The Effect of the Liquid-Crystalline Order on Releasing Dye Molecules from Liquid-Crystalline Nano-Emulsions

Shinji Bono, Masayuki Yokoyama, Yoichi Takanishi & Jun Yamamoto

Published online: 06 Jul 2015.

Submit your article to this journal ⬚

View related articles ⬚

View Crossmark data ⬚

Taylor & Francis
Taylor & Francis Group

The Effect of the Liquid-Crystalline Order on Releasing Dye Molecules from Liquid-Crystalline Nano-Emulsions

SHINJI BONO,[1,*] MASAYUKI YOKOYAMA,[2]
YOICHI TAKANISHI,[1] AND JUN YAMAMOTO[1]

[1]Department of Physics, Graduate School of Science, Kyoto University,
Kyoto, Japan
[2]Faculty of Medicine, The Jikei University School of Medicine, Tokyo, Japan

We fabricated dye-containing liquid-crystalline nano-emulsions (LCNEs) dispersed in water, and studied the controllability of releasingdye molecules from the coreof LCNEs into water. We estimated the concentration of the dye molecules held in the core of LCNEs from transmission spectrum. As a result, it was revealed that the dye molecules are released from the core of LCNEs below the characteristic release-temperature on cooling. Moreover, the depolarized static light scattering measurement was performed to estimate the Isotropic-Nematic(I-N) phase transition temperature of low molecular weight liquid crystals in the core of LCNEs. By controlling mixing ratio of binary liquid crystalline mixture, we tuned theI-N phase transition temperature. The release-temperature completely corresponds to the I-N phase transition temperature in the coreof LCNEswithin the whole mixing ratio. Thus, we confirmed that the emergence of the liquid-crystalline order in the core of LCNEs plays a principal role in releasing the dye molecules from LCNEs.

1. Introduction

The purposes of drug delivery system (DDS) are to hold drugs in carriers and to deliver them to the diseased part in vivo [1–2]. Sincethe stimuli-responsive materials can control releasing loaded drugs by means of external stimuli, they enable us to selectively release drugs [3–5]. Previously, we have succeeded in dispersing the liquid-crystalline nano-emulsions (LCNEs) with diameter of a few hundred nanometers. In such a LCNE system, the shell and the core of LCNEs are occupied by surfactants andnematic low molecular weight liquid crystals(LMWLCs), respectively [6]. The liquid-crystalline (LC) order in the core of LCNEs abruptly emerges at the Isotropic-Nematic (I-N) phase transition. Solubility of solute molecules in LMWLCs also greatly decreases at the I-N phase transition, because the order parameter of LMWLCs couples with the concentration of solute molecules in LMWLCs [7]. Thus, LCNEs can push out the solute molecules from the core of LCNEs into water triggered by the I-N phase transition in the core of LCNEs. Therefore, LCNEs are expected to work as temperature-responsive carriers for DDS.

---

*Address correspondence to Shinji Bono, Department of Physics, Graduate School of Science, Kyoto University, Kita-shirakawa, Kyoto 606-8502, Japan. E-mail: bono@scphys.kyoto-u.ac.jp

In this paper, we adopted a dye as a cargo-molecule, whose absorbance spectrum in LMWLCs differs from that in water, to the water solution of LCNEs [8], and measured temperature dependence of absorbance to estimate concentration of the dye molecules held in the core of LCNEs. To separate the effect of the LC order on releasing the dye molecules from other temperature effects, e.g. solubility [9] and external osmotic pressure [10], we made LCNEs constituted by the binary mixture LMWLCs whose I-N phase transition temperature controlled by their mixing ratio [11]. We confirmed that the dye moleculesare successfully released from the core of LCNEs, and that releasing is triggered by the emergence of the LC order in the core of LCNEs.

2. Experimental

We used the binary LC mixture of 5CB (N-35°C-Iso) and 7CB (N-42°C-Iso). Mixing ratio ϕ is defined as $w_7/(w_5 + w_7)$, where w_5 and w_7 are weight of 5CB and 7CB, respectively. We evaluated the phase transition temperatures of the binary LC mixtures in the bulk state by measuring temperature dependence of retardation of each binary LC mixture. We got the water solutions of LCNEs in the following way. An amphiphilicdiblock copolymer, Poly (ethylene oxicide-b-6-[4′-cyanobiphenyl-4-yloxy]hexyl methacrylate), whose side chain contains mesogenic part and the binary LC mixture are mixed with the constant weight ratio in acetone. After removing acetone by evaporation, we added water into this mixture andsonicated it for more than two hours at 60°C.We purified this solution with a syringe filter whose diameter is 1 μm. As a cargo-molecule, Nile Blue A perchlorate was used [8]. By adding the water solution of Nile Blue A perchlorate into the water solution of LCNEs, we gotdye-containing LCNEs. Concentration of the binary LC mixture and the dye molecules of LCNEs are about 0.1 wt% and about 4×10^{-3} wt%, respectively.

LCNEs are uniformly dispersed in water and freely rotate because of thermally excited Brownian motions. Hence, the macroscopic optical anisotropy completely disappears, even if each micelle has the anisotropy caused by the LC order in the core of LCNEs. To identify the existence of the anisotropy in the core of LCNEs, the light scattering technique was used. We measured temperature dependence of the VH static light scattering intensities (I_{VH}) of LCNEs. I_{VH} reflects the anisotropic order of the binary LC mixtures in the core of LCNEs [6]. According to the theory of light scattering from anematic droplet in isotropic solvent [12], I_{VH} is quadratically proportional to the dielectric anisotropy of LCNEs, $(\varepsilon_\parallel - \varepsilon_\perp)$, where $\varepsilon_\parallel$ and $\varepsilon_\perp$ are the components of dielectric constants parallel and perpendicular to the anisotropic axis, respectively. Since the dielectric anisotropy should indicate the LC order, we can evaluatethe I-N phase transition temperature of the binary LC mixtures confined in the core of LCNEs by measuring I_{VH}.

3. Results and Discussion

Figure 1 shows temperature dependence of I_{VH} of LCNEs with various values of mixing ratio ϕ. I_{VH} was normalized so that maximum and minimum values of I_{VH} become one and zero, respectively. Irrespective of ϕ, I_{VH} increases with decreasing temperature. For LCNEs whose core is composed of pure 7CB ($\phi = 1$), I_{VH} abruptly increasesaround 39.5°C on cooling. Sincethe temperature of abrupt change in I_{VH} was close to the I-N phase transition temperature of 7 CB in the bulk state (~42°C), the result is originated fromthe emergence of the finite LC order due to the I-N phase transition in the core of LCNEs [6]. We defined the phase transition temperature as T_c^{NE}. This abrupt change reflecting the I-N phase transition in the core of LCNEs was observed for all ϕs. It is evident that T_c^{NE} becomes lower with the decrease in ϕ, and is always close tothe phase transition temperature of the binary LC
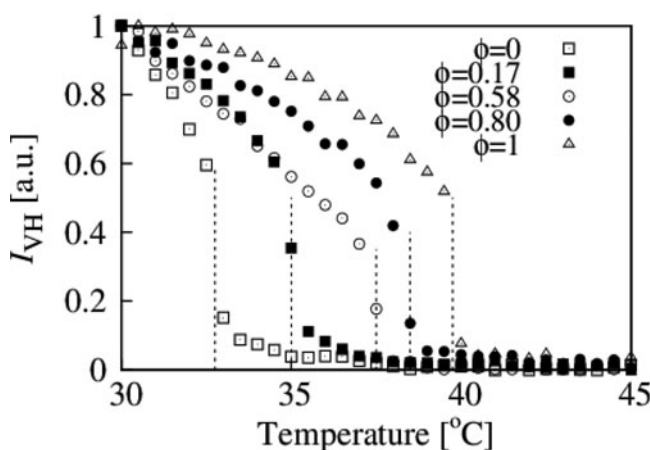
Figure 1. Temperature dependence of I_{VH} of LCNEs with various values of ϕ.

mixture with the same ϕ in the bulk state. Hence, we found that T_c^{NE} can be controlled by changing ϕ, even if the binary LC mixture is confined in the core of LCNEs.

In order to identify whether the dye molecules are held in the core of LCNEs or released into water, we measured transmission spectra of three kinds of samples; dye-containing LCNEs with $\phi = 0.58$ (sample **1**), the water solution of the dye molecules (sample **2**), and the LMWLC (7CB) doped with the dye molecules (sample **3**). We got normalized transmission spectra of the dye-containing LCNE by normalizing spectra of sample **1** by those of LCNEs without dye molecules, because transmittance decreases due to the scattering of LCNEs themselves. For sample **2** and sample **3**, we normalized the maximum value with 100%. Comparing these normalized spectra, we examined whether the dye molecules are dissolved in water or in the core of LCNEs. The normalized transmission spectra of sample **1** at 60°C and 30°C are shown in Fig. 2. We also superimposed transmission spectra of sample **2**
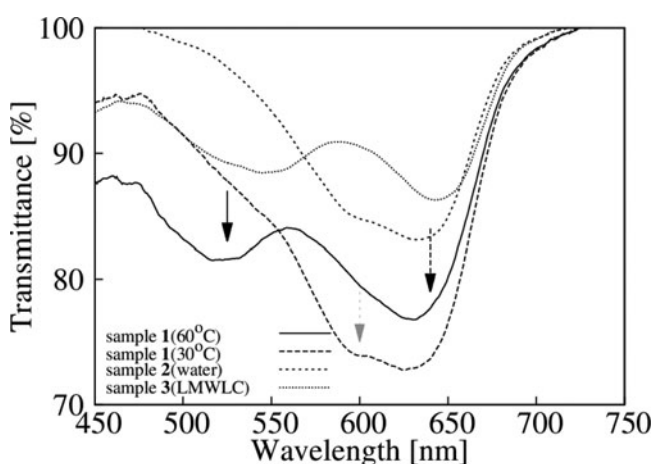

Figure 2. The transmission spectra of the dye-containing LCNE with $\phi = 0.58$ (sample **1**) at 60°C and 30°C. We also superimposed transmission spectra of the dye molecules dissolved in water and in the LMWLCs. The arrows are placed at 525nm (black) and 600nm (dotted gray), 640 nm (broken black).
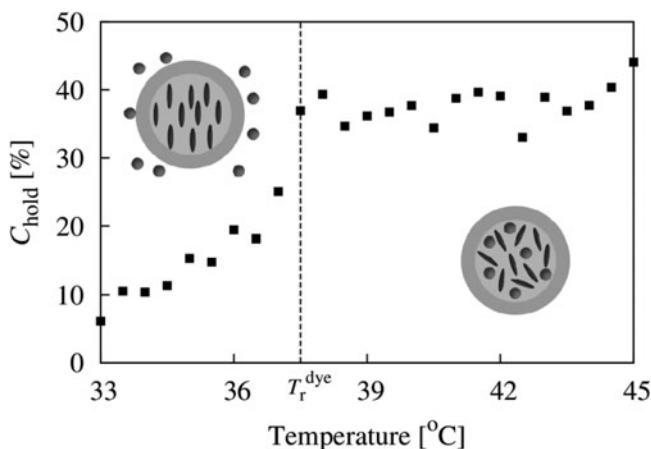
Figure 3. Temperature dependence of the C_{hold} for sample **1**. The broken line shows the release-temperature.

and sample **3**. The dye molecules dissolved in LMWLCs absorb visible light around 525 nm in addition to around 640 nm (sample **3**). Transmission spectrum ofsample **1** at 60°C also has dips due to the absorption of dye moleculesaround 525 nm (indicated by a black arrow) and 640 nm (indicated by a broken black allow) as similar to the spectrum of dye molecules in LMWLCs (sample **3**). Thus, it is confirmed that the dye molecules are held in the core of LCNEs. On the other hands, at 30°C the diparound 525 nm disappears, but appearsaround 600 nm (indicated by adotted gray arrow), as similar to the transmission spectrum of the dye molecules dissolved in water (sample **2**). Finally, it can be concluded that the dye molecules held in the core of LCNEs at 60°C are released into water at 30°C from LCNEs.

We estimated the concentration of the dye molecules held in the core of LCNEs, C_{hold}, from transmittance at 525 nm, $\tau_{\lambda = 525\,\text{nm}}$. According to the Beer-Lambert law [13], $\tau_{\lambda = 525\,\text{nm}}$ is related to C_{hold} as follows,

$$-\frac{\log_{10}\left(I_{\lambda=525\text{nm}}/I_0\right)}{C_{\text{LC}}L} = \alpha\frac{C_{\text{dye}}}{100}C_{\text{hold}} \tag{1}$$

where L, C_{LC} and C_{dye} are thickness of sample ($\sim$1 mm), the concentration of the binary LC mixture and that of the dye molecules, respectively. $\alpha(\sim 6.0 \times 10^{-3}[\mu\text{m}^{-1}])$ is the absorption coefficient of the dye molecules, determined from the transmission measurement of sample **3**. Figure 3 shows temperature dependence of C_{hold} for sample **1**. We can define the release-temperature, $T_{\text{r}}^{\text{dye}}$, where C_{hold} is abruptly changed. Above $T_{\text{r}}^{\text{dye}}$, about 40% of the dye molecules are held in the core of LCNEs. At $T-T_{\text{r}}^{\text{dye}} \sim -5$°C, about 30% of dye molecules are released into water and only 10% of the dye molecules remain in the core of LCNEs.

Figure 4 shows ϕ dependence of the release temperature, $T_{\text{r}}^{\text{dye}}$ and the I-N phase transition temperature of the core of LCNEs, T_{c}^{NE}, associated with the I-N phase transition temperature of the binary LC mixture in the bulk state, $T_{\text{c}}^{\text{bulk}}$. T_{c}^{NE} and $T_{\text{r}}^{\text{dye}}$ increase with the increase in ϕ. Moreover, they are always equivalent to each other within the whole mixing ratio. This result suggests that releasing dye molecules from the core of LCNEs can be controlled by the change of the LC order in the core, and thatemergence of the LC order
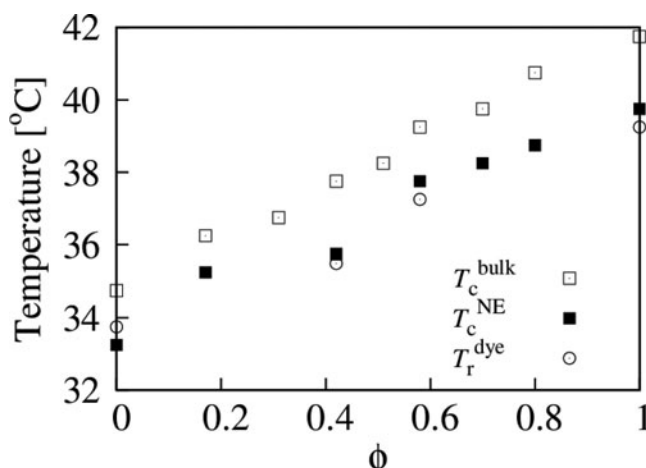
Figure 4. ϕ dependence of the I-N phase transition temperature of the binary LC mixture in the bulk state T_c^{bulk}, and that in the core of LCNEs T_c^{NE}, and T_r^{dye}.

can push out dye molecules into water. On the contrary, the dye molecules are stably held in the core, if the binary LC mixturein the core of LCNEs is isotropic. Furthermore, T_c^{NE} is slightly lower than T_c^{bulk}, which originates from impurity and confined effects as follows. First, hydrophobic chains of surfactants on the surface of LCNEs work as impurities, because they partially mix with the binary LC mixture in the core of LCNEs. Generally speaking, impurities, such as polymers, weaken the LC order parameter, and hence reduce the I-N phase transition temperature [7]. On the other hand, when the uniaxial nematic phase is confined in the spherical nano-emulsions, director needs deformation to match the shape of the inner surface of the container (surfactant). Additionally, defects are introduced under the topological constrainton the director distortion. Both require the penalty of the excess free energy, which causes reduction of the I-N phase transition temperature [6,14].

4. Conclusion

In conclusion, we revealed that the I-N phase transition can trigger offrelease ofthe dye molecules from the core of LCNEs into water, and that LCNEs can work as carriers. The static light scattering measurements give us the correct information about the I-N phase transition of the binary LC mixture in the core of LCNEs, whereas the LCNEs are macroscopically transparent and is otropic.The concentration ratio of the dye molecules held in the core to those released into water was estimated from the transmission spectra of the dye-containing LCNEs. Moreover, we compared I-N phase transition temperature in the core of LCNEs and the release-temperature of the dye molecules, and confirmed that thechange of LC order plays a principal role in releasing the dye molecules.

Funding

References

[1] Iyer, A. K., Khaled, G., Fang J., & Maeda, H. (2006). *Drug Discov. Today, 11*, 812.

[2] Rösler, A.,Vandermeulen, G. W. M. , & Klok, H. A. (2001). *Adv. Drug. Deliv. Rev., 53*, 95.

[3] Nishihara, M., Murakami, Y., Shinoda, T., Yamamoto, J., & Yokoyama, M. (2008). *Chem. Lett. 37*, 1214.

[4] Zhang, Z. X., Qiu, L. Y., & Zhu, Y. J. (2006). *J. Biomed. Mater. Res. A.*, *76*, 773.

[5] Wei, H., Zhang, X., Cheng, C., Cheng, S. X., & Zhuo, R. X. (2007). *Biomaterials*, *28*, 99.

[6] Bono, S., Takanishi, Y., & Yamamoto, J. *in preparation.*

[7] Samitsu, S., Takanishi, Y., & Yamamoto, J. (2010). *Nat. Mater*, *9*, 819.

[8] Jose, J., Ueno, Y., & Burgess, K. (2009). *Chem. Eur. J.*, *15*, 418.

[9] Muschol, M., & Rosenberger, F. (1997). *J. Phys. Chem.*, *107*, 1953.

[10] Petsev, D. N., Wu, X., Galkin, O., & Vekilov, P. G. (2003). *J. Phys. Chem. B*, *107*, 3921.

[11] Demus, D., Fietkau, Ch., Shubert, R., & Kehlen, H. (1974). *Mol. Cryst. Liq. Cryst.*, *25*, 215.

[12] Zumer, S., & Doane, J. W. (1986). *Phys. Rev. A, 34*, 3373.

[13] Boas, D. A., Gaudette, T., Strangman, G., Cheng, X., Marota, J. J. A., & Mandeville, B. (2001). *NeuroImage*, *13*, 76.

[14] Kutnjak, Z., Kralj. S., Lahajnar, G., & Zumer, S. (2003).*Phys. Rev. E, 68*, 021705.