Applications of Liquid Crystals-Based Sensors

Subjects: Chemistry, Analytical | Chemistry, Applied | Others

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liquid crystals LC LC-based sensors

1. Introduction

Liquid crystals (LC) are a class of chemical substances that exist in intermediate states between crystalline solids and liquids [1][2][3][4][5]. They thus share the anisotropic properties of crystalline solids as well as fluid properties of isotropic liquids [5][6][7]. They exhibit various phases due to the noncovalent and orientation-dependent interactions that exist between their molecules [1][2][8][9]. Their anisotropic properties and molecular orientations are responsible for their delicate sensitivity to external stimuli, including light, temperature, mechanical shear, electric field, magnetic field and surface interactions with foreign molecules [10][11][12][13][14][15][16]. Such delicate and exquisite sensitivity is responsible for their exploitation as stimuli-responsive materials in various applications such as display and visualization technology, photovoltaics, optoelectronics, sensors and material science [17][18][19][20][21]. As a consequence, intense research efforts are directed at using LCs as sensitive, fast-response and low-cost sensor materials [7][21][22].

2. LC-Based Glucose Sensors

Glucose is the main source of energy for the proper functioning of cells and organisms [23]. It is an important sugar whose level is maintained through specific mechanisms [21]. The normal level of glucose in the blood ranges from 3.6–6 mM [23], and this normal range is important for proper body function. A blood glucose level (BGL) higher than 11 mM leads to a condition called hyperglycemia, which causes various complications such as blurred vision, extreme thirst and slow wound healing [21][23]. These symptoms may not be noticeable until the BGL reaches a life-threatening level of 15–20 mM. An opposite condition of hypoglycemia refers to abnormally low BGL, which can also produce several complications such as seizures, neuroglycopenia and permanent brain damage. All these complications can be avoided if hypoglycemia and hyperglycemia are identified early enough. Therefore, it is important to detect BGL before it reaches either of the two extreme life-threatening levels. Over the last two decades, there have been numerous reports of LCs being used for the development of label-free glucose

biosensors. These sensors lack the challenges experienced with mainstream diagnostic methods that are based on spectroscopy and electrochemistry such as ion interference, high cost and slow response time. LC-based glucose sensors are robust, cheap, selective and easy to operate. The LCs act as sensitive material for signal amplification such that the signal generated from the sensor can be visualized.

The most widely used glucose detection principle is the oxidation of glucose in the presence of glucose oxidase (GOx) [21][22][23], though glucose detection has also been implemented by means of LC droplets [23]. The enzymatic reaction of glucose oxidase and glucose produces gluconic acid and hydrogen peroxide. Thus, H^+ ions are produced and the pH of the system is lowered. Consequently, certain pH-responsive LC-based sensors can also be adapted for glucose sensing by monitoring the pH changes that accompany the action of glucose oxidase on glucose [24]. Fundamentally speaking, either or both pH and H_2O_2 can be monitored for the detection of glucose. In their glucose sensor development, Zhong and Jang reported a highly sensitive and selective LC-based sensor involving the use of UV-treated 5CB (4-cyano-4′-pentylbiphenyl) to produce amphiphilic 4-cyano-4′-biphenylcarboxylic acid (CBA) [25]. The resulting CBA means that UV-treated 5CB can exhibit pH-dependent optical signals. Therefore, in their experiment, they immobilized GOx on a gold grid and then filled the mesh with UV-treated 5CB, followed by immersion in glucose solution. The H^+ produced from the oxidation of glucose triggered an optical response of the LCs from dark to bright as observed under a polarized microscope. In the absence of glucose, however, a dark image is obtained for there is no glucose oxidation. They were able to achieve a detection limit of 1 pM glucose, which is three orders of magnitude lower than most currently available glucose sensors. Similarly, Qi et al. reported the fabrication of a LC-based sensing platform for the detection of glucose and H_2O_2 [26]. Single-stranded DNA (ssDNA) was adsorbed onto the surface of nanoceria (CeO_2) and the ssDNA gets dislodged from the surface in the presence of H_2O_2. Thus, the oxidation of glucose by GOx to produce H_2O_2 would dislodge the ssDNA from the surface of nanoceria thereby changing the alignment of 5CB from dark to bright. When glucose is absent, no H_2O_2 is produced and 5CB retains its homeotropic alignment at the LC/aqueous interface. This sensor was able to detect both H_2O_2 and glucose. Potentially, it can also detect any biomarker that depends on H_2O_2 concentration. Furthermore, Khan and Park functionalized 5CB with polyacrylic acid (PAA) and mixed polymer brushes of poly(acrylicacid-b-4-cynobiphenyl-4-oxyundecylacrylate) (PAA-b-LCP; LCP stands for liquid crystal polymer) and quaternized poly(4-vinylpyridine-b-4-cynobi-phenyl-4-oxyundecylacrylate) (QP4VP-b-LCP) for glucose detection [27]. According to these authors, the PAA makes the LC–aqueous interphase pH-sensitive while the QP4VP-b-LCP brush immobilized GOx without using coupling agents. The presence of glucose triggers a homeotropic to planar reorientation of the 5CB molecules, giving rise to dark to bright POM image transition accordingly. This sensor has a response linearity between 0.5–11 mM glucose and so it is suitable for BGL monitoring. These authors have also reported a glucose biosensor that uses a backscattering interferometry that gave a detection limit of 0.008 mM [28].

It should be pointed out that LC-based non-enzymatic glucose sensing has also been reported [29]. For instance, 3-Aminophenyl boronic acid (APBA)-decorated 4-cyano-4′-pentylbiphenyl (5CB) microdroplets have been used for non-enzymatic glucose sensing [29]. The binding between glucose and the APBA moiety on 5CB translated into reorientation of the 5CB droplets from radial to bipolar configuration. Such a change in configuration was absent when glucose was not present. This sensor was stable for up to 30 days and it presented high selectivity even in

complex serum samples. The sensor gave a detection limit of 50 µM glucose, however, the limit of linearity was not established and so it is unclear if this sensor will be suitable for glucose monitoring in the normal BGL of 3.6–6 mM. Similarly, Ailincai and Marin also reported a non-enzymatic LC-based glucose sensor [30]. They fabricated a bio-responsive polymer-dispersed LC sensor for glucose and other bio-analytes. By using polymer-dispersed liquid crystal (PDLC) composites prepared by the encapsulation of cholesteryl acetate (L-ChAc) in polyvinyl alcohol boric acid (PVAB), they obtained selective responsiveness of the PDLC to sugars, amino acids and DNA. This was orchestrated by the fact that PVAB produced a uniform distribution of the cholesteric LC as micrometric droplets with moderate wettability. When blood glucose came in contact with the round droplets, the droplets disappeared leaving behind a “chicken-skin texture with rare light spots”, indicating weaker homeotropic alignment, which is attributable to new H-bonds forming between the OH group of glucose and the COO^- group of L-ChAc. LC membranes have also been used for the enhancement of amperometric glucose detection [31], though this sensor is not directly based on interfacial LC-alignment changes that give rise to a homeotropic to planar alignment and POM images. Overall, it is expected that LC-based sensors will continue to dominate the glucose sensing field for the foreseeable future.

3. Detection of Proteins, Peptides and Nucleic Acids

Proteins regulate vital processes in living systems such as immune responses and cell signalling [22][32][33]. Their detection is important in understanding their mode of action and working mechanism. Thus, accurate detection of proteins is also essential for identifying abnormal protein synthesis, which can signal the early stages of diseases. Similar to glucose, there have been several instances where LC-based sensors have been developed for protein detection and on the fundamental level, the composition of the sensor is similar to those of glucose in the sense that a specific functionality within the sensor is involved in some form of interaction with the target protein analyte thereby triggering a realignment of the LC molecules in the system, leading to the transformation of the homeotropic to the planar arrangement or vice versa [22].

Very recently, Xia et al. reported the use of a new immunosensor based on 5CB liquid crystal for the detection of cardiac troponin I (cTnI), which is a protein that regulates the binding of myosin to actin [34]. They developed this LC-based sensor due to the challenges accompanying the use of established detection methods. By tethering cTnI antibody by means of glutaraldehyde (GA) to the surface of glass slides treated with *N*,*N*-dimethyl-*N*-octadecyl (3-aminopropyl) trimethoxysilyl chloride (DMOAP) and (3-aminopropyl) triethoxysilane (APTES), 5CB heated to isotropic phase was then sandwiched between two functionalized glass slides where these LC molecules adopt a homeotropic alignment induced by DMOAP/APTES. This gives rise to a dark image when observed in polarized light. However, if the target cTnI is present, it interacts with the cTnI antibody, thereby triggering a homeotropic to planar realignment of the LC molecules, giving rise to a bright POM image. This immunosensor presented a detection limit of 1 pg/mL, hence of high sensitivity, in addition to being low cost and of high specificity.

Using 5CB decorated with a nonionic surfactant dodecyl β-D-glucopyranoside, Wang et al. recently developed a LC-sensor for the detection of bovine serum albumin (BSA), concanavalin A (Con A) and lysozyme [35]. 5CB was loaded onto gold grids placed on OTS-modified glass slides, an aqueous solution was then placed on the 5CB

layer where the LC molecules assumed planar alignment at the LC/aqueous interface, hence a bright POM image results. When the nonionic surfactant was added to the aqueous layer, it caused the LC molecules to adopt homeotropic orientation where a dark POM image was obtained. This happens due to the formation of a stable self-assembled monolayer of the surfactant. Furthermore, the POM image changed back to bright when each of BSA, Con A and lysozyme was added to the biosensor. Detection limits of 0.001, 0.01 and 0.1 µg/mL were obtained for BSA, Con A and lysozyme, respectively, with this biosensor. Similarly, by monitoring the interaction between sodium polystyrene sulfonate (PSSNa) and a positively charged moiety coated on 5CB placed in a TEM grid cell, Omer and co-workers developed a LC-based biosensor for the detection of BSA, α chymotrypsinogen-A (ChTg) haemoglobin (Hb) and lysozyme [36]. Homeotropic orientation of the 5CB in the TEM grid cell changed to planar orientation when the protein solutions were injected into the cell. The same research group has also reported a similar protein and DNA biosensor based on a similar principle of fabrication [37]. This shows again that it is the interaction between an analyte and recognition molecule in the sensor that triggers reorientation of the LC molecules at the LC/aqueous interface giving rise to visually detectable bright or dark POM image. Ligand/receptor detection is important for analyte and drug screening. Therefore, a LC-based sensor has been reported for detecting avidin-biotin specific binding [38]. Using a microfluidic approach, a LC-based droplet biosensor was fabricated by functionalizing 5CB droplets with PAA-b-LCP (poly(acrylicacid-b-4-cynobiphenyl-4′-undecylacrylate)) with the PAA chains on the LC molecules biotinylated and used for the detection of avidin-biotin binding at the LC/aqueous interface. This binding leads to a configurational change of the LC droplets from radial to bipolar. This biosensor can detect avidin as low as 0.5 g/mL and it can discriminate between the avidin target analyte against other proteins such as BSA, Hb, lysozyme and chymotrypsinogen. Popov et al. has also demonstrated the use of a LC-based biosensor for specific detection of goat Immunoglobulin G (IgG) antigen [39]. 5CB molecules were coated with biotinylated lipids and biotinylated anti-goat IgG. When the analyte goat IgG was applied to the functionalized LC molecules in the TEM grid cell, there was a homeotropic to planar transition that gave rise to dark–bright transition in the POM image. This biosensor did not respond to negative controls of rat or rabbit serum IgG, thus proving the specificity of the sensor for goat IgG. Ren and Jang have also reported a LC-based aptasensor for the detection of the clinically important carcinoembryonic antigen [40]. The analyte binds to a specific aptamer immobilized on the surface of modified glass slides, triggering a reorientation of the 5CB molecules from homeotropic to random alignment (i.e., nematic domains with randomly oriented optical axes). The biosensor was able to discriminate between the analyte and BSA and human serum albumin (HSA).

In a similar vein, various cationic gemini surfactants were used to decorate the LC/aqueous interface in a LC-based protein sensor [41]. The sensor initially produced a dark POM image due to the stable monolayer of surfactants formed at the interface. This dark image then changed to a bright image upon addition of BSA, which is a negatively charged protein in a neutral environment, triggering a realignment of the LC molecules from homeotropic to planar. Similarly, Verma et al. has recently reported the use of a LC-based sensor for the identification of the secondary structure of Cyto, BSA, Hb, Con A and fibronectin (FibN) [42]. They used surfactin, a cyclic lipopeptide, to promote the homeotropic alignment of LC molecules at the LC/aqueous interface to produce a dark POM image initially. However, the colour changed from dark to bright in the presence of nanomolar concentrations of Cyto, BSA, Hb, Con A and FibN at neutral pH, which was interpreted on the basis of interaction

between the anionic headgroups of surfactin and the proteins. The specific patterns observed in the bright POM image is determined by the specific form of interaction between the proteins and surfactin. Wu and coworkers have reported the use of dye liquid crystals (DLC), which exhibits both optical anisotropy and dichroic absorption for the quantification of BSA [43]. The DLC consists of an azobenzene liquid crystal molecule that has been modified with two azo groups to serve as the chromophore. They exploited the dichroic absorption of azobenzene at 470 nm for the transmission spectrometric determination of BSA concentration while using the birefringence characteristics of the LC as the trigger for the transmission intensity change as BSA concentrations varied.

In a somewhat different dimension, a research group has reported the use of LC-based sensors for imaging microcontact printed proteins [44]. A homeotropic to planar transition of the LC confirms the specific binding between a target anti-biotin IgG and biotinylated BSA while such transition does not take place when a control anti-goat IgG was used. This sensor may form the basis for fabricating functional surfaces on which affinity microcontact printed proteins can be imaged. Su et al. reported a LC-based immunosensor for detecting human β-defensin-2 (HBD-2), a cysteine-rich cationic peptide with antimicrobial activity [45]. In this sensor, 5CB was sandwiched between two glass slides whose surfaces had been suitably treated with DMOAP/APTES followed by the addition of HBD-2. When the anti-HBD-2 antibody was then applied, the alignment of the 5CB molecules changed from homeotropic orientation to randomly oriented nematic domains, giving rise to a dark to bright POM image transition that is visually detectable in polarized light. The sensor gave a linear concentration dependence in the range 1–10 ng/mL with a limit of quantitation of 0.53 ng/mL.

Deoxyribonucleic acid (DNA) is the fundamental basis of life and its damage or mutation can lead to lethal consequences. Ribonucleic acid (RNA) is also important in the regulation of various biological processes and changes in the concentration of certain non-coding RNA may be an indicator for disease onset. Therefore, reliable sequence-specific detection of DNA and RNA is important. To this end, several reports have presented the use of LC-based sensors for DNA detection. For example, a research group has presented a highly sensitive LC-based sensor for the detection of p53 mutation gene segment using a dendrimer-mediated approach [46]. Mutation in the p53 gene may signal several diseased states such as brain tumour and liver disease. 5CB doped with SDS was applied to a copper grid cell placed on a DMOAP-coated glass slide. DNA dendrimers applied to the grid created a tilted alignment of the LC molecules at the LC/aqueous interface. However, when the mutant-type target was added, its interaction with the DNA dendrimers induced the rearrangement of the LC molecules from tilted to homeotropic alignment. The target can be detected in the 0.08 to 8 nM concentration regime with high sensitivity. Liu and Yang also reported a LC sensor for the multiplex detection of DNA [47]. 5CB was drawn into the space between two glass slides functionalized by droplets of DNA or PNA (peptide nucleic acid) solutions. The slides were immersed in NaCl solution or other sodium salt solutions such that the sodium ion would complex with the negatively-charged DNA backbone but not with the neutral PNA backbone. The PNA-containing system has the LC molecules in homeotropic alignment so that when a Cy3-DNA target was applied, the interaction between this target and PNA triggers realignment of the LC molecules giving a POM image transition from dark to bright. A limit of detection of 10 fM was reported. Furthermore, Kim and Jang reported the use of a LC-based sensor for the detection of single-strand breaks (SSBs) in DNA [48]. SSBs lead to carcinogenesis and ageing, and so their detection is crucial to human well-being. A single-stranded DNA (ssDNA) adsorbed onto the cationic surfactant

(OTAB) present in the LC/aqueous interface formed by immersing 5CB-filled copper grids in the OTAB solution induces a planar orientation of the LC molecules, giving a bright optical image in polarized light. However, a DNA consisting of SSBs would give a decreased electrostatic interaction with the cationic surfactant, thereby causing a rearrangement of the LC molecules to homeotropic alignment, giving a dark POM image. This sensor makes the detection of SSBs in DNA easier to implement.

4. Gas Sensors

Due to their simplicity, low cost and ease of fabrication, LC-based sensors are now appearing in the literature for the detection of various gaseous substances, including toxic gases. For instance, nitrogen oxide (NO_2), a ubiquitous environmental pollutant is toxic and prolonged exposure to it can lead to death. A LC-based sensor has been reported for this gaseous pollutant by Sen and coworkers [49]. Using LC film supported on a gold-coated substrate, the sensor is able to adsorb NO_2 and the transport of NO_2 molecules to the gold surface induces the orientational transition of the LC molecules at the LC–gold interface. The sensor is selective for NO_2 only while it does not respond to other atmospheric gases over the course of 200 s. Furthermore, a LC-based sensor has been reported for sensing carbon monoxide gas (CO) by using a LC doped with magnetite (Fe_3O_4) nanoparticles and intercalated into porous alumina (Al_2O_3) [50]. The interaction between CO and the nanoparticles dispersed in the LC is the basis for the sensing mechanism. According to the authors, this interaction causes a shift in the selective reflection peak wavelength, which is proportional to CO concentration, which they estimated to be 0.85 nm/(mg/m^3) in air. A highly selective and sensitive optical sensor based on LC has also been reported for ammonia gas [51]. Using chitosan-Cu(II)-decorated glass substrate, the alignment of 5CB on the substrate is disrupted due to competitive binding between ammonia gas and Cu(II) on the glass substrate, thereby causing the orientational transition of the LC molecules from homeotropic to planar state. A detection range of 50–1250 ppm was reported for this ammonia sensor with a detection limit of about 17 ppm.

5. VOCs Sensors

Volatile organic compounds (VOCs) are organic compounds with fairly high vapour pressure such that they easily evaporate under ambient conditions [52]. They cause pollution to the environment and are harmful to humans. Their presence in air can also be used as a biomarker for diseases [53]. Therefore, sensing and monitoring VOC gases is important for people's safety and well-being. To this end, Wang et al. recently reported a LC-based chemical sensor for toluene and acetone vapours [53]. They used LC/polymer composite fibres electrospun and spread out as a mat on a glass substrate. Absorption of these analyte vapours changes the optical properties of the LC/fibre mats producing sensitive and reversible detection. A report has also presented the use of a chiral-nematic LC encapsulated in microscale polyvinylpyrrolidone via electrospinning for gas sensing [54]. Similarly, a fibre-optic VOC gas sensor has been reported by Tang and coworkers [52]. They used a cholesteric LC film coated side polished fibre (CLCFC-SPF) to sense VOC gases such as acetone, methanol and tetrahydrofuran (THF). On applying light to the sensor, they observed selective wavelength coupling from the SPF to the CLCF that resulted in resonant dips in the transmitted spectrum, and the pitch of the CLCF increased as a function of VOC gas concentration.

Similarly, using a LC sandwiched between two modified electrodes, Dadoenkova et al. has also reported a sensor that may be suitable for chemical vapour sensing [55]. It must be mentioned that another LC-based optical sensor was reported for the detection of butylamine vapour in air [56].

6. Detection of Toxic Substances

Substances that are toxic to plants and animals must be continuously monitored in the environment to safeguard people's health and well-being. In that regard, several LC-based sensors have been reported for the detection of toxic substances. For instance, Hu and coworkers recently reported a LC sensing platform for selective detection of uranyl ion (UO_2^{2+}) [57]. The sensor is composed of a UO_2^{2+}–dependent DNAzyme, its substrate, a capture probe and 5CB sandwiched between two treated glass slides. In the presence of the analyte UO_2^{2+}, the DNAzyme cleaves the substrate at the rA site, and the cleaved product hybridizes with a capture probe to form a duplex, which disrupts the original alignment of the LC molecules. This gives a dark to bright transition. This specific and label-free sensing method gave a detection limit of 25 nM and this platform can be adapted for the detection of other radioactive substances.

Organophosphonates are highly toxic chemicals that are used as warfare agents [15]. Therefore, there is a strong interest in reliable methods of monitoring and reporting the presence of organophosphonates at low concentrations on battlefields. Wang et al. has reported a LC-based sensor for dimethyl methylphosphonate (DMMP) vapour [15]. They used 5CB films consisting of Cu(II) ions applied to functionalized substrates. When present, DMMP interacts with Cu(II) ion and this causes a disruption of the LC alignment from homeotropic to planar orientation. They reported a detection limit of 0.51 mg/m^3. A similar experiment was reported by Bungabong and coworkers [58]. Furthermore, a study elucidating the physicochemical phenomena underlying the mass transport of DMMP across the functionalized surface-supported LC film in LC-based sensors has been presented [59].

Using a LC-based sensor, Chen and Yang reported a sensor for detecting organophosphates, which are common ingredients in pesticides and chemical warfare agents [60]. They based the sensing on small pH changes during enzymatic hydrolysis of organophosphates using paraoxonase 1 enzyme, which was immobilized on a copper grid that also contains pH-sensitive 5CB doped with 4′-pentyl-biphenyl-4-carboxylic acid (PBA). Disruption of the LC molecules as a result of the enzymatic reaction causes a dark to bright transition that signals the presence of organophosphates. A limit of detection of 1 µM was found using the naked eye. In a related experiment, Zhou et al. reported a new sensor for detecting organophosphate pesticides [61]. Alkaline phosphatase (ALP) was used for the hydrolysis of dichlorvos (DDVP), an organophosphate pesticide. Using ALP-cleavable surfactant sodium monododecyl phosphate (SMP), an orientational transition was observed in the LC molecules in the presence of DDVP and a dark to bright transition was visible. Wang and Yu also reported a pesticide sensor using acetylcholinesterase (AChE) enzyme and Myr [62]. In the absence of the pesticide, a planar orientation was assumed by the LC molecules in the droplet, which gives a bright image. However, there is a bright to dark transition in the presence of AchE-inhibiting pesticides.

Chuang and Chen also reported a LC-based sensor for melamine [63]. Their sandwich sensor system works on the mechanism that melamine, if present, will bind with anti-melamine adsorbed on the glass substrate, which disturbs the LC orientation. Ren et al. has also reported a LC-based aptasensor for the detection of bisphenol A (BPA), an endocrine-disrupting chemical [64]. The BPA analyte forms a complex with the aptamer and this complex disrupts the orientation of the LC molecules from homeotropic to planar, i.e., dark to bright POM image transition. Such a transition is not evident when BPA is not present. They recorded a detection limit of 0.6 fM for BPA with this sensor.

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