

“Intelligent” Polymers for Biomedical Technologies

Proteins, polysaccharides, and nucleic acids are the basic components of living organic systems. Known as functional biopolymers, they exhibit discrete and reversible changes in form as a response to small changes in their environment. The discovery of such cooperative interactions between segments of biopolymers has led researchers to try to create novel synthetic polymers, which are similarly responsive in a controlled way to stimuli. Scientists say the design, synthesis, and characterization of “intelligent,” environmentally responsive polymeric materials with controllable properties is important for the emerging biomedical technologies of the next decade.

ORNL researchers are working to develop such materials for possible use in biomedical applications. Using the state-of-the-art general purpose-SANS instrument at HFIR, they characterize novel polymeric materials, which are synthesized by materials scientists at ORNL’s CNMS. Neutron scattering allows scientists to study the nanoscale structures and interactions of these novel polymers. The research is being conducted by postdoctoral fellow Gang Cheng, Yuri Melnichenko, and George Wignall, all from the Neutron Scattering Sciences Division, and Kunlun Hong and Jimmy Mays from CNMS.

“ORNL has a proven record of using neutron scattering to investigate the solubility and structure of homopolymers and block copolymers in various solvents,” says Melnichenko, “and these capabilities have been significantly enhanced by the new instruments available at HFIR and SNS. This research will strengthen ORNL’s position as a leader in creating ‘smart’ functional

polymeric materials and characterizing them using advanced neutron scattering methods.”

The project involves the synthesis of biocompatible stimuli-responsive homopolymers, block copolymers, and gels, based on methoxy(oligo(ethylene oxide))styrene and methoxy(oligo(ethylene oxide))norbornene. Says Cheng, “These biomimetic polymers can identify a stimulus (temperature, pH, ionic strength, etc.), evaluate the magnitude of the signal, and then adequately adjust their conformation properties in a direct response.” The figure (next page) shows how the scattering intensity from the polymer solutions increases with temperature, revealing at what temperature the polymers collapse. “Understanding the fundamentals of the conformation response and phase behavior of the ‘intelligent’ polymers is imperative for a variety of applications in biology and medicine,” he says, “such as drug delivery, bioseparation, biometric actuators, and surfaces with reversible hydrophobic and hydrophilic properties.”

SANS has been used largely for investigation of conformation of the polymers in solutions, due to the appropriate length scales (1–100 nanometers) involved, and the significant contrast between hydrogenated polymers and deuterium substituted solvents,” says Melnichenko. “In this project, we use SANS to understand the fundamentals of the conformation response and phase behavior of these polymers, as well as the interplay between the interactions of the backbone and side chains with water molecules. This information is a prerequisite for designing stimuli-responsive materials with desired properties,” he explains.

A rapid response to stimuli and biocompatibility are crucial when designing the molecular structures

Neutron research on developing improved polymers with controllable properties is leading to advances in the biomedical field.

needed for targeted drug delivery inside the human body. To achieve the intended goals, Fengjun Hua and Kunlun Hong, polymer chemists at CNMS, synthesized a series of comblike polymers, consisting of a hydrophobic backbone and hydrophilic oligo ethylene glycol (EG) side chains. The polymers are expected to have low toxicity because of the presence of the EG side chains. By varying the number of EG repeat units in the side chains, the cloud point (temperature at which solids are no longer completely soluble) of their aqueous solutions can be held within the optimal physiological range. And the relative interaction strength of the hydrophobic (backbone—water) and hydrophilic (side chain—water) fragments of the bipolymers can be continuously varied and used to control the solubility and phase behavior of the system.

The comblike architecture allows researchers to vary the length and composition of the backbone and side chains independently of each other to achieve the optimized structures and functions. Both the sizes of the polymers and their shapes can be controlled by increasing the molecular weight of the backbone, while keeping the length of the side chain fixed. As a result, a variety of complex and reversible structural transformations and phase transitions can be induced, including coil-globule in homopolymers, micellization of block copolymers, and swelling—collapse transitions in polymer gels.

“These polymers can be dissolved in water only if a sufficient number of the hydrophilic EG side chains are available,” Cheng explains. “With increasing temperature, the attractive interaction increases due to increased hydrophobic interactions between backbones and weakening hydrophilic interactions between the EG side chains and water. These findings are important for better design and application of stimuli-responsive materials in the future.”

Recent publications resulting from the research include:

G. Cheng, Y. B. Melnichenko, G. D. Wignall, F. Hua, K. Hong, and J. W. Mays, “Small angle neutron scattering study of conformation of oligo(ethylene glycol)-grafted polystyrene in dilute solutions: Effect of the backbone length,” *Macromolecules*, vol. 41(24), pp. 9831-9836, December 2008.

G. Cheng, F. Hua, Y. B. Melnichenko, K. Hong, J. W. Mays, B. Hammouda, and G. D. Wignall, “Association and structure of thermosensitive comblike block copolymers in aqueous solutions,” *Macromolecules*, vol. 41, pp. 4824-4827, July 2008.

