Cell and Molecular Biology

Ninth Edition

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Chapter 9

The Cytoskeleton and Cell Motility

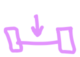
9.1 | Overview of the Cytoskeleton

- Properties of Cytoskeletal Components
- **Cytoskeleton**: "skeletal system" of a eukaryotic cell
  (العظمي ... الجهاز)
- Composed of three filamentous structures:
  - **Microtubules**
  - **Actin filaments**
  - **Intermediate filaments**

Microfilaments (Actin filaments) (Actin)
tensile strength
Special movement
انو ما تتفكك الخلية عن بعضها
لو صار في شد الخلية

لو شديت هدول ما بنفكو عن بعض

Intermediate filaments (Keratin)
tensile strength

Microtubules
Compression strength
movement
هون لو ضغطت الخلية ما بتطعج

لدائرة هون ما بطعج الخيط

9.1 | Overview of the Cytoskeleton (1 of 2)

Properties of Cytoskeletal Components

TABLE 9.1 Properties of Microtubules, Intermediate Filaments, and Actin Filaments

	Microtubules	Intermediate filaments	Actin filaments
Subunits incorporated into polymer	GTP-αβ-tubulin heterodimer	~70 different proteins, likely incorporated as tetramers	ATP-actin monomers
Preferential site of incorporation	+ End (β-tubulin)	Internal	+ End (barbed)
Polarity	Yes	No	Yes
Enzymatic activity	GTPase	None	ATPase
Motor proteins	Kinesins, dyneins	None	Myosins
Major group of associated proteins	MAPs	Plakins	Actin-binding proteins
Structure	Stiff, hollow, inextensible tube	Tough, flexible, extensible filament	Flexible, inextensible helical filament
Dimensions	25 nm outer diam.	10–12 nm diameter	8 nm diam.
Distribution	All eukaroytes	Animals	All eukaryotes
Primary functions	Support, intracellular transport, cell organization	Structural support, mechanical strength	Motility, contractility, intracellular transport
Subcellular distribution	Cytoplasm	Cytoplasm + nucleus	Cytoplasm

9.1 | Overview of the Cytoskeleton (2 of 2)

Functions of Cytoskeletal Components

- *Provides structural support* and maintains cell shape
- تحديد مواقع *Positions* various organelles in the cell
- *Directs the movement* of materials and organelles within the cell
- Generates forces needed for *cellular locomotion* ← الحركة
- Makes up an essential part of the *cell division* machinery

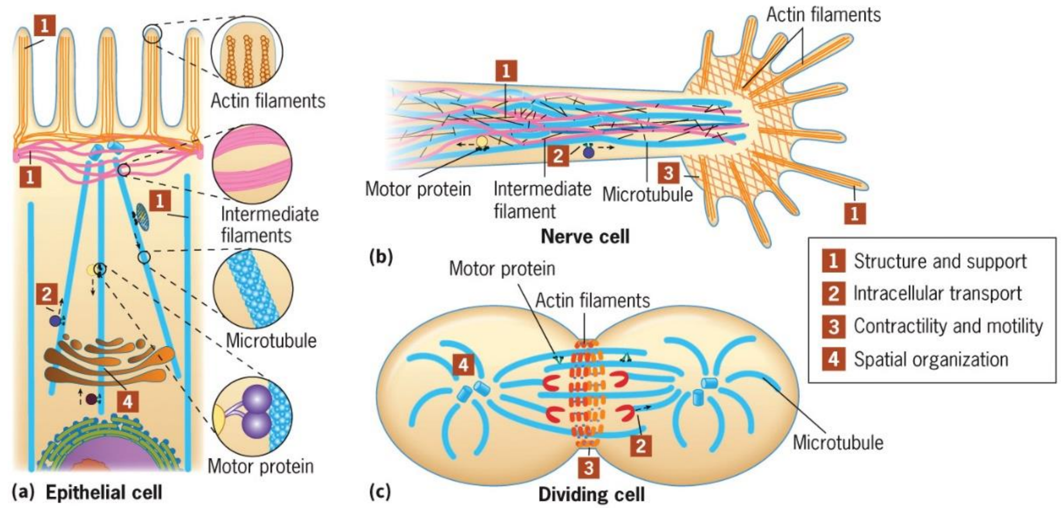


Fig. 9.1 Functions of the cytoskeleton

9.2 | Structure and Function of Microtubules (1 of 5)

Structure and Composition of Microtubules

- Hollow, relatively rigid, tubular (↱ Cylindrical structure)
- Assembled from the protein **tubulin**
- Microtubule proteins are arranged in longitudinal rows called **protofilaments**. (↱ they are a set of globular protein) (العمود الواحد)
- Microtubules have 13 protofilaments aligned side by side in a circular pattern within the wall of the tubule. (لـ بدي 13 عمود عشان اقدر اكون اسطوانة)

Non-Covalent interaction between protofilaments → between the tubules because reversible

Fig. 9.3a Electron micrograph of microtubules

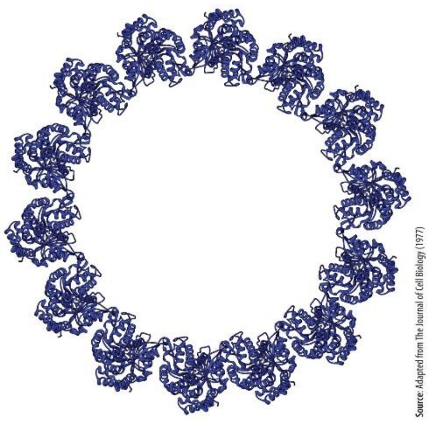


Fig. 9.3b Cross section of a microtubule

9.2 | Structure and Function of Microtubules (2 of 5)

Structure and Composition of Microtubules

Protofilaments are assembled from dimeric building blocks consisting of one **α-tubulin** and one **β-tubulin** subunit. The tubulin subunits:

- Fit tightly together
- Organized in a linear array along the length of each protofilament
- Asymmetric (α-tubulin at one end and β-tubulin at the other) and polar (**plus end** terminated by a row of β-tubulin subunits and the **minus end** terminated by a row of α-tubulin subunits)

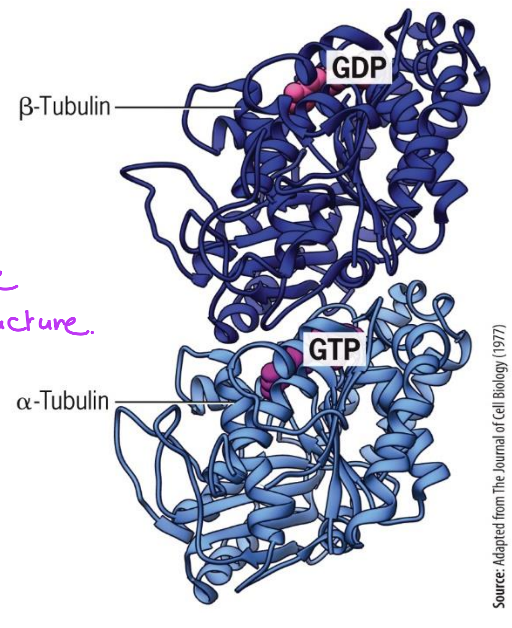


Fig 9.3c 3D structure of the αβ-tubulin heterodimer

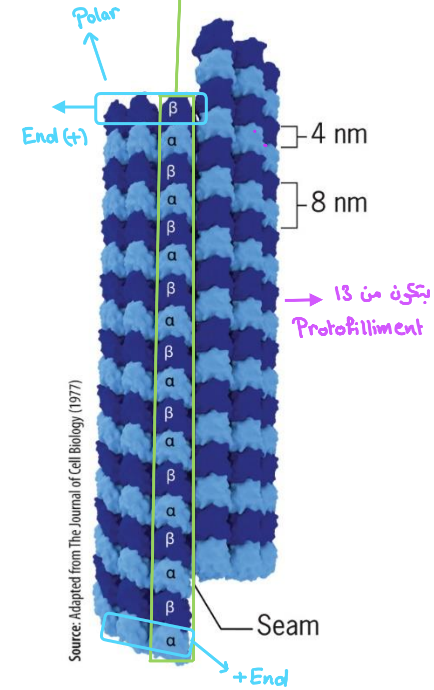


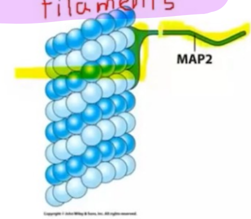
Fig 9.3d Longitudinal section of a microtubule

9.2 | Structure and Function of Microtubules (3 of 5)

Microtubule-Associated Proteins

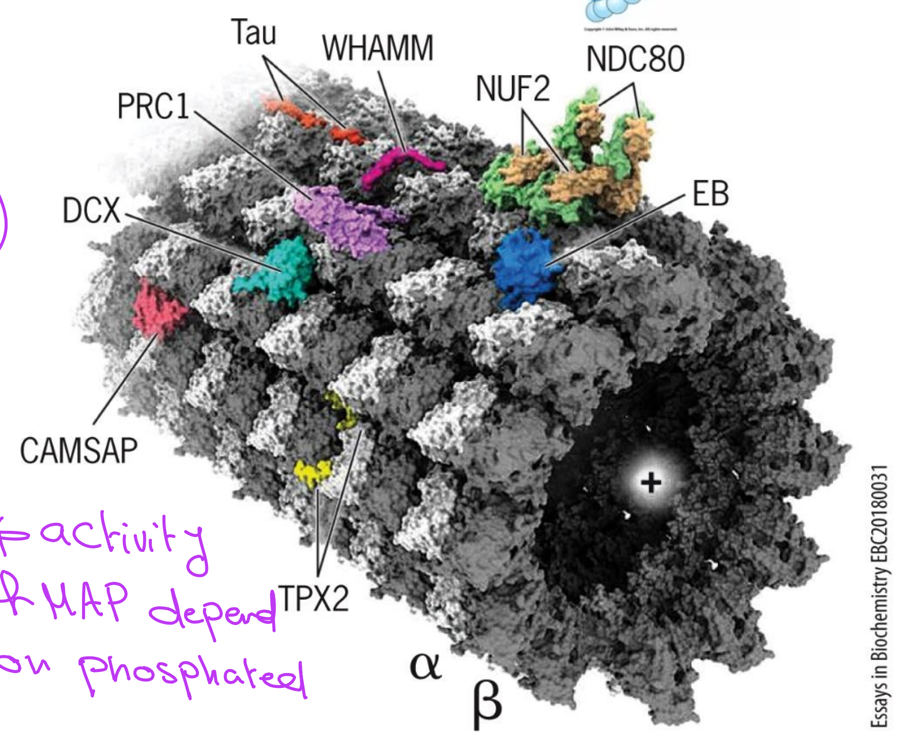
- Microtubules typically contain additional proteins, called **microtubule-associated proteins (MAPs)**. → 2 domain (1 with side of microtubules, 2 with outward as a tail)
- MAPs *increase stability and promote microtubule assembly* by linking tubulin subunits together.
- An abnormally high level of phosphorylation of one particular MAP, called tau, has been implicated in Alzheimer's disease.

بسبب عند حدوث اضافة P تتكتل ولذلك هي هون ما عم تتجمع
عند ازالة P يتجمع اضافة P تتكتل



Tangled filaments

→ tau بسبب الفسفرة التركيبة بتشكل شي Tangled filaments



* activity of MAP depend on phosphated

Fig. 9.4 Microtubule Associated Proteins

9.2 | Structure and Function of Microtubules (4 of 5)

في كثير من الوظائف بكونو كل الانواع مشتركة مع بعض
في نفس الوظيفه ويشتغلو مع بعض زي Network + Support

Function :.

Microtubules as Structural Supports and Organizers

→ Shared by all of the Cytoskeleton

- Provide *mechanical support* by resisting forces that might compress or bend the fiber

→ اهم اشي في تحديد شكل الخلية

- Distribution helps *determine the shape of that cell*. (the most important Function)

□ Internal organized → (اعضاء الخلية بتكون مترتبة عليه
لو جدد اماكن الاعضاء

- Example:
  - In cultured animal cells, microtubules extend (يمتد) in a radial array outward from [near the nucleus], giving cells a round, flattened shape.

قريب من النواة
شكل دائري مسطح

دائماً تمتد من عند النواة وتعطي جهة النواة (-) End

□ Spindle → فصل الخيوط المغزلية
□ Cilia and Flagela

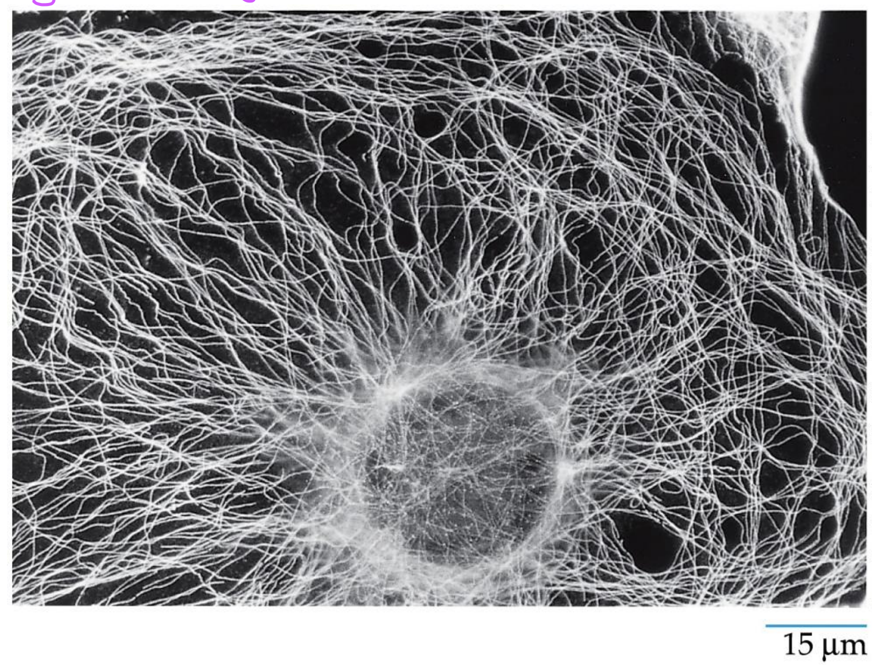


Fig. 9.5 Localization of microtubules

شكل اعضاء الخلية داخلها غير عن المختبر، لانه حسب الالتصاق
الخلية على السطح المجاور + انواع الادوات في المختبر

9.2 | Structure and Function of Microtubules (5 of 5)

the transport is (Anterograde + Retrograde)
Anterograde → From cell body to the terminals
Retrograde → From terminal to the cell body

Mainly in Motility (الحركة الذاتية)

Microtubules as Agents of Intracellular Motility

- *Direct movement* within the cell (Transport inside the cell)
- In nerve cells, directed movement relies on a highly organized arrangement of microtubules and other cytoskeletal components.
  - Nerve cells are extremely long
  - Can stretch from spinal cord to fingertip or toe
  - Directed movement is crucial for delivering neurotransmitters and other essential material
- Defects in transport along microtubules can result in neurological diseases. → اذا صار عنشي اي غلط بنقل السيالات العصبية (Anterograde + Retrograde)
  ↳ ex: CALS

مهم اكثر بس ادرسه

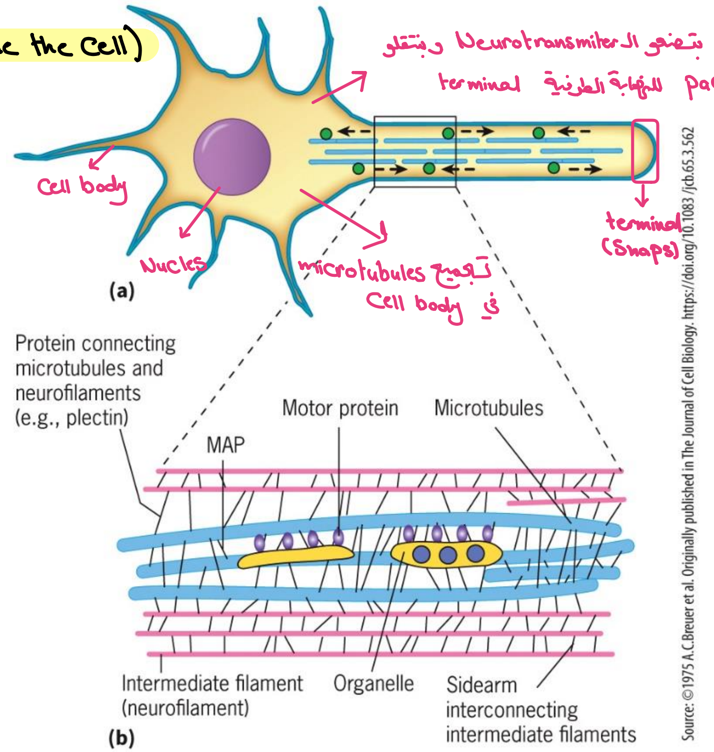


Fig. 9.7a,b Microtubule and intermediate filament organization in an axon.

9.4 | Motor Proteins: Kinesins and Dyneins (1 of 6)

① تحتاج طاقة
② البروتينات تتجه باتجاه واحد فقط
③ تحتاج إلى adaptor يربط بين Cytoskeleton وبين Motor protein

Motor Proteins Traverse the Microtubular Cytoskeleton

Microtubules:

→ Need ATP to Powered by add P and remove it

- Serve as tracks for a variety of **motor proteins** that generate forces required to move objects within a cell.

the intermediate Filaments has No polar end → Motor protein لذلك هي ليس لديها
بوصل العضيات بسبب عدم وجود اتجاه لان النهايتين متساويتان

- Can be grouped into three broad superfamilies:
  - (الذهاب) **Kinesin** and (الرجوع) **Dyneins** which move along microtubules
  - **Myosin** which move along actin filaments

احادي الاتجاه (لها اتجاه واحد) — خطوة بخطوة

- Move unidirectionally along their cytoskeletal track in a stepwise manner from one binding site to the next
- Undergo a series of conformational changes that constitute a mechanical cycle → تغير شكله عن طريق اضافة وازالة P مما يؤدي إلى توليد طاقة ميكانيكية

the mechanical cycle are Coupled to the step of a Chemical Cycle which provide the energy (fuel) ATP binding to the motor Protein, the hydrolosis of ATP ⇝ ∞

9.4 | Motor Proteins: Kinesins and Dyneins (2 of 6)

*_ ينقل المواد من النهاية (–) إلى النهاية (+)
يتجه نحو (+) end

- Smallest and best understood microtubular motor
- A kinesin molecule is a tetramer of two identical heavy and two identical light chains.
- The globular heads bind microtubules and act as ATP-hydrolyzing, force-generating engines.
- Each head is connected to a neck, a rodlike stalk, and a fanlike tail that binds to cargo.

Such as vesicles + need adaptor like Clathren

Kinesins

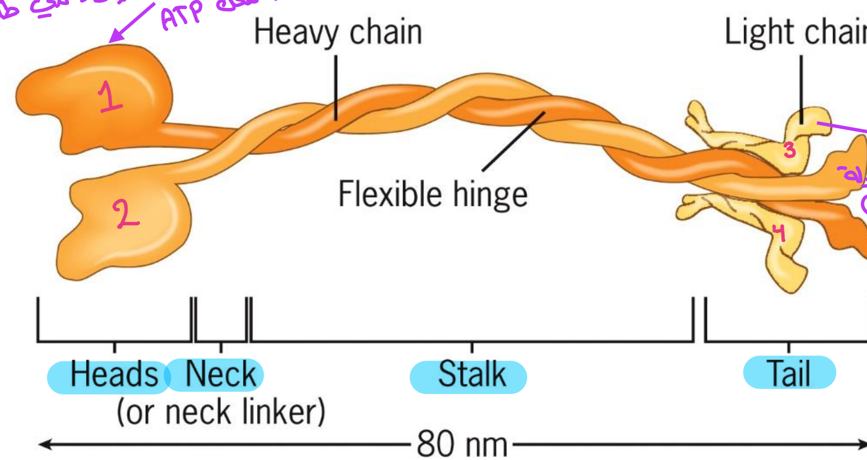


Fig. 9.11a Force-generating heads bind to the microtubule; tail binds to the cargo being transported

a number of different protein have been identified as potential adaptor that like specific (KRPs) and their Cargoes

9.4 | Motor Proteins: Kinesins and Dyneins (4 of 6)

Kinesin-Mediated Organelle Transport

→ on head

- Force-generating agents that drive the movement of cargo and organelles
- Tend to move vesicles and organelles in an *outward direction toward the cell's plasma membrane*

Because the plasma membrane is (+) and the Kinase move to the (+) end

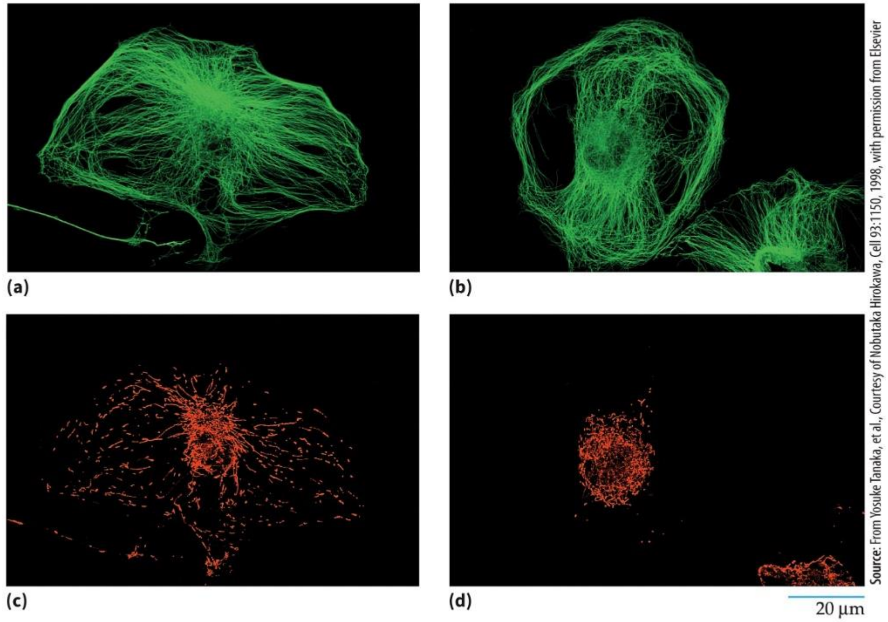


Fig. 9.12 Alteration in the phenotype of a cell lacking a member of the kinesin superfamily

9.4 | Motor Proteins: Kinesins and Dyneins (5 of 6)

Cytoplasmic Dynein

- Huge protein
- Two identical heavy chains
- A variety of intermediate and light chains
- The heavy chain consists of a large globular force-generating head and a microtubule-binding stalk.
- Cytoplasmic dynein moves processively along a microtubule toward the polymer's minus end—*opposite that of most kinesins*.

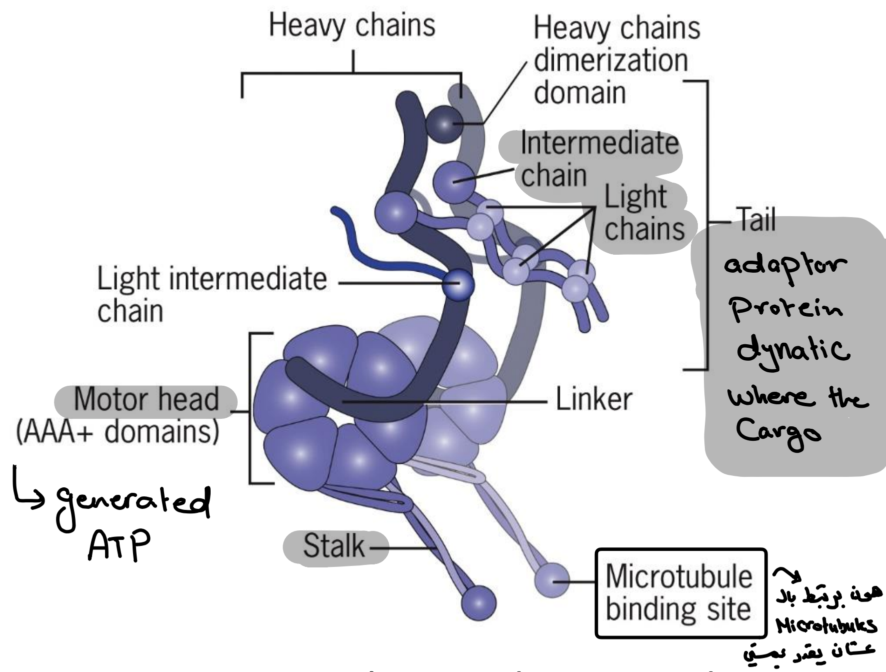


Fig. 9.13a Cytoplasmic dynein and organelle transport by microtubule-tracking motor proteins

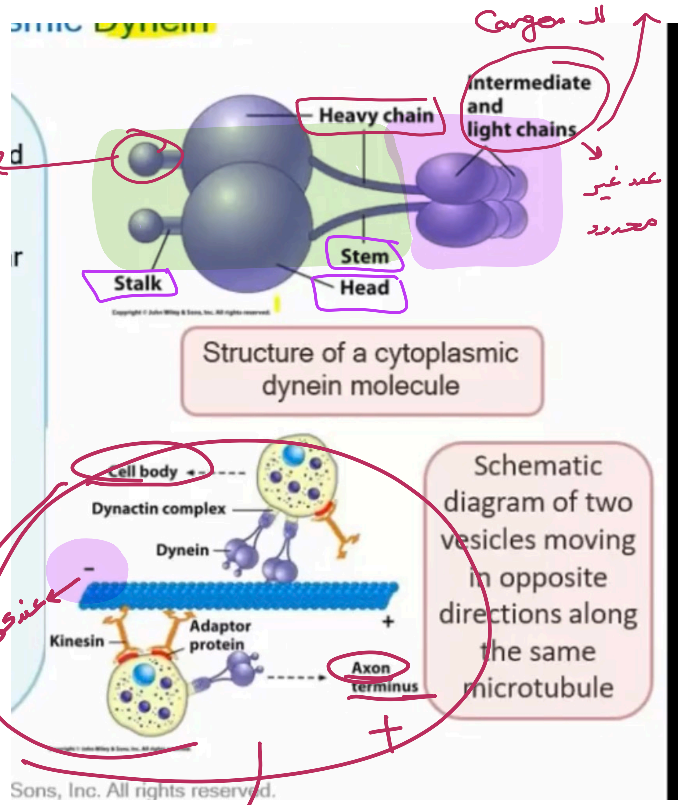
- Need in the Spindle

* يتحرك الي (-) End

Stalk → bind to the microtubles

Head → generated ATP hydrolysis

adaptor → dynactin



هون بيرتبط بال Microtubules

هون بيجي ال adaptor ال Cargo

عدد غير محدود

عشوائي

أول ما يواجه Golgi

مشان (-)

قدم الطريق الرجوع

اتجاه ال microtuble هو الي بتغير اما ال motor protein داخا اتجاهه ثابت

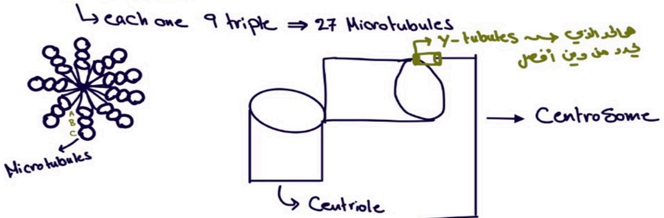
9.4 | Motor Proteins: Kinesins and Dyneins (6 of 6)

Cytoplasmic Dynein

- Positions the spindle and moves chromosomes during mitosis
- Positions the centrosome and Golgi complex
- Moves organelles, vesicles, and particles through the cytoplasm

Microtubules Synthesis:
In Vitro ↳ Nucleation (Slow)
↳ Elongation (Fast)
In Vivo ↳ Nucleation (Fast) ⟶ we don't Need to the Nucleation because of the Centers
↳ Elongation (Fast)

* Centrosome:
x2 Centriole
↳ each one 9 triple ⇒ 27 Microtubules



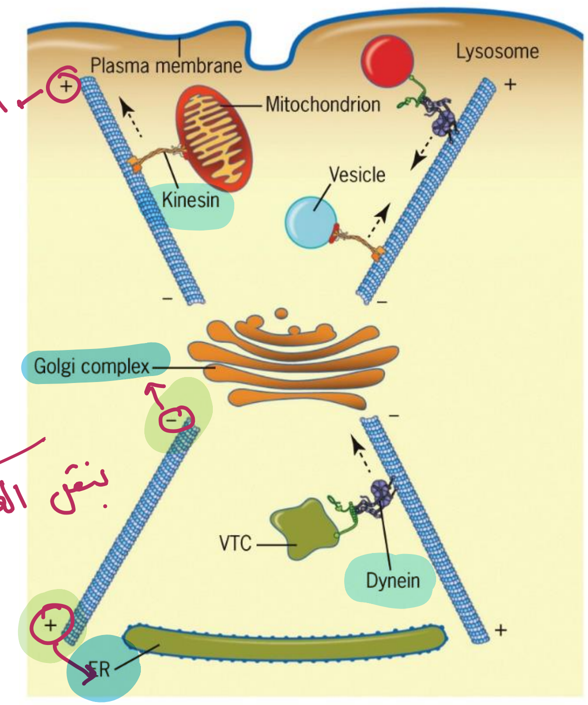


Fig. 9.13c Cytoplasmic dynein and organelle transport by microtubule-tracking motor proteins

9.5 | Microtubule Organizing Centers (MTOCs) (1 of 9)

لم هدول نجدد كيف يتركب الـ microtubles عشان يمشي عليه Motor protein

Centrosomes

- Nucleation of microtubules takes place rapidly inside a cell, where it occurs in association with a variety of specialized structures called **microtubule-organizing centers (or MTOCs)**.
- MTOCs control:
  - Number of microtubules
  - Polarity of microtubules اتجاه + / -
  - Number of protofilaments → 13 واحدة متى الو عددهم
  - Time and location of assembly → متى وقت تقل الحولة
- The best studied MTOC is the **centrosome.**

ممكن الـ microtuble يكون موجود مو ضروري تعمل واحد جديد فقط نعمل عليه استطالة او تقصير

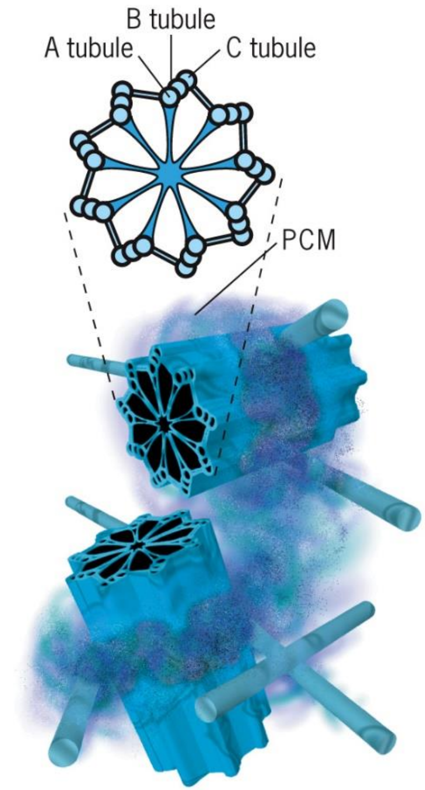


Fig. 9.14a The Centrosome

9.5 | Microtubule Organizing Centers (MTOCs) (2 of 9)

Centrosomes

- Contains two barrel-shaped **centrioles** surrounded by electron dense **pericentriolar material (PCM)**
- Is a major site of microtubule initiation in animal cells and remains at the center of the cell's microtubule network

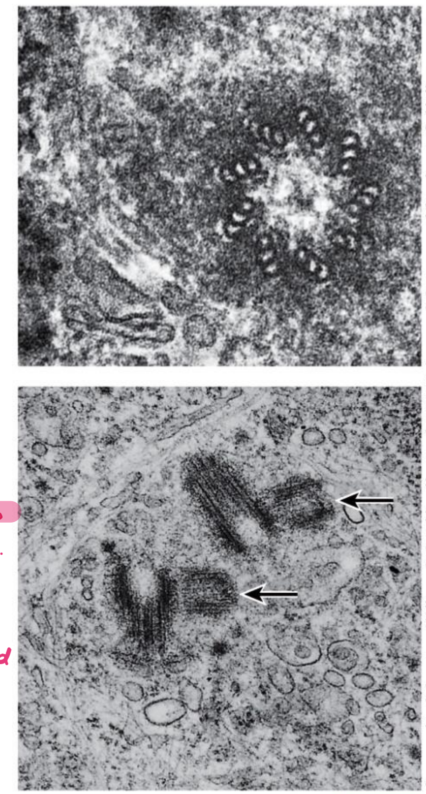
In a vitro, the assembly of microtubules from αβ-tubulin dimers occures in two distinct phases

① Slow phase of Nucleation in which a small portion of the microtubles is initially formed

② much more rapid phase of elongation

In a vivo, Nucleation of microtubules take plase rapidly inside a cell Because of a speciallized structure Called (MTOCs)

Becuase MTOCs Control a Lot of things in the Cell



Source: (top) Courtesy William R. Brinkley (bottom) ©1973 Jerome.B.Rattner and Stephanie G. Phillips. Originally published in The Journal of Cell Biology. https://doi.org/10.1083/jcb.57.2.359

0.3 µm

Fig. 9.14b,c The Centrosome

9.5 | Microtubule Organizing Centers (MTOCs) (4 of 9)

الاصل microtubules يتكون فقط من α,β
لما بدي ابلش Micro-Nucleation ← لازم يدخل فيه γ-tubulin
عشان يحدد اتجاه النمو

Microtubule Nucleation

- MTOCs share a common factor, **γ-tubulin**, a critical protein in microtubule nucleation.
- The PCM serves as attachment sites for ring-shaped structures that contain γ-tubulin, the γ-tubulin ring complexes (γ-TuRCs).
- The γ-TuRC is a helical array of γ-tubulin subunits where αβ-tubulin dimers assemble.

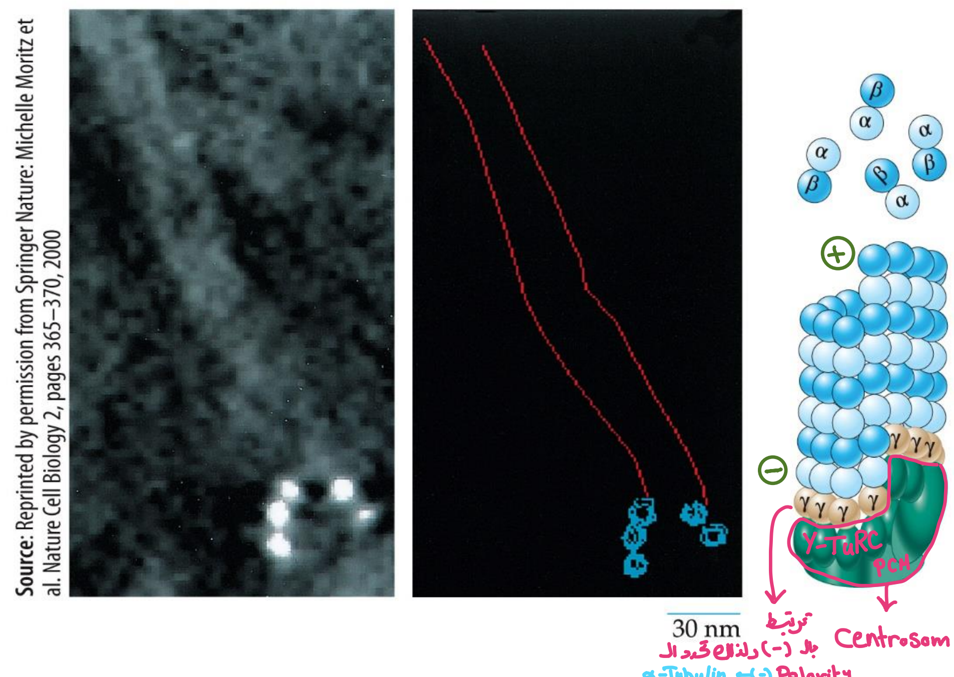


Fig. 9.16b,c Role of γ-tubulin in centrosome function

9.5 | Microtubule Organizing Centers (MTOCs) (5 of 9)

ماعنده branch تفرع لذلك ممكن يعمل تشارك عن طريق Network
لكن هو linear مع باقي الانواع بصير شبكة

The Dynamic Properties of Microtubules

- Can shorten, lengthen, disassemble, and reassemble → due to Non-Covalent bond
- Depending on the cell and location of microtubules (موقعه يحدد اتجاه النقل), their stability is determined by ① microtubule interacting proteins (including MAPs):
  - Stability of Microtubule ② proteins known as +TIPs which bind to the plus-end of growing microtubules
  - ③ enzyme katanin, that severs microtubules into shorter pieces
- Disassembly (of microtubule) can be initiated by:
  - posttranslational modifications
  - cold temperature
  - hydrostatic pressure
  - elevated Ca^{2+} concentration
  - variety of chemicals → عن طريق علاج كيماوي بوقف الـ activity للخلية عن قطع الاشياء الها. Colchicine, taxol, nocodazole متل دواء
- The microtubules of the cytoskeleton are normally subject to depolymerization and repolymerization as the requirements of the cell change from one time to another.

لـ تفكك وتركيب الـ Microtubules يعتمد على حاجة الخلية

9.5 | Microtubule Organizing Centers (MTOCs) (7 of 9)

The Underlying Basis of Microtubule Dynamics

During assembly of tubulin dimers:

- A GTP molecule is bound to the β-tubulin subunit (β-tubulin is a structural protein and a GTPase)
- GTP is hydrolyzed to GDP after the dimer is incorporated, and the resulting GDP remains bound to the assembled polymer

During disassembly of tubulin dimers:

- The dimer enters the soluble pool, the GDP is replaced by a new GTP.
- This nucleotide exchange “recharges” the dimer, allowing it to serve once again as a building block for polymerization.

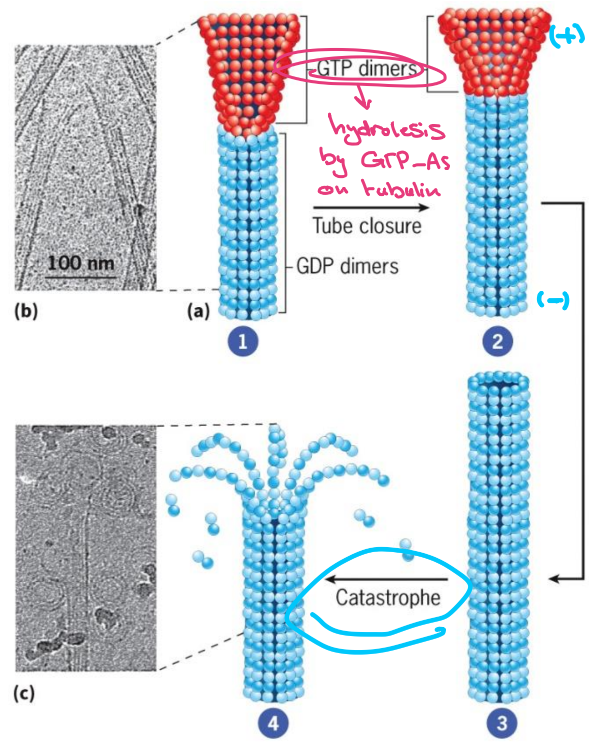


Fig. 9.21 Structural cap model of dynamic instability

Source: (a) Adapted from A.A. Hyman and E. Karsenti, Cell 84:402, 1996, by Cell by Cell Press. (b, c) Courtesy of Thomas Mueller-Reichert, T.U. Dresden, Medical Theoretical Center (MTZ) and Anthony A. Hyman, Max Planck Institute of Molecular Cell Biology and Genetics

9.5 | Microtubule Organizing Centers (MTOCs) (8 of 9)

ratio of hydrolisis more than addition (shorter)

The Underlying Basis of Microtubule Dynamics

Growth or shrinkage of a microtubule depends on the state of the tubulin dimers at the plus end:

1. The tip consists of an open sheet containing tubulin – GTP subunits.
2. The tube begins to close, forcing hydrolysis of the bound GTP.
3. The tube has closed to its end, leaving only tubulin – GDP subunits (GDP-tubulin has a different conformation than GTP-tubulin, which makes them less able to fit into a protofilament).
4. The strain from the GDP-tubulin at the plus end causes a catastrophic shrinkage.

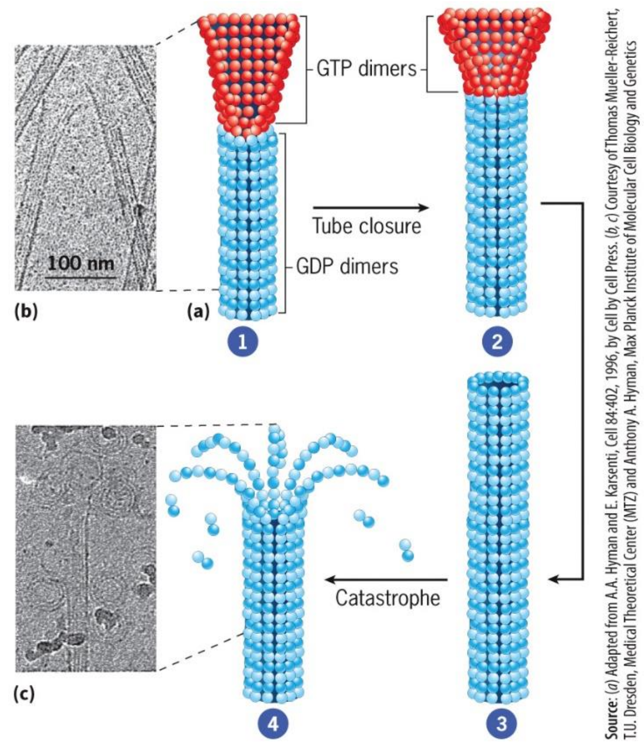
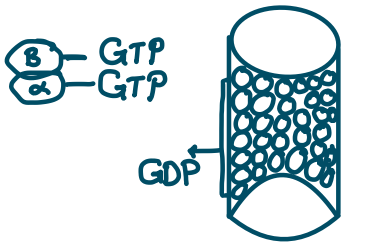


Fig. 9.21 Structural cap model of dynamic instability

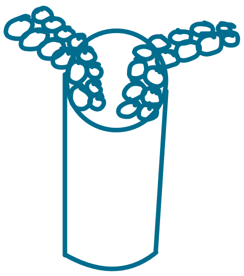
في الاصل → the dimers that are not bind to the proto fillimeuts they are bind ($\alpha + \beta$) to GTP , But the protofilliment are GDP



في البداية عند اضافة dimer بكون مرتبط ب GTP بعد مرور القليل من الوقت بفقد ذرة P ويصبح GDP ⇝ مركب غير قوي لذلك

لدي +TPS → assembly MAP → stabilize

taxol → يمنع نمو الخلايا (السرطانية) → مثل منع Spindle



بعد أن يصبح كل المركب ارتباطه GDP يبدأ المركب بالتفكك

لدي Katatin → dissassembly

(Ca+/ press/ Cold)

assembly =(rescue)

dissassembly =(Catastrophy)

⇝ حالة الجسم

9.5 | Microtubule Organizing Centers (MTOCs) (9 of 9)

The Underlying Basis of Microtubule Dynamics

Dynamic instability is a phenomenon that describes microtubule behavior. It explains that:

↳ Dynamic behavior

1. Growth and shrinkage of microtubules can coexist in the same region of a cell. → due to dynamic behavior
2. A given microtubule can switch back and forth unpredictably between growing and shortening phases.

Dynamic instability is an inherent property of the plus end of the microtubule, where subunits are added during growth and lost during shrinkage.

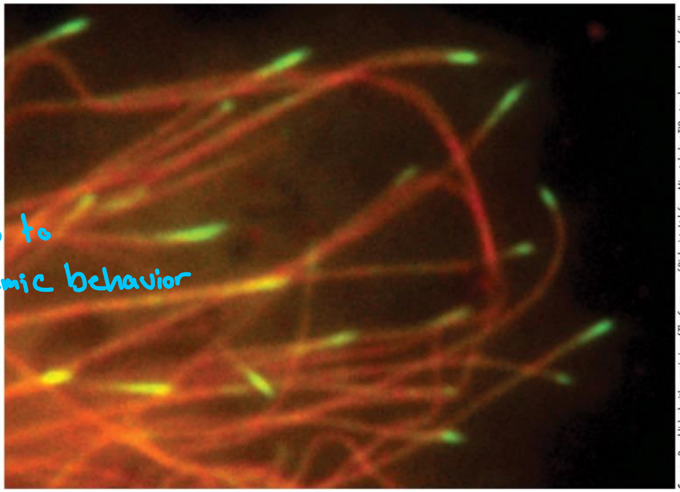


Fig. 9.24 Binding of a microtubule plus end tracking protein (+TIP)

9.7 | Intermediate Filaments (1 of 5)

↳ Identified in animal cells

- Strong, flexible, ropelike fibers that provide mechanical strength to cells (اهم وظيفة) that are subjected to physical stress (للخلايا التي تتعرض ل)
- Chemically heterogeneous group of structures
- Divided into five major classes (based on cell type ① and other criteria) ② structures

TABLE 9.2 Properties and Distribution of the Major Mammalian Intermediate Filament Proteins

IF protein	Sequence type	Primary tissue distribution
Keratin (acidic) (28 different polypeptides)	I	Epithelia
Keratin (basic) (26 different polypeptides)	II	Epithelia
Vimentin	III	Mesenchymal cells
Desmin	III	Muscle
Glial fibrillary acidic protein (GFAP)	III	Astrocytes
Peripherin	III	Peripheral neurons
Neurofilament proteins		Neurons of central and peripheral nerves
NF-L	IV	
NF-M	IV	
NF-H	IV	
Nestin	IV	Neuroepithelia
Lamin proteins		All cell types (nuclear envelopes)
Lamin A	V	
Lamin B	V	
Lamin C	V	ليس للحفظ

More detailed tables can be found in *Trends Biochem Sci.* 31:384, 2006, *Genes and Development* 21:1582, 2007, and *Trends Cell Biol.* 18:29, 2008.

9.7 | Intermediate Filaments (2 of 5)

- Often interconnected to other cytoskeletal filaments by thin, wispy cross-bridges consisting of the protein **plectin**.
- Each plectin molecule has a binding site for an IF at one end (1) and a binding site for another (2) End intermediate filament, microfilament, or microtubule at the other end.

النهايتين ليست Polar لذلك لا يرتبط فيه Motor protein
لكن عنده بروتين يسمى plectin يربطه ويكون شبكة مع
باقي انواع Cytoskeleton

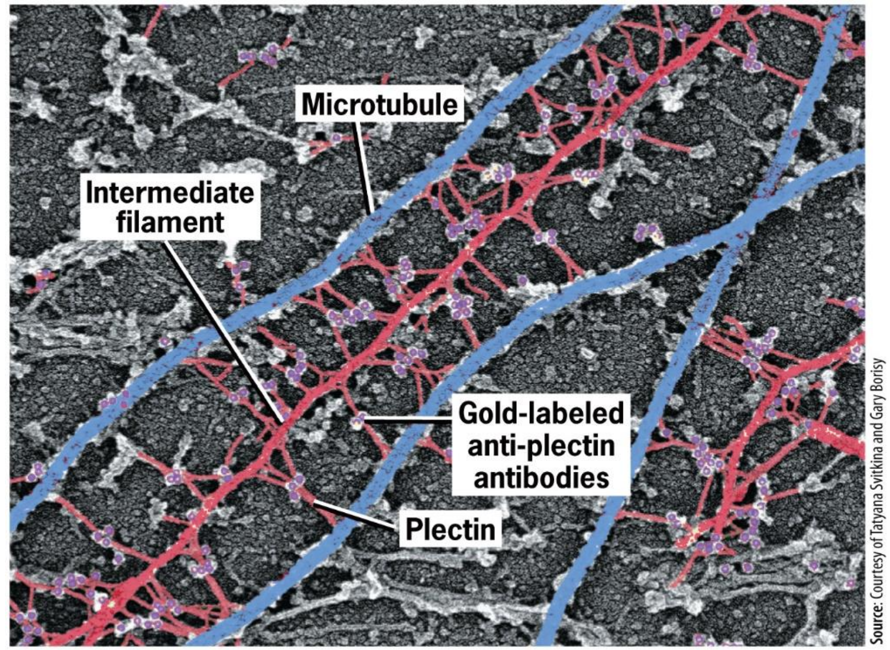


Fig. 9.35 Cytoskeletal elements are connected to one another by protein cross-bridges (plectin).

IF architecture:

1. Each monomer has a pair of globular terminal domains separated by a long alpha-helical region
2. Pairs of monomers are associated in parallel orientation to form dimers
3. Dimers associate in an anti-parallel, staggered fashion to form tetramers (the basic subunit in IF assembly
4. 8 tetramers associate to form a unit length of the IF
5. Elongated Ifs are formed from the end-to end association of these unit lengths

ان IF ترتبط ببعضها البعض وحدة فوق وحدة وطرفاً فوق طرف

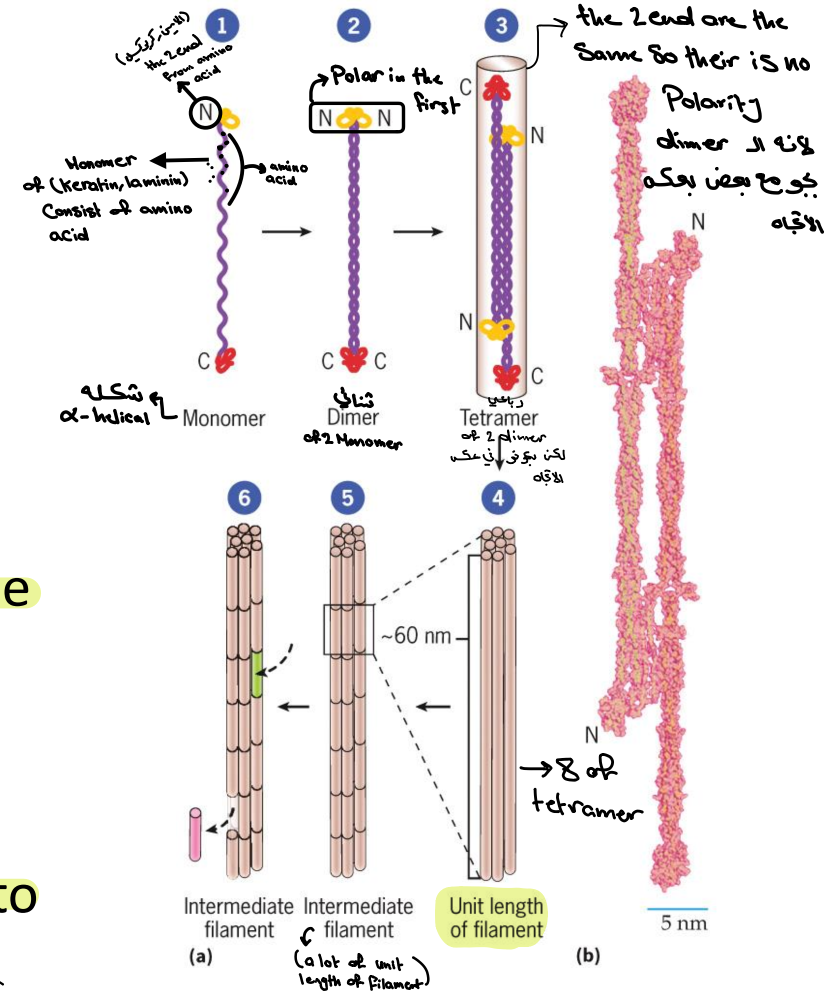


Fig. 9.36 Models of IF assembly and architecture

9.7 | Intermediate Filaments (4 of 5)

Intermediate Assembly and Disassembly

- Assembly steps do not require the direct involvement of either ATP or GTP.
- The tetrameric building blocks *lack polarity* as does the assembled filament, which distinguishes IFs from other cytoskeletal elements.
- The subunits are not incorporated at the ends of the filament but into the filament's interior.

  ↙ الاضافة على IF ممكن تكون من أي جهة وليست فقط الاطراف
  مثلاً ممكن اضيف من المنتصف على عكس باقي الانواع التي فقط الاضافة على الاطراف

- Unlike the other two major cytoskeletal elements, assembly and disassembly of IFs are controlled primarily by subunit phosphorylation and dephosphorylation.

  لما اضافة P تؤدي إلى التفكك نزع P تؤدي إلى ارتباط المركب

  الاضافة لا تكون على IF بل على الحمض الاميني المكون للبروتين وغالباً ما يكون (threonine, Serine)

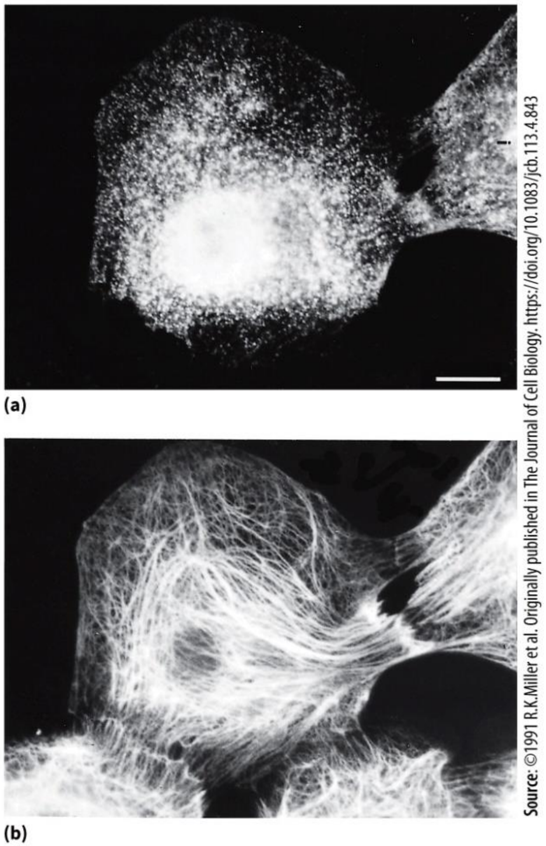


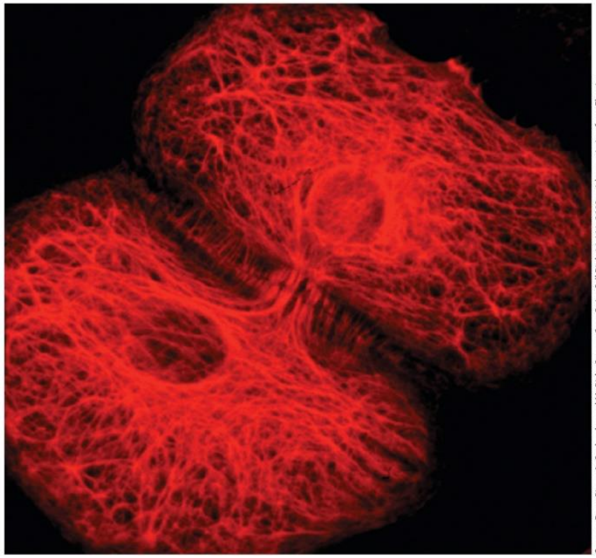
Fig. 9.37 Dynamic character of Intermediate Filaments

9.7 | Intermediate Filaments (5 of 5)

Types and Functions of Intermediate Filaments

- **Keratin containing IFs** – structural proteins of epithelial cells → Cell- Cell adhesion
  - Tethered to the nuclear envelope in the center of the cell and anchored at the outer edge by desmosomes and hemidesmosomes
  - Function to organize and maintain cellular architecture and absorb mechanical stress
- **Neurofilments** – IFs located in the cytoplasm of neurons in bundles oriented parallel to the axon

3) Laminin → In the Nuclear



Source: From Pierre A. Coulombe and M. Bishr Omary, Curr. Opin. Cell Biol. 14:111, 2002, with permission from Elsevier.

Fig. 9.38b The organization of intermediate filaments (IFs) within an epithelial cell.

9.8 | Actin and Myosin (1 of 12)

Microfiliment

Actin Structure

- Third major type of cytoskeletal element that is involved in intracellular motile processes → عمليات الحركة في الخلية
  ↳ More in a specific movement
  ↱ three name but the same things
- An actin filament (F-actin, microfilament) is a two-stranded structure with two helical grooves running along its length.
  ↱ the most abundance protein in the cell.
- Actin filaments can be organized into:
  - ordered arrays → مصفوفات منظمة ومرتبة
  - highly branched networks → شبكات متفرعة جداً (تشبه الشجرة)
  - tightly anchored bundles حزم متراصة و مثبتة بإحكام

helical Shape

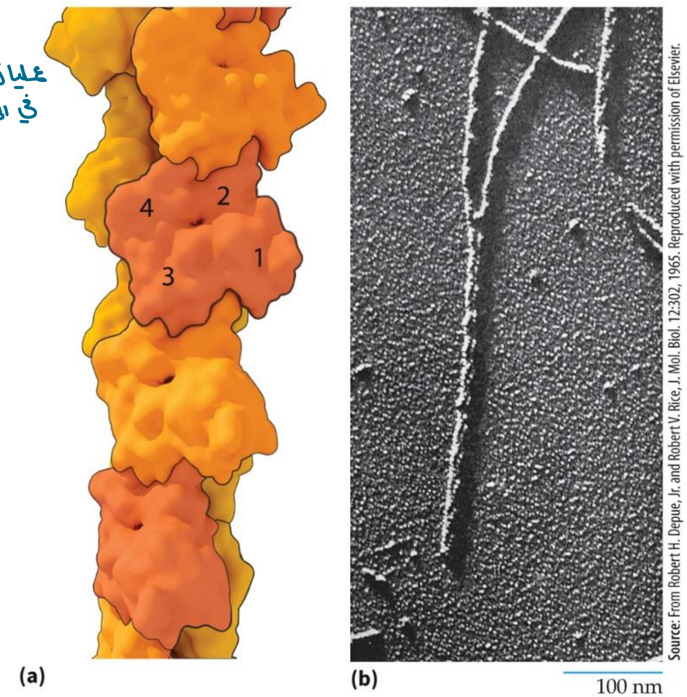
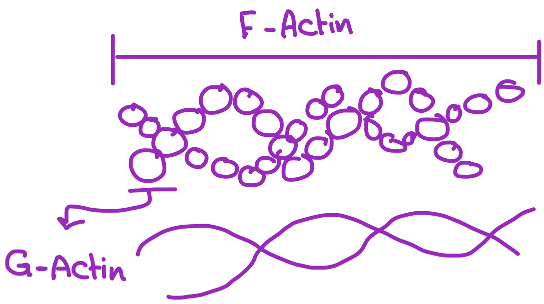
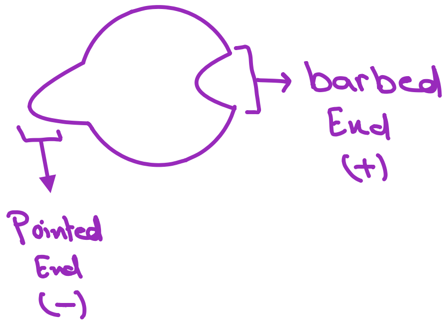
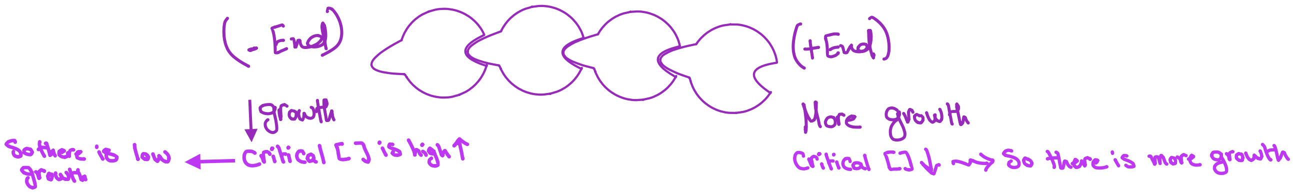


Fig. 9.39 Actin filament structure







growth or not depend on the Concentration (G - Actin)

1 Critical Concentration
- → More of it بناء (growth)
- → below of it تكسير (break)

2 (treadmilling)

loss (-) = growth (+)

length Constant

Poisins :

↳ Cytochalasin (mold) ⇝ block the (+) End

↳ Phalloidin (mushroom) ⇝ prevent the Actin turnover — يبقى الأكتين ثابت حجمه لا يتغير (لا يكبر ولا يصغر)

↳ lantrucutin ⇝ prevent + End to bind to any thing — تمنع النهاية من الارتباط ولكن لا تغلقها

The involvement of these filaments is most readily demonstrated by treating the cells with one of the following drugs that disrupt dynamic actin-based activities:
Cytochalasin, derived from a mold, which blocks the barbed (+) ends of actin filaments and allows depolymerization at the pointed end;
Phalloidin, obtained from a poisonous mushroom, which binds to intact actin filaments and prevents their turnover;
Latrunculin, obtained from a sponge, which binds to free monomers and blocks their incorporation into the polymer.

13.8 | Actin

Cells can be motile: Neural crest cells leave the developing nervous system and migrate across the embryo, to form pigmented skin cells, teeth, and the cartilage of the jaws. White blood cells patrol the body searching for debris and microorganisms.

Cell parts can be motile: Projections of epithelial cells at the edge of a wound act as motile devices that pull the sheet of cells over the damaged area, sealing the wound. The leading edge of a growing axon sends out microscopic processes that survey the substratum and guide the cell toward a synaptic target.

All of these various examples of motility share at least one component: they all depend on actin, the third major type of cytoskeletal element.

Actin is also involved in intracellular motile processes, such as the movement of vesicles, phagocytosis, and cytokinesis.

Actin also plays an important role in determining the shapes of cells and can provide structural support for various types of cellular projections.

9.8 | Actin and Myosin (2 of 12)

Actin Structure

- All of the monomers within an actin filament are pointed in the same direction, resulting in a polar filament with so-called “barbed” (+) and “pointed” (−) ends.
- A major contractile muscle protein → البروتين الاساسي في عملية انقباض العضلات
- A major protein in every eukaryotic cell

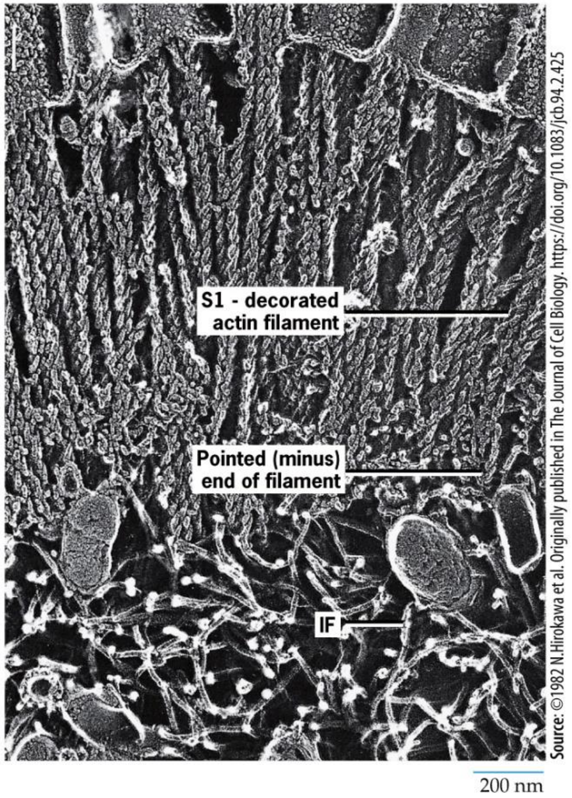


Fig. 9.40 EM: Determining the location and polarity of actin filaments with the S1 subunit of myosin

Actin should be associated with ATP

Actin Filament Assembly and Disassembly

- Before it is incorporated into a filament, an actin monomer binds a molecule of ATP.
- Actin is an ATPase, just as tubulin (Microtubulin) is a GTPase.
- The ATP associated with the actin monomer is hydrolyzed to ADP at some time after it is incorporated into the end of a growing actin filament.
- (في المختبر) The initial nucleation event in filament formation occurs slowly in vitro, whereas the subsequent stage of filament elongation occurs much more rapidly.
- Both ends of a filament become labeled, but the fast-growing barbed (+) end incorporates the monomers at a rate about 10 times that of the pointed (-) end.

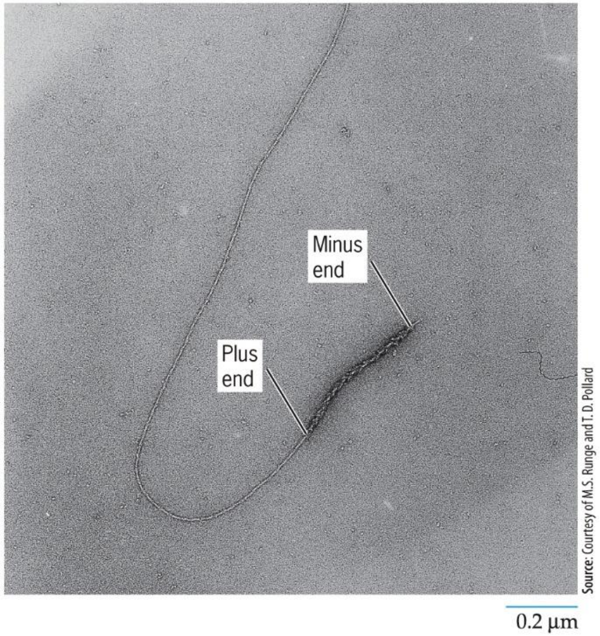


Fig. 9.41a Actin Assembly

End (-) أولا أضعاف الاضافة (10) End (+) الاضافة على

9.8 | Actin and Myosin (4 of 12)

Actin Filament Assembly and Disassembly

Actin assembly/disassembly in vitro:

1. Preformed actin filaments are added in the presence of ATP
2. As long as the concentration of ATP-actin monomers remain high, subunits are added to both ends
3. As monomers are consumed by addition to the ends of the filaments the concentration of free ATP-actin drops, until a point is reached where net addition of monomers continues at the barbed end but stops at the pointed end

مع استهلاك الأكتين الحر، نصل لنقطة حرجة؛ يستمر الطرف المسنن (+) في إضافة الوحدات، بينما يتوقف الطرف المدبب (-) عن ذلك بل ويبدأ بفقدانها

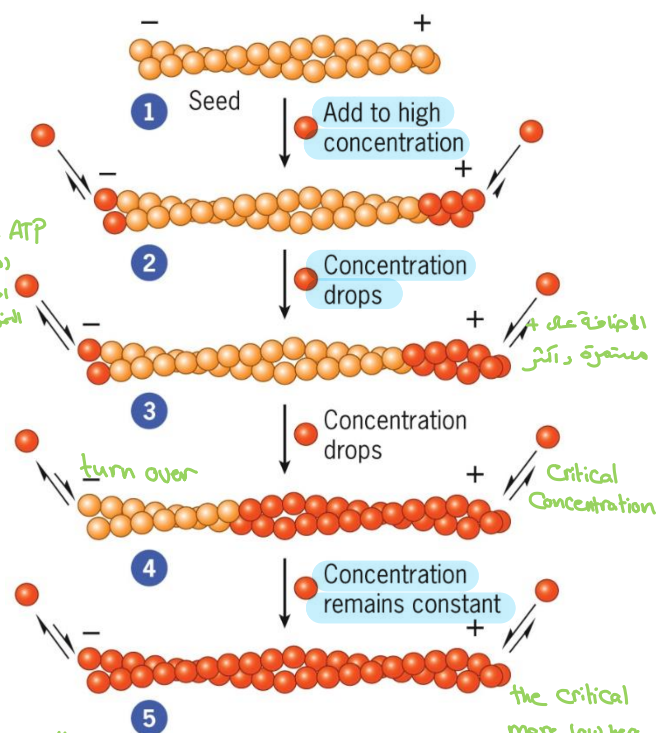


Fig. 9.41b Diagram of the kinetics of actin-filament assembly in vitro to achieve treadmilling

Actin Filament Assembly and Disassembly

4. As filament elongation continues, the free monomer concentration drops, such that monomers continue to be added to the barbed ends of the filaments, but a net loss of subunits occurs at their pointed end.

تركيز G-ATP في السيتوبلازم

5. A point is reached where the two reactions at opposite ends of the filaments are balanced, such that both the lengths of the filaments and the concentration of free monomers remain constant, known as "treadmilling."

عملية الهدم = البناء

اذا ازداد وضع الـ ATP-actin وقل turnover ← يزداد طوله
اذا قل وضع ATP-actin و ازداد turnover ← يقل طوله

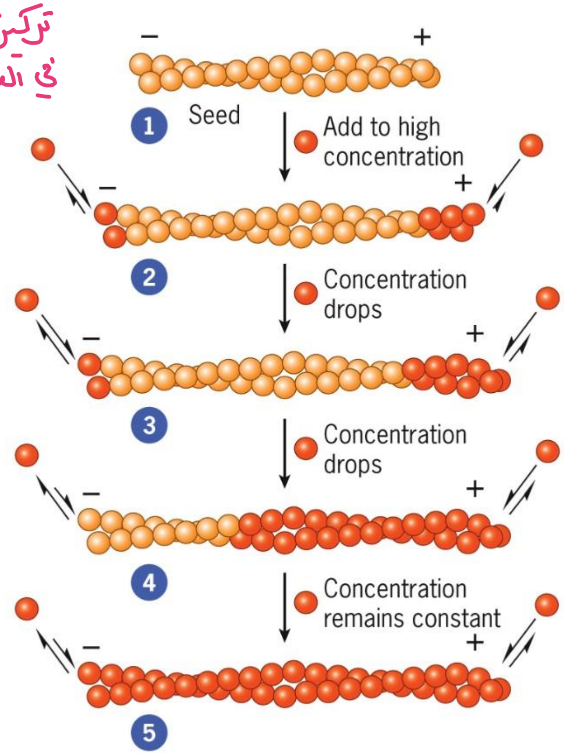


Fig. 9.41b Diagram of the kinetics of actin-filament assembly in vitro to achieve treadmilling

9.8 | Actin and Myosin (6 of 12)

Actin Filament Assembly and Disassembly

- Assembly/disassembly rate can be influenced (متأثر) by a number of different accessory proteins (بروتينات مساعدة).
- By controlling this dynamic behavior, the cell can reorganize its actin cytoskeleton, required for dynamic processes such as:
  - cell locomotion
  - changes in cell shape
  - phagocytosis → (البلعمة) التخلص من الاجسام الغريبة
  - cytokinesis → انقسام السيتوبلازم

9.8 | Actin and Myosin (7 of 12)

→ Motor protein

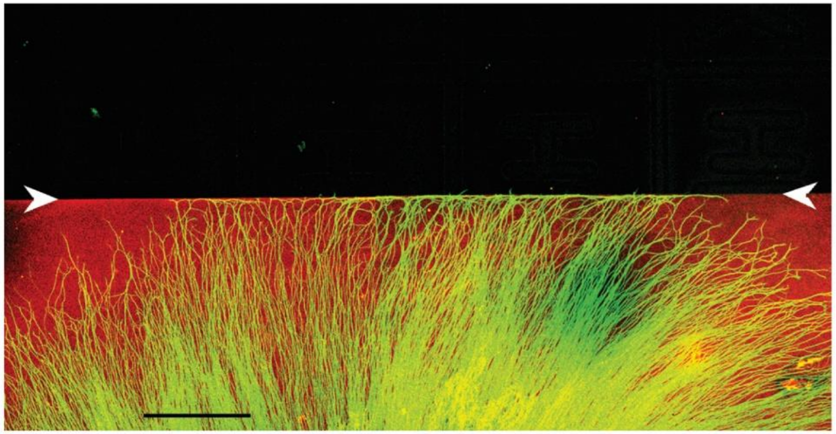
Myosin: The Molecular Motor of Actin

- Molecular motors that operate in conjunction with actin filaments
- Move toward the barbed end (+) of an actin filament → but the Myosin is more heavy so it's pill Actin
- All myosins share a characteristic motor (head) domain.
- The head domain contains two sites:
  - a site that binds an actin filament
  - a site that binds and hydrolyzes ATP to drive the myosin motor
- Whereas the head domains of various myosins are similar (نفس الشكل), the tail domains are highly (للغاية) divergent (مختلفة).
- Generally divided into two broad groups:
  - **conventional (or type II)**
  - **unconventional** ex: microvilli

9.8 | Actin and Myosin (8 of 12)

Conventional (Type II) Myosins

- Primary motors for muscle contraction
- Also found in a variety of nonmuscle cells
- All myosin IIs move toward the barbed end of an actin filament.
- Among their nonmuscle activities, type II myosins are required for:
  - splitting a cell in two during cell division
  - generating tension at focal adhesions
  - cell migration
  - turning behavior of growth cones



Source: Reprinted by permission from Springer Nature: Stephen G. Turney & Paul C. Bridgman. Nature Neuroscience 8, pages 717–719, 2005

Fig. 9.42a Fluorescence micrograph: neurites (green) growing out from mouse embryonic nervous tissue along a coverslip laminin-coated (red)

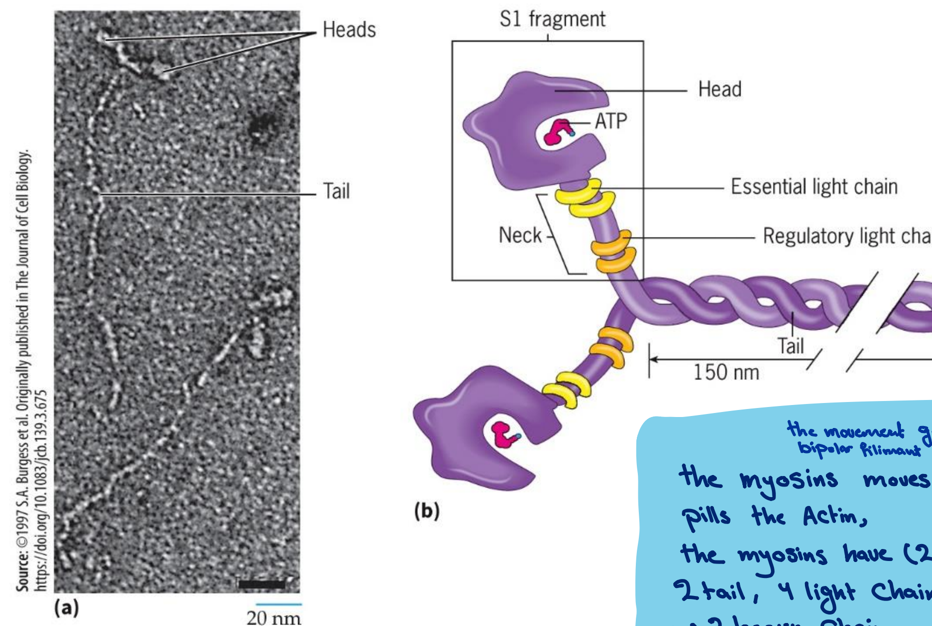
كل الـ Mayosin من الرأس حاصل الفرع (6) ترتبط
على End (+) من Actin

Conventional (Type II) Myosins

Myosin II consists of:

1. a pair of globular heads that contain the catalytic site of the molecule
2. a pair of necks, each consisting of a single, uninterrupted α helix and two associated light chains (خيط غير منقطع)
3. a single, long, rod-shaped tail formed by the intertwining (الالتواء، التفاف) of long a-helical sections of the two heavy chains.

ذيل واحد طويل يشبه العصا، يتكون من التواء خيطين طويلين جدًا مع بعضهما البعض، ويسميان "السلاسل الثقيل



the movement generat bipolar filimant
the myosins moves and pills the Actin,
the myosins have (2head, 2tail, 4 light Chains)
⇒ 2 heavy Chain

Fig. 9.43 Electron micrograph and schematic drawing of a myosin II molecule with one pair of heavy chains (blue) and two pairs of light chains

9.11 | Actin-Binding Proteins (1 of 2)

داخل الخلايا الحية، تترتب خيوط الأكتين في أنماط وأشكال مختلفة. هذه الأنماط تشمل "الحزم" (Bundles) حيث تكون الخيوط متوازية بجانب بعضها، وأيضًا "شبكات متقاطعة" (Crosslinked) و"شبكات متفرعة" (Branched networks) تشبه نسيج العنكبوت

- Patterns in living cells include various types of bundles (حزم) as well as crosslinked (متقاطع) and branched (متفرع) networks.
- The organization and behavior of actin filaments inside cells are determined by the interaction of actin with a variety of **actin-binding proteins**. ← هدول الي بحددو كيف يرتبط Actin وكيف بيتحدد شكله

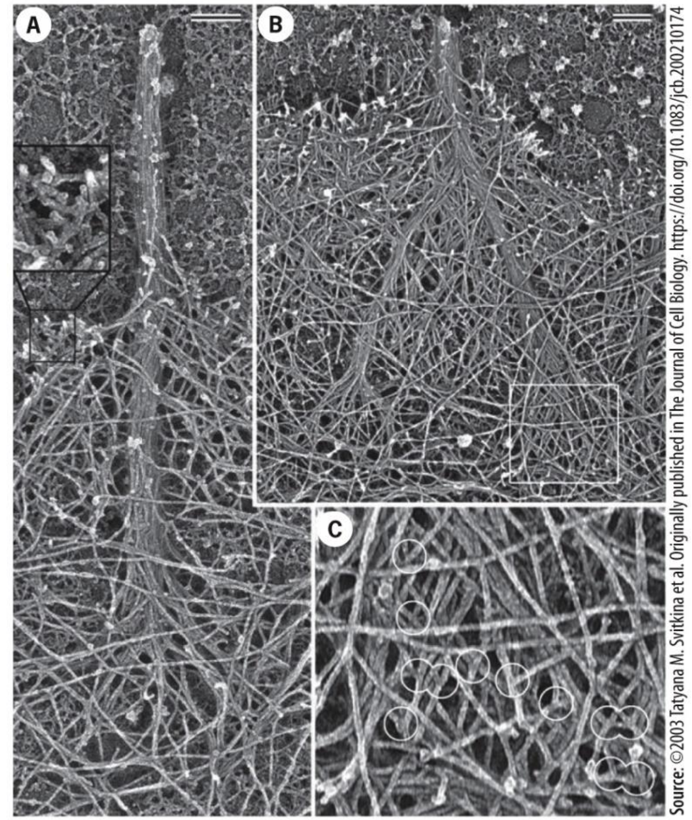


Fig. 9.59 Arrangement of actin filaments

9.11 | Actin-Binding Proteins (2 of 2)

Actin-binding proteins can be divided into categories based on their presumed function in the cell:

1. Nucleating
2. Monomer-sequestering
3. End-blocking (capping)
4. Monomer-polymerizing
5. Actin filament depolymerizing
6. Cross-linking
7. Filament-severing
8. Membrane-binding

درسه من الكتاب في عندهم معلومات دقيقة + امثلة عليهم

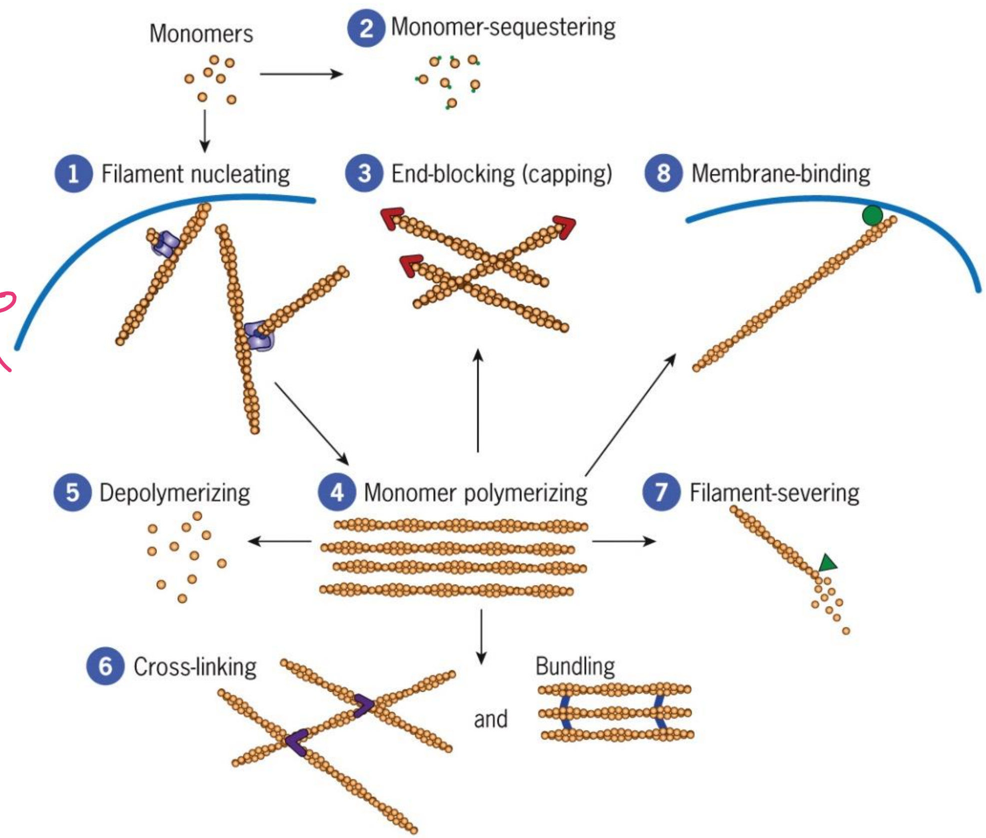


Fig. 9.60 The roles of actin-binding proteins

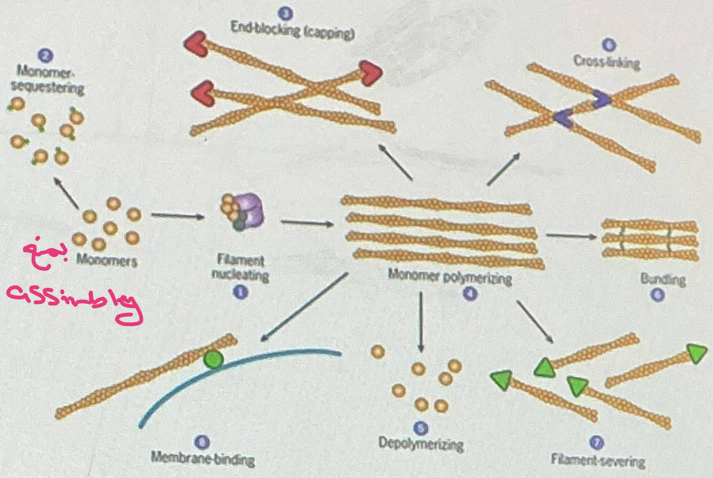
13.11 | Nonmuscle motility

1) **Nucleating proteins** – provide a template for adding actin monomers. Examples: *Arp2/3 complex; formin* branched versus unbranched filaments

2) **Monomer-sequestering proteins** – bind to actin-ATP monomers and prevent them from polymerizing. Example: *thymosin* b_4

3) **End-blocking (capping) proteins** – regulate the length of actin filaments Examples: *capZ; tropomodulin*).

4) **Monomer-polymerizing proteins** –promote the growth of actin filaments. Example: *profilin*



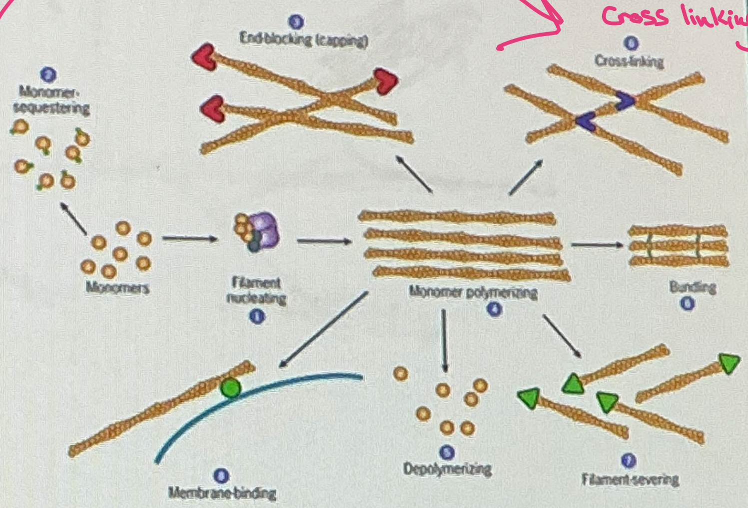
13.11 | Nonmuscle motility

5) **Actin filament depolymerizing proteins** – bind actin-ADP subunits for rapid turnover of actin filaments. Example: *cofilin*

6) **Cross-linking proteins** – alter the three-dimensional organization of actin filaments. Examples: *filamin (X-link), villin, fimbrin (bundling)*

7) **Filament-severing proteins** – shorten filaments and decrease cytoplasmic viscosity. Example: *gelsolin*

8) **Membrane-binding proteins** – link contractile proteins to plasma membrane. Examples: *vinculin, spectrin (dystrophin)*



3 dimintion
Cross linking

Shorting filimant

actin يربط مع plasma membrane

destroy dystrophin

Casbar R ← كاسبر R