FLUIGENT

SHORT NOTE: MONODISPERSE POLYMER PARTICLE SYNTHESIS

INTRODUCTION

Polymer particles find numerous applications in diagnostics, drug analysis and delivery, or DNA purification. For such applications, precise control over the particle size distribution is often required for improving repeatability. Size, for instance, impacts the speed at which drugs or chemicals are delivered and released as well as the dosage.

Conventional methods for microparticle production include solvent evaporation, emulsion polymerization, dispersion polymerization, and spray drying[1]. These usually result in microparticles with large polydispersity, poor reproducibility, limited functionality, and less tunable morphology[2]. To overcome these limitations, droplet microfluidic technology has been implemented. This offers greater control over multiple fluid flows at the microscale. It permits the generation of particles or emulsions with higher monodispersity (~ 5% CV) and complex shapes and structures. Many emulsion droplets can be polymerized (thus usually solidified) upon UV irradiation. This last step can be achieved in a microfluidic system, typically through the downstream channel, where droplets are irradiated with UV light.

	Standard methods	Fluigent microfluidic method
Particle size distribution	Up to 50%	-2%
Reproducibility	Low	High
Live particle size control	No	Precise
Continuous (inline) production	No	Yes

In this short note, we present a Fluigent microfluidic solution for polymer microparticle synthesis with high monodispersity (2% CV). The microfluidic system allows for inline particle generation, spacing, and polymerization by UV light.

This application note was made in collaboration with Secoya

MATERIAL & METHODS

MATERIALS

Microfluidics system:

- **Raydrop** (microfluidic droplet generator)
- **Spacing device** (co flow for droplet spacing)
- **LineUp™ Flow EZ 2 bar** (pressure-based flow controller)
- **Flow Unit M (x2) and L (x1)** (flow sensor)
- **UV light**

Reagents:

Continuous phase and liquid for spacing:

- **Distilled water with 1% Tween 20**

Dispersed phase:

- Radcure Generic 7 - A non commercially available resin. However, any type of biocompatible UV polymerized polymer can be used using the same method
- Ethyl acetate 50%
- Photoinitiator TPO 1% (peak absorbance at 395 nm)

Software:

- All-in-one Fluigent software

SYNTHESIS OF POLYMER PARTICLES

Monodisperse polymer particle synthesis is performed in 3 main steps:

- Generation of monodisperse droplet
- Droplet spacing
- Droplet solidification by UV irradiation

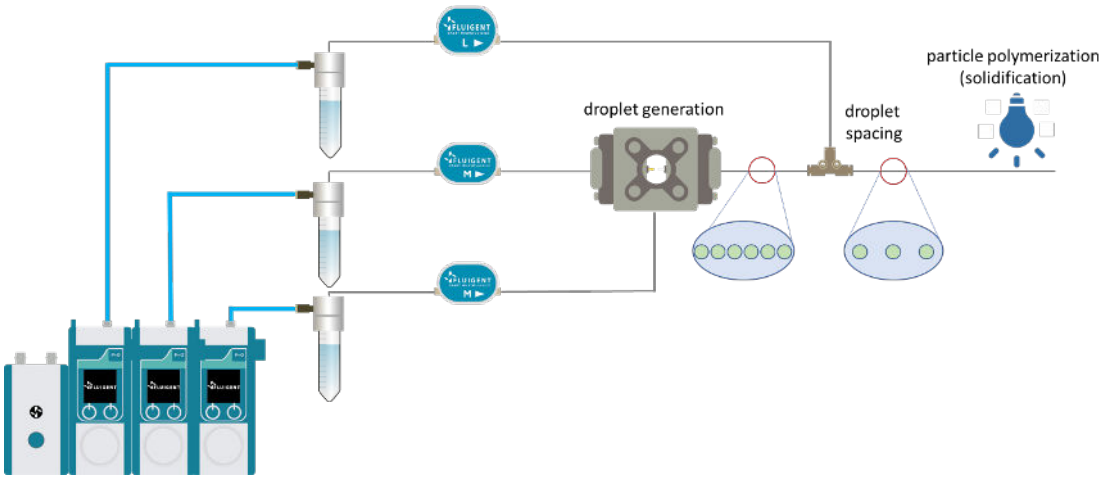

Figure 1: Schematic of the particle polymerization process

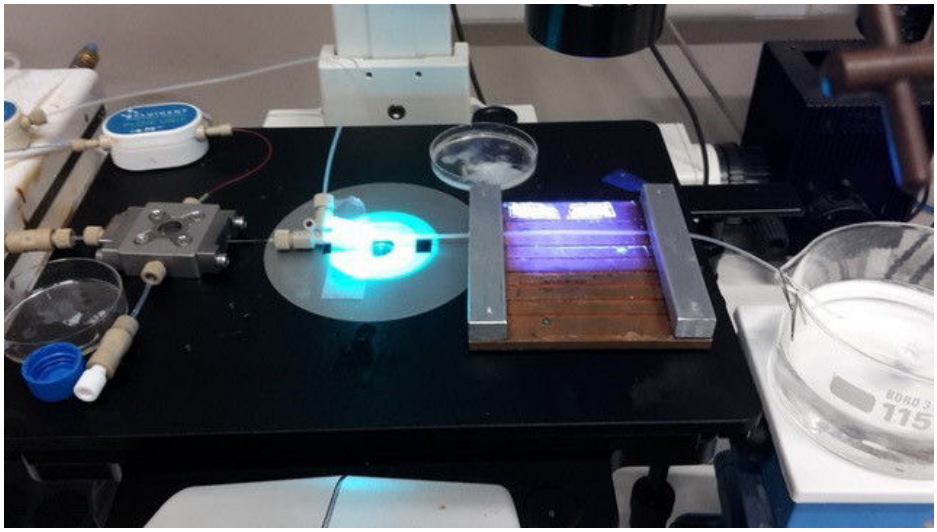

Figure 2: Picture of the particle polymerization process

1. Droplet generation:

For droplet generation, two pressure-based controllers (Flow EZ, 2 bar) are connected to two P-CAP reservoirs containing the polymeric phase (dispersed phase) and distilled water with 1% Tween 20 (continuous phase). The reservoirs are connected to the inlets of the Raydrop using tubing, which passes through Flow Units M for flow rate measurement and control. The dispersed phase is injected through the inner capillary of the Raydrop with a flow rate of 5 µL/min, and the continuous phase is delivered to the Raydrop chamber at a flow rate of 25 µL/min. At the intersection between the two capillaries within the Raydrop, droplets are generated (figure 3). Using the above flow rates, droplets are produced with a frequency of 1 Hz and with an outer diameter of about 100 µm.

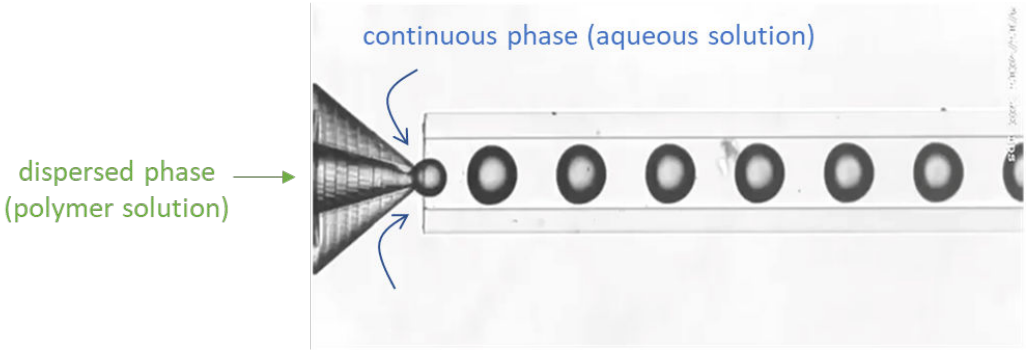

Figure 3: Picture of the particle polymerization process

2. Droplet spacing:

Once generated, droplets exit the Raydrop device with decreased flow velocity (due to the difference between the inner diameter of the downstream channel of the Raydrop and the exit tubing). To avoid clogging during the polymerization by UV, increasing the spacing between droplets is highly recommended. Spacing between droplets can be performed by injecting liquid into the outer tubing in a co-flow manner. To do so, a spacing device (a T-junction) is added to the outlet tubing (figure 1). Distilled water with 1% Tween 20 (same as the continuous phase) is injected into the spacing device with a flow rate of 250 µL/min.

3. Droplet polymerization: particle solidification:

After being spaced, the droplets are exposed to UV light with an irradiance of 95-100 mW /cm², allowing droplet polymerization and subsequent particle solidification.

RESULTS

After particle synthesis, beads are recovered in a petri dish and analyzed under a microscope. Figure 4 shows the polymerized beads after synthesis. We can observe beads with an average diameter of 83 µm, and narrow polydispersity (+/- 1µm). Note that the particle size is smaller than the droplets as they shrink during the polymerization process. We generated particles of 83 µm diameter, but by varying the flow rates of both continuous and disperse phases, it is possible to obtain different particle sizes.

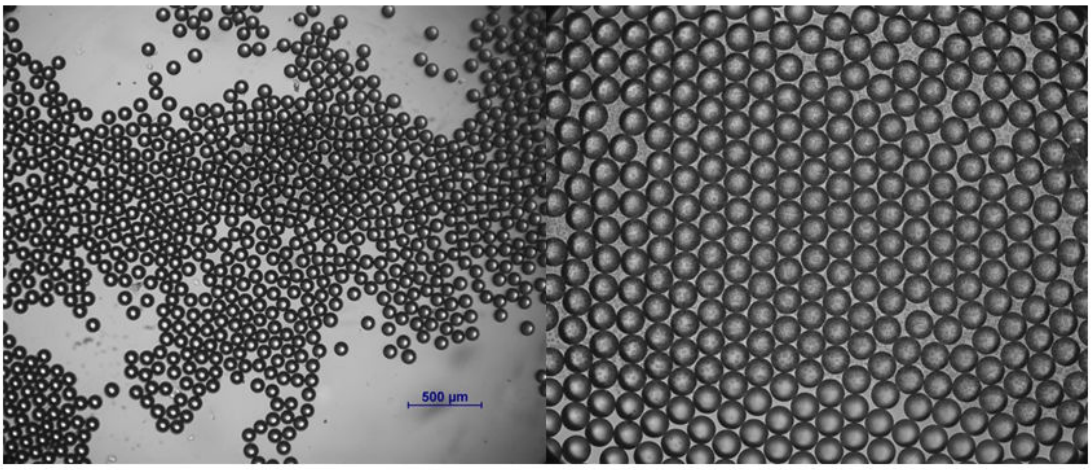

Figure 4: Polymerized beads observed under microscope with magnification (x5 on the left and x10 on the right)

CONCLUSION

Polymer particles find numerous applications in the biomedical field. In this short note, we presented a reproducible solution for polymer particle synthesis that includes inline droplet generation, spacing, and polymerization. The system allows for synthesizing particles with narrow polydispersity, tackling a limitation generally encountered in traditional methods for microparticle production.

REFERENCES

1. Saralidze, K., Koole, L. H. & Knetsch, M. L. W. Polymeric microspheres for medical applications. Materials (*Basel*). 3, 3537–3564 (2010).

2. Li, W. *et al.* Microfluidic fabrication of microparticles for biomedical applications. 47, 5646–5683 (2019).