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SCALE-DEPENDENT RHEOLOGY OF SYNOVIAL FLUID LUBRICATING MACROMOLECULES

Leonardo Martin-Alarcon[1,2], Aleksandra Govedarica[2], Randy H. Ewoldt[3], Steven L. Bryant[2], Gregory D. Jay[4], Tannin A. Schmidt[5], and Milana Trifkovic[2]

[1]Biomedical Engineering Graduate Program, University of Calgary, Calgary, Canada
[2]Chemical and Petroleum Engineering, University of Calgary, Calgary, Canada
[3]Mechanical Science and Engineering, University of Illinois at Urbana-Champaign, Urbana, USA
[4]Emergency Medicine, Brown University, Providence, USA
[5]Biomedical Engineering, University of Connecticut Health Center, Farmington, USA

ABSTRACT

The proper function of free joint motion in the body relies on the biomechanical properties of articular cartilage and synovial fluid (SF), which is a remarkable viscoelastic lubricant. The two major lubricant macromolecules in SF, hyaluronic acid (HA) and proteoglycan 4 (PRG4), synergistically interact to lower cartilage friction during boundary lubrication, but how these physical interactions affect SF rheology is still being debated. In this study, we used laser scanning confocal microscopy, rotational shear rheometry, and optical tweezer microrheology to examine the microstructure and rheological properties of physiologically relevant formulations of HA and recombinant human PRG4 (rhPRG4). Our findings suggest that rhPRG4 forms clusters of stiff, gel-like aggregates that do not interact with the surrounding continuous phase of HA polymers. Although the bulk rheology of HA solutions increased in a dose-dependent manner with the addition of rhPRG4, there was no evidence of a favorable physical interaction between the two that could alter the macroscopic rheology of the solutions. Additionally, we found that the interpretation of macrorheological data was significantly impacted by the interfacial adsorption of rhPRG4 molecules at the air-water interface of the rotational rheometer. Clinically relevant non-ionic surfactants used in the stabilization of rhPRG4 formulations were shown to both suppress the interfacial adsorption of rhPRG4 in rotational rheometers and disrupt the aggregation behavior of rhPRG4 in the bulk. Our results suggest that the macrorheology of this system is not governed by a single length scale, but instead responds as a disordered, hierarchical network with solid-like rhPRG4 aggregates distributed throughout the continuous HA phase. These findings provide important insights into the mechanical functionality of HA and PRG4 during cartilage lubrication and may aid in the development of HA-based viscosupplementation therapies for patients with joint diseases, such as osteoarthritis.