2025 MERIT / MERIT-WINGS Internship (Domestic) Report

Department of Materials Engineering, Graduate School of Engineering
2nd year doctoral student,
12th MERIT-WINGS
Eriko Yamada

Overview

- Period: April 3rd to July 1st, 2025
- Host: Masanobu Naito,
  Data-Driven Polymer Design Group, Polymer Materials Division, Polymer and Biomaterials Research Center, National Institute for Materials Science (NIMS)
- Research topic:
  High-throuphput phase diagram construction for double thermoresponsive polymers
  assisted by machine-learning-based multiple suggestions of experiments

Background

Temperature-responsive polymers are expected to be applied in the medical field. To realize and apply these, precise control of temperature responsiveness is required, but searching for a structure that satisfies the desired temperature range requires a large number of experiments, which remains a major challenge. On the other hand, it is desirable to prepare dual thermoresponsive polymers that exhibit both behaviors, not just the behavior of the lower critical solution temperature (LCST) and the upper critical solution temperature (UCST). This offers the possibility of designing smart materials that respond only within a certain range of the environment, rather than responding by exceeding the critical value of the LCST or UCST.

Therefore, in addition to establishing a method to freely control temperature responsiveness by chemical structure design, a method is required to predict the chemical composition that gives the desired response temperature, temperature range, and response speed.

A machine learning-based support system for creating temperature-responsive "phase diagrams" has been developed. It has been shown to be advantageous not only in accelerating the search, but also in predicting from the raw material charge ratio and in identifying the composition region with a steep change in phase transition temperature early. By utilizing this, a high-speed search for dual thermoresponsive polymers is realized using experimental instructions by machine learning (Fig.1).

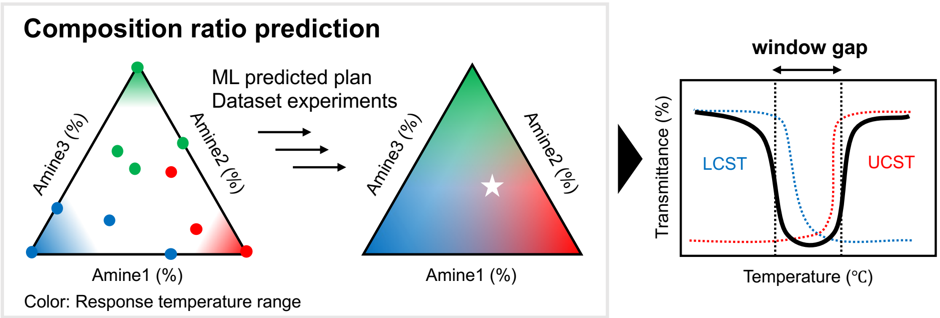

Fig.1 The scheme of this research

Research topic

A thermoresponsive structure was introduced into poly(2-vinyl-4,4-dimethylazlactone) (pVDMA) precursor synthesized by the RAFT method by ring-opening addition reaction with amine to synthesize a thermoresponsive copolymer[1]. By modifying a single precursor, a polymer with a constant molecular weight and different composition can be obtained, eliminating the chain length dependency of temperature responsiveness. In particular, three types of temperature-responsive monomer structures were adopted in this study. As structures that exhibit LCST behavior, acrylamide (R1) with a low phase transition critical temperature (T_c), acrylamide (R_2) with a high Tc, and sulfobetaine group as a structure that exhibits UCST behavior were introduced. In addition, hydrophobic substituted alkyl groups (R_3) were also introduced to adjust the hydrophilicity of the polymer (Fig.2). Polymers with different composition ratios were prepared using a parallel automatic synthesizer to collect temperature response data, and a ternary copolymer temperature-responsive phase diagram was created using machine learning [3] to search for composition ratios that show specific responses.

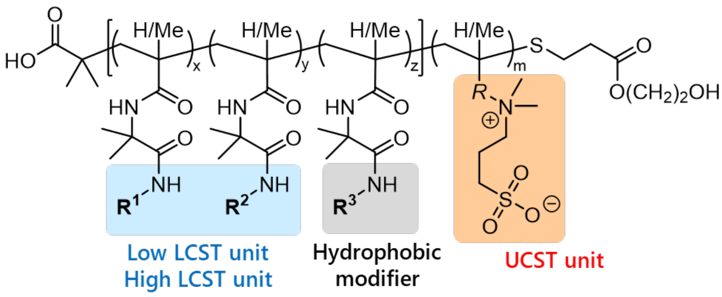

Fig.2 A polymer with a fixed (x+y+z):m was created, and parallel automatic synthesis was performed with different composition ratios (x,y,z).

Results

An aqueous solution of the polymer obtained in the parallel synthesis experiment was prepared, and the transmittance against temperature change was confirmed using UV-vis. The transmittance graph at 500 nm was treated as a turbidity curve to determine the temperature response of the polymer. The temperature responsiveness of the polymers was classified into six types (0: no temperature responsiveness, 1U: UCST type response, 1L: LCST type response, 2A: dual responsiveness with a response center temperature above 37 °C, 2B: dual responsiveness with a response center temperature of 37 °C, 2C: dual responsiveness with a response center temperature below 37 °C). Based on previous research[3], the experimental results were input into the PDC program[4] to calculate the phase diagram, and the seven points with the highest uncertainty scores were adopted as the next experimental points. This cycle was repeated three times, and only 65 points, about 6% of the 1053 experimental points, were investigated to obtain the final phase diagram and discover the region showing dual temperature response. We were able to efficiently discover compositions showing dual temperature response that could not be found at the artificial experimental points in the first cycle.

References

[1] Zhu, Y., *et al*. (2016) *Macromolecules*, 49(2), 672-680.

[2] Hsu, W. H., *et al*. (2019) *RSC advances*, 9(42), 24241-24247.

[3] Matsuoka, N., Nakamura, Y., Tamura, R., Naito, M. "High-throughput phase diagram construction for thermos-responsible polymers assisted by machine-learning-based multiple suggestions of experiments"

[4] Terayama, K., *et al.* (2019) *Phys. Rev. Mater.,* 3(3), 033802.

Review

I carried out research on temperature-responsive polymers, which I had not dealt with before, with the theme of data acquisition and optimization through experimental automation. I was able to spend fulfilling days in a new environment and theme. There were times when I got sick due to the unfamiliar lifestyle, but I think the experience of completing the three months will lead to confidence in the future. It also gave me good material for thinking about my future career. We plan to continue working on this theme with your continued cooperation.

Acknowledgements

I would like to express my sincere gratitude to my host researcher, Professor Masanobu Naito, and to Dr. Yasuyuki Nakamura, who gave me careful guidance. I would also like to express my deep gratitude to everyone in the DDPD group who welcomed me warmly during my internship. Thanks to the support for my accommodation and travel expenses provided by the NIMS internship program, I was able to concentrate on my research and gain valuable experience. Finally, I would like to express my sincere gratitude to my supervisor, Professor Hiroki Ejima, my MERIT-WINGS assistant supervisor, Professor Kyoko Nozaki, the MERIT secretariat, university officials, and everyone in the Ejima Laboratory, who supported me in various ways during this internship.