PLAN

.LEMARCHAND

GÉNERALITES

- Eléments généraux (1,2,3)
- Cytosquelette et phénomènes dynamiques (4,5,6)
- Fonctions

FILAMENTS INTERMEDIAIRES

- Répartition (7,8)
- Structure (9)
- Type de filaments (10)
- Protéines associées (11)
- Rôles (12,13)

MICROTUBULES

- Structure (14,15,16)
- Mécanisme de polymérisation/dépolymérisation (17)
- Polarité (18)
- Protéines associées (19,20, 21,22,23)
- Centrosome - centriole (24,25)
- Cils et flagelles (26,27,28)
- Rôles (29)

MICROFILAMENTS D'ACTINE

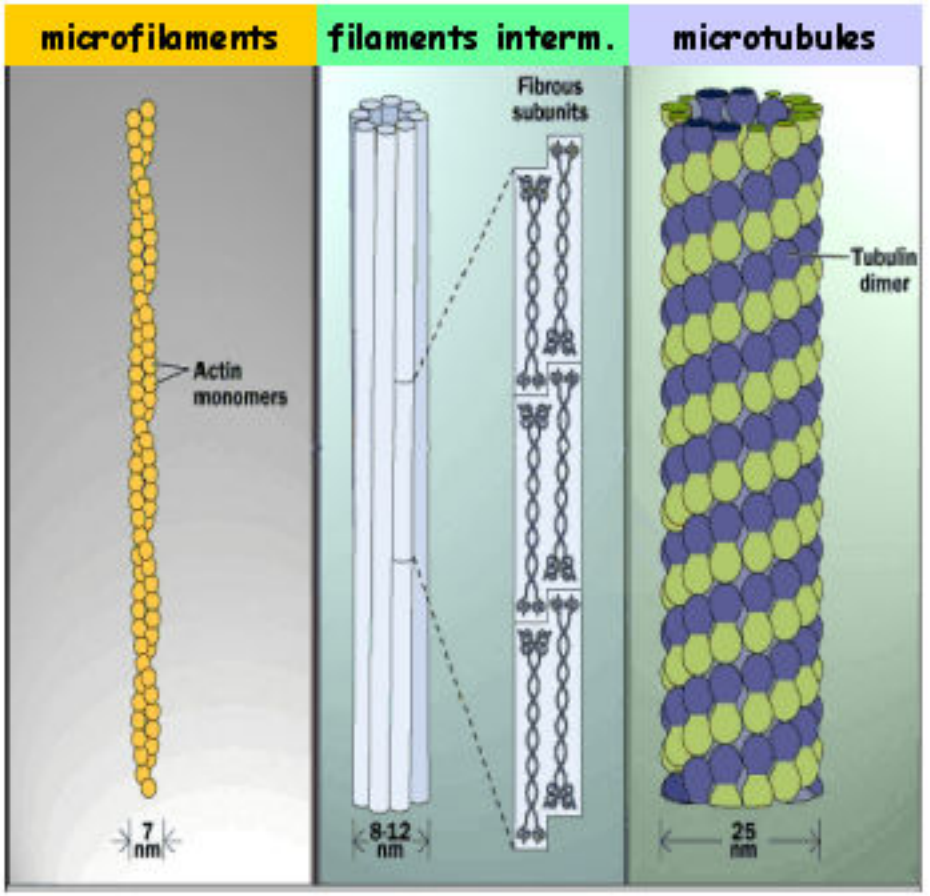
- Caractéristiques (30,31)
- Structure (32)
- Protéines associées (33,34)
- Complexes organisés
    - Cortex (35)
    - Endocytose (36,37), exocytose (38), phagocytose, déplacement (39)
    - **Appareil contractile : généralités (40, 41)**
    - **Appareil contractile des cellules non musculaires (42,43)**
    - **Appareil contractile des cellules musculaires (44-45-46-47-48-49-50-51-52-53)**
- Interaction cytosquelette-membrane (54)
    - Cellules isolées (55)
    - **Jonctions cellulaires (56,57,58)**
    - **Interactions avec la lame basale (59,60,61)**
    - **Interactions avec la MEC (62)**

PATHOLOGIES ASSOCIÉES À DES ANOMALIES DU CYTOSQUELETTE

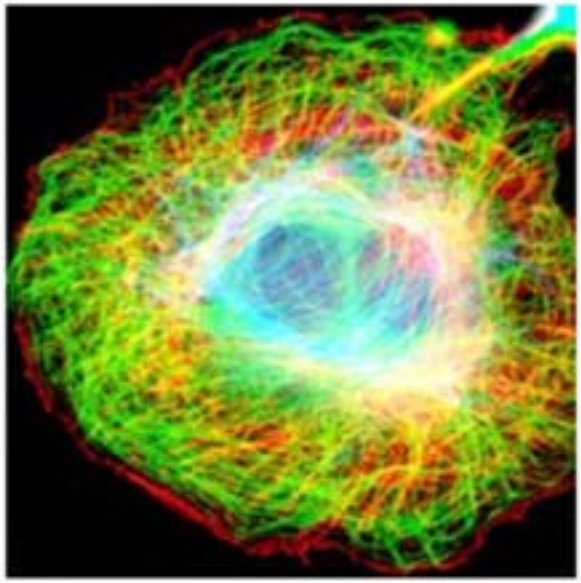
- **Atteinte des constituants du cytosquelette**
    - Maladies génétique : myopathie de Duchenne, Syndrome de Wiskott-Aldrich, Anémies hémolytiques, Epidermolyse bulleuse
    - Maladies acquises : sclérose latérale amyotrophique, maladie d'Alzheimer
- **Maladies infectieuses**

    - Maladies virales : EBV, papilloma virus, virus de la vaccine
    - Maladies bactériennes (63,64)
- **Médicaments et toxiques agissant sur le cytosquelette**
- **Maladies impliquant les kinésines**
- **Autres applications médicales**

Généralités

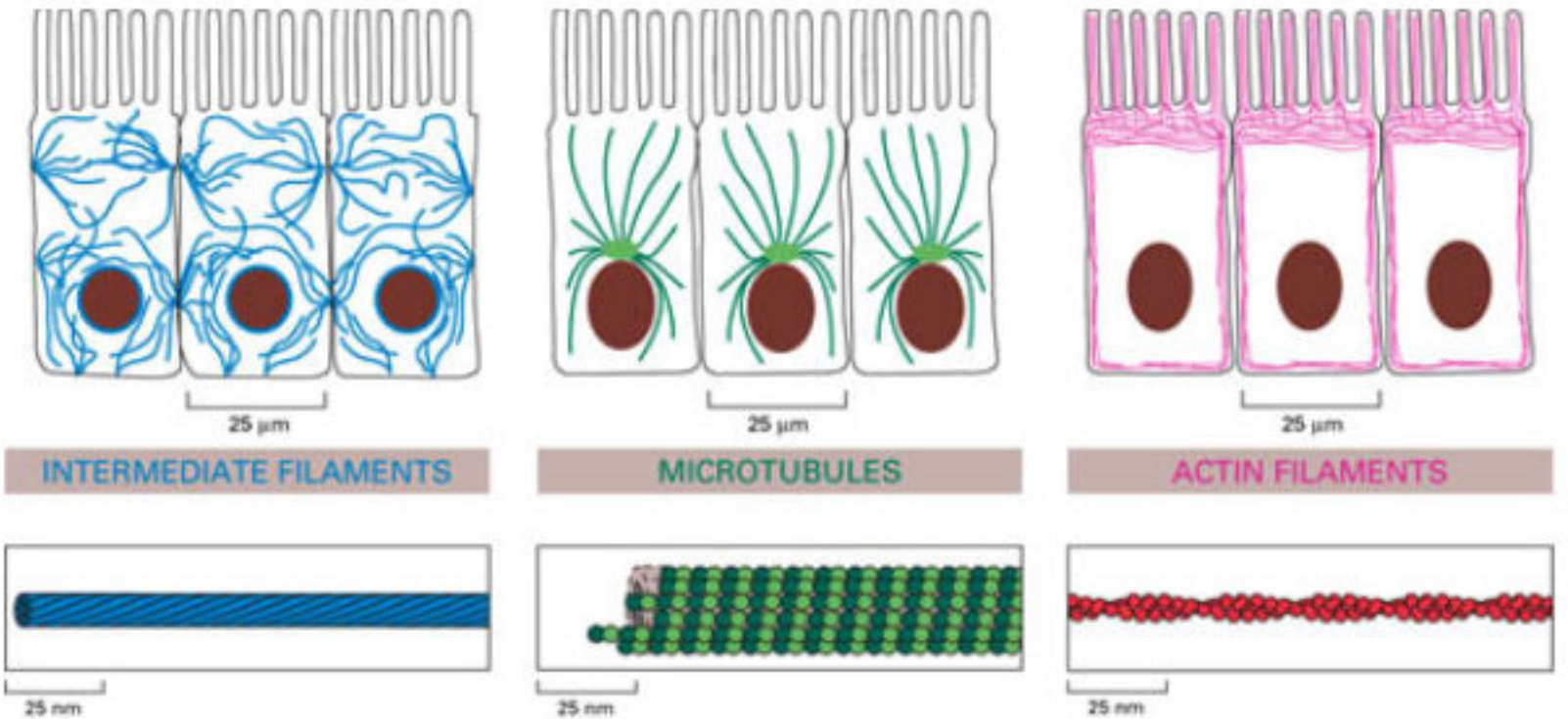


Répartition dans la cellule



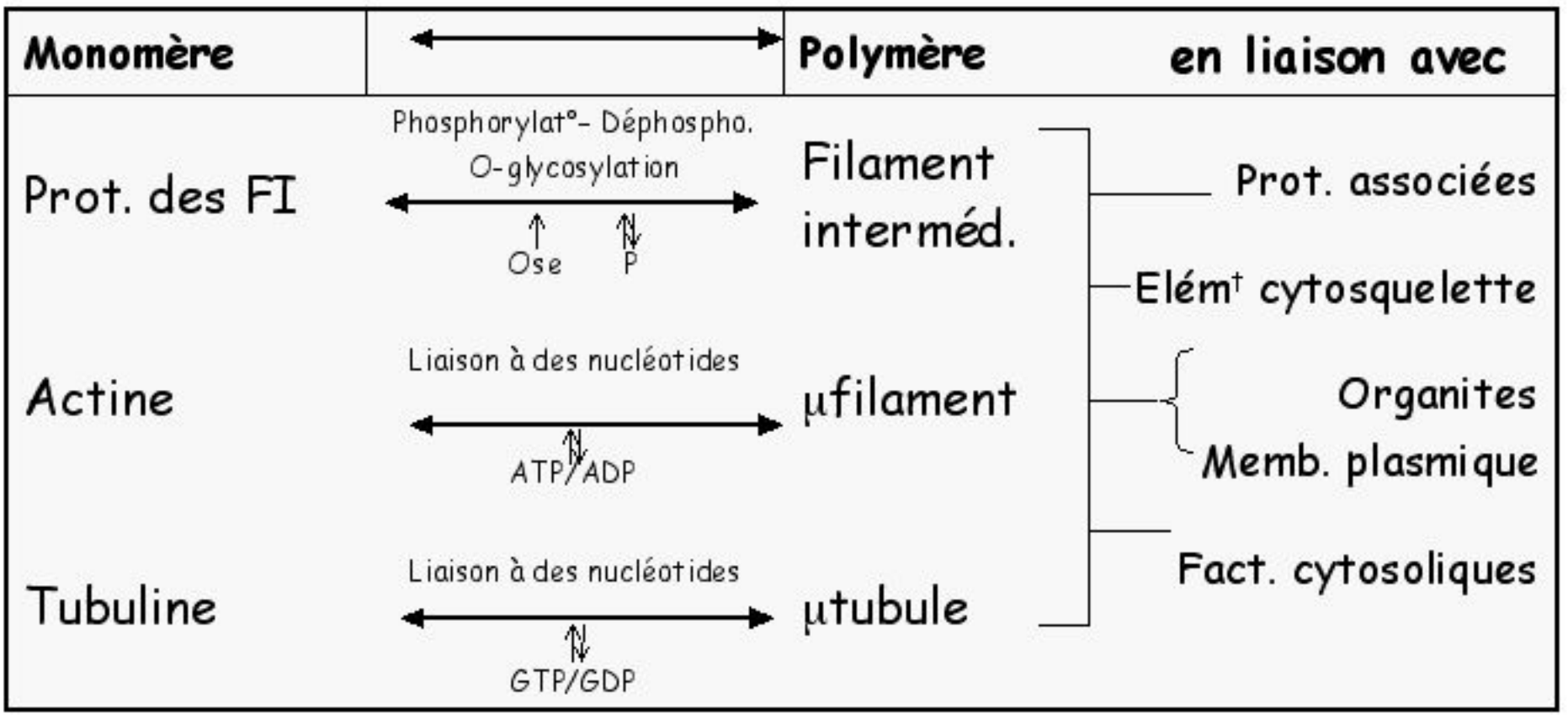
microtubules (vert), actine (rouge), filaments intermédiaires (bleu).

suite

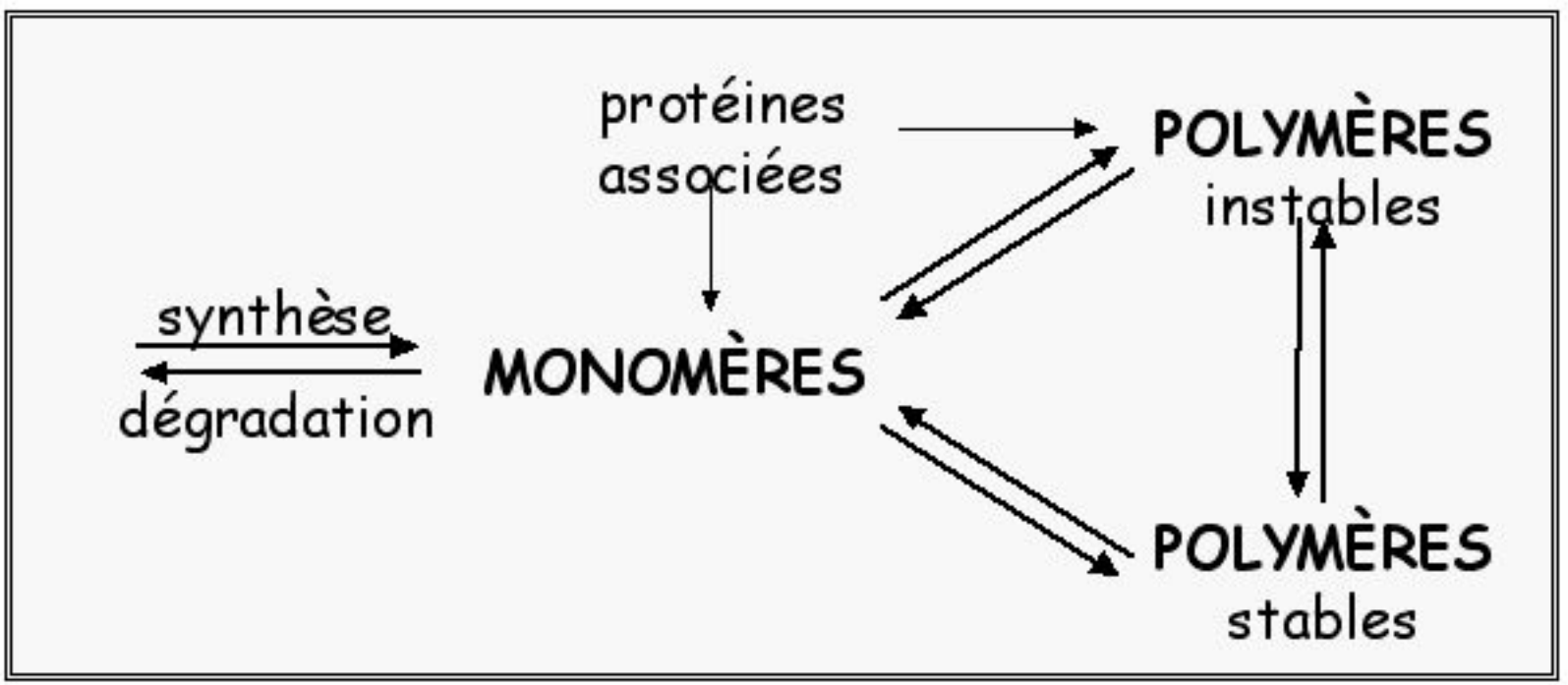


Molecular Biology of the Cell, 3rd edn

suite

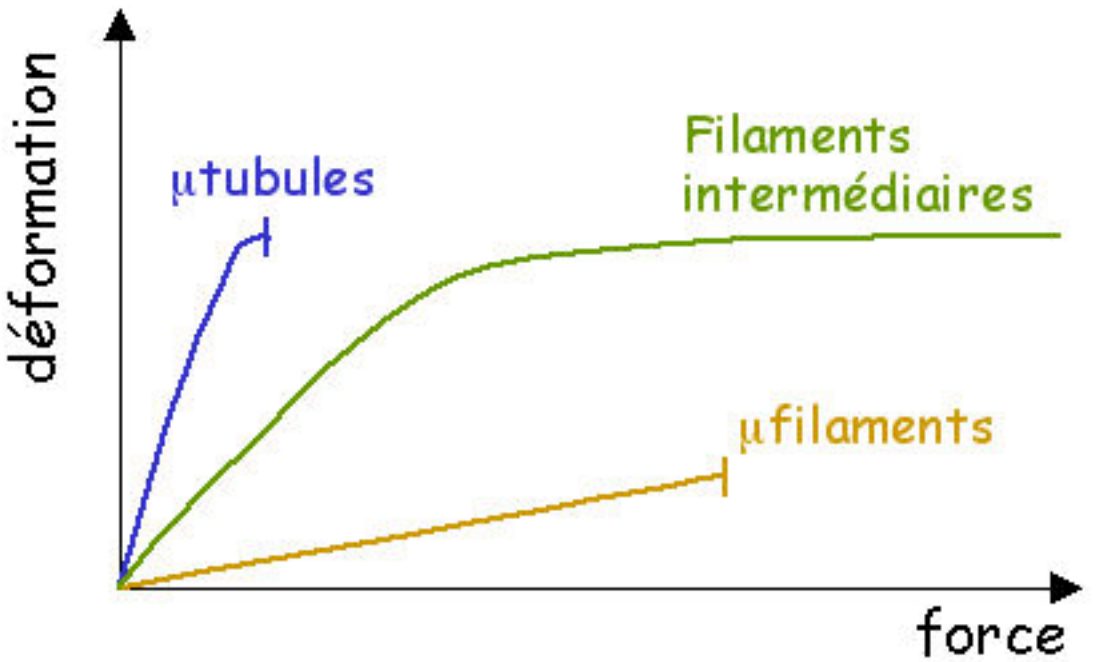


suite

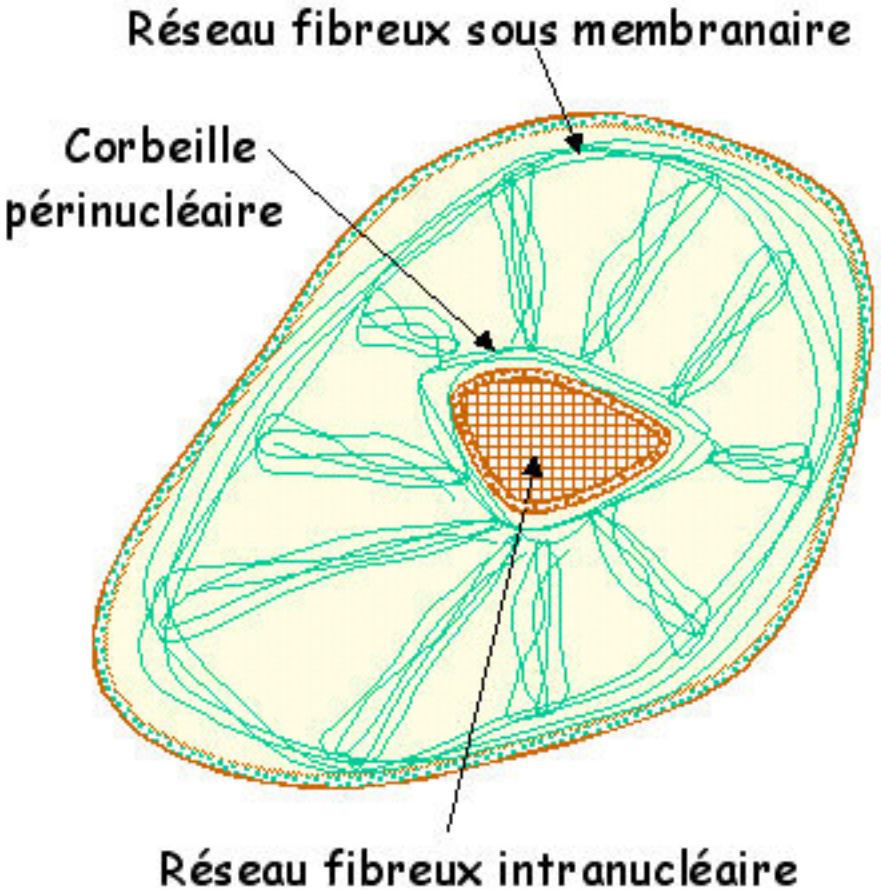

protéines
associées
POLYMÈRES
instables
synthèse
dégradation
MONOMÈRES
POLYMÈRES
stables

suite

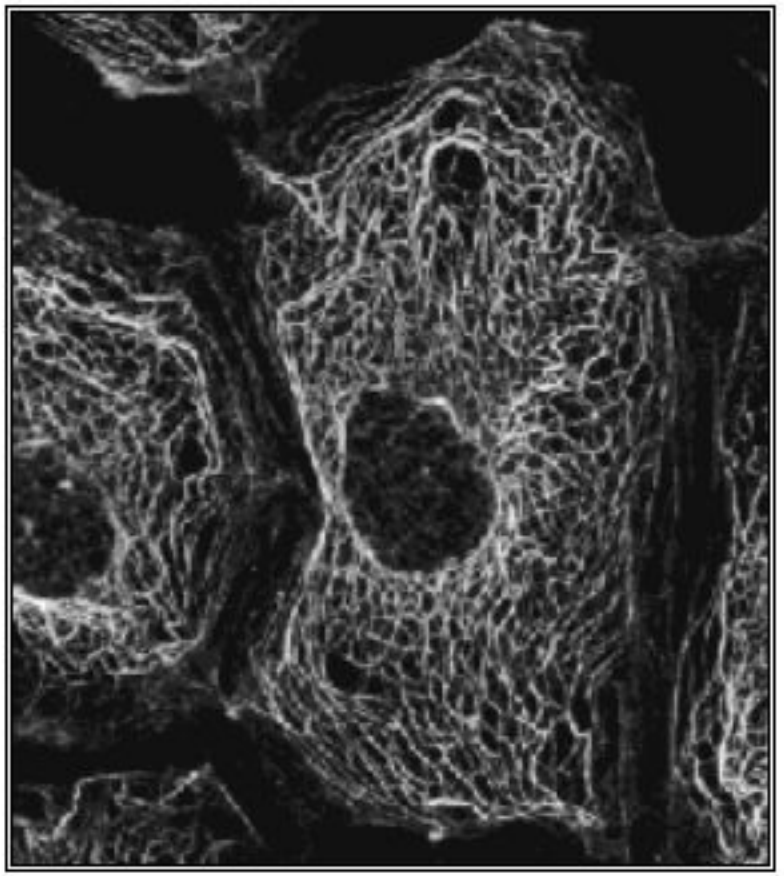
- Résistance des structures du cytosquelette



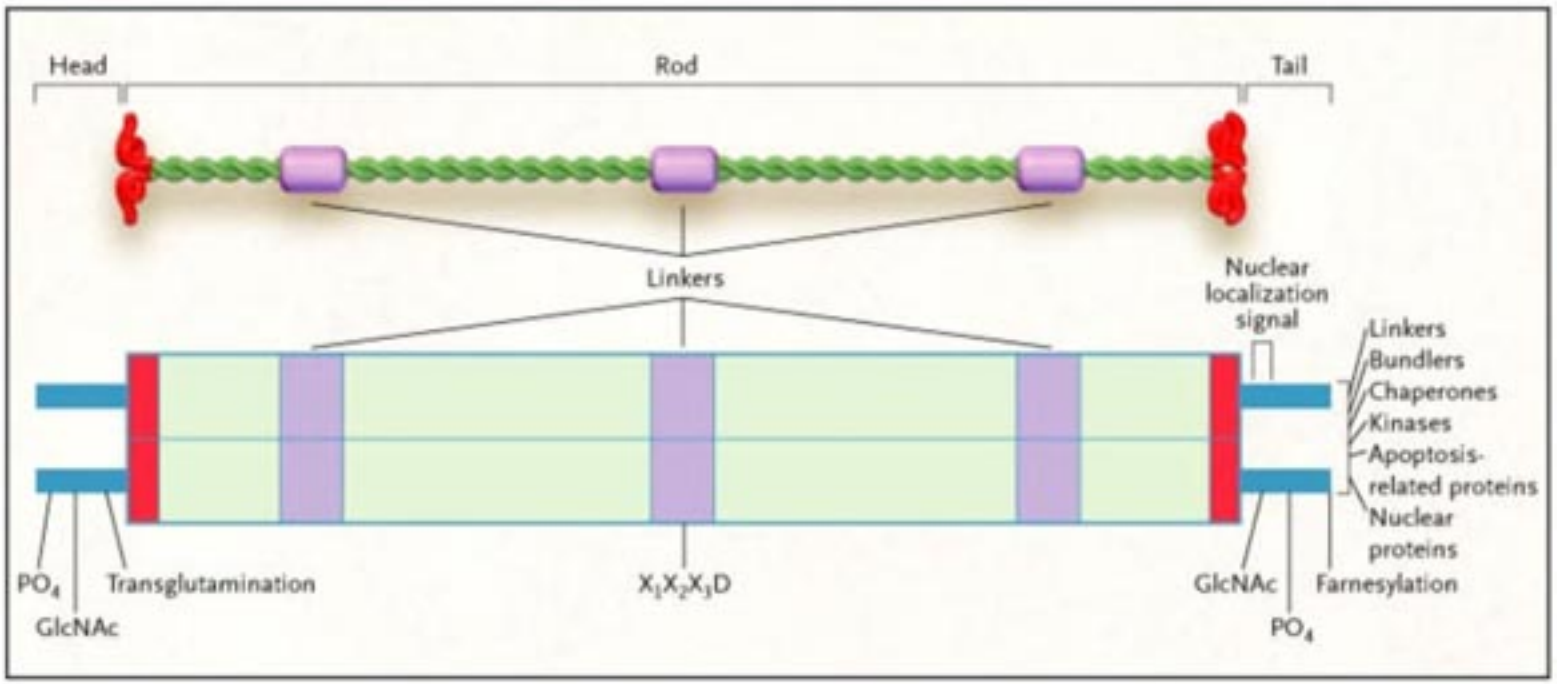
Filaments intermédiaires



suite

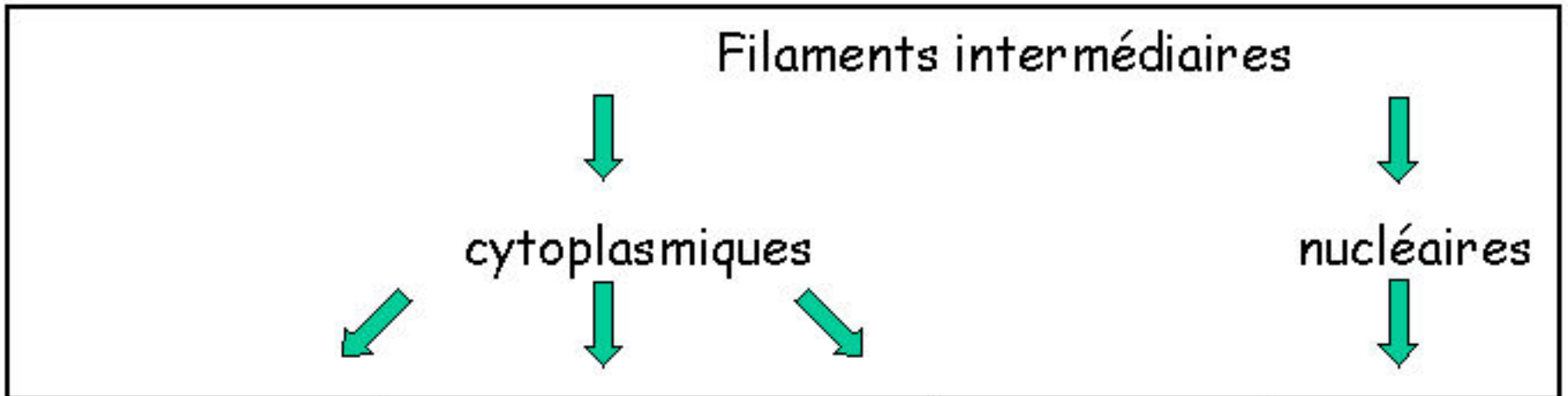


Structure



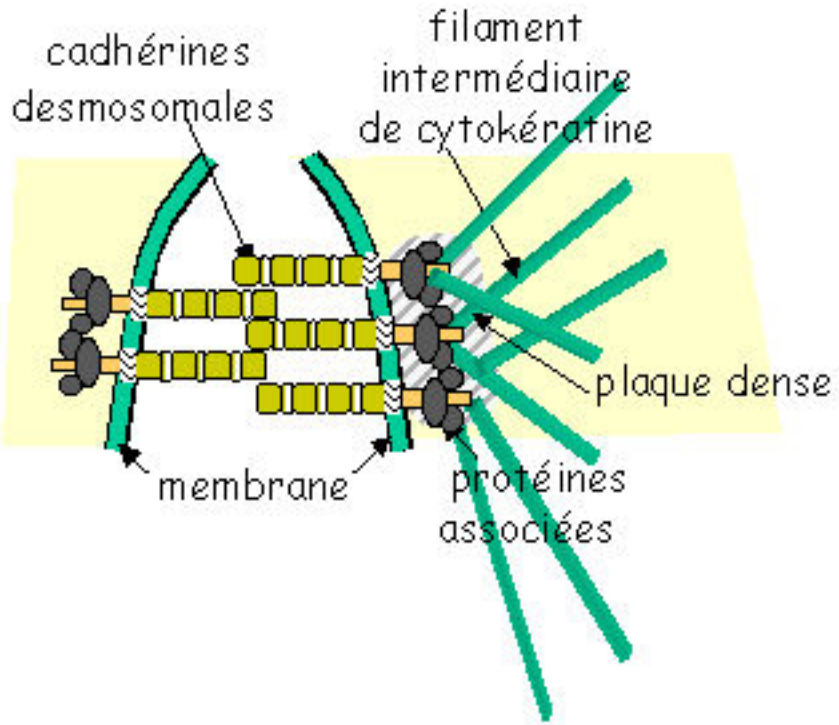
NEJM 2004;351:2087-2100

Type de filaments

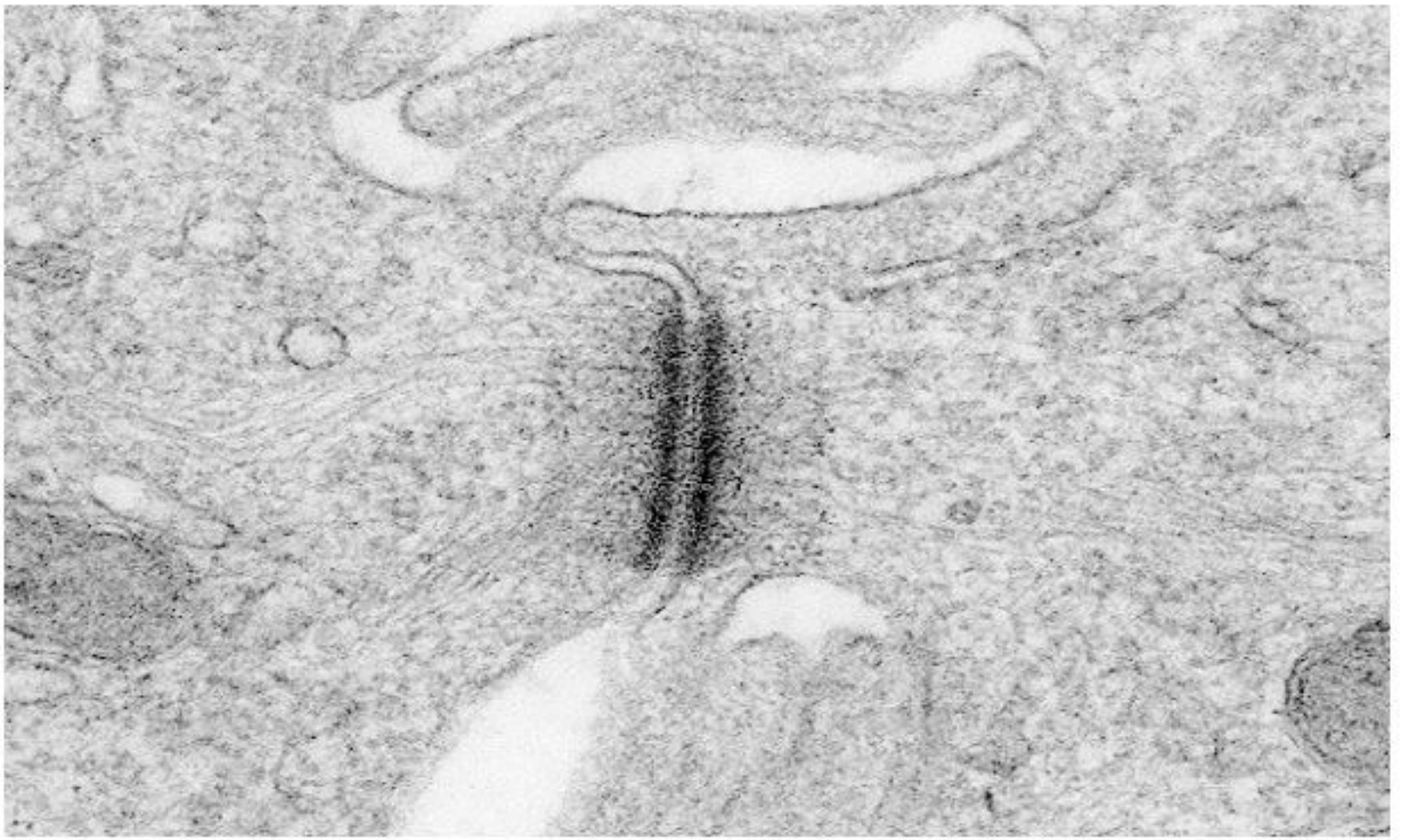


cytokératines	Vimentine & apparenté	Neuro-filaments	Lamines
⊄épithéliales	fibroblastes ⊄musculaires (desmine) ⊄gliales (GFAP)	neurones	noyau de toutes les cellules

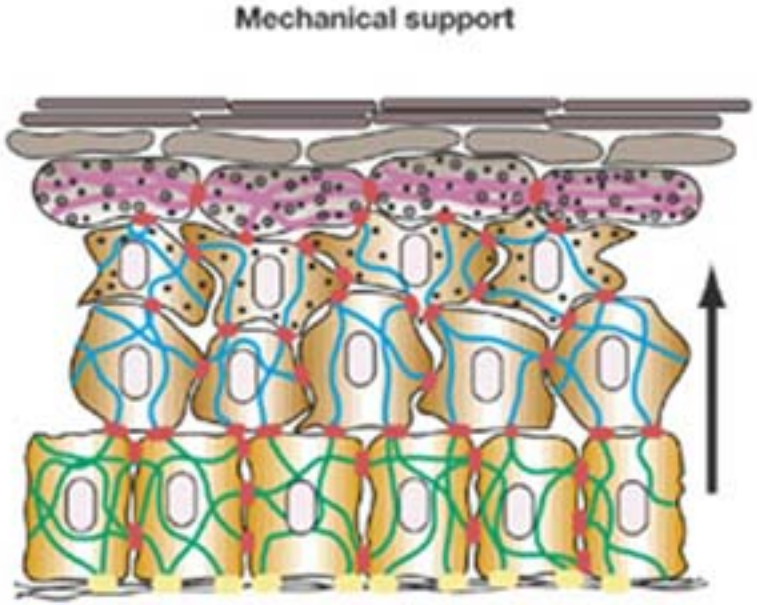
Protéines associées



desmosome



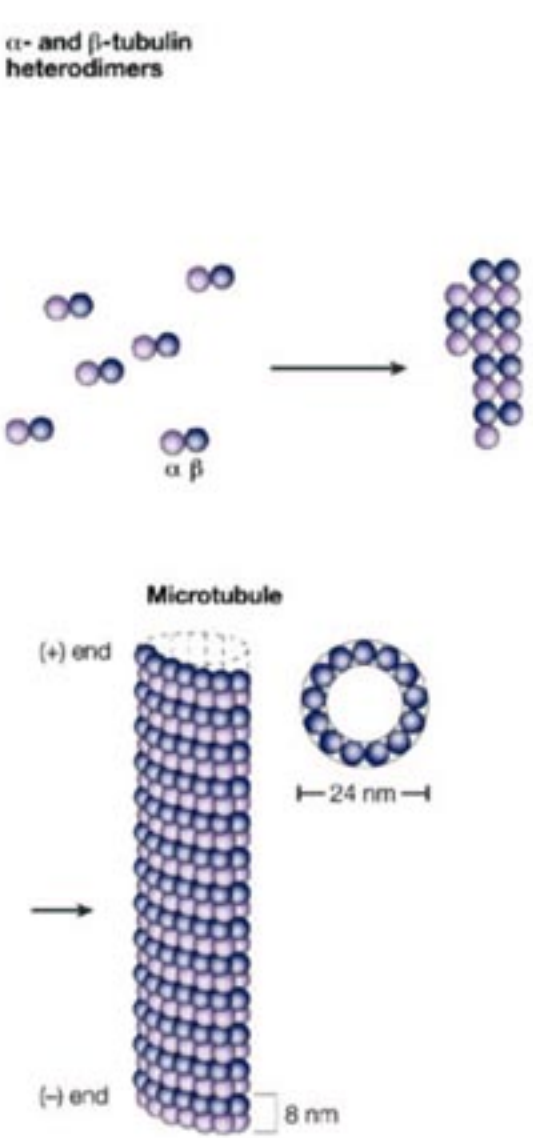
Rôle des filaments intermédiaires



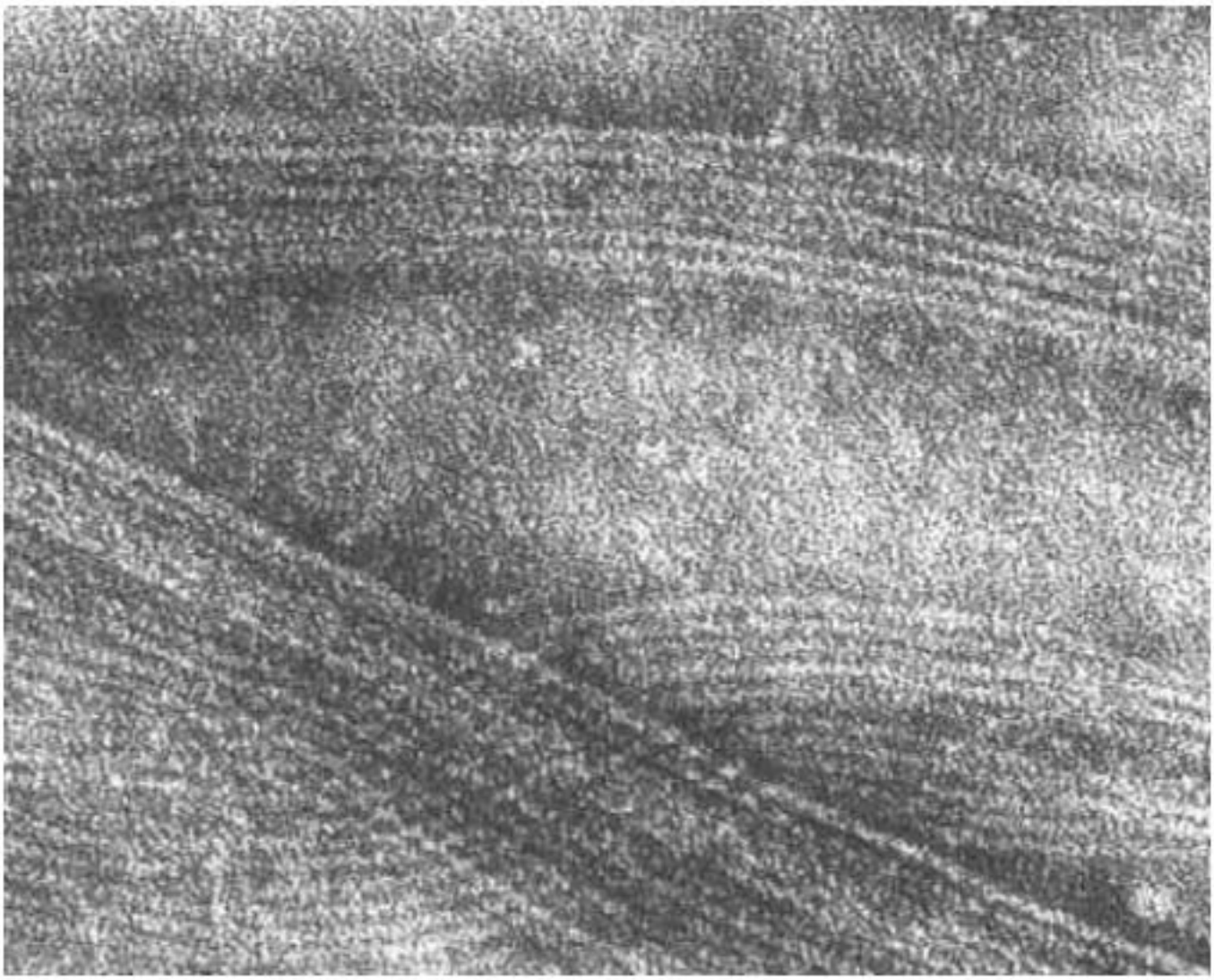
Nature Cell Biology **6**, 699 - 706 (2004)

Filaments intermédiaires (vert, bleu, rose), desmosomes (rouges), hémidesmosomes (jaune)

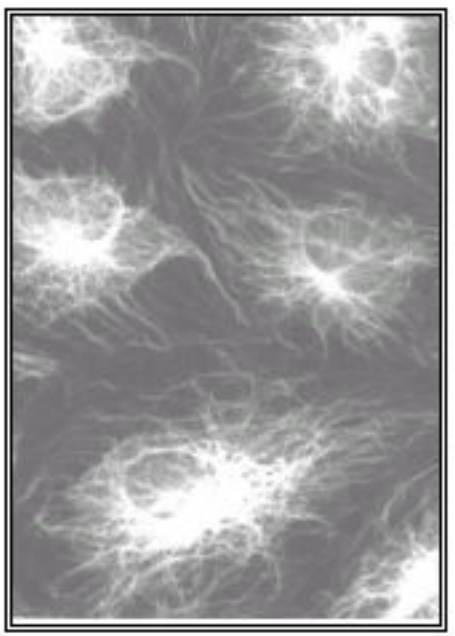
Microtubules

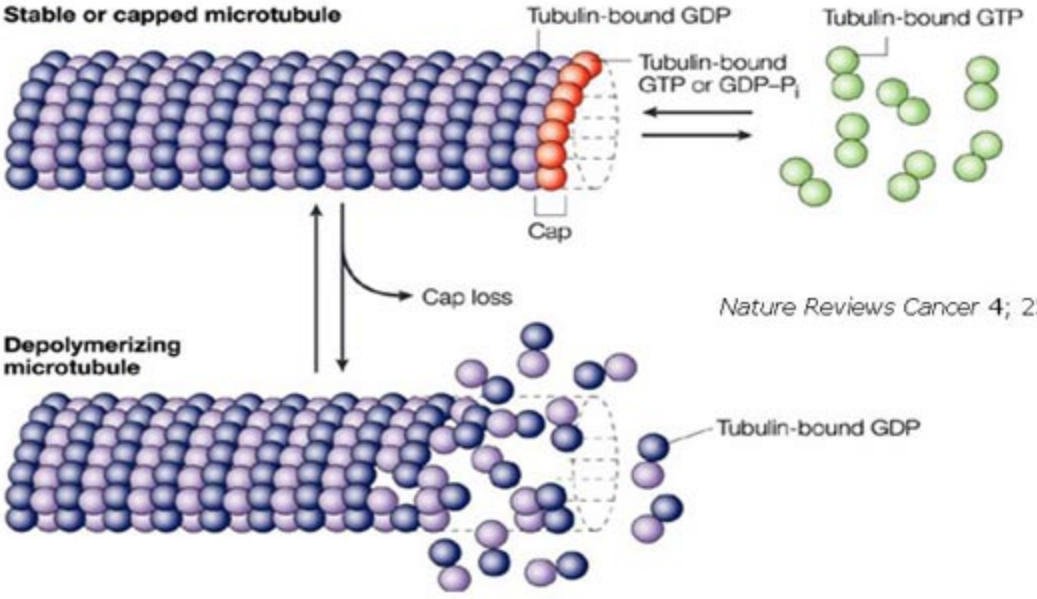


Nature Reviews Cancer **4**; 253-265 (2004)



suite

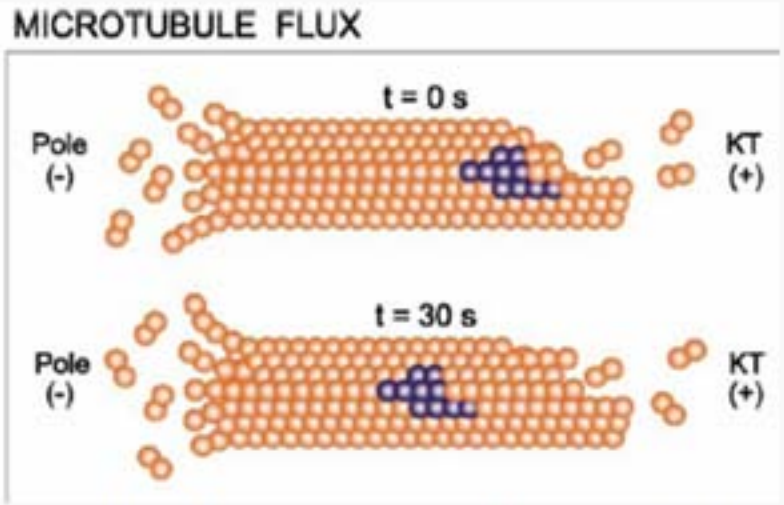




Nature Reviews Cancer 4; 253-265 (2004)

Polarité des microtubules

Extrémité -	Extrémité +
Centre cellulaire (centrosome)	Périphérie cellulaire
Polymérisation lente + dépolymérisation Rôles de COMT et tubuline γ	Polymérisation rapide + dépolymérisation Rôle de la coiffe de tubuline GTP
Stabilité de l'extrémité -	*Allongement rapide, variable*



Molecular Cell, Vol. 15, 317–327, August 13, 2004
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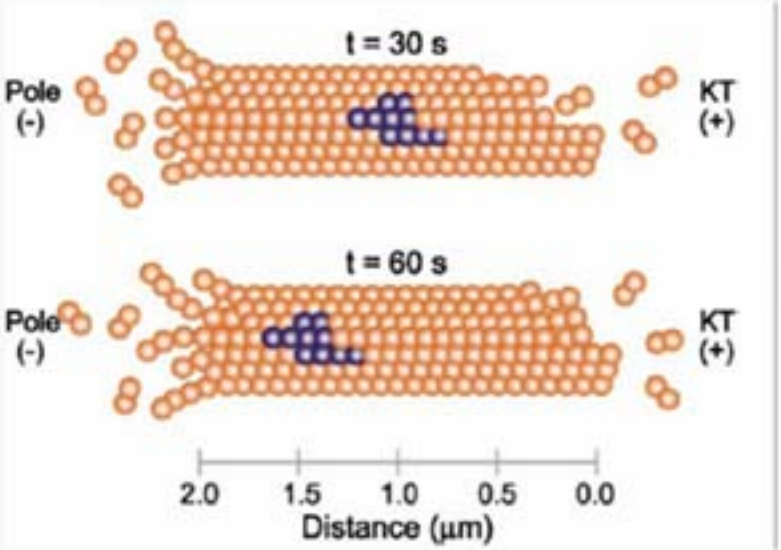
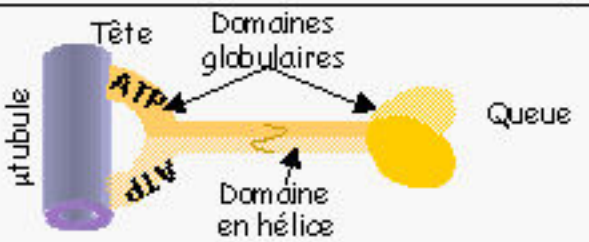
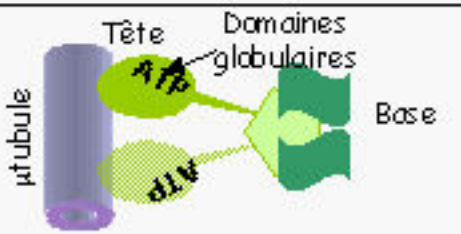
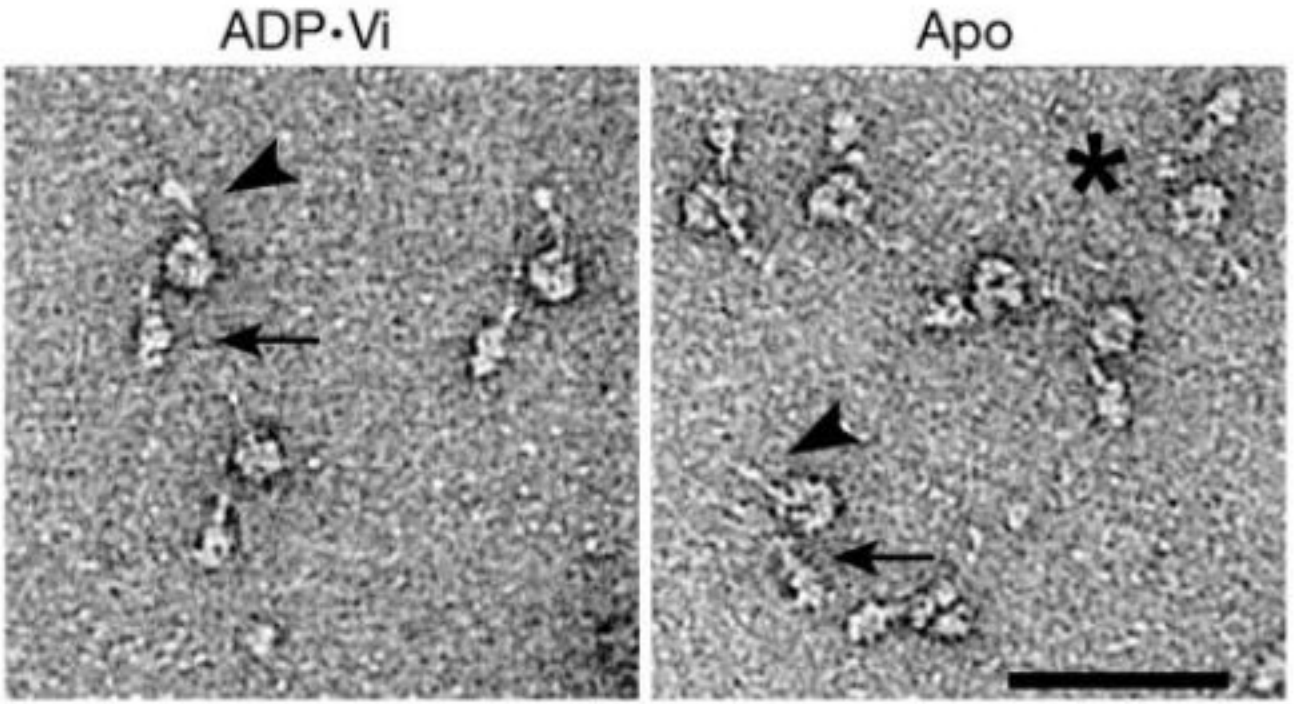


Protéines associées

Kinésines (MW 360 kDa)	Dynéines (MW 2000 kDa)
Tétramère (2x2 sous unités)	Dimère + nbses protéines associées
Têtes globulaires : domaine moteur fixation ATP, liaison aux µtubules (tubuline β)	
Queue : liaison vésicules et organites	Base : liaison vésicules et organites
Se déplace vers extrémité + distale (mécanisme ATP dépendant :	Se déplace vers extrémité - centrale activité ATPase)
	

- Exemple de la dynéine

suite

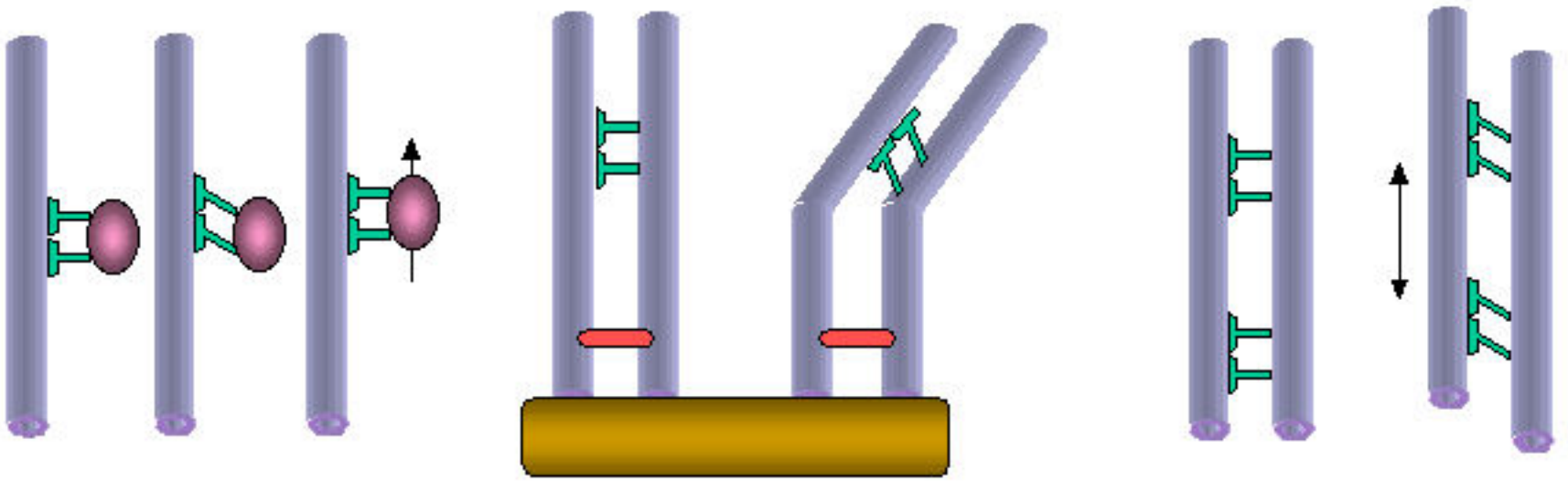


Nature 2003;421:715–718

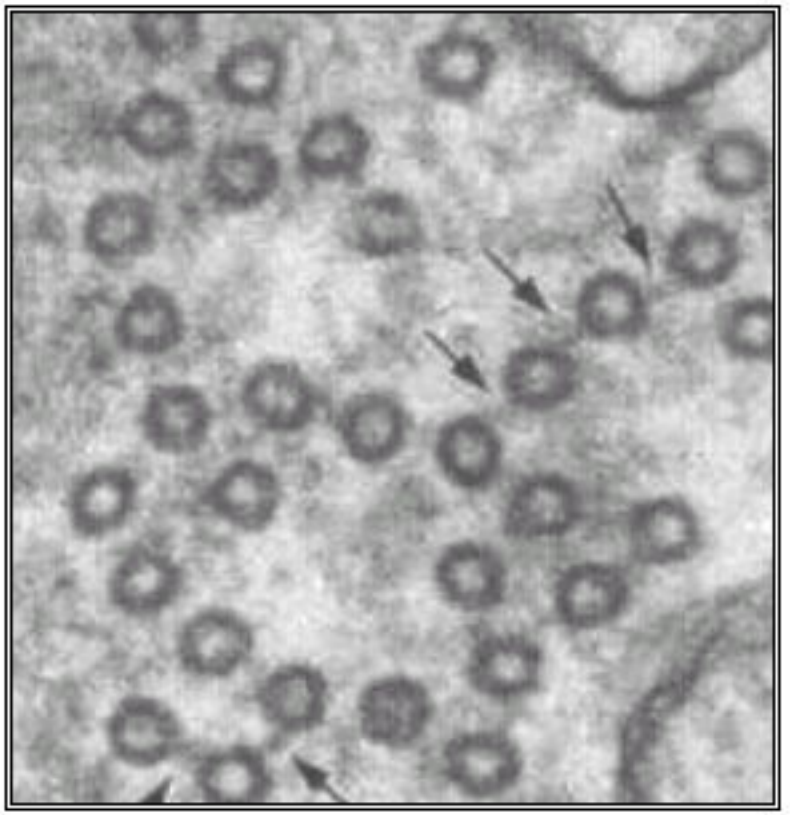
suite

2004;14:233-240

- Principe général des mouvements

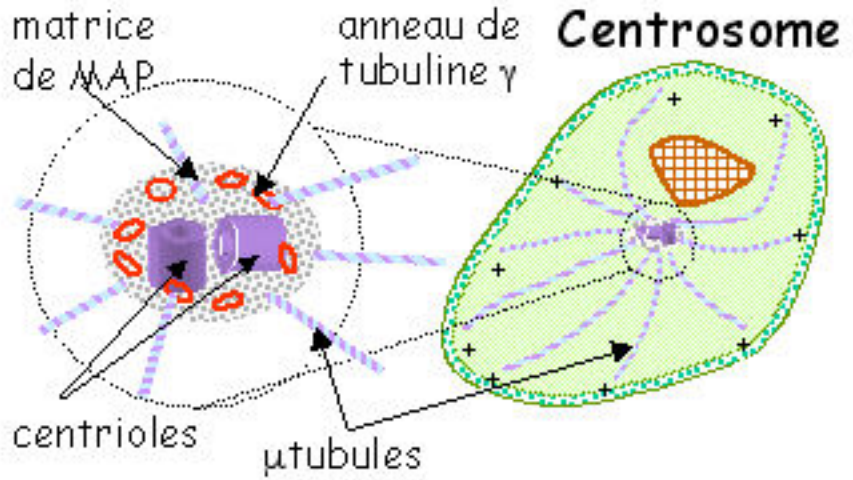


suite

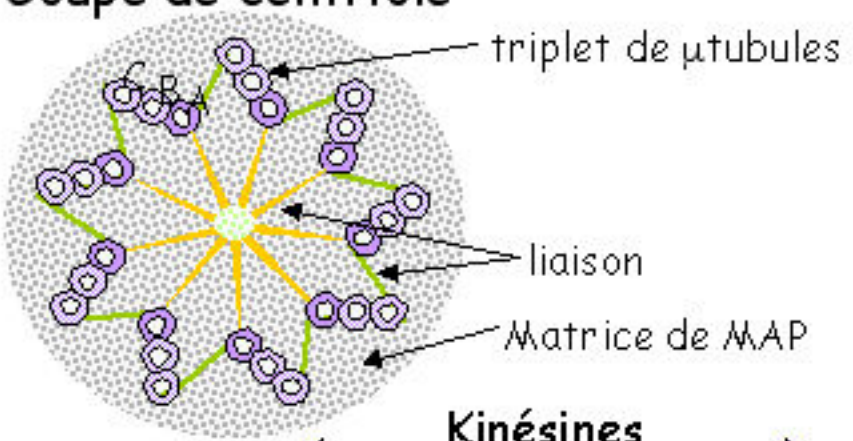


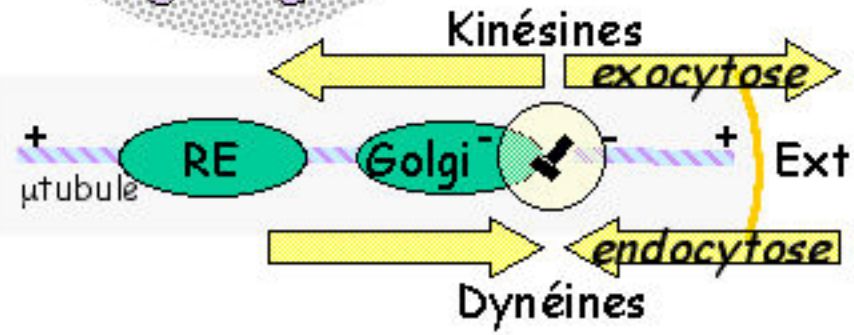
- Coupe de μtubules avec des ponts de MAP. Les flèches indiquent les ponts entre μtubules.

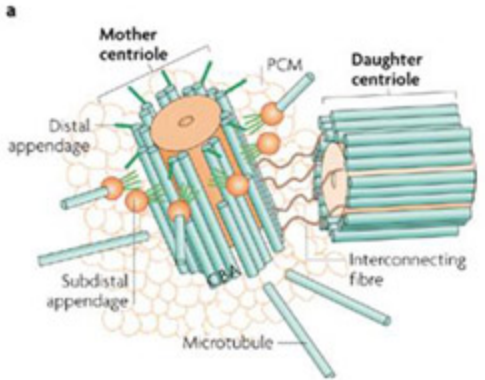
Centrosome

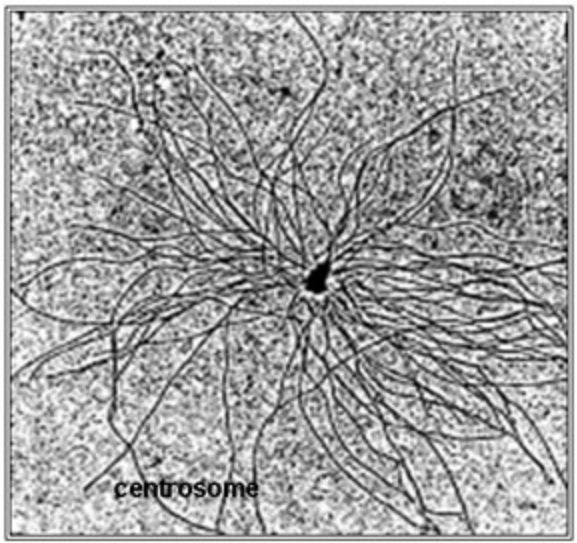


Coupe de centriole







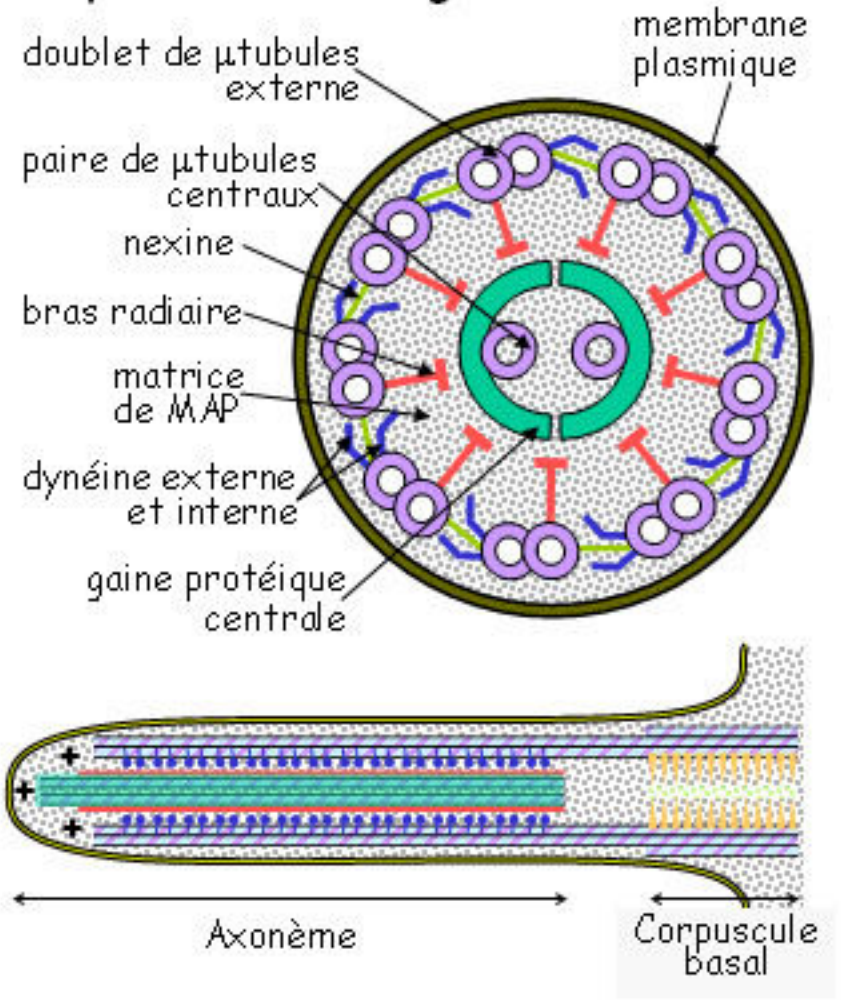


Nature Reviews Molecular Cell Biology 8, 451-463 (2007)

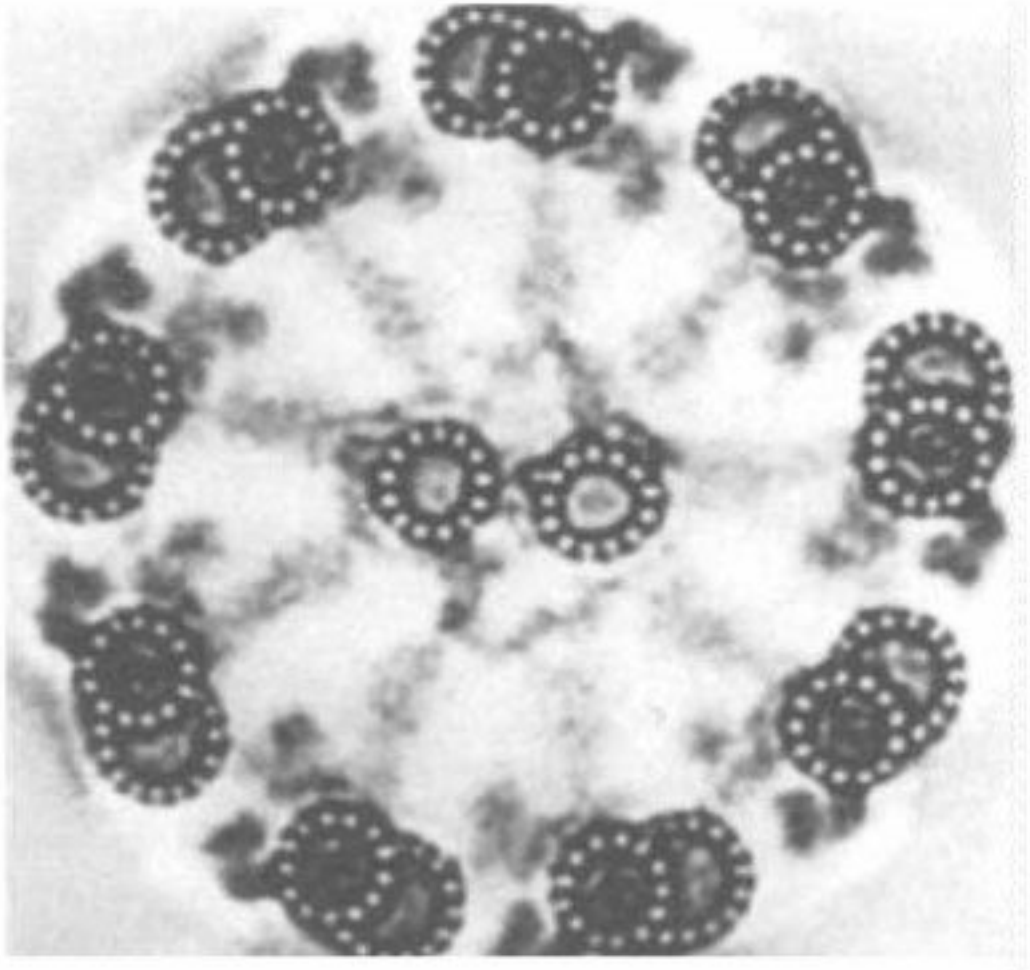
Cils et flagelles

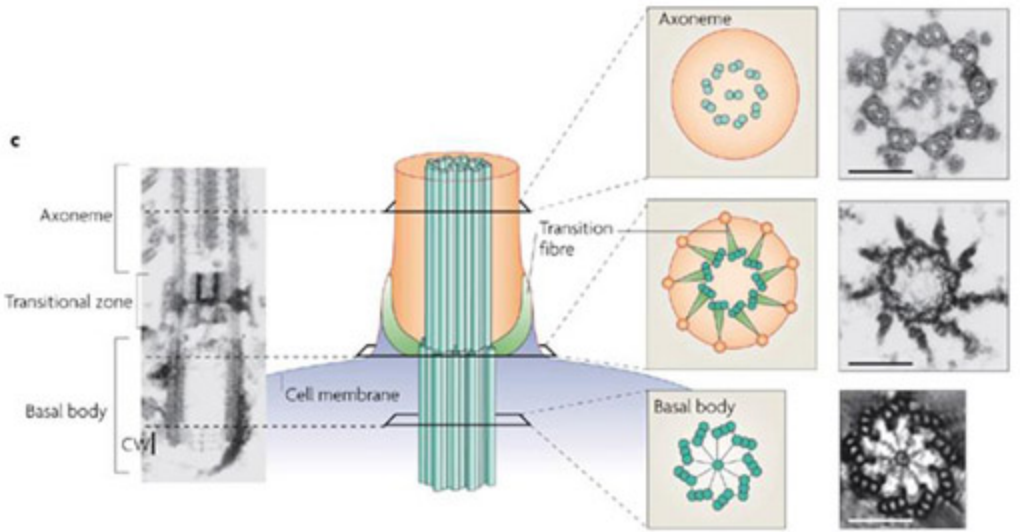
Cils	Flagelles
Nombreux Toute la surface ou toute une face	Peu nombreux Localisation apicale

Coupes de cil ou flagelle



cil

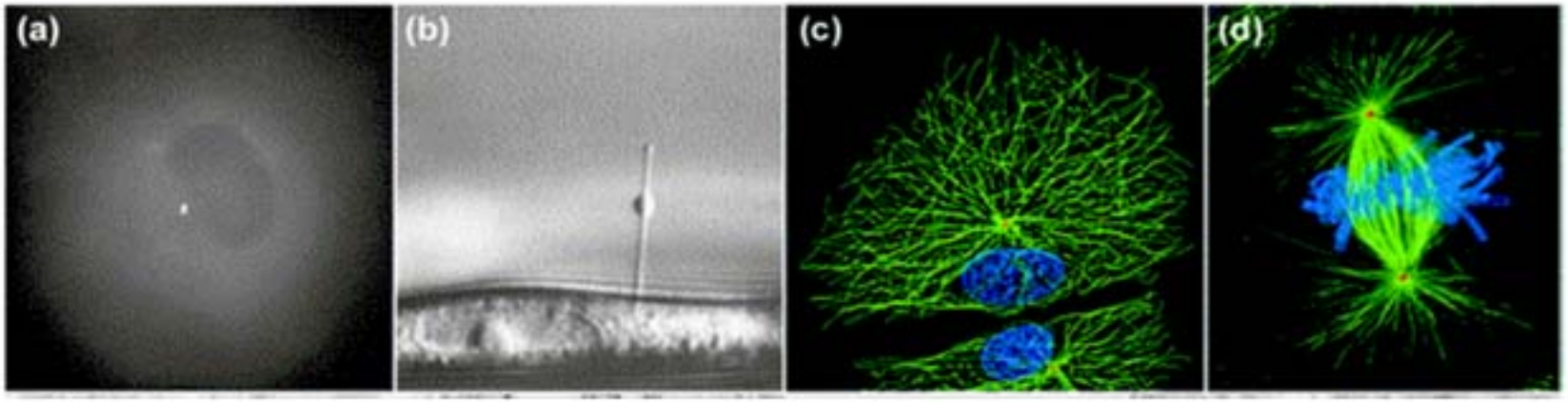




Nature Reviews Molecular Cell Biology 8, 451-463 (2007)

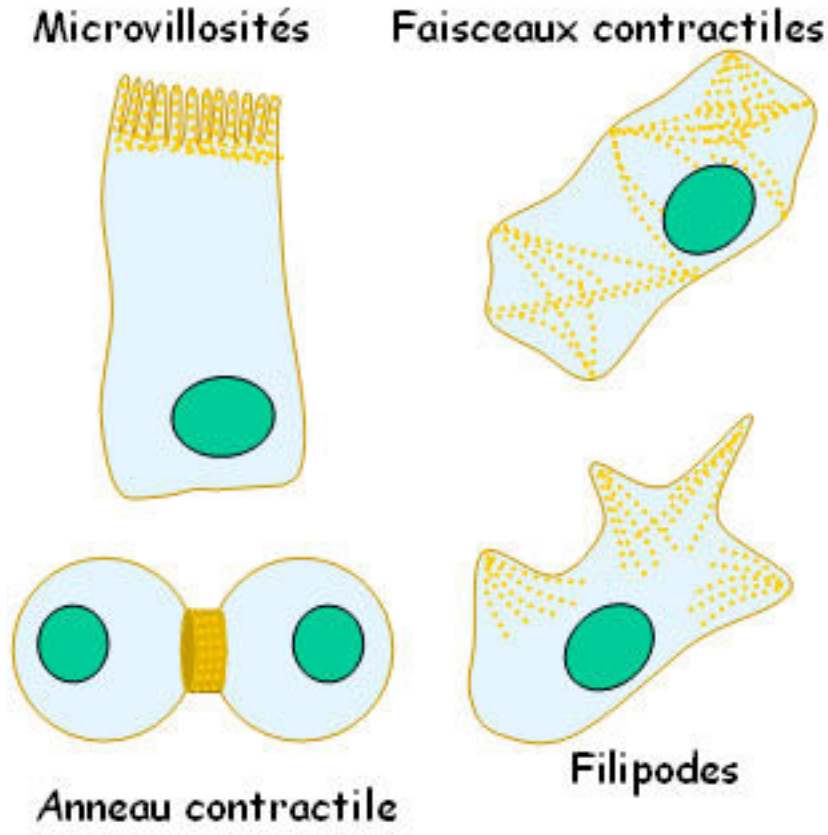
Nature Reviews | Molecular Cell Biology

- Déplacement des chromosomes

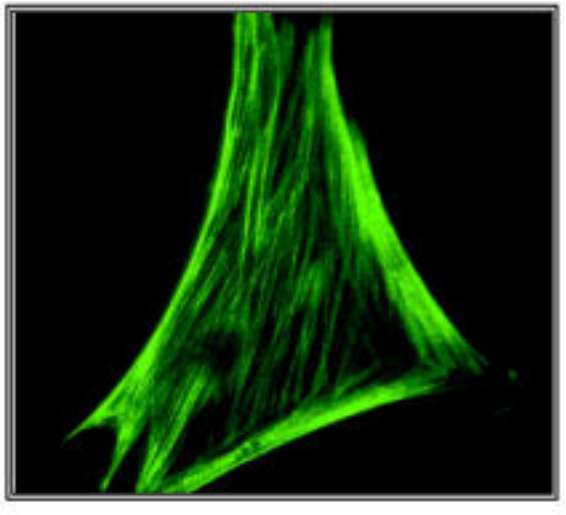


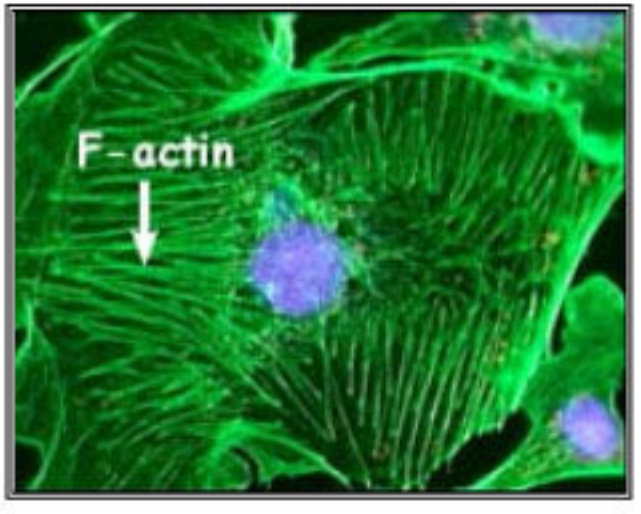
Trends in Cell Biology 2001; 11: 413-419

Microfilaments d'actine

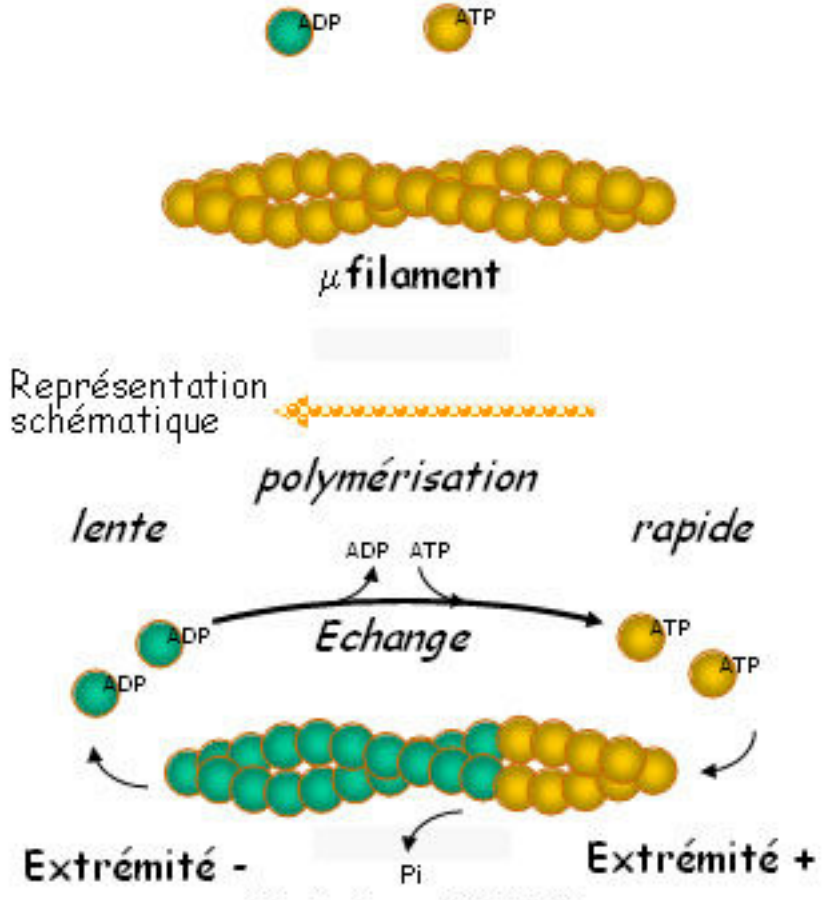


- Microfilaments d'actine marqués par un anticorps fluorescent



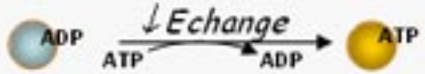
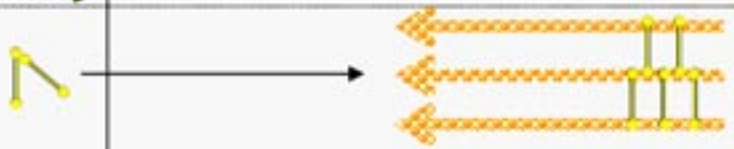


Structure

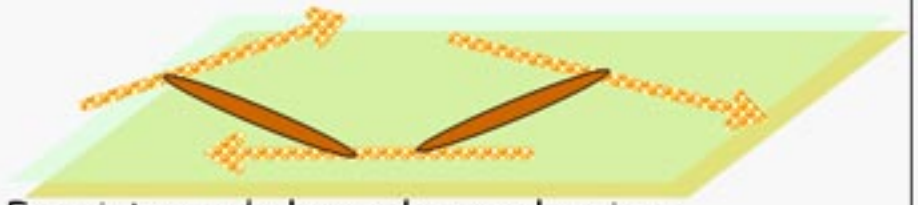


Hydrolyse de l'ATP
↓de l'affinité de liaison
dépolymérisation

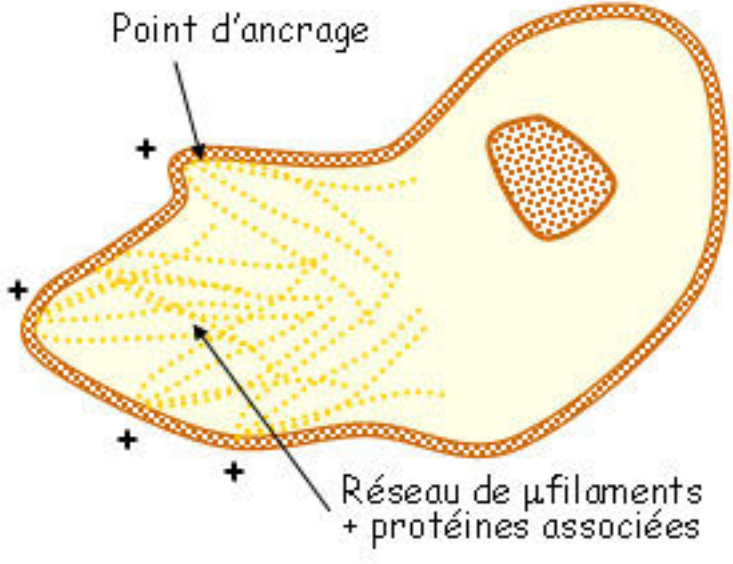
Protéines associées

Protéines	Interaction avec actine	Conséquences
Contrôle polymérisation/dépolymérisation		
Thymosine		Blocage de la polymérisation
Profiline		Diminution de la polymérisation
Caldesmon		Stabilisation des polymères
Organisation des filaments		
Tropomyosine		Stabilisation des µfilaments
e		Formation faisceaux larges
α actinine		Formation faisceaux serrés
Fimbrine		Formation faisceaux serrés
Villine		(microvillosités)
Filamine		Formation de réseaux

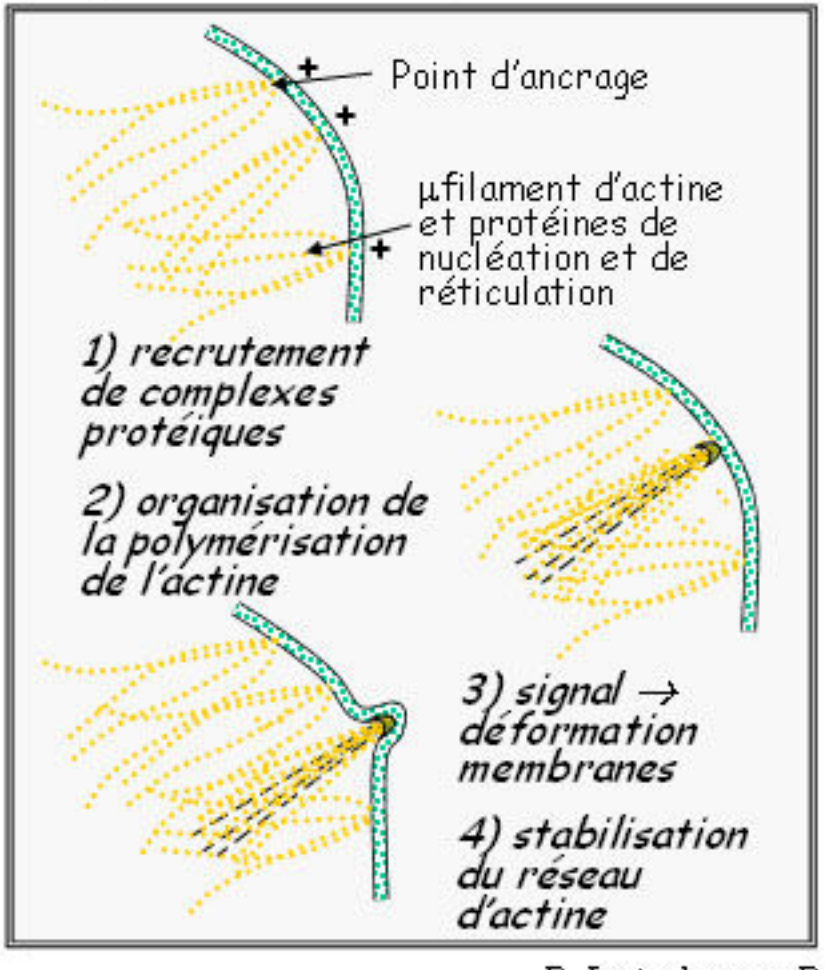
suite

Protéines	Interaction avec actine	Conséquences
Destruction des µfilaments		
Gelsoline		Fragmentation des polymères Transition gel « sol
Mouvements intracellulaires - Contraction		
Myosine I		Déplacement de vésicules
Myosine II		Contraction musculaire
Attachement à la membrane plasmique		
Complexes de nucléation		**Formation des filipodes →déplacement cellulaire**
Spectrine Dystrophine		Nbses Ë (hématies..) Muscles squelettiques

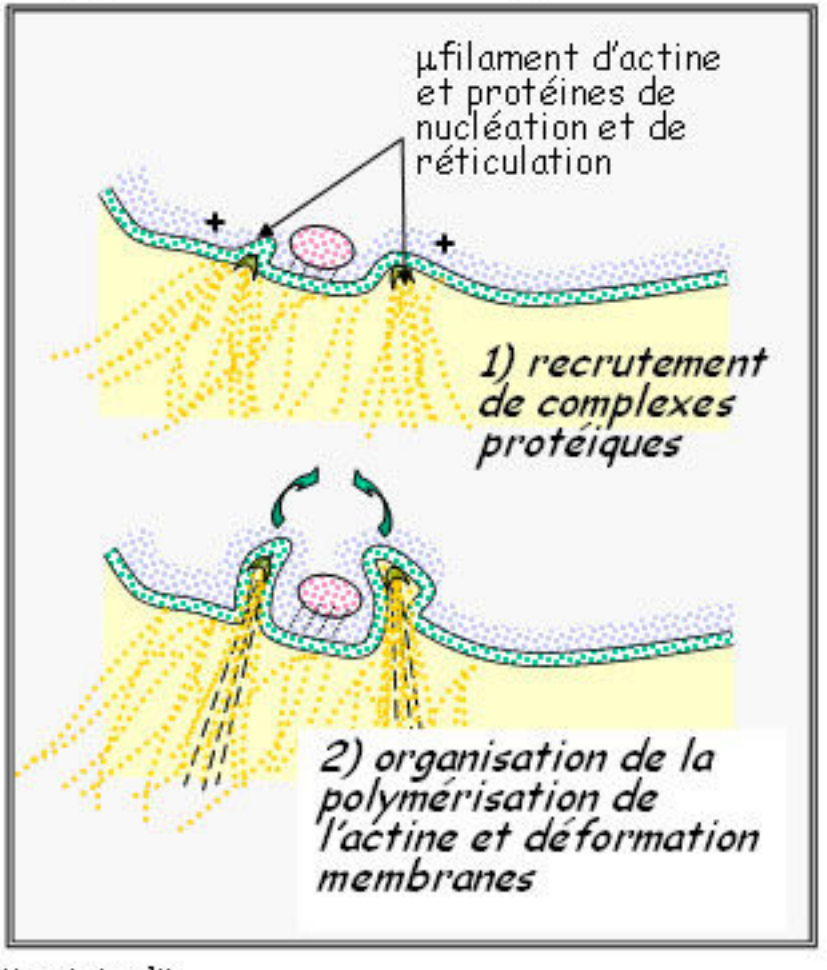
Cortex cellulaire



- Mécanisme d'expansion

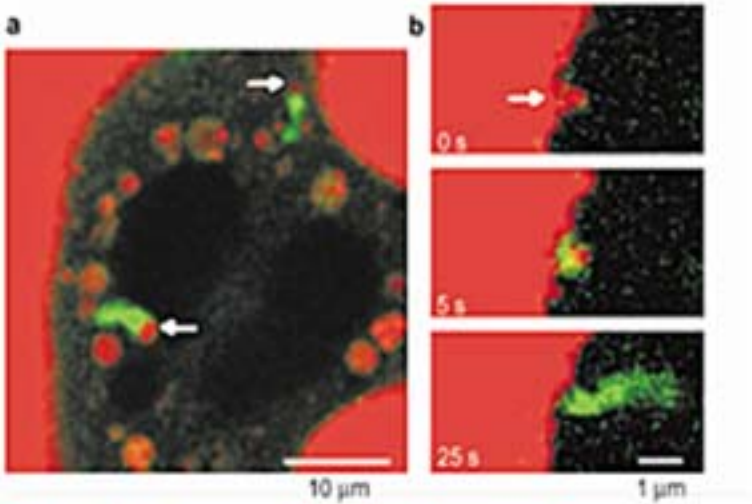


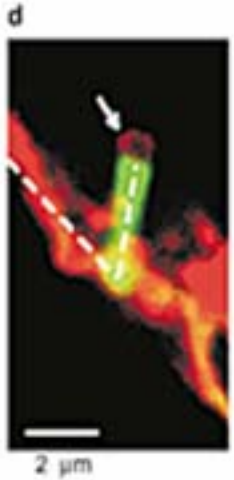
- Mécanisme d'endocytose

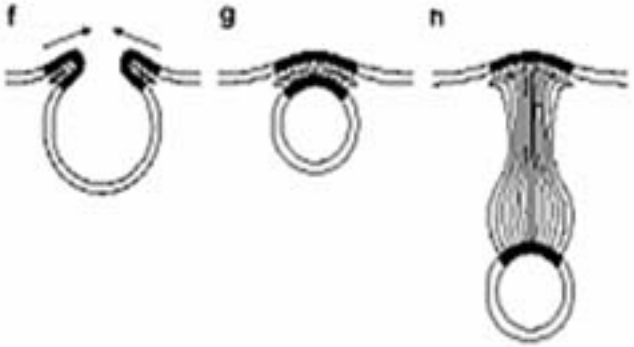


Endocytose

- Formation de la queue d'actine

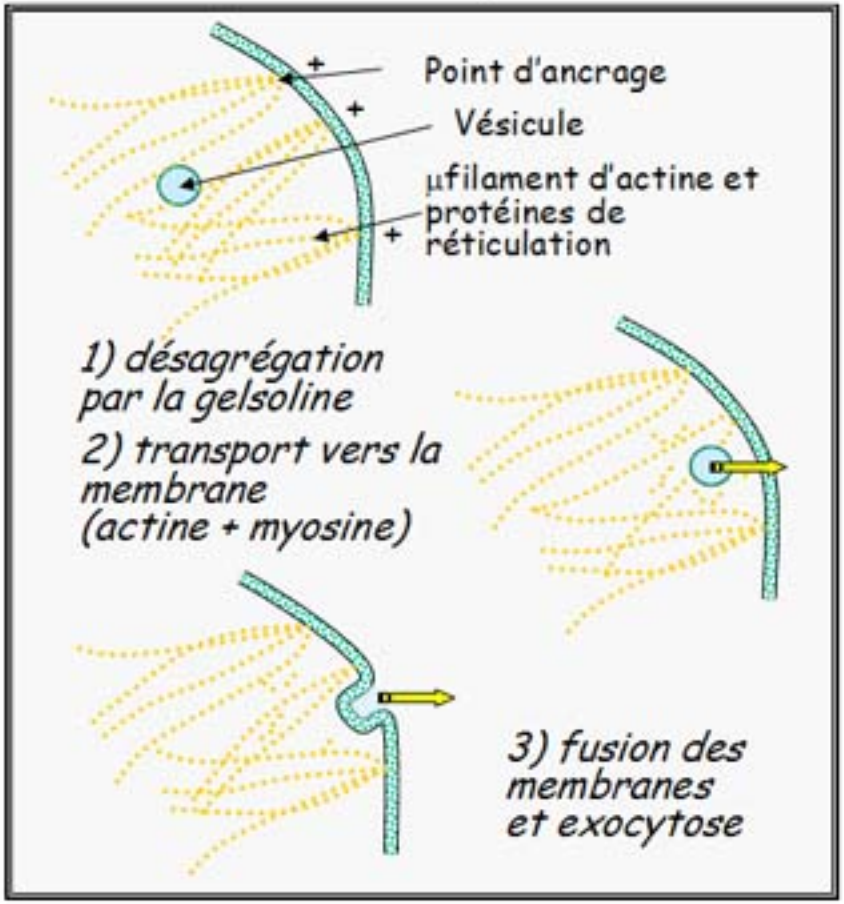




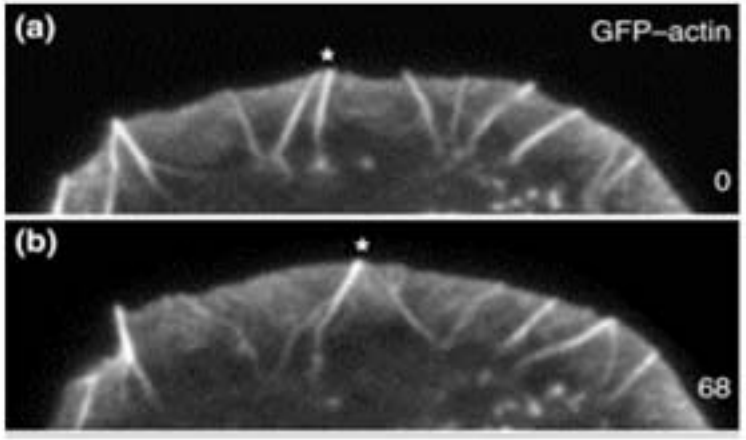


Nature Cell Biology 1999;1:72-74

- Mécanisme d'exocytose



P. Lustenberger. Reproduction interdite



Trends in Cell Biology 2002;12:112
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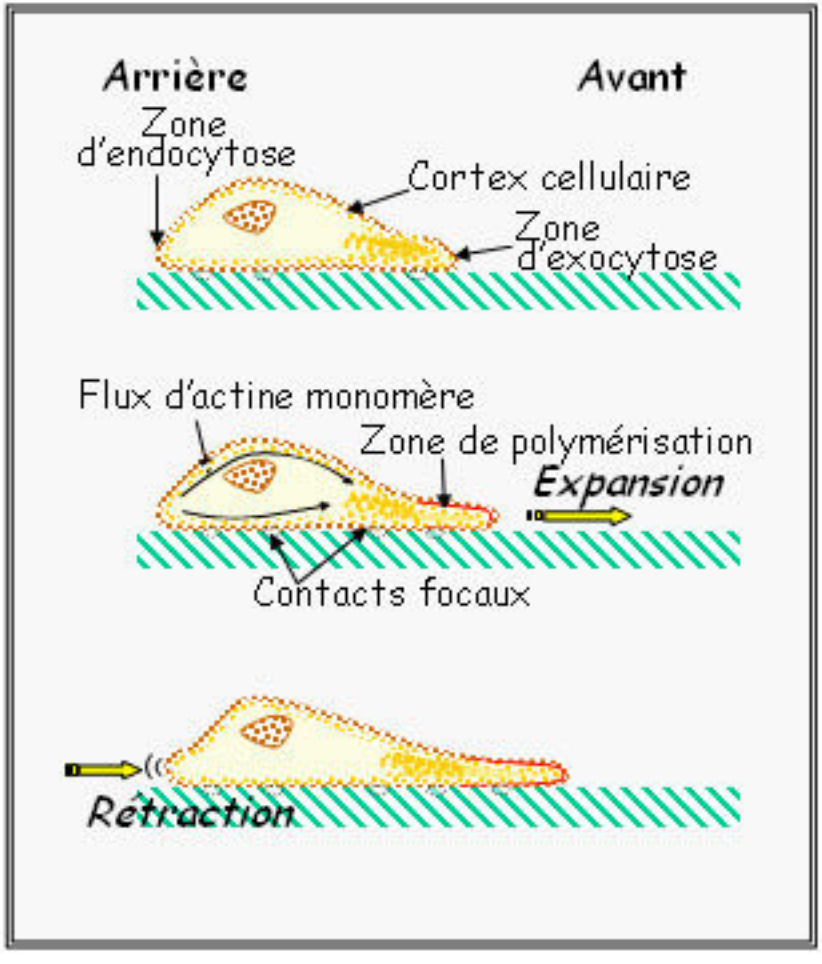
- Déplacement cellulaire

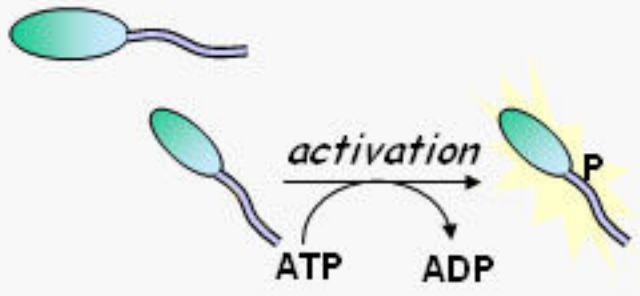


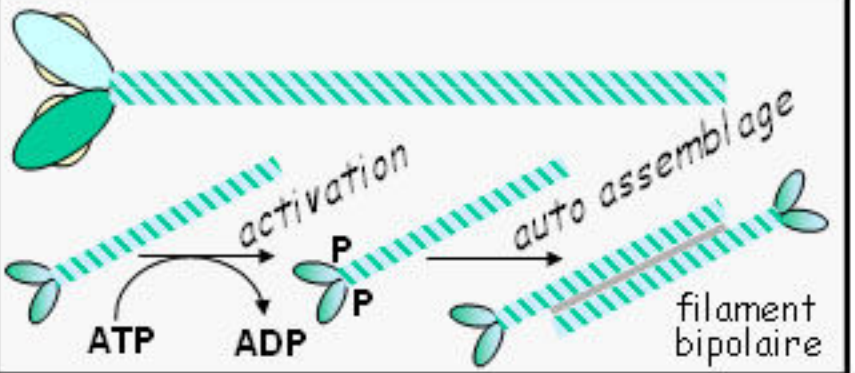
Appareils contractiles des cellules

Myosine I (110 kDa)	**Myosine II** (500 kDa)
Monomère	Dimère de chaînes lourdes + protéines associées

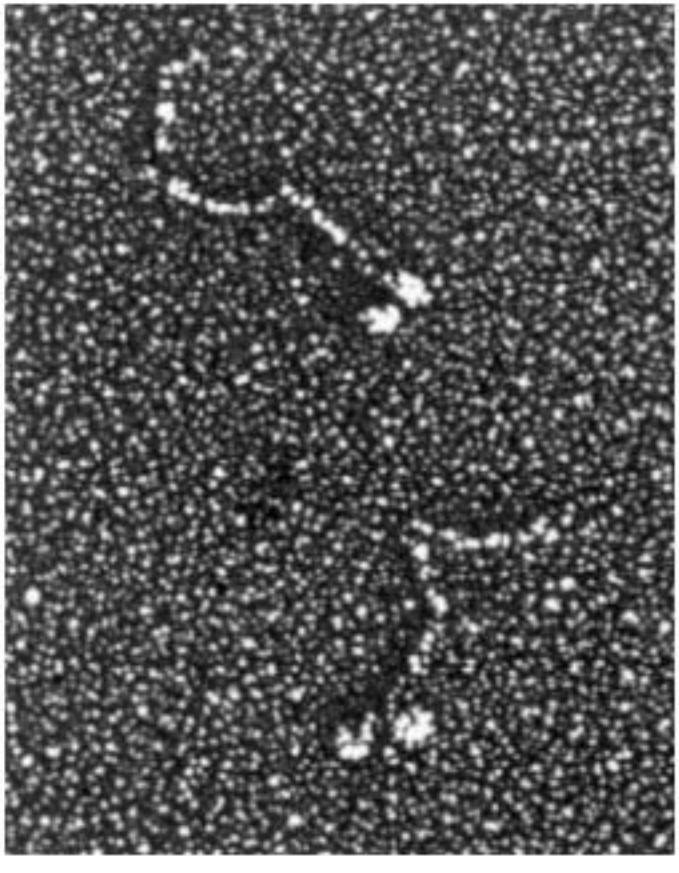
Caractères communs

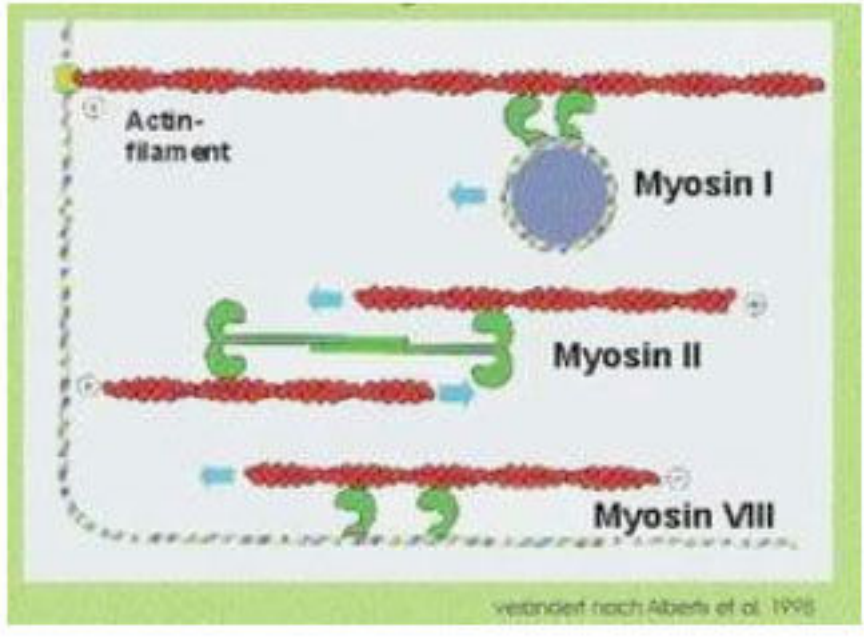
- Ca^{2+} et ATP dépendantes
- Activation par phosphorylation (kinase Ca-dépendante)
- Tête globulaire à activité ATPasique = moteur moléculaire
- Hydrolyse de l'ATP → transconformation et déplacement de la tête le long du μfilament d'actine vers extrémité +



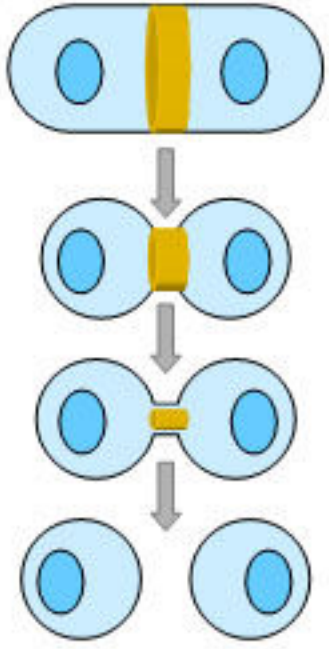


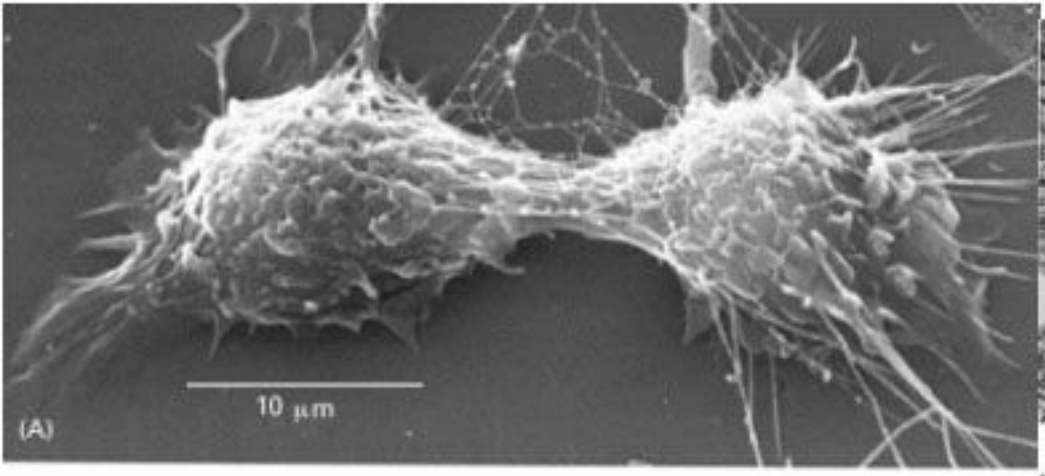
Myosines

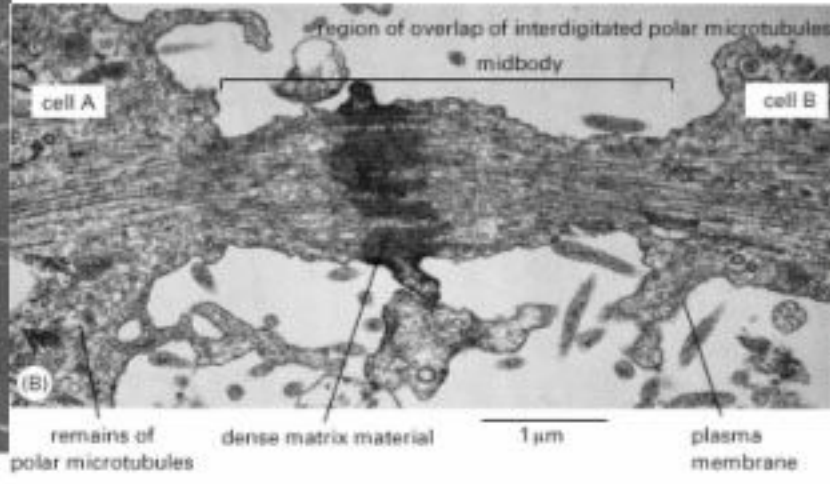




Appareil contractile des cellules non musculaires

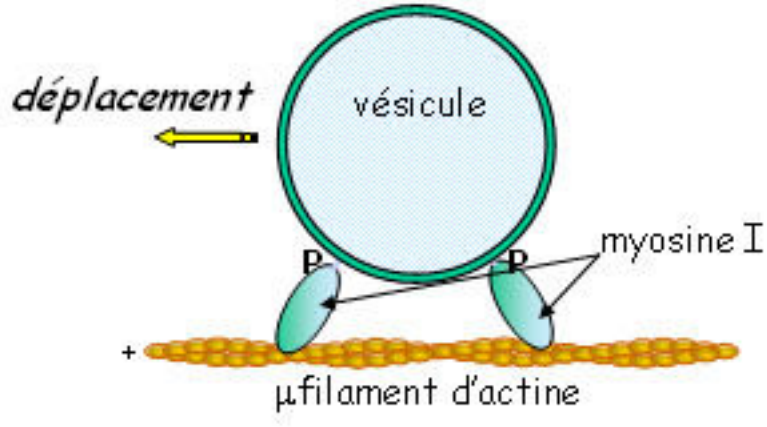




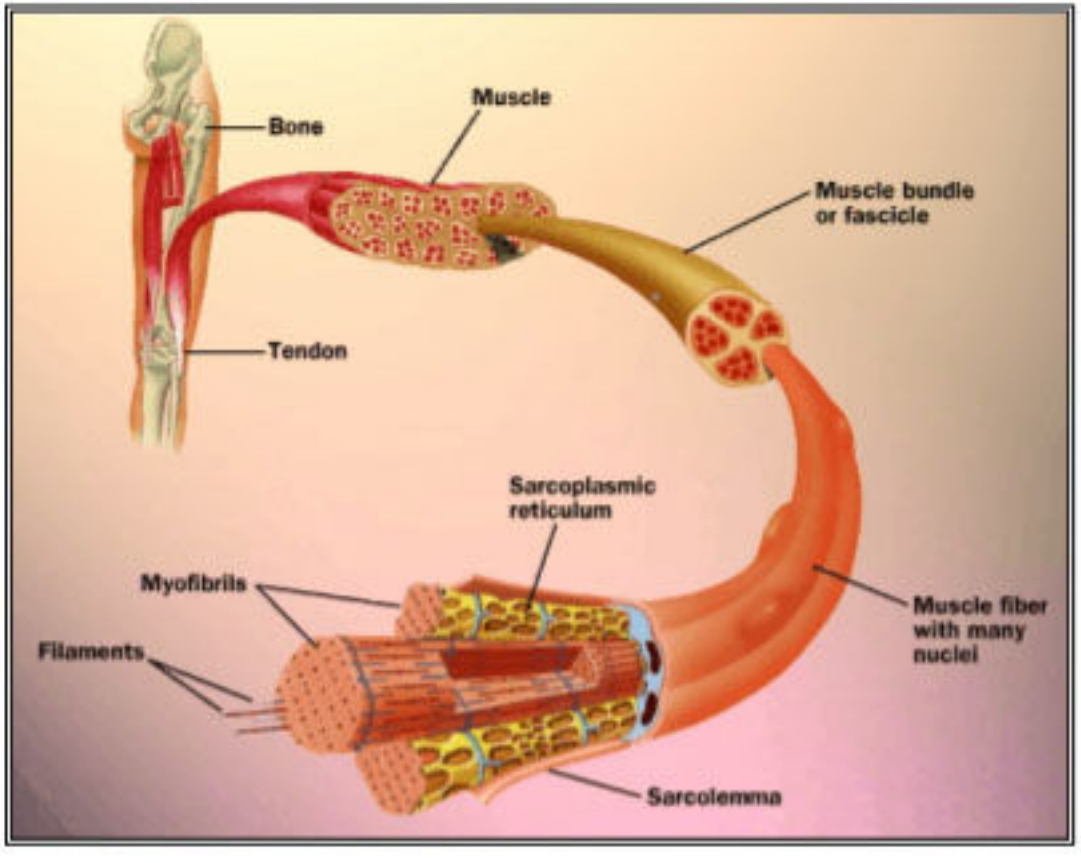


Molecular Biology of the Cell, 3rd edn

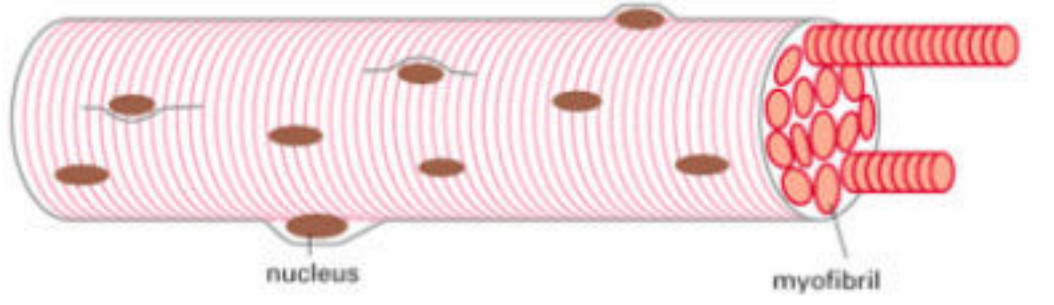
Déplacement des vésicules



Appareil contractile des cellules musculaires

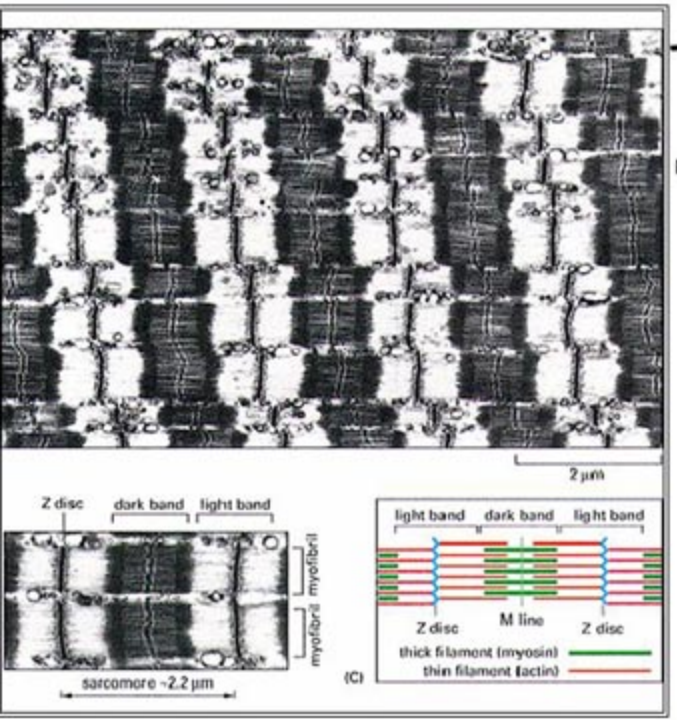


Cellule musculaire

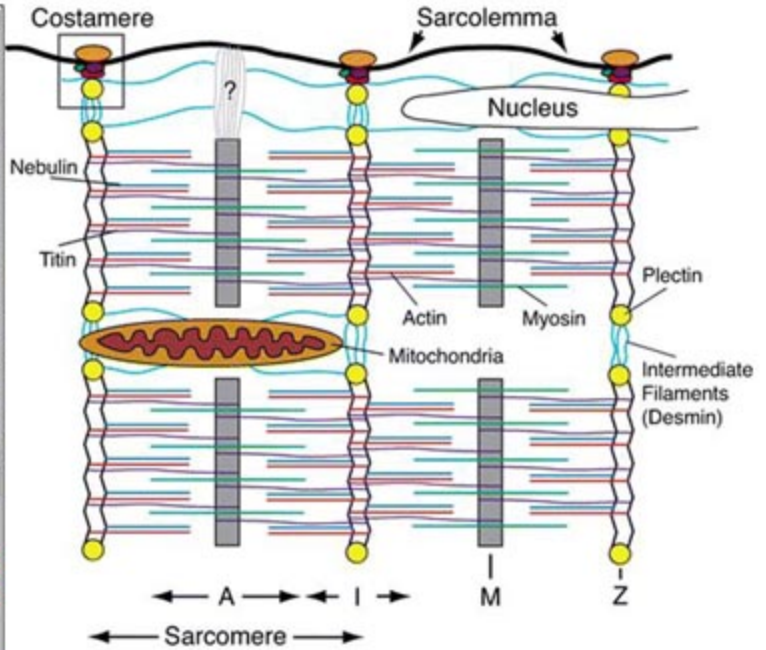


Molecular Biology of the Cell, 3rd edn

Coupe de muscle en microscopie électronique



Molecular biology of the Cell 3rd Ed.



Ann Rev Cell Dev Biology, 2002; 18: 637-706

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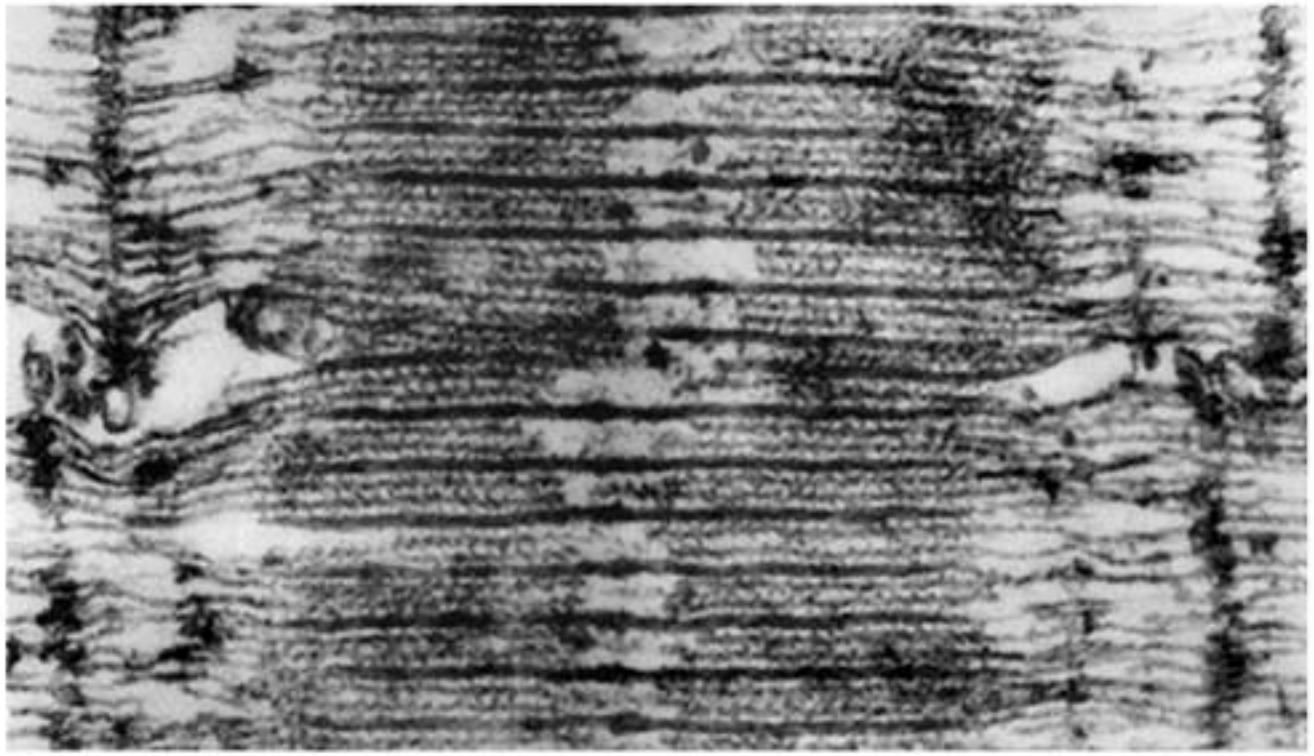
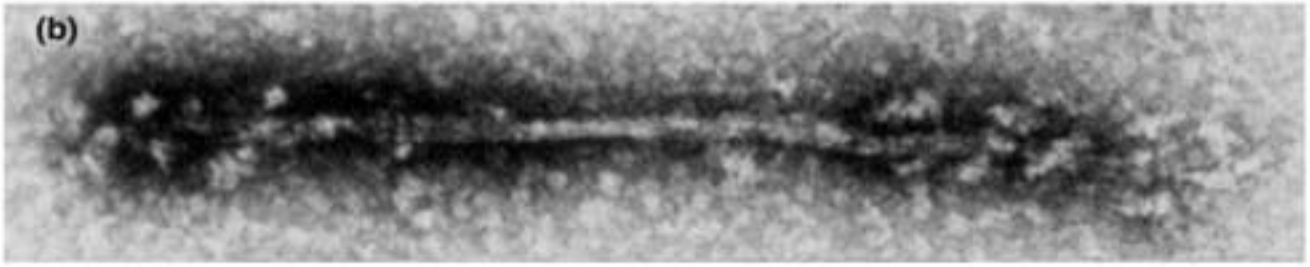
Organisation du sarcomère (1)

sarcomère

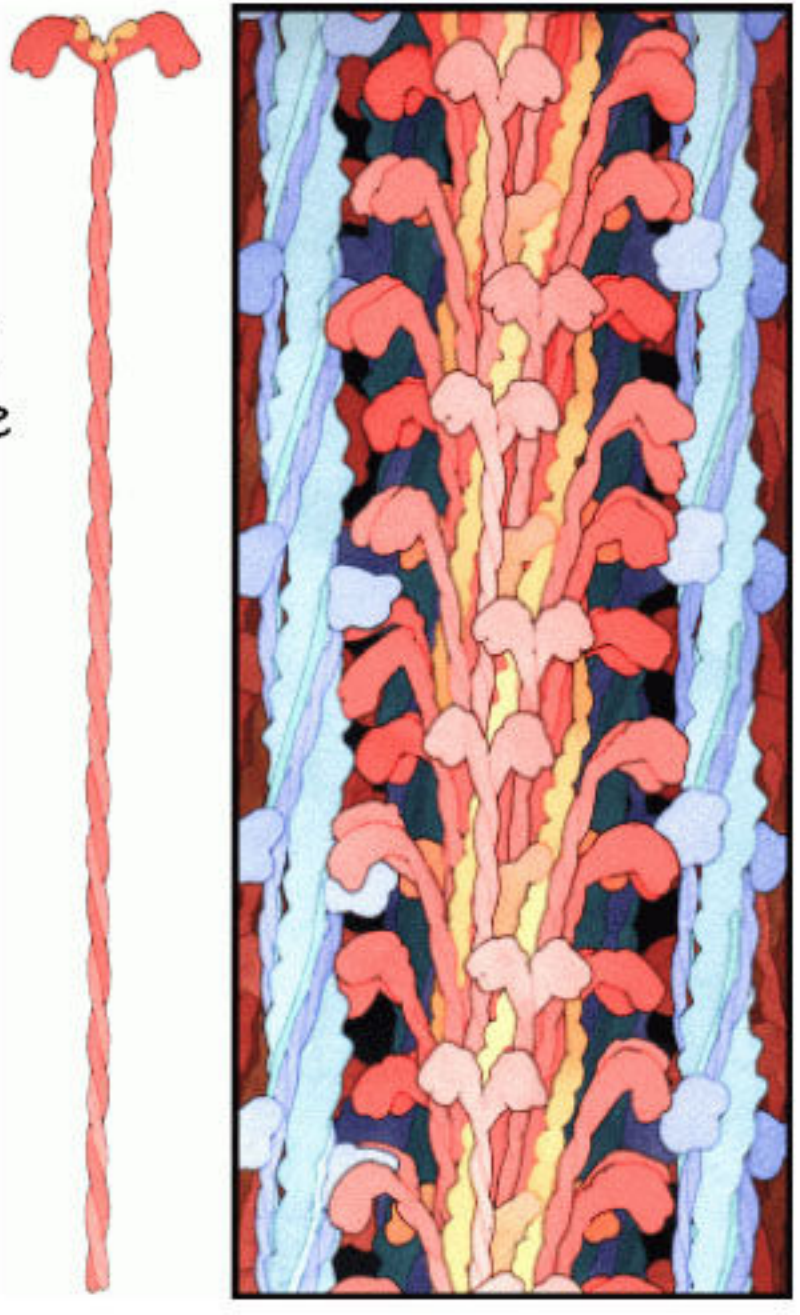


Trends in Cell Biology
2002;12:243

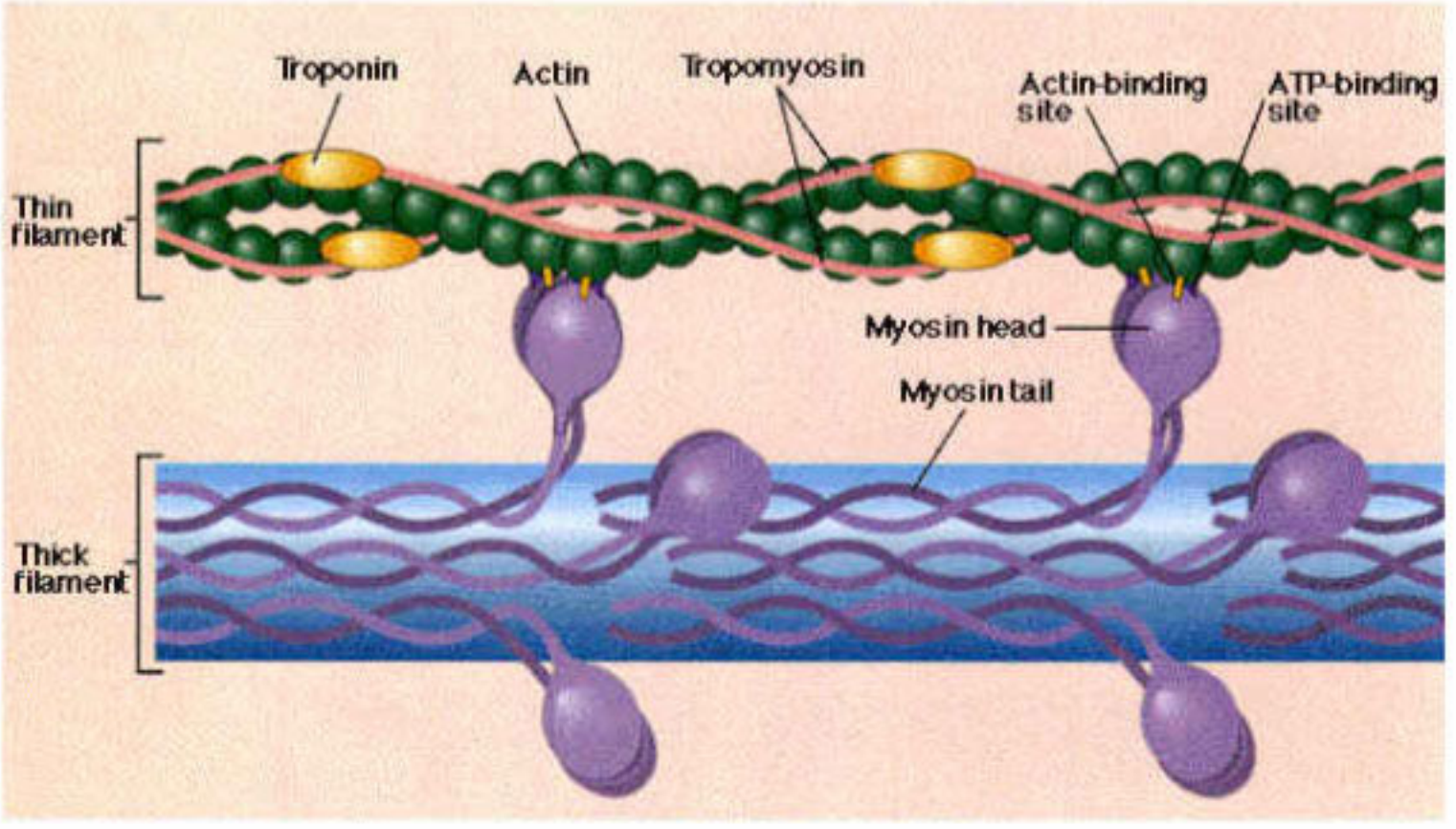
myosine

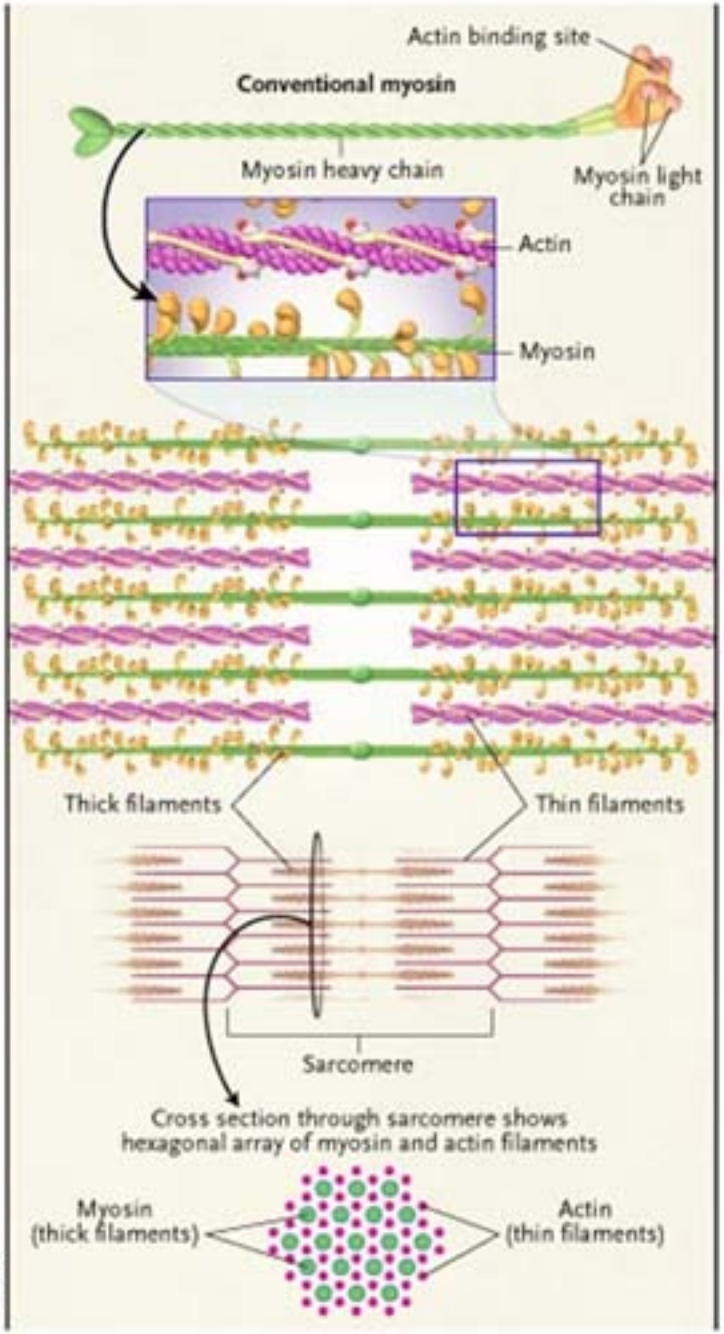


- Représentation des filaments de myosine II et des filaments d'actine dans une cellule musculaire



Accrochage aux filaments d'actine

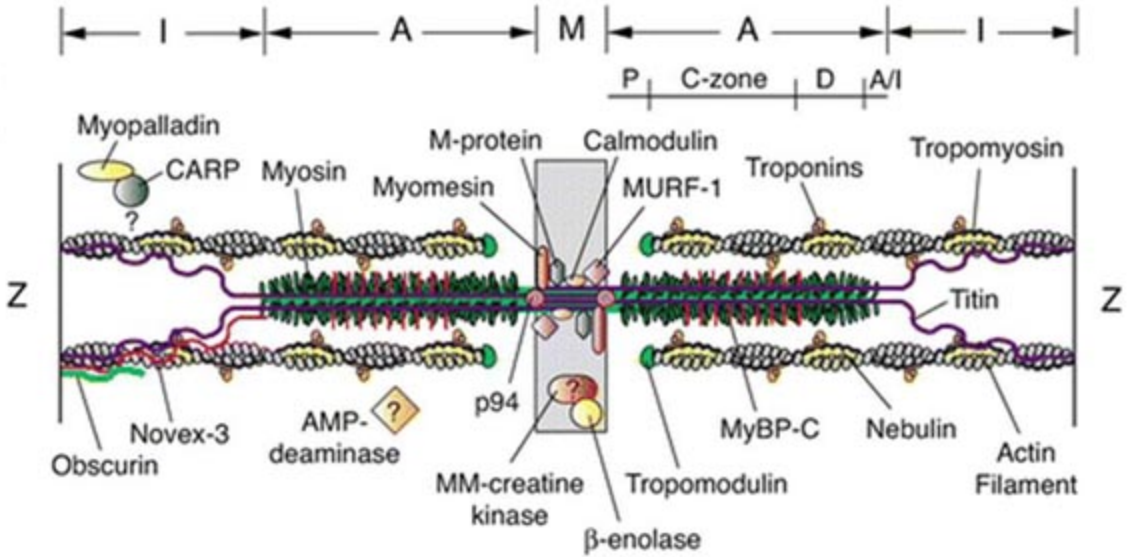




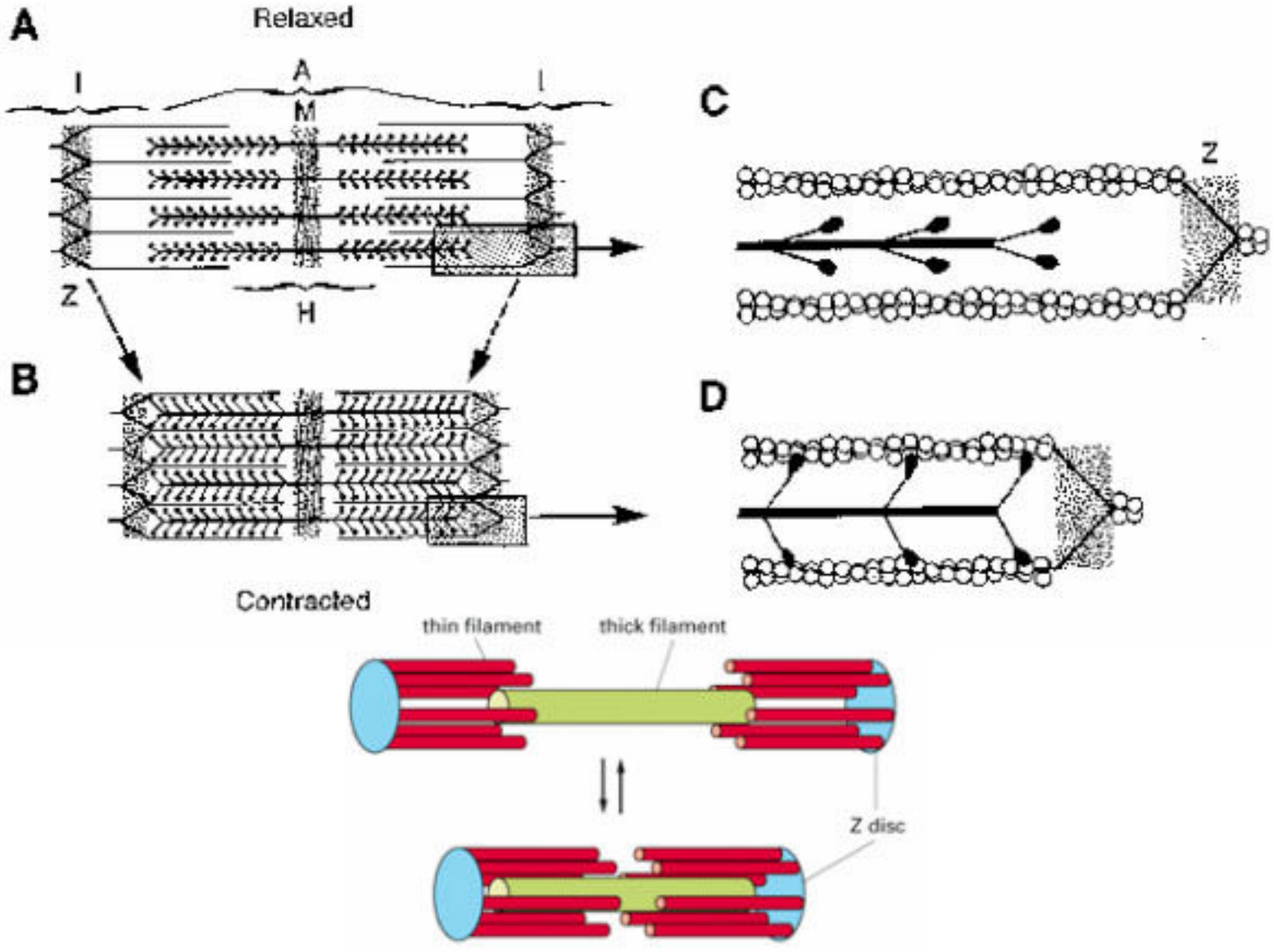
NEJM 2004; 351:424-426

Organisation du sarcomère (2)

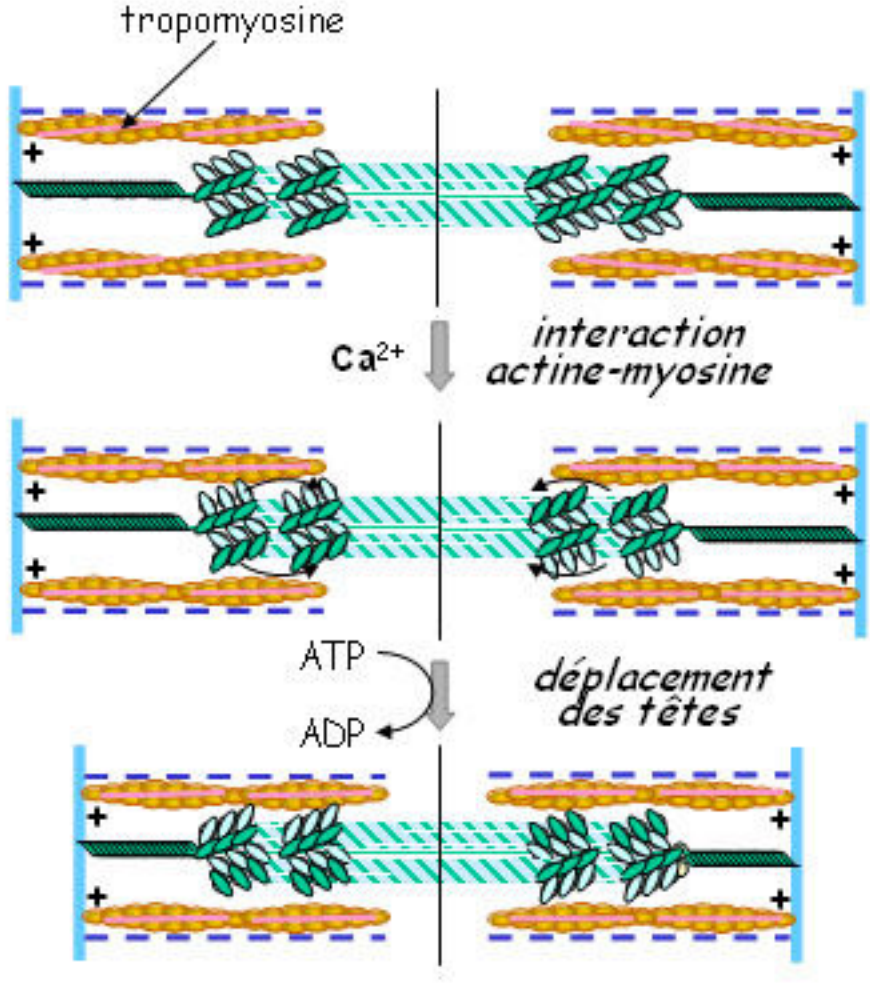
Ann Rev Cell Dev Biology, 2002; 18: 637-706



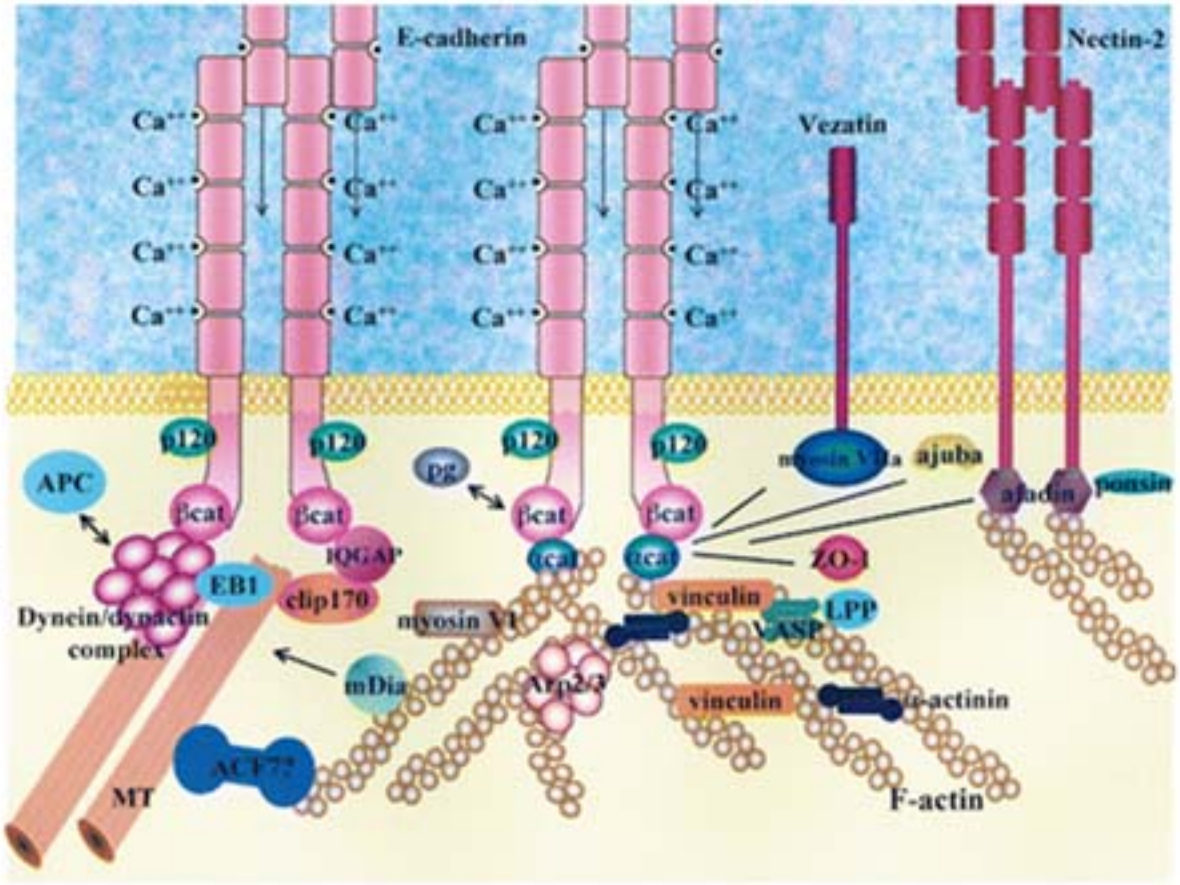
❖ Autre représentation schématique



Aspect moléculaire de la contraction

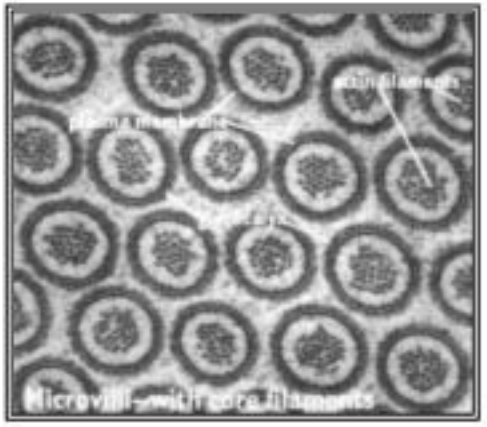


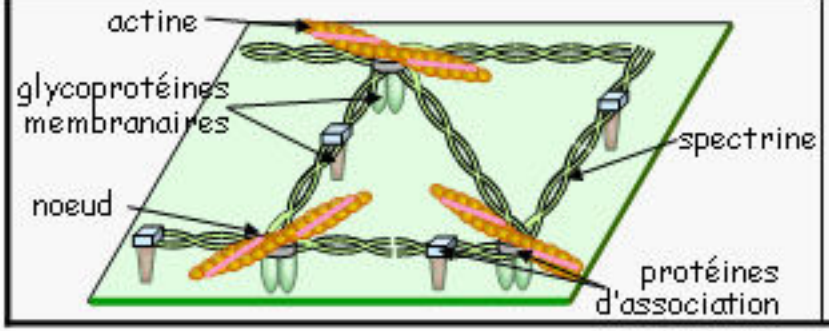
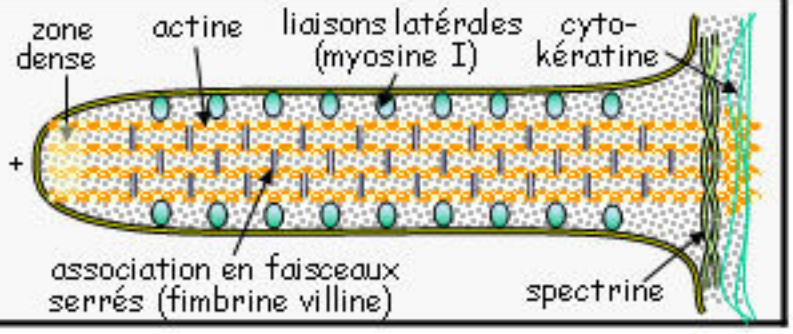
Interactions cytosquelette-membrane plasmique



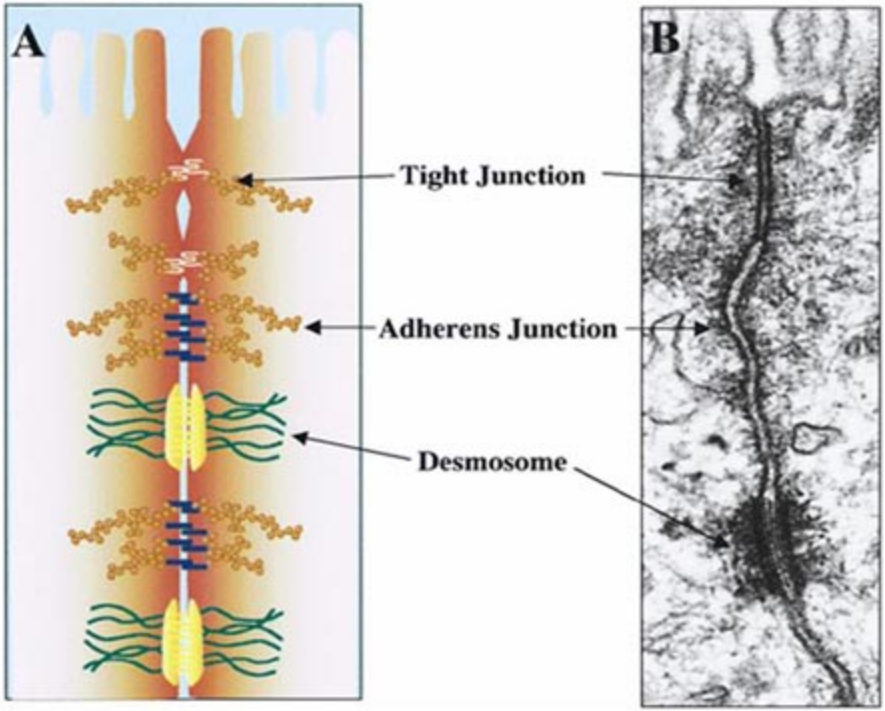
Cell 2003;112:535-546

Cellules isolées



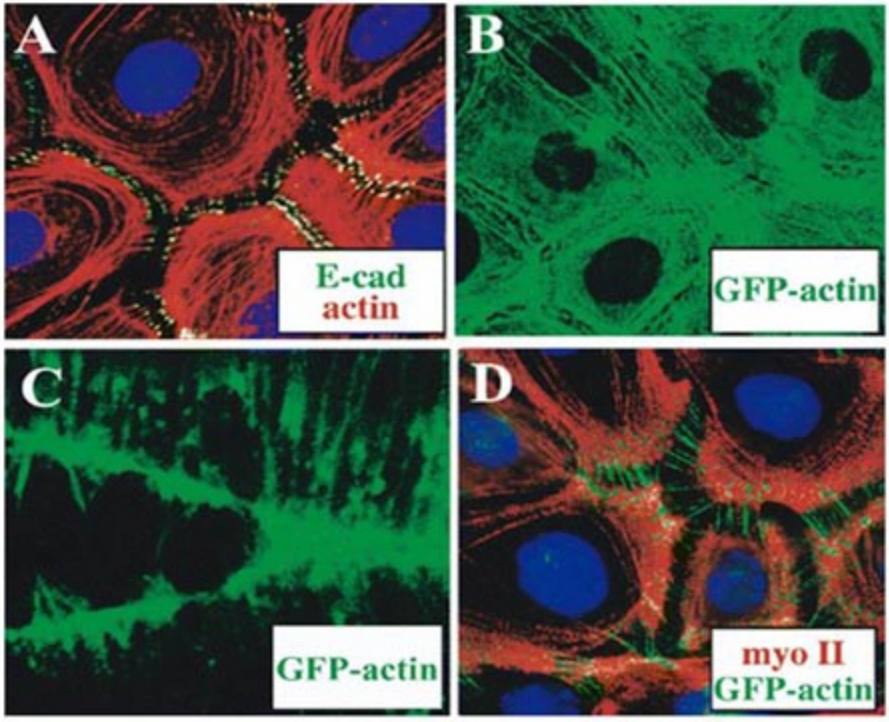
Hématies - squelette	Entérocytes - µvillosités
Organisation **Réseau grillagé de spectrine** **Liaison avec protéines membranaires** (glycophorine, bande 3) **Rôles** **•Forme et déformabilité des hématies**	**Organisation** **Squelette de µfilaments d'actine** **ancrage au sommet** (zone dense) **Base : réseau spectrine + f.i. cytokérat.** **Pontage latéral : myosine I avec memb.** **faisceaux serrés**
	

Classification des jonctions cellulaires



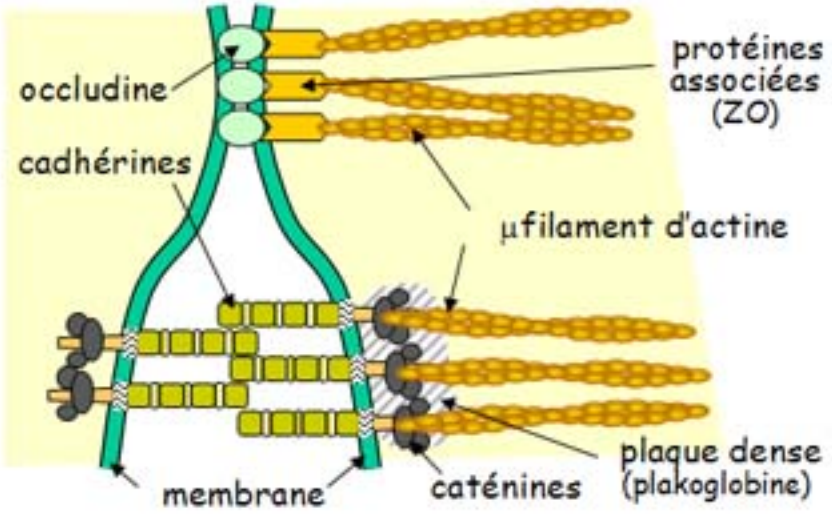
Cell 2003;112:535-546

Exemples de jonctions cellulaires/actine

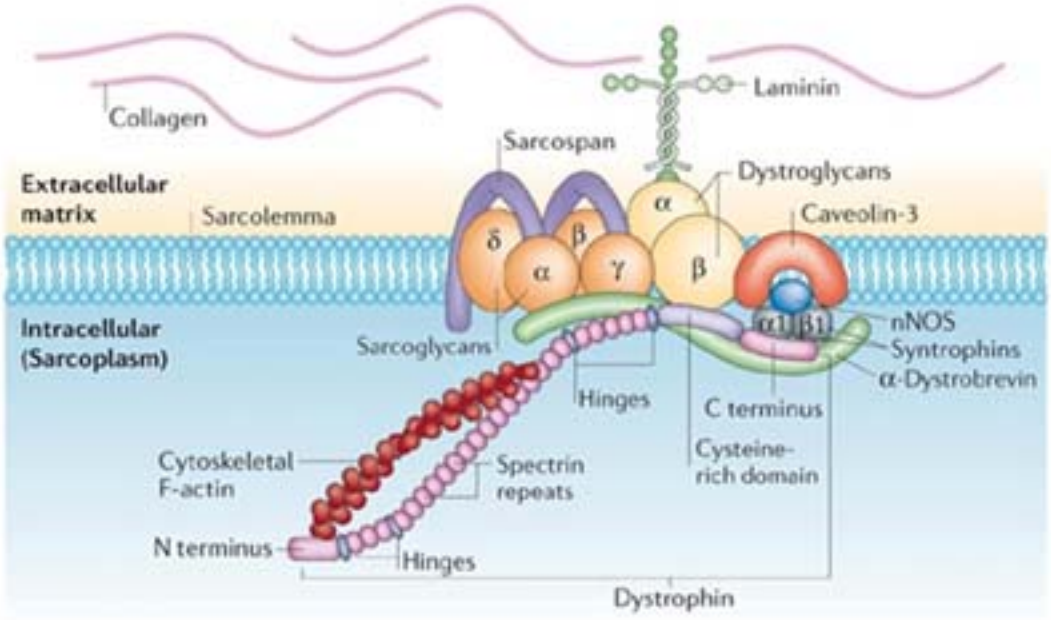


Cell 2003;112:535-546

Jonctions intercellulaires

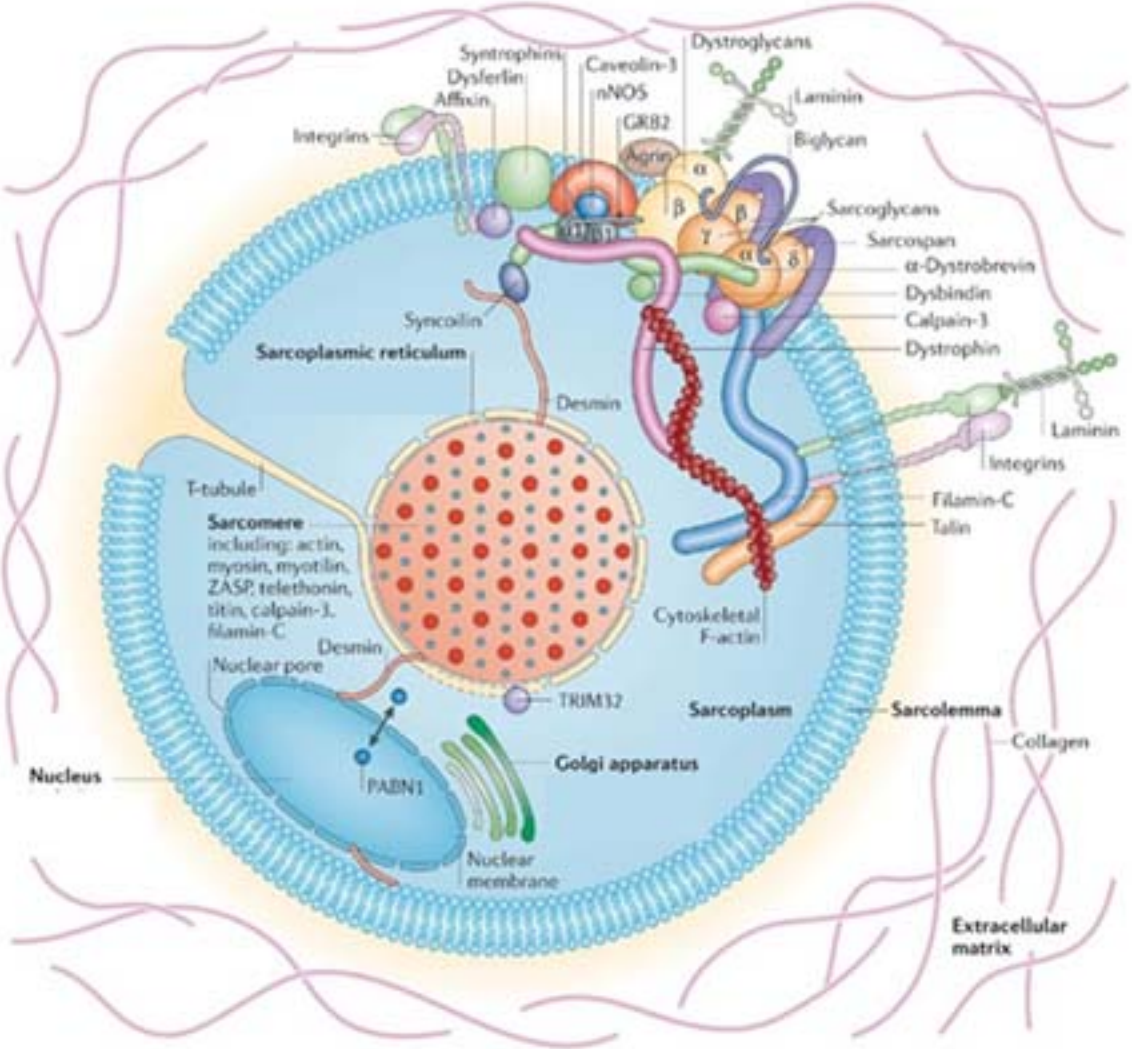


Interactions avec la lame basale



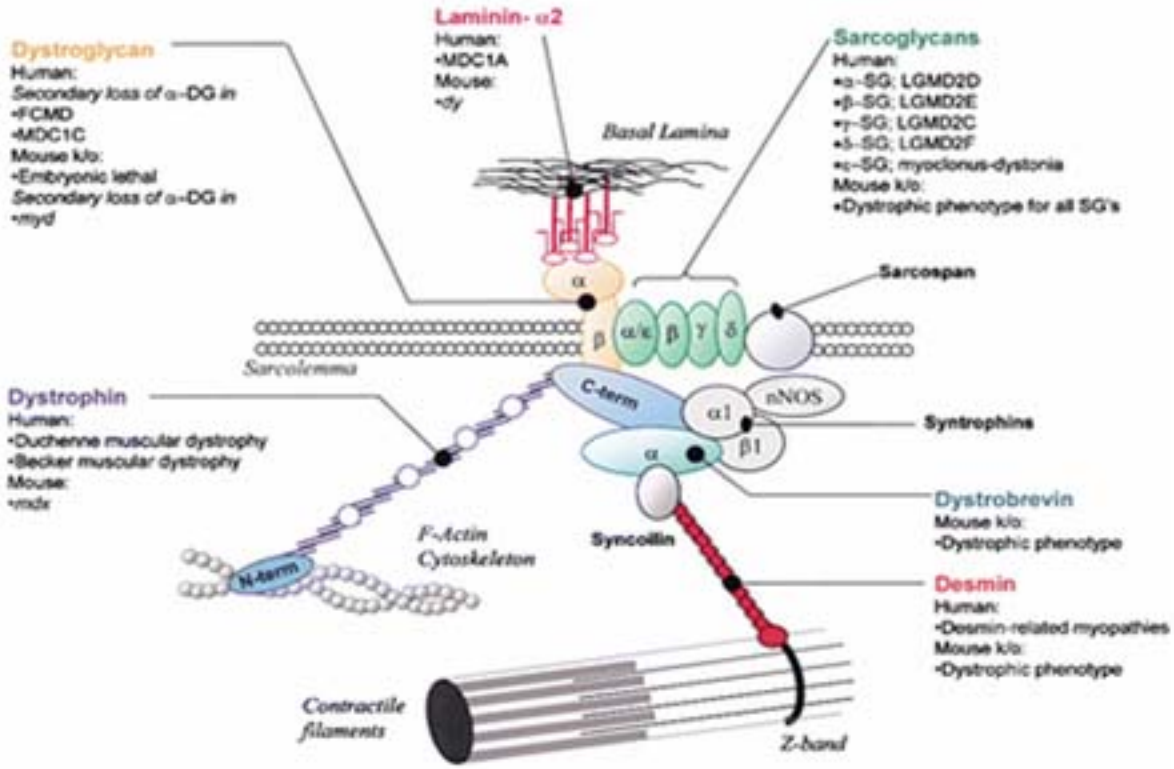
Nature Reviews Molecular Cell Biology 7, 762-773 (2006)

Autre représentation de la dystrophine



Nature Reviews M

Mécanismes moléculaires des maladies neuro-musculaires génétiques



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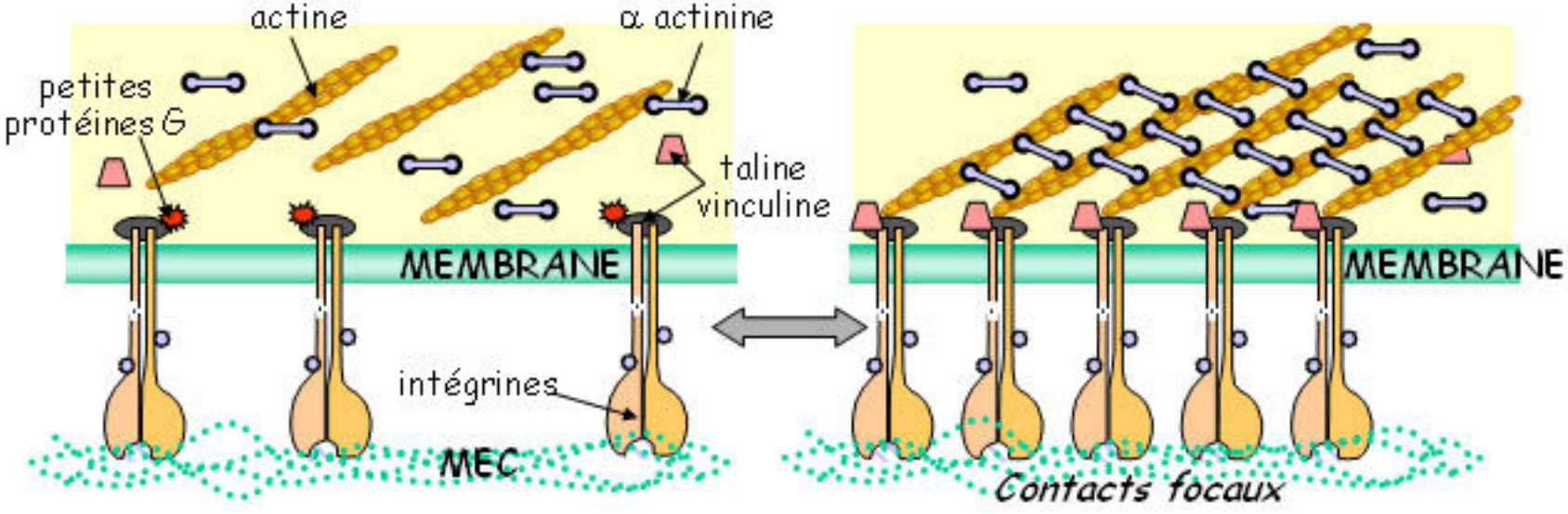
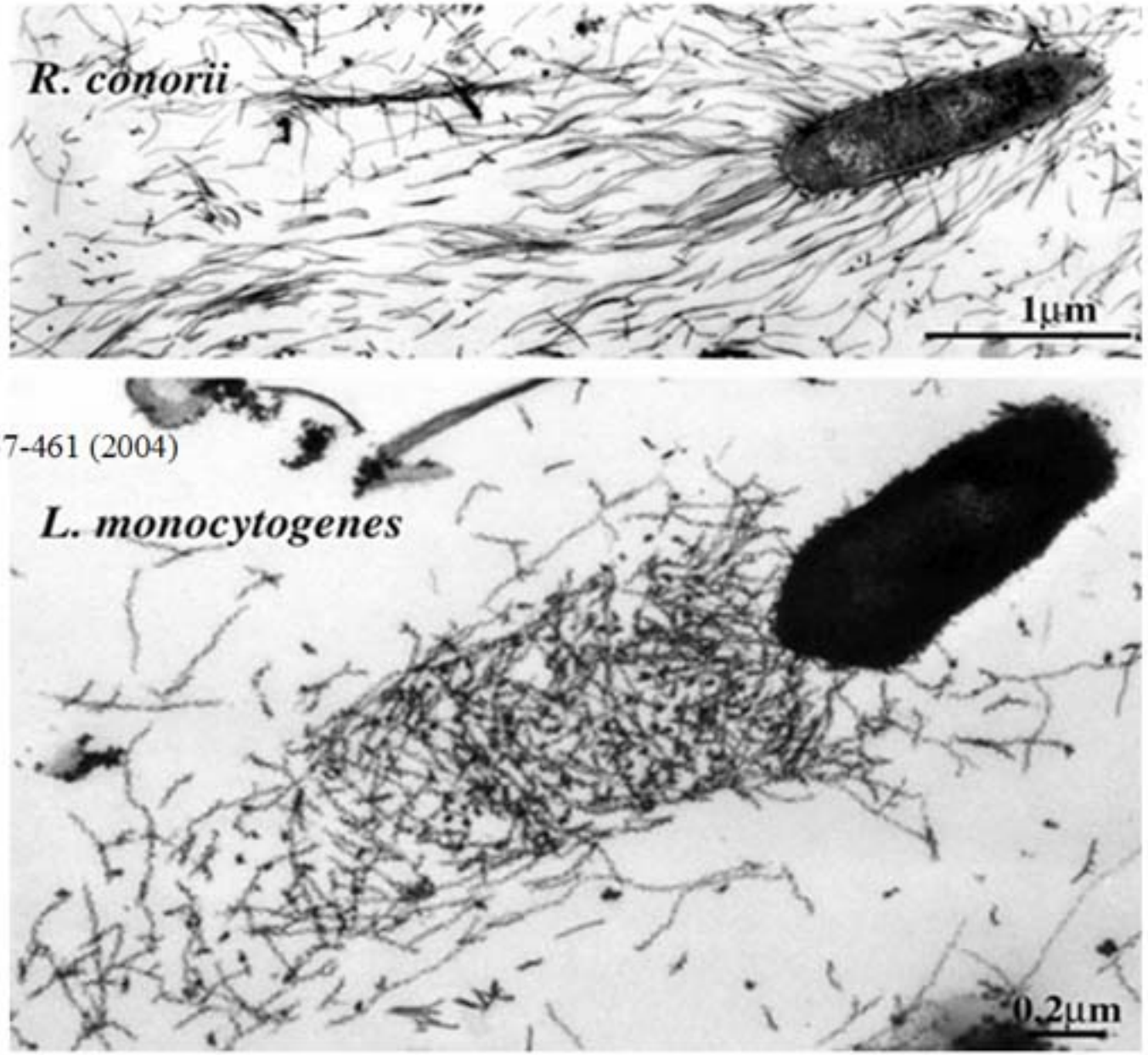
Interactions avec la MEC





Nature **427**, 457-461 (2004)

- Entrée et sortie de Listeria