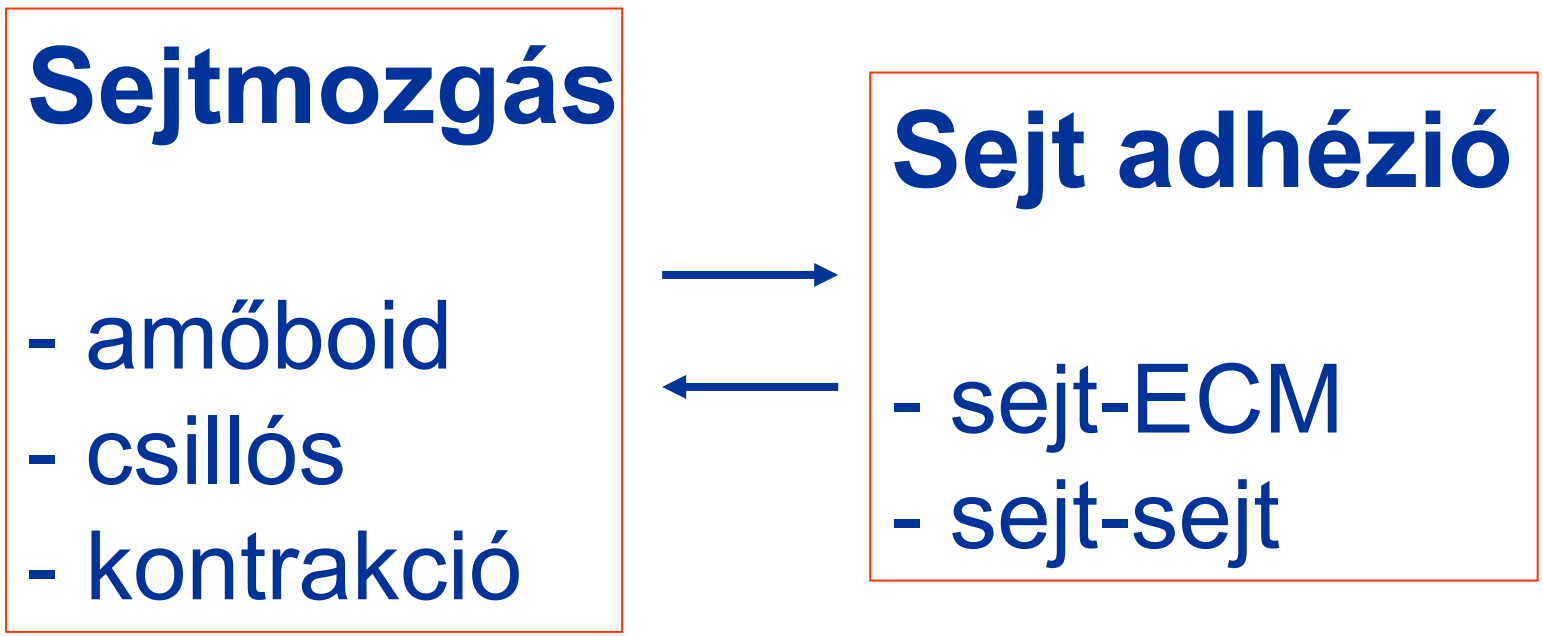
Sejtmozgás és adhézió

Molekuláris biológia kurzus
8. hét

Kun Lídia
Genetikai, Sejt és Immunbiológiai Intézet


Sejtmozgás
- amőboid
- csillós
- kontrakció
Sejt adhézió
- sejt-ECM
- sejt-sejt

MOZGÁS

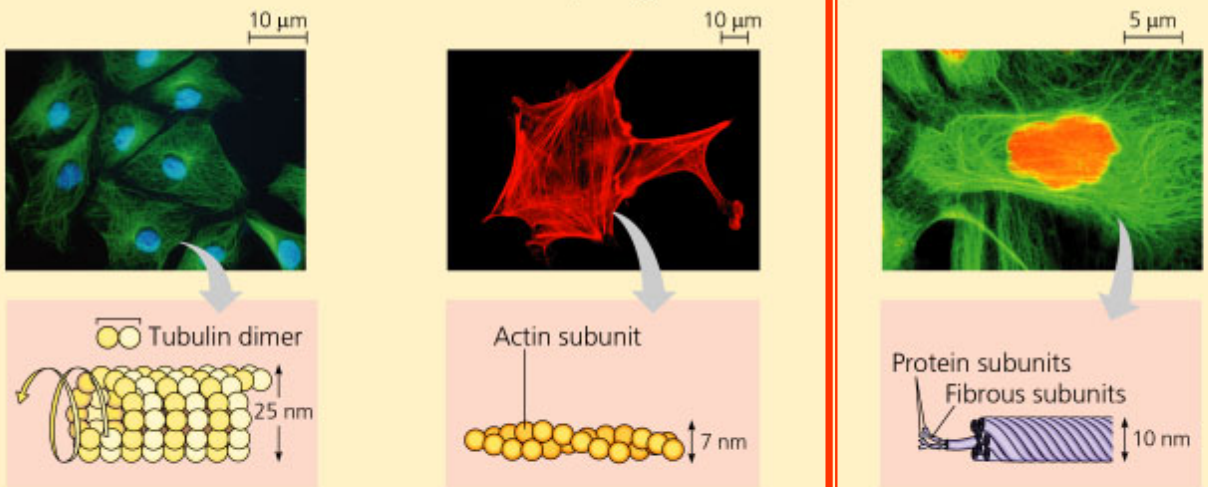
A sejtmozgás szereplői

- **Citoszkeleton** (aktin, mikrotubulus, intermedier filamentum)
- **Motor proteinek** (kinezin, dinein, miozin)
- **Kihorgonyzó ponok** (MTOC, bazális test, fokális adhézió)
- **Szabályozó faktorok** (Ca^{++}, Mg^{++}, kinázok)
- **Energia**: ATP

Citoszkeleton

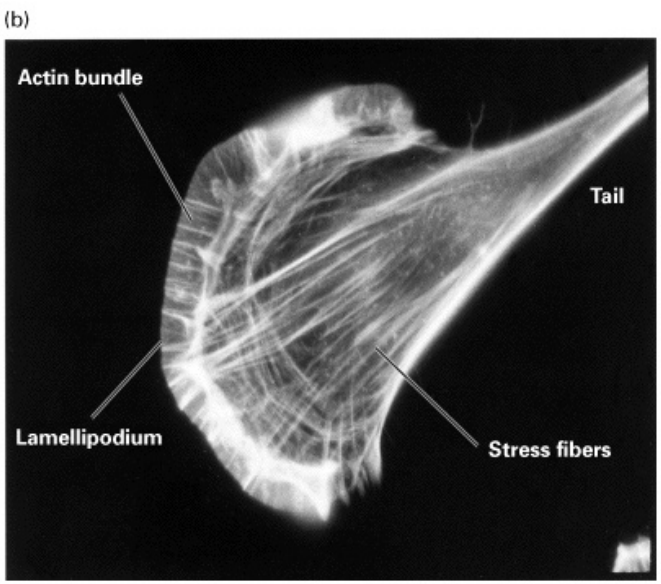
Table 7.2 The Structure and Function of the Cytoskeleton

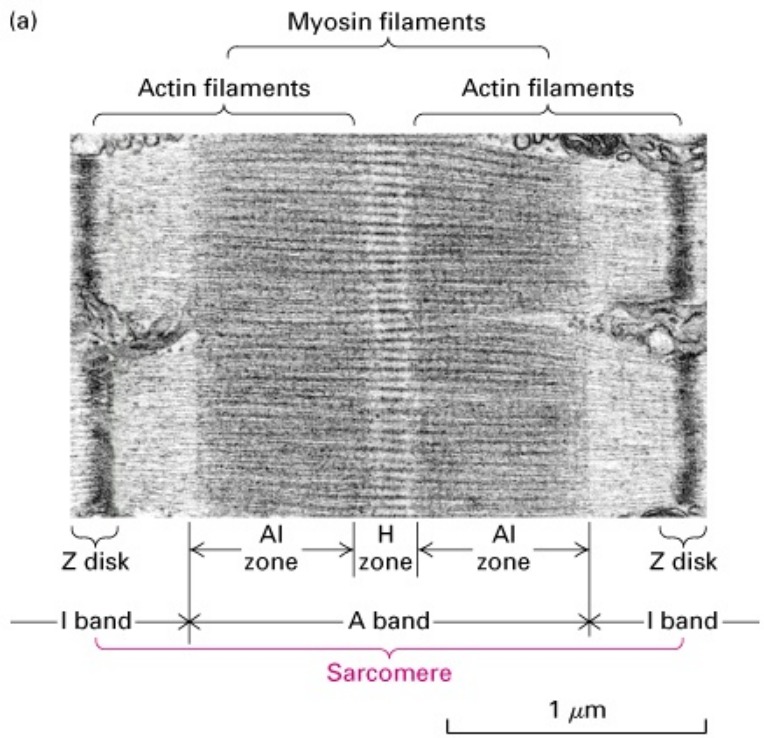
Property	Microtubules	Microfilaments (Actin Filaments)	Intermediate Filaments
Structure	Hollow tubes; wall consists of 13 columns of tubulin molecules	Two intertwined strands of actin	Fibrous proteins supercoiled into thicker cables
Diameter	25 nm with 15-nm lumen	7 nm	8–12 nm
Protein subunits	Tubulin, consisting of α-tubulin and β-tubulin	Actin	One of several different proteins of the keratin family, depending on cell type
Main functions	Maintenance of cell shape (compression-resisting "girders") Cell motility (as in cilia or flagella) Chromosome movements in cell division Organelle movements	Maintenance of cell shape (tension-bearing elements) Changes in cell shape Muscle contraction Cytoplasmic streaming Cell motility (as in pseudopodia) Cell division (cleavage furrow formation)	Maintenance of cell shape (tension-bearing elements) Anchorage of nucleus and certain other organelles Formation of nuclear lamina



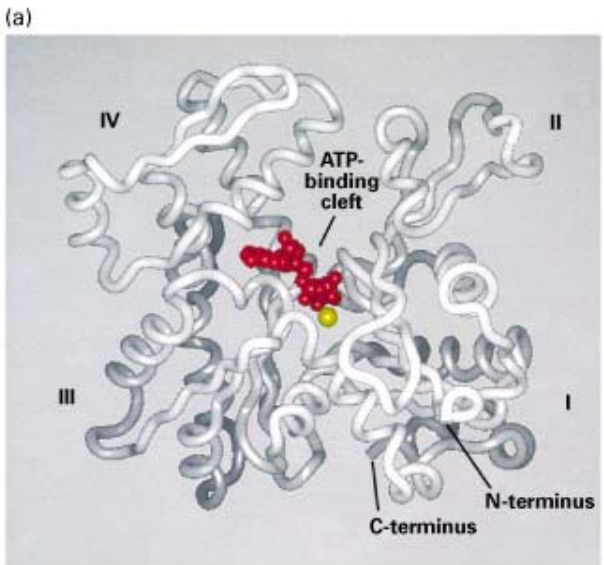
SOURCE: Adapted from W. M. Becker, L. J. Kleinsmith, and J. Hardin, *The World of the Cell*, 4th ed. (San Francisco, CA: Benjamin Cummings, 2000), p. 753.

Sejtmozgás és **aktin**

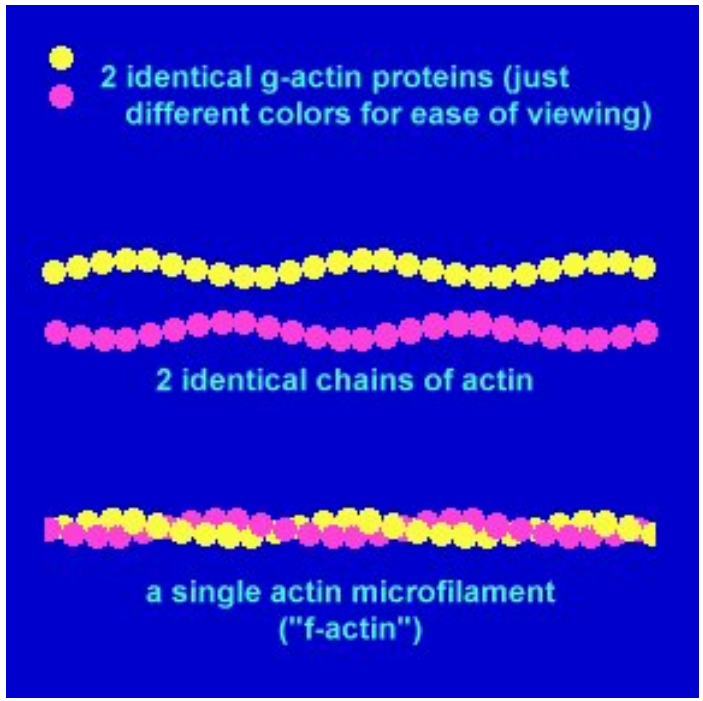




Az aktin filamentumok felépítése



Két G-aktin molekula ATP segítségével kapcsolódik

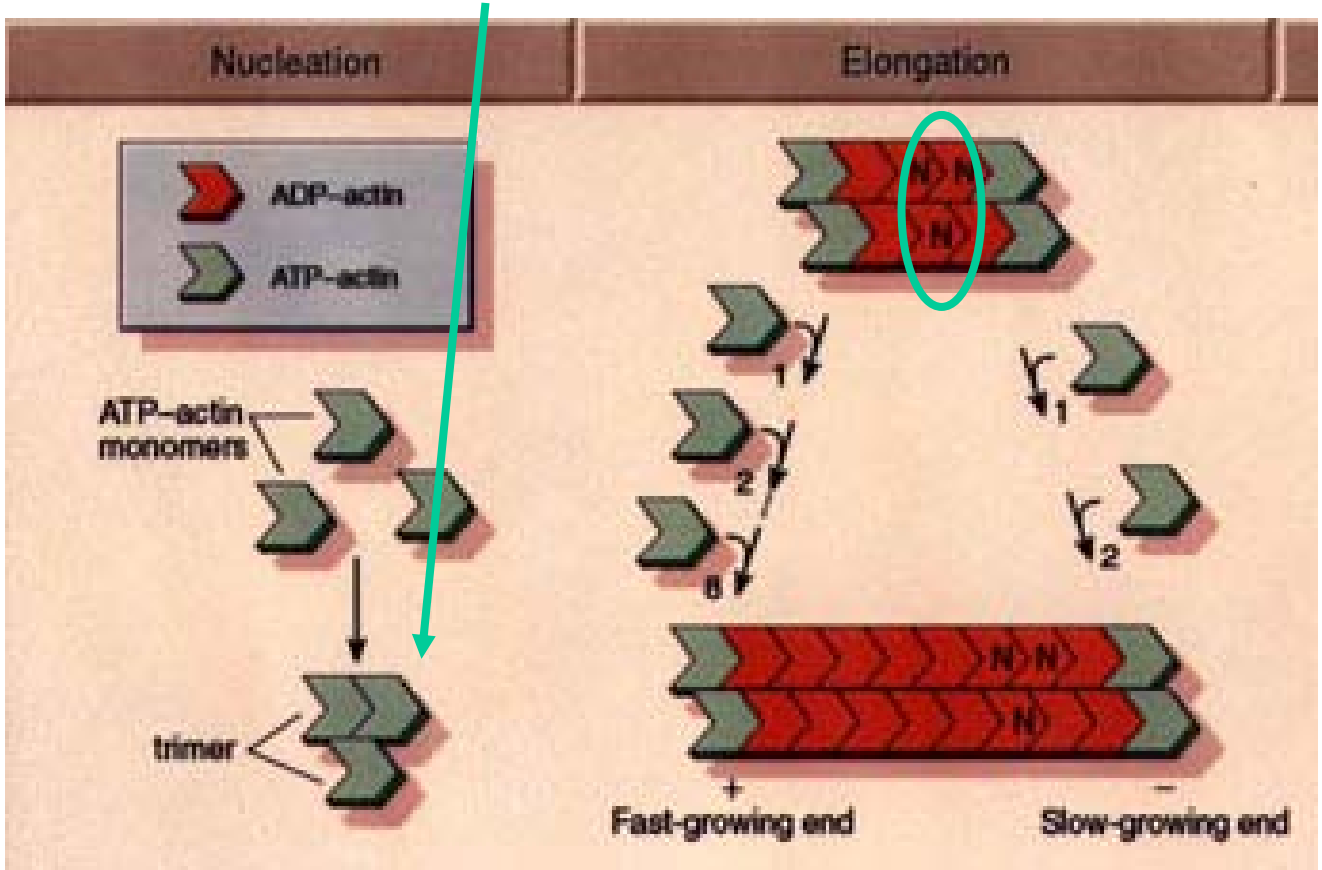


A mikrofilamentum csavaros szerkezete

G-aktin → F-aktin

Mag- képződés

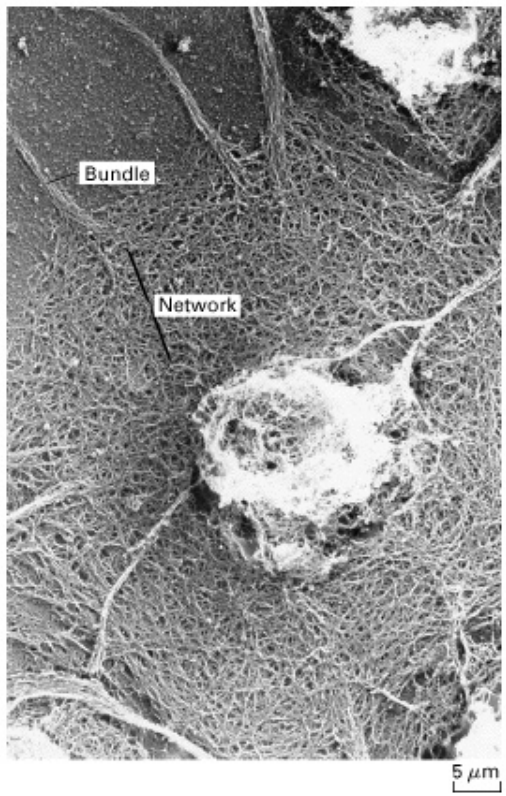
Elongáció (polarizáltan)

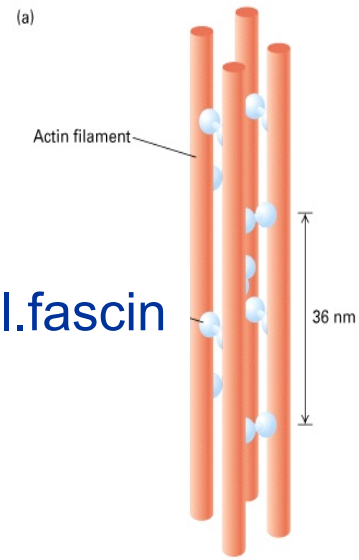


„+” vég:gyorsan növő

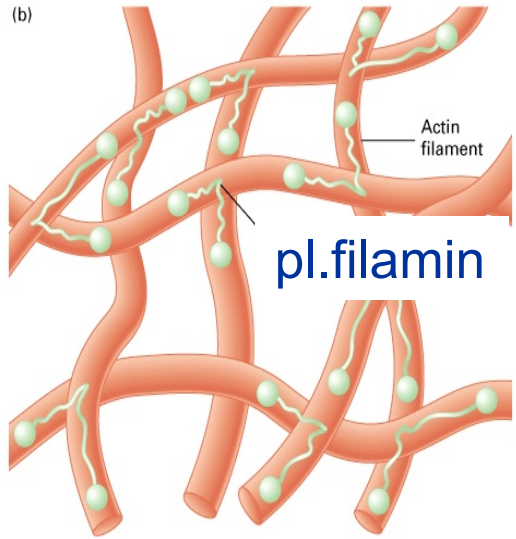
„-” vég lassan növő

Az aktin filamentumok szerveződése





pl.fascin

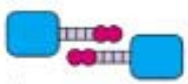
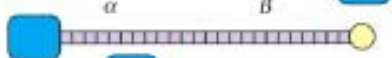
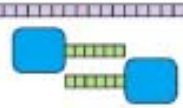


pl.filamin

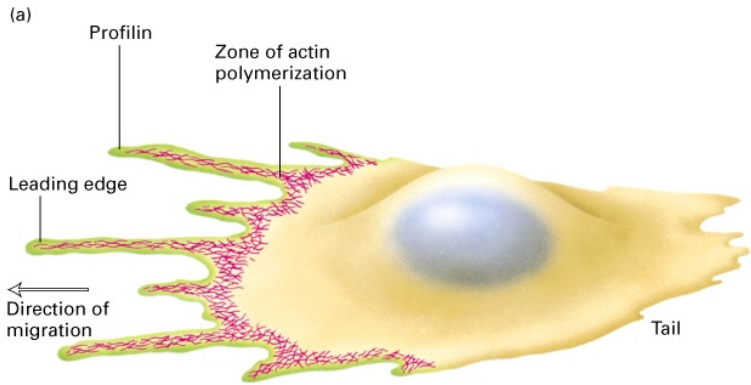
Aktin kötegek, és hálozatok

Aktint keresztkötő fehérjék

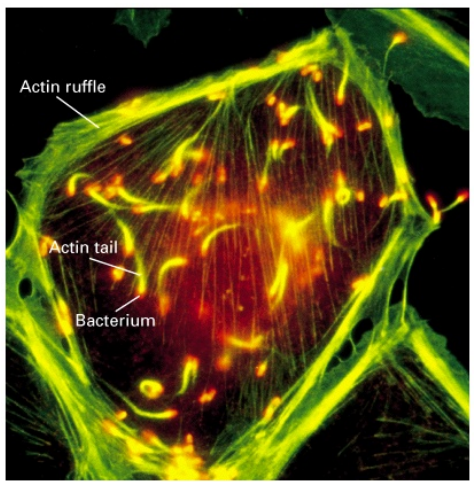
TABLE 18-1 Actin Cross-Linking Proteins

Protein*	MW	Domain Organization†	Location
GROUP I			
30 kDa	33,000		Filopodia, lamellipodia, stress fibers
EF-1	50,000		Pseudopodia
Fascin	55,000		Filopodia, lamellipodia, stress fibers, microvilli, acrosomal process
Scruin	102,000		Acrosomal process
GROUP II			
Villin	92,000		Intestinal and kidney brush border microvilli
Dematin	48,000		Erythrocyte cortical network
GROUP III (CH-domain superfamily)			
Fimbrin	68,000		Microvilli, stereocilia, adhesion plaques, yeast actin cables
α-Actinin	102,000		Filopodia, lamellipodia, stress fibers, adhesion plaques
Spectrin	α: 280,000 β: 246,000–275,000		Cortical networks
Dystrophin	427,000		Muscle cortical networks
ABP 120	92,000		Pseudopodia
Filamin	280,000		Filopodia, pseudopodia, stress fibers

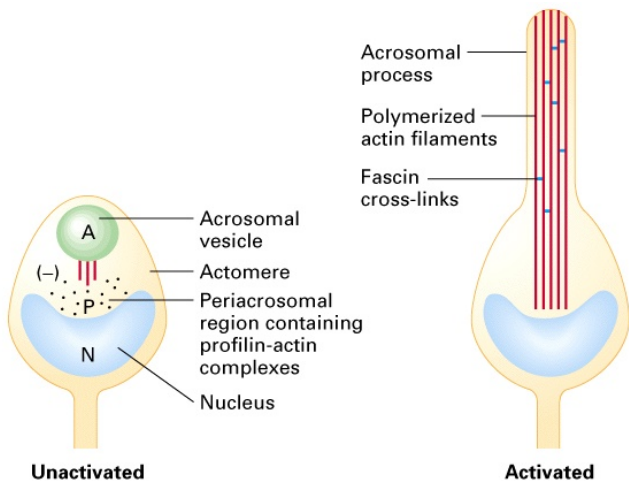
Aktin –polimerizáció és mozgás



Álláb képzés



Leishmania intracelluláris mozg.

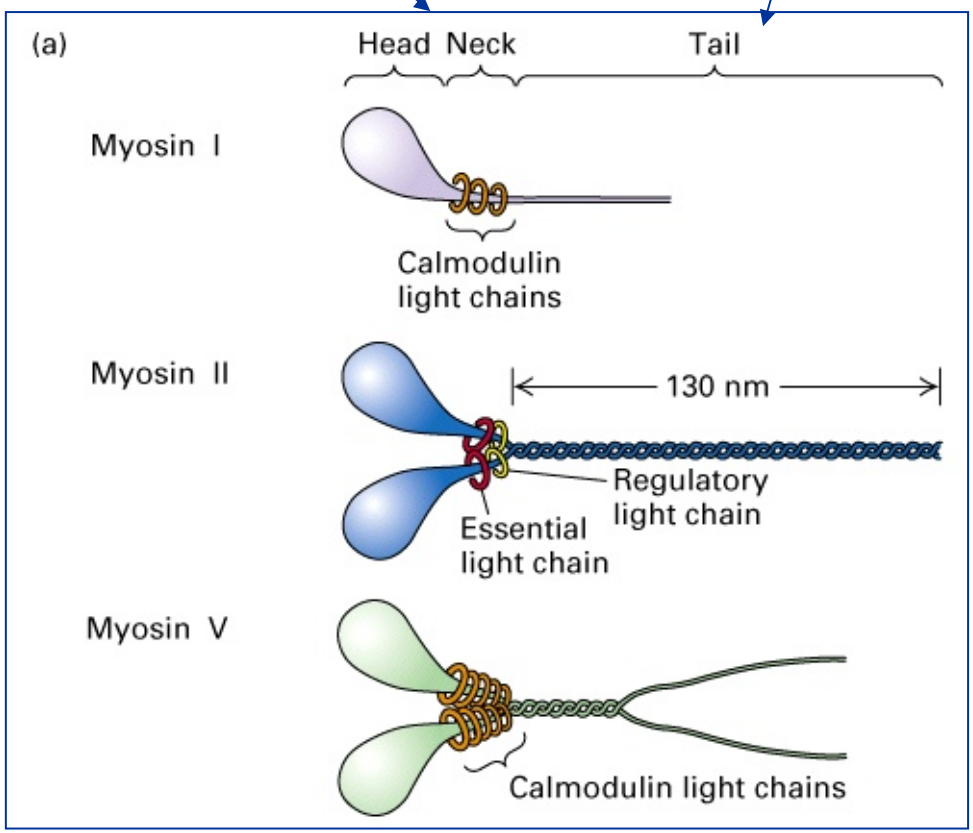


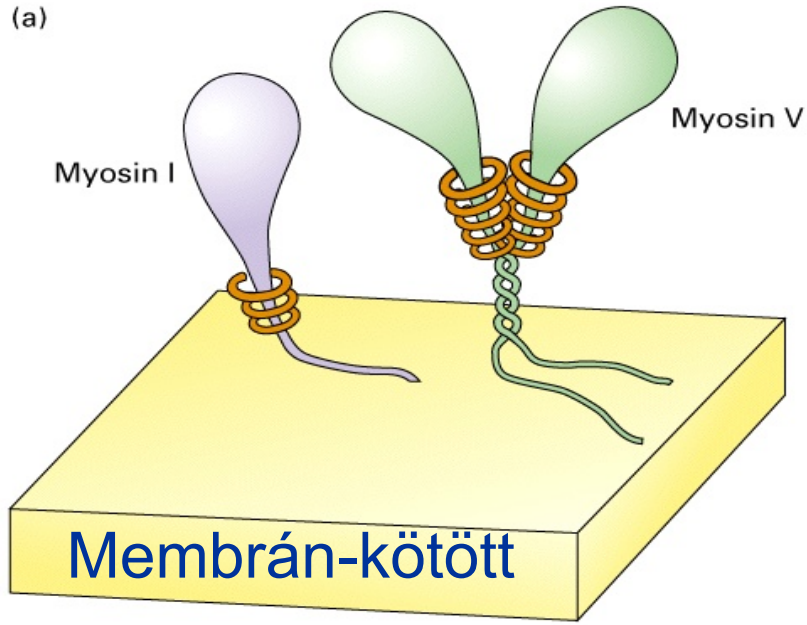
Akroszóma reakció

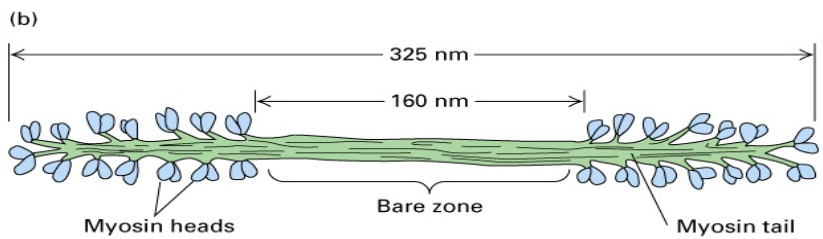
Miozin- az aktin motor fehérjéje

Nehéz lánc
fej + nyak

Könnyű lánc
farok





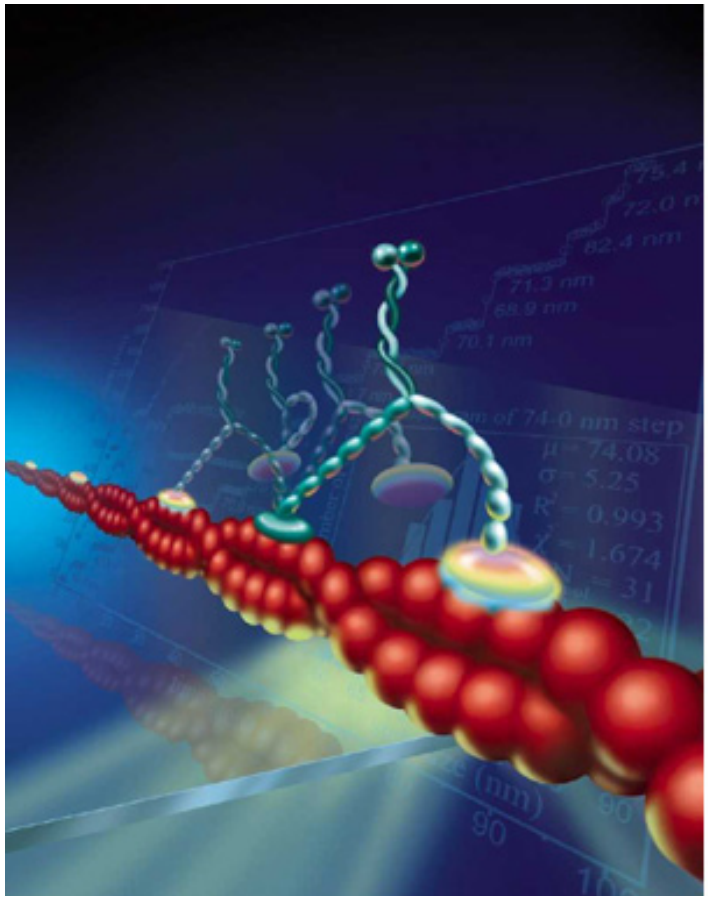


Filamentummá rendeződött

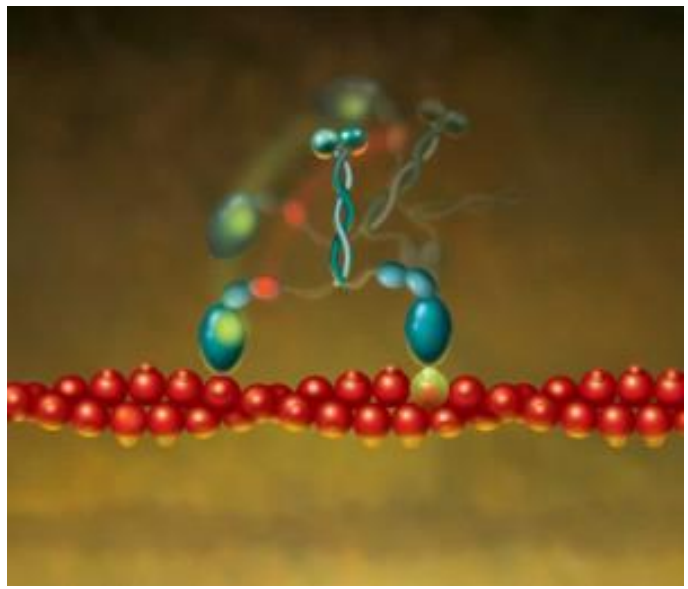
Aktin + miozin

- Sejten belüli szállítás *(pl. miozin I és V)*
- Kontrakció *(miozin II)*
- Amőboid migráció *(miozin I és II)*

Szállítás molekuláris motrokkal

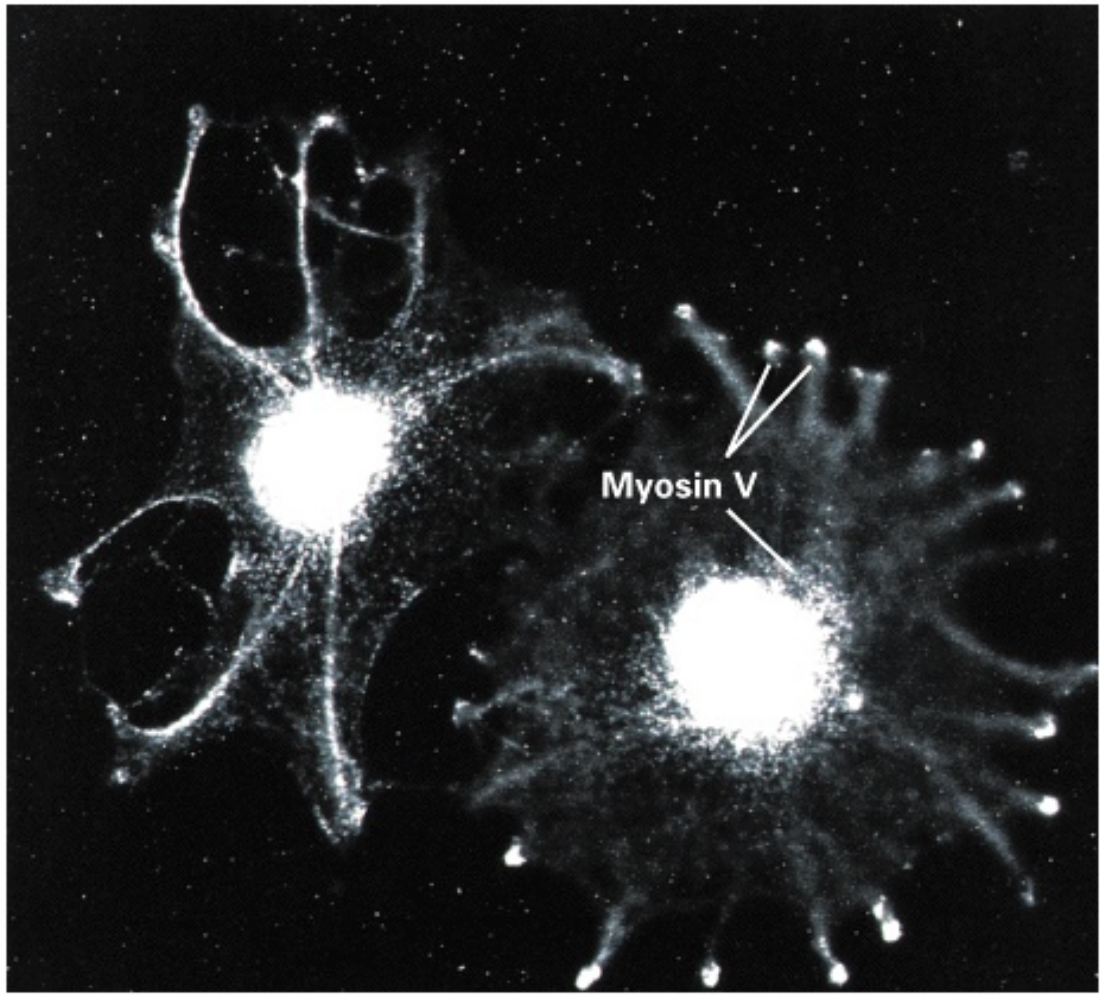


Miozin-V „lépeget” Az egyik „lábát” fluoreszcensen jelölték,és ezt a jelet követték 1 db. mikrofilamentumhoz kapcsoltan.
(Yildiz et al.)

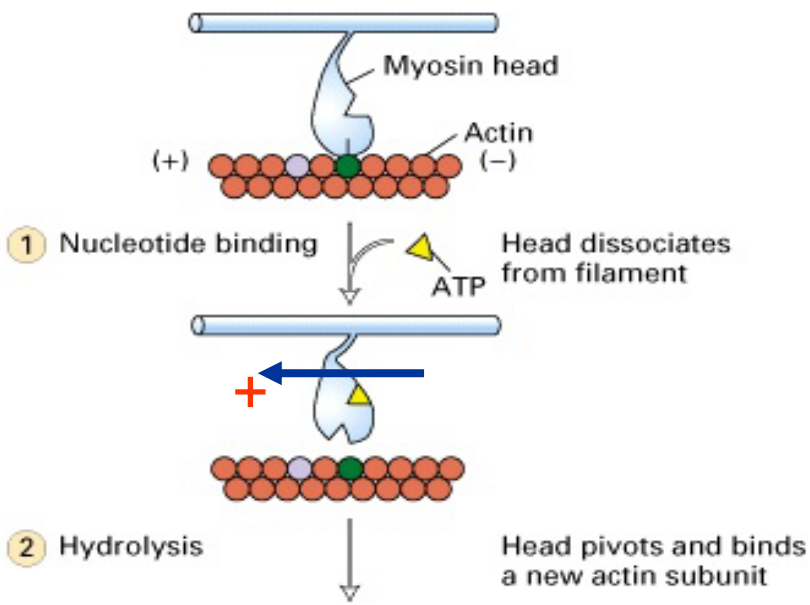


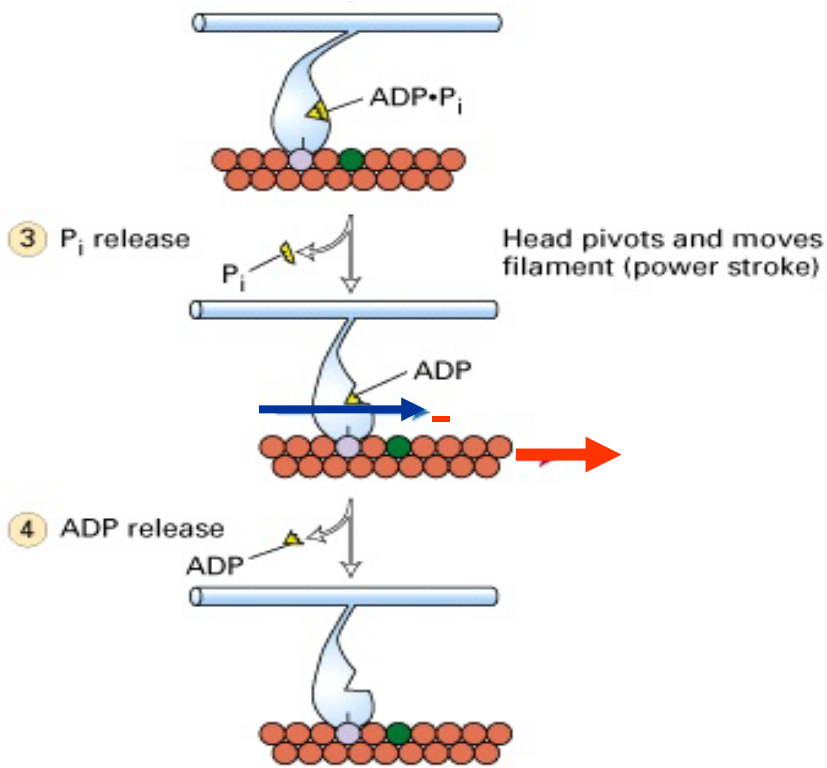
Miozin-VI „cigány kereket vet”
A miozin fejet és nyakat különböző színű flueoreszcens jelzéssel ellátva vált kimutathatóvá a molekula konformáció változása.
(Selvin et al.)

Vezikuláris transzport- Miozin -V.



Miozin-II konformációs változása a sliding során

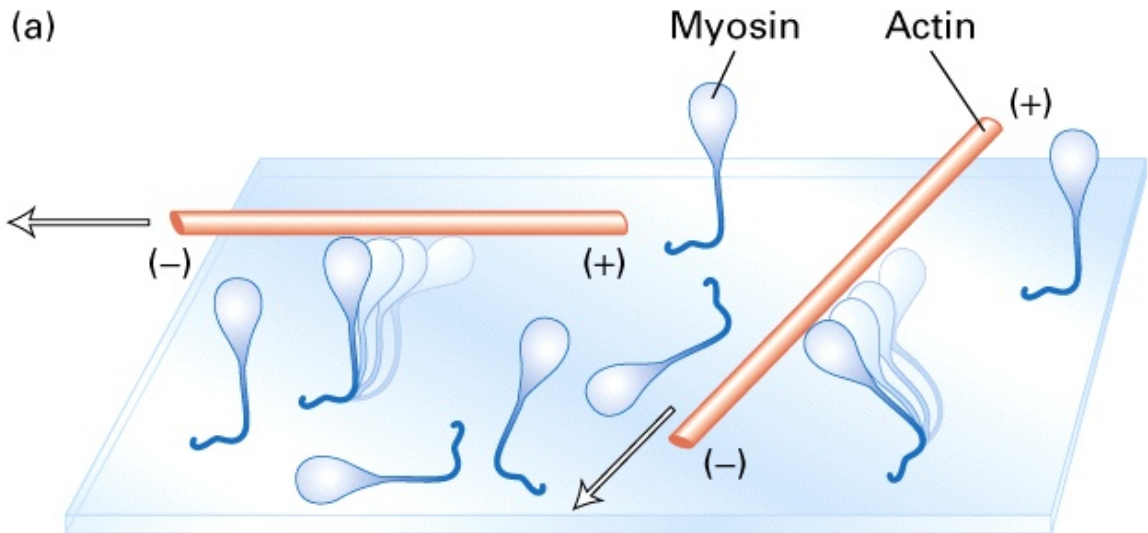


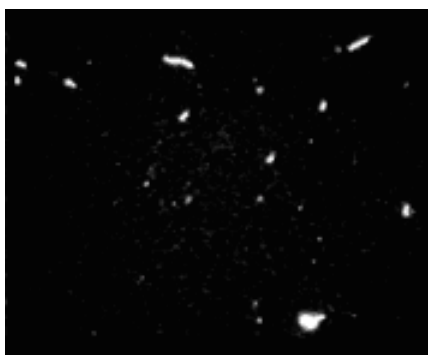


ATP kötödik. A miozin-fej **„hátra hajlik”** és egy (+) vég felé esö aktin részre kerül

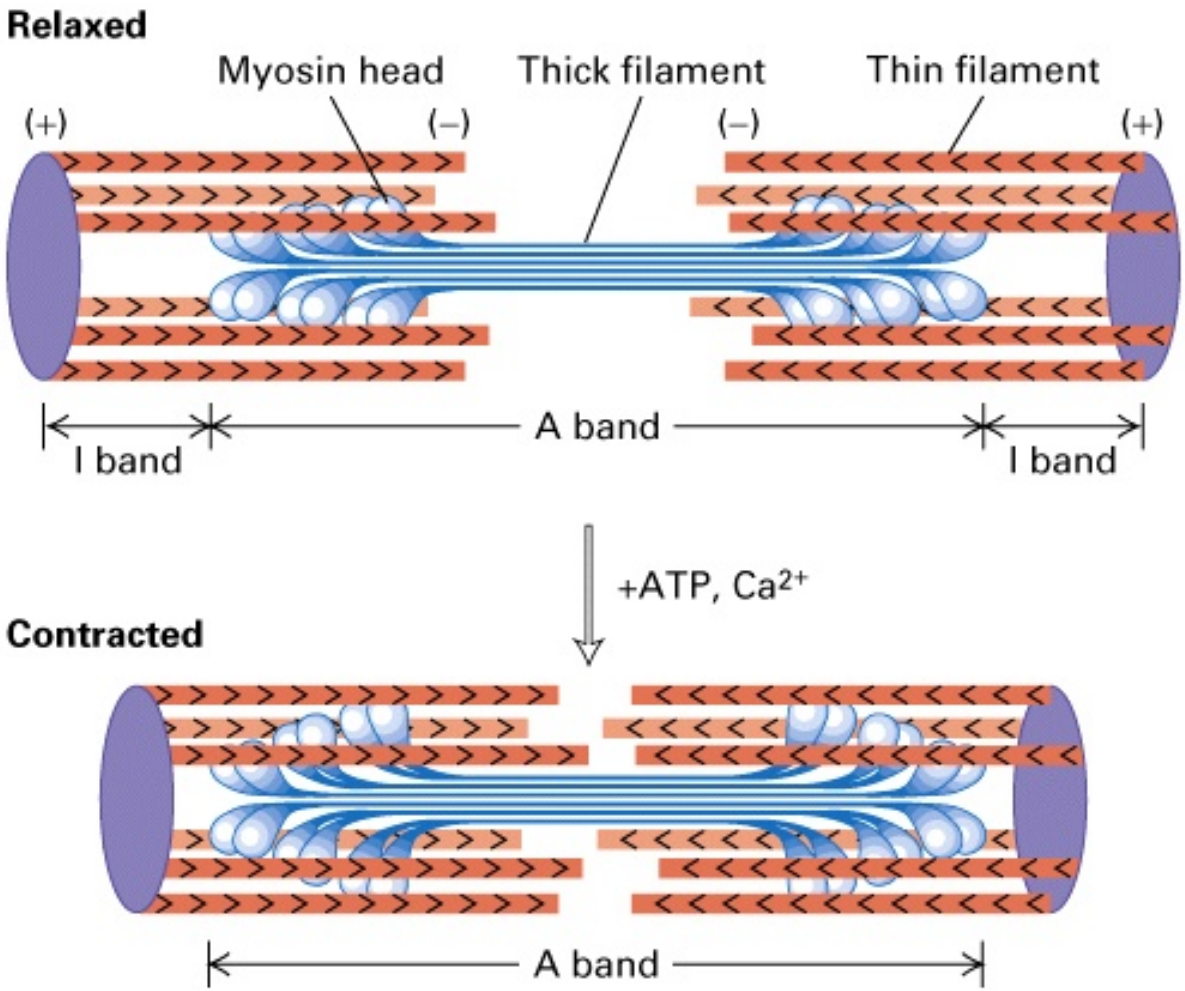
ATP lebomlik. A miozin-fej **„előre billen”** és magával húzza az aktint a(-) vég felel

Az aktin-miozin sliding *in vitro* kimutatása

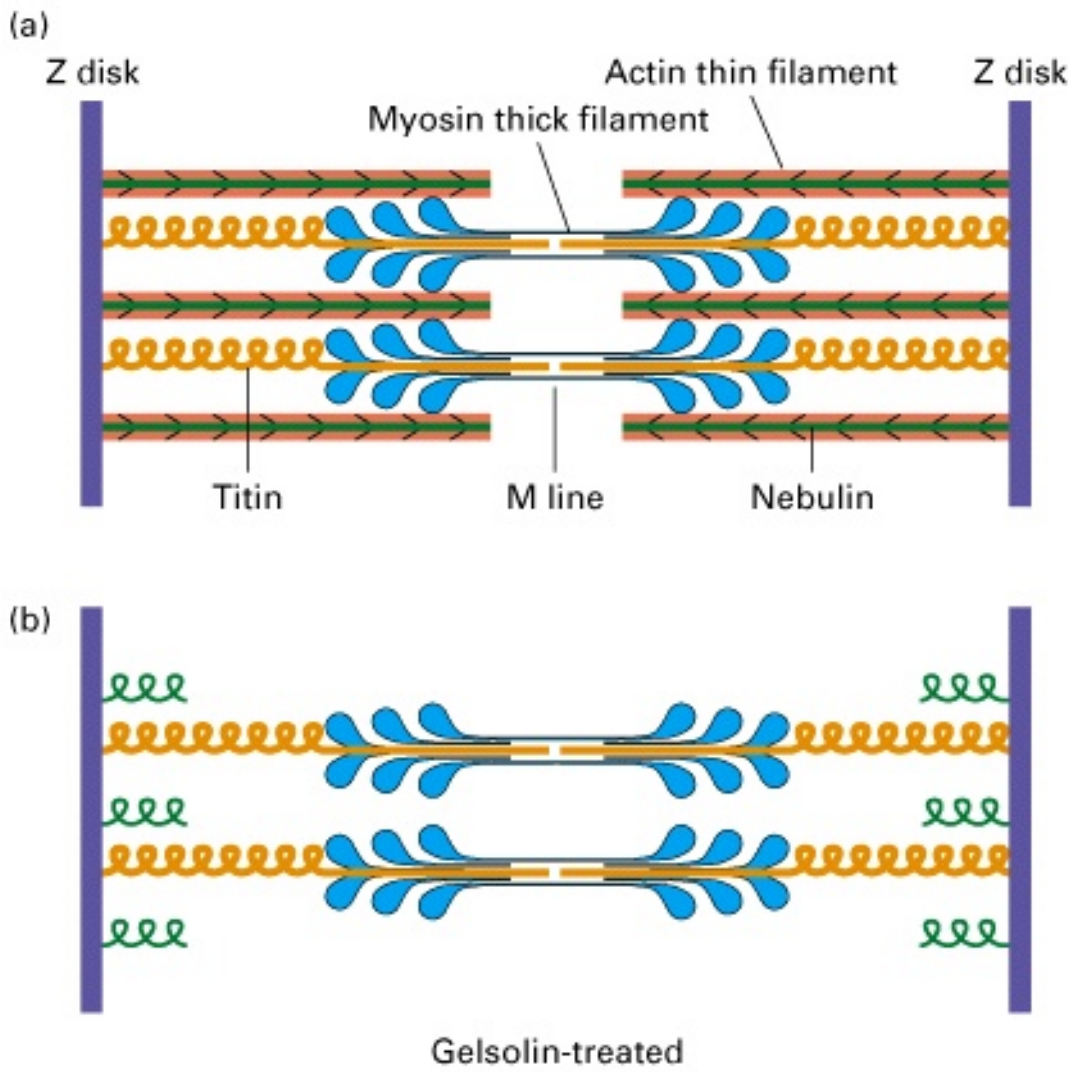




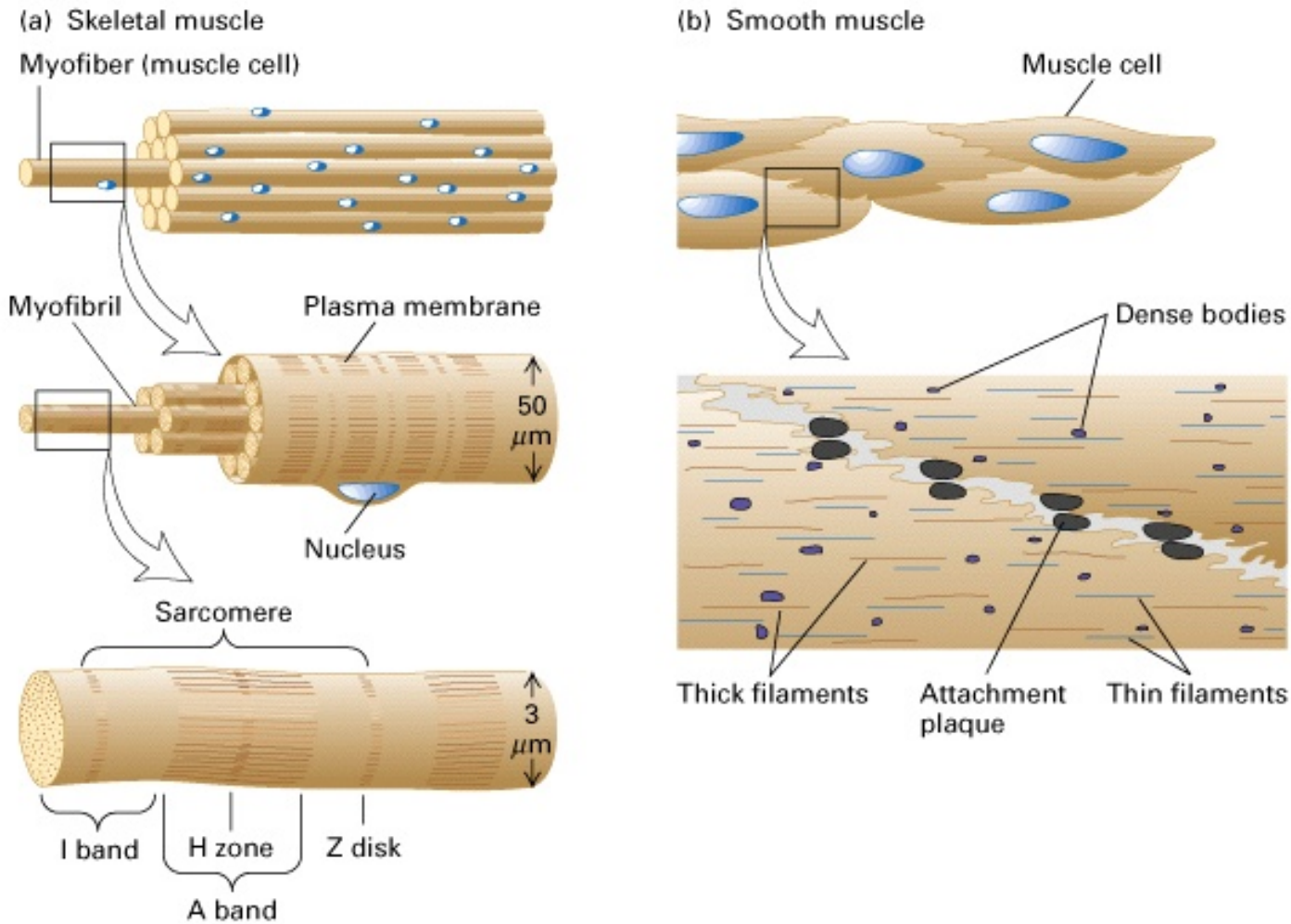
Kontrakció


Relaxed
Myosin head
Thick filament
Thin filament
(+)
(–)
(–)
(+)
I band
A band
I band
+ATP, Ca2+
Contracted
A band

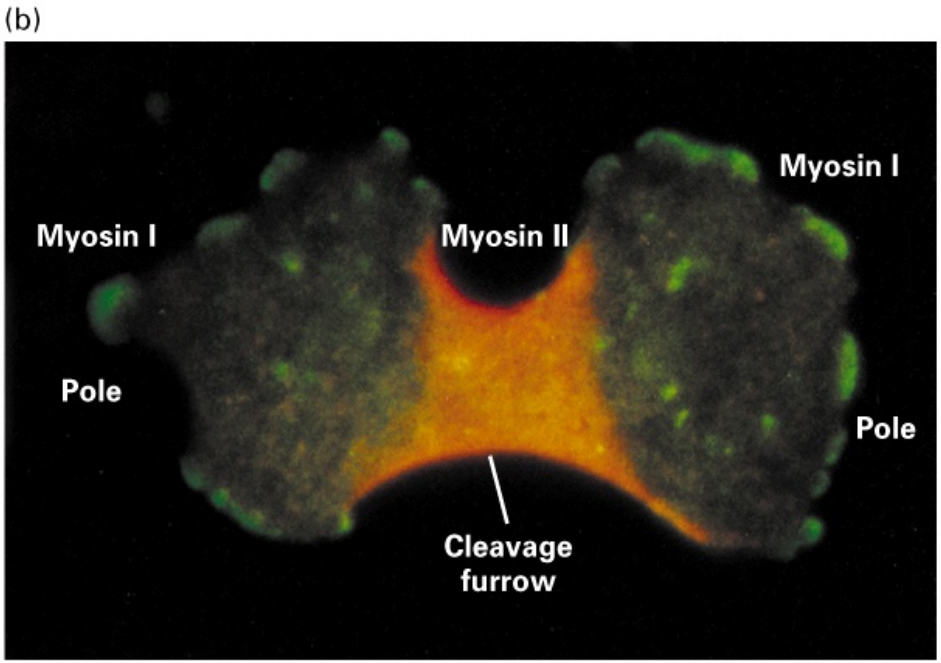
A szarkomer stabilizálása



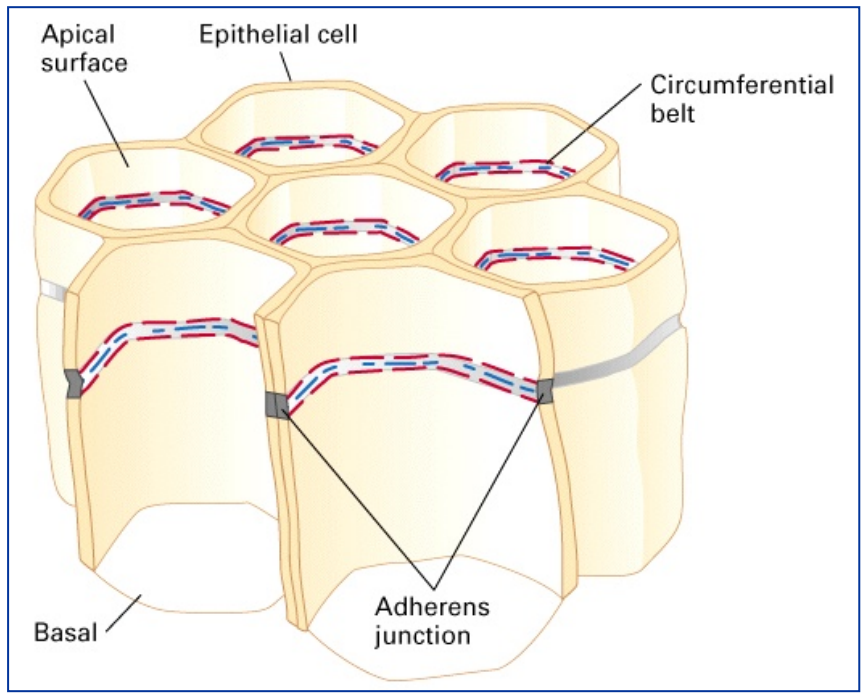
Izomsejtek


(a) Skeletal muscle
Myofiber (muscle cell)
Myofibril
Plasma membrane
50 μm
Nucleus
Sarcomere
3 μm
I band
H zone
Z disk
A band
(b) Smooth muscle
Muscle cell
Dense bodies
Thick filaments
Attachment plaque
Thin filaments

Kontrakció de nem mozgás

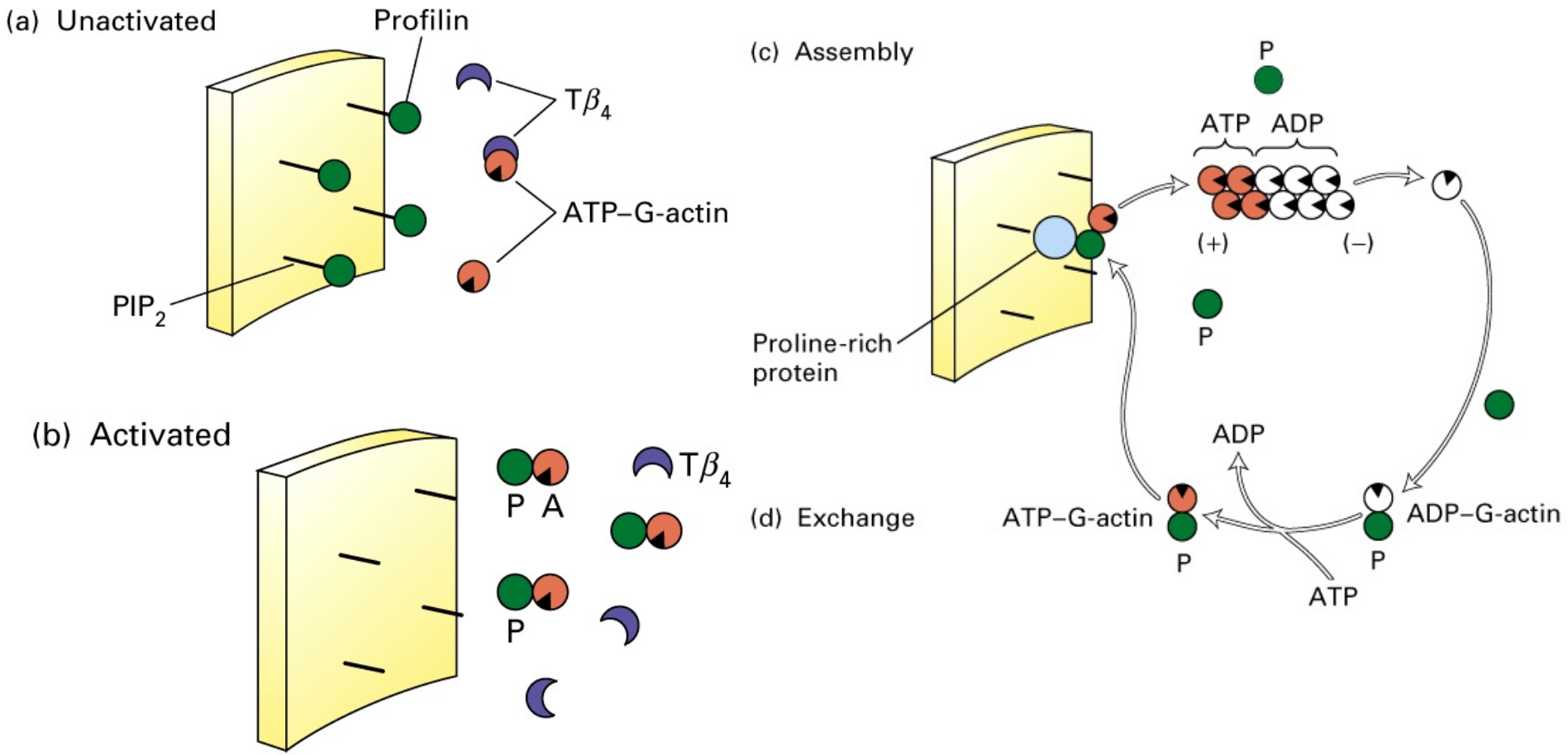


Sejtosztódás:
kontrakciós gyűrű

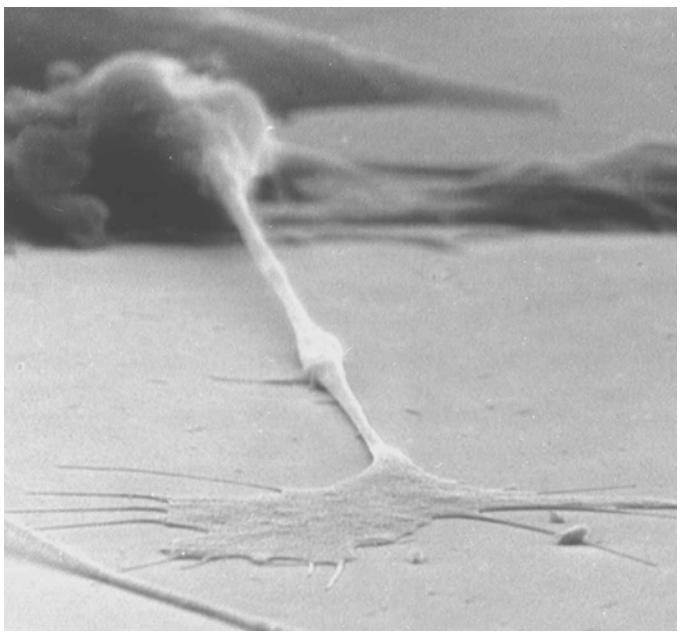


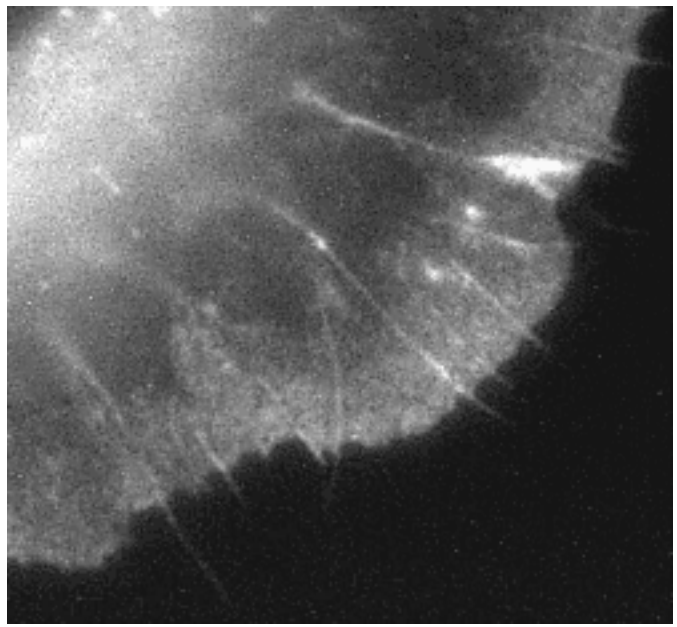
Hámok turgora:
zonula adherenshez kapcsolódó aktin „öv”

Membránhoz kötött aktin polimerizácio→ **álláb képzés**

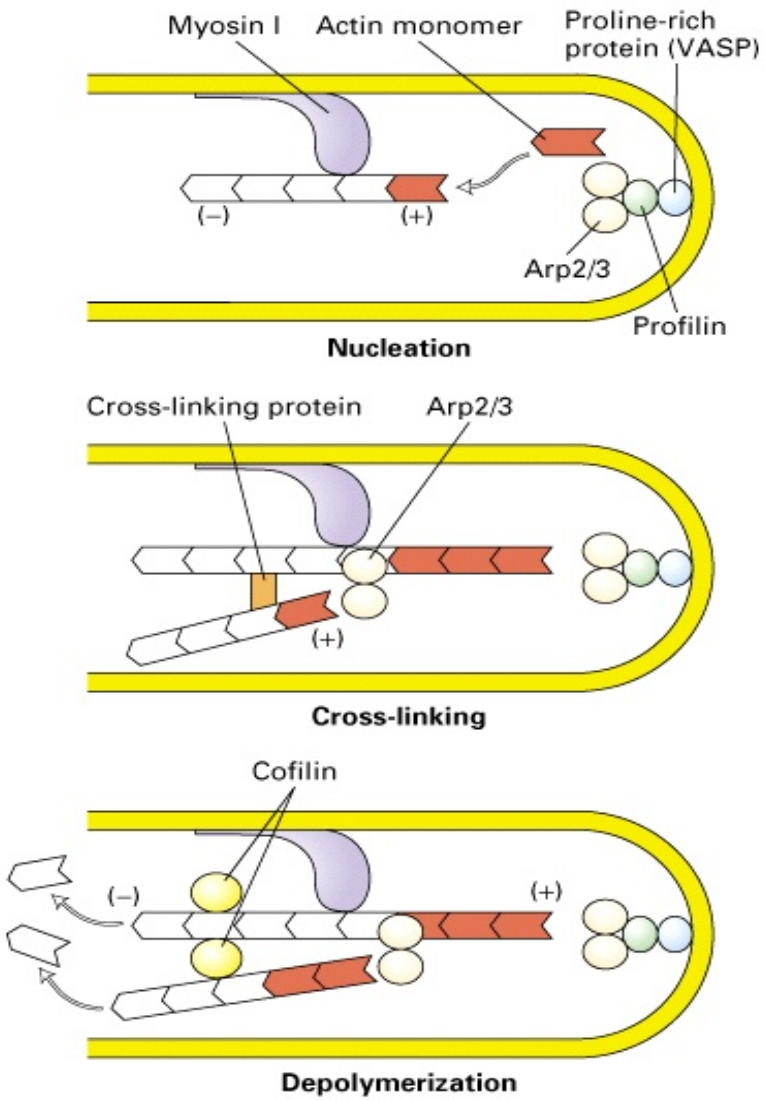


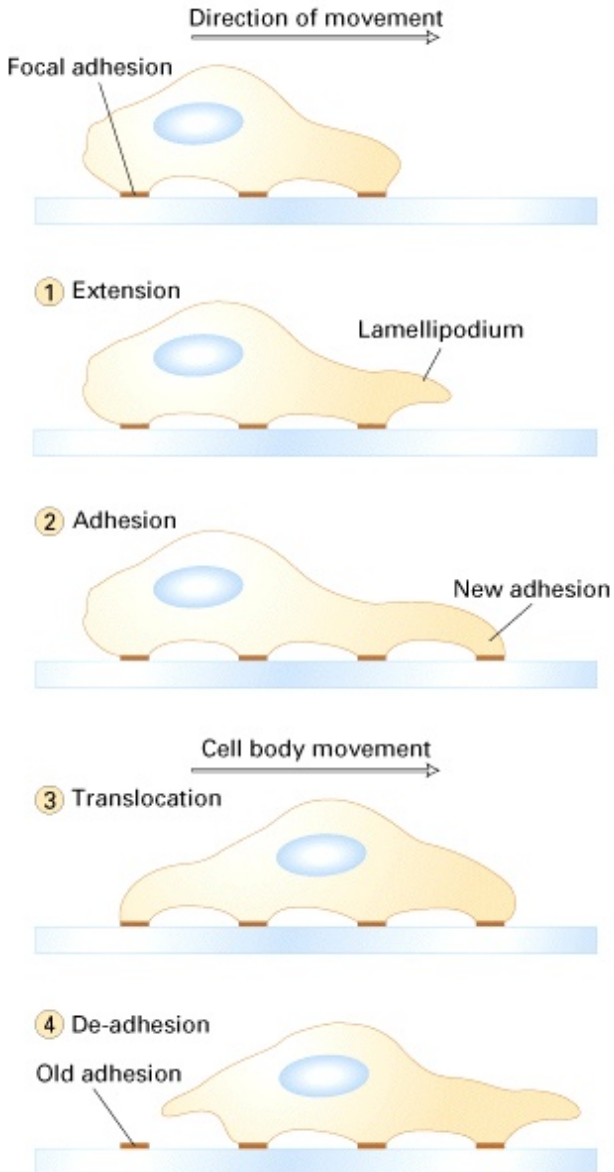
Filopodium, lamellopodium



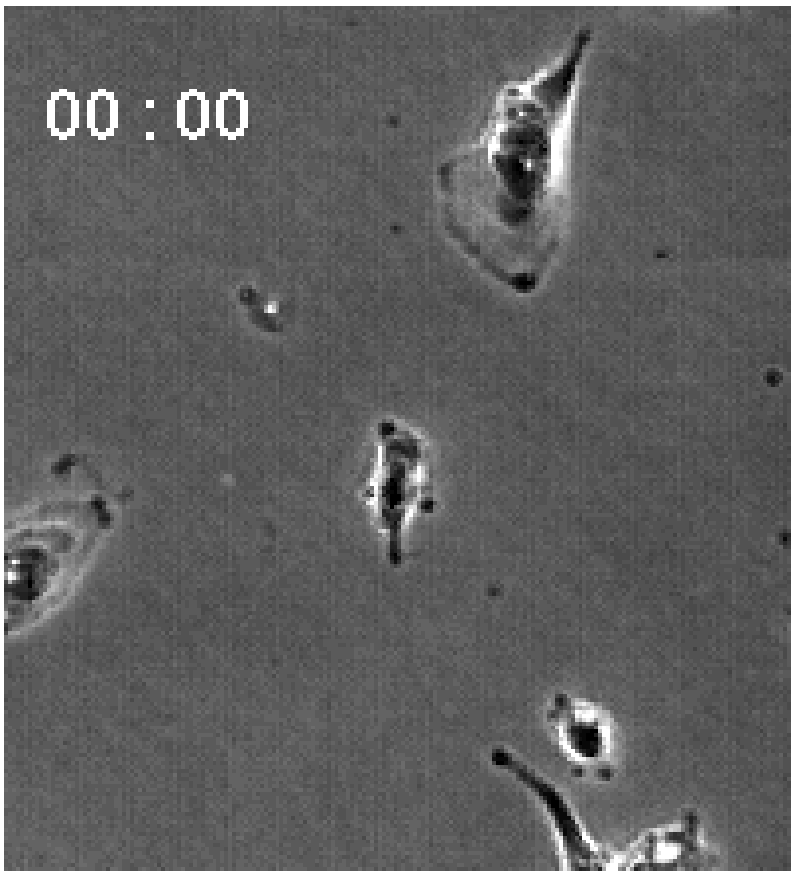


Álláb képzés → amőboid mozgás

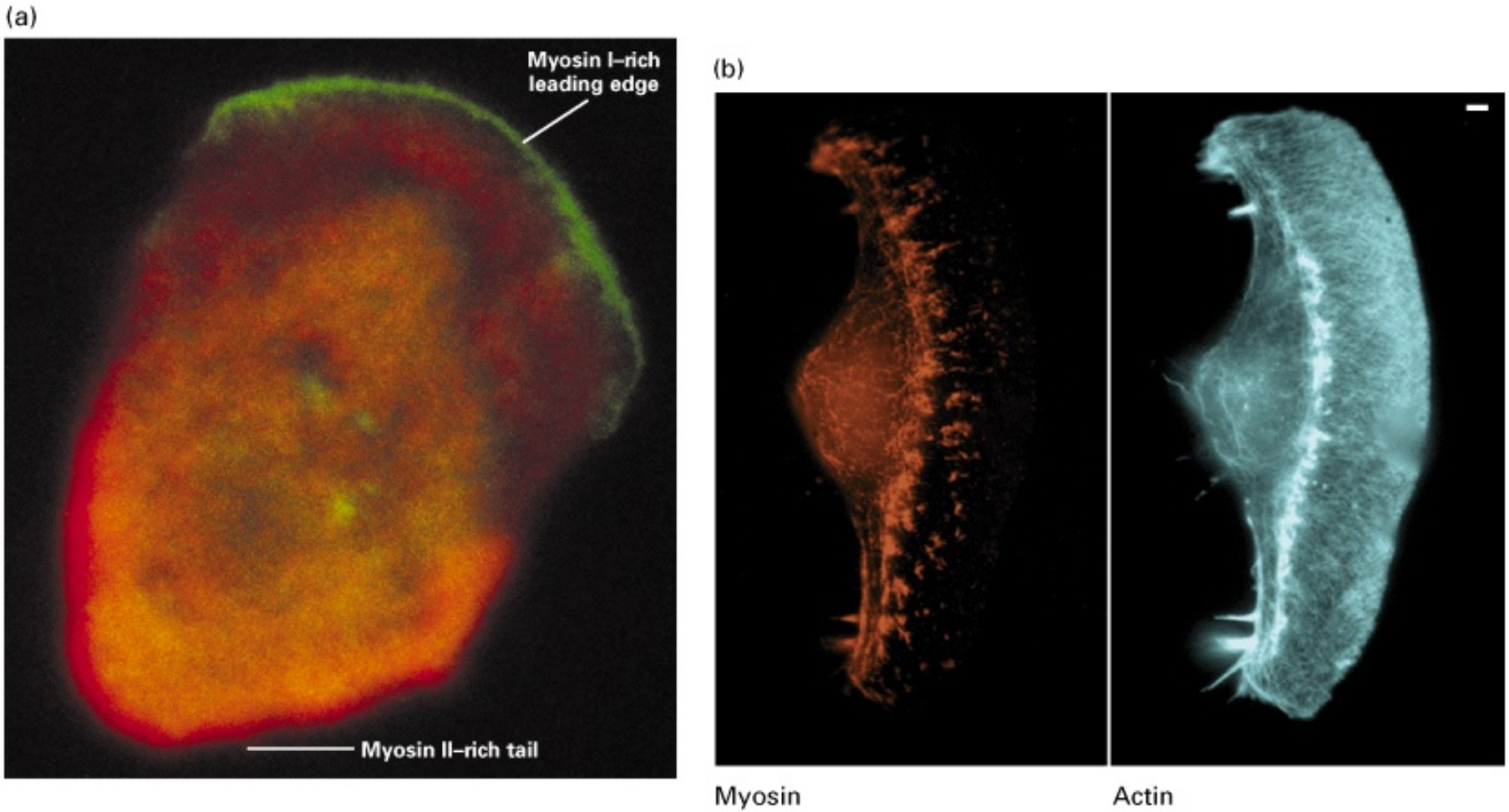




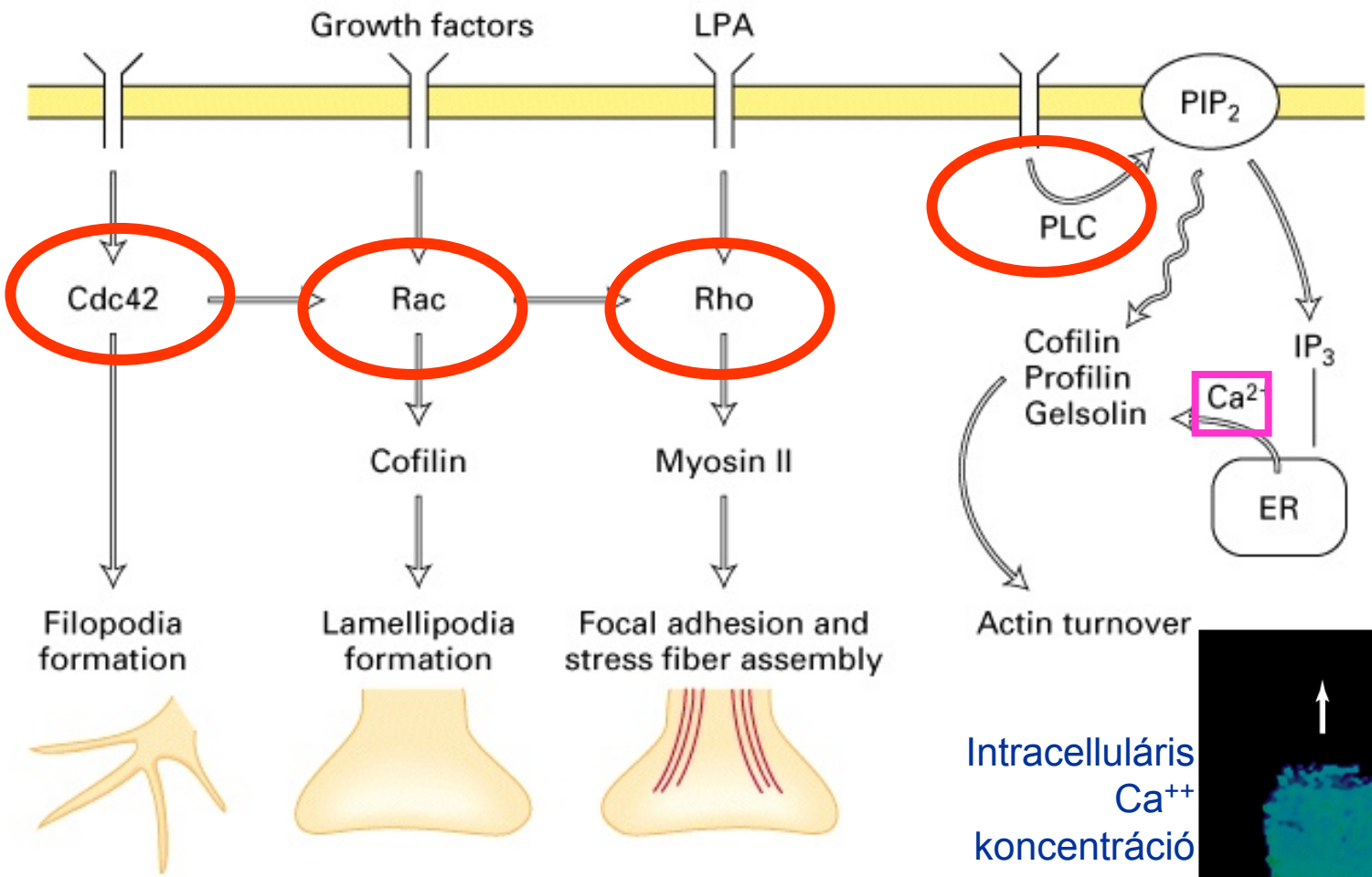
Amőboid mozgás



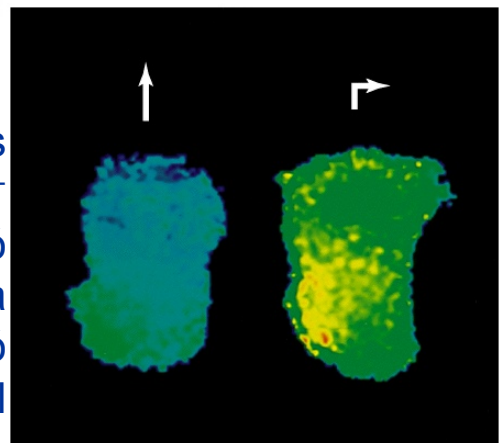
Miozin -I és -II a sejtek migrációjában



A migráció jeltovábbítása

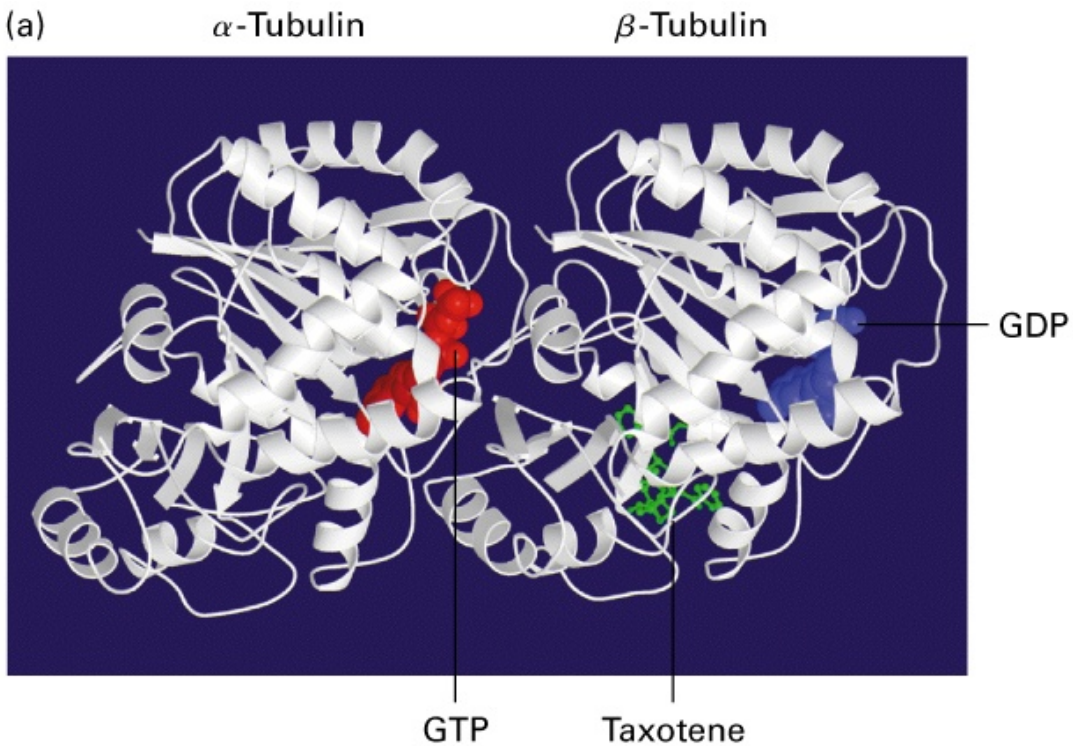


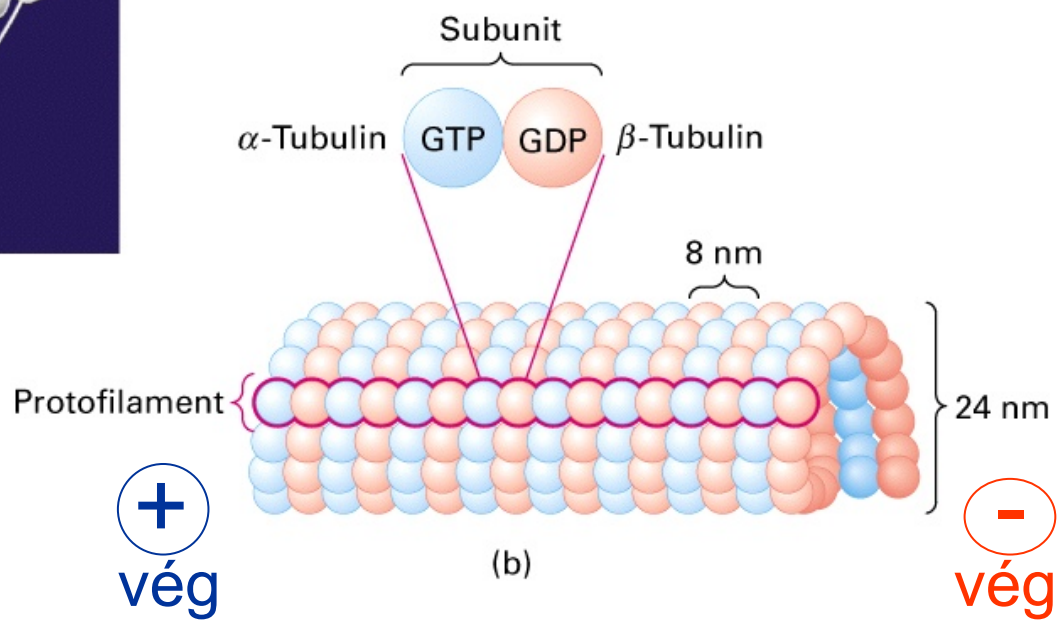
Intracelluláris Ca^{++} koncentráció megoszlása migráló sejtnél



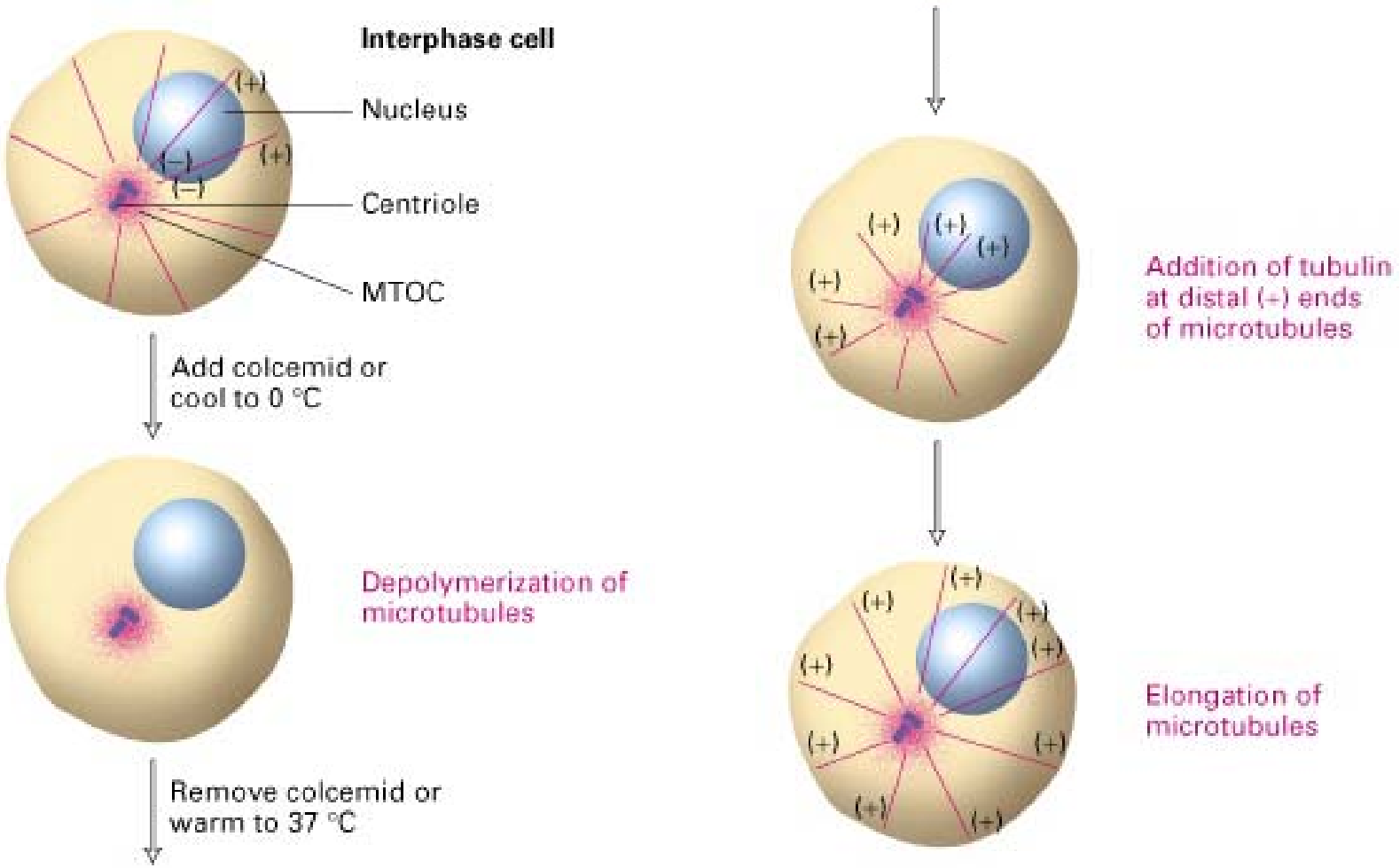
Sejtmozgás és **mikrotubulusok**

A mikrotubulus felépítése

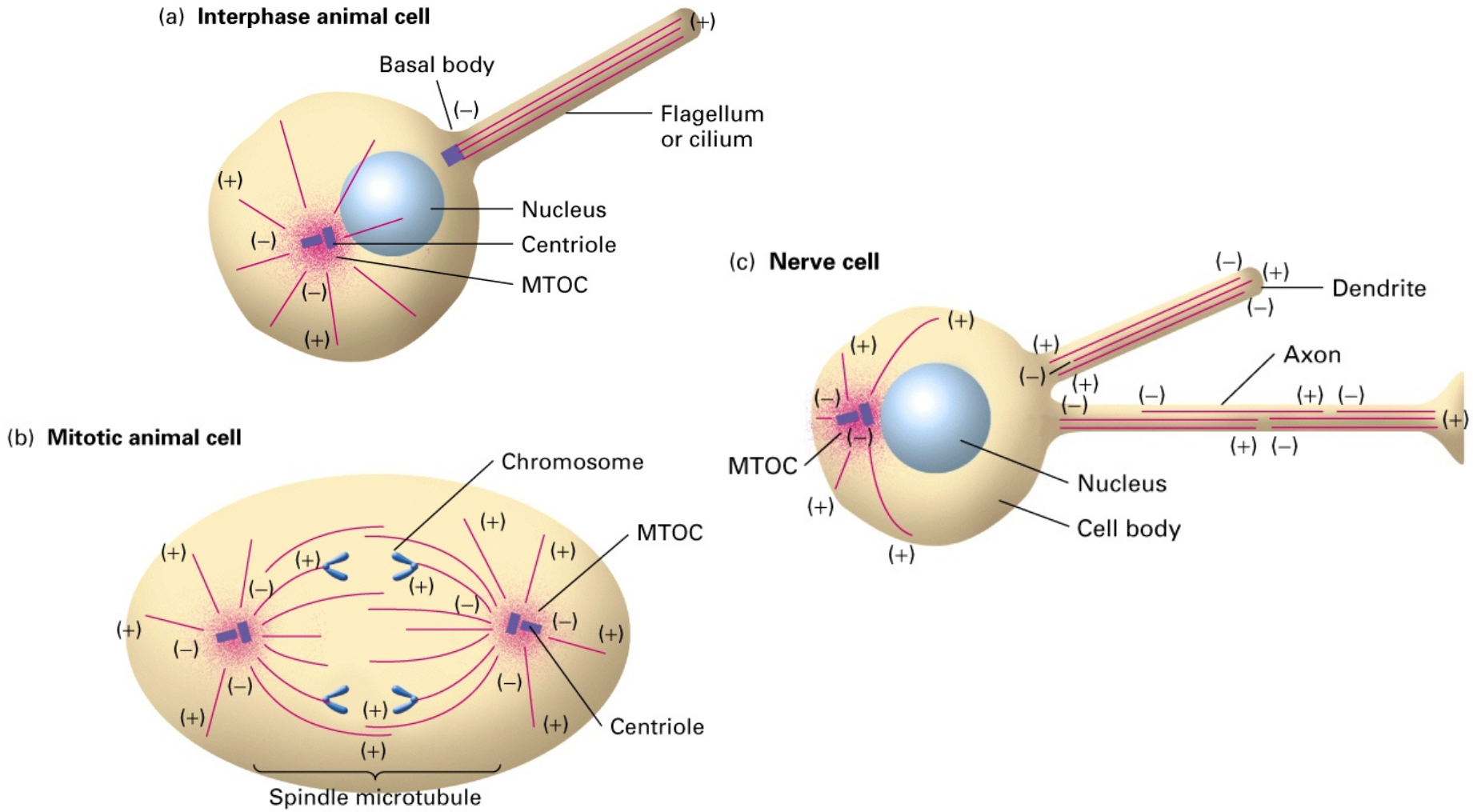




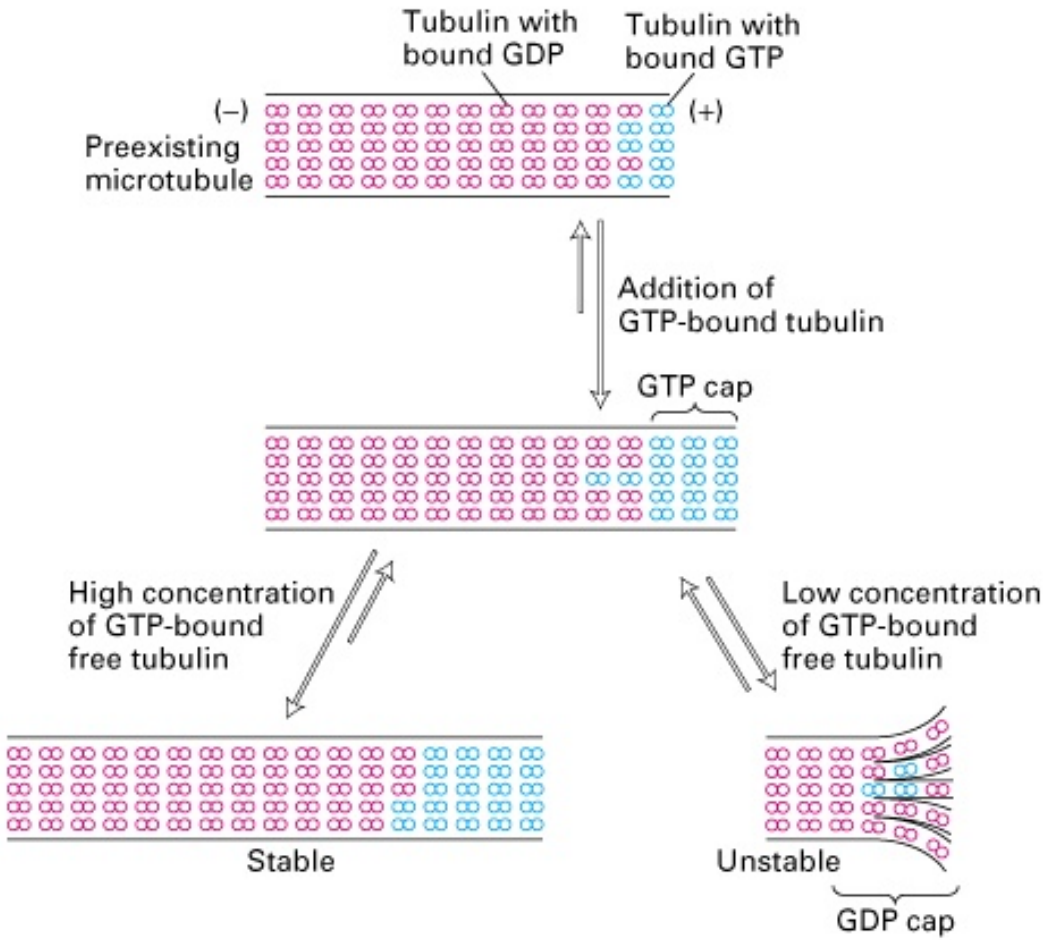
MTOC


Interphase cell
Nucleus
Centriole
MTOC
Add colcemid or cool to 0 °C
Depolymerization of microtubules
Remove colcemid or warm to 37 °C
Addition of tubulin at distal (+) ends of microtubules
Elongation of microtubules

A mikritubulusok polaritása



Dinamikus instabilitás
GTP sapka

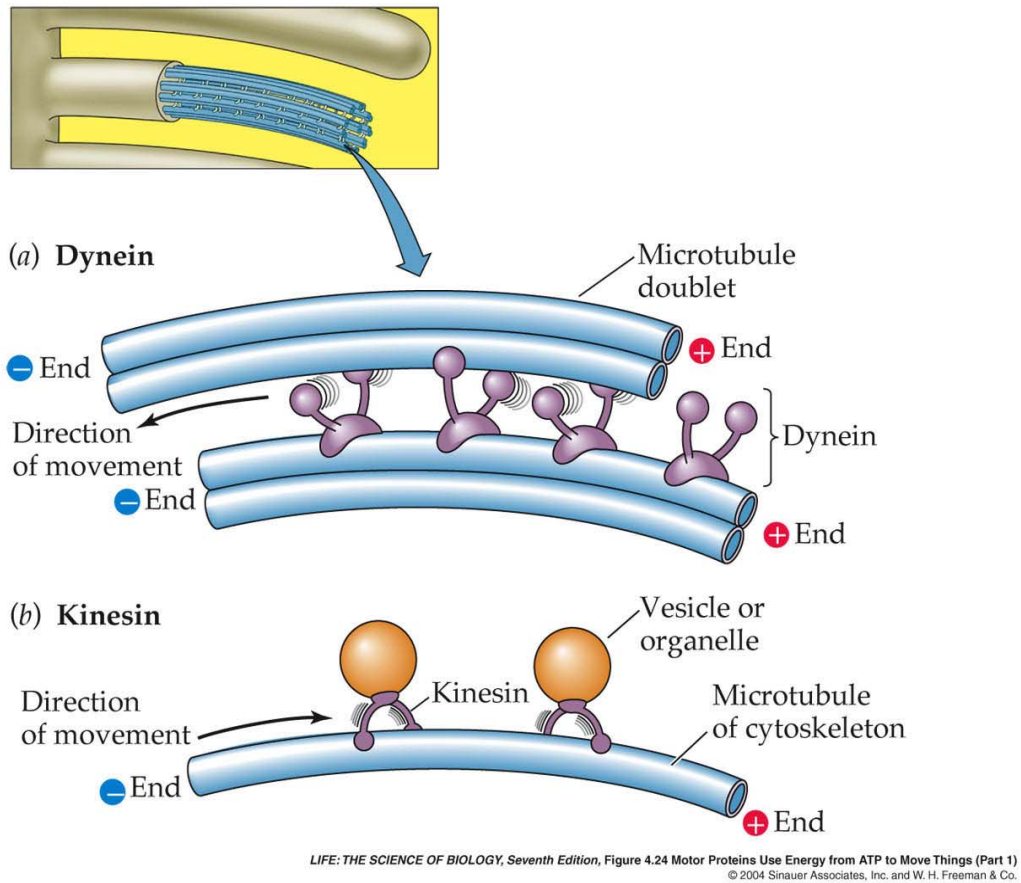


-A + végen épül

-A – végen bomlik

-Ha a GTP koncentráció elég nagy, a + végen stabilizálja a mikrotubulust.

Dinein és kinezin



LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 4.24 Motor Proteins Use Energy from ATP to Move Things (Part 1)

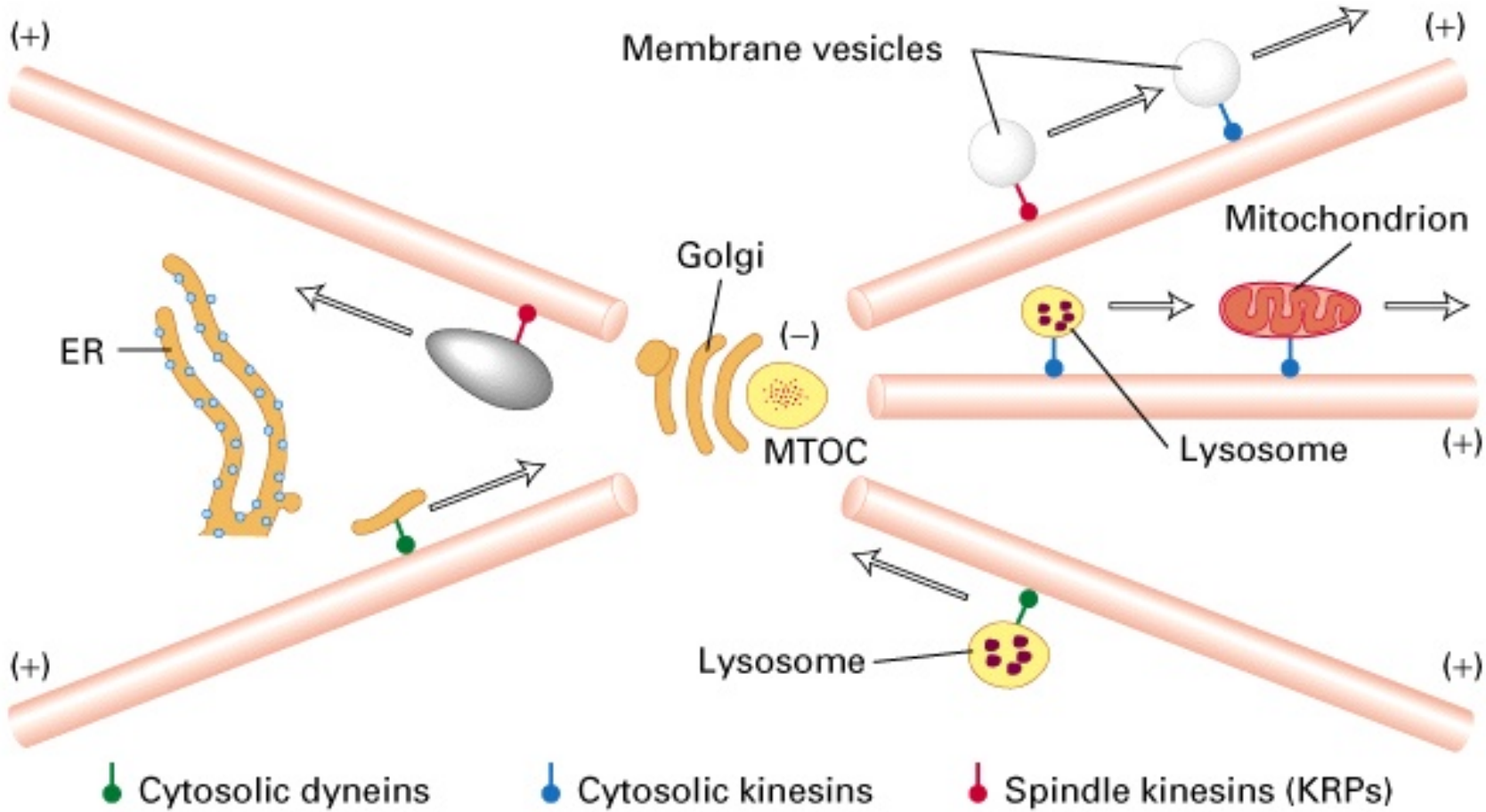
Dinein:

-”szállítás”
(-) vég fele
-mikrotubulusok elcsúsztatása

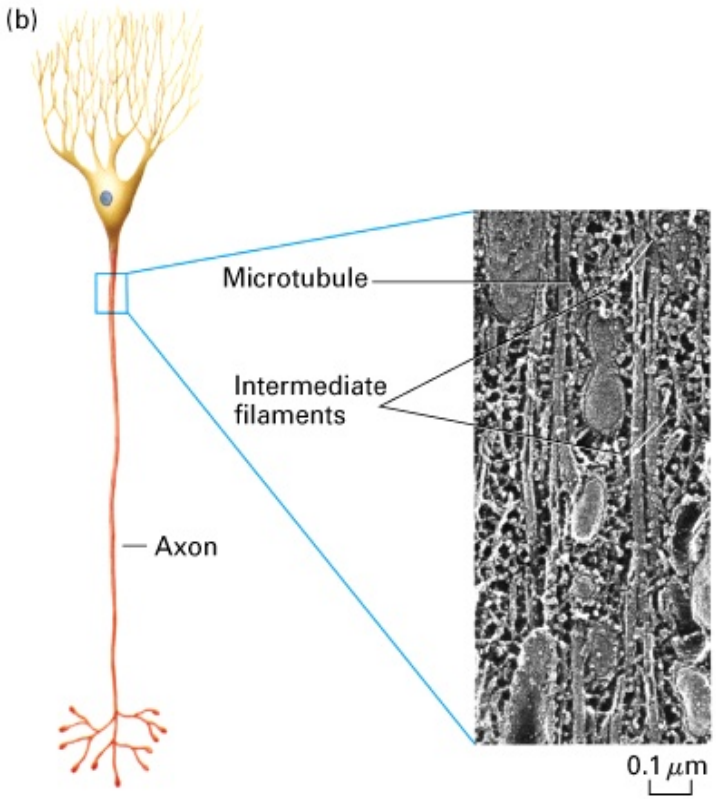
Kinezin:

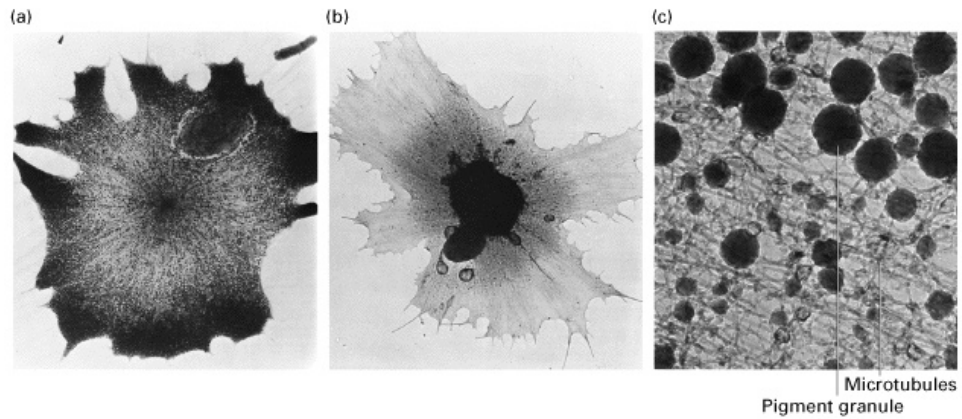
-„szállítás”
-(+) vég fele

A mikrotubulusok a sejt szállító pályái



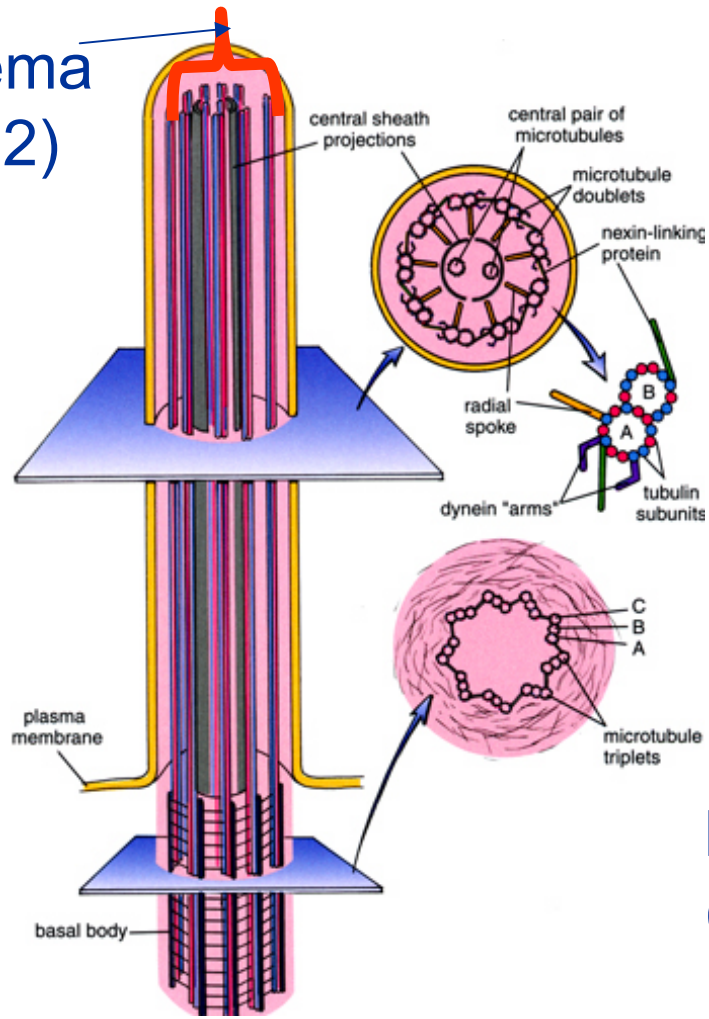
Neuron és pigment sejt





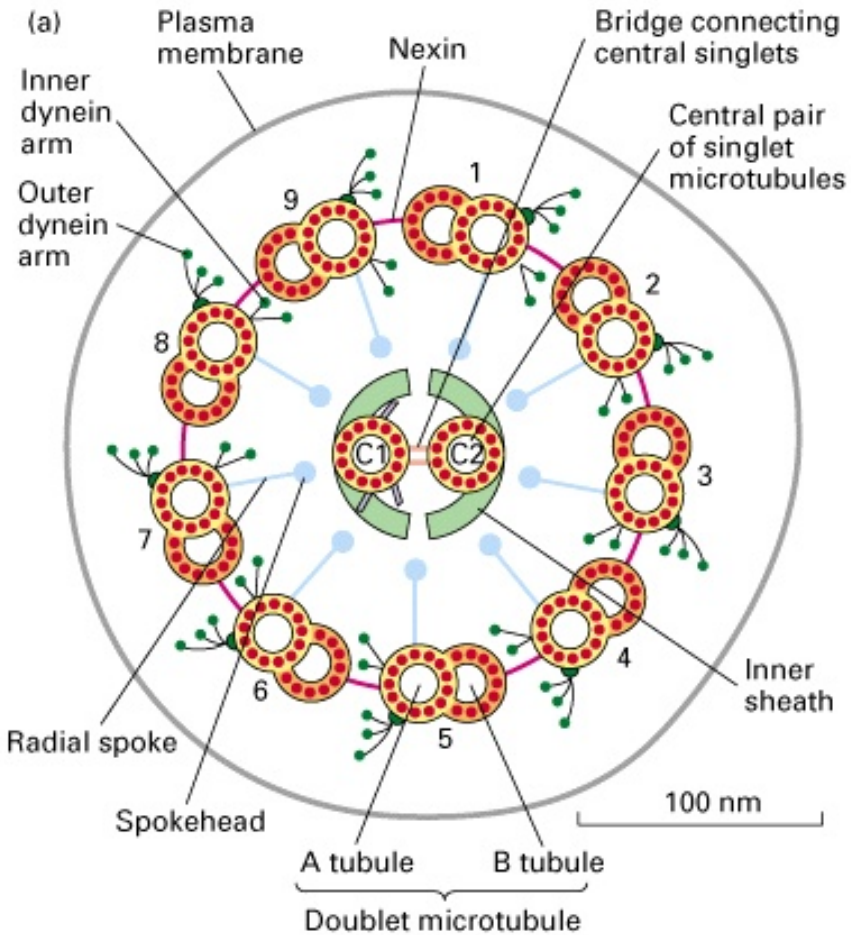
Csillók felépítése

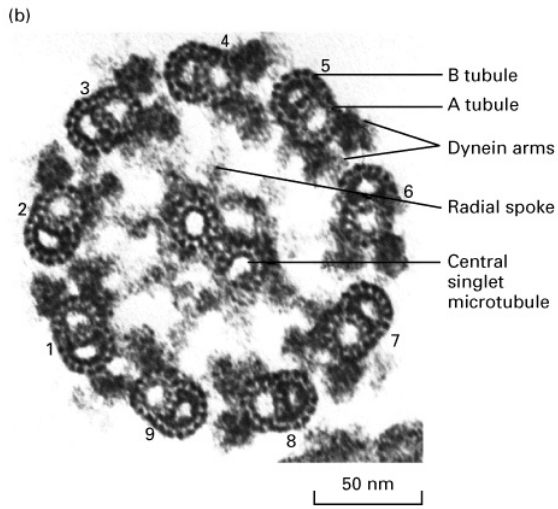
Axonéma
(2x9 +2)



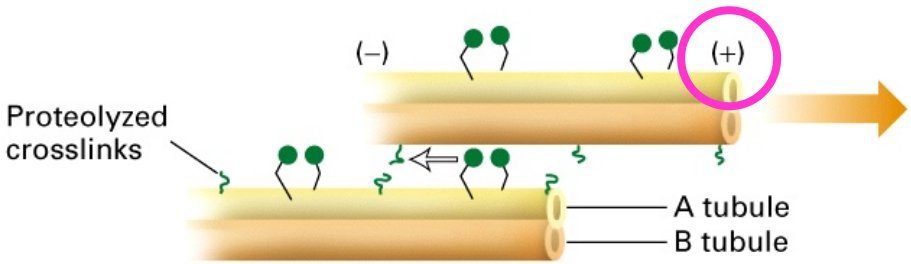
bazális test
(3x9)

Csillók axonémája





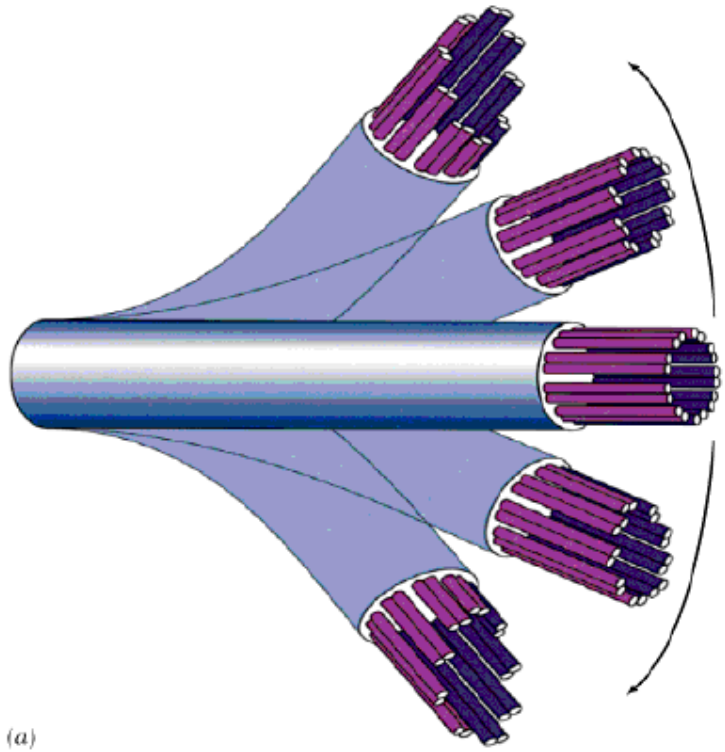
Dinein sliding



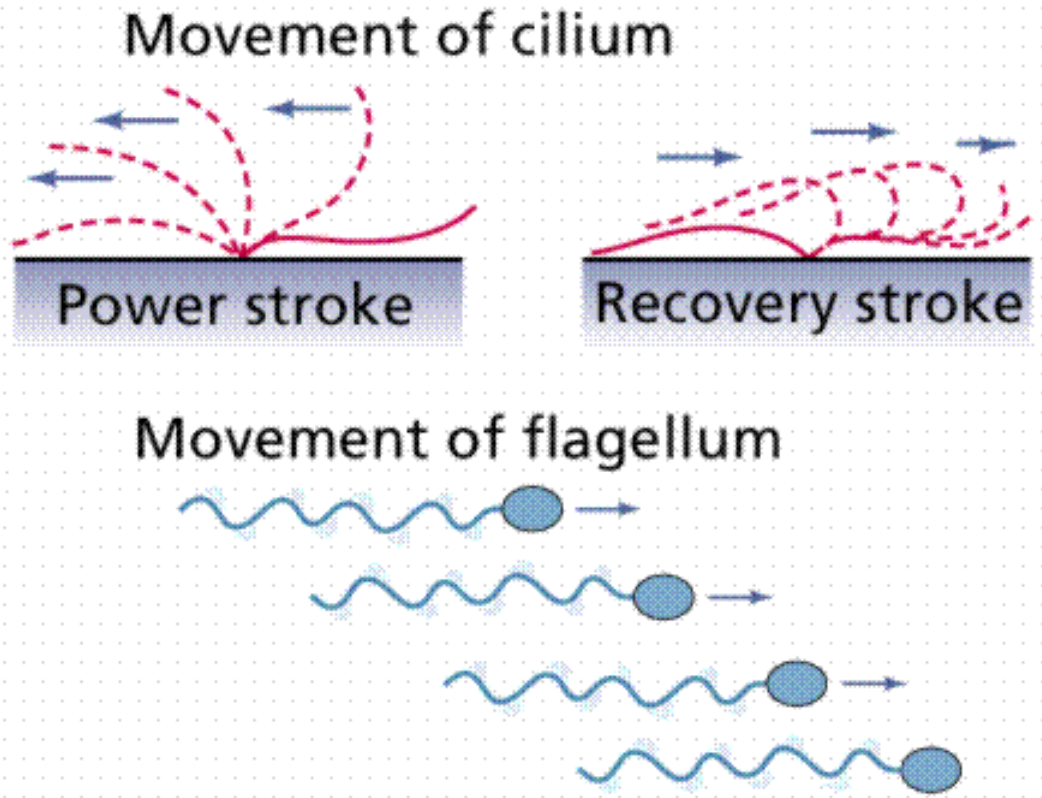
Ez az elcsúszás a nexin és
Küllő fehérjék által korlátozott

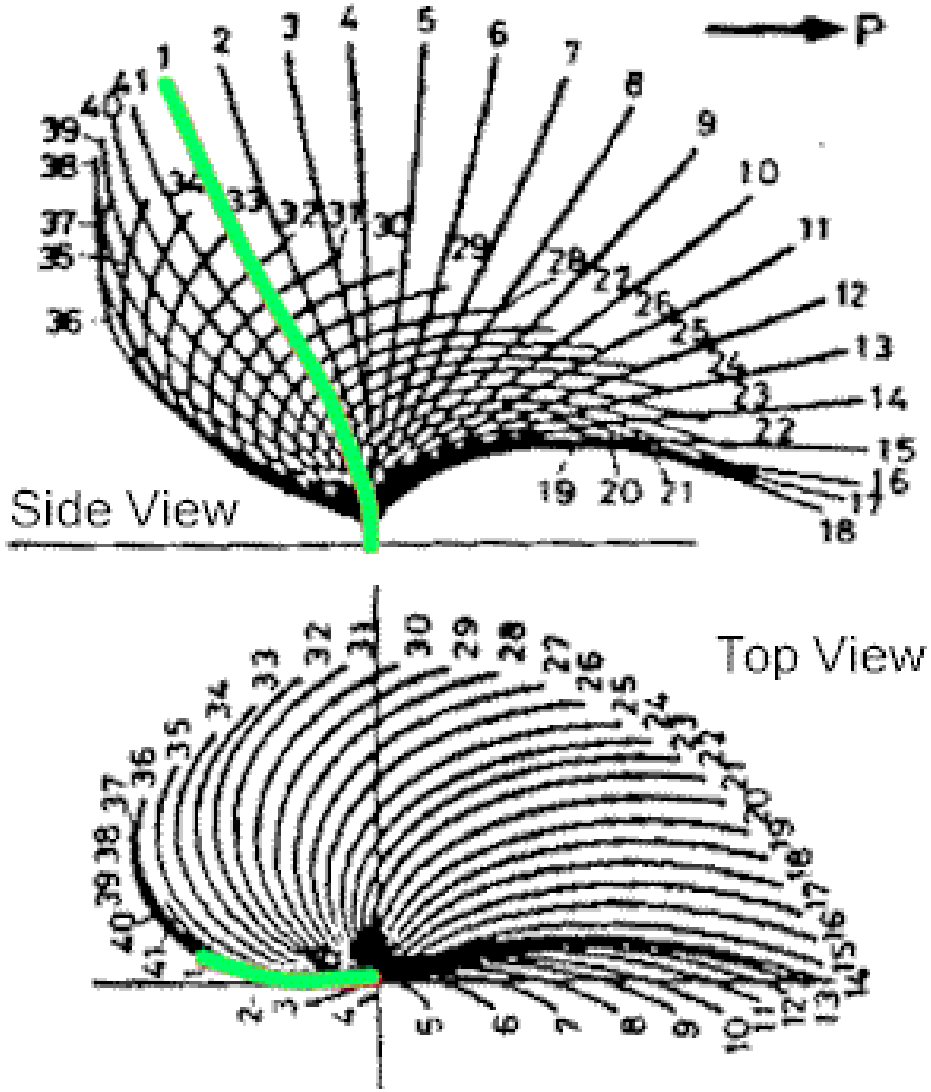
↓

A csilló elhajlik



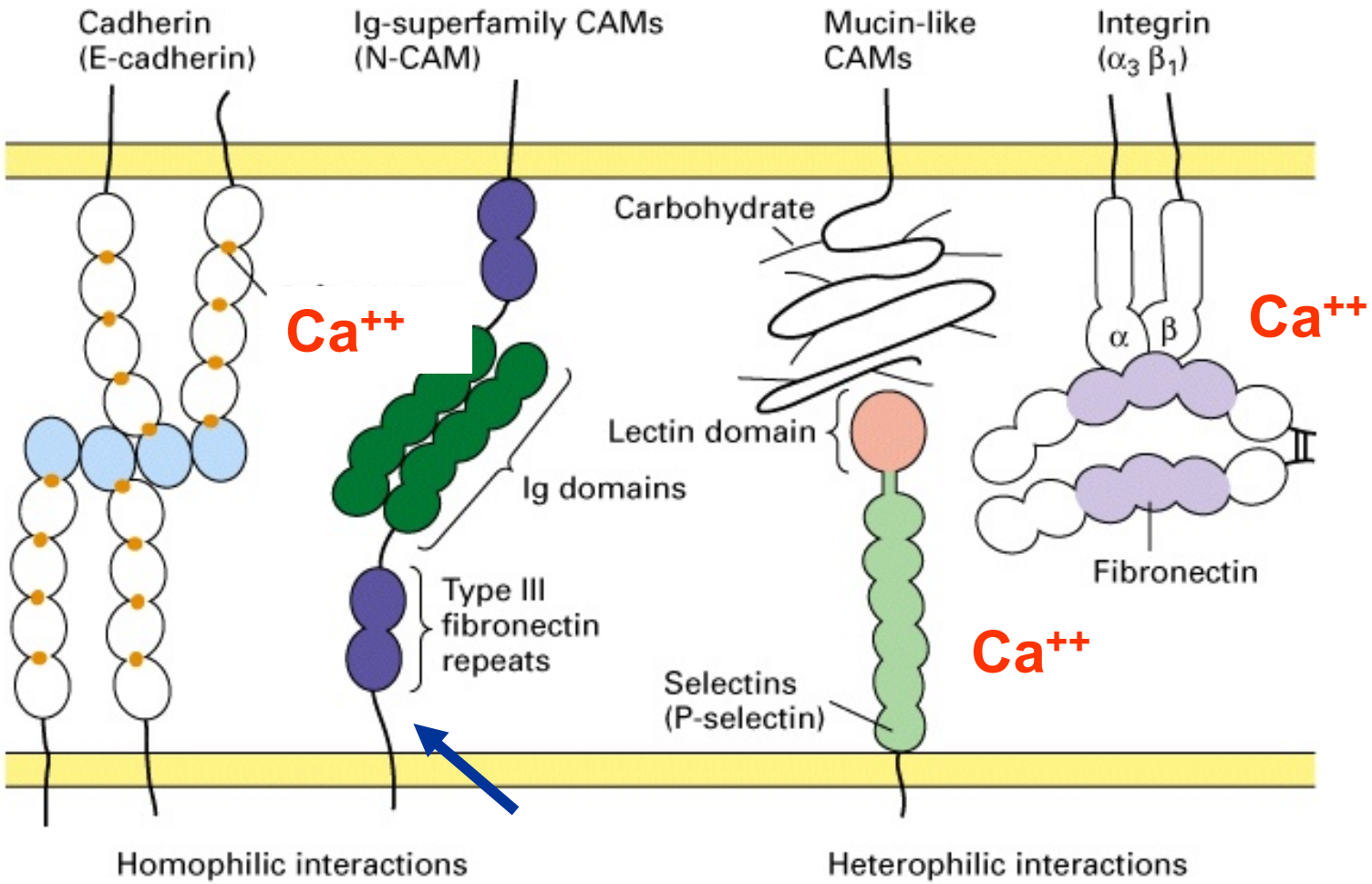
A csilló és ostor mozgás mintázata



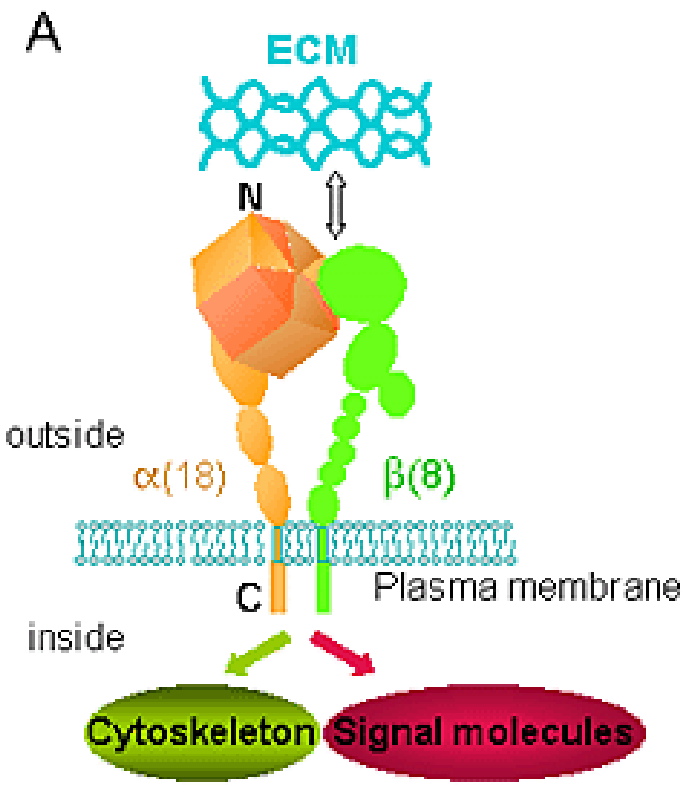

P
Side View
Top View

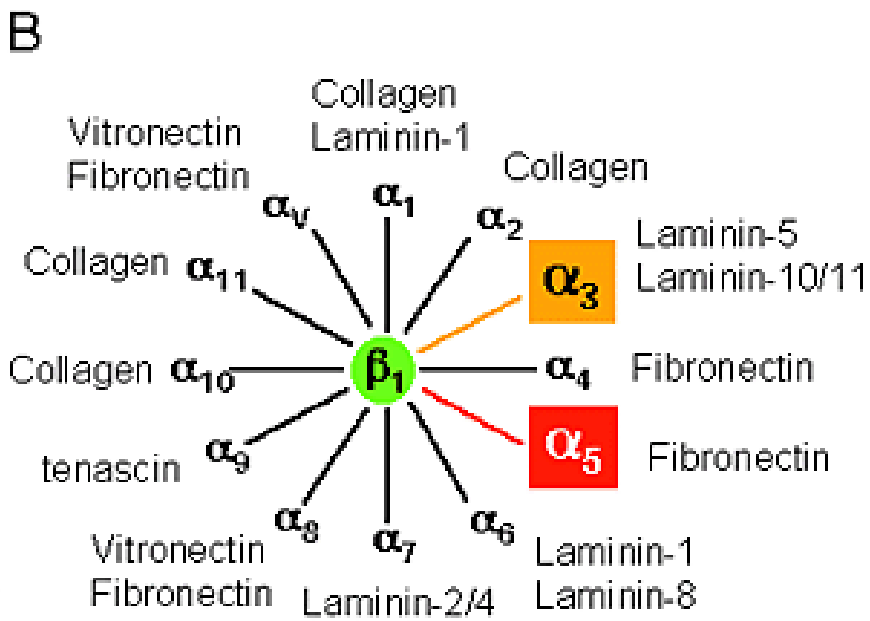
ADHÉZIÓ

Non-junkciónális (átmeneti) adhézió

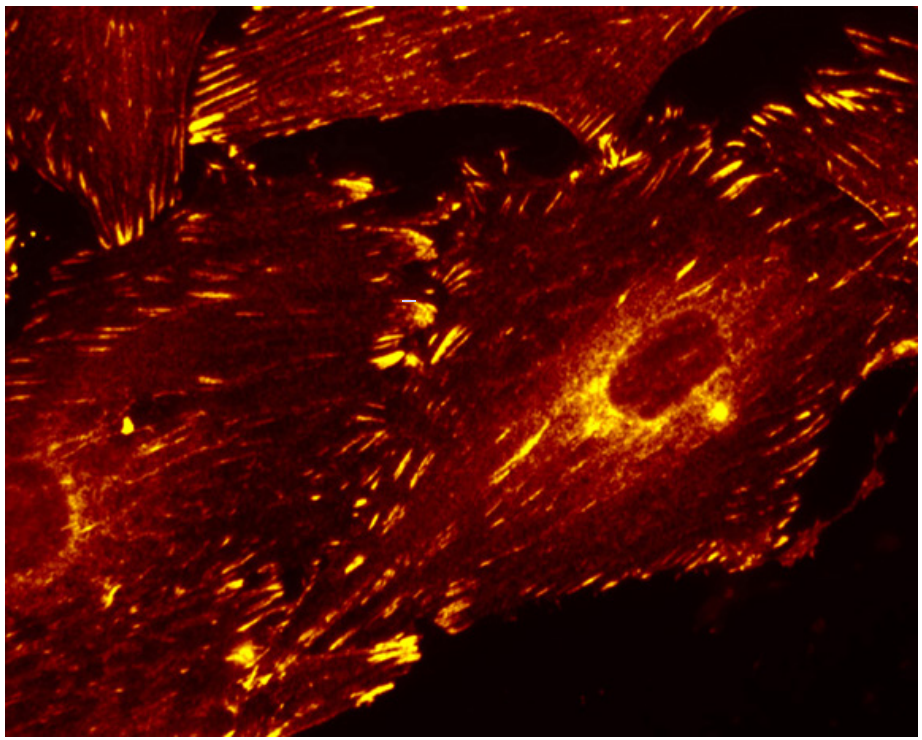


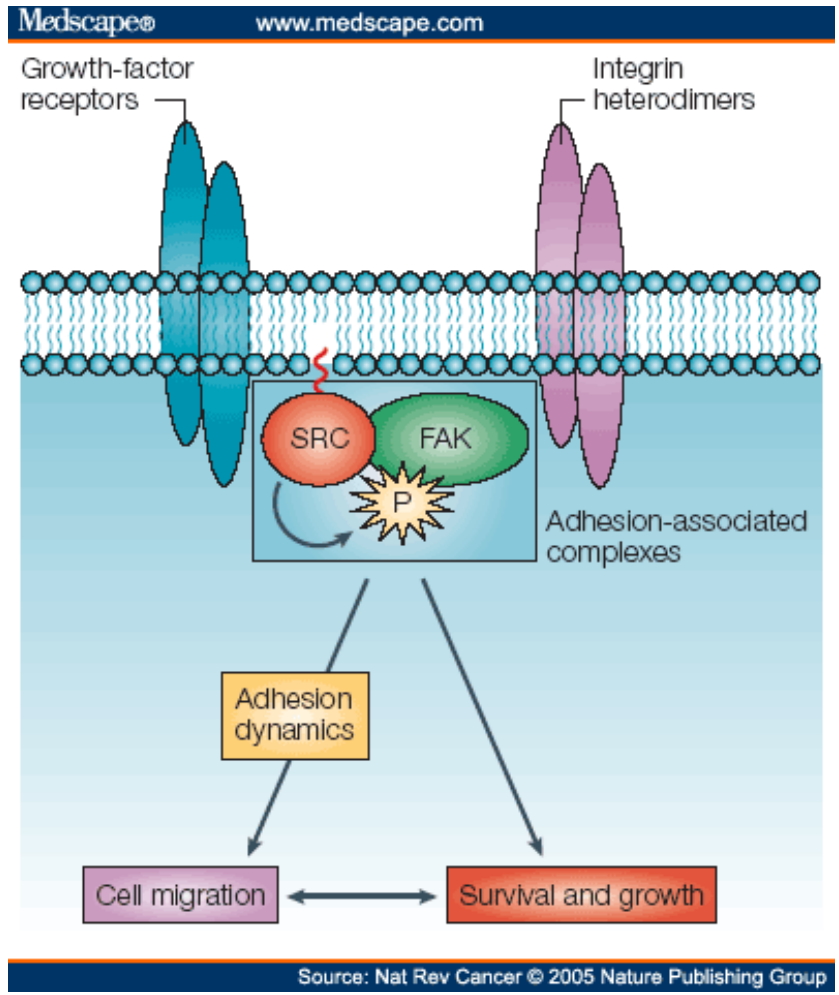
Fokális kontaktus
Integrinek





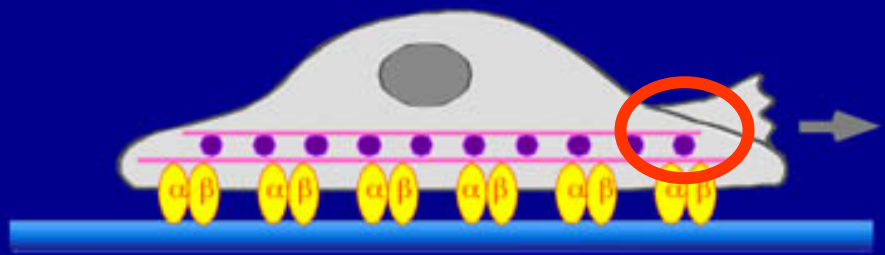
Fokális kontaktus
FAK





Migráció és sejt-ECM kapcsolat

Adhesive Regulation of Cell Migration



Adhesion Release

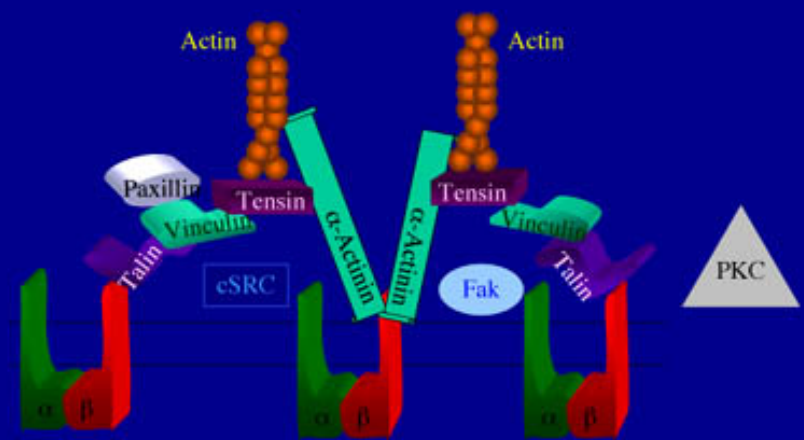
calcineurin
calpain
Rho?
tyrosine phosphorylation?

Adhesion Formati

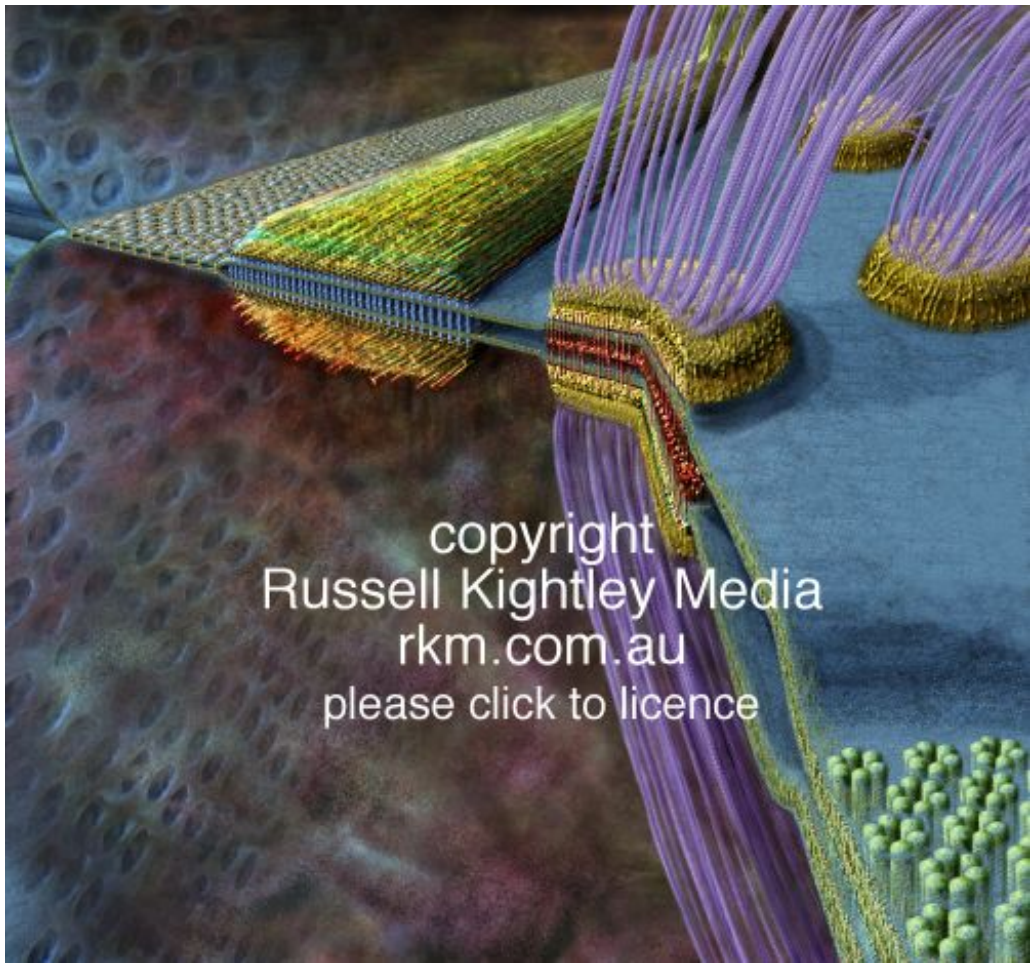
Cdc42, Rac, Rho
FAK
calpain?
paxillin?
CAS / Crk
MAPK?
calcium?

PLC-γ
PI-3-K
PI-5-K
PKC
ERM
Src?
talin?

The Focal Complex



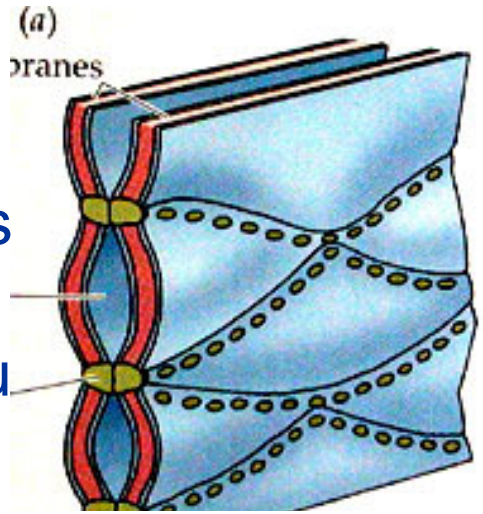
Junkciónális kapcsoló struktúrák

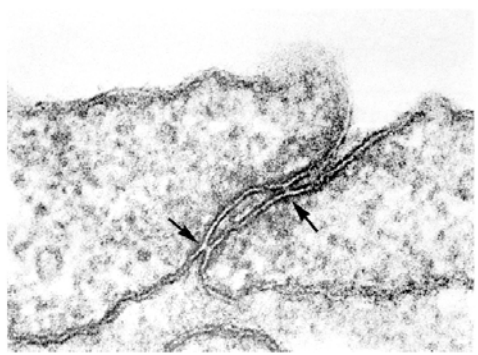


Zonula occludens (szoros kapcsolás)

rés

Occludin

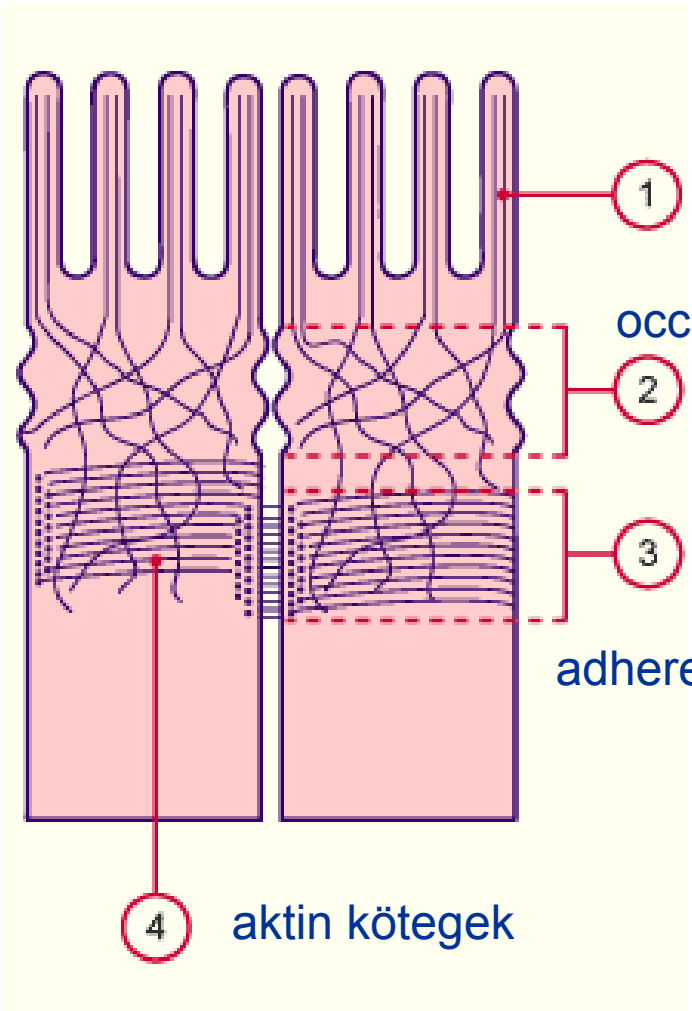




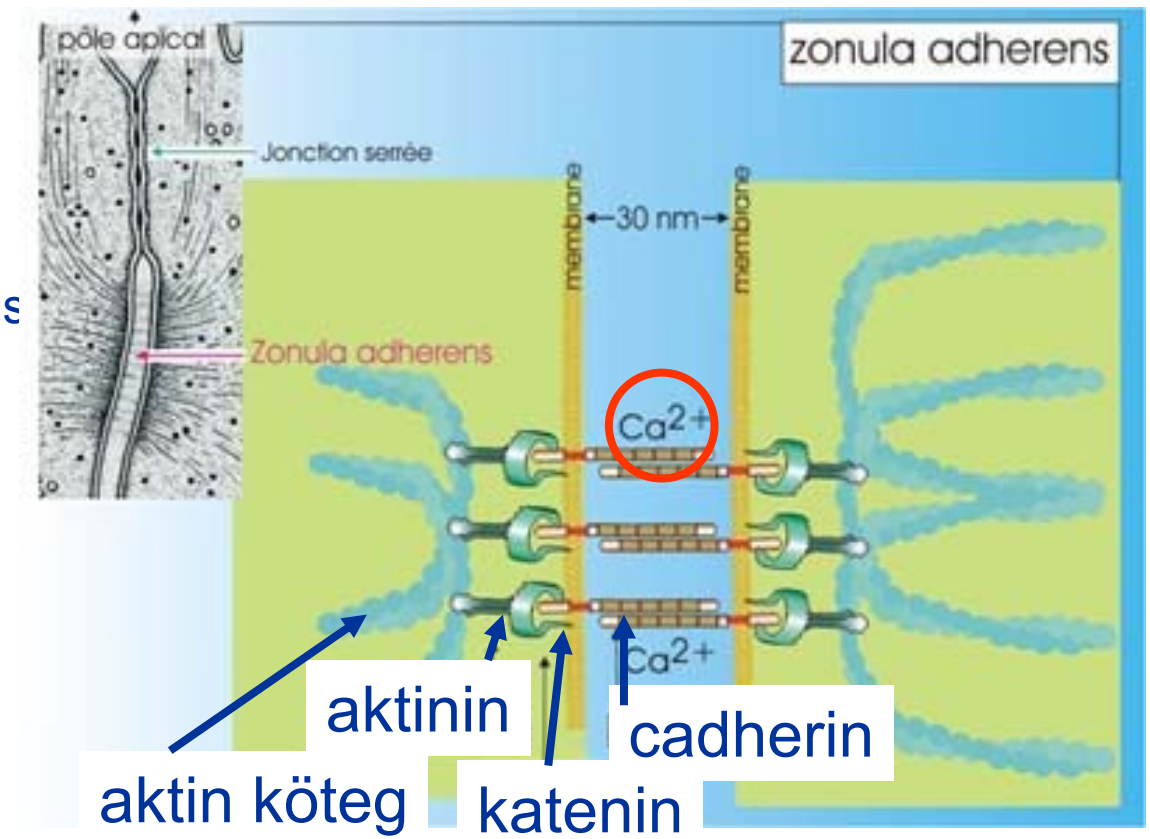
-többszörösen „összevarja” a sejteket (occludin)

-barriert képez

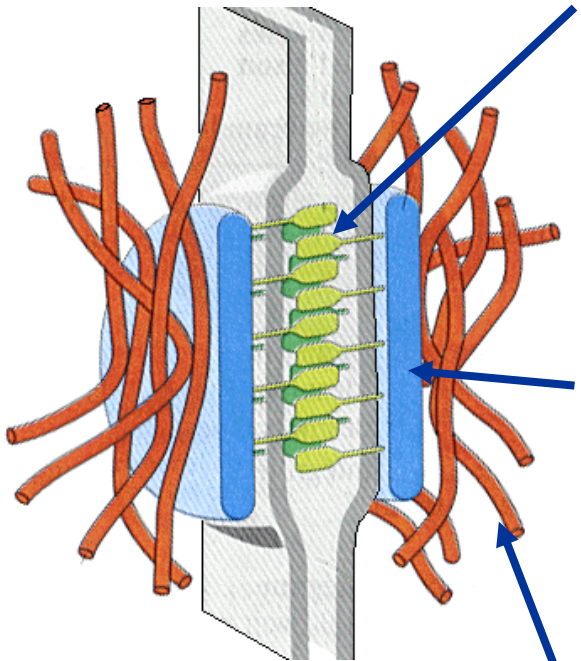
Zonula Adherens



Öv szerüen összekapcsolja a sejteket

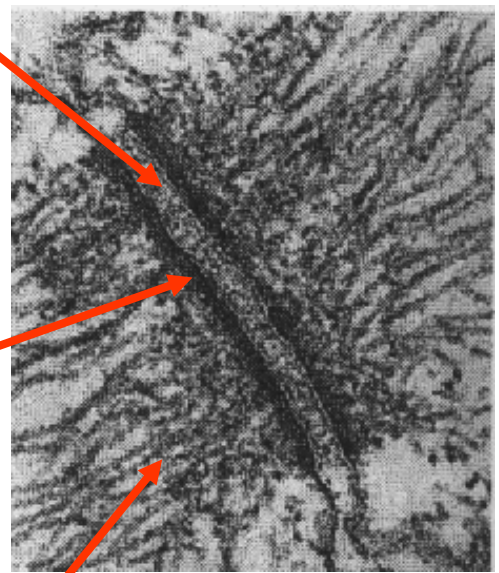


Dezmoszóma



dezmoglein
dezmocollin

dezmoplakin
dezmoglobin

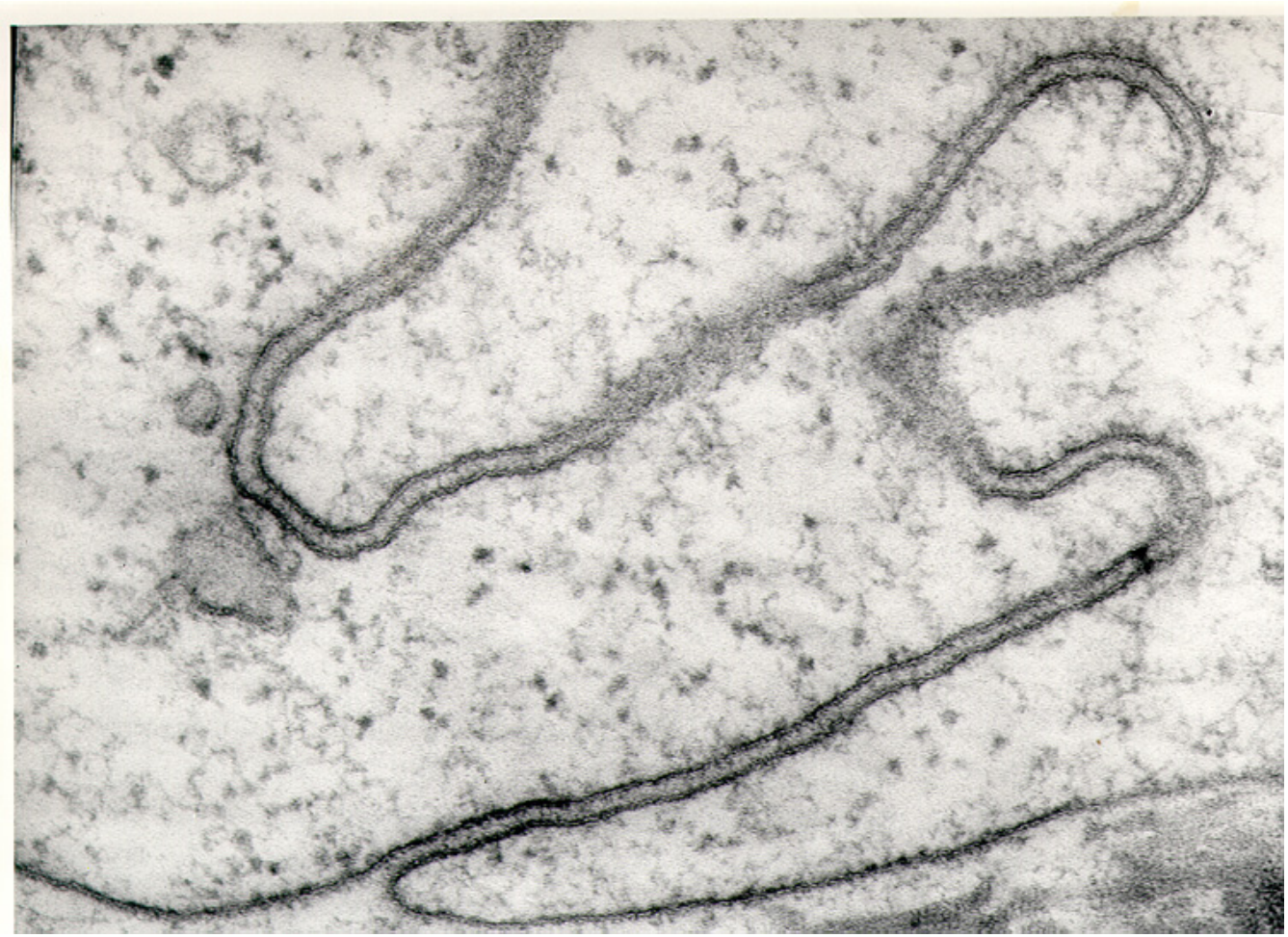


Intermedier filamentumok

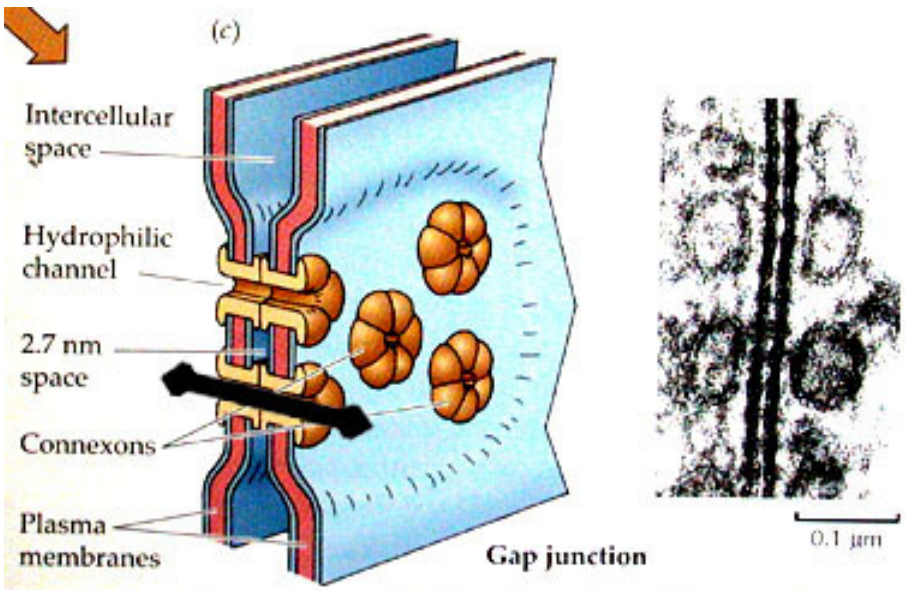
A dezmoszómák a mechanikai stressznek kitett szövetekben a leg jellemzőbb sejtkapcsoló struktúrák

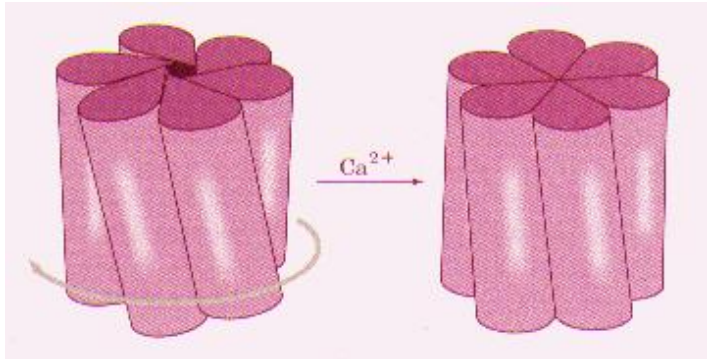
BŐR: STRATUM SPINOSUM

Interdigitació

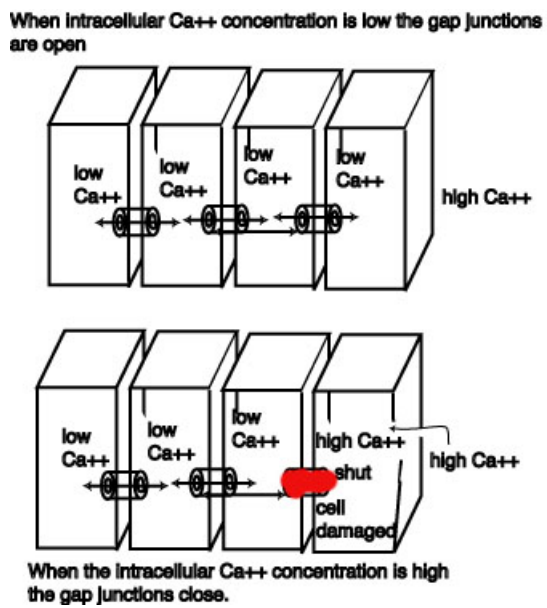


Gap-junction (rés kapcsolat)





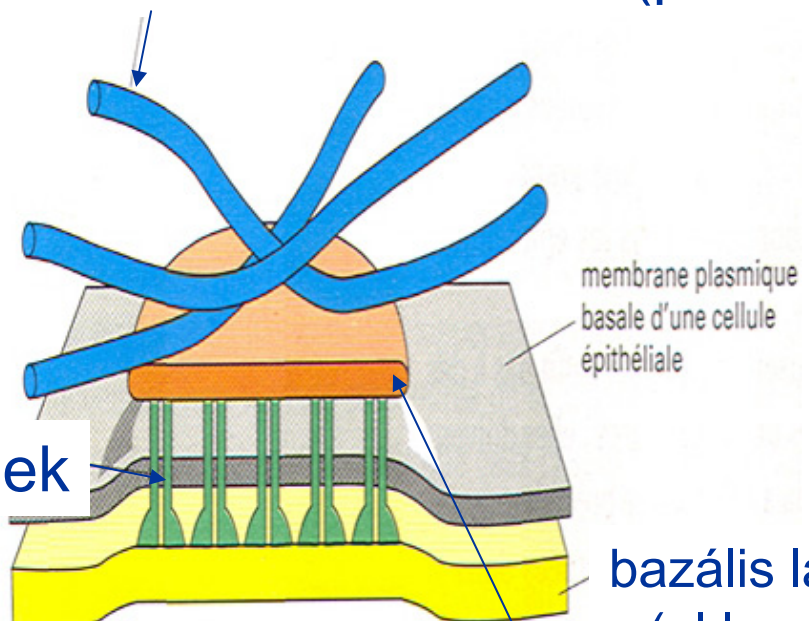
Az intracelluláris viszonyoktól függően nyit, vagy zár a konnexon cstorna



-6 db membrán átérő fehérjéből épül fel
-1,5 nm HIDROFIL csatornát fognak közre
- szinciciális szövetekre jellemző (ahol a sejteknek egyszerre, összehangoltan kell működni

Fél dezmoszóma

Intermedier filamentum (pl. keratin)



integrinek

bazális lamina
(pl.laminin)

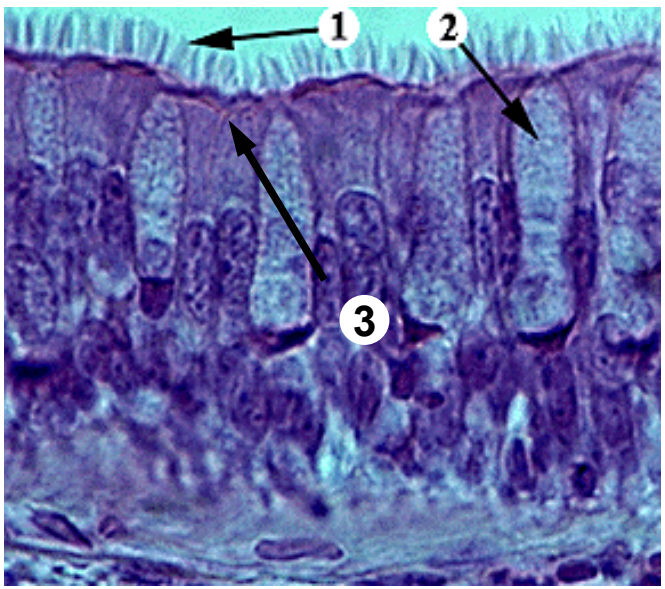
kapcsoló fehérjék

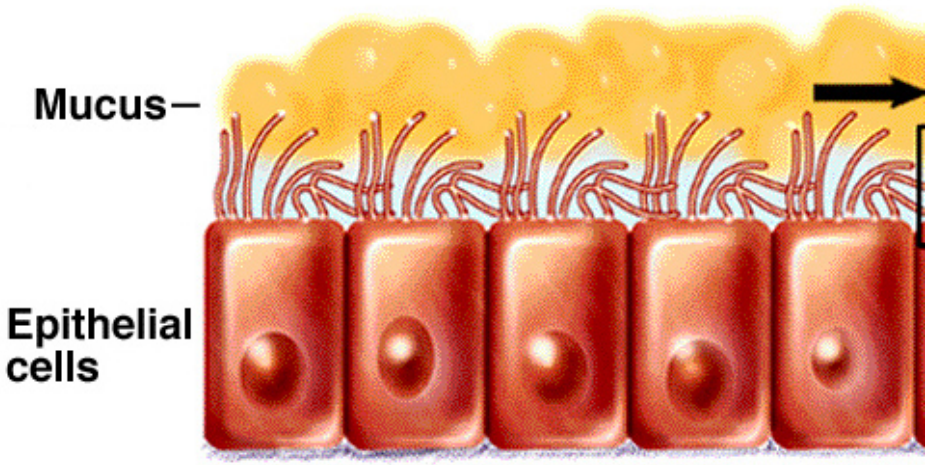
-**ECM-hez** kapcsolja a sejteket (integrinek)

- fokális kontaktustól eltérően az **intermedier** filamentumok horgonyozzák a sejt vázhoz

Mozgás és sejt-sejt kapcsolat 1.

Mozgás és sejt-sejt kapcsolat 2.





1. Csillók
2. Nyák termelő sejtek
3. Zonula adherens kötelék

A tumor-metasztázis adhéziós molekulák mintázatának változásával jár