博士論文

Development of Functional Supramolecular Composites Using Biomolecular Derivatives

（生体分子誘導体を用いた機能性超分子複合体の開発）

榮村　弘希

Supramolecular material chemistry is one of central fields in material science. The dynamic and ordered structures are formed by molecular self-assembly, which leads to novel functions. It is expected that material fabrication based on self-organization gives rise to highly functional and environmental friendly materials for sustainable society.

Liquid crystal is one representative example of supramolecular materials, which is a mesophase between isotropic phase and solid phase. The optical anisotropy and stimuli responsive properties have allowed industrial success of liquid crystals as energy-saving display materials. Moreover, recent advancement has shown that liquid crystal has high potential for a new platform of functional supramolecular materials beyond existing display application. One approach for functionalization of liquid crystalline (LC) materials is to introduce functional molecules to liquid crystals. For example, LC physical gels, which are composed of low molecular weight gelator and liquid crystal, exhibit enhanced functions of liquid crystals due to the microphase-separated structures. Different from conventional display devices using liquid crystal alone, LC physical gels enable us to develop light scattering display without polarizers or rubbed process.

This thesis describes development of functional supramolecular composites by using biomolecular-based molecules and liquid crystals. Based on the concept, biological functions (chapters 1 and 2) and magnetism (chapter 3) of supramolecular composites are studied. For the targeted functions, bioconjugated amphiphilic mesogens and an amino acid-based radical gelator are newly designed and synthesized. It is expected that the well-designed bimolecular derivatives having the biological features form remarkable self-assembled structures in synthetic LC media, leading to the induction of novel functions. A variety of functional LC composites have been developed. However, biomolecules-based materials have not been focused on as components in functional LC composites, though biomolecules achieve remarkable functions in biological system, such as selective protein recognition and ordered nanostructures.

Chapter 1. Aqueous-Liquid Crystalline Interfaces Using Bioconjugated Amphiphilic Mesogens

This chapter describes surface ordering and protein adsorption at aqueous-LC interfaces prepared using LC composites composed of bioconjugated mesogens and abiotic nematic liquid crystals. Liquid crystal is well known to respond to surface environment. The dynamic properties give rise to one emergent approach to develop liquid crystal-based sensors. Specifically, aqueous-LC interfaces have been utilized to detect biological events including specific binding between biomolecules and enzyme reactions. In spite of the high promise of the functional interfaces, liquid crystals tailored for the application have not been widely explored in biological context. Optimized LC materials lead to fully control adsorption of target biomolecules at aqueous-LC interfaces and to couple the biological event to change of LC alignment. In this context, new bioconjugated amphiphilic mesogens were designed and synthesized for functional aqueous-LC interfaces. Biotin and arginine-glycine-aspartic acid (RGD) peptide sequence, respectively, were conjugated with an amphiphilic LC molecule composed of a rod-shaped 2,3-difluoro-4'-(4-*trans*-pentylcyclohexyl)biphenyl-based mesogenic part and a tetraethylene glycol chain. In this study, the author examined self-assembled behaviors of the bioconjugated mesogens at aqueous-LC interfaces and effects of the self-assembly on LC alignment and protein adsorption at the interfaces. Langmuir film measurements indicated that the two bioconjugated mesogens form more highly packed structures at water surfaces than a room temperature nematic liquid crystal, 4-cyano-4’-pentylbiphenyl (**5CB**). Moreover, the bio-recognition moieties have significant effects on self-assembled structures at the aqueous surfaces. Langmuir films of the biotinylated mesogen showed the expanded and condensed states, while only expanded state was observed for the RGD-conjugated mesogen. The different self-assembled behaviors between the two bioconjugated mesogens suggest that the biotinylated mesogens present the biotin group in the aqueous phase, which is an important requirement for induction of biorecognition properties of the aqueous-LC interfaces. The two bioconjugated mesogens exhibited different miscibility with **5CB**. Due to high miscibility of the biotinylated mesogen with **5CB**, LC mixtures containing

the biotinylated mesogen exhibited cholesteric phase at relatively high concentration. In contrast, miscibility of the RGD conjugated mesogen with **5CB** was lower than the biotinylated mesogen, which resulted in no appearance of cholesteric phase in the case of **5CB** containing the RGD mesogen. Due to the low miscibility of the RGD mesogens, following sections in this chapter focus on the surface properties of LC mixture of the biotinylated mesogen. LC mixture containing the biotinylated mesogen showed homeotropic alignment and selective binding of streptavidin at aqueous-LC interfaces, which is consistent with the Langmuir film measurements above. For nematic phase, tilt angle of LC molecules regarding to aqueous-LC interfaces was quantitatively estimated from retardance of the LC films. This measurement revealed that the tilt angle decreases as the concentration of the bioconjugated mesogen in **5CB** increases. This is likely due to spontaneous localization of the biotinylated mesogen at the aqueous-LC interface. In the case of cholesteric LC mixtures containing the biotinylated mesogens, homeotropic anchoring at the aqueous-LC interfaces was also demonstrated by measuring the helical pitch of the optical appearances under crossed polarizers. Moreover, fluorescence microscopic observation of aqueous-LC interfaces adsorbing Texas-Red streptavidin revealed that the LC interfaces prepared using the biotinylated mesogens exhibit higher affinity than that of **5CB** without the biotinylated mesogens due to the specific interaction of streptavidin with the biotin moieties. The details of this study are reported in paper [1].

Chapter 2. Self-Assembly of RGD Peptide Conjugated Mesogens: a Thermotropic Liquid Crystal Having a Biorecognition Moiety

This chapter describes self-assembled behaviors of RGD peptide-conjugated amphiphilic mesogens in the bulk state. While liquid crystals have been widely used in informational flat panel display, the ordered and dynamic assemblies exist in biological system such as biomembrane. In particular, it has been proposed that LC biopolymers are essential as a template in spontaneous formation of tissue structures because many natural biopolymers including DNA, collagen, and cellulose exhibit lyotropic LC

properties. In this context, this chapter studies LC properties of RGD peptide-conjugated amphiphilic mesogens that was reported in chapter 1, to explore a potential of the mesogens as a biological template for regenerated medicine. It is expected that the RGD-mesogen provides a new bioscaffold for macroscopic alignment of cells, which is an important requirement for engineered tissues showing the targeted biological functions, such as high toughness, muscle switch, and signalization. Significantly, the RGD peptide-conjugated mesogen showed thermotropic LC phase, which was confirmed by polarized optical microscopic (POM) observation, different scanning calorimetric (DSC) analysis, and X-ray diffraction (XRD) measurements. The macroscopic alignment of the mesogens was achieved by shearing them at the LC phase.

Chapter 3. Unidirectional Alignment of Radical Fibers in Liquid Crystals

This chapter presents macroscopic alignment and magnetic properties of LC gels containing an amino acid-based radical gelator. Precise control of spatial alignment of stable organic radicals is essential to develop organic magnets showing the targeted magnetism. A previous study reported that an amino acid-based radical gelator forms supramolecular fibers, resulting into induction of antiferromagnetic interactions in the one dimensional radical chain. The intension in this chapter is to explore whether macroscopic ordering of the fibrous structures has influence on the magnetic properties. For the purpose, an isoleucine-based gelator having a TEMPO (2,2,6,6,-tetramethylperidine-1-oxyl) moiety was newly synthesized and mixed with a cyanobiphenyl LC mixture, which exhibits a smectic A phase over wide temperature range. Fibrous aggregates of the radical gelator were unidirectionally aligned in the LC gels, when the LC gel was introduced into a parallel rubbed cell. DSC analysis and POM observation revealed that the fiber formation occurred in the smectic A phase. Specifically, the oriented LC gels were also obtained by magnetic field alignment, which enables us to measure magnetic properties of oriented bulk LC gels with

superconductive quantum interference device (SQUID) because SQUID measurements requires bulk samples, not thin films. SQUID measurements reveal that aligned organic radical fibers show paramagnetic behavior with antiferromagnetic interaction that is almost identical with randomly dispersed radical fibers. From these results, it is anticipated that macroscopic alignment of supramolecular radical fibers has no effects on molecular arrangement of organic radical moieties at molecular scale, which is a key factor of magnetic properties.

Chapter 4. Conclusion and Perspective

This doctor thesis studies LC composites showing biorecognition properties and magnetism, based on an emergent approach that is complexation of functional biomolecular-based molecules with rod-shaped liquid crystals. Chapter 1 reported aqueous-LC interfaces prepared using amphiphilic mesogens with biorecognition epitopes, biotin and RGD peptide sequence. The alignment and protein biding properties at the aqueous-LC interfaces were characterized. Significantly, this work is the first report showing that self-assembly of molecular components in supramolecular materials contribute to specific binding properties on the interface of bulk material, which proposes an alternative approach to surface modification. Chapter 2 focused on mesomorphic properties of a RGD-conjugated mesogen, which is the first report on thermotropic liquid crystal with biorecognition moieties. In Chapter 3, organic radical molecules were unidirectionally aligned by using LC gels of an amino acid-based radical gelator. Magnetic field alignment provides the monodomain LC gels. The oriented radical gels were examined by SQUID, which shows that antiferromagnetic interaction is induced by fibrous assembly of organic radicals.

In conclusion, this thesis pursues the way how self-assembly address to control bulk interface and macroscopic ordering of materials and how the self-organized structures have influence on the material properties. It is expected that fundamental basis obtained in this thesis leads to further functional and structural control of supramolecular materials in order to completely achieve sustainable society.

List of Publications

Original Papers

[1] "Self-Assembly of Bioconjugated Amphiphilic Mesogens Having Specific Binding Moieties at Aqueous-Liquid Crystal Interfaces"
Hiroki Eimura, Daniel S. Miller, Xiaoguang Wang, Nicholas L. Abbott, Takashi Kato,
Chem. Mater. in press DOI: 10.1021/acs.chemmater.5b04736.

[2] "RGD Peptide-Based Thermotropic Liquid Crystal"
Hiroki Eimura, Nicholas L. Abbott, Takashi Kato,
in preparation.

[3] "Self-Assembled Fibers Having Stable Organic Radical Moieties: Alignment and Magnetic Properties in Liquid Crystals"
Hiroki Eimura, Yoshikazu Umeta, Hiroko Tokoro, Masafumi Yoshio, Shin-ichi Ohkoshi, Takashi Kato,
submitted for publication.

[4] "Liquid-Crystalline Gels Exhibiting Electrooptical Light Scattering Properties: Fibrous Polymerized Network of a Lysine-Based Gelator Having Acrylate Moieties"
Hiroki Eimura, Masafumi Yoshio, Yoshiko Shoji, Kenji Hanabusa, Takashi Kato,
Polym. J. **2012**, *44*, 594-599. (Special Issue of Self-Assembled Materials)

References

[5] "Supramolecular approach to the construction of magneto-active physical gels"
Yong Wu, Yuki Hirai, Yoshihide Tsunobuchi, Hiroko Tokoro, Hiroki Eimura, Masafumi Yoshio, Shin-ichi Ohkoshi, Takashi Kato,
Chem. Sci. **2012**, *3*, 3007-3010.

[6] "Supramolecular Effects on Formation of $CaCO_3$ Thin Films on a Polymer Matrix"
Fangjie Zhu, Tatsuya Nishimura, Hiroki Eimura, Takashi Kato,
CrystEngComn **2014**, *16*, 1496-1501.