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Biosensors and bioelectronics on smartphone for portable biochemical detection

Diming Zhang, Qingjun Liu*

Biosensor National Special Laboratory, Key Laboratory for Biomedical Engineering of Education Ministry, Zhejiang Provincial Key Laboratory of Cardio-Cerebral Vascular Detection Technology and Medicinal Effectiveness Appraisal, Department of Biomedical Engineering, Zhejiang University, Hangzhou 310027, PR China

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ABSTRACT

Smartphone has been widely integrated with sensors, such as test strips, sensor chips, and hand-held detectors, for biochemical detections due to its portability and ubiquitous availability. Utilizing built-in function modules, smartphone is often employed as controller, analyzer, and displayer for rapid, real-time, and point-of-care monitoring, which can significantly simplify design and reduce cost of the detecting systems. This paper presents a review of biosensors and bioelectronics on smartphone for portable biochemical detections. The biosensors and bioelectronics based on smartphone can mainly be classified into biosensors using optics, surface plasmon resonance, electrochemistry, and near-field communication. The developments of these biosensors and bioelectronics on smartphone are reviewed along with typical biochemical detecting cases. Sensor strategies, detector attachments, and coupling methods are highlighted to show designs of the compact, lightweight, and low-cost sensor systems. The performances and advantages of these designs are introduced with their applications in healthcare diagnosis, environment monitoring, and food evaluation. With advances in micro-manufacture, sensor technology, and miniaturized electronics, biosensor and bioelectronic devices on smartphone can be used to perform biochemical detections as common and convenient as electronic tag readout in foreseeable future.

Contents

* Corresponding author. Fax: +86 571 87951676.
E-mail address: qjliu@zju.edu.cn (Q. Liu).

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1. Introduction

Biosensors are defined as analytical devices incorporating biological or biological-derived sensing elements either integrated within or intimately associated with physicochemical transducers for analyte detections (Turner, 2000; Banica, 2012; Turner, 2013). Over last decades, various biologically derived materials, such as enzyme, cell, nucleic acid, antigen–antibody, and microorganism, were incorporated into different electrochemical, optical, acoustic, and mechanical detectors to fabricate biosensors with high sensitivity and selectivity (Su et al., 2011; Qureshi et al., 2012; Saha et al., 2012; Liu et al., 2014). By readout devices with associated electronics and signal processors, these biosensor and bioelectronic devices have been successfully used in numerous fields such as clinical diagnostics, drug screening, environmental monitoring, and food quality controlling. They provided powerful detecting and analyzing tools as alternatives of conventional chemical and physical sensors. Currently, much work has focused on miniaturization of biosensor and bioelectronic devices, such as micro-fabricated transducers and compact readout instruments, to achieve real-time, point-of-care, and easy-to-use detections for analytes, especially for clinic and environmental samples (Hu et al., 2014; Tokel et al., 2014; Sang et al., 2015).

With the help of Micro-Electro-Mechanical System (MEMS) and nanotechnology, biosensors can be miniaturized to micro- and nano-scale, and integrated into lab-on-a-chip devices as the sensitive arrays for biosensor detections (Voiculescu and Nordin, 2012; Cao et al., 2014; Ferrier et al., 2015). However, although gaining great improvements in sensitivity and automation, most of micro-/nano- biosensors still require cumbersome readout devices to operate sensing processes, detect response signals, analyze data, and display results. Sometimes, the instruments became even more complex in design and larger in size because of other extra components, such as amplifiers for microelectrodes and pumps for microfluidics, to adapt the micro- and nano-sensors (Han et al., 2013; Kumar et al., 2013; Li and Hu, 2013). Thus, bulkiness and overall cost of the readout devices became new hinders following miniaturization of biosensors for portable and cost-effective detections. To address the challenge, researchers have attempted to integrate smartphone into biosensors and bioelectronics to reduce the overall size and cost of the systems.

Biosensors and bioelectronics on smartphone were developed from biosensing attempts using old simple cellphones, called feature phones. Several researches have proposed biosensor and bioelectronics designs using feature phones for portable healthcare diagnostics outside well-resource laboratories (Martinez et al., 2008; Breslauer et al., 2009; Tseng et al., 2010). However, low computational capability and worse operation interface often limited feature phones to perform biosensing processes independently, and computers were always necessary to analyze signals and report final test results in the designs. Smartphone is the latest generation of cellphones with excellent built-in equipments, such as touch screen, multicore processor, and digital camera. Compared to previous cellphones, smartphone has more advanced computing capability, higher image resolution, and open-source operation system, all of which make the design of biosensors and bioelectronics on smartphone easier and more powerful than those on previous cellphones. The usage of smartphone in biosensor and bioelectronic systems can take place of input button, data analyzer, screen display, and even detectors, which were originally designed in readout devices. It efficiently simplified electronic design, minimized volume size, and lowered overall cost of the systems to allow portable and point-of-care test outside the laboratories. Thus, biosensors and bioelectronics on smartphone can play crucial roles in environmental monitoring, healthcare diagnostics, and food analysis in the foreseeable future. Especially, smartphone is now becoming one of the most widely used mobile devices with approximately 1.75 billion users worldwide, while the number of users is estimated to grow to 2.03 billion (28% of the world's population) by 2015 (MobiThinking, 2014). The ubiquitous availability guarantees a convenient and cost-effective acquisition of smartphone and a large number of potential subscribers for smartphone-based sensor systems. All of these inspire a surge of peripheral apparatus linked to smartphones for biosensing applications.

This review summarizes the latest development of biosensors and bioelectronics on smartphone for biochemical detections. Based on integrated sensor techniques, the biosensors and bioelectronics on smartphone are introduced by optics, surface plasmon resonance, electrochemistry, and near-field communication. Firstly, fabrications of those systems are described with biosensor strategies, methods coupling sensor to smartphone, and usages of built-in functions on smartphone, respectively. Then, performances and advantages of the systems are discussed with their applications in biochemical detections. Finally, current limits and involved challenges of biosensors and bioelectronics on smartphone are highlighted in a brief discussion, while future developing directions and potential opportunities are prospected in outlook.

2. Smartphone-based optical biosensors

Taking advantage of high-resolution camera equipped in smartphone, biosensors and bioelectronics on smartphone were the most commonly designed for optical detections. The pioneer attempt was fabrication of smartphone-integrated microscopies to image bio-components such as blood cells and microorganisms. Now, with advances in imaging technology, nanoscale resolution can be achieved by smartphone with compact devices for detection of nanoparticles, virus, and DNA. Following on the heel of microscopy imaging, fluorescent and colorimetric detections were both developed with light intensity measurement based on digital cameras of smartphone. Especially, colorimetric detections with smartphone have been much reported because of its wide potential applications in point-of-care diagnostics. The typical smartphone-based optical biosensor systems are summarized in Table 1.

2.1. Microscopic bio-imaging on smartphone

Bio-imaging systems on smartphone were developed based on several imaging attempts using feature phones to image cells and bacteria with microscopes. Breslauer et al. (2009) proposed to utilize a camera-enabled mobile phone for microscopy imaging in screening of hematologic and infectious diseases. The microscopic device and imaging results are shown in Fig. 1a. The morphologies of blood cells and microorganisms can be imaged with the cellphone-based microscope in brightfield and fluorescence mode, respectively. Then, several research groups have inserted smartphone into microscope devices for different biomedical applications (Baek et al., 2014; Skandarajah et al., 2014). Using high pixel density camera and advanced computational capacity of the phones, microscopic images can be calculated, overlaid, and analyzed in real time, which can rapidly quantify features such as object size, color, and brightness as signal tags for drug screening and healthcare diagnosis. For instance, application program (App) on smartphone can be used to capture target locations of biosamples and count cell numbers automatically. However, the optical attachments in these designs were often complex and in large size, and sometime, the designs even only directly utilized commercial microscope devices. Therefore, these apparatuses can be