Title	温度応答性両性電解質高分子の液-液相分離の機序解明および応用
Author(s)	廣瀬, 智香
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Description	Supervisor: 松村 和明, 先端科学技術研究科, 博士

Abstract

Tomoka Hirose

Polyampholytes, a class of polyelectrolytes characterized by the presence of both anionic and cationic groups, demonstrate unique pH and temperature responsiveness through interactions the polymers and their surrounding solutions or among the polymers' own functional groups. Such responsiveness enables polyampholytes to undergo phase transitions, making them invaluable in diverse applications ranging from smart materials to biomedical engineering. Due to its high biocompatibility, it is being actively researched as an intelligent material suitable for biomaterials such as drug delivery systems (DDS). Understanding the mechanisms driving these stimulus-responsive phase transitions is crucial for the optimization of polyampholyte-based materials, as it informs the design and functionalization strategies that tailor their properties to specific applications. Furthermore, in recent years, attention has been focused on the behavior of liquid-liquid phase separation (LLPS) in living organisms such as organelles without membranes. This interest is driven by the role of LLPS in critical life processes, including metabolism, where it facilitates the compartmentalization of biochemical reactions without the need for physical barriers. Polyampholytes are also being studied as model compounds for proteins, offering insights into the molecular dynamics underlying phase separation biology.

In this study, I explore the synthesis and evaluation of ampholyte polymers that exhibit both liquid-liquid phase separation (LLPS) behavior and temperature responsiveness. We confirmed that by introducing a benzene ring into an ampholyte polymer that causes phase separation behavior due to electrostatic interactions, stable phase separation behavior can be induced even in salt solvents. Multi-scale measurements revealed that the benzene rings play a crucial role during droplet formation and growth stages likely due to the π-π interaction, thereby stabilizing LLPS behavior. Leveraging the temperature responsiveness of these polymers, we designed a novel DDS carrier using a composite material with photothermal properties derived from liquid metal. This approach aimed to ensure a stable, self-sufficient supply of trigger stimuli, addressing a significant limitation of current DDS technologies. Cell-based experiments demonstrated the carrier's ability to concentrate drugs effectively, suggesting its potential to minimize side effects associated with drug delivery. These findings not only contribute to our understanding of the fundamental principles governing LLPS in ampholyte polymers but also open new avenues for the development of safer, more efficient drug delivery technologies. Future research will focus on further characterizing the interaction mechanisms at play and exploring the clinical applicability of our novel DDS carrier.

Keywords: Polyampholytes, Liquid-Liquid phase separation, Drug delivery system, Temperature response polymers, Liquid metals, Biomaterials