КАЗАНСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ

2025г.

Тема 7. Цитоскелет и молекулярные моторы

лекция

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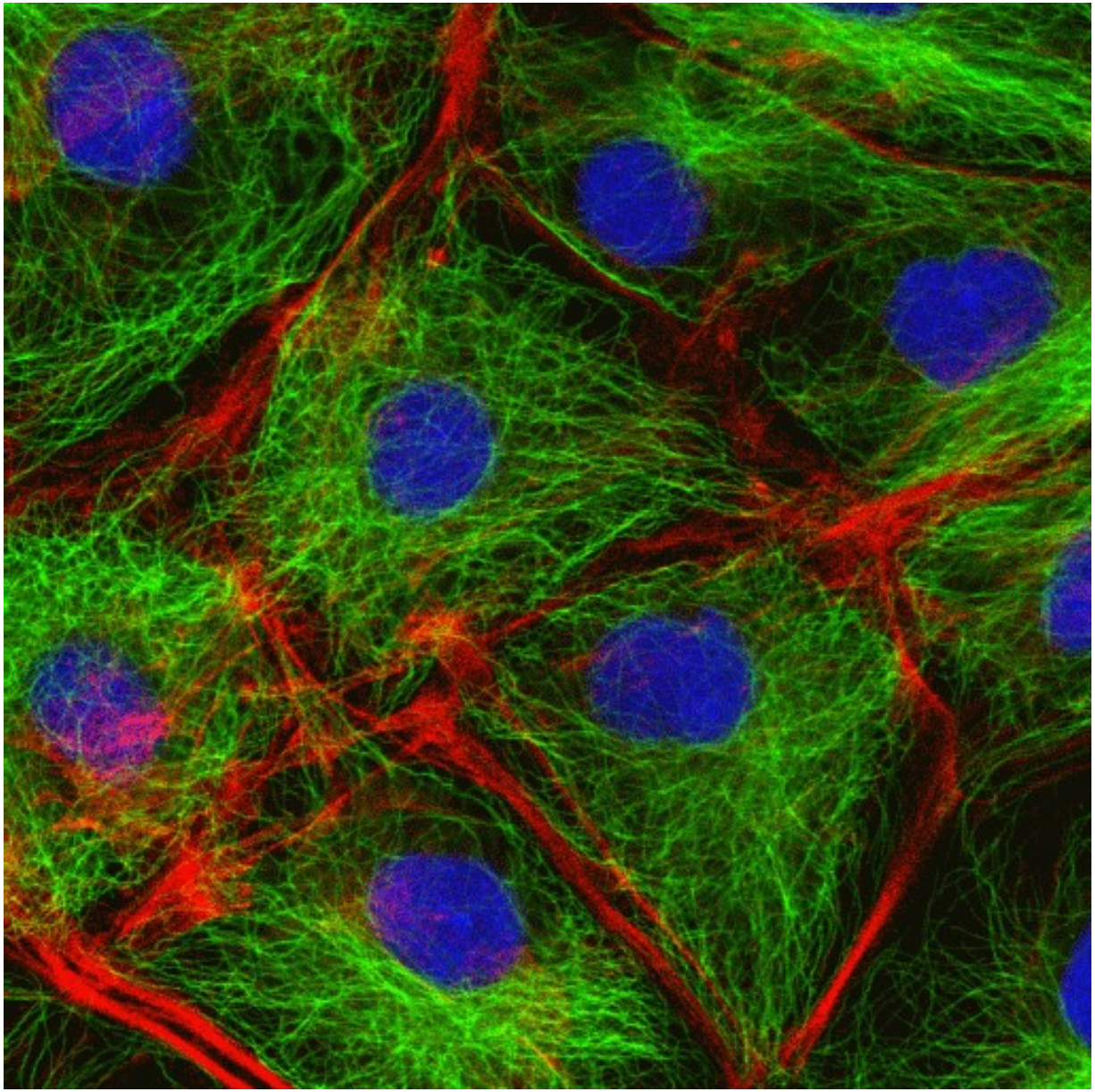
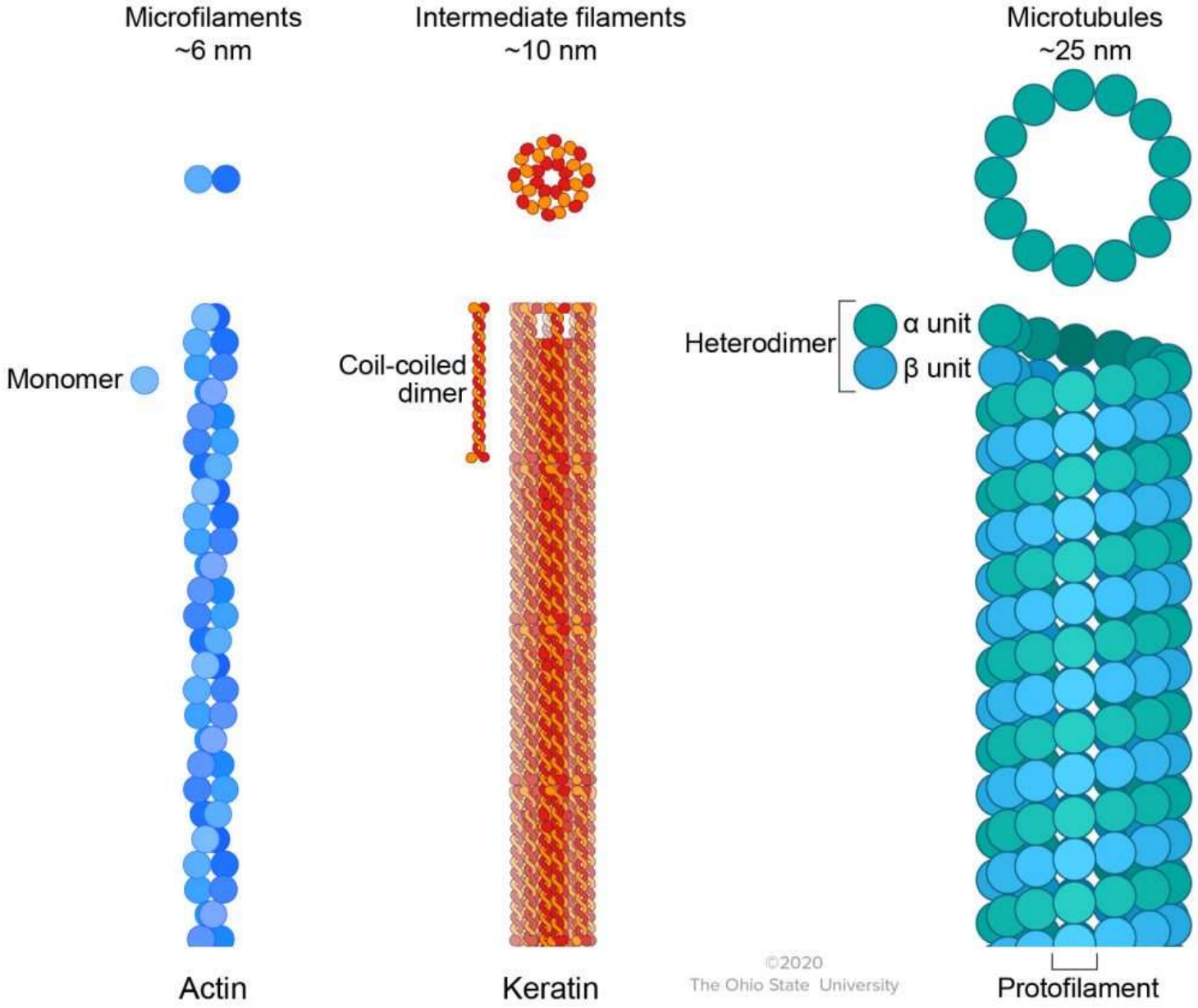
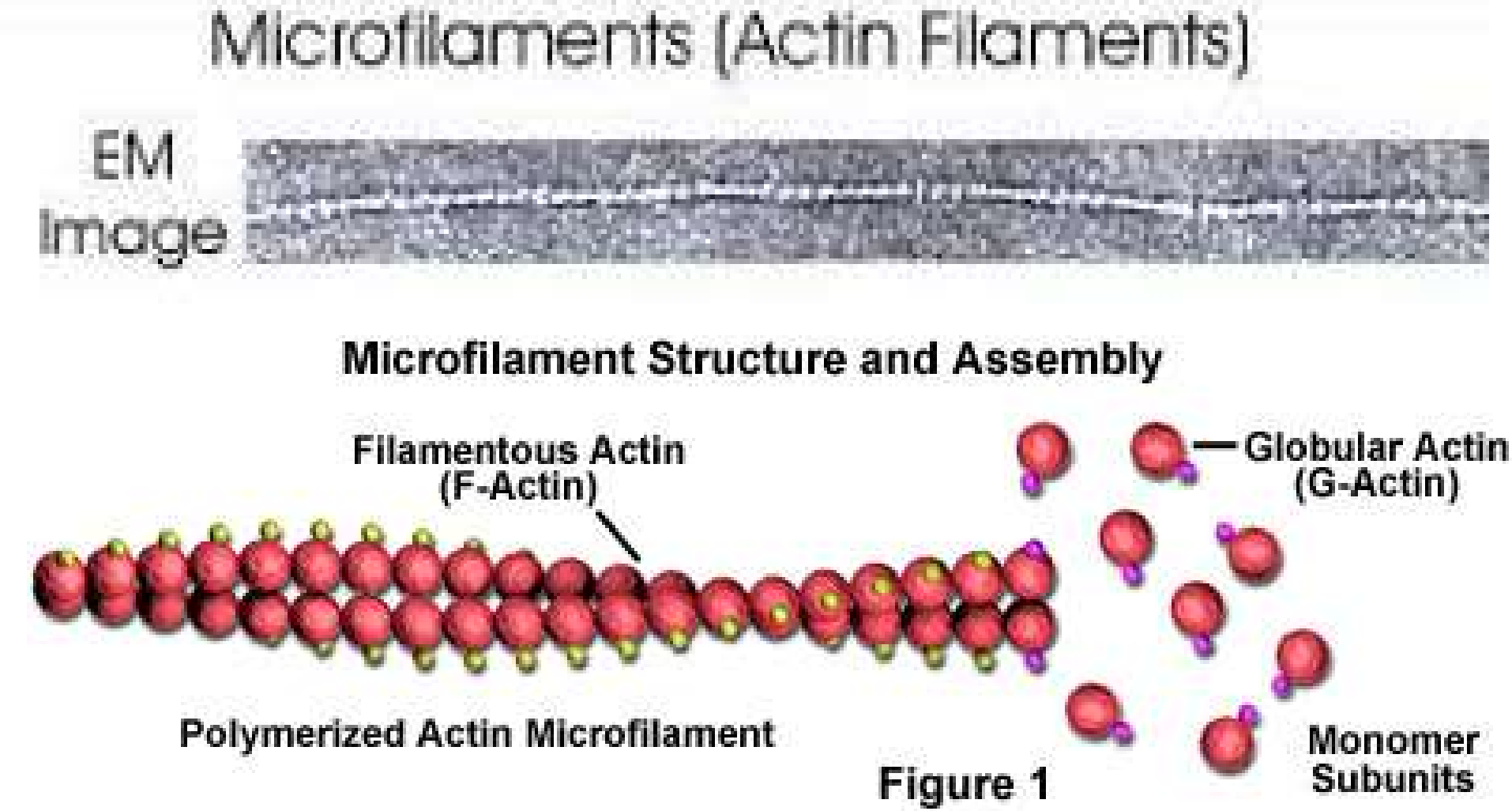
КГМУ

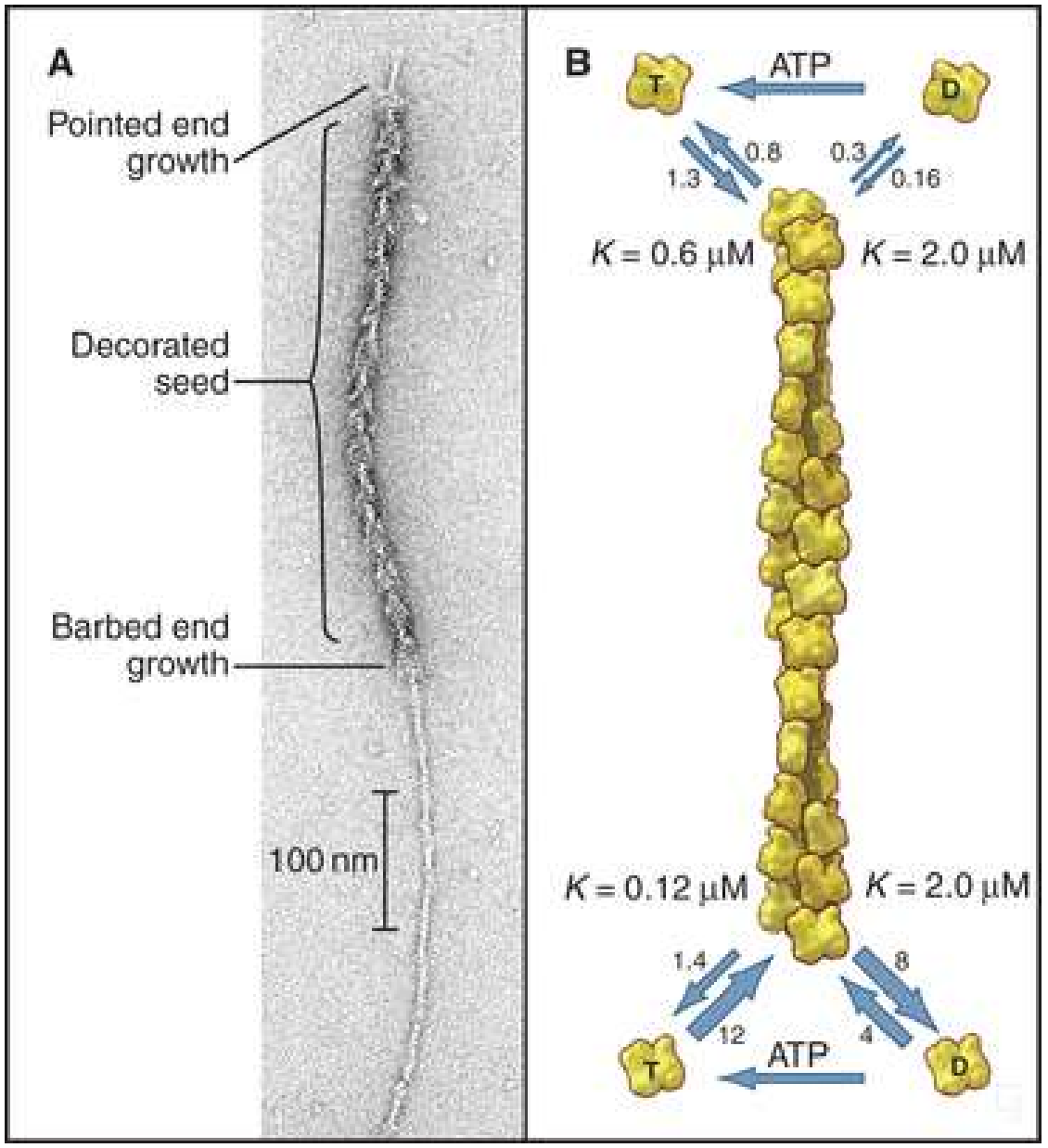
Цитоскелет

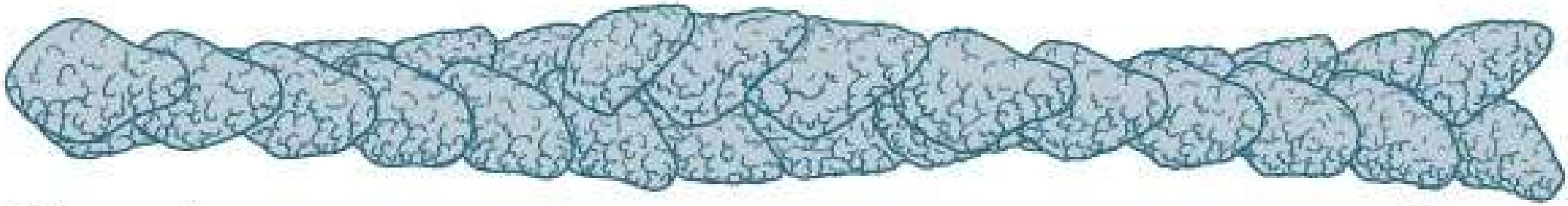




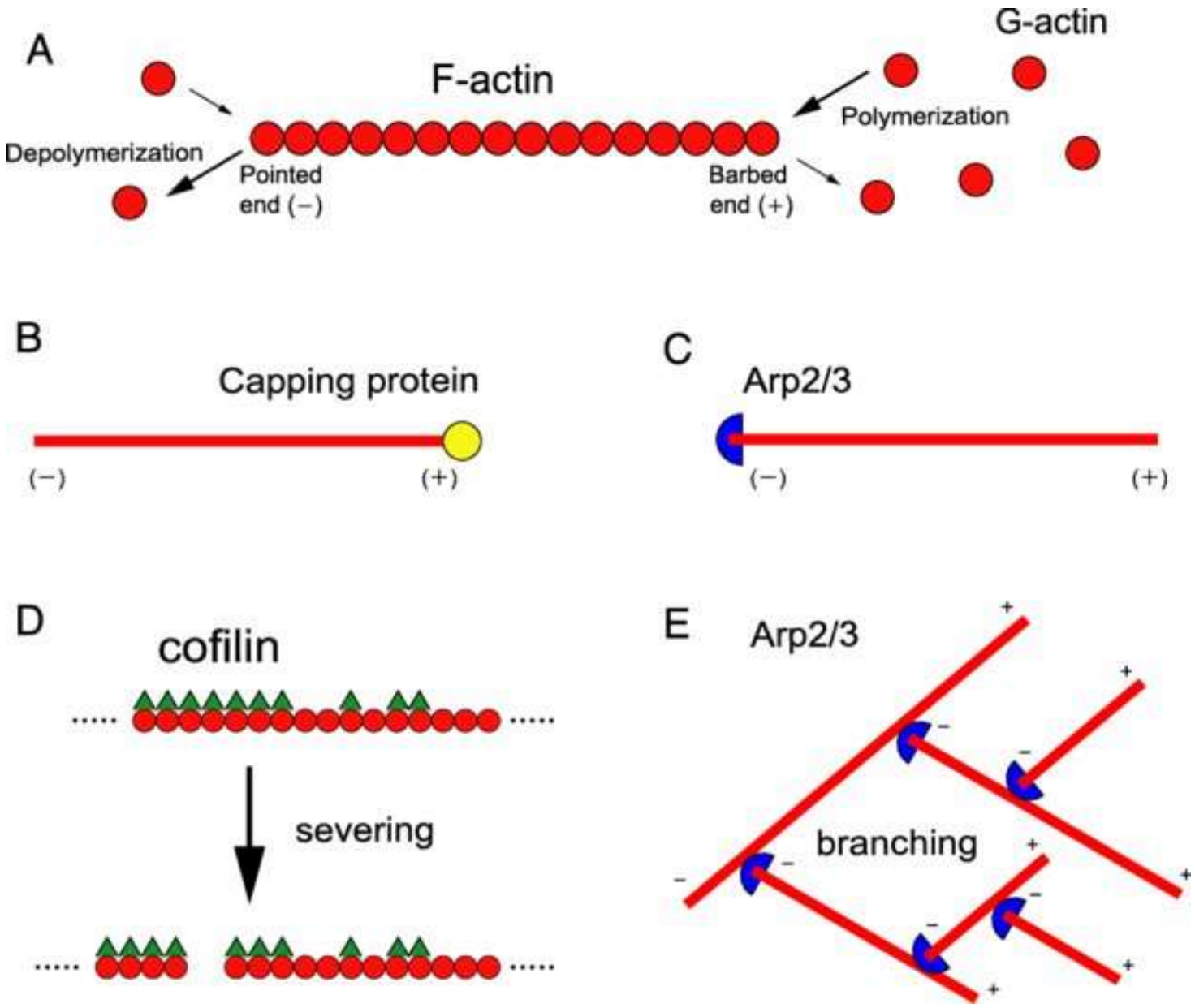
Микрофиламенты

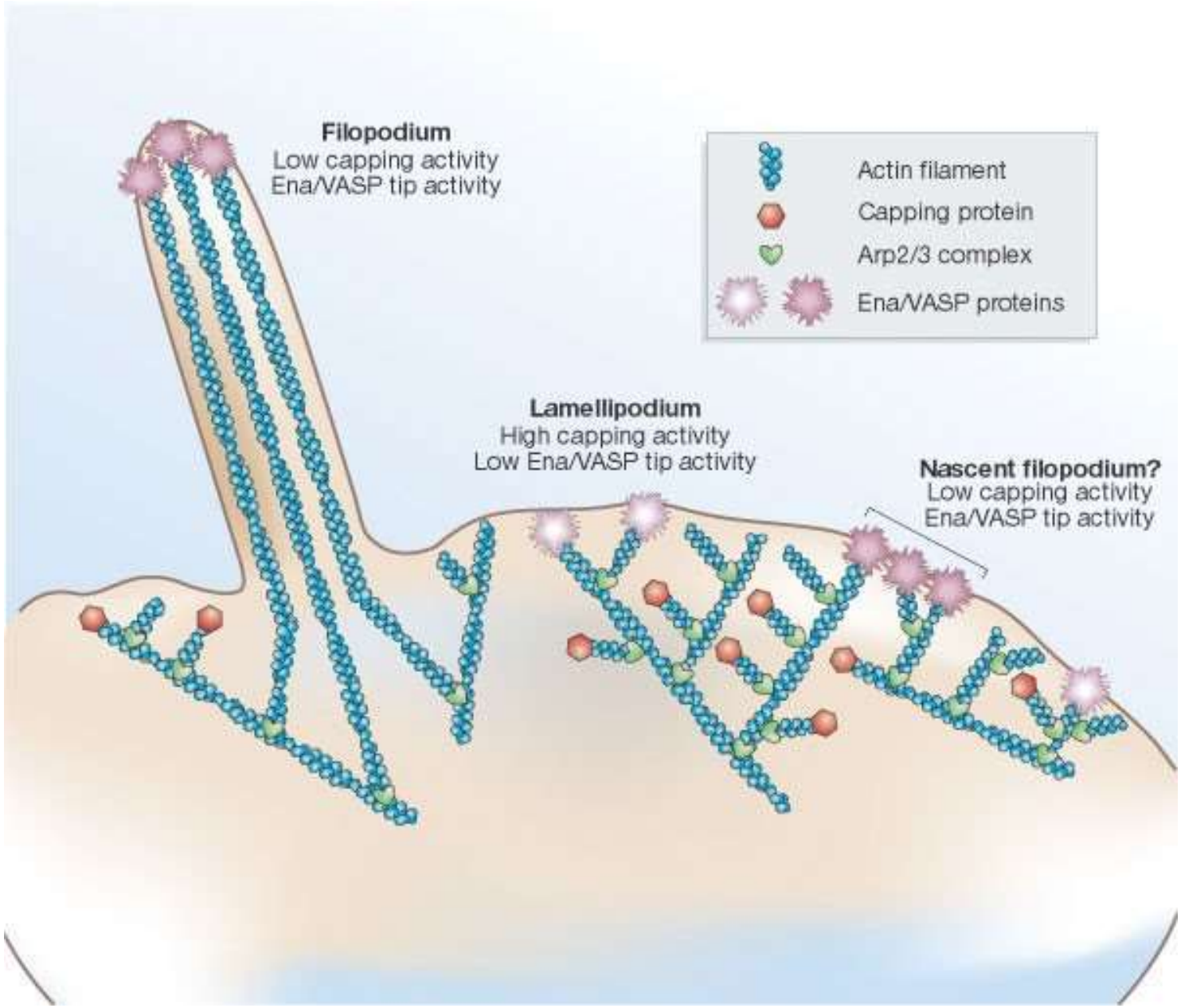



A
Pointed end growth
Decorated seed
Barbed end growth
100 nm
B
T
ATP
D
1.3
0.8
0.3
0.16
K = 0.6 μM
K = 2.0 μM
K = 0.12 μM
K = 2.0 μM
1.4
12
8
4
T
ATP
D



Actin Filament


A
G-actin
F-actin
Polymerization
Depolymerization
Pointed
end (−)
Barbed
end (+)
B
Capping protein
(−)
(+)
C
Arp2/3
(−)
(+)
D
cofilin
severing
E
Arp2/3
branching

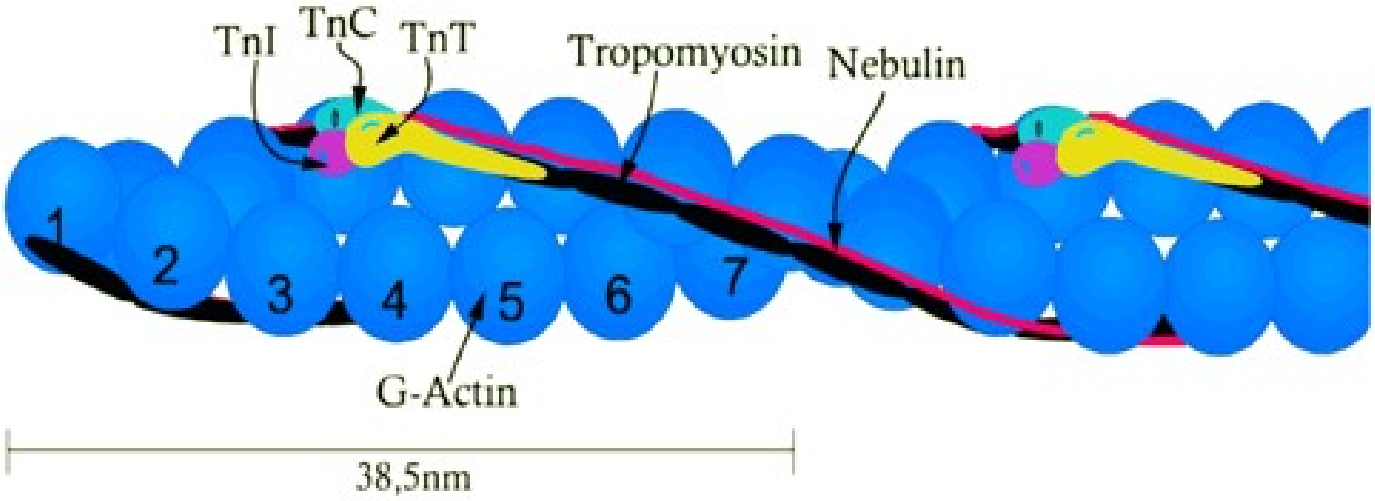

Filopodium
Low capping activity
Ena/VASP tip activity
Actin filament
Capping protein
Arp2/3 complex
Ena/VASP proteins
Lamellipodium
High capping activity
Low Ena/VASP tip activity
Nascent filopodium?
Low capping activity
Ena/VASP tip activity

Actin Isoforms

Six different actin isoforms are expressed in a higher mammal (Vandekerckhove and Weber, 1978). The primary structure of actin is very conservative from birds to humans (Kabsch and Vandekerckhove, 1992). Actin isoforms are coded for by a set of structurally related genes that originate from a common precursor and have highly homologous nucleotide sequences (Hightower and Meagher, 1986). The main differences between isoforms are concentrated at the N-terminus (Vandekerckhove and Weber, 1978). Six human actin genes - α-skeletal (ACTA1), α-cardiac (ACTC1), α-smooth muscle (ACTA2), γ-smooth muscle (ACTG2), β-cytoplasmic (ACTB), γ-cytoplasmic (ACTG1) - are localized on the different chromosomes (Gunning et al., 1984). Recently it has been declared the existence of the seventh actin isoform - β-actin-like protein 2 (ACTBL2), which belongs to the non-muscle actin class, like β-cytoplasmic and γ-cytoplasmic actins, but its expression is very low (Malek et al., 2021). Cytoplasmic actins are expressed in mammalian cells in various proportions and differ by four amino acid residues localized at positions 1, 2, 3, and 9 of the N-terminus (Ampe and Van Troys, 2017). The evolutionary conservatism of actins indicates their fundamental role for the cell survival.

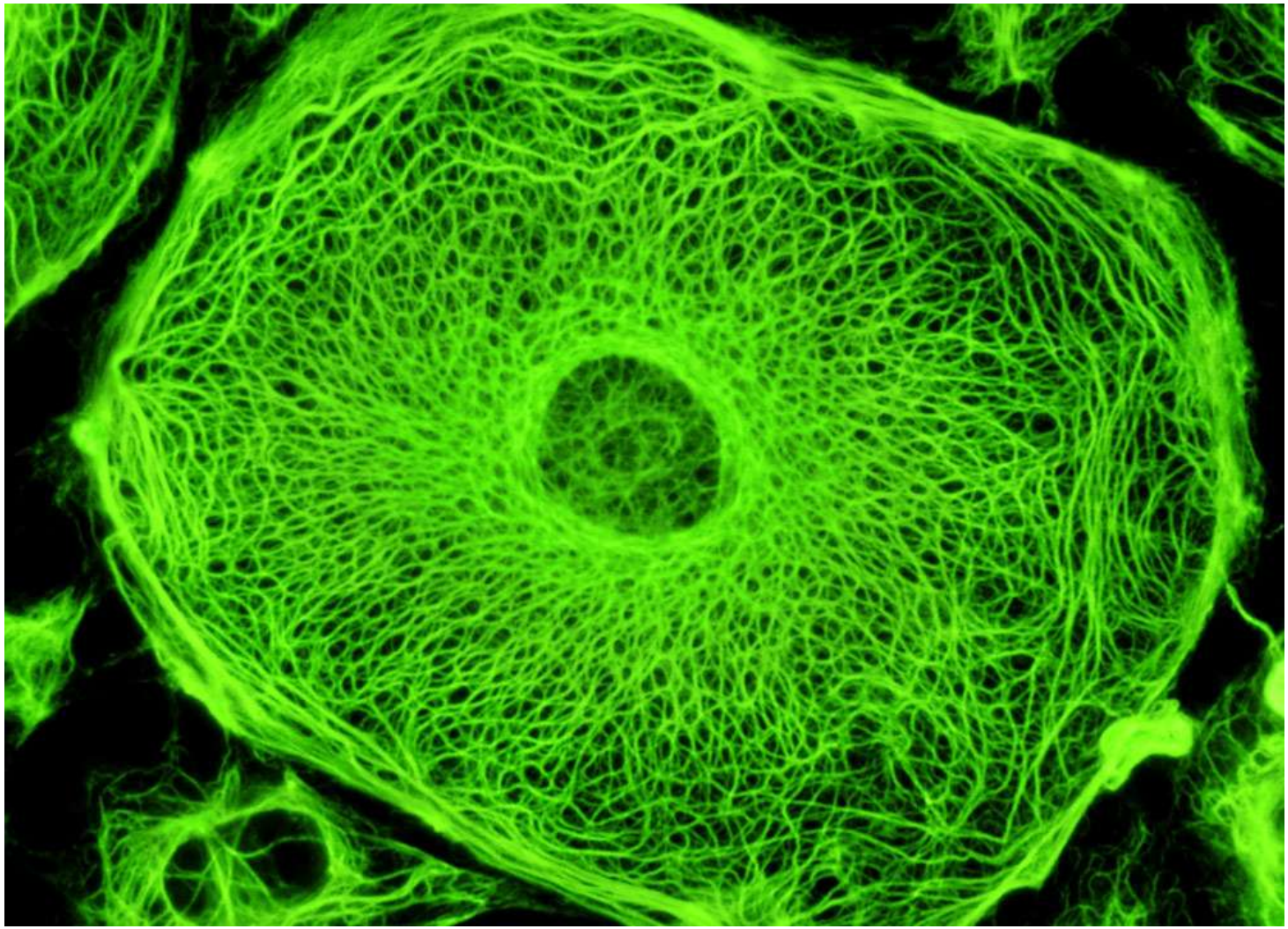
Tropomyosin/Troponin

skeletal muscle



Model of a muscle thin filament showing the localization of laterally aligned tropomyosin in association with the troponin complex.

Промежуточные филаменты



Промежуточные филаменты

Типы I и II – кислые и основные кератины: эпителиальные кератины, трихоцитарные кератины

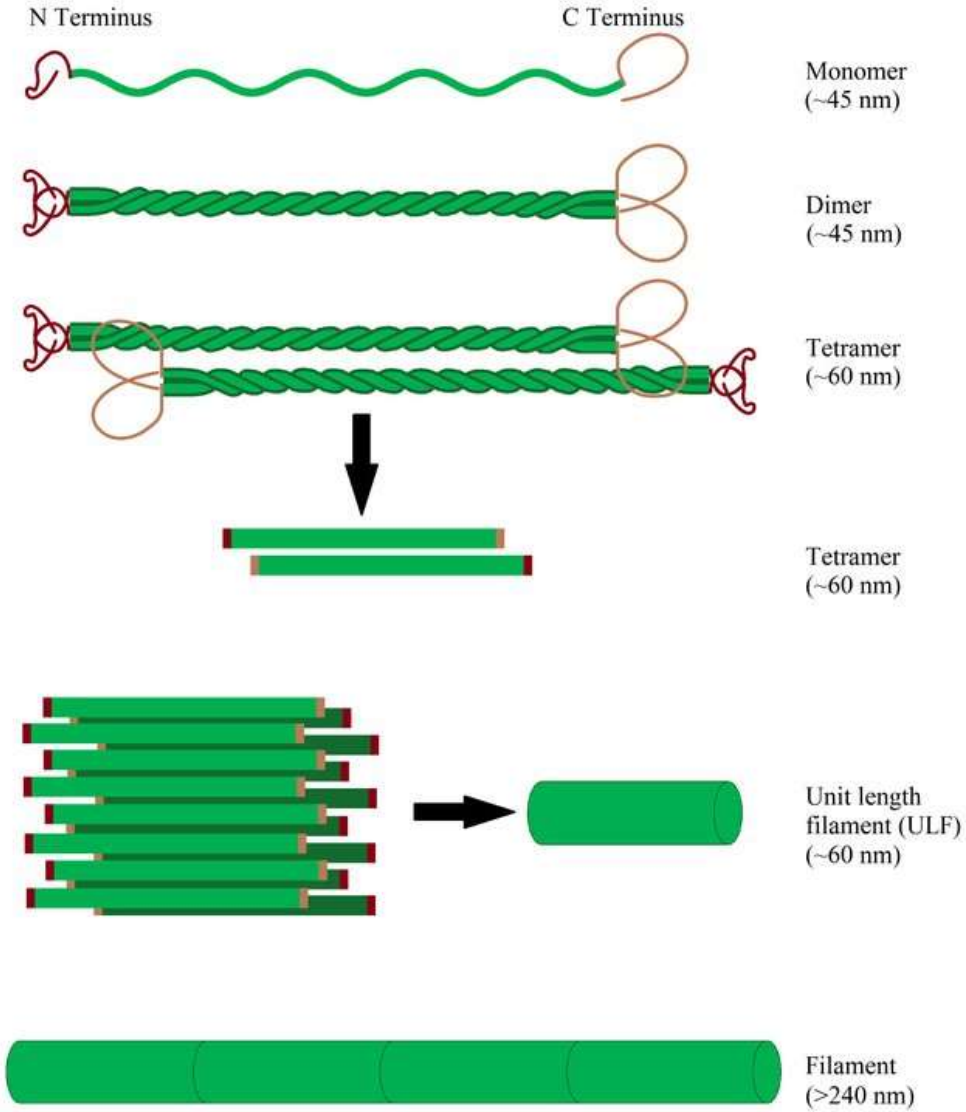
Тип III: Десмин, Глиальный фибриллярный кислый белок (GFAP), Периферин, Виментин, Синкоилин

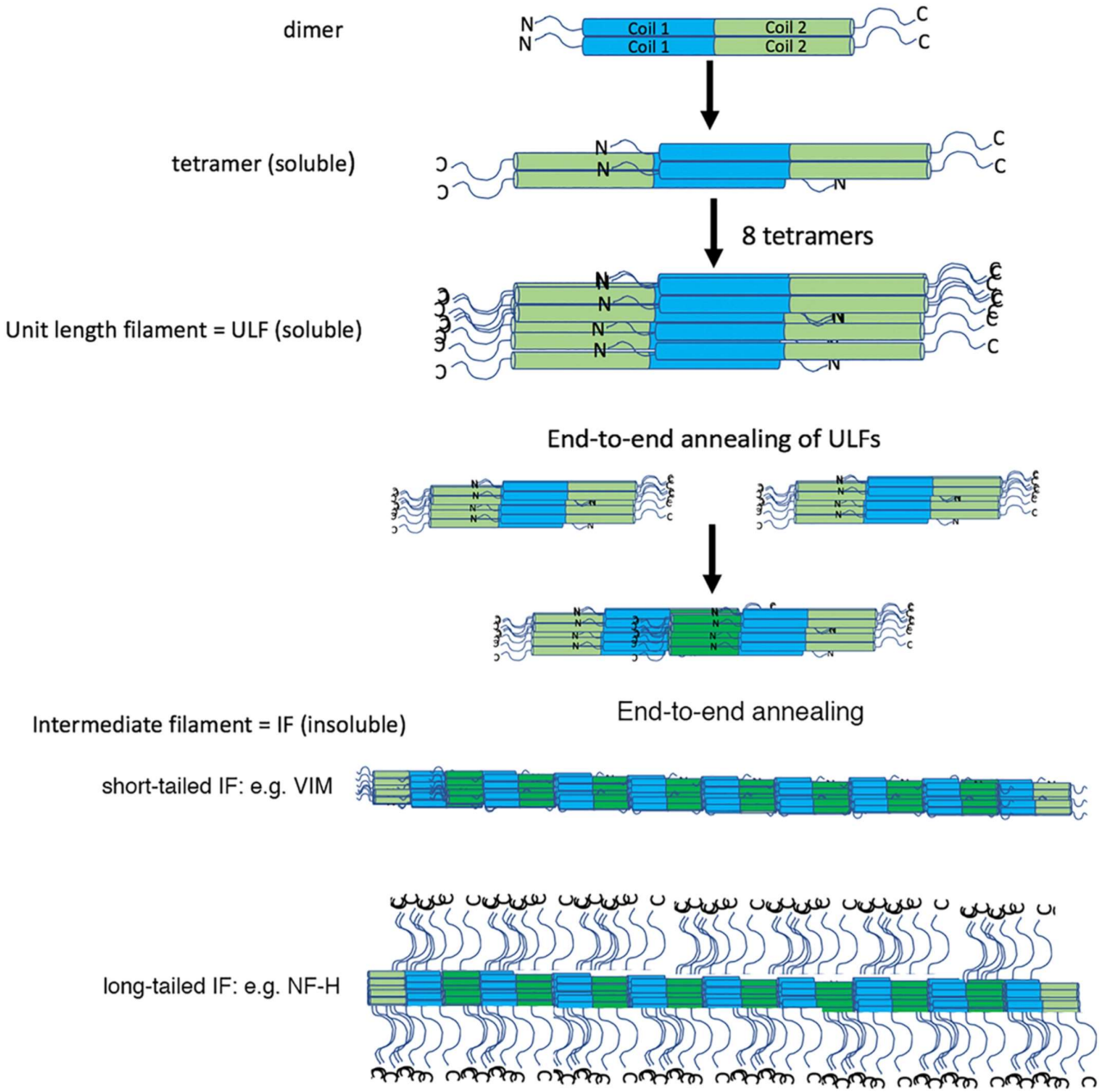
Тип IV: Альфа-интернексин, Нейрофиламенты, Синемин

Тип V – ядерные ламины: Ламины A, B, C

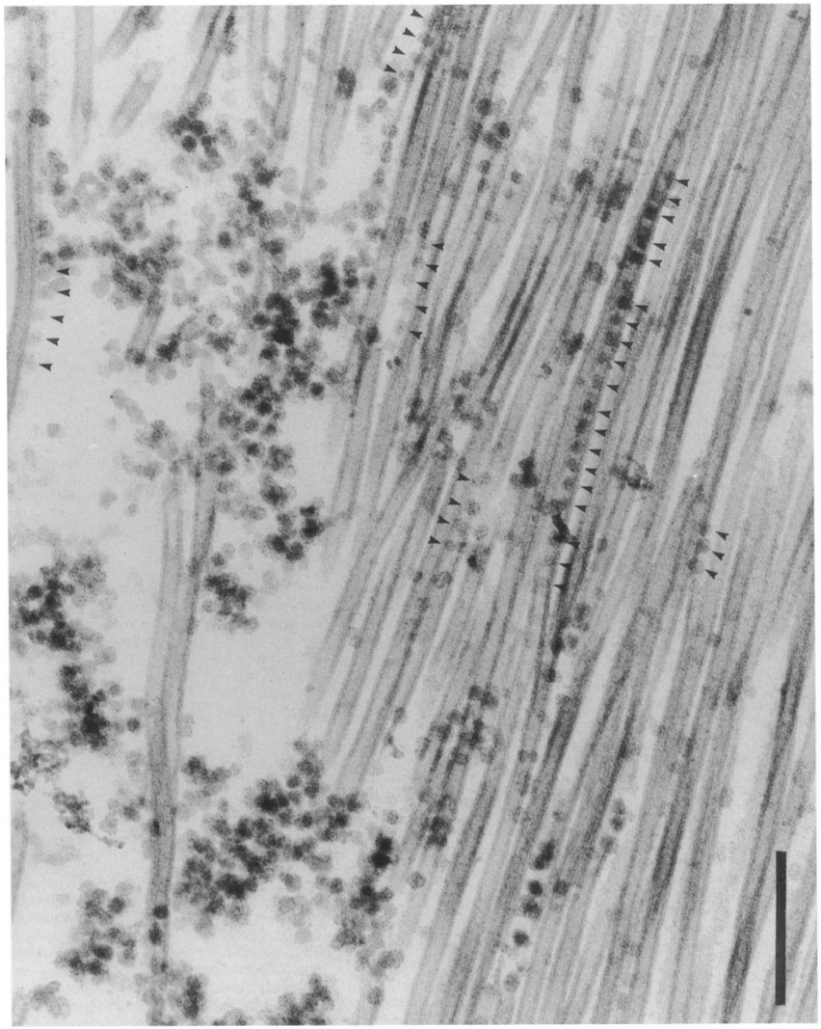
Тип VI: филенсин, факинин, нестин

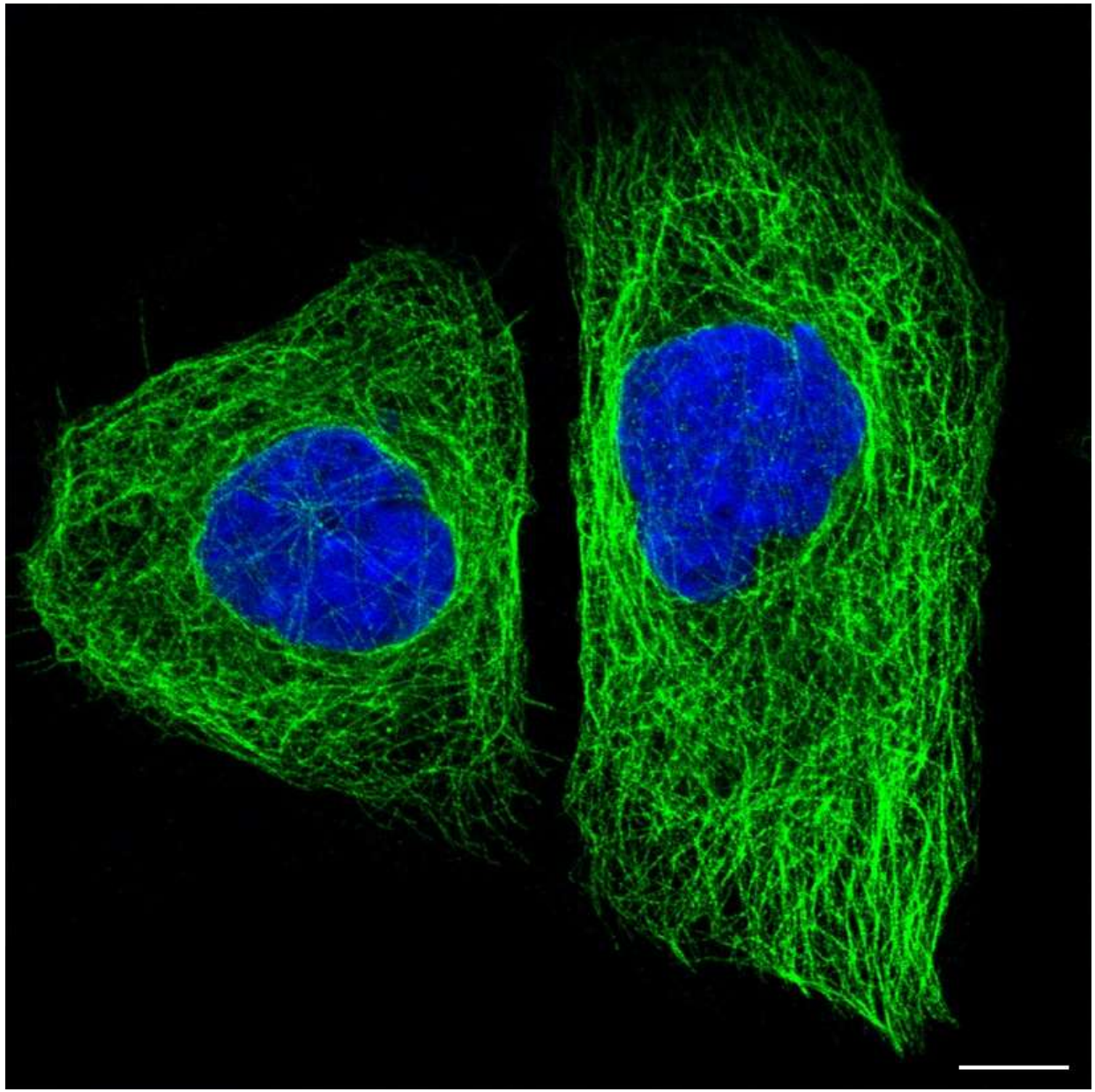
Intermediate filament assembly

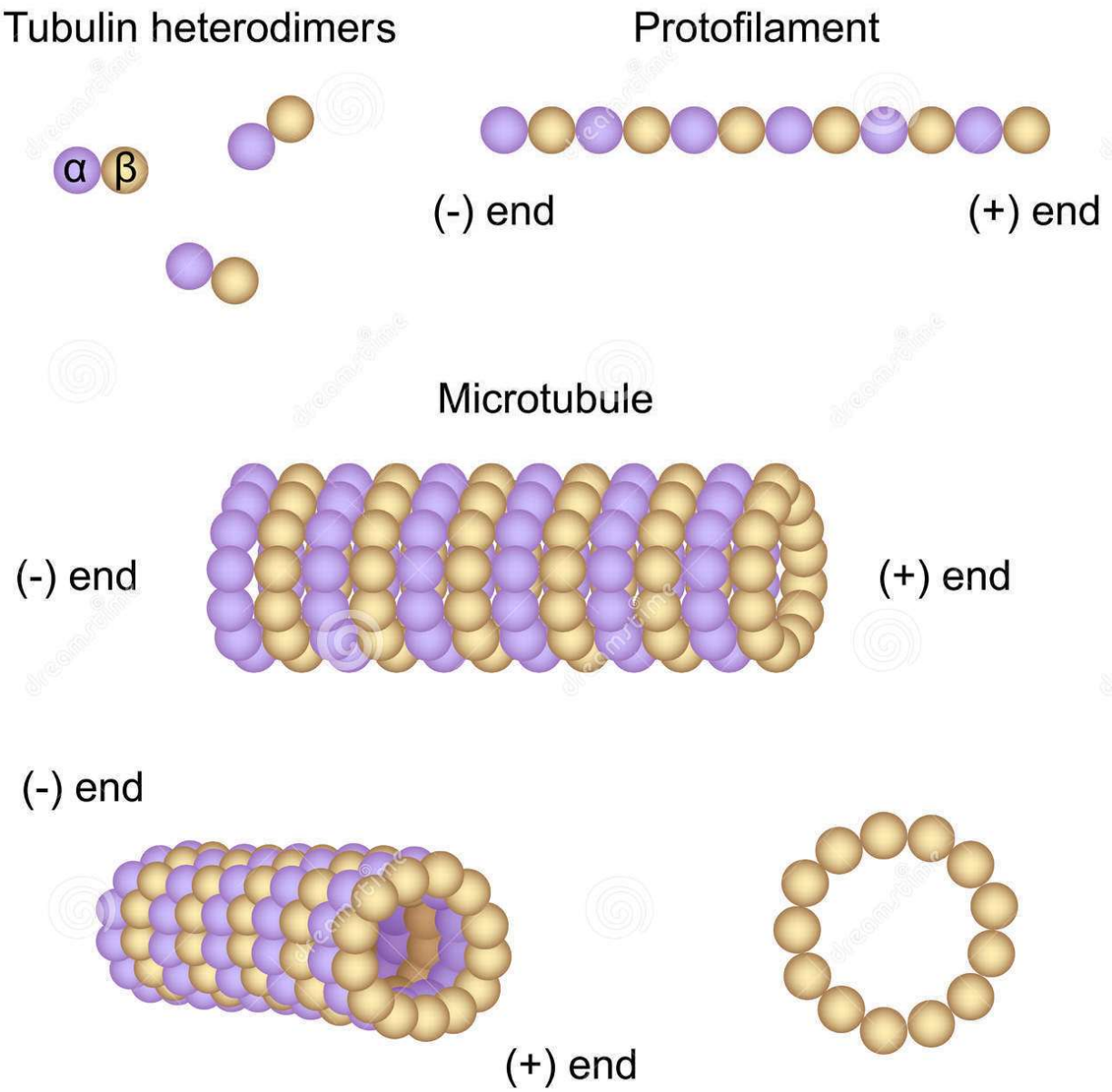


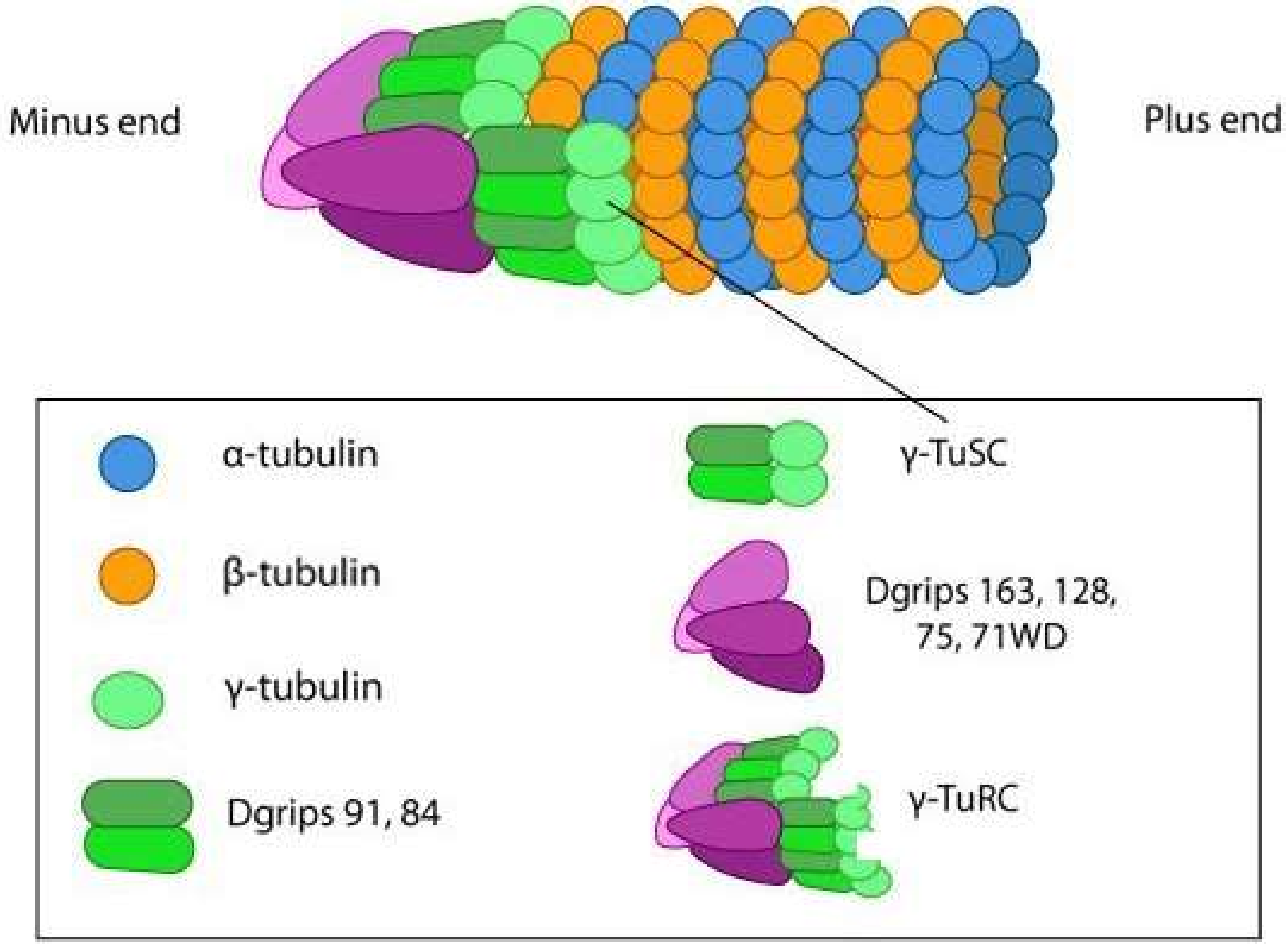

dimer
Coil 1
Coil 2
Coil 1
Coil 2
tetramer (soluble)
8 tetramers
Unit length filament = ULF (soluble)
End-to-end annealing of ULFs
End-to-end annealing
Intermediate filament = IF (insoluble)
short-tailed IF: e.g. VIM
long-tailed IF: e.g. NF-H

Микротрубочки






Tubulin heterodimers
α
β
Protofilament
(-) end
(+) end
Microtubule
(-) end
(+) end
(-) end
(+) end


Minus end
Plus end
α-tubulin
β-tubulin
γ-tubulin
Dgrips 91, 84
γ-TuSC
Dgrips 163, 128, 75, 71WD
γ-TuRC

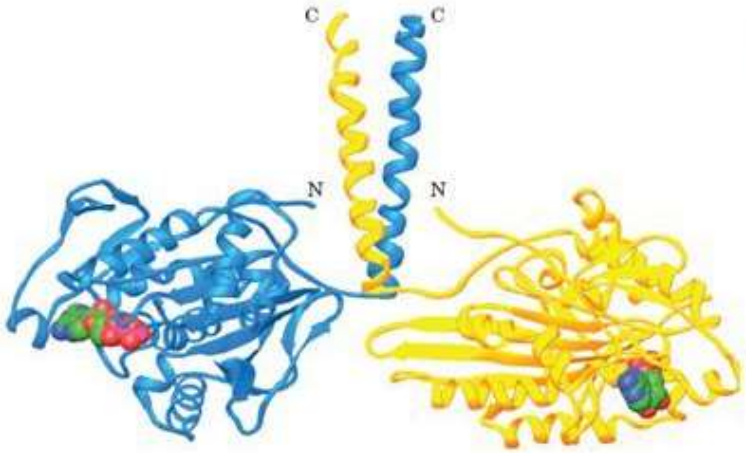
Моторные белки

Motor Proteins convert chemical energy into motion.

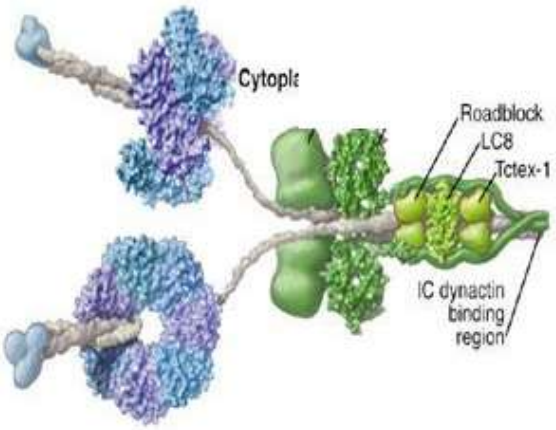
- chemical energy is derived from ATP hydrolysis
- motion is generated by conformational changes depending on the bound nucleotide

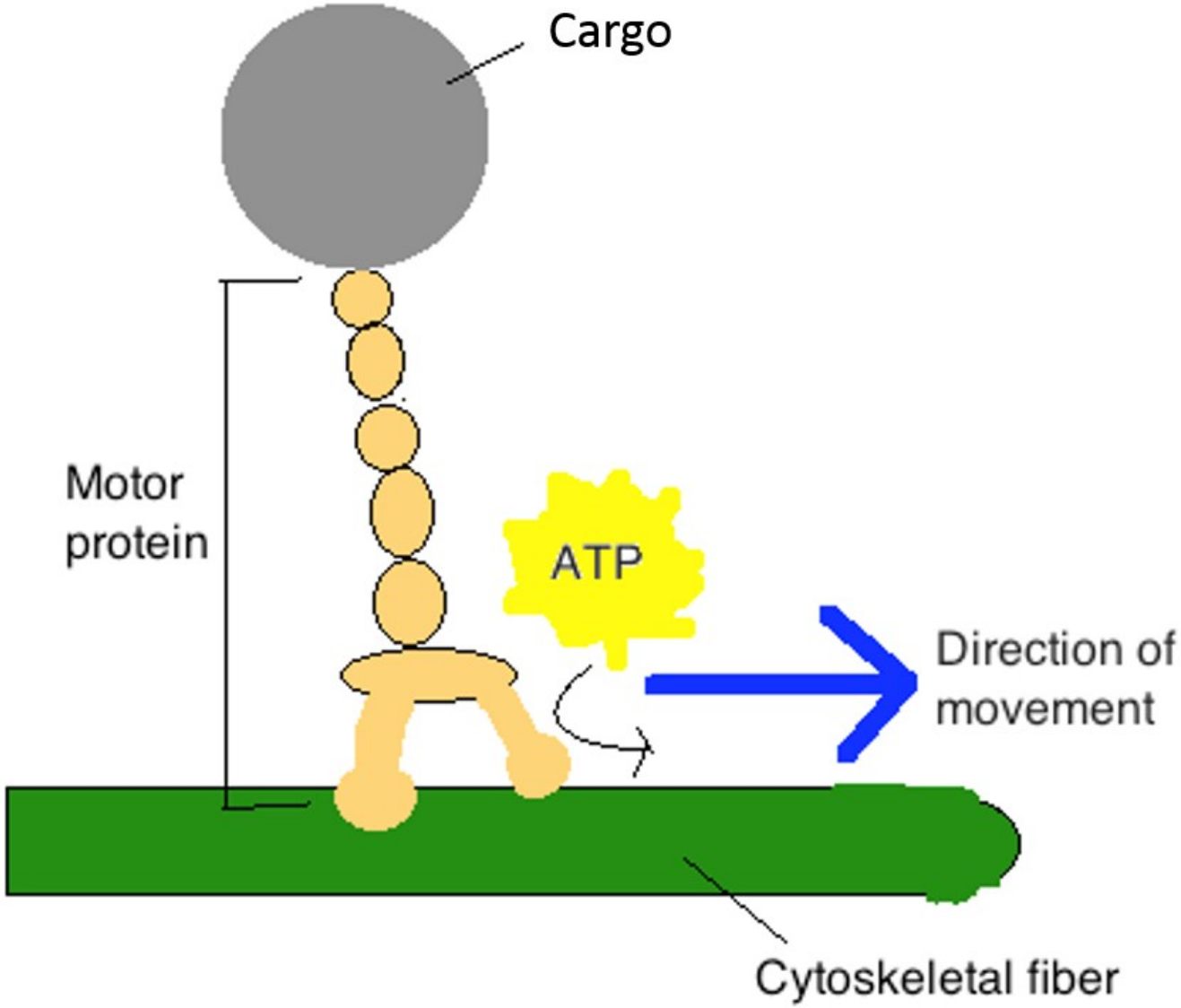
Myosin

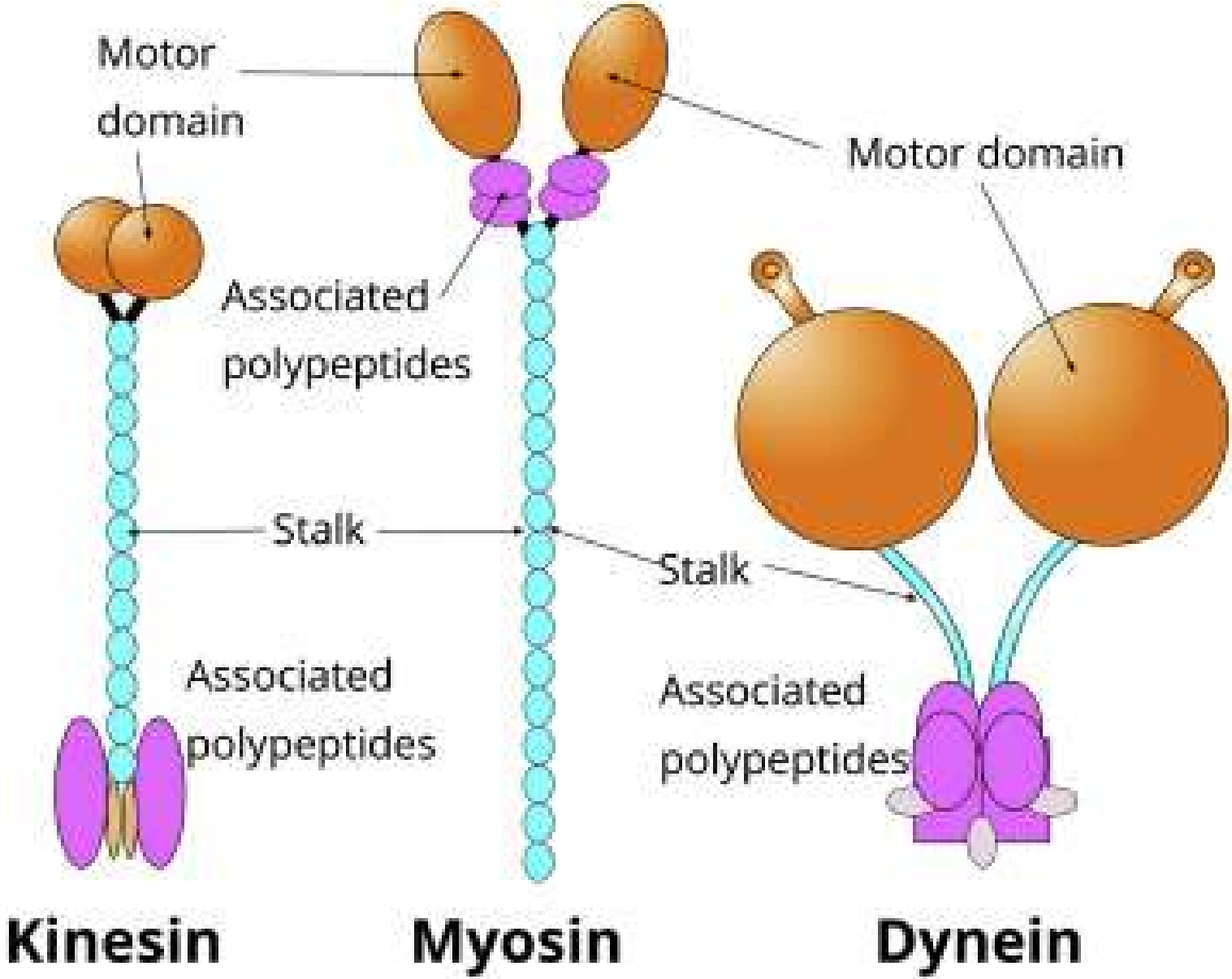
Kinesin

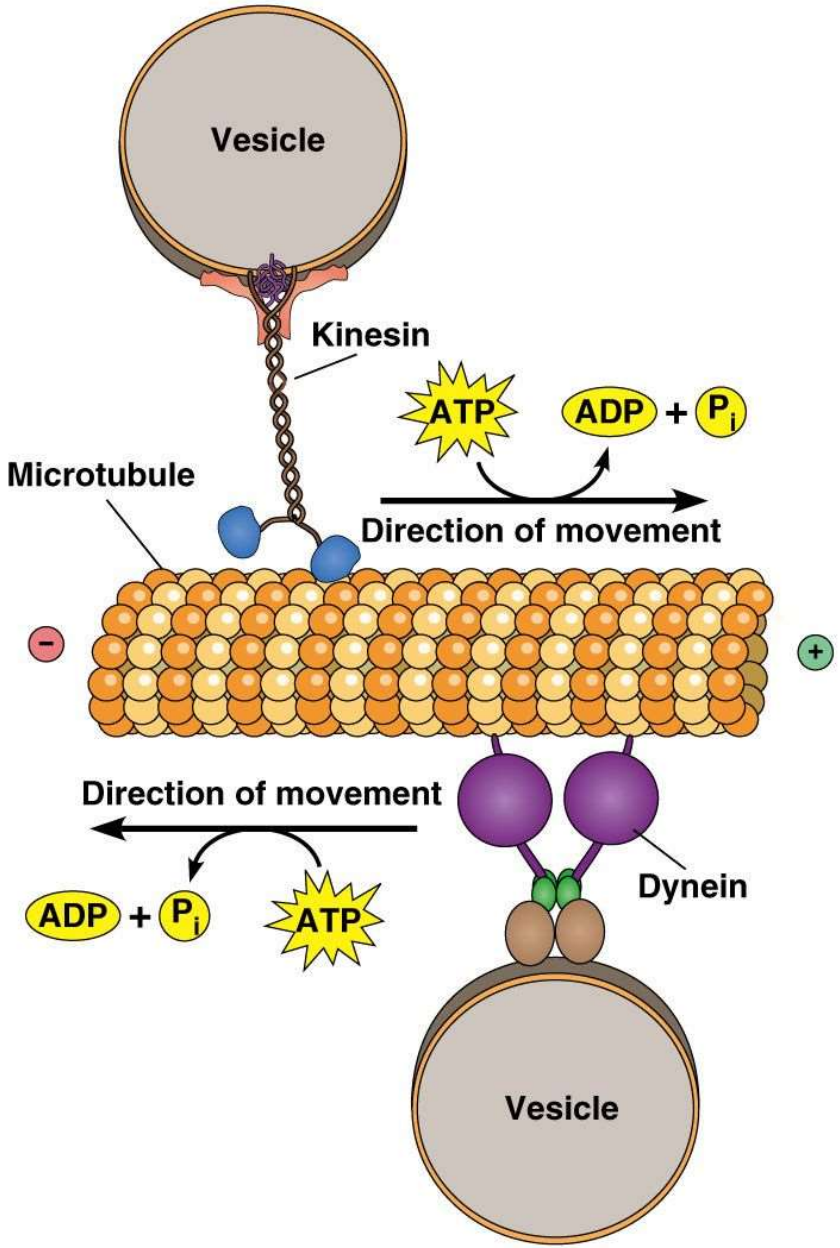


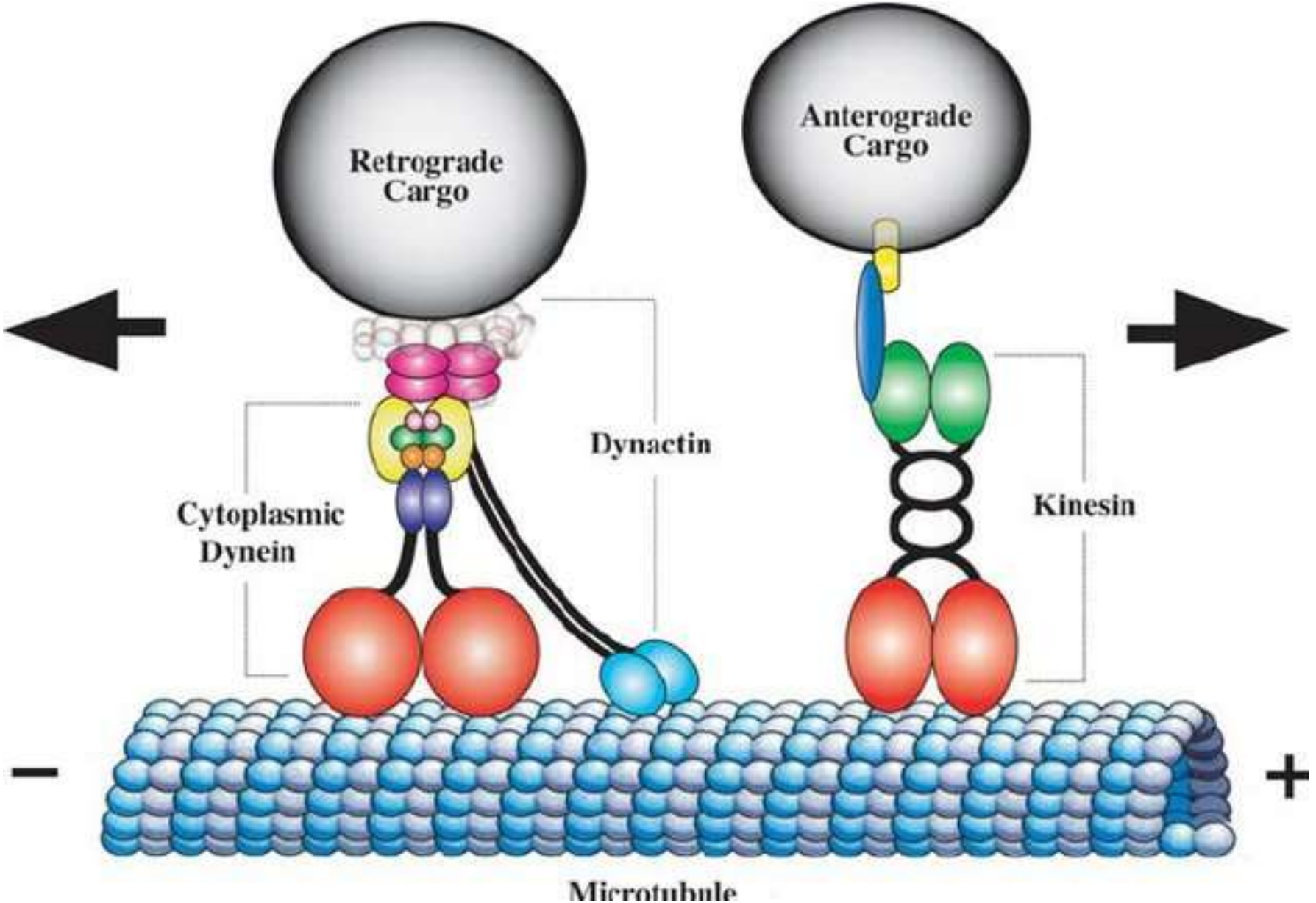
Dynein



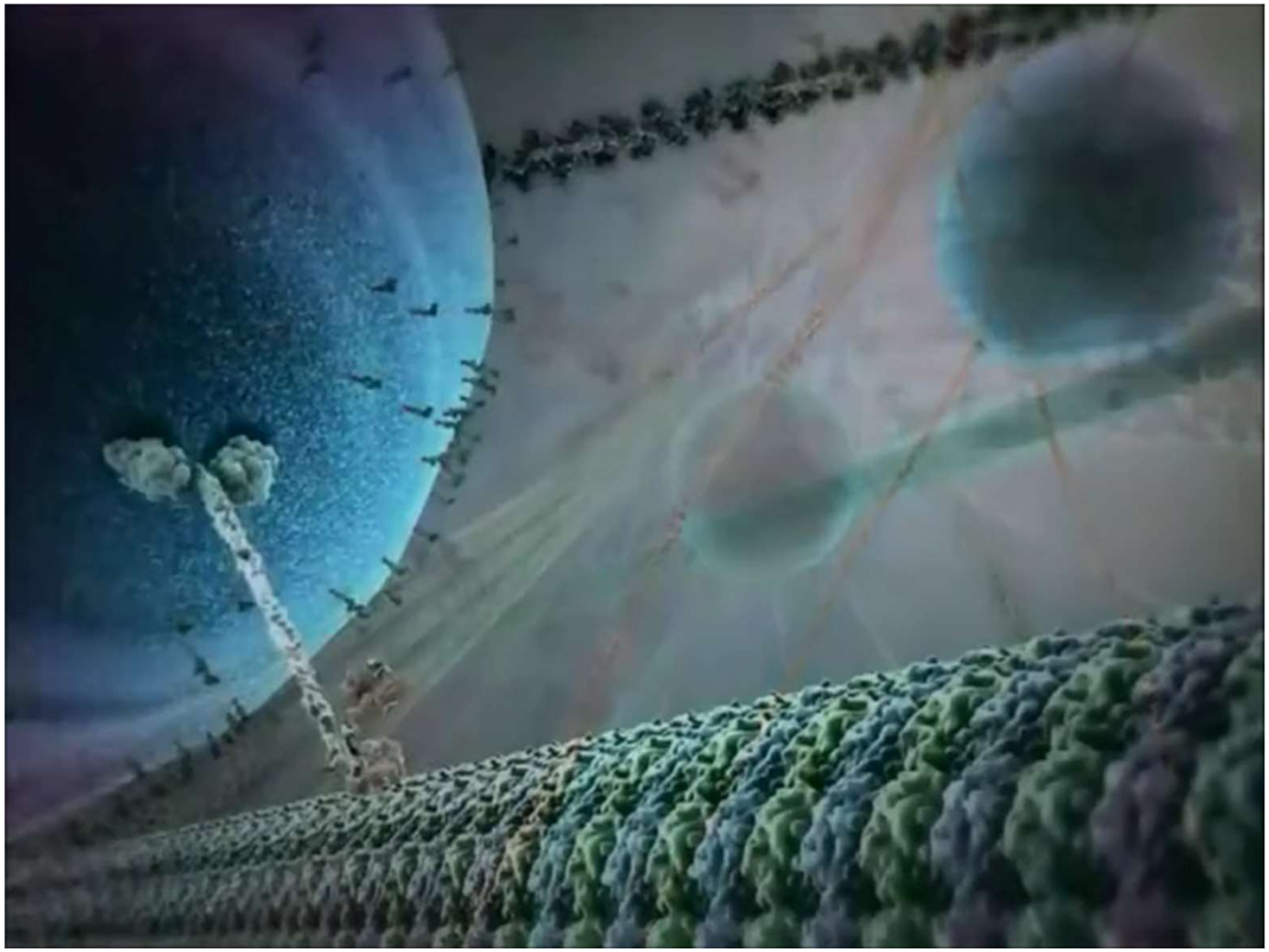

Cargo
Motor protein
ATP
Direction of movement
Cytoskeletal fiber


Motor
domain
Associated
polypeptides
Stalk
Associated
polypeptides
Motor domain
Stalk
Associated
polypeptides
Kinesin
Myosin
Dynein

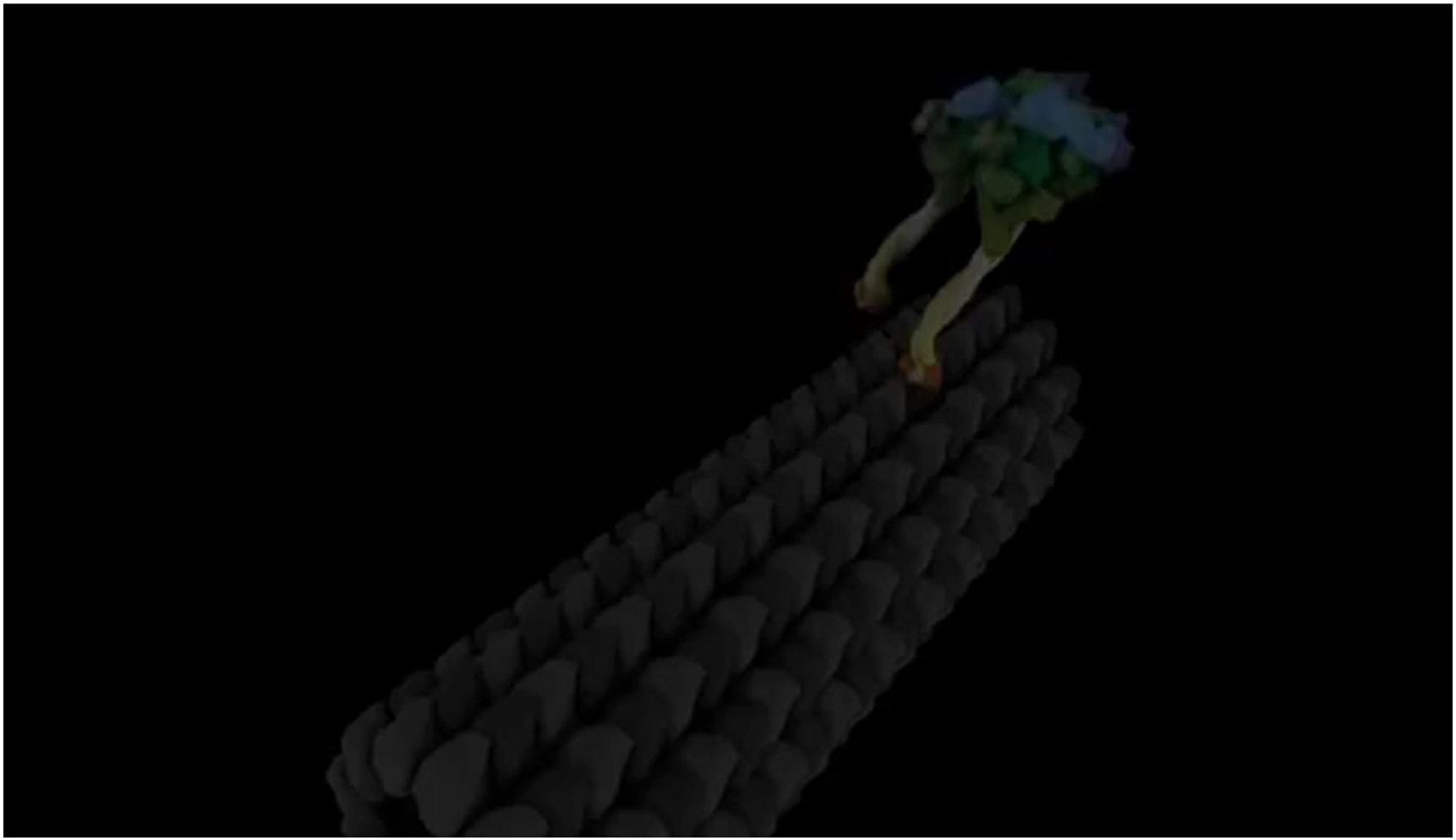

Vesicle
Kinesin
ATP
ADP + P_i
Microtubule
Direction of movement
−
+
Direction of movement
ADP + P_i
ATP
Dynein
Vesicle


Retrograde Cargo
Anterograde Cargo
Dynactin
Cytoplasmic Dynein
Kinesin
−
+
Microtubule

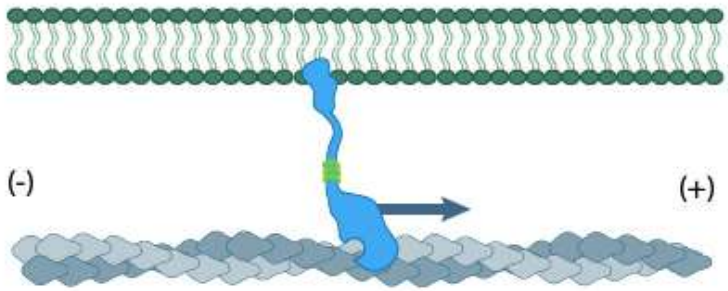
Кинезин



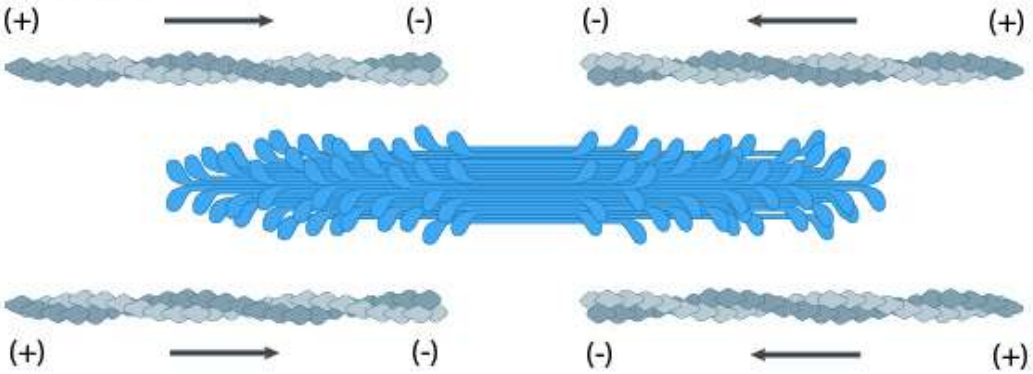
Динеин



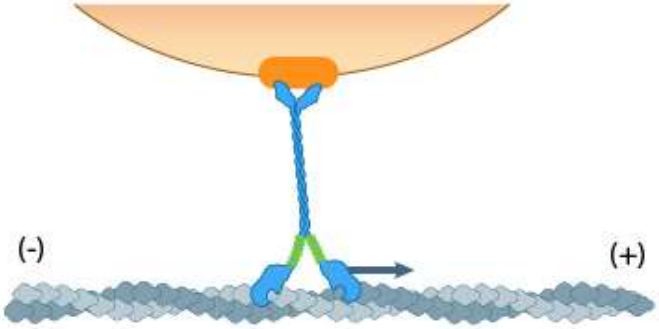
A. Myosin I

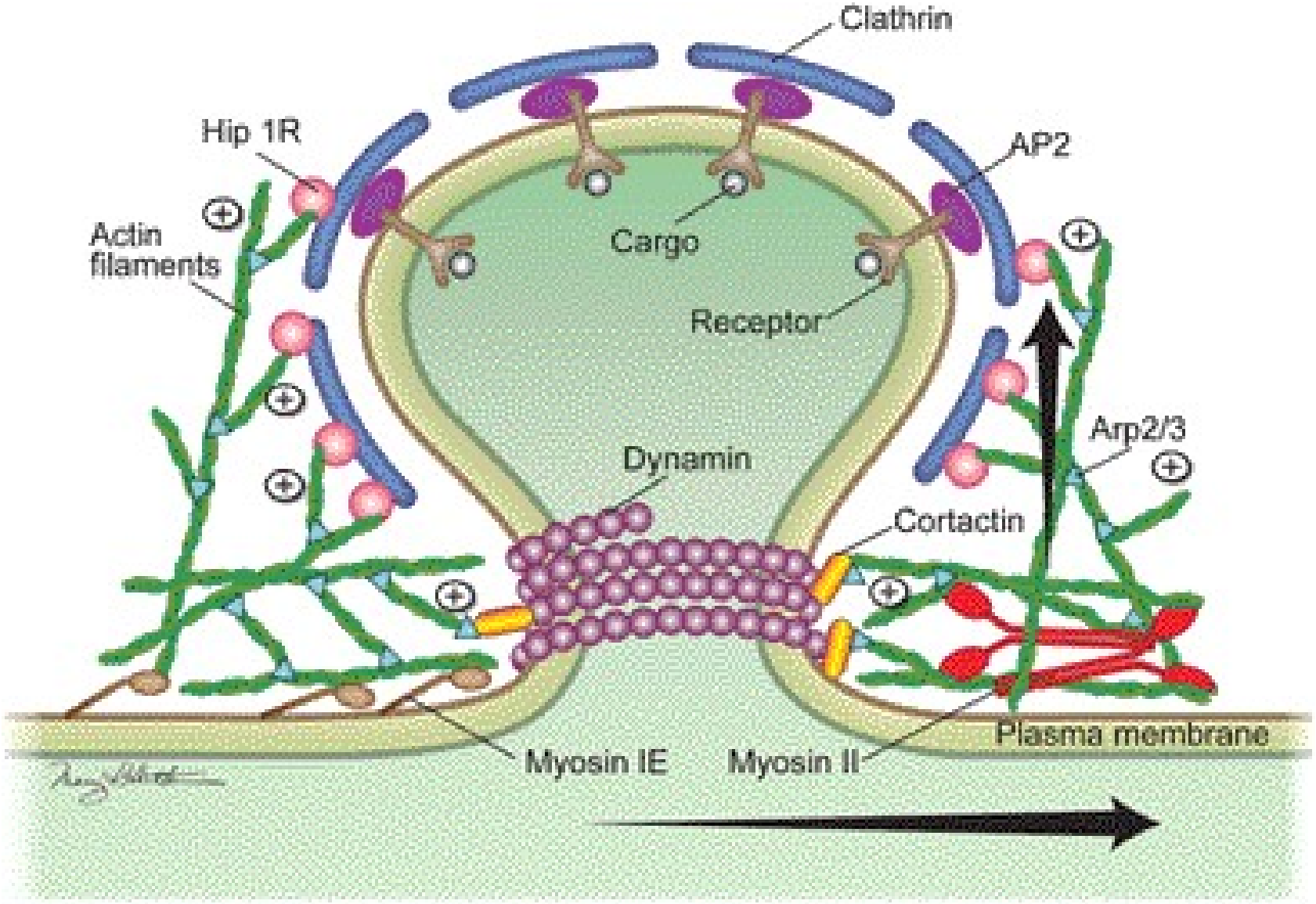


B. Myosin II

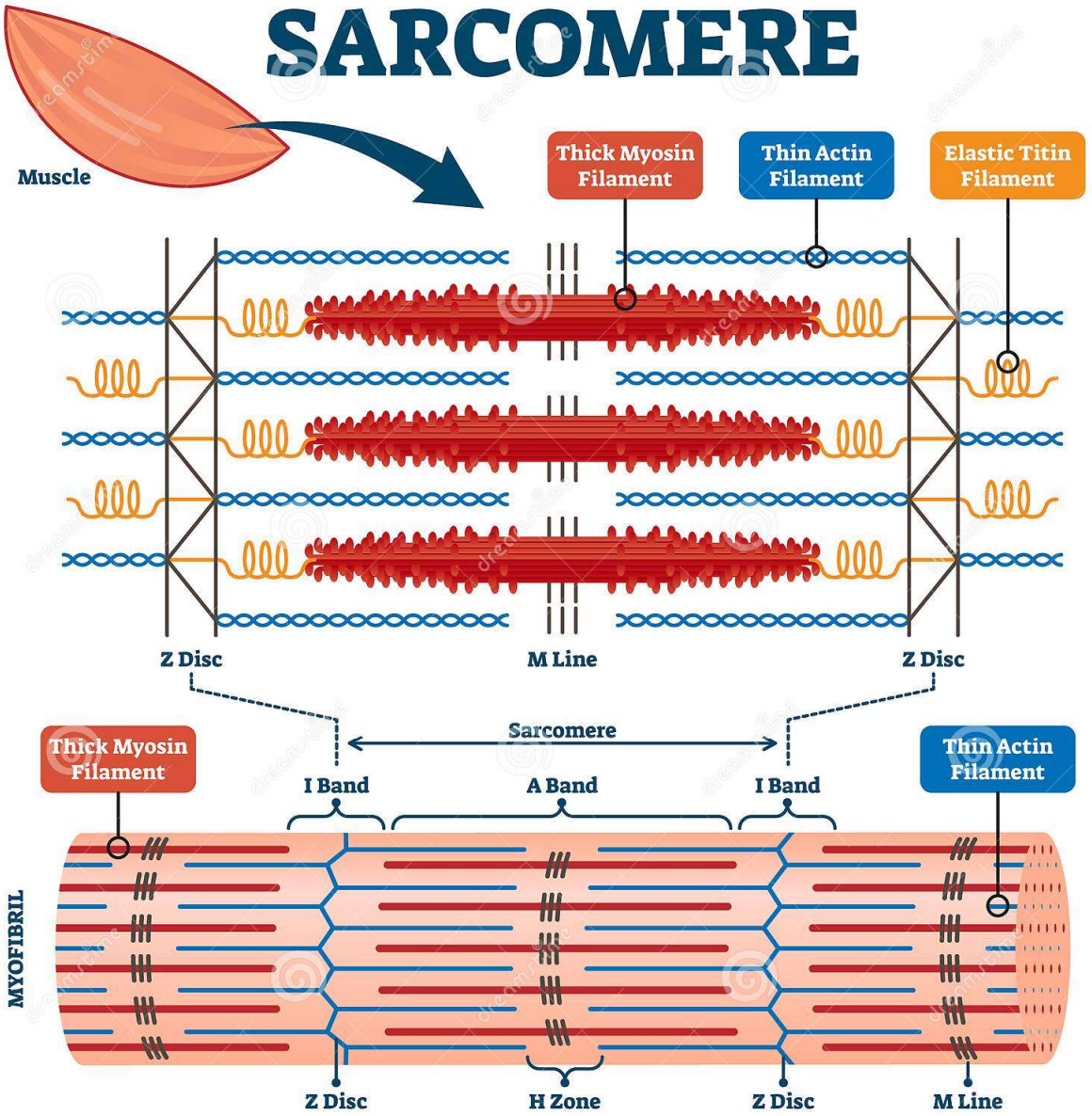


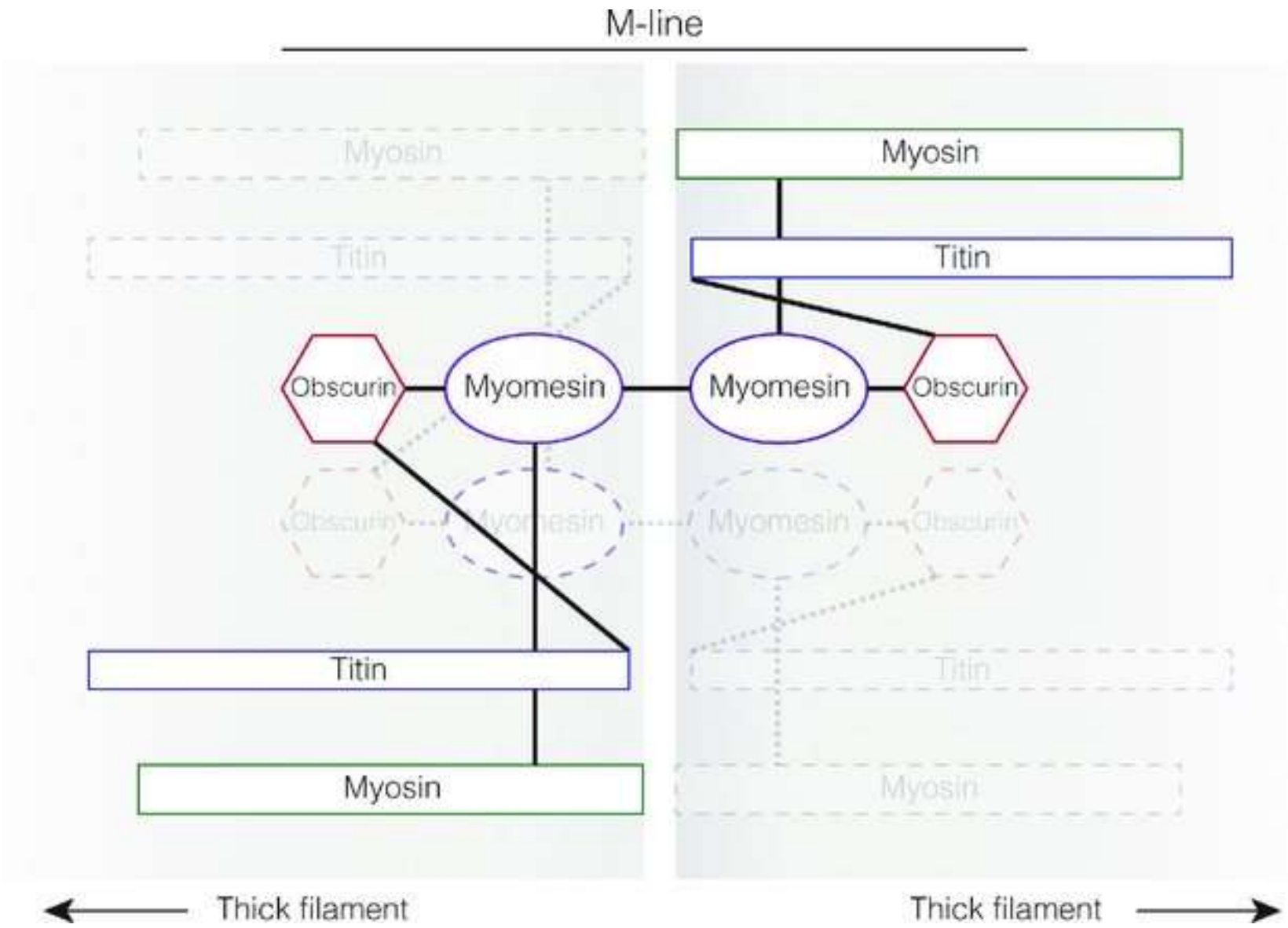
C. Myosin V

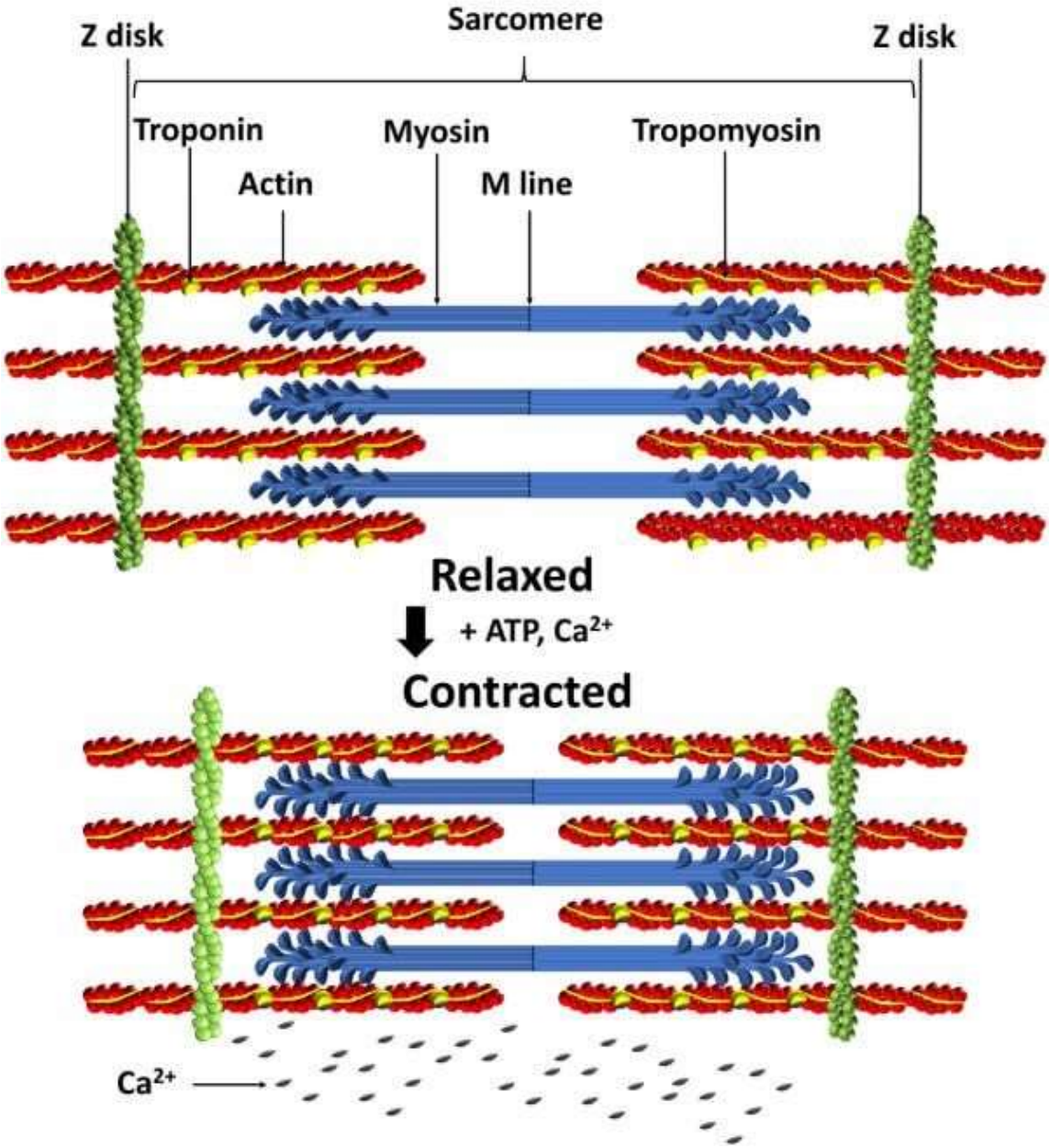




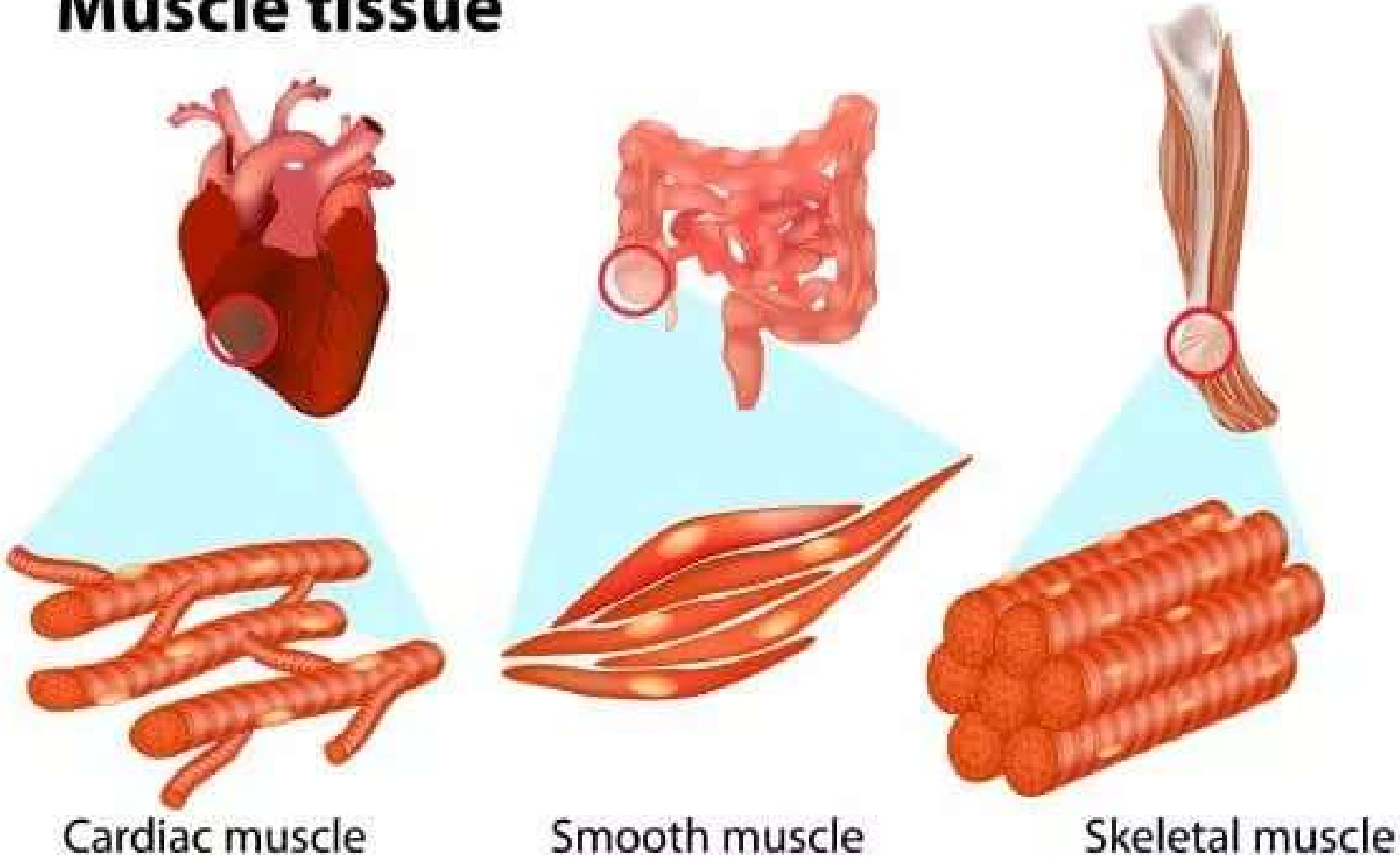
Myosin II Regulates Endocytosis Traffic 2014; 15: 418–432

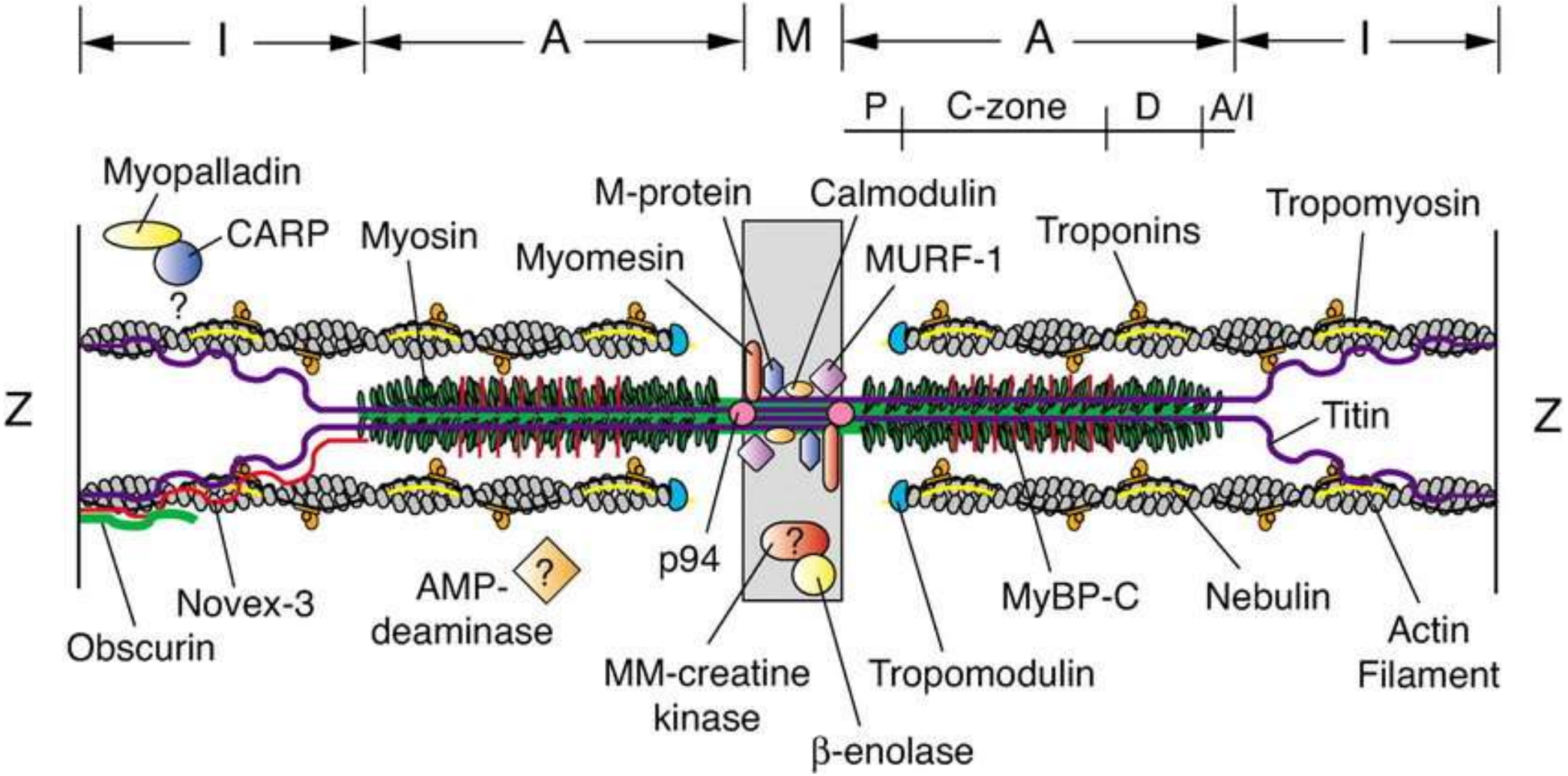

SARCOMERE
Muscle
Thick Myosin Filament
Thin Actin Filament
Elastic Titin Filament
Z Disc
M Line
Z Disc
Sarcomere
Thick Myosin Filament
I Band
A Band
I Band
Thin Actin Filament
MYOFIBRIL
Z Disc
H Zone
Z Disc
M Line

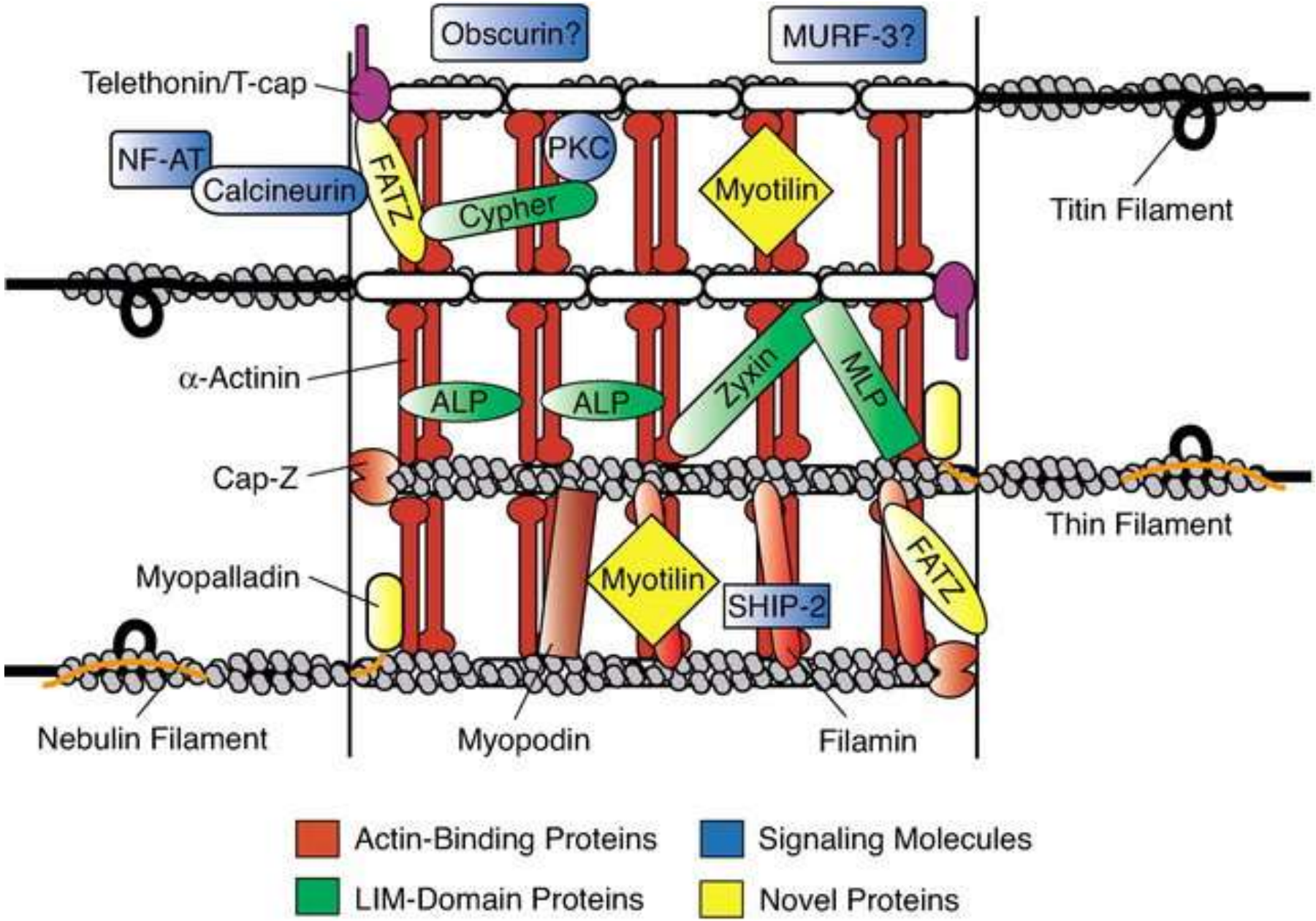

M-line
Myosin
Titin
Obscurin
Myomesin
Myomesin
Obscurin
Titin
Myosin
Thick filament
Thick filament

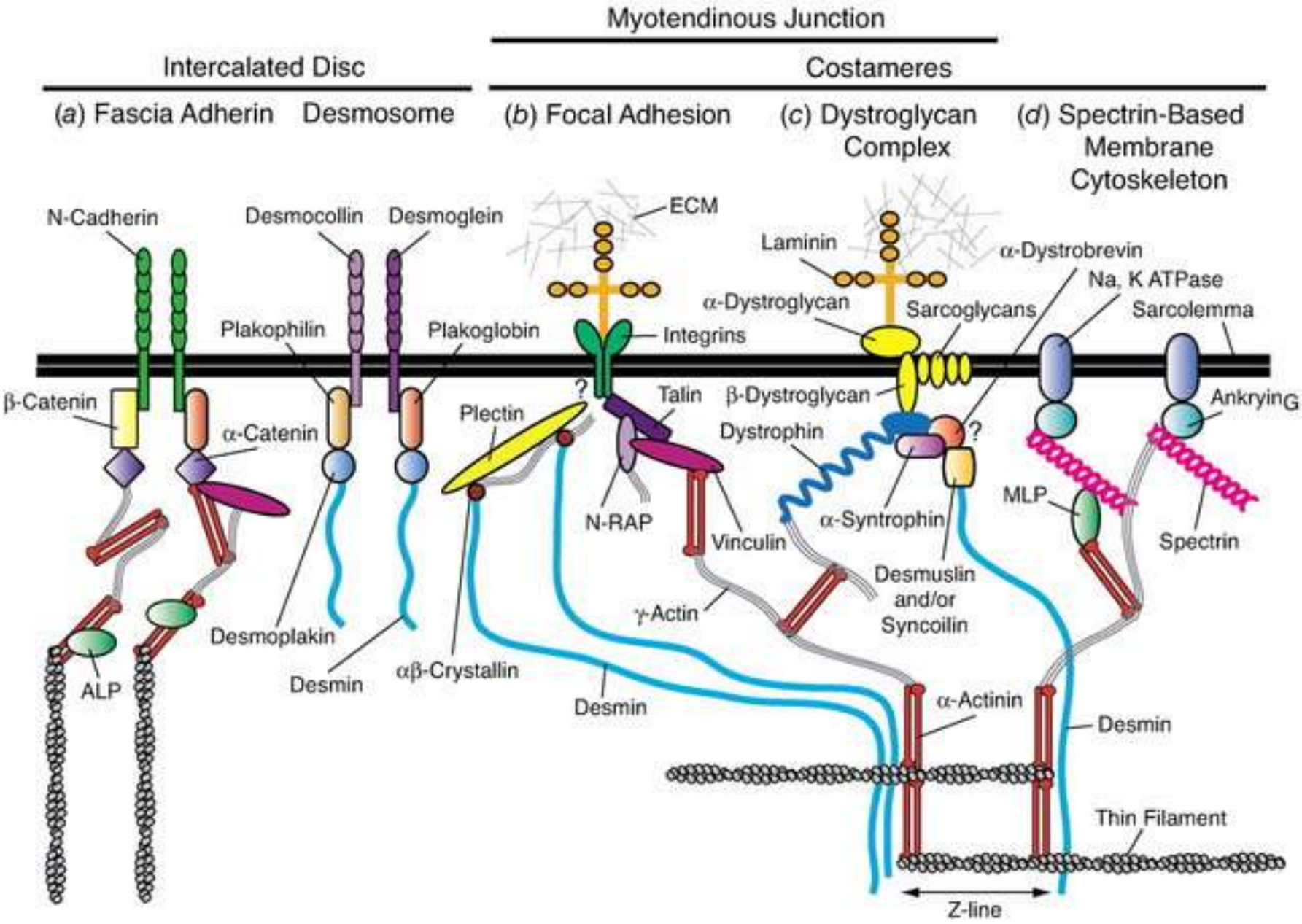

Z disk
Sarcomere
Z disk
Troponin
Actin
Myosin
M line
Tropomyosin
Relaxed
+ ATP, Ca2+
Contracted
Ca2+

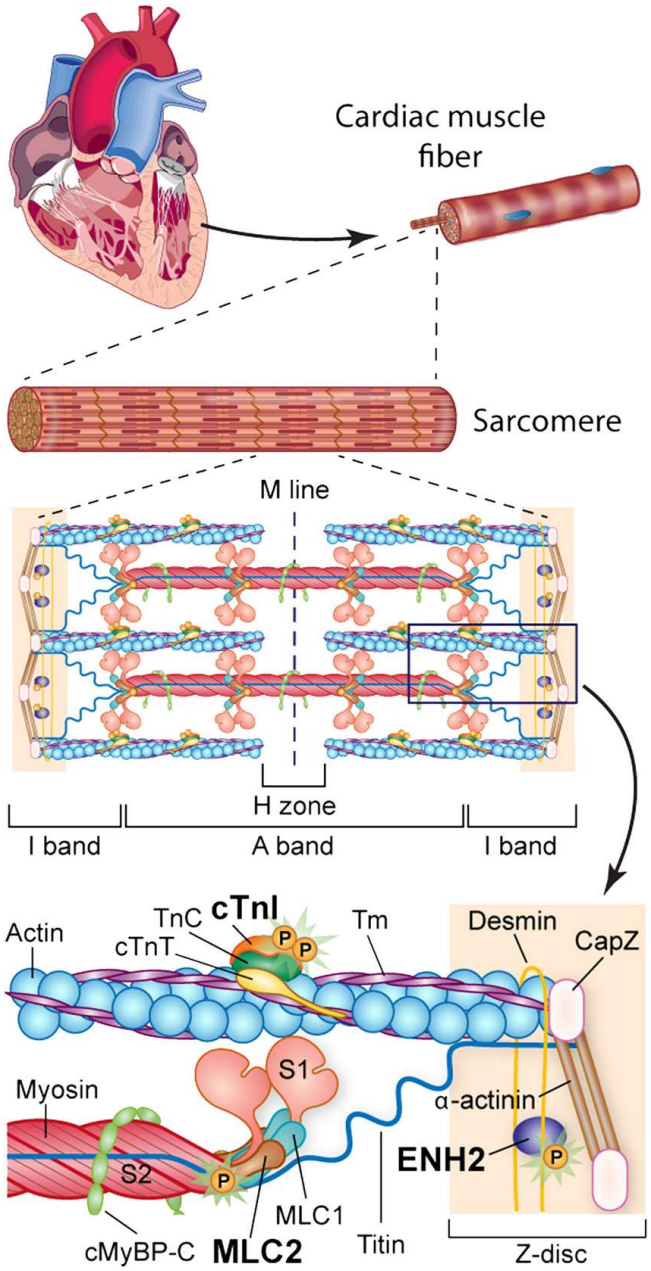
Muscle tissue

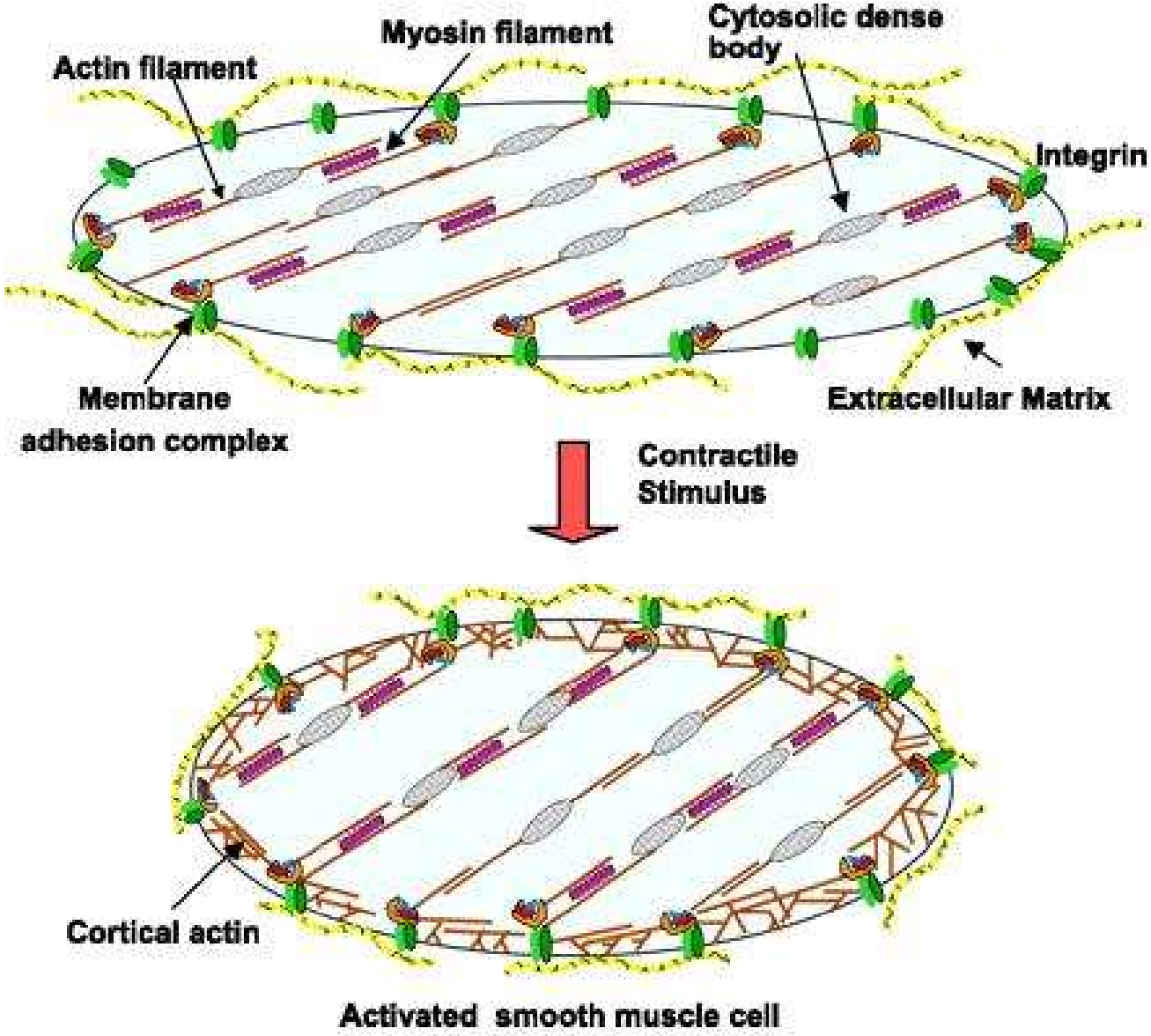


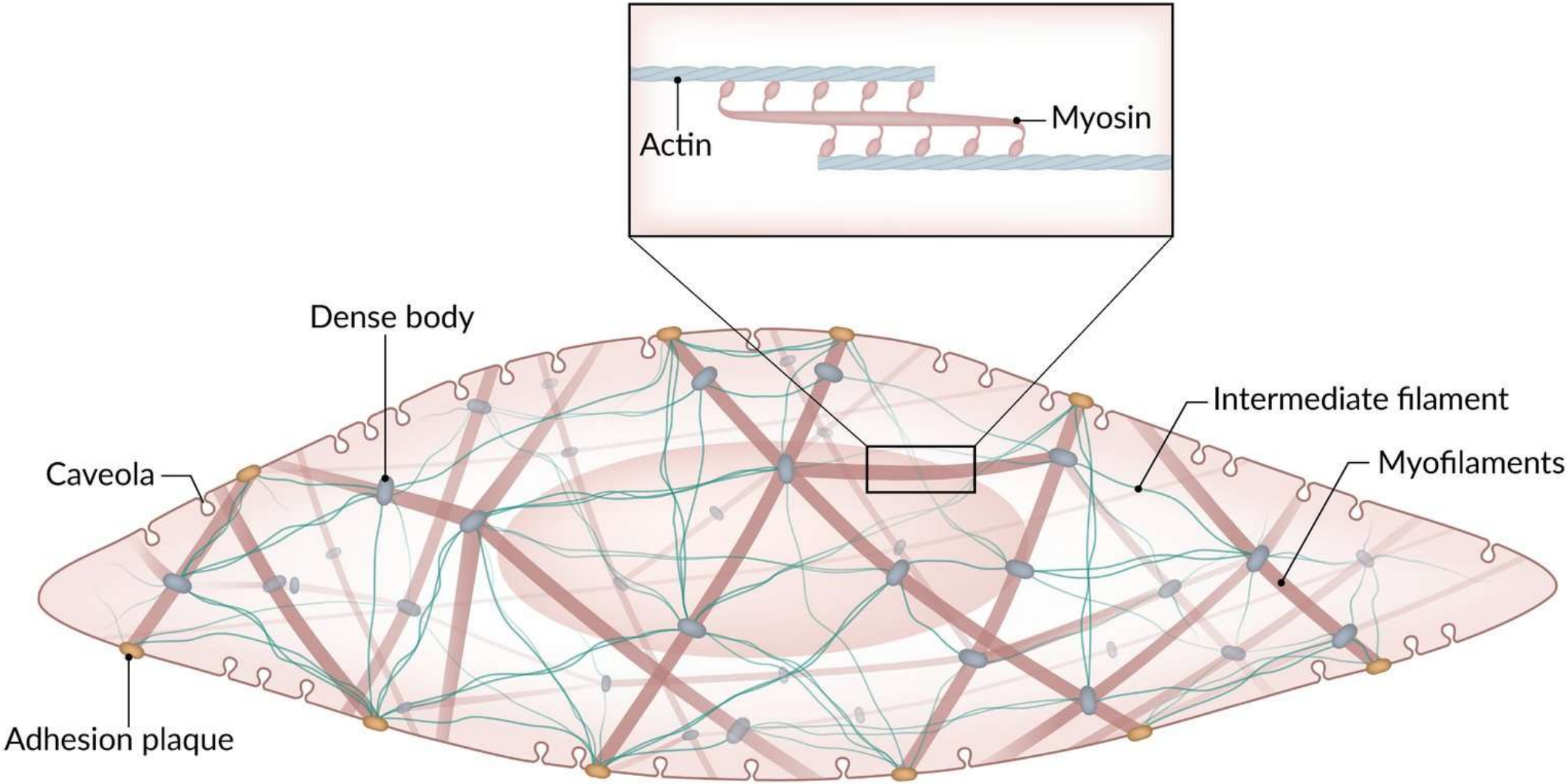

I
A
M
A
I
P
C-zone
D
A/I
Myopalladin
CARP
?
Myosin
Myomesin
M-protein
Calmodulin
MURF-1
Troponins
Tropomyosin
Z
Z
Titin
Obscurin
Novex-3
AMP-
deaminase
?
p94
?
MM-creatine
kinase
β-enolase
Tropomodulin
MyBP-C
Nebulin
Actin
Filament

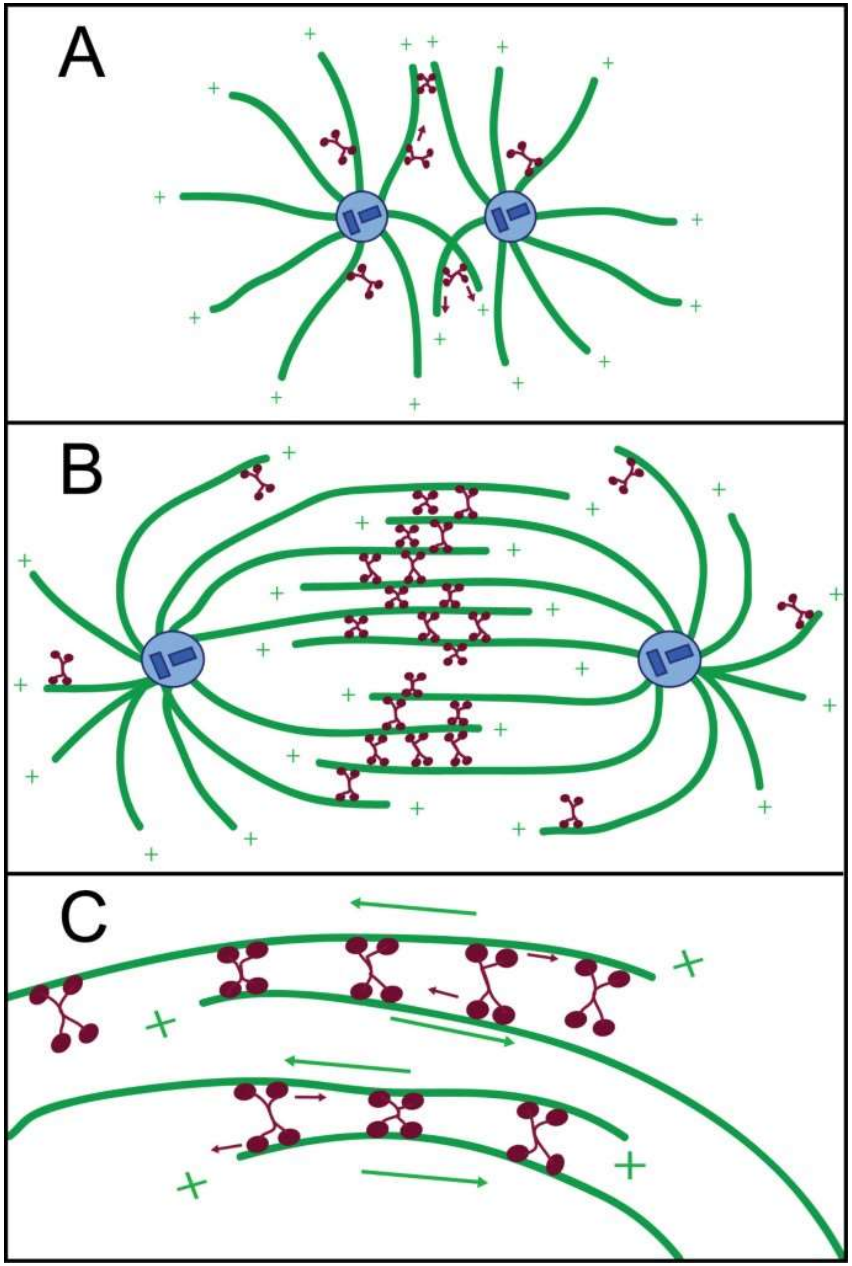

Obscurin?
MURF-3?
Telethonin/T-cap
NF-AT
Calcineurin
FATZ
PKC
Cypher
Myotilin
Titin Filament
α-Actinin
ALP
ALP
Zyxin
MLP
Cap-Z
Thin Filament
Myopalladin
Myotilin
SHIP-2
FATZ
Nebulin Filament
Myopodin
Filamin
Actin-Binding Proteins
Signaling Molecules
LIM-Domain Proteins
Novel Proteins

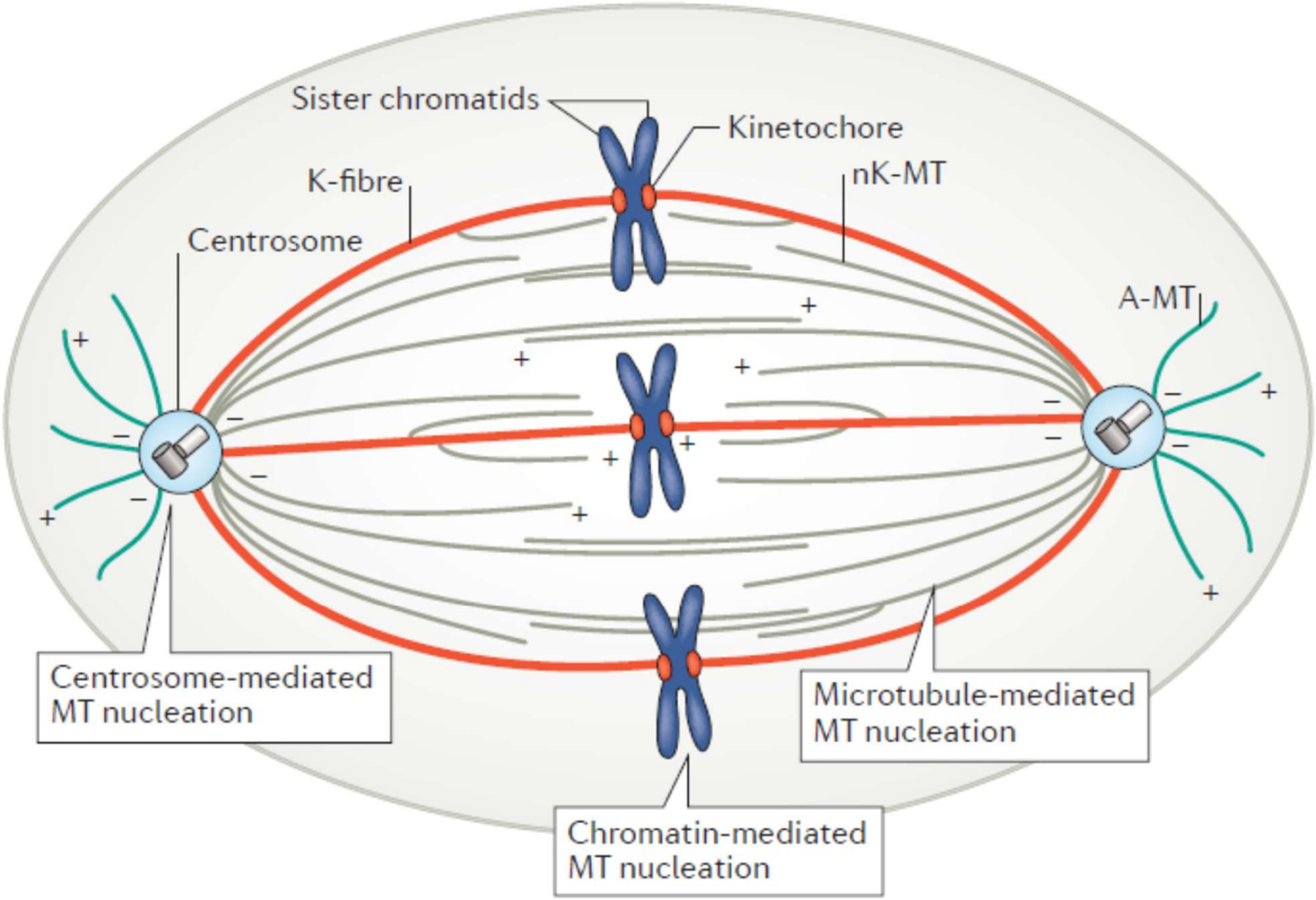

Myotendinous Junction
Intercalated Disc
Costameres
(a) Fascia Adherin
Desmosome
(b) Focal Adhesion
(c) Dystroglycan Complex
(d) Spectrin-Based Membrane Cytoskeleton
N-Cadherin
Desmocollin
Desmoglein
ECM
Laminin
α-Dystrobrevin
Na, K ATPase
α-Dystroglycan
Sarcoglycans
Sarcolemma
Plakophilin
Plakoglobin
Integrins
β-Catenin
α-Catenin
Plectin
Talin
β-Dystroglycan
Ankryin G
Dystrophin
MLP
N-RAP
α-Syntrophin
Vinculin
Spectrin
Desmuslin and/or Syncoilin
γ-Actin
Desmoplakin
ALP
Desmin
αβ-Crystallin
Desmin
α-Actinin
Desmin
Thin Filament
Z-line

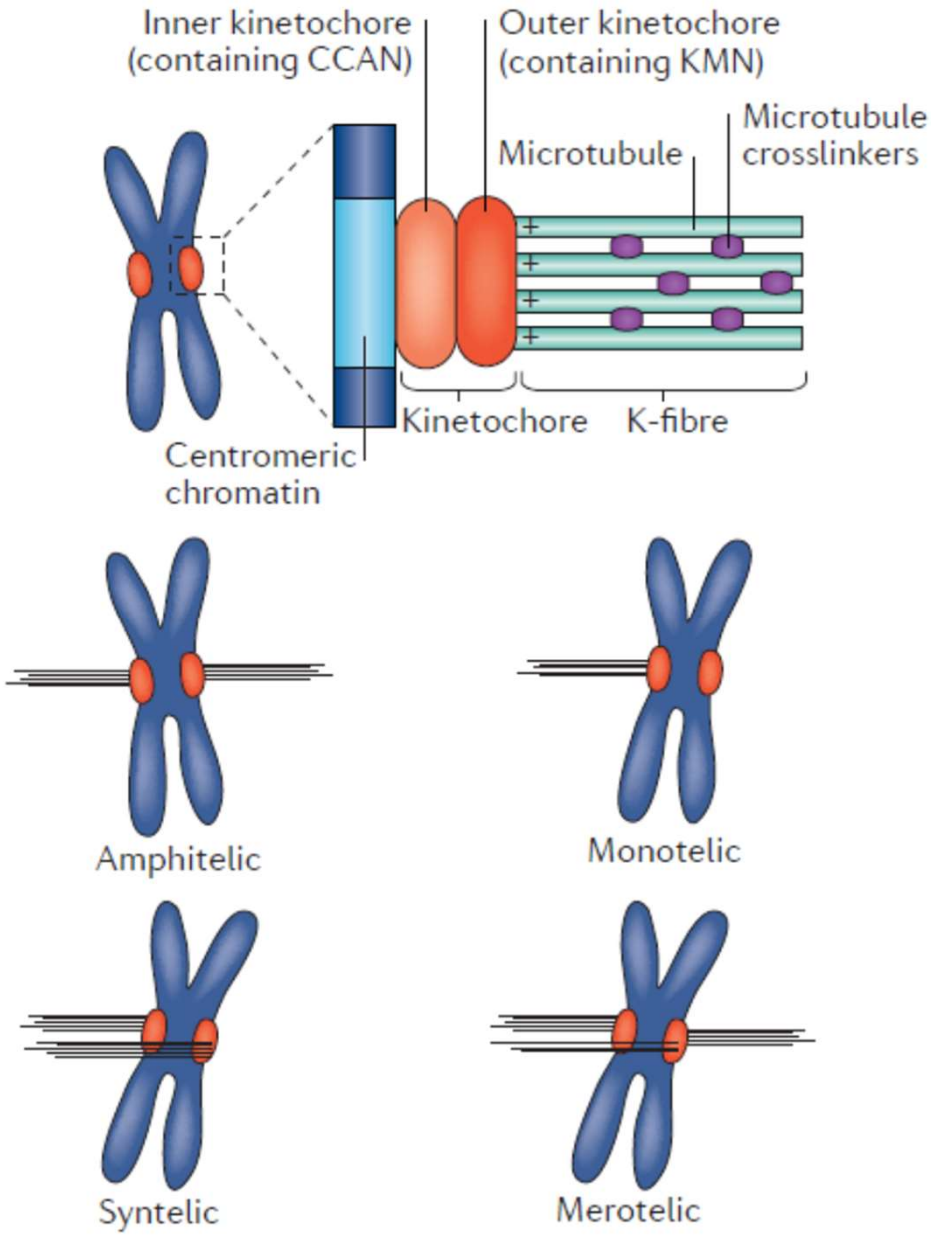

Cardiac muscle fiber
Sarcomere
M line
H zone
I band
A band
I band
Actin
TnC
cTnI
cTnT
Tm
Desmin
CapZ
Myosin
S1
α-actinin
ENH2
S2
MLC1
cMyBP-C
MLC2
Titin
Z-disc

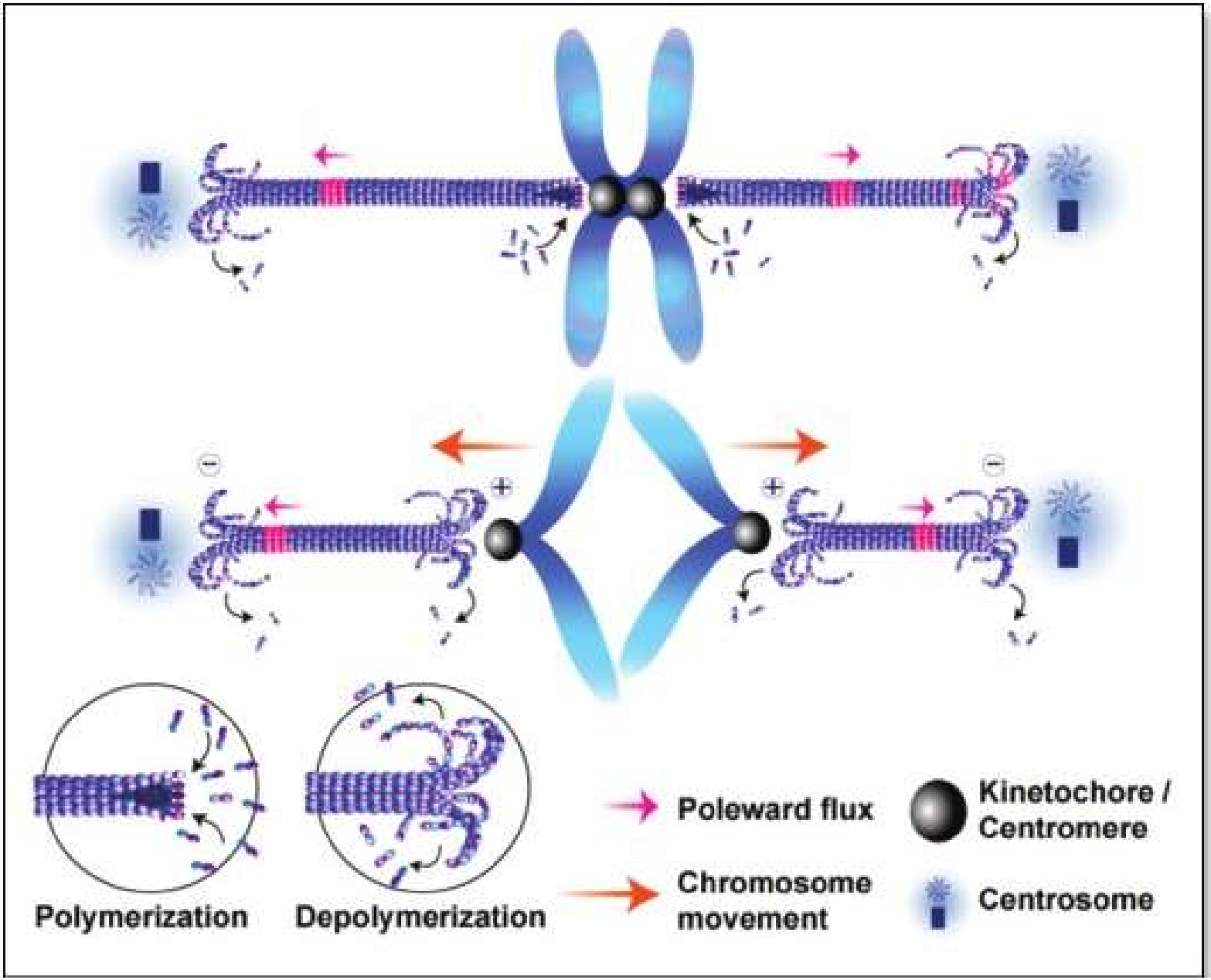

Actin filament
Myosin filament
Cytosolic dense body
Integrin
Membrane adhesion complex
Extracellular Matrix
Contractile Stimulus
Cortical actin
Activated smooth muscle cell

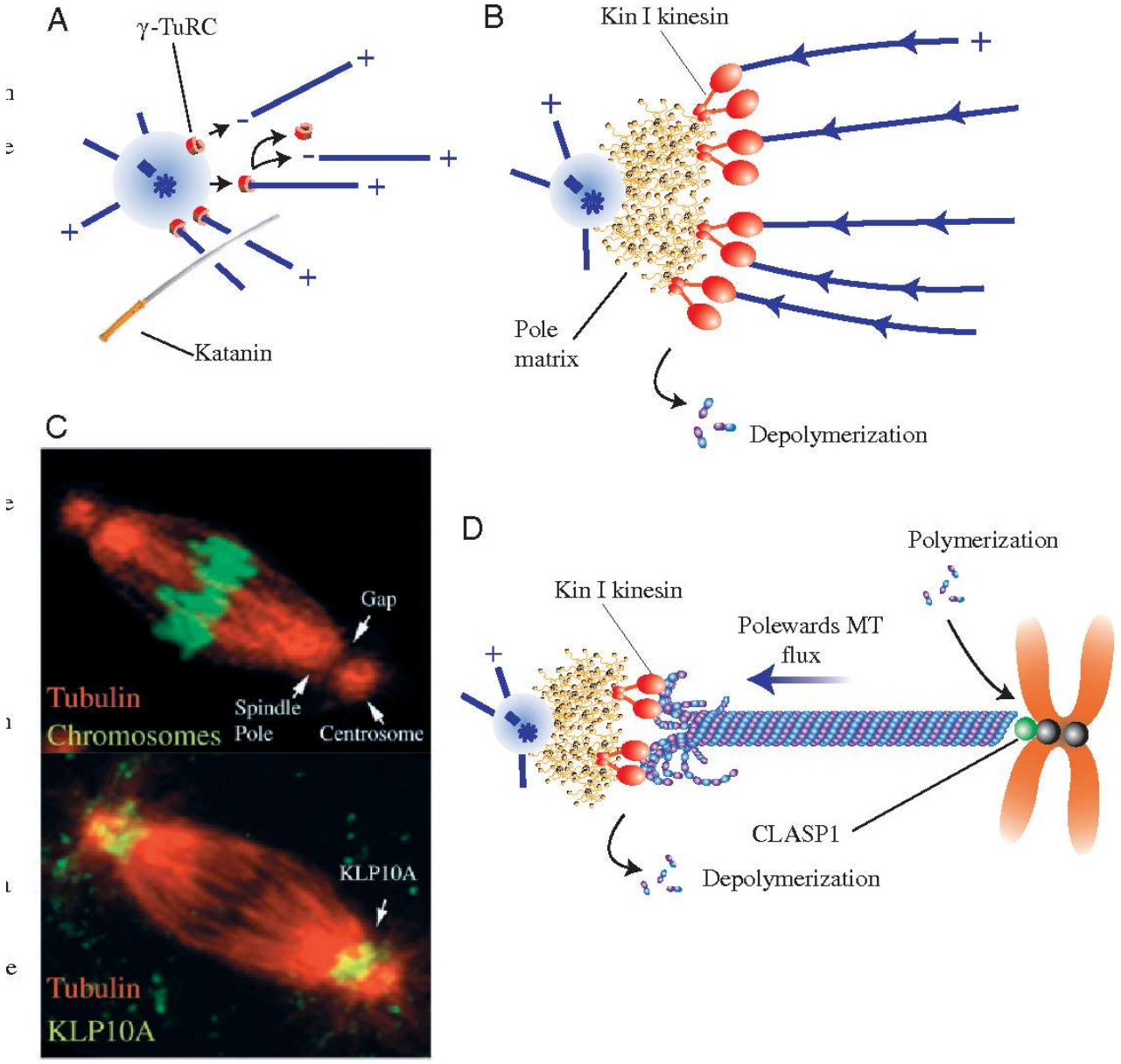

Actin
Myosin
Dense body
Caveola
Intermediate filament
Myofilaments
Adhesion plaque

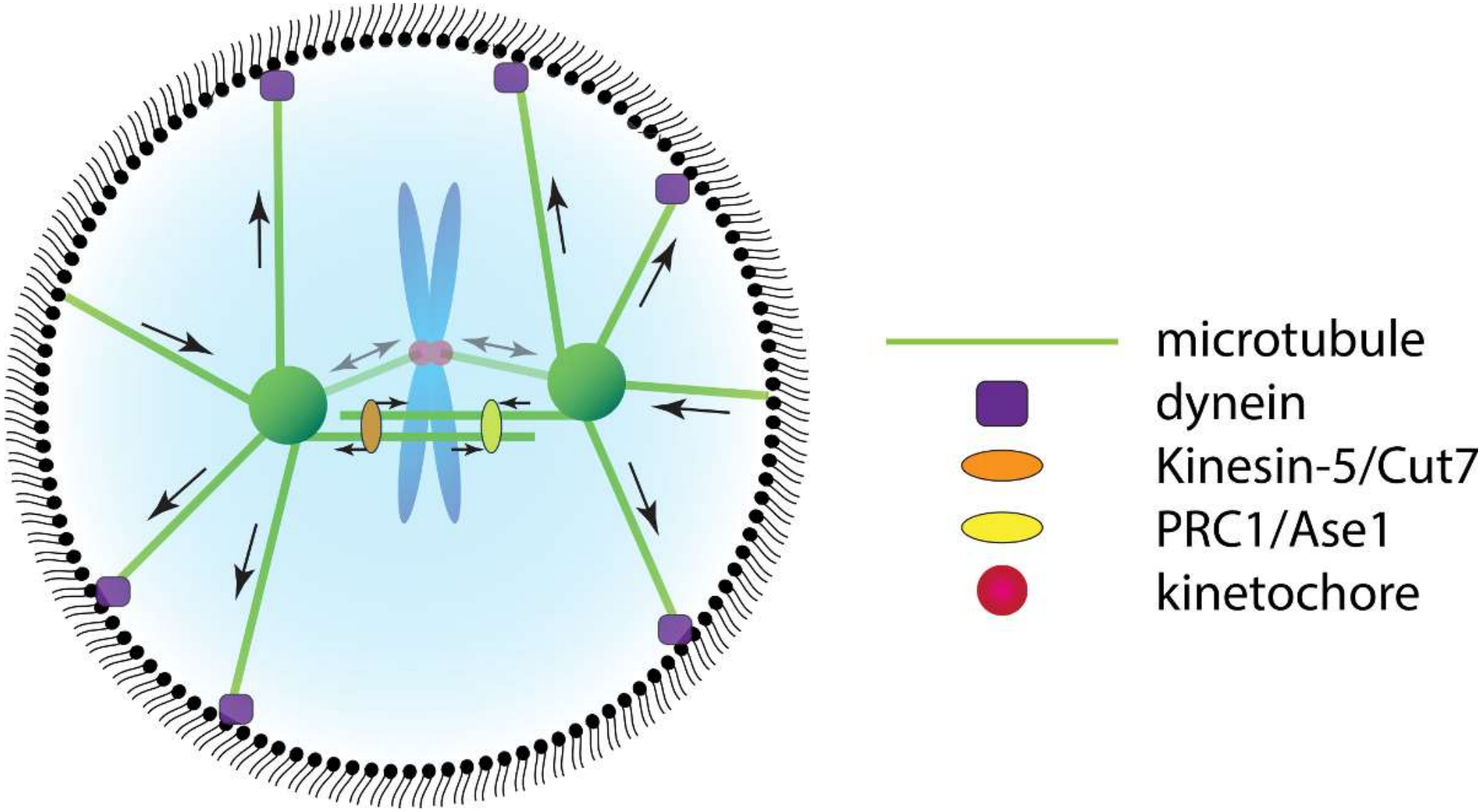

A
B
C

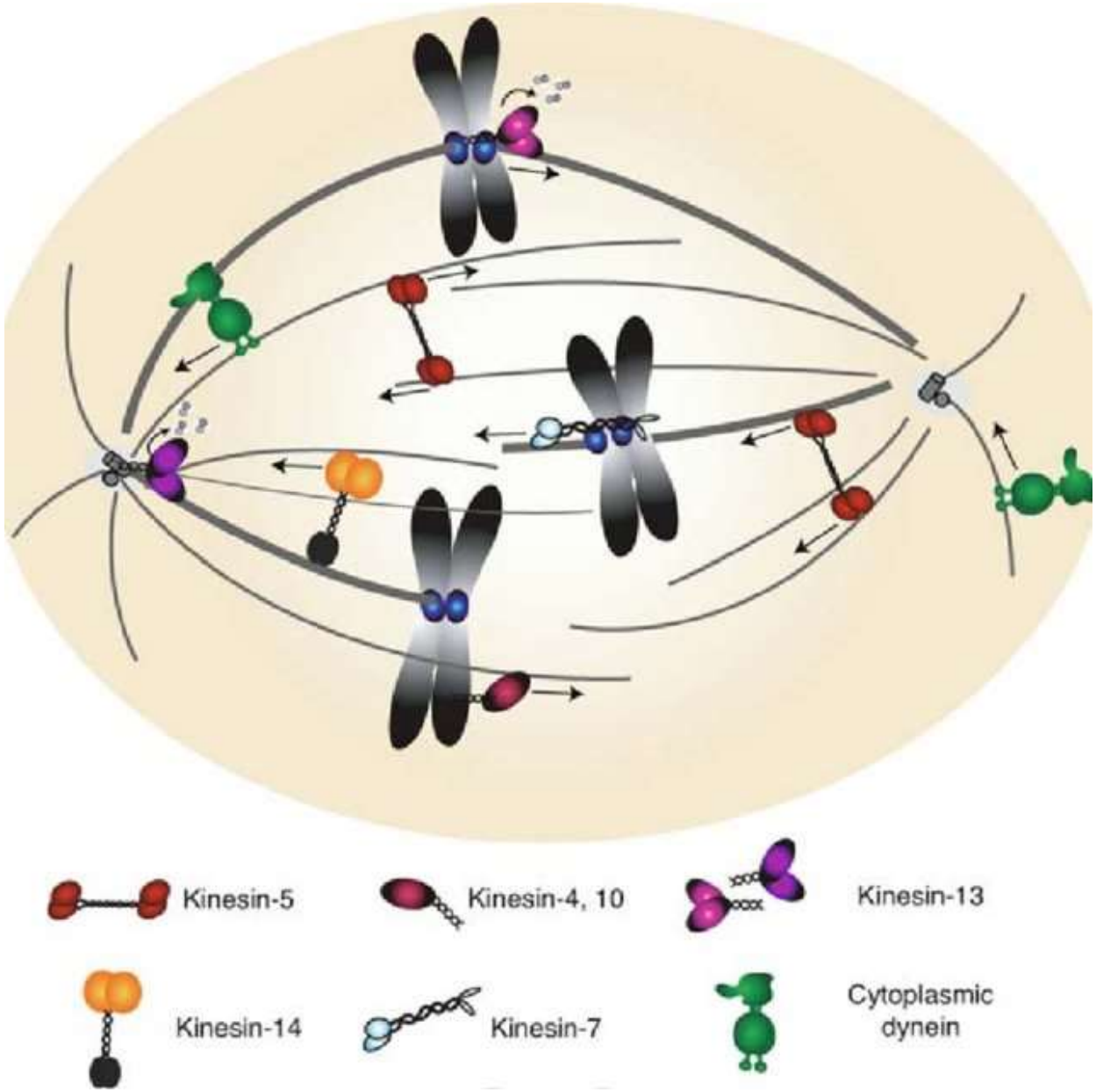

Sister chromatids
Kinetochore
K-fibre
nK-MT
Centrosome
A-MT
Centrosome-mediated
MT nucleation
Microtubule-mediated
MT nucleation
Chromatin-mediated
MT nucleation


Inner kinetochore
(containing CCAN)
Outer kinetochore
(containing KMN)
Microtubule
Microtubule
crosslinkers
Kinetochore
K-fibre
Centromeric
chromatin
Amphitelic
Monotelic
Syntelic
Merotelic

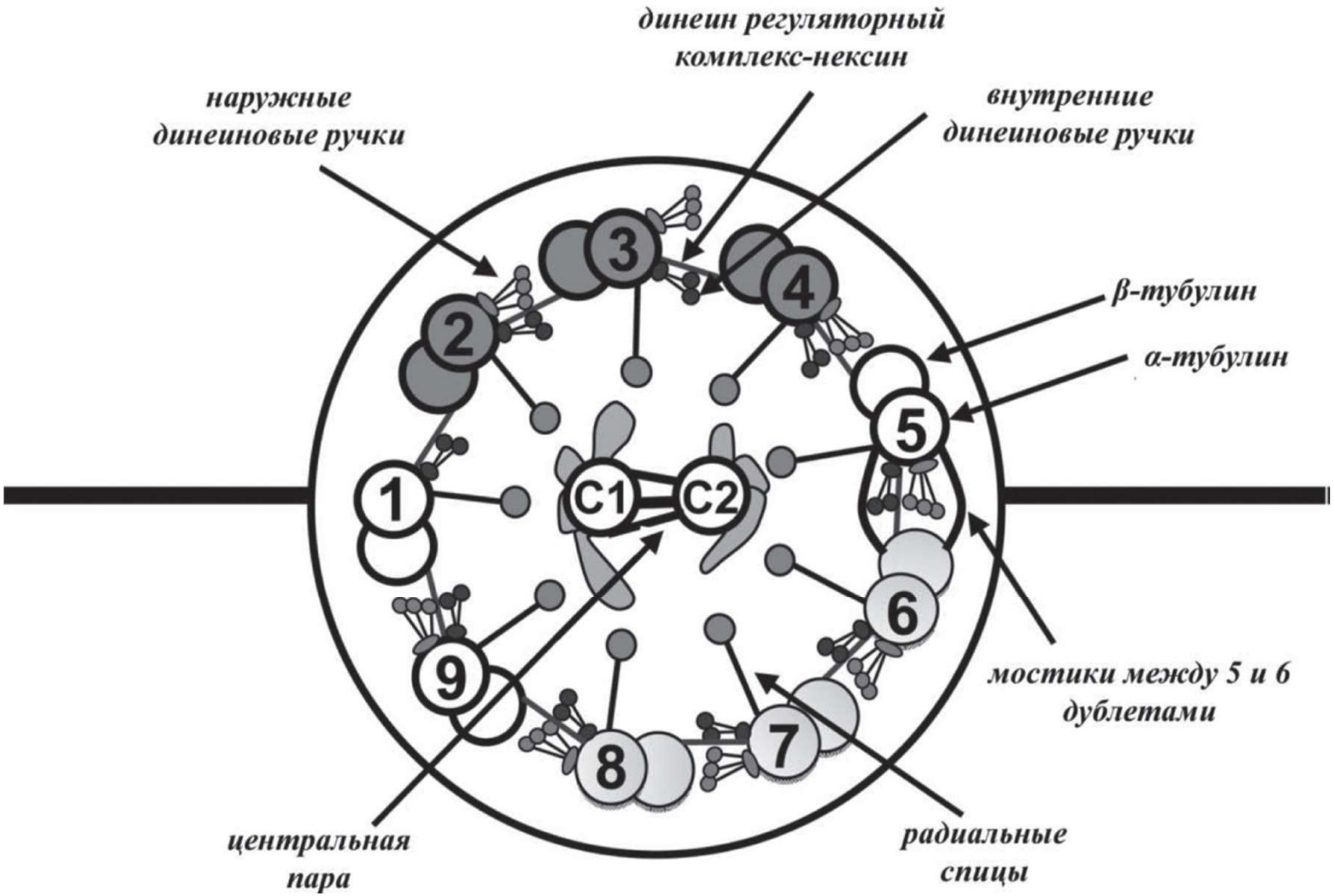

Polymerization
Depolymerization
Poleward flux
Chromosome movement
Kinetochore / Centromere
Centrosome

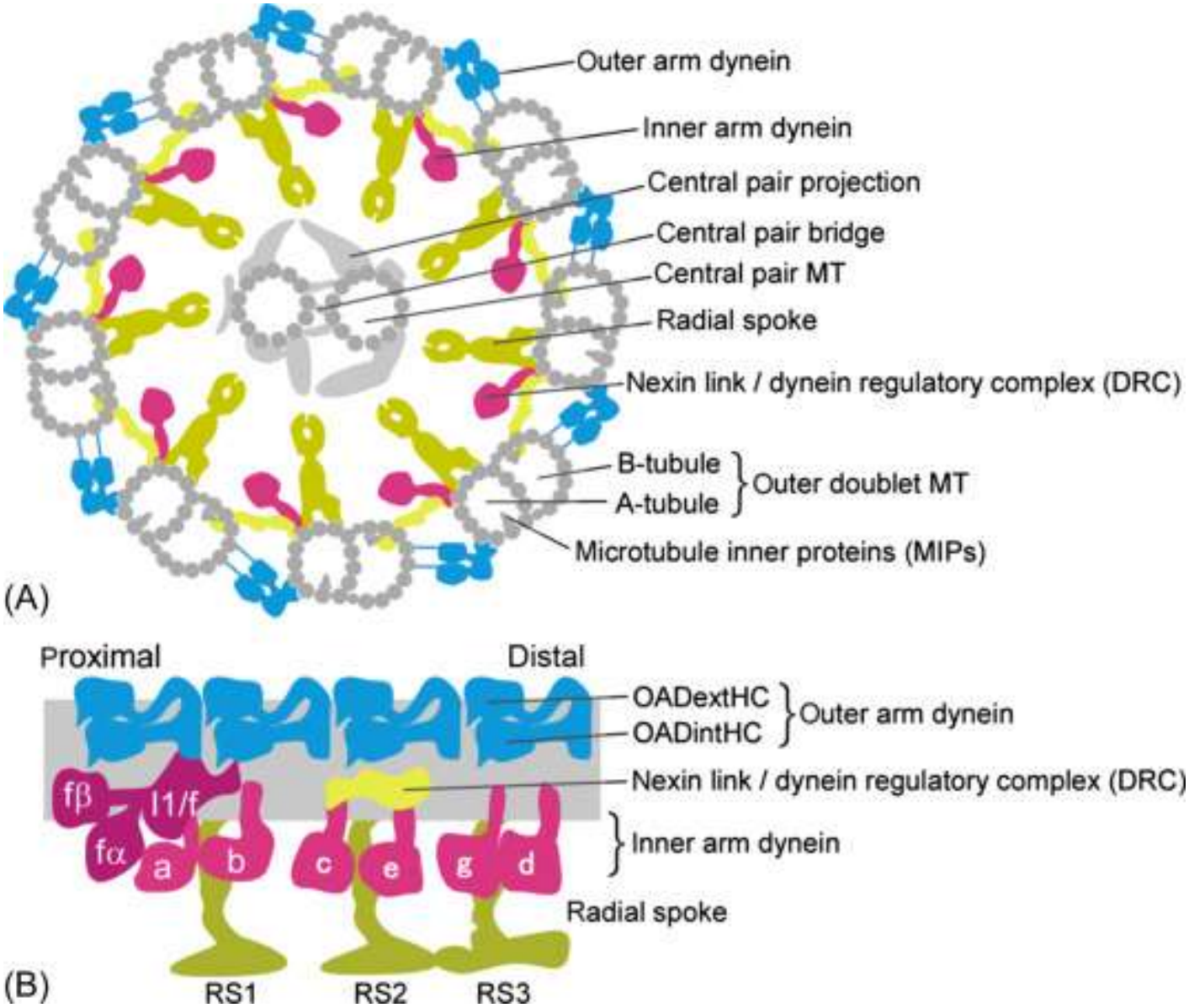

A
γ-TuRC
Katanin
B
Kin I kinesin
Pole
matrix
Depolymerization
C
Gap
Tubulin
Chromosomes
Spindle
Pole
Centrosome
KLP10A
Tubulin
KLP10A
D
Polymerization
Kin I kinesin
Polewards MT
flux
CLASP1
Depolymerization


microtubule
dynein
Kinesin-5/Cut7
PRC1/Ase1
kinetochore


Kinesin-5
Kinesin-4, 10
Kinesin-13
Kinesin-14
Kinesin-7
Cytoplasmic dynein

Аксонема


динеин регуляторный комплекс-нексин
наружные динеиновые ручки
внутренние динеиновые ручки
β-тубулин
α-тубулин
1
2
3
4
5
6
7
8
9
C1
C2
мостики между 5 и 6 дублетами
центральная пара
радиальные спицы


Outer arm dynein
Inner arm dynein
Central pair projection
Central pair bridge
Central pair MT
Radial spoke
Nexin link / dynein regulatory complex (DRC)
B-tubule
A-tubule
Outer doublet MT
Microtubule inner proteins (MIPs)
(A)
Proximal
Distal
OADextHC
OADintHC
Outer arm dynein
Nexin link / dynein regulatory complex (DRC)
fβ
I1/f
fα
a
b
c
e
g
d
Inner arm dynein
Radial spoke
(B)
RS1
RS2
RS3

Благодарю за внимание!