

Liquid Crystals in Medical Applications

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Abstract—Over the past several decades, liquid-crystal (LC) technology has developed rapidly and found applications across a wide range of industries. Its best-known application is in liquid-crystal displays (LCDs). Liquid crystals exhibit properties intermediate between those of conventional liquids and crystalline solids, and many LC materials are stable under suitable storage conditions. This review focuses on the medical and biomedical applications of liquid crystals, with particular emphasis on LC-based biosensors. It introduces the basic concepts, types, and key properties of liquid crystals before discussing their use in biosensing and the detection of biological and chemical targets.

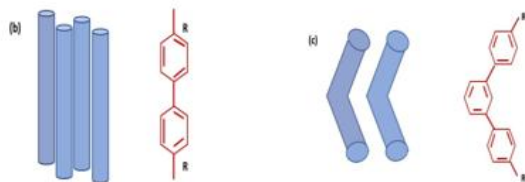
Index Terms—Biomedical applications, liquid crystals, biosensors, 5CB.

I. INTRODUCTION

The study of liquid crystals began in 1888, when Austrian botanist Friedrich Reinitzer observed unusual melting behaviour in cholesteryl

(a) Discotic (b) Calamitic (c) Bent core

Fig. 1. Schematic representation of the molecular geometries of liquid crystals: (a) disc-like or discotic, (b) rod-like or calamitic, and (c) bent-core.



benzoate. Otto Lehmann subsequently investigated these materials and helped establish the concept of the liquid-crystalline state.

During his experiments, Reinitzer heated a solid sample and observed that it first changed into a cloudy liquid and, with further heating, became a clear liquid. The cloudy state represented an intermediate phase

between the crystalline solid and the conventional liquid.

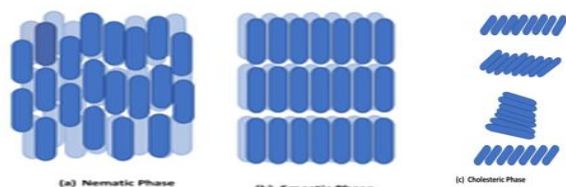
Liquid crystals (LCs) are fascinating materials because they combine certain characteristics of liquids with some of the ordered properties of crystals.

Liquid crystals may be described as a state of matter that exhibits optical anisotropy, similar to crystalline solids, while retaining fluidity, as in isotropic liquids. Their molecules tend to align along a preferred direction, represented by the director, n . Liquid-crystalline behaviour is often associated with molecular shape anisotropy. Common molecular geometries include rod-like (calamitic), disc-like (discotic), and bent-core structures, as illustrated in Fig. 1. Calamitic liquid crystals have been widely studied because of their importance in both fundamental research and technological applications. Disc-like molecules form discotic liquid crystals, whereas bent or banana-shaped molecules form bent-core liquid crystals.

Liquid crystals are commonly classified as thermotropic or lyotropic. Thermotropic liquid crystals exhibit liquid-crystalline phases over particular temperature ranges. Lyotropic liquid crystals form ordered phases when a suitable solvent is added; their phase behaviour depends on concentration as well as other conditions. Systems in which the liquid-crystalline phase changes with solute concentration are therefore described as lyotropic.

Thermotropic liquid crystals may also be classified according to molecular size and architecture. High-molar-mass liquid crystals include main-chain and side-chain liquid-crystalline polymers. Low-molar-mass liquid crystals commonly include rod-like (calamitic) and disc-like (discotic) molecules. Thermotropic calamitic liquid crystals can exhibit several mesophases, including (i) nematic, (ii) chiral nematic (cholesteric), and (iii) smectic phases,

depending on their molecular organization. Nematic and chiral nematic phases primarily exhibit orientational order, whereas smectic phases also possess a degree of positional order. The chiral nematic phase is the chiral counterpart of the nematic phase.



(a) Nematic (N) (b) Smectic (S) (c) Cholesteric

Fig. 2. Schematic representation of the nematic, smectic, and cholesteric mesophases of thermotropic calamitic liquid crystals.

II. BASIC PROPERTIES OF LIQUID CRYSTALS

Liquid crystals occupy an intermediate state between an anisotropic crystalline solid and an isotropic liquid. They can flow like liquids while maintaining a degree of molecular order similar to that of crystals. Two important properties relevant to their applications are dielectric anisotropy and optical anisotropy.

2.1. Dielectric Anisotropy

Dielectric anisotropy describes the directional dependence of a material's dielectric response. In liquid crystals, it determines how the molecules respond to an applied electric field and whether the director tends to align parallel or perpendicular to that field.

2.2. Optical Anisotropy

Optical anisotropy occurs when a material's refractive index depends on the direction of light propagation and its polarization. In liquid crystals, this property gives rise to birefringence and enables optical detection of changes in molecular orientation.

III. MEDICAL APPLICATIONS OF LIQUID CRYSTALS

Liquid crystals have a broad range of applications in medical devices, biomedical imaging, and sensing.

3.1. Medical Displays

One of the most established applications of liquid-crystal technology is the liquid-crystal display (LCD).

LCD technology is used in many devices, including medical instruments and monitors, as well as calculators, thermometers, and telecommunications equipment.

3.2. Liquid-Crystal Lasers

Lasers are important tools in clinical practice and biomedical research. Liquid-crystal lasers may offer tunable emission and could support the development of diagnostic instruments and tunable medical lasers. Broadly tunable LC lasers can operate across a range of wavelengths, potentially overcoming the limited spectral ranges of some conventional laser systems.

3.3. Biomimicry Using Liquid Crystals

Biomimicry involves reproducing structures or functions found in nature. Liquid crystals are promising materials for biomimetic systems because their molecular organization can be controlled by electric fields, polarization conditions, and temperature. These characteristics make them useful for designing responsive structures that imitate selected biological functions.

3.4. Liquid Crystals in Spectroscopy and Microscopy

Biomedical spectroscopy and imaging are important tools in clinical investigations and research. Liquid-crystal devices, including variable retarders, wave plates, and optical filters, have been incorporated into spectrometers and imaging systems. These components can improve system functionality and measurement precision and may enable more compact optical arrangements.

3.5. Liquid-Crystal Biosensors

In 1998, Abbott and colleagues demonstrated that liquid crystals could translate antigen-antibody interactions at a liquid-crystal/solid interface into a visible optical response. This work helped establish an important direction in the development of LC-based biosensors [1, 2].

In 2002, the Abbott group reported that sodium dodecyl sulfonate, an amphiphilic molecule with a long alkyl chain, could adsorb at an LC-aqueous interface and induce a vertically aligned LC arrangement [3]. This finding contributed to the development of biosensors based on LC-aqueous interfaces [4]. Liquid crystals can therefore act as optical transducers for detecting biological and

chemical species, providing a visual sensing approach with potential applications across a range of targets.

3.5.1. Liquid-Crystal Detection Techniques and Principles

Liquid-crystal sensing commonly relies on birefringence, a manifestation of optical anisotropy [2]. A schematic of LC-biosensor detection is shown in Fig. 3. When the liquid-crystal molecules are vertically aligned under suitable crossed-polarizer conditions, the field of view can appear dark. If an interaction with a target molecule disrupts this alignment, the resulting birefringence changes the transmitted light intensity or colour. These optical changes can be observed using a polarized optical microscope and used to indicate the presence of target molecules. Two commonly discussed sensing formats are:

- 1) LC–solid interface sensing
- 2) LC–aqueous interface sensing

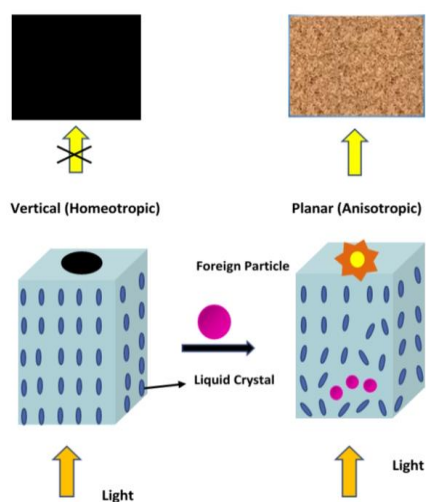
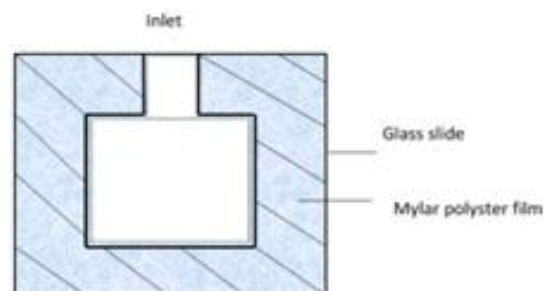


Fig. 3. Schematic representation of liquid-crystal biosensor detection.

3.5.2. LC–Solid Interface Sensing and Its Principle

This approach uses a liquid-crystal cell assembled from glass slides and a Mylar polyester spacer film. An inlet is formed along one side of the spacer to allow the liquid-crystal material to be introduced, as illustrated in Fig. 4.

Fig. 4. Schematic representation of an LC cell used for LC–solid interface sensing.



In LC–solid interface sensing, the surface is first prepared to establish a defined molecular alignment. A substrate is then introduced at the relevant interface, and target molecules are brought into contact with the surface. Interactions between the target molecules and the substrate can disturb the anchoring and orientation of the liquid crystals. This change may produce a visible variation in brightness or colour, which can be used to investigate the target–surface interaction.

3.5.3. LC–Aqueous Interface Sensing and Its Principle

An LC–aqueous interface sensor typically consists of a glass microscope slide, a transmission electron microscopy (TEM) grid or mesh, liquid-crystal material, and a buffer solution for sample analysis.

The glass slide is coated with an alignment agent such as DMOAP (N, N-dimethyl-N-octadecyl-3-aminopropyltrimethoxysilyl chloride), and the TEM mesh is positioned on the prepared surface.

The liquid crystal is introduced into the mesh to form a thin layer. When suitable surfactants, such as phospholipids, promote homeotropic alignment, the observed image may appear dark under crossed polarizers. If target molecules or enzymatic activity alter the interfacial phospholipids, the LC alignment can be disrupted, producing a change in colour or brightness. This response can be used to detect phospholipase activity [5].

3.5.4. Preparation and Alignment of the LC Substrate

Appropriate surface preparation is essential for obtaining a uniform, dark background and reproducible LC alignment. Liquid crystals are sensitive to surface chemistry, topography, and contamination. Methods reported for preparing alignment substrates include (i) obliquely deposited gold films [6, 7], (ii) mechanically rubbed films [8],

and (iii) silanization-based methods [9]. Gold-film preparation can require specialized procedures; mechanical rubbing is a traditional alignment technique but may generate dust or surface debris. Silanization-based approaches are also widely used because they can provide a relatively straightforward means of controlling surface anchoring.

IV. IMPLEMENTATION OF LIQUID-CRYSTAL DETECTION

In recent years, LC-based sensing has been investigated for the detection of cancer cells, infectious agents, small molecules, proteins, DNA, metal ions, and other analytes.

4.1. Detection of Cancer Cells, Viruses, and Bacteria
Yoon and colleagues [10] used an emulsion of 5CB liquid-crystal microdroplets (LCME), exhibiting radial (R) or bipolar (B) configurations, to investigate the detection of KB cancer cells. The interaction between the cells and ligand-functionalized LC droplets was used to generate an optical response [11]. The approach exploits the presence of folate receptors on KB cells and the corresponding recognition by folate ligands.

Choi and colleagues [12] also investigated LC microdroplet emulsions for distinguishing Gram-positive from Gram-negative bacteria and for detecting enveloped and non-enveloped viruses. Interactions involving Gram-negative bacteria and enveloped viruses were associated with changes in LC orientation, including a transition from bipolar to radial configurations. These changes were attributed to lipid transfer from the biological material to the LCME interface.

This sensing approach has been investigated for rapid analysis of different bacteria. The cited studies report detection of small quantities of *E. coli* and viral concentrations as low as 10^4 PFU mL⁻¹ [11]. These values are reported here as described in the cited work. Zafiu and colleagues [13] described a bacterial-sensing approach based on interactions between liquid crystals and lipopolysaccharides (LPS). The LPS–LC system was reported to detect several types of pathogens, with a stated detection threshold of 500 units mL⁻¹ and a detection time of up to 15 minutes. In this approach, liquid crystals act as optical amplifiers of interfacial changes associated with microbial components.

4.2. Detection of DNA and Proteins

Proteins and enzymes play important roles in biological systems, and their detection is relevant to biomedical analysis. Hartono and colleagues [14] developed an LC-based platform for studying phospholipases through molecular interactions at aqueous–LC interfaces. The method was used to identify phospholipase A₂, phospholipase C, and phospholipase D, providing a means of assessing phospholipase activity [2].

Hartono and colleagues [15] subsequently applied a related sensing strategy to beta-bungarotoxin, a toxin with phospholipase-like activity. Hydrolysis of interfacial lipid layers can alter LC alignment and produce a measurable optical response. The cited study reported detection below 5 pg [11]. Such approaches may provide relatively simple, label-free methods for investigating toxins and screening potential inhibitors; their practical performance should be assessed in the context of the specific assay conditions.

LC-based sensing strategies have also been investigated for enzymes such as urease [16, 17], trypsin, catalase, and acetylcholinesterase [18, 19]. In these systems, analyte-dependent changes in the orientation or configuration of 5CB can provide an optical signal. Although these methods show promise for label-free detection, further work is needed to establish their robustness and suitability for practical applications.

Other studies have used 5CB-based biosensors to detect bovine serum albumin (BSA), haemoglobin (Hb), and chymotrypsinogen (ChTg) [11]. The sensing mechanism involved electrostatic interactions between biomolecules and a polyelectrolyte–liquid-crystal block copolymer, poly (2-dimethylaminoethyl methacrylate)-b-(4-cyanobiphenyl-4'-oxyundecyl acrylate) (PDMAEMA-b-LCP). A change in the 5CB alignment from homeotropic to planar was observed at concentrations above 0.02 wt.% under pH conditions between the isoelectric point of BSA and the pK_a of PDMAEMA. Hb and ChTg were also investigated at different pH values using related methods [20].

4.3. Detection of Small Molecules and Ions

Glucose is an important monosaccharide in biological systems, making its detection valuable in biomedical analysis. LC-based glucose biosensors commonly use the specific reaction between glucose oxidase (GOx)

and glucose. Khan and Park [21, 22] reported an LC-based glucose sensor in which a change in 5CB alignment, from vertical to parallel, was observed using a polarized microscope. The reported glucose detection limit was 0.5 mmol L^{-1} , with a response time below 180 s [11]. In subsequent work, GOx and horseradish peroxidase (HRP) were combined on a PAA-b-LCP copolymer to develop a dual-enzyme LC biosensor. The reported GOx:HRP molar ratio was 3:1, and the detection limit was reduced to 0.02 mmol L^{-1} compared with the GOx-only system [23].

Bisphenol A (BPA), a chemical found in some consumer products, has structural features that have raised concerns about its potential to mimic hormone activity. Jang and colleagues developed an LC biosensor for BPA based on the specific interaction between BPA and an aptamer [11].

Park and colleagues [24] reported an LC-based sensor for detecting Ca^{2+} in human saliva. In this system, a PAA-b-LCP compound was incorporated at the 5CB interface and affected the anchoring of the liquid crystal [11]. In a NaCl-containing cell, Ca^{2+} could replace Na^+ associated with the PAA chains, changing the LC orientation from vertical to parallel. This orientation change provided the basis for Ca^{2+} detection.

4.4. Other Liquid-Crystal-Based Sensing Techniques
Conventional LC biosensors mainly use optical anisotropy or birefringence to generate signals at LC–solid or LC–aqueous interfaces. More recently, capacitance, electro-optical, and dielectric measurements have also been explored. Lin and colleagues [25] described a capacitive biosensor in which the LC layer was treated as a parallel-plate capacitor. DMOAP was used to promote homeotropic alignment. In the presence of BSA, interactions at the surface weakened the anchoring and disturbed this alignment; an applied electric field was then required to restore the homeotropic state. The voltage needed for realignment was related to the amount of BSA, providing a basis for quantification. Related studies have also examined electro-optical [26] and dielectric [27] LC biosensors.

These studies broaden the range of methods available for LC-based biosensing. Combining optical observations with electrical, electro-optical, capacitive, and dielectric measurements may help address some of the limitations of texture-based

detection and support the development of more versatile biosensors.

V. CONCLUSION

Over the past two decades, LC biosensors have been investigated for the detection of biological targets, including viruses, bacteria, proteins, amino acids, and DNA, as well as small molecules and ions such as glucose, folic acid, and metal ions. Further research is needed to evaluate additional liquid-crystal materials beyond the widely used 5CB and to expand the range of sensing architectures. In particular, the electrical, electro-optical, and dielectric properties of liquid crystals may provide complementary routes to developing new sensors. With further validation of sensitivity, selectivity, reproducibility, and practical performance, LC-based biosensors may contribute to future advances in biomedical detection.

VI. CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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