Form 2

Dissertation Abstract

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Dissertation title	Control of Morphology and Polymorphism of L-Phenylalanine Crystals by Laser Ablation （レーザーアブレーションによるL－フェニルアラニン結晶の形状および多形の制御）		

Abstract

※ *The abstract should be in keeping with the structure of the dissertation (objective, statement of problem, investigation, conclusion) and should convey the substance of the dissertation.*

Laser have been applied to crystallization fields in the recent years. Among them, we have studied the crystallization behavior by utilizing laser ablation. Thus, we tried to use laser ablation for controlling the crystal growth and crystal nucleation, which are involved in crystallization process. Control of crystal morphology is an indispensable step for various applications of crystalline products, so we have developed an innovative approach for spatiotemporal control of crystal growth of proteins and amino acids by locally modifying crystal structure (e.g., formation of screw dislocations) via femtosecond (fs) laser ablation.

In chapter 1, the purpose of this study, together with scientific history and principles of laser ablation and crystallization, are summarized.

In chapter 2, to clarify the appropriate laser condition for controlling the shape of single crystals with minimized damage, we first systematically investigated the dependence of pulse duration on laser ablation and crystal growth of L-phenylalanine (L-Phe). By using a laser system with tunable pulse durations from fs to nanosecond (ns), we found fs laser ablation can offer nanometer-sized, sharp etching of which diameter was smaller than the diffraction limit. By utilizing such nano-processing via fs laser ablation for promoting the growth of a targeted crystal face, we successfully demonstrated the preparation of a bulky crystal of L-Phe, which are difficult to be obtained by conventional crystallization methods. On the other hand, control of crystal polymorph is also a crucial step for various application especially in drug industry, so we also tried to perform the selective nucleation, which is polymorphism, by using laser ablation.

In chapter 3, we present bidirectional polymorphic conversion of L-phenylalanine by focused femtosecond laser irradiation, which include the phenomena of laser ablation and laser trapping. When the femtosecond laser beam is focused at an air/solution interface of its unsaturated solution, the plate-like anhydrous crystals are generated from the laser focus. This crystal nucleation is realized by local concentration increase achieved by femtosecond laser trapping, which is the first demonstration of femtosecond laser trapping-induced crystallization. Furthermore, the whisker-like monohydrate crystals are produced by the followed laser ablation on the surface of the plate-like crystals. On the contrary, when a focused femtosecond laser irradiation is applied to the whisker-like monohydrate crystals, the plate-like crystals are formed, meaning that an unstable phase is successfully produced from a stable phase. The dynamics and mechanism of the bidirectional polymorphic conversion are explained from the viewpoint of the nucleation rate theory considering solution concentration around the surface of laser ablation induced cavitation bubbles. From this result, we deemed that cooperative effect with laser trapping makes laser ablation promising in

controlling of nucleation stage.

In appendix, we additionally demonstrated the pseudopolymorphism control of L-Phe with laser trapping by tuning laser power, polarization, and initial solution concentration. The absolute control of L-Phe pseudopolymorphism was achieved by changing initial solution concentration. In unsaturated solution, laser trapping always produced only one anhydrous crystal at the focus, which can never be produced on spontaneous nucleation at ordinary temperatures and pressures. While, in supersaturated solution, a number of the monohydrate crystals were densely distributed in an area ranging from 500 μm to 1 mm away from the focus. Moreover, in saturated solution, laser power and polarization contributed to the pseudopolymorphism. As laser power was increased, linearly- and circularly-polarized laser irradiation increased the formation probability of the anhydrous and monohydrate crystals, respectively. The dynamics and mechanism of laser trapping-induced pseudopolymorphism of L-Phe are discussed in view of the formation of highly-concentrated domain consisting of the liquid-like clusters and the stability of the clusters in the domain under electromagnetic field of trapping laser.

In summary, we could say that these advanced laser techniques are very prospective in crystallization field. In the stage of crystal growth, femtosecond laser ablation reacts as a trigger for promotion of target crystal face. Thus, desired crystal morphology (size and shape) can be achieved. In the stage of nucleation, laser ablation also reacts as a tool for increasing local solution concentration. Following this, different crystal polymorph is nucleated based on the different supersaturation value. Thus, the desired crystal form can be purely produced with the interference of other forms. Laser can be used not only for laser ablation but also for laser trapping. In the case of laser trapping, nucleation in unsaturation and polymorphism control are its characteristic features. As a result, we hope that these approaches can be widely applied to various crystallization field and promoting the investigation to higher level.