

Receptor-Mediated and Fluid-Phase Uptake

Cellular housekeeping • Endocytosis, exocytosis, transcytosis and cytoskeletal context

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Learning outcomes

By the end of the session, explain how cells:

- Internalize selected ligands by caveolae- and clathrin-associated routes.
- Sort cargo and receptors within acidified endosomal compartments.
- Balance endocytosis with secretion, recycling, and transcytosis.
- Use cytoskeletal systems for cell structure, movement, and transport.

Three directions of membrane traffic

Endocytosis

Material enters the cell

Surface membrane forms internal vesicles

Exocytosis

Vesicles fuse with the surface

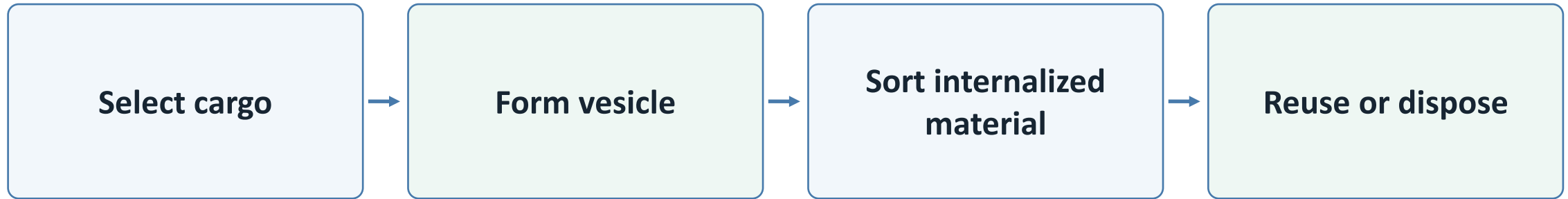
Secreted proteins leave the cell

Transcytosis

Vesicles traverse a cell

Transfer across an epithelial barrier

The basic traffic problem



- Entry, intracellular sorting, and membrane return are linked processes.
- Cargo molecules and their receptors do not necessarily share the same final destination.

Which route is used?

Caveolae

Small receptor-bound molecules, including some vitamins

Caveolin-associated membrane domains

Clathrin-coated pits

Examples: LDL and transferrin receptor cargo

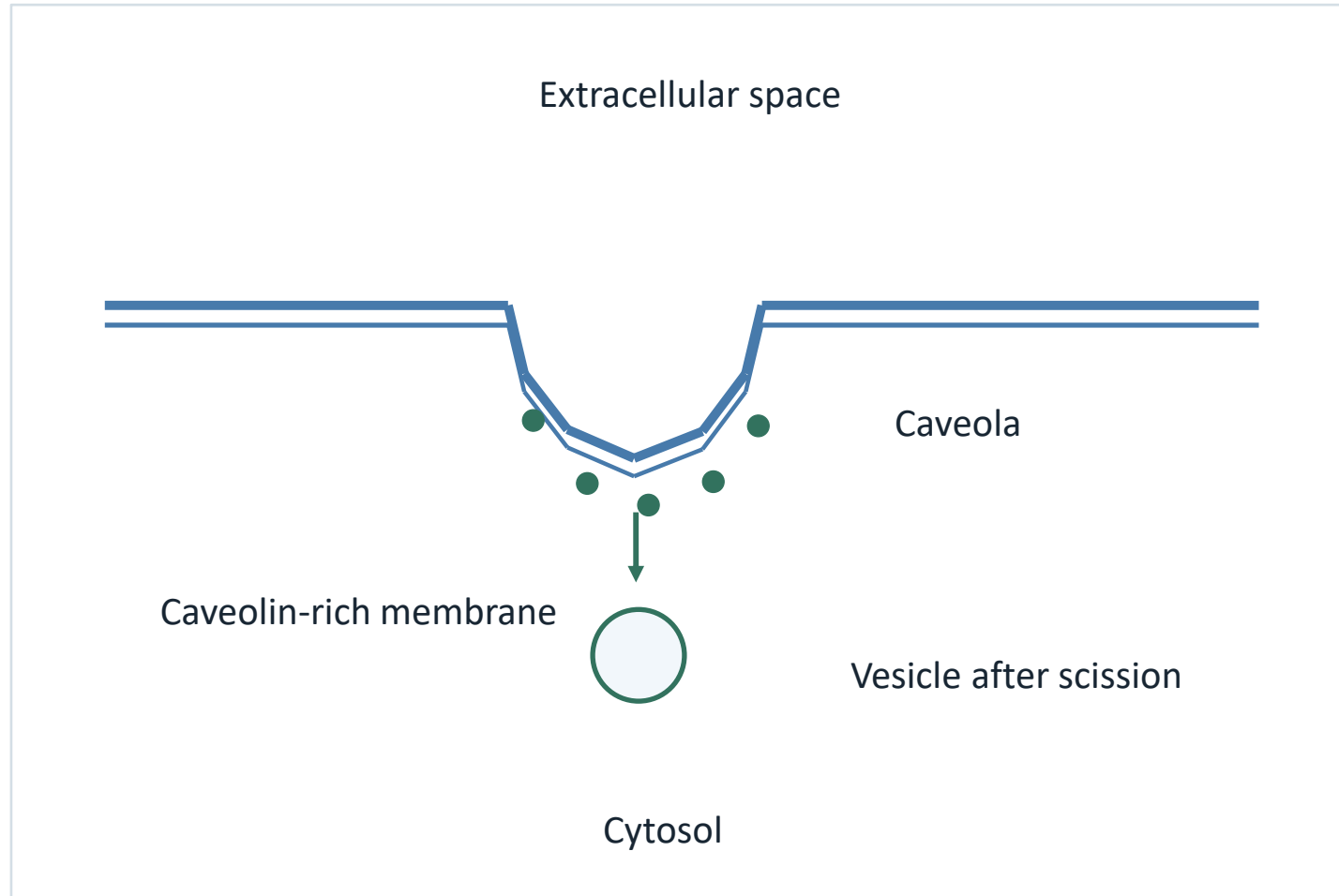
Clathrin-associated internalization

Fluid-phase capture

Extracellular fluid is co-internalized

Can accompany coated-vesicle uptake

Caveolae: Membrane invaginations



Identity

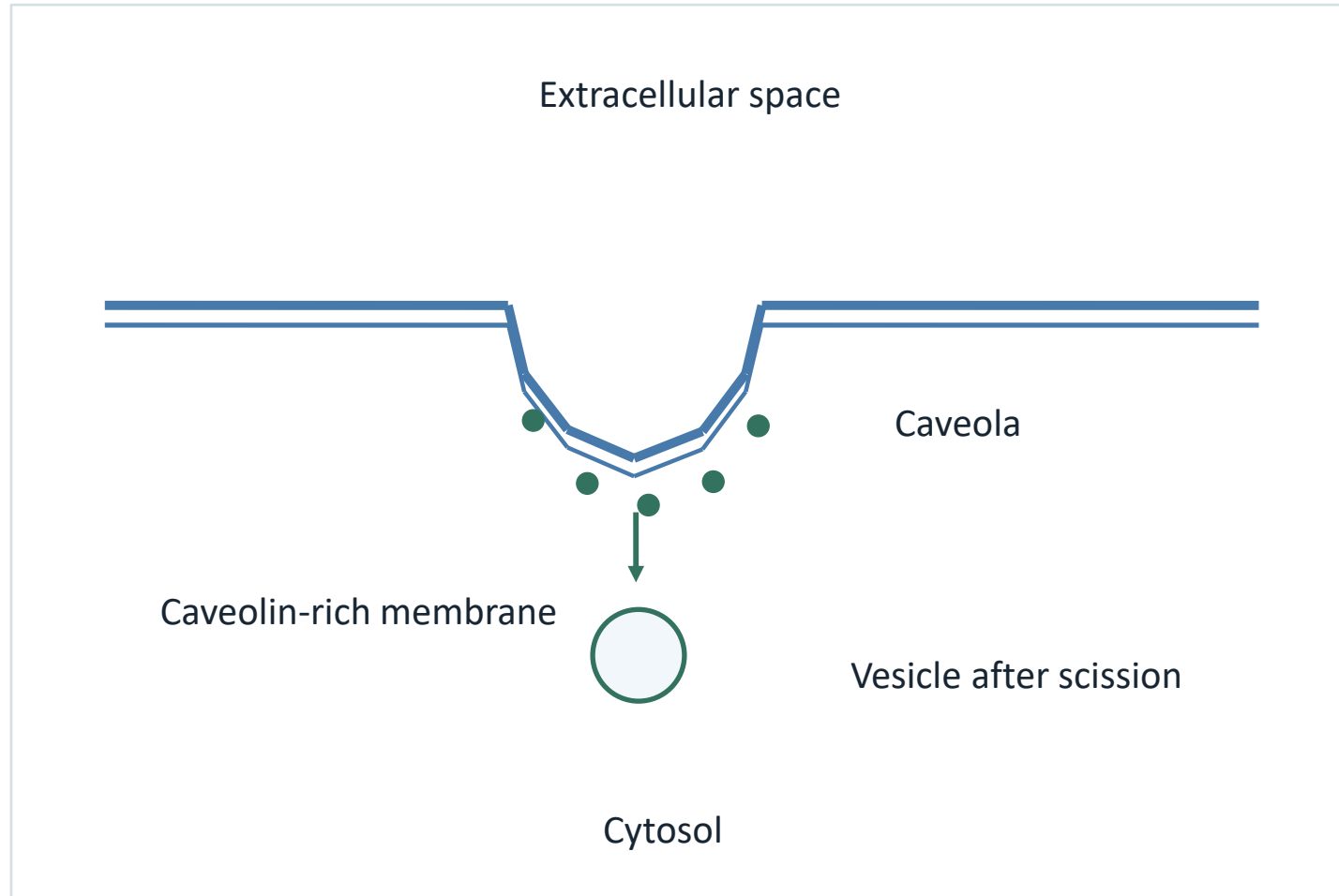
- “Little caves” at the plasma membrane.
- Associated with caveolin rather than a clathrin coat.
- Support uptake of bound molecules and extracellular fluid.

The lipid environment of caveolae

Caveolae share properties with membrane rafts.

- Membrane domains are enriched in cholesterol and glycosphingolipids.
- The lipid setting contributes to localization of specific membrane-associated proteins.
- Caveolin is the major structural protein identified in tissue analysis.

Caveolin and membrane organization



Structural concept

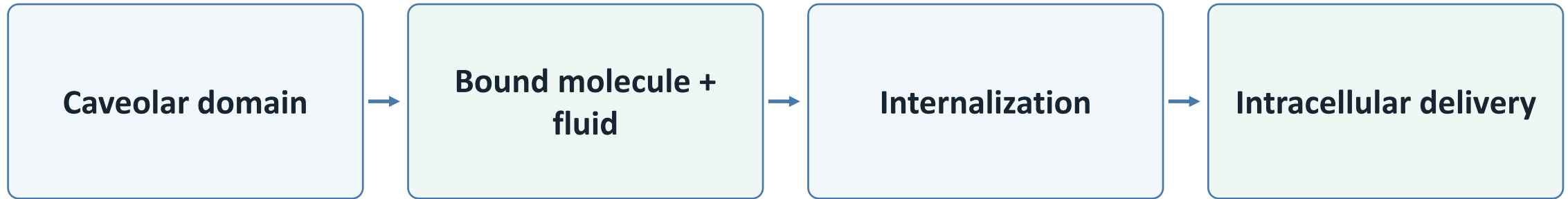
- Caveolin organizes the caveolar membrane domain.
- The domain can internalize associated ligands.
- These are schematic relationships, not a structural micrograph.

Proteins associated with caveolae

Several classes.

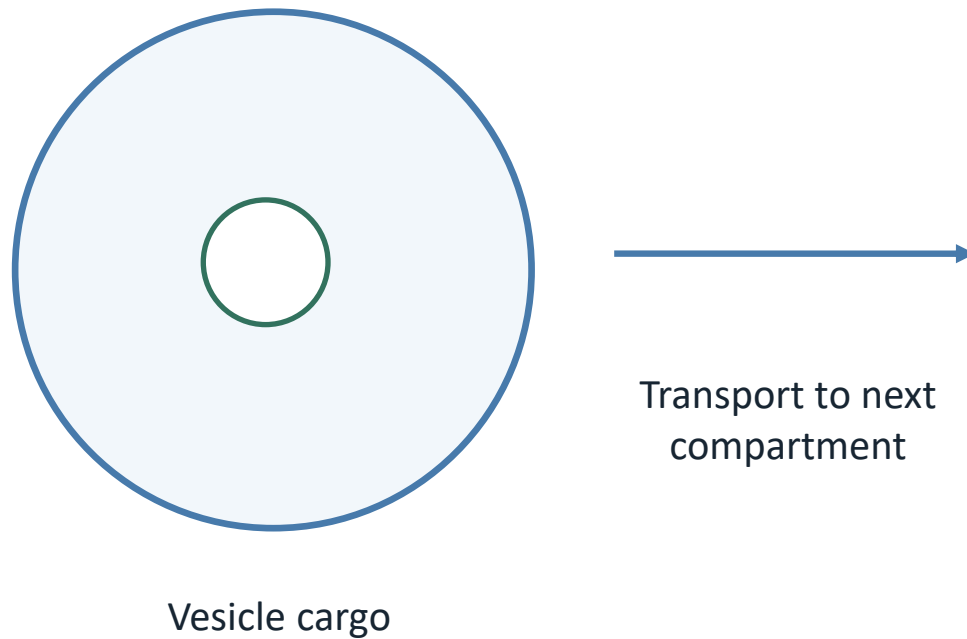
- Glycosylphosphatidylinositol (GPI)-linked molecules.
- CAMP-binding proteins and Src-family kinases.
- Folate receptors involved in uptake of some small molecules.
- Receptors and integrins can be internalized in caveolar pathways.

Potocytosis: “cellular sipping”



- Potocytosis specifically names internalization of caveolae with associated extracellular fluid.

Folate as a caveolar cargo example



Trace the example

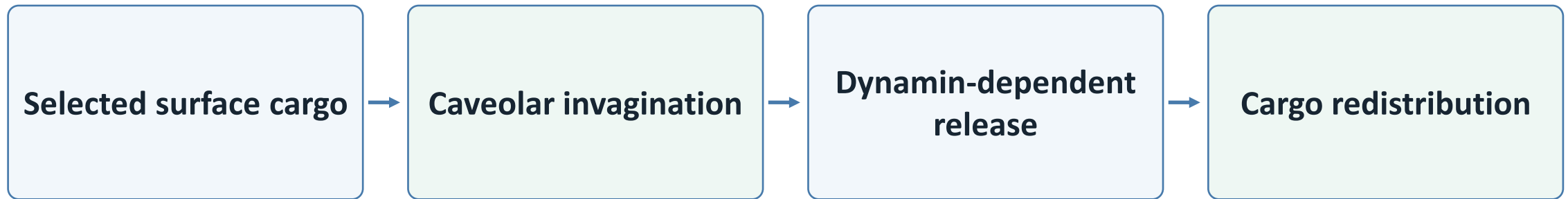
- Folate receptor is associated with caveolae.
- Receptor-associated uptake can deliver folate across the plasma membrane.
- The source treats this as an example, not an exclusive uptake mechanism.

Caveolae extend beyond nutrient uptake

They also participate in cell-surface regulation.

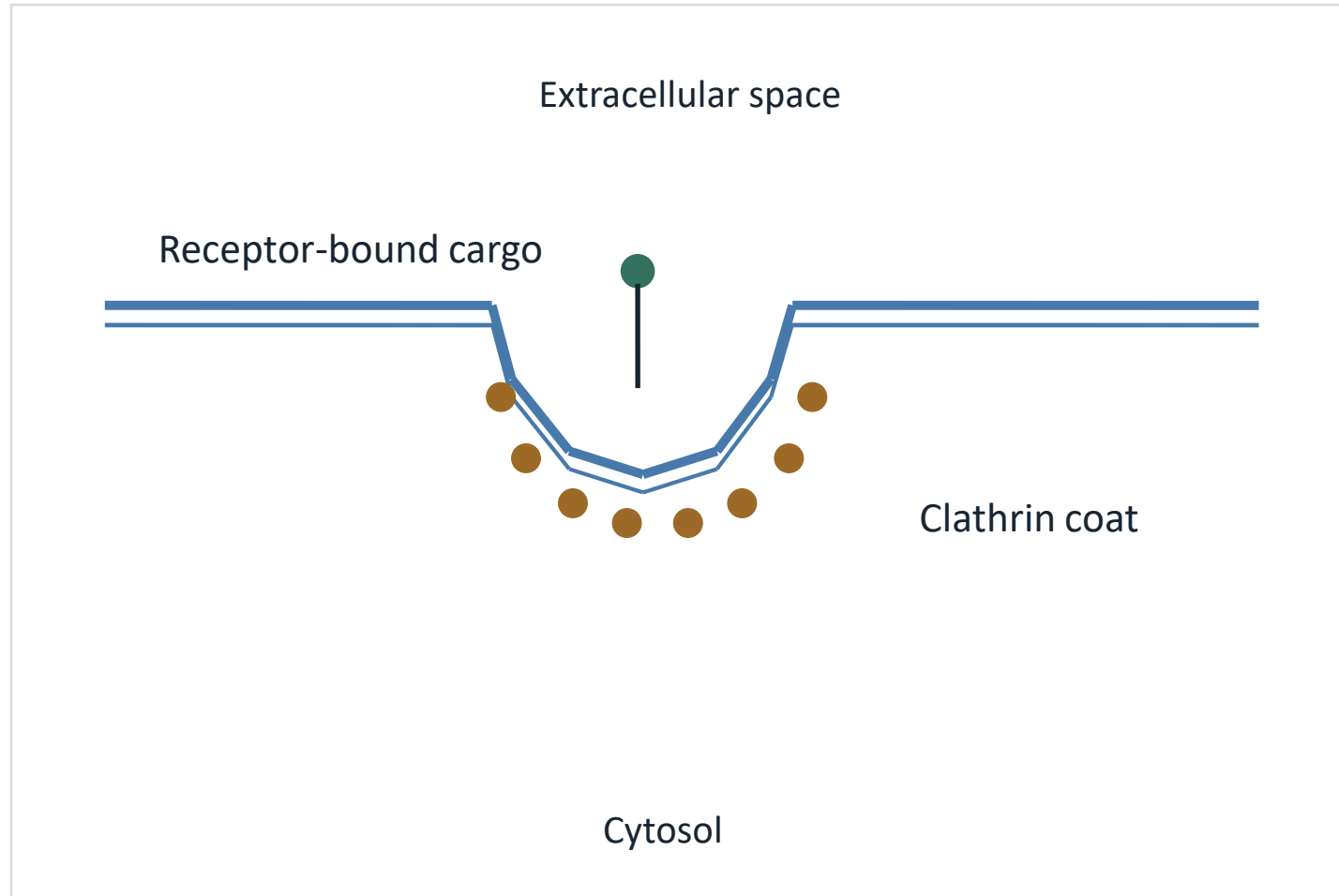
- Internalization of receptors can influence transmembrane signaling.
- Integrin internalization links caveolae to cellular adhesion.
- Membrane transport and surface signaling are mechanistically connected.

One caveolar trafficking sequence



- Dynamin activity is required for the vesicle-release step described for caveolae.

Clathrin-coated pits



Architecture

- Clathrin assembles as an intracellular basket-like lattice.
- The coat helps drive membrane invagination.
- Coated vesicles carry receptor-associated macromolecules.

Two classic receptor-cargo pairs

LDL pathway

LDL receptor binds LDL-associated cargo.

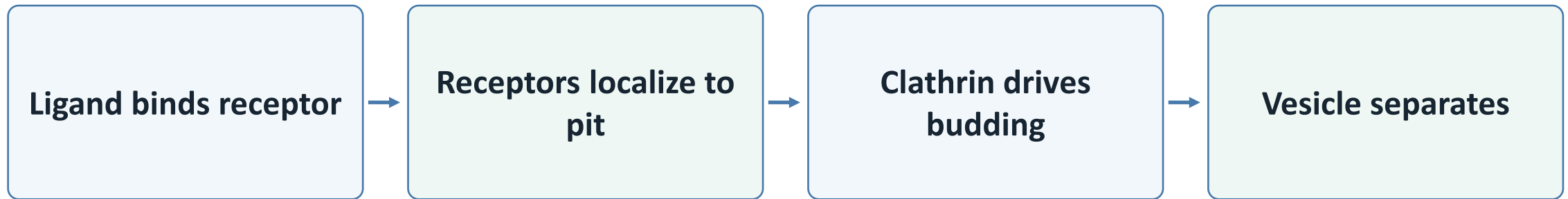
Internalization supports cholesterol delivery.

Transferrin pathway

Transferrin receptor binds transferrin cargo.

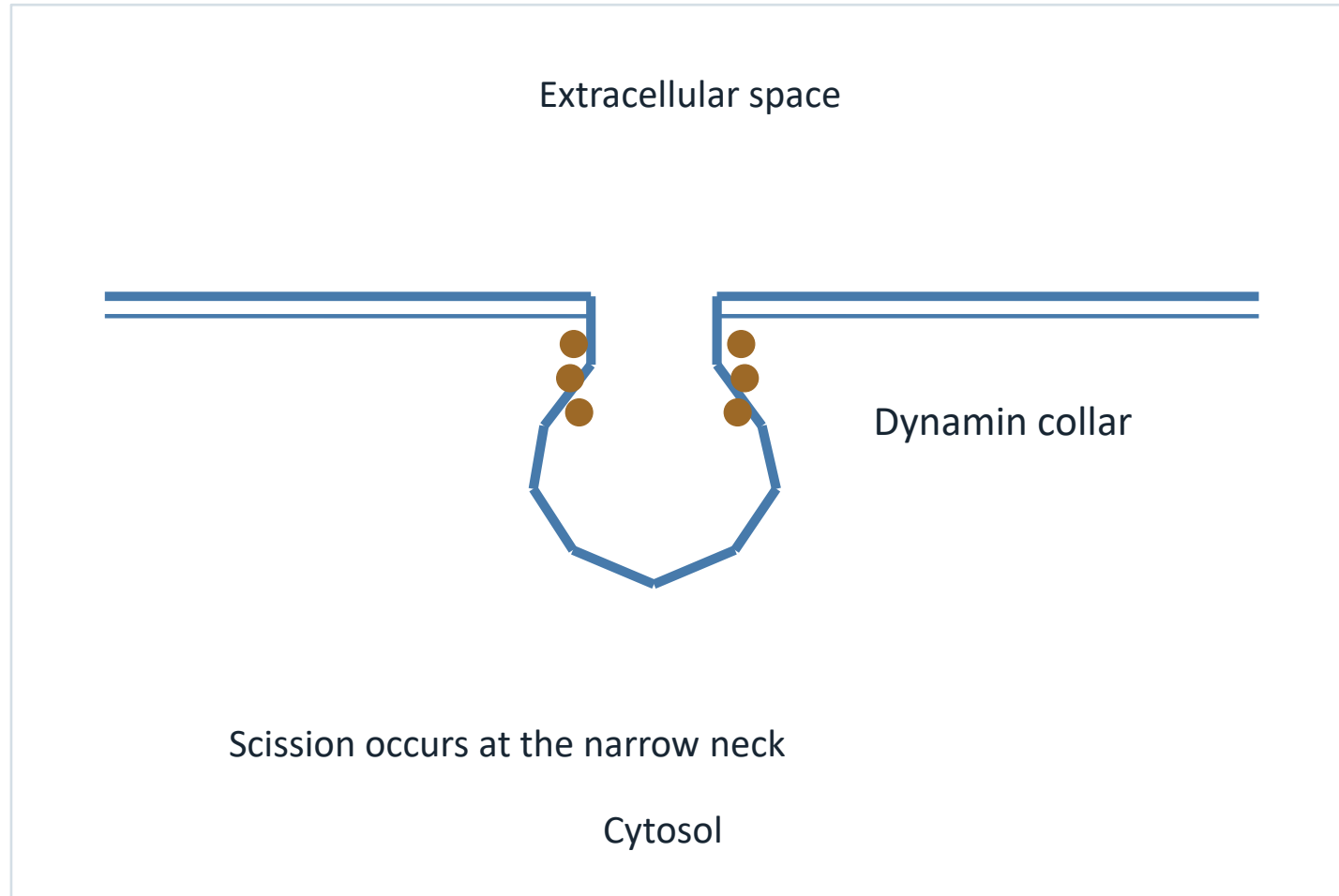
Internalization supports iron delivery.

Formation of a coated vesicle



- Receptor-mediated uptake concentrates bound macromolecules in specialized membrane regions.

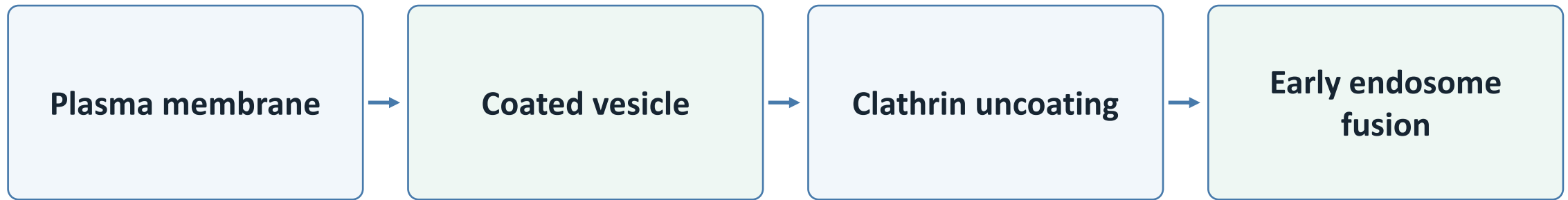
Dynamin: The vesicle scission step



Mechanistic point

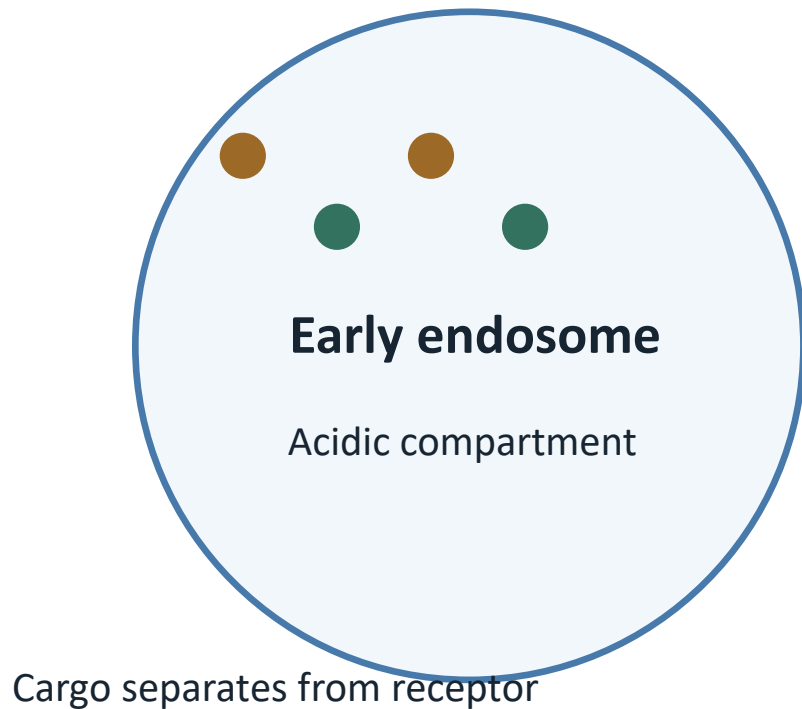
- Dynamin is a GTPase.
- It functions as a molecular scissor at vesicle release.
- Required for the caveolar and clathrin routes described.

Coated vesicles do not stay coated



- Loss of the coat occurs rapidly after release, before endosomal fusion.

Early endosome: First sorting station



Endosomal role

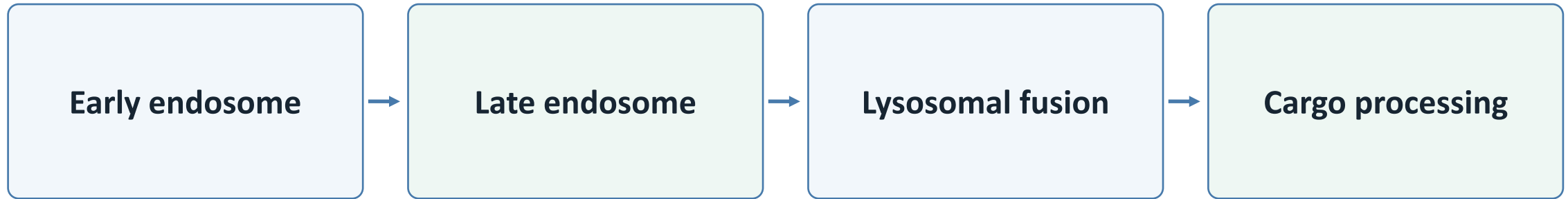
- Receives vesicles after uncoating.
- Maintains an acidic intraluminal environment.
- Provides conditions for ligand-receptor separation.

Why acidic endosomes matter

Low pH changes cargo-receptor association.

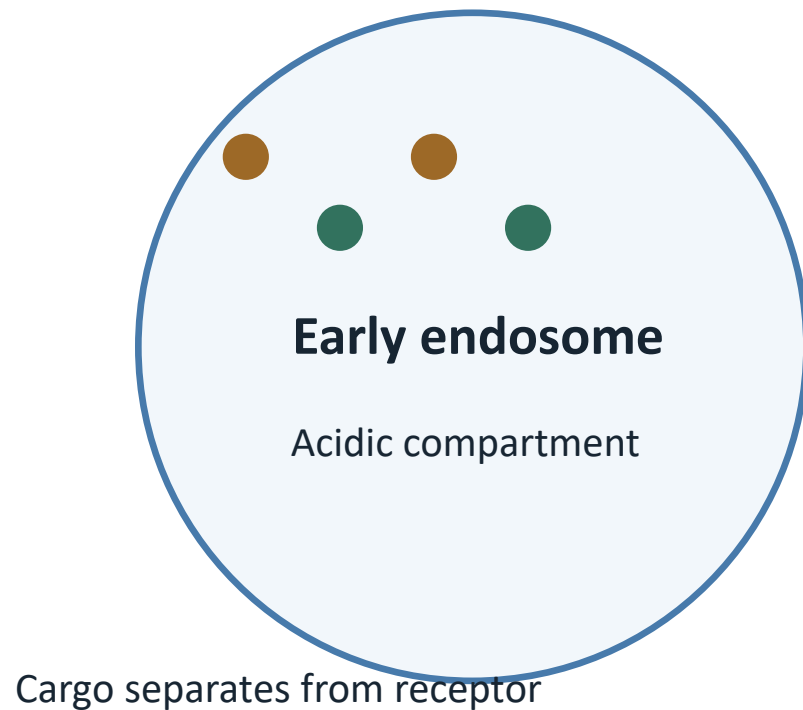
- LDL and transferrin receptors release their transported cargo.
- Cholesterol and iron are then transported into the cytosol.
- The receptor can follow a separate sorting route after ligand release.

Progressive endosomal maturation



- The text describes maturation through a late endosome to eventual lysosomal fusion.

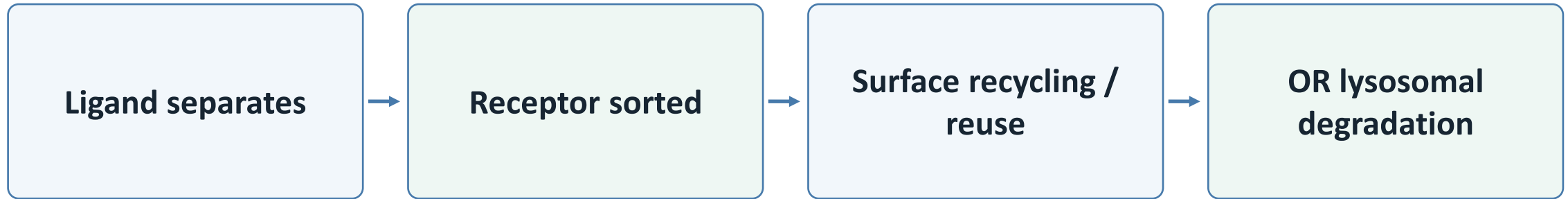
Lysosomes in the endocytic pathway



Terminal destination

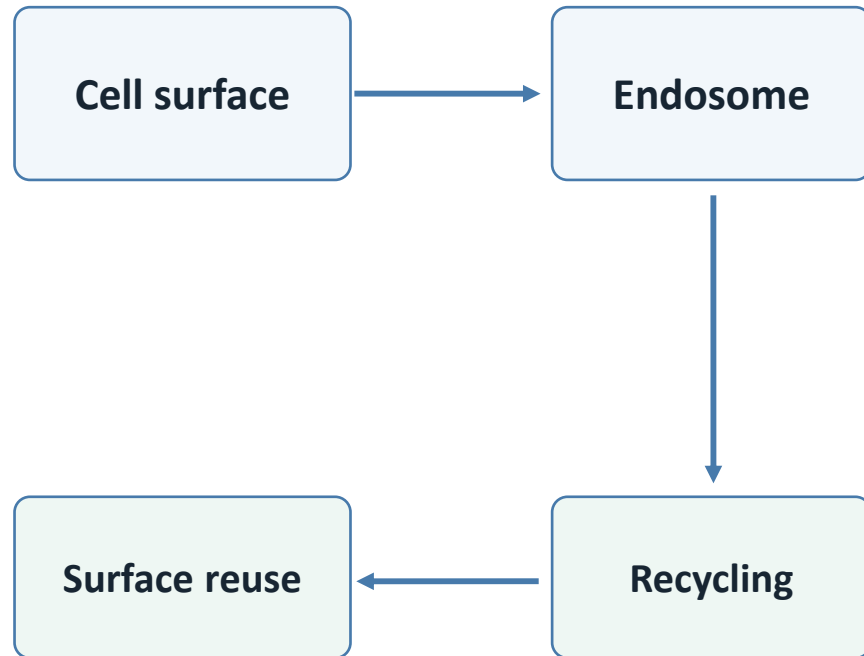
- Late endosomes ultimately fuse with lysosomes.
- Some internalized proteins and receptors are degraded.
- Recycling is a distinct alternative to lysosomal loss.

Receptor fate is a sorting decision



- The two fates have different consequences for cell-surface receptor abundance.

Recycling restores the surface pool



Examples

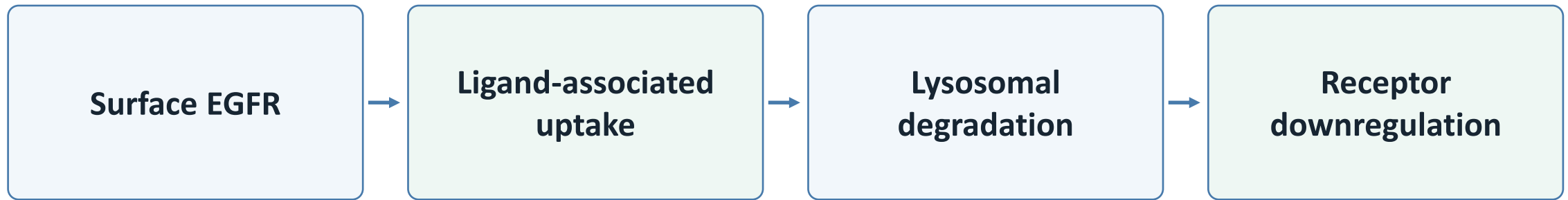
- LDL receptors can be reused.
- Transferrin receptors can be reused.
- Ligand release can precede return to the plasma membrane.

Degradation is a regulatory choice

Not every receptor is returned to the surface.

- Internalized receptors may be directed to lysosomes.
- Receptor degradation reduces the number of available surface receptors.
- The text uses epidermal growth factor receptor (EGFR) as an example.

EGFR internalization limits signaling



- The important consequence is attenuation of receptor-mediated signaling.

Recycling versus downregulation

Return and reuse

- After cargo release, receptor is directed back to plasma membrane.
- Cell preserves a reusable receptor pool.
- Examples in the text: LDL and transferrin receptors.

Removal and degradation

- Endocytic routing can direct receptor toward lysosomal destruction.
- Surface receptor abundance declines.
- EGFR exemplifies signaling control by downregulation.

LDL receptor pathway: Key itinerary

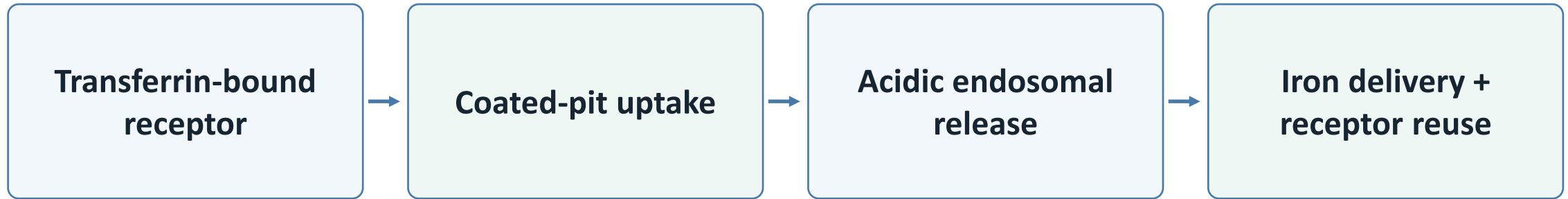


Internalization delivers cholesterol; Defective LDL transport is linked to FH

Follow the cargo

- LDL receptor binds extracellular cargo.
- Clathrin-associated internalization delivers it to endosomes.
- Endosomal release permits cellular cholesterol delivery.

Transferrin receptor: Same overall logic



- The textbook specifically pairs transferrin uptake with iron delivery.

Clinicopathologic bridge: Familial hypercholesterolemia

When LDL receptor-mediated transport is defective:

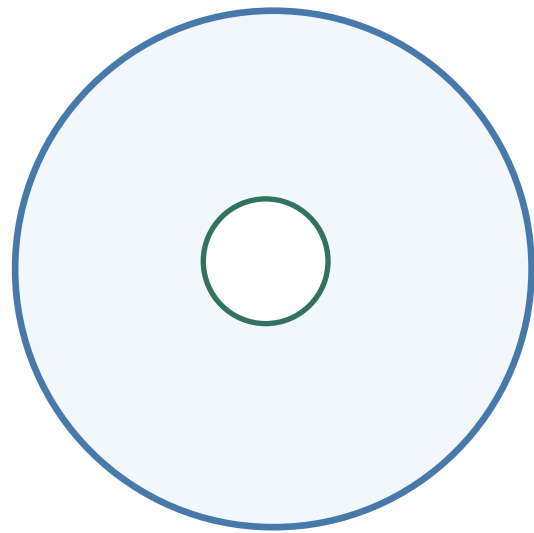
- LDL transport into cells is impaired.
- Familial hypercholesterolemia is identified in tissue analysis as a disease association.
- The source points to Chapter 5 for a fuller description; Detailed genetics are outside this unit.

Fluid-phase pinocytosis

Endocytosis does not carry only receptor-bound cargo.

- As a coated membrane pit closes, it traps extracellular fluid.
- This accompanying fluid uptake is termed fluid-phase pinocytosis.
- Receptor-associated cargo selection and nonspecific fluid capture can occur together.

One vesicle, two types of contents



Vesicle cargo



Transport to next
compartment

Contents

- Selected receptor-bound ligand.
- An aliquot of surrounding extracellular fluid.
- Both can enter the vesicular trafficking pathway.

Pinocytosis and phagocytosis

Pinocytosis

“Cellular drinking”: Fluid/small vesicle uptake.

Includes the fluid captured with coated vesicles.

Phagocytosis

“Cellular eating”: Ingestion of larger material.

Textbook context: Macrophages and neutrophils ingest microbes/debris.

Endocytosis moves substantial volume

10–20%

Of a cell's own volume taken up
from extracellular space per
hour (textbook estimate)

- This is a routine, not exceptional, flux.
- Vesicle trafficking must therefore be sustained.
- Membrane turnover cannot proceed without recycling.

Plasma membrane turns over rapidly

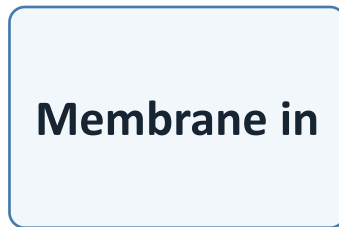
1–2%

Of plasma membrane
internalized each minute
(textbook estimate)

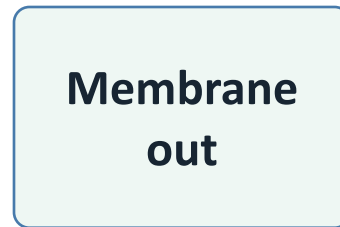
- Unchecked uptake would deplete the cell surface.
- Internalized membrane must be returned.
- Endocytosis and exocytosis are tightly coupled.

Why membrane recycling is essential

Endocytosis



Exocytosis

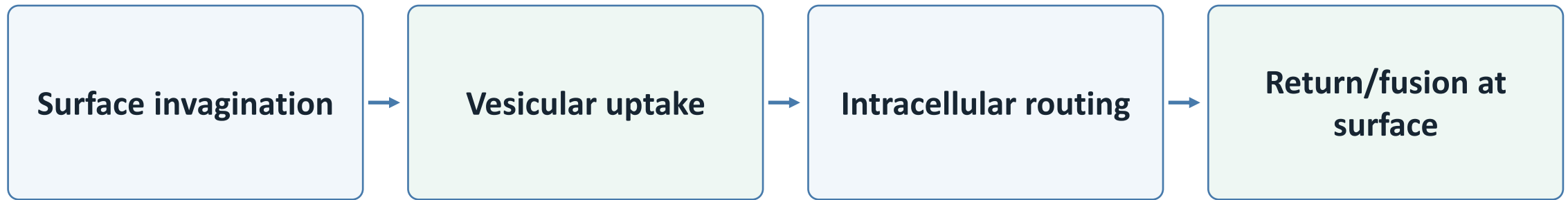


Coupled cycling stabilizes surface area

Conservation

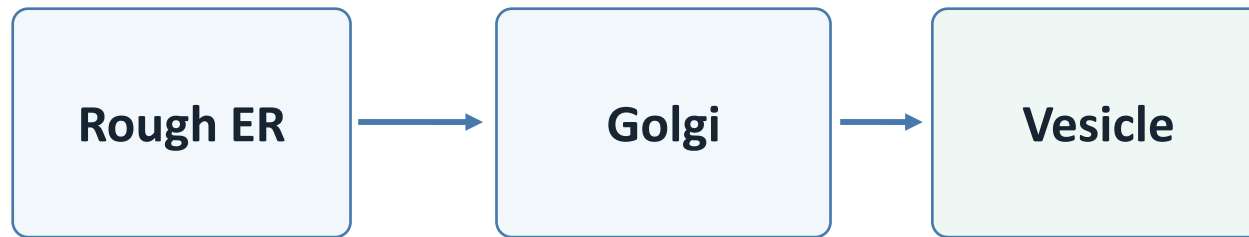
- Endocytosis removes plasma membrane.
- Exocytosis restores membrane to the surface.
- Balance avoids large changes in membrane area.

The membrane conservation cycle



- Multiple rounds of uptake require re-use of membrane after internalization.

Secretory proteins: Preparation for export



Protein synthesis

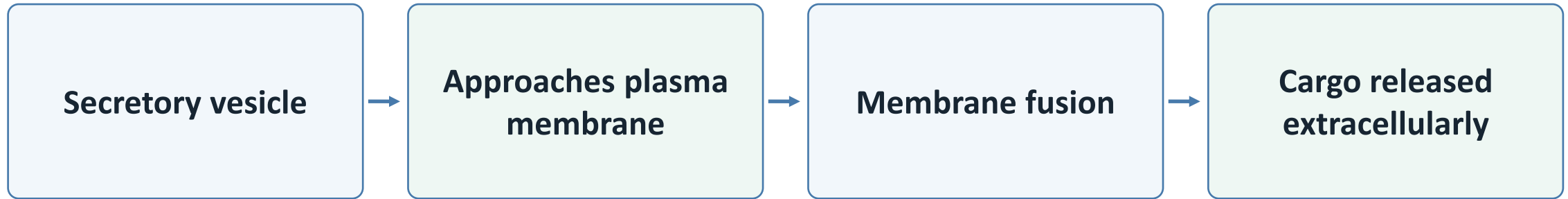
Packaging

Surface fusion

Biosynthetic route

- Secreted proteins originate in rough endoplasmic reticulum (RER).
- Golgi apparatus processes and packages cargo.
- Proteins accumulate in secretory vesicles.

Exocytosis transfers vesicle contents outward



- Vesicle membrane also becomes part of the plasma membrane during fusion.

Two examples of secreted proteins

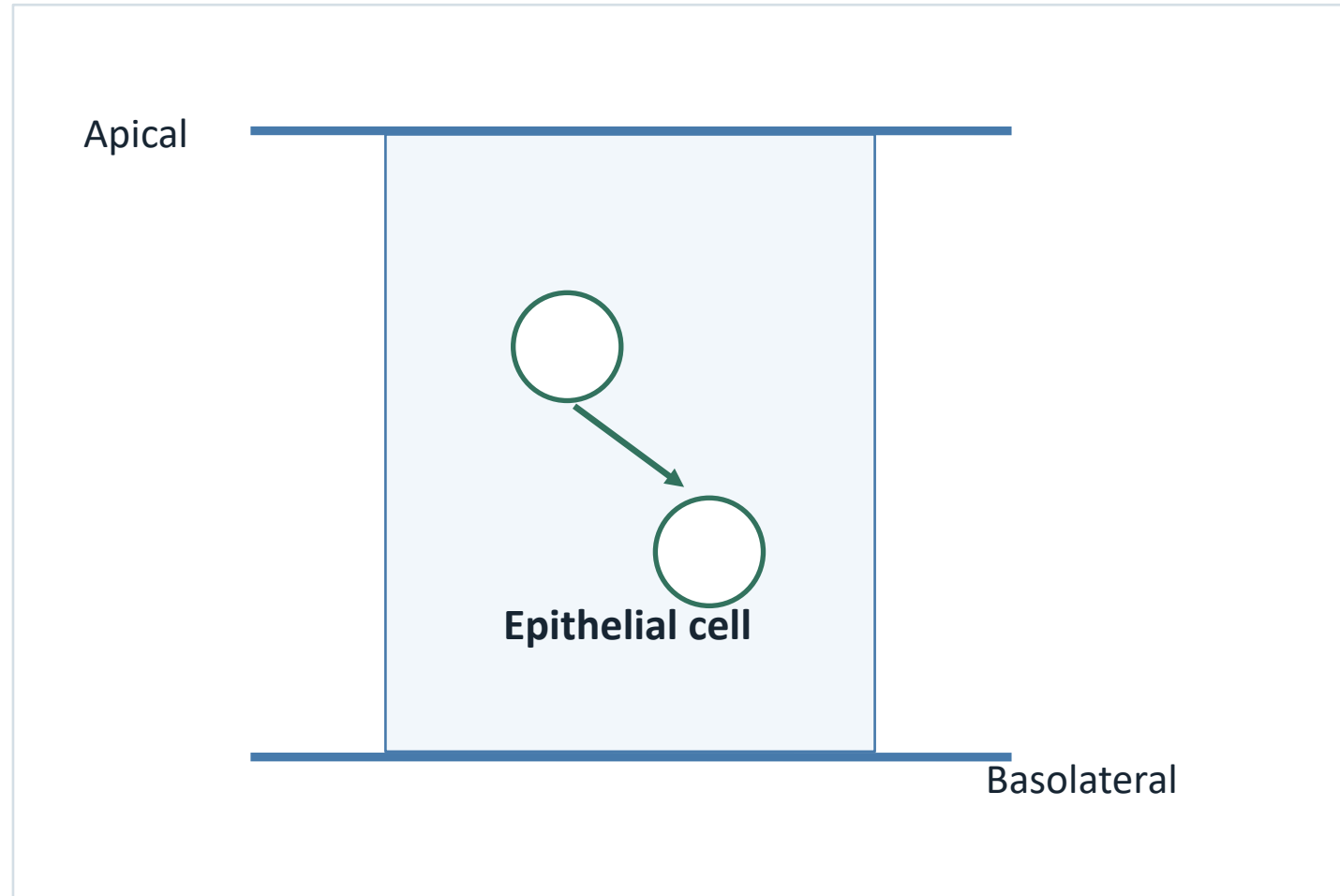
Peptide hormones

- Insulin is an example named in the text.
- Protein is synthesized and packaged before release.
- The vesicle expels its contents after plasma membrane fusion.

Cytokines

- Cytokines are another example named in the text.
- Exocytosis supports export of secreted signaling proteins.
- The cargo exits without crossing the bilayer as an isolated solute.

Transcytosis: Across the cell



Transport direction

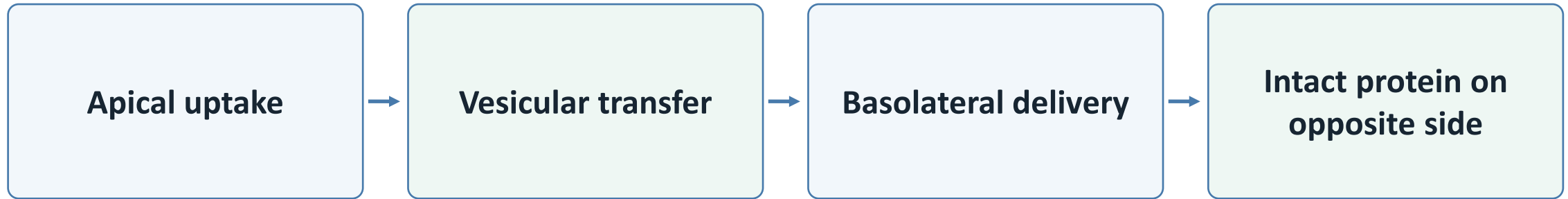
- A vesicle moves between apical and basolateral compartments.
- Transfer can move intact macromolecules across epithelial barriers.
- Transcytosis differs from simple delivery into the cytosol.

Why epithelial polarity matters

An epithelium has distinct membrane domains.

- Apical and basolateral compartments occupy different sides of the barrier.
- Transcytosis links these compartments by intracellular vesicular movement.
- The payload can remain intact during barrier transfer.

Intact proteins cross an epithelial barrier



- The textbook provides maternal milk antibodies as an example of intact-protein transfer.

Transcytosis can also support bulk transport

The text identifies two functional roles.

- Movement of intact proteins across an epithelial interface.
- Rapid movement of large solute volumes.
- The process is distinguished by passage across the cell rather than retention.

Compare the main transport pathways

Caveolae	Clathrin-mediated uptake	Exocytosis	Transcytosis
Caveolin-associated	Clathrin-coated pits	Secretory vesicle fusion	Apical ↔ basolateral
Folate as an example	LDL/transferrin examples	Insulin/cytokines	Maternal antibody example

Clinical application: LDL uptake

Apply the mechanism

A cell has defective LDL receptor-mediated transport. Which trafficking step is most directly compromised?

- Specify the surface recognition and internalization stages.
- Explain the likely consequence for LDL-associated cargo delivery.

Explanation: Defective LDL transport

Reasoning and mechanism

The affected step is receptor-mediated internalization of LDL-associated cargo.

- The textbook connects defects in this process with familial hypercholesterolemia.
- The present unit does not specify individual gene variants or lipid concentrations.

Mechanism check: EGFR

Apply the mechanism

Why can routing an internalized growth factor receptor to the lysosome attenuate cellular signaling?

- Distinguish the fate of the ligand from the fate of its receptor.
- Predict the change in available receptor abundance at the plasma membrane.

Explanation: Receptor downregulation

Reasoning and mechanism

Lysosomal degradation reduces the receptor population available for subsequent signaling.

- This differs from recycling, which returns receptors to the surface.
- EGFR is the source's example of degradation-mediated downregulation.

Mechanism check: Membrane mass

Apply the mechanism

What would happen to plasma membrane area if endocytosis continued without exocytotic return?

- Use the source's rapid uptake rates to justify the direction of change.
- Identify the balancing process that prevents the problem.

Explanation: Membrane homeostasis

Reasoning and mechanism

The plasma membrane would be rapidly depleted unless internalized membrane is returned.

- The source estimates 1–2% membrane internalization each minute.
- Coupled exocytosis and recycling stabilize the surface area.

Endocytic pathways: Five decisions

Ask these questions whenever tracing vesicle traffic.

- What cargo is selected, and by which surface receptor or membrane domain?
- How does budding occur, and what mediates vesicle scission?
- Where does the vesicle deliver its contents?
- Does the receptor recycle or undergo lysosomal downregulation?

Cytoskeleton: Linked Robbins unit

The index groups cytoskeleton with this topic.

- The cytoskeleton governs shape, polarity, organelle organization, and cell migration.
- Its major structural systems are actin microfilaments, intermediate filaments, and microtubules.
- The more dynamic systems reorganize as cellular needs change.

Functions of an intracellular scaffold

Not a static framework.

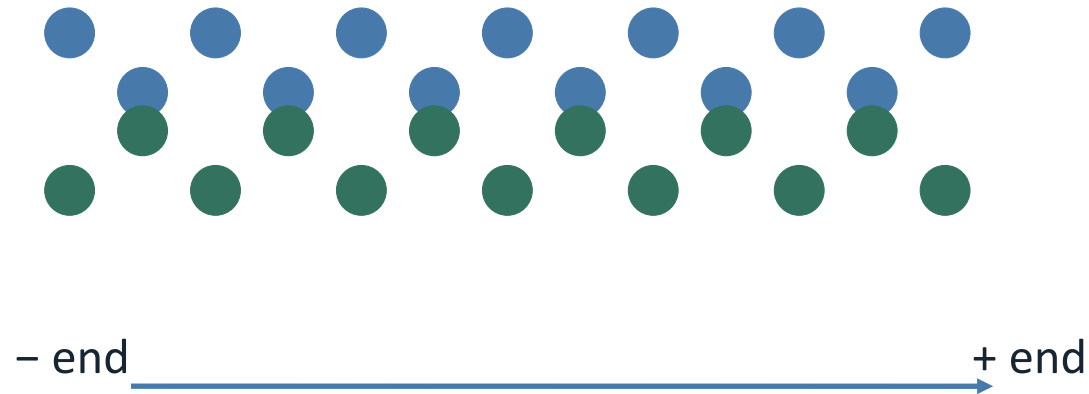
- Establishes cellular shape and mechanical organization.
- Contributes to polarity and intracellular organelle positioning.
- Supports migration and motor-dependent intracellular movements.
- Rapid assembly and disassembly are important to many functions.

Three classes of cytoskeletal polymers

Actin microfilaments	Intermediate filaments	Microtubules
5–9 nm diameter	10 nm diameter	~25 nm diameter
Actin polymers	Protein-family dependent	α/β -tubulin dimers
Dynamic shape/movement	Tensile strength	Tracks and cilia/mitosis

Actin: G-actin to F-actin

F-actin: Intertwined polarized filaments



Molecular architecture

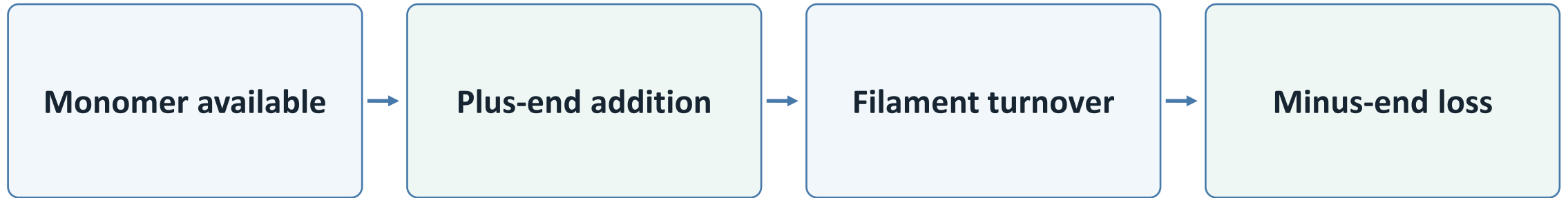
- Globular G-actin monomers polymerize noncovalently.
- F-actin strands intertwine as polarized double helices.
- Actin is a major cytosolic protein.

Polarized actin filaments

Polymer assembly is directional.

- Actin filaments possess plus and minus ends.
- New subunits are typically added at the plus end.
- Removal is commonly associated with the minus end.
- The persistent filament can thus exhibit turnover despite structural continuity.

Actin treadmilling



- Actin nucleation and regulatory proteins control assembly, bundling, and branching.

Actin and myosin

Contractile force requires a motor protein.

- Myosin uses ATP hydrolysis to move actin filaments relative to one another.
- Skeletal and cardiac muscle arrange actin-myosin structures in visible bands.
- Myosin-dependent activity also supports cellular transport and movement.

Actin-related functions

In muscle

Highly organized contractile arrays

Myosin generates relative filament sliding

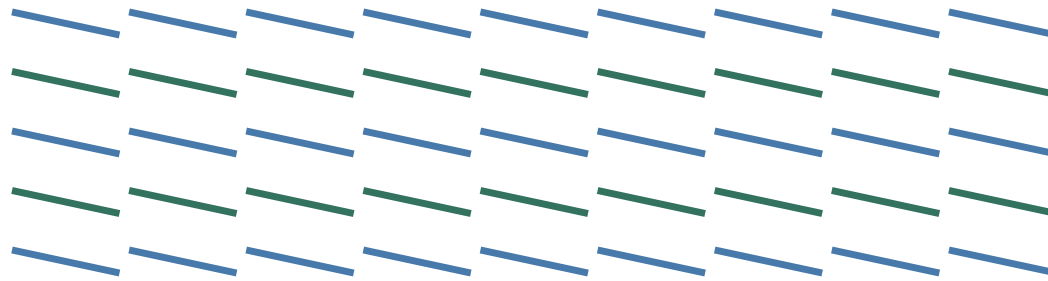
Elsewhere in cells

Vesicular transport and movement

Epithelial barrier regulation and migration

Intermediate filaments: Mechanical resilience

Intermediate filament: Rope-like bundle



Tensile support

Junctional anchorage

Core property

- Rope-like polymers of diverse proteins.
- About 10 nm in diameter.
- Generally less dynamically reorganized than actin and microtubules.

Intermediate filaments support epithelia

Structural integrity depends on anchorage.

- Intermediate filaments connect to desmosomes and hemidesmosomes.
- This network permits tissues to tolerate mechanical stress.
- Cytoskeletal organization is therefore integrated with cell-cell and matrix adhesion.

Examples of intermediate-filament proteins

Epithelial / mesenchymal

Cytokeratins: Epithelial lineages

Vimentin: Mesenchymal cells

Nuclear lamins: Nuclear lamina

Muscle / neural / glial

Desmin: Muscle scaffold

Neurofilaments: Neurons

GFAP: Glial cells

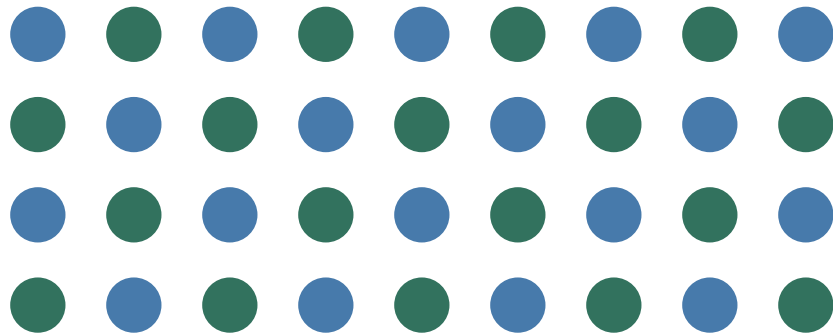
Pathology relevance: Lineage identification

Tissue-specific expression patterns are diagnostically useful.

- Individual intermediate filaments are expressed in characteristic cell populations.
- These patterns can inform assignment of origin in poorly differentiated tumors.
- The text lists cytokeratin, vimentin, desmin, neurofilament, and GFAP lineages as examples.

Microtubules: Tubulin-built cylinders

Hollow tube assembled from α/β -tubulin dimers



Minus end (centrosome)

Plus end (dynamic)

Construction

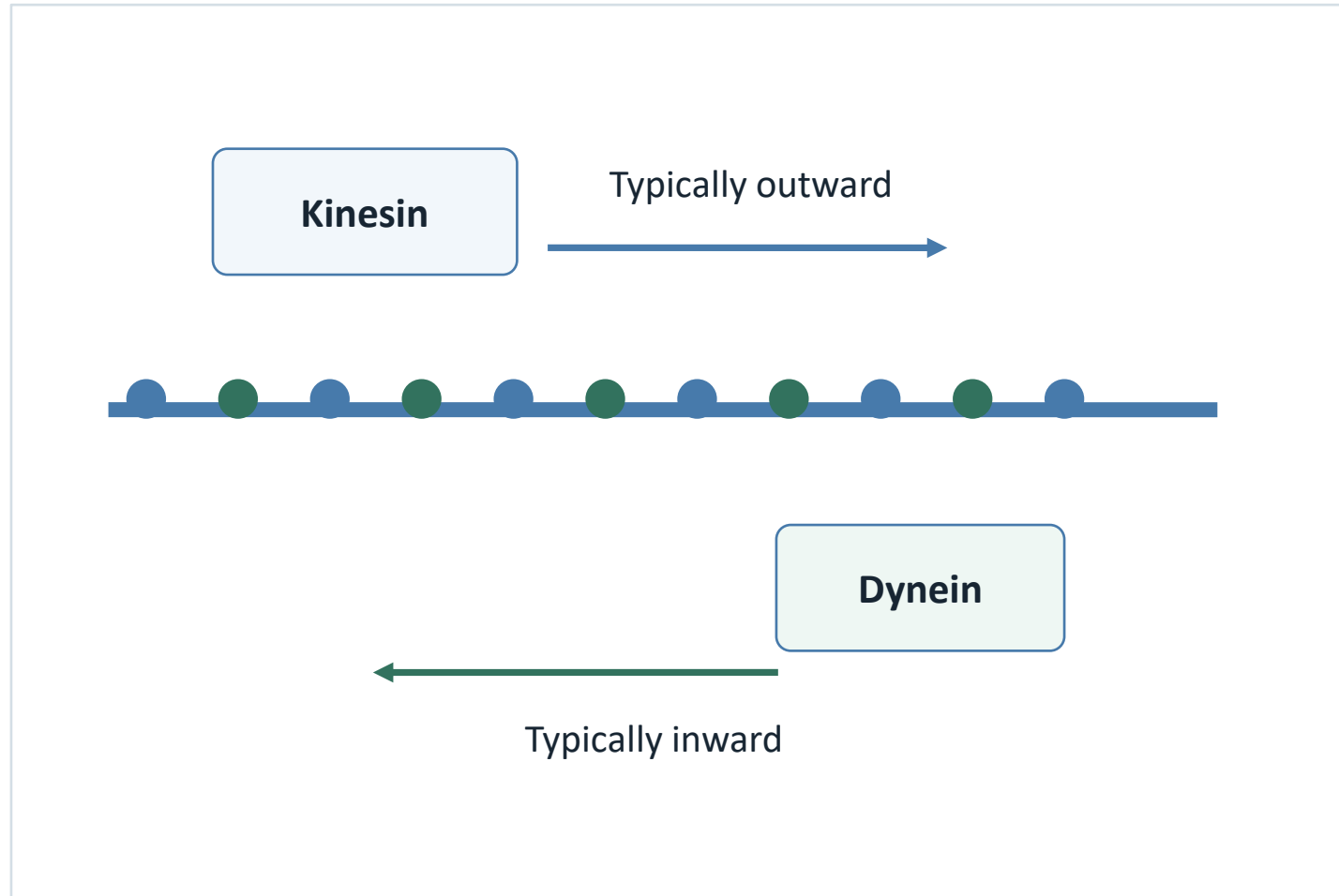
- α - and β -tubulin dimers assemble noncovalently.
- The resulting structure is a hollow tube roughly 25 nm wide.
- Microtubules are polarized and dynamically remodel.

Microtubule polarity and dynamics

The centrosome organizes many microtubules.

- The minus end is typically anchored at a microtubule organizing center.
- The plus end can elongate or retract through tubulin dimer exchange.
- Dynamic behavior permits rapid reorganization of intracellular architecture.

Motor proteins on microtubules



Transport systems

- ATP-dependent motors travel along microtubules.
- Kinesin generally mediates anterograde transport.
- Dynein generally mediates retrograde transport; Exceptions exist.

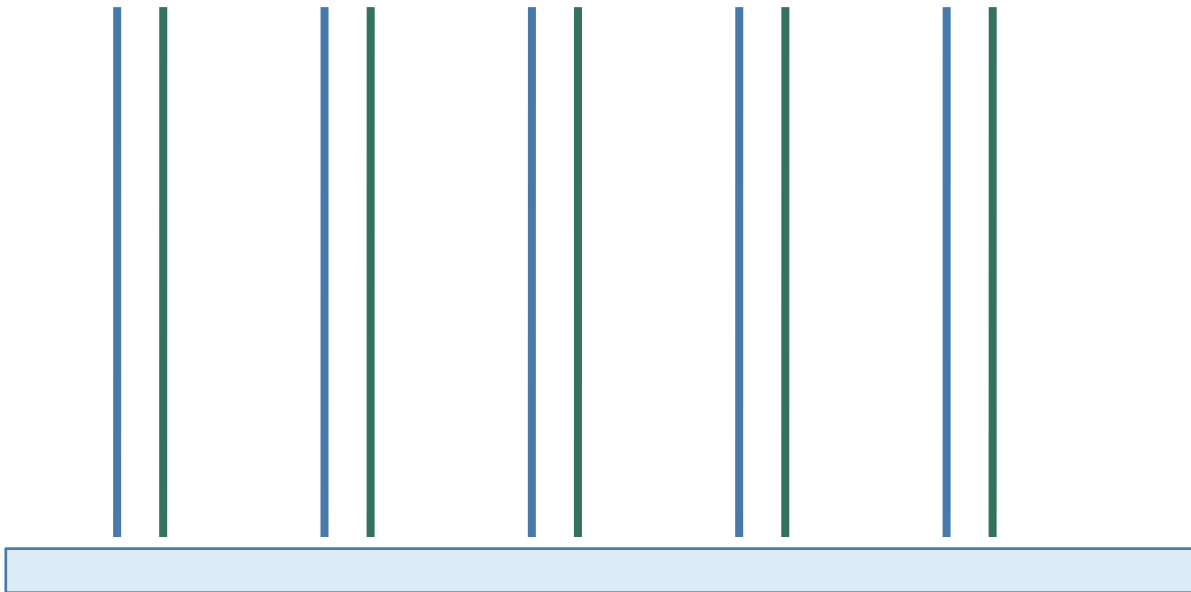
Major functions of microtubules

A dynamic structural scaffold with multiple outputs.

- Serves as tracks for intracellular vesicles and organelles.
- Enables sister-chromatid segregation during mitosis.
- Forms the core of primary cilia.
- Also supports motile cilia and sperm flagella.

Microtubule-based cilia

Microtubule-based surface projections



Primary cilium: Sensory / regulatory

Core idea

- Cilia and flagella depend on microtubular structures.
- Primary cilia are generally nonmotile and regulatory.
- Motile cilia and flagella support movement.

Primary cilia and disease association

The textbook links primary cilia to cellular regulation.

- Primary cilia contribute to proliferation and differentiation signaling.
- Mutations in primary-cilia complex proteins are associated with some polycystic kidney disease forms.
- The mechanism is presented here as a chapter-level connection, not a full renal disease lecture.

Examples of motile microtubular structures

Location helps connect structure with function.

- Bronchial epithelial cells possess motile cilia.
- The sperm flagellum is another microtubule-based motile structure.
- These functions are distinct from the typically nonmotile primary cilium.

Cytoskeletal systems: Distinguishing features

Actin	Intermediate filaments	Microtubules
5–9 nm	10 nm	25 nm
Polar filament network	Rope-like strength	Tubulin-based hollow tube
Myosin interaction	Lineage-specific proteins	Kinesin/dynein tracks
Contraction and movement	Mechanical integrity	Mitosis, cilia, trafficking

Cytoskeleton application

Apply the mechanism

A poorly differentiated tumor is positive for a characteristic intermediate-filament marker. What can that finding contribute?

- Explain what the marker can indicate about cell lineage.
- Identify why a single structural protein is not automatically a complete diagnosis.

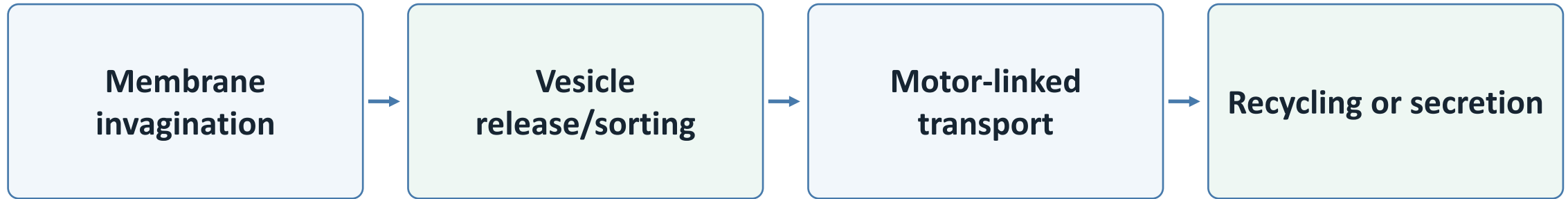
Explanation: Intermediate-filament markers

Reasoning and mechanism

The result can support assignment of a cellular or tissue lineage.

- Intermediate-filament expression follows characteristic tissue patterns.
- This supports diagnosis but does not replace overall morphologic and clinicopathologic assessment.

A connected cellular transport system



- Microtubule motors and actomyosin participate in intracellular transport.
- The membrane and cytoskeleton are integrated, although every step has its own molecular machinery.

Take-home concepts

Six statements to retain.

- Caveolin-rich caveolae and clathrin-coated pits are distinct uptake architectures.
- Dynamin is needed for vesicle release in both routes described.
- Acidic endosomes permit cargo release and receptor sorting.
- Recycling, degradation, and exocytosis determine surface receptor and membrane balance.

Take-home concepts (continued)

Cross-barrier transport and mechanical infrastructure.

- Transcytosis transfers vesicular contents across epithelial compartments.
- Actin, intermediate filaments, and microtubules have distinct dimensions and functions.
- Intermediate-filament patterns can inform tumor cell origin.
- Microtubules support transport, mitosis, and ciliary structures.

Primary source and scope

Primary reference

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 1, “The Cell as a Unit of Health and Disease,” pp. 10–11.

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