LECTURE 16: NANOMECHANICS OF CARTILAGE

Outline :

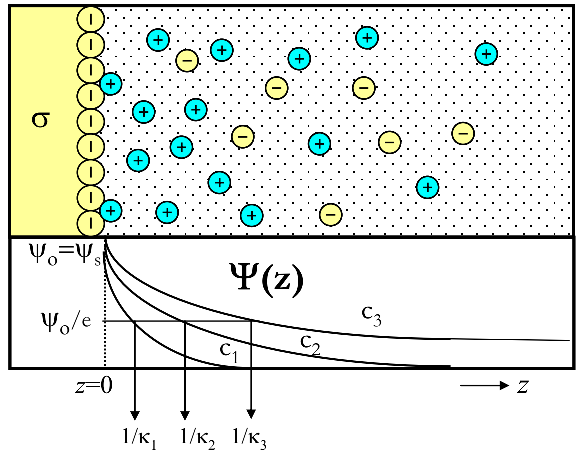
Objectives: To understand the molecular origins of the biomechanical properties of cartilage tissue

Readings: Course Reader Documents 26, 27, Supplements

Multimedia : Cartilage Podcast 2, Ng, et al. *J. Biomech.* **2007** 40, 05 1011.

REVIEW : LECTURE 15 THE ELECTRICAL DOUBLE LAYER BETWEEN TWO CHARGED SURFACES

$$\boxed{\frac{d^2\psi(z)}{dz^2} = \frac{2Fc_o}{\varepsilon}\sinh\frac{F\psi(z)}{RT}}$$ 1D P-B Equation,1:1 monovalent electrolyte



Apply appropriate boundary conditions to solve the P-B equation for $\psi(z)$; constant surface charge or constant surface potential

Linearized approximation;

$$\psi(z) = \psi_o e^{-\kappa z} \; where: \kappa^{-1} = \sqrt{\frac{\varepsilon RT}{2F^2 c_o}}$$ "salt screening"

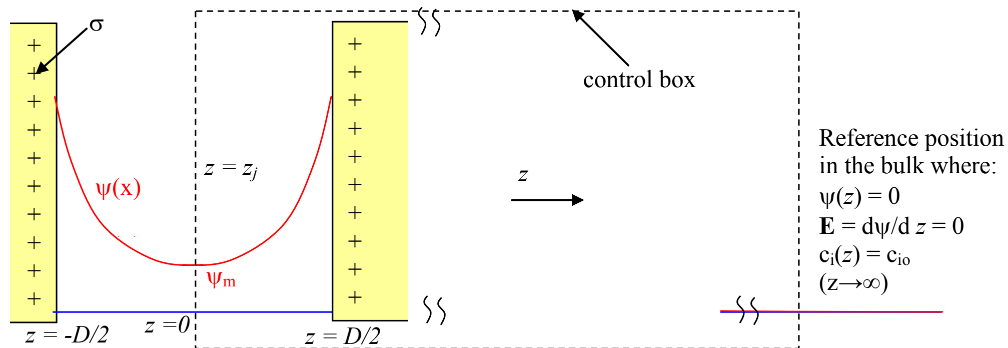
Explored the solution for $\psi(z)$ for two interacting charged surfaces

Calculate pressure (Force/Area) between two charged surfaces :

$$P(z = z_j) - P(\infty) = \text{"electrical"} + \text{"osmotic"}$$

$$P = 2RTc_0\left(\cosh\left(\frac{F\psi_m}{RT}\right) - 1\right)$$ →solve for ψ_m PB equation →linearized approximation

$$P(D)_{ELECTROSTATIC} = C_{ES} e^{-\kappa D}$$



ELECTRICAL DOUBLE LAYER POTENTIALS FOR DIFFERENT GEOMETRIES / DLVO

(From Leckband, Israelachvili, Quarterly Reviews of Biophysics, 34, 2, 2001)

-Monovalent Electrolyte, Linearized P-B formulation, Similarly charged surfaces, Temperature = 37°C

Constant Potential Prefactor:

$$Z\left(J\ m^{-1}\right) = \left(9.38 \times 10^{-11}\right)tanh^2(\psi_o/107)\ ;\psi_o[mV]\ \text{- CR 25,12.16}$$

Conversion to Constant Charge:

$$\sigma\left(Cm^{-2}\right) = 0.116sinh(\psi_o/53.4)\sqrt{c_o}\ ;c_o[M] = mole/L\ \text{- CR 25,12.12}$$

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Table 2 and Figure 6 in Leckband and Israelachvili, Quarterly Reviews of Biophysics, 34, 2, 2001

CARTILAGE TISSUE INTRODUCTION

-Cartilage tissue load bearing tissue in joints that cushions the ends of bones.

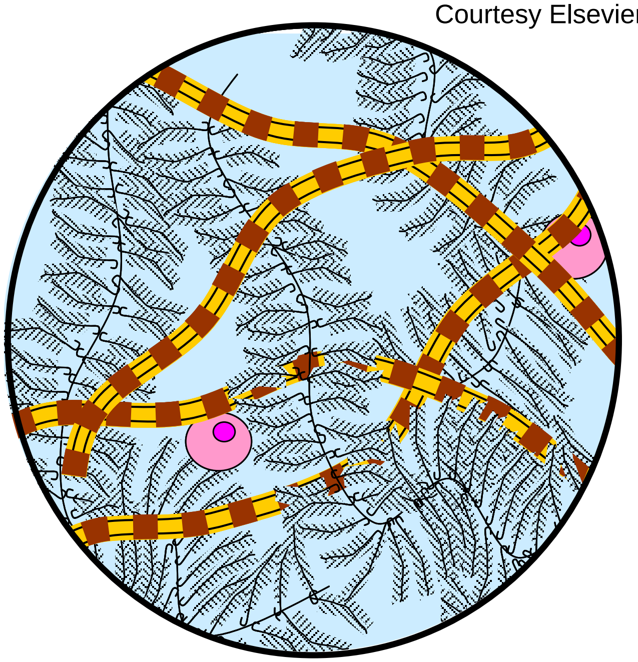
-Osteoarthritis (OA) is a degenerative chronic joint disease characterized by breakdown of the joint's cartilage. Cartilage breakdown causes bones to rub against each other, causing pain and loss of movement.

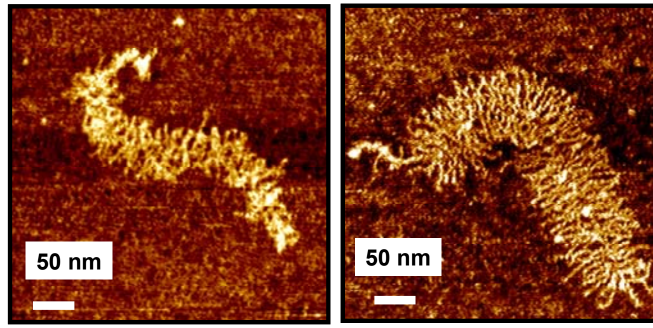
-OA affects 20 - 40 million Americans; 80% of > age 65, 100% of > age 80

- ~80% of torn anterior cruciate ligament (ACL) progress to OA in 14 years (average age 38 years old) *Ann. Rheum. Dis.* **2004**; 63:269-73.

Two photos removed due to copyright restrictions.
Knee joint with cartilage; and a running soccer player whose ACL has just torn.

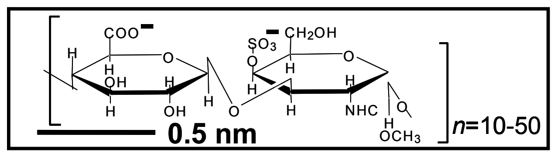
CARTILAGE TISSUE STRUCTURE





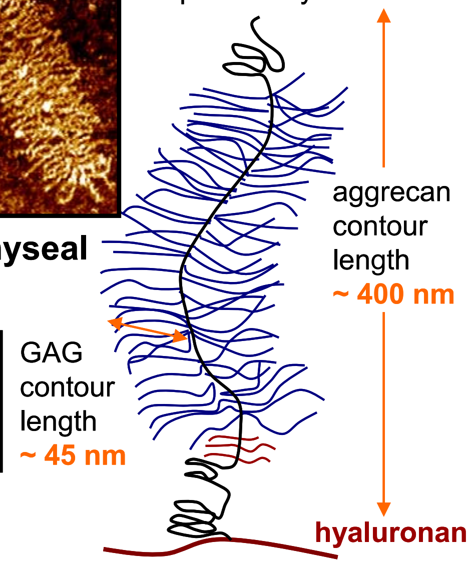
mature nasal **fetal epiphyseal**

(Ng+ *J. Struct. Bio.* 143(3), 242, **2003**)



(*p*Ka COO-= 3.5-4, *p*Ka SO_3^-=2-2.5

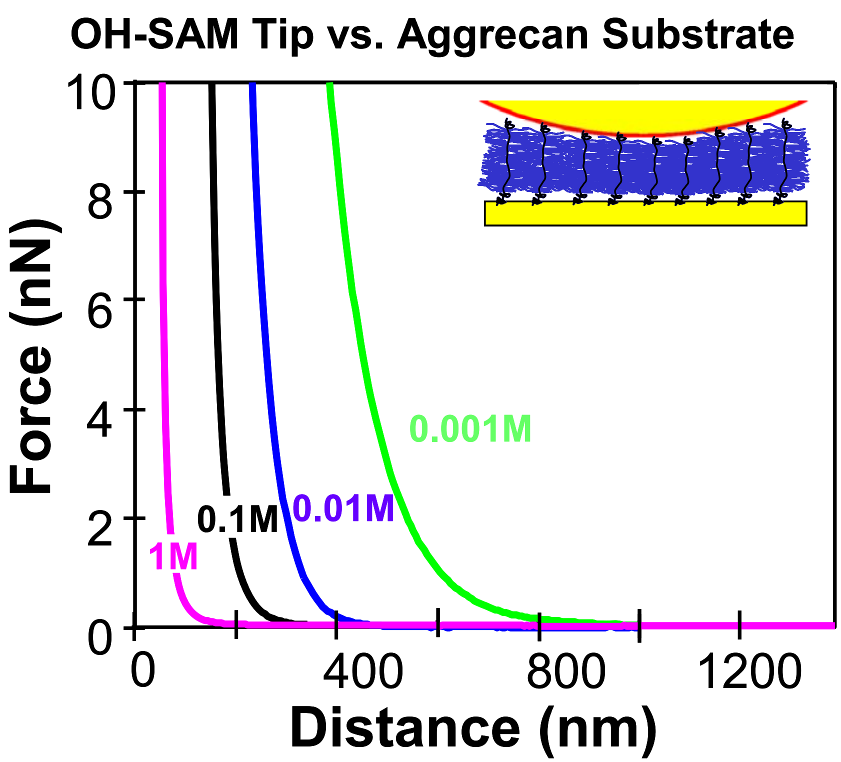
- ● covalent attachment of ~100 glycosaminoglycans (GAGs) to protein core separated by **~ 2-4 nm**

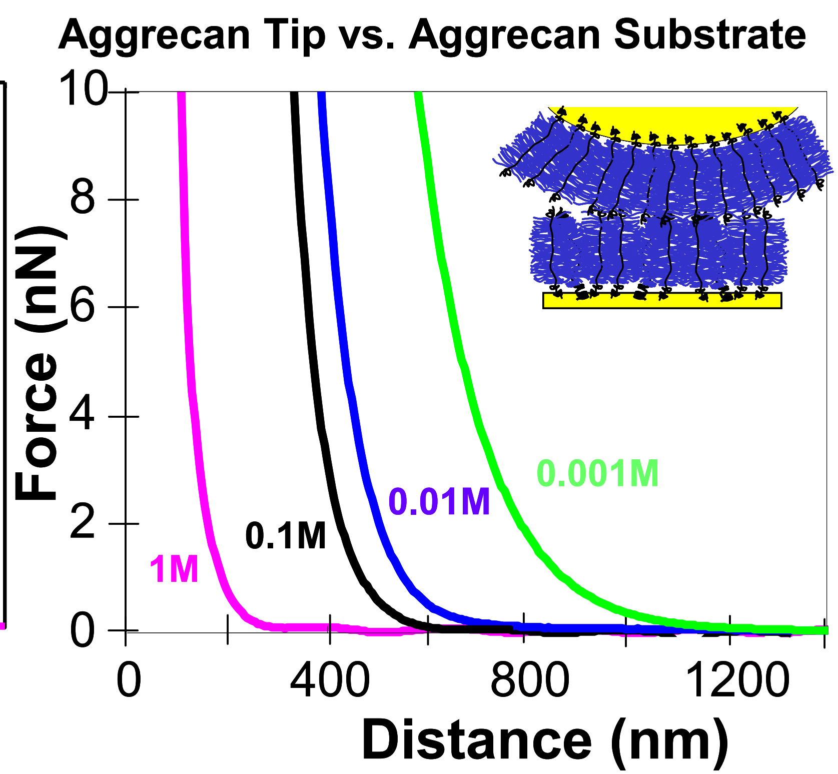


- ● load bearing tissue in joints withstands ~3 MPa compressive stress and 50% compressive strain (static conditions), equilibrium compressive moduli ~0.1-1MPa

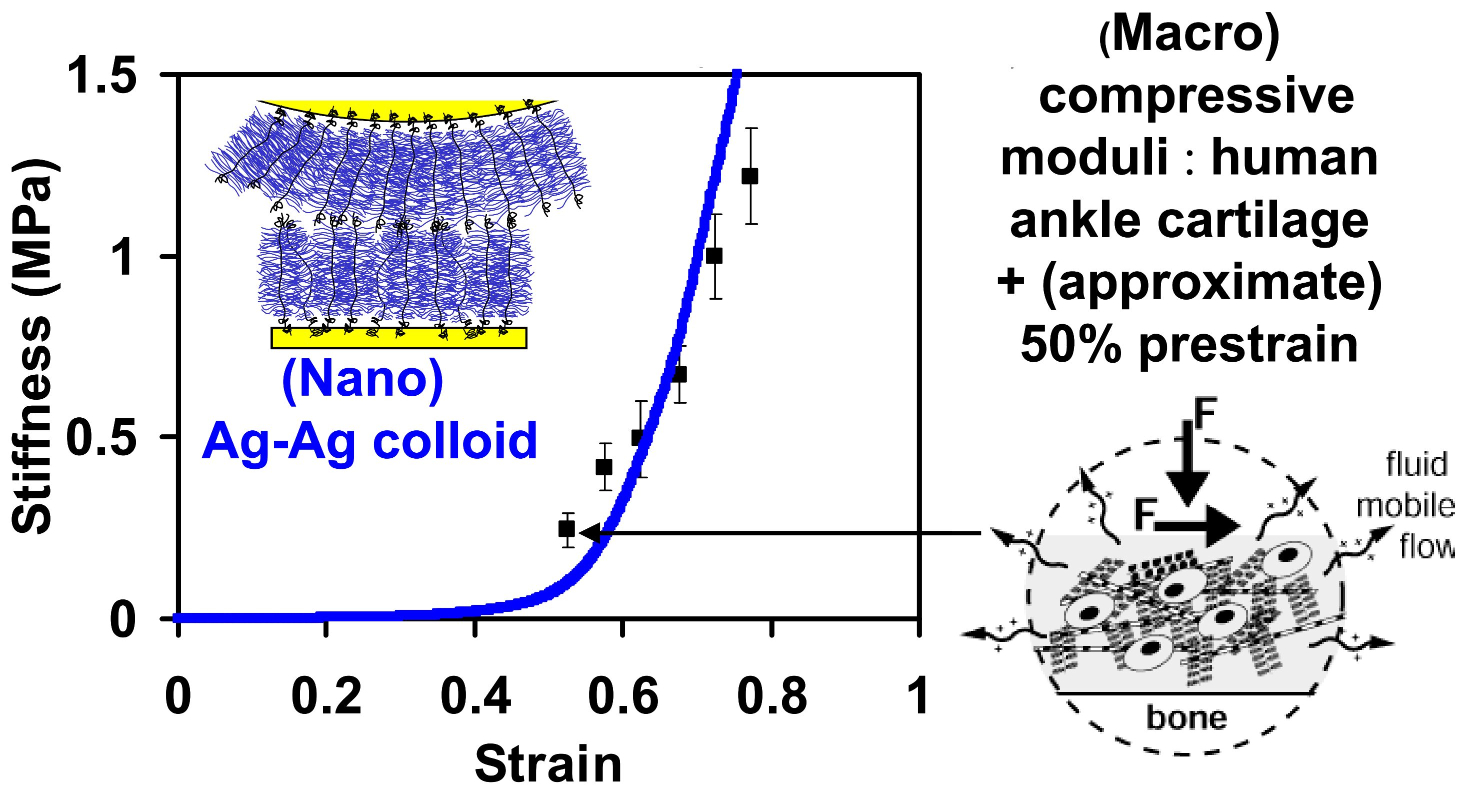
● ~80% HOH, collagen (50-60% solid content, mostly type II), aggrecan (30-35% solid content), hyaluronan, ~3-5% cartilage cells (chondrocytes)

NANOMECHANICS OF OPPOSING AGGRECAN



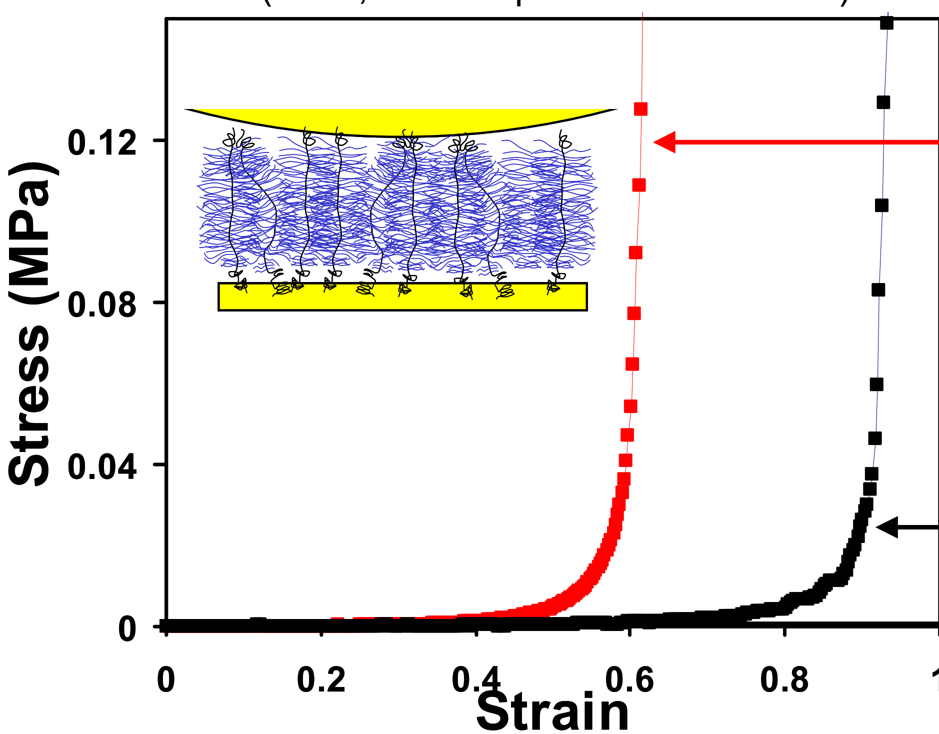


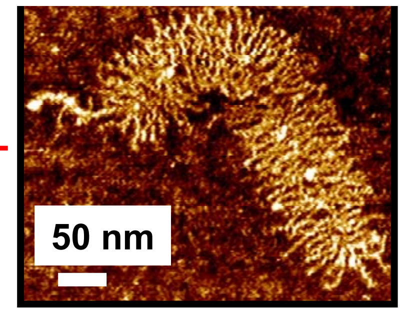
NANOSCALE STIFFNESS VERSUS STRAIN OF CARTILAGE AGGRECAN



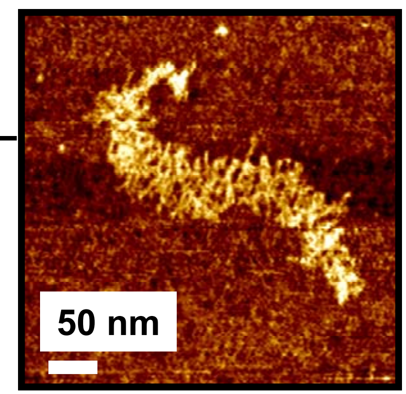
● stiffens nonlinearly with increasing strain at the molecular level→ mechanism to prevent large strains that could result in permanent deformation, fracture, or tearing.

EFFECT OF AGE ON NANOMECHANICAL PROPERTIES OF AGGRECAN: OH-SAM PROBE TIP (0.1M, PH5.6) : STRESS VS. STRAIN





fetal epiphyseal



mature nasal

APPENDIX :

Possion-Boltzman Units :

$$\frac{d^2\psi(z)}{dz^2} = \frac{2Fc_o}{\varepsilon} sinh \frac{F\psi(z)}{RT}$$

$$= \frac{\frac{C}{mole\ electronic\ charge}\frac{mole}{cm^3}}{\frac{C^2}{Jm}} sinh \frac{\frac{C}{mole\ electronic\ charge} mV}{\frac{J}{mole\ K}\mathrm{K}}$$

$$1 Volt = \frac{J}{C}$$

$$= \frac{C}{mole\ electronic\ charge}\frac{mole}{cm^3}\frac{Jm}{C^2} sinh \frac{C}{mole\ electronic\ charge}\frac{J}{C}\frac{mole\ K}{JK}$$

$$= \frac{J}{Cm^2} = \frac{V}{m^2}$$

$$Israelachvili's\ notation; \frac{d^2\psi(z)}{dz^2} = \frac{2en_o}{\varepsilon} sinh \frac{e\psi(z)}{k_B T}$$

$$elementary\ charge, e = 1.60217646 \times 10^{-19}\ coulombs$$

$$= \frac{\mathrm{C}\frac{\#}{m^3}}{\frac{C^2}{Jm}} sinh \frac{\mathrm{C}\frac{\#}{m^3}\frac{J}{C}}{J} = \mathrm{C}\frac{\#}{m^3}\frac{Jm}{C^2} sinh \frac{C}{J}\frac{J}{C} = \frac{V}{m^2}$$

Lecture 16 Nanomechanics of Cartilage: Definitions

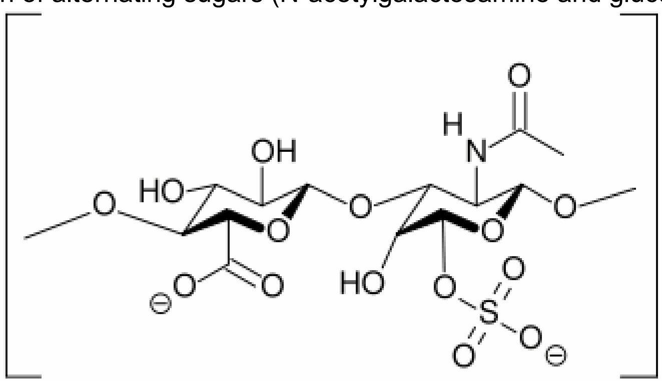
articular cartilage : connective avascular (contains no blood vessels) tissue covering the ends of the bones in synovial joints that allow smooth, low friction, painless motion

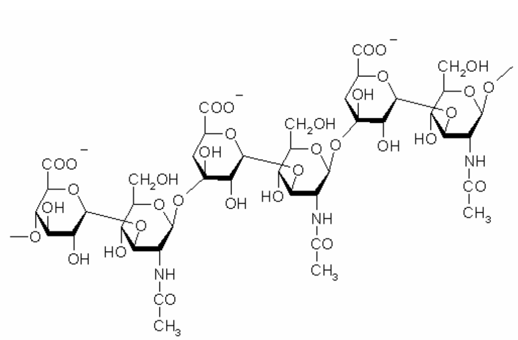
proteoglycan: A molecule that contains both a protein core and glycosaminoglycans, which are a type of polysaccharide. Proteoglycans are found in cartilage and many other connective tissues.

aggrecan: the largest aggregating proteoglycan, found in cartilage tissue and the intervertebral disc, has a bottle-brush configuration composed of a protein core backbone and densely spaces glycosaminoglycans

glycosaminoglycan (GAGs) : Polysaccharides containing repeating disaccharide units that contain either of two amino sugar compounds -- N-acetylgalactosamine or N-acetylglucosamine, and a uronic acid such as glucuronate (glucose where carbon six forms a carboxyl group). Also called mucopolysaccharides in the older literature. GAGs are found in the lubricating fluid of the joints and as components of cartilage, synovial fluid, vitreous humor, bone, and heart valves.

chondroitin sulfate (CS) : One of several classes of sulfated glycosaminoglycans that is a major constituent in various connective tissues, especially in the ground substance of blood vessels, bone, and cartilage. Chondroitin sulfate is a sulfated glycosaminoglycan (GAG) composed of a chain of alternating sugars (N-acetylgalactosamine and glucuronic acid). It is usually found attached to proteins as part of a proteoglycan.

CS→ 

 ← HA

hyaluronan (HA) : Hyaluronan (HA also called hyaluronic acid or hyaluronate) is an anionic polysaccharide composed of repeating disaccharides of beta-1-4-glucuronate-beta-1-3-N-acetylglucosamine distributed widely throughout connective, epithelial, and neural tissues. The polysaccharide appears to be unique amongst glycosaminoglycans as it is synthesized, and exists in vivo, without attachment to any protein. (As such, it is not synthesized via the usual intracellular organelles that involve protein synthesis; rather, it is extruded from the cell membrane, catalyzed by the enzyme hyaluronan synthetase.) It can be synthesized with a very large molecular weight (1,000 - 5,000 kDa). In cartilage, a globular domain at the N-terminus of aggrecan, termed G1 or the hyaluronic acid binding region (HABR). binds to HA in an interaction that is stabilized by link protein.

link protein : A ~45 kDa globular protein that stabilizes the interaction between aggrecan and HA.

chondrocyte : cartilage cells responsible for the synthesis and maintenance of the extracellular matrix; chondrocyte-like cells are also found in the intervertebral disc if the spine

collagen: The fibrous protein constituent of bone, cartilage, tendon, and other connective. Type II is the major fibril-forming collagen in cartilage. (There are currently 28 known, distinct, collagen types.)