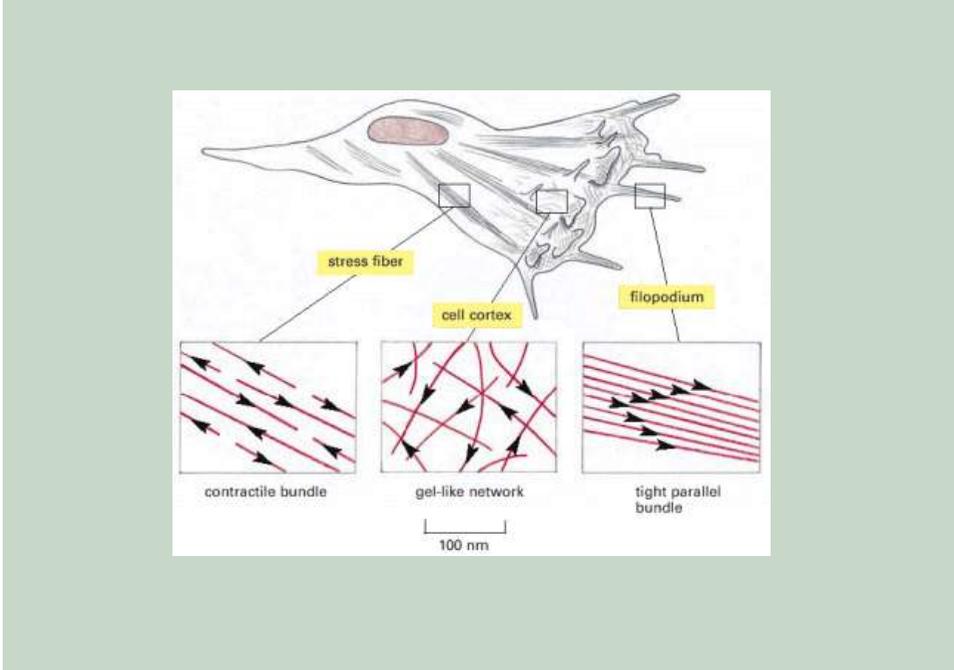
## Filamentos



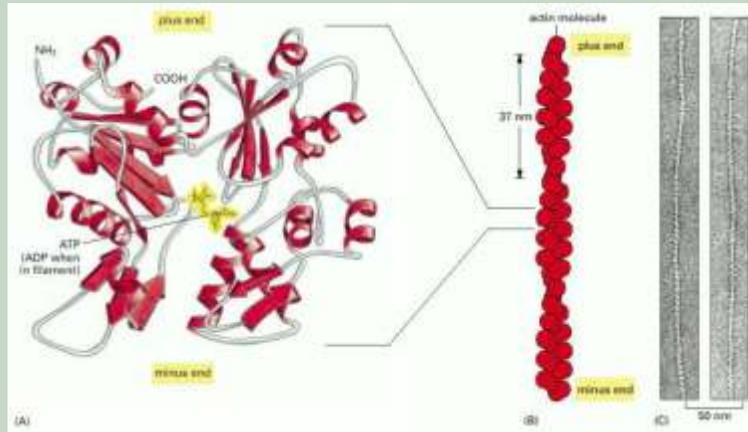
# Actina



# 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 *on-assembly*) 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 linear polymer is initiated 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 molecule to form a trimer makes the entire group more stable.

Further monomer addition can take shape only if the trimer, which therefore acts as a nucleus for polymerization. For actin, the nucleus is larger and has a more complicated structure (usually a ring of 13 or more subunits enclosed) – but the principle is the same.

The assembly of a nucleus is relatively slow, which explains the lag phase when starting polymerization. The lag phase can be reduced or abolished entirely if preformed nuclei, such as fragments of already polymerized microtubules or actin filaments, are added.

### THE CRITICAL CONCENTRATION

The number of molecules that add to the polymer (actin filament or microtubule) per second will be proportional to the concentration of the free subunit ( $[C]$ ), 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 added 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. In this equilibrium,

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

so that

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

When  $C$  is the equilibrium constant for subunit addition (see Figure 2-44).

### TIME COURSE OF POLYMERIZATION

The assembly of a protein into a long linear 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 (see 2-44).

### 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.

The conformational change affects the rate at which subunits will be kinase ends.

Even though  $k_{on}$  and  $k_{off}$  will have different values for the plus and minus ends of the polymer, their ratio  $k_{on}/k_{off}$  – and hence  $C_c$  – must be the same at both ends for an equilibrium reaction like ADP or GTP hydrolysis. This is because exactly the same subunit interactions are broken when a subunit is lost at either end, and the free state of

The subunits after disassembly is identical. Therefore, the  $k_{off}$  is that of free subunits, which does not vary with the equilibrium constant for its association with the end, is identical at both ends. If the plus end grows four times faster than the minus end, it must also shrink four times faster. Thus, for  $C < C_c$ , both ends grow, for  $C > C_c$ , both ends shrink.

The nucleotide hydrolysis hydrolysis that accompanies actin and tubulin polymerization reverses this condition.

### NUCLEOTIDE HYDROLYSIS

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

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

Considering events at the plus end only:

$$F_{actin} + \text{ADP} \rightleftharpoons F_{actin} + \text{GTP} + \text{actin}$$

As before, the polymer will grow until  $C = C_c$ . For this reason, we must not only ignore  $V_p^+$  and  $V_p^-$  since they are usually very small, we also ignore  $V_p^+$  and  $V_p^-$  since they are usually very small, so that polymer growth ceases when  $V_p^+ = V_p^- = 0$ .

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

### 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 those bound nucleotides are hydrolyzed. Under such conditions, the end that is "capped" of subunits outpacing the nucleotide hydrolysis can ATP cap or an actin filament or a GTP cap on a microtubule.

**DYNAMIC INSTABILITY** and **TREADMILLING** are not behaviors observed in crystalline polymers. Both are associated with nucleotide triphosphate hydrolysis. Dynamic instability is believed to predominate in microtubules, whereas treadmilling may predominate in actin filaments.

### TREADMILLING

The consequence of the nucleotide hydrolysis that accompanies polymer formation is to change the critical concentration at the two ends of the polymer. Since  $V_p^+$  and  $V_p^-$  refer to different reactions, they refer to  $C_c^+$  and  $C_c^-$  used not for the same in both ends of the polymer, so that:

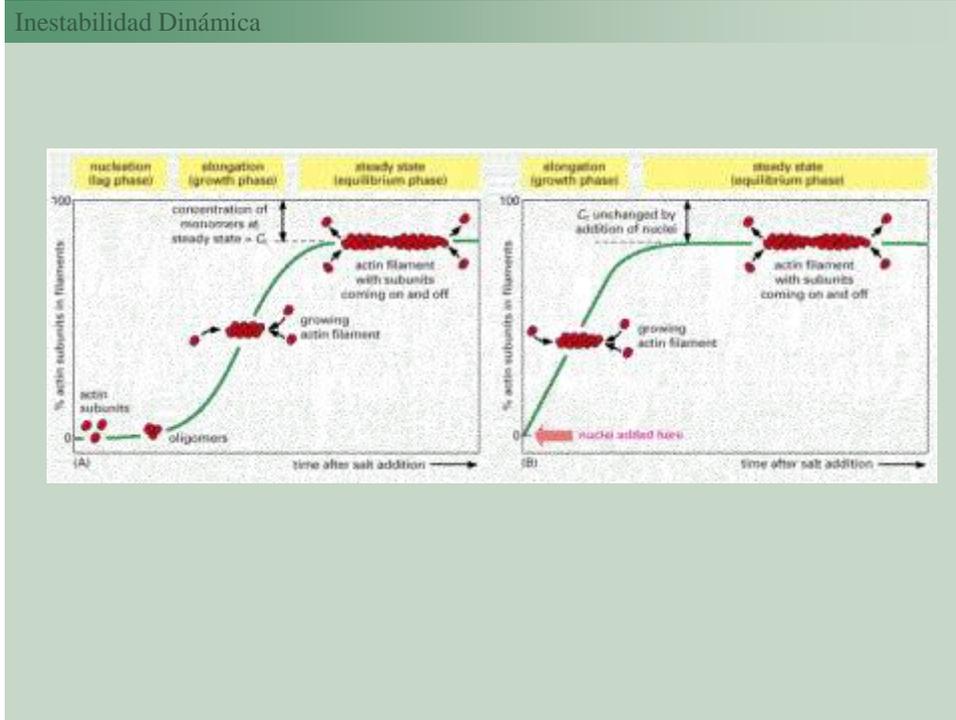
$$C_c^+ \text{ (minus end)} < C_c^- \text{ (plus end)}$$

Thus, if both ends of a polymer are exposed, polymerization ceases and 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. Even so **treadmilling**.

### DYNAMIC INSTABILITY

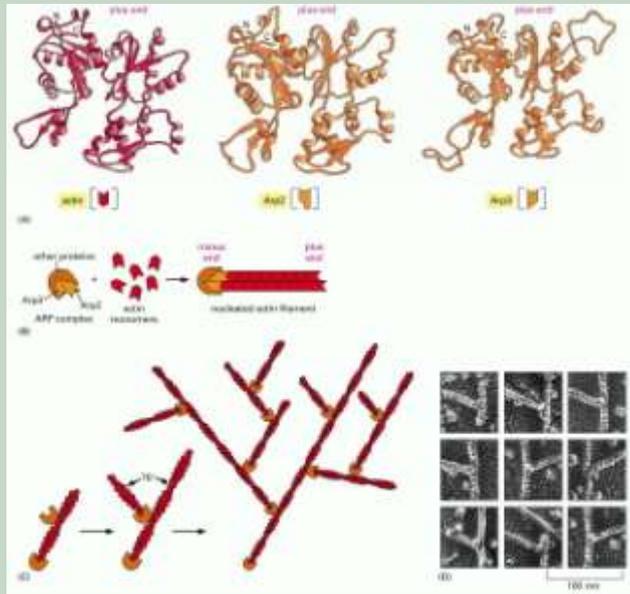
Microtubule depolymerizes about 100 times faster from an end containing GDP subunits than from one containing GTP subunits. A GTP cap hinders growth, but if it is lost, then depolymerization ensues.

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

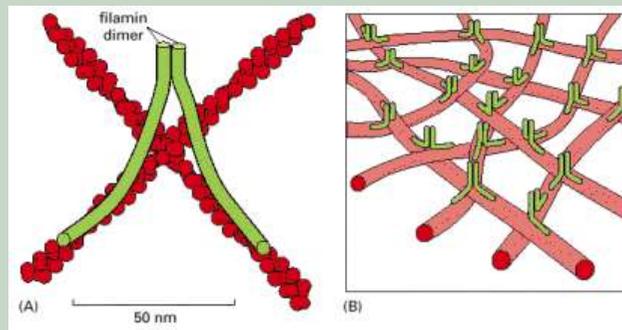




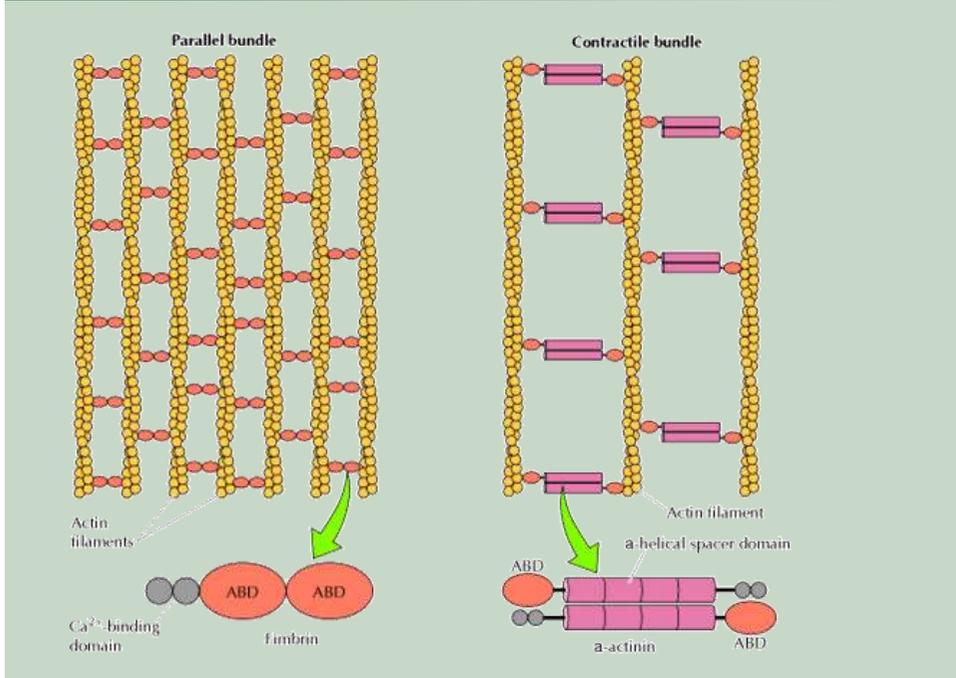
## ARP



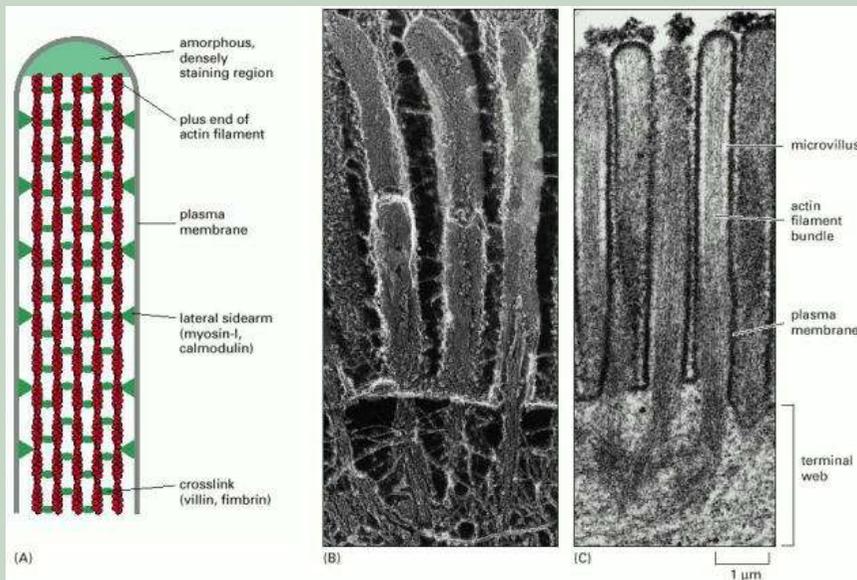
## Filamina



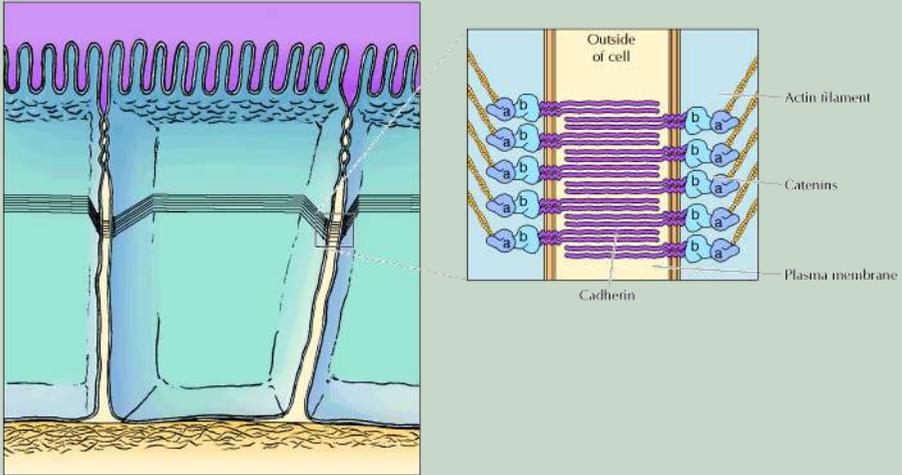
## Haces de Actina



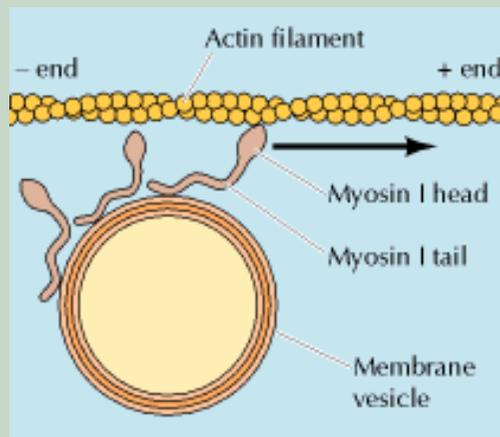
## Microvellosidades



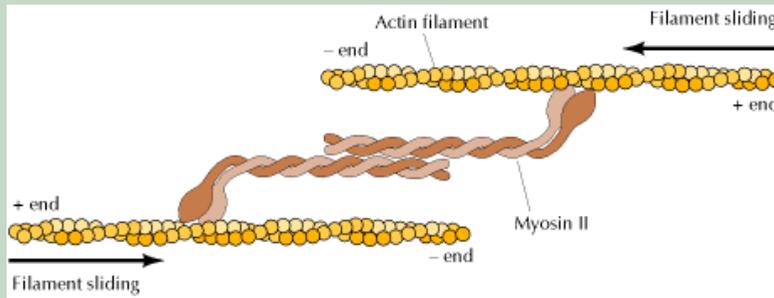
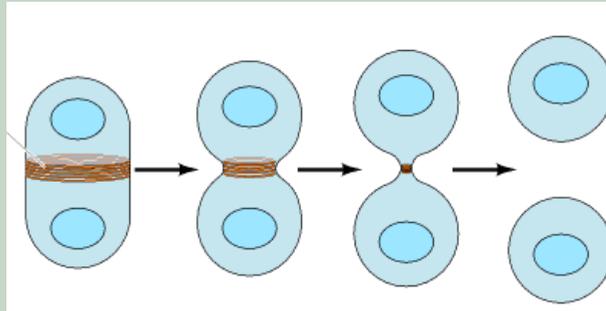
## Uniones adherentes



## Miosina I

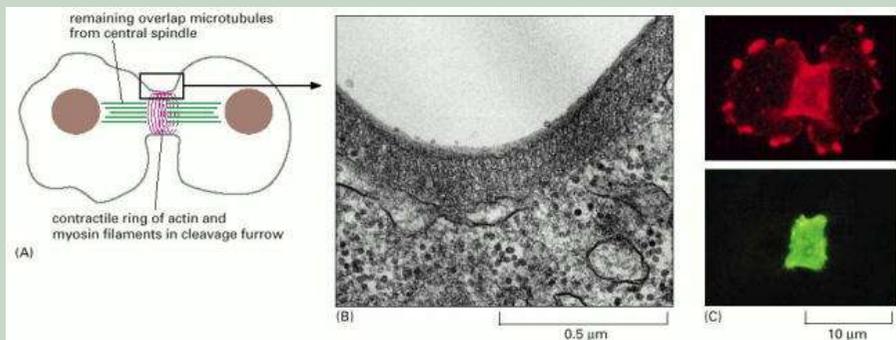


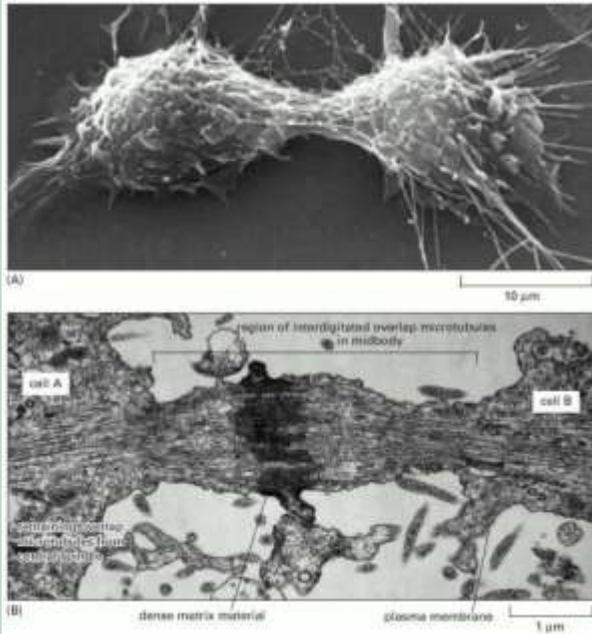
## Miosina II



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

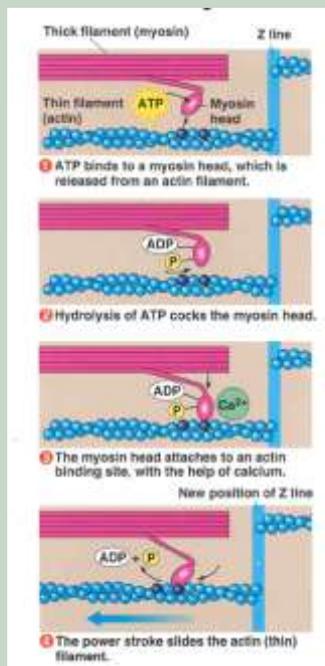
La segmentación se consigue mediante la contracción de un fino anillo compuesto principalmente por una formación superpuesta de filamentos de actina y de filamentos bipolares de miosina II.



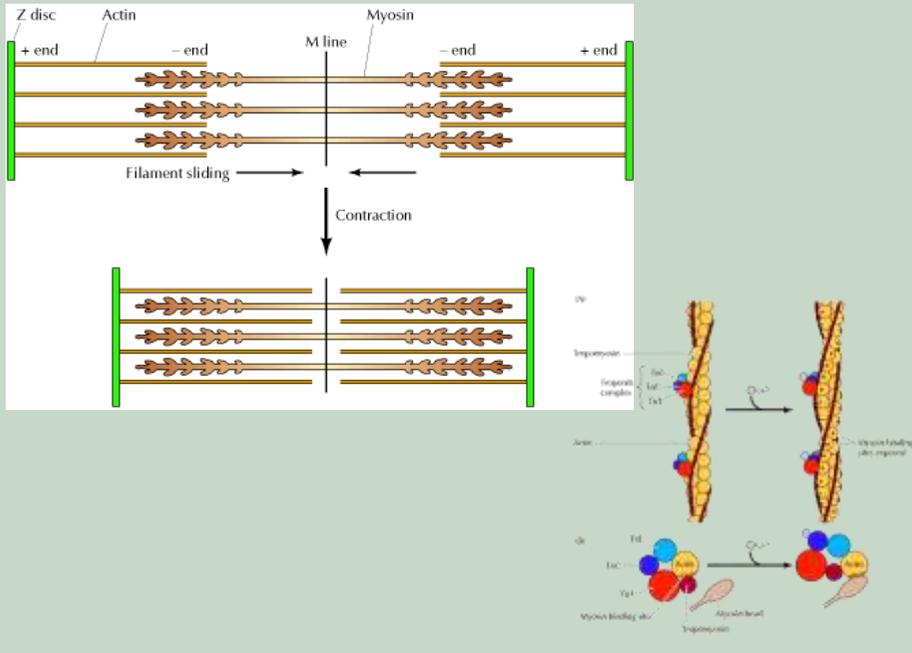


El anillo contráctil se elimina por completo al terminar la segmentación, cuando la membrana plasmática del surco de segmentación se estrecha formando el cuerpo medio, que permanece como un puente entre las dos células hijas.

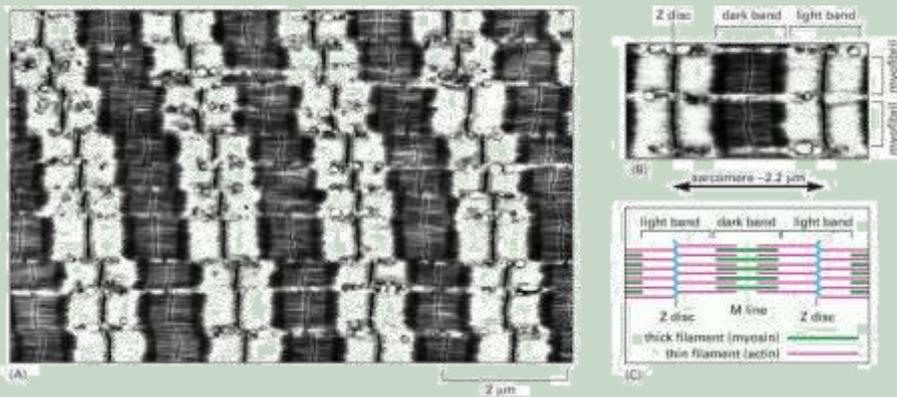
## Contracción Muscular



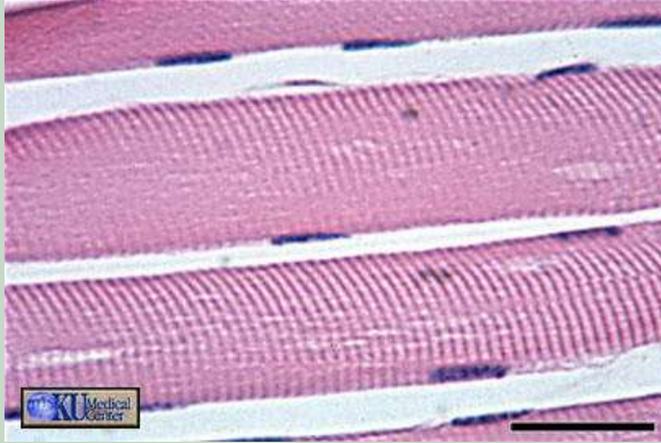
## Contracción Muscular



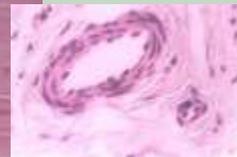
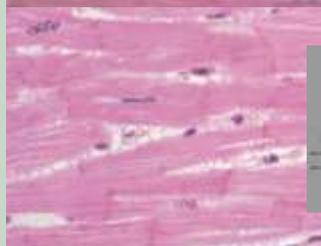
## Sarcómero



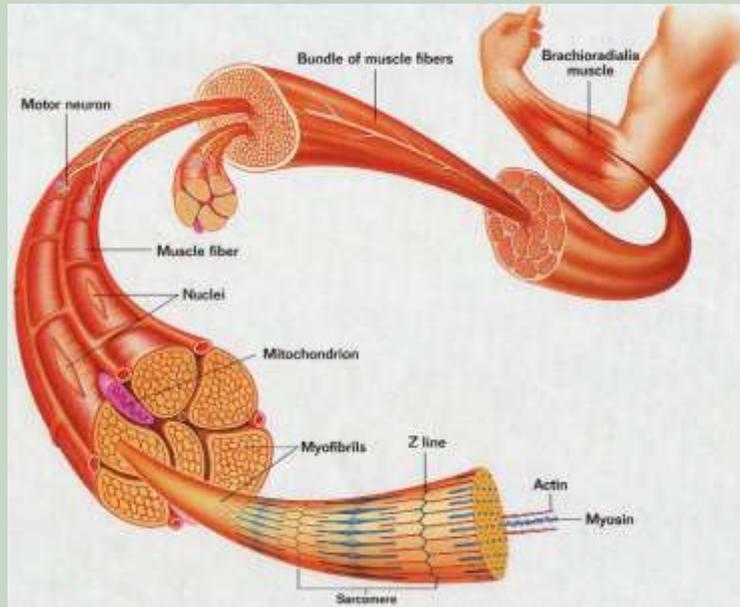
## Miositos esqueléticos



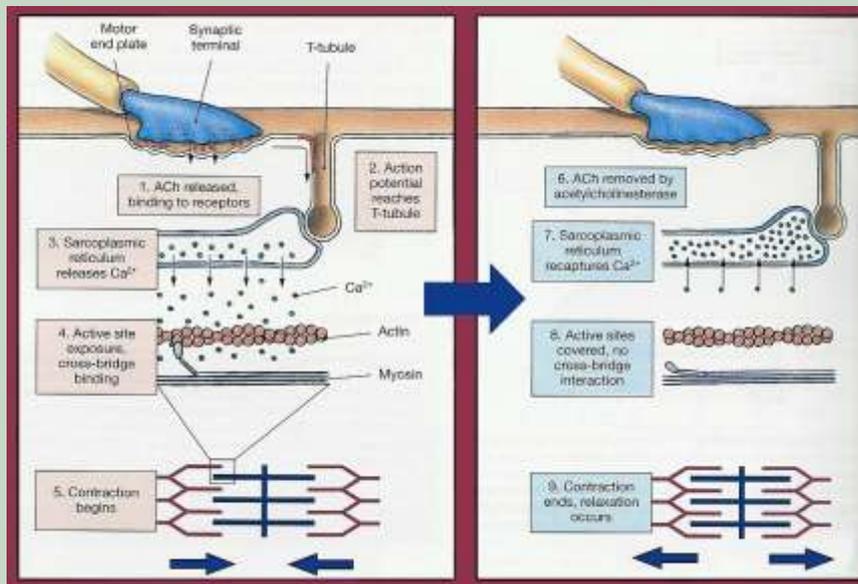
## Músculos



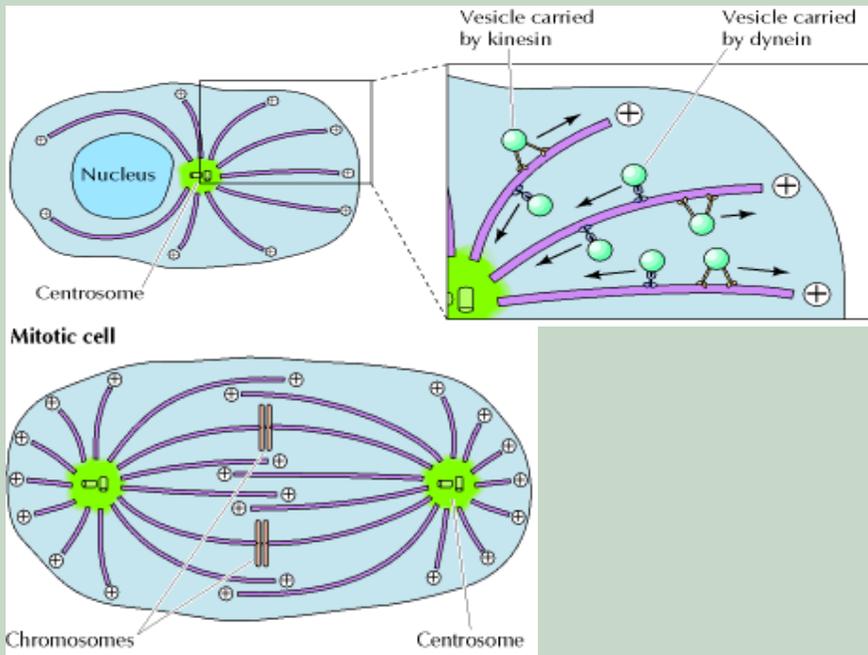
## Músculo esquelético



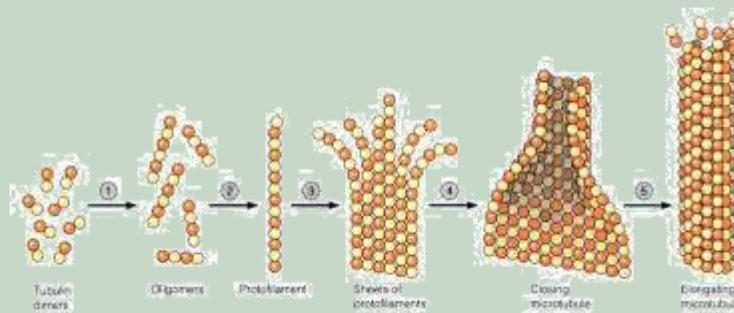
## Placa neuromuscular



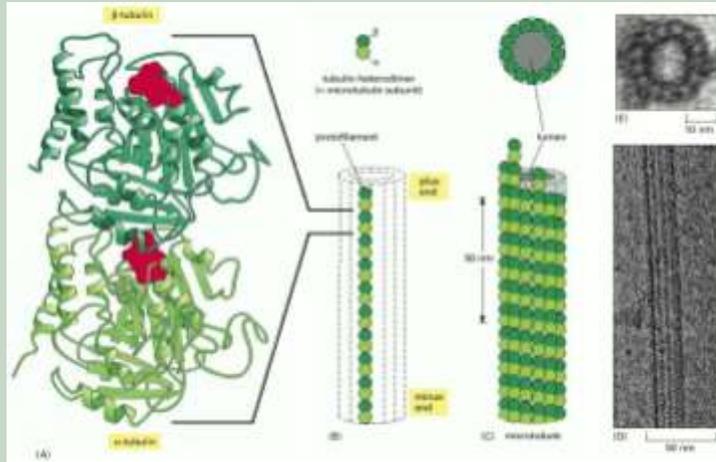
## Microtúbulos



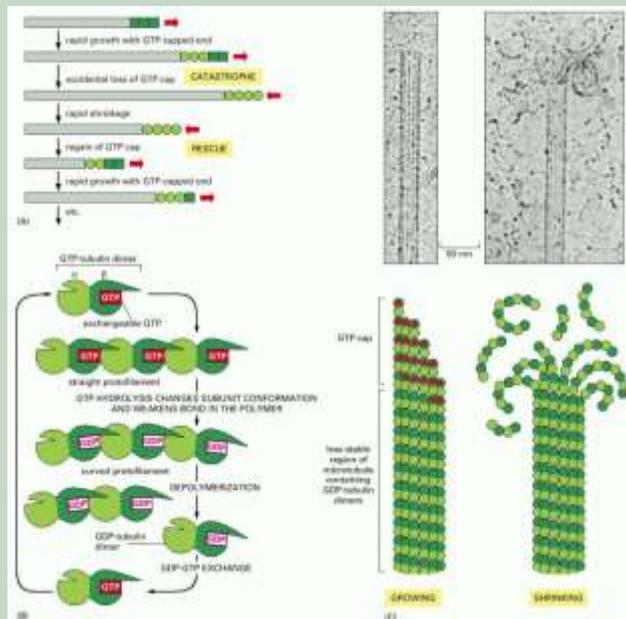
## Microtúbulos



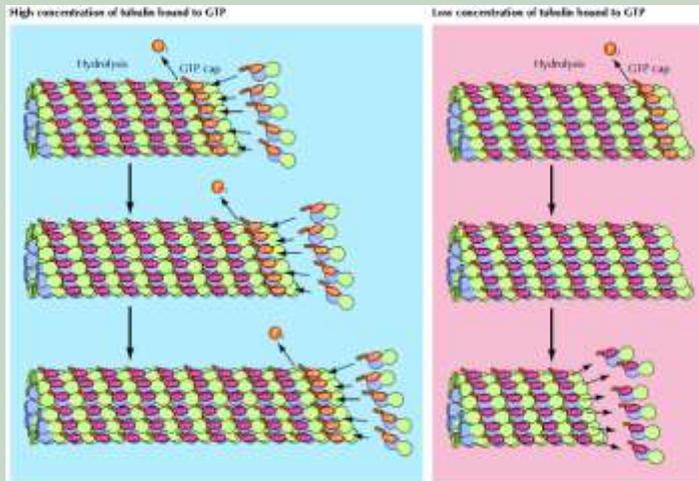
## Microtúbulos



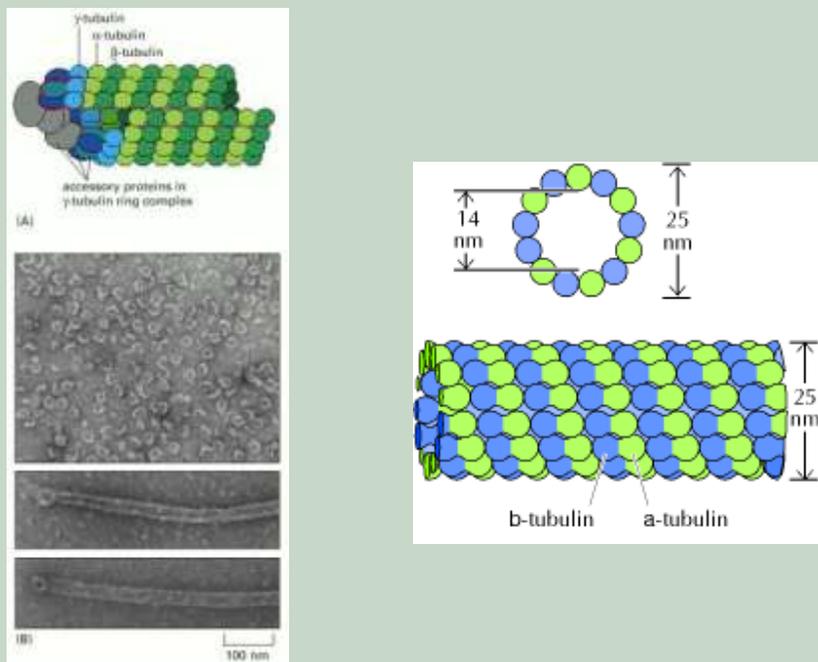
## Inestabilidad dinámica

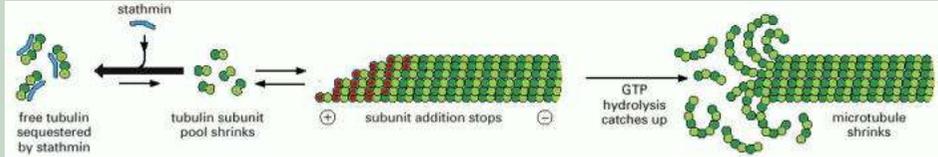


## Inestabilidad dinámica

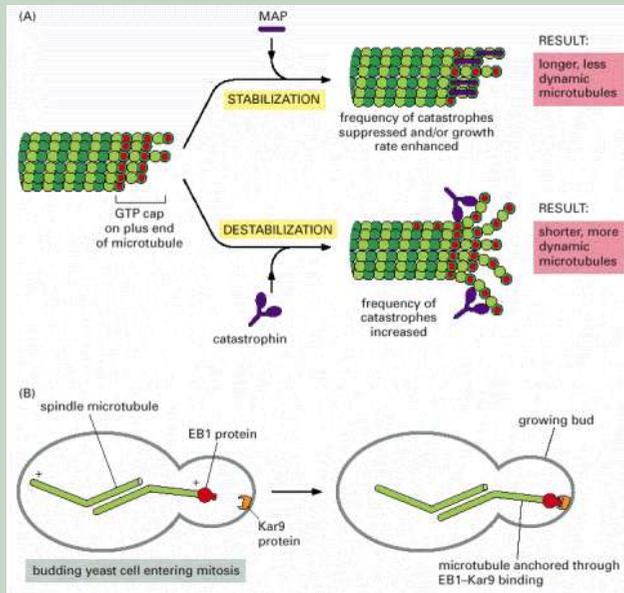


## Inestabilidad dinámica

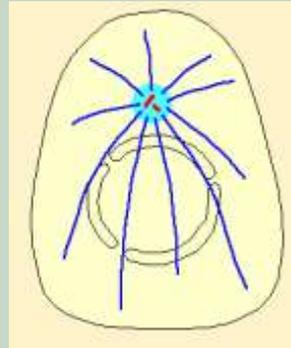
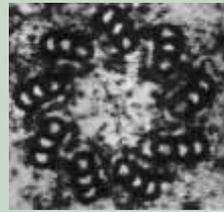
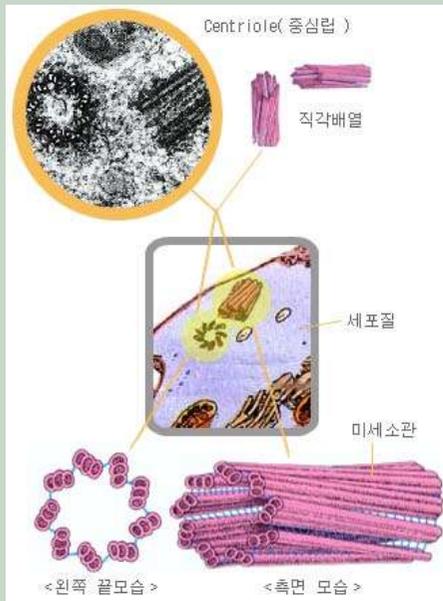




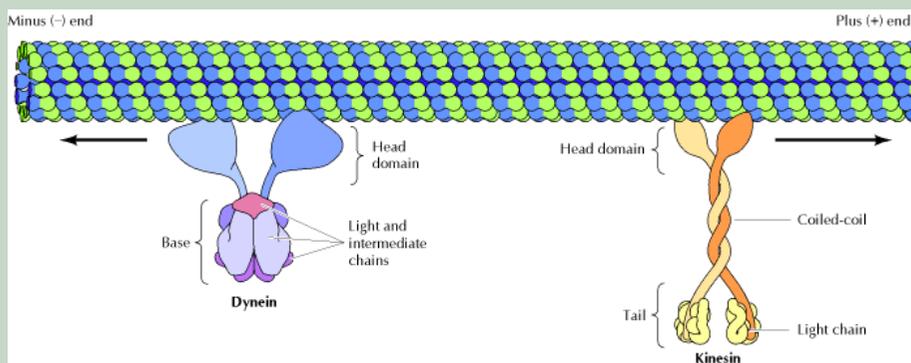
### Inestabilidad dinámica



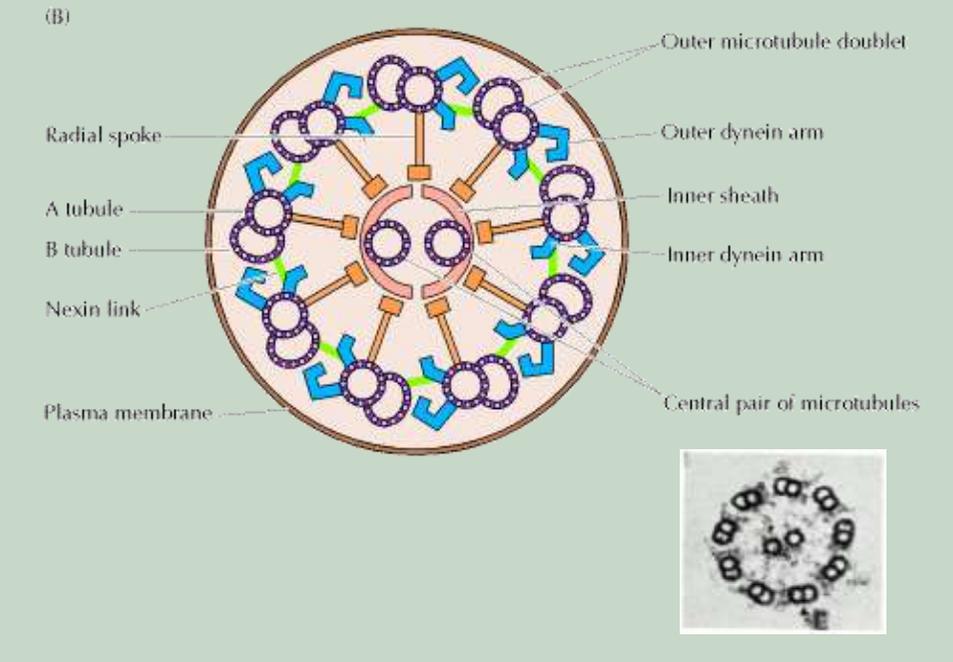
## Centríolos



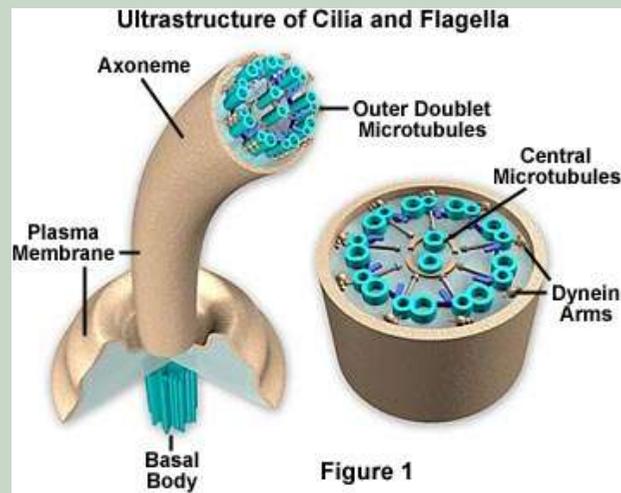
## Dineínas y Quinesinas



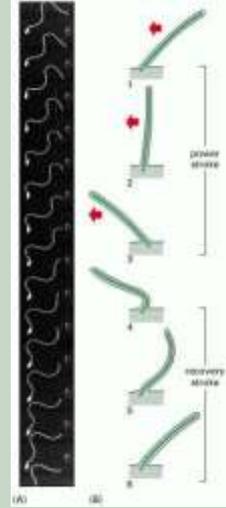
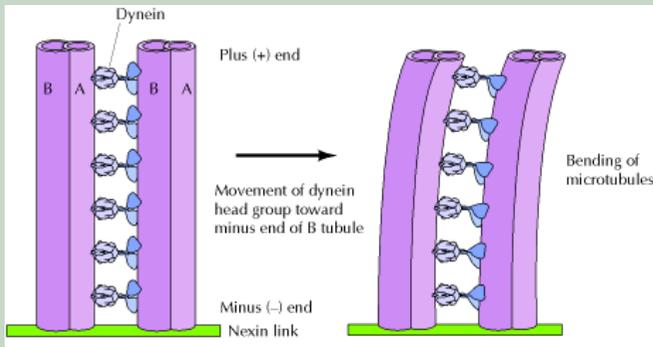
## Cilias y Flagelos



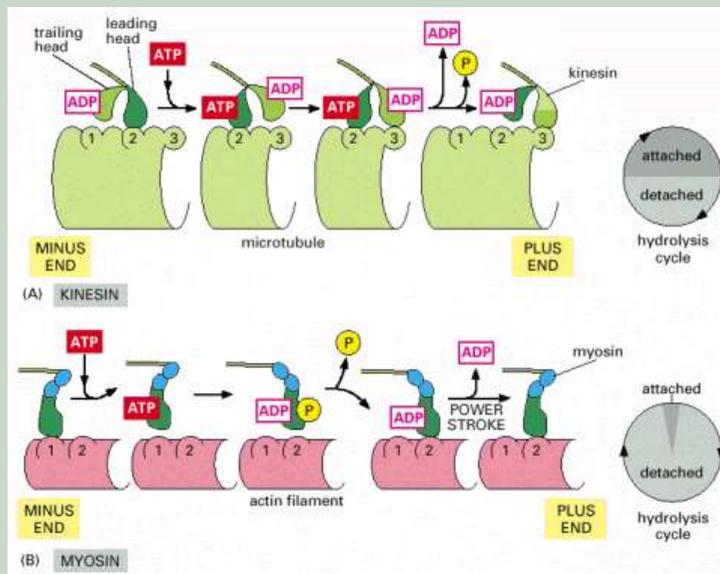
## Cilias y Flagelos



## Cilias y Flagelos



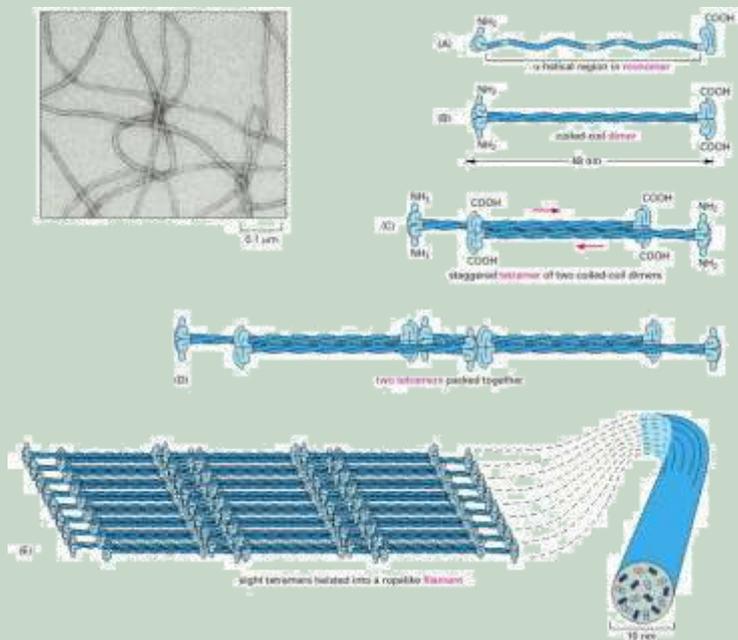
## Miosina vs Quinesina



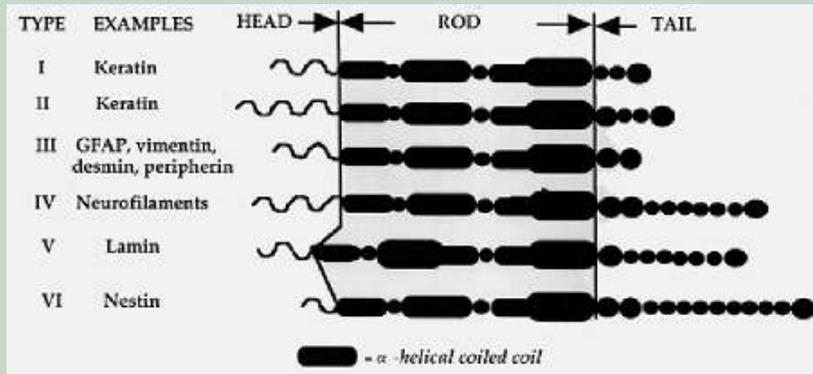
## Filamentos intermedios

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 type I keratins (acidic) type II keratins (basic)	some neurons epithelial cells and their derivatives (e.g., hair and nails)
Axonal	neurofilament proteins (NF-L, NF-M, and NF-H)	neurons

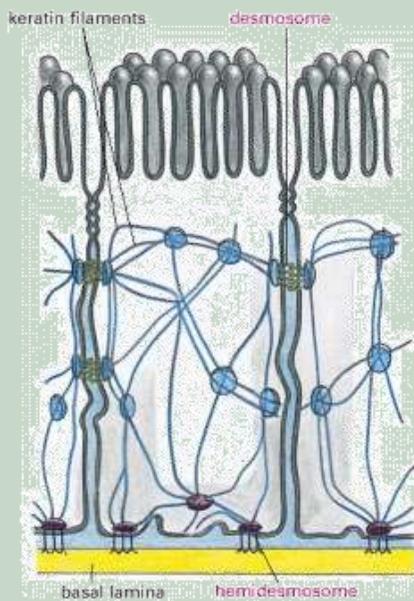
## Filamentos intermedios



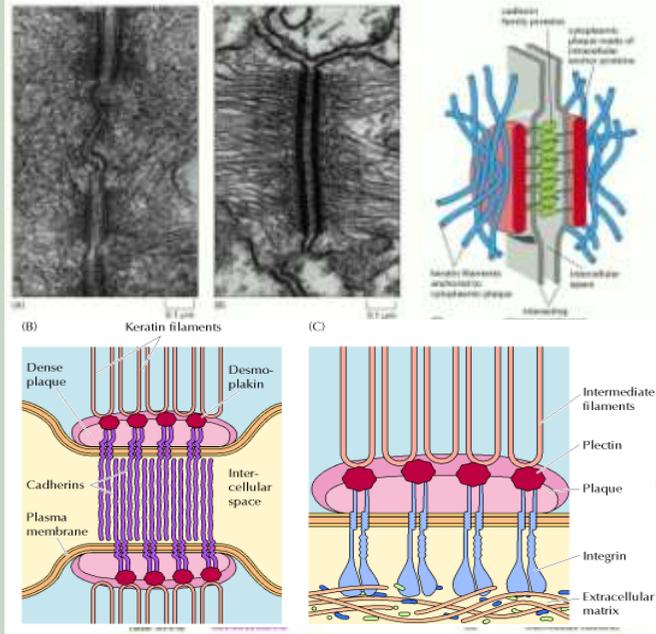
## Filamentos intermedios



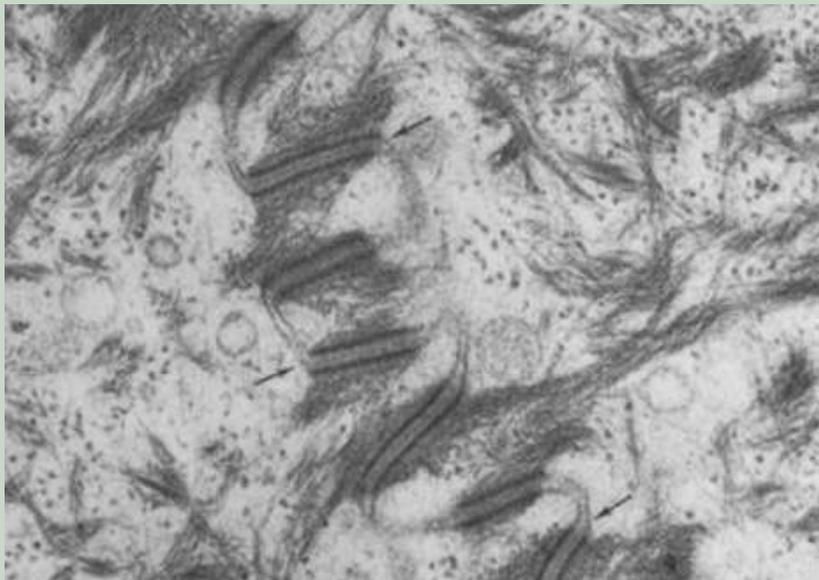
## Desmosomas y Hemidesmosomas



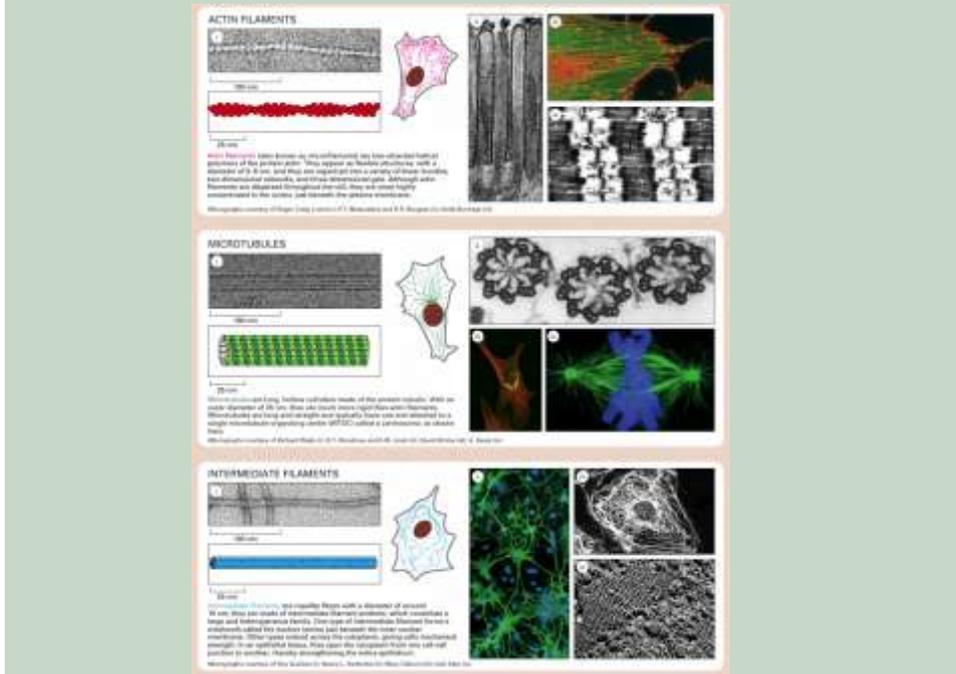
## Desmosomas y Hemidesmosomas



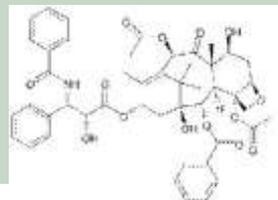
## Desmosomas



## Citoesqueleto



## Drogas y citoesqueleto



**Table 16-2. Drugs That Affect Actin Filaments and Microtubules**

### ACTIN-SPECIFIC DRUGS

Phalloidin	binds and stabilizes filaments
Cytochalasin	caps filament plus ends
Swinholide	severs filaments
Latrunculin	binds subunits and prevents their polymerization

### MICROTUBULE-SPECIFIC DRUGS

Taxol	binds and stabilizes microtubules
Colchicine, colcemid	binds subunits and prevents their polymerization
Vinblastine, vincristine	binds subunits and prevents their polymerization
Nocodazole	binds subunits and prevents their polymerization

