博士論文

Development of Thin-Film Hybrids Comprised of Organic Polymers and Calcium-Based Inorganic Substances

(有機高分子とカルシウム系無機物からなる薄膜状複合体の開発)

Yulai HAN (韓雨来)

Biominerals are organic/inorganic composites synthesized by living organisms. Many composites formed via biomineralization process exhibit elaborate structures that function as structural supports, protection and mineral storage. With the increasing demand on reducing the dependency on fossil-fuel derived materials, biomineralization process has been inspiring researchers for a couple of decades for the development of functional composites under mild conditions. $CaCO_3$ biominerals such as nacre of mollusk shell and coccoliths, and calcium phosphate biominerals in bones and teeth, are considered to be ideal models for material scientists for the rational design and synthesis of functional materials with environmentally benign and eco-friendly processes. Motivated by the functions of biominerals, much efforts have been devoted to a better understanding of the biomineralization mechanism and development of new materials through biomimic strategies.

From the concept of applying biomineralization processes to the design of new functional materials, this research focused on the development of novel polymer/calcium-based inorganic hybrid thin films through the biomimic method. The formation and morphological control of calcium carbonate and calcium phosphate hybrid thin films are studied. Novel polymer/calcium-based inorganic composite thin films formed through biomimic self-aggregation process have been reported in this research.

Chapter 1. Morphology Tuning in the Formation of Vaterite Crystal Thin Films with Thermo-Responsive Poly(*N*-isopropylacrylamide) Brush Matrices

This chapter reported the development of calcium carbonate/polymer hybrid thin film materials by employing thermo-responsive polymer brush matrices. Recent advancement on surface-initiated controlled radical polymerization techniques, such as atom transfer radical polymerization (ATRP), enables the precise control of the thickness, composition and architecture of the polymer brushes. Surface-initiated ATRP allows the modification of various surfaces, such as silicon, metal oxides and polymer surfaces, by covalently attached polymer brushes. Thus, a study of the crystallization behavior of the inorganic minerals on polymer brush matrices may provide useful information toward the design of organic/inorganic functional hybrid coating materials. In this chapter, it is demonstrated that the use of thermo-responsive poly(*N*-isopropylacrylamide) (PNIPAm) brush matrices induced the formation of vaterite crystal thin films in the presence of poly(acrylic acid) (PAA) additives. Moreover, the conformational change of the chains of PNIPAm brush matrices above and below the lower critical solution temperature (LCST) significantly influences the morphologies and preferential orientations of resultant vaterite/PNIPAm hybrid thin films. In addition, the use of PNIPAm brush matrices leads to the formation of strontium carbonate thin-film crystals as well, and the surface patterns of resultant thin films have been tuned by the brush matrices. In this chapter, it is described that polymer brush matrices are effective nucleation and crystallization matrices for inorganic minerals, and the use of stimuli-responsive polymer brush matrices is a promising method for the realization of the morphological and orientational control of hybrid materials. The details of this study are discussed in papers [1] and [2].

Chapter 2. Tuning the Morphology of Calcium Phosphate Crystal Thin Films Using Poly(2-hydroxyethyl methacrylate) Matrices

Calcium phosphate is one of the most important inorganic substances in biological hard tissues. For instance, Hydroxyapatite (HAP), the least soluble and the most thermodynamically stable calcium orthophosphate crystal phase under physiological conditions, has been considered to be the model mineral compound of bones and teeth. This chapter focuses on the development and morphological control of calcium phosphate/polymer hybrid thin films *via* a biomimic method in view of the importance of surface topography for biocompatible and bioactive materials. Bioactive poly(2-hydroxyethyl methacrylate) (PHEMA) has been employed as an organic matrix for the crystallization of calcium phosphate. In this chapter, it is demonstrated that the use of PHEMA matrices leads to the formation of octacalcium phosphate (OCP)/PHEMA hybrid thin films in the presence of PAA additives. The surface morphologies of the resultant thin film have been selectively tuned by changing the amount of acidic polymer additives or the annealing conditions of PHEMA matrices. OCP/PHEMA hybrid thin films with micrometer-scale flower-like or concentric relief patterns have been transformed into HAP/PHEMA thin films while maintaining the surface morphologies. The role of PAA additive in the formation of patterned calcium phosphate crystal thin films on polymer matrices has been investigated in detail. Considering the biological importance of calcium phosphate crystals, the calcium phosphate/PHEMA hybrid thin films with different surface morphologies reported in this chapter have promising application as biomaterials. The details of this chapter are discussed in paper [3].

Chapter 3. Formation of Calcium Phosphate Crystal Thin Films by Employing Cationic Polyelectrolyte Additives

Chapter 3 focuses on the study of the crystallization of calcium phosphate on polymer matrices in the presence of poly(vinyl amine hydrochloride) (PVAmH) and poly(allyl amine hydrochloride) (PAAmH) additives. Although enormous efforts have been directed to anionic polymer additives in previous studies on biomineralization, the existence of moieties such as arginine in biological systems demands the studies on the roles of cationic polymer additives in the biomineralization process of calcium phosphates. In this chapter, it is demonstrated that cationic polymer additives such as PVAmH and PAAmH significantly influence the crystallization of calcium phosphates. The effects of the cationic additives on the crystallization behavior of calcium phosphate have been studied by IR, XRD and time-resolved pH measurements. The use of certain types of insoluble polymer matrices such as PHEMA and poly(vinyl alcohol) in the presence of PVAmH and PAAmH additives leads to the formation of OCP/polymer thin film hybrids. Moreover, crystallization system of calcium phosphate in the presence of cationic polymer additives and PHEMA matrices is pH-dependent. The morphologies and crystal forms of the calcium phosphate crystal thin films have been selectively tuned by the change of pH value. These results show the potential importance of cationic additives in the biomineralization of calcium phosphate and they may contribute to the design of bioactive materials. Paper [4] described this study in detail.

Chapter 4. Conclusion and perspectives

In chapter 1, the potential to synthesize polymer/inorganic hybrid thin films using synthetic polymer brush matrices is described. The use of polymer brushes as nucleation matrices for inorganic materials provides a novel basis towards the development of three dimensional bulky materials with desired hierarchical structures.

In chapters 2 and 3, the potential to control the crystallization and thin film formation of calcium phosphates by anionic as well as cationic polymer additives is described. It is shown that the presence of polymer matrices such as PHEMA leads to the formation of OCP or HAP crystal thin films with controllable morphologies. The use of PHEMA matrices in the presence of certain polyelectrolytes is supposed to be a useful method towards the development of HAP thin films with controllable patterns, which may find applications in cell and tissue engineering.

In conclusion, this thesis reports the development of calcium carbonate and calcium phosphate hybrid thin films *via* biomimic methods by using synthetic polymer templates to control crystal nucleation and growth. The results given in this thesis may provide novel ways towards materials design and they are expected to shed new light on the progress of materials science.

List of publications

Original Papers

[1] "Morphology Tuning in the Formation of Vaterite Crystal Thin Films with Thermo-Responsive Poly(*N*-isopropylacrylamide) Brush Matrices"
Yulai Han, Tatsuya Nishimura and Takashi Kato, *CrystEngComm*, 2014, **16**, 3540

[2] "Biomineralization-inspired Approach to the Development of Hybrid Materials: Preparation of Patterned Polymer/Strontium Carbonate Thin Films by Using Thermo-responsive Polymer Brush Matrices"
Yulai Han, Tatsuya Nishimura and Takashi Kato, *Polymer Journal*, (in press)

[3] "Biomimic Synthesis of Hydroxyapatite Thin Films with Homogeneously Distributed Three-dimensional Concentric Relief Patterns on Polymer Matrices"
Yulai Han, Tatsuya Nishimura, Satoshi Kajiyama and Takashi Kato, to be submitted.

[4] "Cationic Polyelectrolytes Induced Formation of Calcium Phosphate Crystal Thin Films"
Yulai Han, Tatsuya Nishimura and Takashi Kato, to be submitted.