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## **Cartilage Extracellular Matrix: Structure, Interactions and Function**

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Knowledge of the structure and interactions of the polymeric components of cartilage is important for the ultimate understanding of the multiple biological functions of this structurally complex gel-like tissue and for the development of therapeutic treatments for diseases, such as osteoarthritis, in which cartilage loses its functional properties. For example, synovial fluid, which is rich in hyaluronic acid (HA), ‘lubricates’ joints, acting as a viscous liquid over the relatively long timescales involved in slow joint movement and as an elastic material for rapid joint movement. This viscous or elastic response is crucial to the functioning of cartilage in joints. Under mechanical loading, as encountered when standing in place over long times, water and low-molecular mass solutes are driven out from the aggrecan-HA-collagen network permeating cartilage. With increasing age, there is a decrease in the hydration of the matrix, with a corresponding increase in compressive stiffness. This may have implications for the ability of cartilage to undergo reversible deformation. Hardened cartilage makes moving the surrounding joints more difficult. The size of proteoglycan aggregates within the extracellular matrix (ECM) also decreases with age. This may occur as a result of a decrease in the available binding sites of the HA chain or as the result of damage to link proteins and the glycosaminoglycan chains. Aggregation may also affect pore size distribution and solute permeability. In diseases, such as osteoarthritis, the lubricating and load-bearing ability is reduced, however, the mechanisms that lead to loss of cartilage’s key biomechanical properties are still poorly understood. We have quantified the interactions among the major constituents of cartilage ECM using an array of complementary experimental techniques (small angle neutron scattering, neutron spin echo, static and dynamic light scattering, osmotic pressure measurements, etc.) probing the structure and dynamic properties over a broad range of length and time scales.