Environmentally Sensitive Polymer Matrices

Alyssa Panitch and Brandon L. Seal
Harrington Department of Bioengineering, Arizona State University

Statement of Purpose: Both the directed assembly and the nanometer scale of biological polymers have fueled an interest in designing macromolecular materials with controlled architecture and environmental response. We have developed a unique hydrogel network based on physical and covalent crosslinks. Here, we demonstrate that physical interactions coupled with covalent bonds lead to dramatically different dynamic mechanical properties than those of similar covalent systems.

Methods: Our system consists of dynamic physical interactions and stabilizing covalent bonds. Multiarm poly(ethylene glycol) vinyl sulfone (PEGVS) (20,000 g/mol; 5 arms functional) was covalently coupled to dansyl-GKAFAKLAARLYRKAGC (dG-PBD), a heparin-binding peptide derived from antithrombin III. The dG-PBD peptide was added to PEGVS in a 2:1 molar ratio. At room temperature, the addition of heparin (18 kD) facilitated the formation of weak gel-like structures. When the peptide GCRGDSGPQGIAGQGC (crosslinker) was added, the physical matrix was stabilized by the formation of covalent crosslinks. The rheological properties of 10 wt% gels containing a 9:2 molar ratio of PEGVS-dG-PBD:heparin and a 3:2 molar excess of crosslinker:PEGVS were measured by measuring viscoelastic moduli over time at 20°C using a 0.5 Pa oscillatory stress applied at 40 rad/s. After curing the gels for 2 hours, a 0.5 Pa oscillatory stress was applied at 10 rad/s at each temperature integer from 4°C to 45°C.

Results / Discussion: Figure 1 displays the storage modulus, G′, and the loss modulus, G″, for gels with and without heparin. The time to gelation, t_g, of gels without heparin (30.0±4.5 min) was significantly longer ($p<0.05$) than t_g of compositions containing heparin (7.3±0.6 min). Also, both G′ and G″ of the heparin-containing gels were significantly higher than the moduli of similar gels without heparin; after two hours, G′ of heparin-containing gels (2764.3±321.8 Pa) was over ten times larger than the 256.0±61.0 Pa magnitude of G′ recorded for gels without heparin. Since the association of dG-PBD and heparin is rapid, the mechanical properties of the compositions were likely affected by the formation of larger macromolecular chains coordinated by physical bonds. The resulting chain entanglement stabilized the materials, which were further stabilized by chemical crosslinks introduced by the crosslinker. Consequently, the influence of physical interactions resulted in decreased t_g and larger moduli. As seen in Figure 2, G′ of dG-PBD gels without heparin and 10 wt% PEGVS control gels were independent of temperature. In contrast, the viscoelastic properties of dG-PBD gels containing heparin displayed remarkable temperature dependence. G′ at 4°C (5005.3±592.0 Pa) was significantly higher ($p<0.05$) than G′ at 45°C (477.9±150.4 Pa). Since the interaction between heparin and dG-PBD resulted primarily from electrostatic association and hydrogen bonds, the properties imparted by this interaction were transient and dynamic. At low temperatures, the gel components experienced lower diffusion coefficients and lower kinetic rate constants resulting in an increased time of contact between dG-PBD and heparin. When the energy of the system increased, the number of physical bonds decreased until the interaction between heparin and dG-PBD no longer made a significant contribution to the elastic properties of the gels. Consequently, G′ of gels with and without heparin between 36°C and 45°C were not statistically different at each temperature. This temperature-dependent gel weakening followed the same trend seen for previously described physical matrices. However, unlike the moduli of those physical matrices, G′ remained higher than G″ throughout the entire tested temperature range.

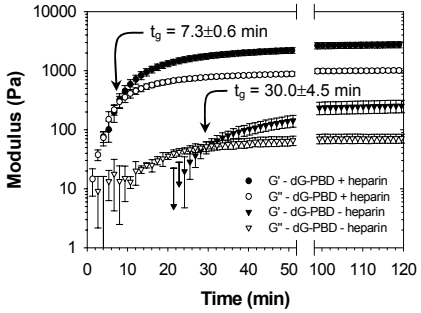

Figure 1. A plot of G′ and G″ as a function of time for various heparin-peptide gels (n=3; ±SD). G′ and G″ are depicted for dG-PBD gels with and without heparin.

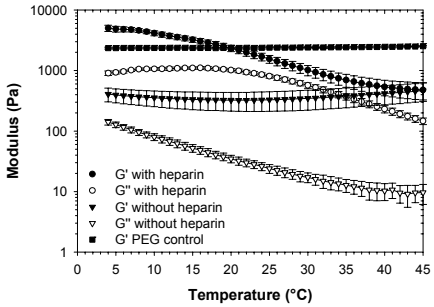

Figure 2. A plot of G′ and G″ as a function of temperature for dG-PBD gels with and without heparin and for PEGVS control gels (n=4; ±SD).

Conclusions: This gel system is a unique material that incorporates properties of both physically and covalently crosslinked hydrogels and that demonstrates that physical interactions can significantly influence the mechanical properties of a polymer matrix. These physical bonds are sensitive to environmental stimuli such as temperature. Consequently, these gels could be tailored to control dynamic mechanical properties, influence swelling behavior, and release molecules based on local temperature. In addition, this system could be useful as a model to better understand how physical and covalent crosslinks interact to influence the behavior of biopolymeric materials.