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Smartphone based bioanalytical and diagnosis applications: A review

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ABSTRACT

A smartphone is a facile, handy-analytical device that makes our lives comfortable and stress-free in terms of health care diagnostic assessments. Due to recent advancements in the technology and the introduction of user friendly operating systems and applications, the smartphones have replaced laptops and desktop computers. Taking this fact into account, researchers have designed sensing systems which are more compatible with smartphones. Consequently, these devices are attracting the attention of researchers from fields such as telemedicine, biotechnology, chemical sciences and environmental sciences. In this review, our focus is on recent advances on smartphone based sensing and diagnosis applications.

1. Introduction

Smartphones have become an essential communication tool. In modern times, these devices are smarter than normal cellular phone and generally recognized as “Feature-Phones” (Becher et al., 2011). The added smartness is adopted by the close similarity to personal computers. Smartphones have drastically changed several features of our lives, ranging from entertainment, banking, shopping to health. Through cloud computing, innovative digital technologies and machine learning, smartphone based medical applications are going to overturn all aspects of conventional health care diagnosis. According to the statistics published in 2017, most used smartphones globally are Chinese and Korean manufactured mobiles (Antutu, 2017). The unique software features such as (i) direct measurement of physical quantities using the integrated sensors (ii) easy wireless connectivity with other devices, and (iii) its easy operation, resulted in more researchers focusing on the smartphones to design portable biosensing devices.

Smartphone sensing applications are categorized as participatory sensing and opportunistic sensing (Khan et al., 2013), enabling smartphones to be used in more analytical applications. For example, the picture angles can be measured with an ‘App’ known as Partometer. Several users have downloaded this ‘App’ from “Google Play”. Moreover, researchers have designed novel Apps for health and environmental applications. By using these Apps various health care tests and environmental monitoring assessments can be made rapidly on-site (Capitán-Vallvey and Palma, 2011; Daponte et al., 2013; Williams et al., 2011). For example, heartbeat, blood oxygen saturation, and respiratory rates can be monitored with ultraviolet indices.

Smartphones are analogous to mini computers with internal memory, high quality cameras and operating systems, thereby providing opportunities to advance analytical sensing systems and their applications as reported in the literature (McCracken and Yoon, 2016; Neubeck et al., 2015; Rateni et al., 2017; Roda et al., 2016; Zhang and Liu, 2016). These are cheaper than the miniaturized analytical devices and are easily available to the public (Vashist et al., 2014). Routine laboratory microscopic and spectrophotometer tests which are generally performed by the trained analysts, could be carried out with these portable and low-cost devices. This system would significantly enhance the diagnostic abilities, particularly in countries with less resources (Bellina and Missoni, 2009; Erickson et al., 2014; Martinez et al., 2008; Xu et al., 2015). The increasing demand in point-of-care instruments have recently led researchers to find alternate ways to use smartphones, especially in pathology tests which are done outside the laboratory (Lee et al., 2011) to diagnose tuberculosis and cancer (Gopinath et al., 2014). Smartphones integrated with complementary metal-oxide semiconductor (CMOS) based cameras were proved as highly potential candidates for portable sensing devices (Smith et al., 2011). Smartphones can be coupled with other accessories to make them complete to use in point-of-care platforms (Kenyon et al., 2011; Wac, 2012).

Recent literature reports suggest that smartphone-based sensing applications have gradually been expanded in the health sectors,

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despite several challenges. For instance, using them as detectors, all optical measurements such as surface Plasmon resonance (SPR), electrochemical luminescence, biochemical luminescence, fluorescence, absorbance and reflectance can be performed. However, there must be additional assessments on the real time analytical performance and practicality of these devices in piloting the point-of-need and point-of-care analysis with limited settings. Additionally, to have a wide outline of the real benefits and scenarios of clinical diagnosis with smartphone-based devices, it is important to point out the challenges in handling the biological fluids sampling. In most of the diagnostic methods, blood or plasma is required even if it is executed with a lancet device. This restricts the possibility of distribution of sample in smartphone biosensing devices, provided they are coupled other sample holders. The sampling of biological samples is simple, however the analysis of cortisol (Zangheri et al., 2015) and lactate (Roda et al., 2014) in saliva and sweat is a bigger challenge, as the concentration of these analytes are lower in saliva than in blood. Therefore, it is highly necessary to have an ultra-sensitive analytical method such as smartphone-based biosensors which have been less explored due to unclear technical reasons. Therefore, it is a good idea to use the smartphone as a detector or as an interface for an instrument. In this review, literature survey is critically performed and presented with the information on integration of smartphones with different accessories. The recent advancements of smartphones and their applications focusing on health care platforms are also discussed in this review.

2. Smartphone-based devices

These devices are classified into two types: (i) smartphone as a detector and (ii) smartphone as an interface for an instrument.

2.1. Smartphone as a detector

In this category, a good quality camera is used as a detector to identify the signal output. For instance, simple and cost-effective smartphone-based luminescence imaging for point-of-care was developed with persistent luminescent phosphors by Paterson and co-workers. According to their study, the smartphone was a sensitive device to detect analytes due to the extremely bright and long-lived emission of persistent phosphor. The device was designed on an iPhone 5s, to slide easily into a protective case as shown in Fig. 1. It has a compartment that positions a lateral flow test cartridge in front of the camera and blocks out background light for sensitive luminescence imaging. The system comprises a few integrated elements into a compact apparatus. In particular luminescence imaging, the simplest system includes a single plano-convex macro lens and a bundle of inexpensive plastic optical fibers. In this study, the iPhone 5s was unable to focus on objects within approximately ≈ 4 cm of the camera. However, macro lens enables the camera to focus at a shorter distance, allowing a more compact and practical attachment design.

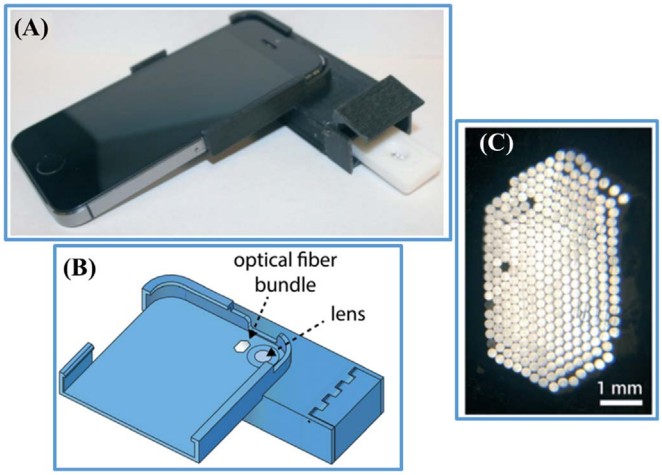

Fig. 1. Frame-A: Image of smartphone attachment with lateral flow assay (LFA) cartridge partially inserted. Frame-B: CAD rendering of attachment noting the lens and optical fiber bundle. Frame-C: Close-up image of optical fibers. Reproduced from Ref: (Paterson et al., 2017) with permission of The Royal Society of Chemistry.

The authors used phone's camera flash to excite phosphors and subsequent luminescence imaging was performed with the camera. The system's performance was demonstrated by detecting human chorionic gonadotropin with strontium aluminate nanoparticles. Interestingly, it was found that the limit of detection (LOD) was ≈ 45 pg mL^{-1} (1.2 pM). The concept could be used to overcome the poor LOD issues and time-gated imaging on a smartphone can be readily adapted for sensitive and potential quantitative point-of-care applications. Additionally, it was done with a variety of persistent luminescent materials (Paterson et al., 2017).

Chloride in sweat is an important diagnostic marker for cystic fibrosis (CF), but the application of point-of-care systems for diagnosis is stalled by the exorbitant costs of existing chloride sensors. To overcome this problem, Zhang and co-workers proposed low cost diagnostic solutions, a citrate-derived synthesis platform for the development of new fluorescence sensors with high selectivity for chloride was designed. In this system, analyte recognition and signal transduction occurred via fluorescence quenching mechanisms. It was noted that the presence of chloride in a solution of CA-Cysteine led to non-radiative relaxation of the excited fluorophore, resulting in visible attenuation of fluorescence. Thereafter, the next signal processing was performed by summation of the total pixel values of the captured fluorescence image to quantify the fluorescence intensity of each measurement followed by the calibration curve as shown in Fig. 2A–D. The sensor material demonstrated a wide linear range of 0.8–200 mM chloride. This test is currently performed with standard sweat diagnostics which is time consuming. However, the clinical validation results demonstrated that the smartphone based chloridometer is a quick and reliable device for the detection of cystic fibrosis and data can be transferred too easily (Zhang et al., 2017).

A first lens-free smartphone spectrometer for the analysis of reaction kinetics and point analyzer that does not use lenses, or other optical components, has been reported by Schäfer et al. (2017). The authors used a light emitting diode (LED) light to illuminate the sample area. As shown in Fig. 3, the smart-phone spectrometer consists of two main parts: the adjustable holding system and the cuvette chamber. The smartphone spectrometer was capable of measuring reaction rates by monitoring changes in the absorbance at wavelengths ranging from 425 to 560 nm and 625–675 nm. The authors demonstrated the device performance by urease bioassay for the detection and measurement of enzyme inhibition caused by heavy metals. It was noted that urease activity was measured to a minimum activity of approximately 1 U mL^{-1}. In addition, the smartphone spectrometer could be used to investigate the mechanism of single-component inhibition in enzyme kinetics in school or basic university laboratories. It could be used as well for community engagement programs to enhance student's interest in the field of science and technology.

On the other hand, Zhu and co-workers have designed a wide-field fluorescent and darkfield imaging device coupled with the smartphone. This device has several important features, including compactness, lightweight and cost-effective optical components that are mechanically integrated to the existing camera unit of the cell-phone as shown in Fig. 4. In this device, battery powered LED was adopted to pump the sample from the side using butt-coupling, where the pump light was directed within the sample cuvette to uniform excitation. The fluorescent emission from the sample was then imaged using an additional lens that was positioned right in front of the existing lens of the cell-phone camera. Since the excitation occurred through guided waves that propagate perpendicular to detection path, an inexpensive plastic color filter was sufficient for fluorescent imaging. In this study, device

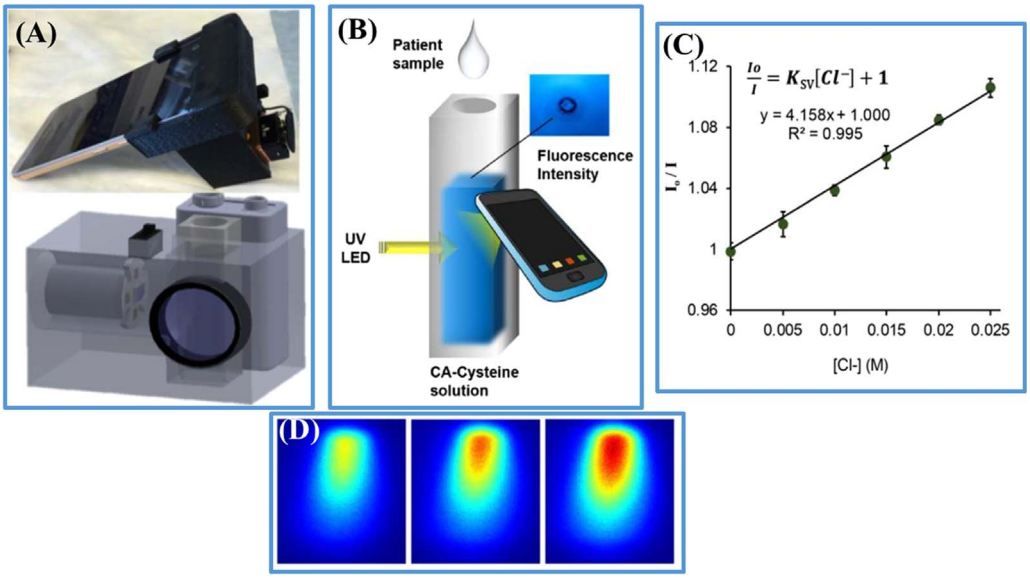

Fig. 2. Frame-A to B: Photo and schematic diagram of the chloridometer system. Frame-C: Calibration curve obtained by the Stern-Volmer relation to linearize fluorescence quenching rates (I_0/I) over chloride concentration to determine the KSV (slope). Frame-D: Raw images of CA-Cysteine fluorescence captured by a smartphone camera in the presence of increasing chloride concentrations. Reproduced from Ref: (Zhang et al., 2017) with permission from Elsevier.

performance was carried out by imaging various fluorescent micro-objects in two colors (i.e., red and green) over a large field-of-view (FOV) of 81 mm^2 with a raw spatial resolution of 20 mm as depicted in Fig. 5. Interestingly, it was found that by using compressive sampling theory, the resolving power was enhanced by two-folds without a trade-off in FOV as one of the features of the device. It should be noted that, the capability of imaging a wide FOV would be exceedingly important to probe large sample volumes (> 0.1 mL) of blood, urine, sputum or water. The authors also demonstrated the fluorescent imaging of labeled white-blood cells from whole blood samples and water-borne pathogenic protozoan parasites such as *Giardia lamblia cysts* detected using the same device (Zhu et al., 2011), making it suitable for decentralized point-of-care use, particularly in developing areas.

Mudanyali and co-workers designed a smartphone-based rapid-diagnostic-test (RDT) reader that could work with various lateral flow immuno-chromatographic assays. This device was used to sense the presence of a target analyte in a sample. The device has several benefits including compactness, low-cost digital RDT reader, light weight (65 g) and automatically integrated to the existing camera. The advantage of this device was that various types of RDTs can be used to capture images in reflection or transmission modes under LED illumination. Then, the captured raw images were digitally processed (within less than 0.2 s per image) through a smart application running on the smartphone for validation of the RDT, as well as for automated reading of its diagnostic result. Due to a dedicated App, the resulting data together with the RDT images and other related information were communicated to a central server, which presents the diagnostic results on a world map through geo-tagging (Mudanyali et al., 2012). A smartphone based device for the detection of cholesterol in blood was developed based on the reflectance photometry using the iPhone iOS platform. This device consists of a strip (sample-stick) on which color change based assay occurred. In this system, a smartphone built-in flash light was used as a light source to irradiate the sample area for further cholesterol enzymatic reaction. A screenshot of the App is depicted in Fig. 6A.

When a user selected the “analyze” button on the App, an image of colorimetric color change was acquired through the iPhone camera. As illustrated in Fig. 6B, the App then execute several processing steps such as the selection of calibration area, taking average of Red Blue Green (RBG) and its conversion to Hue Saturation Lightness (HSL) before the cholesterol value is displayed on the screen. It was found that the average HSL value could be compared to a reference value and a background shift could be computed. Furthermore, algorithm verification was generated to confirm the validation of the obtained value with the typical cholesterol value. Authors demonstrated the device's performance for cholesterol colorimetric reaction that occurred on a dry

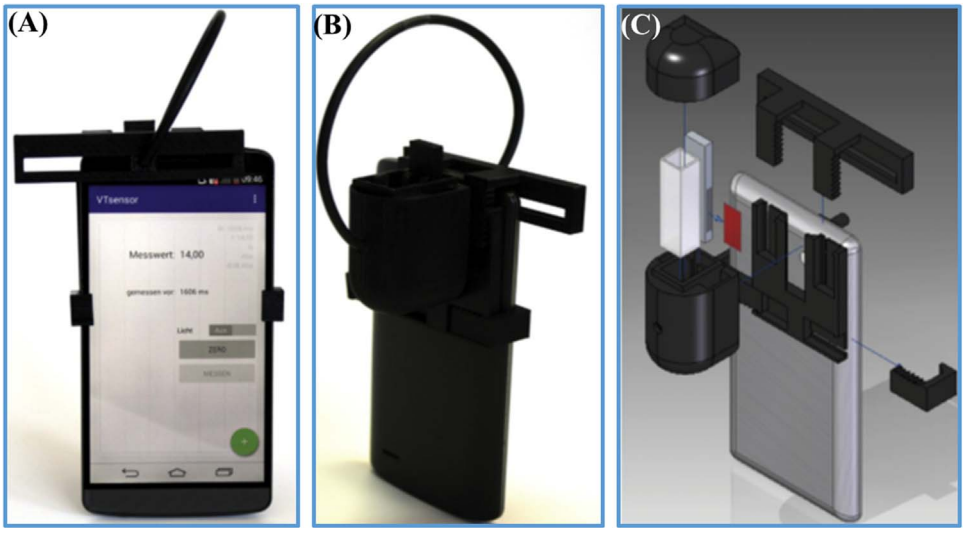

Fig. 3. Frames-A to C: Depicted is the smartphone spectrometer for the measurement of enzyme kinetics and heavy metal ion concentrations with the user interface of the custom-made android app (left) and its exploded-view drawing (right). Reproduced from Ref: (Schäfer et al., 2017) with permission from Elsevier.

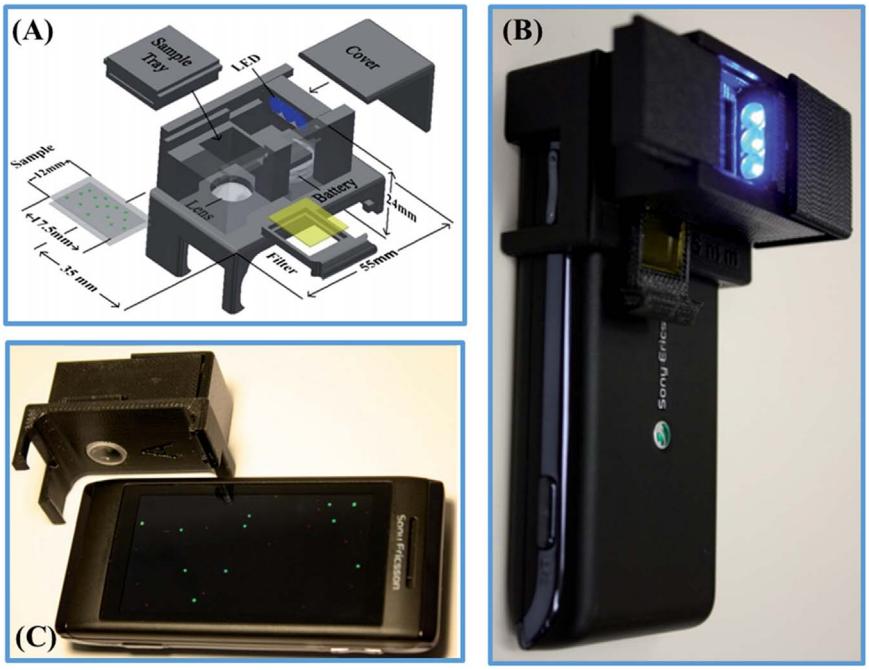

Fig. 4. Frame-A: Schematic diagram of the designed optical attachment for wide-field fluorescent imaging on a cell-phone. Frames-Band C: Different views of the fluorescent imager prototype. This entire attachment to the cell-phone. Reproduced from Ref: (Zhu et al., 2011) with permission of The Royal Society of Chemistry.

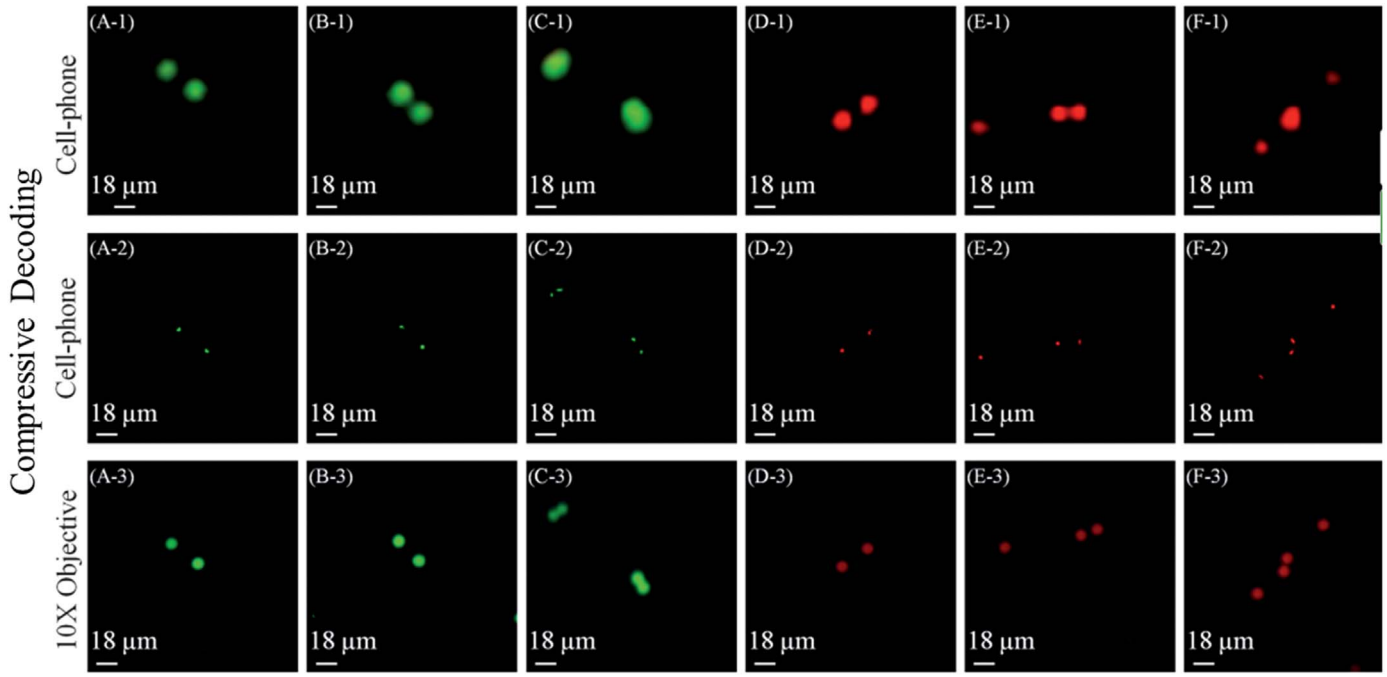

Fig. 5. Spatial resolution of the cell-phone fluorescent microscope illustrated using green and red fluorescent beads. The top row shows raw cell-phone images of the particles which demonstrate 20 mm resolution in both of the fluorescent colors, e.g., the particles in B-1 and E-1 can be resolved from each other by our cell-phone microscope. The middle row illustrates the compressive decoding results of the top row cell-phone images which can now resolve 10 mm spaced fluorescent particles in both green and red colors, as shown in C-2 and F-2, respectively. The bottom row illustrates, for comparison purposes, 10 microscope-objective (NA = 0.25) images of the same samples acquired with a conventional fluorescent microscope. Note that because the samples were suspended in a solution, their relative orientations might be slightly shifted in microscope comparison images. Markers were used on the sample slides to be able to conveniently match the microscope images to their corresponding cell-phone images phone. Reproduced from Ref: (Zhu et al., 2011) with permission of The Royal Society of Chemistry.

reagent test strip. Interestingly, it was noted that the entire range of physiological cholesterol with the actual cholesterol level was 178 mg dL^{-1} (Oncescu et al., 2014). These results further confirmed that this device could be used for reliable and quick results compared to the standard laboratory methods.

Chemiluminescence (CL) has been widely used in several applications, however it is rarely used in a simpler, economical and more effective way. In this study, for the first time, authors have proposed CL cloth-based glucose test sensors (CCGTSs) as a new class of CL glucose sensors, with no need for complicated, expensive device fabrication and peripheral equipment. This device was integrated with a desirable hydrophobic barrier in the flow channel and gravity/capillary flow induced by a difference in height between the loading zone and the detection zone, a single cloth based device was performed in two enzyme reaction steps. The wax screen printed approach was used to fabricate ultra-cheap CCGTSs, the glucose detection involves the enzymatic

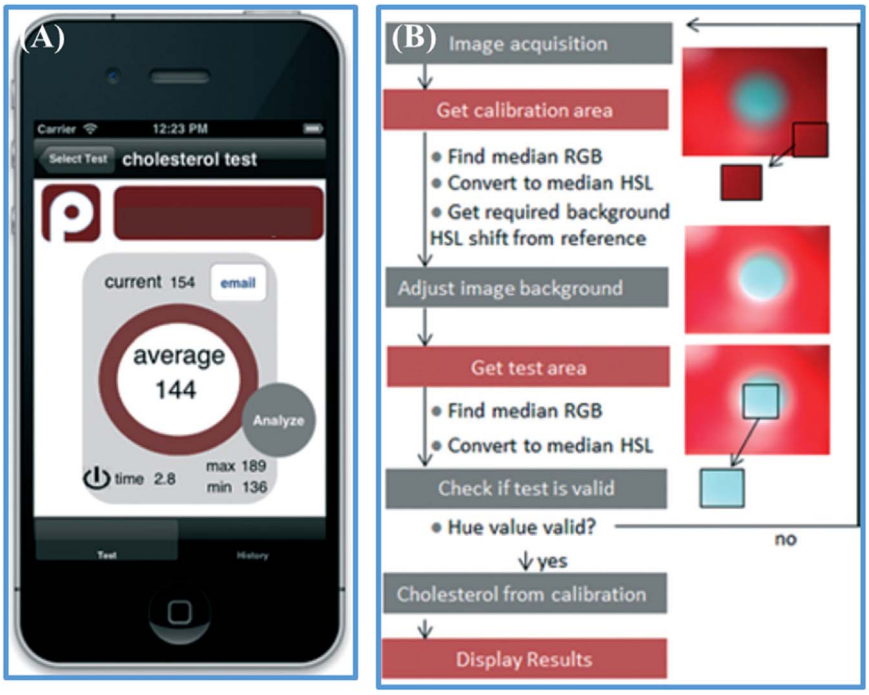

Fig. 6. Frame-A: Screenshot of the app showing current cholesterol reading as well as average reading for one user, Frame-B: Algorithm used for image processing and implemented in iOS app. Reproduced from Ref: (Oncescu et al., 2014) with permission from The Royal Society of Chemistry.

oxidation of glucose to gluconic acid and H_2O_2 followed by the horseradish peroxidase (HRP)-catalysed oxidation of luminol by H_2O_2, and the emitted CL signals are enhanced with p-iodophenol (PIP) and imaged using an inexpensive, portable charge-coupled device (CCD) camera. It was found that, under optimized conditions, glucose can be determined over the range of 0.1–100 mM, with an LOD of 0.0948 mM in less than 5.5 min. The authors demonstrated the device's performance for real sample analysis such as urine and serum samples. Thus, the proposed sensors could provide great promise in applications in many areas, and may facilitate the achievement of point-of-care testing (Li et al., 2017).

Im et al., reported a novel diffraction based approach that enables molecular and cellular diagnostics. This system consists of microbeads, which were used to generate unique diffraction patterns imaged by smartphones. Furthermore, this device was used to screen precancerous or cancerous cells in cervical specimens and also to detect human papillomavirus (HPV) DNA within 45 min. Due to its potential novelty, we believe that this system shows excellent agreement with gold-standard pathology of HPV. Hence, this approach could have favourable global health applications where medical access is limited or when pathology bottlenecks challenge prompt diagnostic readouts (Im et al., 2015).

2.2. Smartphone as instrumental interface

This section focuses on the exploitation of smartphones as an interface device via Wi-Fi, Bluetooth and microUSB with analytical instruments. In this set-up, all the experimental parameters and test results are controlled through the smartphone similar to the laptop. Very few laboratory reports were available in the literature, however, several commercial instruments are available in the market.

Wang et al. developed a compact electrochemical white blood corpuscles (WBC) counting device on microporous paper with patterned gold microelectrodes coupled with a label-free smartphone (Wang et al., 2017b) as illustrated in Fig. 7. The generated voltammetry signal was measured with differential pulse voltammetry (DPV) and transmitted via Bluetooth to the smartphone (see Fig. 7A) within a min. Moreover, the smartphone App collected the data and calculated the concentration value of WBC with internal calibration. Additionally, this system has three gold electrodes, patterned on a polyvinylidene fluoride (PVDF) by e-beam evaporation (see Fig. 7B). Fig. 7C showed the scanning electron microscopy (SEM) image of trapped WBC (white blood cell) on PVDF and microporous structure with a pore size of 5.0 μm. The PVDF membrane surface with thin gold layer electrode appeared to be porous, rough and adsorptive and provided an ideal platform for cell trapping and signal amplification. Further in this study, electrochemical impedance spectroscopy (EIS) measurements were performed in which an upward bending of diffusion impedance appeared at lower frequencies, indicated depletion of ions arriving at the electrode (Fig. 7D). The advantages of porous membrane were measured with Tafel plots as shown in Fig. 7E. In comparison, the slope in the Tafel plot of the membrane electrode was more flattened even at small over-potential due to relatively strong diffusion limit in membrane electrodes, conforming smaller background diffusion coefficient (Fig. 7F). The authors demonstrated the sensor's performance by applying it to human WBC counting in the concentration range of 195–25 kuL^{-1}. The LOD was found to be 195 μL^{-1}, which was 30 times lower than normal concentration (~ 6000 μL^{-1}) in blood. The high accuracy and precision of this system, especially in low WBC concentrations are crucial for applications such as monitoring therapy effects for cancer or immune-deficiency patients.

Recently, to overcome the poor sensitivities and specificities of antibody based point-of-need devices, a low-cost and reliable latent tuberculosis infection (LTBI) screening system based on enzyme linked aptamers was developed. In this study, direct and indirect dot-blot approaches have been reported for the simultaneous quantification of multiple samples and identification of mycobacterial strains. This system has a dedicated, user-friendly interface installed on a Huawei honor 3C (H30-C00) smartphone (Fig. 8A–B). Using an App, the red, green and blue (RGB) information was extracted from JPEG digital images captured by a smart-phone built-in camera or images imported from other equipment. Therefore, an algorithm was established based on the relationship between the concentration of *Mycobacterium tuberculosis* (MTB) and the darkness of the dots. Other research groups also reported that the RGB information extracted from digital images could be converted to grayscale values in two ways: (i) averaged RGB algorithm and (ii) weighted RGB algorithm (Almuntashri and Agaian, 2010). In their study, two algorithms were compared using the optical darkness ratio (ODR) obtained by Adobe Photoshop as a standard. To

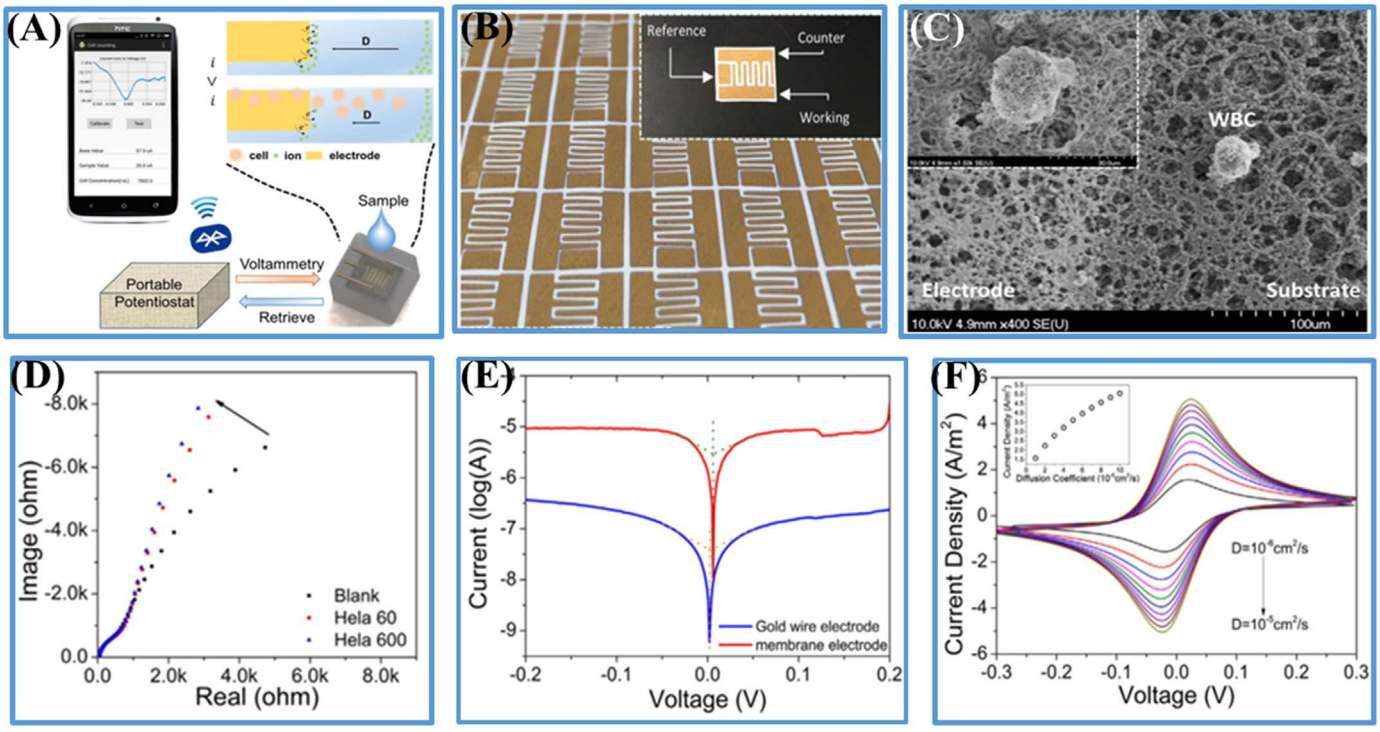

Fig. 7. Cell counting sensor design and principle. Frame-A: System diagram and electrochemical principle for WBC count. D is diffusion coefficient. i is the electrochemical current. Frame-B: Gold three-electrodes on PVDF (polyvinylidene fluoride) membrane paper. Frame-C: Scanning electron microscopy image of trapped WBC (white blood cell) on PVDF and microporous structure of PVDF membrane. Frame-D: Nyquist plot of electrochemical impedance spectroscopy (EIS) showing the diffusion impedance upward bending by adding more Hela cells on the membrane electrode. The over-potential in EIS is − 0.5 V with frequency sweeping from 10 Hz to 100 kHz. Frame-E: Tafel plot of the membrane electrode and wire electrode in 1 mM $[Fe(CN)_6]^{3-}/[Fe(CN)_6]^{4-}$ and 10 mM PBS at the scan rate of 0.1 mV/s. Frame-F: Simulation of cyclic voltammetry method at different diffusion coefficient in the environment of 1 mM $[Fe(CN)_6]^{3-}/[Fe(CN)_6]^{4-}$ and the inset is the peak current density change with diffusion coefficient. Reproduced from Ref: (Wang et al., 2017b) with permission of Elsevier.

this end, area of interest within a dot was selected by a square frame (Fig. 8C) and color information of each pixel inside the selected area was recorded without any external color reference. The concentration of the bacteria was calculated in the unit of CFU mL^{-1} using the calibration curve embedded in the App (Fig. 8D).

Compared with traditional acid-fast staining assay used for LTBI screening, the direct dot-blot system has offered a lower limit of quantitation (LOQ) at 104 CFU mL^{-1} and higher accuracy. In contrast to the traditional bacterial culture approach which takes 3–5 weeks, the present assay can be completed within 5 h, which is a remarkable increase in assay efficiency. The dynamic range and the LOQ of direct dot-blot and indirect dot-blot systems with color spots for different concentration of MTB were shown in Fig. 9A–C. Fig. 9B–D showed calibration plots and the other fitting parameters for MTB sensor of direct and indirect dot-blot systems. To maximize the portability and completeness of LTBI screening device in developing countries, an Android

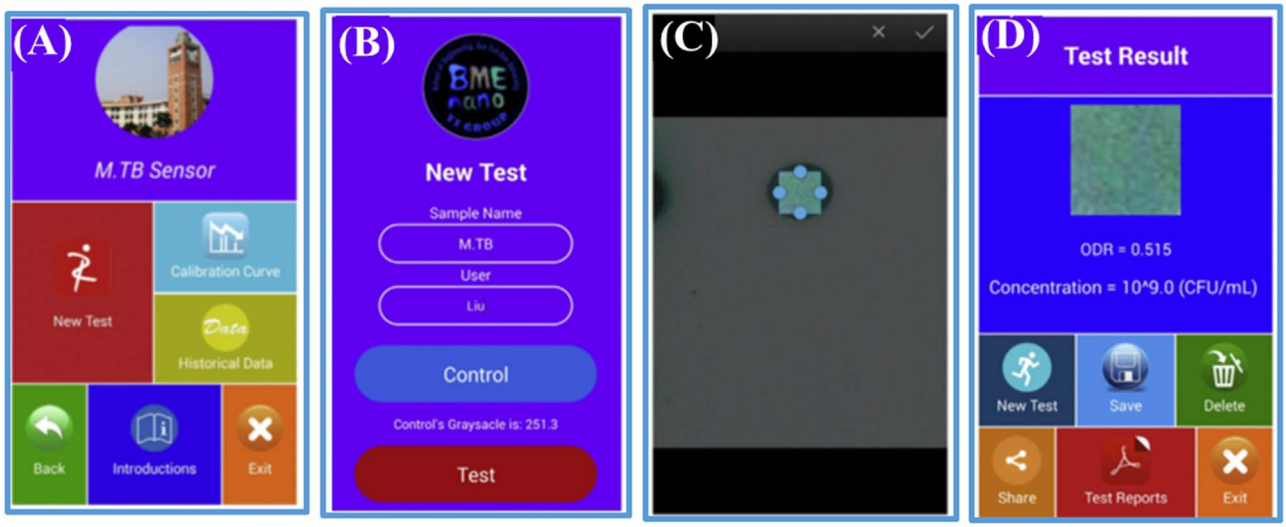

Fig. 8. The main interface of the APP, M.TB Sensor. Frame-A: Main menu. Frame-B: Sample and user information interface: Background grayscale information was obtained by clicking the "Control" button before sample testing. Frame-C: The interface with acquired color images and the selection zone were presented. Frame-D: Interface with processed image and the results after interpolation. The application was run on a Huawei honor 3C (H30-C00) smartphone. Reproduced from Ref: (Li et al., 2018) with permission of Elsevier.

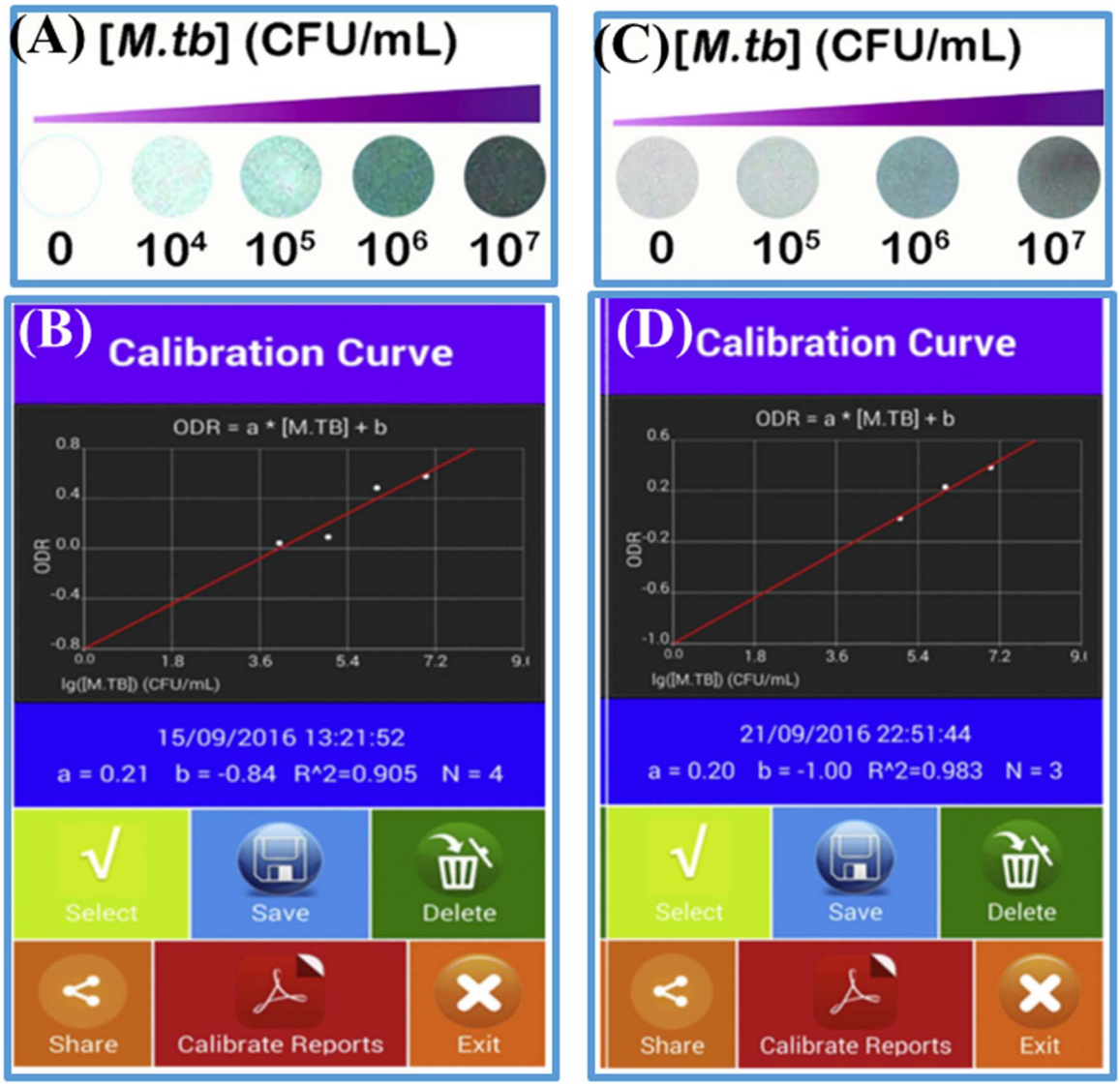

Fig. 9. Dynamic range and limit of quantitation of direct dot-blot and indirect dot- blot systems. Frames-A and C: The color spots with different M.tb concentration in the direct and the indirect dot-blot system, respectively. Frames-B and D: Interface of the M.TB sensor of direct and indirect dot-blot systems showing the calibration plot and the other fitting parameters. Ref: (Li et al., 2018) with permission of Elsevier.

App was developed. In this system, colorimetric analysis of images was captured by a smartphone camera and diagnostic reports were shared via internet connectivity. Due to its low-cost and effectiveness, LTBI screening system would be used to control the outspread of tuberculosis and save many lives, particularly in developing countries (Li et al., 2018).

Of the commercially available sensing systems that can be connected to a smartphone, we essentially find electrocardiogram (ECG), glucometer and HIV dongle. AliveCor Kardia Mobile ($99.00) ECG is a single-channel cardiac recorder operated with an App that enables medical practitioners to record and review electrocardiograms (ECG's) anywhere, anytime (Fig. 10A). This device attaches to the back of smartphone, and communicates via Kardia App (see Fig. 10B). It is very easy to operate by simply resting on fingers or on chest to record an ECG. This device is quick and efficiently transmits signals resulting in minimal battery drain. Interestingly, it is noted that the 4th generation AliveCor Kardia Mobile ECG is compatible with most iOS and Android devices, including iPhone 4S or later, iPad 2 or later, and iPod Touch (5th gen) as shown in Fig. 10C. The smartphone ECG had excellent correlation with the gold standard 12-lead ECG in patients (AliveTec, 2017; Muhlestein et al., 2014; Waks et al., 2015).

MyDario has developed a pocket-sized glucometer controlled via an App to manage diabetes quickly, efficiently and accurately (Fig. 11A). The glucometer was plugged into a smartphone and blood sugar levels were monitored using the company's all-in- one-meter lancets and strips (Fig. 11B) in seconds. The MyDario plugs do not required standalone batteries as they get power source from smartphone. Through the App, users can see blood glucose levels, carbohydrates and insulin intake, as well as physical activity thereby offering a fuller picture of a person's health (Health, 2017).

A research group from New York City's Columbia University developed and commercialized an inexpensive ($1.44 for each test) tool, a small dongle that attaches to a smartphone (Fig. 12). The dongle uses an App to run three assays in one simple test, and employs microfluidics, powered by the smartphone. This is an in-situ method due to its stable gold and silver nanoparticles instead of enzymes that would require special laboratory conditions. The App and dongle diagnose syphilis or an HIV infection by detecting antibodies in a blood sample taken from a finger prick. After successful testing of 96 HIV patients' workers in Rwanda, it was confirmed that the obtained results were remarkably similar to full lab-run HIV or syphilis assays with 92–100% sensitivity for detecting the sexually transmitted diseases. This device is

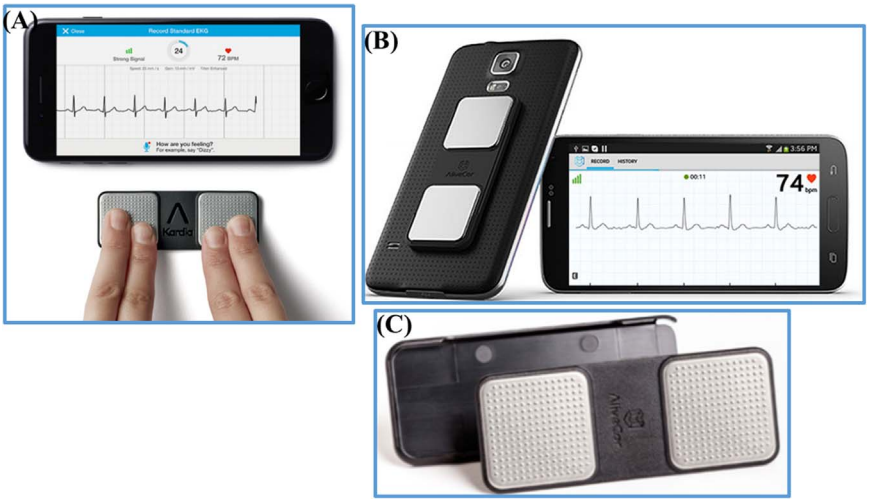

Fig. 10. Frame-A: AliveCor Kardia Mobile ECG, single-channel cardiac recorder. Frame-B: The device attaches to the back of most iOS and Android devices, and communicates wirelessly with the free Kardia App. Frame-C: The 4th generation AliveCor Kardia Mobile ECG, compatible with most iOS and Android devices. Reproduced from Ref: (AliveTec, 2017) with permission of AliveTec.

Fig. 11. Frame-A: Pocket Dario glucometer. Frame-B: The all-in-one meter contains the lancets and strips. Reproduced from Ref: (Health, 2017) with permission of Mydario.

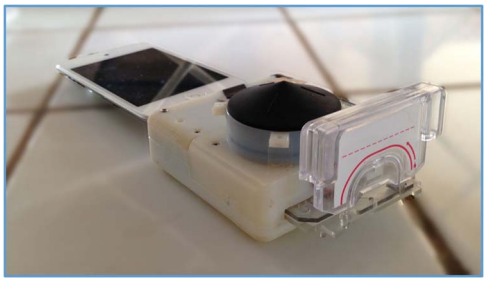

Fig. 12. The smartphone coupled to small dongle for the detection of HIV, developed by The New York City's Columbia University researchers. Reproduced from Ref: (Imtiyaz, 2017) with permission of Labcritics.

useful to developing countries where access to testing labs are limited (Imtiyaz, 2017).

Food and Drug Administration approved smartphone based sensing systems are also available on the market. For example, iBGStar® glucometer and AliveCor® ECG are available to monitor the glucose levels and heart beat respectively (AliveCor, 2017). The world's smallest glucometer was developed by iHealth lab Inc. This company had designed two glucometers which are connected to smartphones or tablets via direct standard audio jack (iHealthlabs, 2017a) and Bluetooth respectively (iHealthlabs, 2017b). These two devices are controlled by an App and the results are automatically stored in a smartphone. It is also easy to share data with the family physician or caretaker.

3. Different smartphone techniques

In this study, smartphone sensors are classified into different types based on their physical principles and materials used. The recently reported different sensor systems and their applications are presented in Table 1.

3.1. Colorimetric chemical sensors

Traditional methods require complicated instrumentation and critical environment. Optical analytical methods can be affected by intrinsic adsorption of a complicated sample such as serum.

The smartphone based colorimetric detection system offers a novel method to healthcare applications (Barbosa et al., 2015; Lai et al., 2017; Mthembu et al., 2017). In general, the pixel intensity of the captured images is determined by an image processing algorithm.

Shin and co-workers recently reported a Smart Forensic Phone for age estimation based on colorimetric analysis of a bloodstain as shown in schematic diagram in Fig. 13. Briefly, for the blood sample on five different materials namely, A4 paper, fabric, wallpaper, glass and wood. The intensity of RGB values were monitored and thereafter the age of the bloodstain was calculated from the plot of brightness (V) values against time. The shortfall of this method is that estimation of the age of the bloodstain is limited to less than 42 h old samples (Shin et al., 2017).

Other colorimetric based application uses gold nanoparticle (AuNPs) which are stabilized by anionic albumins from aggregation, thus, remaining red in color even in salty solutions. However, in the

Table 1
Quick glance on the different smartphone based sensing systems reported in the literature.

Sensor system	Detection source	LOD/LOQ	Applications	Citation
Colorimetry	Smartphone integrated camera	0.1%	Detection of Blood hematocrit	(Kim et al., 2017a)
Colorimetry	Integrated digital camera	0.1 U L^{-1}/–	Detection of alkaline phosphatase activity in milk	(Yu et al., 2015)
Colorimetry	Flash LED	70 μg mL^{-1}/900 μg mL^{-1}	Detection of humanC-reactive protein	(Vashist et al., 2015a)
Colorimetry	Flash LED	–/–	Analysis of a bloodstain for age estimation	(Shin et al., 2017)
Colorimetric smartphone-based immunosensor	Flash LED	0.1 μM/–	Detection of cancer antigen 125 (CA125).	(Hosu et al., 2017)
Colorimetric smartphone-based immunoblotting assay	Illumination sensor	0 to 5 × 10^{-3} μg mL^{-1}/–	Detection of type II collagen (uCTX-II)	(Park et al., 2017)
Lateral flow immunoassay	Chemiluminescence	8.27 × 10^{6} μM/–	Salivary cortisol	(Zangheri et al., 2015)
Immunoassay	Flash LED	10 μg mL^{-1}/10^{5} M^{-1} S^{-1}	Detection of Hepatitis B and HIV	(Giavazzi et al., 2014)
Biological assay	Surface plasmon resonance imaging	1330 μM/–	Point-of-care	(Guner et al., 2017b)
Immunoassays	Fluorescence and electrochemical impedance spectroscopy	12.3 × 10^{-6} μM/–	Detection of Hepatitis C virus core antibody	(Aronoff-Spencer et al., 2016)
Lab on smartphone	Electrochemical	–/–	Gender verification	(Deng et al., 2016)
Smartphone-controlled electrochemical impedance spectroscopy	Electrochemical impedance spectroscopy	1.78 μg mL^{-1}/2970 μg mL	Detection of bull serum albumin (BSA) and thrombin	(Zhang et al., 2016)
Paper-based bipolar electrode	Smartphone for the read-out of ECL signal	1.75 μM/–	Detection of glucose in artificial urine	(Chen et al., 2016)
Chloridometry	Fluorescence	800 μM/–	Detection of Cystic fibrosis	(Zhang et al., 2017)
Fluorescence analyzer	Smartphone camera	4.95 μM/–	Detection of Ochratoxin A in beer samples	(Bueno et al., 2016)
Dual-wavelength fluorescent detection	Smartphone imaging-based fluorescence microscopy	1 × 10^{-6} μg mL^{-1}/–	17-β-estradiol in water	(Lee et al., 2017)
Nanoplasmonic biochips	Commercially available plastic lens,	1000 μg mL^{-1}/–	Detection of imidacloprid pesticides	(Lee et al., 2016)
Smartphone-based portable biosensing system using cell viability biosensor	Illumination provider	0.0422 μM/–	Detection of Okadaic acid	(Su et al., 2017)
Paper-based analytical device (PAD)	Flash LED	20 μM/60 μM	Glucose and lactate concentrations in the cell culture medium	(Im et al., 2016)
Smartphone based microfluidic paper analytical device(mPAD)	–	10^{6} CFU mL^{-1}/–	Detection of urinary tract infection and gonorrhea	(Cho et al., 2015)

absence of adsorbed albumins, AuNPs aggregate and change color to blue. These colorimetric changes can be documented using a smart phone camera acquiring the concentration images which should depict a linear relation between the red color intensity and the logarithm values of albumin concentration to quantify albumin. Lai and co-workers proposed a colorimetric smart phone based assay to determine human serum albumin from samples of the artificial urine matrix containing creatinine and urine (Lai et al., 2017). Although there has been significant advancements in bio-molecular detection and fluidic systems integration, the insight of smartphone performance devices for colorimetric diagnostic applications still presents major difficulties, mostly because of the need to combine adequate sensitivity with the low cost of production and operational simplicity and speed (Barbosa et al., 2015; Gopinath et al., 2014; Kim et al., 2017a).

The smartphones have been used for image-processing program for rapid and sensitive hematocrit determination from 10% to 65% in human blood. The hematocrit determination to an LOD of 0.1% with a sensitivity of 0.53 Gy scale value (GSV) (a.u.)/hematocrit%. Hence, the hematocrit of human blood could be conveniently and accurately determined using the disposable microfluidic device, and then processed by the smartphone camera (Kim et al., 2017a).

A hybrid-biosensor system that works in immunoassay for both protein markers and the enzyme assays have been reported by Kim and co-workers. The system minimizes the interference by the use of pre-determined membrane site etched in a pattern and mounted with a biochemical-reaction pad. This allows for a loaded sample to stay in the pad for entire immunoassay. A serum sample was analyzed according to the vertical direction flowing along the strip and the color signal that was produced from each assay was detected at a pre-determined time and quantified on a smartphone-based detector (Fig. 14). The dynamic ranges for the analytes covered the respective clinical ranges, and the total coefficient of variation was between 8.6% and 13.3% with a high correlation ($R^2 > 0.95$) to other reference systems (Kim et al., 2017b).

A power-free and flexible detection system named Microcapillary Film (MCF) phone for portable colorimetric and fluorescence quantitative sandwich immunoassay detection of prostate specific antigen (PSA) was presented. The entire setup included a smartphone integrated with a magnifying lens, a simple light source and a miniaturized immunoassay platform, the MCF. The excellent transparency and flat geometry of fluoropolymer MCF allowed quantitation of PSA in the range 0.9–60 ng mL^{-1} with < 7% precision in 13 min using enzymatic amplification and a chromogenic substrate with LODs of 0.08 ng mL^{-1} in whole blood samples (Barbosa et al., 2015). Combining the Reflective Phantom Interface to smart phone system enables the realization of novel hand held biosensing devices suitable for those applications where multiple targets have to be rapidly detected. The Reflective Phantom Interface based on measuring the intensity of light reflected by the surface of an amorphous fluoropolymer substrate, which has a refractive index very close to that of the aqueous sample solution and hosts various antibodies immobilized within spots. The reflectivity of dozens of spots is monitored in real time by the phone's camera using the embedded flash LED as the illumination source. The device was able to target heterologous immunoglobulins and antigens for low concentrations in the ppb range (Gopinath et al., 2014).

A colorimetric smartphone-based immunosensor for the detection of cancer antigen 125 (CA125) was designed based on a sandwich strategy whereby the primary antibody was immobilized by spotting onto the 3D nitrocellulose membrane. The antibody-AuNPs captured onto immunospots after being incubated with CA125 solutions induced the silver deposition from a silver enhancer solution leading to the formation of gold-silver nanoparticles of different grey color spots depending on CA125 concentration. The color image acquisition and data handling performed with an 8 megapixels smartphone camera was able to detect up to 30 U mL^{-1} CA125 (Hosu et al., 2017).

A good example of how efficient the smartphone-based colorimetric reader (SBCR) can be was demonstrated by Vashist et al., where SBCR

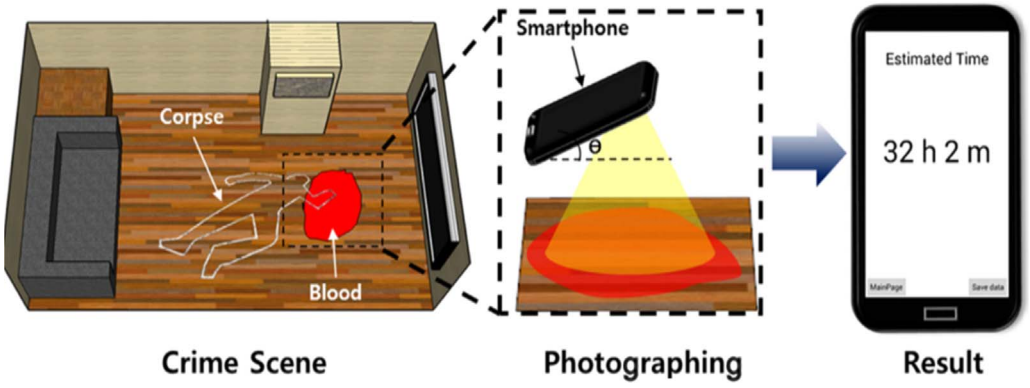

Fig. 13. Illustration stating the blood strain's RBG variation using smartphone for forensic application. Reproduced from Ref: (Shin et al., 2017) with permission of Elsevier.

was compared with a commercial MTP reader (MTPR) for three model assays. The SBCR had the same precision, dynamic range, LOD and sensitivity as MTPR for all three assays (Vashist et al., 2015b).

Park and co-workers developed smartphone-embedded illumination sensor that is integrated with immunoblotting assay method. Interestingly, this system could respond to the ambient light in a wide range of wavelengths, including visible and infrared. In principle, the immunoblotting assay, produced insoluble precipitates at the end of an enzymatic reaction which was then fabricated and mounted on the illumination sensor of the smartphone. The intensity of penetrating light on the illumination sensor is inversely proportional to the amount of precipitates. The efficiency of the system was tested by measuring urinary C-terminal telopeptide fragment of type II collagen (uCTX-II), in the concentration ranging 0–5 ng mL^{-1}. This system was proven to be highly sensitive and accurate under various light conditions (Park et al., 2017).

Although there has been significant advancements in bio-molecular detection and fluidic systems integration, the insight of smartphone performance devices for colorimetric diagnostic applications still presents major difficulties, mostly because of the need to combine adequate sensitivity with low cost of production and operational simplicity and speed (Barbosa et al., 2015; Gopinath et al., 2014; Kim et al., 2017a).

3.2. Spectroscopy sensing

De Oliveria and co-workers recently reported the design for a hand held smartphone-based spectrometer that works in both absorption and emission modes. The device, has a user-friendly home-made software which decompose the pixels from shots of spectral images into their RGB and hue (H) values which are then processed by a simple algorithm developed to convert H values to their corresponding wavelengths. Analytical signals for the absorption mode are provided by an empirical equation based on RGB vector norms (||vRGB||) directly used to acquire

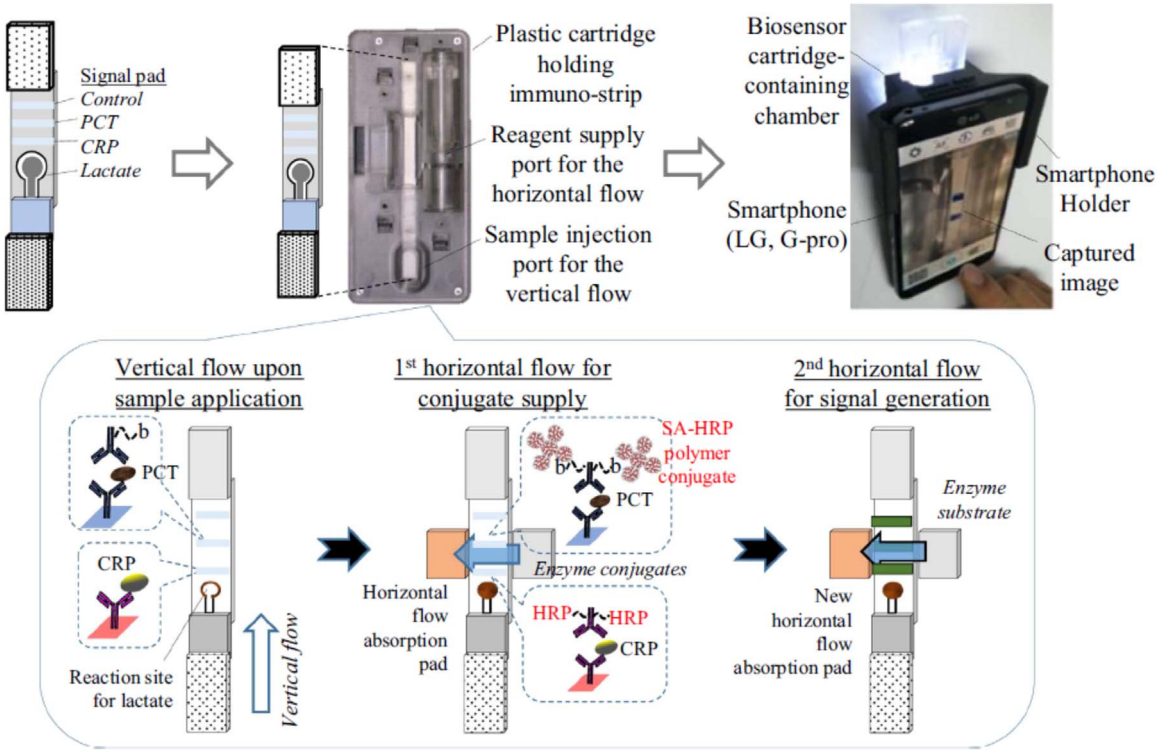

Fig. 14. Analytical concept of the simultaneous biosensing for the biochemical as well as the protein markers in an independent manner. The immune-strip prepared by immobilizing the captured antibodies for procalcitonin (PCT) and C-reactive protein (CRT) on the signed pad and also a secondary antibody at the control site. The biochemical-reaction site for lactate was fabricated on the bottom of the signal pad in a manner that created a surrounding barrier. For the analysis, a clinical sample was applied to the cartridge in the vertical direction and the enzyme tracers for the immunoassays were subsequently supplied using the horizontal flow. The enzyme substrate for HRP was finally supplied along the identical path and the color of the signal intensities were determined using the smartphone-based detector. Reproduced from Ref: (Kim et al., 2017b) with permission of Elsevier.

emission signals taken in blank and after light absorption. The Spectrophone was applied to determine Fe^{2+} in medicine samples and Na^{+} in saline solution and natural water samples (de Oliveira et al., 2017). The method showed no statistically significant differences when compared to commercial instruments (α = 5%). With limits of quantification of 70 μg L^{-1} for absorption and 60 μg L^{-1} emission modes, respectively, and high linearity ($R^2 > 0.9995$). Zangheri and co-workers developed a simple and accurate biosensor based on a chemiluminescent (CL)-lateral flow immunoassay (LFIA) method integrated in a smartphone for quantitative detection of salivary cortisol. The direct competitive immunoassay using peroxidase–cortisol conjugate, is detected by adding the chemiluminescent substrate luminol/enhancer/hydrogen peroxide while the smartphone camera was used for image acquisition and data handling. The system comprises of a cartridge, which houses the LFIA strip, and a smartphone adaptor with a plano-convex lens and a cartridge-insertion slot. The method is simple and fast, with a quantitative analysis in the range of 0.3–60 ng mL^{-1}, and LOD of 0.3 ng mL^{-1} which is adequate for detecting salivary cortisol in the clinically accepted range (Zangheri et al., 2015).

The presence of false signals from non-specific reactions as well as a high background and low signal-to-noise ratios for complementary metal oxide semiconductor image sensors has always been a challenge for bioassay based smartphone-integrated fluorescent biosensors. With the intention to mitigate such a challenge, Lee et al., developed a dual-wavelength fluorescent detection of biomolecules. Whereby one wavelength decreases and the other increases, as the target analytes bind to the split capture and detection aptamer probes. The smartphone imaging-based fluorescence microscopy was performed using a microarray platform on a substrate with metal-enhanced fluorescence (MEF). The authors demonstrated an improvement on the sensitivity and specificity for the target biomolecule 17-β-estradiol in water with LOD of 1 pg mL^{-1} (Lee et al., 2017).

For the first time, Wang and co-workers reported a multichannel smartphone spectrometer (MSS) operating as an optical biosensor for simultaneously detecting of human cancer biomarker. The MSS captured images were converted to the transmission spectrum in the visible wavelength range from 400 to 700 nm with the high resolution of 0.2521 nm per pixel (Wang et al., 2017a).

A smartphone label-free biosensor platform based on grating-coupled surface plasmon resonance (GC-SPR) has been reported by Zhang et al. The sensor system consists of a disposable sensor chip with Au diffraction grating modified with a synthetic peptide receptor and spectra dispersive unit in a form of a compact disk (CD). The GC-SPR sensor was able to detect lipopolysaccharides (LPS) with a limit of detection (LOD) of 32.5 ng mL^{-1} in water. Interestingly the GC-SPR sensor was able to detect LPS in clinical-grade 0.9% sodium chloride intravenous infusion, sodium lactate intravenous infusion and insulin (Zhang et al., 2018).

The rapid detection of antibiotic residual activity in everyday life is very important for food safety, thus confirming the on-site and visual detection of antibiotics. A smartphone-based on the indirect quantification of streptomycin, a model compound for antibiotics, provides fluorescence measurements has been reported. In principle, the excess streptomycin aptamer is hybridized with the complementary DNA to form the dsDNA which then combines with SYBR Green I, emitting green fluorescence (see Fig. 15). Eventually, increasing streptomycin concentration results in a decrease in fluorescence intensity monitored through the RGB values of the images. The streptomycin was detectable at low concentration levels (94 nM), with a linear relationship to G values ranging from 0.1 to 100 μM (Lin et al., 2018).

Another smartphone based SPR imaging platform integrated with biological assays, demonstrated by Gunner et al., to capture mouse IgG antibodies by an immobilized layer of rabbit anti-mouse (RAM) IgG antibody with LOD in the nanomolar level (Guner et al., 2017a). Overall these assay shows us that the illumination sensor-based optical biosensor, miniaturization of SPR biosensing has led to evolution of suitable devices for point-of-care testing (POCT) offering the advantage of portability and simplicity. There is also a potential for multichannel smartphone spectrometer (MSS) biosensors to be useful for high-throughput point-of-care diagnostics with its miniaturized size, light weight, low cost and rapid data transmission.

3.3. Electrochemical sensors

Rapid, sensitive, selective and portable detection through electrochemical sensing platforms are in high demand for public safety, health diagnosis and environmental monitoring through point-of-care (POC) testing. Consequently, there are numerous reports on smartphone-based systems using impedance monitoring applications is demonstrated (Jiang et al., 2014; Liu et al., 2017; Wang et al., 2015; Zhang et al., 2015). These systems include miniaturized biosensors, hand-held EIS detector, and smartphones. Some applications demonstrated the smartphone-controlled electrochemical biosensor system provided a portable and cost-effective platform that allowed integration of diverse biosensor formats for different kinds of quantifications for bio related testing. For instance, a smartphone-controlled biosensor system that was developed by Zhang and co-workers coupled with electro-chemical impedance spectroscopy (EIS) to detect serum albumin (BSA), thrombin and 2,4,6-trinitrotoluene(TNT) (Zhang et al., 2015, 2016).

In their first report they used screen-printed electrodes modified with analyte-specific peptides to produce impedance responses monitored by a hand-held device sent to smartphone through Bluetooth technology. Then, the smartphone was used to display 2,4,6-trinitrotoluene (TNT) responses in real time for concentration as low as 10 μM (Zhang et al., 2015). Later, the protocol was advanced using printed carbon electrodes and interdigital gold electrodes, modified with bio-components for the detection of bovine serum albumin (BSA) and thrombin concentrations as low as 1.78 g mL^{-1} and 2.97 ng mL^{-1} respectively. The impedance measurement shown in Fig. 16, demonstrated an analytical performance for the quantification of the protein binding and enzyme activities by special antibodies and peptides immobilized onto the electrodes (Zhang et al., 2016).

An interesting application of smartphone-based devices is the smartphone-interfaced electrochemical chip device for on-site gender verification. The detection is based on the known difference of biomarkers (creatine kinase (CK) and alanine transaminase (ALT)) between male and female groups. Enzyme cascade reactions converted the enzyme level in the biofluids to the consumption of NADH, detected by an electrochemical chip. Interestingly, this device was capable to perform gender verification when used in serum and serum stains (Deng et al., 2016). Chen and co-workers reported a hand held paper-based bipolar screen-printed electrode-electrochemiluminescence (P-BPE-ECL) system which consists of a rechargeable battery power supply and a smartphone as a read-out of the ECL signal. The P-BPE-ECL system demonstrated impressive detection of glucose in phosphate buffer solution (PBS) and artificial urine (AU) samples, with LOD values of 0.017 mM and 0.030 mM, respectively (Chen et al., 2016). A smartphone-based cyclic voltammetry system with a simple method of electrode modification for the electrochemical detection has great potential in public health, water and food quality monitoring. Ji and co-workers reported on a smartphone with an App, used as a controller and display of the system as shown in Fig. 17. The researchers were able to control the scan rates, and perform cyclic voltammetric (CV) studies with errors < 3.8% in contrast to commercially available electrochemical workstations. Interestingly the screen printed electrodes modified with reduced graphene oxide (rGO) and 3-amino phenylboronic acid (APBA) were used to fabricate a glucose sensor with good linearity, sensitivity and specificity responses to glucose for different doses, even in blood serum as low as about 0.026 mM with 3δ/slope calculation (Ji et al., 2017). Thus, the system could show great potential for the detection and modification of electrodes in various fields.

The results obtained with the smartphone-based electrochemical

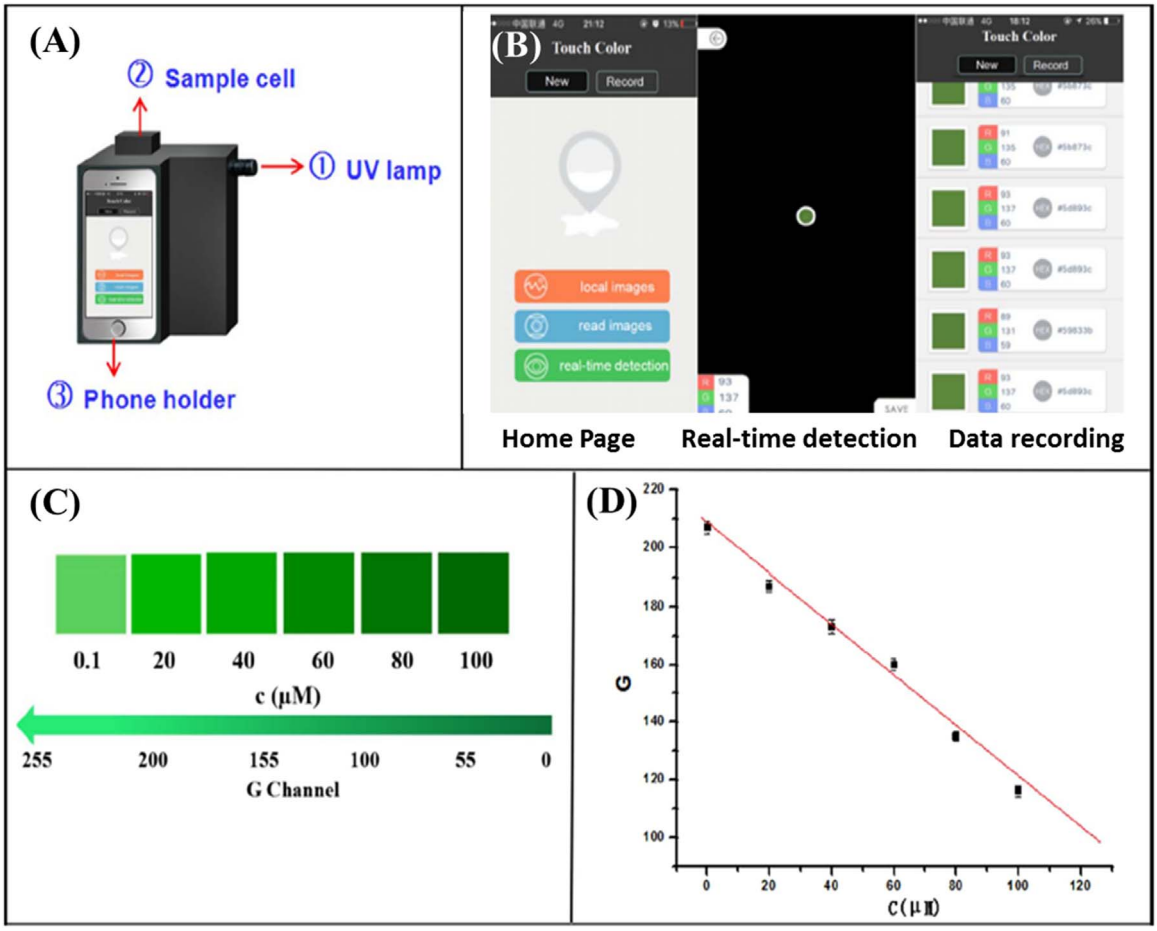

Fig. 15. Frame-A: Construction of the smartphone-based device. Frame-B: The touch Color APP installed in smart phone. Frame-C: Images of sample solutions containing various concentrations of streptomycin. Frame-D: The linear relationship between the G value and the streptomycin concentration. Reproduced from Ref: (Lin et al., 2018) with permission of Elsevier.

measurements are in close correlation with those from traditional instruments, this shows a great potential for a simple, cheap and less invasive monitoring health applications. It is evident in these reports that electroanalytical systems with miniaturized battery-based electronic device and a smartphone app can replace the conventional potentiostat and microcomputer as the analytical system is totally portable.

4. Conclusions and future perspectives

Smartphone-based sensing devices are rapidly gaining recognition in the market with emerging new technologies. More physical quantities can now be measured using smartphones by embedding new sensor Apps and also several wired and wireless connection methods are available to share the recorded data. Camera detectors are also used as a main embedded component in the case of optical sensors. The advantage of using smartphone-based analysis, is that the results can be automatically saved on secure cloud servers or can be shared on several public social media platforms. Since large measurement errors are associated with the mobile sensors, the simplicity, a user-friendly application and low-cost renders this handheld device an attractive alternative for absorption/emission measurements in spectroscopy. It is envisaged that the demonstrated smartphone-based sensing systems will realize the fabrication of highly-sensitive and rapid in-field quantification of multiple species of bacteria and pathogens. With methods such as MCF phone, capable of performing rapid colorimetric quantitative and highly sensitive fluorescence tests with good recovery, this is a major step for the integration of a new generation of inexpensive and portable devices with commercial immunoassay reagents and off-the-shelf smartphone technology. The added advantage of smartphone-based systems, is that they can be used even without the presence of a trained personnel.

Therefore, smartphone-based sensing devices could be a powerful point-of-care tool for the next generation technology for detecting and monitoring of cancer biomarkers at early stages by taking advantage of devices with enhanced features such as smartphones. The future of diagnostics and health monitoring will potentially have cell-phone based or portable readers sipping saliva or blood and thus, continuously monitoring human health. Following an initial publication on the smartphone-based sensing systems, there were huge number of patents and publications that discuss various principles, technologies and transducers coupled to smartphones. In this field, most of the researchers are interested in patenting their devices rather than real time applications. Having such sensitive biosensing capabilities in the field could enable on-the-spot tracking of groundwater contamination, combine the phone's GPS data with biosensing data to map the spread of pathogens, or provide immediate and inexpensive medical diagnostic tests in clinical field or contaminant checks in the food processing and distribution chain. It is challenging to envisage the real awareness of smartphone-based biosensors into the public domain. However, researchers should be motivated and visionary as Bill Gates' dream of "A computer in every home" by exploiting the potential use of technology. All of these sensors, if successfully integrated into the existing smartphones or smart watch products, promises to transform lives. The possibilities are endless, and the only thing holding it back is really just the development of practical sensors themselves. Many of them are very

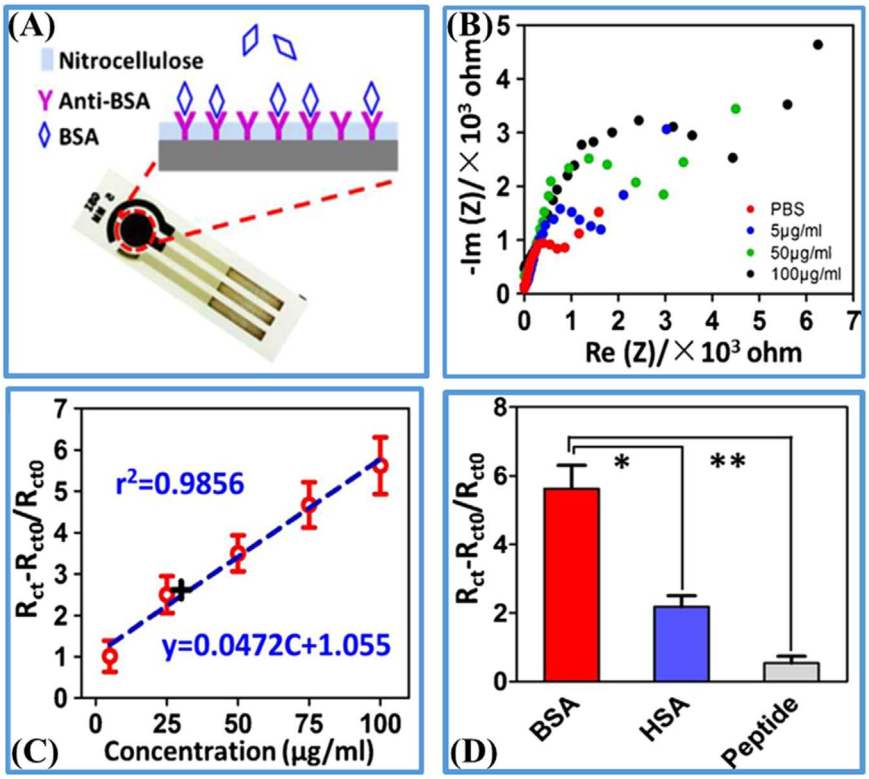

Fig. 16. Images demonstrating the immunosensor coupled to smartphone Frame-A: Screen printing electrode modified with anti-BSA on membrane containing nitrocellulose for the detection of BSA. Frame-B: Nyquist plots for BSA at increasing concentrations. Frame-C: Linear dose-dependent responses. Frame-D: Selective responses of the smartphone-controlled system to BSA. Reproduced from Ref: (Zhang et al., 2016) with permission of Elsevier.

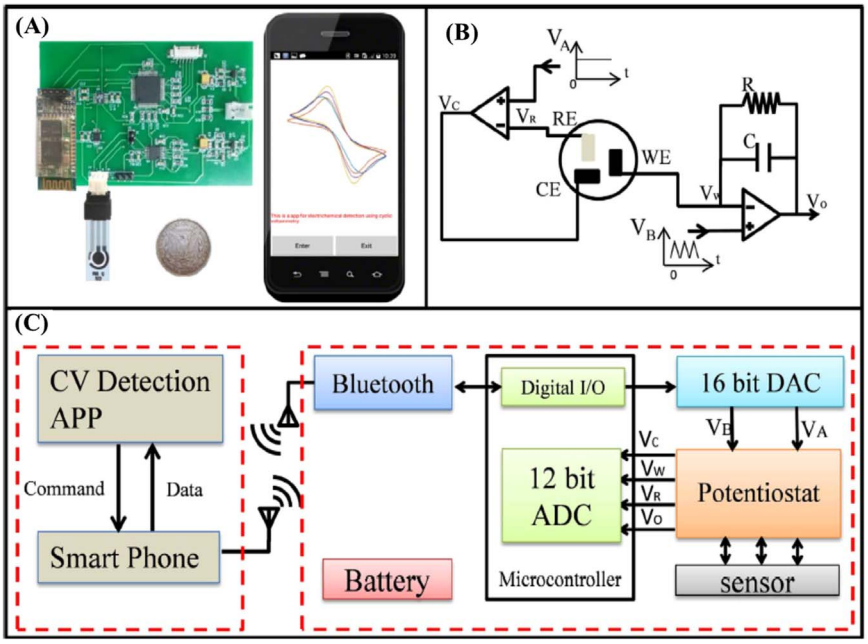

Fig. 17. The schematic and the design of the smartphone-based CV system. Frame-A: The image of the hand-held detector connected with SPE and the welcome interface of the App and the smartphone. Frame-B: The circuit design of the potentiostat based on a resistive feedback transimpendance amplifier. Frame-C: A schematic diagram of the smartphone-based CV system. Reproduced from Ref: (Ji et al., 2017) with permission of Elsevier.

close to viable, while others are already available and only needed to be integrated into new smartphone-based platforms.

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Conflict of interest

All authors declare no conflict of interest.

References

AliveCor, 2017. AliveCor ⟨https://www.alivecor.com/⟩ (12 July 2017).
AliveTec, 2017. AliveCor Kardia Mobile ECG for iPhone and Android. ⟨http://www.alivetec.com/alivecor-heart-monitor/⟩ (06 October 2017).
Almuntashri, A., Agaian, S., 2010. An algorithm for visualizing and detecting edges in RGB color images using logarithmic ratio approach. In: IEEE International Conference on Systems, Man and Cybernetics, Istanbul, pp. 3942–3947.
Antutu, 2017. Top 10 Most Popular Smartphones Around the World of 2016. ⟨http://www.antutu.com/en/doc/107774.htm⟩ (02 November 2017).
Aronoff-Spencer, E., Venkatesh, A.G., Sun, A., Brickner, H., Looney, D., Hall, D.A., 2016. Biosens. Bioelectron. 86, 690–696.
Barbosa, A.I., Gehlot, P., Sidapra, K., Edwards, A.D., Reis, N.M., 2015. Biosens. Bioelectron. 70, 5–14.

Becher, M., Freiling, F.C., Hoffmann, J., Holz, T., Uellenbeck, S., Wolf, C., 2011. Mobile security catching up? Revealing the nuts and bolts of the security of mobile devices, Security and Privacy (SP). In: IEEE Symposium on Security and Privacy, IEEE Computer Society, Berkeley, CA, USA, pp. 96–111.
Bellina, L., Missoni, E., 2009. Diagn. Pathol. 4, 19–22.
Bueno, D., Muñoz, R., Marty, J.L., 2016. Sens. Actuator B-Chem. 232, 462–468.
Capitán-Vallvey, L.F., Palma, A.J., 2011. Anal. Chim. Acta 696, 27–46.
Chen, L., Zhang, C., Xing, D., 2016. Sens. Actuator B-Chem. 237, 308–317.
Cho, S., Park, T.S., Nahapetian, T.G., Yoon, J.-Y., 2015. Biosens. Bioelectron. 74, 601–611.
Daponte, P., De Vito, L., Picariello, F., Riccio, M., 2013. Measurement 46, 3291–3307.
de Oliveira, H.J.S., de Almeida Jr, P.L., Sampaio, B.A., Fernandes, J.P.A., Pessoa-Neto, O.D., de Lima, E.A., de Almeida, L.F., 2017. Sens. Actuator B-Chem. 238, 1084–1091.
Deng, W., Dou, Y., Song, P., Xu, H., Aldalbahi, A., Chen, N., El-Sayed, N.N., Gao, J., Lu, J., Song, S., Zuo, X., 2016. J. Electroanal. Chem. 777, 117–122.
Erickson, D., O'Dell, D., Jiang, L., Oncescu, V., Gumus, A., Lee, S., Mancuso, M., Mehta, S., 2014. Lab Chip 14, 3159–3164.
Giavazzi, F., Salina, M., Ceccarello, E., Ilacqua, A., Damin, F., Sola, L., Chiari, M., Chini, B., Cerbino, R., Bellini, T., Buscaglia, M., 2014. Biosens. Bioelectron. 58, 395–402.
Gopinath, S.C., Tang, T.H., Chen, Y., Citartan, M., Lakshmipriya, T., 2014. Biosens. Bioelectron. 60, 332–342.
Guner, H., Ozgur, E., Kokturk, G., Celik, M., Esen, E., Topal, A.E., Ayas, S., Uludag, Y., Elbuken, C., Dana, A., 2017a. Sens. Actuator B-Chem. 239, 571–577.
Guner, H., Ozgur, E., Kokturk, G., Celik, M., Esen, E., Topal, A.E., Ayas, S., Uludag, Y., Elbuken, C., Dana, A., 2017b. Sens. Actuator B-Chem. 239, 571–577.
Health, D., 2017. Diaro Health: Dario Blood Glucose Management System. ⟨https://mydario.com/⟩ (06 October 2017).
Hosu, O., Ravalli, A., Lo Piccolo, G.M., Cristea, C., Sandulescu, R., Marrazza, G., 2017. Talanta 166, 234–240.
iHealthlabs, 2017a. iHealth Align. ⟨http://www.ihealthlabs.com/glucometer/ihealth-align⟩ (12 July 2017).
iHealthlabs, 2017b. iHealth Smart: Wireless Gluco-Monitoring System. ⟨https://ihealthlabs.com/glucometer/wireless-smart-gluco-monitoring-system/⟩ (12 July 2017).
Im, H., Castro, C.M., Shao, H., Liong, M., Song, J., Pathania, D., Fexon, L., Min, C., Avila-Wallace, M., Zurkiya, O., Rho, J., Magaoay, B., Tambouret, R.H., Pivovarov, M., Weissleder, R., Lee, H., 2015. Proc. Natl. Acad. Sci. USA 112, 5613–5618.
Im, S.H., Kim, K.R., Park, Y.M., Yoon, J.H., Hong, J.W., Yoon, H.C., 2016. Sens. Actuator B-Chem. 229, 166–173.
Imtiyaz, M., 2017. Labcritics: Quick Smartphone Based HIV Test ⟨http://www.labcritics.com/quick-smartphone-based-hiv-test-3708/⟩. (7 February 2015).
Ji, D., Liu, L., Li, S., Chen, C., Lu, Y., Wu, J., Liu, Q., 2017. Biosens. Bioelectron. 98, 449–456.
Jiang, J., Wang, X., Chao, R., Ren, Y., Hu, C., Xu, Z., Liu, G.L., 2014. Sens. Actuator B-Chem. 193, 653–659.
Kenyon, J.I., Poropatich, R., Holtel, M.R., 2011. Otolaryngol. Clin. North Am. 44, 1351–1358.
Khan, W.Z., Xiang, Y., Aalsalem, M.Y., Arshad, Q., 2013. IEEE Commun. Surv. Tutor. 15, 402–427.
Kim, S.C., Jalal, U.M., Im, S.B., Ko, S., Shim, J.S., 2017a. Sens. Actuator B-Chem. 239, 52–59.
Kim, S.W., Cho, I.H., Lim, G.S., Park, G.N., Paek, S.H., 2017b. Biosens. Bioelectron. 98, 7–14.
Lai, T.-S., Chang, T.-C., Wang, S.-C., 2017. Sens. Actuator B-Chem. 239, 9–16.
Lee, D., Chou, W.P., Yeh, S.H., Chen, P.J., Chen, P.H., 2011. Biosens. Bioelectron. 26, 4349–4354.
Lee, K.-L., You, M.-L., Tsai, C.-H., Lin, E.-H., Hsieh, S.-Y., Ho, M.-H., Hsu, J.-C., Wei, P.-K., 2016. Biosens. Bioelectron. 75, 88–95.
Lee, W.-I., Shrivastava, S., Duy, L.-T., Yeong Kim, B., Son, Y.-M., Lee, N.-E., 2017. Biosens. Bioelectron. 94, 643–650.
Li, H., Liu, C., Wang, D., Zhang, C., 2017. Biosens. Bioelectron. 91, 268–275.
Li, L., Liu, Z., Zhang, H., Yue, W., Li, C.-W., Yi, C., 2018. Sens. Actuator B-Chem. 254, 337–346.
Lin, B., Yu, Y., Cao, Y., Guo, M., Zhu, D., Dai, J., Zheng, M., 2018. Biosens. Bioelectron. 100, 482–489.
Liu, L., Zhang, D., Zhang, Q., Chen, X., Xu, G., Lu, Y., Liu, Q., 2017. Biosens. Bioelectron. 93, 94–101.
Martinez, A.W., Phillips, S.T., Carrilho, E., Thomas III, S.W., Sindi, H., Whitesides, G.M., 2008. Anal. Chem. 80, 3699–3707.
McCracken, K.E., Yoon, J.-Y., 2016. Anal. Methods 8, 6591–6601.
Mthembu, L., Sabela, M.I., Mlambo, M., Madikizela, L.M., Suvardhan, K., Gumede, H., Mdluli, P.S., 2017. Anal. Methods 9, 5943–5951.
Mudanyali, O., Dimitrov, S., Sikora, U., Padmanabhan, S., Navruz, I., Ozcan, A., 2012. Lab Chip 12, 2678–2686.
Muhlestein, J.B., Le, V., Albert, D., Moreno, F.L., Anderson, J.L., Yanowitz, F., Vranian, R.B., Barsness, G.W., Bethea, C.F., Severance, H.W., Ramo, B., Pierce, J., Barbagelata, A., Muhlestein, J.B., 2014. J. Electrocardiol. 48, 249–259.
Neubeck, L., Lowres, N., Benjamin, E.J., Freedman, S.B., Coorey, G., Redfern, J., 2015. Nat. Rev. Cardiol. 12, 350–360.
Oncescu, V., Mancuso, M., Erickson, D., 2014. Lab Chip 14, 759–763.
Park, Y.M., Han, Y.D., Chun, H.J., Yoon, H.C., 2017. Biosens. Bioelectron. 93, 205–211.
Paterson, A.S., Raja, B., Mandadi, V., Townsend, B., Lee, M., Buell, A., Vu, B., Brgoch, J., Willson, R.C., 2017. Lab Chip 17, 1051–1059.
Rateni, G., Dario, P., Cavallo, F., 2017. Sensors 17, 1453.
Roda, A., Guardigli, M., Calabria, D., Calabretta, M.M., Cevenini, L., Michelini, E., 2014. Analyst 139, 6494–6501.
Roda, A., Michelini, E., Zangheri, M., Di Fusco, M., Calabria, D., Simoni, P., 2016. Trends Analyt Chem. 79, 317–325.
Schäfer, M., Bräuler, V., Ulber, R., 2017. Sens. Actuator B-Chem. 255, 1902–1910.
Shin, J., Choi, S., Yang, J.-S., Song, J., Choi, J.-S., Jung, H.-I., 2017. Sens. Actuator B-Chem. 243, 221–225.
Smith, Z.J., Chu, K., Espenson, A.R., Rahimzadeh, M., Gryshuk, A., Molinaro, M., Dwyre, D.M., Lane, S., Matthews, D., Wachsmann-Hogiu, S., 2011. PLoS One 6, e17150.
Su, K., Pan, Y., Wan, Z., Zhong, L., Fang, J., Zou, Q., Li, H., Wang, P., 2017. Sens. Actuator B-Chem. 251, 134–143.
Vashist, S.K., Marion Schneider, E., Zengerle, R., von Stetten, F., Luong, J.H., 2015a. Biosens. Bioelectron. 66, 169–176.
Vashist, S.K., Mudanyali, O., Schneider, E.M., Zengerle, R., Ozcan, A., 2014. Anal. Bioanal. Chem. 406, 3263–3277.
Vashist, S.K., van Oordt, T., Schneider, E.M., Zengerle, R., von Stetten, F., Luong, J.H., 2015b. Biosens. Bioelectron. 67, 248–255.
Wac, K., 2012. Yearb. Med. Inform. 7, 83–93.
Waks, J.W., Fein, A.S., Das, S., 2015. JAMA Intern. Med. 175, 437–439.
Wang, L.J., Chang, Y.C., Sun, R., Li, L., 2017a. Biosens. Bioelectron. 87, 686–692.
Wang, X., Gartia, M.R., Jiang, J., Chang, T.-W., Qian, J., Liu, Y., Liu, X., Liu, G.L., 2015. Sens. Actuator B-Chem. 209, 677–685.
Wang, X., Lin, G., Cui, G., Zhou, X., Liu, G.L., 2017b. Biosens. Bioelectron. 90, 549–557.
Williams, A.J., Ekins, S., Clark, A.M., Jack, J.J., Apodaca, R.L., 2011. Drug Discov. Today 16, 928–939.
Xu, X., Akay, A., Wei, H., Wang, S., Pingguan-Murphy, B., Erlandsson, B.E., Li, X., Lee, W., Hu, J., Wang, L., Xu, F., 2015. Proc. IEEE 103, 236–247.
Yu, L., Shi, Z., Fang, C., Zhang, Y., Liu, Y., Li, C., 2015. Biosens. Bioelectron. 69, 307–315.
Zangheri, M., Cevenini, L., Anfossi, L., Baggiani, C., Simoni, P., Di Nardo, F., Roda, A., 2015. Biosens. Bioelectron. 64, 63–68.
Zhang, C., Kim, J.P., Creer, M., Yang, J., Liu, Z., 2017. Biosens. Bioelectron. 97, 164–168.
Zhang, D., Jiang, J., Chen, J., Zhang, Q., Lu, Y., Yao, Y., Li, S., Logan Liu, G., Liu, Q., 2015. Biosens. Bioelectron. 70, 81–88.
Zhang, D., Liu, Q., 2016. Biosens. Bioelectron. 75, 273–284.
Zhang, D., Lu, Y., Zhang, Q., Liu, L., Li, S., Yao, Y., Jiang, J., Liu, G.L., Liu, Q., 2016. Sens. Actuator B-Chem. 222, 994–1002.
Zhang, J., Khan, I., Zhang, Q., Liu, X., Dostalek, J., Liedberg, B., Wang, Y., 2018. Biosens. Bioelectron. 99, 312–317.
Zhu, H., Yaglidere, O., Su, T.-W., Tseng, D., Ozcan, A., 2011. Lab Chip 11, 315–322.