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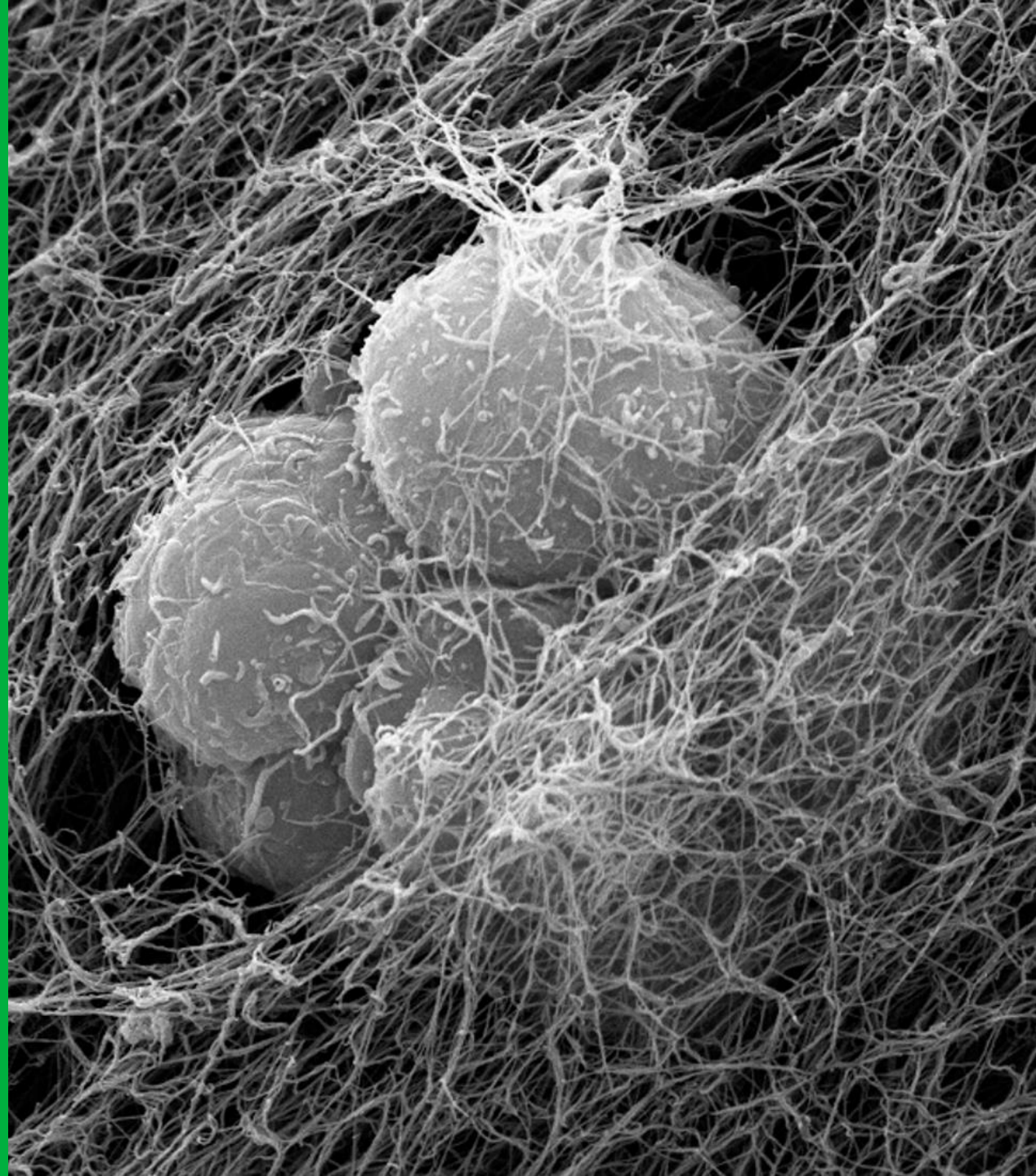
Extracellular matrix and cell-cell interactions

RNDr. Jan Škoda, Ph.D.
Department of Experimental Biology



Outline

- Supportive extracellular structures
- Cell wall in prokaryotes
- Cell wall in plants and fungi
- Extracellular matrix (ECM) in animals
- Cell-ECM interactions
- Cell-cell interactions

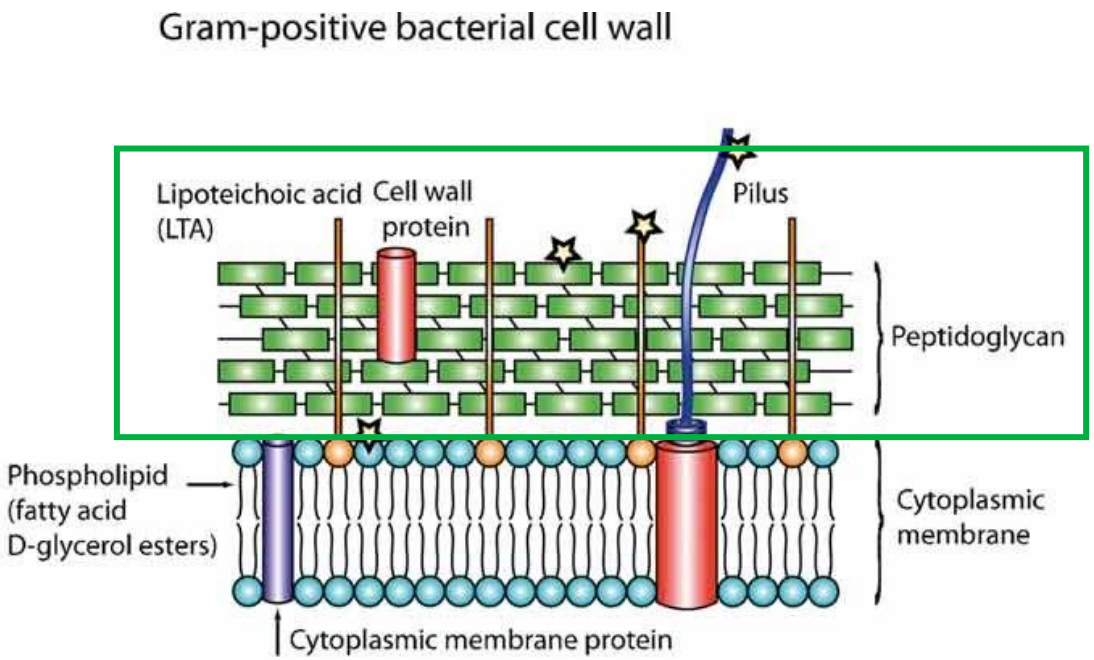
Supportive extracellular structures

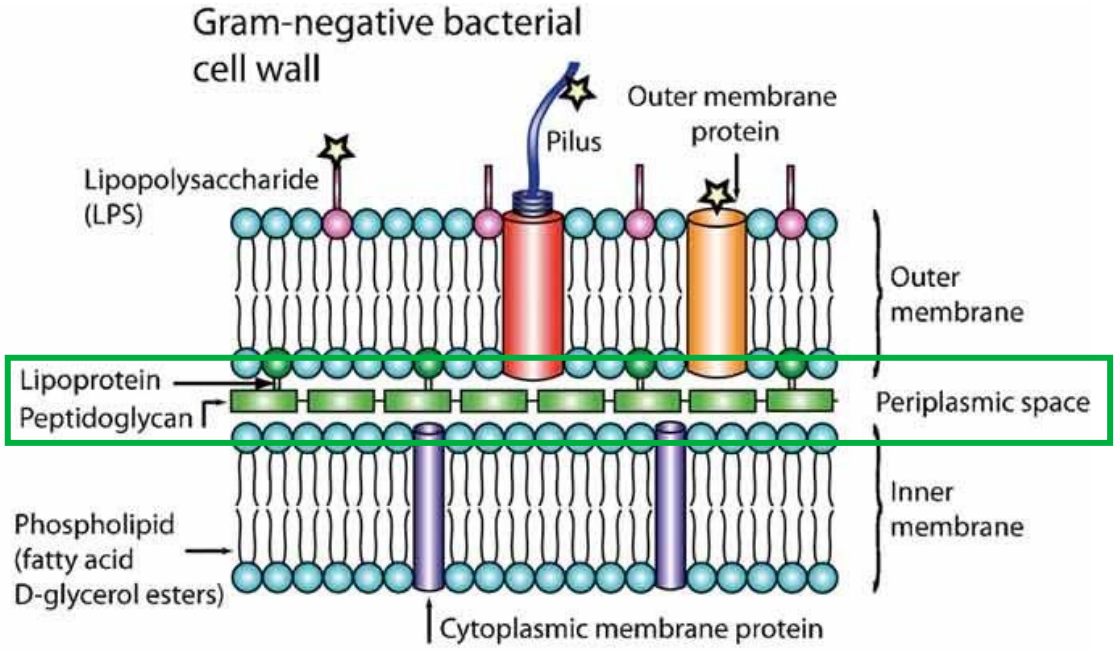
- **Cell wall** (Bacteria, Archea, plants, fungi)
- **Glycocalyx** (animals)

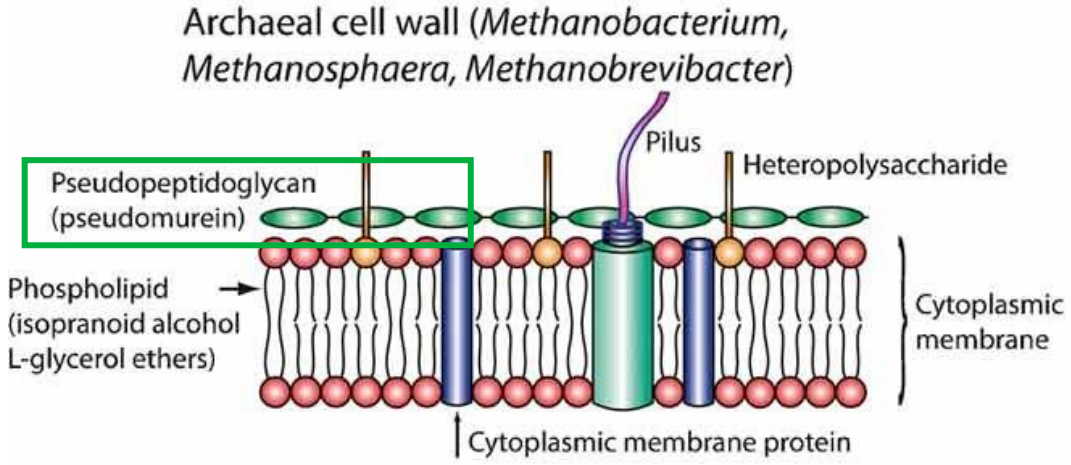
Multicellular eukaryotic organisms

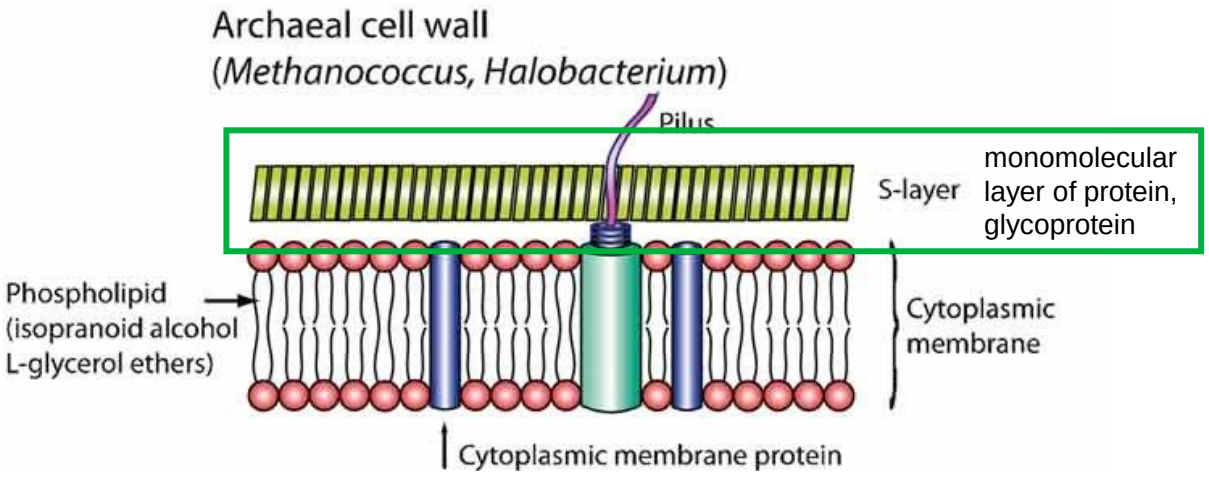
- Interactions among cells:
  tissues = **cells + extracellular matrix (ECM)**
- **Interconnection of cells – direct contact or via ECM**
  - Cell growth, migration, proliferation, differentiation

Cell wall in prokaryotes


Gram-positive bacterial cell wall
Lipoteichoic acid (LTA)
Cell wall protein
Pilus
Peptidoglycan
Phospholipid (fatty acid D-glycerol esters)
Cytoplasmic membrane
Cytoplasmic membrane protein


Gram-negative bacterial cell wall
Outer membrane protein
Pilus
Lipopolysaccharide (LPS)
Outer membrane
Lipoprotein
Peptidoglycan
Periplasmic space
Phospholipid (fatty acid D-glycerol esters)
Inner membrane
Cytoplasmic membrane protein

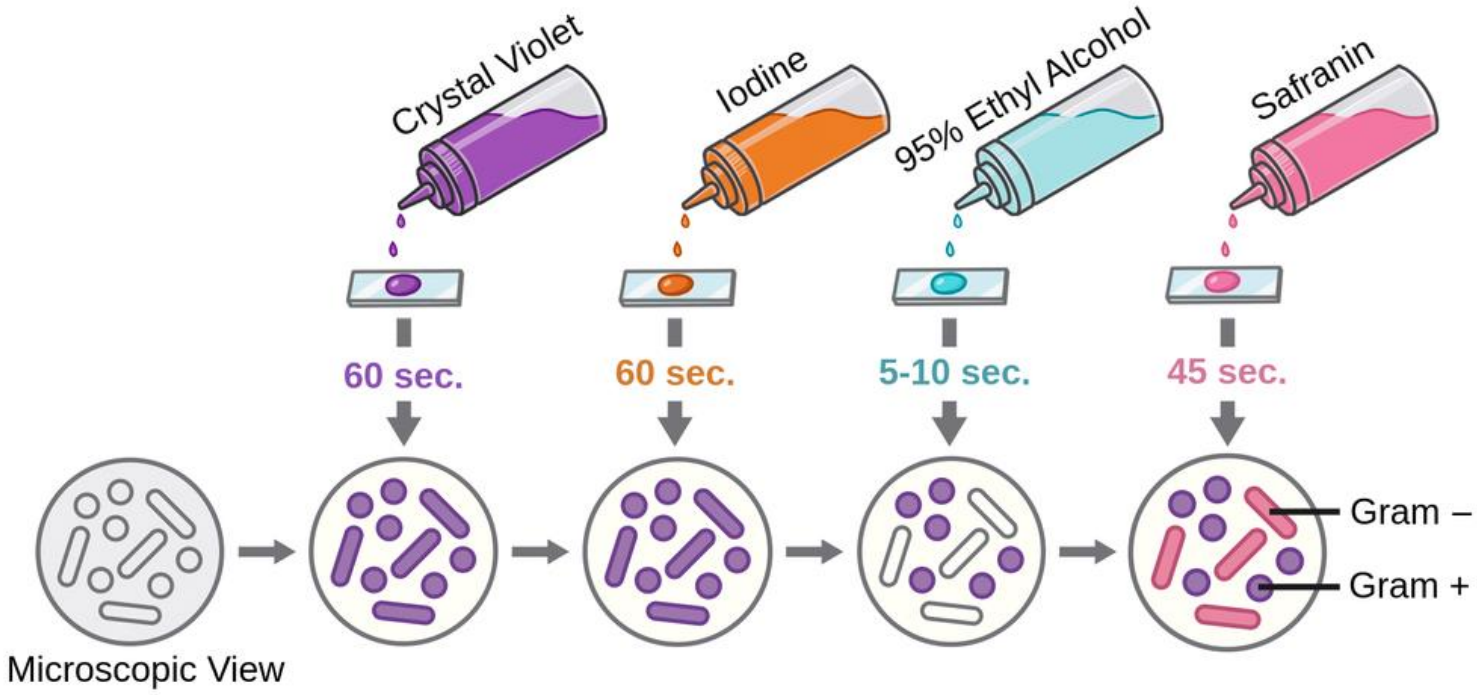

Archaeal cell wall (Methanobacterium, Methanosphaera, Methanobrevibacter)
Pilus
Heteropolysaccharide
Pseudopeptidoglycan (pseudomurein)
Phospholipid (isopranoid alcohol L-glycerol ethers)
Cytoplasmic membrane
Cytoplasmic membrane protein


Archaeal cell wall (Methanococcus, Halobacterium)
Pilus
S-layer
monomolecular layer of protein, glycoprotein
Phospholipid (isopranoid alcohol L-glycerol ethers)
Cytoplasmic membrane
Cytoplasmic membrane protein

Gram staining

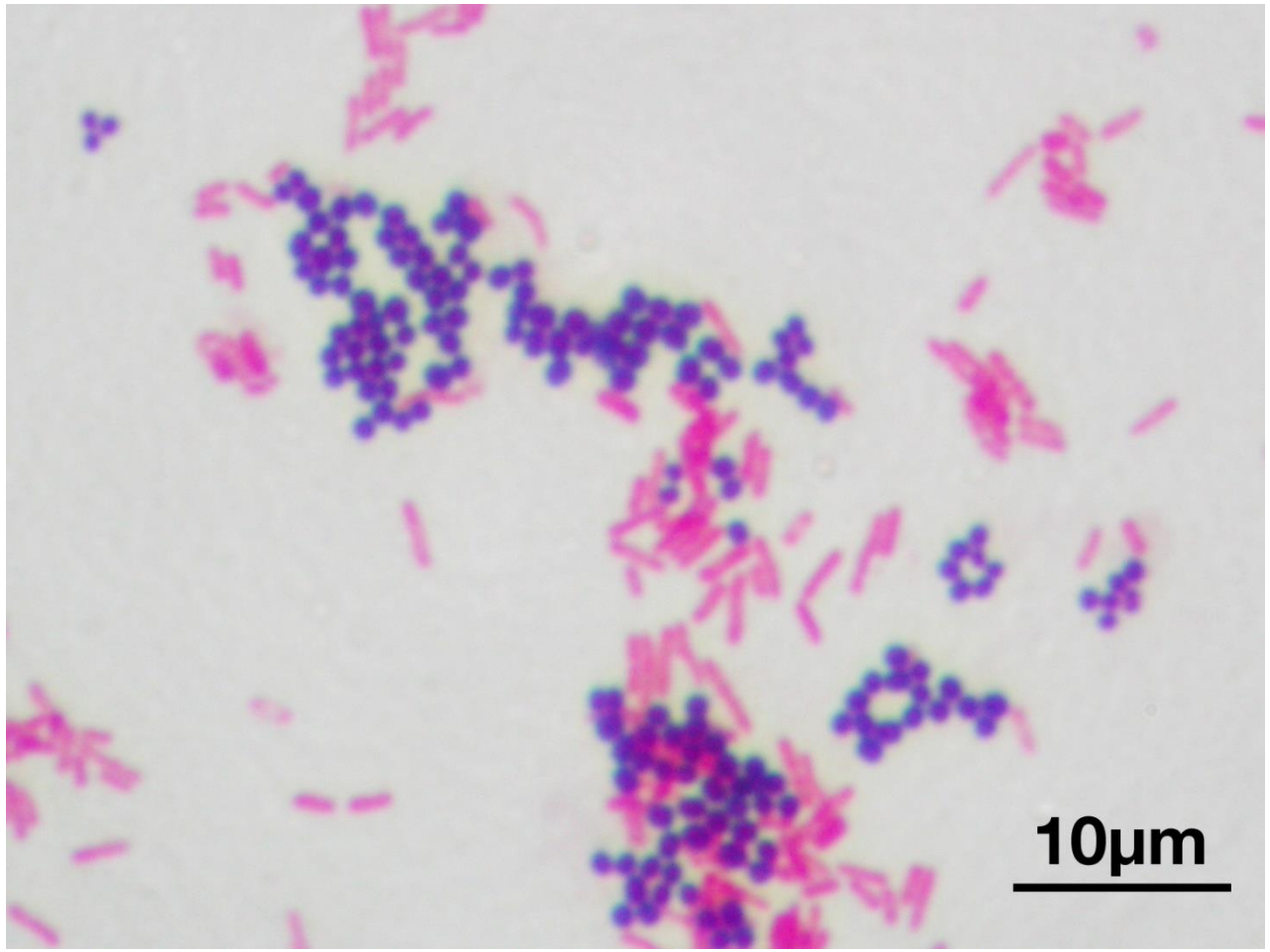
Hans Christian Gram

- **G+: thick peptidoglycan walls retain crystal violet**



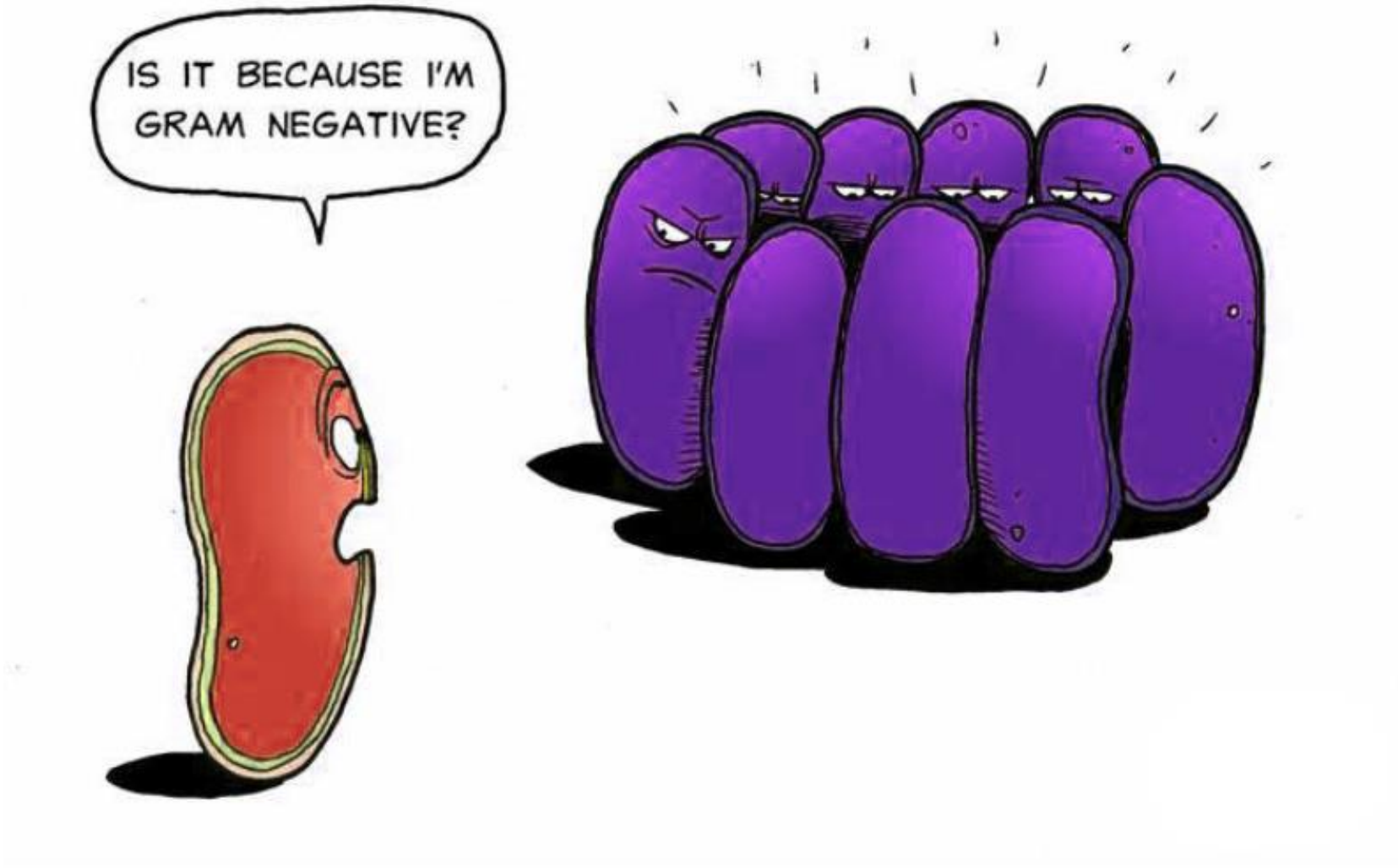
- Iodine (potassium iodine) forms complexes with crystal violet
- Ethanol (acetone) dehydrates peptidoglycan layer
- Crystal violet trapped and insoluble in water
- Safranin counterstain all bacteria
- G+ purple; G- pink/red

Gram staining result



- Purple:
  G+ *Staphylococcus aureus*

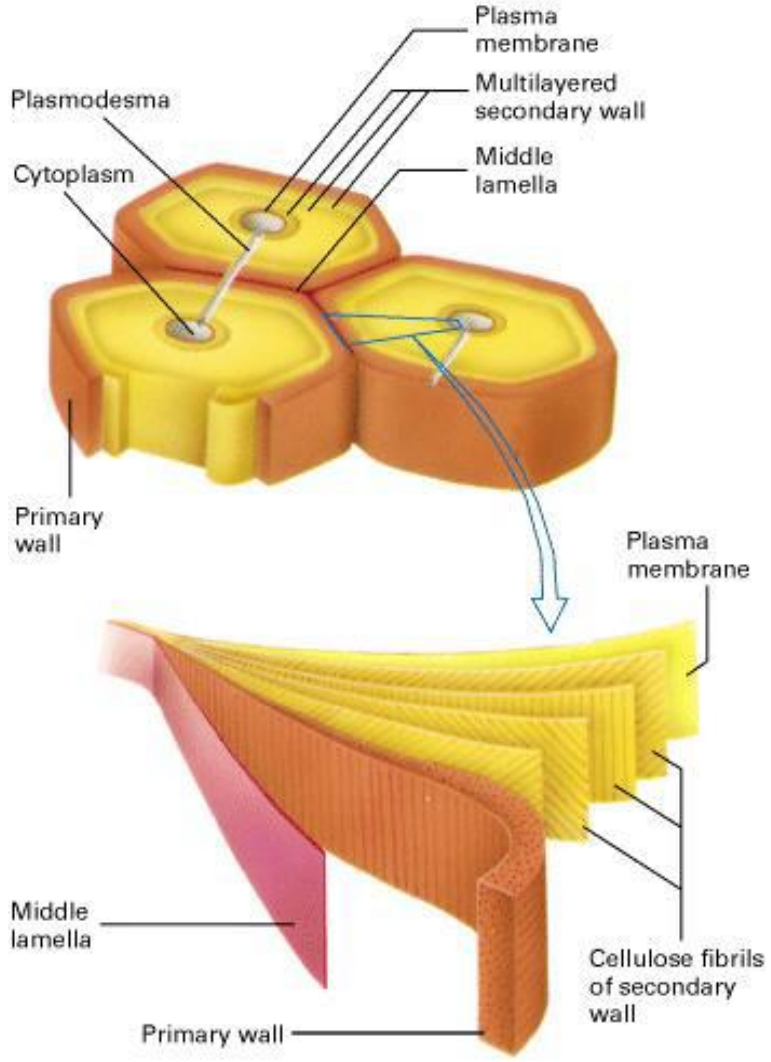
- Pink:
  G- *Escherichia coli*

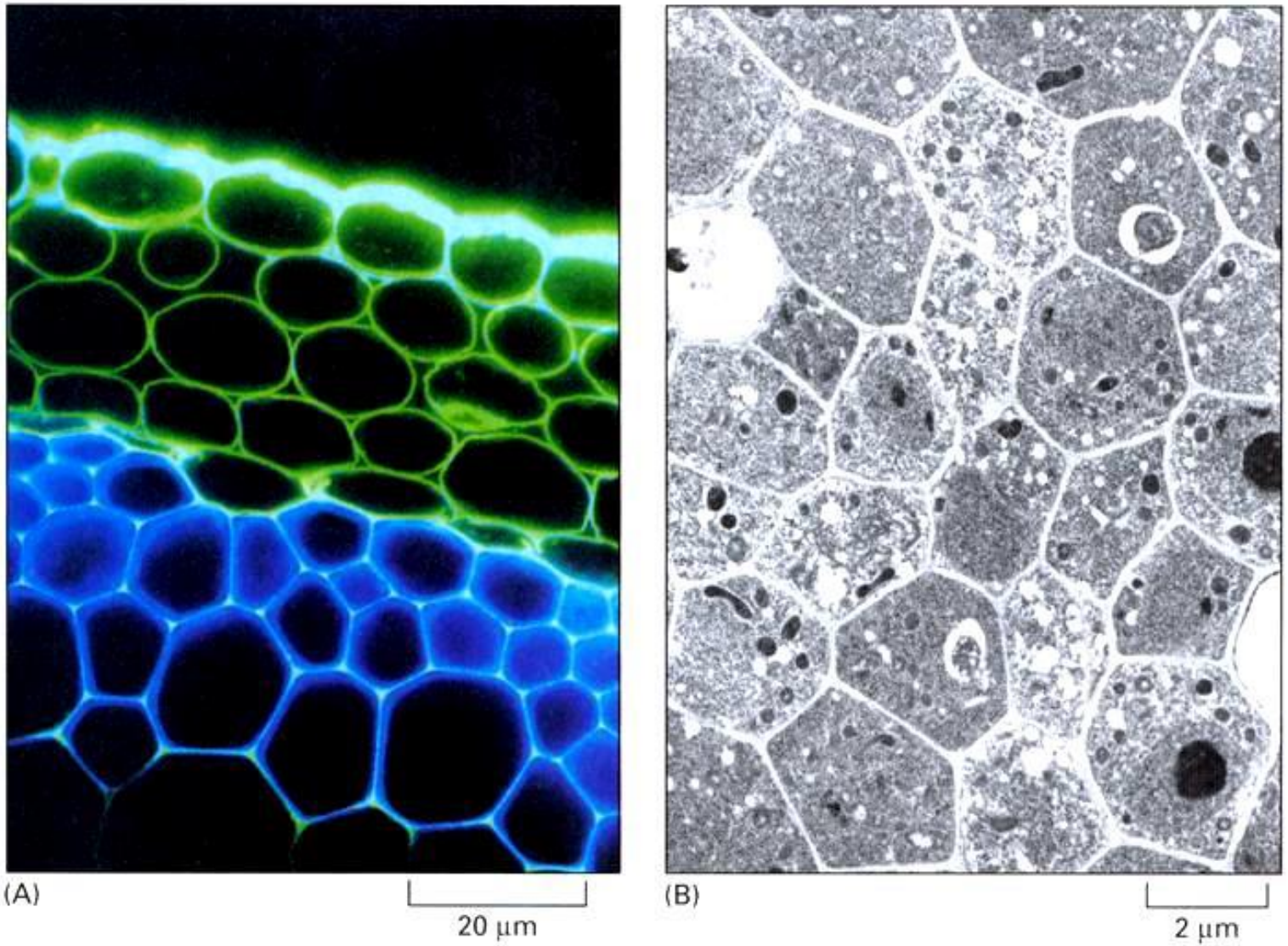

IS IT BECAUSE I'M GRAM NEGATIVE?

Cell wall in plants and fungi

Cell wall in plants

- **Primary cell wall**
  - Thin, flexible, extensible
  - **Cellulose, hemicelluloses, pectin**
- **Secondary cell wall**
  - Additional layers underneath the primary cell wall (always produced by the cell itself)
  - Thick layer, strengthens and/or waterproofs
  - Additional components: **lignin (xylem), suberin (cork)**
- **Middle lamella**
  - Between cell walls of neighboring cells
  - Calcium and magnesium pectates



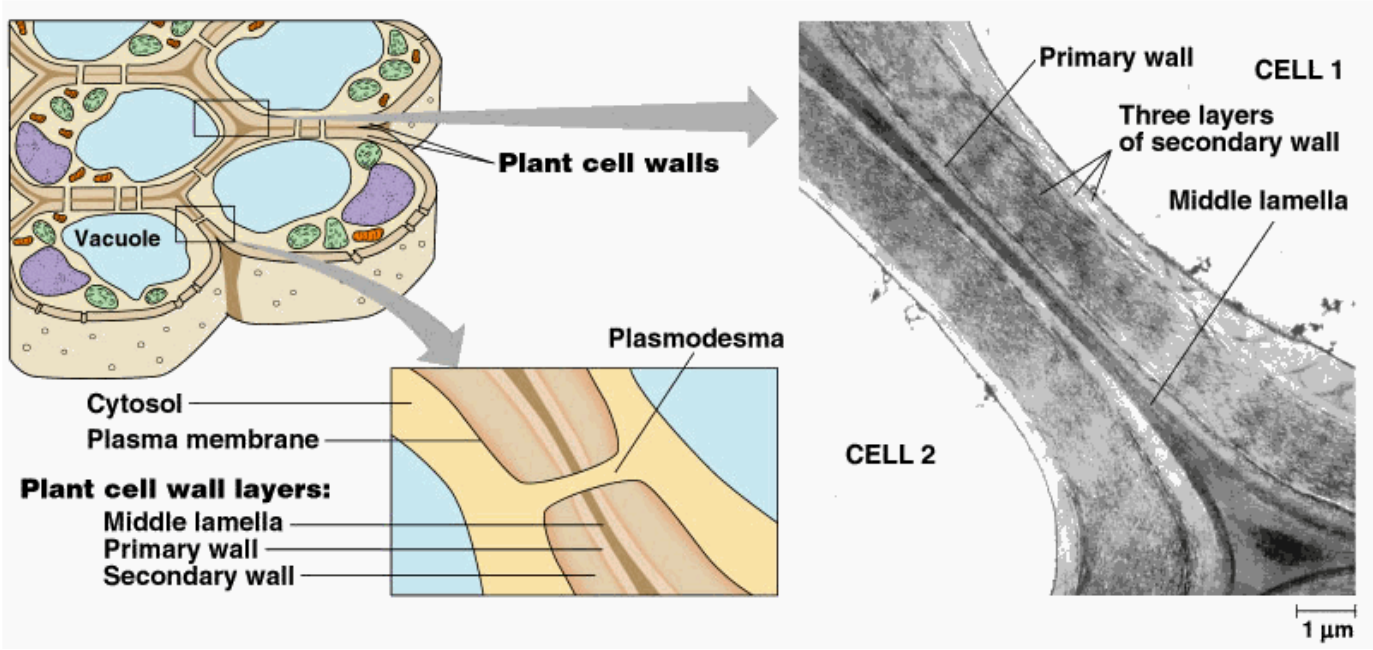


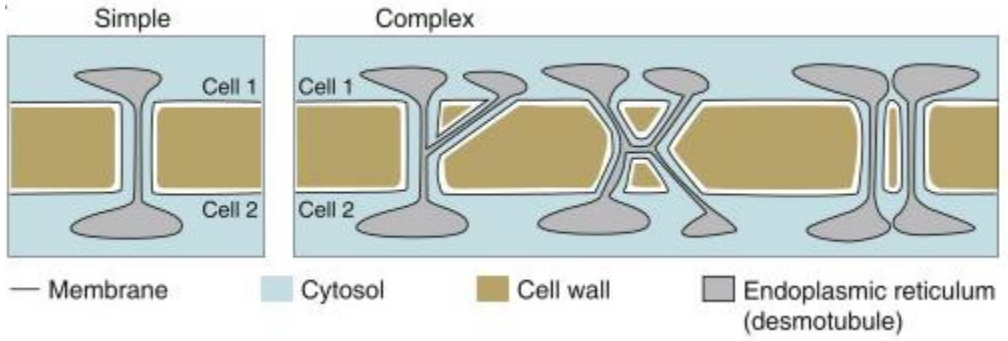
– *Arabidopsis thaliana* stem cross section

Cellulose, pectin

Plasmodesmata

- **Plasmodesma**
  - A channel interconnecting cytosol of two cells; **cell-cell communication**
- **Primary**
  - Forms during cell division, around ER trapped between the dividing cells = **desmotubule**
- **Secondary**
  - Between non-dividing cells, unknown mechanism





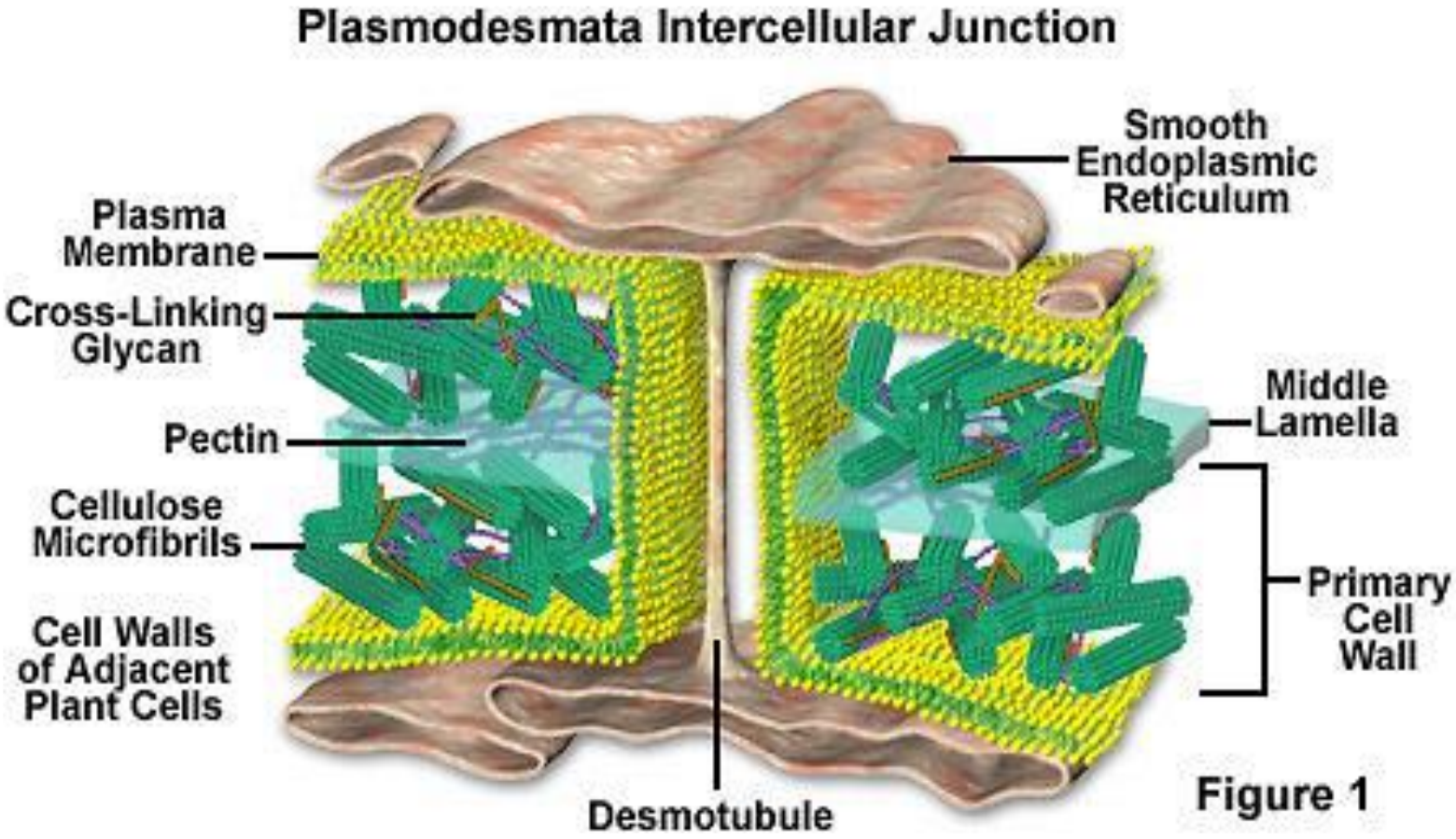
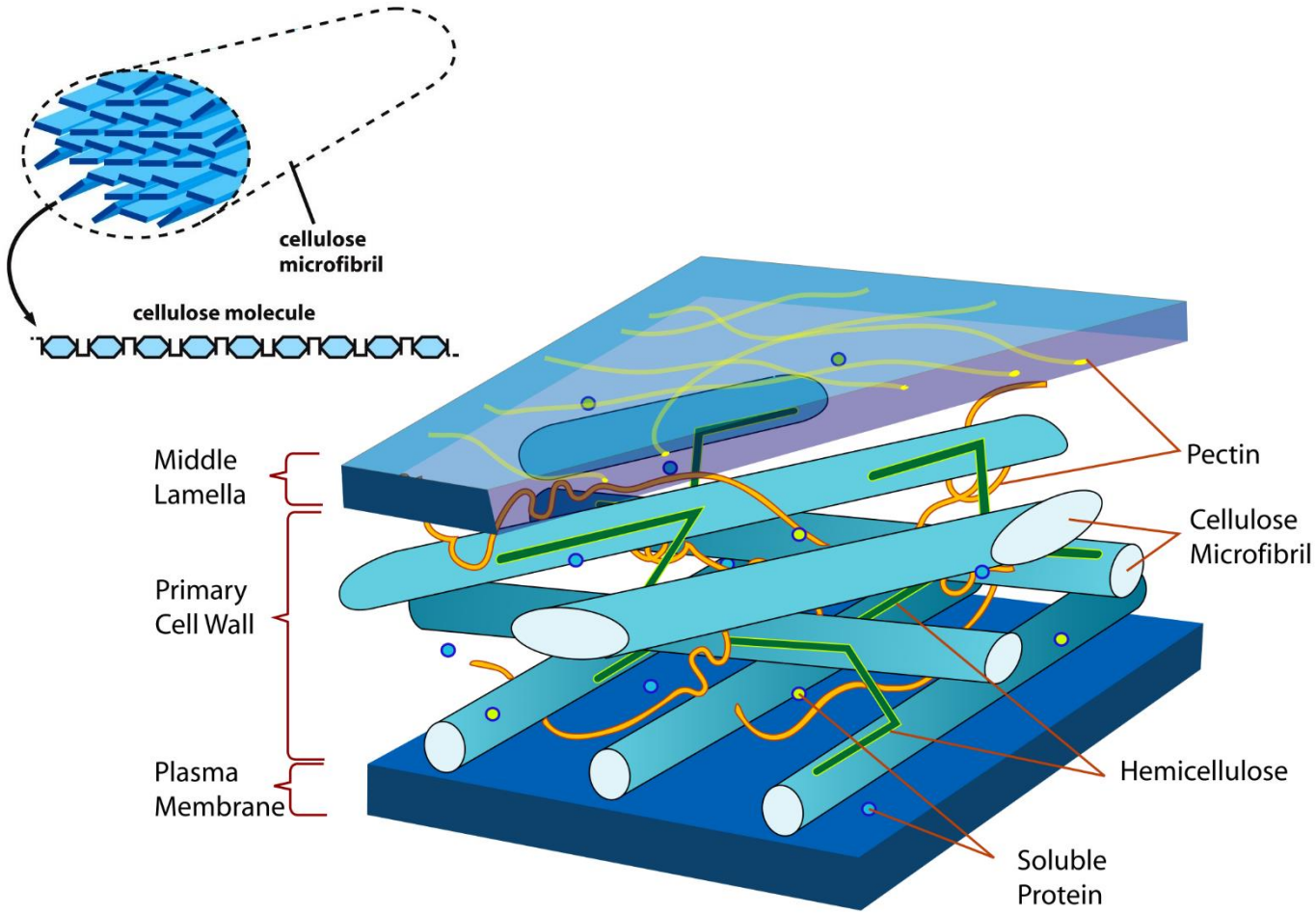

Plasmodesmata Intercellular Junction
Smooth Endoplasmic Reticulum
Plasma Membrane
Cross-Linking Glycan
Pectin
Cellulose Microfibrils
Cell Walls of Adjacent Plant Cells
Middle Lamella
Primary Cell Wall
Desmotubule

Figure 1

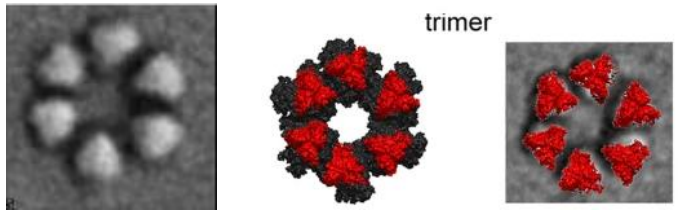
Cell wall composition and synthesis

- **Cellulose microfibrils cross-linked with other polysaccharides, hemicellulose and pectin**
- Specific components: lignin (xylem ~ wood), cutin (epidermis), suberin (cork), silica crystals (in grasses)

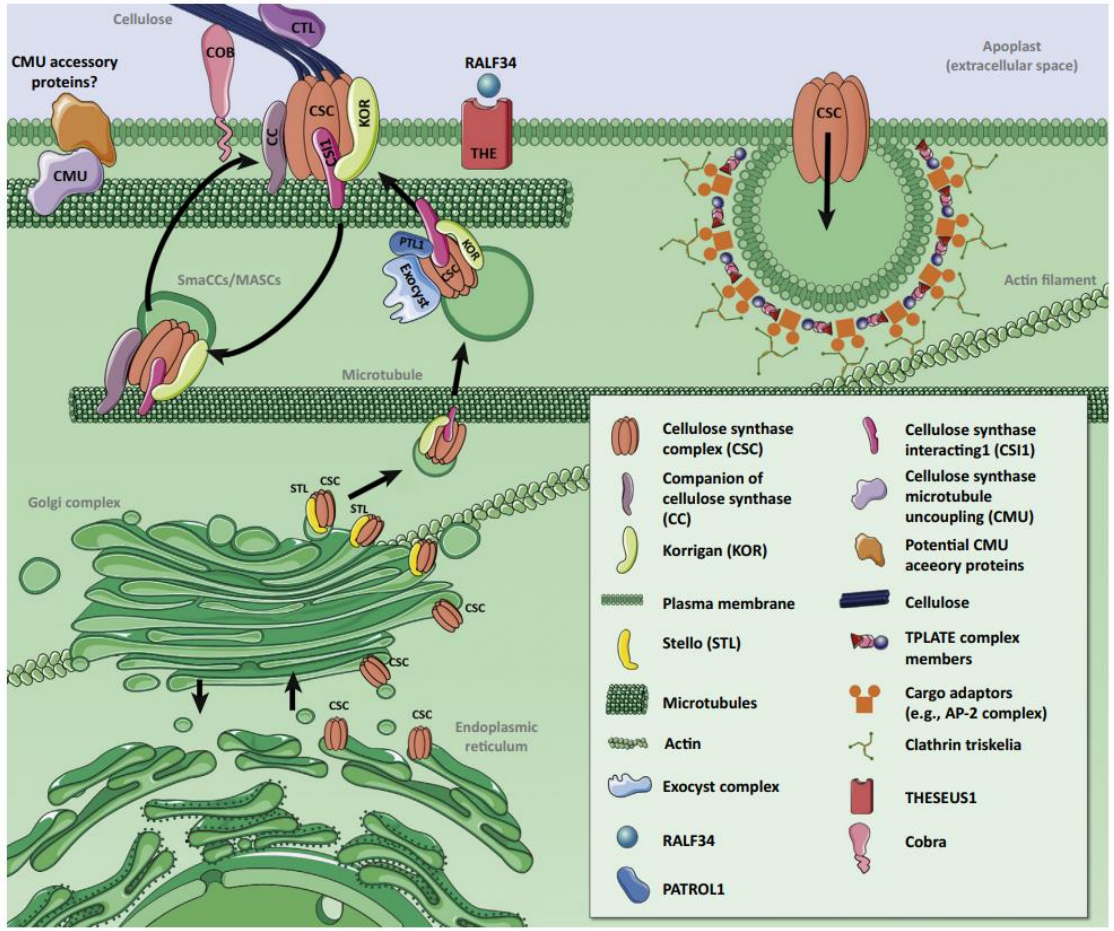


Cell wall composition and synthesis

- **Cellulose synthesis: proteins embedded in the plasma membrane**
- **Cellulose synthase (CESA)**
  - Oligomers form complexes – rosettes



  - Transport of saccharide monomers across the plasma membrane
  - Microfibril orientation – microtubules

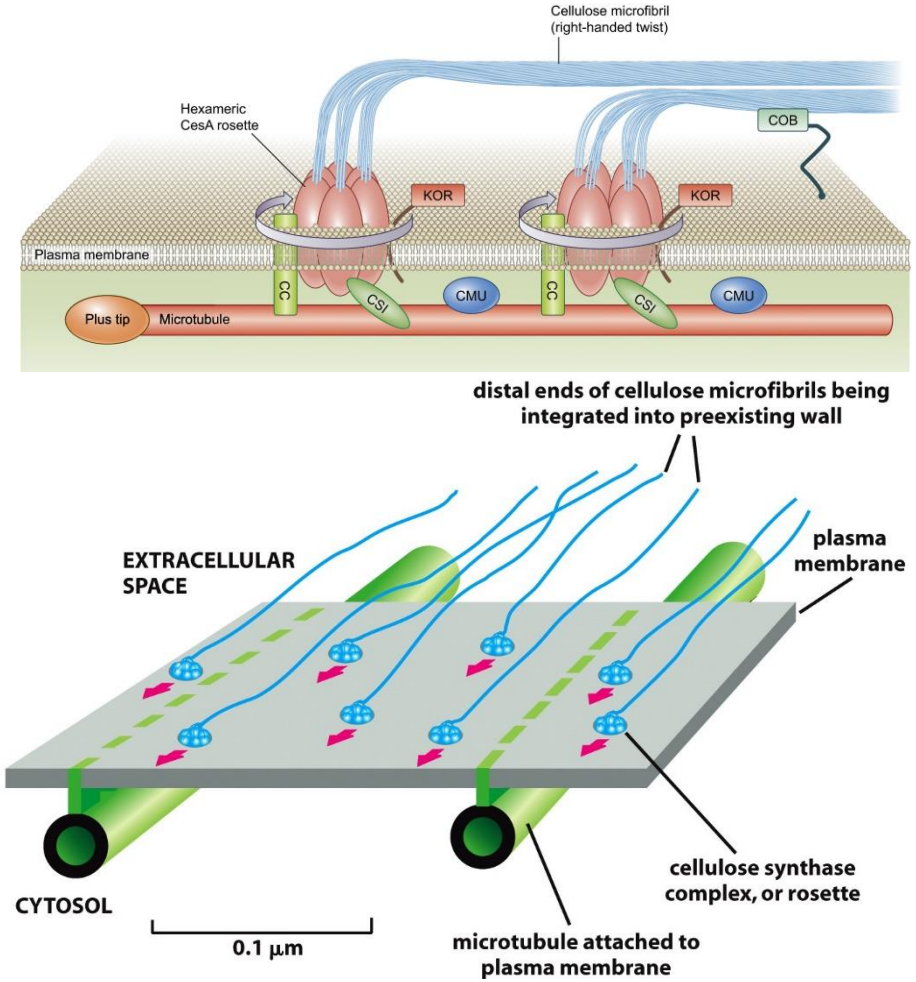


Trends in Plant Science

Cell wall composition and synthesis

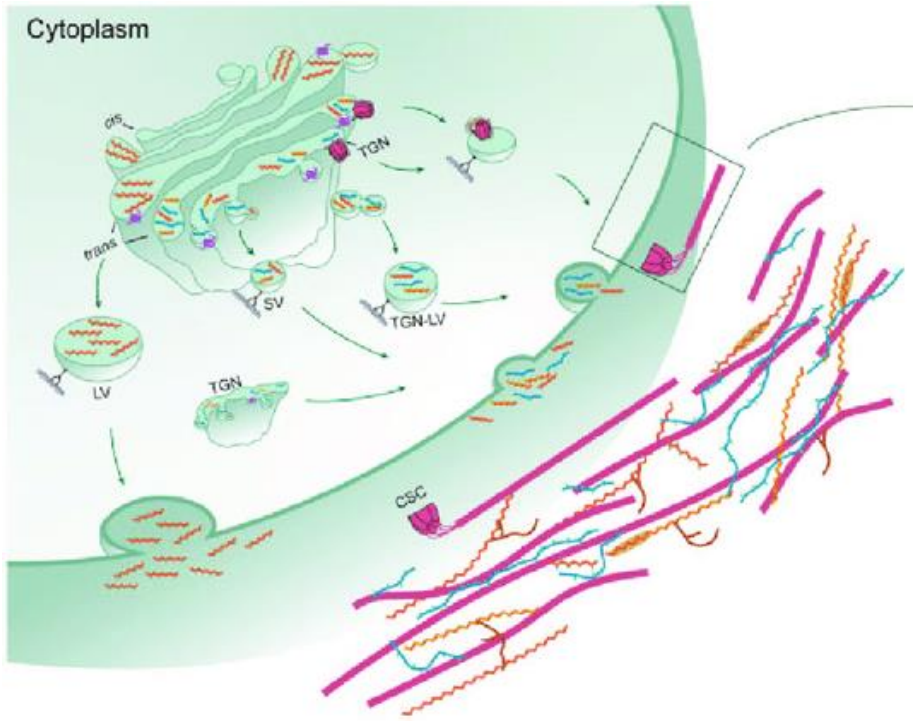
Cellulose synthesis

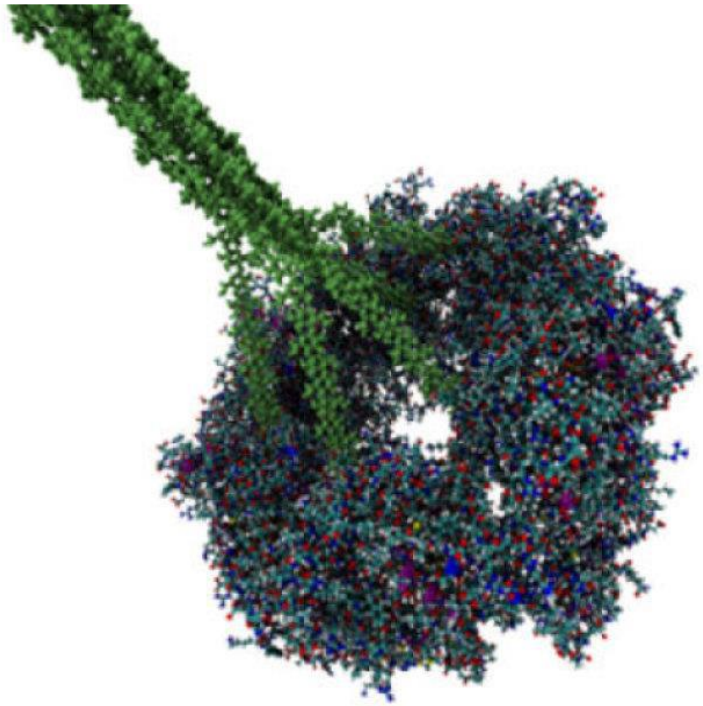
– Probable model: **cellulose microfibrils synthesized as the complexes move along the microtubules**

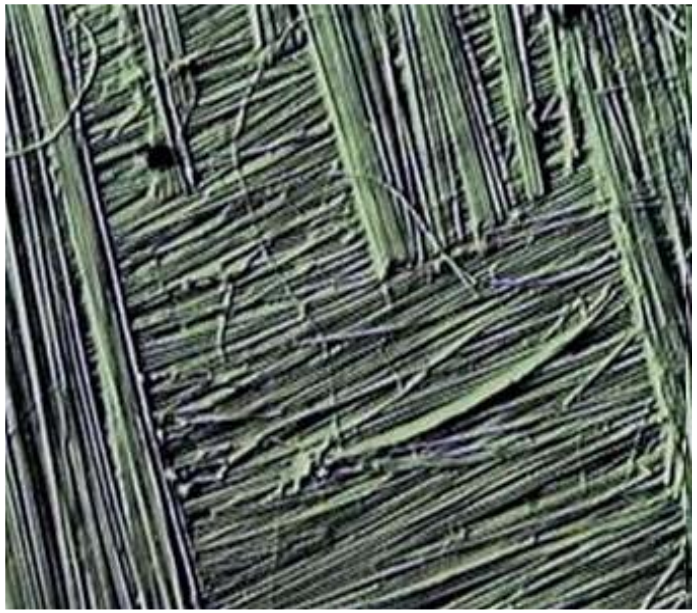


Other cell wall components

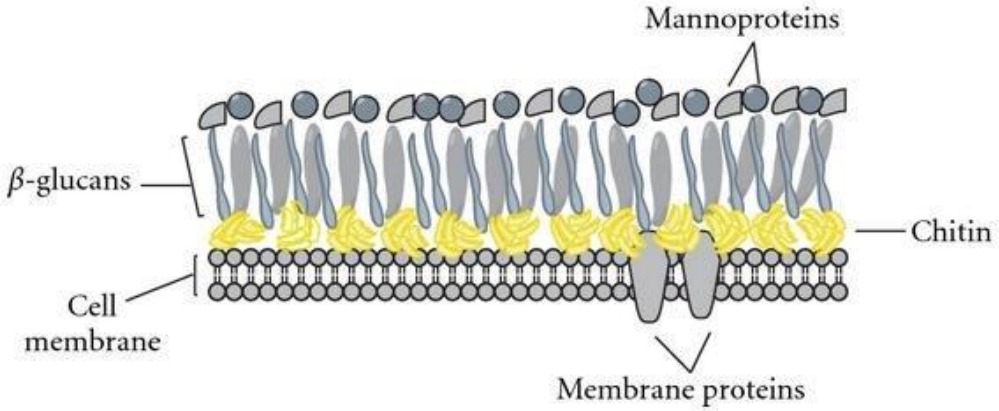
– Synthesized inside the cell and secreted by exocytosis

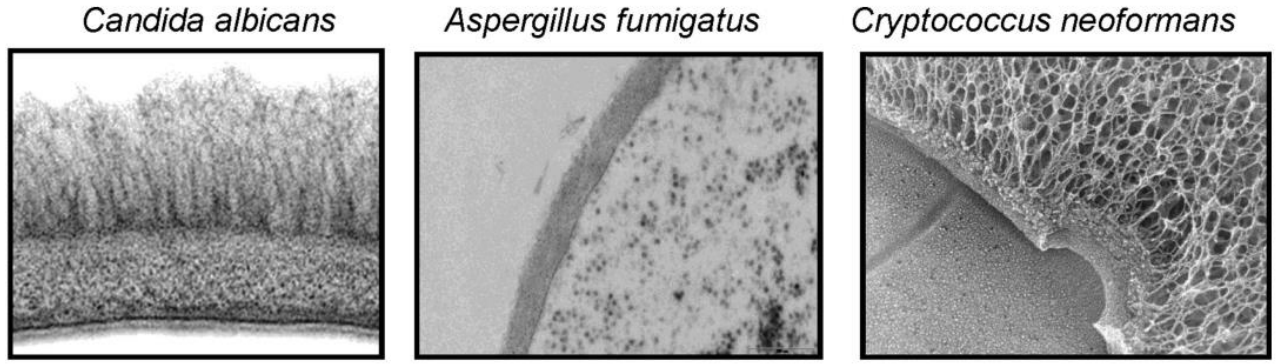

Cytoplasm
cis
TGN
trans
SV
TGN-LV
LV
TGN
CSC



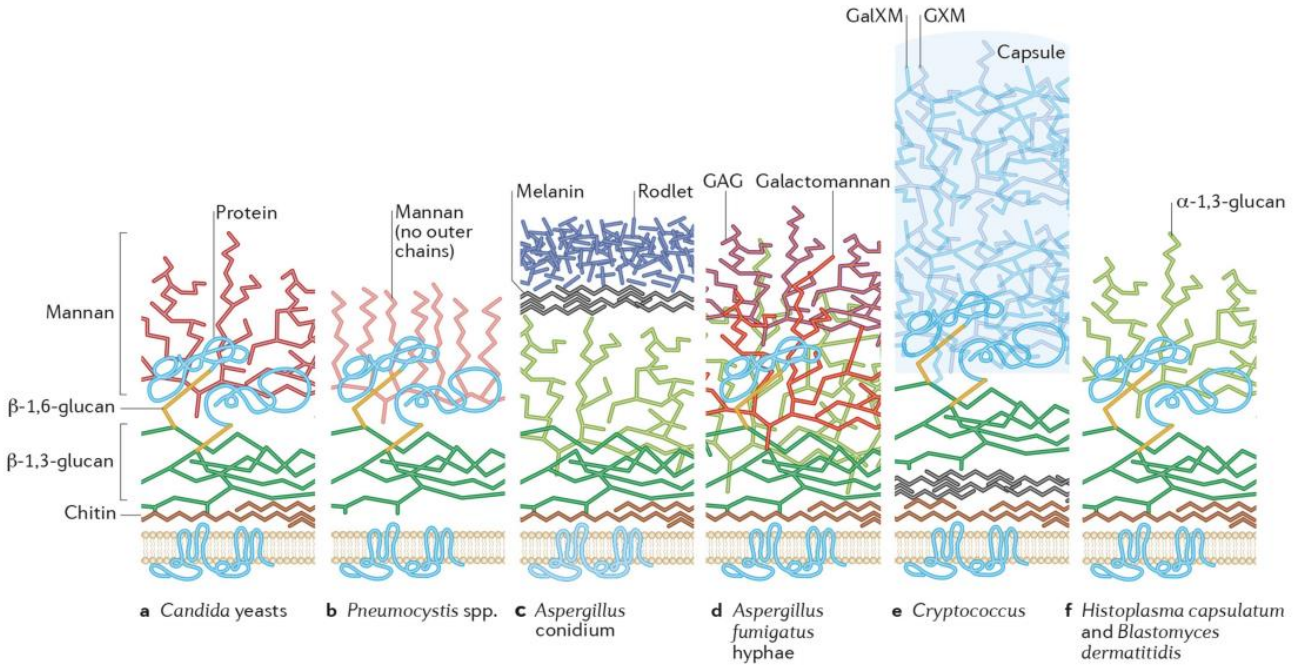


Fungal cell wall





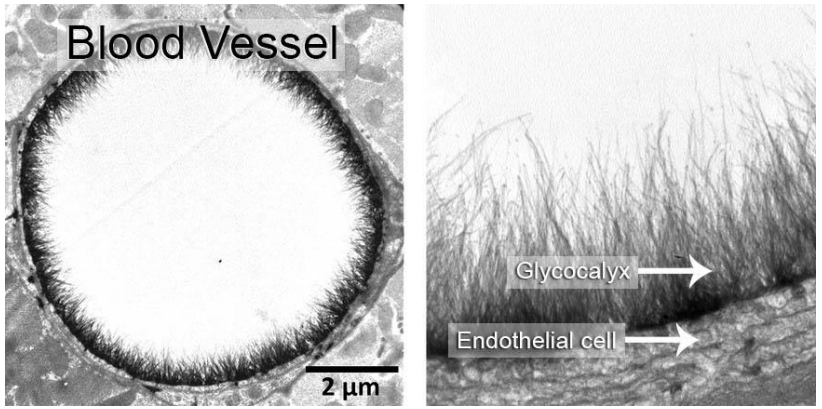
- **Chitin,** chitosan
- **Glucans** (mostly β-glucans)
  - Differ between species
- **Mannoproteins**
- Melanin

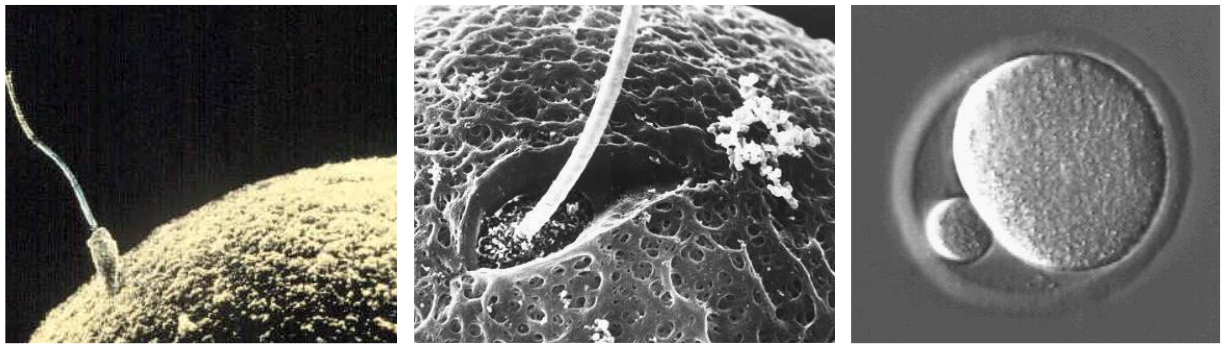


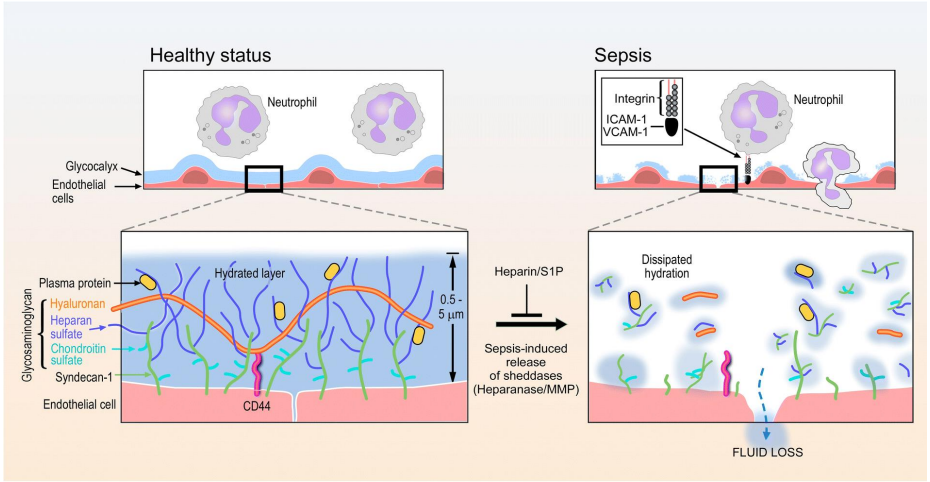
Extracellular matrix in animals

Glycocalyx

- Pericellular matrix (vs. extracellular matrix!)
- **Dense glycoprotein and glycolipid cover**
- Plasma membrane components
- **Physical barrier, involved in regulation of cell-cell interactions**
- e.g., zona pellucida in oocytes, endothelial cells





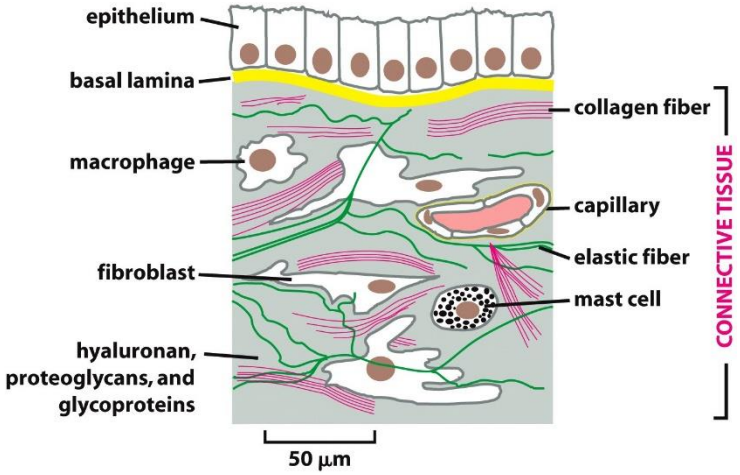


Extracellular matrix (ECM)

- Organization and composition based on the tissue type
- **Connective tissue** (bone, tendon, cartilage, vitreous body): predominance of ECM (mechanical strength and support)
- **Muscle and epithelial tissue**: minimal ECM – basal lamina (mechanical support provided by cytoskeleton)

Roles of ECM:

1. Mechanical support
2. Tissue-specific functions and cell adhesion signaling
3. Regulation of developmental processes



ECM composition

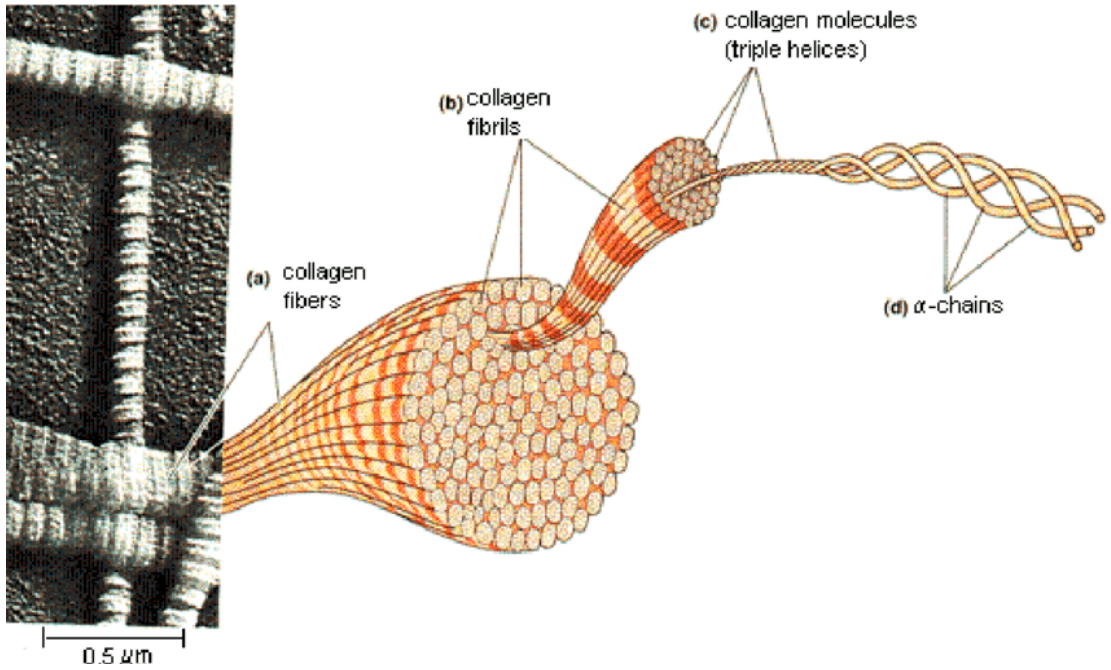
– Components produced by cells and secreted by exocytosis:

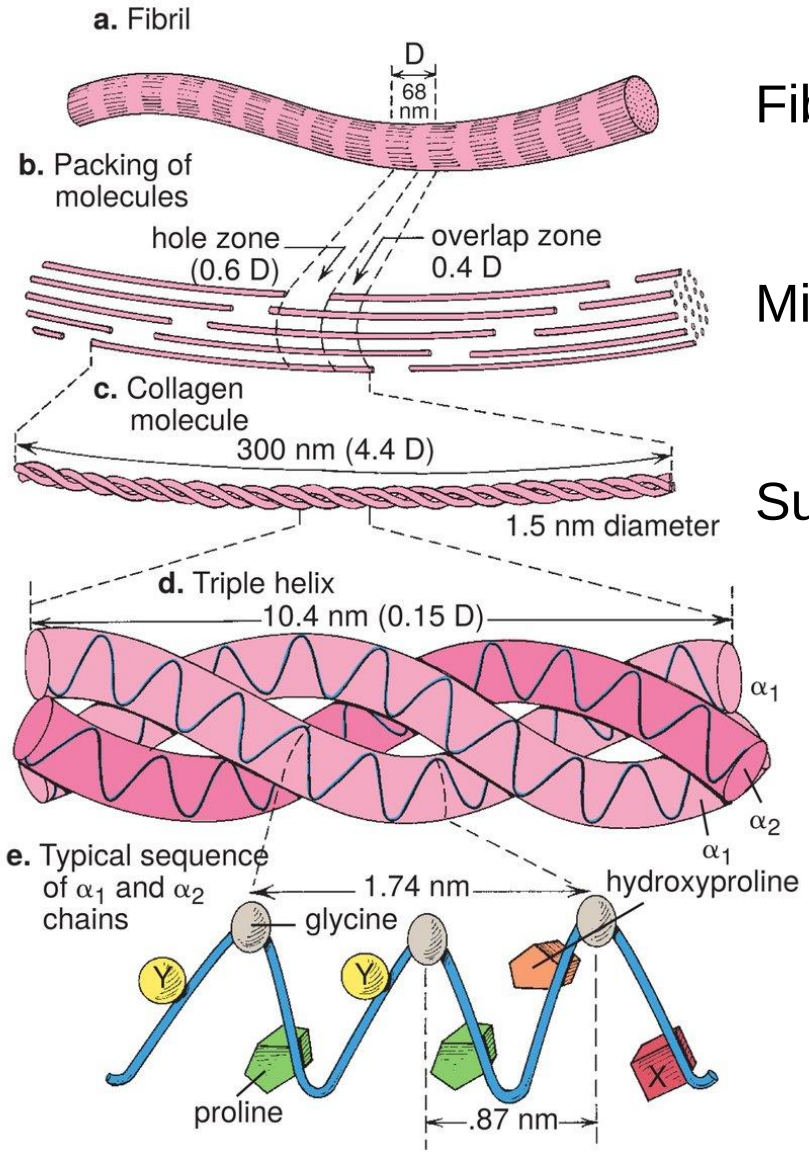
1. **Collagen fibers** (provide tensile strength; **collagens)**
2. **Elastic fibers** (provide elasticity; **elastin** and **fibrillin**)
3. **Space filling components** (prevents compression; **glycosaminoglycans**: **hyaluronan** and **proteoglycans**)
4. **Adhesive molecules** **(glycoproteins)**

Different types of ECM in different tissues

Collagen fibers

- **Collagens** – in mammals ~40 genes, 25% of the total protein mass
- Triple-stranded helical structure of three collagen α chains
- Rich in proline and glycine: **superhelix** → **collagen microfibril** → **collagen fibril** (10-300 nm in diameter) → **collagen fiber**
- **Organization of fibrils – tissue- and function-dependent:**
  - **Skin** – plywood-like arrangement: different layers laid at nearly right angles; withstand tension stress in multiple directions
  - **Tendons** – fibrils organized in parallel; withstand tension in the major axis
- Synthesis by **fibroblasts** and **epithelial cells**

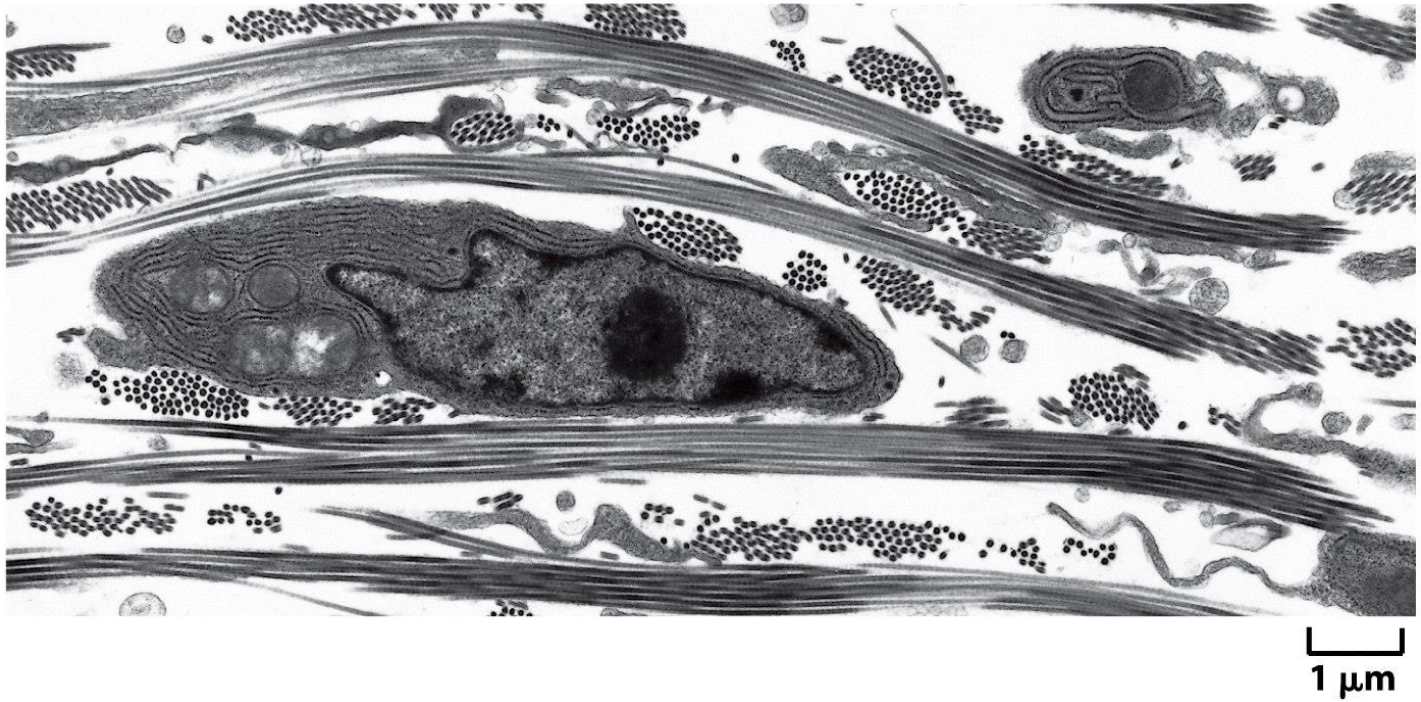




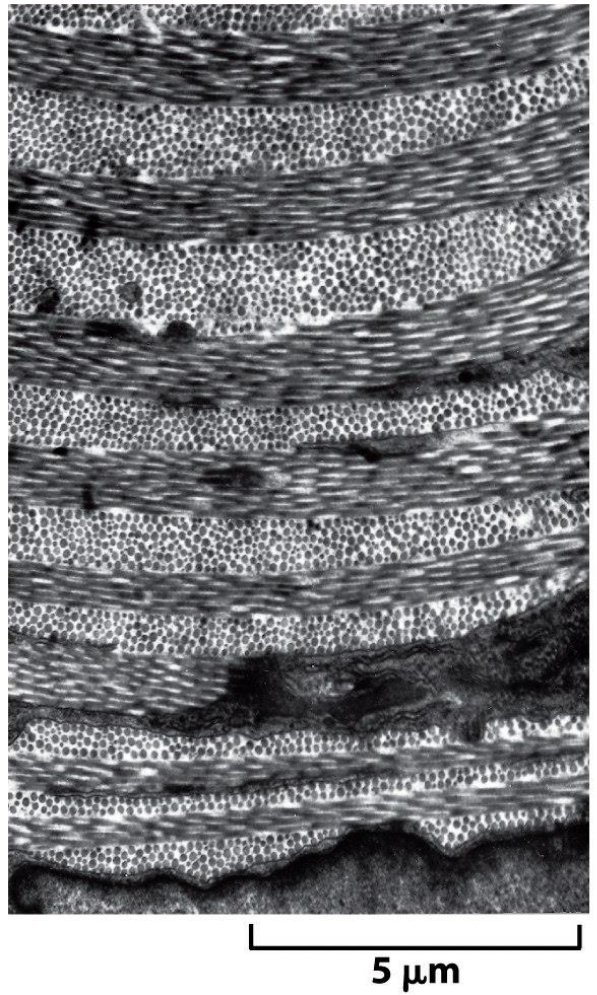
Fibril

Microfibril

Superhelix



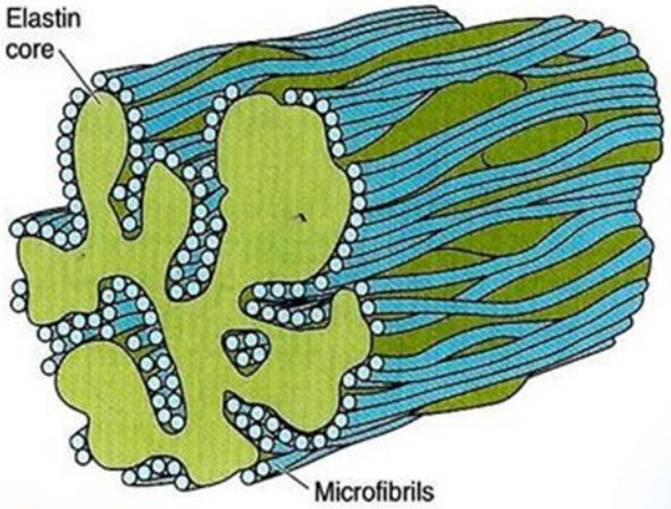
Collagen fibrils produced by a fibroblast

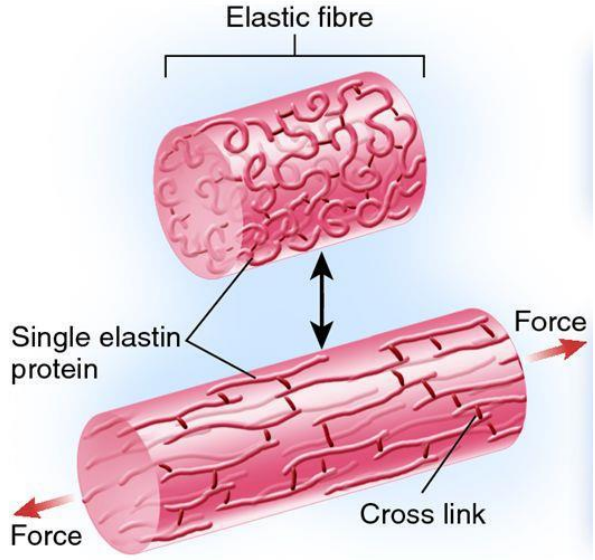


Collagen fibrils in the skin

Elastic fibers

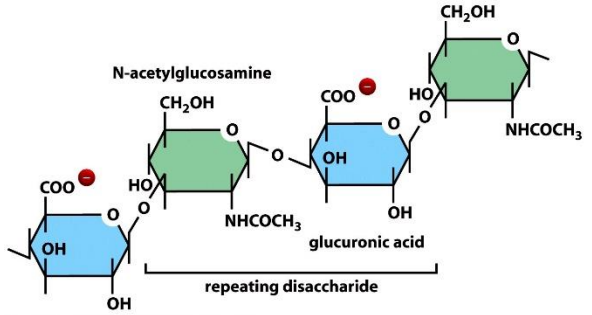
- **Elastin** and **fibrillin**
- Synthesis limited to embryonal and juvenile fibroblasts
- Skin, blood vessels, lungs
- Network of elastin molecules (core) and glycoprotein microfibrils (sheath; fibrillin)
- Elastin network recoils after stretch: elasticity



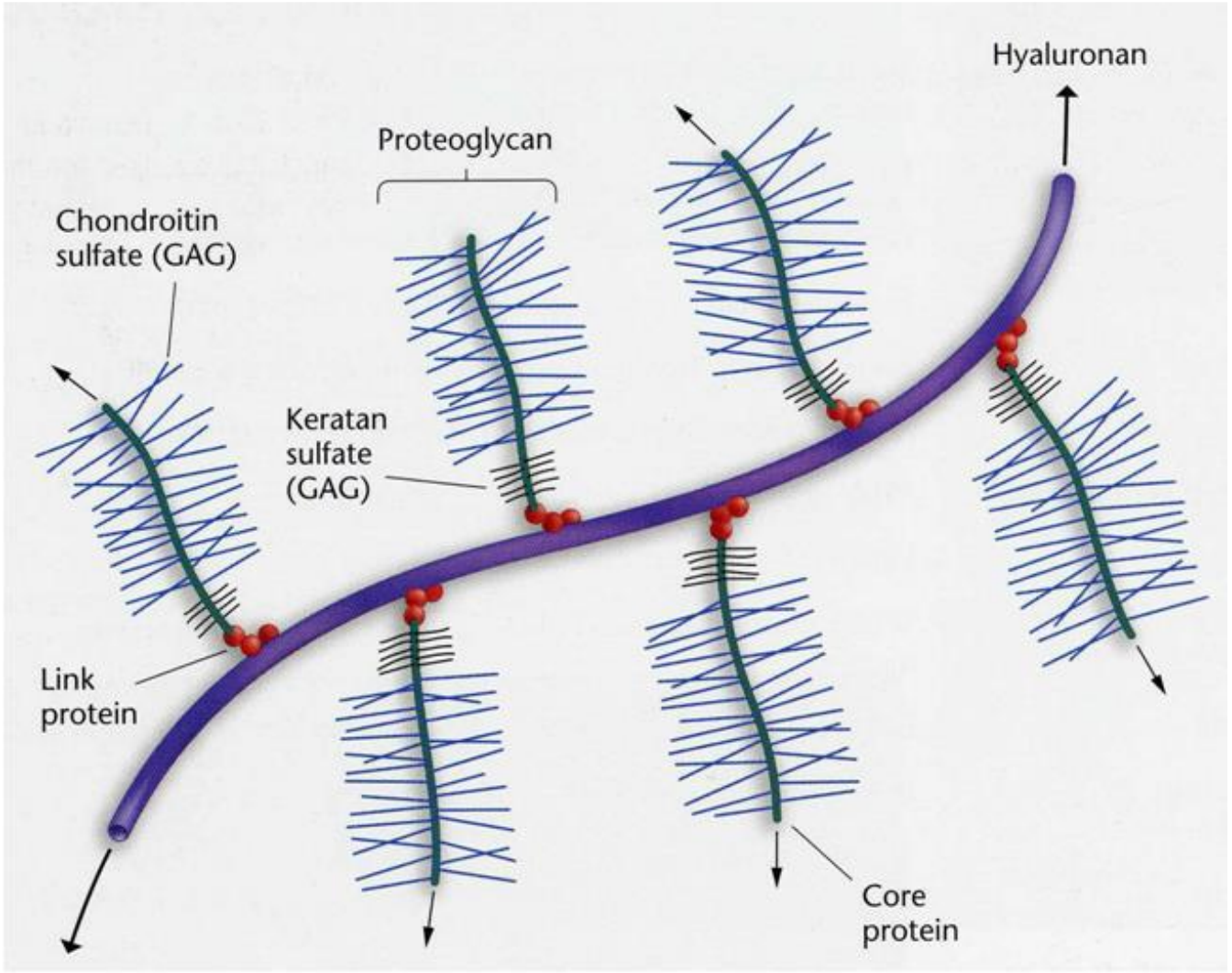


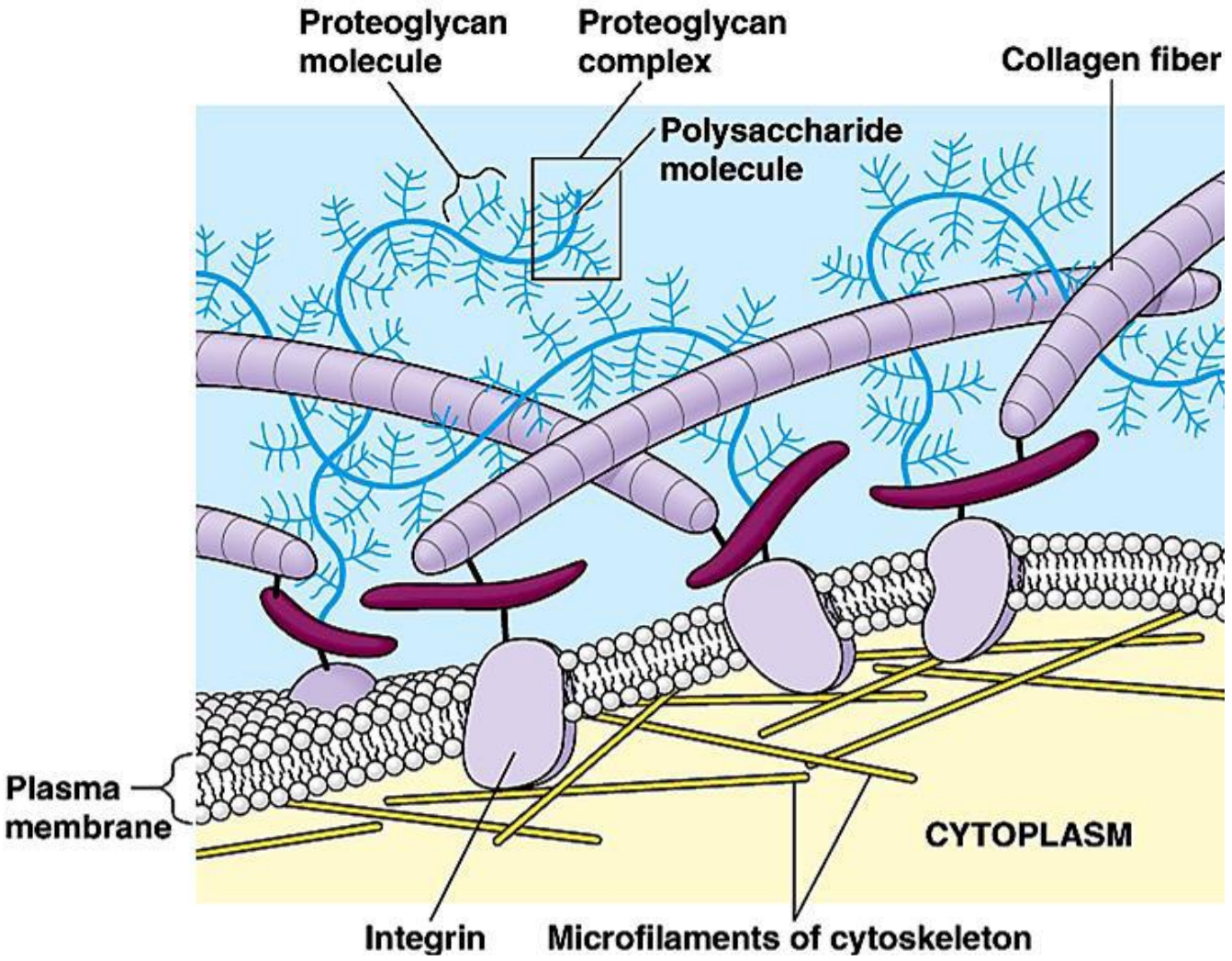
Tropocollagen (pre-collagen) / elastin

Space filling components



- Glycosaminoglycans (GAG)
- **Hyaluronan:** glucuronic acid & *N*-acetylglucosamine; up to 50 K disaccharide units in one molecule
- **Proteoglycans**: core protein and covalently bound GAG chains
- **Highly polar = attract water – form viscous hydrogels**
  - Attain large volumes – lubricants or shock absorbers
- **Hyaluronan surface receptors** (e.g., CD44): activation promote cell proliferation, migration, and invasion


Hyaluronan
Proteoglycan
Chondroitin sulfate (GAG)
Keratan sulfate (GAG)
Link protein
Core protein


Proteoglycan molecule
Proteoglycan complex
Collagen fiber
Polysaccharide molecule
Plasma membrane
CYTOPLASM
Integrin
Microfilaments of cytoskeleton

Adhesive glycoproteins

- Mediate interactions in the ECM, important for cell-ECM interactions

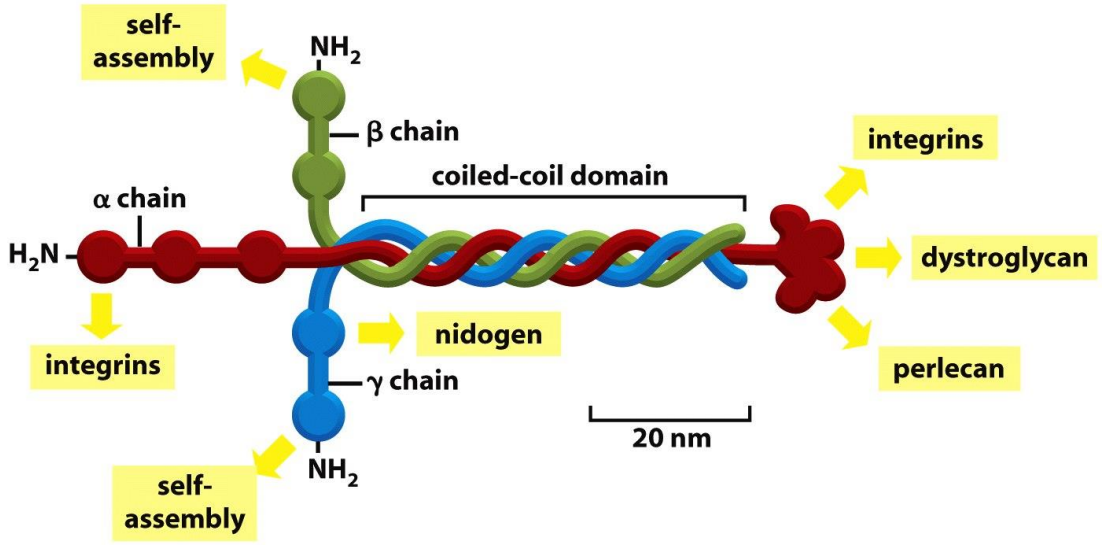
4 major types:

- **Laminins:** basal lamina glycoprotein
- **Fibronectins:** binds to integrin, cell-ECM attachment
- **Tenascins:** antiadhesive effects, often overexpressed in tumor stroma (metastasis), connective tissue, brain, bone, smooth muscles
- **Fibrinogen:** thrombocyte aggregation (coagulation factor)

Adhesive glycoproteins interact with other ECM components

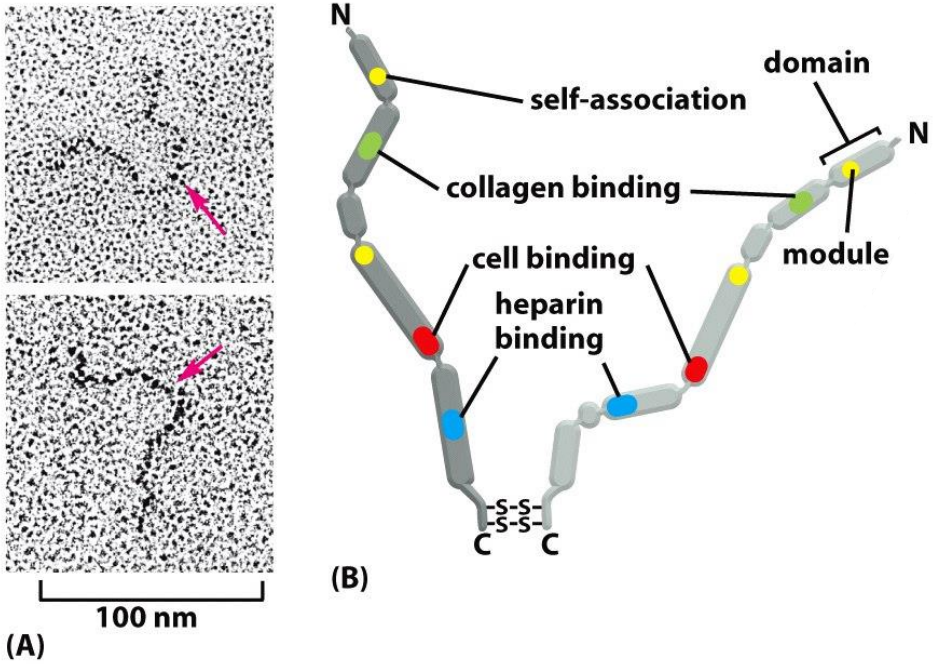
Laminin

- Three polypeptide chains
- Crosslinked by disulfide bonds to cross-like structure

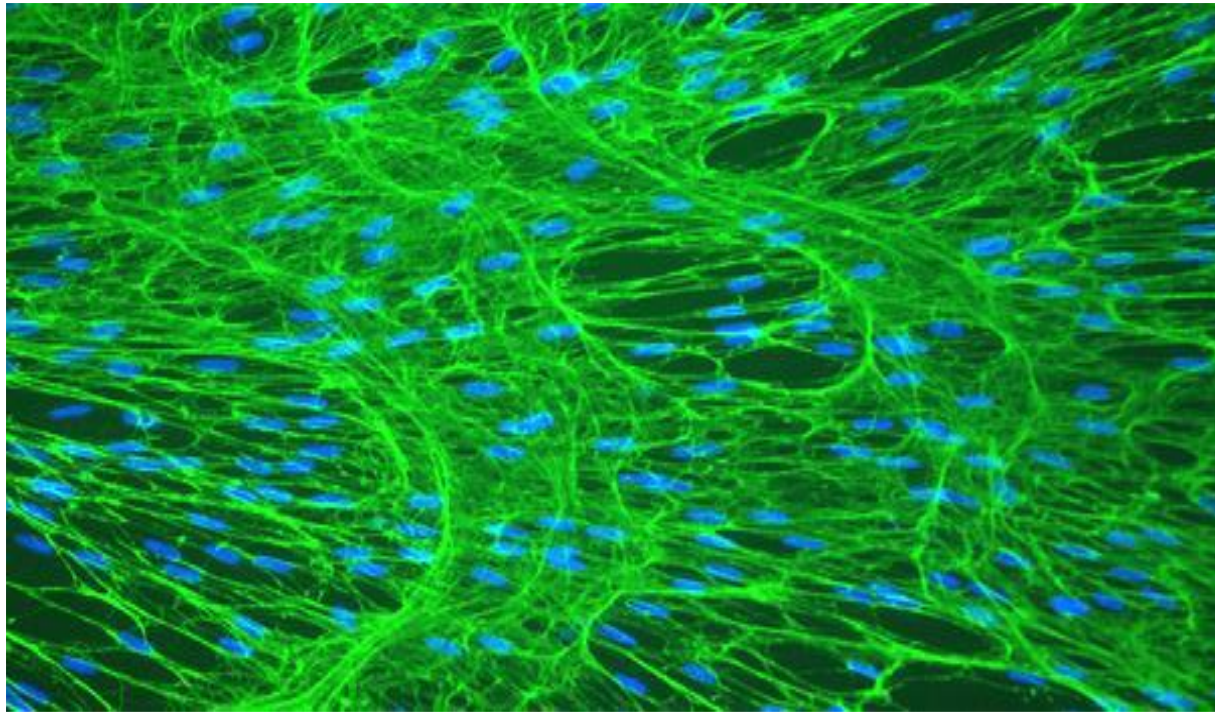


Fibronectin

- Dimeric structure, disulfide bonds
- Cell binding: trough integrins

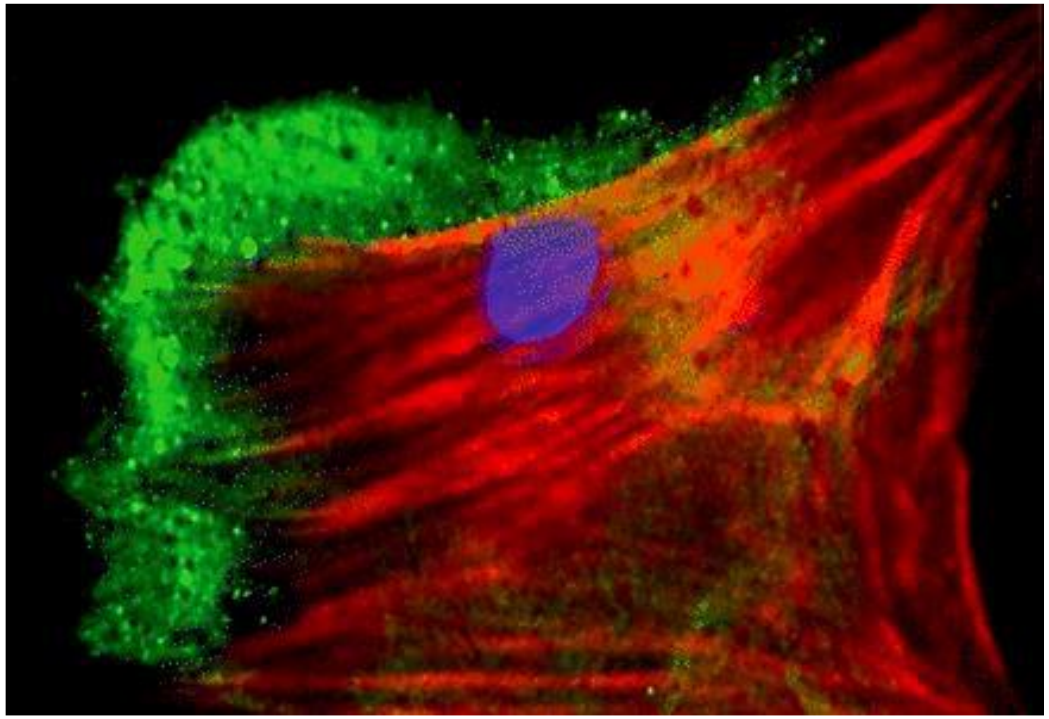


Human lung fibroblasts



Nuclei / fibronectin-GFP (ECM)

Rat pulmonary artery smooth muscle cell

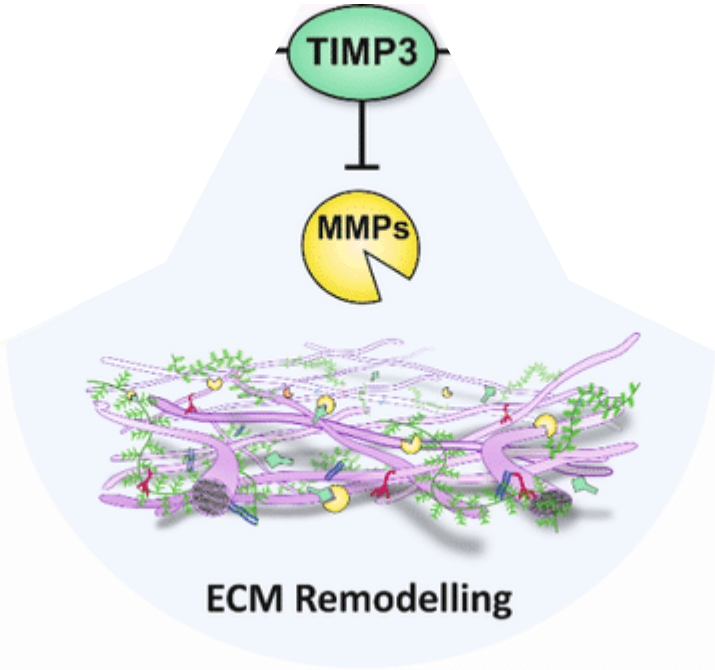


Nuclei / tenascin (ECM) / F-actin

ECM remodeling

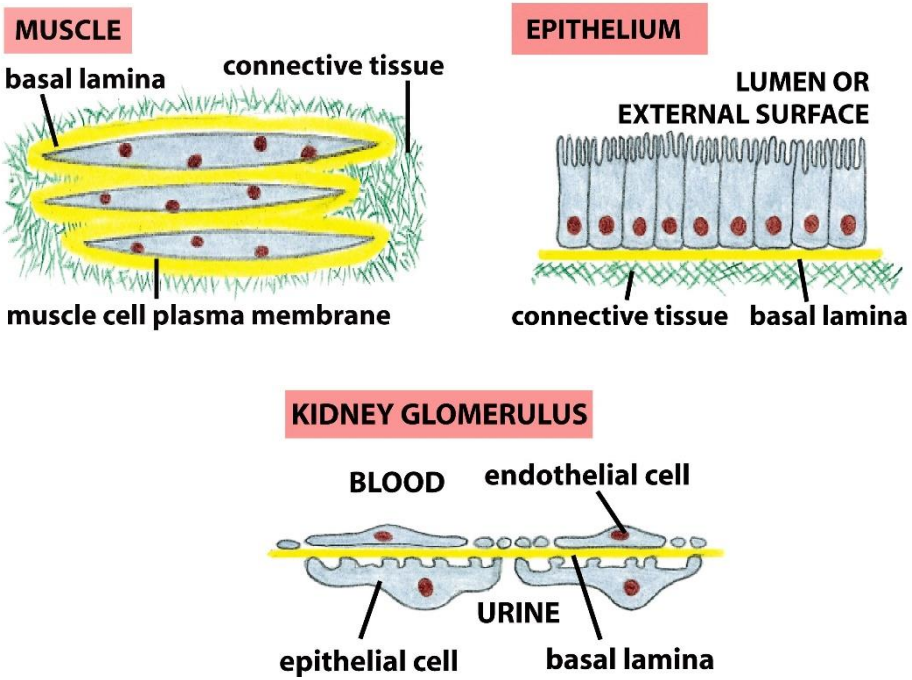
- Mechanisms of degradation and re-organization
- Important during development, wound healing, inflammation etc.
- Exploited by cancer cells (metastasis)

- **Matrix metalloproteinases** (MMPs) and **tissue inhibitors of metalloproteinase** (TIMPs)

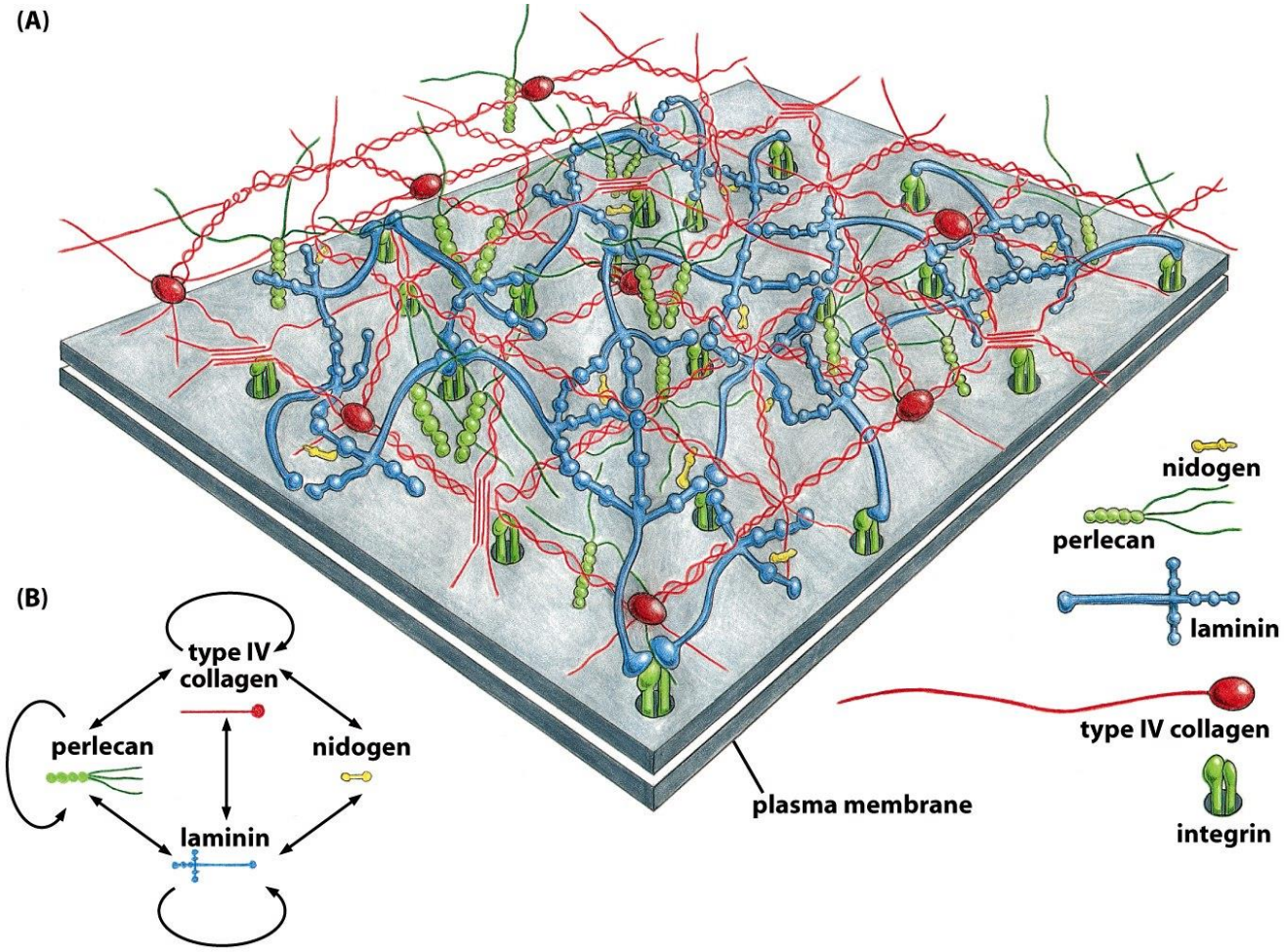


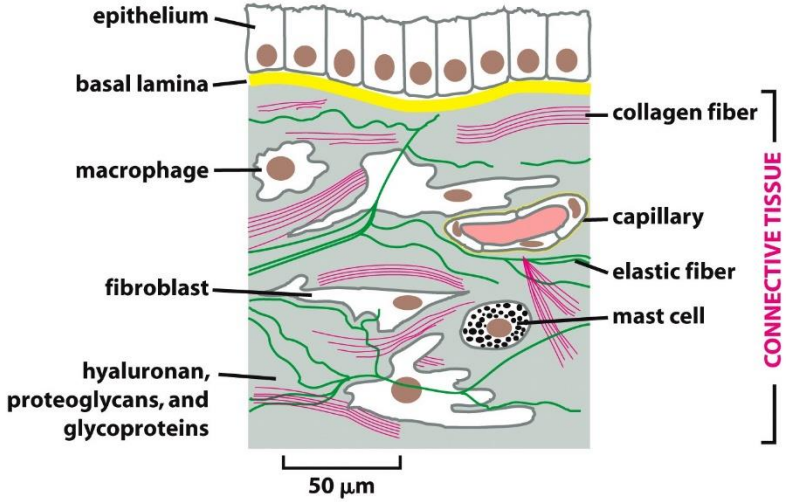
Basal lamina – basement membrane

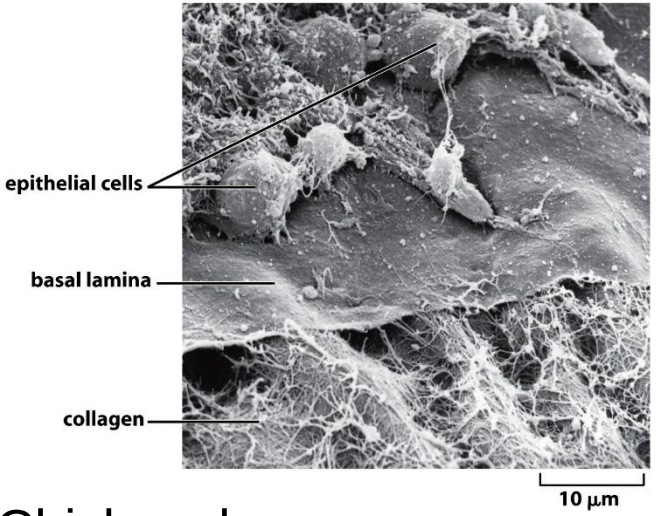
- Underlies epithelial cells, surrounds muscle, fat and Schwann cells
- Cell polarity, mechanical connection with connective tissue, filter (kidney)
- Relatively thin ECM layer: 50-200 nm



- **Collagen type IV, laminins, nidogens** (linker proteins; formerly entactin), **perlecan**







Chick embryo cornea

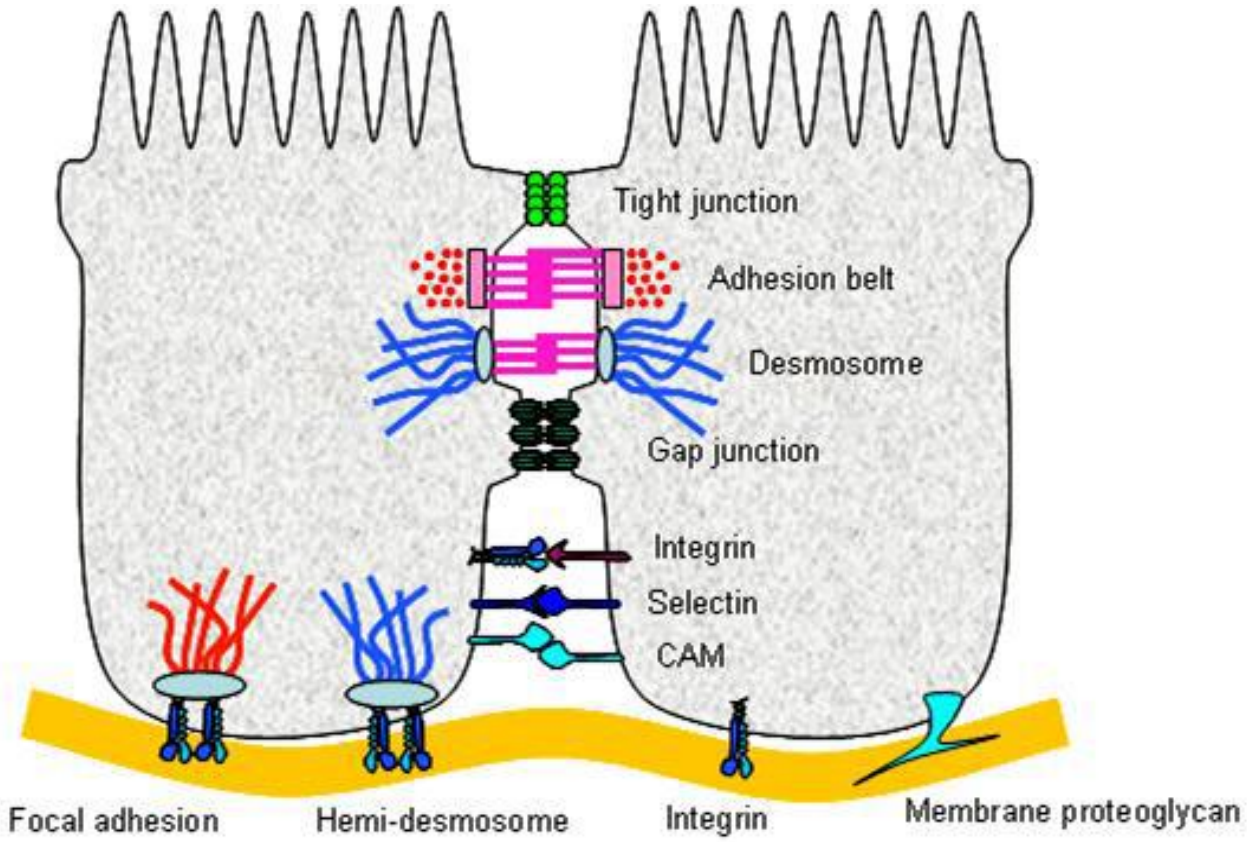
Cell interactions

Cell interactions

- Expression of specific receptors: **cell adhesion molecules (CAM)**
  - **CAM interactions**: cell-cell interactions & cell-ECM interactions
  - **Intracellularly linked with cytoskeleton** (stability and signaling)
  - Regulation by translocation (membrane vs. vesicles; secretory vs. endocytic pathway)

4 major CAM classes:

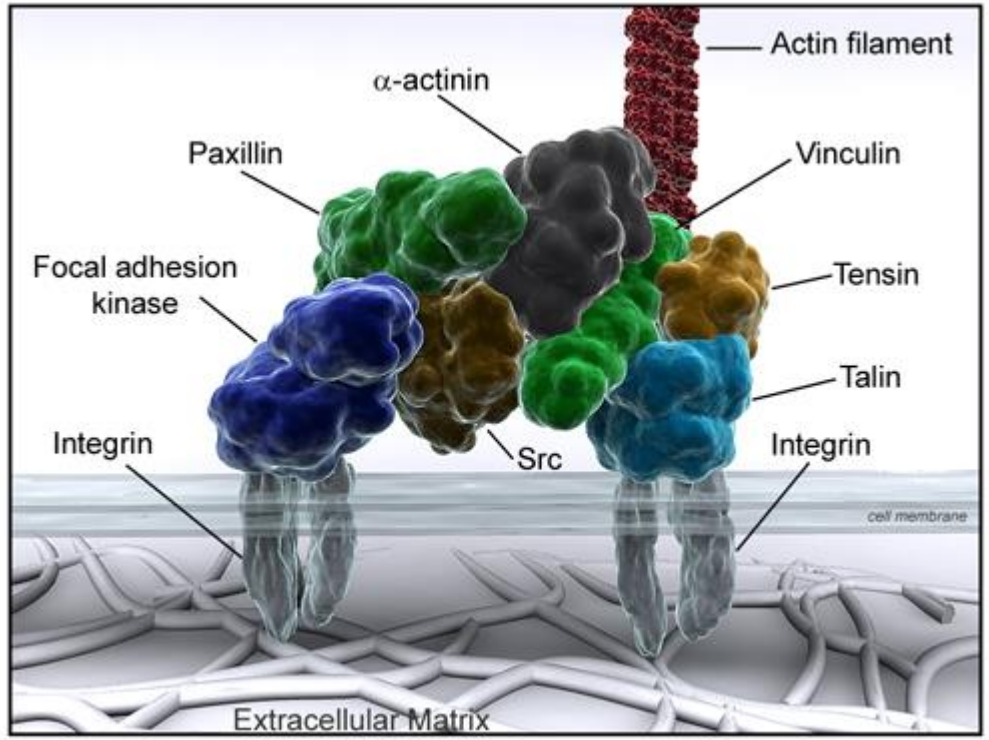
- **Integrins (cell-ECM)**
- **Cadherins (cell-cell)**
- **Selectins**
- **Immunoglobulin-like CAMs (ICAMs)**

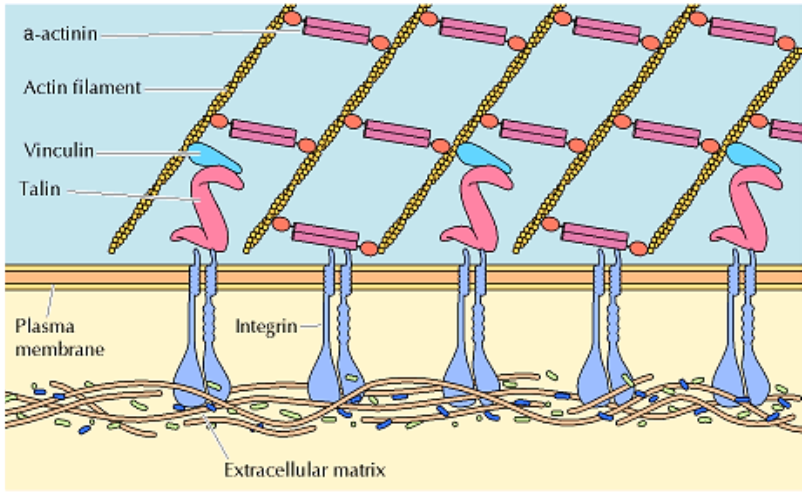

Tight junction
Adhesion belt
Desmosome
Gap junction
Integrin
Selectin
CAM
Focal adhesion
Hemi-desmosome
Integrin
Membrane proteoglycan

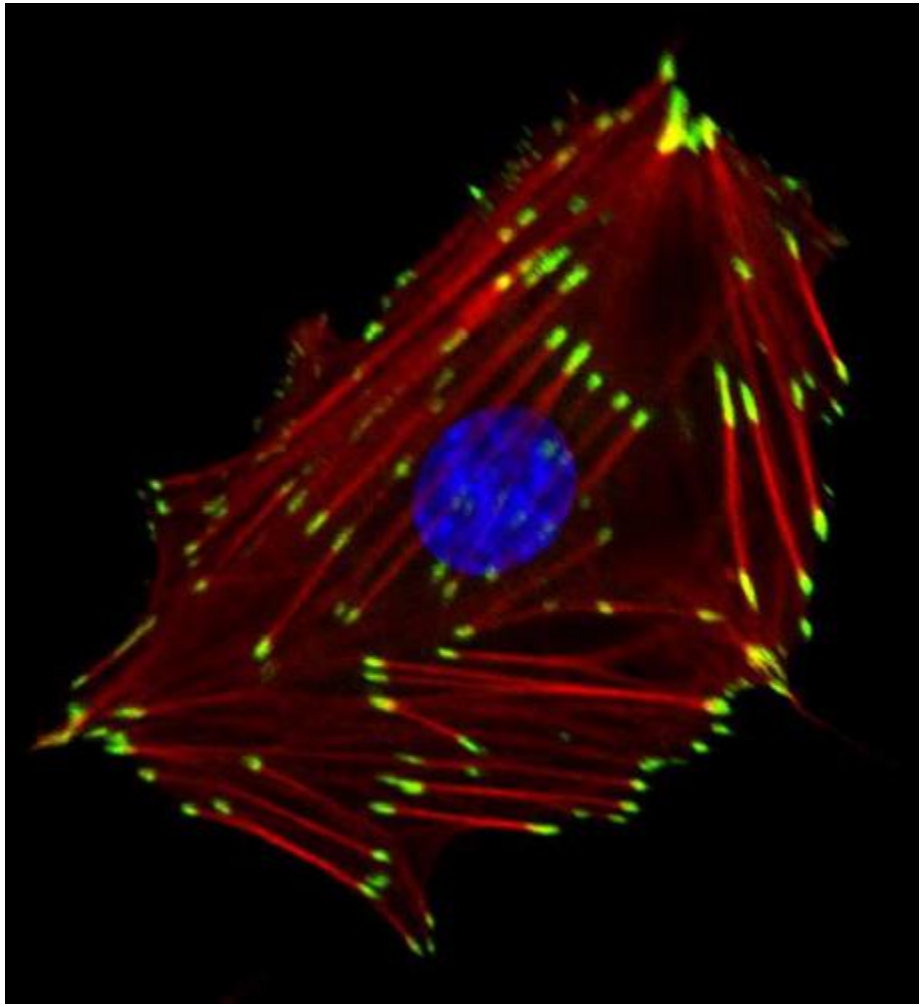
Cell-ECM interactions

Focal adhesions

- Connecting **actin filaments to ECM** through **integrins**
- Important for **cell signaling** (FAK/Src): cell survival, migration, proliferation…



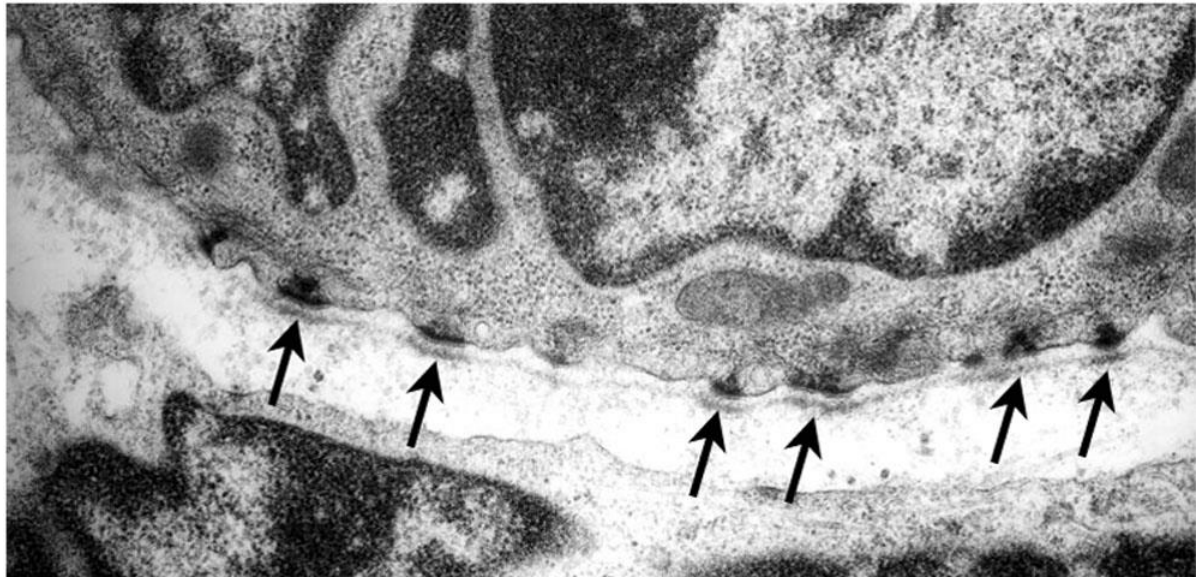


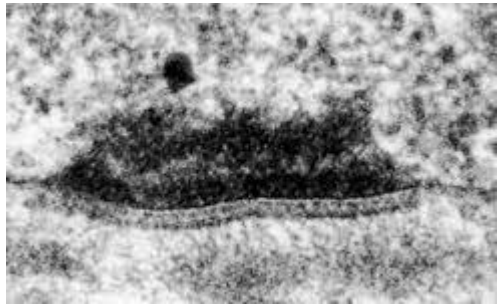


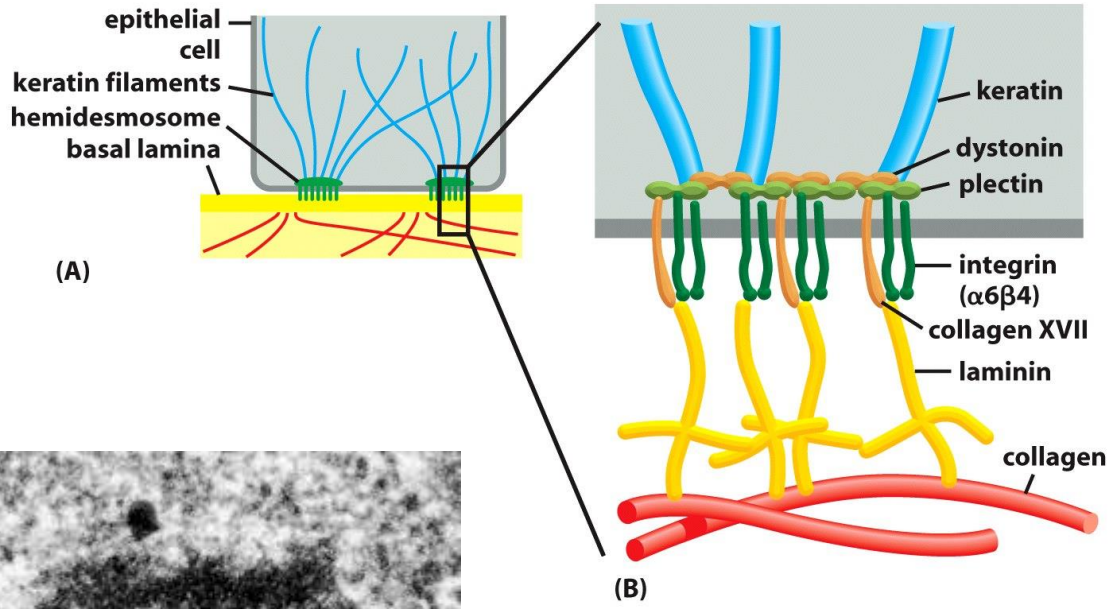
Vinculin (focal adhesions) / F-actin / nuclei

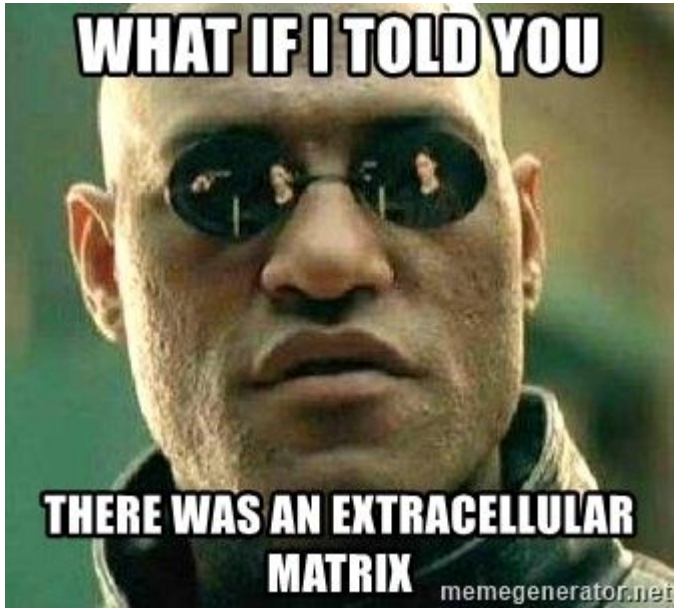
Hemidesmosomes

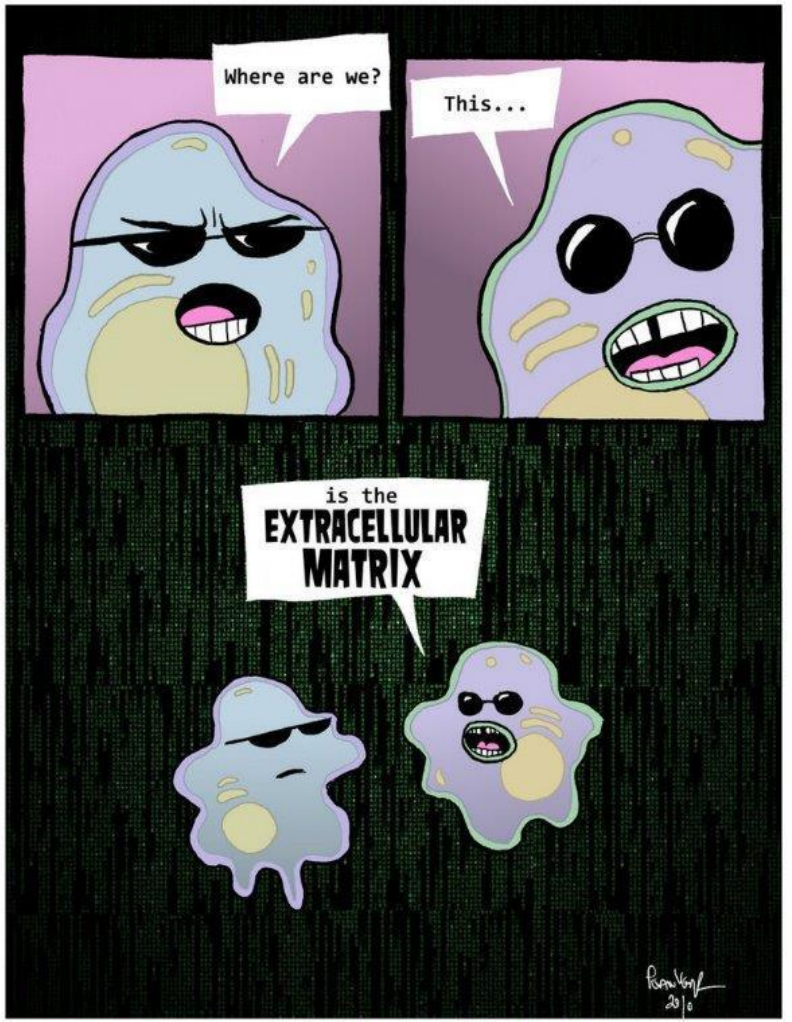
- Connecting **intermediary filaments to ECM** through **integrins**
- **Anchor epithelial cells to basal lamina**








WHAT IF I TOLD YOU
THERE WAS AN EXTRACELLULAR MATRIX
memegenerator.net


Where are we?
This...
is the
EXTRACELLULAR MATRIX

Cell-cell interactions

Types of cell-cell interactions

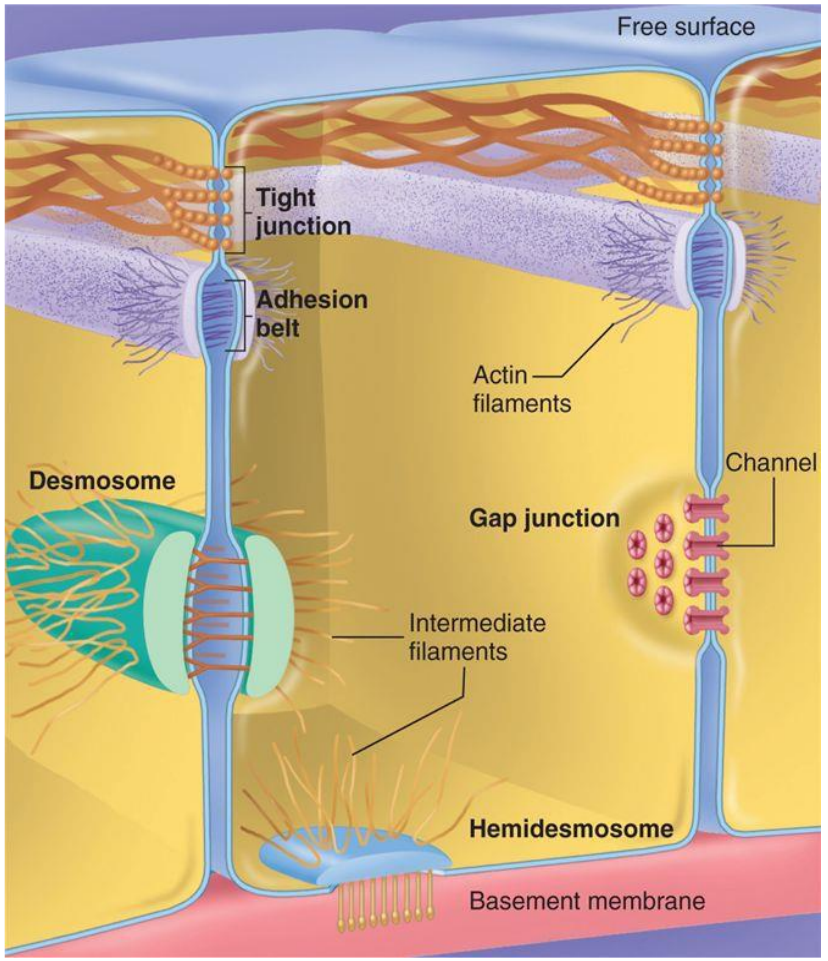
Cell adhesions

- **Adherens junctions (adhesion belt)**
- **Desmosomes**

Tight junctions

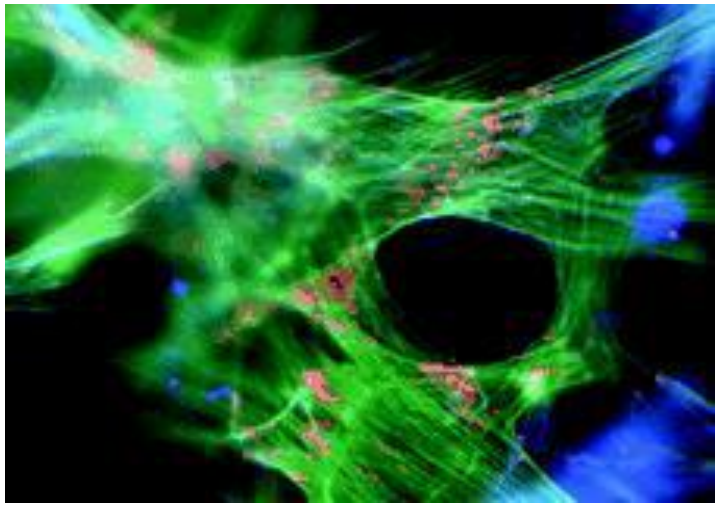
Channel-forming junctions

- **Gap junctions**
- **Plasmodesmata** (plants)

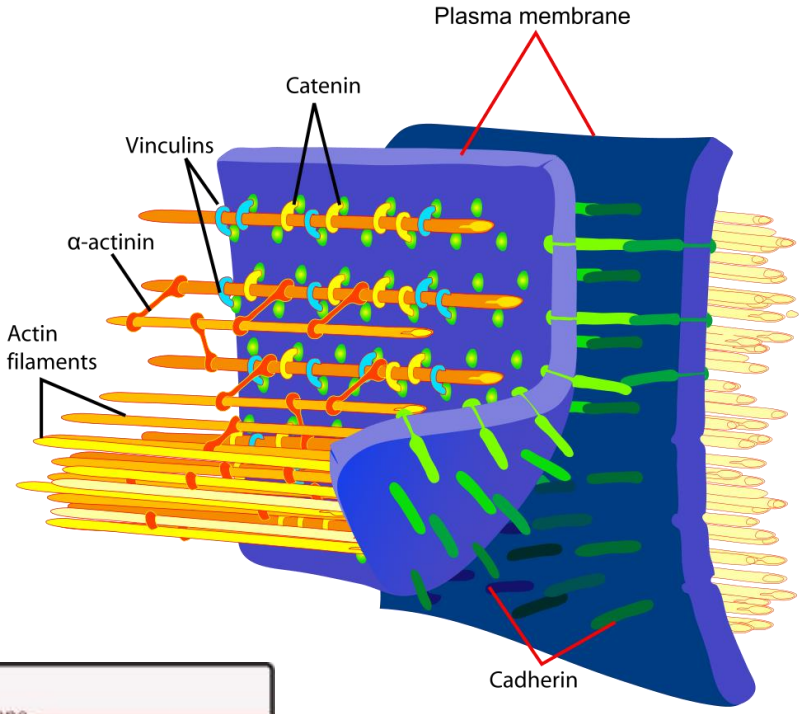


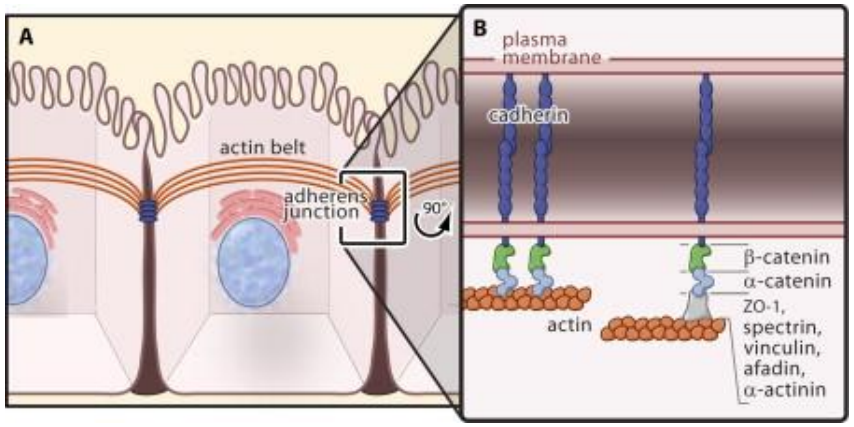
Adherens junctions

– Connect **actin filaments** in neighboring cells via **cadherins**



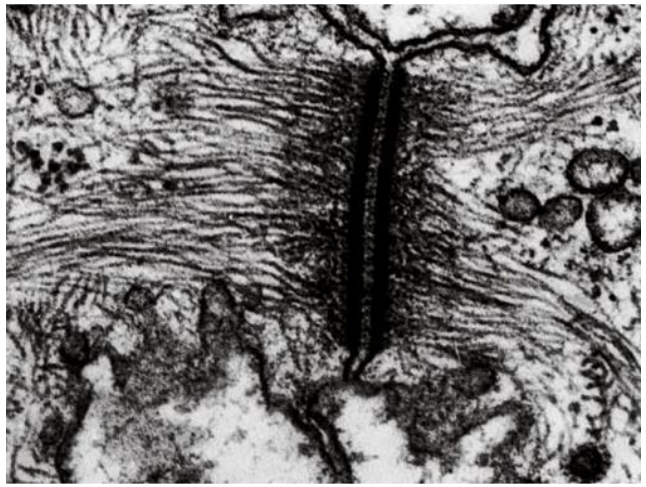
F-actin / β-catenin

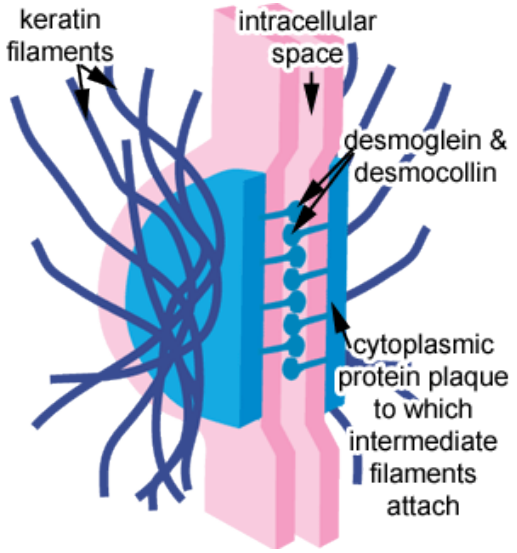




Desmosomes

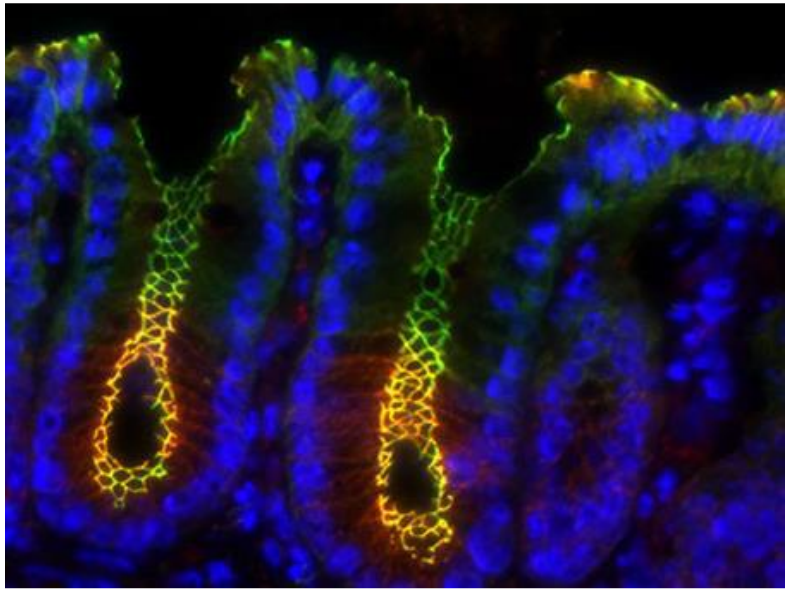
- Connect **intermediary filaments** in neighboring cells via desmosomal **cadherins**
- **Dense cytoplasmic plaque** within cells

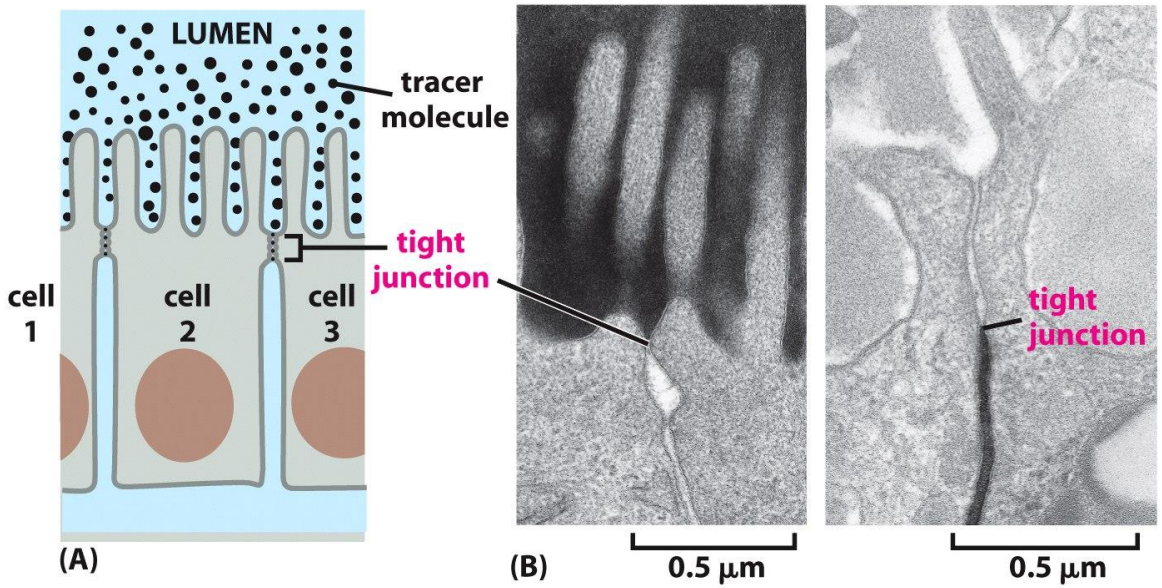


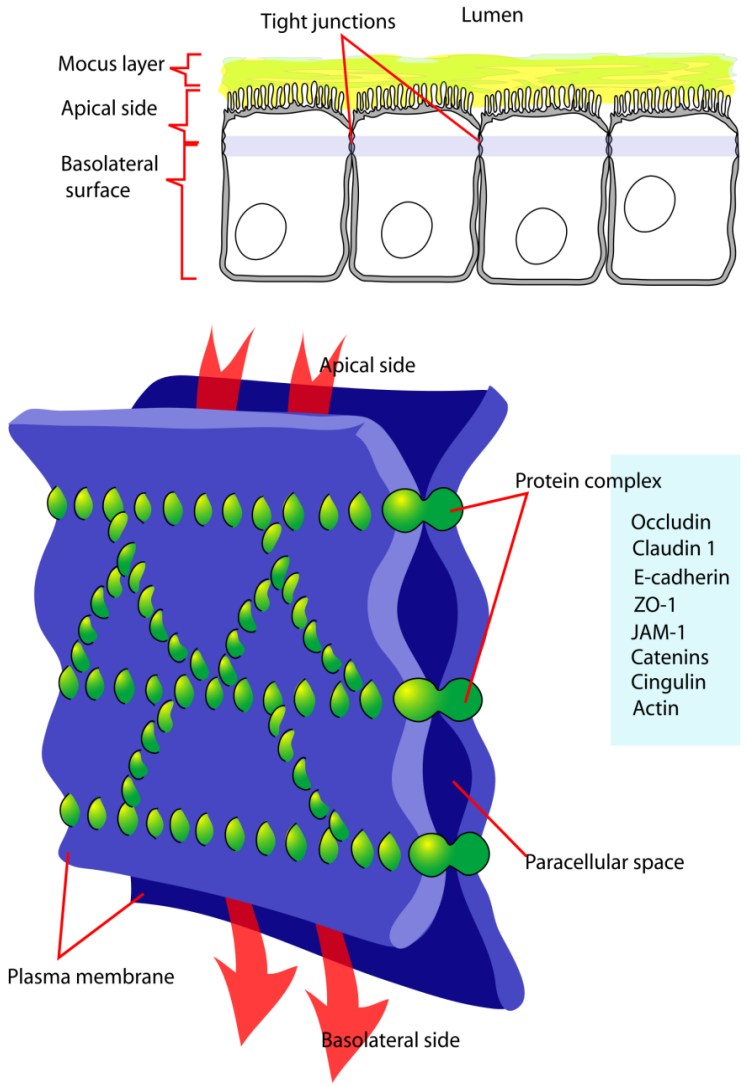


Tight junctions

- **Seal gaps between epithelial cells** close to apical membrane
- **Impermeable (selectively permeable) barrier**
- **Claudin, occludin, JAMs (junction adhesion molecules)**



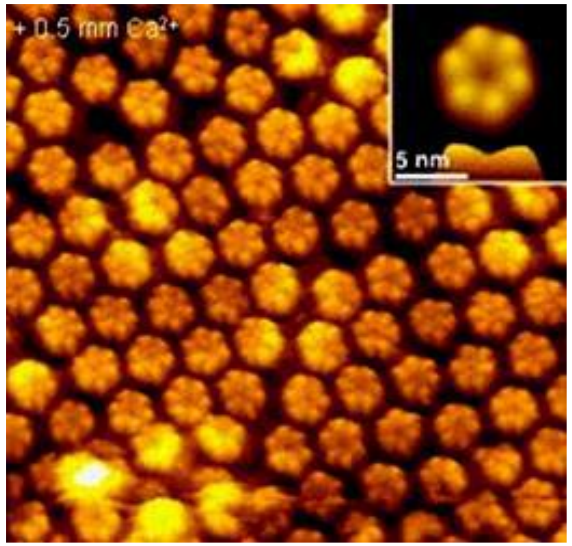


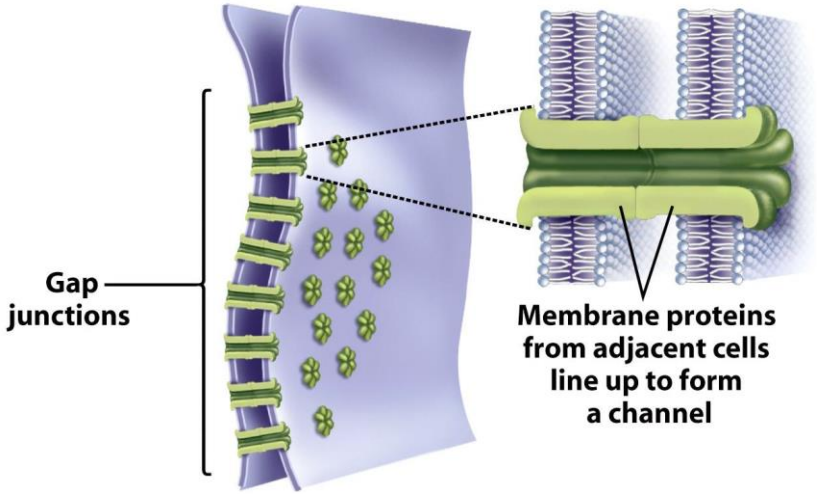

Tight junctions
Lumen
Mocus layer
Apical side
Basolateral surface
Apical side
Protein complex
Occludin
Claudin 1
E-cadherin
ZO-1
JAM-1
Catenins
Cingulin
Actin
Paracellular space
Plasma membrane
Basolateral side

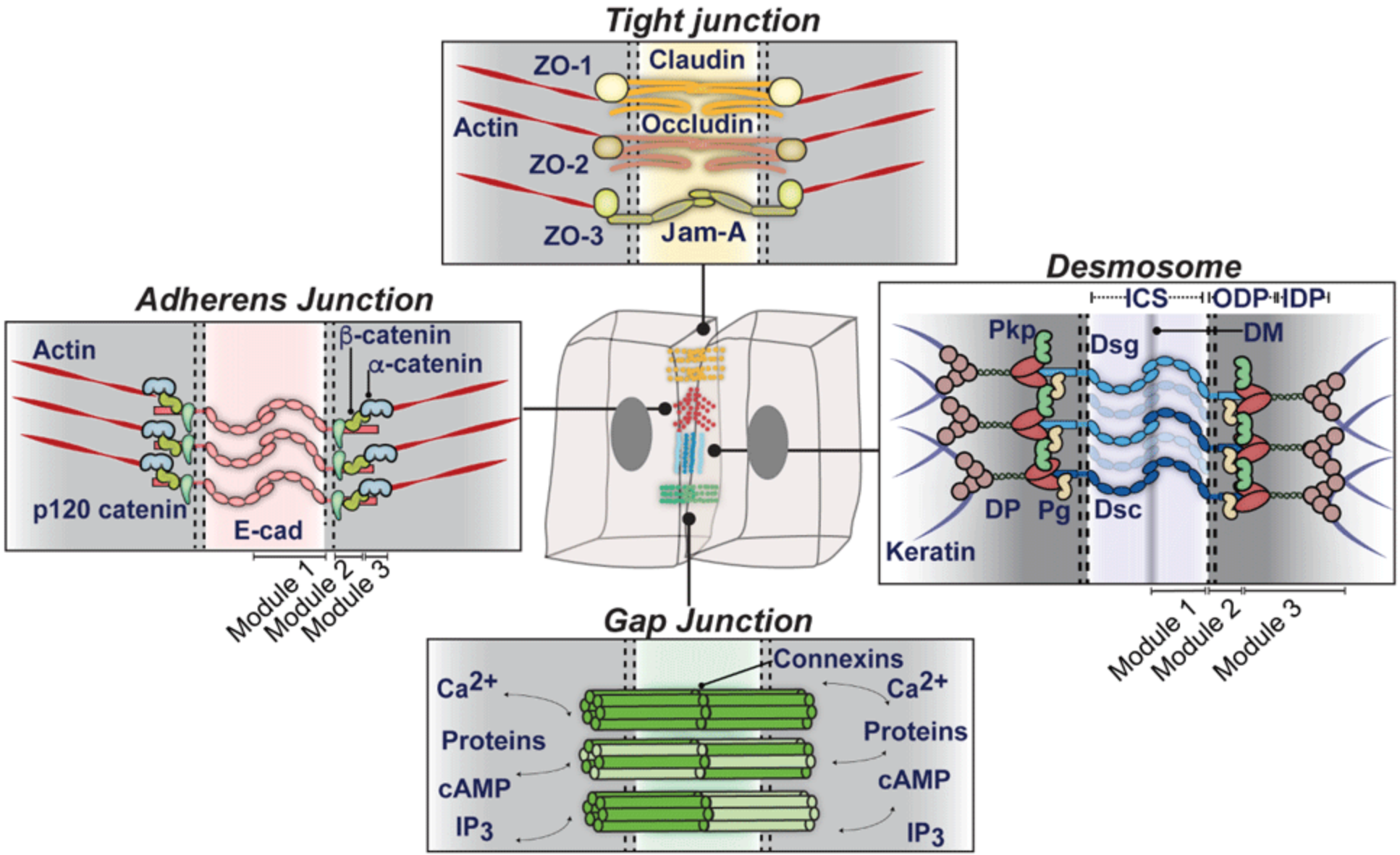
Gap junctions

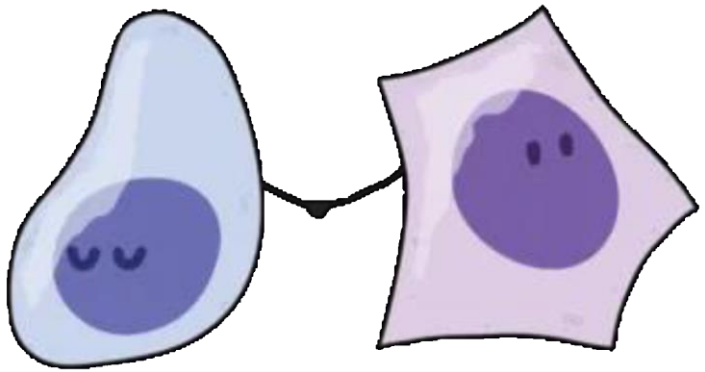
(parallel: plasmodesmata in plant cells)

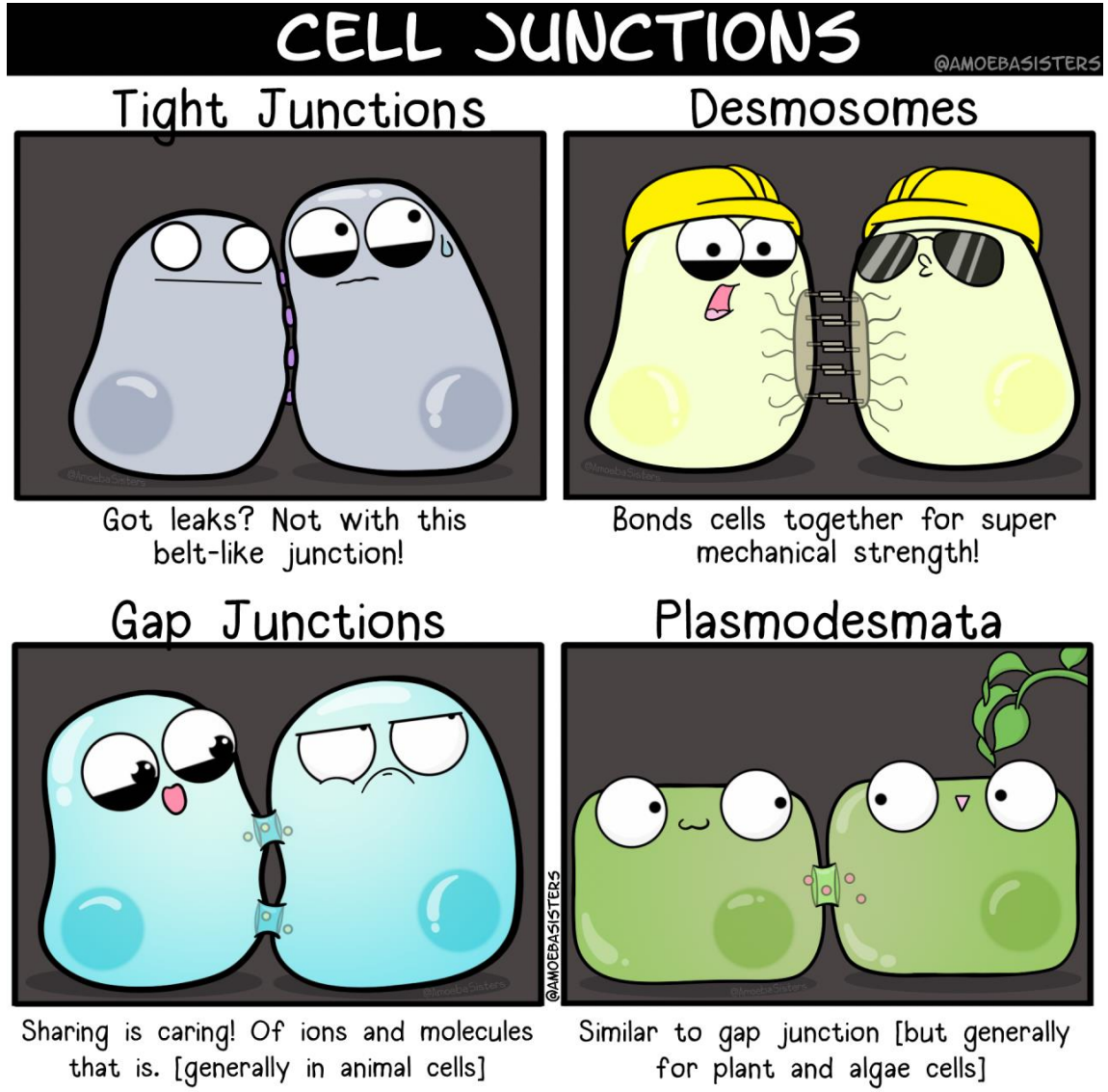
- **Directly link cytoplasms** of adjacent cells; **animal cells**
- Diffusion of water, ions, small molecules: cell-cell communication
- Hexamer of **connexin** proteins = **connexons** (1.5 nm wide channels)






Tight junction
ZO-1
Claudin
Actin
Occludin
ZO-2
ZO-3
Jam-A
Adherens Junction
Actin
β-catenin
α-catenin
p120 catenin
E-cad
Module 1
Module 2
Module 3
Desmosome
ICS
ODP
IDP
Pkp
Dsg
DM
DP
Pg
Dsc
Keratin
Module 1
Module 2
Module 3
Gap Junction
Connexins
Ca2+
Ca2+
Proteins
Proteins
cAMP
cAMP
IP3
IP3




CELL JUNCTIONS
@AMOEBASISTERS
Tight Junctions
Got leaks? Not with this belt-like junction!
Desmosomes
Bonds cells together for super mechanical strength!
Gap Junctions
Sharing is caring! Of ions and molecules that is. [generally in animal cells]
Plasmodesmata
Similar to gap junction [but generally for plant and algae cells]
@AMOEBASISTERS