

Synthesis of Dimpled and Submicron-Sized Polymer Particles of Different Morphologies Using Free Micromixer

*AUTHOR NAMES. Yusuke Kawai, Tetsuya Yamamoto**

*AUTHOR ADDRESS. Department of Materials Design Innovation Engineering,
Nagoya University,*

Furo-cho, Chikusa-ku, Nagoya, 464-8603, Japan

AUTHOR EMAIL ADDRESS. yamamoto.tetsuya@material.nagoya-u.ac.jp

*CORRESPONDING AUTHOR FOOTNOTE. Phone: +81-52-789-3378, Fax: +81-52-
789-3271,*

E-mail: yamamoto.tetsuya@material.nagoya-u.ac.jp

Abstract

Dimpled polymer particles are attracting significant attention because of their immense potential in varied applications. **In this report, we propose a new method for synthesizing dimpled and submicron-sized polystyrene (PS) particles using a novel microfluidic device called the free micromixer (FMM).** We could successfully synthesize **dimpled and submicron-sized** particles of various morphologies by controlling the concentration of PS and the temperature of the poor solvent used before mixing within the FMM. Formation of the particles can be attributed to the electrical charge of the polymer used for forming the particles.

Keywords: Dimpled Particles, Polystyrene, Microfluidic Device, Zeta Potential

In recent years, **dimpled** particles have attracted significant attention because of their potential for use in a range of applications such as in drug delivery and preparing inks, cosmetics, battery anodes, and various micro/nanostructures. Several methods have therefore been developed for synthesizing them [1-6], of which the most common ones are the microfluidic method, the water release method, and the swelling method. In the microfluidic method [2-6], an organic solvent that can dissolve one or more different polymer(s) is introduced under a flow of a poor solvent (usually pure water) in the form of solvent droplets. The polymer particles form a solid shell on the surface of **solvent** droplets because of the precipitation caused by the decrease in the polymer(s)' solubility owing to the interdiffusion of water. The shells are then collected as dimpled or hollow particles. In the water release method [7, 8], a monomer is made to grow into a polymer in an aqueous system and water is stored within the particles owing to the hydrophilic groups or three-dimensional network of the polymer. As the polymerization phenomenon progresses, the stored water is released, and the cavities become dimples or hollows. In the swelling method [1, 9-14], pre-synthesized spherical particles are dispersed in the bulk such that they absorb an organic solvent and swell. After swelling, the bulk is gradually cooled or freeze dried, and the swollen particles release the captured solvent, owing to which the cavities turn into dimples or hollows. In all these cases, though, controlling the precipitation or polymerization of the polymer(s) and releasing the contents of the particles is critical to obtaining particles of the desired morphology. **However, these particle sizes synthesized using microfluidic devices were more than one micro meter.**

In this study, we developed a method for synthesizing dimpled and submicron-sized polymer particles of different shapes using a free micromixer (FMM). The FMM is

a microfluidic device in which a microscale flow pass is formed using a metal ball and a spring [15]. **Fig. 1** shows a schematic of the FMM. This device generates a microscale flow based on the force balance between the fluid, which is pushed by a pump, and the spring. Within the FMM, a pipe for introducing the solvent phase is installed just before the microscale flow pass, which causes the oil phase to mix with the water phase, resulting in the formation of solvent droplets. **By controlling the concentration of polystyrene (PS) and the temperature of the poor solvent before mixing within the FMM, we could successfully synthesize dimpled and submicron-sized particles of various morphologies.**

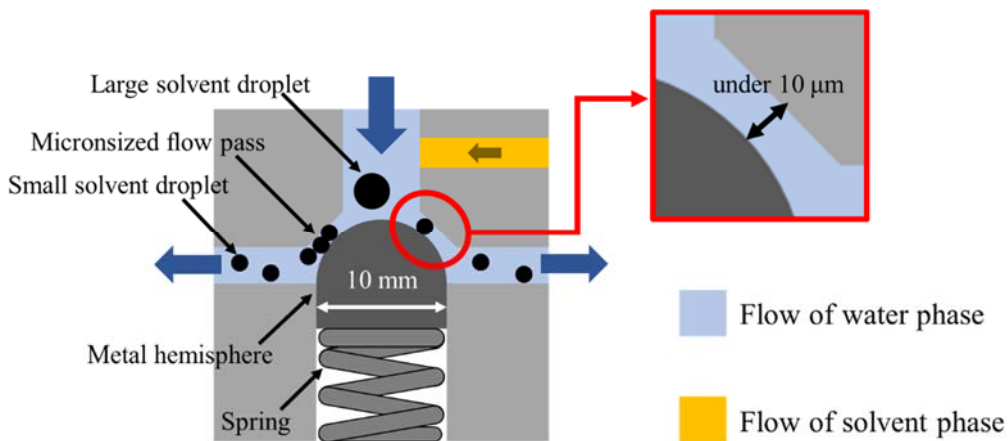


Fig. 1. Schematic illustration of the FMM.

In this study, styrene monomer (St, Tokyo Chemical Industry), methyl methacrylate monomer (MMA, Tokyo Chemical Industry), benzyl methacrylate monomer (BMA, FUJIFILM Wako Pure Chemical), 2,2'-szobis(isobutyronitrile) (AIBN, FUJIFILM Wako Pure Chemical), 2,2'-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride (VA-044, FUJIFILM Wako Pure Chemical), potassium peroxydisulfate (KPS, Sigma Aldrich Co. LLC.), and acetone (FUJIFILM Wako Pure

Chemical) were used as received. The water used was purified using a purification system (Auto Still WG250, Yamato).

First, PS was synthesized by radical polymerization: 1 mL of St and 10 mg of AIBN were added to a reactor, which was heated at 70 °C for 4 h, resulting in the formation of the PS. The reactor was then cooled to room temperature and the reaction was stopped.

Next, the PS was dissolved in acetone to prepare a PS/acetone solution. Here, 30 mL of acetone was added to the reactor, and the synthesized PS was mixed in it. The reactor was left in a refrigerator overnight and the PS that did not dissolve was removed by centrifugation at 5 °C. The concentration of PS dissolved in the acetone was measured by the change in the weight of the PS/acetone solution and the precipitated PS after volatilization of the acetone. The PS/acetone solution was diluted with pure acetone, and the concentration of PS was adjusted to a predetermined level. **The molecular weight M_w of the PS dissolved in the acetone was determined to be 19,300 by gel permeation chromatography (GPC-8020, TOSOH, Japan).**

Then, dimpled and **submicron-sized** particles were synthesized using the FMM. The diluted PS/acetone solution and a poor solvent (50% w/w of water) were mixed in the FMM and the resulting PS/acetone droplets were made to flow in the poor solvent. We used 50 vol% acetone as the poor solvent to descending intrusion of water into the PS/acetone droplets and to stabilize the particle formation process. The experimental conditions used are listed in **Table 1**. The flow rates of the poor solvent and the PS/acetone solution were kept constant, while the concentration of PS in the PS/acetone solution and the temperature of the poor solvent before mixing in the FMM were varied. After mixing in the FMM, the solution mixture turned white immediately.

Finally, the mixture was heated using a hotplate at 90 °C for 6 h, and the acetone in the bulk was volatilized, resulting in a suspension containing the dimpled particles.

Table 1. Experimental conditions for synthesis of dimpled particles

Sample number	1	2	3	4	5	6
PS concentration [mg/mL]	0.1	0.3	0.5	0.1	0.3	0.5
Temperature of poor solvent before mixed [°C]	20	20	20	30	30	30
Flow rate of poor solvent [mL/min]				240		
Flow rate of PS/acetone solution [mL/min]				120		

The synthesized particles were observed using field-emission scanning electron microscopy (FE-SEM, JSM-7500FA, JEOL). The average particle diameter D_p and dimple diameter ratio R_d (= average diameter of dimple (D_d)/average particle diameter (D_p)) were calculated from the FE-SEM images. The zeta potentials of the particles in the bulk were measured using a ZETASIZER Nano-ZS system (MALVERN Co., Ltd.).

By varying the concentration of PS and the temperature of the poor solvent, particles of various morphologies could be synthesized successfully. **Fig. 2** shows FE-SEM images of the synthesized particles, while **Fig. 3** shows the D_p and R_d values of the particles. All the particles of sample 1 did not exhibit large dimples and a lens-like shape. However, when viewed from the top or bottom, they appeared spherical. Considering that the particles of samples 2–6 had **dimpled** morphologies, it can be said that the particles of sample 1 were almost all shaped like lenses. Regardless of the temperature of the poor solvent before mixing in the FMM, an increase in the PS concentration increased the D_p and decreased the R_d . This can be attributed to the release of acetone from the PS particles. If the concentration of PS in the PS/acetone solution decreased, the amount of acetone captured per PS particle increased. This induced a greater degree of shrinkage of the PS particles because it resulted in the release of more acetone, owing to which the R_d

increased. Further, an increase in the temperature of the poor solvent resulted in decreasing D_p and R_d . This was because of the difference in the solubility of PS in the mixture at different temperatures. In general, at higher temperatures, a solvent will dissolve more of a polymer than at lower temperatures. Therefore, when the temperature of the poor solvent was 30 °C, the precipitation rate of the PS was lower, and the particle generation process was more stable than at 20 °C. As a result, both D_d and R_d as well as the standard deviation of D_d decreased.

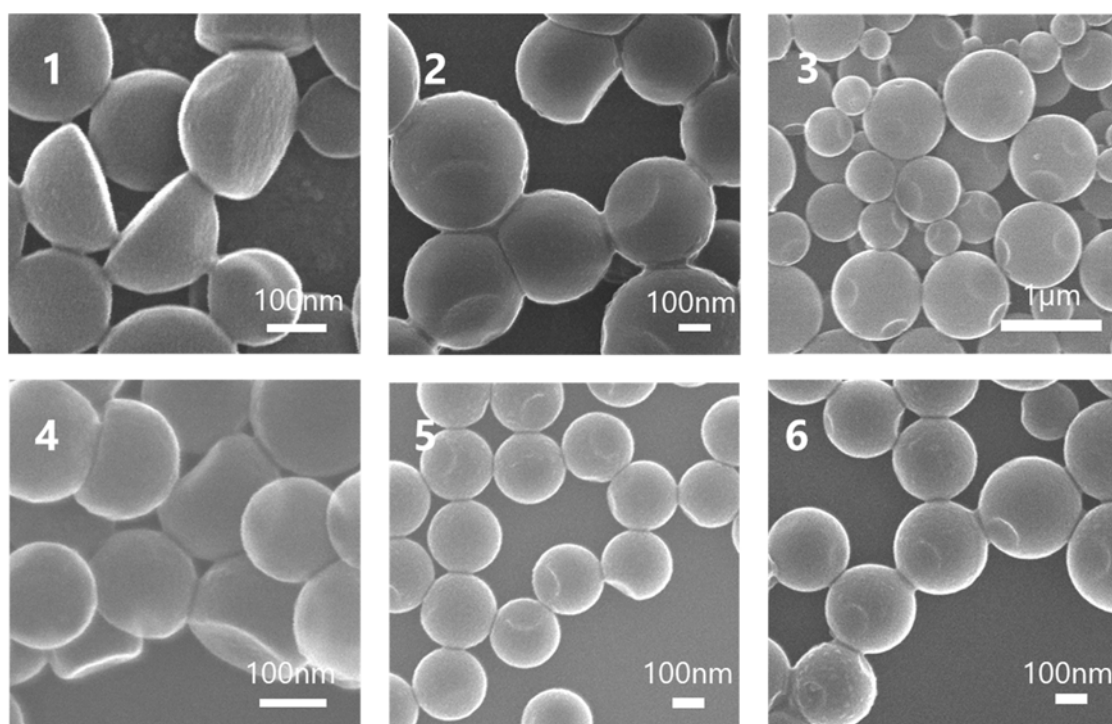


Fig. 2. FE-SEM images of synthesized particles. White numerals in upper-left corner indicate sample numbers. Scale bars represent 100 nm for samples 1, 2, 4, 5, and 6 and 1 μm for sample 3. **SEM images with lower magnifications are shown in Fig. S1.**

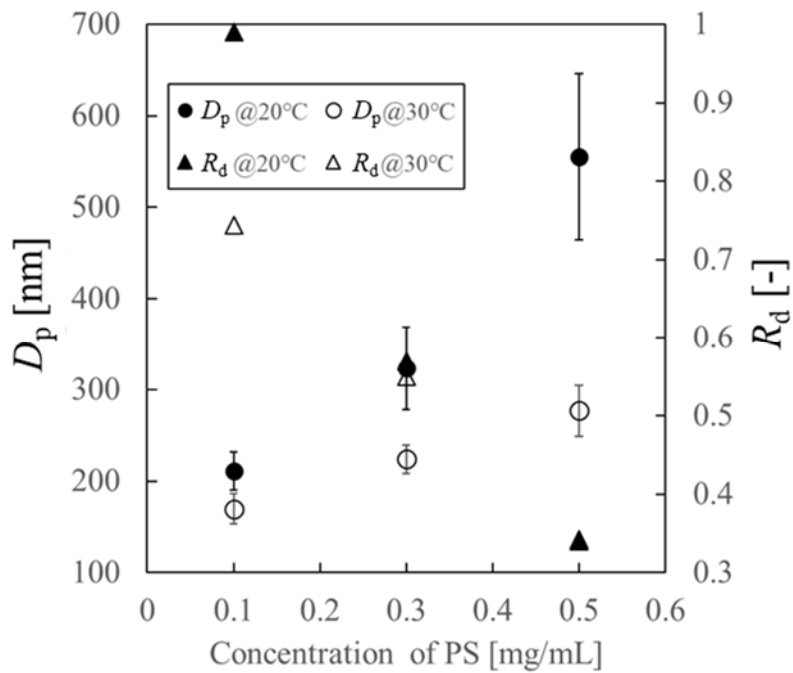


Fig. 3. Effects of concentration of PS and temperature of poor solvent before mixing by FMM on D_p and R_d .

Table 2 shows the zeta potentials of the synthesized particles. Even though the PS particles did not contain any ionic groups and the bulk did not contain any surfactant, the synthesized particles had a negative zeta potential. This was because of the phenyl ring of PS. Recent studies have reported that the π -electron cloud of PS is responsible for the observed negative charge [16-19].

Table 2. Zeta potentials of the particles.

Sample number	1	2	3	4	5	6
Zeta potential [mV]	-50.1	-49.2	-52.5	-46.8	-48.0	-49.3

The charge of the polymer is an important factor in the generation process of the particles. **Table 3** lists the zeta potentials of the particles synthesized from different

monomers and initiators. When the polymer changed from PS to poly(methyl methacrylate) (PMMA), owing to soap-free polymerization using AIBN as an initiator [20], no particle formation was observed. In contrast, when the initiator changed to VA-044 (cationic water-soluble initiator) [21-23] or KPS (anionic water-soluble initiator), particle formation was observed. Further, in these two cases, the zeta potential was positive (VA-044) and negative (KPS), respectively. Moreover, when the polymer changed to poly(benzyl methacrylate) (PBMA), which is an acrylate polymer with a phenyl ring, and was polymerized by AIBN, particle formation was observed. Thus, it can be concluded that the charge of the polymer stabilizes the particle dispersion and inhibits the aggregation of semisolid particles before the evaporation of acetone.

Table 3. Zeta potentials of PMMA or PBMA particles.

Monomer	MMA		BMA	
	AIBN	VA-044	KPS	AIBN
Zeta potential [mV]	—	17.0	-36.6	-31.5

In conclusion, we have developed a new method for the synthesis of dimpled and **submicron-sized** particles of various shapes using an FMM. The D_p and R_d values of the particles can be controlled based on the concentration of PS in the PS/acetone solution and the temperature of the poor solvent. The electrical charge of the polymer used also has a critical effect on the particle formation process.

Acknowledgment

We thank OHKAWARA KAKOHKI CO., LTD. for providing us with the FMM used in this study. Dr. N. Nomura, Associate Professor at the Graduate School of Bioagricultural Sciences, Nagoya University, provided us the M_w data of PS.

References

- [1] S. Hyuk Im, U. Jeong, Y. Xia, Polymer hollow particles with controllable holes in their surfaces, *Nat Mater*, 4 (2005) 671-675.
- [2] M. Mizuno, T. Toyota, M. Konishi, Y. Kageyama, M. Yamada, M. Seki, Formation of monodisperse hierarchical lipid particles utilizing microfluidic droplets in a nonequilibrium state, *Langmuir*, 31 (2015) 2334-2341.
- [3] Z. Nie, S. Xu, M. Seo, P.C. Lewis, E. Kumacheva, Polymer particles with various shapes and morphologies produced in continuous microfluidic reactors, *J Am Chem Soc*, 127 (2005) 8058-8063.
- [4] R. Vasiliauskas, D. Liu, S. Cito, H. Zhang, M.A. Shahbazi, T. Sikanen, L. Mazutis, H.A. Santos, Simple Microfluidic Approach to Fabricate Monodisperse Hollow Microparticles for Multidrug Delivery, *ACS Appl Mater Interfaces*, 7 (2015) 14822-14832.
- [5] T. Watanabe, Y. Kimura, T. Ono, Monodisperse polylactide microcapsules with a single aqueous core prepared via spontaneous emulsification and solvent diffusion, *RSC Advances*, 4 (2014).
- [6] Y. Wang, C. Li, X. He, J. Zhu, Preparation and assembly of concave polymer microparticles, *RSC Advances*, 5 (2015) 36680-36686.
- [7] Y. Hu, G. Azadi, A.M. Ardekani, Microfluidic fabrication of shape-tunable alginate microgels: effect of size and impact velocity, *Carbohydr Polym*, 120 (2015) 38-45.
- [8] T. Yamamoto, S. Kim, Anomalous particle through soap-free emulsion polymerization of styrene using oil-soluble initiator, *J Polym Res*, 24 (2017).
- [9] S.H. Kim, A.D. Hollingsworth, S. Sacanna, S.J. Chang, G. Lee, D.J. Pine, G.R. Yi, Synthesis and assembly of colloidal particles with sticky dimples, *J Am Chem Soc*, 134 (2012) 16115-16118.
- [10] H. Minami, H. Kobayashi, M. Okubo, Preparation of hollow polymer particles with a single hole in the shell by SaPSeP, *Langmuir*, 21 (2005) 5655-5658.
- [11] M. Okubo, H. Kobayashi, C. Huang, E. Miyanaga, T. Suzuki, Water Absorption Behavior of Polystyrene Particles Prepared by Emulsion Polymerization with Nonionic Emulsifiers and Innovative Easy Synthesis of Hollow Particles, *Langmuir*, 33 (2017) 3468-3475.
- [12] C. Huang, H. Kobayashi, M. Moritaka, M. Okubo, Hollow particles are produced by the burying of sulfate end-groups inside particles prepared by emulsion polymerization of styrene with potassium persulfate as initiator in the absence/presence of a nonionic emulsifier, *Polymer Chemistry*, 8 (2017) 6972-6980.
- [13] J. Liang, H. Hu, H. Park, C. Xiao, S. Ding, U. Paik, X.W. Lou, Construction of hybrid bowl-like structures by anchoring NiO nanosheets on flat carbon hollow particles with enhanced lithium storage properties, *Energ Environ Sci*, 8 (2015) 1707-1711.
- [14] S. Hosseinzadeh, Y. Saadat, H. Eslami, F. Afshar-Taromi, A. Hosseinzadeh, M. Rimaz, V. Hooshangi, Effect of second monomer and initiator type, mixing method, and stabilizer content on the shape of the particles produced by seeded dispersion polymerization in the presence of saturated hydrocarbon droplets, *Colloid and Polymer Science*, 290 (2012) 1713-1719.

- [15] T. Tanaka, G. Nemoto, M. Matsushita, K. Higashitani, A Newly-Developed Device for Emulsification and Dispersion of Particles, *Journal of the Society of Powder Technology, Japan*, 54 (2017) 470-472.
- [16] T. Yamamoto, K. Higashitani, Size Control of Polymeric Particle in Soap-Free Emulsion Polymerization, *KONA Powder and Particle Journal*, 35 (2018) 66-79.
- [17] T. Yamamoto, Soap-free emulsion polymerization of aromatic vinyl monomer using AIBN, *Colloid and Polymer Science*, 290 (2012) 1833-1835.
- [18] T. Yamamoto, K. Kawaguchi, Relationship between surface potential and particle size in soap-free emulsion copolymerization of styrene and methyl methacrylate using a water- or oil-soluble initiator, *Colloid Polym Sci*, 294 (2015) 281-284.
- [19] T. Yamamoto, Effect of the Amount of pi Electrons in Aromatic Monomer on the Surface Potential of Polymeric Particles Obtained through Soap-free Emulsion Polymerization Using AIBN, *Chemistry Letters*, 44 (2015) 1555-1556.
- [20] T. Yamamoto, Synthesis of nearly micron-sized particles by soap-free emulsion polymerization of methacrylic monomer using an oil-soluble initiator, *Colloid Polym Sci*, 291 (2013) 2741-2744.
- [21] T. Yamamoto, Y. Takahashi, Design of polymer particles maintaining dispersion stability for the synthesis of hollow silica particles through sol-gel reaction on polymer surfaces, *Colloid Surface A*, 553 (2018) 66-70.
- [22] T. Yamamoto, Y. Takahashi, Synthesis of polystyrene@silica particles through soap-free emulsion polymerization and sol-gel reaction on polymer surfaces, *Adv Powder Technol*, 30 (2019) 214-218.
- [23] T. Yamamoto, R. Furuta, Y. Kawai, Effect of initiator charge on dispersion stability of polymer particles formed by soap-free emulsion polymerization of 4-vinylaniline or 4-vinylpyridine, *Chemistry Letters*, 48 (2019) 208-210.