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Liquid crystals: emerging materials for use in real-time detection applications

Ding Wang, Soo-Young Park, Inn-Kyu Kang*

Department of Polymer Science and Engineering, School of Applied Chemical Engineering, Kyungpook National University, Daegu 702-701, South Korea

E-mail: ikkang@knu.ac.kr

ABSTRACT

With the rapid advances in liquid crystal (LC) materials technology over recent decades, many different practical devices have been developed and commercialized. LC devices have found numerous applications in fields such as imaging, microscopy, spectroscopy, and optical probing. Multifarious LC-based sensors have been developed to analyze label-free polyelectrolytes, ions, molecules, and biological systems. The detection principle in these LC sensors is based on the highly sensitive orientational response of LC molecules to minute changes in surface structures. Moreover, due to their potential applications in fields such as chemistry, biomedicine, and environmental science, scientists have been attracted to the research and development of LCs because of their potential use in real-time sensors. This review presents a brief overview of the historical background on the research progress of LCs and recent trends in their use in real-time detection applications.

1. Introduction

Liquid crystals (LCs) are responsive to external electric and magnetic fields, and will reposition themselves into collective alignment in the presence of an applied field. Today, LCs are well known for their applications in display technology. Liquid crystal display (LCD) technology has dominated international research efforts in display applications for quite a long time, driven by consumer demand. LCD technology is so much better today that continued research and development for day-to-day applications is conducted mainly in industrial laboratories.

LCs, which assemble with polymers and aqueous solutions, have attracted much attention

1 in recent years because of their large surface areas and unique optical properties.¹ In bulk, LC
2 molecules arrange themselves in arbitrary orientations. However, blended with various
3 surfactants, polymers, and other materials, and confined by space, LC molecules are forced to
4 assume a specific directional orientation dictated by local intermolecular forces within the
5 aqueous phase. Due to long-range orientation correlations, the energy required to perturb the
6 molecular order of LCs is very small.²⁻⁴ The alignment of LC molecules is therefore very
7 sensitive to the type, strength, and concentration of surfactants and/or polymers existing in
8 the aqueous phase. The orientation of LCs acts as an amplifier for local perturbations caused
9 by foreign molecules adsorbed on the interface.⁵ The LCs at the surface can then
10 communicate their orientations through the bulk, causing changes in orientations throughout
11 the LC matrix. This process then can generate optical textures that are visible to the naked
12 eye under crossed-polarizers in real time.¹

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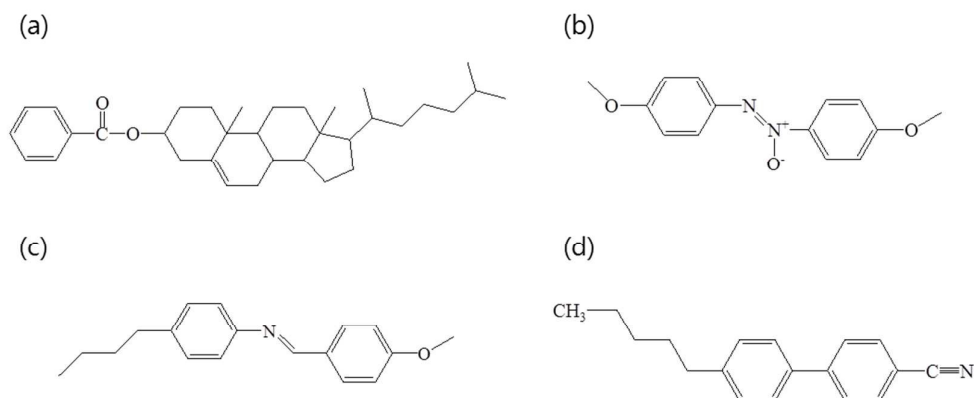
14 **2. Historical perspective**

15 From 1850 to 1888, researchers in physics, chemistry, biology, and biomedical science
16 found that some materials demonstrated very unusual properties near their melting points. It
17 was observed further that the optical properties of these materials changed continuously with
18 increasing temperatures. In 1850, W. Heintz reported that stearin melted from a solid to a
19 cloudy liquid at 52 °C, changed to an opaque liquid at 58 °C, and then to a clear liquid at
20 62 °C.^{6,7} In 1888, an Austrian botanical physiologist named Friedrich Reinitzer⁶ observed
21 “double melting” behavior for cholesteryl benzoate (Fig. 1a). (The chemical structure of
22 cholesterol was still unknown. Today we know that the observed compound was cholesteryl
23 benzoate.)

24 Research in the area of LCs continued to grow and expand in the years after 1888. In the
25 beginning, every LC substance that had been identified and researched was naturally
26 occurring. It was not until 1890 that Gatterman and Ritschke prepared the first synthetic LC,
27 p-azoxyanisole (Fig. 1b).⁷ However, between World War II and 1958, researchers thought
28 they had learned everything possible about LCs and that there was nothing new to be
29 explored. New young scientists did not have any contact with liquid crystal research.

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Fig. 1 Molecular structure of the typical LC: (a) cholesteryl benzoate, (b) p-azoxyanisole, (c) 4-methoxybenzylidene-4-butylaniline (MBBA), (d) 4-pentyl-4'-cyanobiphenyl (5CB).

5 Until 1969, the first room-temperature nematic substance, 4-methoxybenzylidene-40-
 6 butylaniline (MBBA) (Fig. 1c), was synthesized by Hans Kelker.⁸ This material became one
 7 of the most heavily researched materials in the LC field of study. Additional milestones in the
 8 development of LC materials were reported as below. In 1973, George Gray synthesized a
 9 new class of LCs, which continues to be commercially important today: 4-n-alkyl-4'-
 10 cyanobiphenyl (CB, n=5-8). An example of this type of LC, 4-pentyl-4'-cyanobiphenyl
 11 (5CB), is illustrated in Fig. 1d.⁹ Along with Ken Harrison and the UK Ministry of Defense
 12 (UK MOD) located at R. R. E. Malvern, Gray led design efforts for materials that were
 13 rapidly adopted for use in small LCDs for electronic devices. Then, W. MacMillan¹⁰ and R.
 14 Meyer¹¹ proposed the mean-field theory for smectics in 1974.

15 In 1991, Pierre-Gilles de Gennes, a theoretical physicist working at the University of Paris
 16 XI in France, became interested in LCs and soon found amazing analogies between LCs and
 17 superconductors as well as magnetic materials, and received the Nobel Prize in physics "for
 18 discovering that methods developed for studying order phenomena in simple systems can be
 19 generalized to more complex forms of matter, in particular to liquid crystals and polymers".

20 The future of LCs has just begun. There are still many unsolved physical problems to
 21 investigate. LC materials are still used as a key component in simple inexpensive displays for
 22 common calculators and mobile phones. As research in this field continues and as new
 23 applications are developed, LCs will play an important role in chemistry, physics, biology,
 24 medicine, electronic engineering, and many other fields. Today, LCs are finding new

1 applications in detection technology. In this review, we look at LCs as emerging materials for
2 use in real time detection. New LC materials and devices will no doubt drive forward new
3 research in these fundamental and applied sciences.

5 **3. LCs and surfactants**

6 Nematic LCs are composed of calamitic or rod-like organic molecules which have no
7 positional order, but they self-align to have long-range directional order with their long axes
8 roughly parallel.¹² Nematic LCs are characterized by their director field, \vec{n} , which can be
9 seen using polarized optical microscopy. A number of previous researchers have reported the
10 influence of surfactants adsorbed at the interface between the liquid crystal layer and the
11 aqueous phase on the orientation of LCs.¹³⁻¹⁵

12 A systematic study of the anchoring of nematic LCs in contact with the aqueous phase
13 containing surfactants has shown that the orientation of LCs was affected by its molecular
14 architecture, alkyl chain length and concentration of surfactant.¹⁶ A surfactant responds to the
15 presence of LCs at the LC-aqueous interface by extending its non-polar alkyl chain
16 homeotropically into alignment with the LC, causing the LC molecules to align in a
17 homeotropic orientation (Fig. 2a). This homeotropic orientation is called a radial
18 configuration when in LC droplets (Fig. 3a). LC droplets in this configuration have a point
19 hedgehog disclination at the droplet center. Examples of surfactants that work this way
20 include bolaform surfactants, which are ionic surfactants like sodium dodecyl sulfate (SDS)
21 and dodecyltrimethylammonium bromide (DTAB).¹⁷ However, polyvinylalcohol (PVA) or
22 polyvinylpyrrolidone (PVP) adsorb at the interface in a more or less random coil
23 conformation, imposing tangential anchoring at the surface. This conformation leaves the LC
24 molecules in a planar orientation (Fig. 2b), which is called a bipolar configuration in LC
25 droplets (Fig. 3b). This bipolar configuration then creates two point defects, referred to as
26 “boojum” when occurring in LC droplets.¹⁸⁻²⁰ The most favorable configuration at an
27 interface occurs when a polar phase such as water is used. An example of the experimental
28 geometry used to create stable interfaces between aqueous phases and thermotropic LCs is
29 shown in Fig. 4.¹³

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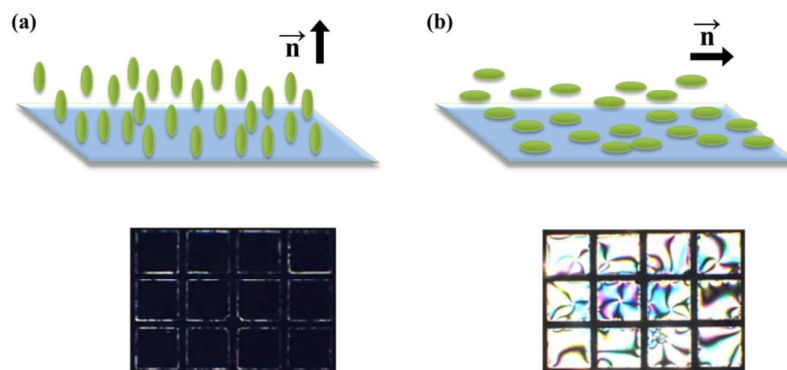


Fig. 2 Schematic representation of (a) homeotropic and (b) planar anchoring of LC molecules on a solid substrate

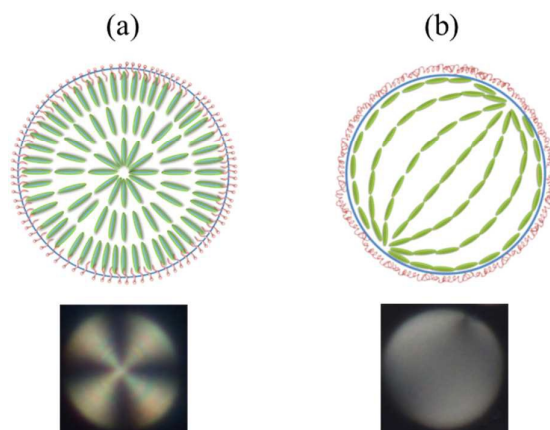
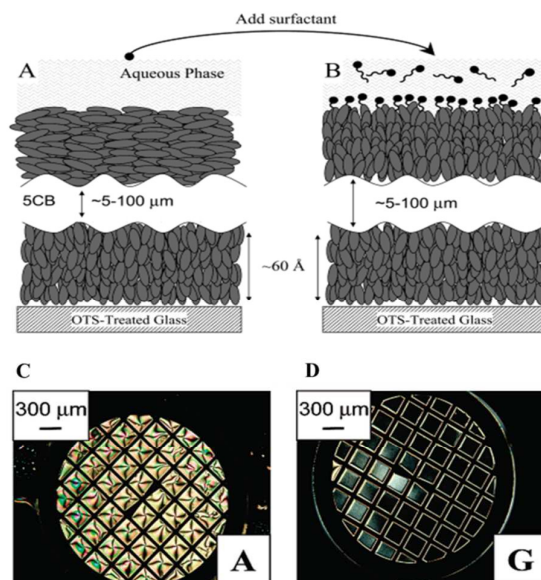


Fig. 3 Schematic representation of a typical LC droplet orientation: (a) radial, (b) bipolar.



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2 Fig. 4. A–B) Schematic illustration of the director profiles of 5CB induced by adsorption of SDS at the 5CB-
 3 aqueous interface: (A) SDS-free interface (planar anchoring of the LC at the interface with the aqueous phase) ;
 4 (B) SDS-laden interface (homeotropic anchoring of the LC at the interface with the aqueous phase). Note that the
 5 orientation of the 5CB at the grid surface is normal to the grid-5CB interface. C–D) Optical images (crossed
 6 polars) of 5CB confined to a copper grid with a spacing of 292 μm that was supported on an OTS-coated glass
 7 slide and immersed under pure water (C) or an aqueous solution of 2.2 mM SDS (D). Reprinted with permission
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10 In addition, J M Brake et al.¹⁶ explained that the decreased bulk concentration of SDS and
 11 DTAB anchored at the interface changed the orientation of the LC molecules from planar to
 12 homeotropic. Hence, the dominant role of the surfactant headgroup is that of determining the
 13 interfacial density of the adsorbed surfactant (via headgroup-headgroup repulsion).
 14 Surfactants with short aliphatic chain lengths did not cause homeotropic anchoring of 5CB at
 15 any bulk concentrations of surfactant. The choice of surfactant is quite important because it
 16 will influence the alignment of the director at the interface and, later, when used in an actual
 17 detection device.

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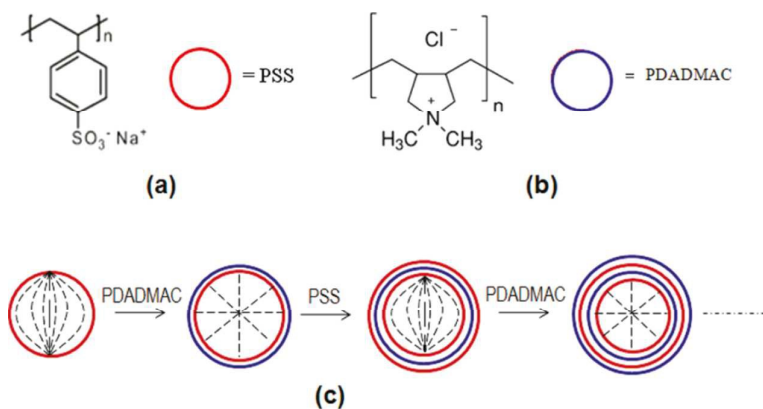
19 4. LCs and polyelectrolytes

20 The interactions of species at the LC/water interface result in variation of the LC director
 21 that causes detection of chemical and biological events occurring at the surface in contact

1 with the LCs.²¹⁻²⁵ There has been recent interest in extending the application of LCs to
 2 imaging the molecular ordering of self-organized systems.²⁶⁻³¹ For this application, the
 3 interface of the LC was modified by adsorbing surfactants or polymers. Properties of these
 4 physically adsorbed species such as molecule density,³² charge³⁰ and pH^{33,34} may accomplish
 5 this change in LCs, resulting in a different orientation.^{35,36} Hence, such chemically modified
 6 LC droplets were found to be a more useful option for the detection of chemicals and
 7 biological species.

8 4.1. Homopolymers as polyelectrolytes

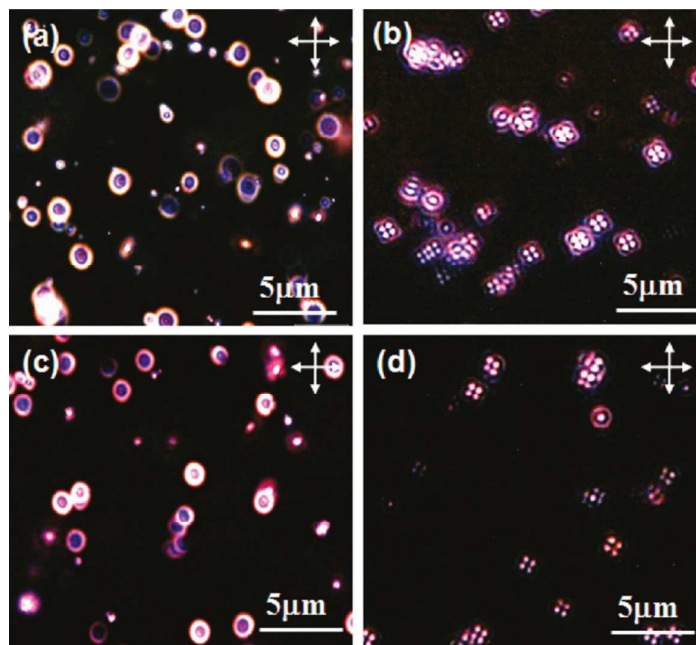
9 Recently, Jianhua Zou et al.³⁰ reported that negatively charged poly(styrenesulfonate
 10 sodium salt) (PSS) and positively charged poly(diallyldimethylammonium chloride)
 11 (PDADMAC) multilayer-coated LC droplets had been successfully prepared. These materials
 12 can trigger bipolar/radial orientation transitions inside 5CB droplets (shown in Fig. 5, 6).



13

14 Fig. 5 (a) Chemical structures of poly(styrenesulfonate sodium salt) (PSS), (b) poly(diallyldimethylammonium
 15 chloride) (PDADMAC), and (c) a schematic illustration of the alternating bipolar/radial transitions of 5CB in
 16 droplets triggered by the layer-by-layer coating of PSS and PDADMAC on the droplet surface. Reprinted with
 17 permission from ref. from ref. 30. Copyright (2011) American Chemical Society.

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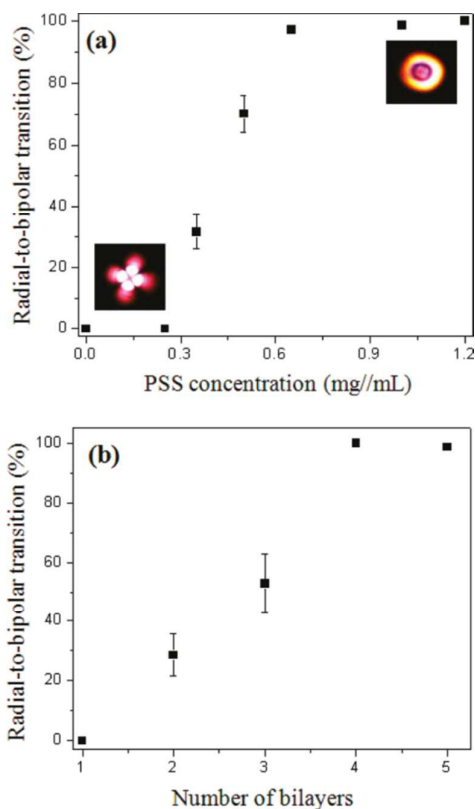
2 Fig. 6 (a) Polarizing optical microscopy images of poly(styrenesulfonate sodium salt)(PSS)-coated 5CB droplets,
3 (b) poly(diallyldimethylammonium chloride)(PDADMAC)/PSS-coated 5CB droplets, (c) PSS/PDADMAC/PSS-
4 coated 5CB droplets, and (d) (PDADMAC/PSS)₂-coated 5CB droplets. All images were taken in water. The
5 direction of the polarizer and analyzer is indicated by white arrows. Reprinted with permission from ref. from ref.
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8 The orientational transition was found to be dependent on the amount of dendrimer coated
9 on LC droplets. Hence, the sensitivity of the transition from bipolar to radial could be
10 controlled using different amounts of the electrolyte or dendrimer on the surface of the LC
11 (Fig. 7).³⁰ The layer-by-layer deposition of material for the modification of LC droplet
12 surfaces was the easiest and most flexible approach, as it provided opportunities to deposit
13 different materials, e.g., polymers,³¹ proteins,³⁷ DNA,³⁸ multivalent cations,³⁹ and anions.⁴⁰
14 The surface of the LC provided ample opportunities for transformation of interfacial
15 interactions and events⁴¹⁻⁴⁴ in ways for detection and quantification by analyzing orientational
16 transitions in the LCs. The properties of LC emulsions in real-time detection depend on their
17 size and topological defects. Monodispersed LC emulsions of different sizes and topologies
18 have been prepared and characterized for their stability by containing a single droplet in a
19 core-shell geometry⁴⁵ or by using the microfluidics technique.⁴⁶ A remarkable property of
20 low molecular weight LCs is their ability to orient due to interactions at the interface. Clare et
21 al.⁴⁷ calculated that a mass density of an oligopeptide of less than 1 ng/cm² can lead to a

1 measurable change in the anchoring energy of 5CB. This result indicated that measurements
2 of interfacial anchoring energies of LCs on surfaces may offer the basis of quantitative and
3 label-free methods for real time detection of biomolecules on surfaces.

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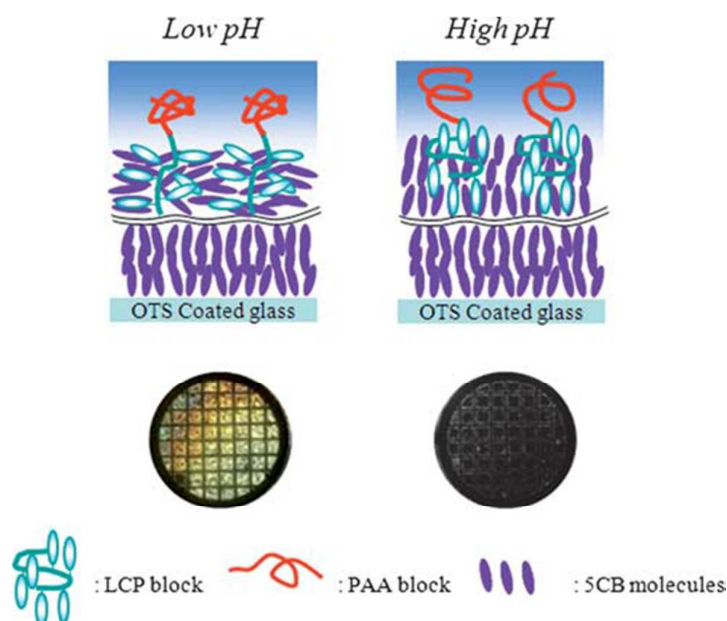
7 Fig. 7 (a) The director configuration transition of 5CB in poly(diallyldimethylammonium
8 chloride)(PDADMAC)/poly(styrenesulfonate sodium salt)(PSS)-coated droplets after being exposed to PSS
9 solutions with different concentrations for 20 min, (b) the director configuration transition of 5CB in
10 PDADMAC/PSS multilayer-coated droplets after being exposed to a PSS solution with a concentration of 0.25
11 mg/mL for 20 min. The data points were obtained from averaging the result of 100 droplets for each sample.
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14 4.2. Copolymers as polyelectrolytes

15 Over the past ten years, researchers have shown a great interest in the synthesis of
16 amphiphilic block copolymers due to their various applications in both academic and
17 industrial settings. Block copolymers containing a polyelectrolyte block carrying ionizable
18 groups with electrostatic charges have been widely studied and even incorporated into

1 sensors.^{48, 49} Abbott and co-workers²¹ reported an amphiphilic diblock copolymer
 2 functionalized with hydrophobic (N-decyl acrylamide) and hydrophilic (N-{3-
 3 (dimethylamino) propyl} acrylamide) side groups that assembled at the aqueous/LC interface.
 4 Amphiphilic diblock copolymers were designed to anchor at the aqueous/5CB interface and
 5 respond reversibly to changes in the pH of the aqueous phase, resulting in an orientational
 6 change, which can be observed under a polarized microscope. Additionally, 5CB assembled
 7 with polyacrylic acid block liquid crystalline polymers have been used to facilitate
 8 examination of the effects of diverse stimuli, which has been reported by Park et al.^{33, 50, 51} A
 9 compact coil of hydrophilic polyacrylic acid (PAA) block (e.g., at pH = 2) could spread over
 10 a small area on the aqueous/LC interface. Also, the connected hydrophobic poly(4-
 11 cyanobiphenyl-4-oxyundecylacrylate) (LCP) block might be miscible with 5CB, so that there
 12 are extensive interactions between 5CB and the LCP block (see Fig. 8, left). The LCP block
 13 (perpendicular to the main chain) would therefore be parallel to the interface, increasing the
 14 usual assembling ability at an aqueous/LC interface. However, the expanded coil of the PAA
 15 block (e.g., at pH = 12) would spread over a larger area on the interface, and the connected
 16 LCP block might relax and adopt an oblate configuration, resulting in LCs vertical to the
 17 interface (Fig. 8, right).³³



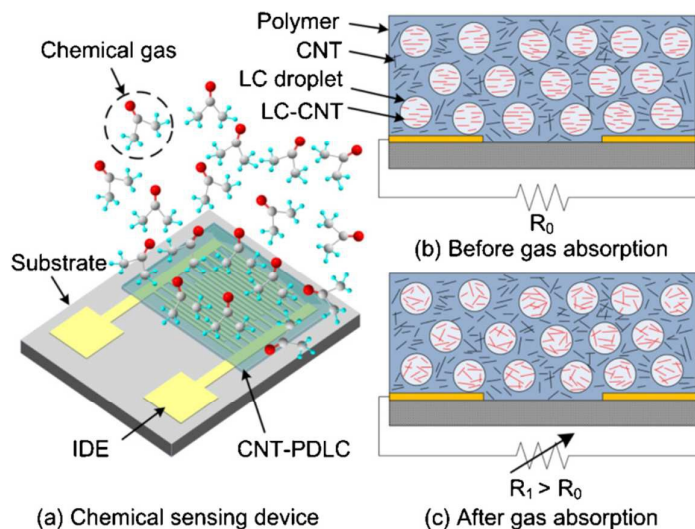
19 Fig. 8 A schematic diagram of director orientation in a cell, indicating the conformation of the polyacrylic acid
 20 (PAA)-b-poly(4-cyanobiphenyl-4-oxyundecylacrylate) (LCP) on an aqueous 5CB interface at pH 2 (left) and pH
 21 12 (right). Reprinted with permission from ref. 33. Copyright (2010) Royal Society of Chemistry.

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2 **4.3. Electro-optical responses to polymer-encapsulated LCs**

3 Electro-optical devices based on two- and three-dimensional arrays of polymer-
4 encapsulated nematic LCs have been developed for large area flexible displays on plastic
5 substrates.^{43, 52-54} The polymer-dispersed LC (PDLC) devices switch reversibly between
6 strongly scattering and transparent states by the application of large electrical fields in the
7 droplets. In the off-state, the PDLC appears opaque as they strongly scatter light due to a
8 mismatch of the refractive index between the LC droplets and the polymer matrix. In the
9 presence of an electrical field, however, PDLCs becomes transparent because they allow light
10 to pass due to matching of refractive indices of the LC and polymer.⁵⁵ Yu-Tse Lai et al.⁵⁶
11 reported a novel gas detector that uses a sensing film consisting of a PDLC doped with
12 carbon nanotubes (CNT) for acetone detection (see Fig. 9). Fig. 9b shows a schematic
13 representation of the CNT orientation in the CNT-PDLC-sensing film before chemical gas
14 absorption. The orientations of CNTs and LC molecules are aligned parallel to the substrate
15 because the LC media normally are strongly anchored to the CNT surface.⁵⁷ Consequently,
16 the concentrations of chemical or biological agents that change the orientation of the LCs can
17 be detected by measuring the conductivity of the CNT-LC material along a specific direction.
18 Therefore, as shown in Fig. 9c, the gas molecules permeate through the CNT-PDLC film, and
19 when the sensor is exposed to these gas molecules, the gas molecules destroy the alignment
20 of the LC phase, resulting in an isotropic liquid phase. The gaseous acetone can be easily
21 detected by measuring the changes in the electrical resistance of the sensing film. A linear
22 sensor response was achieved for gas concentrations from 100 ppm (0.65% resistance change)
23 to 1500 ppm (20.15% resistance change) and the response time was approximately 32 s.
24 Hence, PDLCs have been developed as a shear stress sensor that offer many advantages over
25 conventional single-point measurement systems, offering an ideal 2-dimensional mapping of
26 shear stresses across a surface and showing a great signal-to-noise ratio with a high temporal
27 bandwidth. Furthermore, the PDLCs allow for a reversible sensor that is self-adherent to
28 testing surfaces.⁵⁸⁻⁶⁰

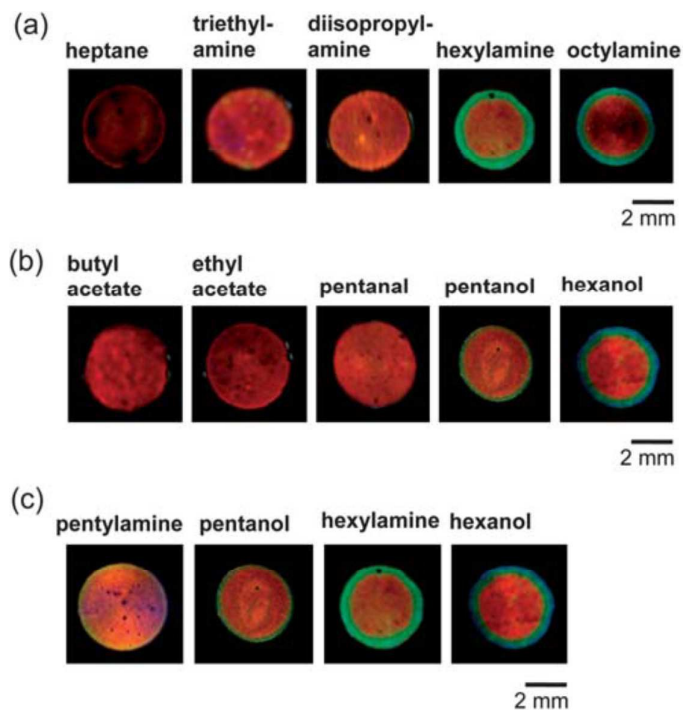
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2 Fig. 9 Schematic diagram of (a) carbon nanotube (CNT)-polymer-dispersed liquid crystal (PDLC) chemical
 3 sensing device, (b) random LC droplets in a polymer and the orientation of CNT-LC, and (c) the sensor reactions
 4 when the CNT-PDLC material absorbs chemical gas. The CNT-conducting networks within the CNT-PDLC film
 5 are rearranged. Reprinted with permission from ref. 56. Copyright (2014) The Institute of Electrical and
 6 Electronics Engineers.

7 Cholesteric liquid crystal (CLC) is a type of the nematic liquid crystal, in which the LC
 8 molecules are ordered in a helical pattern.^{61, 62} It is well known that CLCs have a unique
 9 optical property, selective reflection in a wavelength due to their helical structure.⁶³ When the
 10 wavelength of the reflected light corresponds to the visible light, the CLC appears iridescent
 11 colors to the naked eye.⁶⁴ Past studies have demonstrated the utilization of functional CLCs
 12 as portable and low-cost detection methods for volatile organic compounds (VOCs).^{65, 66}
 13 Sutarlie et al.⁶⁷ reported the utility of a colorimetric polymer stabilized cholesteric liquid
 14 crystal (PSCLC) array for detecting vaporous amines. The addition of polymer supports the
 15 fluid CLC and increases its portability. The PSCLC with miscellaneous polymer
 16 concentrations (5–20% w/w) is made into an array which shows visible color changes upon
 17 exposure to 400 parts-per-million (ppm) octylamine vapor at 23–35 °C. Intriguingly, PSCLC
 18 shows stronger response to vapors through hydrogen bonding with cholesteryl derivatives
 19 such as primary amine over secondary amine, tertiary amine, ester, aldehyde, and alkane
 20 having similar molecular weights (Fig. 10). Thin films of PSCLC also show capability to
 21 detect vapor with faster response times and better reversibility at room temperature. Hence,
 22 they can be coated on windows or safety goggles to offer real-time, power free protection
 23 against amine vapors.



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2 Fig. 10 Response of PSCLC (20% NOA61) to a variety of organic vapors at 400 ppmv including (a) alkane and
 3 various amines; (b) esters, aldehyde, and primary alcohol vapors. (c) Comparison of the colorimetric response of
 4 PSCLC (20% NOA61) to primary amine and primary alcohol vapors of similar molecular weight at 400 ppmv.
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6 In addition, Sutarlie et al.⁶⁸ reported a new sensing utilization of a thin layer of a polymer
 7 dispersed cholesteric liquid crystal (PDCLC) or a free CLC separated from the microfluidic
 8 device by using a thin film of poly(dimethylsiloxane) (PDMS) for monitoring ethanol inside
 9 microfluidic channels. They show distinct colorimetric response to ethanol solutions with a
 10 detection limit of 4% (v/v). These microfluidic channels with embedded PDCLC or
 11 embedded CLC also have potential for detecting other VOCs which are difficult to detect by
 12 using other chemical sensors.

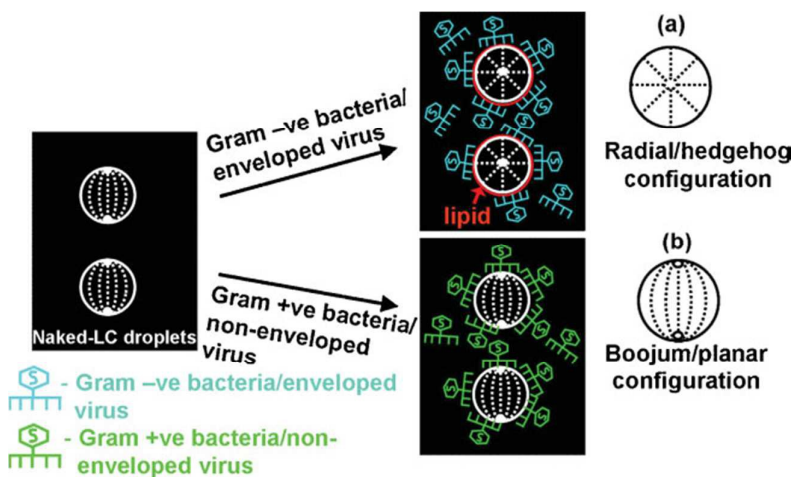
13 5. LCs and biosensors

14 5.1. Detection of microorganisms

15 Brake et al.¹⁶ demonstrated the detection of biomolecular interactions at fluid interfaces
 16 decorated with self-assembled phospholipid monolayers between LCs and aqueous solutions.
 17 Specific binding and enzymatic events could cause reorganization of the phospholipid
 18 membranes and result in a change in the orientation of the LCs. Additionally, poly(allylamine
 19 hydrochloride) (PAH)/poly(styrenesulfonate sodium) (PSS) multilayer-coated LC droplets

1 have been used successfully in detection of lipid-enveloped viruses.⁶⁹ The orientational
 2 transition in the LC is due to the transfer of lipids from the viruses to the PAH/PSS
 3 multilayer-coated LC droplets (Fig. 11).

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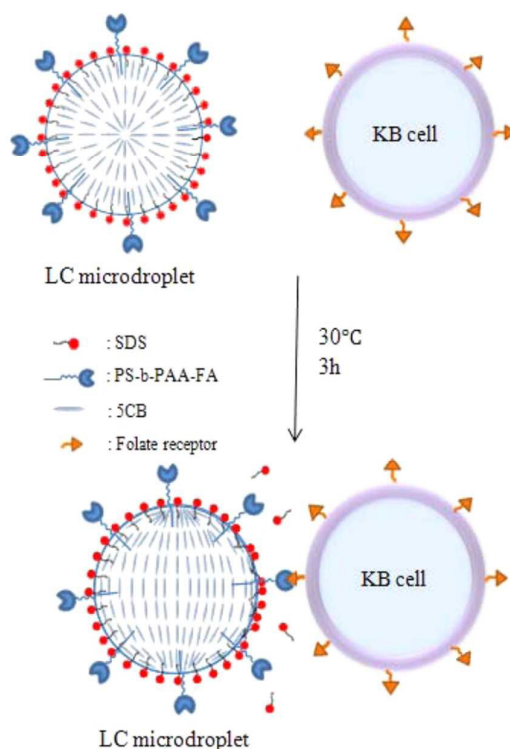
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6 Fig. 11 Schematic representation of the interaction of viruses or bacteria with naked LC emulsions. The cartoons
 7 depict a) radial and b) bipolar configurations of LC droplets. Reprinted with permission from ref. 69. Copyright
 8 (2009) John Wiley and Sons.

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10 Interfacial interactions have been a basis for molecular screening of diseases, toxins in
 11 food, narcotics in blood, and novel drugs. Most of these interfacial interactions and events
 12 depend on the immobilization of specific proteins that control ligand-receptor interactions
 13 (Fig. 12).^{70, 71} Yoon et al.⁷² reported a ligand-receptor interaction sensor for detection of KB
 14 cancer cells (mouth epidermal carcinoma cells). 5CB LC molecules were encapsulated by
 15 folic acid-conjugated block copolymers (PS-b-PAA-FA) and sodium dodecyl sulfate (SDS)
 16 as a mediator to cause an orientational change from radial to bipolar when contacted with KB
 17 cells, which has a specific folate receptor on its membrane as shown in Fig. 12. In addition, to
 18 confirm the selectivity of folate ligand-anchored 5CB microdroplets for recognition of KB
 19 cancer cells in the presence of other control cells, a set of co-cultured experiments was done
 20 in a phosphate-buffered saline solution (PBS, pH 7.4) at 30 °C in the presence of 5% CO₂ for
 21 3 h by incubating LC microdroplets with KB cancer cells with a mixture of fibroblast (FB)
 22 and osteoblast (OB) cells, which were stained with methylene blue to distinguish⁷³ them from
 23 KB cancer cells (Fig. 13). The interaction of a KB cell (white) with a LC microdroplet

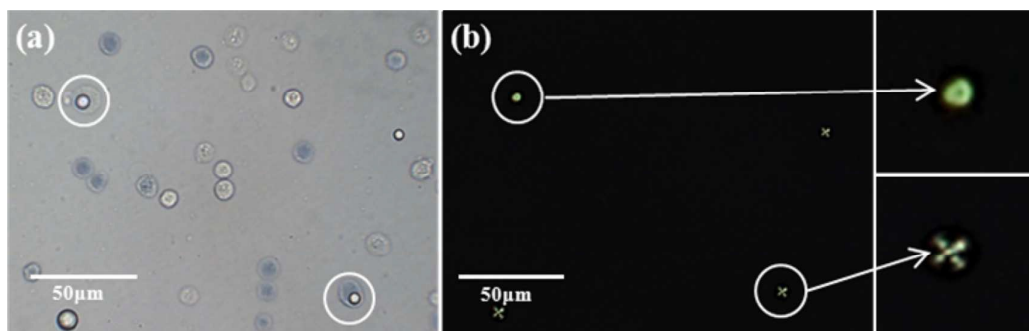
1 induced the orientational transition from radial to bipolar is shown by the circle on the top
 2 side of the micrograph in Fig. 13a and 13b, whereas the interaction of control cells (blue)
 3 with LC microdroplets remained ineffective in inducing any orientational transition in LC
 4 microdroplets as shown by the circle on the bottom of the micrograph. Thus, folate ligand-
 5 anchored LC microdroplets have shown a potential for use in in-vitro detection of KB cancer
 6 cells in the early stage of tumor development.



7

8 Fig. 12 KB cancer cell (mouth epidermal carcinoma cell) interactions with LC microdroplets containing folic acid-
 9 conjugated block copolymers (PS-b-PAA-FA). Reprinted with permission from ref. 72. Copyright (2014)
 10 American Chemical Society.

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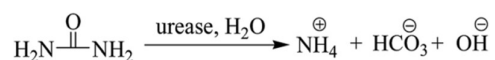
12 Fig. 13 (a) Bright field micrograph of LC microdroplets incubated for 3 h with KB cancer cells (mouth epidermal

1 carcinoma cells) and methylene blue-stained fibroblast (FB) and osteoblast (OB) cells. The contact of LC
2 microdroplets with KB cells is shown by circles at left top and methylene blue-stained FB or OB cells at bottom
3 right, and (b) polarized light micrograph of LC microdroplets ($2.1 \times 10^6/\text{mL}$) after contact for 3 h with KB, FB, and
4 OB cells at a total density of 8000 cells/mL in 1:1:1 ratio. The polarized light micrograph of LC microdroplets after
5 contact with KB cells for 3 h showed a bipolar configuration (left top circle) and a radial configuration after contact
6 with FB or OB cells (right bottom circle). Conditions of tests: temperature 30 °C, pH 7.4 and medium PBS for all
7 images. Reprinted with permission from ref. 72. Copyright (2014) American Chemical Society.

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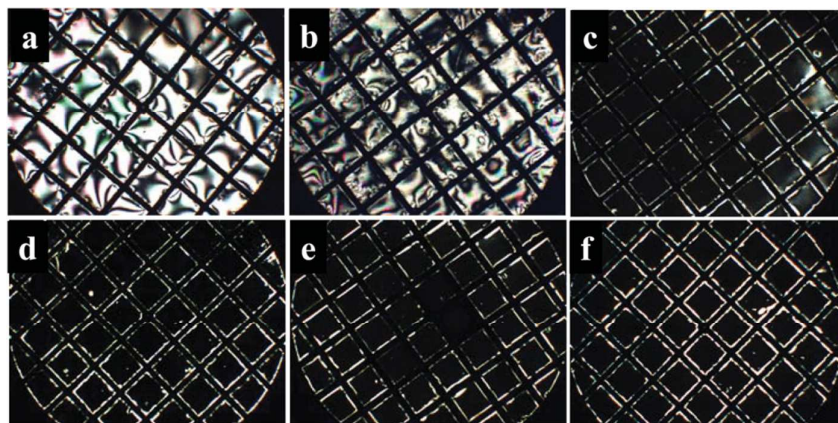
9 5.2. Detection of biomolecules

10 The long-range orientational ordering transition and fluidity of LCs triggered by the
11 response of the assembled molecules at the LC/water interface to external stimuli has
12 received a great deal of attention due to its application to biosensors. Surfactant-decorated
13 LC-based sensors have been developed to detect competitive binding of cholic acid,⁷⁴
14 specific enzymatic reactions,⁷⁵⁻⁸¹ protein absorption,⁸²⁻⁸⁵ environmental pollutants,^{86, 87}
15 antigen-antibody immunoassay,^{1, 88, 89} DNA hybridization^{90, 91} and DNA interaction with
16 immobilized oligonucleotides.^{92, 93} Mashooq Khan⁹⁴ reported a LC-based urea biosensor
17 functionalized with mixed PAA and 4-cyanobiphenyl-4-oxyundecylacrylate brushes, which
18 was tested for stability, enzyme activity (see Scheme 1), and sensitivity towards urea
19 detection. A transmission electron microscopy (TEM) grid filled with 5CB on an
20 octadecyltrichloro silane-coated glass substrate in aqueous media was prepared and then
21 coated with poly(acrylic acid-b-4-cyanobiphenyl-4-oxyundecylacrylate) (PAA-b-LCP) at the
22 aqueous/LC interface at which immobilizing urease was covalently bound to the PAA chains.
23 Urea was detected from the planar-to-homeotropic (P–H) orientational transition of 5CB
24 molecules at concentrations as low as 5 mM by polarized optical microscopy with crossed
25 polarizers (Fig. 14).



26
27 Scheme 1 Hydrolysis of urea by urease.

28



1

2 Fig. 14 Polarized Light Microscopy (POM) images of transmission electron microscopy (TEM) grids under
3 crossed polarizers with different urea concentrations (C_0 s) of (a) 2, (b) 3, (c) 5, (d) 8, (e) 20, and (f) 80 mM.
4 Reprinted with permission from ref. 94. Copyright (2014) Royal Society of Chemistry.

5

6 The immobilized proteins can have random or well-defined orientations depending on the
7 physical binding/chemical linkages between the functionalized surfaces and the proteins.
8 However, a well-defined orientation of the protein is found useful to prevent denaturation and
9 preserve the biological functions of the immobilized proteins.^{78, 95, 96} Well-defined proteins
10 are immobilized in a number of ways such as i) chemoselective immobilization via
11 Staudinger ligation, Diels-Alder cycloaddition reactions, or native chemical ligation, and ii)
12 fusion protein immobilization via popular fusion tags. The orientations of LCs are very
13 sensitive to minute changes on the surfaces, which can be amplified to the LC bulk phase up
14 to 100 μm within tens of milliseconds, and the orientation of the birefringence can be readily
15 seen under crossed polarizers.²¹

16

17 6. Conclusion

18 LC materials and technology can contribute to the assembly of label-free, high-sensitivity
19 real-time detectors without the need for complex and expensive instrumentation. LC
20 materials have been found to be simple, convenient, and efficient in making sensing devices
21 for transduction of various chemical and biological events into optical responses visible by
22 the naked eye. LC-based sensors were found to be useful in a variety of sensing applications
23 under ambient light conditions, including the detection of environmental pollutants,
24 enzymatic reactions, protein interactions, ligand-receptor interactions, antigen-antibody

1 immunoassay interactions, and DNA hybridization. LC-based sensing techniques are simple
2 and useful for development of portable, low-cost screening assays for rapid evaluation of
3 samples away from the central laboratory.

4

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9



Ding Wang

Ding Wang is an engineering graduate student at the School of Applied Chemical Engineering, Major in Polymer Science and Engineering, Kyungpook National University. She received her BS degree in the School of Chemistry and Materials Science at Nanjing Normal University. In fall 2013, she began her graduate studies with Prof. Inn-Kyu Kang. Her research interest lies in the application of liquid crystal biosensor.



Soo-Young Park

Soo-Young Park is a professor in the Department of Polymer Science and Engineering at the Kyungpook National University (KNU). He obtained his Ph.D. degree in the Department of Macromolecular Science at the Case Western Reserve University in 1998, and joined in the Department of Polymer Science and Engineering at the KNU in 2002 as a professor. He is currently a director of Polymeric Nano Materials Laboratory (PNML) and a principal investigator of Basic Research Laboratory (Ultra-

1 sensitive LC-based Sensors) sponsored by Korean Research Foundation. He has published
2 more than 120 articles and his research is focused on structure analysis using
3 WAXS/SAXS/SANS, nanocomposites, and liquid crystal sensors.



Inn-Kyu Kang

Inn-Kyu Kang is a professor of Department of Polymer Science and Engineering at the Kyungpook National University. He obtained his Ph.D. degree in Polymer Chemistry Department at Kyoto University in 1987, and joined in the Department of Polymer Science and Engineering, Kyungpook National University in 1988 as a professor. He is currently a director of Center for Intelligent Hybrid Nanomaterials and Processes supported by the Brain Korea 21+ National Program. He has published more than 190 articles and his research is focused on surface modification, nanofiber scaffolds, functionalization of nanoparticles, and liquid crystal sensors.

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