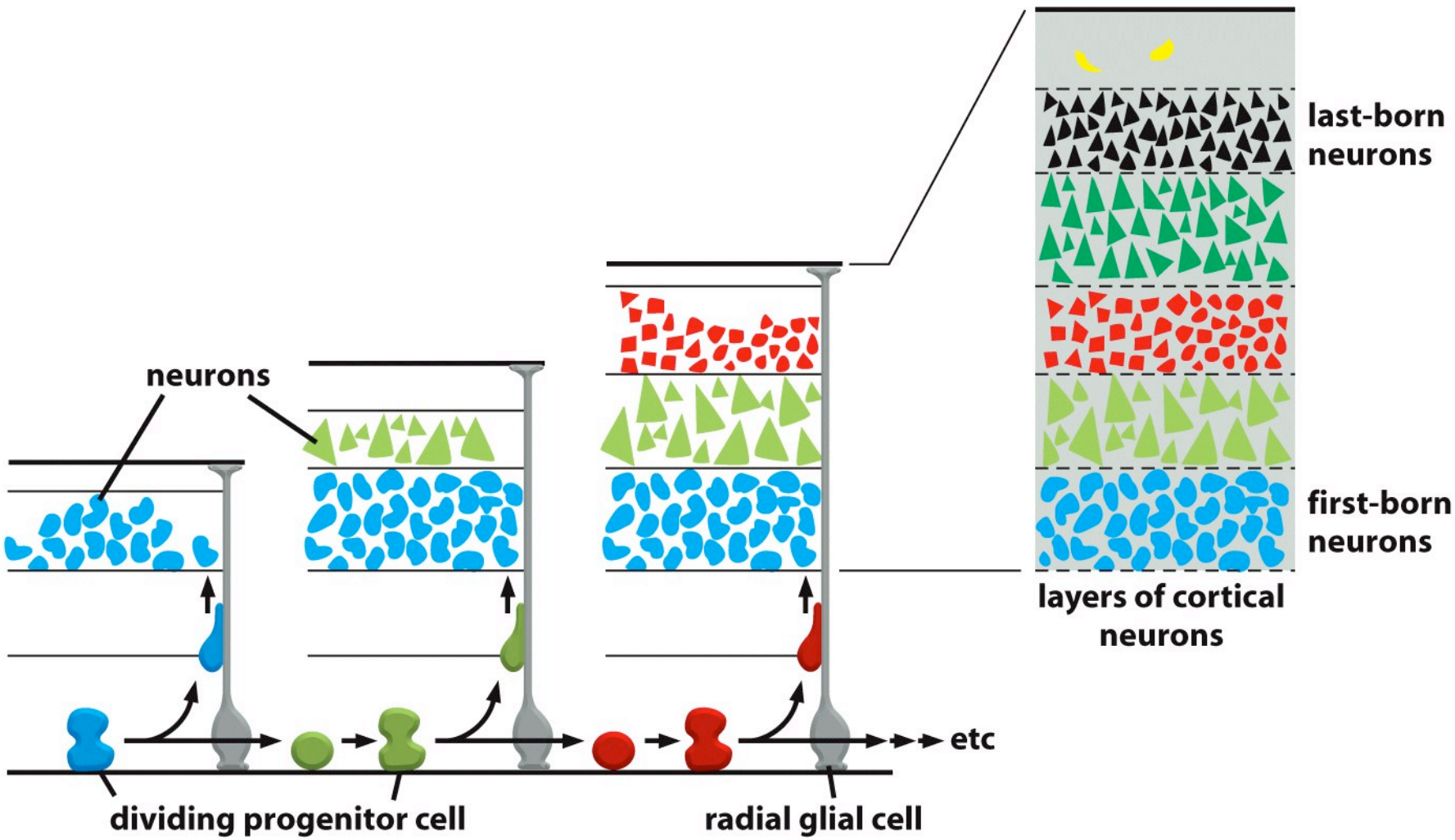



Figure 22-99 *Molecular Biology of the Cell* (© Garland Science 2008)

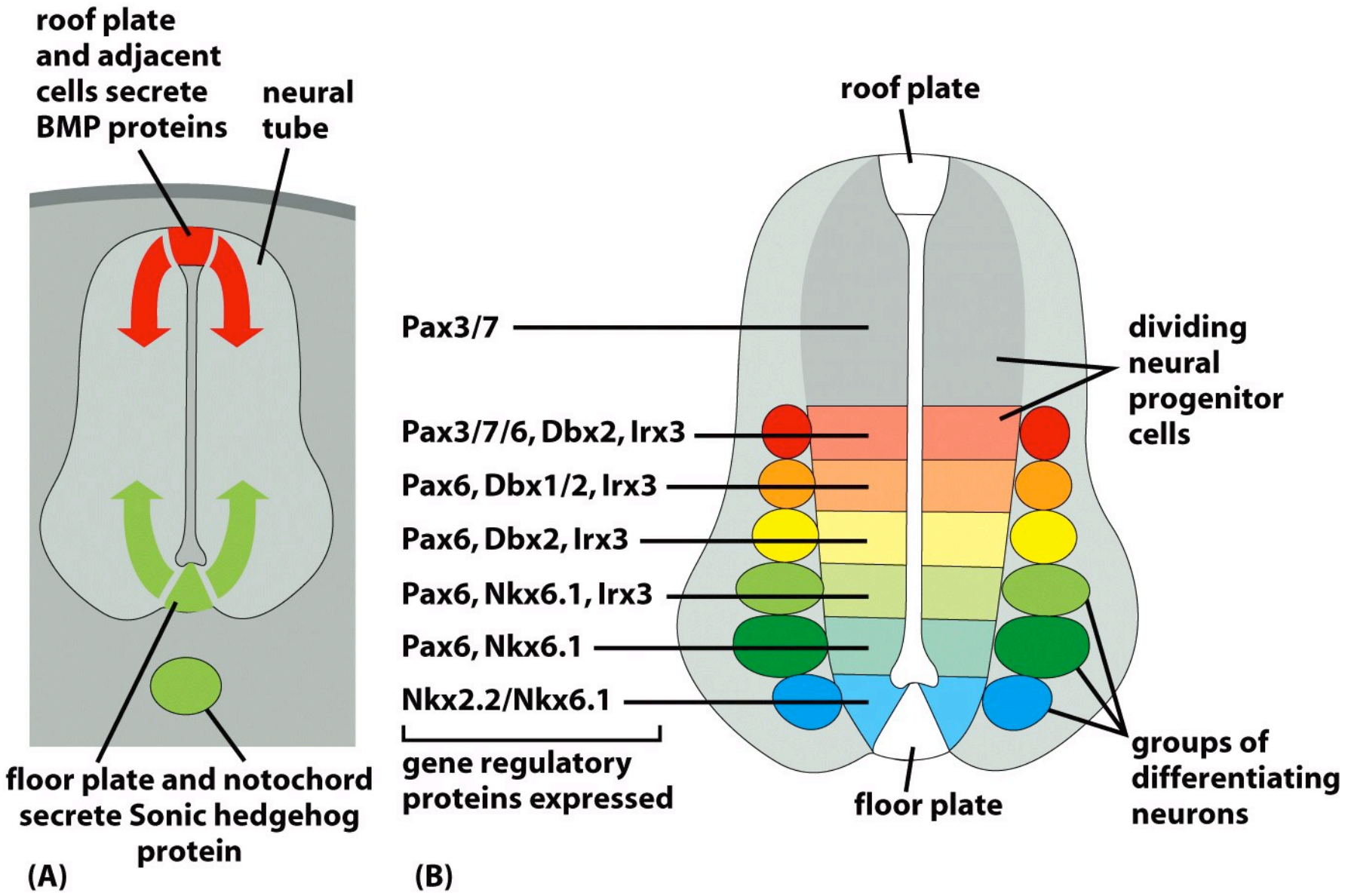



Figure 22-80 *Molecular Biology of the Cell* (© Garland Science 2008)

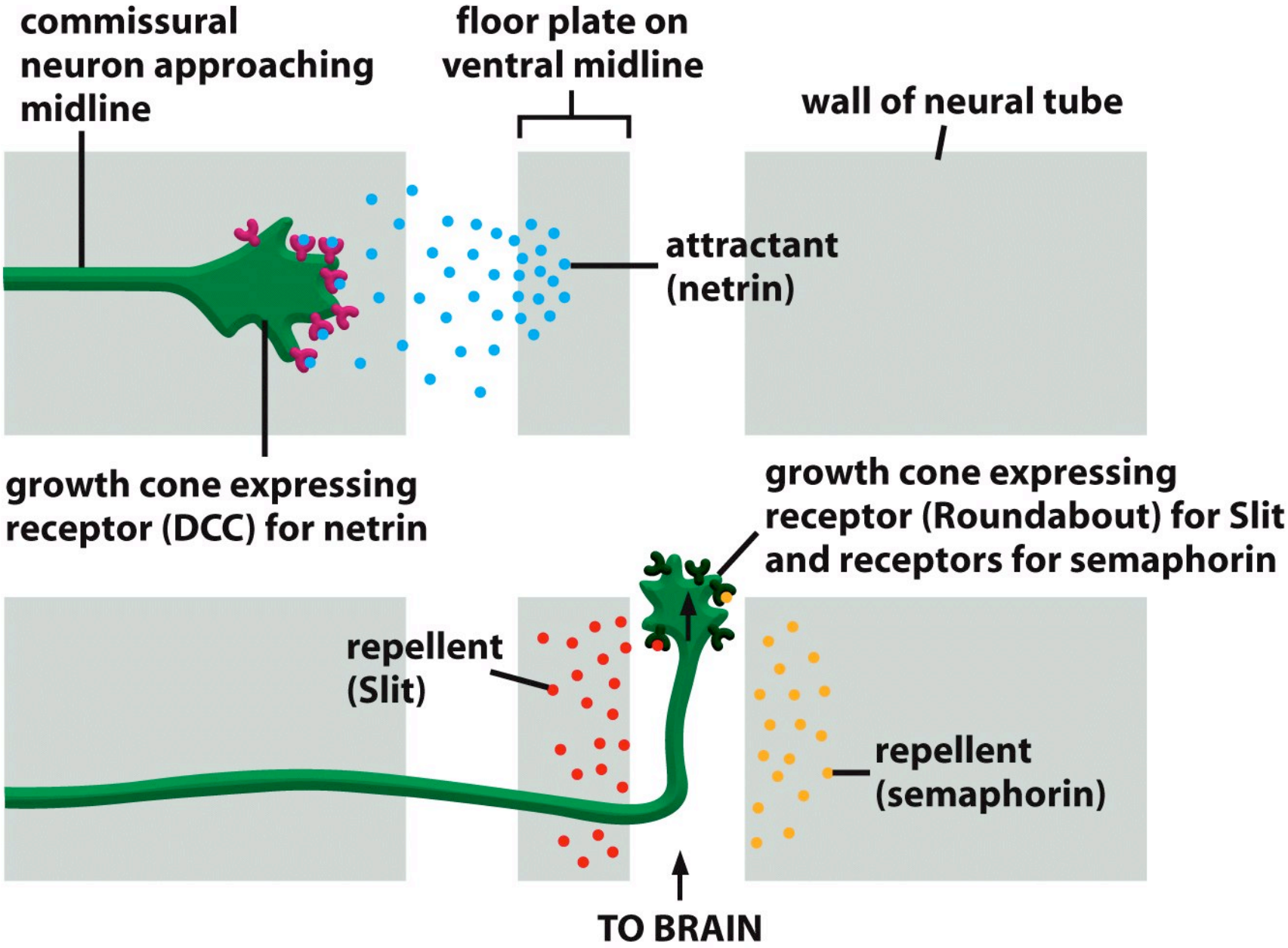



Figure 22-102b *Molecular Biology of the Cell* (© Garland Science 2008)

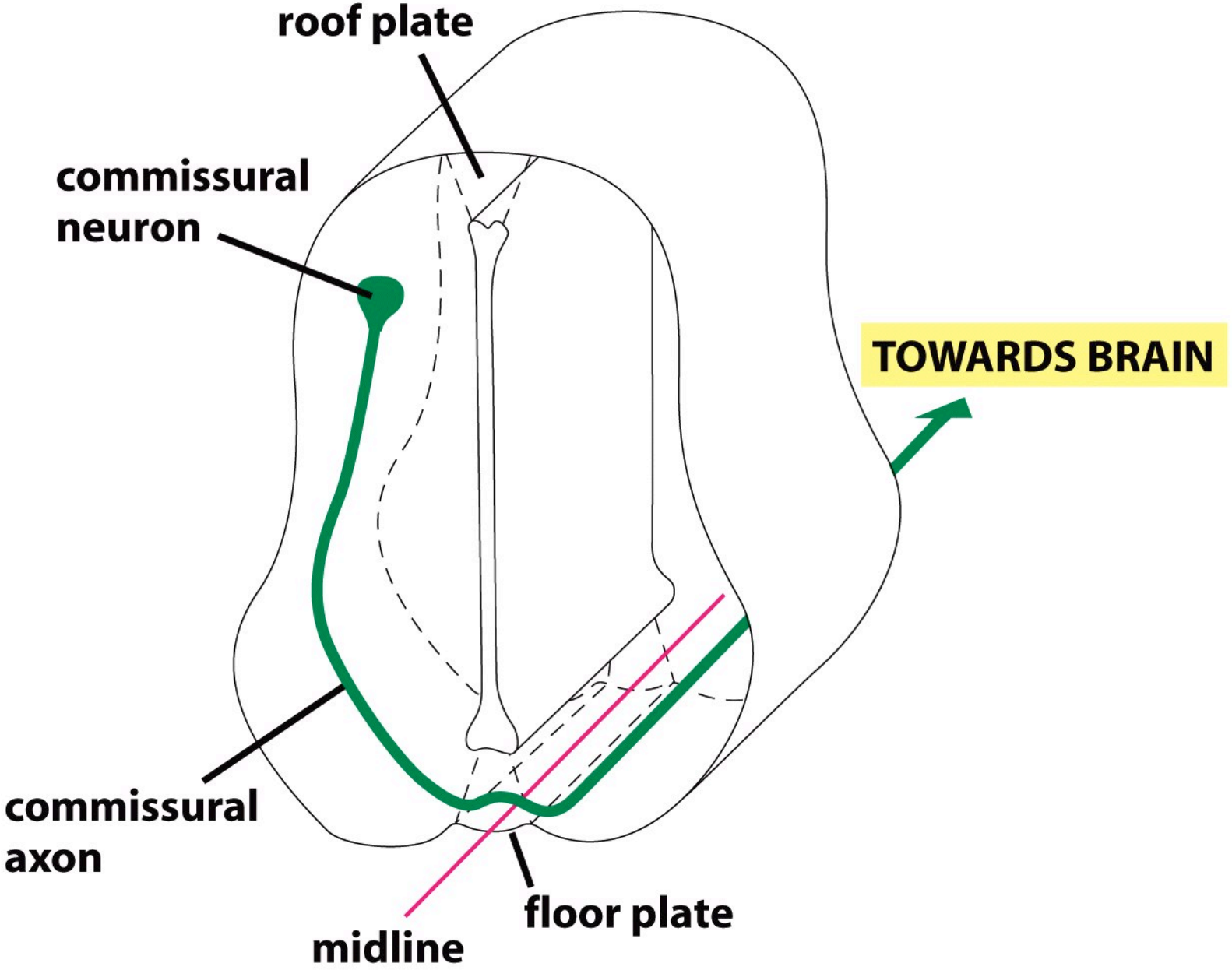
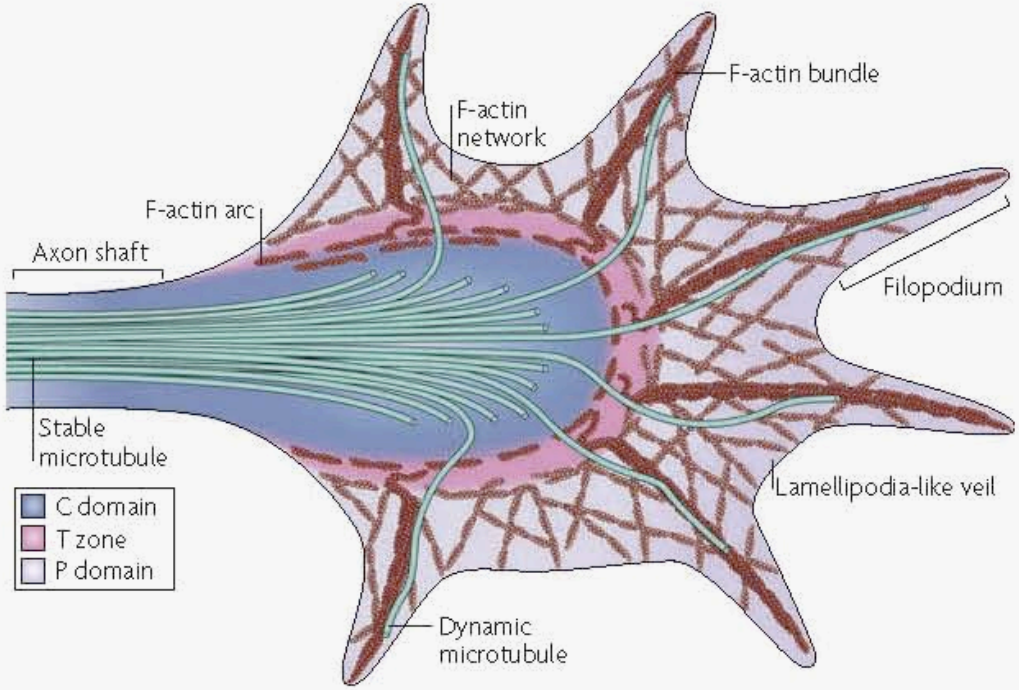



Figure 22-102a *Molecular Biology of the Cell* (© Garland Science 2008)

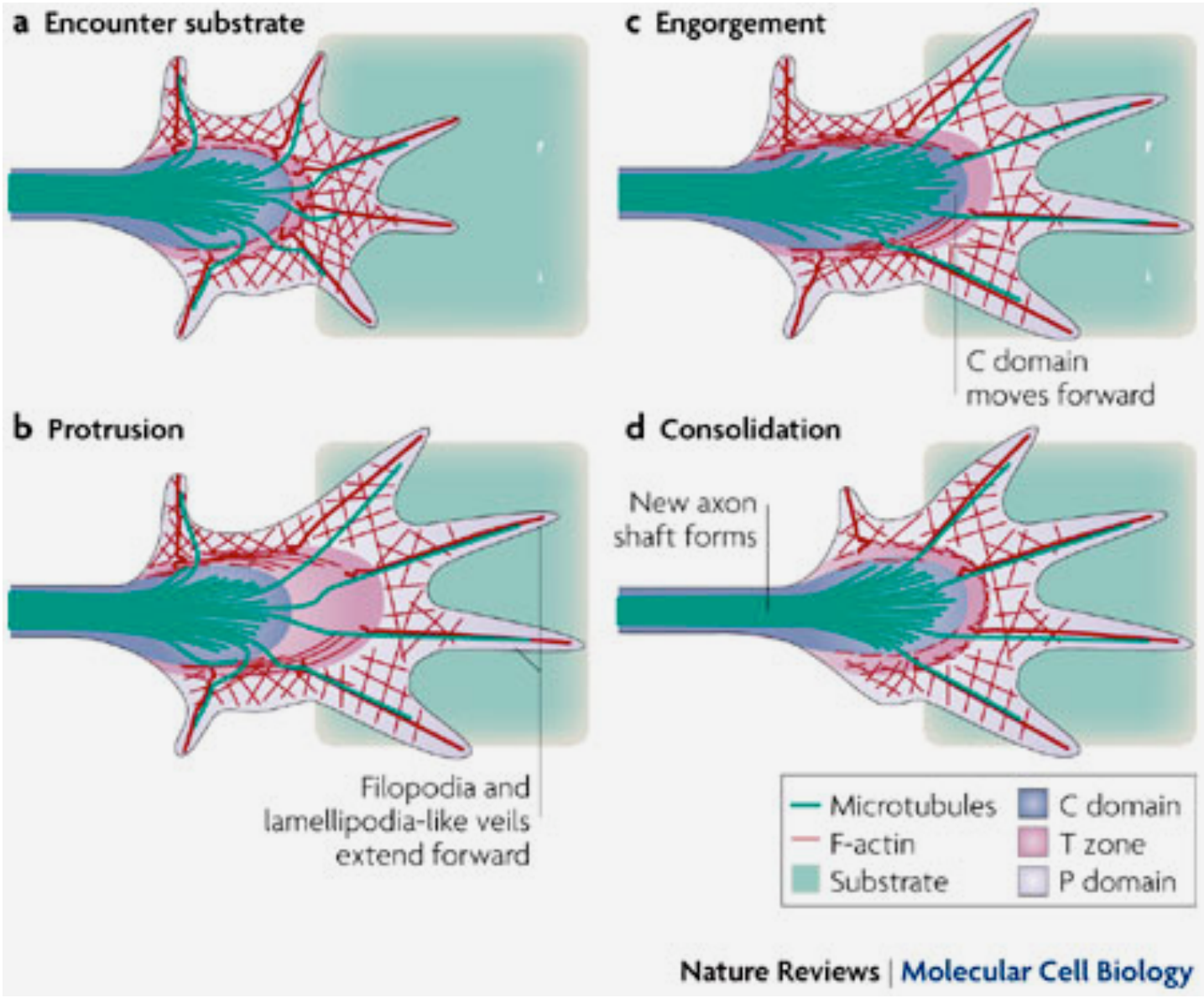
Box 1 | **The structure of the growth cone**




The structure of the growth cone is fundamental to its function. The leading edge consists of dynamic, finger-like filopodia that explore the road ahead, separated by sheets of membrane between the filopodia called lamellipodia-like veils (see the figure). The cytoskeletal elements in the growth cone underlie its shape, and the growth cone can be separated into three domains based on cytoskeletal distribution[1,4]. The peripheral (P) domain contains long, bundled actin filaments (F-actin bundles), which form the filopodia, as well as mesh-like branched F-actin networks, which give structure to lamellipodia-like veils. Additionally, individual dynamic 'pioneer' microtubules (MTs) explore this region, usually along F-actin bundles. The central (C) domain encloses stable, bundled MTs that enter the growth cone from the axon shaft, in addition to numerous organelles, vesicles and central actin bundles. Finally, the transition (T) zone sits at the interface between the P and C domains, where actomyosin contractile structures (termed actin arcs) lie perpendicular to F-actin bundles and form a hemicircumferential ring[33]. The dynamics of these cytoskeletal components determine growth cone shape and movement on its journey during development.

# Growth cone

- Growth cone propulsion: protrusion, engorgement and consolidation
- Growth cone motility and protrusion of the leading edge membrane depend on the dynamic properties of actin


a Encounter substrate
c Engorgement
C domain
moves forward
b Protrusion
d Consolidation
New axon
shaft forms
Filopodia and
lamellipodia-like veils
extend forward
Microtubules
F-actin
Substrate
C domain
T zone
P domain
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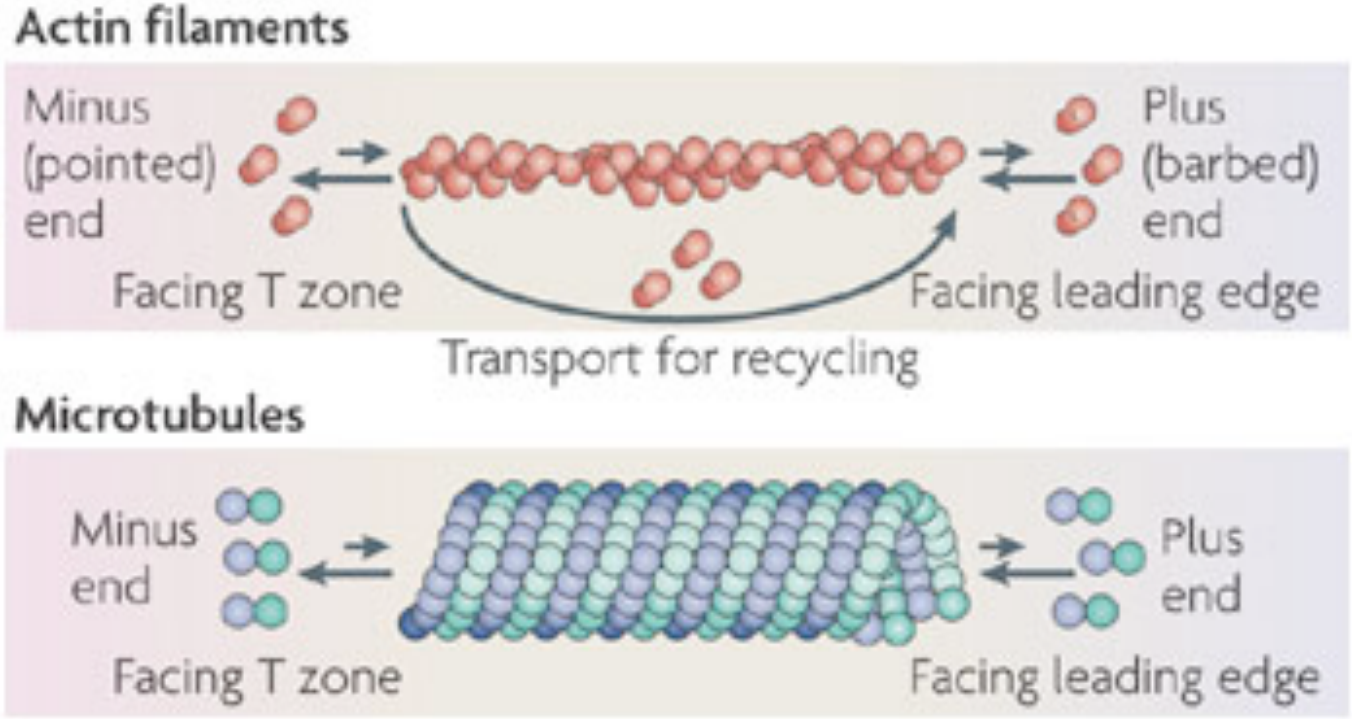
# Growth cone

- Growth cone propulsion: protrusion, engorgement and consolidation
- Growth cone motility and protrusion of the leading edge membrane depend on the dynamic properties of actin

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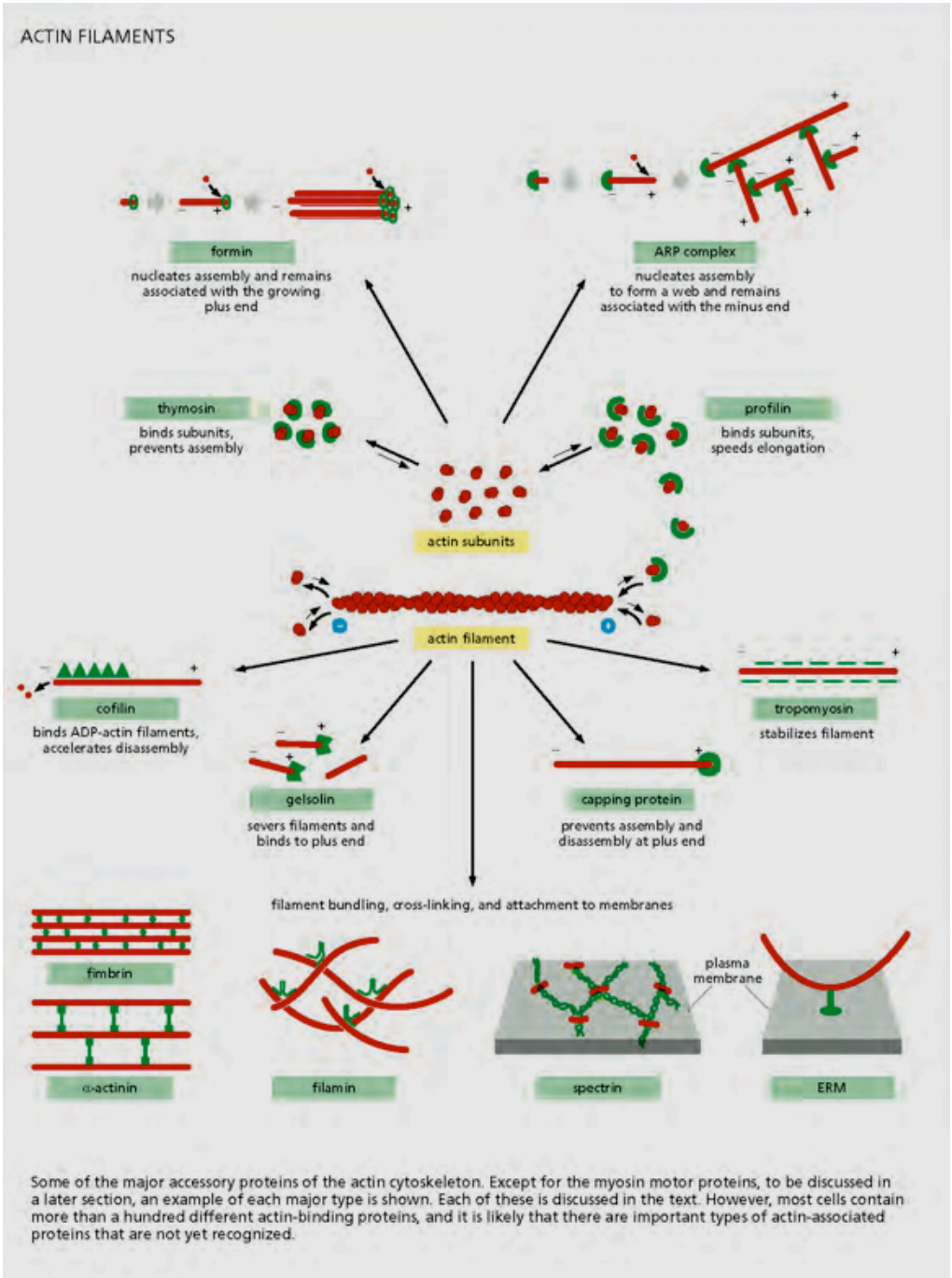



Some of the major accessory proteins of the actin cytoskeleton. Except for the myosin motor proteins, to be discussed in a later section, an example of each major type is shown. Each of these is discussed in the text. However, most cells contain more than a hundred different actin-binding proteins, and it is likely that there are important types of actin-associated proteins that are not yet recognized.

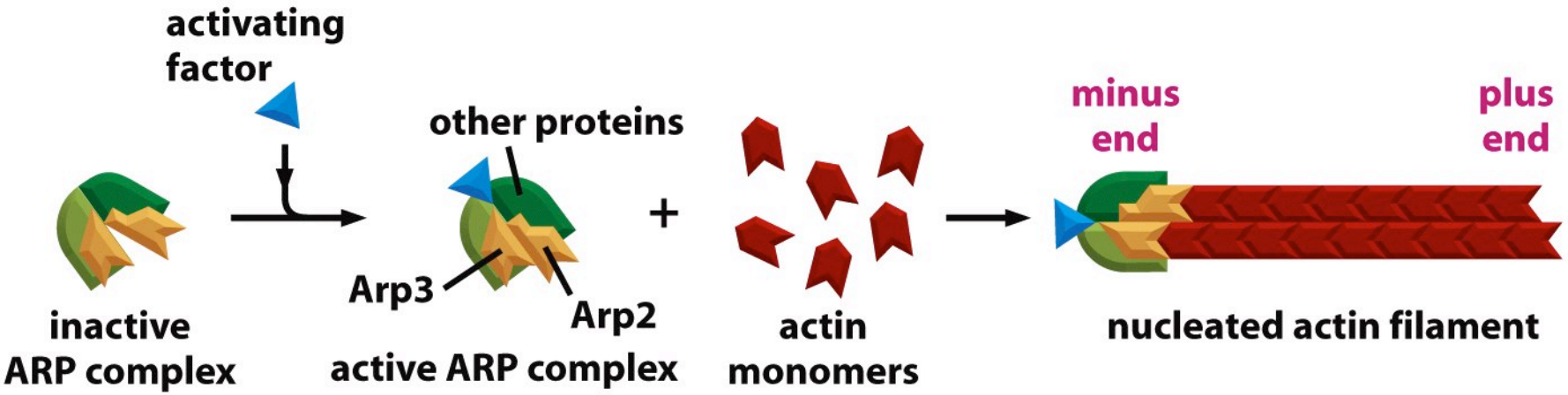



Figure 16-34b *Molecular Biology of the Cell* (© Garland Science 2008)

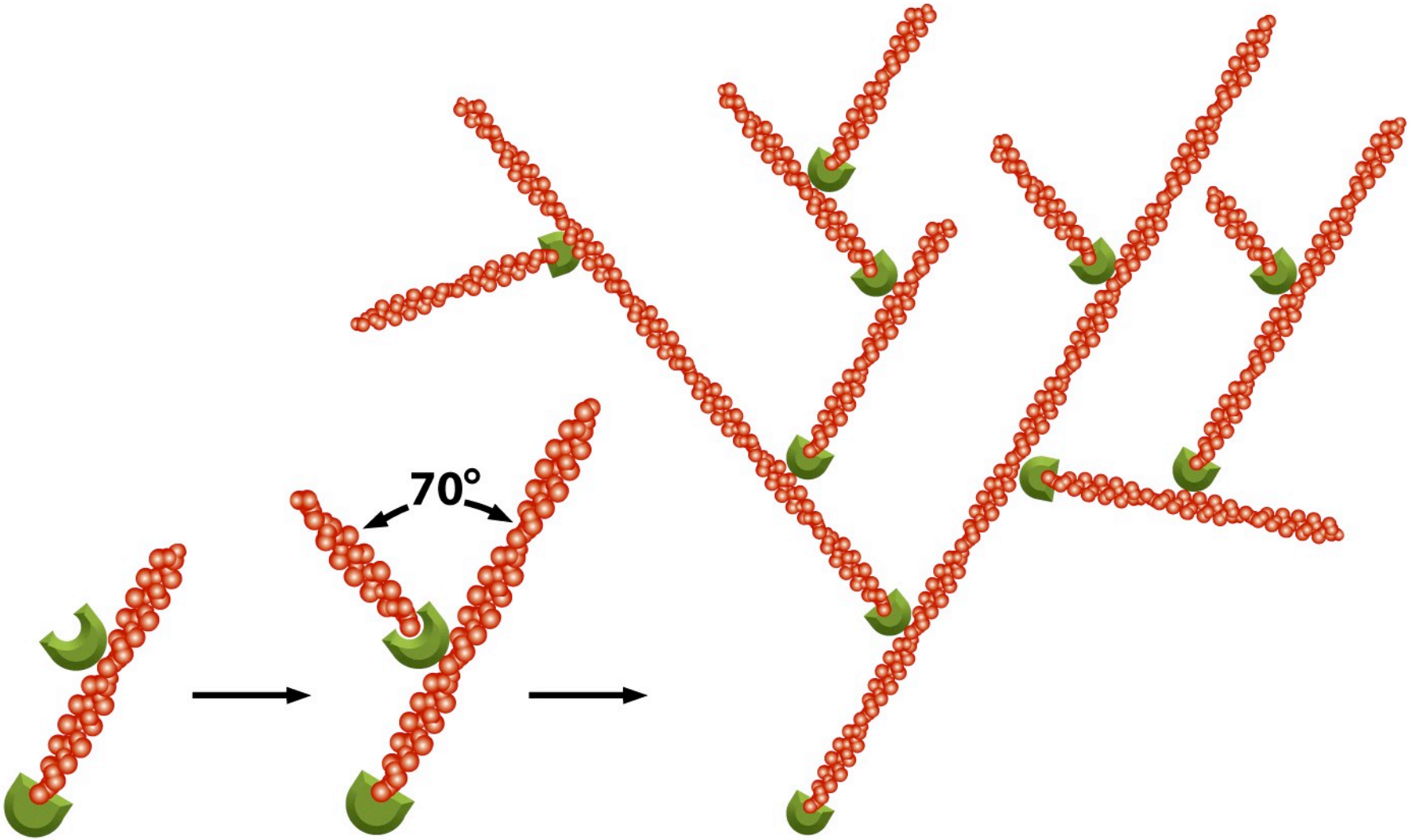



Figure 16-34c *Molecular Biology of the Cell* (© Garland Science 2008)

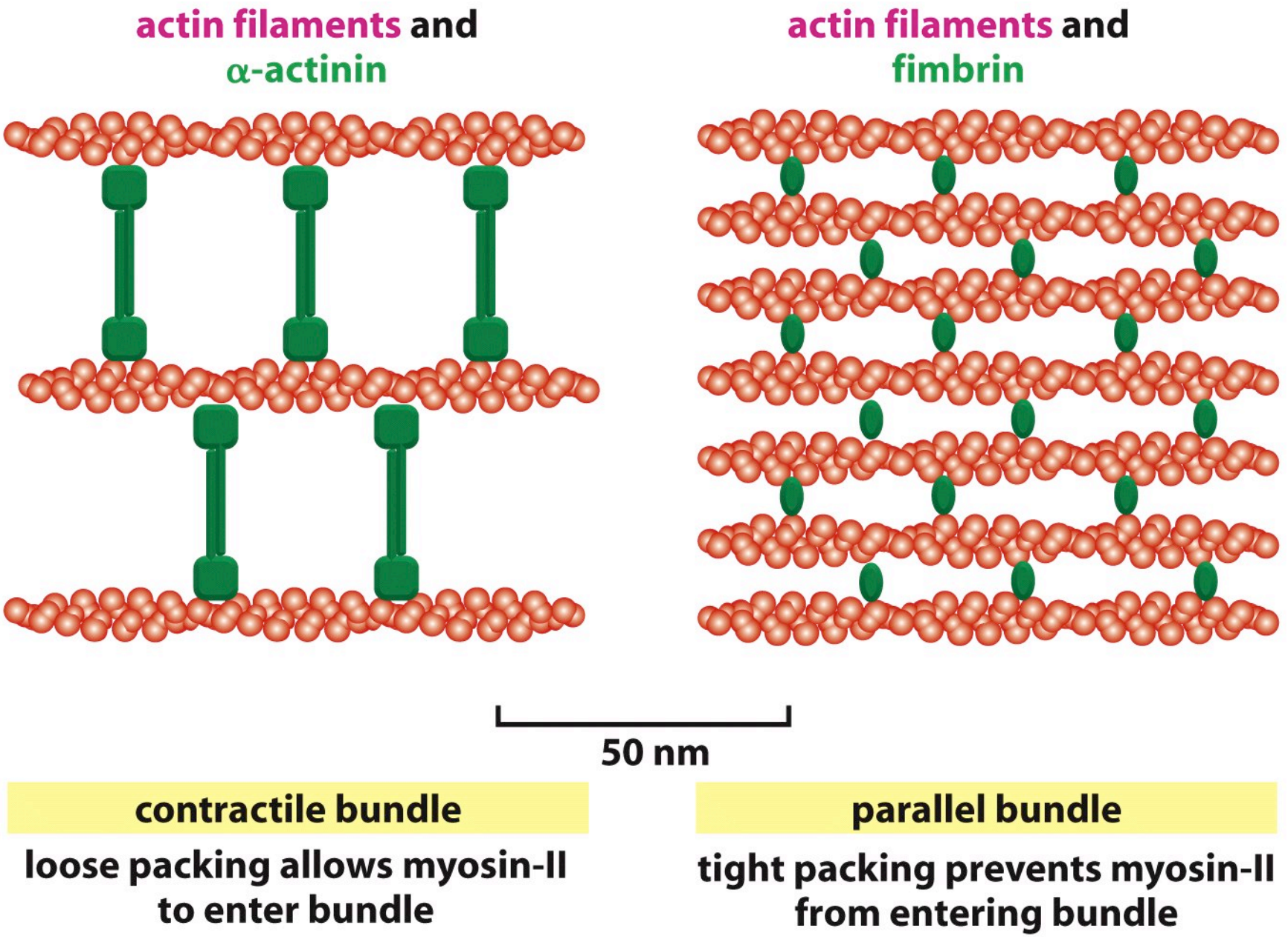



Figure 16-49a *Molecular Biology of the Cell* (© Garland Science 2008)

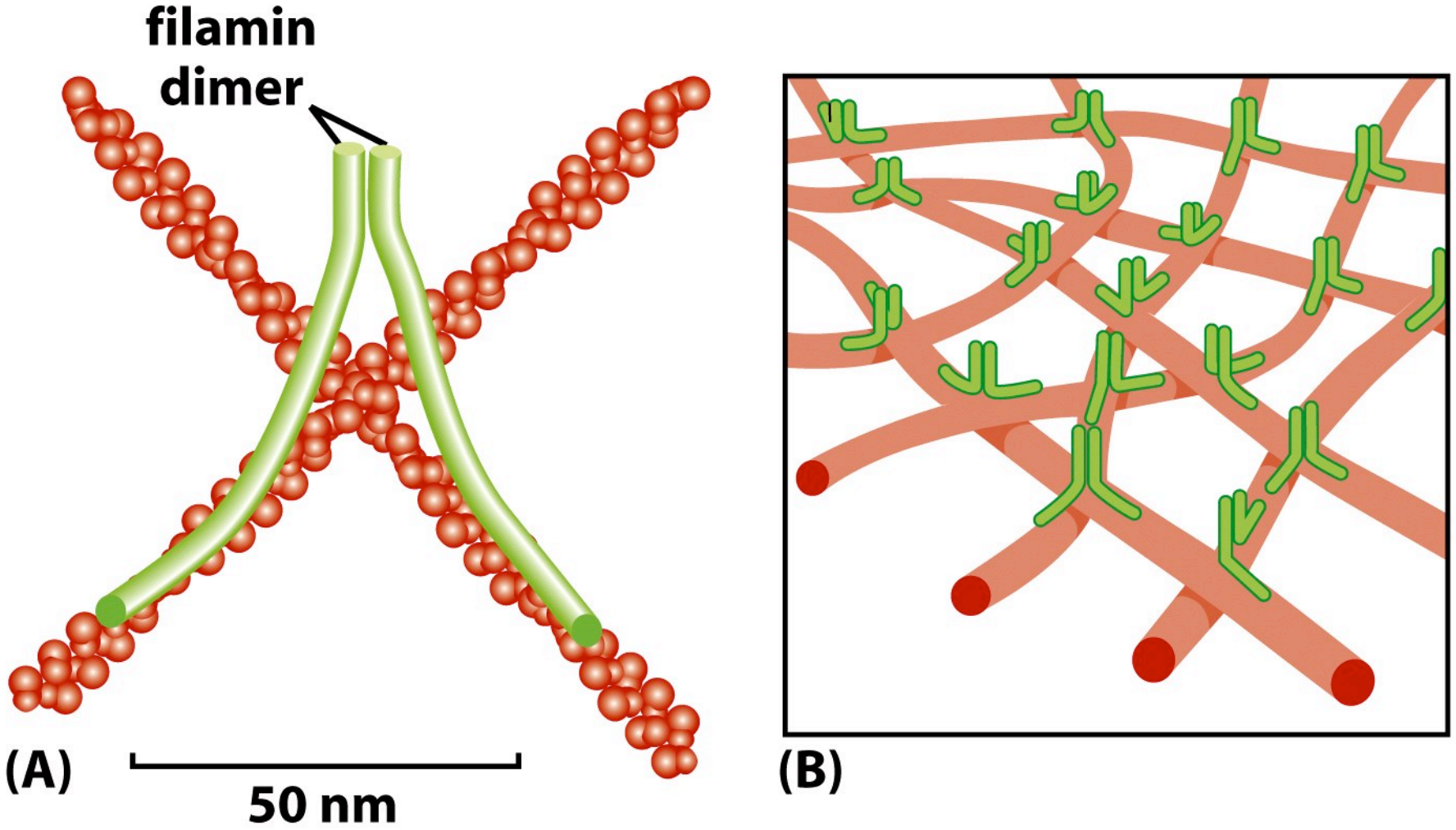



Figure 16-51 *Molecular Biology of the Cell* (© Garland Science 2008)

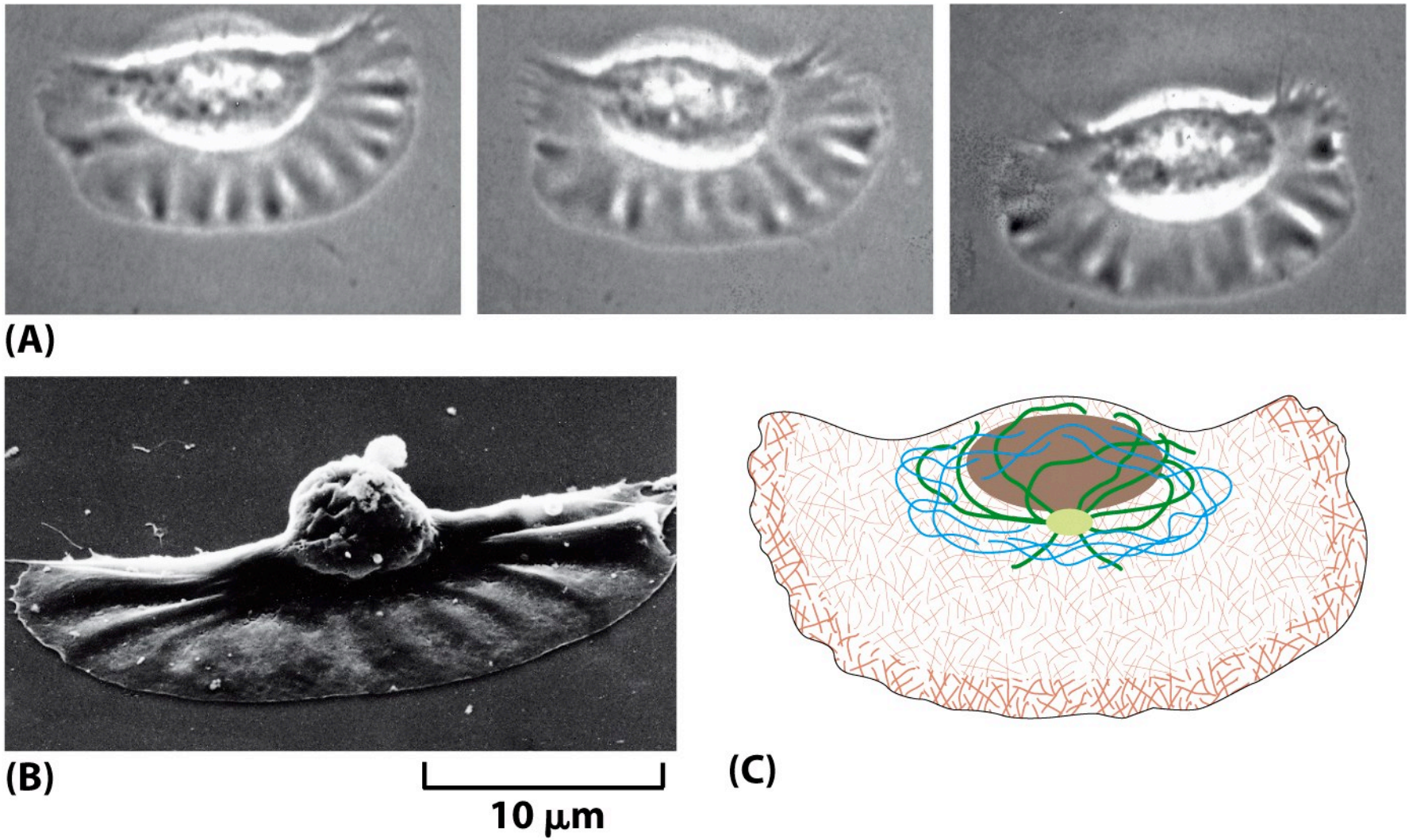



Figure 16-87 *Molecular Biology of the Cell* (© Garland Science 2008)

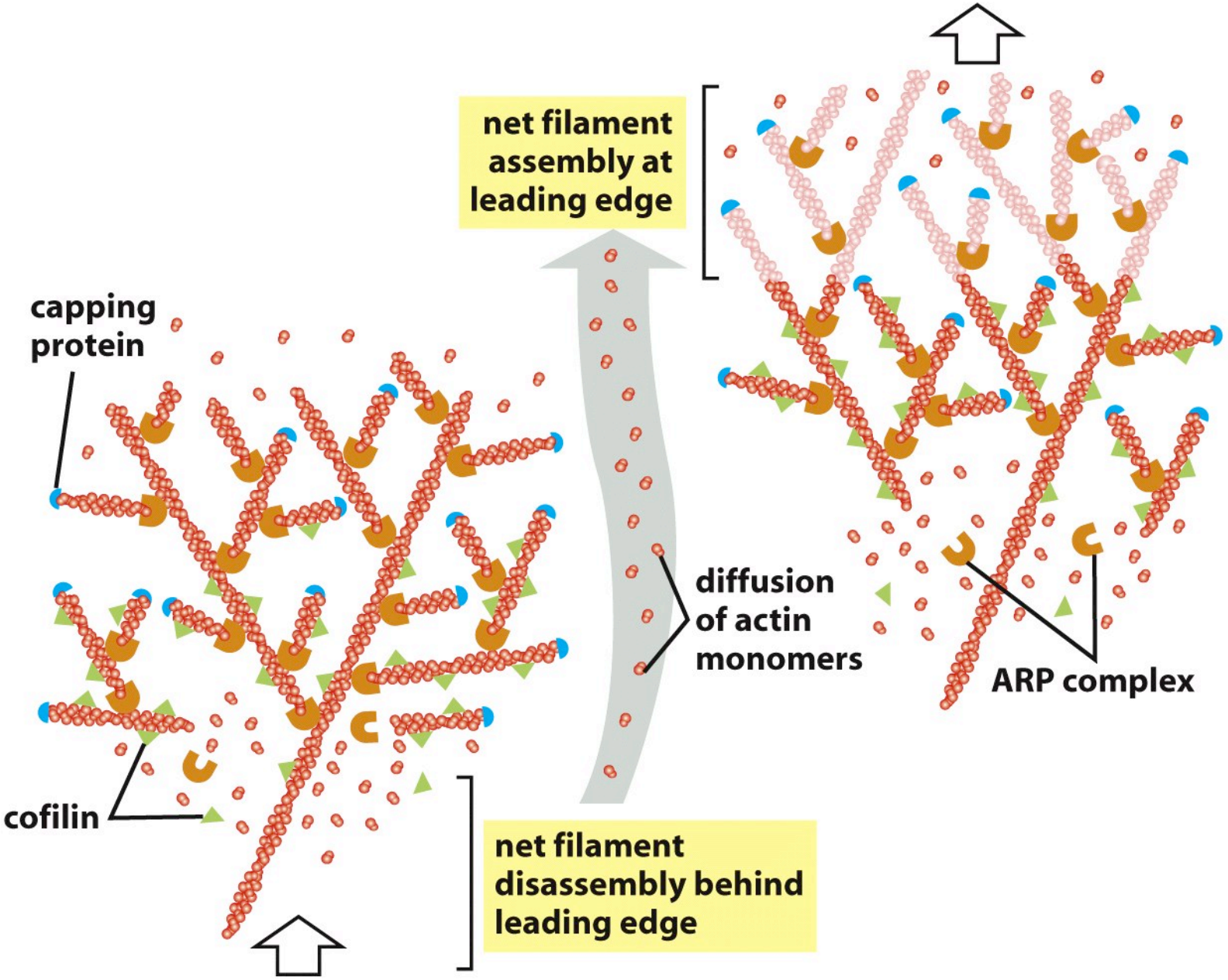



Figure 16-90 *Molecular Biology of the Cell* (© Garland Science 2008)

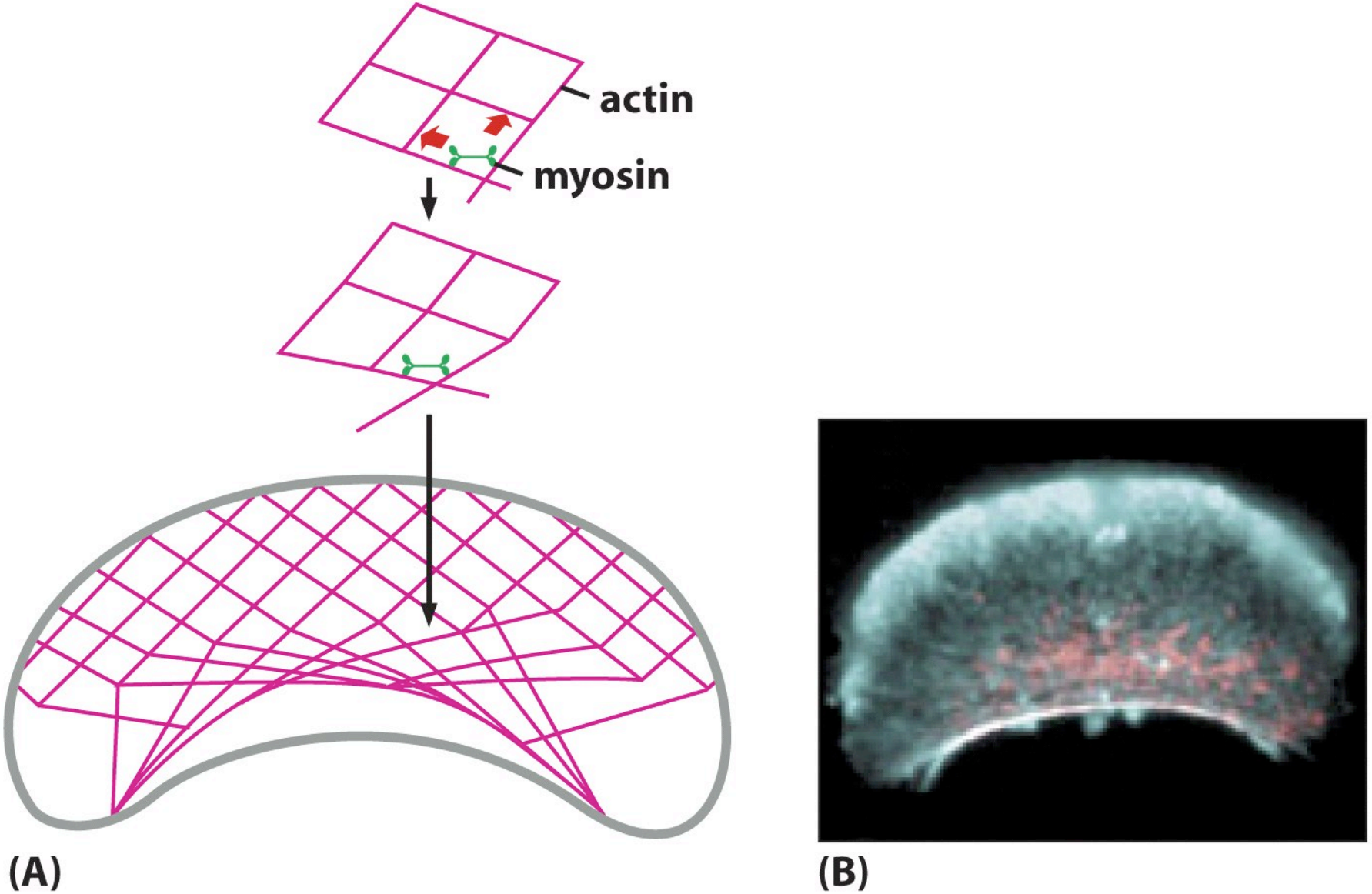



Figure 16-91 *Molecular Biology of the Cell* (© Garland Science 2008)

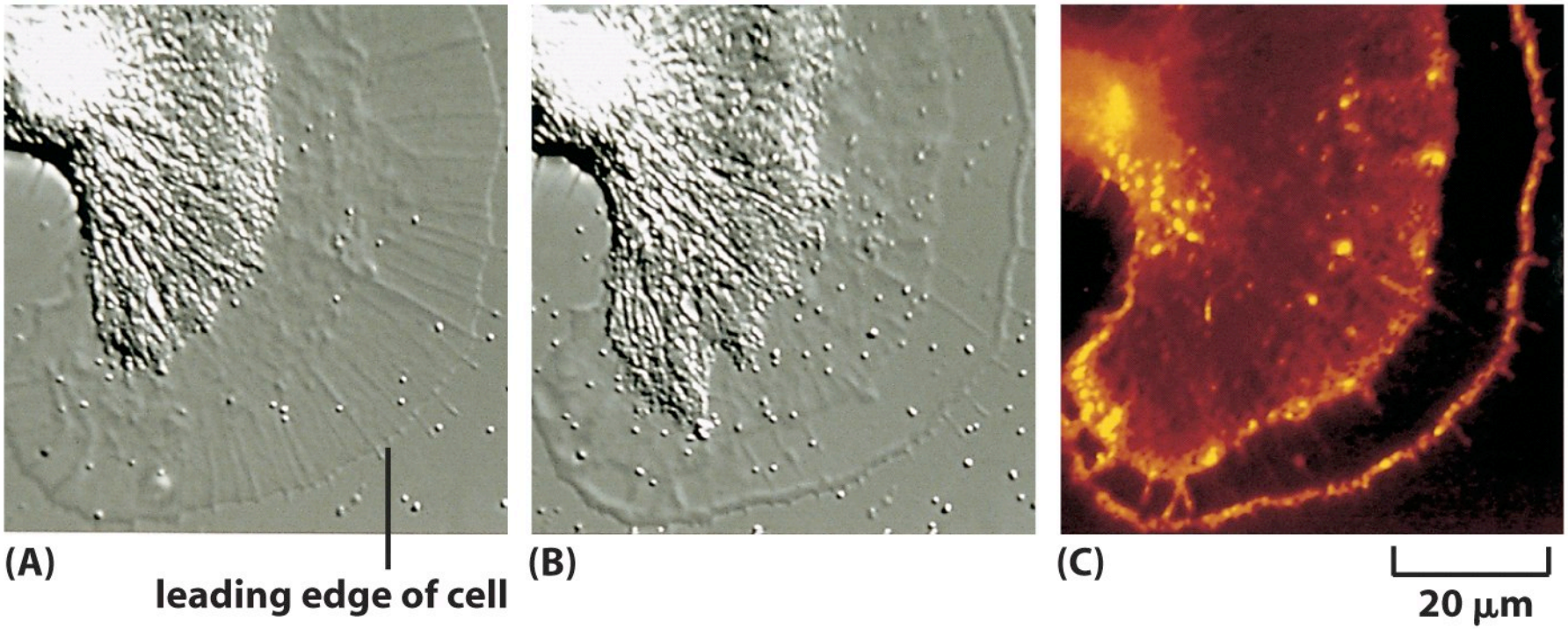



Figure 16-92a–c *Molecular Biology of the Cell* (© Garland Science 2008)

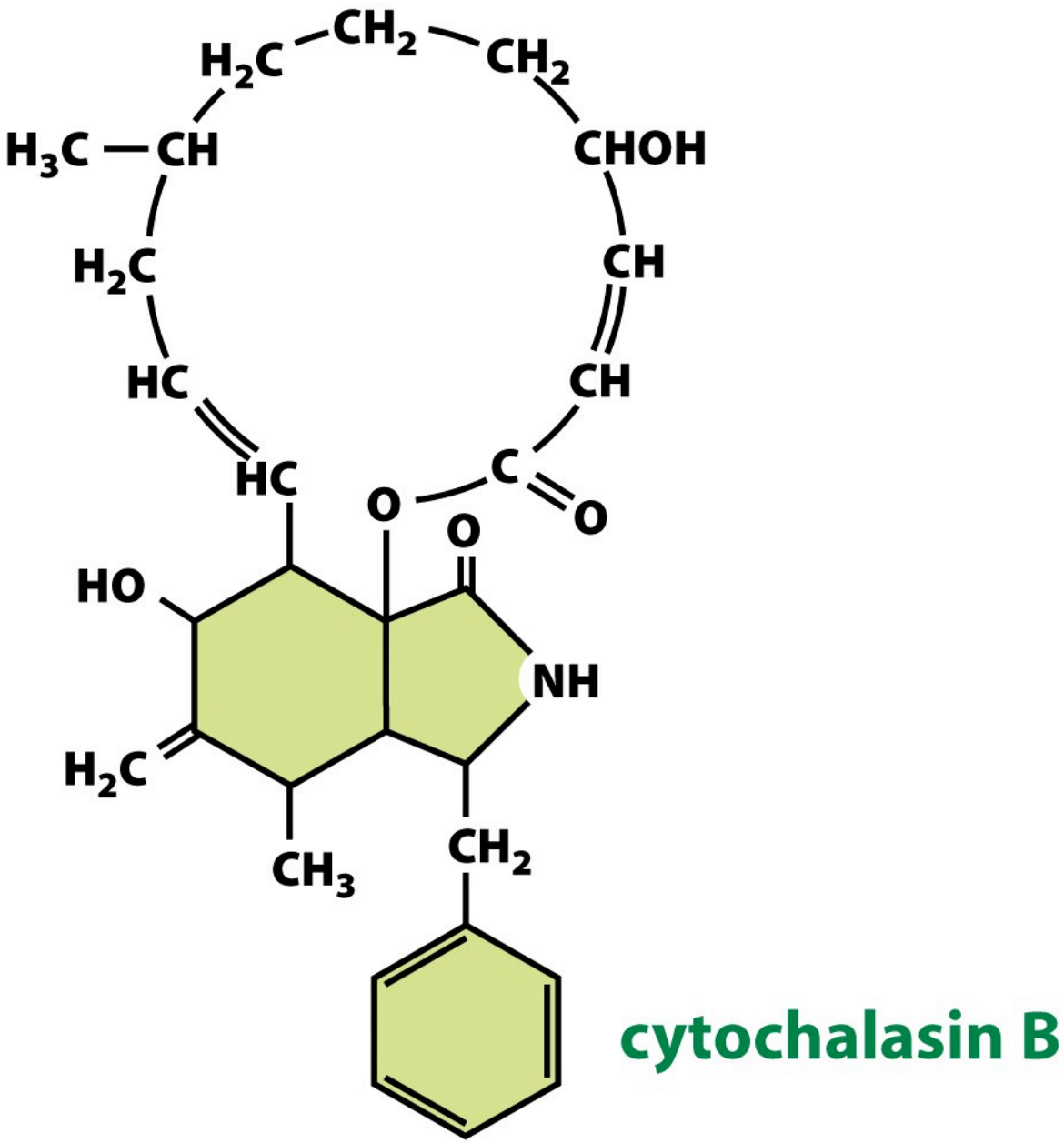



Figure 16-92d *Molecular Biology of the Cell* (© Garland Science 2008)

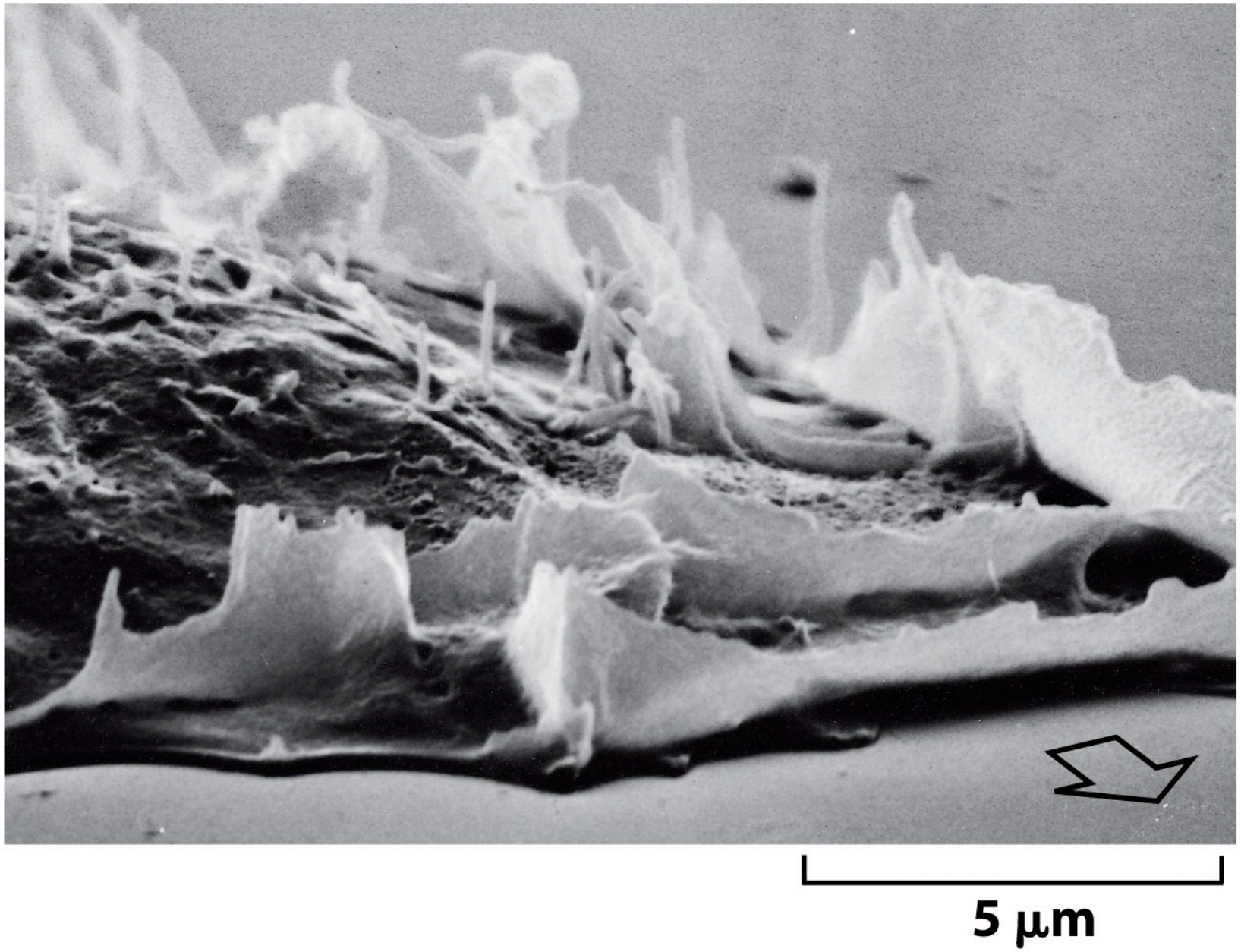
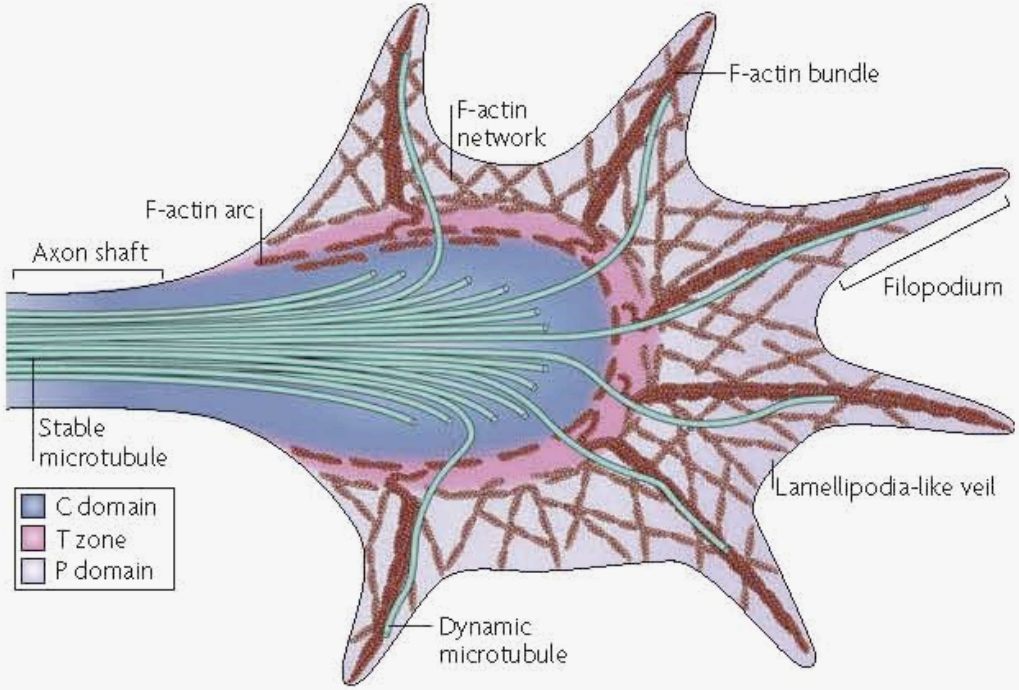
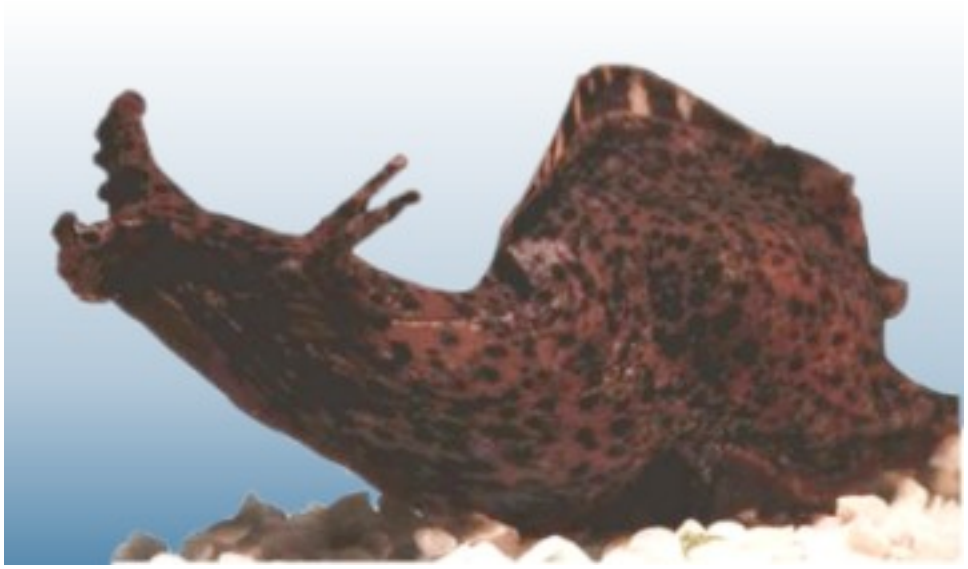



Figure 16-93 *Molecular Biology of the Cell* (© Garland Science 2008)

Box 1 | **The structure of the growth cone**




The structure of the growth cone is fundamental to its function. The leading edge consists of dynamic, finger-like filopodia that explore the road ahead, separated by sheets of membrane between the filopodia called lamellipodia-like veils (see the figure). The cytoskeletal elements in the growth cone underlie its shape, and the growth cone can be separated into three domains based on cytoskeletal distribution[1,4]. The peripheral (P) domain contains long, bundled actin filaments (F-actin bundles), which form the filopodia, as well as mesh-like branched F-actin networks, which give structure to lamellipodia-like veils. Additionally, individual dynamic 'pioneer' microtubules (MTs) explore this region, usually along F-actin bundles. The central (C) domain encloses stable, bundled MTs that enter the growth cone from the axon shaft, in addition to numerous organelles, vesicles and central actin bundles. Finally, the transition (T) zone sits at the interface between the P and C domains, where actomyosin contractile structures (termed actin arcs) lie perpendicular to F-actin bundles and form a hemicircumferential ring[33]. The dynamics of these cytoskeletal components determine growth cone shape and movement on its journey during development.



*Aplysia californica*

APCAM (NCAM)

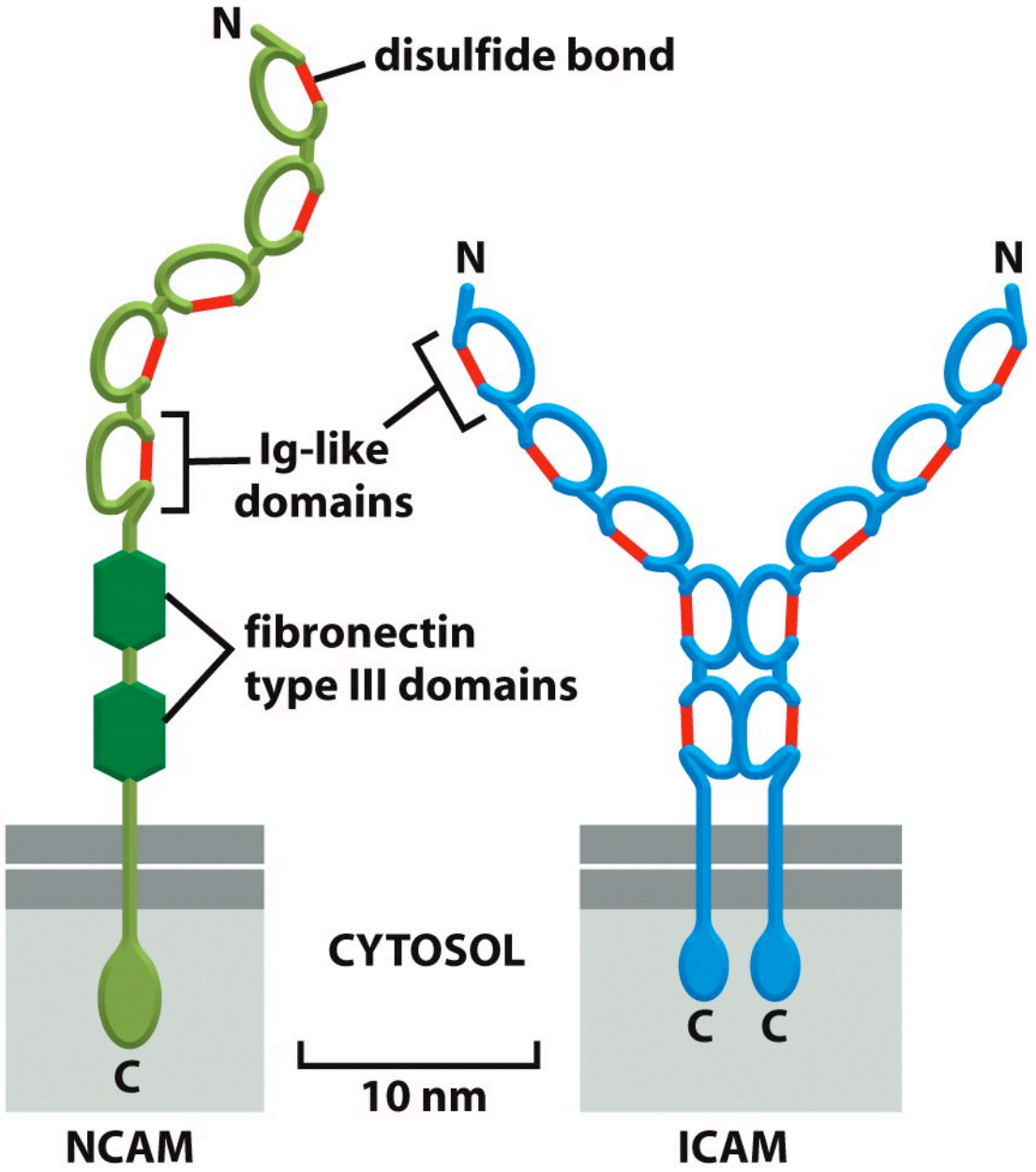



Figure 19-20 *Molecular Biology of the Cell* (© Garland Science 2008)

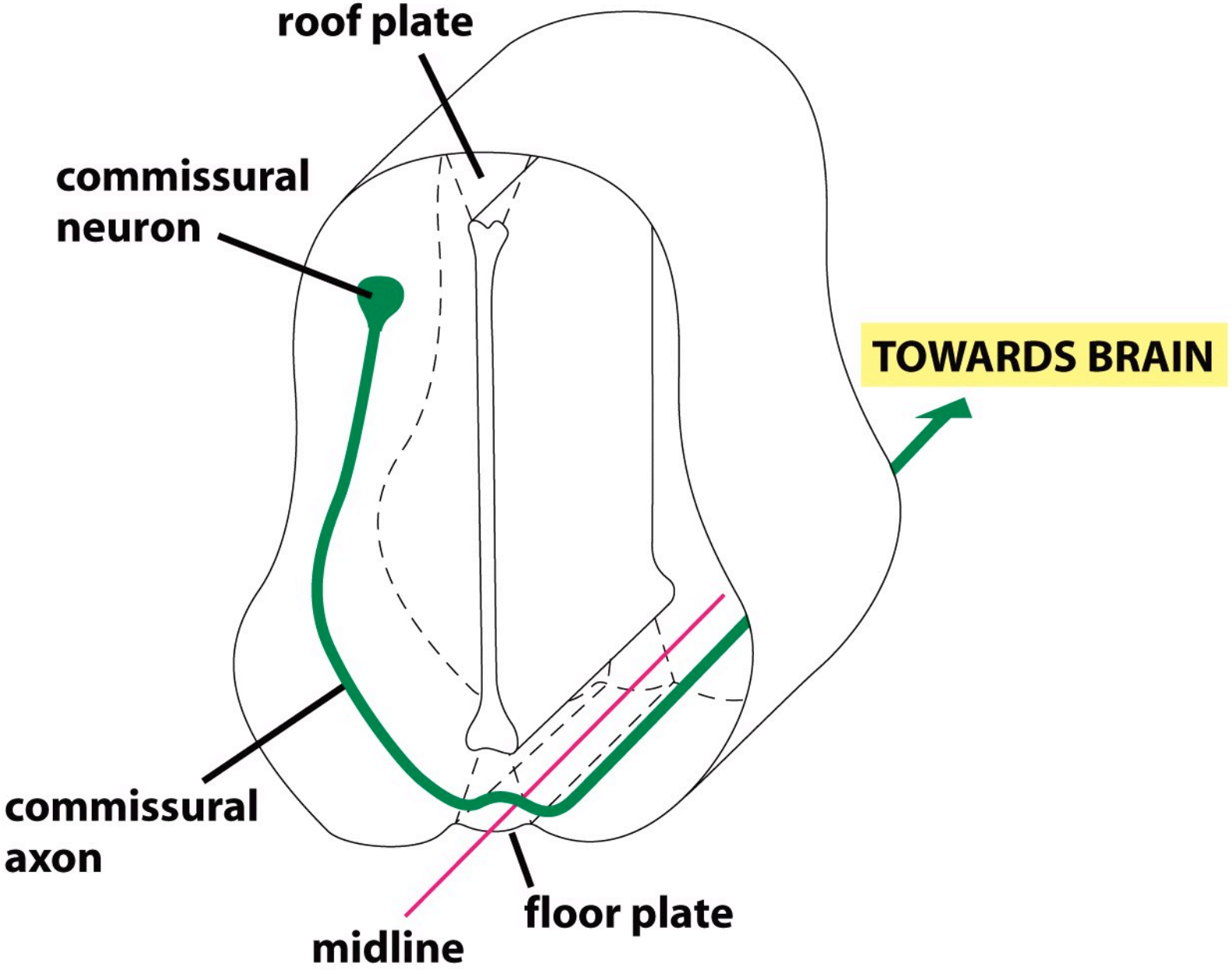



Figure 22-102a *Molecular Biology of the Cell* (© Garland Science 2008)

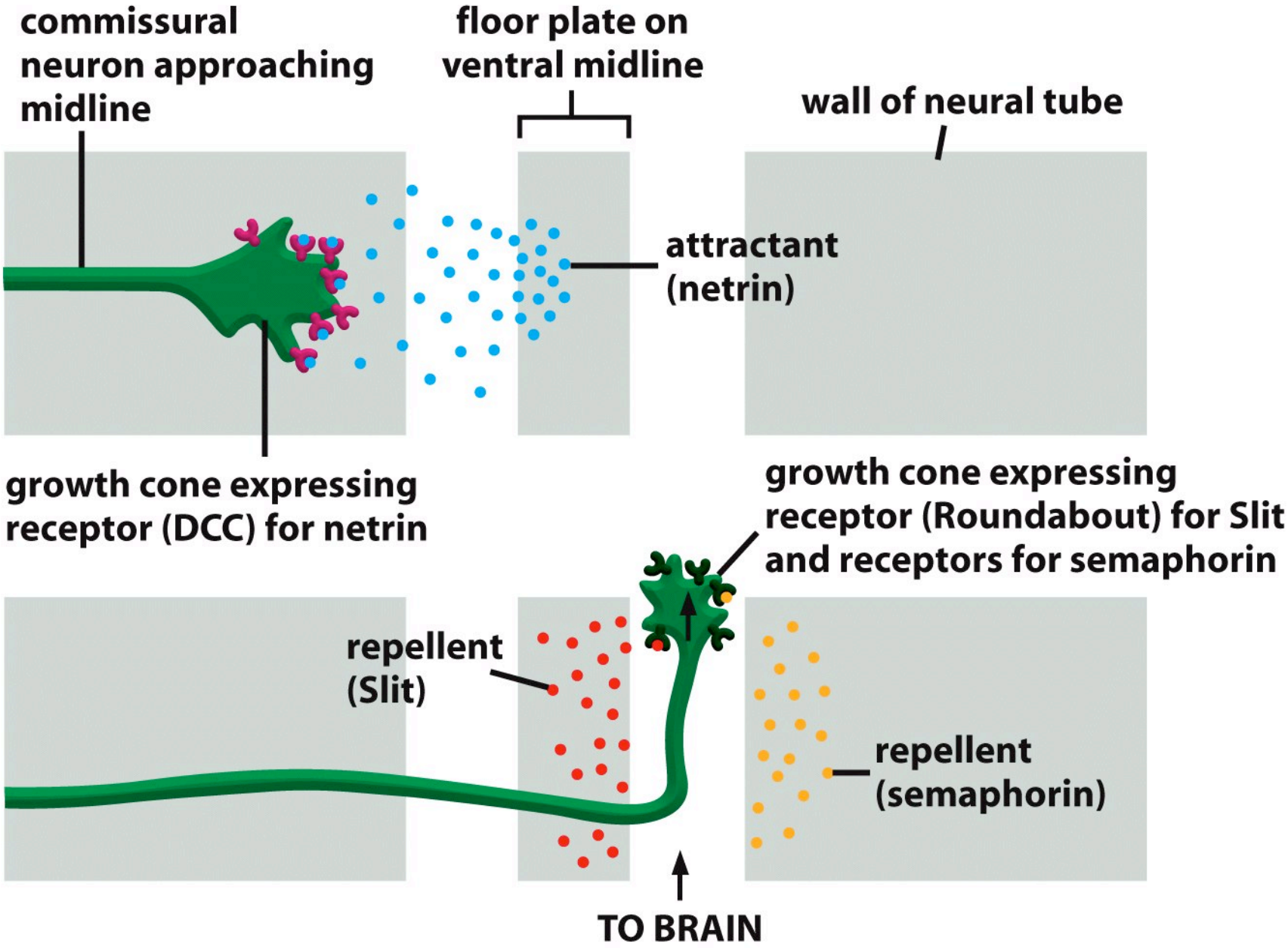
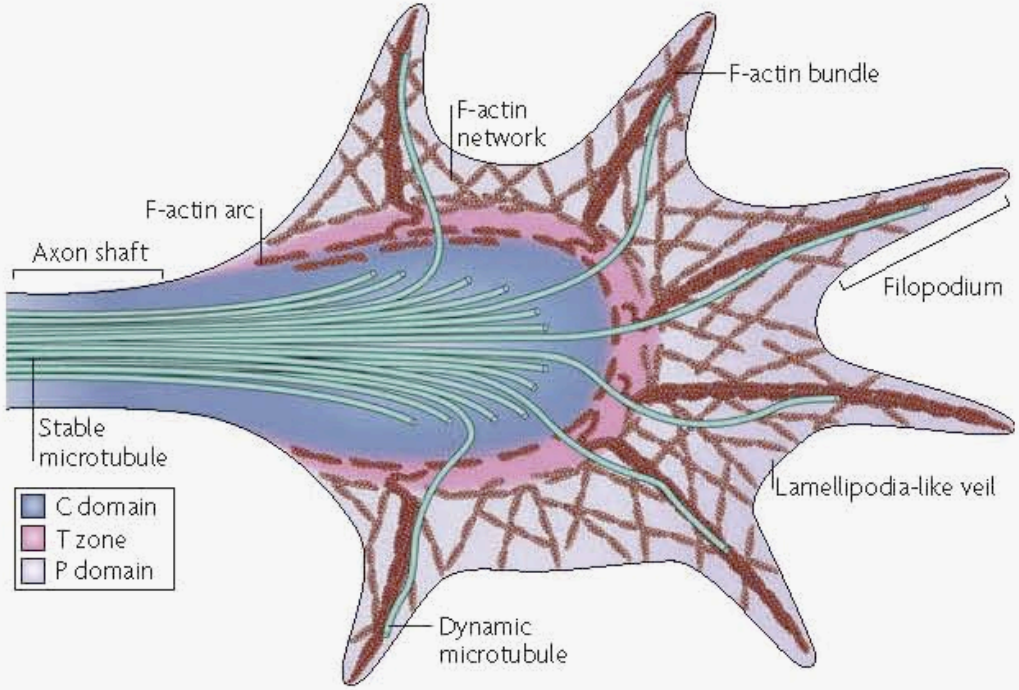



Figure 22-102b *Molecular Biology of the Cell* (© Garland Science 2008)

# Axonal guidance

- *Unc6, codes for the homolog of netrin*
- *Unc40, codes for its transmembrane receptor – homolog DCC*
- Localized activation of DCC by netrin leads to opening of a specialized class of ion channels (Ca ++) in the plasma membrane – TRCP
- Noncommissural neurons in the neural tube, lacking DCC, are not attracted to the floor plate
- *Unc5 (Unc5H)*, a different netrin receptor actively repelled by the floor plate and send their axons instead toward the roof plate.

Box 1 | **The structure of the growth cone**

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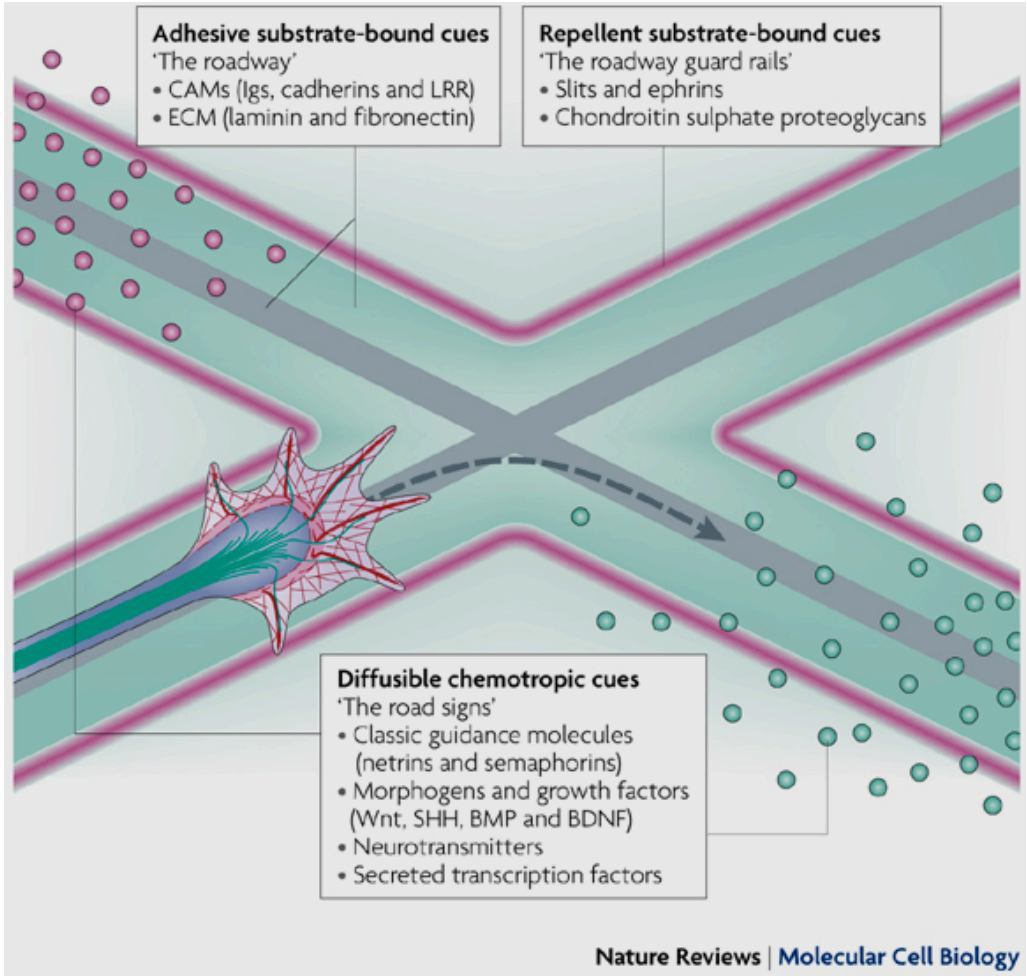
Adhesive substrate-bound cues
'The roadway'
• CAMs (Igs, cadherins and LRR)
• ECM (laminin and fibronectin)
Repellent substrate-bound cues
'The roadway guard rails'
• Slits and ephrins
• Chondroitin sulphate proteoglycans
Diffusible chemotropic cues
'The road signs'
• Classic guidance molecules (netrins and semaphorins)
• Morphogens and growth factors (Wnt, SHH, BMP and BDNF)
• Neurotransmitters
• Secreted transcription factors
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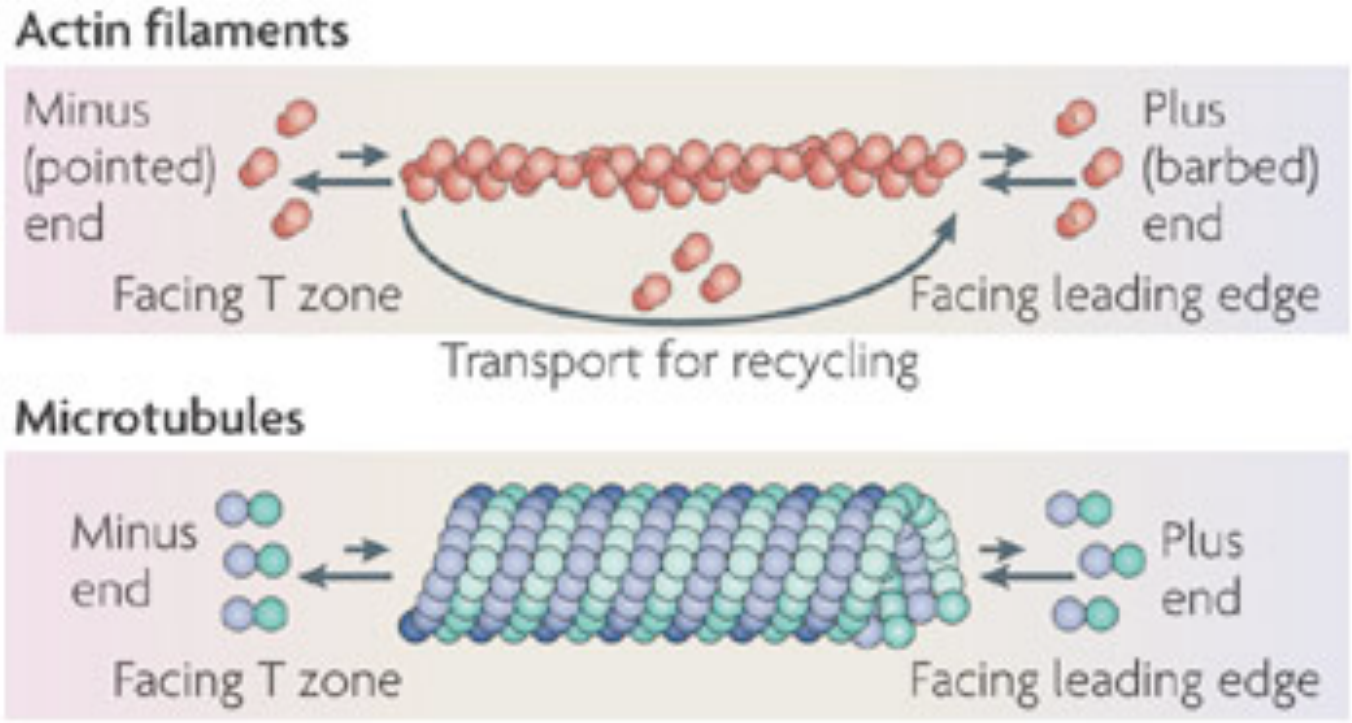


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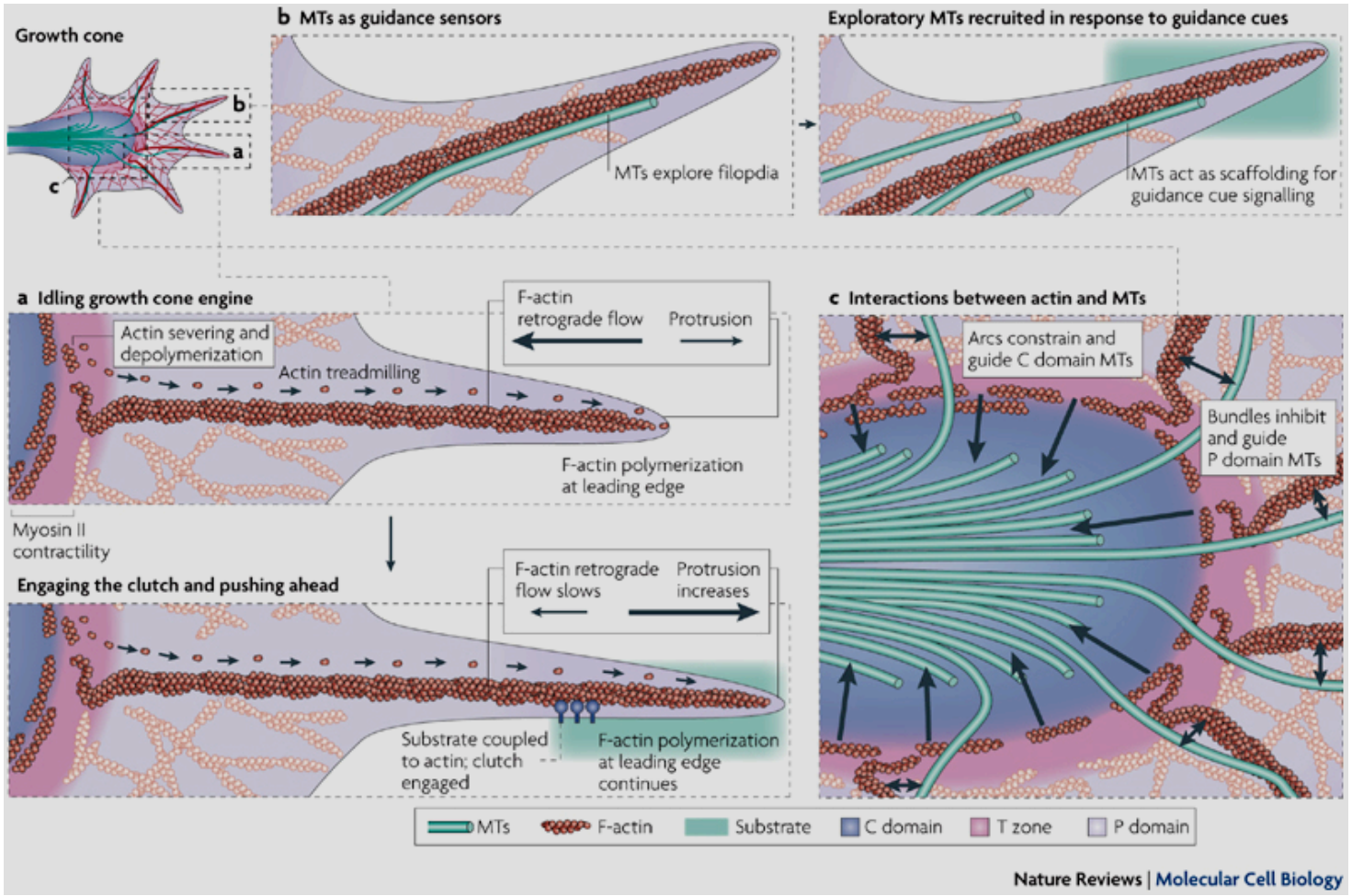
MTs involved in the localization of Src family of proteins

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# Environmental cues the direct growth cone

- -Adhesive molecules like  transmembrane cell adhesion molecules (CAMs)
- Complex extracellular matrix (ECM) like laminin and fibronectin.
- Anti-adhesive surface-bound molecules such as slits, ephrins and chondroitin sulphate proteoglycans
- Diffusible chemotropic cues such as netrins and semaphorins
- Morphogens such as Wnt, sonic hedgehog (SHH) and bone morphogenetic protein (BMP)
- Growth or neurotrophic factors such as brain-derived neurotrophic factor (BDNF), and neurotransmitters

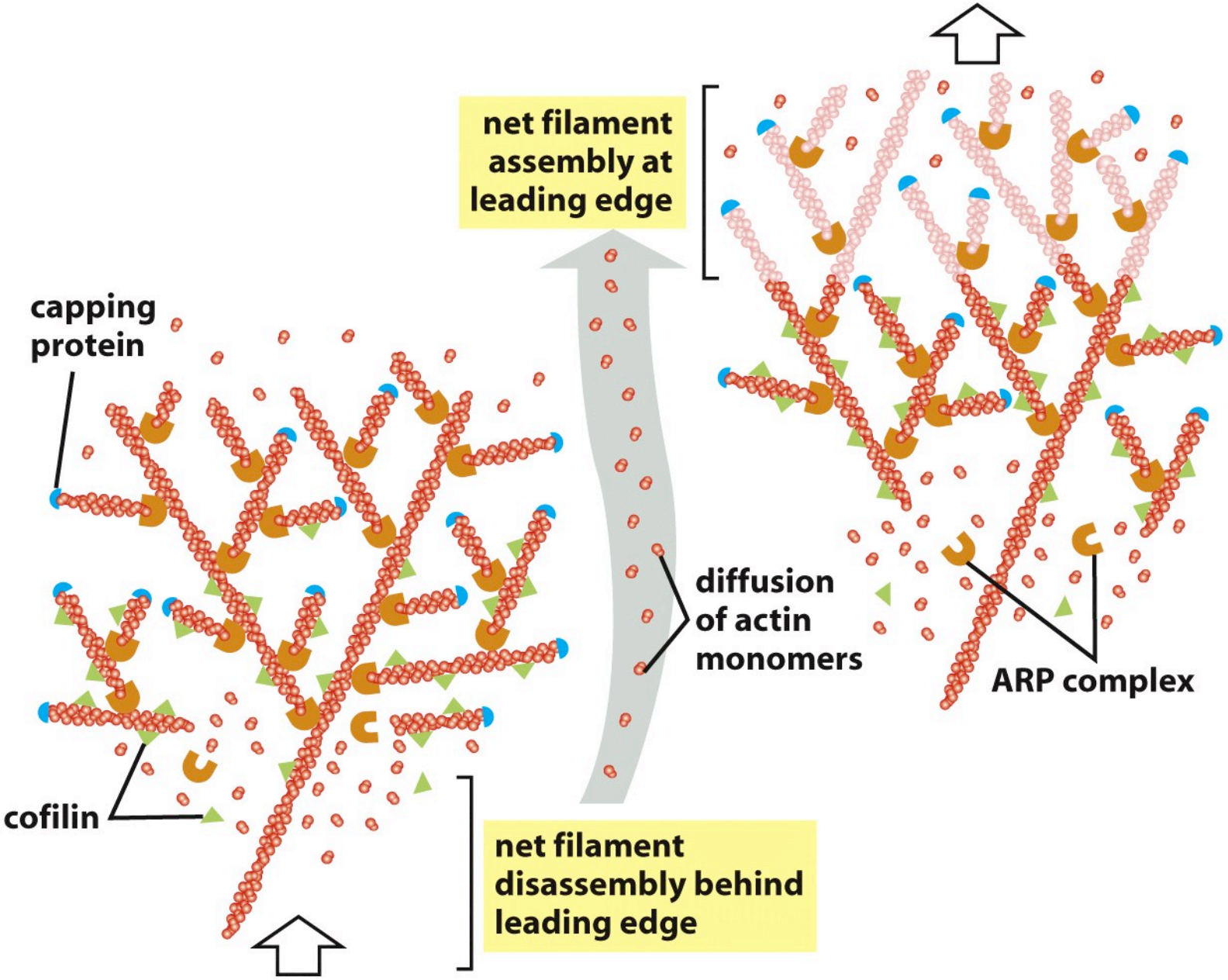



Figure 16-90 *Molecular Biology of the Cell* (© Garland Science 2008)

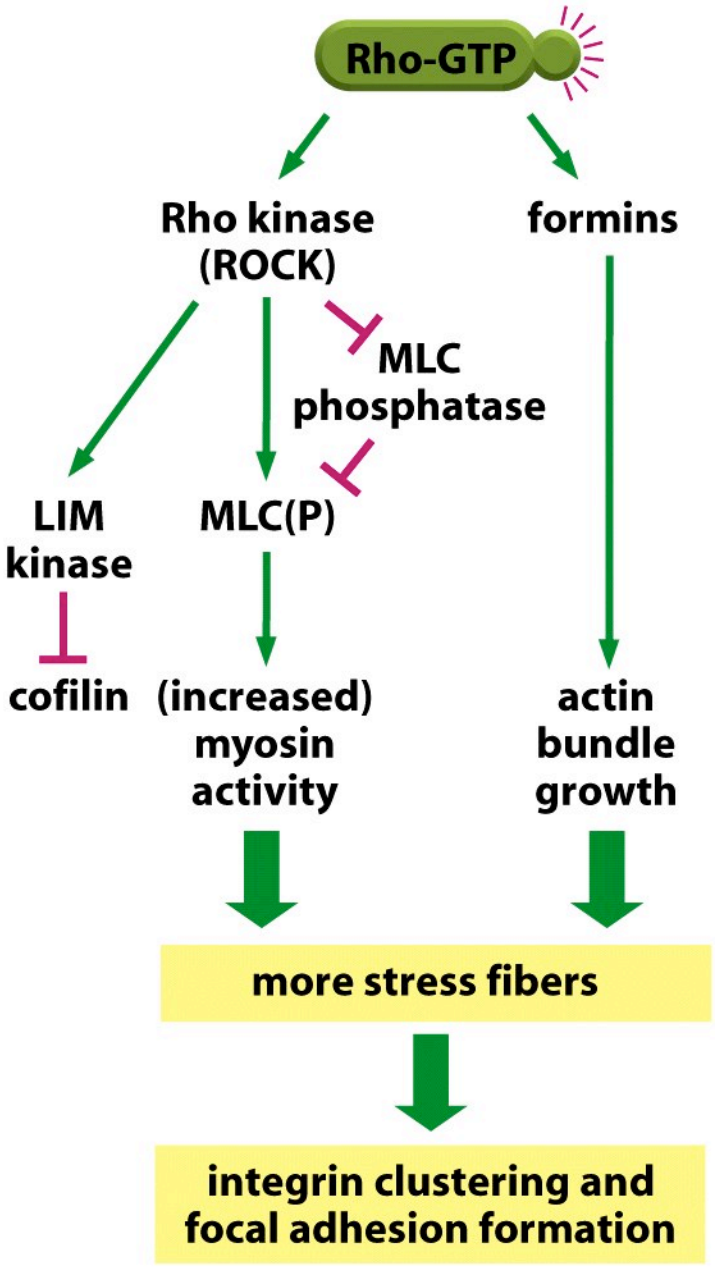
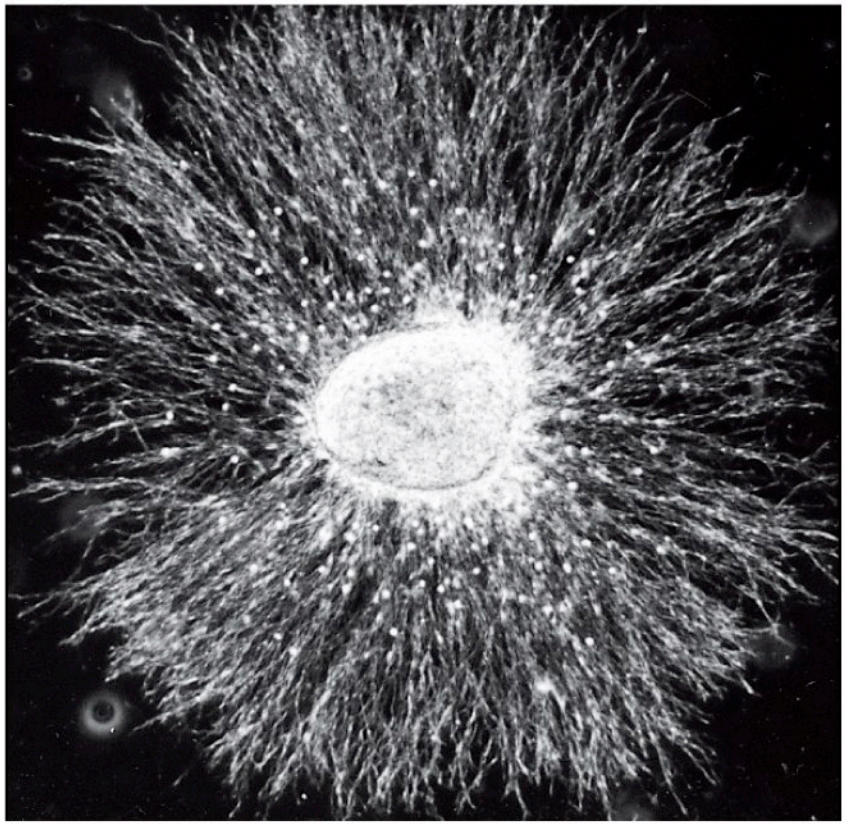
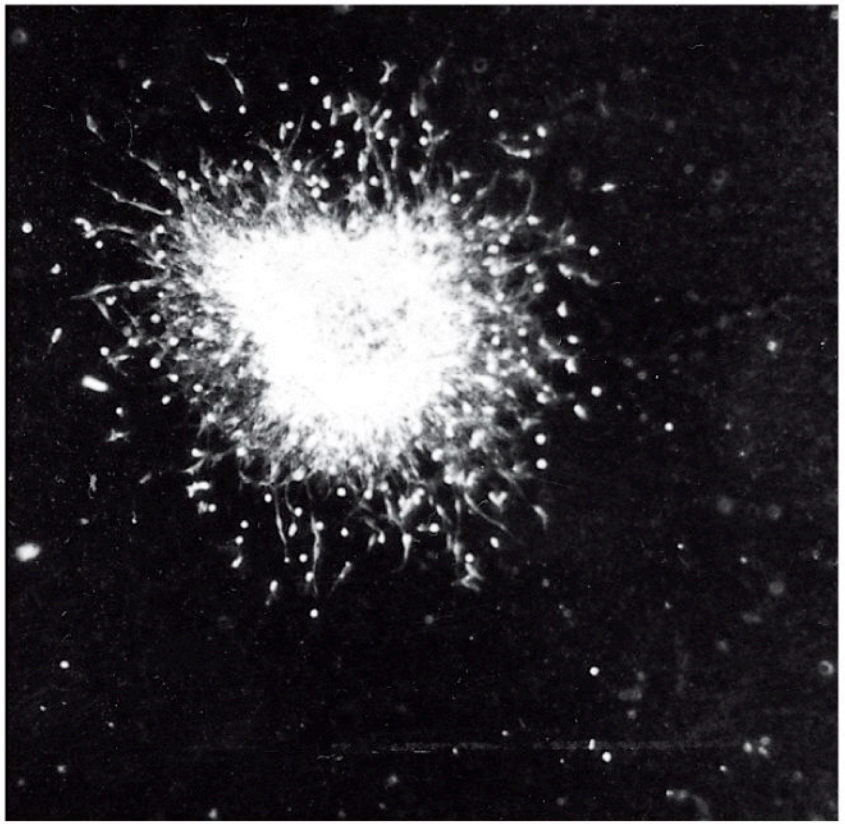



Figure 16-98b *Molecular Biology of the Cell* (© Garland Science 2008)

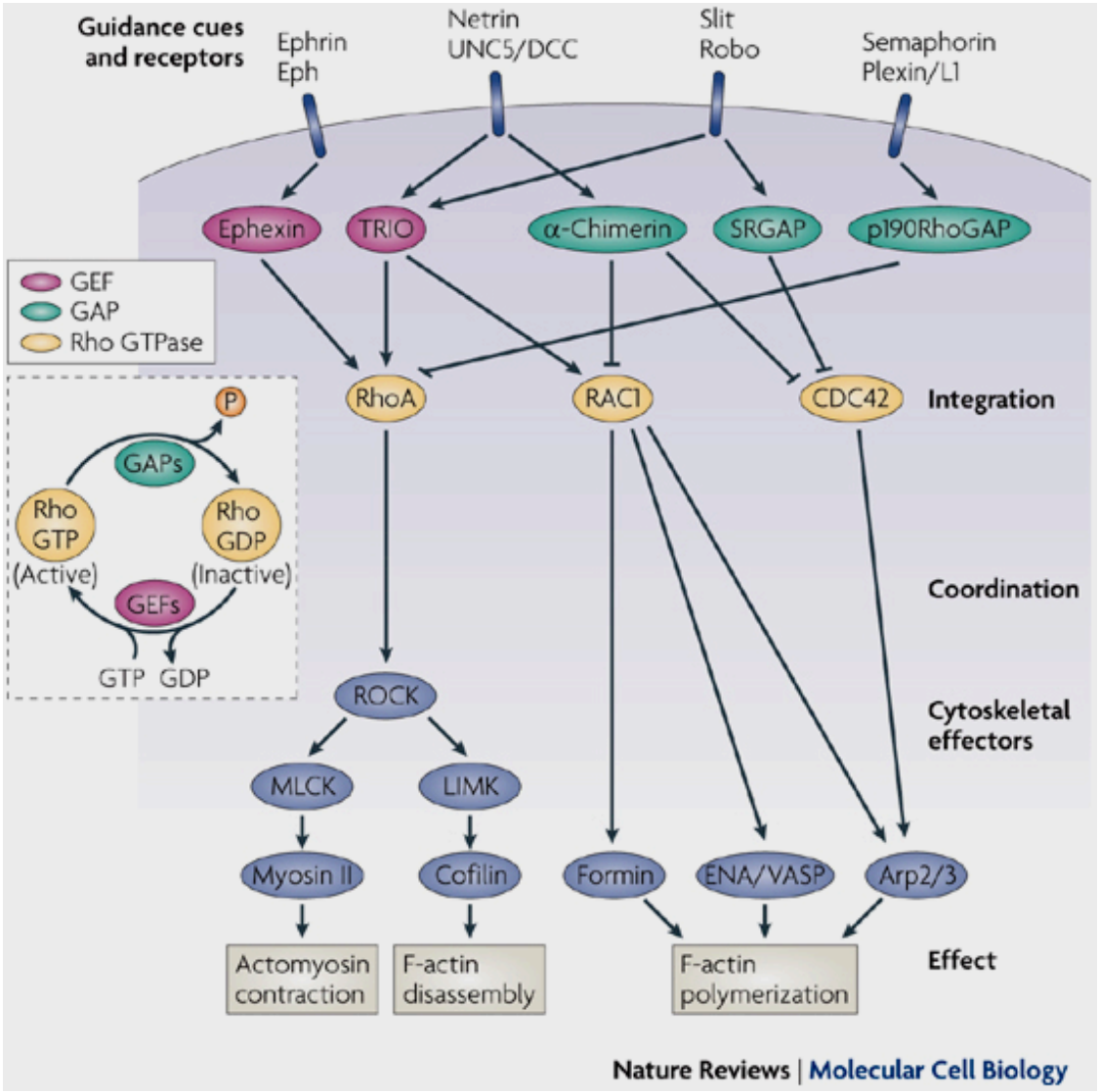


NGF



control

Figure 22-103 *Molecular Biology of the Cell* (© Garland Science 2008)


Guidance cues and receptors
Ephrin Eph
Netrin UNC5/DCC
Slit Robo
Semaphorin Plexin/L1
Ephexin
TRIO
α-Chimerin
SRGAP
p190RhoGAP
GEF
GAP
Rho GTPase
P
GAPs
Rho GTP
(Active)
Rho GDP
(Inactive)
GEFs
GTP GDP
RhoA
RAC1
CDC42
Integration
Coordination
Cytoskeletal effectors
Effect
ROCK
MLCK
LIMK
Myosin II
Cofilin
Formin
ENA/VASP
Arp2/3
Actomyosin contraction
F-actin disassembly
F-actin polymerization
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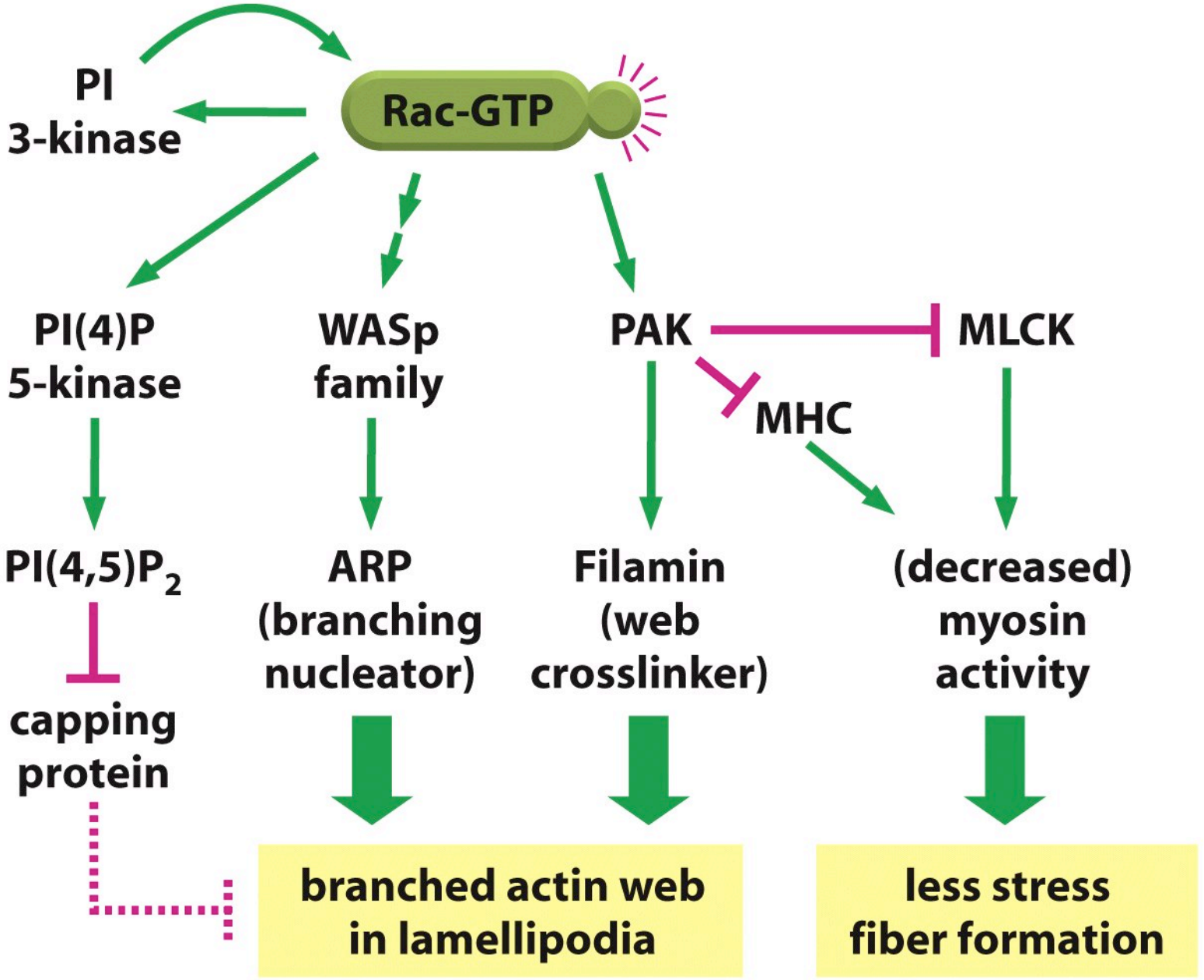


Figure 16-98a *Molecular Biology of the Cell* (© Garland Science 2008)

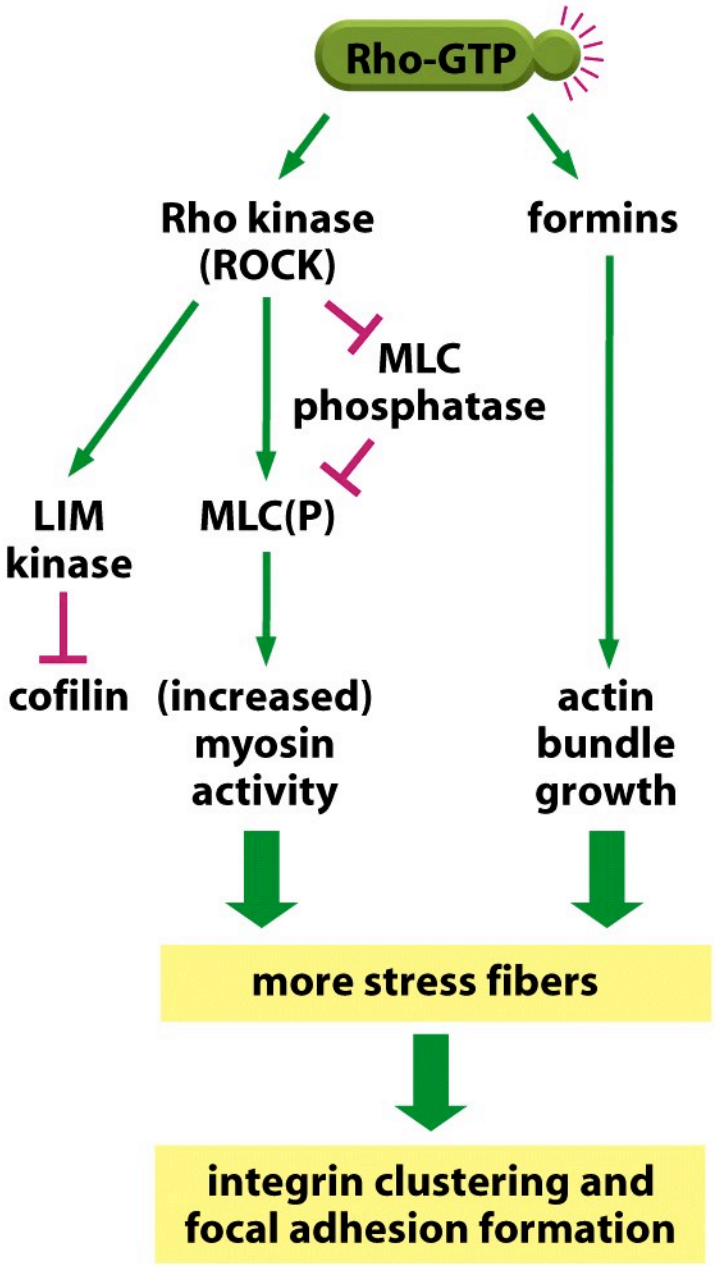


Figure 16-98b *Molecular Biology of the Cell* (© Garland Science 2008)