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| <b>REPORT DOCUMENTATION PAGE</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                             |                                                            | Form Approved<br>OMB NO. 0704-0188                                             |                                                                    |
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| 13. ABSTRACT (Maximum 200 words)<br><br>The objectives of this work are to create nanostructured polymer gels, to correlate such structures to their physical properties, and to use them for sensors and controlled drug release. Under ARO sponsorship, the most important results are summarized in seven areas: (i) Synthesized nanostructured polymer gels that display striking iridescence like precious opal. (ii) Developed a new route to make crystalline hydrogels in neutral pH and aqueous environment. They can be used as sensors that change their colors in response to external stimuli. (iii) Developed new carriers for controlled drug delivery. Biodegradable hydrogel nanoparticles based on FDA approved biopolymers have been synthesized. The biocompatibility of hydrogel nanoparticles has been tested. (iv) Studied conformation changes of long-chain branched polymers synthesized by ARL scientists. (v) Understanding of phase behavior of aqueous suspension of gel nanoparticles has been achieved using thermodynamic perturbation theory combined with light scattering measurements. (vi) Synthesized hydrogel nanoparticles with different functionalities. (vii) Improved performance of hydrogels by incorporating hydrogels with Na-montmorillonite layered silicates. The major accomplishments include 18 peer-reviewed publications, 19 presentations in various meetings, 2 granted patents and 3 pending patents. Five graduate students received their Ph.D., participating in this ARO sponsored research. |                                                             |                                                            |                                                                                |                                                                    |
| 14. SUBJECT TERMS<br>Polymer gels, hydrogels, nanostructured polymers, smart materials, sensors and devices, light scattering, nanoparticles, long chain-branched polymers, controlled drug delivery                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                             |                                                            | 15. NUMBER OF PAGES<br>8                                                       |                                                                    |
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**(1) Forward (optional): none**

**(2) Table of Contents (if report is more than 10 pages, N/A)**

**(3) List of Appendixes: None**

**(4) Statement of the problem studied**

This proposed project seeks novel, fundamental polymer research that may provide nanomaterials technology for chemical and biological defense. Most current research on polymer gels has focused on either bulk gels or microgels. The objectives of this work are to create nanostructured polymer gels, to correlate such structures to their physical properties, and to use them for sensors and controlled drug release. The central idea is to first synthesize monodispersed polymer gel nanoparticles, then self-assemble them into 3D networks, and eventually covalently bond them. In contrast to conventional gels that are colorless, the new gels invented here exhibit colors and these colors can change with external stimuli. This project has also included studying another nanomaterial, a long chain-branched polymer, developed at ARL, with an emphasis on their conformation changes under various solvents. This work has provided a framework to generate stable periodic 3D structures with varying feature sizes in polymer gel materials. It allows us to obtain useful functionality not only from the constituent building blocks but also from the long-range ordering that characterizes these structures. Creating such nanostructured materials is of great importance in technological applications including controlled drug delivery, sensors, devices, and displays.

**(5) Summary of the most important results**

Under ARO sponsorship, the most important results are summarized in following seven areas: (i) Made a conceptual breakthrough in synthesis of nanostructured polymer gels that display a striking iridescence like precious opal but are soft and flexible like gelatin. (ii) Developed a new route to make high strength crystalline hydrogels in neutral pH and aqueous environment. They can be used as sensors that change their colors in response to external stimuli such as temperature, pH and protein concentration. (iii) Developed new carriers for controlled drug delivery. These carriers have a unique two-level structural hierarchy: the primary network consists of crosslinked polymer chains inside each nanoparticle, while the secondary network is a crosslinked system of the nanoparticles. The primary and the second networks have been used to entrap small and large biomolecules, respectively. New biodegradable hydrogel nanoparticles based on FDA approved biopolymers have been synthesized as building blocks for these carriers. The biocompatibility of hydrogel nanoparticles have been tested and compared with commercially available biopolymers. (iv) Studied conformation changes of long-chain branched polymers synthesized by ARL scientists under various solvents using light scattering techniques. These results can be used as a guide to prepare high performance long-chain branched polymers that may detect the presence of biological warfare agents at extremely low concentrations. (v) Fundamental understanding of phase behavior of poly-N-isopropylacrylamide (PNIPAM) nanoparticles dispersed in water has been achieved using thermodynamic perturbation theory combined with light scattering and spectrometer measurements. (vi) Developed various schemes to synthesize hydrogel nanoparticles with different functionalities. (vii) Improved performance of hydrogels by incorporating hydrogels with Na-montmorillonite layered silicates.

**(i) Conceptual breakthrough**

***“Hydrogel opals,” Z. B. Hu, X. Lu & J. Gao, Advanced Materials 13 (Cover), 1708-1712 (2001). This work was reported by Chemical & Engineering News (Nov. 2001).***

Hydrogels have been studied extensively because of their abilities to simulate biological tissues and to swell or collapse reversibly in response to external stimuli. They usually consist of a randomly crosslinked polymer chains and contain a large amount of water filling interstitial spaces of the network, resulting in amorphous structures. Without adding a coloring agent, the hydrogels are clear when they fully swell in water. Here we show a new class of bulk hydrogels with mesoscopically crystal structures. The central idea is to covalently bond self-assembled hydrogel nanoparticles. The covalent bonding contributes to the structural stability, while self-assembly provides them with crystal structures that diffract light, resulting in colors. As a result, these novel materials, which contain up to 97 wt % water, display a striking

iridescence like precious opal but are soft and flexible like gelatin. In this report, three simple applications based on the crystal hydrogels are presented: a gel sensor with environmentally-tunable colors, a gel “opal” that displays a striking iridescence but is elastic and soft, and a gel display whose iridescent pattern can be made either visible or invisible by simply switching temperature.

**(ii) Developing novel gel sensors**

***“A new route to crystalline hydrogels as guided by a phase diagram,” Z. B. Hu and G. Huang, Angewandte Chemie, Int. Ed., 42, 4799 (2003).***

Here we show a new route towards the fabrication of crystalline hydrogels following a phase diagram. The central idea is to synthesize monodispersed nanoparticles of PNIPAM-co-allylamine and measure the phase diagram of their water dispersion. Taking the advantage that the thermally sensitive nanoparticles in colloidal glasses can be converted into ordered crystals via particle based volume transition as reported by Lyon and co-workers, a crystalline hydrogel could be obtained by initiating the crystallization process near the colloidal crystal melting temperature while subsequently bonding the PNIPAM-co-allylamine particles below the glass transition temperature. This can increase the polymer concentration, resulting in a crystalline hydrogel with higher mechanical strength. Furthermore, the allylamine contributes amine groups that can be covalently bonded in water at a neutral pH but does not significantly affect the volume phase transition of the PNIPAM polymer. Hydrogels are well known for their unique hydrophilic and environmentally responsive properties that lead to fascinating applications including controlled drug delivery, artificial muscles, devices and sensors. Tailoring hydrogels with periodic structures under mild synthesis conditions could open a new avenue for these applications.

**(iii) Novel carriers for Controlled drug delivery and their biocompatibility**

***“Synthesis and study of and controlled release from nanoparticles and their networks based on functionalized hydroxypropylcellulose,” T. Cai, Z. B. Hu, B. Ponder, J. St. John, and Moro, Macromolecules 36, 6559-6564 (2003).***

The structure of hydroxypropylcellulose (HPC) has been modified by covalently attaching either vinyl groups linked by degradable esters, or methacrylate groups. The vinyl groups allow for chemical linking of the HPC chains into nanoparticles through a free radical polymerization process above its low critical solution temperature (LCST). The HPC nanoparticles with degradable moieties in aqueous solution have been monitored using dynamic light scattering technique as a function of time. The degradation rate increased at either low or high pH values. Residual, uncrosslinked vinyl groups on the surface of the nanoparticles have been further linked together forming a network of nanoparticles. The controlled release of biomolecules from this network has been correlated with the primary structure that comprises crosslinked polymer chains in each individual particle and the secondary structure that is a system of crosslinked nanoparticles.

***“Controlled drug release from hydrogel nanoparticle networks,” G. Huang, J. Gao, Z. B. Hu, J. V. John, B. C. Ponder D. Moro, J. Controlled Release 94, 303-311 (2004).***

Two hydrogel nanoparticle networks have been synthesized by co-polymerizing N-isopropylacrylamide (NIPA) with allylamine or co-polymerizing NIPA with acrylic acid to form particles that are then crosslinked into a secondary network. The secondary networks of nanoparticles are formed at room temperature and at neutral pH; factors which make these networks amicable for drug loading and release. Controlled release studies have been performed on the networks using dextran markers of various molecular weights as model macromolecular drugs. Drug release was quantified under various physical conditions including a range of temperature, particle size, and concentrations.

***“Tissue responses to thermally-responsive hydrogel nanoparticles,” H. Weng, J. Zhou, L. P. Tang, Z. B. Hu, J. Biomaterials Sci.–Polymer Ed. 15, 1167-1180 (2004).***

Thermally-responsive hydrogel nanoparticles of poly(N-isopropylacrylamide) (PNIPAM) and hydroxypropyl cellulose (HPC) have been synthesized. The particle size has been correlated to surfactant concentration and polymer concentration using dynamic laser light scattering techniques. The tissue compatibility of these hydrogel nanoparticles has been evaluated by comparing with poly-L-lactic acid and polystyrene nanoparticles using a mouse implantation model. Our results suggested that both PNIPAM and HPC nanoparticles triggered lesser inflammatory and fibrotic responses among all nanoparticles tested. It is likely that these hydrogel nanoparticles may be suitable for tissue augmentation or drug-delivery devices.

**(iv) Fruitful collaboration with ARL Scientists on Long Chain branched polymers**

***“Light scattering study of self-association behavior of long chain polymers in solvents,” X. H. Xia, Z. B. Hu, J. Gao, D. J. Qin, H. D. Durst and R. Yin, Langmuir 18, 8300 (2002)***

Self-association behavior and conformation variation of long chain branched (LCB) poly (2-ethyloxazoline) (PEOx) with a  $\text{CH}_3-(\text{CH}_2)_{17}(\text{C}_{18})$  modified surface are investigated using light scattering techniques in various solvents. It is found that this LCB-PEOx self-associates in less polar solvents to form meta-stable nano-aggregates instead of undergoing precipitation. The critical aggregation concentration (C.A.C.) of this LCB was obtained from the sharp increase of both hydrodynamic radius ( $R_h$ ) and scattering light intensity measured in dynamic light scattering. The C.A.C. strongly depends on solvent polarity, decreasing as the solvent becomes more hydrophobic. As polarity of the solvent increases,  $\text{C}_{18}$  chains move from the outside surface to the interior. Inward movement of  $\text{C}_{18}$  chains can cause coupled LCB-polymer chains to move with them, resulting shrinkage of the particle size. The self-association process in the LCB-PEOx involves intra-chain ( $\text{C}_{18}$  chains) collapse and inter-chains association. Combining dynamic and static light scattering, average density of individual LCB-PEOx molecules in ethanol was estimated below the C.A.C. The hydrodynamic radius of the LCB-PEOx in ethanol was found to shrink upon increasing temperature, indicating the solvent becomes poorer. During the heating process, self-association did not occur.

**(v) Correlating the phase diagram with thermodynamic calculations.**

***“Phase behavior of thermally responsive microgel colloids,” J. Z. Wu, B. Zhou, Z. B. Hu, Phys. Rev. Lett. 90, 048304 (2003).***

The phase behavior of poly-N-isopropylacrylamide (PNIPAM) nanoparticles dispersed in water is investigated using a thermodynamic perturbation theory combined with light scattering and spectrometer measurements. It is shown how the volume transition of PNIPAM particles affects the interaction potential and determines a novel phase diagram that has not been observed in conventional colloids. Because both particle size and attractive potential depend on temperature, PNIPAM aqueous dispersion exhibits phase transitions at a fixed particle density by either increasing or decreasing temperature.

***“Inter-particle potential and the phase behavior of temperature-sensitive microgel dispersions,” J. Z. Wu, G. Huang, Z. B. Hu, Macromolecules 36, 440-448 (2003).***

Molecular-thermodynamic models assisted with experimental measurements are applied to correlate and predict the volume transition and structural ordering of poly-N-isopropylacrylamide (PNIPAM) microgel particles dispersed in pure water. The effective pair potential between neutral PNIPAM particles is represented by a Sutherland-like potential where the size and energy parameters are correlated with particle radius and the solution osmotic second virial coefficients attained from static and dynamic light scattering experiments. Using a first-order perturbation theory for the fluid phase and an extended cell model for the crystalline solid, the calculated phase diagram indicates that an aqueous dispersion of PNIPAM particles may freeze at both high and low temperatures. At low temperature, the freezing occurs at large particle volume fraction, similar to that in a hard-sphere system; while at high temperature, the freezing is driven by strong van der Waals attraction due to the increase in the Hamaker constant of the microgel particles when they collapse. The phase diagram of PNIPAM dispersions predicted from the molecular-thermodynamic models agrees favorably with experimental observations.

***“Volume transition and internal structures of small poly(N-isopropylacrylamide) microgels,”***

***L. Arleth, X. H. Xia, R. P. Hjelm, J. Z. Wu, & Z. B. Hu, Journal of Polymer Science, Polym. Phys. Ed., 43, 849-860 (2005).***

Poly(N-isopropylacrylamide) (PNIPAM) undergoes a phase transition from a low temperature swelled to a high temperature unswelled state close to  $34^\circ\text{C}$ . We have prepared monodispersed PNIPAM microgels, with hydrodynamic radius  $R_h$  of 50 nm in the swollen state. The volume transition and structure changes of the microgel particles as a function of temperature is probed by laser light scattering and small angle neutron scattering (SANS) with the objective of unveiling the small particle internal structure, particle-particle and particle-solvent interaction. We find that, within the resolution of the experiments, the particle has a constant cross-link density as a function of the radius. This is in contrast to previous reports on the heterogeneous structures of larger PNIPAM microgel particles but in good agreement with

recent reports based on computer simulation. Furthermore, a large repulsive particle-particle interaction potential is observed below the transition temperature, while the potential becomes attractive above the transition temperature.

**(vi) Gel nanoparticles with new functionalities**

***“Optical properties of N-isopropylacrylamide microgel spheres in water,” J. Gao and Z. B. Hu, Langmuir 18, 1360-1367 (2002).***

Optical properties of *N*-isopropylacrylamide (NIPA) microgel spheres in water have been investigated using light scattering and turbidity methods. Two batches of NIPA microgel spheres were synthesized with their hydrodynamic radii of 132 and 216 nm in water at 25 °C. The concentrations ranging from ~ 0.01 wt% to ~ 14 wt% were obtained by dilution/condensation of the dispersions. The hydrodynamic radius distribution, the radius of gyration, the molar mass of the microgel spheres and the polymer volume fraction in spheres were determined by combining dynamic and static light scattering. As polymer concentration increases, the microgel spheres in dispersions exhibit the liquid, the crystal and the glass states, while the optical appearance of the dispersions changes from transparent to cloudy, then to colored (pink, green, blue and purple gradually), and eventually to transparent. The formation of large colloidal crystals in a very narrow concentration range (ca. 3~5 wt%), at room temperature (18 ~ 22 °C), yields iridescent patterns from typical Bragg diffraction. For a colored dispersion, the turbidity (as the function of wavelength  $\lambda$ ) exhibits a sharp shoulder-shape increase at a certain  $\lambda_c$  with decreasing wavelength.  $\lambda_c$  shifts linearly to a lower wavelength with the decrease of inter-particle distance. Heating a concentrated NIPA microgel dispersion from room temperature to 35 °C leads to a continuous increase of turbidity.

***“Formation and volume phase transition of hydroxypropyl cellulose microgels in salt solution,” X. H. Xia, S. J. Tang, X. H. Lu, Z. B. Hu, Macromolecules 36, 3695-3698, (2003)***

Surfactant-free hydroxypropyl cellulose (HPC) microgels have been synthesized in salt solution. The average size and size distributions of microgel particles have been correlated with polymer concentration, salt concentration and reaction temperature using light scattering techniques. It is found that the low critical solution temperature (LCST) of HPC polymer chains decreases upon the increase of sodium chloride concentration. In a narrow sodium chloride concentration range from 1.3 M to 1.4M, HPC chains can self-associate into colloidal particles at room temperature. These particles remained stable in solution for weeks without changing their sizes. The microgel particles were then obtained *in situ* by bonding self-associated HPC chains at 23°C using divinylsulfone as a crosslinker. The volume phase transition of the resultant HPC microgels has been studied as a function of temperature at various salt concentrations. A theoretical model based on Flory-Huggins free-energy consideration has been used to explain the experimental results.

**(vii) Phase transitions in bulk hydrogels**

***“Swelling and mechanical behavior of poly(N-isopropylacrylamide)/Na-montmorillonite layered silicates composite gels,” X. H. Xia, J. Yih, N. D’souza, and Z. B. Hu, Polymer 44, 3389-3393 (2003)***

Clay-polymer hydrogel composites have been synthesized based on poly(*N*-isopropylacrylamide) (PNIPAM) gels containing 0.25 to 4 wt% of the expandable smectic clay Na-montmorillonite layered silicates (Na-MLS). The morphology of the composite gels has been studied using a polarized optical microscope. The size of Na-MLS aggregates increases with Na-MLS concentration. The swelling ratio of the Na-MLS/PNIPAM composite in water is increased at the low Na-MLS concentration but decreases as the concentration increases. Correspondingly, the shear modulus of the gel is found to exhibit a distinct minimum against clay concentration. For Na-MLS concentrations ranging from 2.0 to 3.2 wt%, the composite gels have larger swelling ratio and stronger mechanical strength than those for a pure PNIPAM. The presence of Na-MLS does not affect the value of the lower critical solution temperature (LCST) of the PNIPAM. However, the gel volume change at the LCST is first increased and then decreased upon the increase of the Na-MLS. No pH induced phase transition is observed for the Na-MLS/PNIPAM composites. The experimental results can be explained by considering that Na-MLS is physically entrapped inside rather than chemically bonded into the gel.

**(6) Listing of all publications and technical reports supported under this grant or contract. Provide the list with the following breakout, and in standard format showing authors, title, journal, issue, and date.**

**(a) Papers published in peer-reviewed journals**

- 1 “Hydrogel opals,” Z. B. Hu, X. Lu & J. Gao, *Advanced Materials* **13** (Cover), 1708-1712 (2001).
- 2 “Self-association of hydroxypropyl cellulose in water,” J. Gao, G. Haidar, X. H. Lu, and Z. B. Hu, *Macromolecules* **34**, 2242-2247 (2001).
- 3 “Spinodal decomposition in N-isopropylacrylamide gel,” Z. B. Hu, C. J. Wang, Y. Y. Chen, X. M. Zhang, & Y. Li, *J. Polym. Sci., Part B: Polym. Phys.* **39**, 2168-2174, (2001).
- 4 “Optical properties of N-isopropylacrylamide microgel spheres in water,” J. Gao and Z. B. Hu, *Langmuir* **18**, 1360-1367 (2002).
- 5 “Light scattering study of self-association behavior of long chain polymers in solvents,” X. H. Xia, Z. B. Hu, J. Gao, D. J. Qin, H. D. Durst and R. Yin, *Langmuir*, **18**, 8300-8306 (2002).
- 6 “Phase transition behavior of hydroxypropylcellulose under interpolymer complexation with poly(acrylic acid),” X. H. Lu, Z. B. Hu, J. Schwartz, *Macromolecules* **35**, 9164-9168 (2002).
- 7 “Inter-particle potential and the phase behavior of temperature-sensitive microgel dispersions,” Wu, J. Z., Huang, G., Hu, Z. B. *Macromolecules* **2003**, *36*, 440-448.
- 8 “Phase behavior of thermally responsive microgel colloids,” Wu, J. Z.; Zhou, B.; Hu, Z. B. *Phys. Rev. Lett.* **2003**, *90*, 048304.
- 9 “Swelling and mechanical behavior of poly(N-isopropylacrylamide)/Na-montmorillonite layered silicates composite gels,” X. H. Xia, J. Yih, N. D’souza, and Z. B. Hu, *Polymer* **44**, 3389-3393 (2003)
- 10 “Formation and volume phase transition of hydroxypropyl cellulose microgels in salt solution,” X. H. Xia, S. J. Tang, X. H. Lu, Z. B. Hu, *Macromolecules* **36**, 3695-3698, (2003)
- 11 “Synthesis and study of and controlled release from nanoparticles and their networks based on functionalized hydroxypropylcellulose,” T. Cai, Z. B. Hu, B. Ponder, J. St. John, and D. Moro, *Macromolecules* **36**, 6559-6564 (2003)
- 12 “A new route to crystalline hydrogels as guided by a phase diagram,” Z. B. Hu and G. Huang, *Angewandte Chemie, Int. Ed.*, **42**, 4799(2003).
13. “Nanostructured polymer gels,” Z. B. Hu, *Macromolecular Symposia* **207**, 47-55 (2004)
- 14 “Microgel Dispersions: Colloidal Forces and Phase Behavior,” J. Z. Wu and Z. B. Hu, *Encyclopedia of Nanoscience and Nanotechnology*, J. A. Schwarz, C.I. Contescu, and K. Putyera, Editors. Marcel Dekker, Inc. 1967 – 1976 (2004). (Invited Contribution).
- 15 “Controlled drug release from hydrogel nanoparticle networks,” G. Huang, J. Gao, and Z. B. Hu, J. V. John, B. C. Ponder D. Moro, *J. Controlled Release* **94**, 303-311 (2004).
- 16 “Tissue responses to thermally-responsive hydrogel nanoparticles,” H. Weng, J. Zhou, L. P. Tang, Z. B. Hu, *J. Biomaterials Sci.–Polymer Ed.* **15**, 1167-1180 (2004).
- 17 “Physically bonded nanoparticle networks: A novel drug delivery system,” X.H. Xia, Z. B. Hu, and M. Marquez, *Journal of Controlled Release*, **103**, 21–30(2005).
- 18 “Volume transition and internal structures of small poly(N-isopropylacrylamide) microgels,” L. Arleth, X. H. Xia, R. P. Hjelm, J. Z. Wu, & Z. B. Hu, *Journal of Polymer Science, Polym. Phys. Ed.*, **43**, 849-860 (2005).

**(b) Papers published in non-peer-reviewed journals or in conference proceedings**

None

**(c) Papers presented at meetings, but not published in conference proceedings**

- 1 “Polymer gel nanoparticle networks,” December 5-7, 2001, Polymer gel symposium, 7<sup>th</sup> Pacific polymer Conference, Oaxaca, Mexico.
- 2 “Phase transition in nanostructured gels,” Z. B. Hu, X. Lu, J. Gao, IUPAC, July 20, 2002, Beijing, China
- 3 “Smart Gels,” Z. Hu (invited) Symposium of Nanotechnology and Smart Materials organized by Kraft Food, Inc., September 26, 2002, Glenview, IL.
- 4 “Hydrogel opals,” Z. B. Hu, A symposium in honor of the 70<sup>th</sup> birthday of professor Allan S. Hoffman, December 17-20, 2002, Maui, Hawaii
- 5 “Phase behavior of thermally responsive microgels,” Z. Hu (Invited) Workshop on Neutron Scattering and Light Scattering on Colloidal Systems, Los Alamos National Laboratory, Los Alamos, NM, June 11-12, 2003.
- 6 “Hydrogel opals,” Z. Hu, Invited speaker in the first annual meeting of strategic partnership research in nanotechnology, UT-Austin, August 25-27, 2003.
- 7 “Smart Hydrogel Nanoparticles and Their Application in Biotechnology,” Z. Hu (invited), Annual Convention of the Chinese Institute of Engineers, Dallas-Fort-Worth Chapter, September 20, 2003.
- 8 “Nano-fabrication of polymer gels,” Z. Hu, (invited) The 5th International Gel Symposium (GelSympo 2003), Kashiwa, Japan, Nov. 18-Nov. 20, 2003.
- 9 “A new route to crystalline hydrogels as guided by a phase diagram,” Z. Hu, (invited) *Particles 2004*, 6-9 March 2004, Orlando, FL
- 10 “Novel polymer gel nanoparticle dispersions,” Z. Hu, (invited), Third Annual Meeting of Texas and Southwest Section of the North American Thermal Analysis Society, April 29 and 30, 2004, Dallas, Texas.
- 11 “Volume transition and internal Structures of small poly-N-isopropylacrylamide microgels,” R. P. Hjelm, X. Xia, Lise Arleth, J. Wu and Z. B. Hu, European-MRS Spring Meeting 2004, May 24-28, 2004, Strasbourg, France.
- 12 “Polymer gel nanoparticle dispersions with inverse thermo-reversible gelation,” Z. B. Hu, and X. H. Xia, 2004 Polymer Network Conference, August 15-19, 2004, NIH Campus, Bethesda, MD.
- 14 “Synthesis and Study of Photo-responsive Microgels,” M. Marquez, Antonio A. Garcia, Rohit Rosario, Devens Gust, Mark Hayes, Joseph Springer, Tom Picraux, Bruce Bunker, Tong Cai, and Zhibing Hu, The 18th European Colloid and Interface Society Conference, Almería, Spain. September 19-24, 2004.
- 16 “Laser Light Diffraction Study of Temperature Stimuli in Self-Assembling Colloidal Crystals,” Ryan Bosca, S. Tang, Z. B. Hu, 2004 Fall Meeting of Texas Section of the American Physical Society, Baylor University, Waco, TX, Oct 9-11, 2004
- 17 “Synthesis and Light Scattering Study of Microgels with Interpenetrating Polymer Networks,” X. Xia and Z. B. Hu, 2004 Materials Research Society Fall Meeting, Nov 29-Dec 3, 2004, Boston, MA

- 18 “Controlled drug release from hydrogel nanoparticle networks,” Z. Hu, (invited), First Interdisciplinary Network of Emerging Science and Technologies Meeting: Droplet NanoEngineering, May 15, (2005)
- 19 “Polymer gel nanoparticles and their networks,” Z. Hu, (invited) Symposium in Pacificchem 2005, Honolulu, Hawaii, December 15-20, 2005

**(d) Manuscripts submitted, but not published**

“Hydrogel nanoparticle dispersions and their tissue response,” Z. B. Hu, X. H. Xia, M. Marques, H. Weng, and L. P. Tang, Macromolecular Symposia (invited) (2005).

**(e) Technical reports submitted to ARO**

Technical reports submitted to ARO in 2002, 2003, 2004

**(7) List of all participating scientific personnel showing any advanced degrees earned by them while employed on the project**

**Dr. X. Lu**, Ph. D. Dissertation in Materials Science and Engineering, 2002, entitled “Synthesis and study of polymer gel nanoparticles and their networks”.

**Dr. X. Xia**, Ph.D. Dissertation in Chemistry, 2003, entitled “Fabrication and light scattering study of multi-responsive nanostructured hydrogels and water-soluble polymers”.

**Dr. C. Wang**, Ph. D. Dissertation in Physics, 2003, entitled “Polymer gels: Kinetic and dynamic studies and their applications as biomaterials.”

**Dr. G. Huang**, Ph. D. Dissertation in Chemistry, 2004, entitled “A new route to crystalline hydrogels as guided by phase diagrams.”

**Dr. B. Zhou**, Ph.D. Dissertation in Materials Science and Engineering, Dec. 2004, entitled “Synthesis and characterization of crystalline assembly of poly(N-isopropylacrylamide)-co-acrylic acid nanoparticles.”

**Postdoctoral research fellows:** Dr. X. Lu and Dr. Y. Zhang

**Some students have received awards:**

Ms. Jessica Yih was selected as a semifinalist in the 2003 Intel Science Talent Search.

X. Xia received the Office of the Research Vice President’s 2004 Dissertation Award for Research Achievement in the Natural Sciences, Mathematics, or Engineering.

G. Huang received 2004 Spurlock Scholarship Award- given for outstanding research achievement by a graduate student in Chemistry.

**(8) Report of Inventions (by title only)**

1. Z. B. Hu, X. H. Lu, and J. Gao, B. Ponder, & J. St. John, “Synthesis and use of polymer gel nanoparticle networks,” U.S. Pat. Appl. Publ. US 20030138490, A1 (July 2003).
2. Z. B. Hu, X. H. Lu, J. Gao, T. Cai, G. Huang, and B. Zhou, “Synthesis, uses and compositions of crystal hydrogels.” U.S. Pat. Appl. Publ. US 2004018160 A1 (2004).
3. K. D. Nelson, A. A. A. Romero-Sanchez, G. M. Smith, N. Alikacem, D. Radulescu, P. Waggoner and Z. B. Hu, “Drug releasing biodegradable fiber implant,” U. S. Patent 6,596,296, (July 2003)
4. K. D. Nelson, A. A. A. Romero-Sanchez, G. M. Smith, N. Alikacem, D. Radulescu, P. Waggoner and Z. B. Hu, “Fabrication of drug loaded biodegradable polymer fibers,” U.S. Patent 6,858,222 (February, 2005)
5. Z. B. Hu, X. H. Xia and L. P. Tang, “Improved process and apparatus for synthesizing of surfactant-free hyaluronic acid nanoparticles and microparticles,” U. S. Patent Application (USPTO Serial No.: 60/516,707)

**(9) Bibliography (None)**

**(10) Appendixes (None)**