Extracellular Matrix

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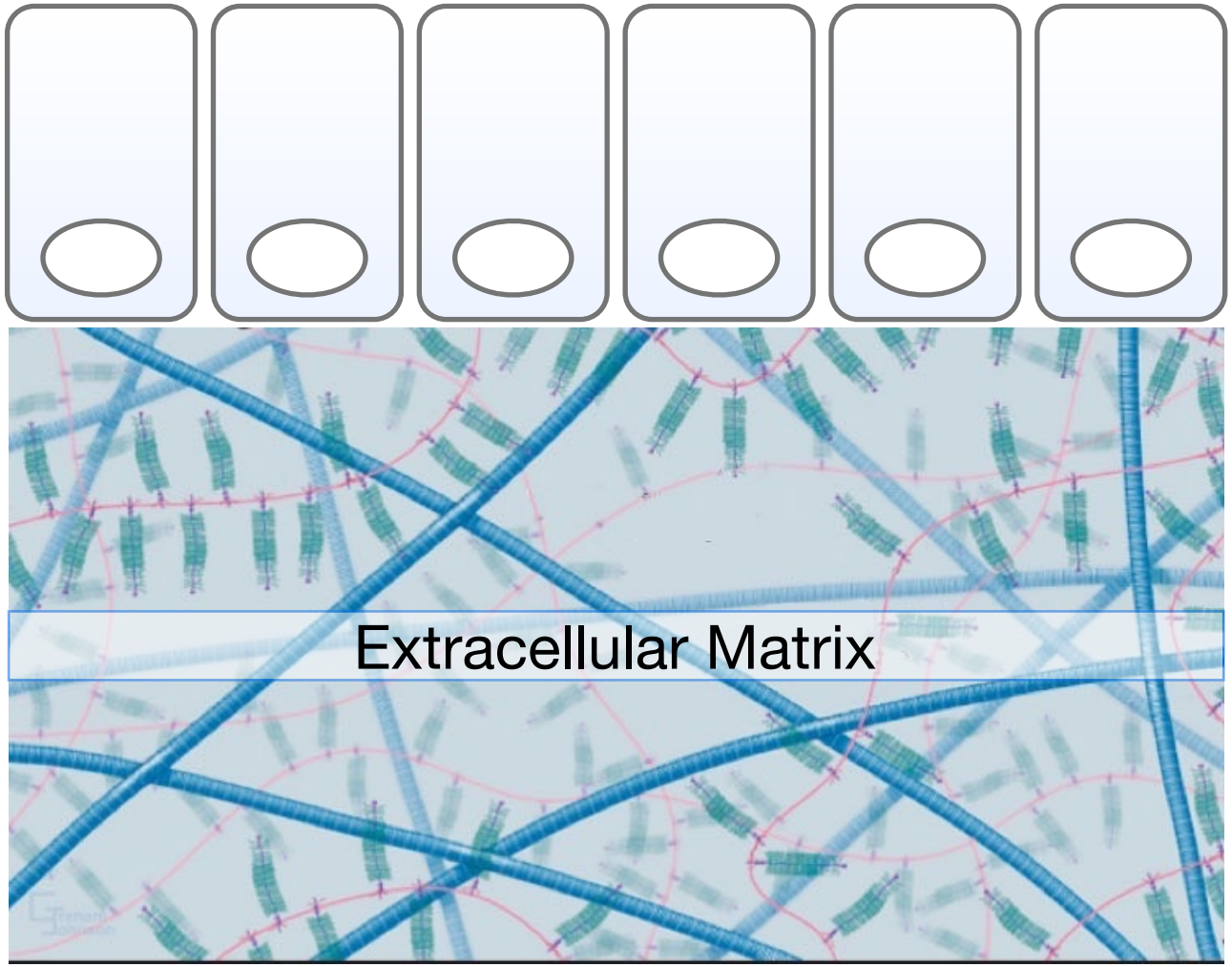
MD CURRICULUM

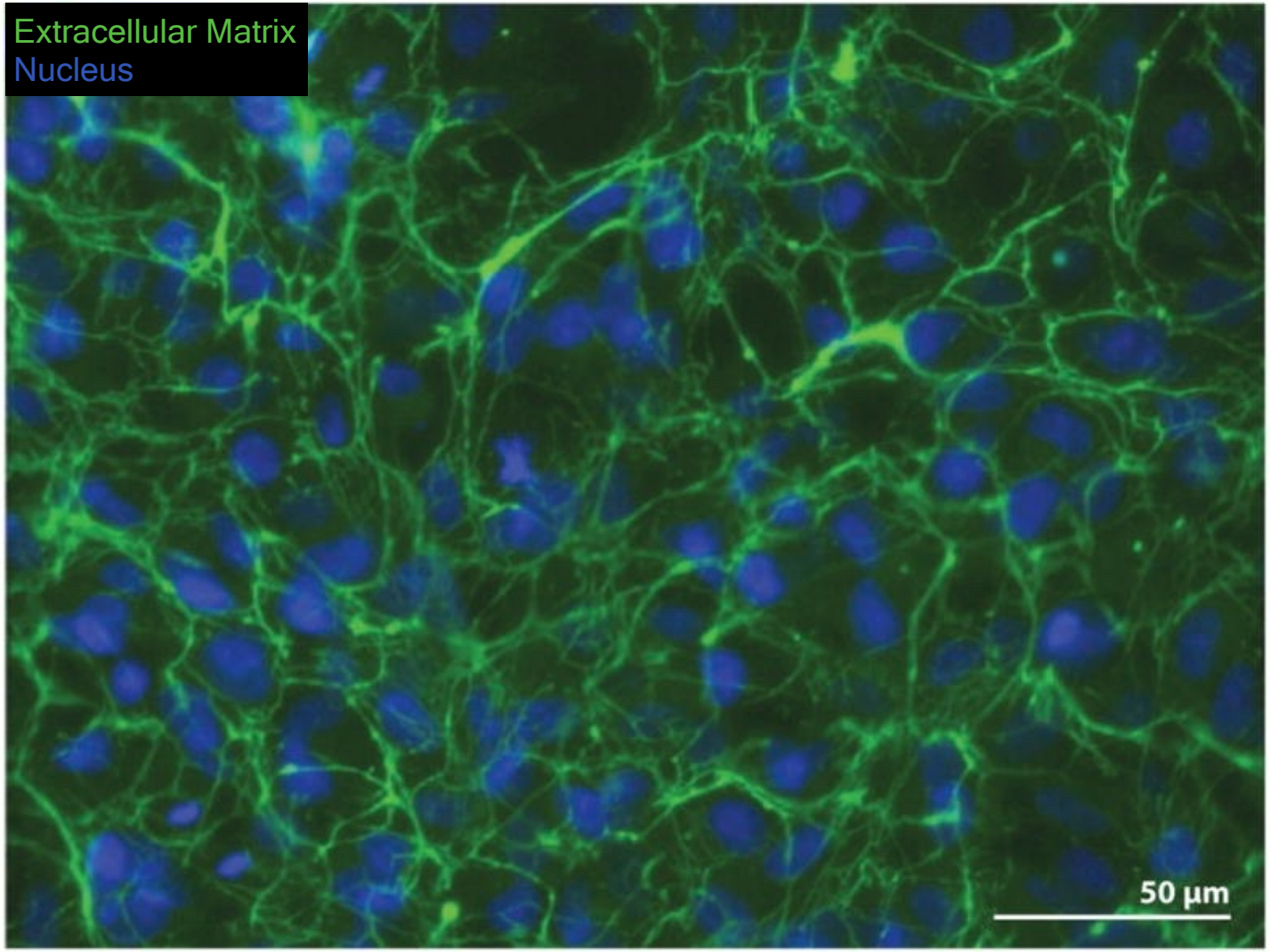
What we will talk about…

- Overview of functions
- Components
- Turnover

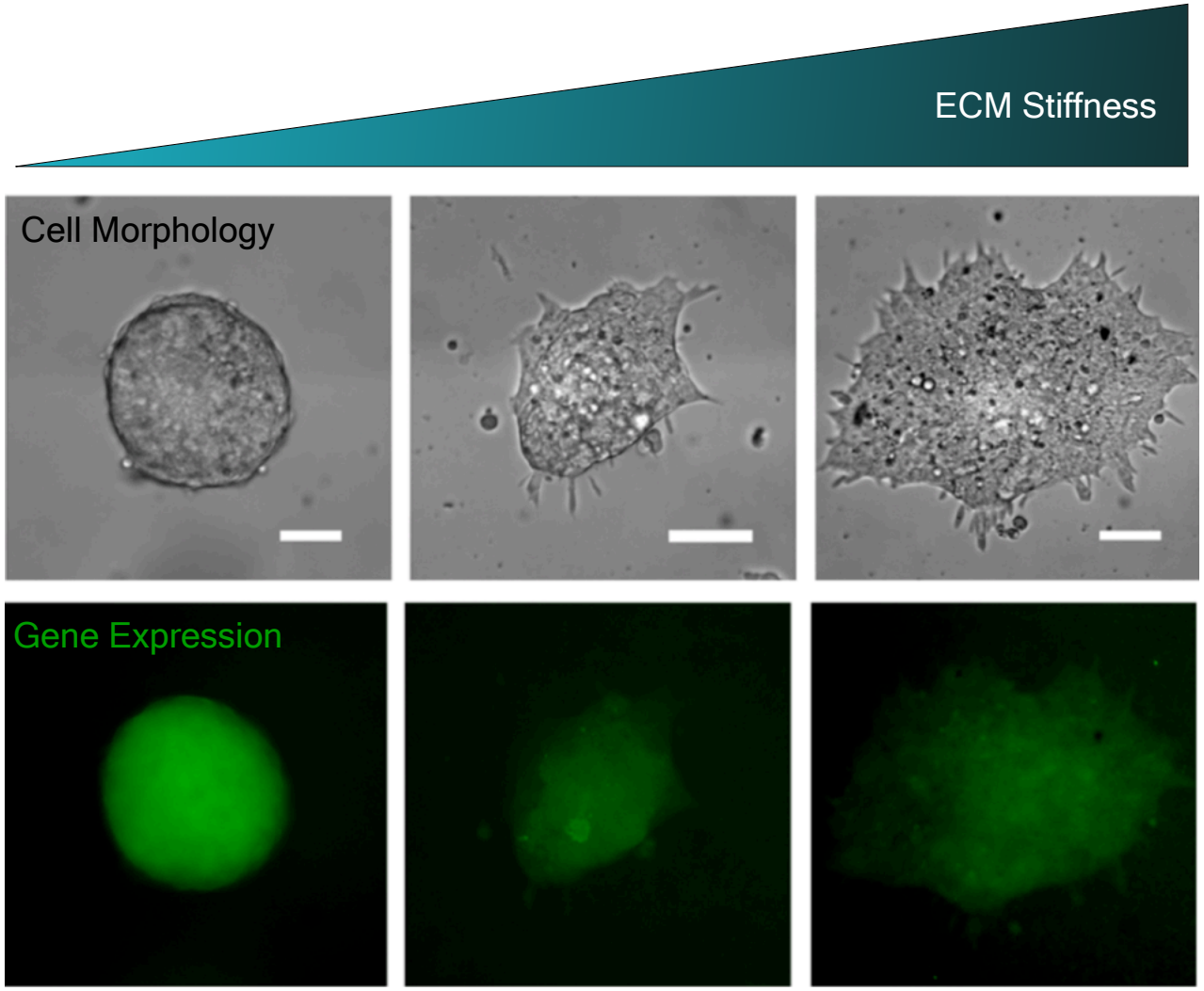
ECM provides structural support to cells.



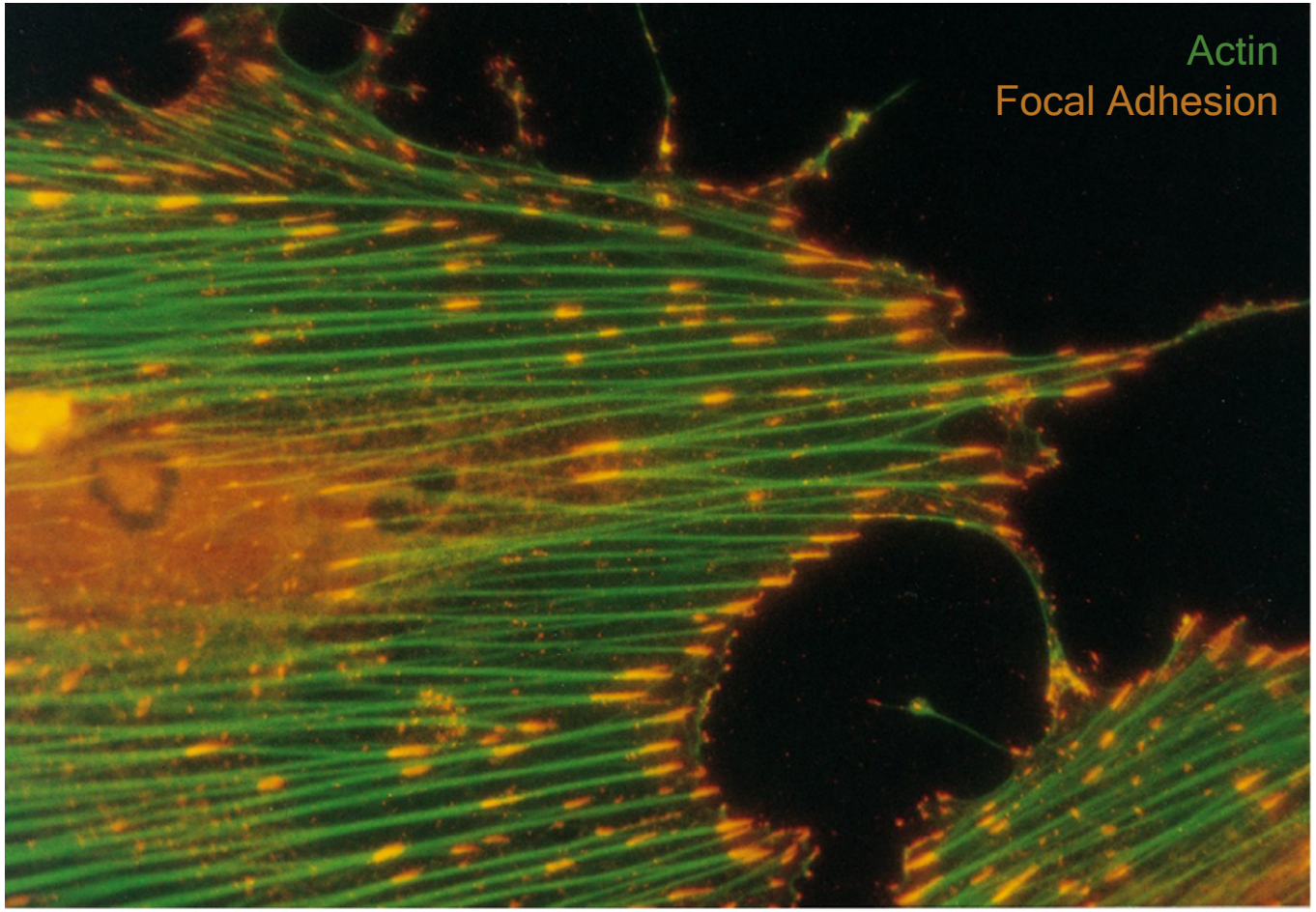
ECM provides structural support to cells.



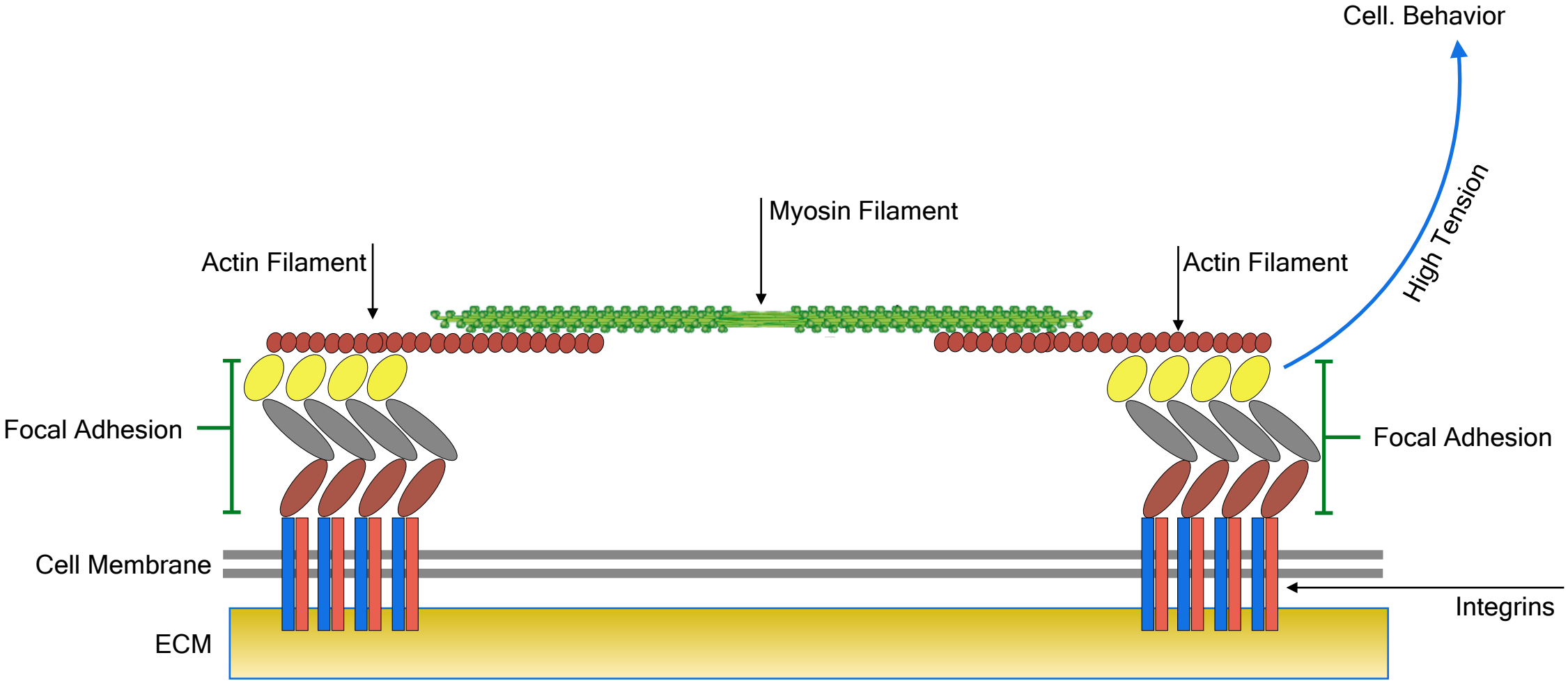
Extracellular matrix regulates cell behavior.



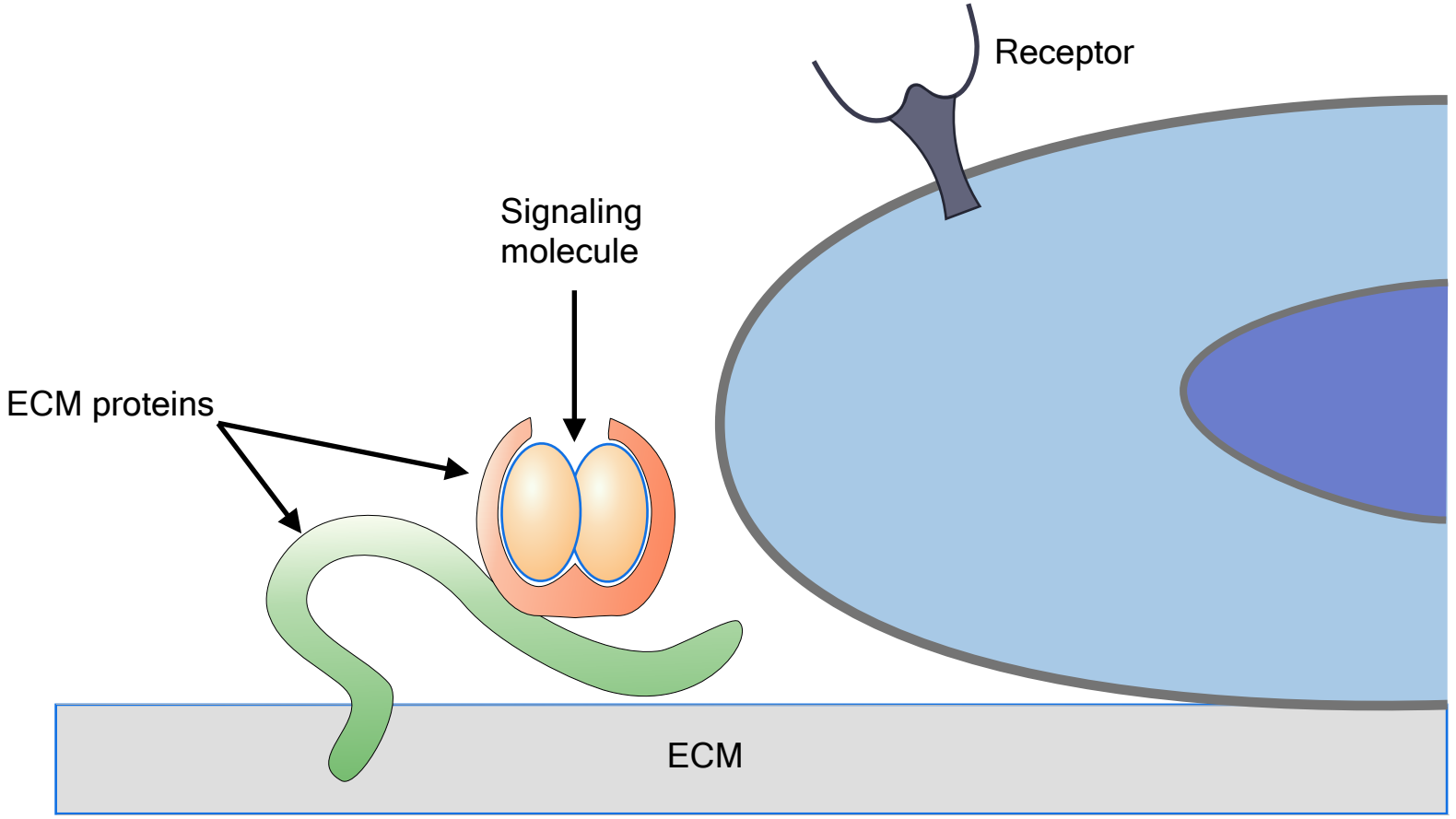
Cells connect to extracellular matrix at sites called focal adhesions.



Cells measure ECM stiffness through tension generated by myosin and actin.

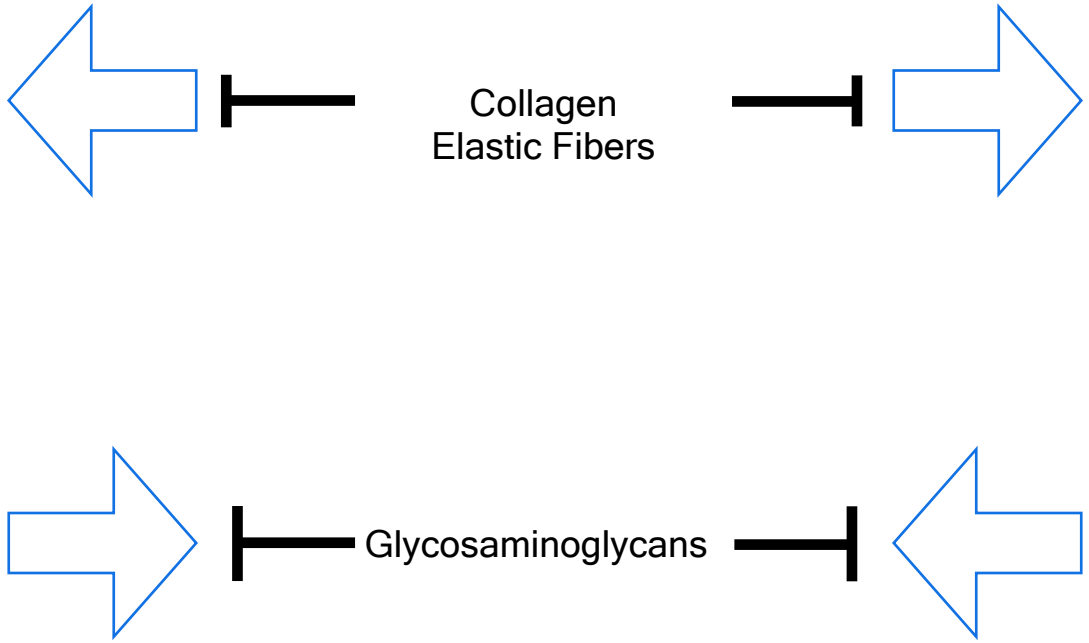


ECM regulates cell behavior by controlling the concentration of signaling molecules.



Components of the Extracellular Matrix

Extracellular matrix resists tension and compression.

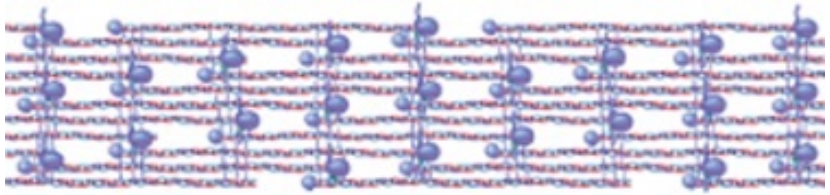


Collagen

Collagens are a large family of proteins that form different structures and have different mechanical properties.

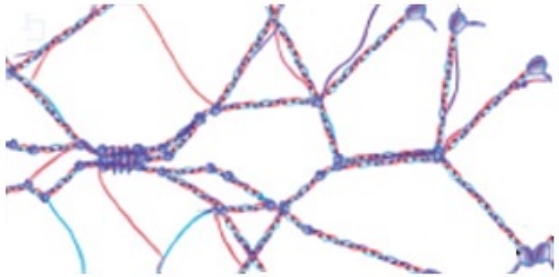
Fibrillar:

- Type I: Bone, ligament, skin, tendon
- Type II: Collagen
- Type III: Reticular fibers

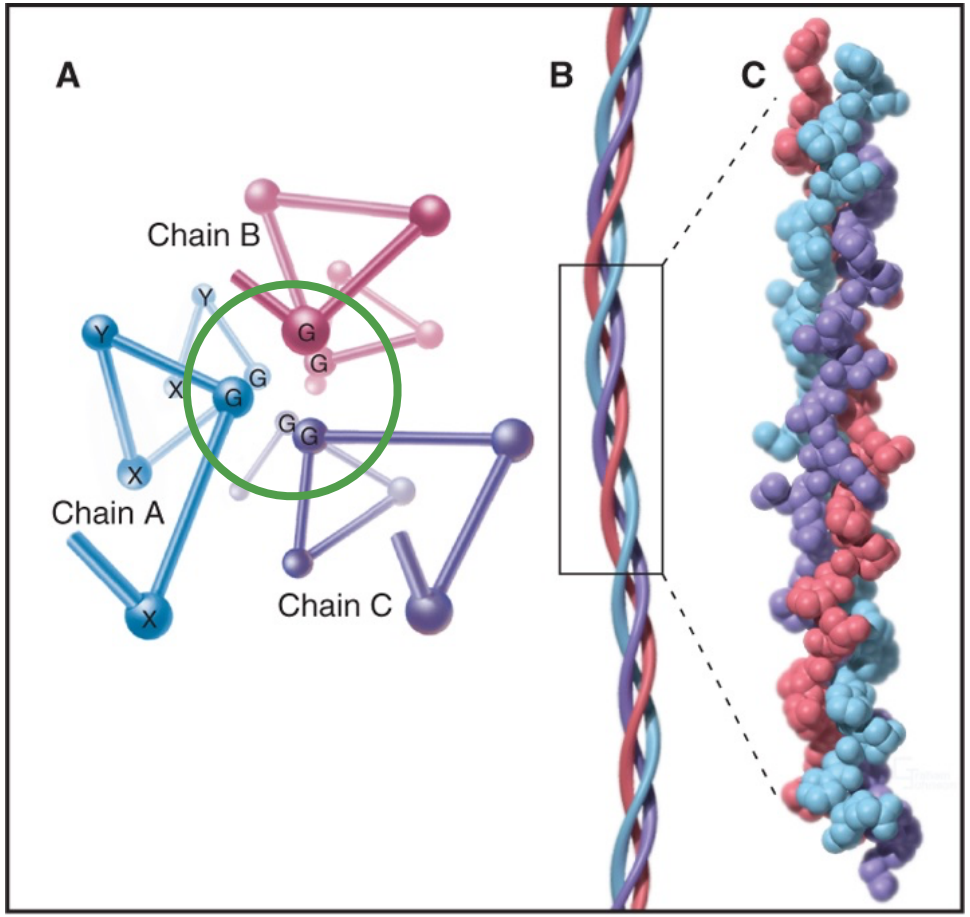


Network

- Type IV: Basement membrane



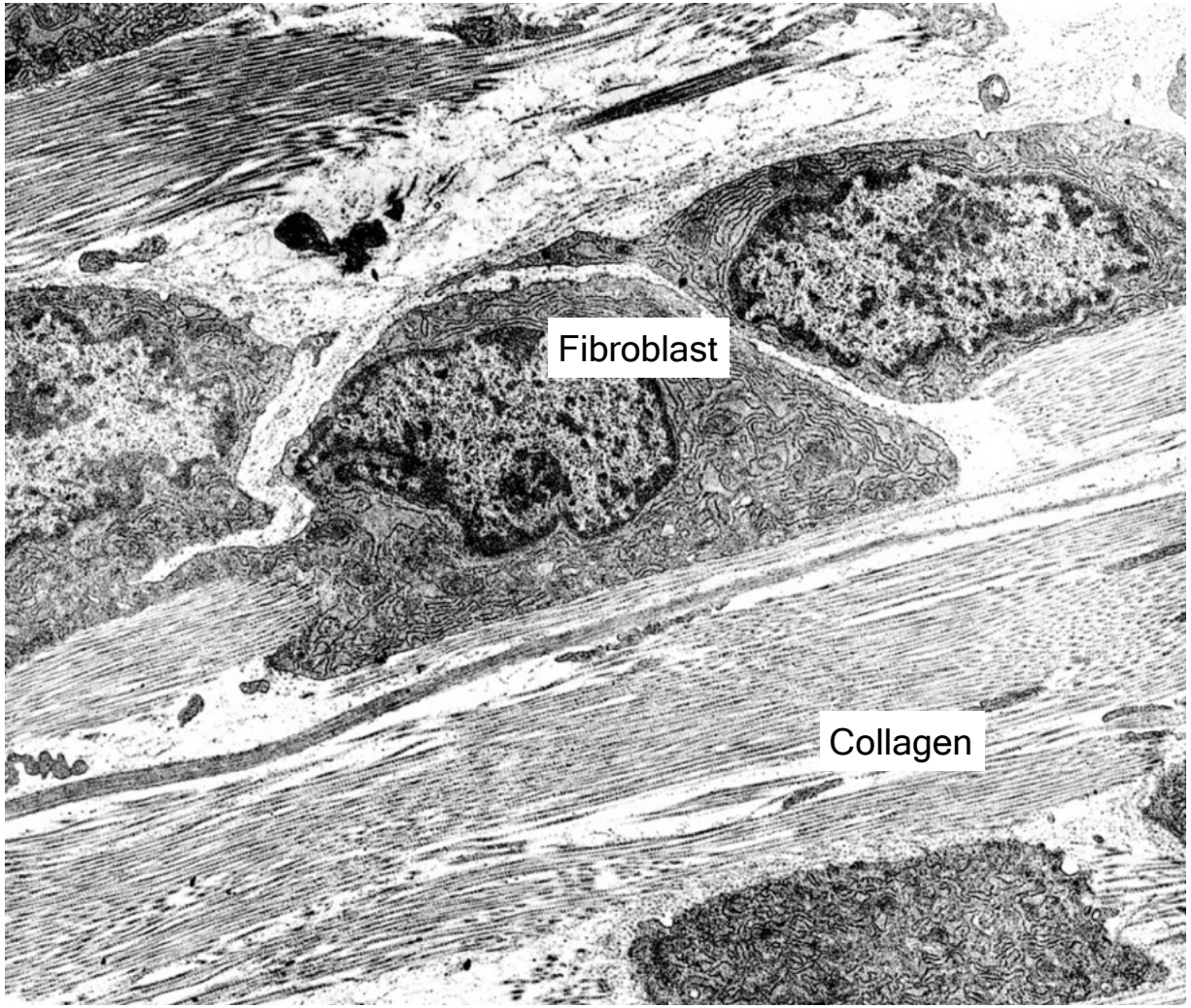
Three collagen polypeptides associate to form rope-like structures.



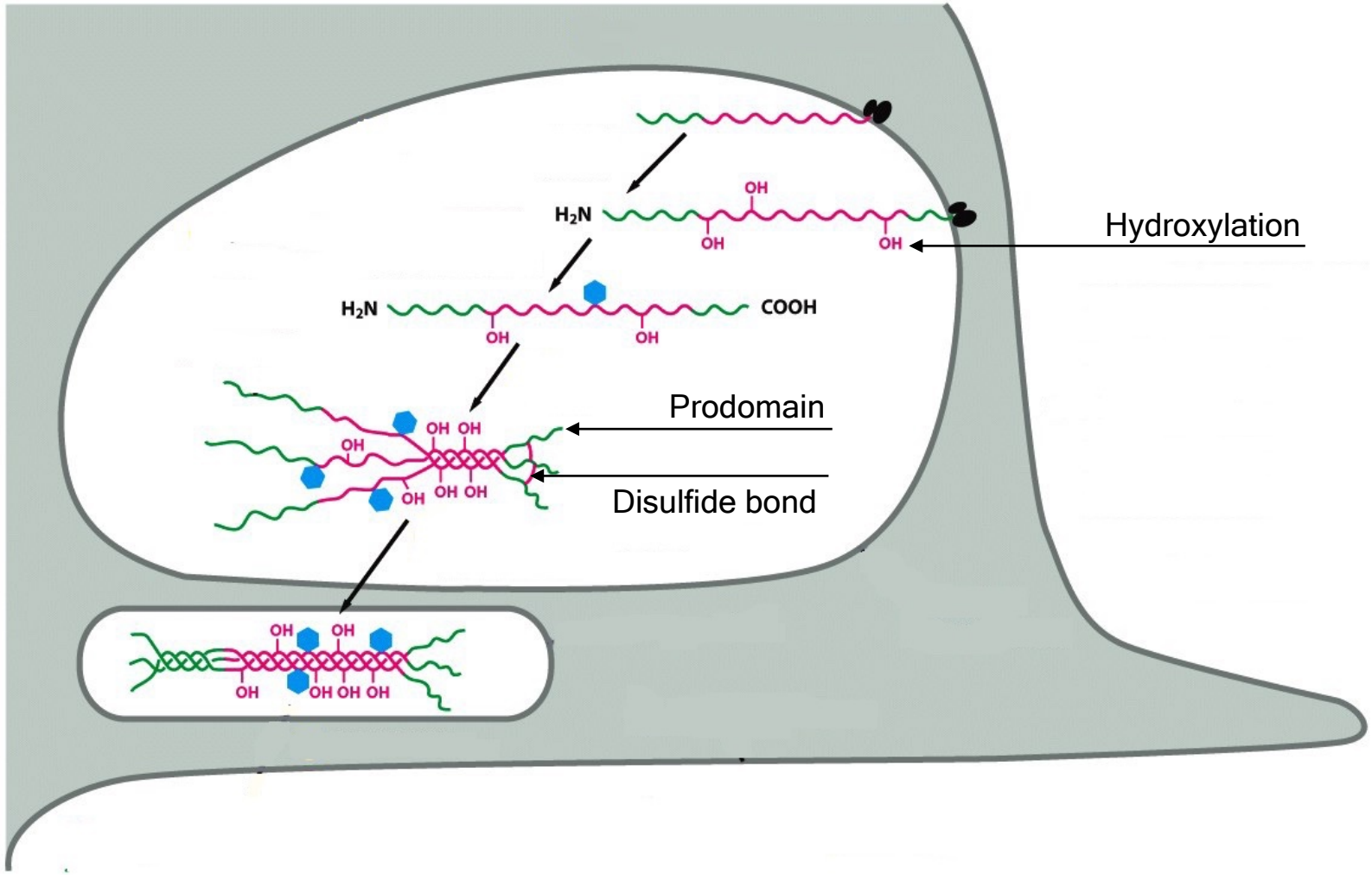
Collagen Genes

- Type I Collagen: *COL1A1* and *COL1A2*
- Type II Collagen: *COL2A1*
- Type III Collagen: *COL3A1*
- Type IV Collagen: *COL4A1 - COL4A6*

Fibroblasts synthesize and process collagen.



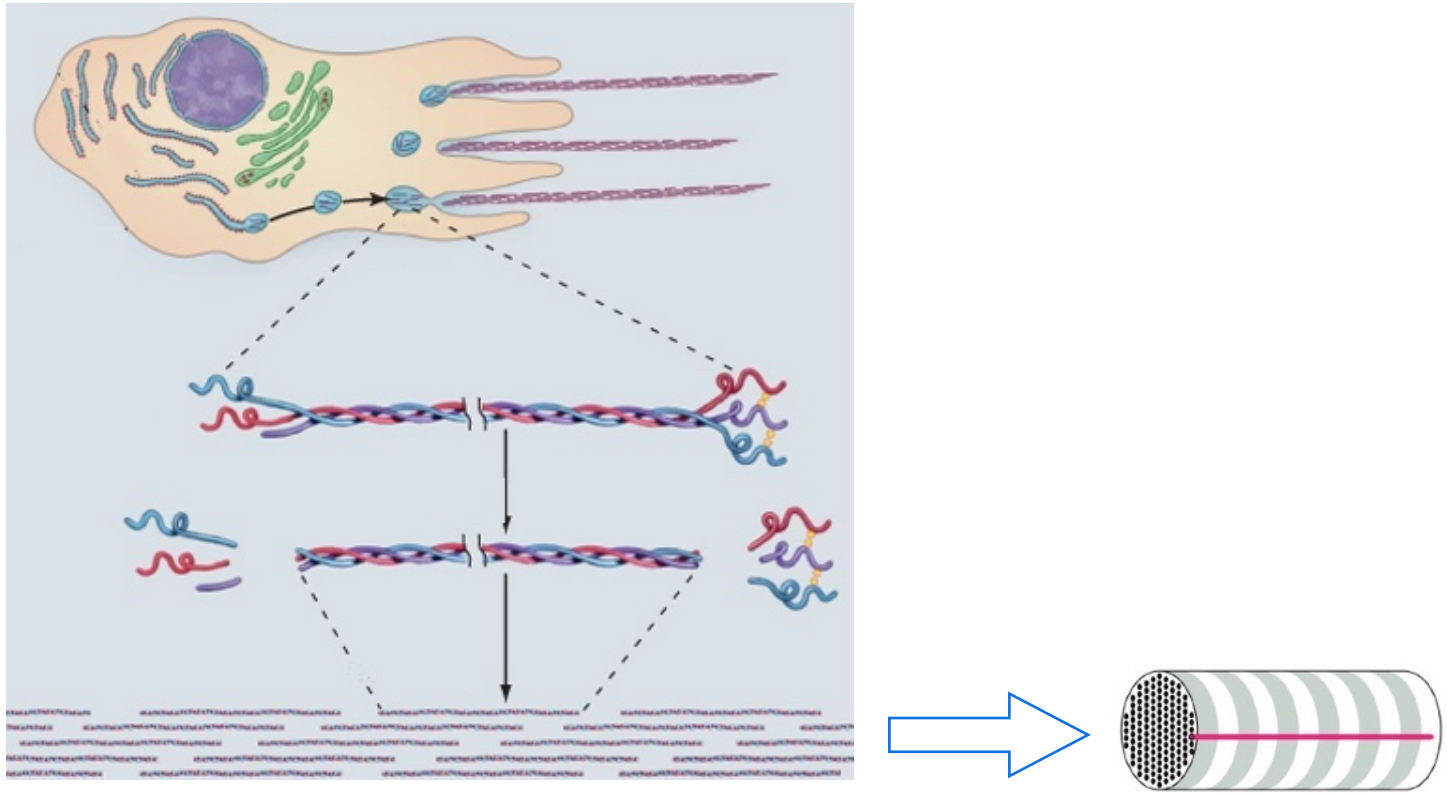
Fibroblasts synthesize and secrete collagen via secretory pathway.



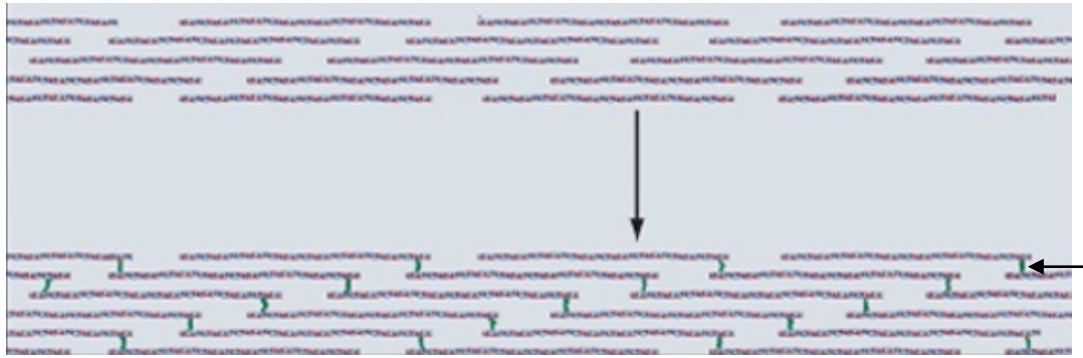
Removal of prodomains outside the cell allows collagen to assemble into fibrils.

Remove prodomains

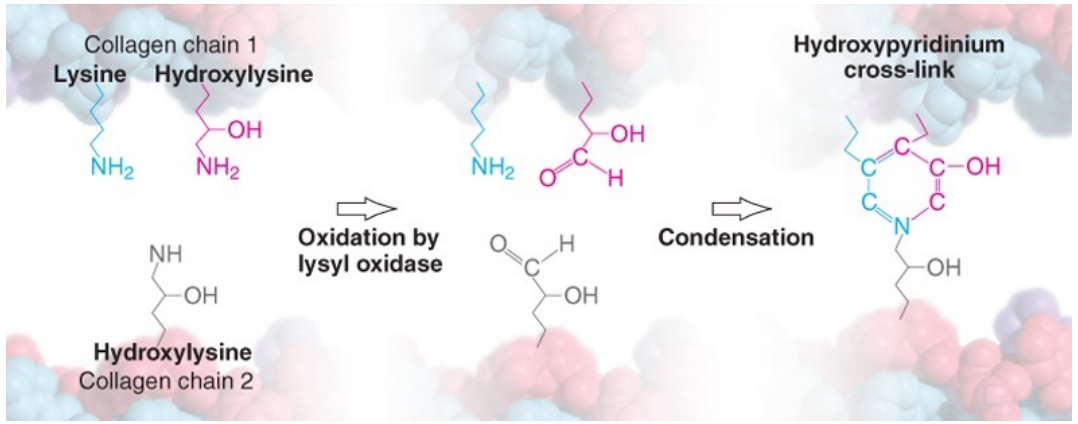
Assemble into a fibril



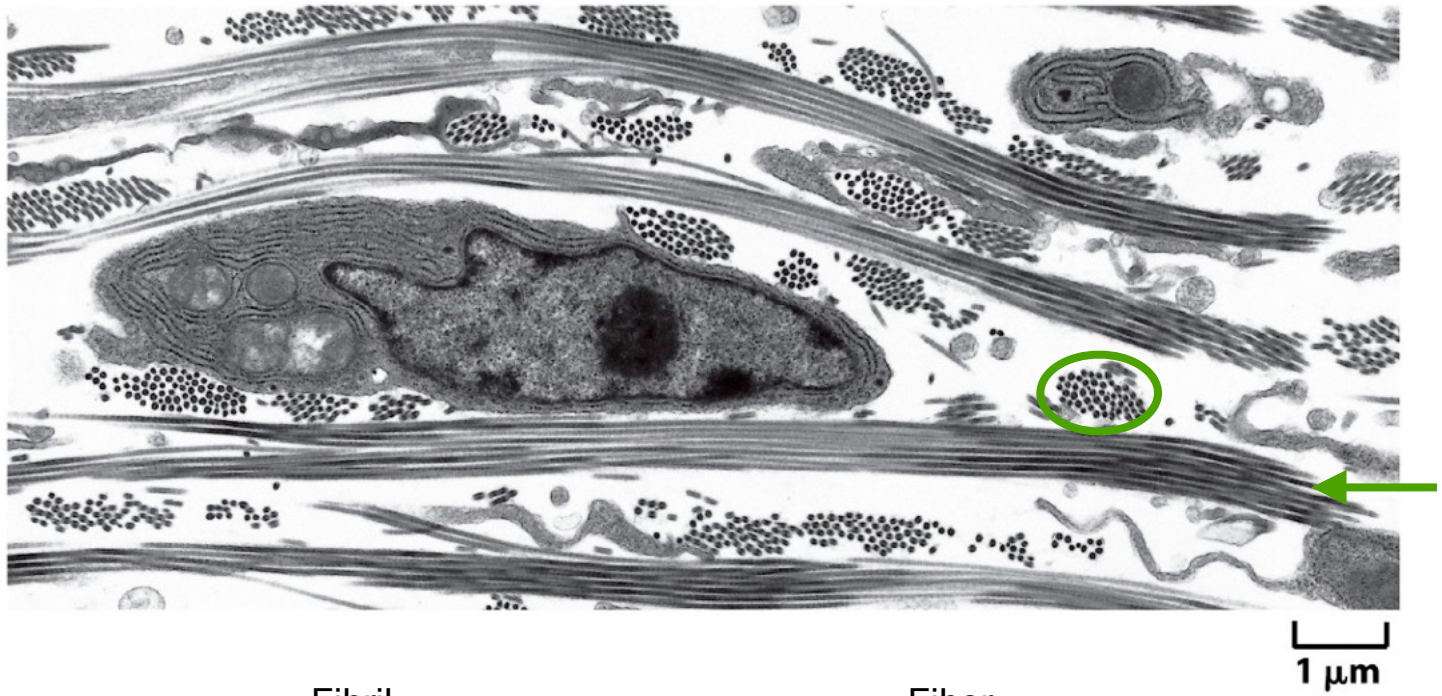
Lysyl oxidase catalyzes covalent bonds between hydroxylated amino acids in adjacent trimers.



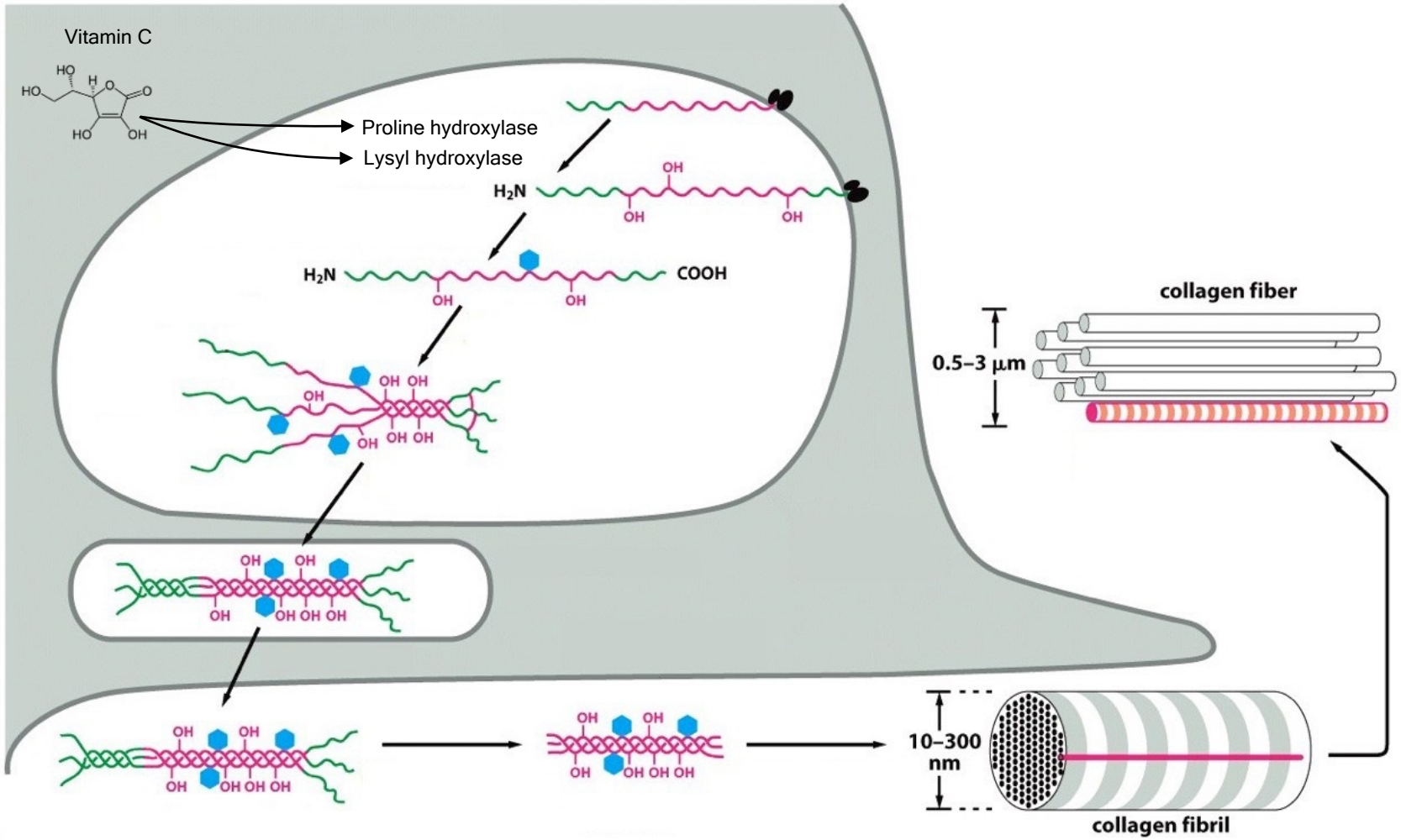
Covalent attachment



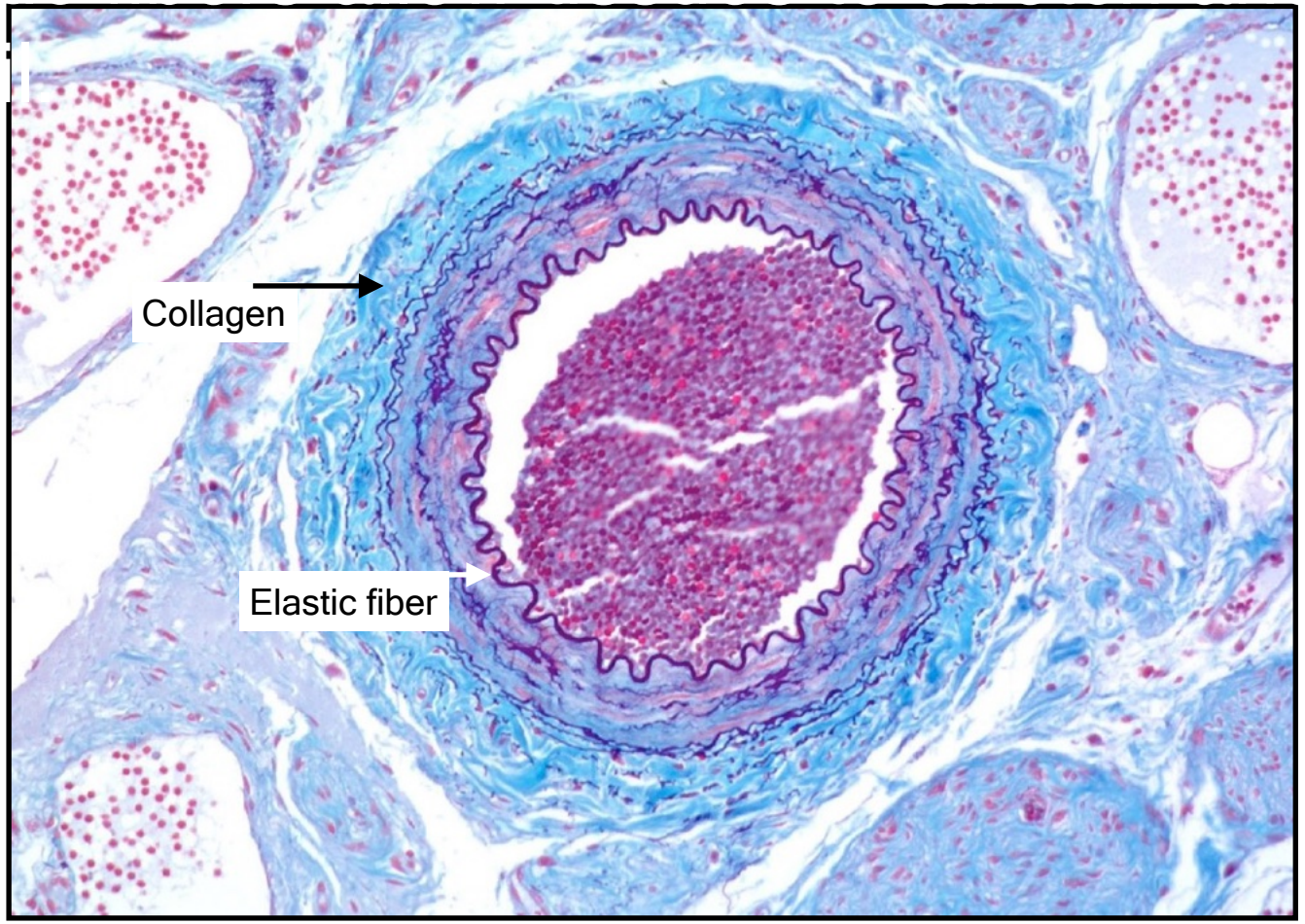
Type I collagen fibrils aggregate to form fibers.



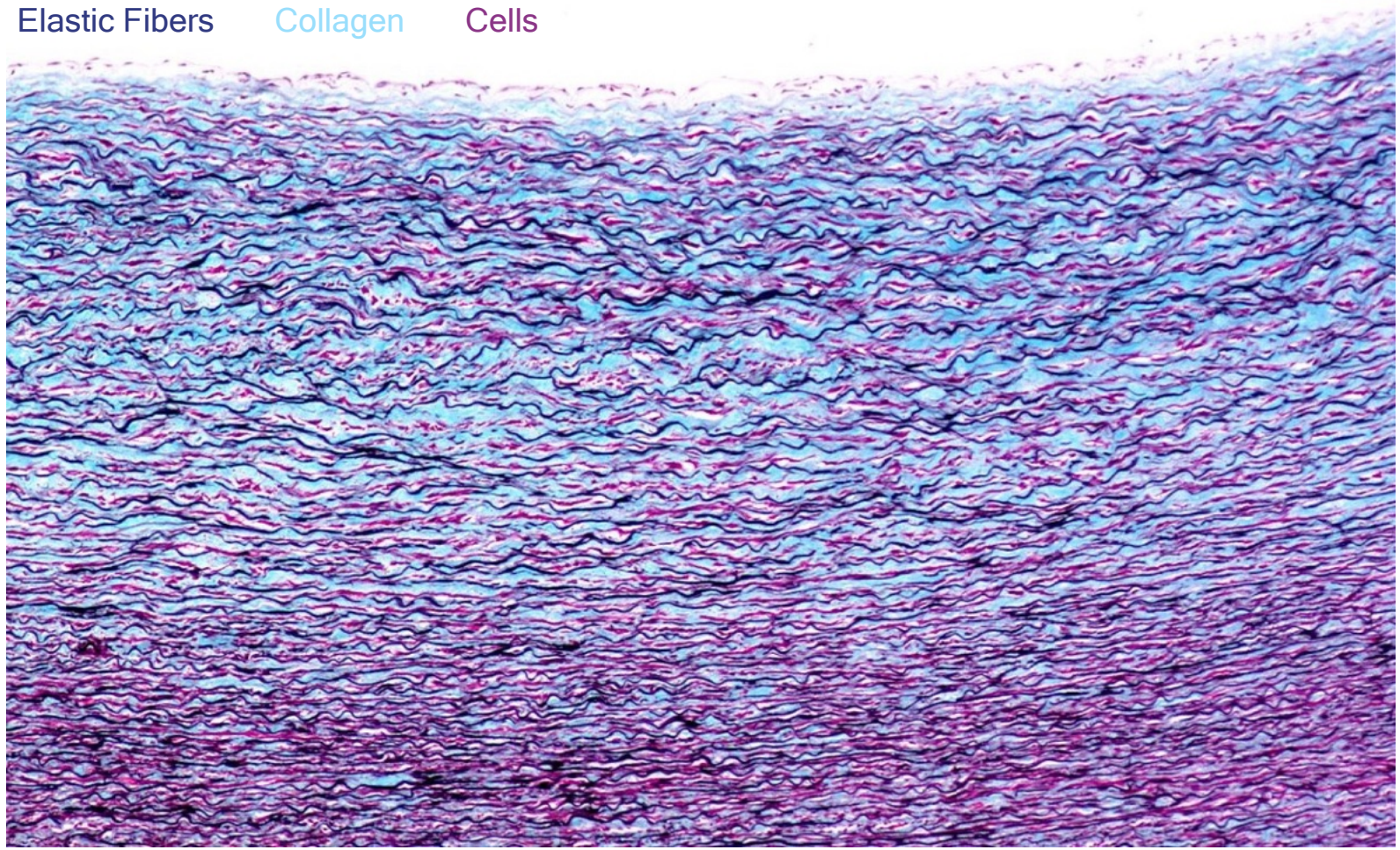
Vitamin C is a critical cofactor in the assembly of collagen fibrils.



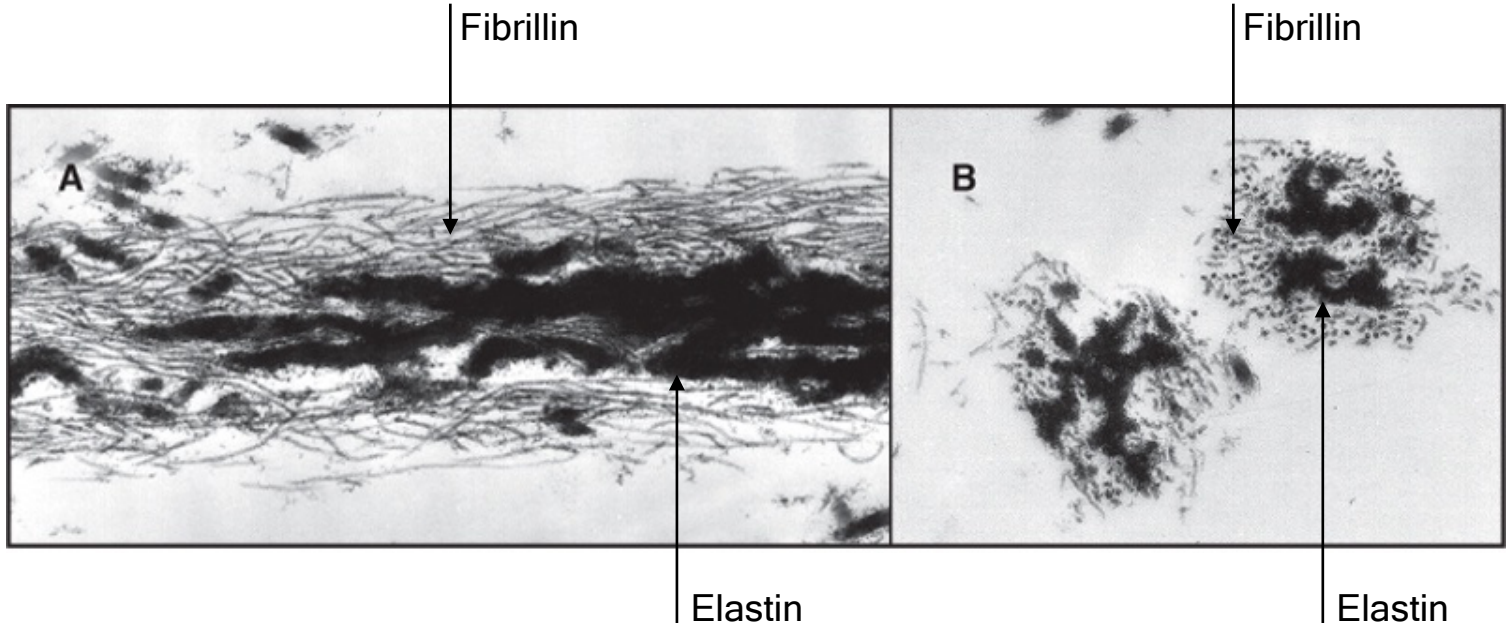
Elastic Fibers


Collagen
Elastic fiber

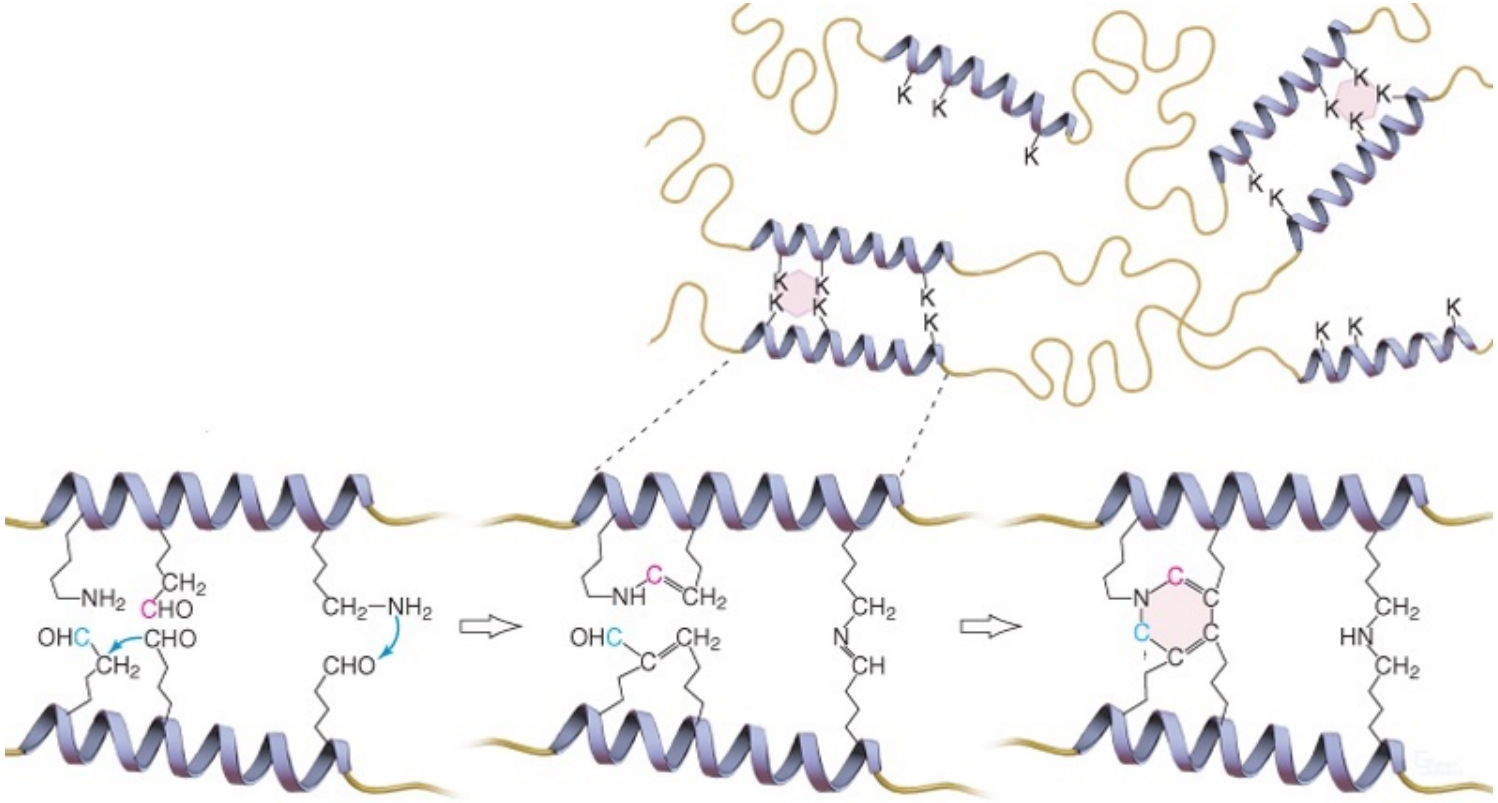
Wall of the aorta has a high concentration of elastic fibers.



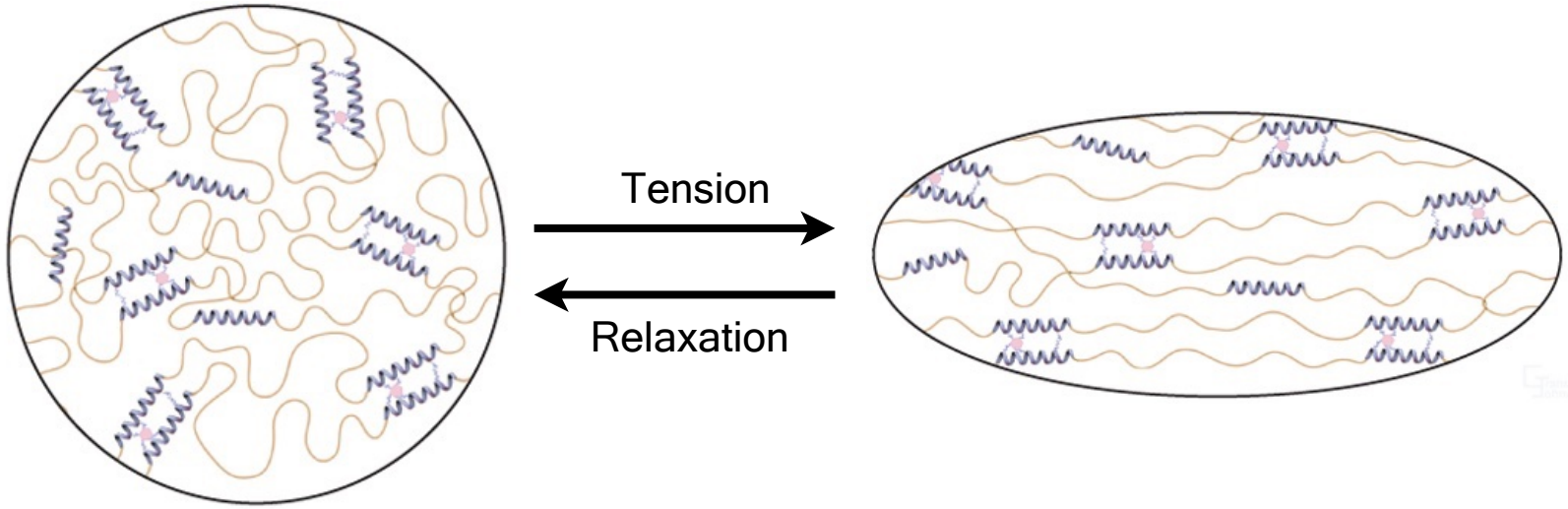
Elastic fibers are a composite of elastin and fibrillin.



Elastin is an unstructured protein that is crosslinked into networks.



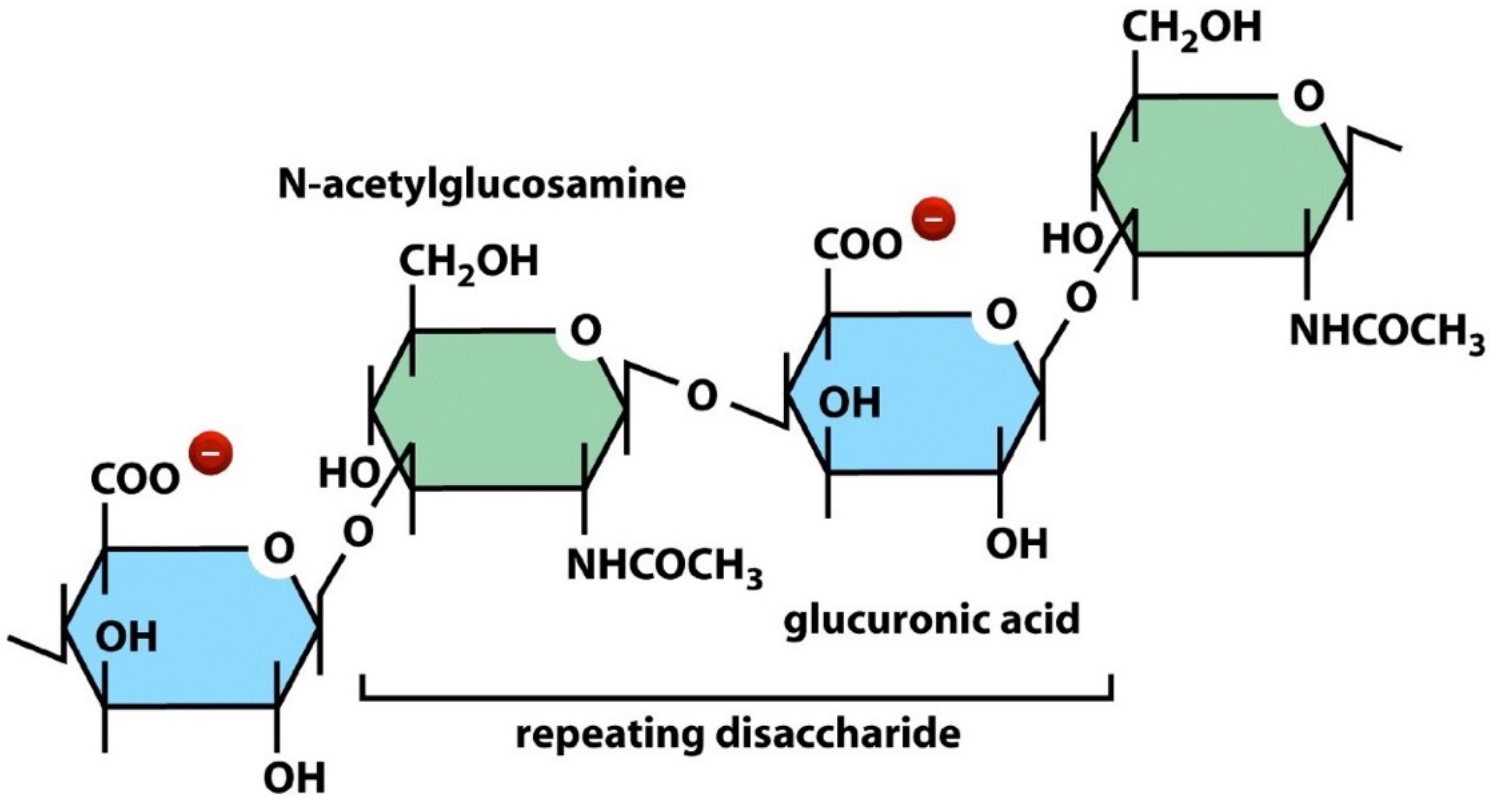
Tension generates order in elastin networks that provides energy for recoil.



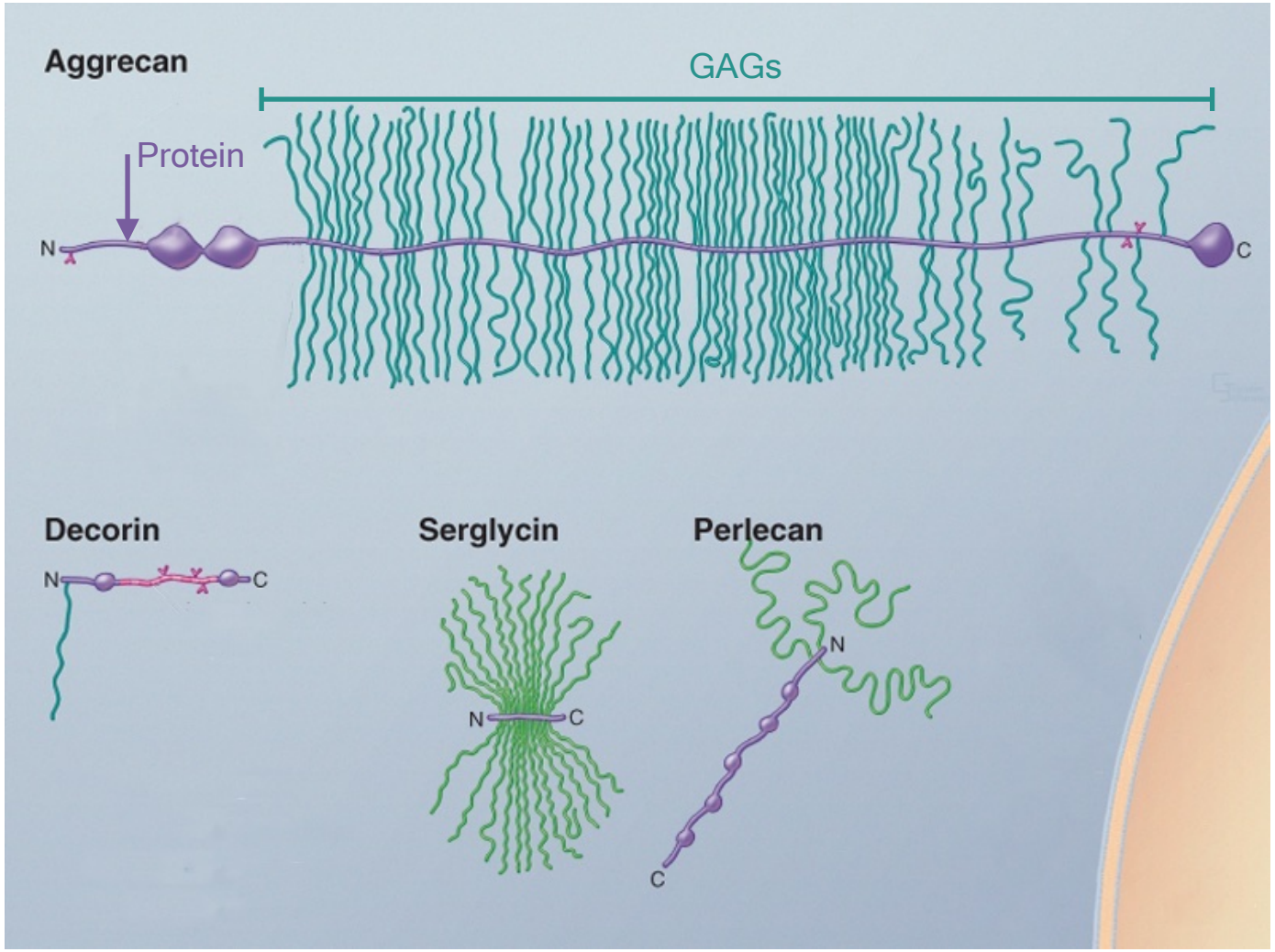
Glycosaminoglycans

Glycosaminoglycans (GAGs) in connective tissue resist compression by retaining water.

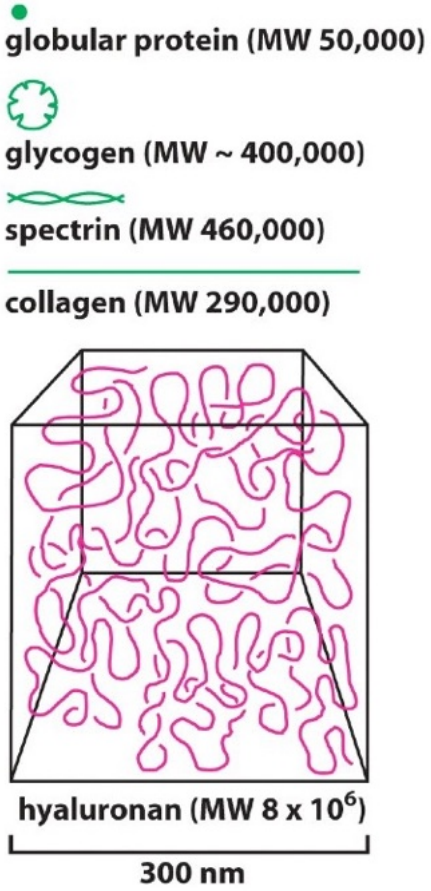
Glycosaminoglycans are long chains of repeating disaccharides.



Proteoglycans are single polypeptide with several attached glycosaminoglycans.

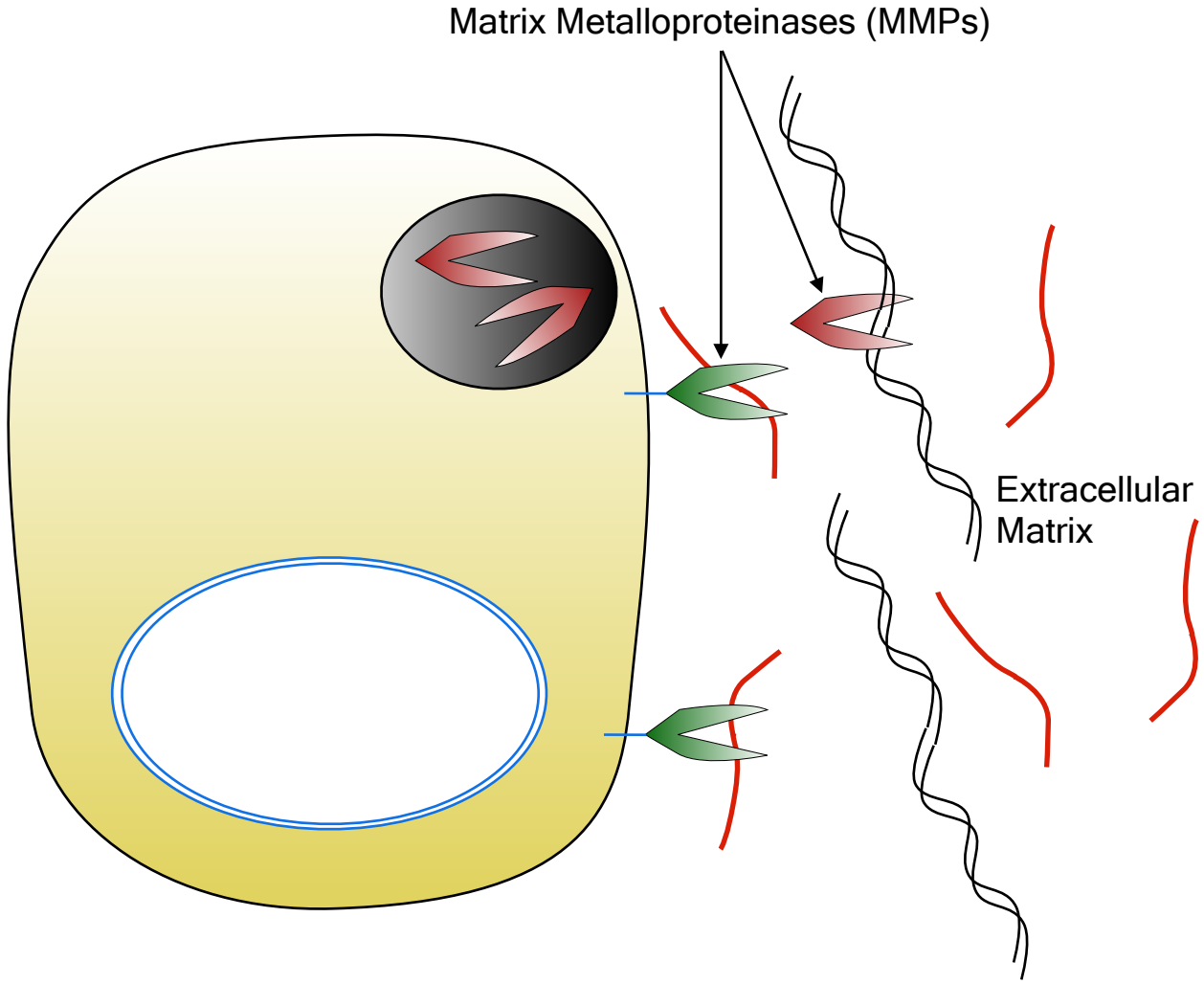


Hyaluronan is a long polymer of disaccharides that occupies a large volume.

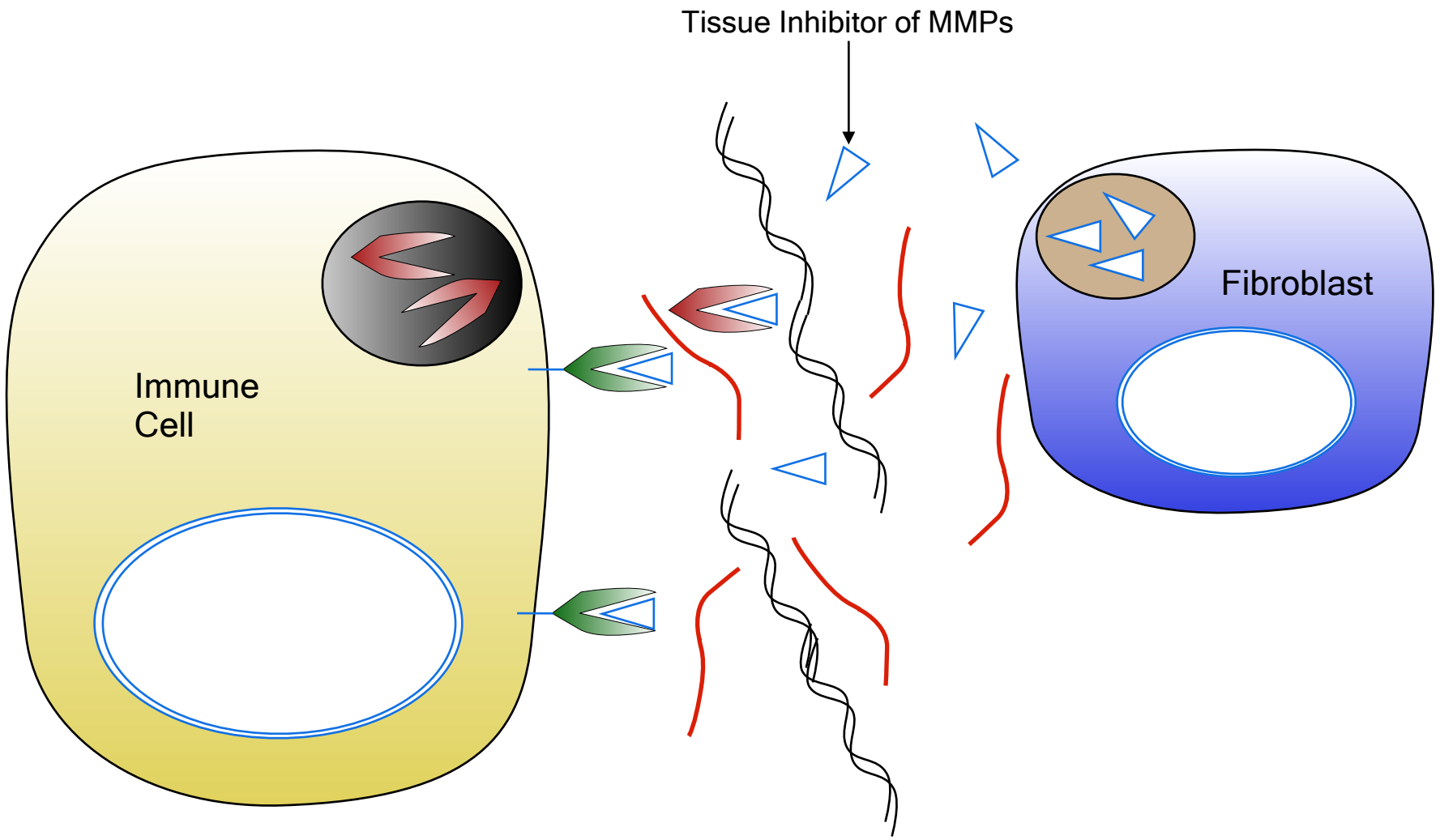


Turnover of ECM

Some cells produce enzymes that digest components of extracellular matrix.



Fibroblasts secrete tissue inhibitors of metalloproteases (TIMPs) to limit digestion.



Take home points...

- Mechanical properties of connective tissue is determined by amount and arrangement of collagen, elastic fibers and glycosaminoglycans.
- Fibril collagens resist tensions and are formed from parallel arrays of collagen trimers.
- Elastic fibers allow tissues to stretch and recoil and contain elastin and fibrillin.
- Glycosaminoglycans contain large amounts of disaccharide chains and resist compression.
- Regulation of turnover of ECM is critical for maintaining structural integrity.