

What the Joint Tells the Brain and Immune System

Joint Proprioception and Osteoimmunology

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Anatomy

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Movement

Self-Awareness



Mind and Movement

<https://www.mindandmovement.com.au/self-awareness-why-bother/>

Proprioception - The Sixth Sense*

Three Major Sources of Proprioception

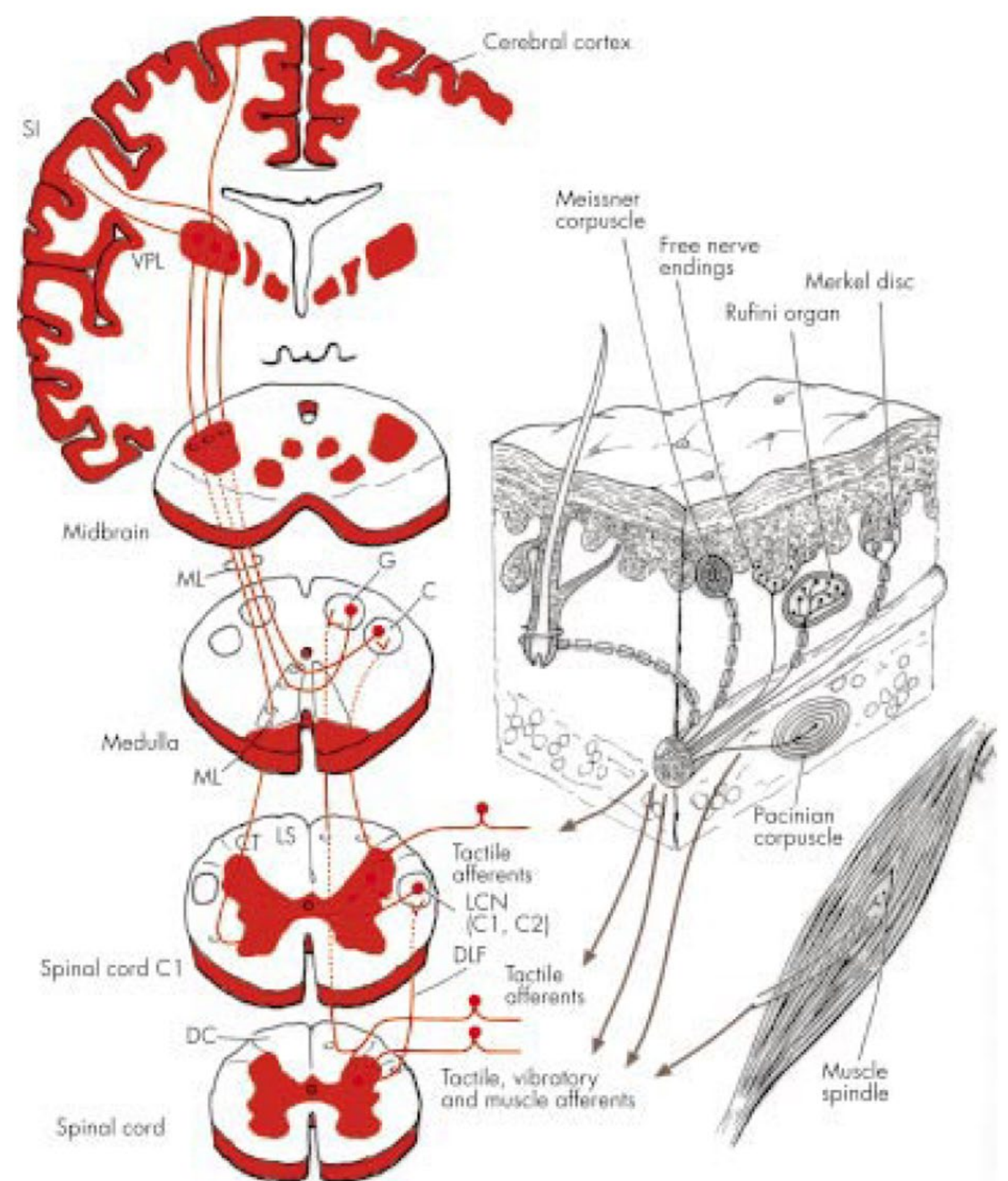
- Somatic sensory system
 - Muscle spinal apparatus
 - Cutaneous touch corpuscles
 - Joint receptor endings
- Vestibular system
- Visual system

* Sir Charles Bell, 1833

Proprioception

Three Major Sources of Proprioception

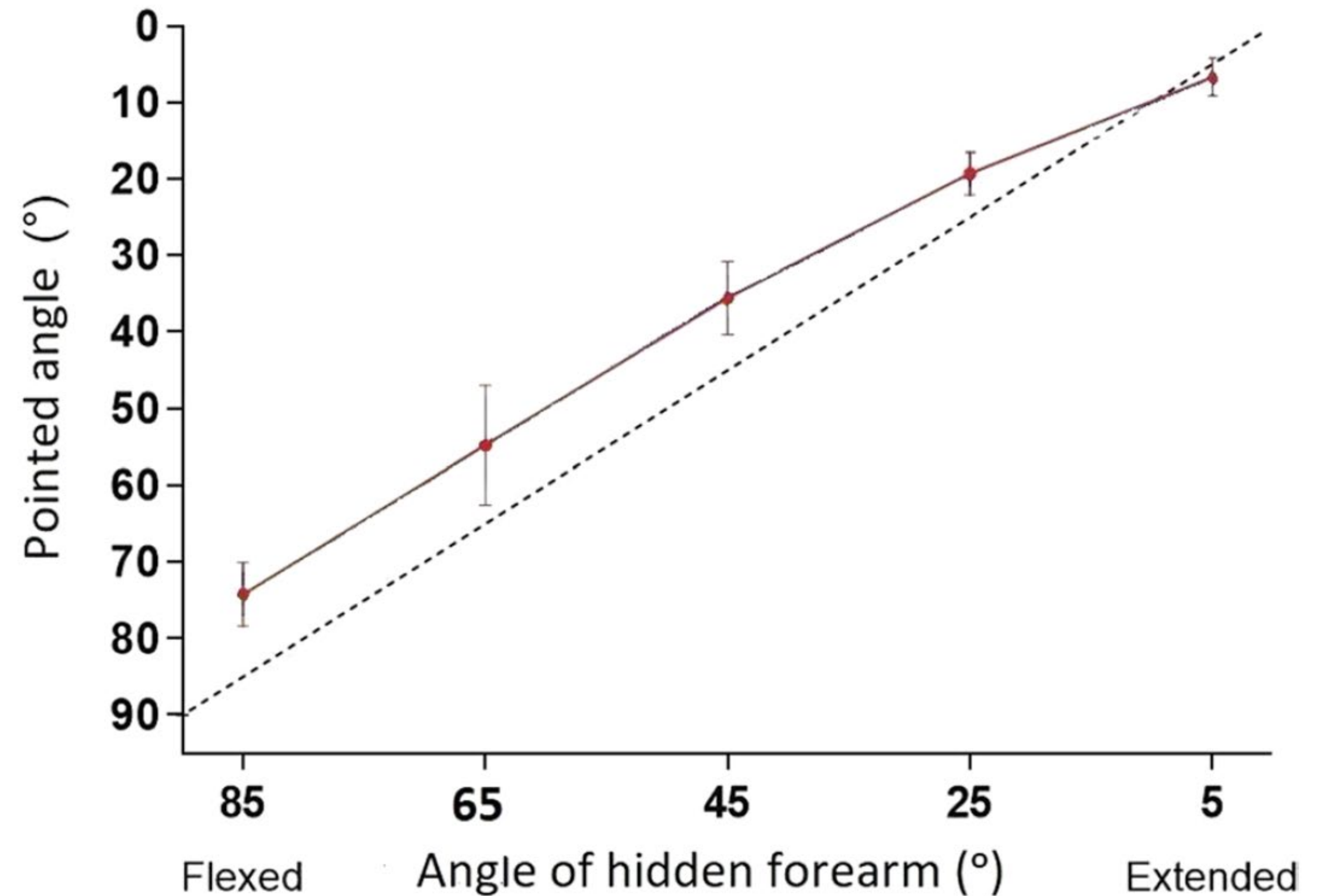
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 - ~~Joint receptor endings~~
- Vestibular system
- Visual system



Proprioception

End-range of Joint Function

- Hypothesis: End-range precision is facilitated by the joint receptors



Proske U. 2023. A reassessment of the role of joint receptors in human position sense. *Exp Brain Res* 241: 943-49

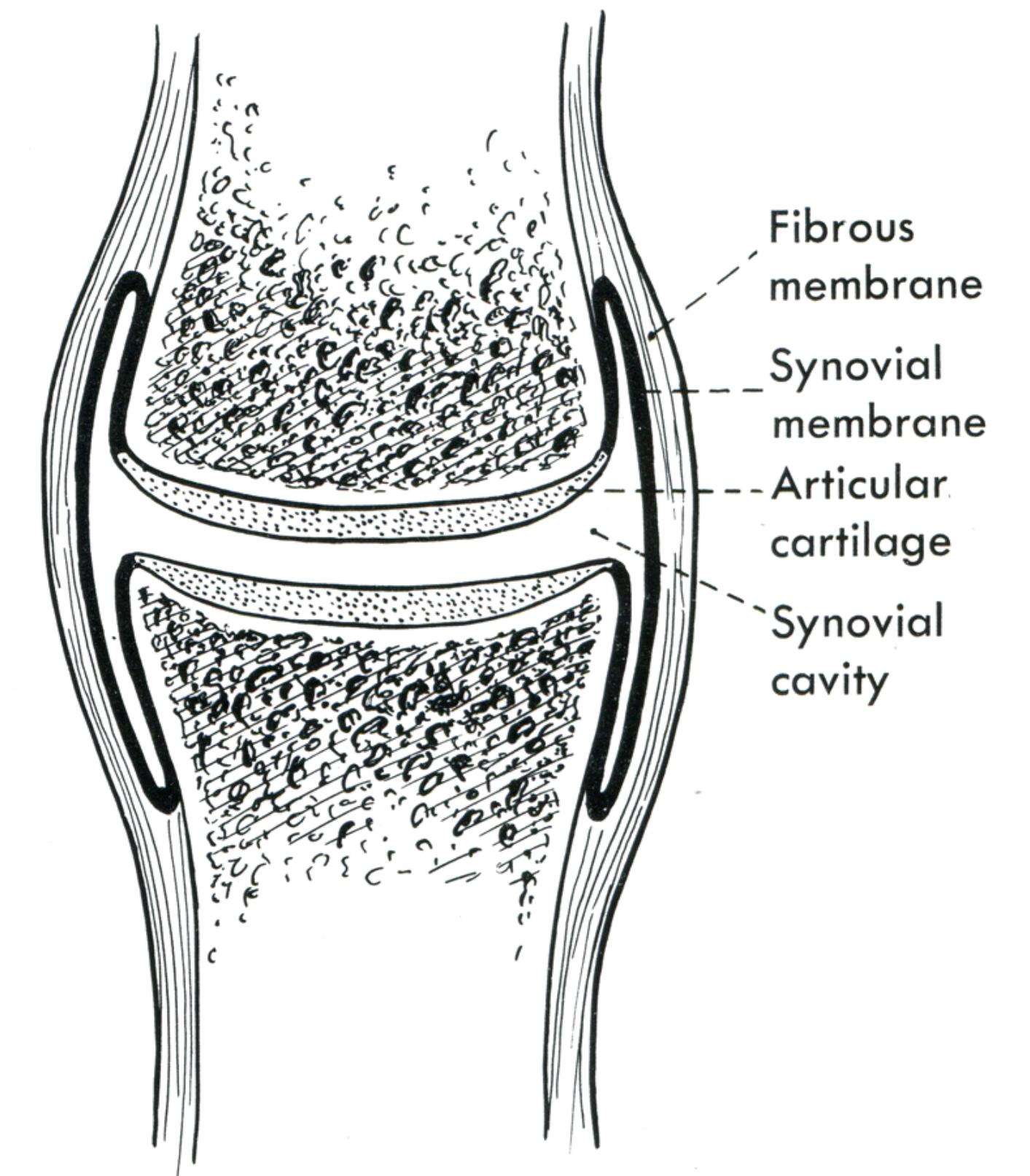
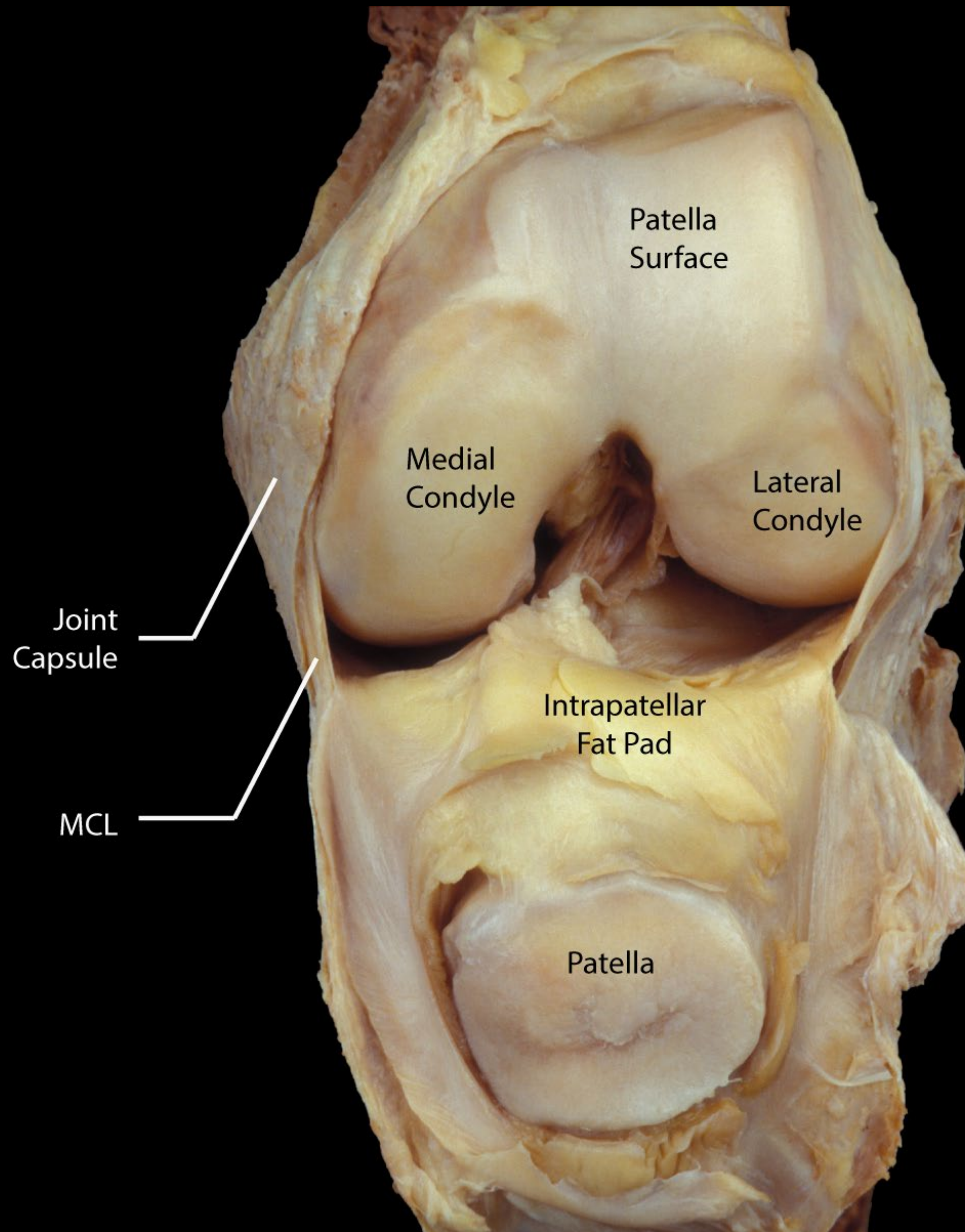
Synovial Joint

Diarthroses

Capsule

Synovial membrane

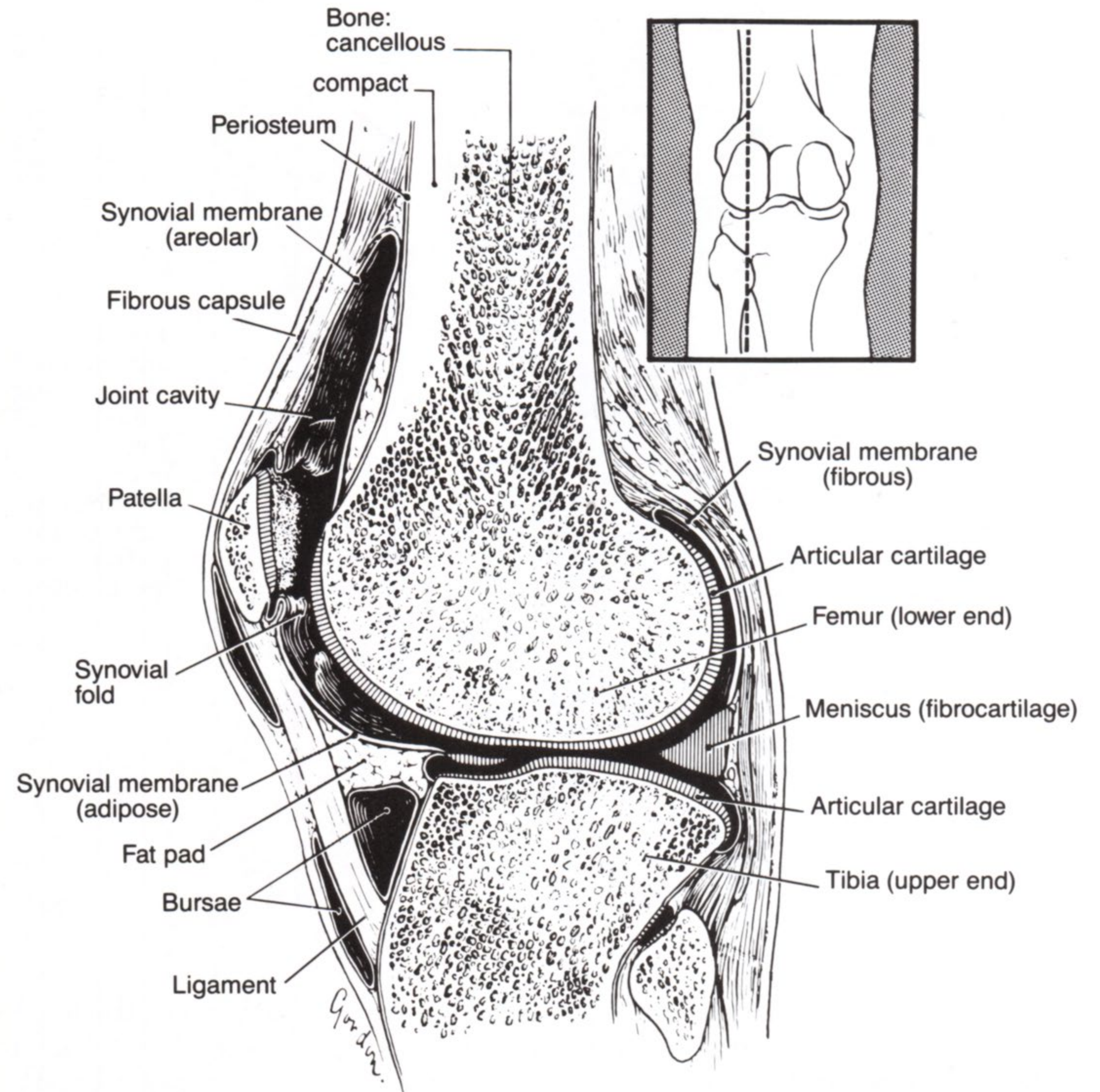
Articular surface



Joint Anatomy

Synovial joint

Capsule
Space
Synovium
Bursa
Fat pad
Menisci
Ligaments
Articular surfaces

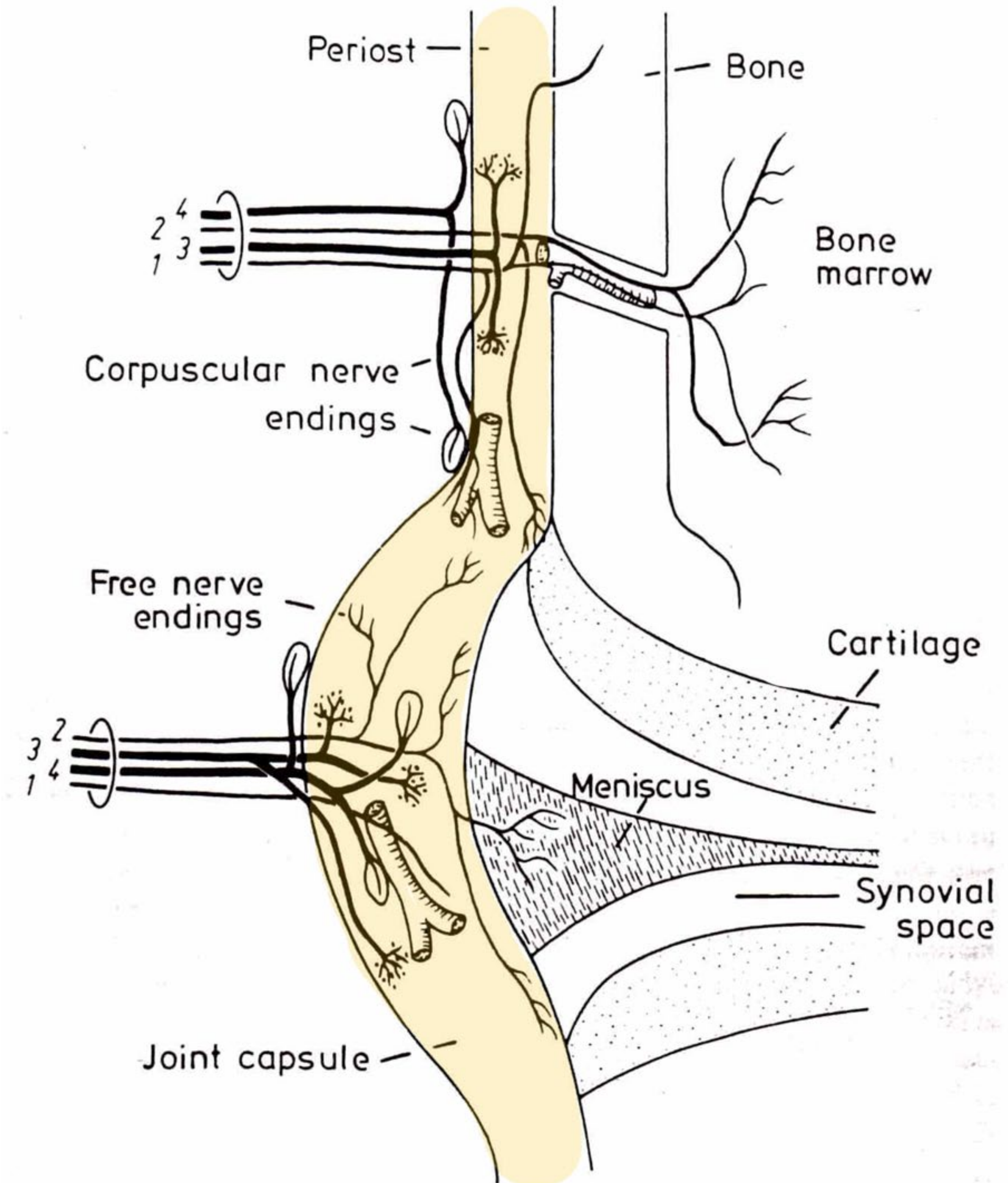


Proprioception

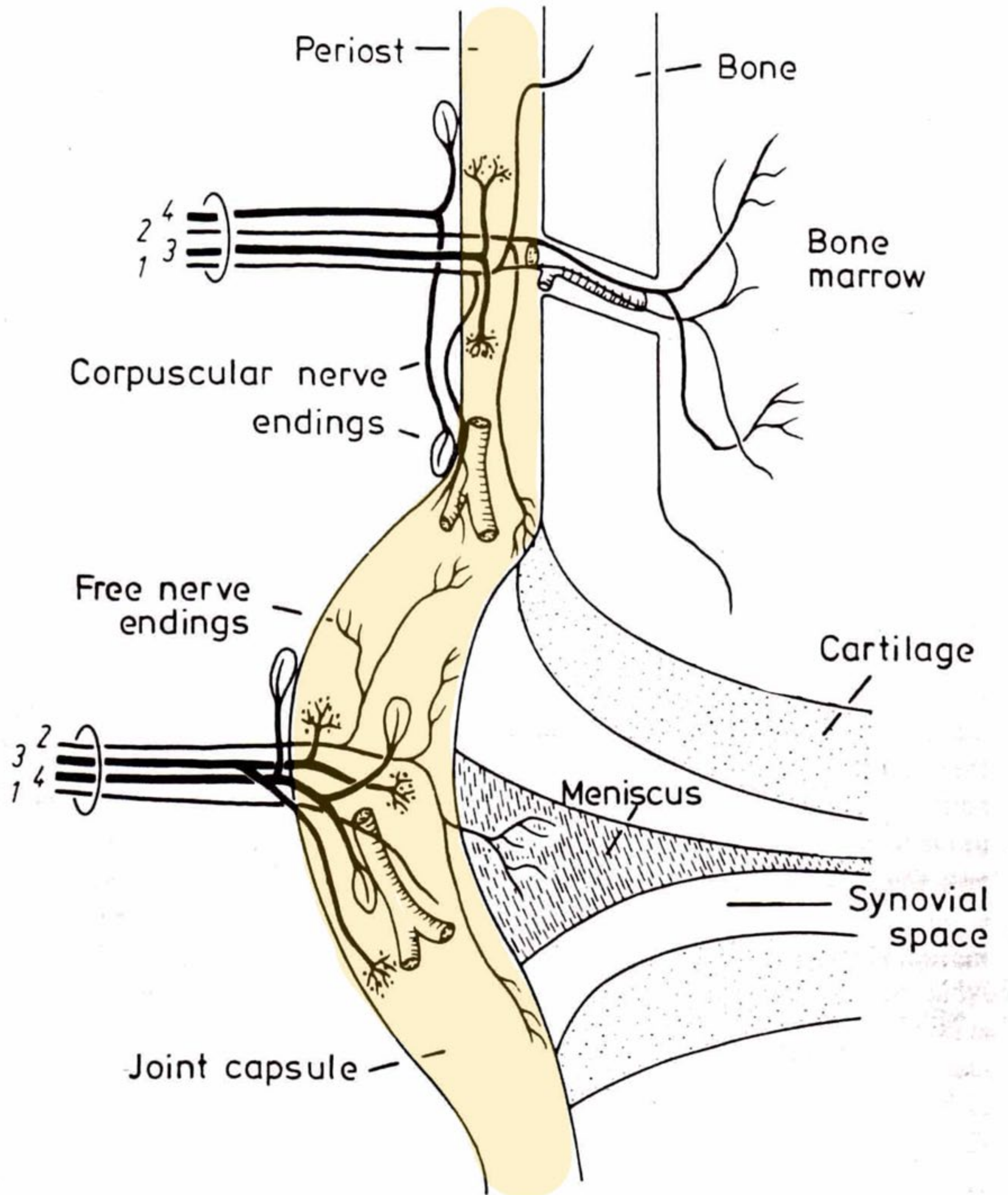
Joint Innervation

1 & 2 Non-myelinated C-fibers

3 & 4 Large myelinated A-beta fibers



Modified from: Zimmermann, M. 1989. Pain mechanisms and mediators in osteoarthritis. *Seminars in Arthritis and Rheumatism*. 18:22-29.



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Joint Innervation

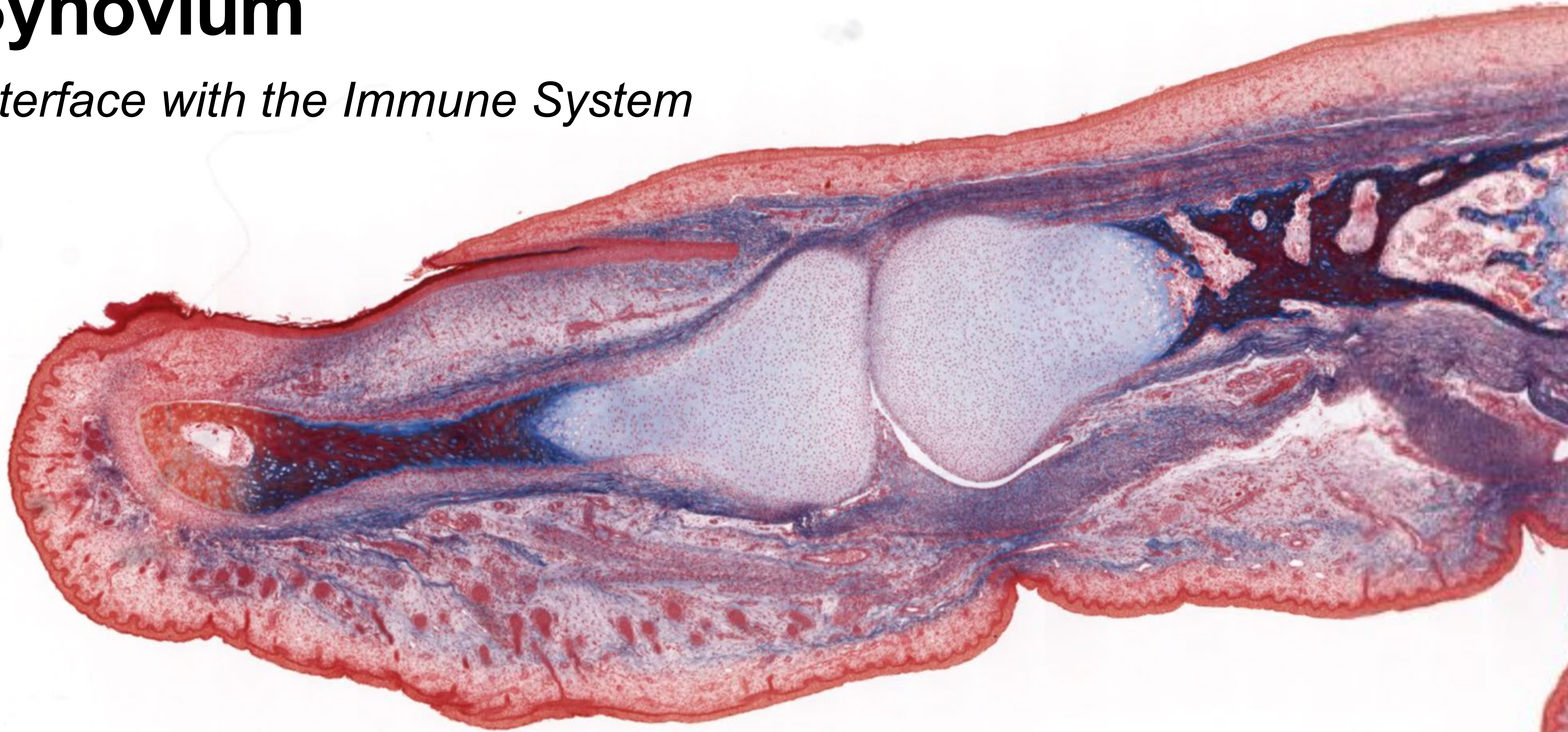
Receptor Types

- Ruffini endings
 - Slowly adapting, located in the joint capsule
- Pacinian corpuscles
 - Rapidly adapting, located in the periosteum of the bone
- Golgi Tendon Organ-like receptors
 - Located in the ligaments of the joint
- Free nerve endings
 - Joint capsule, vascular adventitia, synovium

Wyke, B. D. (1981). A neurology of joints: a review of general principles. *Clinics in Rheumatic Diseases of North America*, 7, 223-239.

Synovium

Interface with the Immune System



Synovium

Interface with the Immune System

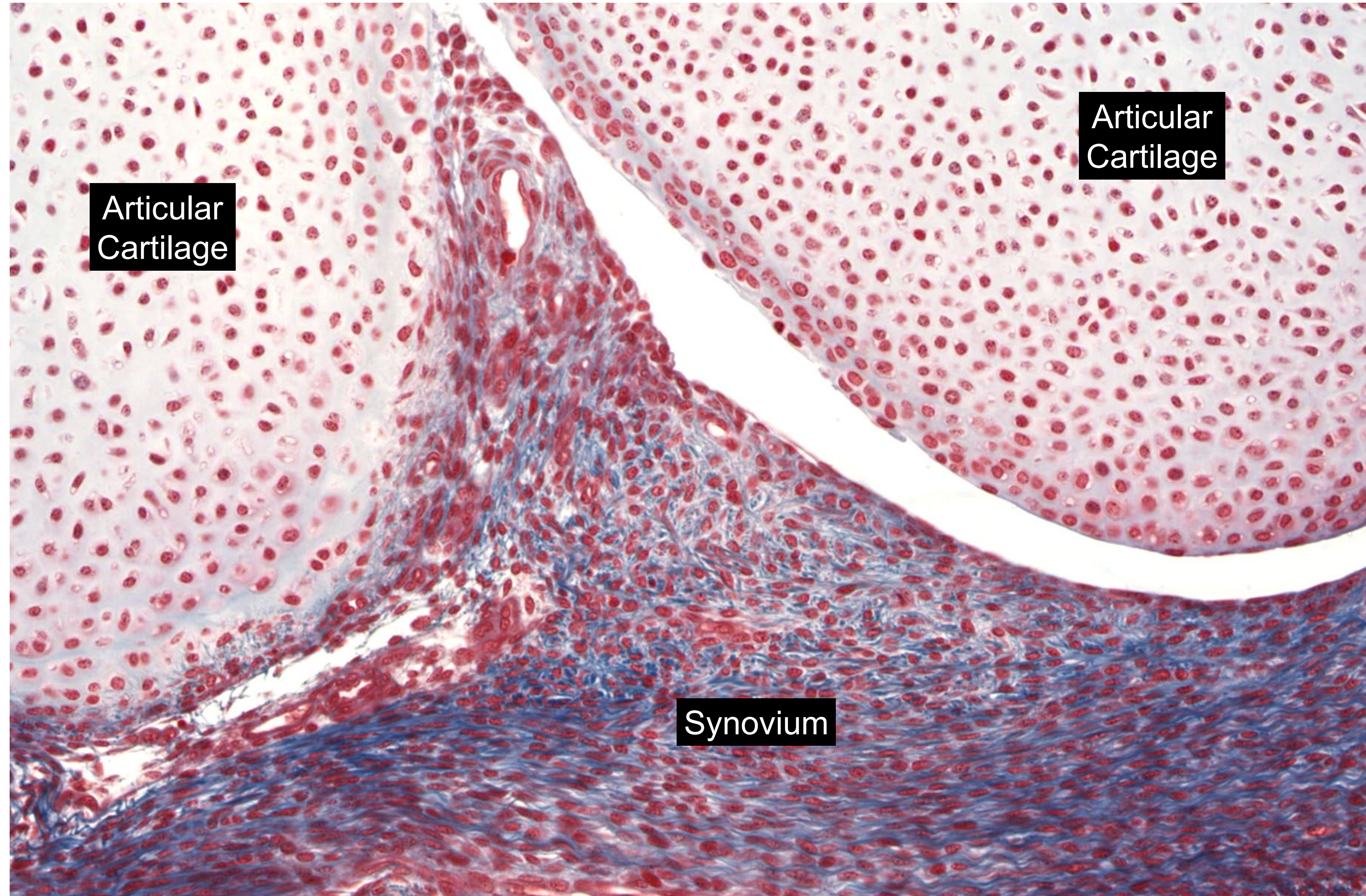
Lines the joint cavity

Secretes hyaluronic acid
and lubricin

Maintains the viscosity and
elasticity of the articular
cartilage

Tunica intima

Tunica subintima



Articular
Cartilage

Articular
Cartilage

Synovium

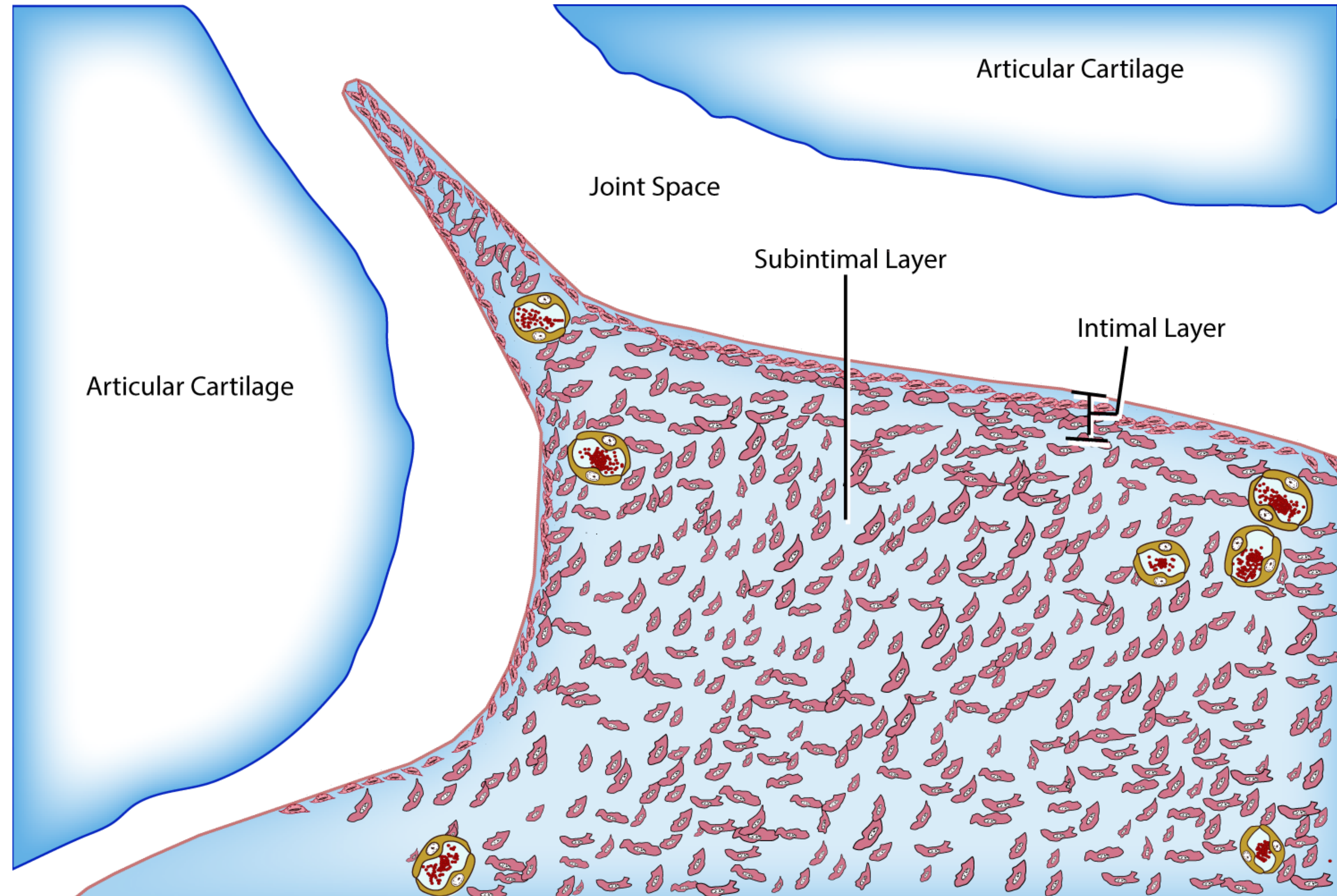
Inflammation

Synovial lining

Lacks epithelial cells,
basement membrane, tight
junctions or desmosomes

Intimal layer
Subintimal layer

Loose association of cells
in a bed of ECM



Synovium

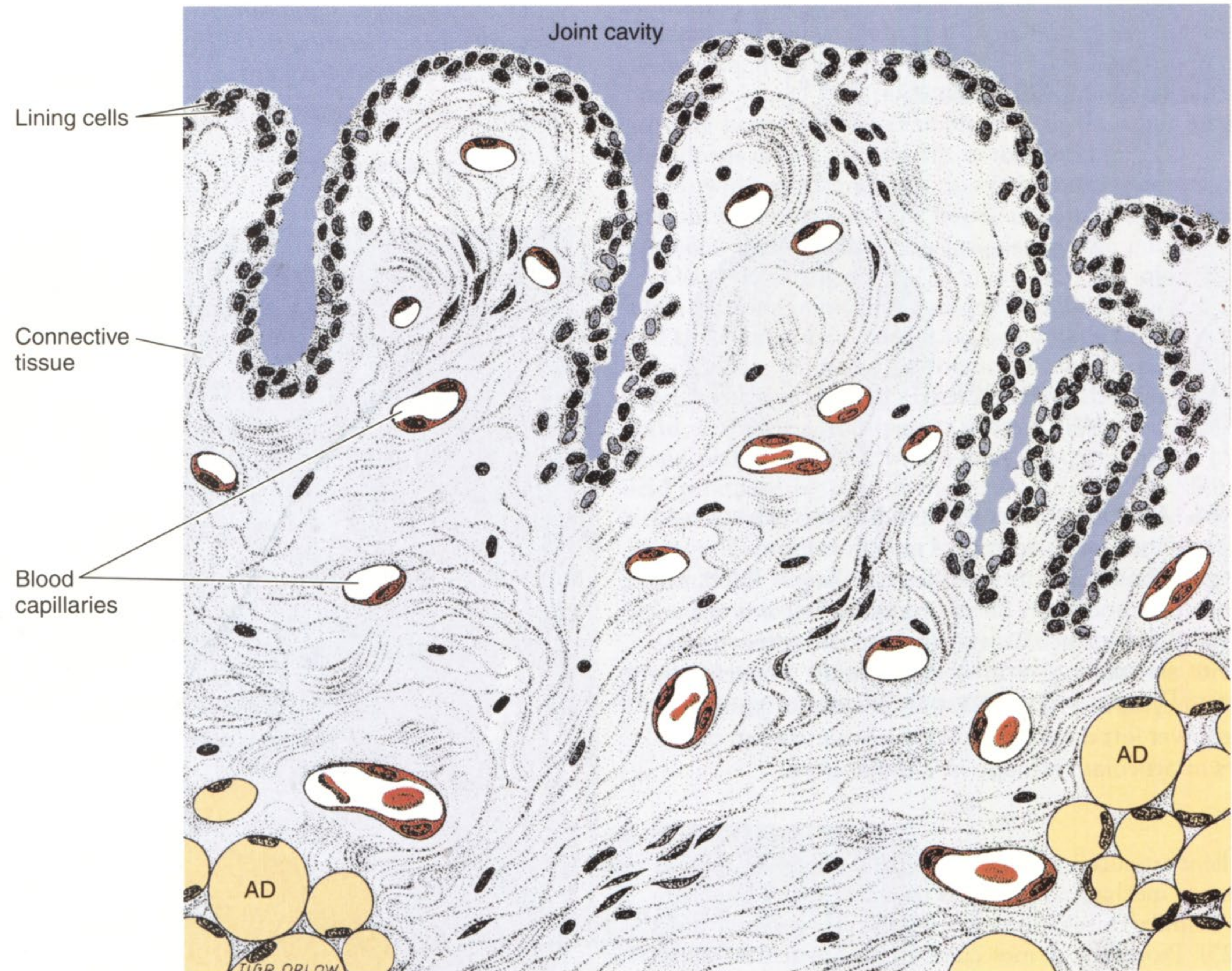
Layers

Intimal layer

Epithelial-like, Macrophage-type synoviocytes

Subintimal layer

Fibroblast-type synoviocytes
Macrophage-type synoviocytes
Adipose tissue
Vascular tissue

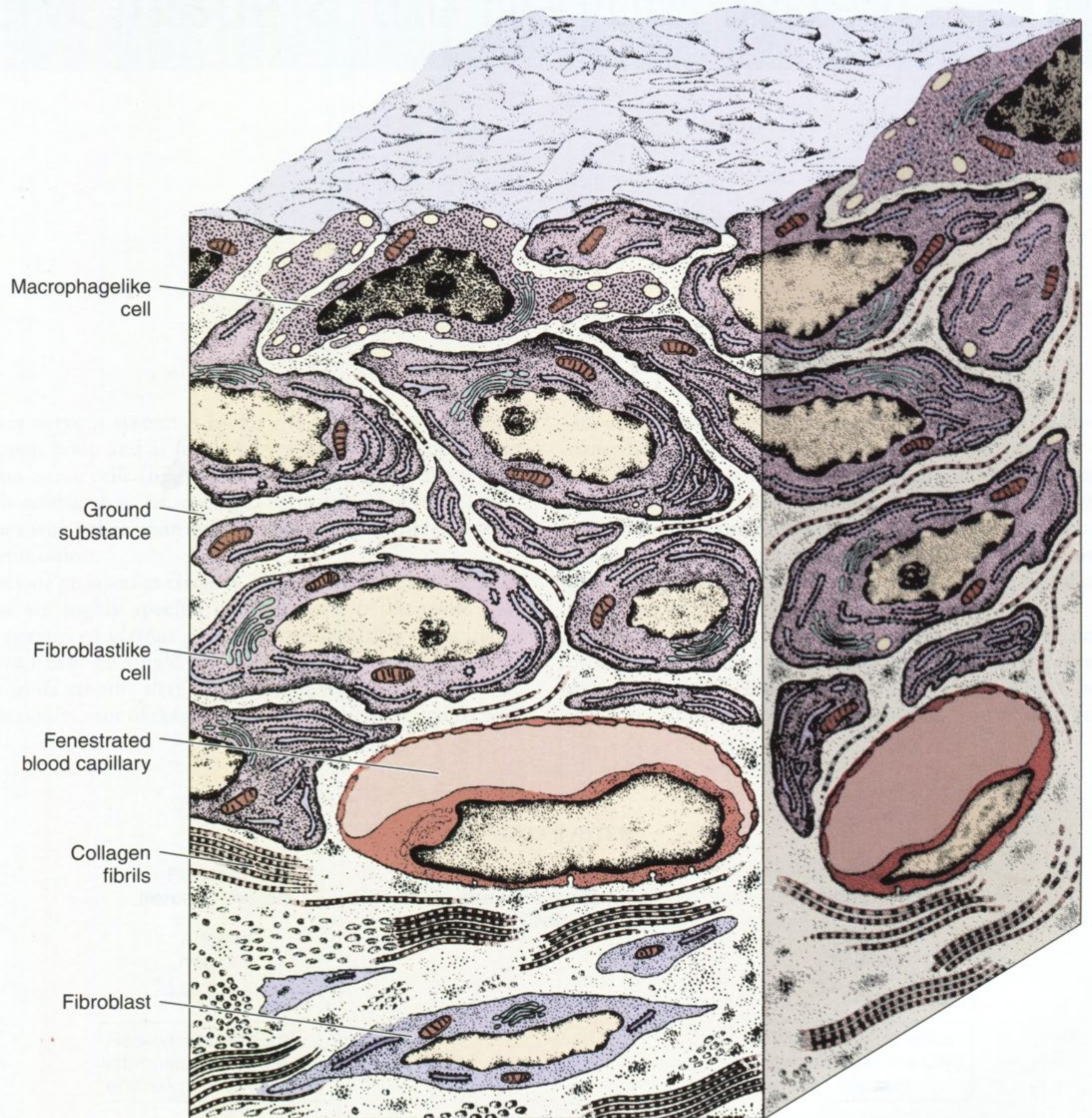


Synovial Cell-type

*Epithelial-type Macrophage
Synovocytes*

*Fibroblast-type
Synovocytes*

*Macrophage-type
Synovocytes*



Synovial Cell-types

Fibroblast-like Synoviocyte

- Health
 - Forms the initial basis for the development of the joint
 - Stromal cell producing collagen and ECM molecules
 - Major source of hyaluronic acid
 - Small amounts of matrix metalloproteinases
- Pathology
 - Hyperproliferation
 - Growth factors driving neoangiogenesis
 - Proinflammatory cytokines including RANK ligand

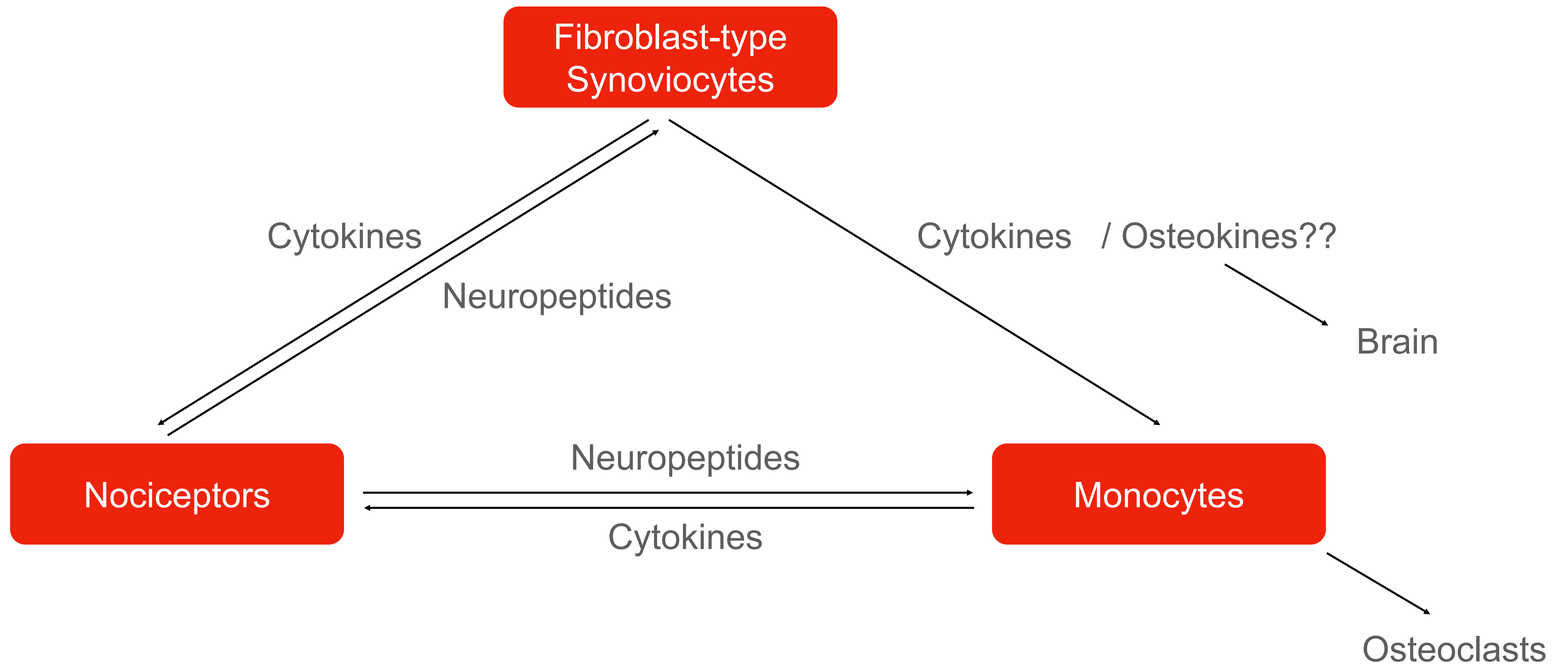
Synovial Cell-types

Macrophage-type synoviocyte

- Resident macrophages under normal conditions
- Make up the intimal layer
 - Epithelial-like macrophages: differentiated from subintimal macrophages
 - Tight junctions
- Scattered macrophage-type synoviocytes in the subintimal layer

Osteoimmunology

Bidirectional Communication



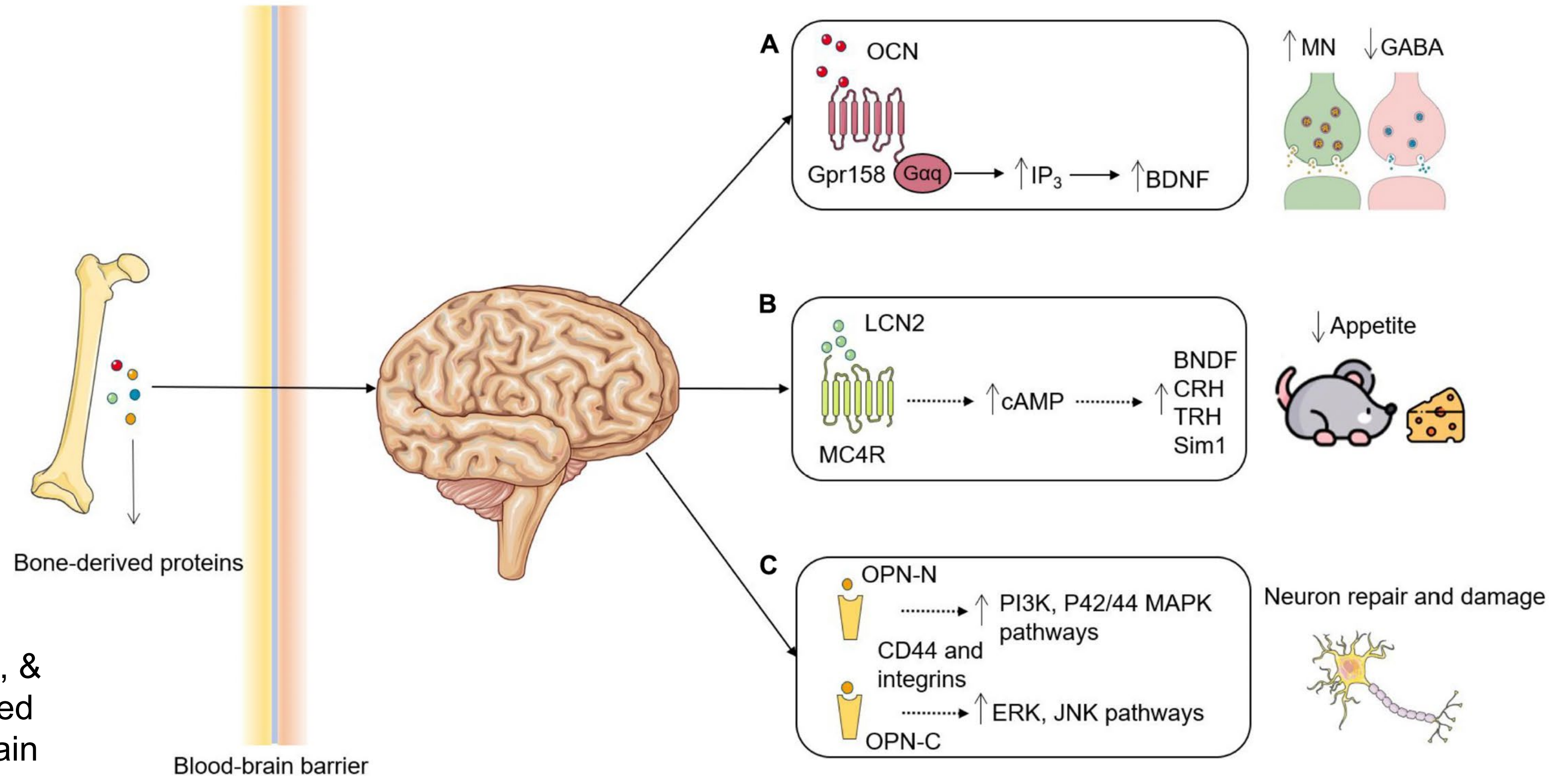
Osteoimmunology

Bone-Brain Axis

- Numerous “osteokines” can also be found in the brain
- At least one - Osteocalcin - is known to cross the BBB to enter the brain
- Weight-bearing movement increases Osteocalcin in circulation
- Osteocalcin increases cognitive performance in rodents

Osteoimmunology

Bone-Brain Axis



Chen, H., Shang, D., Wen, Y., & Liang, C. (2021). Bone-Derived Modulators That Regulate Brain Function: Emerging Therapeutic Targets for Neurological Disorders. *Front Cell Dev Biol*, 9, 683457.

Summary

Osteo-Neuroimmunology

Integration of multiple systems in to a dynamic molecular network of signaling pathways that function to maintain homeostasis and health