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Topical Review

Disposable chemical sensors and biosensors made on cellulose paper

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Abstract

Most sensors are based on ceramic or semiconducting substrates, which have no flexibility or biocompatibility. Polymer-based sensors have been the subject of much attention due to their ability to collect molecules on their sensing surface with flexibility. Beyond polymer-based sensors, the recent discovery of cellulose as a smart material paved the way to the use of cellulose paper as a potential candidate for mechanical as well as electronic applications such as actuators and sensors. Several different paper-based sensors have been investigated and suggested. In this paper, we review the potential of cellulose materials for paper-based application devices, and suggest their feasibility for chemical and biosensor applications.

Keywords: cellulose, disposable, chemical sensor, biosensor, paper, flexibility

(Some figures may appear in colour only in the online journal)

1. Introduction

Biosensors and chemical sensors are detecting electrochemical devices, which can react with different biological as well as chemical components. However, due to complicated electronic-based structures and high manufacturing costs, cheap and mobile devices with light and flexible substrates, e.g. plastic or paper-like materials, are required to improve current sensor devices [1–3]. Paper, as a substrate, is composed of multiple layers of cellulose fibers which can form an inner network structure. Already, there have been attempts to use cellulose in innovate paper-based electronic applications [4–6]. Since paper is flexible, lightweight, cheap and disposable, once electronic devices are made with and on paper, it will bring a broad technological impact. Recently a new approach for semiconducting logic devices based on cellulose paper was reported [7].

Cellulose, the chain of glucose residues which form the principal component of the plant cell wall, is the most abundant and widespread biopolymer. Every year, plants make more than 10^{11} tons of cellulose [8]. Besides of its abundance, biodegradability, biocompatibility and renewable behavior, cellulose, especially nanocrystal cellulose, has unique material properties: high Young's modulus, transparency, dimensional stability and low thermal expansion coefficient. Since cellulose can be easily modified by chemicals, a variety of functionalities can be given. For a fascinating application of cellulose, paper-based flexible and disposable sensors have been suggested.

For chemical sensor applications, the chemically interactive properties of conventional polymers have been systematically studied by functionalizing polymer–metal oxide hybrid composites, resulting in significant enhancement of optical, thermal and mechanical properties due to the synergistic effects via physical or chemical interactions between the organic and inorganic elements [9]. However, conventional polymers, especially petroleum-based polymers, cost more than natural materials and prohibit practically their recycling after usage. Thus, it is beneficial to use natural polymer materials for chemical sensors. However, functionality of the materials should be improved.

To enhance the cellulose material properties for electronic and sensor applications, a hybrid modification or functionalization of cellulose has been recently studied for biosensors and chemical sensors [10–15]. By adding metal oxide into a cellulose matrix, the material properties in terms of chemical stability, electrical conductivity, photo-catalytic activity and

photosensitivity can be enhanced [16, 17]. In this paper, we review recently reported paper-based application devices including field effect transistors, biosensors and chemical sensors.

2. Cellulose–carbon nanotube-based paper transistor and sensor applications

Cellulose itself possesses an insulating material property due to the lack of intrinsic free electrons and holes. However, similar to Si technology, where we can modify the electronic properties of Si as n-type or p-type by dopants, we can form electronic channels or paths into cellulose structures by chemical bonding (similar to doping) of metallic or semiconducting nanostructures to cellulose chains. Therefore it is possible to use cellulose for electronic devices, such as printable and flexible transistors which can control the electronic current passing through the devices by applying an electric field. Unlike the earlier approach, where cellulose was used for a dielectric insulating layer [7], a paper transistor made with regenerated cellulose–multiwalled carbon nanotube (RC–MWCNT) covalently bonded was demonstrated [18]. As shown in figure 1, the inter-digit transducer (IDT) patterns can act as source and drain electrodes and a top gate electrode is used to control the electric current flow through nanotube channels in the cellulose matrix. Here, MWCNT plays a role to allow an electron channel path within the cellulose substrate. The result proves the feasibility of flexible paper-based transistors, namely 'paper-tronics', for future electronic devices. However, the low transfer characteristics and on/off ratio should be improved up to the performance of polymeric transistors.

Using the basic concept of a papertronic device, a novel chemical vapor sensor with MWCNT–cellulose (M/C) composite was reported to have detected four different polar solvents—methanol, ethanol, 1-butanol and 1-propanol [19]. Because cellulose, as a matrix polymer of M/C composite, has good affinity to hydrophilic polar molecules and related volumetric change by polar molecule adsorption, the M/C composite shows a good response to polar solvents. In particular, the linear response of the M/C composite for 1-propanol indicates that it can be used as a chemical sensor to differentiate the concentration of 1-propanol. Figure 2 shows the suggested paper-based chemical sensor.

3. Cellulose–SnO-based biosensors and pH sensors

Using cellulose paper, glucose oxidase (GO_x) immobilized cellulose–SnO_2 hybrid nanocomposite has been developed as a glucose biosensor by Mahadeva *et al* [20]. Porous GO_x was attached to the cellulose–SnO_2 hybrid nanocomposite via covalent bonding between GO_x and SnO_2. Upon exposing the GO_x immobilized cellulose–SnO_2 hybrid composite to glucose, an enzymatic reaction occurs between GO_x and glucose which is presented in figure 3.

Paper based on the tin-oxide-coated cellulose was also investigated for a urea detecting sensor [21]. When the urease immobilized sample comes into contact with a urea solution, the urea molecules can be adsorbed to the urease sites. By a

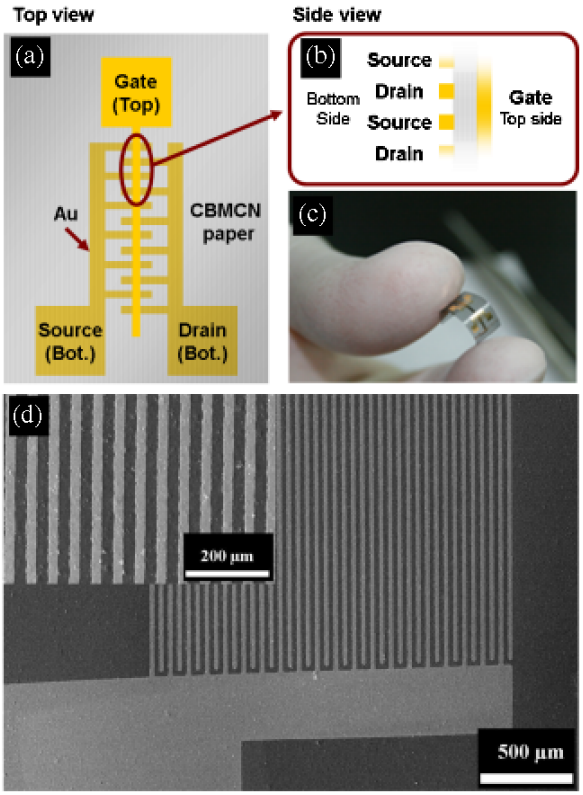

Figure 1. (a) Schematic of RC–MWCNT paper transistor, (b) configuration of gate, source and drain electrodes, (c) the bendable flexible paper transistor, and (d) detailed image of inter-digit structure of electrodes on the paper transistor. (Reproduced with permission from [18]. Copyright 2009 AIP.)

catalytic reaction occurring between urease and urea, the sensitivity curve shows three regions: (i) a highly sensitive region up to 10 mM, (ii) transition up to 42 mM and (iii) saturation above 50 mM. Cellulose–tin oxide nanocomposite is found to be sensitive in the 0–42 mM urea concentration and can detect as low as 0.5 mM. The sensitivity of urea sensors as a function of urea concentration is depicted in figure 4. Another paper-based chemical sensing approach using a microfluidic paper-based *chemi*luminescence analytical device (uPCAD) was proposed by Yu *et al* [22]. This lab-on-paper biosensor based on oxidase enzyme reaction and the *chemi*luminescence reaction is an easy to use and inexpensive as well as portable alternative.

Generally, pH paper can be used for disposable and quick qualitative pH indication. Each color on the pH paper can indicate a certain pH value and the color is reliable within a range. Therefore, a paper-based pH indicator can provide a color response if the solution is acidic, neutral or basic. Also, a pH meter has a membrane to allow acidic ions to pass, which can produce a voltage. Compared to previous pH sensors, shown in figure 5, a simple and novel paper-based pH sensor based on the tin-oxide–cellulose hybrid composite was studied [23]. The paper-based pH sensor shows increases of its conductance, and the sensitivity, defined as the change of resistance with respect to the pH level, is associated with three response regions with different slope rates depending on the pH value. The relatively good sensitivity in the pH

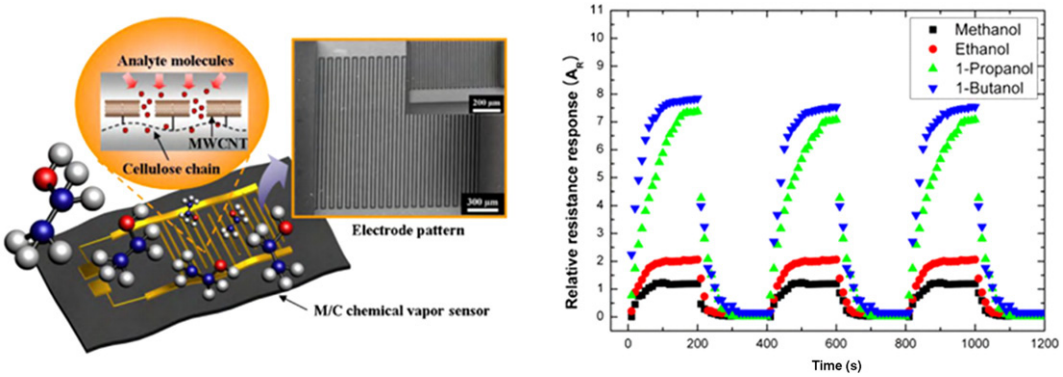

Figure 2. Schematic of paper-based chemical sensor made with M/C composite and IDT shaped electrode, and electrical response to selected chemicals. (Reproduced with permission from [19]. Copyright 2010 Elsevier.)

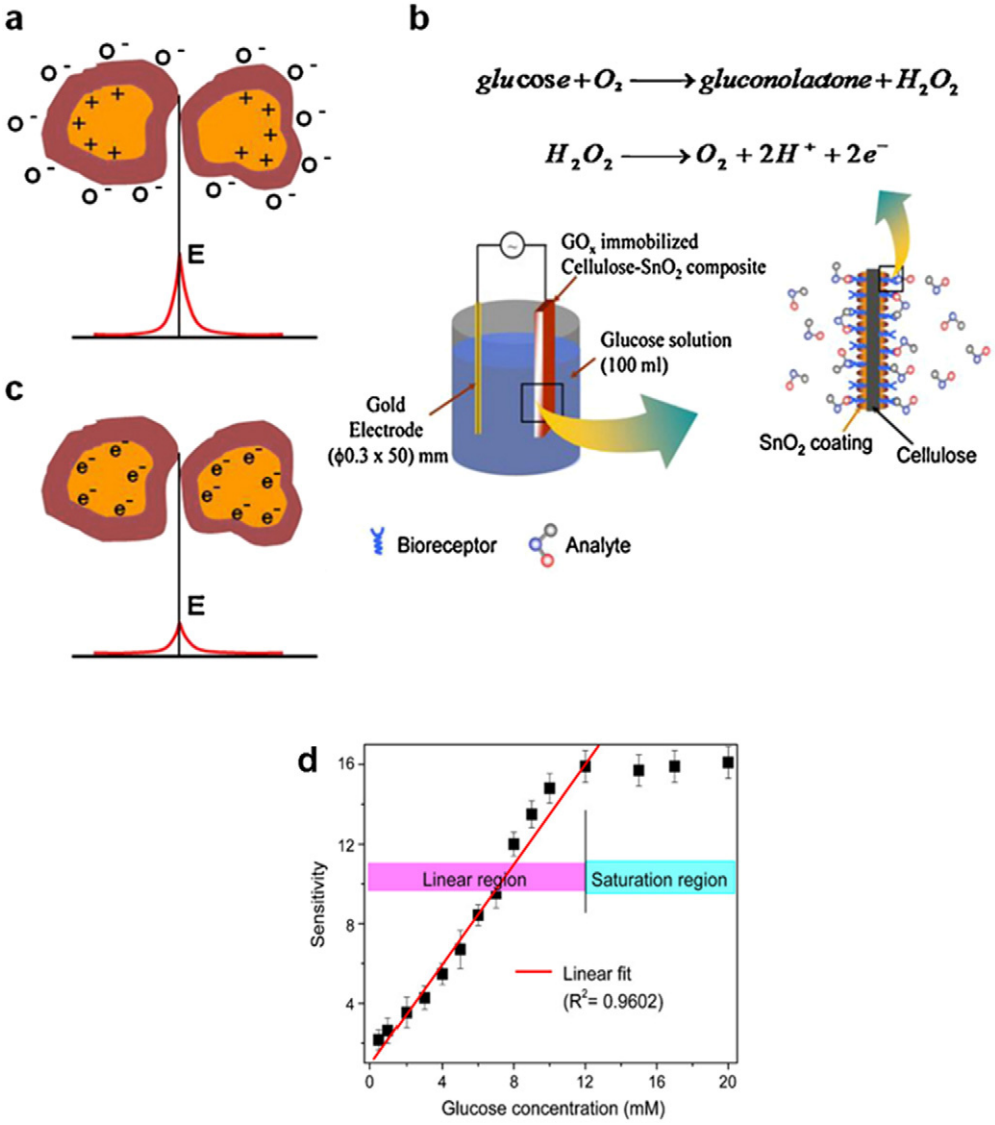

Figure 3. (a)–(c) Schematic representation of the detection mechanism of a cellulose–SnO_2 hybrid nanocomposite glucose biosensor, and (d) sensitivity results of the glucose biosensor. (Reproduced with permission from [20]. Copyright 2011 Elsevier.)

range of 4–8 indicates the feasibility and potential of the tin-oxide–cellulose hybrid composite for disposable, cheap and environment-friendly pH sensor applications.

4. TiO_2–cellulose composite for sensor applications

For gas detection, such as explosive, toxic and harmful gases, semiconducting metal oxides are widely used in sensor

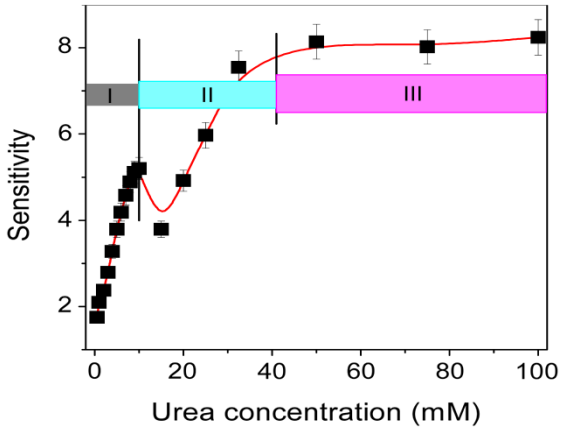

Figure 4. Sensitivity of the urea biosensor. (Reproduced with permission from [21]. Copyright 2013 IEEE.)

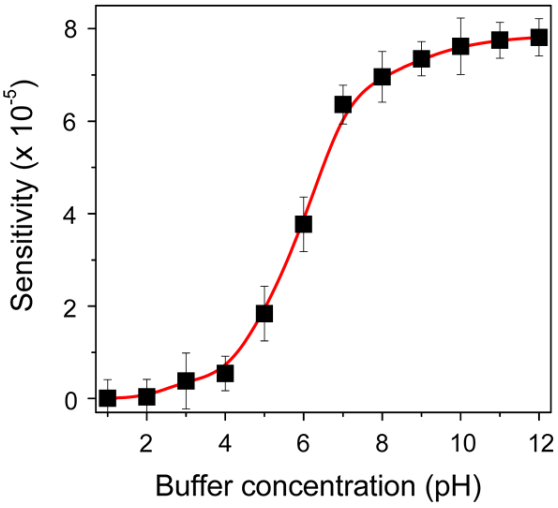

Figure 5. Conductance response of cellulose–tin oxide hybrid composite based pH sensor with different pH levels. (Reproduced with permission from [23]. Copyright 2013 Oldenbourg Wissenschaftsverlag.)

applications. Because ammonia gas is colorless, caustic and hazardous, the concentration in air must be regulated within the recommended exposure limits. As a cheap paper-based gas sensor, TiO_2–cellulose hybrid nanocomposite (TCHN) was prepared by blending TiO_2 nanoparticles into cellulose solution for a glucose biosensor [24]. The successful immobilization of glucose oxidase into TCHN via covalent bonding between TiO_2 and GO_x was confirmed by x-ray photoelectron analysis. The current level of the TCHN conductometric biosensor increased with increasing the weight ratio of TiO_2 in the cellulose. The calibration curve portrays two regions which consist of a linear region up to 10 mM and a saturation region above 10 mM. The linear region demonstrates that the proposed biosensor can easily detect the clinical range of 4.4–6.6 mM glucose. Figure 6 shows the good linearity of the behavior in a relatively lower range of glucose concentration. Titanium dioxide (TiO_2)–multiwall carbon nanotube (MWCNT) nanocomposite with cellulose film was synthesized by a hydrothermal process [25]. From the result, the cellulose–TiO_2–MWCNT (CTM) hybrid nanocomposite exhibited much higher response and faster recovery behavior to detect NH_3 gas when the gas concentration changed from 50 to 500 ppm (figure 7). This gas sensor showed potential for monitoring traces of NH_3 with good sensitivity and repeatability in the range of 50–500 ppm at room temperature. This result is a comparable performance to previous reports of WO_3 sensors on Pt electrode and TiO_2 film/Si devices operated at 250 °C [26].

Due to the photo-catalytic behavior of TiO_2, Ye *et al* presented homogeneous and non-aggregated TiO_2 immobilization on cellulose fibers by bioconjugation with fusion protein CBM2a-Strep-tagII/streptavidin/biotinylated TiO_2 [27]. As shown in figure 8, the photo-catalytic capability of the TiO_2-containing paper was able to completely photo-degrade 1.7 ml of RB5 aqueous solution with a concentration of 23 ppm, by 365 nm irradiation at intensity of 23 W m^{-2} for 12 h.

Also, in figure 9, a prototype 3D μPAD system to test with four different analytes and visualize the results of the assays in a side-by-side configuration for easy comparison was studied by Martinez *et al* [28].

5. GaN–cellulose composite for sensor applications

GaN is a wide band gap semiconducting material which is promising for power electronics and light emitting devices

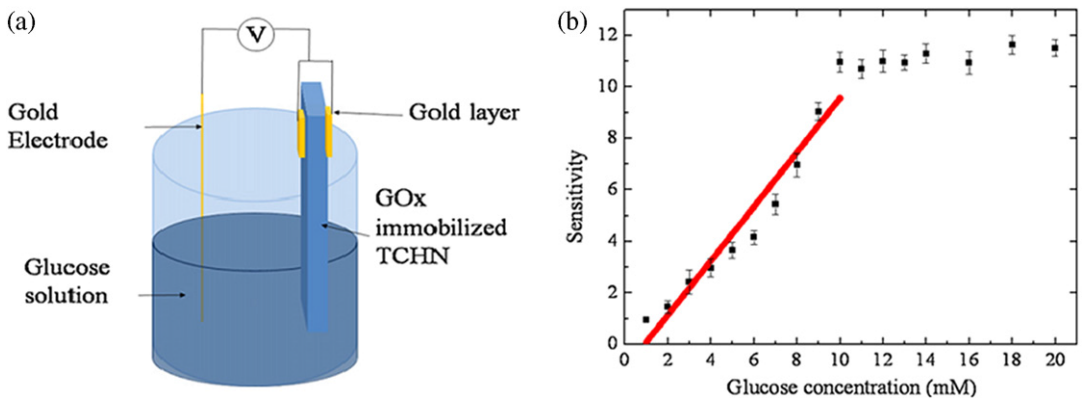

Figure 6. (a) Schematic of TCHN biosensor, and (b) its sensitivity with varying glucose concentrations. (Reproduced with permission from [24]. Copyright 2012 Elsevier.)

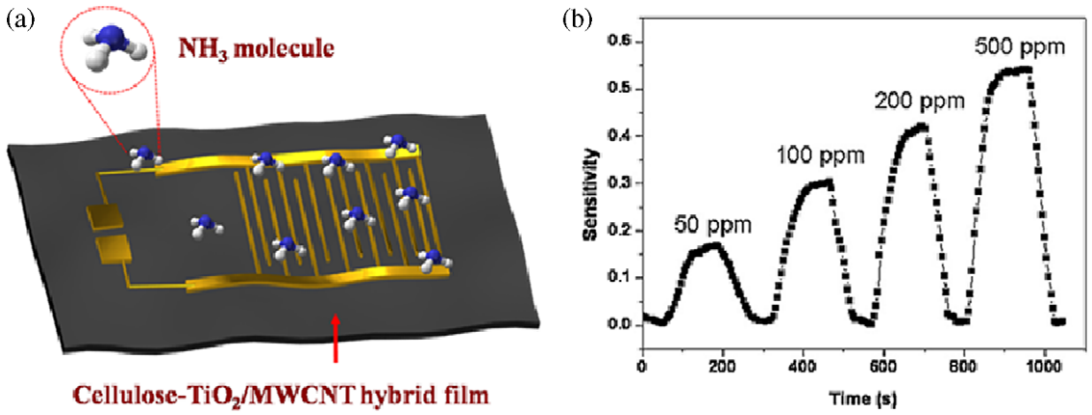

Figure 7. (a) Schematic of NH_3 detecting gas CTM sensor, and (b) its response curve and sensitivity. (Reproduced with permission from [25]. Copyright 2012 Elsevier.)

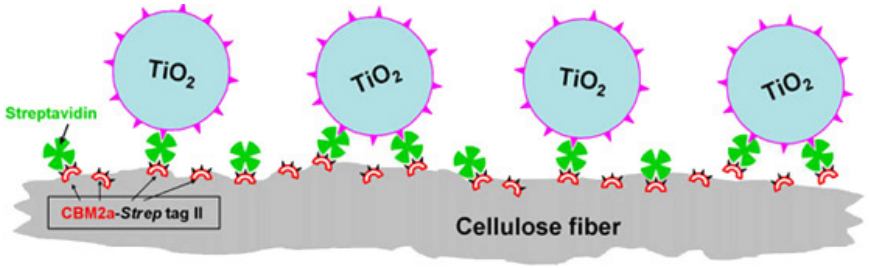

Figure 8. Cellulose-binding-module protein used to attach TiO_2 to cellulose. (Reproduced with permission from [27]. Copyright 2009 RSC.)

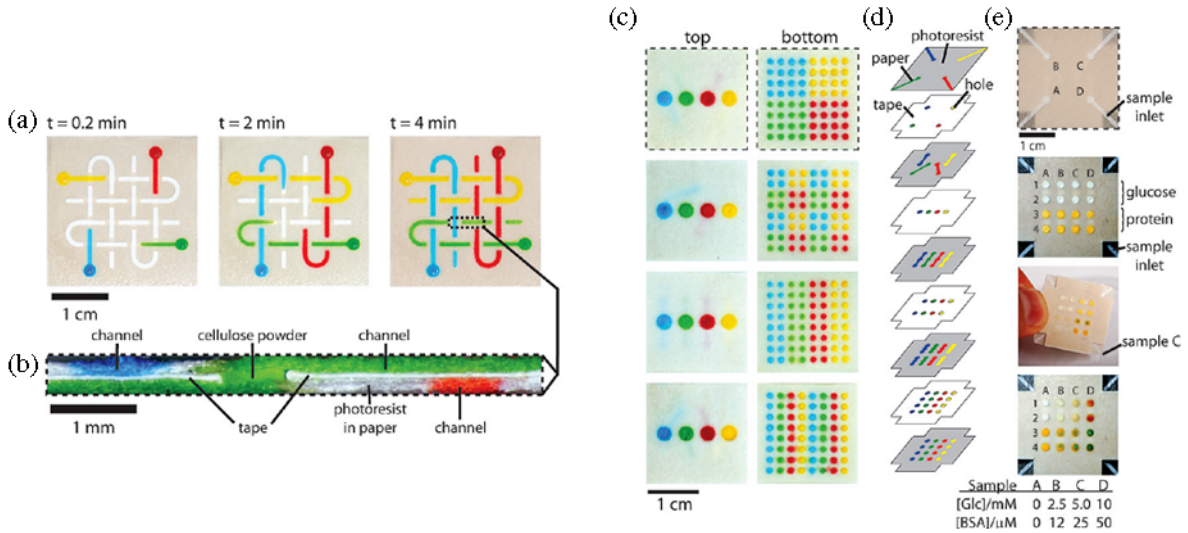

Figure 9. 3D μPAD with four channels that cross each other multiple times in different planes without mixing their contents. (Reproduced with permission from [28]. Copyright 2008 National Academy of Sciences.)

as well as piezoelectric applications due to its strong polarization [29, 30]. Using these interesting material properties, Chen *et al* reported new gas sensing properties with hybrid gallium nitride (GaN)-coated cellulose nanocomposite for chemical gas sensor applications [31]. The GaN nanoparticles were coated on a cellulose paper, then IDT gold electrodes were patterned to make a paper-like gas sensor for NO_2 and NH_3 gases (figure 10). The sensor shows good sensitivity and fast response and recovery times. The gas sensing mechanism of the GaN–cellulose gas sensor is explained as a defect-related charge depletion layer for NO_2 gas and a surface adsorption of oxygen species of GaN nanoparticles for NH_3 gas. Figure 10 depicts the schematic of GaN substrate and GaN nanoparticle-based paper chemical gas sensors and corresponding sensitivity results.

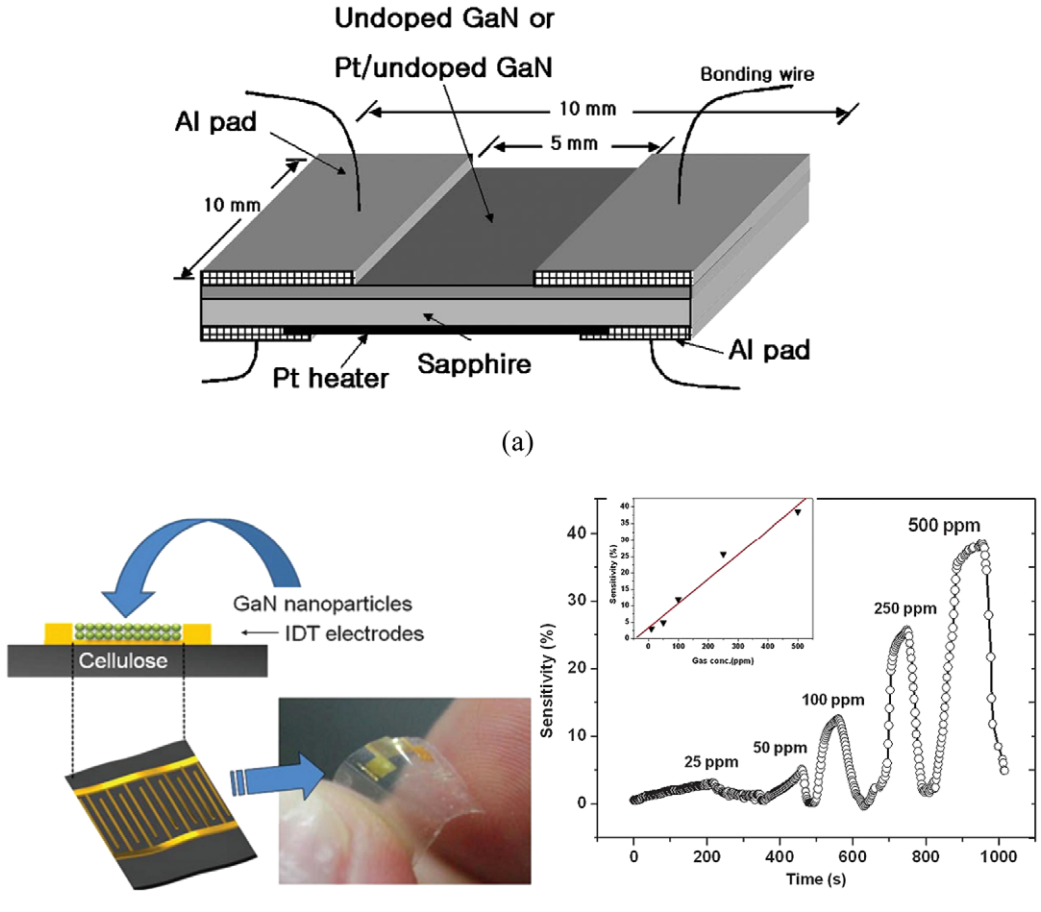

Figure 10. (a) GaN substrate-based gas sensor, and (b) suggested GaN nanoparticle–cellulose paper-based chemical sensor and its sensitivity with NH_3 gases. (Reproduced with permission from [30]. Copyright 2003 Elsevier.) (Reproduced with permission from [31]. Copyright 2012 American Scientific Pub.)

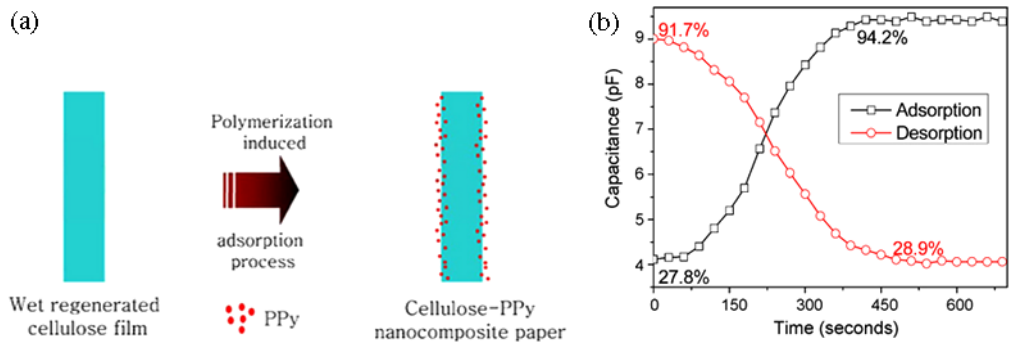

Figure 11. (a) Schematic of cellulose–PPy nanocomposite; (b) response and recovery behavior of cellulose–PPy composite based flexible humidity sensor. (Reproduced with permission from [32]. Copyright 2011 Elsevier.)

6. Paper-based humidity sensor applications

The humidity sensor is a very common device in our daily life. Due to the chemical structure of cellulose, cellulose itself is also relatively sensitive to humidity in air, with the desorption of water molecules. A cellulose-based flexible humidity and temperature sensor has also been demonstrated [32]. As a humidity and temperature sensitive layer, nanoscaled polypyrrole (PPy) was introduced onto a cellulose surface via an *in situ* polymerization technique without disrupting the cellulose structure. Cellulose–PPy nanocomposite was fabricated by nanocoating layer deposition onto cellulose membrane with varying polymerization times (figure 11(a)). For all the cases, the measured capacitance of the paper-based humidity sensor increases with increasing the humidity. Due to the polymerized surface, the adsorption and of

desorption of water molecules shows good repeatability with cyclic humidity testing (figure 11(b)). Thus, a flexible paper-based humidity sensor is made using the cellulose–polypyrrole nanocomposite.

7. Conclusions

In this paper, we reviewed recent achievements and the progress of cellulose paper-based application devices. By hybridizing and covalent bonding carbon nanotubes as well as functional metal oxides with cellulose substrates, the potential and feasibility of nature-friendly, cost-effective and disposable sensor devices with good sensing performance was investigated. However, still more efforts on research and development of the hybrid materials in conjunction with sensor devices are necessary to move forward to real applications. Also long term stability in harsh environments as well as industrial detection protocols to provide complementary sensing information will be additional issues. However, based on the modified current integration technology, cellulose-based paper sensors have great potential for cheap, disposable and biocompatible sensors, with even recycling available after usage.

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