Anisotropic Stimuli-Responsive Polymeric Nanoparticles: Synthesis and Characterization

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ANISOTROPIC STIMULI-RESPONSIVE POLYMERIC NANOPARTICLES: SYNTHESIS AND CHARACTERIZATION

A Dissertation
Presented to
the Graduate School of
Clemson University

In Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy
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Chunliang Lu
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Accepted by:
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ABSTRACT

This dissertation focuses on the design, synthesis and characterization of stimuli-responsive anisotropic nanoparticles with various morphologies. Size- and shape-tunable Janus nanoparticles consisting of poly(methyl methacrylate/n-butyl acrylate) (p(MMA/nBA)), poly(pentafluorostyrene/nBA) (p(PFS/nBA) and poly(2-(N,N'-dimethylamino) ethyl methacrylate/nBA) (p(DMAEMA/nBA)) phases were synthesized via consecutive seeded emulsion polymerization. These Janus nanoparticles are capable of changing size and morphology in response of temperature and/or pH changes, which may have potential applications as solid surfactants.

Gibbous and inverse-gibbous nanoparticles were synthesized via copolymerization of fluorinated monomers in the presence of pMMA or polystyrene (pSt) seed particles. The morphology of the gibbous nanoparticles can be controlled by polymerization conditions. Incorporation and copolymerization of methacrylic acid (pMAA) components results in pH-responsive gibbous nanoparticles with numerous size-tunable bulges. In addition, the gibbous and inverse-gibbous nanoparticles can be controlled to self-assemble in solutions but upon evaporation of solvents form two- and three-dimensional assemblies stabilized by electrostatic interactions and shape-matching topographies.

Taking advantage of the heterogeneous nature of emulsion polymerization, surfactant free heterogeneous radical polymerization (SFHRP) was developed to synthesize ultra-high molecular weight amphiphilic block copolymers. This is one-step
process of preparing block copolymer morphologies. The amphiphilic block copolymers can form thermochromic inverse micelles in organic solvents, capable of selectively scattering light as a function of temperature. The approach was also utilized to synthesize polymer nanowires via in-situ self-assembly of amphiphilic block copolymers. This kinetically controlled directional growth may lead to many industrial applications, including synthesis of other block copolymers, polymeric nanowire latexes and other morphologies.
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INTRODUCTION

Colloidal particles are fundamental components of many macrostructures, polymeric films and fibers that serve as precursors to many technologies. Therefore, understanding behavior of these building blocks is critical in the development of new materials with desirable properties. This is particularly challenging when chemical or physical anisotropy as well as stimuli-responsiveness are required. Although scientific interests and application needs for the development of controllable and rationally designed nanoparticles with tunable properties are critical to future technologies, precise control of stimuli-responsiveness and shape anisotropy are challenging. In spite of the fact that emulsion polymerization offers attractive and simple methods of synthesizing colloidal particles, it is not capable of achieving desirable nanoparticle properties. The objectives of this dissertation are:

- Synthesis of triphasic size- and shape-tunable Janus nanoparticles (JNPs) by seeded emulsion polymerization, followed by investigation of their stimuli-responsive behavior as well as interfacial properties as a function of temperature and pH.

- Design and synthesis of gibbous and inverse-gibbous nanoparticles with well-defined surface topographies by surfactant-free emulsion polymerization, and the controlled self-assemblies by the topography-matching nanoparticles.

- Control of copolymer morphologies and in-situ formation of nano-objects by one-step surfactant-free heterogeneous radical polymerization.
This dissertation is concerned with synthesis and characterization of stimuli-responsive colloidal nanoparticles with anisotropic shape and consists of two parts: Part 1 (Chapters II-IV) outlines the synthesis of Janus, gibbous and inverse gibbous nanoparticles via seeded emulsion polymerization, and Part 2 (Chapters V-VI) focuses on the synthesis of amphiphilic block copolymers and their in-situ self-assemblies.

Chapter I reviews the polymer nano-objects capable of altering size, color, and shape in response of external stimuli. Design and synthesis of nano-objects with precisely controlled and responsive shapes as well as chemical functionalities are not only challenging in the development of spatial anisotropies, but also asymmetrical responses to stimuli. The morphology control during any synthetic process as well as the local responsiveness to external stimuli resembles biological behaviors. This chapter discusses recent advances in the development of stimuli-responsive anisotropic nano-objects and their applications. Synthesis of Janus and gibbous nanoparticles that are capable of asymmetrically changing size, shape, and color are demonstrated. Stimuli-responsive nanowire and nanotubes with morphology changes in axial and two-dimensional lateral directions are also discussed.

Chapter II shows the synthesis of triphasic size- and Janus balance (JB)-tunable nanoparticles (JNPs) utilizing a two-step emulsion polymerization of pentafluorostyrene (PFS) and 2-(dimethylamino)ethyl methacrylate (DMAEMA) and n-butyl acrylate (nBA) in the presence of poly(methyl methacrylate (MMA)/nBA) nanoparticle seeds. Each JNP consists of three phase-separated copolymers: p(MMA/nBA) core, temperature, and pH-responsive (p(DMAEMA/nBA)) phase capable of reversible size and shape changes, and
shape-adoptable (p(PFS/nBA)) phase. Due to built-in second-order lower critical solution temperature (II-LCST) transition of p(DMAEMA/nBA) copolymer, macromolecular segments collapse when temperature increases from 30 to 45 °C, resulting in size and shape changes. The p(DMAEMA/nBA) and p(MMA/nBA) phases within each JNP assume concave, flat, or convex shapes, forcing p(PFS/nBA) phase to adopt convex, planar, or concave interfacial curvatures, respectively. As a result, the JB can be tuned from 3.78 to 0.72. The presence of pH-responsive DMAEMA component also facilitates the size and JB changes due to protonation of the tertiary amine groups of p(DMAEMA/nBA) backbone. Synthesized in this manner, JNPs are capable of stabilizing oil droplets in water at high pH to form Pickering emulsions, which at lower pH values release oil phase. This process is reversible and can be repeated many times.

Chapter III shows the synthesis of copolymer nanoparticles with controlled stimuli-responsive phase-separated gibbosities using a simple free radical polymerization process. The topography of the gibbous phase can be controlled by the copolymer composition and polymerization conditions. When pH-sensitive monomers were copolymerized onto surface bulges, pH changes resulted in dimensional changes of the localized gibbous phases. Facilitated by radical and monomer diffusion into the seed particle surfaces, localized polymerization near the surface is responsible for the formation of phase-separated gibbous topographies. This general approach may offer a number of possibilities for controllable design of ordered heterogeneous copolymer morphologies for a variety of applications.
Chapter IV describes the synthesis of gibbous and inverse-gibbous colloidal nanoparticles by taking advantage of the localized phase separation and surface tension differences within hydrophobic-hydrophilic environments during colloidal synthesis. The topography-matching nanoparticles stabilized by opposite charges are capable of forming “gear-like” directional assemblies due to short-range electrostatic interactions and long-range “gear-like” mechanical interlocking. Guided by surface charges, these nanoparticles form 2D directional arrays. Upon a surface deposition process, 3D crack-free colloidal structures develop, facilitated by the combined short-range electrostatic repulsions and long-range “gear-like” mechanical interlocking.

Chapter V shows the synthesis of ultra-high molecular weight (> 10^6 g/mol) amphiphilic block copolymers using one-step surfactant-free heterogeneous radical polymerization (SFHRP). The polymerization initially involves formation of water-soluble homopolymer blocks, followed by copolymerization of a hydrophobic monomer, resulting in ultra-high molecular weight block copolymers. The process is controlled by facilitating heterogeneous reaction conditions and continuous supply of an initiator. Using this synthetic approach, we synthesized amphiphilic block copolymers of poly(2-(N,N-dimethylamino) ethyl methacrylate)-block- poly(n-butyl acrylate) (pDMAEMA-b-pnBA), pDMAEMA-block-poly(tert-butyl acrylate) (pDMAEMA-b-ptBA) and pDMAEMA-block-polystyrene (pDMAEMA-b-pSt) with molecular weights of 1.98 x10^6, 1.18 x10^6, and 0.91 x10^6 g/mol, respectively. These ultrahigh molecular weight block copolymers are able to self-assemble in non-polar solvents to form thermochromic inverse polymeric micelles as well as other shapes.
Chapter VI investigates the in-situ synthesis of block copolymer nanowires via one-step surfactant-free heterogeneous radical polymerization (SFHRP) of DMAEMA and St in an aqueous phase. Under heterogeneous reaction and initiator-starvation conditions, the sequential copolymerization of DMAEMA and St leads to the formation of amphiphilic block copolymers, which instantaneously form polymeric micelles that consist of hydrophobic pSt block core and hydrophilic pDMAEMA block corona. Upon continuous polymerization and micellar growth, initially formed spherical micelles will extend in one dimension due to the high repulsive forces of the pDMAEMA blocks in a localized region and subsequent chain extension to form pSt blocks. The high glass transition temperature of pSt blocks facilitates the stabilization of this kinetically controlled morphology formation. As a result, block copolymer nanowires with the aspect ratio greater than 100 can be obtained.
CHAPTER ONE

STIMULI-RESPONSIVE COLLOIDAL NANO-SCIENCE: ANISOTROPY
OF SHAPE AND RESPONSIVENESS

1.1 Introduction

Basic structural components of living organisms are cells. Although there are many types of cells which consist of several bioactive components serving multiple functions and interacting with each other, their common feature is cellular metabolism. These sequential chemical reactions facilitate the mechanisms for growth and reproduction, while maintaining living functions. The cell sizes may vary from 0.1 – 100 \( \mu \text{m} \), and while most cells exhibit spherical or oval shapes, other morphologies also exist.[1] Moreover, their morphologies may change, depending upon external stimuli. For example, when experiencing disruptions, the red blood cells shown in Figure 1-1-A, may transform to echinocytes of an abnormal shape with many small thorny projections sticking out of the membrane.[2] This is shown in Figure 1-1-B. On the other hand, the filamentous cells depicted in Figure 1-1-C usually exhibit long visible chains or filaments. One of the filamentous cells is the filamentous algae that intertwine to form a mat on a substrate in water. Another illustrative example are high aspect ratio Filoviruses cells with a diameter of 80 nm and a few microns in length.[3]
Except unicellular organisms, cells are organized into complex structures to support living functions. To sustain these functions, cells require selectively tailored molecular structures and assemblies enabling the control of specific chemical and physical reactions in their environments. For example, phospholipids may control selective transport of proteins, but inhibit transport of other components.⁴ These responsive biointerfacial boundaries have inspired numerous studies to develop of stimuli-responsive nanomaterials with various shapes. Although significant efforts will be necessary to achieve biological functions, shape and shape changes combined with stimuli-responsiveness represent the first step in this direction. The first attempts towards this goal focused on the development of stimuli-responsive nanomaterials that may selectively release cargo at a targeted site.⁵ For that purpose, various phospholipid and nanoparticles were synthesized in order to increase the drug-loading capacity (hollow...
particles or vesicles),\[6, 7] while avoiding renal clearance and cellular uptake (worm-like micelles, nanowires, or nanotubes),\[8] and to achieve dual/multiple drug-delivery (Janus or multi-compartment particles).\[9]

Among attractive nanomaterials that may potentially mimic biological cells are colloidal nanoparticles capable of responding to chemical/physical stimuli.\[10] External stimuli may be applied to control particle structures, dimensions, morphologies, interactions as well as self-assemblies. The striking resemblance between the shape of cells and colloidal synthetic assemblies is depicted in Figure 1-1, A/A’, B/B’, and C/C’. Also, aside from the visual similarities, stimuli-responsive behavior stimulated many attempts to mimic biological systems.

While a spherical shape is perhaps the most common anticipated outcome of colloidal synthetic efforts, the main challenge is to control physical and chemical anisotropy. These anisotropic features not only inspired new shape developments, but also resulted in the imbedding responsive of chemical functionalities into diversified shapes. This is particularly apparent for soft matter materials, whereby precisely controlled chemical reactions may control morphologies and anisotropy of responsiveness. In contrast, the control of morphologies of inorganic nanoparticles is limited by processing conditions. Thus, the primary responses to electric and magnetic fields as well as electromagnetic radiation results from intrinsic materials properties that rarely results in morphological changes.
1.2 Anisotropy of Responses

Numerous efforts have been placed into the synthesis of colloidal nano-objects with various morphologies and functionalities. The responsiveness of individual nanostructures in a controllable manner represents another level of complexity. Figure 1-2-(a-c) depicts isotropic spherical, core-shell, and hollow nanoparticles capable of uniformly altering size, shape, color as well as other properties which were summarized in the several review articles.[5, 11-13] Figure 1-2-(d-g) depicts anisotropic nano-objects that are capable of changing size and morphologies asymmetrically in three directions (3D), thus enabling orientation or self-assembly of heterogeneous and hierarchical structures. Stimuli-responsive anisotropic nanoparticles, such as gibbous and Janus nanoparticles, nanowires, and nanotubes are of particular interest not only in the context of mimicking biological organisms, but also due to potential lithographic and biomedical applications. While numerous efforts were given to the synthesis and applications of these materials, the precise size and morphology control still remains to be of a significant challenge. It should be noted that limited analytical tools are available to elucidate the origin of molecular processes responsible for their properties, thus making the measurements of asymmetric responses to external stimuli troublesome. Another exciting challenge is to imbed stimuli-responsive components, facilitating directional interactions, and multi-dimensional encoded signaling that resemble the activity of biological cells.
Nanoparticles with structural and compositional gradients capable of selective dimensional responses at the nanoscale levels are of particular interest. For isotropic shape nanoparticles (spherical, core-shell and hollow) shown in Figure 1-2-(a-c), the property changes in response of external stimuli typically exhibit isotropic dimensional restrictions, in which the size and porosity of nanoparticles can be locally altered\textsuperscript{[5, 11, 14]}. For anisotropic nanoparticles, which typically exhibit asymmetrical distribution of chemical and/or physical properties, the responsiveness will be directional. As shown in
Figure 1-2-d, stimuli-responsive bulges on the surface of gibbous nanoparticles may alter their individual shape, while maintaining the shape of the spherical core, thus offering the adjustment of topography and surface roughness.[15] Another example are the Janus nanoparticles shown in Figure 1-2-e. The size, color, and physical or chemical properties of each hemisphere can be modulated by external stimuli.[16-18] The cylindrical nanoparticles shown in Figure 1-2-f are capable of altering flexibility,[19] or transform to spherical nanoparticles under certain conditions.[20] As shown in Figure 1-2-g, nanotubes that exhibit stimuli-responsive walls will expand or shrink, and the inner diameter as well as the wall thickness can be altered by temperature changes.[21]

For thermal and pH responsive nano-objects morphology changes of these nano-objects are driven by conformational changes, hydrogen-bonding and/or protonation-deprotonation induced rearrangements. The thermo-responsive polymers have lower critical solution temperature (LCST) in aqueous environments, and typical examples includes poly(N-isopropyl arylamide) (PNIPAM), poly(ethylene oxide) (PEO), poly(propylene oxide) (PPO), and poly(vinylcaprolactone) (PVCL). Above the LCST, homopolymers or copolymers containing these monomer units will experience the coil-to-globule transitions due to loss of hydrogen bonding (H-bonding) between polymers and water molecules. The pH-responsive polymers usually realize on the reversibly ionizable functional groups within the side chains that induce electrostatic repulsions between charged polymer units upon environmental pH changes. As a result, polymer segments are able to extend or collapse, depending on the extent of ionization. Typical pH-responsive polymers include poly(acrylic acid) (PAA), poly(methacrylic acid)
(PMAA), poly(N,N’-dimethyl aminoethyl methacrylate) (PDMAEMA) and poly(vinyl pyridine) (PVP).

There is also an increasing demand for developing photo-chromic nanoparticles that are capable of changing morphologies and color/fluorescence in response of electromagnetic irradiation. This is achieved by attaching or copolymerizing photo-responsive chromophores on the surface of inorganic nanoparticles, or along the polymer chains of soft-matter nanoparticles. The most common chromophores \cite{22} capable of changing dimensions and absorption/emission of light in response to electromagnetic irradiation are azobenzene, \cite{23} spiropyran,\cite{24, 25} and triphenylmethane.\cite{14}

The pH responsive nanoparticles usually exhibit ionic strength-responsiveness, typically due to manipulation of electrostatic interactions between polymer units and ions.\cite{11} Biologically responsive nanomaterials are usually triggered by the presence of biologically active enzymes, which are often utilized in targeted drug-delivery systems.\cite{26, 27} For example, liposomes consisting of polypeptide-functionalized polymers demonstrated targeted release of drugs in the presence of cancer-associated protease.\cite{28} Colloidal nanoparticles containing conducting polymers \cite{29, 30} or gold nanoparticles \cite{31} have been utilized for controlled drug-releasing devices in response of weak electric fields. Due to “remote” control of responses by external magnetic fields and other unique properties, magnetic nanoparticles have been widely studied and utilized in biomedical applications.\cite{32-36} Electrochemical-responsive colloidal systems typically consist of gold nanoparticles, enabling the redox reactions of the media which found potential applications as electrochemical sensors.\cite{37} Several reviews are available.\cite{38-41}
1.3 Synthesis of Stimuli-Responsive Nanoparticles

Although colloidal synthesis have been known for many decades and the most known commodity products are latex paints, sophisticated synthesis of isotropic nanoparticles and manipulation of their symmetrical responsiveness have formulated the foundation for the development of anisotropic morphologies as well as anisotropic responsiveness. Anisotropic colloidal particles can be synthesized by several methods,[42-44] but the most common approaches are seeded growth,[45-47] self-assembly,[48-51] controlled fusion,[52] designed phase-separation,[53] selective deposition,[54, 55] partial surface modification,[56-58] and seeded emulsion polymerization.[15, 59, 60] Of particular interest are the Janus particles with two sides of different chemistry/polarity and directional assemblies. The synthesis of Janus particles has been achieved using several approaches, which are categorized into four major strategies: masking, phase-separation, seeded growth, and self-assembly. As shown in Figure 1-3, the most versatile strategy is the selective chemical modification of exposed surface on temporarily immobilized spherical particles on 2D planar substrates, or at the interface of the Pickering emulsion droplets. The top surfaces of particles immobilized on 2D substrates can be chemically modified by metal deposition,[54, 61, 62] plasma treatments,[63] ligand exchanges,[64-66] chemical reactions,[67] electrostatic binding,[68] electrochemical growth,[69] and other means.[44] The particles can be also immobilized on the surface of electrospun fibers[70] or the Pickering emulsion droplets,[58, 71] followed by chemical modifications and release of the resulting asymmetric particles.
Figure 1-3. Synthetic strategies of Janus particles. Adapted from Ref. [72].

Another widely utilized synthetic procedure is the phase-separation of two component mixture in one single particle, which can be realized through electrohydrodynamic co-jetting,[53] microfluidic co-flow,[73, 74] and solvent assisted phase-separation in polymer solution droplets.[75, 76] Janus particles can be also obtained through the phase-separation between the growing secondary components and seed particles. For the synthesis of inorganic Janus nanoparticles, seed particles stabilized by ligands facilitate the growth of the secondary phase on one side to form the Janus morphologies. Polymeric Janus nanoparticles can be obtained by seeded emulsion polymerization of phase-separated copolymers. In addition, the Janus nanoparticles can be synthesized via
the self-assembly of triblock copolymers into various multi-compartment micelles or films, followed by cross-linking of the middle block and dissolution of the assembled structure.\cite{51, 77, 78}

![Figure 1-4](image)

Figure 1-4. (A) Control of heterogeneous nanoparticle morphologies by tuning MMA content of p(MMA/nBA) seed particles; (B) Synthesis of Color changing Janus nanoparticles; (C) UV-Vis spectra of the colloidal dispersion and (D) nanoparticles with various morphologies exhibiting yellow and red color at neutral and acid conditions, respectively. Reproduced with permission from Ref.\cite{16, 79}.

Emulsion polymerization can be utilized to synthesize variable morphologies,\cite{80-82} including recently developed synthetic methods of obtaining Janus nanoparticles.\cite{60}

Using a step-wise seeded emulsion polymerization, PFS and nBA can be copolymerized on the p(MMA/nBA) core and the phase-separation between the two copolymers results in acorn-shape Janus nanoparticles consisting of p(MMA/nBA) and p(PFS/nBA) hemispheres.\cite{60} By tuning the $T_g$ of the seed particles \textit{via} copolymerization of MMA and nBA with various ratios, followed by copolymerization of PFS/nBA in the presence of p(MMA/nBA) seed particles, heterogeneous nanoparticles with various morphologies.
were obtained due to glass transition temperature ($T_g$) difference and interfacial surface tension between fluorinated and acrylic copolymer phases.\cite{79} As shown in Figure 1-4-A, when $T_{\text{reaction}} > T_g$ of the seed, core-shell nanoparticles are obtained. As $T_{\text{reaction}}$ is close to or smaller than the $T_g$ of the seed and the interfacial surface tension ($\gamma$) between the two phases increase, acorn-shape or inverse acorn-shape morphologies can be obtained. Furthermore, upon incorporation of pH-responsive azobenzene compounds (AZO) during synthesis (Figure 1-4-B), the Janus nanoparticles exhibit color responses depending upon pH changes, as demonstrated by the UV-vis absorbance spectra shown in Figure 1-4-C and illustrated in Figure 1-4-D.\cite{16} Furthermore, when the p(MMA/nBA)-p(PFS/nBA) Janus nanoparticles were utilized as seed particles, and DMAEMA and nBA were copolymerized semicontinuously, triphasic Janus nanoparticles with a stimuli-responsive hemispherical shell were synthesized.\cite{17} These triphasic Janus nanoparticles are capable of changing shape by varying temperature and/or pH. Potential applications of these nanoparticles are numerous, ranging from lithographic to rheological applications.

Figure 1-5. Synthesis of “mushroom-like” amphiphilic Janus particles. Reproduced with permission from Ref. [18].
As shown in Figure 1-5, internal phase-separation between two polymers (pSt and pMMA) solubilized in an organic solvent microdroplets can be utilized to synthesize Janus particles with one hemisphere modified with ATRP macro-initiators (2-(2-(Bromoisobutyryloxy)ethyl methacrylate, BIEM). This, in turn, can further induce surface-initiated polymerization of DMAEMA to create T- and pH-responsive Janus particles.\[75, 76\] The pSt-pAA Janus particles obtained from seeded emulsion polymerization of tBA in the presence of pSt seed and subsequent hydrolysis of t-butyl ester groups, are capable of stabilizing Pickering emulsions and phase-inversions at selected pH conditions.\[18\]

Figure 1-6. Triblock copolymer assemble into multicompartiment micelles, followed by crosslinking of the middle block and dissolution of the micellar structure, leading to formation of Janus micelles, which adopt different aggregated structures in different solvents. Reproduced with permission from Ref. [77].
Janus nanoparticles can be also obtained by utilizing self-assembly of block copolymers.\cite{51, 77, 78, 83-86} For example, amphiphilic pSt-pMAA Janus micelles were synthesized by dissolution of self-assembled pSt-block-pBD-block-pMMA films with cross-linked pBD blocks followed by hydrolysis of ester side groups.\cite{83} These Janus micelles are capable of forming supermicelles above a critical aggregation concentration in aqueous environment facilitated by basic conditions and NaCl. Upon self-assembly in solution, the pSt-block-pBD-block-pMMA triblock copolymers can also form multicompartment micelles, which upon cross-linking of each compartment and dissolution can generate Janus-balance tunable nanoparticles. As shown in Figure 1-6, such Janus nanoparticles are capable of forming dumbbell-shape assemblies in chloroform and raspberry-like assemblies in water.\cite{77}

Figure 1-7. Synthetic strategies of gibbous nanoparticles.
Multicompartment micelles exhibit similar structure as gibbous (raspberry-like) nanoparticles, which possess high surface roughness and hierarchical nanostructures. Figure 1-7 depicts anisotropic nanoparticles which usually consist of a spherical core and multidirectional bulges. With the incorporation of stimuli-responsive components in the core and/or the bulges, nanoparticles may be able to alter their size and properties in multiple directions. The common method of producing these nanoparticles is to attach a large number of smaller nanoparticles on the surface of a spherical particle through chemical reactions,\cite{87-89} electrostatic attraction,\cite{90-92} or hydrogen-bonding.\cite{93} Inorganic nanoparticles that stabilize monomer droplets forming Pickering emulsions can be immobilized upon polymerization to obtain raspberry-like nanoparticles. Emulsion polymerization of hydrophobic monomers in the presence of surface-functionalized inorganic nanoparticles with a small size also leads to the formation of raspberry-like nanoparticles. Furthermore, seeded emulsion polymerization was utilized to obtain raspberry-like nanoparticles owing to the localized phase-separation of secondary phase on seed particles. These particles can be utilized to the fabrication of superhydrophobic surfaces.\cite{87,91}

1.4 Synthesis of Stimuli-Responsive Nanowires and Nanotubes

Synthesis of anisotropic shapes represents another level of complexity in designing stimuli-responsive nanomaterials. Typically, this was accomplished by molecular design of copolymer blocks that in specific environments will self-assemble to form anisotropic shapes. Block copolymers with well-defined architectures (diblock,
triblock, star-like, etc.) and block lengths are usually synthesized using living cationic/anionic, ring-opening metathesis \[94\] and controlled free radical polymerizations (CRPs).\[95\] If designed appropriately, they may self-assemble in solutions to form colloidal nano-objects. Block copolymers consist two or more blocks and each block exhibits specific characteristic properties; for example, non-compatible hydrophobic-hydrophobic,\[83\] hydrophilic-hydrophobic,\[48\] cationic-anionic,\[96\] rod-coil,\[97, 98\] or crystalline-amorphous blocks.\[99-101\] These block copolymers have an affinity to phase-separate to aggregate to form colloidal assemblies upon the manipulation of solution conditions, such as cosolvent ratios, pH, temperature, ionic strength, the presence of organic counter ions, or inorganic nanoparticles. Different approaches have been utilized to facilitate self-assembly of block copolymers. The most common approach is to dissolve block copolymers in a common solvent, followed by slow addition of a poor solvent (solvent displacement), and removal of the common solvent upon evaporation or dialysis. As a result, various heterogeneous morphologies can be obtained. The well-defined block copolymer structures facilitate thermodynamically or kinetically controllable self-assembly by solvent displacement method.\[102\] The other approach involves direct dispersion of block copolymers in selective solvents upon sonication.
The most common morphologies obtained by block copolymer self-assembly are spheres, nanowires (worm-like micelles, cylinders, nanofibers), and vesicles. The major forces governing the formation of well-defined structures in aqueous solutions are the degree of stretching of the core-forming hydrophobic blocks driven by entropic energy, the interfacial tension between the core and the solvent environments, facilitated by enthalpic contribution, and the repulsive interactions within the corona-forming hydrophilic blocks resulting from electrostatic forces or steric interactions. The packing parameter, $P$, is often utilized to predict the resulting morphologies, where

$$P = \frac{v}{a \cdot l}$$

For an amphiphilic AB diblock copolymer, $v$ and $l$ are the volume and length of the hydrophobic block, respectively, and $a$ is the interfacial area between two blocks.\cite{104}
As illustrated in Figure 1-8, it is generally accepted that block copolymers having \( P < 1/3 \) will form spherical micelles, whereas \( 1/3 < P < 1/2 \) will favor nanowire formation. For \( 1/2 < P < 1 \), vesicles will be formed.

Aside from the three favorable morphologies, a wide variety of other morphologies can be produced. For example, lamellae\(^\text{106}\) segmented (striped) nanowires\(^\text{50}\), nanotubes\(^\text{107}\), multi-lamellar vesicles\(^\text{108}\), helical micelles\(^\text{109}\) to name just a few, can be generated. The complexity of the block copolymer assembly are magnified by a number of factors, such as polymer structure, molecular weight, block length and dispersity, crystallization, concentration, solubility in cosolvents, temperature, \( \text{pH} \), stirring rate, and solvent displacement speed, etc.\(^\text{102, 106}\) For example, linear poly(acrylic acid)-block-poly(methyl acrylate)-block-polystyrene (pAA-b-pMA-b-pSt) triblock copolymers were kinetically controlled to form segmented worm-like micelles in tetrahydrofuran (THF)/water mixture and the presence of 2,2'-(ethylenedioxy)diethylamine (EDDA) as organic counter ions by manipulating the solvent-displacement protocols.\(^\text{50}\) The initial spherical micelles formed during self-assembly procedure form one-dimension aggregation upon abrupt addition of THF. As a result, cylindrical micelles consist of alternating segments of the hydrophobic and hydrophilic blocks can be obtained.
By taking advantage of incompatibility of fluoropolymers and nonfluorinated polymers, triblock copolymers containing hydrophilic, hydrophobic, and fluorophilic blocks, capable of forming various multicompartment micellar morphologies through self-assembly driven by the interfacial tension,[49] can be obtained. Figure 1-9 illustrates micellar morphologies assembled from ABC triblock copolymers, where A represents hydrophilic block, B is the hydrophobic block, and C is the fluorophilic block. Typically, all the micellar structures produced by self-assembly of these block copolymers have a hydrophilic corona resulting from the solvation of hydrophilic blocks in water, and a heterogeneous core which may exhibit morphologies ranging from core-shell, gibbous, segmented worm-like, hamburger-like, disc-like, and others. ABC triblock copolymers primarily form the core-shell-corona structures, capable of minimizing interfacial energy,
whereas BAC triblock copolymers tend to form gibbous core-corona morphologies. Due to the contact between each polymer blocks, μ-ABC miktoarm star copolymers usually form hamburger-like, segmented worm-like cores, and a hydrophilic corona.

Although self-assembly of block copolymers through post-polymerization solvent displacement in dilute solutions offers control over various morphologies, the time-consuming procedure as well as dilute conditions (usually < 1 wt%) represent a significant drawback for industrial scale synthesis. Recently, considerable progress has been reported for in-situ assembly of block copolymer nano-objects during extending soluble macroinitiator upon dispersion \[111-117\] and emulsion \[118-120\] polymerization, where the propagating blocks are not soluble in a continuous phase. Typically, this polymerization-induced self-assembly (PISA) results in spherical and worm-like micelles (nanowires, nanofibers) and vesicles, as solvophobic block length increases. For example, as shown in Figure 1-10-a, RAFT dispersion polymerization of hydrophobic core-forming monomer hydroxypropyl methacrylate (HPMA) using poly(glycerol monomethacrylate) (PGMA) macro-CTA and will result in various intermediate morphologies as polymerization conversion increases (Figure 1-10-b).\[121\] For the synthesis targeting at PGMA\textsubscript{47}-PHPMA\textsubscript{200} diblock composition, spherical micelles ~ 20 – 30 nm were formed at conversion ~ 46% due to micellar nucleation of the resulting PGMA\textsubscript{47}-PHPMA\textsubscript{92}. As polymerization continues, the spherical micelles undergo 1D fusion to form nanowires, and then become branched nanowires, which transform to 2D bilayers. At conversion ~ 70 %, the bilayers begin to wrap-up to form “jelly-fish” with hemi-vesicles and nanowires, which eventually lead to formation of vesicles at
conversion > 80%. This morphology transformation is attributed to the increase of packing parameter as DP of hydrophobic block increases.

Figure 1-10. (a) RAFT aqueous dispersion polymerization of hydroxypropyl methacrylate (HPMA) using poly(glycerol monomethacrylate) (PGMA) macro-CTA at 10 w/w % and 70 °C; (b) Suggested mechanism for the sphere-to-worm-to-vesicle transformation during the in-situ synthesis; (c) Thermoresponsive aqueous solution behavior of a 10% w/w aqueous dispersion of diblock copolymer particles. TEM studies of grids prepared from a dilute aqueous dispersion of G54-H140 dried at either 21 or 4 °C showing the reversible worm-to-sphere transition. Reproduced with permission from Ref. [20, 121].

An interesting phenomenon was observed for the PGMA$_{47}$-PHPMA$_{140}$ block copolymer nanowires which can undergo reversible morphological transitions upon
temperature changes.[20] As shown in Figure 1-10-c, the block copolymer dispersion consists of nanowires and exhibits gel-like behavior at 21 °C. On cooling from 21 to 4 °C, the dispersion become free-flowing and nanowires transform to spherical micelles, as confirmed by DLS and TEM measurements. The rheological behavior showed that at lower temperature the storage (G’) and loss (G”) moduli decrease due to the transformation of nanowires to nanospheres. At higher temperature, the G’ maintains at ~100 Pa due to gel network formation resulting from physical contacts between nanowires. Similar worm-to-sphere transitions can be also achieved in PGMA-block-PHPMA copolymers synthesized using a carboxylic acid based RAFT agent.[122] Ionization of the block copolymer end groups induces the morphological transition of the block copolymer assemblies as a function of pH.

Initially, the interest in tubular morphologies was stimulated by the development of phospholipid tubules.[123, 124] As shown in Figure 1-11, the biologically active phospholipids with a hydrophilic head group and two hydrophobic tails can self-assemble to form multilayered nanotubes upon chiral molecular packing induced by hydrophobic interactions at specific solvent conditions.[125] Such phospholipid nanotubes can be utilized as a template to produce ferromagnetic nanotubes. For example, redox reactions of ammonium iron (II) sulfate hexahydrate ((NH₄)₂Fe(SO₄)₂) and hydrogen peroxide (H₂O₂) in the presence of nanotube dispersions lead to the formation of iron oxide layers on the inner and outer layer of the phospholipid nanotubes.[126, 127] Furthermore, upon calcination at 550 °C, the amorphous iron oxide phases convert to nanocrystalline magnetite (Fe₃O₄) and the sandwiched phospholipid layer become amorphous carbon. As
a result, iron oxide/carbon/iron oxide concentric nanotubes consisting of ferromagnetic inner and outer layers and an electrically conductive carbon layer were obtained. The morphology of the nanocomposite nanotubes can be controlled by reactant concentration and solvent conditions.\textsuperscript{[128]}

![Figure 1-11. Schematic diagram of ferromagnetic nanotubes. Adapted from Ref. [126-128].](image)

Furthermore, diameter- and wall thickness-tunable nanotubes can be obtained by incorporating temperature-responsive polymers between the multilayers of phospholipid nanotubes. As shown in Figure 1-12, upon the free radical polymerization of N-isopropylacrylamide (NIPAAm) in the presence of 1,2-bis(tricosa-10,12-diynoyl)snglycero-3-phosphocholine diacetylenic phospholipid (DC\textsubscript{8,9}PC) self-assembled nanotubes, reversibly expandable polymeric nanotubes can be obtained.\textsuperscript{[21]} The NIPAM monomers diffuse into the hydrophilic regions of the PL bilayers and polymerized in-situ to form temperature-responsive polymer layers. As temperature increased to above 37 °C, the outer diameter and the wall of PNTs shrink by 20 and 55%, respectively. In the meantime, the inner diameter increases by 16%. This size changing behavior of the PNTs is attributed to the PNIPAM backbone buckling induced by temperature-induced conformational changes.
Polymeric nanotube can be also obtained from block copolymer self-assembly in nonpolar solvents \cite{101, 129, 130} as well as aqueous environments\cite{131-133}. Such block copolymer nanotubes incorporated with stimuli-responsive monomer units can alter their morphologies in response to environmental adjustments. For example, as shown in Figure 1-13, pH and CO$_2$ responsive nanotubes can be prepared from poly(ethylene oxide)-b-poly((N-amidine)dodecylacrylamide)-b-polystyrene triblock copolymers (PEO-PADA-PS), which are dissolved in THF and self-assembled by solvent displacement with water to form microtubules\cite{134}. In the presence of CO$_2$ gas as stimulus, amidine-containing blocks will be protonated, thus resulting in morphology changes, from microtubules to vesicles to spheres.
Figure 1-13. (a) Gas-switchable amidine-containing triblock copolymer PEO-PADA-PS, (b) representation of its CO$_2$-driven controlled self-assembly and shape transformation behavior, and (c) representation of block copolymer chain rearrangements induced by the CO$_2$ stimulus. Reproduced with permission from Ref. [134].
1.5 Applications of Stimuli-Responsive Nano-Objects

Although nanotechnology has dominated many branches of science and technology, it should be realized that back in mid-1950s, monodispersed colloidal latexes enabled myriad industrial uses in paper, paint, coatings, films and other industries. Considered to be the first lecture on modern nanotechnology, Feynman anticipated that “there’s plenty of room at the bottom,” which encouraged new research in this area and striking developments of buckyballs and carbon nanotubes are the manifestation of these statements. Various applications and impact that nanotechnology has made on daily lives is attributed to the higher strength and light weight materials, multiple functions, and programmed behaviors. Inorganic nanoparticles, nanorods and nanofibers with high strength and low density have been widely used in matrix reinforcement.\textsuperscript{135} Nanoparticles made of silicate, silica, titanium dioxide, zinc oxide, silver, and others, are utilized as gas barriers, fillers, UV protectors, UV blockers, anti-microbial agents, and fillers.\textsuperscript{136} Semiconductor nanoparticles including quantum dots (QDs) are applied in manufacture of ion batteries, fuel cells, LEDs, diode lasers, solar cells and imaging sensors.\textsuperscript{137, 138} Metal nanoparticles are used in catalysis, conductive components of circuit boards, transistors, sensors, and many other applications.\textsuperscript{139} Gold \textsuperscript{140} and iron oxide magnetic nanoparticles \textsuperscript{141} found applications in bioimaging and biosensors, plasmonic and hyperthermia therapy, and targeted delivery carriers. With respect to organic/polymeric nanoparticle, latexes and colloidal dispersions have been vastly manufactured for large-scale synthesis of polymers and direct application to coatings, paints, and pressure-sensitive adhesives.\textsuperscript{142} Polymeric nanoparticles with various
morphologies have been used in biomedical applications, drug-delivery carriers, self-healing materials.\textsuperscript{[143]} The size and morphology of nanoparticles plays an important role in determination of the final properties. For example, micro- or meso-porous catalyst nanoparticles with high total surface area usually demonstrate optimum catalytic properties.

Figure 1-14. Applications of nanoparticles, nanowires, and nanotubes in various economic sectors.
1.6 References


CHAPTER TWO

TRI-PHASIC SIZE- AND JANUS BALANCE-TUNABLE COLLOIDAL JANUS
NANOPARTICLES

2.1 Introduction

While imparting distinctly different physical and/or chemical properties into colloidal solution, Janus particles (JPs) have attracted attention due to their numerous technological advantages. Various approaches have been utilized in their synthesis, including microfluidics, block copolymer assembly, masking technique, heterogeneous nucleation, flame synthesis, and emulsion polymerization. Of particular interest, and perhaps most challenging, is the synthesis of large quantities of Janus nanoparticles (JNPs) with precisely defined morphologies capable of responding to a variety of external or internal stimuli. The presence of stimuli-responsive components built into each individual JNP may be beneficial in a variety of applications, particularly if self-assembly into complex hierarchical morphologies are sought. Building upon our prior controllable synthesis of “acorn-shape” JNPs using seeded emulsion polymerization, not only shape evolution control of JNPs can be achieved by adjusting the glass transition temperature (T_g) via compositional gradients during copolymerization, but tunable color changes were developed by incorporating photochromic entities into shape-adjustable JNPs.
One of the intriguing properties of JPs is their enhanced interfacial activities.\textsuperscript{[24]} The ratio of hydrophilic and hydrophobic components defined by the Janus balance (JB), defined as the ratio of hydrophilic and hydrophobic components, is introduced to quantify the geometry of the JPs as well as their interfacial activities.\textsuperscript{[25]} However, only a few studies have demonstrated procedures capable of controlling JB values of JPs during the synthesis process, such as controlling the flow rate of monomers in microfluidic synthesis of JPs,\textsuperscript{[5]} controlling the exposed area of particles to be chemically modified,\textsuperscript{[25-28]} or controlling of the block lengths of block terpolymers that self-assemble into JNPs.\textsuperscript{[29]} However, introducing stimuli-responsive components into JNPs with the capable of tuning JB values will offer numerous advantages.

In these studies we focused on the synthesis of triphasic shape-tunable JNPs, where p(DMAEMA/nBA) phase within each nanoparticle is capable of reversible shape tunability induced by temperature and/or pH changes, while p(MMA/nBA) and p(PFS/nBA) phases remain passive, yet capable of adapting to shape changes of the adjacent phases. Finally, we demonstrate the interfacial activities of JNPs by stabilizing oil droplets in water at different pH values.

\textbf{2.2 Experimental}

Preparation of stimuli-responsive JNPs: MMA, nBA, PFS, DMAEMA and sodium dioctylsulfosuccinate (SDOSS), 2,2’-azobis(isobutyronitrile) (AIBN), 0.1 N volumetric standard solutions of sodium hydroxide (NaOH) and hydrochloride acid (HCl)
were purchased from Aldrich Chemical Co. Water-soluble initiator 2,2’-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (AIPD, or VA-44) was purchased from Wako Pure Chemicals Ind. Ltd. The particles shown in Figure 2-1 were synthesized via conventional emulsion polymerizations. (1) p(MMA/nBA) colloidal dispersion was synthesized using a semicontinuous process outlined elsewhere.[17] The reaction flask was immersed in a water bath preheated to 75 °C and purged continuously with N₂ gas. The reactor was first charged with 15 mL of double deionized water (H₂O), and after purging N₂ for 30 min, the content was stirred at 350 rpm. At this point, pre-emulsion (H₂O, 15 mL; SDOSS, 0.18 g, MMA, 3.0 g; nBA, 3.0 g) was fed continuously over 4 h while initiator solution (VA-044, 0.012 g; H₂O, 5 mL) was fed over 4.5 h. After completion of pre-emulsion feeding, the reaction was continued for additional 10 h. (2) Withdraw half of the p(MMA/nBA) seed emulsion, and pre-emulsion (H₂O, 15 mL; SDOSS, 0.12 g; PFS, 1.8 g; nBA, 1.8 g) was fed continuously over 4 h into the remained half p(MMA/nBA) emulsion while initiator solution (VA-044, 0.008 g; H₂O, 5 mL) was fed over 4.5 h. After completion of pre-emulsion feeding, the reaction was continued for additional 10 h. (3) Withdraw 2/3 of the S2 emulsion and 30 mL H₂O was added into the remained p(MMA/nBA)-p(PFS/nBA) emulsion, and pre-emulsion (H₂O, 15 mL; SDOSS, 0.15 g; DMAEMA 0.8 g; nBA, 0.8 g; AIBN, 0.01 g) was fed continuously over 3 h. After completion of pre-emulsion feeding, the reaction was continued for additional 10 h.

Particle size analysis was performed using a Microtrac Nanotrac particle size analyzer (model ULTRA) with an accuracy of ±1 nm. Potentionmetric titrations were performed at 25 °C using Orion pH meter model 350 with a glass combination electrode.
(Orion 9202 BN). Autocalibration against standard buffer solutions was done before titration. Standard HCl and NaOH solution were utilized to adjust pH values of the Janus colloidal solutions.

Morphologies of the Janus particles were investigated using a JEOL TEM-2100 transmission electron microscope (TEM) operated at 200 kV, where the samples were diluted and deposited on a Formvar/carbon copper grid (EMS). In order to enhance the contrast of the TEM images of JNPs, each specimen was stained using osmium tetroxide vapors, as described in ref 29. This procedure allowed us to differentiate between p(DMAEMA/nBA) and p(MMA/nBA) phases by oxidizing tertiary amine groups in p(DMAEMA/nBA) copolymer, thus, giving higher electron densities. In a typical experiment, each specimen was exposed for four hours and the TEM images were collected. Since the gray scale obtained from TEM analysis is often highly subjective in the analysis, we also utilized image analysis using The Environment for Visualizing Images (ENVI; v. 3.5, Research Systems, Inc.).

Static contact angle measurements were conducted using a sessile drop technique and a Ramé-Hart goniometer coupled with a DROP image data analysis software. 10 µL drops were placed onto the flat surfaces coated by each copolymer film while an image of the drop was captured and the contact angle measured. Each copolymer was synthesized by surfactant-free emulsion polymerization with monomer composition and initiator ratio constant. These copolymers were precipitated, dissolved in toluene and spin-coated on glass slide.
Grazing-angle attenuated total reflectance Fourier transform infrared (GATR FT-IR) spectroscopy measurements were conducted on the film–substrate (F-S) interfaces using a Bio-Rad FTS-6000 FT-IR single-beam spectrometer set at 4 cm\(^{-1}\) resolution. A 2 mm Ge crystal with a 45° angle maintaining constant contact pressure between the crystal and the specimens was used. All spectra were corrected for spectral distortions by Q-ATR software using the Urban-Huang algorithm. The spectra are shown in Appendix A, Figure A-4.

Thermal analysis of copolymers synthesized during each step of emulsion polymerization was conducted using TA Instruments DSC Q-100. The calibration was carried out using indium and sapphire standards. Heating and cooling rates of 5 °C/min were used over the studied temperature range.

Computer modeling simulations were conducted using a classical (Newtonian) molecular dynamic theory combined with the COMPASS force field conditions on Material Studio software (Accelrys Inc., Version 5.5). Three kinds of random copolymers p(MMA/nBA), p(PFS/nBA) and p(DMAEMA/nBA) were created. Each of them has 50 repeating units and was energy-minimized by Forcite calculations. In the phase-separation simulation, an amorphous cell was created by constructing two of each kind of energy-minimized copolymer chains under 3D periodic boundary conditions. And then this amorphous cell was allowed to do thermodynamic simulations, including NPT (constant number, pressure and temperature) and NVT (constant number, volume and temperature) processes to reach an energy-minimized state.
2.3 Results and Discussion

Figure 2-1-A illustrates a two-step synthesis of stimuli-responsive JNPs from p(MMA/nBA) colloidal seed particles. During the first step, PFS and nBA were copolymerized under monomer-starvation conditions in the presence of previously synthesized spherical p(MMA/nBA) seed emulsions with an average particle size of 86 nm (Figure 2-1-B-a). Due to substantial interfacial energy differences between fluorinated and acrylate phases, this process favors the formation of phase-separated JNPs with an average particle size of 110 nm shown in TEM images of Figure 2-1-B-b. Compared with the p(MMA/nBA) phase, p(PFS/nBA) phase in the JNPs appears darker due to higher electron density of fluorine components. The second step involved copolymerization of temperature and/or pH responsive DMAEMA along with nBA monomers on the top of phase-separated p(MMA/nBA)-p(PFS/nBA) JNPs, giving a three phase system: p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA). Figure 2-1-B-c illustrates the final product which exhibits an average particle size of 147 nm. The choice of p(DMAEMA/nBA) was dictated by temperature and/or pH responsiveness, whereas p(MMA/nBA) and p(PFS/nBA) copolymers are able to form phase-separated JNP cores.
It is well-established that during semicontinuous emulsion polymerization under monomer-starvation conditions monomers and growing oligomeric radicals continuously diffuse into existing particles instead of forming new particles. As a result, the particle size increases. As noted in the earlier studies, the shape of the resulting particles is dictated by the ability of individual phases to minimize total interfacial energy during polymerization. To correlate synthetic efforts responsible for morphological features shown in TEM images in Figure 2-1, let us consider the surface energy differences within this tertiary copolymer system. To determine surface energy values of the individual copolymer phases, surfactant-free colloidal particles of the same composition were synthesized. Upon being centrifuged, dried, dissolved in toluene and spin-coated, p(MMA/nBA), p(PFS/nBA) and p(DMAEMA/nBA) films were produced. While the
results of static contact angle measurements using water and hexadecane are summarized in Table 2-1, Appendix A (Sections 1 and 2) provide further details regarding determination of surface energies.

Table 2-1-A. Static contact angle measurement data and surface energy results of the copolymer films.

<table>
<thead>
<tr>
<th>Copolymers</th>
<th>Static Contact Angle</th>
<th>$\gamma_{sv}^d$ (mN/m)</th>
<th>$\gamma_{pv}^p$ (mN/m)</th>
<th>$\gamma$ (mN/m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(MMA/nBA)</td>
<td>71.2° 0°</td>
<td>27.5</td>
<td>11.0</td>
<td>38.5</td>
</tr>
<tr>
<td>p(PFS/nBA)</td>
<td>97.0° 42.3°</td>
<td>20.8</td>
<td>2.2</td>
<td>23.0</td>
</tr>
<tr>
<td>p(DMAEMA/nBA)</td>
<td>69.5° 0°</td>
<td>27.5</td>
<td>11.9</td>
<td>39.4</td>
</tr>
</tbody>
</table>

Table 2-1-B. Interfacial surface tension between p(MMA/nBA) and p(PFS/nBA), p(PFS/nBA) and p(DMAEMA/nBA), p(MMA/nBA) and p(DMAEMA/nBA), respectively.

<table>
<thead>
<tr>
<th>Copolymers</th>
<th>Interfacial Surface Tension $\gamma_{12}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(MMA/nBA) - p(PFS/nBA)</td>
<td>6.80</td>
</tr>
<tr>
<td>p(DMAEMA/nBA) - p(PFS/nBA)</td>
<td>7.43</td>
</tr>
<tr>
<td>p(MMA/nBA) - p(DMAEMA/nBA)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

As shown in Table 2-1-A, surface energies of p(MMA/nBA), p(PFS/nBA) and p(DMAEMA/nBA) are 38.5, 23.0 and 39.4 mN/m, respectively. It is quite apparent that p(PFS/nBA) exhibits significantly smaller surface energy values compared to p(MMA/nBA) and p(DMAEMA/nBA). The surface energies for each copolymer as well as polar and dispersive contributions shown in Table 2-1-A allow us to estimate the interfacial surface tension between two phases in individual JNPs. The results summarized in Table 2-1-B show that the interfacial surface tension between p(MMA/nBA) and p(PFS/nBA), p(DMAEMA/nBA) and p(PFS/nBA), p(MMA/nBA) and p(DMAEMA/nBA) are 6.80, 7.43, 0.04 mN/m, respectively. These data indicate that when PFS/nBA was copolymerized in the presence of p(MMA/nBA) seed (Figure 2-1-B-
a), significant interfacial surface tension (6.8 mN/m) between the two copolymers favors the minimum contact area within each particle, resulting in the formation of phase-separated JNPs (Figure 2-1-B-b).\[17-19\] Furthermore, when DMAEMA and nBA monomers were copolymerized on the p(MMA/nBA)-p(PFS/nBA) core under monomer-starvation conditions, p(DMAEMA/nBA) also phase-separates from p(PFS/nBA) fluorinated hemisphere and resides near the least hydrophobic nonfluorinated p(MMA/nBA) copolymer phase in order to minimize the total interfacial surface energy within the tri-phasic JNPs. Also, instead of diffusing into p(MMA/nBA) phase and forming inverse core-shell morphologies, higher hydrophilicity of p(DMAEMA/nBA) facilitates polymerization on the surface of p(MMA/nBA) hemispherical core. As a result, stimuli-responsive JNPs shown in Figure 2-1-B-c are produced. Although similarities of p(MMA/nBA) and p(DMAEMA/nBA) copolymer electron densities make the two phases of the half core-shell hemisphere not easily distinguishable by TEM, the particle size analysis shows the particle growth from 110 to 147 nm further substantiating the formation of stimuli-responsive JNPs during stage III illustrated in Figure 2-1-A.
Figure 2-2. Computer simulations illustrating tri-phase copolymers in one amorphous cell: p(MMA/nBA) yellow, p(PFS/nBA) green, and p(DMAEMA/nBA) (white for H, grey for C, red for O, blue for N). As shown, phase separation between p(PFS/nBA) and p(MMA/nBA) as well as p(DMAEMA/nBA) occurs. In contrast, p(MMA/nBA) and p(DMAEMA/nBA) are compatible.

Molecular thermodynamics simulations were also employed in which three random copolymers p(MMA/nBA), p(PFS/nBA) and p(DMAEMA/nBA) containing 50 repeating units were allowed to equilibrate to reach the minimum energy state. The results of these simulations are shown in Figure 2-2, where p(PFS/nBA) polymer chains (green) are apart from both p(MMA/nBA) (yellow) and p(DMAEMA/nBA) segments due to their incompatibility leading to phase-separation within one colloidal particle. In contrast, p(DMAEMA/nBA) and p(MMA/nBA) segments remain compatible manifested by the presence of entanglements, indicating that p(DMAEMA/nBA) phase prefers to remain on the nonfluorinated p(MMA/nBA) hemisphere. Appendix A, Table A-1 provides energy values between each copolymer after the unit cell has been equilibrated.
As shown, the unfavorable equilibrium state for copolymers is manifested by highest energy values which are 9164 and 9467 kcal/mol for p(MMA/nBA)-p(PFS/nBA) and p(DMAEMA/nBA)-p(PFS/nBA), respectively. It should be pointed out that these modeling exercises do not take into account the interfacial energy considerations during polymerization, thus neglecting the role of solvent (water) and surface active components (surfactants).
Figure 2-3. (a) TEM (A–E and A′–E′) images of p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA) nanoparticles at 25 (A/A′), 35 (B/B′), 38 (C/C′), 40 (D/D′), and 45 (E/E′) °C; Images A″–E″ were obtained using image analysis, as described in the Experimental Section; Dimensional changes of the JNPs at 25, 35, 38, 40, and 45 °C are schematically depicted in A‴–E‴, respectively. (b) TEM (A–D and A′–D′) images of p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA) nanoparticles at pH = 4 (A/A′), 6 (B/B′), 8 (C/C′), and 10 (D/D′). Images A″–D″ were obtained using image analysis, as described in the Experimental Section; Dimensional changes of the particles at pH = 4, 6, 8, and 10 are schematically depicted in A‴–D‴, respectively.
To illustrate stimuli-responsiveness and the ability to form tunable shapes, p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA) JNPs were exposed to pH = 8 at 25 °C, 35 °C, 38 °C, 40 °C, 45 °C, respectively. TEM images in Figure 2-3-a-(A-E) as well as their close-ups shown in Figure 2-3-a-(A’-E’) illustrate that when temperature increases from 25 °C to 45 °C, the JNP shape changes from spherical to ellipsoidal. At 25 °C, the interfacial tension between p(MMA/nBA)-p(DMAEMA/nBA) and p(PFS/nBA) phases forces JNPs to form equilibrated hemispherical morphologies with a convex shape of p(PFS/nBA) phase. Upon temperature increase to 35 °C, p(DMAEMA/nBA) phase begin approaching the second-order low critical solution temperature (II-LCST) transition, resulting in the collapsed p(DMAEMA/nBA) phase.\[^{30}\] As a consequence, the temperature increase from 30 to 46 °C causes the JNPs to shrink gradually from 147 to 131 nm (Appendix A, Figure A-1). It should be noted that the three copolymers exhibit glass transition temperature (Tg) below 25 °C (Appendix A, Figure A-2), which facilitates free rotation of polymer backbones and rearrangement of polymer chains during II-LCST temperature range in order to reach equilibrated particle morphologies. The collapse of p(DMAEMA/nBA) segments also increase the magnitude of hydrophobic interactions within this phase, causing shrinkage of p(MMA/nBA) hemisphere core as well as expansion of the outer p(PFS/nBA) hemisphere layer. As a result, JNPs assume a new shape with a less convex interface of the p(PFS/nBA) phase. Because p(DMAEMA/nBA) random copolymers exhibit a II-LCST transition over a broad temperature range, as temperature increases further, p(DMAEMA/nBA) backbones
continue to collapse, leading to an almost planar interface at 38 °C. At the same time, the volume of single stimuli-responsive particle decreases by ~ 19 %. When temperature reaches 40 °C, a concave interface is assumed, which is further expanded at higher temperatures with shrinkage values as high as ~ 29 %. This shape-tunable behavior can be repeated many times in aqueous environments.

During this temperature induced process particle morphologies and the interfacial curvature between the two phase-separated hemispheres of the JNPs is being continuously altered, resulting in the hydrophilic-to-hydrophobic surface area ratio known as the Janus Balance (JB) tunability induced by temperature changes. Appendix A, section 4, provides further details regarding the JB determination. As shown in Figure 2-3-a-(A″–E″), at 25 °C, the JB is 3.78 (79.1/20.9) and is dominated by hydrophilic hemisphere. However, as a result of p(DMAEMA/nBA) collapse at elevated temperatures, the relative surface area of hydrophilic hemisphere decreases while the relative area of hydrophobic hemisphere increases, leading to the decrease of the JB to 1.60 (61.6/38.4) at 38 °C. When temperature reaches 40 °C, the relative surface areas of hydrophilic and hydrophobic hemispheres become almost the same and the JB is 0.98 (49.5/50.5), which upon temperature increase to 45 °C, further decreases to 0.72 (41.7/58.3).

Due to the expansion of p(DMAEMA/nBA) phase induced by protonation of the tertiary amine functional groups in acidic environments, particle size of the JNPs increases from 145 to 163 nm as pH decreases from 10 to 4 at 25 °C (Appendix, Figure A-2). Figure 2-3-b illustrates the size and morphology changes of these same JNPs as a
function of pH. As seen, when pH decreases from 10 to 4, the interface for p(PFS/nBA) hemisphere becomes more convex while its size remain almost unchanged whereas the nonfluorinated p(MMA/nBA)-p(DMAEMA/nBA) hemisphere size increases, which means that hydrophilic–hydrophobic hemisphere ratio increases. As a result, JB values of the JNPs increase from 3.42 (77.4/22.6) at pH = 10 to 4.24 (80.9/19.1) at pH = 6 and further increase to 4.52 (81.9/18.1) at pH = 4. These relatively small changes are likely attributed to the limited penetration of acid groups during protonation by aqueous HCl as well as the decrease of protonation during TEM sample preparation due to evaporation of HCl.

One of the intriguing applications of tunable JB is the ability of JNPs to stabilize oil droplets in water known as Pickering emulsions. After removing excess surfactant molecules (3 days dialysis), 5% w/w JNPs solutions were utilized to stabilize dodecane droplets in water to form Pickering emulsions. Figure 2-4-(A–F) shows the photographs of Pickering emulsions prepared under magnetic stirring at 2000 rpm for 10 min at 25 °C which were oil-in-water determined by drop tests showing that the Pickering emulsions disperse readily in water. As shown, while p(MMA/nBA) particles are not capable of stabilizing oil droplets (Figure 2-4-A) and p(MMA/nBA)-p(PFS/nBA) can stabilize only 15% of oil droplets (Figure 2-4-B), the p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA) JNPs are able to stabilize the Pickering emulsions for more than 2 months (Figure 2-4, D–F), which is attributed to higher adsorption energy of amphiphilic JNPs at oil/water interface than that of spherical particles.[24] Figure 4C′–F′ show the optical images of dodecane-in-water droplets stabilized by JNPs at pH = 3, 4, 8, and 10, respectively. As
seen, JNPs with smaller JB values (3.42 at pH = 10) are able to generate stable smaller oil droplets. However, as the JB value increase to 4.52 under acidic conditions (pH = 4), the oil droplets become larger (Figure 2-4-D). And when the JB increased further at pH = 3, oil droplets become even larger (Figure 2-4-C’) and the oil phase starts to separate from the Pickering emulsion phase. As a result, 35% of the dodecane is released in one day (Figure 2-4-C), which is attributed to desorption of JNPs from the oil–water interface into water phase due to protonation of the pDMAEMA component. As pH decreases further to pH = 2, all oil droplets can be released in less than 1 h.

It should also be noted that insignificant droplet size changes were observed when Pickering emulsions were subjected to 30, 35, 45, and 50 °C temperatures for over 2 months. As we recall, individual JNPs exhibit significant temperature sensitivity manifested by the size and JB changes, but acidic and/or basic environments have relatively small influence on their responsiveness. In contrast, temperature changes do not significantly influence the stability of oil-in-water emulsions, whereas the residual surface charges on JNPs do, signifying that interfacial energy plays a major role on stability of Pickering emulsions.
2.4 Conclusions

In summary, these studies show the synthesis of triphasic stimuli-responsive JNPs that consist of phase-separated p(MMA/nBA), p(PFS/nBA), and p(DMAEMA/nBA) copolymers. These JNPs are capable of shape and size changes as a function of pH and temperature. As the temperature increases, the particle size of JNPs decreases from 147 nm at 25 °C to 131 nm at 45 °C and the particle morphology of the JNPs also changes from spherical with a convex p(PFS/nBA) phase to ellipsoidal with a concave p(PFS/nBA) phase while the JB decreased from 3.78 to 0.72. As pH decreases from 10 to 4, the particle size of JNPs increases from 145 to 163 nm while the JB increased from
3.42 to 4.52. The use of size- and JB-tunable JNPs may offer many applications ranging from stabilization of oil in water at high pH environments to environmentally compliant petroleum recovery processes, or multi-drug delivery applications in which each phase may serve as a delivery and release vehicle under desired physiological conditions.
2.5 References


CHAPTER THREE
RATIONALLY DESIGNED GIBBOUS STIMULI-RESPONSIVE COLLOIDAL NANOPARTICLES

3.1 Introduction

Processes occurring in nature lead to a variety of heterogeneous morphologies with often amazing shapes at various length scales. While mimicking molecular events leading to the formation of different shapes and scaled up morphologies are challenging, recent attempts successfully showed that an interplay of dynamic reactions combined with diffusion processes may facilitate the growth of well-defined, complex and unique microstructures.[1, 2] The challenge is to facilitate desirable thermodynamic and kinetic conditions that will lead to controllable heterogeneities and anisotropies.[3-6] At nanoscales, these challenges are amplified by the limited ability to measure highly localized events at or near inter and intra molecular bond scales.[7] Although previous studies have developed irregular nanoparticles utilizing electrostatic forces,[8, 9] emulsion-evaporation,[10, 11] hydrogen-bonding,[12] capillary forces,[13] covalent bonding,[14-16] or acid-base interactions,[17, 18] the precise control of chemico-physical events facilitating hierarchical build-ups leading to highly organized 3D arrays[19, 20] with stimuli-responsive attributes have not been shown. Although tri-phasic stimuli-responsiveness Janus nanoparticles were prepared,[7] controllable stimuli-responsive nanoparticle gibbosity has not been exploited. In these studies we developed colloidal nanoparticles with tunable gibbousness that change size upon pH environmental changes. These
materials may offer numerous future opportunities for technological advances in the areas where high surface-to-volume properties are needed, such as multi-stage drug delivery systems, nanoporous materials for energy storage, thermal barrier materials, or remarkably high surface area catalysts with high yields, just to name a few; there are others.

3.2 Experimental

Tetraethoxysilane (TEOS) and ammonia (28-32% in water), methyl methacrylate (MMA), n-butyl acrylate (nBA), t-butyl acrylate (tBA), styrene (St), methacrylic acid (MAA), pentafluorostyrene (PFS), potassium persulfate (KPS), 3-(methacryloyloxy) propyl trimethoxysilane (MPS), aluminum oxide (Al₂O₃) were purchased from Aldrich Chemical Co. MMA, nBA, MAA, St and PFS were allowed to pass through Al₂O₃ column to remove inhibitors prior to use and all other chemicals used as received.

Preparation of p(MMA/nBA), p(MMA/MAA), or pSt particles by surfactant-free emulsion polymerization. 90 mL deionized water (H₂O, 5 mol) was added into a reaction flask maintained at 75 °C, purged continuously with N₂ gas and stirred mechanically at 400 rpm. 3 g MMA/nBA (or MMA/MAA, St) monomer mixture and 5 mL KPS aqueous solution (0.01 g/mL, 37 mM) were added and the reaction was allowed to continue for 5 h (15 h for pSt to ensure full conversion). The seed particles were purified by centrifugation at 1500 g for 3 h. Upon completion, they were redispersed in 95 mL deionized water. Monomer molar ratios, particle sizes and % monomer conversions are listed in Appendix B, Table B-2.
Preparation of silica particles. The colloidal silica particles were synthesized according to the well-known Stöber method.\textsuperscript{[23]} 10 g TEOS (0.048 mol), 200 mL absolute ethanol (3.43 mol) and 10 mL ammonium hydroxide (0.09 mol) were introduced into a 500 mL round-bottom flask while stirring at 350 rpm at room temperature for 24 h. The colloidal dispersion was purified by repeated centrifugation redispersion cycles with deionized water for more than 3 times. The final SiO$_2$ particles (particle size ~ 95 nm) were collected by centrifugation at 1000 g for 3 h. Yield: 63%

Preparation of SiO$_2$-pMMA core-shell nanoparticles. The surface of MPS silica particles (95 nm) was modified by MPS to attach C=C double bond, which facilitates the formation of SiO$_2$-pMMA core-shell nanoparticles. 60 mL colloidal silica dispersion (0.5 w/w\%) was added into a reaction flask maintained at 75 °C, purged continuously with N$_2$ gas and stirred mechanically at 350 rpm. 0.6 mL KOH 1\% aqueous solution (0.107 mmol) was then introduced into the colloidal dispersion. 30 min later 0.07 g MPS (0.28 mmol) was added dropwise into the flask to modify silica particle surface with methacrylate groups. The monomer MMA and KPS initiator were continuously fed into the system over 2 h and the reaction was continued for 5 h. The seed particles were purified by centrifugation at 1000 g for 3 h and redispersed in 65 mL deionized water. Appendix B, Table B-3 provide a list of synthesized particles, monomer and initiator feed amounts, and % monomer conversions.

Preparation of gibbous composite particles. Monomers (compositions as shown in Appendix B, Table B-4) were added into 5 g seed particle dispersions stirred at 600 rpm. After the monomers completely diffused into the seed particles (over 15 h), the colloidal
dispersion was deoxygenated by purging N\textsubscript{2} for 30 min and KPS aqueous solution (feed amounts shown in Table D-4) was added. The reaction was continued for 2 hours at 75 °C. The gibbous particles synthesized using this procedure are monodispersed and agglomerates/aggregates are rarely observed. No separation was needed for TEM/SEM experiments. Monomer compositions, KPS feed amounts, and conversions are listed in Table D-4.

Particle size measurements were performed using a Malvern Zetasizer Nano ZS at 25°C. Particle morphologies were examined using a Hitachi H-9500 Transmission Electron Microscope (TEM) operated at 300 kV and Hitachi HD-2000 Scanning Transmission Electron Microscope (STEM) with Energy Dispersive X-ray Spectroscopy function operated at 200 kV. Each colloidal dispersion at \~5 w/w % solids, upon 1:10\textsuperscript{4} dilution, was deposited on a Carbon film Cu grid (EMS) and TEM and SEM analyses were performed. The pH-responsiveness of pMMA-p(PFS/MAA) nanoparticles was determined by depositing the diluted nanoparticles on a Carbon film Cu grid and initial SEM analysis was performed. In the next step, the specimen was dipped into an aqueous solution of KOH (0.1mM; pH = 10) for 30 min. Upon removal and drying for 30 min., the same SEM analysis was repeated.

### 3.3 Results and Discussion

Synthesis of gibbous nanoparticles consists of three steps: (1) synthesis of a seed, (2) swelling the seed with monomers, followed by (3) polymerization of the monomers swollen in the seed. Figure 3-1 illustrates how nanoparticle morphologies are controlled
by minute modifications of reaction conditions. For example, TEM images in Figure 3-1(a-d), illustrate the seeds which may consist of homopolymer, such as pMMA (a), or an inorganic core and polymer shell, such as SiO$_2$-pMMA core-shell nanoparticles with shell thickness of ~ 10, 30, 100 nm (b-d). TEM images in Figure 3-1-a'/a”/a”” illustrate particle morphologies resulting from copolymerization of pentafluorostyrene/n-butyl acrylate (PFS/nBA, wt. ratio = 2:1; molar ratio = 1.32:1) with various feed amounts in the presence of pMMA seed particles. As shown, a large number of protuberances are produced and as the monomer feed amount increases, fewer but larger protuberances are formed. The series of TEM images b’/b”/b””-d’/d”/d”” illustrate the morphology changes of the inorganic-organic core-shell gibbous particles as a function of monomer feed amount as well as the shell thickness of SiO$_2$-pMMA seed particles. When the pMMA shell thickness of the seed particles > 30 nm, as shown in Figure 3-1, c’/c”/c””-d’/d”/d””, gibbous nanoparticles containing well-spaced and round protuberances are formed and as the monomer feed amount increases, the number of protuberances decreases while the size increases, which is confirmed by the SEM images shown in Appendix B, Figure B-2. The composition of core-shell gibbous particles is also manifested by the SEM images and the corresponding spatial elemental analysis of nanoparticles in Appendix B, Figure B-3. It can be seen that the silica core is not involved in this process. However, when the pMMA shell thickness is ~ 10 nm, as shown in Figure 3-1-b”, copolymerization of 144 mM PFS/nBA results in anisotropic particles with 3 or 4 bulges on the surface. Two-fold increase of the monomer feed (288 mM) results in dumbbell-like (two bulges) morphologies (Figure 3-1-b””).
Figure 3-1. TEM images of pMMA seed (~250 nm) (a) and SiO$_2$-pMMA seed nanoparticles with a shell thickness of ~10 (b), 30 (c), 100 nm (d); TEM images a'-d', a'”-d”, and a’”-d’” represent individual nanoparticles synthesized by the swelling and polymerization process using PFS/nBA monomers. TEM images a'-a’”/b’-b’”/c’-c’”/d’-d’” correspond to the following monomer feed amounts (PFS/nBA, molar ratio: 1.32:1): 72, 144, and 288 mM, respectively. Appendix B, Figure B-1 illustrate TEM images of larger populations of the same nanoparticles.

In view of these data, two questions need to be addressed: what drives the formation of gibbosity and what are molecular processes responsible for this behavior.
For that reason, we extracted aliquots during polymerization and conducted the particle size analysis (Appendix B, Figure B-4). The particle size rapidly increases during the first 10 min of polymerization from 250 to 297 nm, to reach the maximum at ~ 318 nm after 120 min. As shown in Figure 3-2-a, pMMA seed particles are uniform compositionally and topographically. As PFS/nBA monomers swell pMMA, their surface softens, as shown in Figure 3-2-b. As polymerization is initiated after 2 min, phase-separated regions are formed (Figure 3-2-c), which become larger and spherical (4 min). At the same time, bulges begin to form and after 6 min become larger, but their quantities remains constant. As polymerization continues (10 – 120 min), the size of bulges keeps increasing and adjacent phase-separated bulges may merge to a larger bulge. During this process, it can be seen that both the deformation of seed particles and bulges play an important role in gibbous morphology formation.

Figure 3-2. Morphologies developed during swelling and polymerization of 288 mM PFS/nBA (molar ratio: 1.32:1) in the presence of pMMA seeds (a) as a function of polymerization time: 0 (b), 2 (c), 4 (d), 6 (e), 10 (f), and 120 min (g).
The role of deformability of seeds was examined by tuning the Tg of p(MMA/nBA) and p(MMA/methacrylic acid(MAA)) particles. TEM images shown in Figure 3-3(a-d), illustrate images of resulting gibbous particle from p(MMA/nBA) seed particles with the Tg of 50 to 75, 90, and 105 °C, and show that protuberances are more pronounced at higher Tgs. As a matter of fact, seed nanoparticles with the Tg < Tp (Tp: polymerization temperature) will lead to core-shell inversion, as demonstrated in Figure 3-3-a and predicted in earlier studies.[21] When the Tg of the core is ~75 °C, protuberances form (Figure 3-b) and when Tg > Tp, gibbosity is produced (Figure 3-3-c, d). Similar morphologies are observed when p-MMA/nBA-SiO2 seed particles are utilized (Appendix B, Figure B-5). As the Tg of the seed further increases, by copolymerizing MMA with MAA, to 114 and 117 °C, significantly larger protuberances are produced.

Figure 3-3. TEM images of gibbous nanoparticles synthesized by utilizing 144 mM PFS/nBA (1.32:1 molar ratio) in the presence of p(MMA/nBA) seeds (particle size 250 ± 5 nm) with the Tgs of ~ 50 (a), 75 (b), 90 (c) and 105 °C (d), and p(MMA/MAA) seeds (particle size 250 ± 5 nm) with the Tg of ~ 114 (e) and 117 °C (f). The insets are SEM images of respective nanoparticles. Scale bar 50 nm.
The role of mobility of growing fluorinated polymer chains on the gibbosity formation was examined by tuning p(PFS/nBA) (or p(PFS/MAA)) to desired $T_g$s. As shown in Figure 3-4-a, when PFS/nBA ratio is 1:1, the resulting copolymers exhibit the $T_g = -5 \, ^\circ C$ below room temperature and no bulges are formed due to enhanced chain mobility. As PFS/nBA ratio increases to 1.5:1 and the $T_g$ of the resulting copolymers (25 $\, ^\circ C$) reaches room temperature, bulges begin to form (Figure 3-4-b). More pronounced bulges are formed with the increase of PFS/nBA ratio (Figure 3-4-c). However, when only PFS monomer ($T_g=80 \, ^\circ C$) or PFS/MMA (wt. ratio 10:1, $T_g = 82 \, ^\circ C$) is utilized,
irregular protuberances with sharp edges are formed (Figure 3-4, d and e). Further increase of the $T_g$ to 102 °C results in the formation of significantly greater number of small bulges, which is likely due to restricted mobility of phase-separated copolymer regions.

Figure 3-5. Schematic representation of the mechanism responsible for the formation of raspberry-like morphologies by seeded emulsion polymerization (a); and the representation of the formation of core-shell raspberry-like (b) and dumbbell-like (c) particles.

Based on these experimental results, the following mechanism of the gibbosity development in nanoparticles is proposed. As depicted in Figure 3-5-a-1, at a given polymerization temperature, hydrophilic initiator-derived radicals approach seed particle surfaces to initiate polymerization of monomers (PFS and nBA) near the surface. Upon initiation, polymerization continues as long as monomer supplies last, and hydrophobic
bulges are formed. Their growth is driven by a greater surface tension difference between p(PFS/nBA) and water than that between seed and aqueous phase. (Appendix B, Table B-1). At the same time, the limited free volume within the seed inhibits diffusivity of p(PFS/nBA) chains inward particles. As a result, they form protuberances on seed nanoparticle surfaces (Figure 3-5-a-2). Another driving force for supplying monomers to the seed particle surface is the higher solubility of reactive monomers in copolymerized protuberances compared to the seed (Figure 3-5-a-3). As polymerization proceeds, the protuberances form gibbous surfaces (Figure 3-5-a-4). The same process is responsible for the formation of protuberances when SiO$_2$-pMMA particles with thick pMMA shell (> 20 nm) are utilized as seeds (Figure 3-5-b). However, when SiO$_2$-pMMA has a thin pMMA shell (~ 10 nm), seeded emulsion polymerization results in the formation of particles with fewer protuberances as well as dumbbell-shaped particles (Figure 3-5-c). Since pMMA layer is not sufficiently thick, adjacent growing protuberances merge to form two protuberances on opposite sides of the core, resulting in dumbbell-shaped particles.
The gibbous particles containing MAA components exhibit different surface topographies at neutral and basic conditions. As shown in Figure 3-6-a, at pH = 7, the particles exhibit a large number of small bulges with fairly distinct edges. However, when pH = 10, carboxylic acid groups of pMAA side chains are deprotonated, thus carrying negative charges along the copolymer backbone. As a result, the overall diameter of the gibbous particles increases from 260 to 290 nm (Figure 3-6) due to expansion, manifested by the development of rounded edges. In an effort to illustrate the size changes of the bulges each SEM image of Figure 3-6 show magnified individual bulges as a function of pH. On average, the bulge diameter increases by ~15 %. To further justify the stimuli-responsiveness and stability of gibbous nanoparticles zeta potential measurements were conducted as a function of pH. The results are shown in Appendix B, Figure B-8, which illustrate zeta potential and particle size changes plotted.
as a function of pH. As seen, when the degree of neutralization increases, zeta potential values decrease which parallels the particle increase. The apparent dissociation constant (pK$_a$) of poly(methacrylic acid) component is $\sim$3.6,$^{[22]}$ and Appendix B, Figure B-8 clearly illustrates that above that value zeta potential levels off at $\sim$ -40-45 mV, thus stabilizing the particles which parallels their size increase.

3.4 Conclusion

Gibbous nanoparticles with controlled morphologies and surface topographies were synthesized via seeded emulsion polymerization. The gibbosity of the particles can be easily controlled by altering monomer composition/concentration. Furthermore, incorporation of pH-responsive components into the bulges results in stimuli-responsiveness manifested by size changes under different pH conditions. These controlled heterogeneous and topographies will lead to the development of complex, high surface colloidal crystals with lowest symmetries, an opportunity for entrapment of nano-objects inside gibbous cavities and others.
3.5 References


CHAPTER FOUR

“GEAR-LIKE” ASSEMBLIES OF GIBBOUS AND INVERSE-GIBBOUS COLLOIDAL NANOPARTICLES

4.1 Introduction

Many biological processes rely on shape recognition. The basic mechanism by which enzymes catalyze chemical reactions begins with the physical fit between an enzyme and a substrate, where the substrate fits in a key-like fashion to its lock, the enzyme. While macroscopic analogies of these interactions have been well documented, due to many potential applications in medicine, materials chemistry, and engineering, precisely designed shapes and sizes of organic and inorganic nanoparticles continue to be of scientific interests and technological importance. The synthesis of well-defined nanoparticles with various morphologies, such as cubes,\(^1\) clustered spheres,\(^2\) dimpled,\(^3,4\) and gibbous particles,\(^5\) is particularly relevant when designing 2D/3D hierarchical structures, requiring directional guidance.\(^6-8\) Due to the absence of anisotropic directional bonds, the most challenging and intriguing aspects of nanoparticle constructs is encoding directional guided arrays. Typically, van der Waals,\(^9\) electrostatic,\(^10,11\) depletion,\(^12\) and DNA hybridization\(^13\) were utilized. Other examples are “lock-and-key” shape matching colloids resulting in the higher organized structures,\(^12,14\) or assemblies of biotin/DNA decorated particles via “patch-patch” interactions.\(^13\) While the formation of organized 2-3D nanoarrays is not trivial, theoretical studies suggested that the attractive interactions between nanoparticles are balanced by the entropy for surface
non-adsorbing polymers, whereas adsorbing polymers are of the enthalpic origin.\textsuperscript{[15]} It has also been theorized that to achieve programmable self-assembly of colloidal nanostructures, two general strategies should be considered: puzzle and folding approaches, which rely on short-range (for example, electrostatic) and long range (for example, geometrical) interactions, respectively.\textsuperscript{[16]}

4.2 Experimental

Materials. Tetraethoxysilane (TEOS, 98\%) and ammonium hydroxide (28–32\% in water), methyl methacrylate (MMA, 99\%), n-butyl acrylate (nBA, 99\%), styrene (St, 99\%), anionic initiator potassium persulfate (KPS, 99\%), 3-(methacryloyloxy)propyl trimethoxysilane (MPS, 98\%), and aluminum oxide (Al\textsubscript{2}O\textsubscript{3}, 98\%) were purchased from Aldrich Chemical Co. Pentafluorostyrene (PFS, 99\%), and heptafluorobutyl acrylate (HFBA, 97\%) were purchased from Fisher Scientific Co. Cationic initiator 2,2' -azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (AIPD or VA-44) was purchased from Wako Pure Chemicals Ind. Ltd. MMA, nBA, St, and PFS were allowed to pass through an Al\textsubscript{2}O\textsubscript{3} column to remove inhibitors prior to use, and all other chemicals were used as received.

Preparation of Gibbous Nanoparticles. Gibbous nanoparticles were synthesized according to the procedures described in Chapter 3.

Preparation of “-” and “+” pSt Seed Nanoparticles. In a typical synthesis, 90 g deionized water was placed in a flask and heated to 75 °C under protection of N\textsubscript{2} gas and magnetic stirring at 400 rpm. St (3 g, 28.8 mmol) and 5 mL anionic initiator KPS
aqueous solution (0.01 g/mL, 37 mM) (or 5 mL cationic initiator AIPD aqueous solution (0.012 g/mL, 37 mM)) were added, and the reaction was allowed to continue for 15 h. The seed particles were purified by centrifugation at 1500g for 3 h. Upon completion, they were redispersed in 95 mL of deionized water. Conversion > 99%.

Preparation of Inverse-Gibbous Nanocomposite Particles. In a typical synthesis, 5 g pSt seed particle dispersions were stirred at 600 rpm and 0.16 g HFBA/nBA mixture (molar ratio 1:1) were added. After the monomers completely diffused into the seed particles (over 15 h), the colloidal dispersion was deoxygenated by purging N₂ for 30 min, and KPS (AIPD for “cationic” seeds) aqueous solution (0.007 mmol) was added. The reaction was continued for 1 h at 75 °C. The inverse-gibbous particles synthesized using this procedure were monodispersed, and agglomerates/aggregates were rarely observed. No separation was needed for TEM/SEM experiments.

Self-Assembly of Oppositely Charged Gibbous and Inverse-Gibbous Particles. In a typical procedure, negatively charged “-” gibbous nanoparticles and positively charged “+” inverse gibbous particles were diluted by deionized water with a ratio of 1: 10,000. Equal amount dispersions were quickly mixed and TEM samples were prepared by putting 2 µL of the colloidal mixtures. The sample was controlled to dry at room temperature and relative humidity of 80 %.

Preparation of Colloidal Films. In a typical procedure, negatively charged “-” gibbous and inverse-gibbous nanoparticle dispersions with topography-matching surfaces (determined by TEM) were diluted to 0.5 wt% using deionized water, respectively. Equal amount (2.5 mL each) of the two dispersions were mixed and put in a 20 mL vial and
sonicated for 5 min. Glass slides (pre-cleaned with by sonication in acetone and water) were vertically positioned in these vials. Subsequently, the colloidal particles were self-assembled on the glass slides at 60 °C and relative humidity of 50 %.

Characterization. Particle size measurements were performed using a Malvern Zetasizer Nano ZS at 25 °C. Particle morphologies were examined using a Hitachi H-9500 transmission electron microscope (TEM) operated at 300 kV and a Hitachi HD-2000 scanning transmission electron microscope (STEM) with energy-dispersive X-ray spectroscopy function operated at 200 kV. Each colloidal dispersion at ~5 w/w % solids, upon 1:10 dilution, was deposited on a carbon film Cu grid (EMS), and TEM and SEM analyses were performed. Colloidal films were first sputter-coated with Pt (~5 nm thick) and observed by using a Hitachi S-4800 SEM operated at 5 kV. The glass transition temperature (Tg) was measured using differential scanning calorimetry (DSC) (TA instruments Discovery Series) in the temperature range of -55 °C – 150 °C at a heating rate of 10 °C/min.
4.3 Results and Discussion

Figure 4-1. TEM, SEM images and graphical representations of gibbous (a-a’”) and inverse-gibbous particles (b-b’’’).

In view of these considerations we designed and synthesized gibbous (Figure 4-1-a) and inverse-gibbous nanoparticles (Figure 4-1-b) with geometrically matching surfaces that facilitate “gear-like” particle mechanical interlocking which, as will be shown later, will be guided by surface ionic interactions. As shown in Figures 4-1, a and a’, TEM and SEM images of gibbous nanoparticles exhibit well-defined bulges. The nanoparticles consist of poly(methyl methacrylate) (pMMA) core and poly(pentafluorostyrene(PFS)/n-butyl acrylate(nBA)) shell. Using the same polymerization procedure, we synthesized inverse-gibbous particles which consist of polystyrene (pSt) core and poly(heptafluoro-n-butyl acrylate(HFBA)/nBA) shell. TEM and SEM images of the inverse-gibbous nanoparticles are shown in Figure 4-1, b and b’. Figures 4-1, a’”/a’’” and b’”/b’’” depict the particle’s geometrical features obtained from the TEM and SEM images. The radius of the nanoparticles is ~ 145 nm, whereas the bulges (gibbous) and dimples (inverse-
gibbous) are ~ 15 nm ($r_a$ and $r_b$, respectively). In designing and synthesizing these surface
topographies, it was critical to match the $r_a$ and $r_b$ values in order to facilitate shape
matching to obtain “gear-like” assemblies guided by ionic interactions.

To produce gibbous and inverse-gibbous nanoparticles, hydrophobic monomers
were allowed to diffuse into the particle seeds, followed by their polymerization initiated
by a water-soluble initiator. Using this approach, phase-separated copolymer domains
were produced on the seeds. In order to guide an essential phase-separation during
polymerization we utilized monomers with specific solubility parameters (Appendix C,
Table C-1) for each polymer/monomer composition. According to the previous studies \(^5\)
as well as the results of control experiments (Appendix C, Figure C-1, C-2, and C-3), the
solubility parameters of given two polymers need to be distinctly apart (> 2 cal\(^{0.5}\)cm\(^{1.5}\))
to obtain significant phase-separation and distinct surface heterogeneities. Another
important factor governing the morphology development is the rigidity of the
copolymerizing macromolecules reflected by the glass transition temperature ($T_g$). The
deformation of forming copolymers during polymerization will significantly influence
the resulting particle morphologies.\(^{[17]}\)

Figure 4-2 depicts the mechanism responsible for the synthesis of gibbous and
inverse-gibbous nanoparticles which were produced by the same synthetic procedures,
but the choice of starting materials was dictated by their solubility parameter and the $T_g$
of the forming copolymers tuned by copolymer composition. Thus, the process involves
the seed formation, monomer diffusion, and localized copolymerization. Initially,
copolymerization of pentafluorostyrene (PFS) and n-butyl acrylate (nBA) (molar ratio
1.5:1) on a pMMA seed results in the formation of phase-separated gibbous bulges with the glass transition temperature ($T_g$) of 70 °C (Figure 4-2-a). The gibbous morphology is attributed to the fact that the forming fluorinated copolymers cannot diffuse into the seed particles and thus become immobilized and form phase-separated bulges. In contrast, when HFBA and nBA in a molar ratio of 1.5:1 are copolymerized onto a hydrophobic pSt seed (Figure 4-2-b and Appendix C, Figure C-4, C-5, C-6 and C-7), phase-separation leads to the formation of dimples resulting in inverse-gibbous morphologies. Since p(HFBA/nBA) copolymers exhibit the $T_g$ of ~ -20 °C, they will collapse on the seed particle surfaces and maintain their phase-separation to form dimples. Furthermore, being hydrophobic, these copolymers will minimize the surface area to lower the interfacial energy. As copolymerization proceeds, localized fluorocopolymer indentations are formed on the surface due to the higher surface tension, resulting in dimple morphologies. The number and the size of the dimples can be tuned by altering the monomer feed ratio as well as the reaction times. This is illustrated in Appendix C, Figure C-4, C-5, C-6 and C-7.
Figure 4-2. Schematic representation of the mechanism responsible for the formation of gibbous (a) and inverse-gibbous (b) nanoparticles using seeded emulsion polymerization.

An ultimate objective of these studies is to develop nanoparticles capable of 2D and 3D assemblies via short- and long-range directional interactions. While long-range interactions can be achieved by mechanical interlocking of gibbous and inverse-gibbous morphologies to form “gear-like” assemblies, short-range interactions can be introduced by incorporating the opposite electrostatic charges on the surfaces of the seeds as well as gibbous and inverse-gibbous nanoparticles. For polymeric nanoparticles synthesized
using surfactant-free emulsion polymerization, cationic “+” or anionic “−” surface charges can be incorporated by the choice of an initiator and the surface charge density is proportional to the number of polymer chains in each particle.[18] In order to obtain nanoparticles stabilized by positive or negative charges, cationic “+” (2,2’-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride, AIPD) or anionic “−” (potassium persulfate, KPS) initiators were utilized. The “−” seeds and gibbous nanoparticles have the zeta potential of ~ -35 and -49 mV, respectively. In contrast, the “+” seeds and inverse-gibbous nanoparticles have the zeta potential of +39 and +52 mV, respectively. The increase of the absolute values of the zeta potentials indicates higher charge densities on the bulges/dimples of the gibbous/inverse-gibbous surfaces.[19]
Having secured short- and long-range interactions schematically depicted in Figure 4-3-a, we combined oppositely charged ("+" and "-" ) polymeric nanoparticles in an aqueous phase. The premise behind this approach is to form directional mechanical interlocking guided by attractive electrostatic forces. When such assemblies are formed, the arrangement and orientation of these assemblies will enhance the probability of the next particle to be attracted to oppositely charged end of this “dipole”, thus forming gear-
like alignment. Because these alignments can be affected by nanoparticle concentration levels, we examined various concentrations of nanoparticles and analyzed TEM images. At the concentration levels of ~ $10^{-7}$ g/mL, the particles link to form 2D directional “gear-like” assemblies. This is illustrated in Figure 4-3, c and d. This is attributed to geometrical interlocking guided by enhanced electrostatic attractions between “-” gibbous particles and “+” inverse-gibbous nanoparticles. As illustrated in Figure 4-3-b, the attractive forces between oppositely charged particles as well as repulsive forces between the particles with the same charges will favor “gear-like” directional assemblies. It should be noted that while van der Waals attractive forces may also contribute to the stability of the assemblies, attractive and repulsive electrostatic forces facilitate the directional alignment of nanoparticles. At higher concentration levels ~ $10^{-6}$ g/mL, gibbous and inverse-gibbous nanoparticles form multi-gear-like assemblies (Appendix C, Figure C-8), whereas spherical particles and oppositely charged nanoparticles (~ $10^{-7}$ g/mL) with spherical, gibbous and inverse-gibbous topographies result in random assemblies (Appendix C, Figure C-9).
One of the challenges in forming 3D nanoparticle assemblies are stresses that develop during film formation that result in crack formation. The unique feature of gibbous and inverse-gibbous nanoparticles is their ability to interlock during film formation, thus forming 3-D crack-free colloidal assemblies. These conditions are facilitated by vertical deposition of concentrated interlocking nanoparticles stabilized by the same electrostatic charges (anionic) during water evaporation.\textsuperscript{[20]} This is illustrated in Figure 4-4, a-a”. Usually, self-assemblies of spherical nanoparticles lead to undesired crack formation (Figure 4-4, b-b”) resulting from mechanical stresses developed during drying,\textsuperscript{[21]} and in order to prevent cracking, templates,\textsuperscript{[22]} superhydrophobic substrates \textsuperscript{[23]} or in-situ reactions \textsuperscript{[24]} are required. Notably, self-assembly of gibbous particles (Figure 4-4, c-c”) prevents the development of cracks along the horizontal direction, which is likely due to
the bulges that fit into the space between neighboring particles, thus alleviating stresses along the horizontal direction. For self-assembly of inverse-gibbous particles (Figure 4-4, d-d”), both horizontal and vertical cracking occur due to their spherical shape. However, when gibbous and inverse-gibbous nanoparticles are simultaneously assembled to form colloidal films (Figure 4-4, a-a”), crack formation is completely eliminated. This is attributed to mechanical interlocking between the bulges on gibbous and dimples on inverse-gibbous nanoparticles as well as electrostatic short-range inter-particle interactions.

4.4 Conclusion

In summary, these studies show the synthesis of gibbous and inverse-gibbous colloidal nanoparticles using seeded emulsion polymerization. The formation of these controllable morphology and topography nanoparticles is driven by the surface tension differences at the phase-separated regions of the forming copolymers on seed particles. The gibbous and inverse-gibbous topography is driven by the solubility parameters, miscibility, and chain rigidity of the forming copolymers. The topography-matching nanoparticles stabilized by opposite charges are capable of forming “gear-like” directional assemblies due to short-range electrostatic interactions and long-range “gear-like” mechanical interlocking. Furthermore, topography-matching gibbous and inverse-gibbous nanoparticles are capable of forming 3D crack-free colloidal films.
4.5 References


CHAPTER FIVE
ONE-STEP SYNTHESIS OF AMPHIPHILIC ULTRAHIGH MOLECULAR WEIGHT BLOCK COPOLYMERS BY SURFACTANT-FREE HETEROGENEOUS RADICAL POLYMERIZATION

5.1 Introduction

For almost two decades, controlled radical polymerization (CRP) has dominated the field of polymer synthesis. Due to pseudo-living features, nitroxide-mediated (NMP),\(^1\,^2\) atom transfer radical (ATRP),\(^3\,^4\) and reversible addition-fragmentation chain transfer (RAFT) polymerizations\(^5\,^7\) facilitated thermodynamically controlled conditions for the synthesis of well-defined block copolymers with a narrow dispersity. These advances enabled many applications, ranging from drug delivery systems\(^8\) to diagnostic imaging processes,\(^9\,^10\) new separation membranes\(^11\,^12\) and others. One of the drawbacks of CRPs is the time-consuming synthesis, purification steps, and molecular weight limitations.\(^13\) In contrast, emulsion polymerization is technologically well suited for the synthesis of ultra-high molecular weight polymers, but limited copolymer composition control and high dispersity are the main drawbacks. Due to fast kinetics of initiation, propagation, and termination steps, copolymer structural control during this statistical polymerization is difficult to achieve. However, heterogeneous nature of emulsion polymerization facilitates an opportunity for controlling the diffusion of propagating polymeric radicals into separated phases. Taking advantage of these environments, several colloidal nanoparticles with well-defined morphologies and surface topographies
have been successfully synthesized. Capitalizing on these findings, it was reasonable to consider that the kinetic control of copolymerization of hydrophilic and hydrophobic monomers in heterogeneous environments may lead to ultra-high molecular weight amphiphilic block copolymers.

5.2 Experimental

Materials. 2-(Dimethylamino)ethyl methacrylate (DMAEMA, 98%), n-butyl acrylate (nBA, 99%), t-butyl acrylate (tBA, 99%), Styrene (St, 99%), N,N-Dimethylformamide (DMF, 99.8%), DMF-d7 (99.5 atom %D), and aluminum oxide (Al₂O₃, activated, basic) were purchased from Aldrich Chemical Co. Water-soluble initiator 2,2’-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (AIPD) was purchased from Wako Pure Chemicals Ind. Ltd. Inhibitors in monomers were removed by passing through Al₂O₃ column.

Synthesis of p(DMAEMA-block-nBA) copolymers. Deionized water (50 mL) was stirred at 600 rpm, deoxygenated by bubbling N₂ for 30 min, and heated up to 75 °C. DMAEMA (3.93 g, 25 mmol) was added and dissolved into a homogeneous solution. Then, nBA (3.2 g, 25 mmol) was added and AIPD aqueous solution (3 mL X 0.005 g/mL, 0.046 mmol) was fed over 3 h. After the beginning of initiator addition, polymerization solution became bluish in 2 min and turned milky white in 5 min, indicating the formation of colloidal nanoparticles with hydrophobic core. The reaction was allowed to run for another 30 min. The resulting emulsion was dialyzed (molecular weight cutoff (MWCO) = 6-8 kDa) against water for 24 h and ethanol for 5 h to remove
oligomers and unreacted monomers. The resulting polymers were precipitated in diethyl ether and dried in vacuum oven overnight at 65 °C. Yield: 69%.

Preparation of inverse polymeric micelles. pDMAEMA-b-pnBA copolymers (0.6 g) and H₂O (0.02 g) were added to 20 mL toluene. The mixture was sonicated overnight and purple/blue clear solution was obtained.

Synthesis of p(DMAEMA/(tBA or St) block copolymers using SFHRP. Deionized water (50 mL) was stirred at 600 rpm, deoxygenated by bubbling N₂ for 30 min, and heated up to 75 °C. DMAEMA (25 mmol) was added and dissolved into a homogeneous solution. Then, tBA (or St) (25 mmol) was added and AIPD aqueous solution (3 mL X 0.005 g/mL, 0.046 mmol) was fed over 3 h. After the beginning of initiator addition, polymerization solution became bluish in 2 min and turned milky white in 5 min, indicating the formation of colloidal nanoparticles with hydrophobic core. The reaction was allowed to run for another 30 min. The resulting emulsion was dialyzed (molecular weight cutoff (MWCO) = 6-8 kDa) against water for 24 h and ethanol for 5 h to remove oligomers and unreacted monomers. The resulting polymers were precipitated in diethyl ether and dried in vacuum oven overnight at 65 °C. Yield: 65-68%.

Synthesis of p(DMAEMA/(nBA, tBA or St)) statistical copolymers. Ethanol (50 mL) was stirred at 600 rpm, deoxygenated by bubbling N₂ for 30 min, and heated up to 75 °C. DMAEMA (25 mmol) and nBA/tBA/St (25 mmol) were added, forming homogeneous solution. Then, AIPD aqueous solution (3 mL X 0.005 g/mL, 0.046 mmol) was fed over 3 h. The reaction was allowed to run for another 30 min. The resulting solution was dialyzed (molecular weight cutoff (MWCO) = 6-8 kDa) against water for 24
h and ethanol for 5 h to remove oligomers and unreacted monomers. The resulting polymers were precipitated in diethyl ether and dried in vacuum oven overnight at 65 °C. Yield: 76%.

Synthesis of pDMAEMA homopolymers. Water (50 mL) was stirred at 600 rpm, deoxygenated by bubbling N2 for 30 min, and heated up to 75 °C. DMAEMA (25 mmol) was added, forming transparent solution. Then, AIPD aqueous solution (3 mL x 0.005 g/mL, 0.046 mmol) was fed over 3 h. The reaction was allowed to run for another 30 min. The resulting polymers were precipitated in acetone and dried in vacuum oven overnight at 65 °C. Yield: 81%.

Synthesis of pnBA (ptBA, or pSt) homopolymers. Water (50 mL) was stirred at 600 rpm, deoxygenated by bubbling N2 for 30 min, and heated up to 75 °C. Hydrophobic monomer nBA (tBA or St) (25 mmol) was added. Then, AIPD aqueous solution (3 mL x 0.005 g/mL, 0.0046 mmol) was fed over 3 h. The reaction was allowed to run for another 30 min. The milky white polymer emulsions were precipitated by centrifugation and dried in vacuum oven overnight at 65 °C. Yield: 75-79%.

Molecular weight determination. The molecular weight of SFHRP block copolymers were determined by AF2000 Multiflow Organic Asymmetrical field flow fractionation (FFF) system equipped with a PN5300 autosampler for injection, a PN3621 Multi Angle Light Scattering detector and a PN3150 RI detector using DMF as the solvent.

Characterization. Particle size measurements are performed using a Malvern Zetasizer Nano-ZS equipped with a 633 nm laser, at a constant backscattering angle of
173° at 25 °C. Inverse micelle morphologies were investigated using a Hitachi H-9500 transmission electron microscope (TEM) operated at 300 kV, where the samples were diluted and deposited on a Carbon-film supported Copper grid (EMS). $^1$H NMR spectra were obtained using a JOEL ECX-300 spectrometer operating at 300 MHz. All spectra were collected at 25 °C and referenced to tetramethylsilane or residual protium in the NMR solvent (DMF-d7: 8.00). UV-Vis spectra were obtained on PerkinElmer Lambda 950 UV/Vis/NIR spectrometer.

5.3 Results and Discussion

These studies report one-step surfactant-free synthesis of amphiphilic ultrahigh molecular weight block copolymers, which is achieved by sequential copolymerization of phase-separated hydrophilic and hydrophobic monomers controlled by the initiator-starvation conditions. Figure 5-1-A depicts a schematic diagram of this surfactant-free heterogeneous radical polymerization (SFHRP). Initially, water-soluble monomer $M_1$ is dissolved in an aqueous phase, whereas hydrophobic monomer $M_2$, due to poor water solubility, forms phase-separated droplets (Figure 5-1-A-1). Polymerization of $M_1$ in an aqueous phase is initiated by hydrophilic radicals resulting from thermal decomposition of a water-soluble initiator (Figure 5-1-A-2). The first propagation stage involves polymerization of $M_1$ to form hydrophilic radical-terminated $pM_1^\cdot$ blocks in an aqueous phase, followed by the second stage copolymerization of a hydrophobic monomer $M_2$ (Figure 5-1-A-3). The growing $p(M_1)_m-M_2^\cdot$ polymer chain ends become hydrophobic, resulting in the formation of polymeric micelles composed of polymerized $pM_1$ blocks.
and interior pM₂* ends.¹⁹ The continuous diffusion of M₂ into the reaction loci facilitates the second stage copolymerization of hydrophobic blocks (Figure 5-1-A-4). Since the polymerizing hydrophobic radicals are protected by hydrophilic pM₁ segments, the possibility of bimolecular termination is minimized. The termination may occur by disproportionation and combination, resulting in the pM₁-pM₂ diblock or pM₁-pM₂-pM₁ triblock copolymers, respectively (Figure 5-1-A-5).²⁰

Similarly to CRP, the key controlling parameter of SFHRP is to maintain low concentration levels of free radicals. However, in contrast to CRP, SFHRP does not rely on reversible deactivation. Instead, it utilizes kinetically controlled propagation stages involving the sequential polymerization of M₁ and M₂, thus the statistical copolymer growth can be eliminated. However, if high concentration levels of initiators are added at the onset of the reaction, polymerization and termination will occur in an aqueous phase. Thus, it is critical to slowly and continuously supply an initiator (Appendix D, Figure D-1), which kinetically controls SFHRP. The continuous diffusion of M₂ from the monomer droplets into the polymerization site is driven by chemical potential differences and a high surface area of the forming polymeric micelles.²¹ Also, as pointed out above, SFHRP should not be allowed to reach the high monomer conversion rates in order to maintain significantly higher concentration levels of M₁ (C_M₁) in an aqueous phase. In the typical polymerization, C_M₁ > 10 C_M₂ at ~ 70 % conversion. Also, water solubility of monomers M₁ and M₂ should be significantly different (Appendix D, Table D-3). In regards to the reactivity ratios, it is preferable that M₁ exhibits higher reactivity towards itself (r₁ > 1 and r₂ < 1), thus facilitating the initial polymerization of M₁ to form the pM₁
blocks in an aqueous phase. Furthermore, hydrophilic pM$_1$ blocks should maintain the stability to form polymeric micelles by electrostatic repulsions. In view of these requirements, due to its high water solubility and reactivity as well as colloidal stability provided by tertiary amine groups upon partial protonation, a good candidate for M$_1$ is 2-(N,N-dimethylamino) ethyl methacrylate (DMAEMA). Since monomer M$_2$ should be hydrophobic and exhibit low water solubility, suitable candidates are nBA, tert-butyl acrylate (tBA), and styrene (St).

![Figure 5-1](image-url) (A) Schematic illustration of SFHRP synthesis of amphiphilic block copolymers. Water-soluble radicals initiate polymerization of water-soluble monomer M$_1$ first, followed by phase-separation and sequential propagation of hydrophobic monomer M$_2$ in the polymeric micelles. (B) Schematic representation of SFHRP of pDMAEMA-b-pnBA block copolymers.
Using SFHRP approach, we synthesized pDMAEMA-b-nBA, pDMAEMA-b-tBA and pDMAEMA-b-St block copolymers with molecular weights of 1.98x10^6, 1.18x10^6, 0.91x10^6 g/mol with dispersity of 2.55, 4.84, 1.29, respectively (Appendix D, Table D-1). While Appendix D discloses experimental details of their synthesis and characterizations, here we briefly outline key elements and conditions facilitating SFHRP synthesis of pDMAEMA-b-nBA block copolymers. Starting with 0.51 M aqueous solution of DMAEMA, after polymerization was completed, 0.15 M of the monomer was left. The reason for ~70% monomer conversion was to maintain high levels of water soluble monomers in an aqueous phase. In contrast, the initial concentration levels of hydrophobic nBA (solubility in water: 2 g/L) in water were < 0.015 M. Under these conditions, the initiation and first propagation stage of DMAEMA occur in an aqueous phase, whereas the second propagation stage of nBA takes place within hydrophobic moiety of polymeric micelles. Considering the initial monomer concentration levels at ~70% conversion rate and the final molecular weight of the polymer, we estimated that the initiator efficiency is ~0.26.

The block copolymer structures were verified by solubility measurements, differential scanning calorimetry (DSC), and 1H NMR analysis. While experimental details for all copolymers are provided in the Appendix D, the following features are characteristics of a pDMAEMA-b-pnBA copolymer: (1) The presence of two T_g's at -39 and 47 °C. In contrast, the solution polymerized p(DMAEMA-stat-nBA) exhibits one T_g at -10.5 °C (Figure 5-2); (2) The α-methyl protons in the 1H NMR spectrum clearly show no shielding by α-protons of the nBA units, indicating the block copolymer formation.
NMR spectrum of solution polymerized p(DMAEMA-stat-nBA) copolymers show significant shielding of α-methyl protons \(^{22}\) (Figure 5-3); (3) The solubility differences between the SFHRP and solution polymerized p(DMAEMA/nBA) copolymers show that pDMAEMA-b-pnBA block copolymer is soluble in DMF (a common solvent for both blocks), whereas p(DMAEMA-stat-nBA) is soluble in many organic solvents (Appendix D, Table D-2). The block copolymer morphologies of SFHRP synthesized pDMAEMA-b-pSt and pDMAEMA-b-pSt are also confirmed by Appendix D, Figures D-(2-5) and Table D-2.

Figure 5-2. DSC analysis of (a) homogeneous solution polymerized p(DMAEMA-stat-nBA) and (b) SFHRP synthesized pDMAEMA-b-pnBA copolymers.

\(^1\)H NMR spectra of hydrophobic (Trace A) and hydrophilic (Trace B) homopolymers, statistical (Trace C), and block (Trace D) copolymers are shown in
Figures 5-3, and Appendix D, Figure D-3, and D-5. As seen, the resonance profile in the range of 1.05 - 1.25 ppm of block copolymers (Traces D) exhibits characteristic features of α- methyl protons in a continuous DMAEMA unit sequence. In contrast, the resonance of the corresponding statistical copolymers (Trace C) shows significant shift to 0.9 - 1.1 ppm, indicating that α-methyl groups are in a random sequence of DMAEMA and nBA (Figure 5-3), DMAEMA and tBA (Figure D-3), and DMAEMA and St (Figure D-5).

Furthermore, as shown in Figure D-5, the resonance in the range of 6.3 – 7.5 ppm of pDMAEMA-b-pSt (Trace D) is characteristic of the protons in monosubstituted benzene rings of the continuous St unit sequence. In contrast, as compared to the corresponding statistical 7 copolymer (Trace C), the shift to 6.7 – 7.8 ppm is detected due to resonances with randomly distributed DMAEMA units.

Due to ultrahigh molecular weight of block copolymers, the detection of single M1-M2 interface in a pM1-b-pM2 copolymer is difficult. In essence, if an average molecular weight of the ideal block copolymer is 2x10^6 g/mol, there are virtually no characterization methods that would detect the single M1-M2 interface between two ~10^6 molecular weight blocks. Considering that the percentage of hydrophilic and hydrophobic homopolymer impurities during the synthesis was in the 0.3-0.8 w/w% range, as determined by the solvent fractionation method, combined analysis using 1H NMR, DSC, and solubility measurements, confirm that amphiphilic block copolymers can be successfully synthesized using SFHRP.
One of the characteristic features of high molecular weight block copolymers is their ability of forming inverse polymeric micelles. For that reason, we utilized toluene (containing 0.1 vol% water) as a solvent in which pDMAEMA-b-pnBA was sonicated and dispersed to form nanoparticles. The polymer concentration in toluene was 0.03 g/mL. Figure 5-4-A illustrates optical images of the solutions at 10, 20, 30, 40, 50, and 60 °C. As seen, at 10 °C the solution exhibits blue color, which gradually changes to yellow upon increasing temperature. This thermochromic behavior is fully reversible. The UV-vis spectra of the dispersions at various temperatures shown in Figure 5-4-B illustrate that polymeric micelles at 10 °C extensively scatter blue/purple light (λ < 450 nm). As the temperature increases, the absorption curve shifts to shorter wavelengths. This is
attributed to smaller particle size, which decreases from ~ 250 to ~ 200 nm due to the lower critical solution temperature of pDMAEMA blocks (LCST= ~ 40 °C), when temperature increases from 10 to 60 °C. This is depicted in Figure 5-4-C. At the same time, a new absorption band is detected in the ~ 500 - 650 nm visible range of the spectrum (Figure 5-4-B). This is attributed to the refractive index changes as a function of temperature. As shown in Figure 5-4-D, the refractive index of toluene decreases with increasing temperature, thus the refractive index difference between the solvent and the copolymer is larger, resulting in the enhanced scattering of the visible region. The thermochromic behavior of pDMAEMA-b-ptBA and pDMAEMA-b-pSt block copolymers is shown in Appendix D, Figure D-8.
Figure 5-4. (A) Optical images and (B) UV-vis spectra of pDMAEMA-b-pnBA inverse polymeric micelle dispersions in the 10 – 60 °C temperature range; (C) Schematic illustration of reversible size and color changes from 10 – 60 °C; (D) the wavelength dispersion of the refractive indices for toluene in the 10 – 60 °C temperature range.
5.4 Conclusion

In summary, these studies demonstrate one-step SFHRP of ultrahigh molecular weight amphiphilic block copolymers, which is achieved by kinetically controlling propagation stages of hydrophilic and hydrophobic monomers using initiator starvation conditions facilitated by slow and continuous initiator addition. The block copolymers form thermochromic inverse polymeric micelles in suitable organic solvents. SFHRP is the one-step synthesis of high molecular weight amphiphilic block copolymers, and this process can be potentially employed on the industrial large scale. It requires no additional reagents and can be potentially explored in numerous in-situ copolymer higher-order self-assemblies with well-defined morphologies in aqueous environments.
5.5 References


CHAPTER SIX

BLOCK COPOLYMER NANOWIRES BY IN-SITU SELF-ASSEMBLY DURING SURFACTANT-FREE HETEROGENEOUS RADICAL POLYMERIZATION

6.1 Introduction

Flexible worm-like micelles formed by surfactant molecules have been of interests and technological importance for many decades. While unique static and dynamic properties \cite{1} and widespread applications in emulsion/disersion industry \cite{2} are the primary targets, diversified micellar morphologies have been also extended to the self-assembly of amphiphilic block copolymers, which can be seen as macromolecular surfactants. \cite{3} The resulting worm-like polymeric micelles, often termed as cylindrical nanoparticles, nanowires, or nanofibers, with a high aspect ratio, exhibit excellent stability, versatile functionality, unique rheological properties and well-defined morphologies, facilitating potential applications in drug-delivery and biomedical fields. \cite{4}

Although polymer nanoparticles dispersed in aqueous environments have been utilized in a wide range of applications, \cite{4-7} precise morphology control is critical for desired functions. \cite{8} Various morphologies, such as spherical, \cite{9, 10} hollow, \cite{11} Janus, \cite{12, 13} gibbous, \cite{14} and tubular \cite{15} nanoparticles, have been synthesized by emulsion polymerization and other synthetic approaches. \cite{16-18} Nevertheless, worm-like polymeric micelles have been exclusively obtained from self-assembly of block copolymers synthesized by living cationic/anionic/ring-opening or controlled radical polymerizations (CRPs). \cite{19-26} In a typical experiment, self-assembly was performed by slowly adding a
non-solvent for one block into the block copolymer solution.\textsuperscript{[23]} Although solvent displacement method may facilitate both thermodynamic and kinetic control over the final morphologies,\textsuperscript{[19]} this approach requires multi-step synthesis and purification as well as time-consuming assembly process and low concentration disadvantages (usually < 1 wt%). Recently, polymerization-induced self-assembly (PISA) have been developed to instantaneously obtain block-copolymer nano-objects by in-situ polymerization in the presence of a hydrophilic macromolecular reagent (macroinitiator or chain transfer agent).\textsuperscript{[27-31]} However, time-consuming synthesis and purification of macromolecular reagents is one of the limiting factors in applications on industrial large-scale level.

\textbf{6.2 Experimental}

Materials. 2-(Dimethylamino)ethyl methacrylate (DMAEMA, 98\%) and styrene (St, 99\%), were purchased from Aldrich Chemical Co. Water-soluble initiator 2,2’-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (AIPD) was purchased from Wako Pure Chemicals Ind. Ltd. Inhibitors in monomers were removed by passing through Al\textsubscript{2}O\textsubscript{3} (activated, basic) column.

Synthesis of pDMAEMA-b-pSt micelles. For the typical emulsion synthesis, deionized water (25 mL) was stirred at 300 rpm, deoxygenated by bubbling N\textsubscript{2} for 30 min, and heated up to 75 °C. DMAEMA (2.0 g, 12.5 mmol) was added and dissolved into a homogeneous solution. Then, St (feed amount according to the DMAEMA/St molar ratio) was added and 0.5 mL AIPD aqueous solution (0.0025 g/mL, 7.7 mM) was fed
over 30 min. The reaction was allowed to run for additional 5 min and the resulting emulsion was directly used for characterizations.

Self-assembly of the pDMAEMA-b-pSt block copolymer in water. The pDMAEMA-b-pSt copolymers corresponding to Figure 2, C-E, were collected by centrifugation at 13500 rpm for 30 min and dried in vacuum oven at 70 °C overnight. Then, the dried block copolymers were dissolved at a concentration of 1.0 wt% in 1 mL DMF, which is a good solvent for both polymer blocks. The homogeneous solution was stirred at 500 rpm using a magnetic stir bar for 15 h to equilibrate and then (DI) water (5 mL) were dropwise added into the solution at a feed rate of 0.5 mL/h. After the addition, the mixture was allowed to equilibrate for 2 h. Then, the micellar dispersion was dialyzed (molecular weight cutoff (MWCO) = 6-8 kDa) against deionized water for 3 days to remove DMF. The morphologies of the final micelles were observed by TEM directly.

Characterization. The morphologies of block copolymer micelles were investigated using a Hitachi H-9500 transmission electron microscope (TEM) operated at 300 kV, where the samples were diluted and deposited on a Carbon-film supported Copper grid (EMS). 1H NMR spectra were obtained using a JOEL ECX-300 spectrometer operating at 300 MHz. All spectra were collected at 25 °C and referenced to tetramethyilsilane or residual protium in the NMR solvent (DMF-d7: 8.00).

6.3 Results and Discussion

Using recently developed surfactant-free heterogeneous radical polymerization (SFHRP), we developed one-step synthesis of ultra-high molecular weight block
copolymers by copolymerizing water-soluble monomer $M_1$ and hydrophobic monomer $M_2$ in an aqueous phase, while maintaining low concentration levels of radicals by slow addition of water-soluble initiators to facilitate the kinetic control. Figure 6-1-A depicts a diagram of the directional growth of amphiphilic block copolymer nanowires during SFHRP, which involves the formation of $p(M_1)_n \cdot$ blocks in an aqueous phase initiated by hydrophilic radicals (Figure 6-1-A-1), followed by phase-separation of $p(M_1)_n-M_2\cdot$ radical end, diffusion and successive copolymerization of $M_2$ to form $-pM_2$ blocks (Figure 6-1-A-2). The resulting amphiphilic $pM_1$-block-$pM_2$ copolymers self-assemble to form polymeric micelles with a hydrophobic core and a hydrophilic corona (Figure 6-1-A-3). The formation of polymeric micelles requires the presence of attractive hydrophobic interactions that facilitate aggregation of hydrophobic $pM_2$ blocks as well as repulsive forces between the hydrophilic $pM_1$ blocks stabilizing the micelle. The morphology development of the polymeric micelles can be driven by the repulsive interactions of the $pM_1$ blocks in a localized region and chain arrangements of the $pM_2$ blocks in the core,\textsuperscript{[32]} which may facilitate the kinetic control over anisotropic growth of the polymeric micelles.
In order to obtain block polymer nanowires during SFHRP synthesis, it is preferable to have distinct solubility differences in aqueous phase between $M_1$ and $M_2$ (facilitating synthesis of $pM_1$-$b$-$pM_2$ and micelle formation with $pM_1$ corona and $pM_2$ core), partially charged hydrophilic $pM_1$ blocks (increasing the repulsive forces in the corona), and hydrophobic $pM_2$ blocks with $T_g > T_{\text{reaction}}$ (75 °C) (maintaining the kinetically controlled morphologies). With this in mind, we copolymerized water-soluble
2-(N,N-dimethylamino) ethyl methacrylate (DMAEMA, concentration in water 0.51 M) and hydrophobic styrene (St, water solubility 0.5 g/L, 0.48 x 10^{-2} M) using a water-soluble initiator 2,2’-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (AIPD). As illustrated in Figure 6-1-B, amphiphilic pDMAEMA-block-pSt block copolymers with molecular weight of ~ 0.91 x 10^6 g/mol and dispersity of 1.27 were obtained, and the block copolymer structure was confirmed by DSC, \(^1\)H NMR analysis and solubility measurements. During the in-situ formation of pDMAEMA-block-pSt micelles, chain extension of the continuously formed p(DMAEMA)\(_n\)-St· and the chain arrangements of the resulting pSt blocks in the micelles can be controlled by monomer feed ratio and initiator feed rate. Therefore, as DMAEMA and St with different monomer ratios are copolymerized in SFHRP, block copolymer micelles with spherical, worm-like and hollow morphologies can be obtained.
Figure 6-2. TEM images of p(DMAEMA-block-St) micelles obtained from one-step SFHRP of DMAEMA (0.51 M) and St with various molar ratios: 1:0.1 (A), 1: 0.16 (B), 1: 0.2 (C), 1: 0.33 (D), 1:0.5 (E), and 1:1 (F). Inset scale bar: 100 nm.

Figure 6-2, A-F illustrates the TEM images of pDMAEMA-block-pSt copolymer morphologies produced by the following DMAEMA/St ratios: 1: 0.1 (A), 1: 0.16 (B), 1: 0.2 (C), 1: 0.33 (D) 1:0.5 (E), and 1:1 (F), while keeping DMAEMA feed constant at 0.51 M. As shown, when DMAEMA and St in the molar ratio of 1:0.1 are copolymerized, spherical polymeric micelles with diameter of ~ 80 nm are formed (Figure 6-2-A). Reduction of the hydrophobic St feed ratio to < 0.07 leads to almost transparent solution, indicating the lack of significant micelle formation due to low St content in the feed. As the St feed ratio increases to 0.16, as shown in Figure 6-2-B, short length (~ 1 µm) nanowires with blurred boundaries are formed. This is attributed to the hydrophilic corona consisting of long pDMAEMA blocks. As shown in Figure 6-2-C, when the
DMAEMA/St feed ratio is 1: 0.2, linear nanowires with a diameter of ~ 68 nm and the length from a few to tens of microns are produced. When higher feed amount of St is utilized (DMAEMA:St = 1: 0.33), as shown in Figure 6-2-D, copolymerization results in branched nanowires (diameter ~ 68 nm) interconnected by lamellar structures, resulted from one and two dimensional growth. Further increase of the St feed amount leads to the formation of a mixture of nanowire, lamellar micelles and vesicles (Figure 6-2-E), and hollow nanoparticles (Figure 6-2-F).

In view of these experimental data, it is quite apparent that the formation of nanowires is attributed to desirable DMAEMA/St feed ratio. To elucidate the origin of the nanowire formation, we took aliquots during the SFHRP of DMAEMA:St (molar feed ratio, 1: 0.2) and examined the resulting polymeric micelle morphologies at a given time of the reaction. Figure 6-3, A-F shows TEM images of the block copolymer micelles at different reaction times: 2.5, 5, 10, 15, 20, 30 min, respectively. As the initiator solution was dropwise added into the reactor, the polymerization mixture turned bluish within 2 min, indicating that the formation of phase-separated polymeric micelles. As shown in Figure 6-3-A, the block copolymers assembled into spherical polymeric micelles with diameter of ~ 85 nm at 2.5 min. The polymerization mixture gradually turned to a white milky solution at ~ 5 min and the TEM image in Figure 6-3-B shows that the diameter of the polymeric micelles increased to ~ 100 nm, and at the same time 70% of these micelles had a “worm-like tail” with diameter of ~ 30 nm and length of 100 – 500 nm. As polymerization proceeds, the diameter of the worm-like tail increased to ~ 43 nm (10 min), 56 nm (15 min), 68 nm (20 min) and maintained at ~ 68 nm during
further polymerization, whereas the length of the tail kept increasing from a few to tens and hundreds of microns. It should be noted that polymerization after 30 min may result in the formation of undesired spherical micelles due to secondary nucleation of newly formed micelles with shorter pDMAEMA blocks resulted from lower DMAEMA concentration in water (Appendix, Figure E-2).

Figure 6-3. TEM images of p(DMAEMA-block-St) nanowires obtained from one-step emulsion synthesis of DMAEMA/St (molar ratio 1: 0.2) as a function of time: 2.5 (A), 5 (B), 10(C), 15 (D), 20 (E), 30 (F) min, respectively.

From these nanowire development data, it can be seen that the nanowire formation is due to one dimensional growth of the initially spherical micelles. Due to the lack of deformability of the pSt blocks ($T_g \sim 100 \, ^\circ\text{C}$) at reaction temperature (75 $^\circ\text{C}$), the formation of polymer nanowires may not be attributed to the thermodynamically driven
self-assembly of the amphiphilic block copolymers. In order to verify this, the pDMAEMA-b-pSt copolymers were collected by centrifugation of the nanowire dispersion (shown in Figure 6-4-A), followed by purification. Such block copolymers were dissolved in DMF (1 wt %) and stirred at 500 rpm, and deionized (DI) water were dropwise added into the solution at a rate of 0.5 mL/h to facilitate the self-assembly of the block copolymers in a thermodynamically controlled manner.[32] As a result, spherical micelles with diameter of ~ 73 nm as shown in Figure 6-4-A’ were obtained, indicating that spherical micelles are the most favorable morphologies of the block copolymers synthesized during SFHRP and that the nanowire formation is a kinetically controlled process. It should be also noted that the diameter of the spherical micelles is similar to the diameter of the nanowires (~ 68 nm), which means that the pSt blocks in the hydrophobic core of the nanowire adopted favorable arrangements (along the cross-sections) and that isotropic growth of the micelles (diameter may increase to > 73 nm) is unfavorable during SFHRP.
Figure 6-4. TEM images of pDMAEMA-block-pSt micelles obtained from one-step SFHRP of DMAEMA (0.51 M) and St with various molar ratios: 1: 0.2 (a), 1: 0.33 (b), 1:0.5 (c), and the corresponding thermodynamically self-assembled micelles from the pure pDMAEMA-block-pSt through solvent displacement method (a’-c’).

Based on these experimental results, the following mechanism for the in-situ formation of block copolymer nanowires is proposed. At the initial stages of SFHRP, pDMAEMA-b-St is synthesized by sequential copolymerization of DMAEMA and St. The polymerization leads to the assembly of amphiphilic block copolymers into phase-separated spherical polymeric micelles, whereby the core consists of hydrophobic pSt blocks and the corona consists of solvated pDMAEMA blocks (Figure 6-5, A and B). At the same time, hydrophobic monomers St diffuse into the phase-separated polymeric micelles to facilitate the chain extension of the amphiphilic polymeric radicals. As SFHRP synthesis continues, more pDMAEMA-b-pSt copolymers are formed in the micelles, resulting in the growth of the spherical micelles. However, the diffusion of newly formed pDMAEMA-St into the spherical micelles may lead to significant high density and repulsive forces of the pDMAEMA blocks in the localized region. Consequently, the chain extension in the localized region may lead to formation of a protuberance (Figure 6-5-C), and as a result, the localized high repulsive forces in the
corona will be relieved. The continuous formation and diffusion of p(DMAEMA)$_n$-St• and the sequential chain extension in the protuberance facilitated the directional growth to form a “tail” (Figure 6-5-D). During this process, the pSt blocks can also remain favorable arrangements along the cross-sections of the tail. As polymerization proceeds, block copolymer nanowires with high aspect ratios can be obtained (Figure 6-5-E).

![Figure 6-5. Schematic representation of the block copolymer nanowire formation.](image)

### 6.4 Conclusion

In summary, amphiphilic block copolymer nanowires were synthesized by one-step SFHRP. This is attributed to the localized chain extension of newly formed polymeric radicals and directional growth of the polymeric micelles, driven by repulsive forces between pDMAEMA blocks in the localized regions and chain arrangements of the hydrophobic pSt blocks in the core.
6.5 References


CONCLUDING REMARKS AND OUTLOOK

In this dissertation, the control of particle and copolymer morphologies by emulsion polymerization were developed. In Chapter I, the recent developments of stimuli-responsive anisotropic nanoparticles capable of asymmetrically changing size, shape, color and other physical and/or chemical properties in response of external stimuli were reviewed. Chapter II demonstrated the synthesis of stimuli-responsive triphasic Janus nanoparticles by seeded emulsion polymerization. Each particle has a fluorinated hemisphere, an acrylic hemispherical core and a responsive hemispherical shell. Upon temperature and pH changes, the Janus nanoparticles are able to reversibly change size and shape, and thus facilitating the interfacial property changes. Such Janus particles may have potential applications of solid surfactants and oil recovery materials. In Chapter III, the synthesis of gibbous nanoparticles with controlled morphologies and surface topographies by surfactant-free seeded emulsion polymerization was developed. Furthermore, pH responsive gibbous nanoparticles with shape-tunable bulges were synthesized and their properties were investigated. Chapter IV describes newly developed synthesis of shape-matching gibbous and inverse gibbous nanoparticles using seeded emulsion polymerization. The mechanism of forming completely opposite topographies using the same procedure was investigated and revealed that solubility parameters, polymer miscibility and chain rigidity of the copolymers in each phase are critical in this synthesis.

In the second part, Chapter V demonstrated for the first time one-step synthesis of amphiphilic block copolymers with ultrahigh molecular weight. This kinetically
controlled process is facilitated by initiator starvation conditions and phase-separation between the hydrophilic and hydrophobic components in aqueous environments. Such block copolymers were self-assembled in toluene to form thermochromic inverse polymeric micelles. Chapter VI investigated the in-situ growth of block copolymer nanowires during the surfactant-free emulsion polymerization. The localized chain extension of polymeric radicals and the favorable chain arrangement of the hydrophobic blocks facilitated the one-dimensional growth of the initially spherical micelles to form nanowires. As a result, block copolymer nanowires consisting of hydrophilic block corona and hydrophobic block core were produced.

Although emulsion polymerization has been known for many decades, many aspects of this complex system still remain unknown and debatable. There are many undiscovered synthetic paths which may open new scientific opportunities and practical applications. Thus, continuous efforts in elucidating mechanistic aspects of emulsion polymerization may lead to new discoveries. While the development of controllable and rationally designed nanoparticles continues to be of scientific interests and technological needs, the precise control of nano-object morphologies still remains challenging due to the small size and inherent dispersity of colloidal nanoparticles. Specifically, during fabrication of anisotropic colloidal particles, the phase-separation and interfacial surface tension between each phase may impact final morphologies. The challenge is to thermodynamically and kinetically control physical processes and chemical reactions that lead to specific heterogeneities and anisotropies. Furthermore, understanding long-term
stability of colloidal nano-objects under various solvent, temperature, pH, light exposure, shear rate conditions, are also critical.

Stimuli-responsive polymer nano-objects can be used in a variety of applications, ranging from responsive surfaces and interfaces utilized in flexible displays, or coatings capable of changing color and properties in response to the environments, artificial tissues, biosensors and other biomedical applications. Incorporation of multiple responsive components into single nano-object may also offer unique properties, facilitating multi-dimensional control, leading to the development of new materials for advanced composite applications. The use of multi-responsive components incorporated into different parts of anisotropic nanoobjects will lead to synergistic responsive behaviors.

Another opportunity is to produce anisotropic nanoparticles at an industrial scale. Since most of the synthetic strategies require elaborate synthesis and purification procedure, and time-consuming assembly process, one-step colloidal synthesis will overcome several hurdles of conventional solvent displacement method for self-assembly of block copolymers synthesized by CRPs. In addition, polymerization-induced self-assembly through in-situ chain extension by CRPs is also a promising concept for facile and efficient fabrication of block copolymer nano-objects at high concentration levels. In this context, less expensive reagents and less time-consuming procedures should be investigated. Therefore, surfactant-free heterogeneous radical polymerization is one of the options which is worth exploring and may lead to well-defined nano-objects with large scale and low cost synthesis capability.
APPENDICES
Appendix A

SUPPORTING INFORMATION FOR CHAPTER II

1. Determination of surface free energy through contact angle measurements:

$$W_A = \gamma_{lv} (1 + \cos \theta) = 2\left[ (\gamma^p_{lv} * \gamma^p_{sv})^\frac{1}{2} + (\gamma^d_{lv} * \gamma^d_{sv})^\frac{1}{2}\right]$$

$$\gamma_s = \gamma^d_s + \gamma^p_s$$

where $\gamma_{lv}$ and $\gamma_{sv}$ are liquid-vapor and solid-vapor interfacial tensions, $\theta$ is the contact angle. $\gamma^p_{sv}$ and $\gamma^d_{sv}$ are polar and dispersive contributions to the surface free energies of the copolymer films. For water, $\gamma_{lv} = 72.8$ mN/m, $\gamma^p_{lv} = 21.8$ mN/m, $\gamma^d_{lv} = 51.0$ mN/m; for hexadecane, $\gamma_{lv} = 27.5$ mN/m, $\gamma^p_{lv} = 27.5$ mN/m, $\gamma^d_{lv} = 0$ mN/m.

2. The relationship allowing determination of interfacial tension:

$$\gamma_{12} = \gamma_1 + \gamma_2 - \frac{4\gamma^d_1 \gamma^d_2}{\gamma^d_1 + \gamma^d_2} = \frac{4\gamma^p_1 \gamma^p_2}{\gamma^p_1 + \gamma^p_2}$$

where $\gamma_{12}$ is the interfacial tension, $\gamma_1$ the surface tension, $\gamma^d_1$ and $\gamma^p_1$ the dispersion and polar components of $\gamma_1$, respectively.

3. Table A-1 lists the total energy values for two copolymers A and B placed into an amorphous cell and allowed to equilibrate to reach a thermal equilibrium. The higher the energy values, the greater the degree of phase separation is observed, as illustrated in Figure 2-2 in Chapter II.
Table A-1. The total energy values of equilibrated amorphous cell containing A and B copolymer pairs.

<table>
<thead>
<tr>
<th>Copolymer 1</th>
<th>Copolymer 2</th>
<th>$E_{total}$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(MMA/nBA)</td>
<td>p(MMA/nBA)</td>
<td>5035</td>
</tr>
<tr>
<td>p(MMA/nBA)</td>
<td>p(PFS/nBA)</td>
<td>9164</td>
</tr>
<tr>
<td>p(MMA/nBA)</td>
<td>p(DMAEMA/nBA)</td>
<td>5628</td>
</tr>
<tr>
<td>p(PFS/nBA)</td>
<td>p(PFS/nBA)</td>
<td>6012</td>
</tr>
<tr>
<td>p(PFS/nBA)</td>
<td>p(DMAEMA/nBA)</td>
<td>9467</td>
</tr>
<tr>
<td>p(DMAEMA/nBA)</td>
<td>p(DMAEMA/nBA)</td>
<td>4931</td>
</tr>
</tbody>
</table>

4. The Janus balance (JB) (hydrophilic-to-hydrophobic surface area ratios) was determined from TEM images in the following manner. Assuming a spherical shape of the JNPs, the surface area ratio between non-fluorinated and fluorinated phases is equal to the height of each phase, as depicted in Figure A-1. Blue and red lines represent the height of the non-fluorinated and fluorinated phases and by ratioing the length of blue and red lines, the JB was estimated. The listed values represent an average of the approximately one hundred measurements on different JNPs under specific temperature and pH conditions. Table A-2 lists an average standard deviation for measurements conducted at different temperature and pHs.
Figure A-1. Calculation of Janus balance from TEM images of the JNPs.
Table A-2. Janus balance (JB) of JNPs as a function of temperature and pH.

<table>
<thead>
<tr>
<th>JNPs at Temperature/pH conditions</th>
<th>Janus Balance (JB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>at 25 °C, pH 8</td>
<td>3.78 ± 0.46</td>
</tr>
<tr>
<td>at 35 °C, pH 8</td>
<td>2.07 ± 0.32</td>
</tr>
<tr>
<td>at 38 °C, pH 8</td>
<td>1.60 ± 0.25</td>
</tr>
<tr>
<td>at 40 °C, pH 8</td>
<td>0.98 ± 0.34</td>
</tr>
<tr>
<td>at 45 °C, pH 8</td>
<td>0.72 ± 0.37</td>
</tr>
<tr>
<td>at 25 °C, pH 4</td>
<td>4.52 ± 0.28</td>
</tr>
<tr>
<td>at 25 °C, pH 6</td>
<td>4.24 ± 0.29</td>
</tr>
<tr>
<td>at 25 °C, pH 10</td>
<td>3.42 ± 0.20</td>
</tr>
</tbody>
</table>

5. JNP size plotted as a function of temperature and pH.

Figure A-2. Size of p(MMA/nBA-PFS/nBA-DMAEMA/nBA) JNPs as a function of temperature and pH.
From the particle size measured by dynamic light scattering, it can be seen that the particle size increased from 145 to 177 nm when pH increase from 10 to 2. By assuming that the shape of p(PFS/nBA) does not change upon pH, it can be estimated that the Janus balance (JB) increased from 3.78 to 4.81. However, the JB values determined from TEM images is changed to 4.52, which is probably due to the shrinkage of the p(DMAEMA/nBA) phase upon evaporation of water during TEM sample preparation.

6. Differential scanning calorimetric (DSC) analysis

Figure A-3. DSC diagram of p(MMA-nBA) (S1), p(MMA-nBA)-p(PFS-nBA) (S2) and p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA) (S3), respectively.
7. FT-IR analysis

Figure A-4. FT-IR spectra of p(MMA-nBA) (S1), p(MMA-nBA)-p(PFS-nBA) (S2) and p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA) (S3), respectively.

In an effort to confirm the chemical makeup of the polymers at different stage, IR analyses were performed. As shown in Figure A-4, all three traces show the characteristic bands at 2958 cm\(^{-1}\) (CH\(_3\) asym str), 2932 cm\(^{-1}\) (CH\(_2\) asym str.), 2874 cm\(^{-1}\) (CH\(_3\) sym str), 1732 cm\(^{-1}\) (C=O str) and 1165 cm\(^{-1}\) (C-O-C str). However, the spectra of both p(MMA/nBA)-p(PFS/nBA) sample and p(MMA/nBA)-p(PFS/nBA)-p(DMAEMA/nBA) sample show 1524 and 1502 cm\(^{-1}\) (Ar C=C str), which confirms the existence of PFS component. Finally, the spectra of S3 polymers show the characteristic bands at 2773 (\(-\)N(CH\(_3\))\(_2\)/N-CH\(_2\)), 1333 and 1300 cm\(^{-1}\) (N-CH\(_3\)), which confirms the existence of DMAEMA component on the three-phase Janus particles.
Figure B-1. Control of nanoparticle morphologies: TEM images of pMMA seed (250 nm) (a) and pMMA-SiO\textsubscript{2} nanoparticles with a shell thickness of 10 (b), 30 (c), 100 nm (d); TEM images a’-d’, a”-d”, and a”’-d”’ represent individual nanoparticles synthesized by swelling and polymerization process using PFS/nBA monomers. TEM images a’-a”'/b’-b”’/c’-c”'/d’-d”’ correspond to the following monomer feed amounts (PFS/nBA, molar ratio: 1.32:1): 72, 144, and 288 mM, respectively. Scale bar 200 nm. (Inset: corresponding representative SEM images, scale bar 100 nm.)
Figure B-2. Comparison of the gibbous particle morphologies by TEM and SEM. (a and b) TEM images of SiO$_2$-pMMA(shell thickness: 30nm)-p(PFS/nBA) particles with PFS/nBA feed of 144, and 288 mM; and (a’ and b’) their corresponding SEM images.

Figure B-3. SEM image of raspberry-like nanoparticles (a) shown in Figure 3-1-c” and corresponding EDX dark field mapping of the following elements: C (b), F (c), Si (d), and O (e).
Figure B-4. Particle size vs reaction time during swelling and polymerization of 288 mM PFS/nBA (2:1) in the existence of pMMA seed particles. One droplet of the reaction emulsion was withdrawn and immediately dispersed into 5 mL cold deionized water (~ 0 °C) in order to preserve the particles size and morphologies. Particle size was measured for sample taken at 0, 1, 2, 4, 6, 8, 10, 30, 60, 120 min.

Figure B-5. TEM images of core-shell nanoparticles by swelling and polymerization of 144 mM PFS/nBA (2:1 wt/wt) in the existence of SiO$_2$-p(MMA/nBA) seeds (shell thickness ~ 60 nm) with glass transition temperature ($T_g$) at approximately 50 °C (a), 75 °C (b), 90 °C (c) and 105 °C (d).
Figure B-6. DSC curves of p(MMA/nBA) or p(MMA/MAA) seed particles with various $T_g$s.

Figure B-7. DSC curves of the gibbous nanoparticles obtained by copolymerization of PFS/nBA with weight ratios of 1:1 (a), 1.5:1 (b), 11:1 (c), and 1:0 (d), and of PFS/MMA with weight ratio of 10:1 (e) and PFS/MAA weight ratio of 10:1 (f) in the presence of pMMA seeds (particle size ~ 250 nm). The copolymer shells have estimated $T_g$ of -5, 25, 60, 80, 82, 102 °C, respectively.
Figure B-8. Zeta potential and particle size of the p(MMA-PFS/MAA) gellous particles at various pH.

Table B-1. Static contact angle measurement data and surface energy results of the copolymer films.

<table>
<thead>
<tr>
<th>Copolymers</th>
<th>Static Contact Angle</th>
<th>(\gamma_{SV} (\text{mN/m}))</th>
<th>(\gamma_{SV} (\text{mN/m}))</th>
<th>(\gamma (\text{mN/m}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(MMA)</td>
<td>70.5(^\circ)</td>
<td>0(^\circ)</td>
<td>27.5</td>
<td>11.4</td>
</tr>
<tr>
<td>p(PFS/nBA)</td>
<td>98.6(^\circ)</td>
<td>43.1(^\circ)</td>
<td>20.6</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Surface tension difference \(\gamma_{p(PFS/nBA)-H_2O} = 72.8 - 22.5 = 50.3 \text{ mN/m}\)

\(\gamma_{pMMA-H_2O} = 72.8 - 38.9 = 33.9 \text{ mN/m}\)

Table B-2. Composition, conversion, particle size and \(T_g\) of p(MMA/nBA) and p(MMA/MAA) seed particles.

<table>
<thead>
<tr>
<th>Sample</th>
<th>MMA [mmol]</th>
<th>nBA [mmol]</th>
<th>MAA [mmol]</th>
<th>Conversion [%]</th>
<th>Particle Size [nm]</th>
<th>(T_g) [(^\circ)C]</th>
</tr>
</thead>
<tbody>
<tr>
<td>pMMA seed</td>
<td>30.0</td>
<td>-</td>
<td>-</td>
<td>97.5</td>
<td>250</td>
<td>105</td>
</tr>
<tr>
<td>Seed for Figure 3-3-a</td>
<td>24.6</td>
<td>4.2</td>
<td>-</td>
<td>96.4</td>
<td>245</td>
<td>50</td>
</tr>
<tr>
<td>Seed for Figure 3-3-b</td>
<td>27</td>
<td>2.3</td>
<td>-</td>
<td>96.5</td>
<td>248</td>
<td>75</td>
</tr>
<tr>
<td>Seed for Figure 3-3-c</td>
<td>28.8</td>
<td>9.4</td>
<td>-</td>
<td>97.3</td>
<td>251</td>
<td>90</td>
</tr>
<tr>
<td>Seed for Figure 3-3-e</td>
<td>27</td>
<td>-</td>
<td>3.5</td>
<td>97.3</td>
<td>252</td>
<td>114</td>
</tr>
<tr>
<td>Seed for Figure 3-3-f</td>
<td>24</td>
<td>-</td>
<td>7.0</td>
<td>97.5</td>
<td>254</td>
<td>117</td>
</tr>
</tbody>
</table>
Table B-3. Monomer and initiator feed amounts, shell thickness and conversions of SiO$_2$–pMMA seed particles.

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 3-1-b</td>
<td>5</td>
<td>0.28</td>
<td>20</td>
<td>0.11</td>
<td>~ 10</td>
<td>95.4</td>
</tr>
<tr>
<td>Figure 3-1-c</td>
<td>5</td>
<td>0.28</td>
<td>70</td>
<td>0.35</td>
<td>~ 30</td>
<td>94.9</td>
</tr>
<tr>
<td>Figure 3-1-d</td>
<td>5</td>
<td>0.28</td>
<td>120</td>
<td>0.60</td>
<td>~ 100</td>
<td>93.6</td>
</tr>
</tbody>
</table>

Table B-4. Monomer compositions, KPS amounts, and conversions of gibbous particles synthesized using seeded emulsion polymerization.

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 3-1(a’-d’), Figure 3-3(a-f)</td>
<td>0.21</td>
<td>0.16</td>
<td>-</td>
<td>-</td>
<td>0.01</td>
<td>95.5 – 96.8</td>
</tr>
<tr>
<td>Figure 3-1(a’”-d””), Figure 3-2</td>
<td>0.82</td>
<td>0.62</td>
<td>-</td>
<td>-</td>
<td>0.04</td>
<td>95.0 – 96.8</td>
</tr>
<tr>
<td>Figure 3-4-a</td>
<td>0.31</td>
<td>0.47</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
<td>96.4</td>
</tr>
<tr>
<td>Figure 3-4-b</td>
<td>0.37</td>
<td>0.37</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
<td>97.1</td>
</tr>
<tr>
<td>Figure 3-4-c</td>
<td>0.57</td>
<td>0.08</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
<td>95.8</td>
</tr>
<tr>
<td>Figure 3-4-d</td>
<td>0.62</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
<td>97.1</td>
</tr>
<tr>
<td>Figure 3-4-e</td>
<td>0.57</td>
<td>-</td>
<td>0.10</td>
<td>-</td>
<td>0.02</td>
<td>97.3</td>
</tr>
<tr>
<td>Figure 3-4-f</td>
<td>0.52</td>
<td>-</td>
<td>-</td>
<td>0.23</td>
<td>0.02</td>
<td>96.7</td>
</tr>
</tbody>
</table>
Due to close proximity of the solubility parameters of p(St/nBA) and pMMA seeds, copolymerization of St/nBA monomers on pMMA seed particles results in nanoparticles with smaller bulges. This is illustrated in the TEM images shown in Figure C-1.

Figure C-1. TEM images of pMMA seed particles (a) and pMMA-p(St/nBA) composite nanoparticles synthesized with the following St/nBA)/pMMA (w/w) monomer feed ratios: 0.25:1 (b), 0.5:1 (c), 1:1 (d).
Figure C-2 illustrates that copolymerization of PFS/nBA on pSt seed particles results in phase-separated spherical particles due to the close proximity of solubility parameters of between p(PFS/nBA) and pSt seeds (similar structure).

Figure C-2. TEM images of pSt seed particles (a) and pSt-p(PFS/nBA) composite nanoparticles synthesized with the following PFS/nBA/pSt (w/w) monomer feed ratios: 0.25:1 (b), 0.5:1 (c), 1:1 (d).
Figure C-3 illustrates that copolymerization of HFBA/nBA on pMMA seed particles results in nonspherical core-shell nanoparticles with incomplete and non-symmetrical soft shells due to the close proximity of solubility parameters of between p(HFBA/nBA) and pMMA seeds.

Figure C-3. TEM images of pMMA seed particles (a) and pMMA-p(HFBA/nBA) composite nanoparticles with the following HFBA/nBA/pMMA (w/w) monomer feed ratios: 0.25:1 (b), 0.5:1 (c), 1:1 (d).
Figure C-4 shows the synthesis of inverse-gibbous nanoparticles with variable number and size of dimples on pSt seed particle surface which is accomplished by varying the monomer feed ratio.

Figure C-4. TEM images of pSt-HFBA/nBA nanoparticles with the following HFBA/nBA/pSt (w/w) monomer feed ratios: 0.25:1 (a), 0.5:1 (b), 1:1 (c), 2:1 (d).
Figure C-5 shows that at the initial stages of HFBA/nBA copolymerization, numerous evenly distributed indentations begin to form on a pSt seed. However, as polymerization progresses, the number of indentations decreases with the increase of their size. During this process, the diameter of the particles continuously increases.

Figure C-5. Particle morphologies that develop during swelling and polymerization of HFBA/nBA (molar ratio = 1:1, monomer feed amount: seed = 1:1, w/w) in the presence of pSt nanoparticles as a function of time: 0 (a), 2 (b), 4 (c), 8 (d), 15 (e), and 60 min (f), respectively.
Figure C-6 shows that when HFBA and nBA were copolymerized on SiO$_2$-pSt core-shell seed particles, inorganic-organic inverse-gibbous nanoparticles were obtained and the silica core is not involved in the dimple formation.

Figure C-6. TEM images of SiO$_2$-pSt-HFBA/nBA nanoparticles synthesized with the following nHFBA/nBA)/pSt (w/w) monomer feed ratios: 0.25:1 (a), 0.5:1 (b), 1:1 (c), 2:1 (d). In these experiments SiO$_2$-pSt core-shell particles with the shell thickness of 50 nm were utilized.
Figure C-7 shows the morphology development of SiO$_2$-pSt-p(HFBA/nBA) core-shell inverse-gibbous nanoparticles as a function of reaction time.

Figure C-7. TEM images illustrating morphologies development as a function of time during polymerization of HFBA/nBA nanoparticles (HFBA/nBA molar ratio = 1:1, monomer feed amount/seed = 1:1, w/w) in the presence of SiO$_2$-pSt nanoparticles: 0 (a), 2 (b), 4 (c), 8 (d), 15 (e), and 60 min (f), respectively.

Figure C-8. TEM images of the assemblies of gibbous(-)/inverse-gibbous(+) particles with concentrations of $10^{-6}$ g/mL. Three figures are taken from the same sample with different magnifications.
In contrast to 2D colloidal assemblies shown in Figure 4-3, which showed linear assemblies of nanoparticles, Figure C-9 shows that oppositely charged colloidal nanoparticles without shape curvature matching form random assemblies.

Figure C-9. TEM images of assemblies of 10^7 g/mL spherical pMMA(-)/pSt(+) (a), gibbous(-)/spherical pSt(+) (b), and spherical pMMA(-)/inverse-gibbous(+) (c) nanoparticles.

Table C-1. Estimated solubility parameters of monomers and homopolymers utilized in the studies.[1]

<table>
<thead>
<tr>
<th></th>
<th>ΔE_v (cal/mol)</th>
<th>ΔV (cm^3/mol)</th>
<th>δ(cal^{1/2} cm^{-3/2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>pMMA</td>
<td>8080</td>
<td>89.9</td>
<td>9.48</td>
</tr>
<tr>
<td>pnBA</td>
<td>10965</td>
<td>122.9</td>
<td>9.45</td>
</tr>
<tr>
<td>p(HFBA)</td>
<td>10540</td>
<td>160.7</td>
<td>8.10</td>
</tr>
<tr>
<td>pSt</td>
<td>9630</td>
<td>94.5</td>
<td>10.09</td>
</tr>
<tr>
<td>pPFS</td>
<td>14630</td>
<td>89.5</td>
<td>12.78</td>
</tr>
</tbody>
</table>

\[ \delta = (\Delta E_v / \Delta V)^{1/2} \]

Additional experimental details

Preparation of ‘cationic’ and ‘anionic’ pMMA seed nanoparticles. In a typical synthesis, 90 g deionized water was placed in a flask and heated to 75 °C under protection of N_2 gas and magnetic stirring at 400 rpm. MMA (3 g, 30 mmol) and 5 mL anionic initiator KPS aqueous solution (0.01 g/mL, 37 mM) (or 5 mL cationic initiator AIPD aqueous solution (0.012 g/mL, 37 mM)) were added, and the reaction was allowed
to continue for 5 h (conversion > 99 %). The seed particles were purified by centrifugation at 1500g for 3 h. Upon completion, they were redispersed in 95 mL of deionized water.

Preparation of pMMA-(St/nBA) composite nanoparticles. In a typical synthesis, 5 g pMMA seed particle dispersions were stirred at 600 rpm and St/nBA (molar ratio 1:1) mixture were added. After the monomers completely diffused into the seed particles (over 15 h), the colloidal dispersion was deoxygenated by purging N₂ for 30 min, and KPS aqueous solution (0.007 mmol) was added. The reaction was continued for 1 h at 75 °C. Conversion > 98 %.

Preparation of pMMA-(HFBA/nBA) composite nanoparticles. In a typical synthesis, 5 g pMMA seed particle dispersions were stirred at 600 rpm and HFBA/nBA (molar ratio 1:1) mixture were added. After the monomers completely diffused into the seed particles (over 15 h), the colloidal dispersion was deoxygenated by purging N₂ for 30 min, and KPS aqueous solution (0.007 mmol) was added. The reaction was continued for 1 h at 75 °C. Conversion > 98 %.

Preparation of pSt-(PFS/nBA) composite nanoparticles. In a typical synthesis, 5 g pSt seed particle dispersions were stirred at 600 rpm and PFS/nBA (molar ratio 1:1) mixture were added. After the monomers completely diffused into the seed particles (over 15 h), the colloidal dispersion was deoxygenated by purging N₂ for 30 min, and KPS aqueous solution (0.007 mmol) was added. The reaction was continued for 1 h at 75 °C. Conversion > 98 %.
Preparation of silica particles. The colloidal silica particles were synthesized according to the well-known Stöber method. Ten grams of TEOS (0.048 mol), 200 mL of absolute ethanol (3.43 mol), and 10 mL of ammonium hydroxide (0.09 mol) were introduced into a 500 mL round-bottom flask while being stirred at 350 rpm at room temperature for 24 h. The colloidal dispersion was purified by repeated centrifugation redispersion cycles with deionized water for more than three times. The final SiO\textsubscript{2} particles (particle size ∼95 nm) were collected by centrifugation at 1000g for 3 h (63% yield).

Preparation of SiO\textsubscript{2}-pSt core–shell nanoparticles. The surface of MPS silica particles (95 nm) was modified by MPS to attach a C=C double bond, which facilitates the formation of SiO\textsubscript{2}-pSt core–shell nanoparticles. Sixty milliliters of colloidal silica dispersion (0.5 w/w%) was added into a reaction flask maintained at 75 °C, purged continuously with N\textsubscript{2} gas, and stirred mechanically at 350 rpm. Then 0.6 mL of 1% KOH aqueous solution (0.107 mmol) was introduced into the colloidal dispersion. Thirty minutes later, 0.07 g of MPS (0.28 mmol) was added dropwise into the flask to modify the silica particle surface with methacrylate groups. Monomer St 3.12 g (30 mmol) and 4 mL KPS (0.01 g/mL, 37 mM) aqueous solution were continuously fed into the system over 2 h, and the reaction was continued for 5 h (conversion > 98 %). The seed particles were purified by centrifugation at 1000g for 3 h and redispersed in 65 mL of deionized water.

Preparation of SiO\textsubscript{2}-pSt-p(HFBA/nBA) composite inverse-gibbous nanoparticles. Five gram SiO\textsubscript{2}-pSt seed particle dispersions were stirred at 600 rpm and 0.16 g
HFBA/nBA mixture (molar ratio 1:1) were added. After the monomers completely diffused into the seed particles (over 15 h), the colloidal dispersion was deoxygenated by purging N\(_2\) for 30 min, and KPS aqueous solution (0.007 mmol) was added. The reaction was continued for 1 h at 75 °C (conversion > 98 %).

Reference:

Figure D-1 shows the monomer conversion as a function of time during SFHRP of DMAEMA and nBA (0.025/0.025 mol) when different initiator addition rates are used. As shown, when initiator is added at the rate $> 3.3 \times 10^{-7}$ mol/min, the monomer conversion reaches 60% in 30 min, and > 18 wt % of the resulting polymers are water-soluble, indicating the formation of pDMAEMA homopolymers. When the initiator addition rate is $< 2.58 \times 10^{-7}$ mol/min, the monomer conversion increases continuously as polymerization progresses, resulting in the formation of ultra-high molecular weight amphiphilic block copolymers.

Figure D-1. Overall monomer conversion vs. reaction time during SFHRP synthesis of pDMAEMA-b-pnBA (0.025/0.025 mol) using different initiator addition rates: $3.3 \times 10^{-7}$ (a), $2.58 \times 10^{-7}$ (b), $1.67 \times 10^{-7}$ (c), and $0.83 \times 10^{-7}$ (d) mol/min.

1. Block Copolymer Morphology.
To verify block copolymer morphologies synthesized via SFHRP, solubility tests, DSC measurements and \(^1\)H NMR analysis were performed. All results were compared with statistical copolymers synthesized by solution polymerization in in ethanol as well as homopolymers synthesized in an aqueous phase.

1-a. pDMAEMA-b-nBA block copolymer

Figure 5-2 shows the results of the DSC analysis of p(DMAEMA-stat-nBA), and pDMAEMA-b-pnBA. For p(DMAEMA-stat-nBA) copolymer, one glass transition temperature at \(T_g = -10\) °C (trace a) is observed. In contrast, pDMAEMA-b-pnBA shows two distinct \(T_g\)s at -39 and 46 °C (trace b), indicating the formation of p(nBA) and p(DMAEMA) homopolymer blocks. The physical properties of both copolymers are also distinctly different: While p(DMAEMA-stat-nBA) is soluble in common organic solvents (toluene, THF, chloroform, DMF), pDMAEMA-b-pnBA is only soluble in DMF (Table D-2).

Figure 5-3 (trace A-D) shows \(^1\)H NMR spectra of p-nBA, pDMAEMA, p(DMAEMA-stat-nBA), and pDMAEMA-b-pnBA, respectively. As shown in trace B, the spectra of the \(\alpha\)-methyl protons on pDMAEMA homopolymer exhibits three resonances at 1.27, 1.19 and 1.11 ppm (trace B), which correspond to iso- (mm), hetero- (mr or rm), and syndiotactic (rr) triads. As shown in \(^1\)H NMR spectra of p(DMAEMA-stat-nBA) (trace C), the \(\alpha\)-methyl protons appear in the lower field (1.15, 1.07, and 1.01 ppm, respectively), and ~ 60% of the resonance shifts to lower field and overlays with the \(-\text{CH}_3\) groups on butyl groups of pnBA (based on peak integration). This is attributed to the shielding of \(\alpha\)-methyl protons by \(\alpha\)-protons of nBA units. In contrast, pDMAEMA-b-
pnBA shows distinctly different $^1$H NMR spectroscopic features shown in trace D: $\alpha$-methyl protons resonances correspond to the same ppm region as in pDMAEMA homopolymers, and the only difference is the negligible shift of rr triads to lower field (by 0.03 ppm).

1-b. pDMAEMA-b-tBA block copolymers

Figure D-2 shows the DSC analysis of solution polymerized p(DMAEMA-stat-tBA) (trace a) and pDMAEMA-b-pStBA (trace b). The statistical and block copolymers exhibit one and two $T_g$s, respectively, indicating the formation of statistical and block (or separate homo-) polymers. $^1$H NMR spectra in Figure D-3 show that the chemical shift of the protons on $\alpha$-methyl groups of DMAEMA units ($\delta = 1.1, 1.0, 0.93$ ppm) of p(DMAEMA-stat-tBA) (trace C) shift from their original $\delta = 1.26, 1.20, 1.12$ ppm (trace B) due to the shielding effect by $\alpha$-protons of the neighboring nBA units. In contrast, SFHRP block copolymers (spectra D) do not exhibit the shielding effect, indicating the formation of pDMAEMA and ptBA blocks.

1-c. pDMAEMA-b-pSt block copolymers

The DSC analysis in Figure D-4 shows that p(DMAEMA-stat-St) (trace a) and pDMAEMA-b-pSt (trace b) have one and two $T_g$s respectively, again indicating the formation of statistical and block polymers. $^1$H NMR spectra in Figure D-5 shows that the protons on $\alpha$-methyl groups of DMAEMA units ($\delta = 1.0, 0.8, 0.5$ ppm) of p(DMAEMA-stat-St) (trace A) are shifted to lower ppm values due to the shielding effect of $\alpha$-protons of the neighboring St units. At the same time, the chemical shift of the ortho-protons of benzene rings of St units ($\delta = 6.7$ ppm) is shifted upper field due to the
deshielding effect by α-methyl groups on the neighboring DMAEMA units. These data indicate the formation of pDMAEMA and pSt blocks.

2. Control Experiments.

   In an effort to examine potential formation of separate homopolymers during SFHRP, the following control experiments were conducted.

   2-a. During SFHRP, a milky-white dispersion is formed within initial 3 min of reaction and the dispersion retains its stability throughout. In contrast, when polymerizing DMAEMA under the same conditions, transparent solutions are obtained.

   2-b. As shown in Table D-2, SFHRP block copolymers exhibit limited solubility, whereas the corresponding statistical copolymers as well as each homopolymer are readily soluble in many organic solvents. The solubility behavior of SFHRP copolymers is characteristics of a block copolymer morphology.

   2-c. pDMAEMA-b-pnBA (or pDMAEMA-b-ptBA) block copolymers can self-assemble in toluene to form thermochromic inverse polymeric micelles. In contrast, their statistical counterparts dissolve readily in toluene to form transparent solutions. When pnBA (or ptBA) and pDMAEMA homopolymer mixtures are dissolved in toluene, transparent solutions of pnBA in toluene are obtained while pDMAEMA phase-separates.
Figure D-2. DSC analysis of (a) homogeneous solution polymerized p(DMAEMA-stat-tBA) and (b) SFHRP synthesized pDMAEMA-b-ptBA copolymers.

Figure D-3. $^1$H NMR spectra of (A) p-tBA, (B) p-DMAEMA, (C) solution polymerized p(DMAEMA-stat-tBA) and (D) pDMAEMA-b-ptBA in DMF-d$_7$ (Letters and numbers correspond to chemical shift of specific protons on tBA and DMAEMA units, respectively, and * indicates solvent resonance).
Figure D-4. DSC analysis (a) homogeneous solution polymerized p(DMAEMA-stat-St) and (b) SFHRP synthesized pDMAEMA-b-pSt.
Figure D-5. $^1$H NMR spectra of (A) pSt, (B) p(DMAEMA), (C) homogeneous solution (ethanol) polymerized p(DMAEMA-stat-St) and (D) SFHRP synthesized pDMAEMA-b-pSt in DMF-d$_7$. (Letters and numbers correspond to chemical shift of specific protons on St and DMAEMA units, respectively, and * indicates solvent resonance).
It should be noted that the average particle size is ~250 nm, which corresponds to theoretical molecular weight of fully extended copolymer of ~70,000 g/mol. Thus, it is reasonable to conclude that the actual molecular weight is significantly higher, as measured by FFF with a multi-angle light scattering detector providing absolute values of molecular weight.
3. Thermochromic Behavior of block copolymers.

Figure D-8 illustrates thermochromic behavior of pDMAEMA-b-ptBA and pDMAEMA-b-pSt micellar dispersions. As shown, the pDMAEMA-b-ptBA dispersed in toluene exhibits almost the same color at 10 and 60 °C as pDMAEMA-b-pnBA. However, pDMAEMA-b-pSt block copolymers dispersion exhibits much lighter color. This is attributed to the increased phase-separation between hydrophilic (pDMAEMA) and hydrophobic (pSt) domains, thus leading to less dispersible block copolymers and lower scattering intensities.

As shown in Figure D-9, the cumulative weight fraction of the SFHRP copolymers gradually increases along with the molecular weight of the polymers, indicating the molecular weight distribution is unimodal. The dispersity of pDMAEMA-b-pnBA, pDMAEMA-b-ptBA, and pDMAEMA-b-pSt are 2.55, 4.84, 1.29, respectively. The broad distribution is due to the nature of conventional radical polymerization. The pDMAEMA-b-pSt exhibits lower dispersity is likely due to significantly lower solubility of St in water (0.0029 M), as compared to nBA and tBA (0.015 M), facilitating the control over the SFHRP synthesis. Since SFHRP is one step process, individual block length cannot be determined.
Figure D-9. Cumulative molecular weight distribution of pDMAEMA-b-pnBA (a), pDMAEMA-b-ptBA (b), and pDMAEMA-b-pSt (c).
5. Percentage of Homopolymer Impurity.

The weight percentage of pDMAEMA oligomers for SFHRP synthesis was ~ 0.8 wt%, which was determined by measuring the weight percentage of the polymers that pass through a 0.2 µm filter in the original dispersion. The weight percentage of pnBA, ptBA, and pSt homopolymers in the corresponding SFHRP block copolymer products were ~ 0.3 %, 0.3 % and 0.1 %, respectively. Similarly, these values were obtained by measuring the weight percentage of polymers that dissolve in acetone and pass through a 0.2 µm filter. The block copolymer DMF solutions (2 wt%) were precipitated in acetone (good solvent for the hydrophobic homopolymers), followed by the same filtration process. Also, the theoretical transfer limit of butyl acrylates in emulsion polymerization is < 2%. Here in SFHRP synthesis, the branching effect of the chain transfer reaction is neglected due to not reaching of high conversions.

Table D-1. Synthesis of solution polymerized statistical copolymers: p(DMAEMA-stat-nBA), p(DMAEMA-stat-tBA), and p(DMAEMA-stat-St); and SFHRP block copolymers: pDMAEMA-b-pnBA, pDMAEMA-b-ptBA, and pDMAEMA-b-pSt.

<table>
<thead>
<tr>
<th></th>
<th>Mn (g/mol)</th>
<th>Mw (g/mol)</th>
<th>PDI</th>
<th>Monomer Feed m_{DMAEMA} : n_{nBA}</th>
<th>Final Ratio m_{DMAEMA} : n_{nBA}</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(DMAEMA-stat-nBA)</td>
<td>1.85 x 10^4</td>
<td>3.46 x 10^4</td>
<td>1.87</td>
<td>50 : 50</td>
<td>49 : 51</td>
</tr>
<tr>
<td>p(DMAEMA-stat-tBA)</td>
<td>1.47 x 10^3</td>
<td>3.81 x 10^4</td>
<td>2.59</td>
<td>50 : 50</td>
<td>50 : 50</td>
</tr>
<tr>
<td>p(DMAEMA-stat-St)</td>
<td>2.67 x 10^4</td>
<td>9.23 x 10^4</td>
<td>3.46</td>
<td>50 : 50</td>
<td>52 : 48</td>
</tr>
<tr>
<td>pDMAEMA-b-pnBA</td>
<td>1.98 x 10^6</td>
<td>5.05 x 10^6</td>
<td>2.55</td>
<td>50 : 50</td>
<td>54 : 46</td>
</tr>
<tr>
<td>pDMAEMA-b-ptBA</td>
<td>1.18 x 10^6</td>
<td>5.71 x 10^6</td>
<td>4.84</td>
<td>50 : 50</td>
<td>47 : 53</td>
</tr>
<tr>
<td>pDMAEMA-b-pSt</td>
<td>0.91 x 10^6</td>
<td>1.17 x 10^6</td>
<td>1.29</td>
<td>50 : 50</td>
<td>48 : 52</td>
</tr>
</tbody>
</table>
Table D-2. Solubility of homopolymers, homogeneous solution synthesized statistical copolymers and HRP block polymers.

<table>
<thead>
<tr>
<th></th>
<th>Water</th>
<th>Acetone</th>
<th>Ethanol</th>
<th>Toluene</th>
<th>Chloroform</th>
<th>DMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(nBA)</td>
<td>-</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>p(DMAEMA)</td>
<td>++</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>p(tBA)</td>
<td>-</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>p(St)</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>p(DMAEMA-stat-nBA)</td>
<td>-</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>p(DMAEMA-stat-tBA)</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>p(DMAEMA-stat-St)</td>
<td>-</td>
<td>+++</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>pDMAEMA-b-pnBA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>pDMAEMA-b-pnBA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>pDMAEMA-b-pSt</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

“-” Insoluble; “+” soluble; “++” readily soluble

Table D-3. Solubility of monomers in water at 75 °C.

<table>
<thead>
<tr>
<th></th>
<th>Solubility in water (g/L) at ~75 °C</th>
<th>Molar Concentration (mol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMAEMA</td>
<td>~ 80</td>
<td>0.51</td>
</tr>
<tr>
<td>nBA</td>
<td>~ 2</td>
<td>0.015</td>
</tr>
<tr>
<td>tBA</td>
<td>~ 2</td>
<td>0.015</td>
</tr>
<tr>
<td>St</td>
<td>~ 0.5</td>
<td>0.0048</td>
</tr>
</tbody>
</table>
Figure E-1. TEM images of pDMAEMA-block-pSt micelles obtained from one-step SFHRP with different DMAEMA/St ratios: 1: 0.07 (a), 1: 0.4 (b).
Figure E-2. TEM images of p(DMAEMA-block-St) nanowires obtained from one-step emulsion synthesis of DMAEMA/St (molar ratio 1: 0.2) as a function of time: 40 (A) and 60 (B) min, respectively.
Figure E-3. TEM images of pDMAEMA-block-pSt micelles obtained from one-step SFHRP of DMAEMA (0.51 M) and St with various molar ratios: 1: 0.33 (A), 1:0.5 (B), and the corresponding thermodynamically self-assembled micelles from the pure pDMAEMA-block-pSt through solvent displacement method (A’, B’).
Figure E-4. TEM images of pDMAEMA-block-pSt micelles obtained from one-step SFHRP of DMAEMA (0.51 M) and St (molar ratio: 1: 0.2) as a function of initiator AIPD (feeding rate: 1 mL/h) concentration: 15.5 (A) and 10.2 (B) mM.

Table E-1. Monomer feed ratios and final composition of pDMAEMA-b-pSt polymers shown in Figure 6-2.

<table>
<thead>
<tr>
<th>Feed Ratio DMAEMA:St</th>
<th>Final Composition * DMAEMA:St</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 6-2-a</td>
<td>1 : 0.1</td>
</tr>
<tr>
<td>Figure 6-2-b</td>
<td>1 : 0.16</td>
</tr>
<tr>
<td>Figure 6-2-c</td>
<td>1 : 0.2</td>
</tr>
<tr>
<td>Figure 6-2-d</td>
<td>1 : 0.33</td>
</tr>
<tr>
<td>Figure 6-2-e</td>
<td>1 : 0.5</td>
</tr>
<tr>
<td>Figure 6-2-f</td>
<td>1 : 1</td>
</tr>
</tbody>
</table>

* Determined from $^1$H NMR spectra.