Biosensors

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A Touchscreen as a Biomolecule Detection Platform**

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In recent years, considerable effort has been dedicated to the development of a simple, instrument-free detection method that enables point-of-care testing (POCT) and decentralized clinical diagnosis of diseases.[1–3] One of the most promising approaches to this goal involves the use of an electrical detection strategy. Owing to operational simplicity and ability to be miniaturized, this approach has been subjected to very extensive studies.[2–5] Nevertheless, except for a glucose sensor or i-STAT blood analyzer,[3] no practical portable POCT device has been developed to date because of the lack of success in readily integrating detection elements into electrical devices.

A touchscreen is an input device, generally used in kiosk systems, PDAs (personal digital assistants), or smart phones, that can detect the presence and location of a touch within the device area.[6] Among other touchscreen technologies, including those that employ resistive, infrared, and surface acoustic wave (SAW) signaling, the capacitive touchscreen has been widely used recently owing to the recent increasing popularity of smart phones.[6,7] Basically, a capacitive touchscreen detects small capacitance changes of electrodes in the device that are induced by a human finger touching event in accord with the relationship shown in Equation (1):

$$C_t = C_p + C_f \quad (1)$$

where C_t is the total capacitance, C_p is the touch panel capacitance, and C_f is the finger capacitance.

Capacitive touchscreens, consisting of touch panels and controllers, currently utilize two types of technologies.[6,7] The first employs a surface capacitive response in which a human body capacitively couples to the touch panel surface, creating a path for the flow of very small amounts (20–500 μA) of electrical current from the surface of a touchscreen to ground. The induced current flow is detected by the controller and the touch location is determined by calculating the distances from the touch point to electrodes located at the four corners of the panel. In this manner, the touchscreen recognizes a single touch point caused by a single touching event.

In contrast, projected capacitive technology relies on the detection of changes in the charge storage capacities of the electrodes separately patterned on the panel. This is performed by measuring charging pulse numbers, which represent the time period required to accomplish a certain number of charging/discharging cycles of the electrode (capacitor). The charging pulse number generally increases when a finger touch takes place because the charging/discharging time of the electrode increases in accord with the increased capacitance. Therefore, by using this technique, multiple touch points can be simultaneously identified. Since both types of touchscreens detect very small capacitance changes (pF level), they could serve as highly sensitive detection platforms for the analysis of various biomaterials that have dielectrical properties. In particular, as a consequence of their "handheld" size and operational convenience, touchscreen-based instruments should be applicable to novel POCT systems and personalized medical devices.

Herein, we have devised and tested a surface-capacitive touchscreen-based strategy that utilizes signal location as the foundation for detection and quantification of DNA. As the surface capacitive touchscreen identifies only a single point touched by a sample, a strategy is used in which the location of an in-between point is recognized when more than two points are touched by samples simultaneously. The location of the point in-between that is observed on the display varies in a geometrically dependent manner with the conductivities of the touching materials, being closer to the point touched by a sample with higher conductivity. Owing to the fact that DNA displays increasing conductivity as a function of increasing concentration,[8–11] a device employing this principle was constructed to determine the concentrations of DNA samples based on the location of the touch signal of samples in the presence of a reference DNA solution of known concentration. The results of this effort, in which concentrations of unknown DNA samples were accurately determined in a manner that is comparable to the detection performance of a conventional absorbance-based method, and the potential of this technology in the biosensor area was verified.

In a proof-of-concept experiment, 1 μL of a reference solution of DNA (50 ng μL^{-1}) and two test DNA samples A and B were applied to three fixed points on a touchscreen panel surface (Figure 1). The samples were covered with an ITO-coated cover glass in a manner that enabled the ITO layer to make contact with all three samples. A conducting wire was connected to the ITO layer so that electrical current would flow through the samples from the touch panel to a human finger when the conducting wire is touched. In this system, the three DNA samples, including the reference

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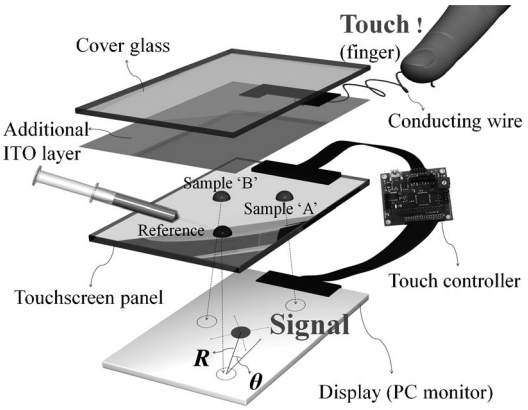

Figure 1. Illustration of the signal-location-based DNA detection method with a surface-capacitive touchscreen (see text for details).

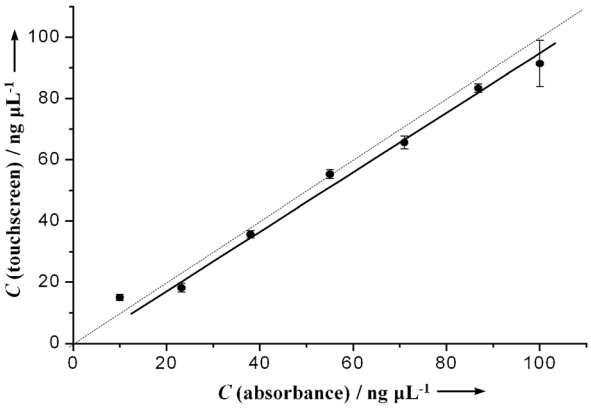

Figure 2. Comparison of DNA concentrations determined by the signal location-based DNA detection method utilizing a surface-capacitive touchscreen and the conventional absorbance-based method.

solution and A and B, serve as triple touch points on the touchscreen when the conducting wire is touched with a finger. Importantly, the specific location of the touchdown signal that appears is dependent on the relative concentrations of the three DNA samples.

Equations to correlate DNA concentrations of samples A and B with the signal location were determined by using the response surface analysis experimental design with Minitab statistical analysis software. The distance R between the locations of the touch signal and the reference solution and the angle θ between the location of touch signal, reference solution, and unknown DNA sample point can be mathematically correlated with the DNA concentrations in the test samples (see the Supporting Information). Application of this technique when a 50 ng μL^{-1} reference solution of DNA is used leads to Equations (2) and (3) for the length R in pixels and the angle θ in degrees, respectively:

$$R = 88.0426 + 1.5454[\mathrm{A}] + 0.8669[\mathrm{B}] - 0.0042[\mathrm{A}]^2 - 0.0015[\mathrm{B}]^2 - 0.0086[\mathrm{A}][\mathrm{B}] \quad (r^2 = 0.91) \tag{2}$$

$$\theta = 14.1944 - 0.2398[\mathrm{A}] + 0.3802[\mathrm{B}] + 0.0012[\mathrm{A}]^2 - 0.0013[\mathrm{B}]^2 - 0.0008[\mathrm{A}][\mathrm{B}] \quad (r^2 = 0.98) \tag{3}$$

By solving the equations using R and θ values determined from the touch signal location, the concentrations of DNA in the two unknown samples "A" and "B" can be determined. The results obtained by applying this method to known solutions show that concentrations of DNA samples in a range from 10–100 ng μL^{-1} can be accurately measured.

It is significant that the level of quantification is nearly the same as that associated with a system that employs a conventional absorbance-based method (Figure 2). Owing to the fact that ratios of DNA concentrations in the test and reference solutions governs the location of the touch, the detection range of test samples is determined by the concentration of reference solution. It should be noted that this signal-location-based method cannot be utilized to quantify samples that contain 200 times higher or lower DNA concentrations than the reference solution because the touch signals in these extreme situations is coincident with that of the sample with the higher concentration. Furthermore, the concentration (50 ng μL^{-1}) of reference DNA solution used in this study is in the range of those found in common PCR-amplified target DNA. Finally, when two variables (length and angle) are used in the analysis, two unknown DNA samples can be simultaneously analyzed. However, if more variables, such as signal intensity, are incorporated into the mathematical treatment, more samples can be simultaneously analyzed.

Following successful demonstration of the conceptual basis of the new touchscreen strategy, a signal intensity-based multiplexed DNA detection method utilizing a projected capacitive touchscreen was explored. The strategy relies on capacitance changes of electrodes patterned on a touch panel when they are placed in contact with DNA solutions, which exhibit capacitances that depend on their concentrations.[12–14] Because this projected capacitive touchscreen detects contact points of the capacitive materials with the electrode layer patterned on the touch panel, it can be activated by simply applying test samples to the touchscreen panel surface without the need for a human touching event. Furthermore, the projected capacitive touchscreen method should enable multiplexed detection because it simultaneously recognizes multiple touchdown events.

In the experiment illustrated in Figure 3, six DNA samples (10 μL solutions, with concentrations in the range of 9.2×10^{-4}–9.2×10 ng μL^{-1}) were applied to a projected capacitive touchscreen and the capacitance changes of separately patterned electrodes that occurred were simultaneously measured. In this system, the charging pulse numbers of each electrode increase with increasing DNA concentrations because the capacitance of the electrodes increases in accord with the capacitance of the contacting test samples (see the Supporting Information). In this case, the determination is performed by analysis of the equation $Y = 23.77 + 3.19 \log(X)$, where X and Y are the respective concentration of a DNA sample and the change of charging pulse number ($r^2 = 0.92$). Using a standard curve obtained by plotting the change in charging pulse number as a function of the DNA concentration, the DNA concentrations of the six unknown samples were determined simultaneously. The results were

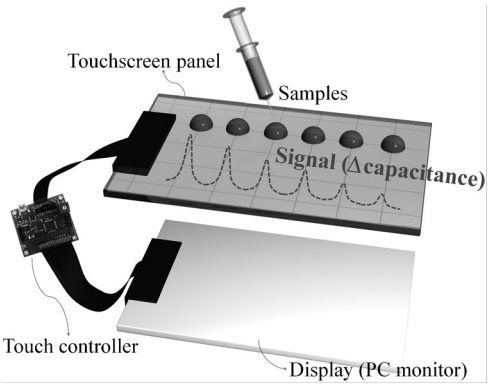

Figure 3. Illustration of the signal-intensity-based multiplexed DNA detection method on a projected capacitive touchscreen and the capacitance change in the presence of target sample.

found to be in excellent agreement with those obtained by using the conventional absorbance-based method (Figure 4).

To demonstrate the potentially widespread utility of the projected capacitive touchscreen strategy, it was applied to

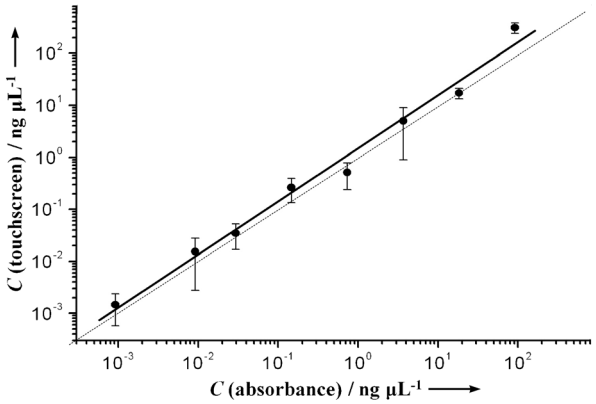

Figure 4. Comparison of the DNA concentration determined by the signal-intensity-based multiplexed DNA detection method utilizing the projected capacitive touchscreen and the conventional absorbance-based method.

the detection of capacitance changes of a polypyrrole (PPy) conducting polymer, which has different dielectric constants depending on its oxidation/reduction state. The capacitance C of this material is controlled by its dielectric constant ε according to the equation $C = \varepsilon \varepsilon_0 A d^{-1}$, where ε_0 is the dielectric permittivity of free space, A is the electrode area, and d is the electrical double-layer thickness. Analysis of impedance spectra of an electrochemically polymerized PPy film on a gold electrode (Figure 5a), fitted by using the corresponding equivalent circuit model (Figure 5a, inset), reveals that the oxidized state of PPy has higher capacitance value (ca. five-fold in this case) than its reduced state under the same concentration and contact-area conditions. The capacitance change of the bound PPy film was successfully detected on the touchscreen, showing that a sufficient signal

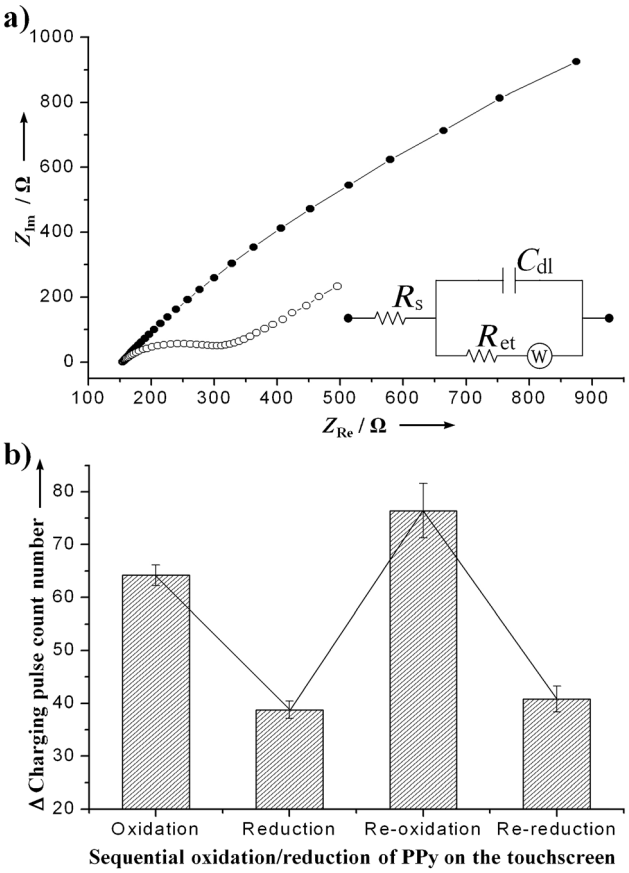

Figure 5. a) Impedance spectra of a polypyrrole (PPy) film on a gold electrode measured at oxidative (●, 0.4 V vs Ag/AgCl) or reductive potentials (○, −0.6 V vs Ag/AgCl) with 10 mV alternating voltage from 100 kHz to 50 mHz. Inset: An equivalent circuit corresponding to a PPy-coated electrode surface consisting of solution resistance R_s, electron-transfer resistance R_{et}, Warburg impedance W, and double-layer capacitance C_{dl}. b) Signal change of the capacitive touchscreen promoted by the sequential state change of PPy film on the touchscreen in the course of successive oxidation and reduction process.

change is promoted by successive oxidation and reduction of PPy film (Figure 5b). Likewise, binding of biomaterials also can be definitively detected by utilizing the new system containing a properly modified touchscreen surface with specific probe molecules. Consequently, it appears that the touchscreen technology should serve as a new detection platform for the analysis of a range of biomaterials including amino acids, peptides, proteins, DNA, membranes, and cells, all of which typically have dielectric properties.[15–17]

In conclusion, a new technology based on capacitive touchscreen strategies has been developed and its biomolecular detection capabilities have been demonstrated through the reliable analysis of the concentrations of DNA solutions. The potential of this technology in the biosensor area has also been verified. This new technology as part of touchscreen-equipped smart-phone or smart-pad devices should advance the goal of producing personalized diagnostic devices that are suitable for point-of-care testing or ubiquitous healthcare.

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