Biosensing Using Liquid Crystals*

Ariba Parveen and Jai Prakash

Liquid crystals (LCs) based biosensors are promising systems to detect several bioanalytes and diseases as they are simple yet highly sensitive, and low-cost. These biosensors are based on the ordering transformations of LC molecules due to the specific binding of molecules. In this article, we present the principle and fabrication process of LC-based biosensors and their signal detection by probing different interfacial interactions. Compared to conventional biosensors available, LC-based biosensors provide rapid, cost-effective, and selective detection of various chemicals and biological analytes for better healthcare.

1. Introduction

Liquid crystals (LC) refers to an intermediate state between highly ordered crystalline solids and isotropic liquids. It is also known as ‘mesophase’ or ‘mesostate’. LCs share several common characteristics with both solids and liquids. While macroscopically, they look like liquids, at a microscopic level, they possess some order between their molecules [1]. Such materials have very interesting optical properties as they are birefringent\(^1\) in nature [2]. If we look intrinsically at the LC materials, they evince different other phases due to the orientation-dependent and non-covalent interactions between molecules. There are several emerging applications of LCs because of their adequate molecular order units, high sensitivity to temperature, external electric and magnetic fields, light, mechanical shear, surface interactions, etc., [3, 4]. Due to their ability to self-assemble through changes in their orientational parameters, LCs can be reorganized and find applications in modern

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Apart from all these applications, from the last few years, it can be used as a biosensor to detect and sense different bioanalytes such as DNAs, glucose, bacteria, viruses, specific proteins, etc., and their interaction with other analytes in case of severe diseases and health issues—in human beings as well as plants. A biosensor is an analytical sensor that can detect different types or species of biological analytes. Various analytical biosensors have been developed based on the principle of transferred biological response in the form of measurable signals. LC-based biosensors are based on the absorption/desorption of the LC molecules at the interface due to molecular interactions. Compared to traditional conventional methods, biosensors provide high sensitivity, selectivity, and label-free detection of the analytes without the help of any other complicated methods and instruments. Different biological substances such as glucose, bile acid, cholesterol, endotoxins, urea, DNA molecules, etc., and several diseases such as cancer, stroke, blood pressure, etc., have been sensed using such LC-based biosensors [6–9]. This type of biosensor fabricates easily as it consumes only a low electric power in detection process, and are cost-effective, simple, and well-suited for the advanced world [10]. The detection mechanism basically depends on the optical appearances/textures and electrical signals. Scientists are also working on detection through dielectric spectroscopic techniques. This article describes the advancements in LC-based biosensors using different strategies and techniques and through the development in the detection limit.

Detection Methods of LC-based Biosensors

LC-based biosensors use the characteristics of birefringence, optical anisotropy, and the obtained spectra to sense the presence of different bioanalytes. A novel LC-based biosensor is available to detect plant pathogens using dielectric spectroscopic tech-
niques [11]. Almost all the biosensors based on LCs depend on the change in the orientation alignment at different interfaces such as LC-aqueous interfaces [12], LC-solid interfaces [13], etc.

(i) Dielectric Measurement

Plant pathogen detection through LC-based biosensors is very advantageous and helpful in the agriculture sector. Nematodes are plant pathogenic, free-living roundworms. They are abundant in nature and cause severe diseases in plants. While resisting nematode-infection, the productivity of the crops reduces, and so does the quality of fruits. We recently developed a LC-based biosensor that detects root-knot nematodes (Meloidogyne species) infection in cowpea (Vigna unguiculata) [11]. The principle behind this type of sensor is the realignment of the LC molecules due to interaction with fresh and infectious plant extract. Dielectric studies were performed for different samples cells that are made with pure nematic LC (NLC)\(^2\) material namely ZLI; mixtures with NLC with fresh and diseased plant extract. The dielectric variations observed in the samples are illustrated in Figure 1(a)–(c).

As demonstrated from Figure 1, in the case of pure ZLI, the value of dielectric permittivity is around 4, which is nearly the same as the value for the composites of ZLI/fresh plant extract. When the dielectric permittivity is measured for the mixture of ZLI/infectious plant extract, there is a drastic change (clearly reflected in Figure 1(a)). This change is detected due to the infectious extract present in the mixture that changes the ordering of NLC molecules, and the dielectric permittivity increases abruptly. The loss factor and absorption in different samples are also illustrated accordingly (Figure 1(b)–(c)). This comparative study can be used to detect other hazardous pathogens. Based on this principle, some futuristic portable and label-free biosensors can be designed for food safety and quality purposes.

(ii) Optical Detection at LC-Solid Interfaces

Our group has fabricated an LC-solid interface-based biosensor to detect cholesterol [14]. This work is based on the principle that the LC materials are sandwiched between two glass plates

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\(^2\)Nematic LC (NLC) is the simplest LC phase, which is characterized by only long-range orientational order with no positional order. The orientational ability of the director of NLCs under the external applied electric, as well as, magnetic fields coupled with other interesting features such as low power consumption and large cell gap tolerance make them potential candidates for various display applications.

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Our group has fabricated an LC-solid interface-based biosensor to detect cholesterol.
Figure 1. (a) Dielectric permittivity, (b) Dielectric loss factor, (c) Dielectric absorption for pure ZLI, ZLI with fresh plant, and ZLI with nematode affected plant at room temperature (Adapted with permission from [11]).

3In which the molecules are aligned perpendicular to the substrates.

coted with different substrates and enzymes. Different concentrations of cholesterol are loaded on the self-assembled monolayer (SAM) surfaces, and cells are made by joining two glass plates (with coated side). LCs are filled inside these sample cells for further investigations. The schematic representation of the whole biosensing procedure is represented in Figure 2.

From Figure 2, it is reflected that the alignment of LC depends on the different substrates and enzymes coated. When the glass plate is coated with dimethyloctadecyl[3-(trimethoxysilyl)propyl]ammonium chloride (DMOAP) and (3-aminopropyl)trimethoxy-silane (APTMS) film, a homeotropic\(^3\) alignment in NLC, namely 4’-pentyl-4-biphenylylacetonitrile (5CB) molecule is observed, and no light passes through the LC cell (Figure 2(a)). The dark background is detected through the polarizing optical microscope (POM).
This cell is used as a reference cell for the whole experiment. When the glass plates are incorporated with the cholesterol oxidase enzyme, the alignment of the LC changes, and low-intensity light is observed (Figure 2(b)). In the presence of cholesterol at enzyme-loaded SAM surface, the enzymatic reaction takes place, the molecules of LCs tend to align homogeneously, and more intense light is observed (Figure 2(c)).

(iii) Optical Detection at LC: Aqueous Interfaces

More recently, we have designed a new LC-based biosensor using LC-aqueous interfaces. Compared to the LC-solid interfaces, the aqueous interfaces provide high mobility and adaptability for targeted bioanlytes. We have detected different concentrations of histamine (e.g., 20 mg/L and 100 mg/L) using this technique. Histamine (β-aminoethylimidazole) is a dibasic vasoactive amine present in most body tissues of animals and plants. The word ‘histamine’ is derived from the Greek word *histos* meaning ‘tissue’. It is a chemical messenger released by the cells in certain situations, and it acts upon other types of tissues based

**Figure 2.** Illustration of detection process of LC biosensor (a) No transmission of light in homeotropically aligned cell, (b) A very low transmission when cholesterol oxidase enzyme is present, (c) Intense light transmission in the presence of cholesterol (Adapted with permission from [14]).
**Figure 3.** Polarizing optical micrographs images of (a) reference cell, (b) enzyme cell, (c) biosensing cell with cholesterol concentrations 10 mg/dl, (d) 50 mg/dl, (e) 150 mg/dl, and (f) 250 mg/dl. Scale bar: 200 μm. Crossed arrows show crossed polarizer (P) and analyzer (A). Adapted with permission from [14]. The POM textures are given in Figure 3 illustrating the alignment towards homeotropic to homogeneous. (a) represents the proper homeotropic alignment of LC molecules in the presence of DMOAP/APTMS. In the presence of the cholesterol oxidase enzyme, there was some disturbance in the alignment of 5CB molecules, and bright images with low intensity were observed. But the LC molecules change towards homeotropic to homogeneous with the increasing concentrations of cholesterol (from 10–250 mg/dl) ((c)–(f)) and improved contrast with different colors are reflected with concentrations. On their receptors. It mediates cellular responses, including inflammatory reactions, allergic reactions, gastric acid secretion, limited neurotransmitter action in the brain, etc. In this experiment, we first placed the TEM grid over a polyamide-coated glass. After that 4 octyl-4-cyanobiphenyl (8CB) was filled in the TEM grid and put in the aqueous solution containing sodium dodecyl sulphate (SDS). SDS is used to change the NLC to align homeotropically [15, 16]. Following this, we added an aqueous solution containing the enzymes of histamine. Finally, we added different concentrations of histamine, first 20 mg/L and then 100 mg/L. The complete observations are depicted in Figure 4.

**Figure 4(a)** shows the optical appearance of 8CB inside the TEM grid; a bright color was observed in this case. In the presence of SDS, the alignment became totally homeotropic after 70 secs, and a dark pattern was observed at this stage (Figure 4(b)). When it came in contact with the enzymes, the disruption of the LC molecular alignment started, and a bright color was observed (Figures 4(q)–(r)). In the presence of histamine (20 mg/L), molecules started turning homogeneous, and the observed texture was with improved brightness (Figure 4(s)). When the histamine concentration was increased to 100 mg/dl, the texture became intense bright (Figure 4(t)). In this scheme, the bioanalytes in the aqueous solution are arrested at the interface, leading to a change in the alignment of LC molecules. The performances with the detection limit of different LC-based biosensors to detect various
biomolecules are summarized in Table 1 [10]:

**Abbreviations**: IM: immobilizing matrix; DT: detection techniques; DR: detection range; DL: detection limit; RT: response time; IB: immobilizing biomolecule; TA: target analyte.

**Future Outlook**

LC-based biosensors technology promises many salient applications in the field of infectious diseases in plants and human beings. LCs as biological sensors with portable, sensitive, specific, and point-of-care diagnostic platforms will be more affordable and adopting sensing mechanisms in next-generation diagnostic techniques. The aforementioned outcome of LC-based biosensors provides new scope for the development of more advanced and efficient biosensors.

**Conclusions**

In summary, LCs are promising materials for detecting different proteins, enzymes, nucleic acids, cells, microorganisms, and

**Figure 4.** Polarized optical microscopy images of (a) TEM$_{\text{pureCB}}$ (b)–(p) TEM$_{\text{SCB/SDS}}$ (q)–(r) TEM$_{\text{ASCB/SDS/enzyme}}$ (s)–(t) TEM$_{\text{SCB/SDS/enzyme/EHistamine}}$ (Scale bar: 200 μm); Crossed arrows show crossed polarizer (P) and analyzer (A).
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<td>2.</td>
<td>SAM = dimethylthacodicyl[3-(trimethoxyxyl)propyl]ammonium chloride (DMOAP) and (3-Aminopropyl)trimethoxyxylamine (APTMS) DT=polarizing optical microscope IB=cholesterol oxidase TA=cholesterol</td>
<td>DR=10-250 mg/dL DL = 10mg/dl</td>
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<td></td>
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<td>Label-free detection of specific pathogen DNA.</td>
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<td>Low production cost and easy detection through the naked eye</td>
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<td>7.</td>
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<td>Simpler and less expensive</td>
<td>Kaze D., Gidwell et al. (2007)</td>
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<td>9.</td>
<td>SAM (coated)= octadecyltrichlorosilane (OTS) DT=polarized light microscope IB=ssDNA TA= mercercule (lig +)</td>
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<td>First precise and selective detection of metals with a very low detection limit</td>
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<td>10.</td>
<td>SAM = polyurethane acrylate)-coated silica substrates into 1 mM ethanesulfonic acid solution consisting of 0.5 mM mercaptothebenedic acid and 0.5 mM decanedioic DT=Polarization Light Microscope, Ellipsometry, Atomic Force Microscopy IB= tuberculosis antigen EBT-4 TA=tuberculosis</td>
<td>0.015-15 μg/mL</td>
<td>Label-free detection of anti-tuberculosis antibodies</td>
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<td>11.</td>
<td>SAM = triethoxysilylbutylrotenone/N, N-dimethyloctadecyl (3-aminopropyl) trimethoxyxyl chloride (TEA/DMOAP) DT=polarized optical microscopy IB= single-strand ATP aptamer TA=adenosine triphosphate</td>
<td>DR &gt;10 nM/mL DL = 10 nM/mL</td>
<td>Simple and sensitive detection</td>
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Table 1. Potential of LC-based biosensor.

other biomolecules critical to human health. Several severe diseases have been detected through different sensing platforms based on various interfacial structures as LC-solid interfaces and LC-aqueous flat interfaces. LC-based biosensors are dominant tools to
sense bioanalytes with high-density integration, a rapid response, low cost, and high sensitivity compared to conventional technologies that require high-precision instruments for detection.

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Suggested Reading


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