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Research Article

Smartphone-based portable wireless optical system for the detection of target analytes

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Rapid and accurate on-site wireless measurement of hazardous molecules or biomarkers is one of the biggest challenges in nanobiotechnology. A novel smartphone-based Portable and Wireless Optical System (PAWS) for rapid, quantitative, and on-site analysis of target analytes is described. As a proof-of-concept, we employed gold nanoparticles (GNP) and an enzyme, horse radish peroxidase (HRP), to generate colorimetric signals in response to two model target molecules, melamine and hydrogen peroxide, respectively. The colorimetric signal produced by the presence of the target molecules is converted to an electrical signal by the inbuilt electronic circuit of the device. The converted electrical signal is then measured wirelessly via multimeter in the smartphone which processes the data and displays the results, including the concentration of analytes and its significance. This handheld device has great potential as a programmable and miniaturized platform to achieve rapid and on-site detection of various analytes in a point-of-care testing (POCT) manner.

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1 Introduction

Point-of-care testing (POCT) is defined as medical testing conducted near the location of a patient whenever medical care is necessary [1]. In recent years, POCT devices have attracted a great deal of attention because they facilitate near-patient testing, broaden convenient access to diagnostics, and provide immediate results with simple and cost-effective instrumentation [2, 3]. POCT systems are normally based on electrochemical [3, 4], optical [3, 5], thermal [6] or piezoelectric [7] detection. Among these techniques, optical platforms have been widely utilized due to their simplicity [8, 9], visual response capability [10, 11], accuracy [9], and high sensitivity [9]. Currently, various types of optical POCT devices are commercially available and most of the popular ones are being produced by leading companies such as Hach [12], LaMotte [12], Roche Diagnostics [12], and Abbott Diagnostics [3]. They are portable and comprised of cheaper components compared to bulky lab-based conventional spectrophotometers. However, the devices have several remaining drawbacks. First, they are still expensive. Second, they do not possess the advanced functionalities found in most portable smart devices, which routinely include computing power, wireless and internet connectivity, intuitive touch-based display and Global Positioning System (GPS) tagging, all of which can facilitate several key activities, such as analyzing the measured data and then informing relevant authorities of the results.

With the goal of overcoming the drawbacks of the aforementioned systems, many researchers are trying to develop POCT devices by integrating smartphones, which harness their advanced computational ability and communication functions. Most of the smartphone-integrated POCT devices include software that can analyze

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Abbreviations: GNP, gold nanoparticles; **GPS,** Global Positioning System; **HRP,** horse radish peroxidase; **LDR,** light dependent resistor; **LED,** light emitting diode; **LOD,** limit of detection; **PAWS,** portable and wireless optical system; **POCT,** point-of-care testing; **TMB,** 3,3',5,5'-tetramethylbenzidine

the data obtained from the sensing system. Representatively, Pelegris et al. [13] reported an application that checks the heartbeat of a user based on the color change of a finger placed on the smartphone's camera. Shen et al. developed a pH sensor utilizing a smartphone to take images of pH test strips [14]. Recently, Wei et al. developed a novel strategy to detect mercury ions [15] by analyzing a photo captured by the smartphone camera; similar strategies have been presented by Vashist et al. and Garcia et al. for the detection of c-reactive protein (CRP) [16] and potassium [17], respectively. Priye et al. developed a smartphone-based platform to detect nucleic acids that can be deployed for the inflight detection [18]. The core of their strategies involves a target-specific colorimetric reaction followed by quantification of the resulting color by analyzing a photo of the solution. These strategies, unlike conventional techniques, are applicable to POCT instrumentation to achieve on-site detection. However, these approaches have limitations in terms of repeatability and detection sensitivity, both of which depend on undesirable variations in ambient light conditions (e.g. day vs. night), alignment and/or user operation (angle of taking photo) while capturing the photo. Moreover, their detection results vary according to the smartphone chosen because the detection accuracy depends on the quality of the smartphone camera (e.g. 2 megapixels vs. 10 megapixels).

We herein report a lightweight (≈350 g), standalone, cost-effective, field-portable, wireless and smartphone-based device for the sensitive and quantitative on-site detection, taking melamine and hydrogen peroxide as the proof-of-concept target analytes by promoting the colorimetric reactions of the respective colorimetric substrates, gold nanoparticles (GNP) and 3,3',5,5'-tetramethylbenzidine (TMB). The smartphone is installed with a custom-modified application that analyzes and displays the detection result and its significance.

2 Materials and methods

2.1 Construction of PAWS

To construct the PAWS circuit, a transistor (MPS 2222a), LDR (light dependent resistor) (GL55), LED (light emitting diode) (3 mm, White), resistors (EPX34LM4 and EPX34LNG), battery (AAA), capacitor (100 μF), and red laser pointer (emission at 650 nm) were purchased from eLePARTS, South Korea. The wireless multimeter (Mooshimeter, Bluetooth: 4.0) was purchased from Mooshim Engineering. The LED works as an indicator to check the functioning of the circuit. The wireless mulitmeter was connected in parallel to the LED to measure the changes in voltage drop according to the resistance of the LDR. Darlington transistors were employed to amplify the current from the LDR, and batteries (6 V) were the power source of the circuit. The capacitor was connected parallel to the power source to reduce voltage fluctuations in the circuit. The mulitmeter was connected to the circuit, which measures the voltage wirelessly and sends the signal to the smartphone. The smartphone (Samsung Galaxy S4 mini) detects the wireless signal and displays the voltage and measurement details. Disposable cuvettes were used to load samples and a red laser pointer was used as the light source. The laser is placed ≈10 mm away from the cuvette and the cuvette is ≈16 mm away from LDR. The sizes of the cuvette, multimeter, circuit and battery are approximately 10 mm × 10 mm, 105 mm × 40 mm, 25 mm × 25 mm, and 50 mm × 25 mm, respectively.

We modified the application of the multimeter to detect the target analytes. We first measured the voltage change in response to the concentration of the analyte, which was then used to plot a standard curve of voltage change vs. concentration of the analyte. Finally, we calculated the equation correlating the analyte concentration with the voltage change, which was saved in the application. Based on the equation of the curve, the application automatically calculated the unknown concentration of target analytes from the measured voltage. In order to detect other analytes, standard curves of the analytes can be constructed and stored in the application. When a specific target analyte under measurement is selected, it refers to the corresponding curve and calculates the unknown concentration. The equations for standard curves used to quantify melamine and hydrogen peroxide were $y = -0.0034x + 1.9562$ and $y = -0.0042x + 1.9213$, respectively, where "x" is the concentration of target analyte and "y" is the voltage measured by PAWS. We used these equations to calculate the unknown concentrations of melamine and hydrogen peroxide. We further programmed the application to show the significance of the measured concentrations of the analytes, so that users can determine whether the milk is edible, inedible or to be reported to the relevant authorities.

2.2 GNP-based melamine detection

GNP was synthesized based on the procedure of Grabar et al. with slight modifications [19]. 50 μL of $HAuCl_4$ (1 mM) was prepared in a flask, which was then stirred continuously until boiling. 5 mL of sodium citrate (38.8 mM) was added to the boiling solution resulting in a color change from pale yellow to blue and slowly to red. Boiling was continued for 7 min; the hot plate was removed but stirring was maintained for additional 15 min. Finally, GNP with 13 nm in diameter was prepared and used for the detection of melamine in milk.

Milk and melamine were bought from the local supermarket in Daejeon, South Korea, and Sigma Aldrich, respectively. Melamine was spiked in the whole milk followed by dilution with milk to prepare the different concentrations of melamine in milk. Melamine-spiked milk

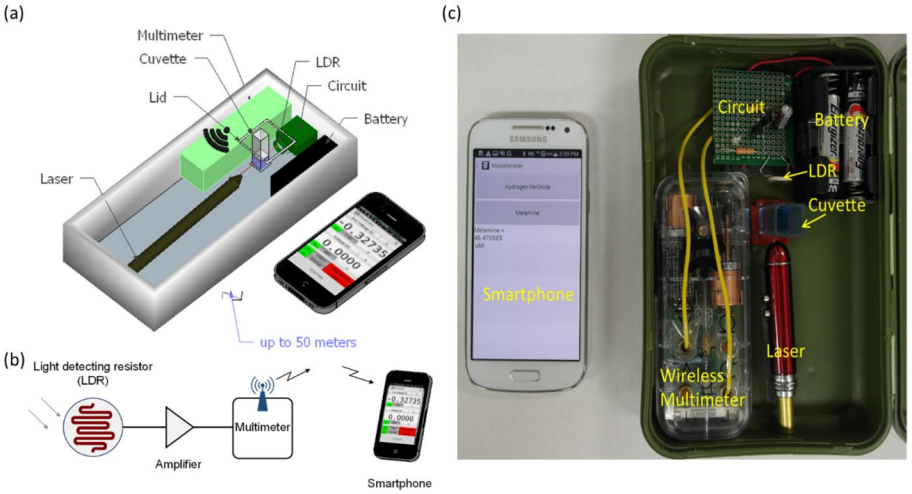

Figure 1. Design of PAWS. (**a**) 3D schematic illustration of the internal structure of PAWS. The upper cover of the system is transparent to illustrate the internal structure (in reality, it is opaque to block the ambient light.). (**b**) Procedure for wireless signaling on the smartphone. The LDR converts the optical signal to an electrical signal and the multimeter measures the voltage wirelessly in the smartphone, which analyses it and shows the result. (**c**) Photograph of the actual PAWS device.

was then centrifuged down in Millipore Amplicon centrifugal tubes (3K) for 10 min at 14 000 rpm. The filtrate was mixed with the GNP solution in a ratio of 1:10 v/v and incubated for 10 min to promote the colorimetric reaction, followed by three times dilution with distilled water, followed by the absorbance measurement. Absorbance was measured by Tecan Infinite 200 Pro and PAWS.

2.3 TMB-based hydrogen peroxide detection

HRP (P8735) and TMB were bought from Sigma Aldrich. Typically, 20 µL of TMB (5 mM), 10 µL of HRP (1 U/mL), and 50 µL of hydrogen peroxide spiked with different concentrations in lake water were added into 20 µL of Tris-acetate (25 mM, pH 4). Then, the final mixture was incubated at 40°C for 30 min and the measurement was done via PAWS and UV-Vis spectrophotometer.

3 Results

3.1 Design and working principle of PAWS

The PAWS system consists of four major components (Fig. 1a): a red laser pointer as a light source, cuvette holder to hold the sample, a circuit including LDR to convert the optical signal to an electrical signal and wireless multimeter to send the electrical signal to the smartphone. The light from the laser pointer first passes through the sample and a certain amount of the light is absorbed by the sample, depending on the concentration of the target analyte. The target analyte with higher concentration would lead to higher absorption of light, reducing its intensity. After absorption, this reduced intensity of light then hits the LDR in the circuit, whose resistance is inversely proportional to the intensity of the light (Fig. 1b). The small round shaped LDR has a high spectral response at a wavelength similar to that of red light from a laser pointer (Supporting information, Fig. S1). Next, the current from the LDR passes through an amplifier and is amplified exponentially, consequently increasing the voltage in the circuit (Fig. 1b). Thus, the small change in the intensity of the incoming light leads to a large change in voltage, which achieves the enhanced sensitivity of our system. We employed an advanced multimeter, which is capable of wirelessly measuring the voltage and displays in the smartphone (Fig. 1b). The custom-modified application installed in the smartphone finally utilizes the voltage signal, analyzes it, and displays the measurement results on the screen.

As a proof of concept, GNP and TMB were employed as colorimetric substrates to detect two model targets, melamine and hydrogen peroxide, respectively. We exploited the feature that GNP, which is originally red in color, becomes blue (absorbance around 625 nm) [20] in the presence of melamine, and TMB forms oxidized TMB (oxy-TMB) with absorbance around 650 nm by HRP in the presence of hydrogen peroxide. Therefore, a red laser pointer was employed as a light source which yielded red light at the wavelength analogous to the absorption wavelengths of the two substrates.

In our prototype, all the components were combined in an opaque cuboidal box as shown in Fig. 1a, which is drawn to approximately the same scale as the real setup (165 mm × 115 mm, Fig. 1c). The size and weight of the system can be further reduced by using button cells and a smaller cuvette, and arranging the components more compactly. The device has a lid (Fig. 1a) on top of the cuvette holder. Closing the lid is very crucial during the measurement because the resistance of the LDR will be reduced by stray light, which might lead to incorrect results. In this work, we have used a Samsung Galaxy 4 mini (Fig. 1c); however, other phones can be also used for the analysis and display of the data. Of note, a smartphone can easily detect the wireless signal from up to 50 meters away, which eases the detection process.

3.2 Android-based smartphone application for the analysis and display of the data

We developed a custom-designed android application which analyzes the voltage measured in response to the analyte concentration, and displays the results. The android application can be installed on smartphones available after mid 2013 (we checked that the Samsung Galaxy S4 mini, S4, S3, and Note 3 could be employed for our system). After installation, the smartphone needs to be connected to the system via Bluetooth network by pressing the "Connect" button on the starting screen (Fig. 2a).

In order to detect a target analyte, users put a sample into a cuvette in the cuvette holder, close the lid, and run the application. Pressing the "Detection" button on the main screen of the application (Fig. 2b) will show the voltage obtained from the circuit and direct the application to the next page (Fig. 2c), where users are supposed to select the target analyte. Since "Melamine" and "Hydrogen Peroxide" were employed as the model analytes in this study, the screen shows these two corresponding buttons (Fig. 2c). Finally, the application will calculate the concentration of the target analyte by using a previously uploaded equation, and display the determined concentration together with the proper instructions (Fig. 2d and 2e). The instructions will instruct users about the significance of the results by informing them, for example, of the desired action for that particular analyte concentration.

3.3 GNP-utilized detection of melamine

In order to prove the detecting capability of PAWS, melamine was first employed as a target analyte. Melamine is an organic compound widely used in polymer industries; however, it is illegally added to adulterate protein rich foods due to its high nitrogen content (66% nitrogen by mass) [21]. It is estimated that more than 50 000 babies and 300 000 victims were hospitalized and hundreds of pets died of renal failure by consuming melamine-adulterated milk products in 2007 and 2008 [21]. Until now, various techniques such as capillary electrophoresis [22], gas/mass chromatography [23], ionization mass spectroscopy [24], electrochemical methods [25], ELISA-based methods [26], and colorimetric sensors [27] have been reported to identify the presence of melamine, but none of them provides miniaturized and on-site sensing interfaced with wireless connectivity.

To achieve a novel system capable of the on-site sensing of melamine, coupled with an intuitive touch-based display and wireless connectivity, GNP was employed as a colorimetric substrate. GNP has unique colorimetric properties which can tune by particle size; it is originally red in color, but changes to blue after aggregation. This property of GNP has been intensively studied [28–32], and utilized in various colorimetric detection systems including those for DNA [33–36], proteins [33, 37], small molecules [33, 38], heavy metal ions [33, 39–41], hazardous materials [42, 43], disease biomarkers [44], bacteria [45], and cancerous cells [46]. Melamine has electron rich amine and ring nitrogen groups that bind onto the electron deficient surfaces of metal nanoparticles [47, 48]. The three exocyclic amine

Figure 2. Screenshots of our android-based application. (**a**) Start screen on the smartphone after installation of the android application. (**b**) Main screen of the application. The number in the second lane is the voltage measured in response to the analyte concentration, while the number in the first lane is the current. (**c**) Detection menu. Screen displayed after pressing the "Detection" button in the main menu. (**d**) Melamine detection menu. The detected concentration of melamine and its significance are displayed on the screen. (**e**) Hydrogen peroxide detection menu. The detected concentration of hydrogen peroxide and its significance is displayed on the screen.

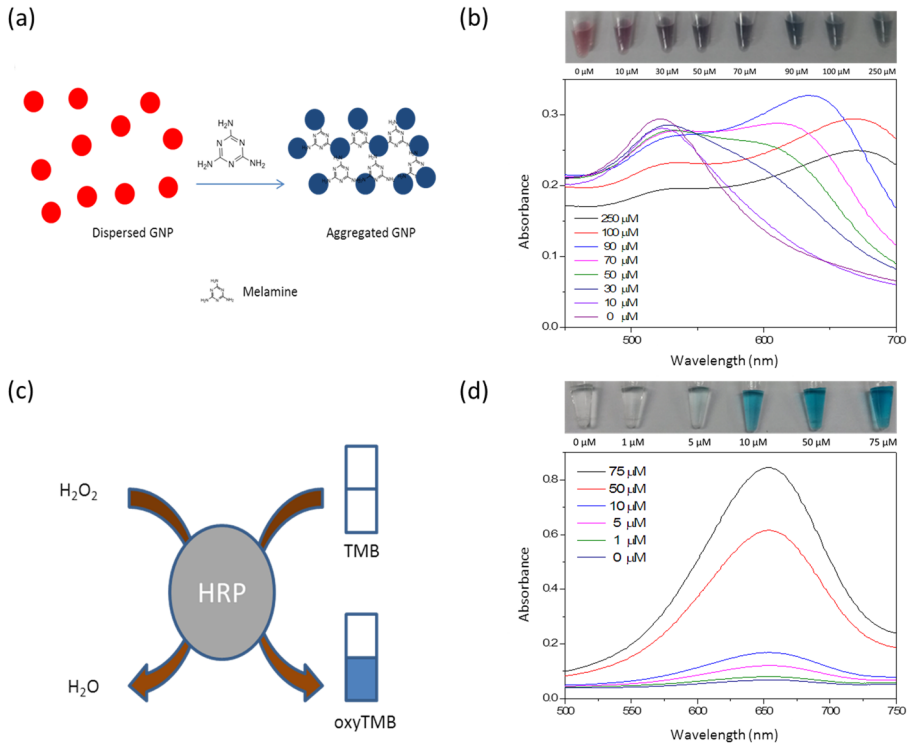

Figure 3. Schematic illustrations of colorimetric reactions. (**a**) Aggregation of GNP in the presence of melamine. (**b**) UV-Vis absorption spectra of GNP incubated with milk spiked by melamine at varying concentrations. Inset shows the corresponding photographs. (**c**) Oxidation of TMB in the presence of hydrogen peroxide. (**d**) UV-Vis spectra obtained from the HRP-catalyzed oxidation product of TMB in the presence of hydrogen peroxide at varying concentrations. The final concentrations of TMB and HRP were 1 mM and 0.1 U/mL, respectively. Inset shows the corresponding photographs.

groups within a melamine molecule can bind to three GNPs at the same time and crosslink them, consequently inducing the aggregation of GNPs (Fig. 3a) [49].

In this study, we prepared GNP with about 13 nm particle diameters (Supporting information, Fig. S2), which exhibited little variation in size, by ±2 nm, and a narrow absorbance peak at 520 nm, and then incubated the GNP with milk spiked by melamine. As a result, we observed the color change from wine red to purple or blue depending on the concentration of melamine (Fig. 3b). Since the target samples were melamine-adulterated milk products, it was possible that the results might be affected by interfering compounds in the milk, including amino acids such as glycine and L-alanine, small molecules such as glucose, and salts such as Na^+ and K^+. Therefore, we examined the selectivity of our system by employing 100-fold higher concentrations of these compounds compared to melamine. As a result, as shown in Fig. 4, a quite sig-

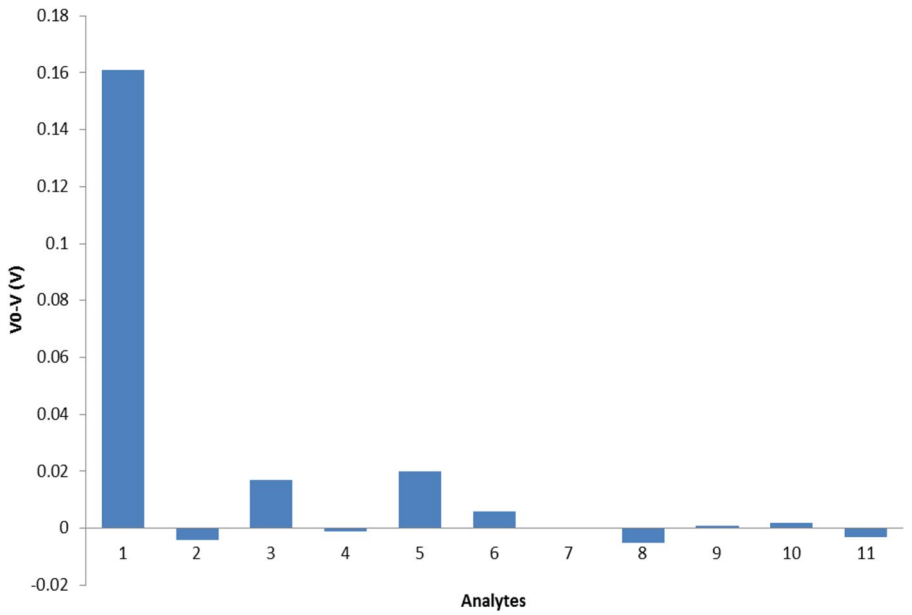

Figure 4. Selectivity of GNP-based melamine detection in whole milk. The voltage change (V0-V) measured by PAWS in the presence of different analytes, where V0 and V are the voltages measured in the absence (control) and presence of analytes, respectively. Analytes: 1, melamine; 2, glycine; 3, L-alanine; 4, L-aspartic acid; 5, L-histidine; 6, cyanuric acid; 7, glucose; 8, galactose; 9, L-ascorbic acid; 10, sodium chloride; 11, potassium hydroxide. Concentrations of melamine and other analytes were 10 μM and 1 mM, respectively.

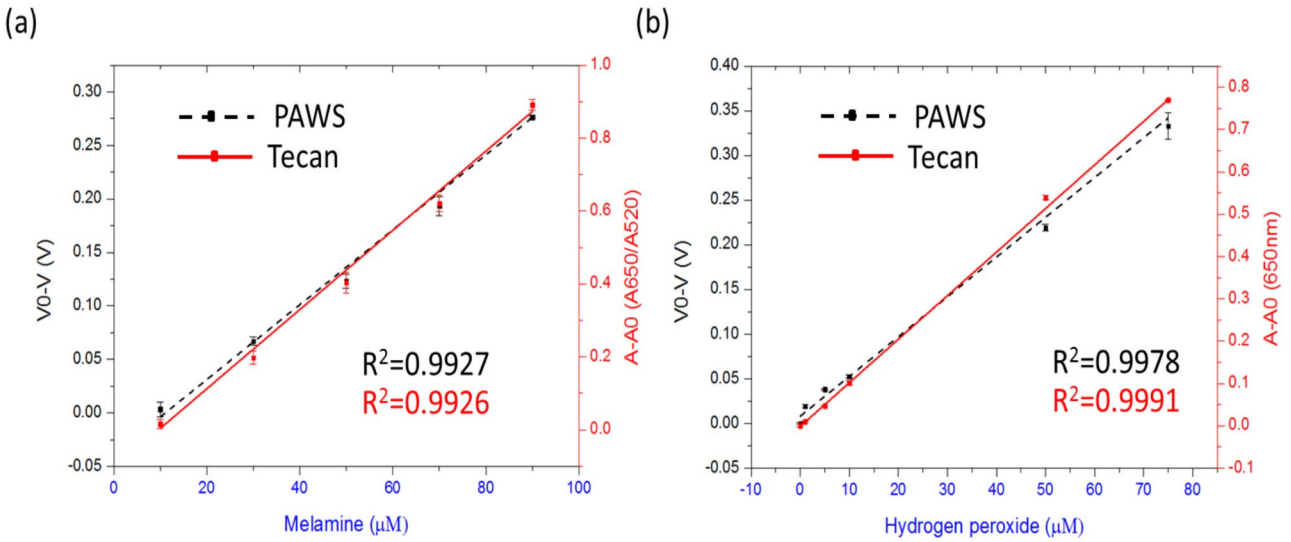

Figure 5. Sensitivity and accuracy of the PAWS system. The detecting performance of the PAWS system was compared with that of the commercial UV-Vis spectrophotometer, Tecan Infinite 200 Pro, for the detection of (**a**) melamine and (**b**) hydrogen peroxide using GNP and TMB, respectively, as the colorimetric substrates.

nificant signal was observed only from the presence of the target melamine, which confirms the excellent selectivity of our system.

We next checked the sensitivity of our system. The limit of detection (LOD) for the detection of melamine in whole milk was determined to be 6.12 μM, and the linear range was observed from 10 to 90 μM (Fig. 5a). According to the Food and Drug Administration of United States and the European Union, the safety limit of melamine in milk and dairy products is 20 μM [49], which is much higher than our LOD, and lies within the linear range of our system. Therefore, PAWS could actually be employed for the on-site quantification of melamine in whole milk.

We next evaluated the detection precision of our system by analyzing three independent milk samples spiked with melamine. The recovery rates were in the range from 96.18% to 106.4% and the CVs of all datasets were less than 7.05%, indicating the high precision of our system (Table 1a).

We also examined the performance of a typical large benchtop UV-Vis spectrophotometer, a Tecan Infinite 200 Pro, and compared it with that of our system (Fig. 5a). The absorbance observed from the benchtop system showed almost the same pattern and linear range from 10 to 90 μM (Fig. 5a), and its LOD was determined to be 3.24 μM (Fig. 5a) which is comparable to that of our system. These results confirm that our system is as sensitive and accurate as the commercially dominant benchtop spectrophotometers.

Table 1. Detection precision of PAWS for (**a**) GNP-based detection of melamine in whole milk and (**b**) TMB-based detection of hydrogen peroxide in lake water. Recovery (%) = measured value/expected value × 100.

(**a**)

Sample	Melamine added (μM)	Melamine recovered (μM)	CV (%)	Recovery (%)
1	0	0	–	–
2	25	25.5 ± 1.4	5.40	102.1
3	40	42.5 ± 3.0	7.05	106.4
4	55	52.9 ± 1.9	3.60	96.18

(**b**)

Sample	H_2O_2 added (μM)	H_2O_2 recovered (μM)	CV (%)	Recovery (%)
1	0	0	–	–
2	30	30.17 ± 0.11	0.37	100.52
3	35	35.79 ± 0.54	1.53	102.27
4	55	55.39 ± 1.02	1.85	100.71

3.4 TMB-utilized detection of hydrogen peroxide

To further demonstrate the detecting capability of our system, we applied the PAWS system to the detection of our second model analyte, hydrogen peroxide, by employing TMB as a colorimetric substrate. TMB forms a stable and insoluble blue colored product after oxidation (Fig. 3c). Since hydrogen peroxide is produced as a byproduct of various metabolic and enzymatic reactions including the signal transduction pathways [50] and oxidative reactions [51–53], it's detection could be used to monitor these reactions and identify the corresponding substrate molecules, such as glucose [54], galactose [55], choline [56], and acetylcholine [57]. We examined the sensitivity of PAWS for the detection of hydrogen peroxide in the same manner as the first model analyte, melamine, and the LOD was determined to be 0.70 μM (Fig. 5b), which is even slightly lower than that of a standard benchtop UV-Vis spectrophotometer (0.81 μM, Fig. 5b and Fig. 3d). All the absorbance measured by PAWS were quite consistent with those obtained with the benchtop spectrophotometer. The recovery rates were in the range from 100.52% to 102.27% and the CVs of all the datasets were less than 1.85%, indicating the high precision of our system (Table 1b).

3.5 Stability of PAWS

For our system to be actually applied for the on-site detection of target analytes, it should be stable enough for a certain period of time and reproduce results consistently. Our system employs a battery, and measures the circuit's voltage to quantify the analyte. Since a battery has a certain lifetime and voltage might fluctuate during the measurement, it is necessary to confirm the stability of the device when measuring the circuit's voltage. We examined the stability of our device and confirmed that the circuit's voltage, measured by PAWS, was quite consistent for up to two months (Supporting information, Fig. S3a) and that the time dependent fluctuation of the voltage was negligible during the measurement (Supporting information, Fig. S3b, green number on the right), assuming that clicking the button does not take more than 90 seconds.

4 Discussion

In summary, we have developed a simple, portable, cost effective and smartphone-based PAWS platform capable of wirelessly sending the electrical signal resulting from the colorimetric assay to a smartphone, which finally quantifies the amount of target analytes. We demonstrated the capability and utility of our PAWS prototype by successfully detecting melamine spiked in milk and hydrogen peroxide spiked in lake water, and demonstrated the PAWS prototype was as sensitive as a bulky, expensive and highly advanced benchtop spectrophotometer. Notably, PAWS is very cheap compared with the currently available representative portable optical devices and the typical benchtop spectrophotometer, Tecan Infinite 200 Pro (Supporting information, Table S1), and its measurement is very fast (within a few seconds).

Our system can be further improved with advanced system hardware and software. Our ongoing endeavor to enhance the system's detection sensitivity includes utilization of a photodiodes array, and optimization of amplification with respect to voltage for an enhanced signal. Moreover, our device can be also extended to quantify other target molecules, including hazardous molecules [58], proteins [58], bacteria [58], and cancerous cells [59] by labelling the GNP with target-specific ligands [58] or by employing a laser with a different wavelength and the corresponding LDR.

PAWS is an excellent example of building a new system by utilizing pre-existing individual technical components, including multimeter-based measurement and wireless signal transfer to the smartphone, and the computing and communication capability of the smartphone. By taking advantage of its computational capability and internet connectivity, our device could be used to detect hazardous materials and dangerous pathogens while simultaneously conducting their spatial mapping. Furthermore, PAWS could be also applied to continuously monitor harmful chemicals and pathogens found in different parts of the world, and to upload that information to the internet to warn people.

In fact, mobile phone subscriptions by 2013 reached more than seven billion worldwide and smartphone penetration was expected to be more than 60, 45, and 25% in North America, Europe, and Africa, respectively, at the end of 2015 [15]. Therefore, smartphone-based bioanalytical applications can be widely deployed and used quite effectively even in resource-limited regions, including third world countries, where on-site measurement of hazardous materials or food additives is very important because of deep-rooted problems such as famine and lack of clean drinking water. To date, in these places, samples such as water or food need to be sent away to a laboratory in order to verify their purity, despite the immediate necessity. Therefore, we believe that the PAWS system could be widely utilized for the on-site sensing of various target analytes and serve as a good model to construct a novel POCT device capable of computational works and communication functions.

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Cover illustration

The cover of this regular issue of BTJ shows fluorescence microscopy images of bacteria along with their processed counterparts after CellShape analysis. While the former are simple raw images, the latter reveal important quantitative information e.g. intensity contours and spots. Altogether, they form a complete dataset from which we can accurately interpret cellular fluorescent signals. The cover is prepared by Ángel Goñi-Moreno, Juhyun Kim and Víctor de Lorenzo authors of the article "CellShape: A user-friendly image analysis tool for quantitative visualization of bacterial cell factories inside". (http://dx.doi.org/10.1002/biot.201600323).

Biotechnology Journal – list of articles published in the February 2017 issue.

Review
Bringing 3D tumor models to the clinic – predictive value for personalized medicine
Kathrin Halfter and Barbara Mayer
http://dx.doi.org/10.1002/biot.201600295

Research Article
Metabolic engineering of *Mannheimia succiniciproducens* for succinic acid production based on elementary mode analysis with clustering
Won Jun Kim, Jung Ho Ahn, Hyun Uk Kim, Tae Yong Kim and Sang Yup Lee
http://dx.doi.org/10.1002/biot.201600701

Research Article
Genome analysis of a hyper acetone-butanol-ethanol (ABE) producing *Clostridium acetobutylicum* BKM19
Changhee Cho, Donghui Choe, Yu-Sin Jang, Kyung-Jin Kim, Won Jun Kim, Byung-Kwan Cho, E. Terry Papoutsakis, George N. Bennett, Do Young Seung and Sang Yup Lee
http://dx.doi.org/10.1002/biot.201600457

Research Article
Camelid V_HH affinity ligands enable separation of closely related biopharmaceuticals
Timothy M. Pabst, Michaela Wendeler, Xiangyang Wang, Sandra Bezemer, Pim Hermans and Alan K. Hunter
http://dx.doi.org/10.1002/biot.201600357

Research Article
Combination of two epitope identification techniques enables the rational design of soy allergen Gly m 4 mutants
Heide Havenith, Karolin Kern, Paul Rautenberger, Holger Spiegel, Michael Szardenings, Elke Ueberham, Jörg Lehmann, Matthias Buntru, Simon Vogel, Regina Treudler, Rainer Fischer and Stefan Schillberg
http://dx.doi.org/10.1002/biot.201600441

Research Article
A versatile modular bioreactor platform for Tissue Engineering
Sebastian Schürlein, Thomas Schwarz, Steffan Krziminski, Sabine Gätzner, Anke Hoppensack, Ivo Schwedhelm, Matthias Schweinlin, Heike Walles, Jan Hansmann
http://dx.doi.org/10.1002/biot.201600326

Research Article
Immobilized hematopoietic growth factors onto magnetic particles offer a scalable strategy for cell therapy manufacturing in suspension cultures
Matthew J Worrallo, Rebecca LL Moore, Katie E Glen and Robert J Thomas
http://dx.doi.org/10.1002/biot.201600493

Research Article
Integrated genome and protein editing swaps α-2,6 sialylation for α-2,3 sialic acid on recombinant antibodies from CHO
Cheng-yu Chung, Qiong Wang, Shuang Yang, Bojiao Yin, Hui Zhang and Michael Betenbaugh
http://dx.doi.org/10.1002/biot.201600502

Research Article
Smartphone-based portable wireless optical system for the detection of target analytes
Shreedhar Gautam, Bhagwan S Batule, Hyo Yong Kim, Ki Soo Park and Hyun Gyu Park
http://dx.doi.org/10.1002/biot.201600581

Research Article
High-throughput downstream process development for cell-based products using aqueous two-phase systems (ATPS): A case study
Sarah Zimmermann, Christian Scheeder, Philipp K Zimmermann, Are Bogsnes, Mattias Hansson, Arne Staby and Jürgen Hubbuch
http://dx.doi.org/10.1002/biot.201600587

Research Article

Improved production of propionic acid using genome shuffling

Carlos H Luna-Flores, Robin W Palfreyman, Jens O Krömer, Lars K Nielsen and Esteban Marcellin

http://dx.doi.org/10.1002/biot.201600120

Biotech Method

CellShape: A user-friendly image analysis tool for quantitative visualization of bacterial cell factories inside

Ángel Goñi-Moreno, Juhyun Kim and Víctor de Lorenzo

http://dx.doi.org/10.1002/biot.201600323

Biotech Method

A simplified procedure for antibody engineering by yeast surface display: Coupling display levels and target binding by ribosomal skipping

Julius Grzeschik, Steffen C. Hinz, Doreen Könning, Thomas Pirzer, Stefan Becker, Stefan Zielonka and Harald Kolmar

http://dx.doi.org/10.1002/biot.201600454

Biotech Method

Predictive glycoengineering of biosimilars using a Markov chain glycosylation model

Philipp N. Spahn, Anders H. Hansen, Stefan Kol, Bjørn G. Voldborg and Nathan E. Lewis

http://dx.doi.org/10.1002/biot.201600489