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Self-Assembly of Aggrecan Molecules in Solution

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Aggrecan is a biologically important high molecular weight bottlebrush shaped proteoglycan. It forms large complexes with hyaluronic acid (HA), which provide the osmotic properties necessary for cartilage to resist deswelling under compressive load. The aggrecan-HA complex is a hydrated, viscous gel that gives cartilage its resilience and high compression modulus. The compressive properties of cartilage are closely correlated with the fixed charge density of the glycosaminoglycan (GAG) chains and hence with the proteoglycan concentration.

The biochemistry of cartilage formation has been extensively studied in the last couple of decades. Aggrecan contains three globular domains. Two of these bind the GAG chains. The N-terminal domain interacts specifically with hyaluronic acid to form large aggregates present in the extracellular matrix. Imaging techniques (e.g., electron microscopy, atomic force microscopy) have revealed the size and structural pattern of large distinct aggrecan-hyaluronic acid complexes. Such methods yield detailed information on spatial arrangements within a selected area of the sample. However, the interactions that govern the equilibrium morphology and dynamics of aggrecan assemblies remain poorly understood.

In solutions, where a very large number of molecules interact, knowledge of the statistical properties of the system is of paramount importance in order to describe the conformation and motion of the elements. Scattering techniques provide such information, since they explore a large volume of the specimen simultaneously. The aim of this work is to investigate the spatial organization in solutions of pure aggrecan and aggrecan-HA complexes in the length scale range between 10 and 5000 Å. The static properties are studied by small angle neutron scattering and static light scattering, while the dynamics are probed by dynamic light scattering.

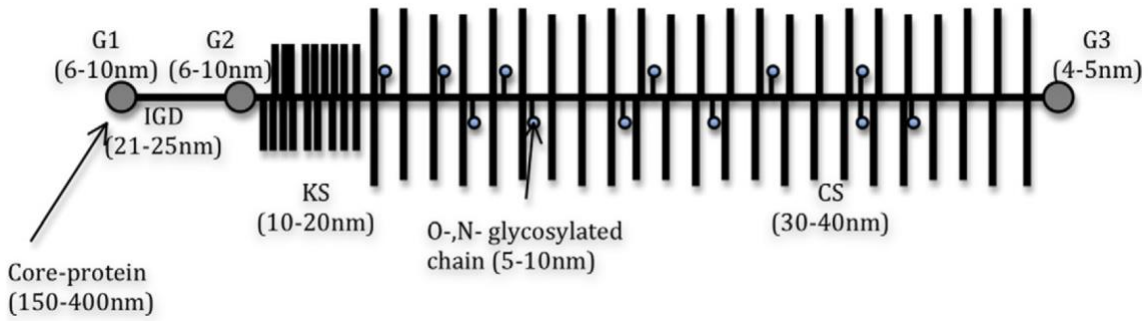

Figure 1. Schematic representation of the structure of the aggrecan bottlebrush.