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Emotion-on-a-chip (EOC): Evolution of biochip technology to measure human emotion using body fluids

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ABSTRACT

Recent developments in nano/micro technology have made it possible to construct small-scale sensing chips for the analysis of biological markers such as nucleic acids, proteins, small molecules, and cells. Although biochip technology for the diagnosis of severe physiological diseases (e.g., cancer, diabetes, and cardiovascular disease) has been extensively studied, biochips for the monitoring of human emotions such as stress, fear, depression, and sorrow have not yet been introduced, and the development of such a biochip is in its infancy. Emotion science (or affective engineering) is a rapidly expanding engineering/scientific discipline that has a major impact on human society. The growing interest in the integration of emotion science and engineering is a result of the recent trend of merging various academic fields. In this paper we discuss the potential importance of biochip technology in which human emotion can be precisely measured in real time using body fluids such as blood, saliva, urine, or sweat. We call these biochips emotion-on-a-chip (EOC). The EOC system consists of four parts: (1) collection of body fluids, (2) separation of emotional markers, (3) detection of optical or electrical signals, and (4) display of results. These techniques provide new opportunities to precisely investigate human emotion. Future developments in EOC techniques will combine social and natural sciences to expand their scope of study.

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Introduction

Over the last decade, advances in nano/micro technologies have enabled researchers to increase the focus biochip development. Comprehensively, the biochip includes a biosensor, an integrated electric circuit, or functionalized microchannels for analyzing analyte properties in an aqueous solution. A biosensor is a device that consists of a molecular recognition component (or a bioreceptor) and a signal transfer component (or a transducer). The specific interaction between analytes (e.g. DNA, protein, enzymes, hormone, antibodies, cells, or microbes) and the bioreceptor can produce a measurable output such as optical, electrical, mechanical, or thermal signals. Typical biochips consist of an array of independent biosensors in which the sensor signal can be individually monitored and is generally used for the analysis of multiple analytes [1]. Examples of representative and commercially available biochips are DNA, protein, and cell chips, including a lab-on-a-chip. Such technologies have the potential to identify physiological biomarkers in body fluids such as blood, saliva, and urine which are indicative of many diseases. In particular, because point-of-care testing (POCT) has attracted a lot of attention from medical industries, applications for biochips have become increasingly important. Examples of POCT include the well-established glucose and pregnancy test kits that have been on the market for decades. These tests are time-saving, self-monitoring, and do not require experts to interpret results [2]. Biochip technologies for the diagnosis of severe physiological diseases have been increasingly studied in academia and in industry, but biochips to monitor human emotions such as stress, fear, depression, and sorrow have not yet been introduced, and the development of such technology is in its infancy. In addition to conventional biochip technologies, biochips that can precisely measure human emotion in real-time, which we call "emotion-on-a-chip (EOC)" should be considered for development (Fig. 1).

For the past several years, researchers from various fields have attempted to define emotion. Although a clear definition has not been reached, emotion can be summarized as an individual's physiological and instinctive phenomena, including the cognitive, social-cultural property of an individual's psychological, physical, and psychic experiences and reactions to external stimulation. There has been growing interest in the measurement of human emotion since emotion is central to many of the political, social, educational, industrial, and medical problems of human society [3]. Among various types of human emotion, stress is an important

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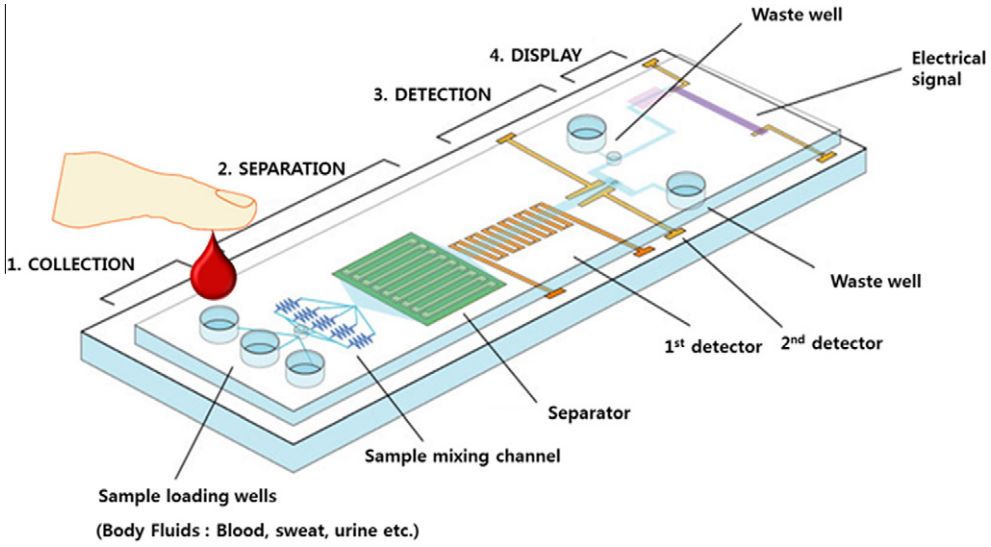

Fig. 1. Schematic drawing of emotion-on-a-chip (EOC).

factor in understanding human behavior and physiological conditions. Indeed, many researchers have investigated the effects of the stress response on various diseases and the effects of psychological stress on physiological conditions [4–6]. Currently, emotion is mainly measured using self-reporting, interview, electroencephalogram (EEG), electrocardiogram (ECG), electrooculography (EOG), and body temperature. Such techniques have been generally accepted as scientific measurements in that physiological responses to external stimuli can be monitored by changes in electronic signals. It is generally accepted that detection of an individual's emotional status could be achieved through easy and economical methods. While conventional measurement techniques exploiting bio-electronic signals have been extensively developed, biochips for the precise analysis of human emotion in real-time have not yet been developed. In this review, we suggest for the first time the potential of developing and applying an emotion-on-a-chip (EOC). EOC will enable analysis of the psychological status of an individual to be easily accomplished by merely taking a drop of body fluid.

General background and examples of conventional biochip technology

Notable developments in micro-electromechanical systems (MEMS) technology have made it possible to fabricate microdevices for analytical purposes. These devices (e.g. DNA chips and lab-on-a-chip) have many advantages, including high speed, high throughput, low cost, disposability, low sample consumption, and portability in various fields of diagnosis and research. Since Fodor invented the DNA chip [7], there has been great progress in the field of biochip technology. The DNA chip is the most developed technology for analyzing DNA molecules on a chip surface and the technique has already been commercialized. After the success of DNA chip technology, the protein chip technology has become a potential tool for providing a direct information on protein function and analyzing protein molecules in biological samples. In the past years, protein chip technology has been studied for the analysis of multiple biomolecular interactions including protein–protein, antibody–antigen, protein–lipid, protein–nucleic-acid, protein–small-molecule interactions, and enzyme–substrate interactions [8]. Recently, functional protein chips which comprehend surface chemical treatments, capture molecule attachment, protein labeling and detection methods are ideal tools for protein profiling, drug discovery, clinical prognosis, diagnosis, and drug target identification [8]. For example, Sauer was able to present a protein chip for diagnosis of sepsis that combines both a sandwich and a binding inhibition format in order to quantify high (C-reactive protein) and low abundant proteins (cytokines, procalcitonin, neopterin) in parallel [9].

Chips which analyze and handle cells for various purposes are called cells-on-a-chip or a cell chip [10,11]. Especially, microsystems allow the spatial and temporal control of cell growth and stimuli with complex microfluidic channels by mimicking the extracellular matrix [10]. For example, studies of cell behavior and exploratory factors have been performed in order to analyze factors that promote cellular growth. Kim et al. (2009) observed cells using physical stimulation with micro-beads [12]. They also demonstrated correlations between growth rate and stimulated conditions, but such conditions are detrimental to MC3T3 cells. Song et al. (2009) suggested a novel device based on the trapping and sorting of cells labeled with magnetic beads [13]. They developed a new system of Joule heating to control thermal energy and applied it to the active area of a microfluidic device to increase/decrease the internal temperature of the device from ambient to the biocompatible temperature of 37 °C. Since then, they have developed a novel microfluidic cell culture device that contains magnetic beads to generate pulsed electromagnetic fields for observing specific phases of the cell cycle [14]. These studies are important in advancing analysis techniques in the field of tissue engineering.

At the beginning of 1990, the concept of a lab-on-a-chip was introduced as a means of separating the reaction, mixing, synthesis, and analysis onto the surface of a single chip [15]. Specifically, the micro total analysis system (μ-TAS), which contains sample collection, separation, detection, and display, is an important technology for analysis. Jung's group has used labs-on-a-chip to separate circulating tumor cells (CTC) from whole blood using a novel hydrodynamic method. They also developed a biochip to improve the purity using methods for size-based particle separation, multi-orifice flow fractionation (MOFF) and dielectrophoresis (DEP). They achieved a high recovery rate, purity, and throughput by integrating the two independent techniques of hydrodynamic separation (primary) and DEP separation (secondary) for CTC separation [16,17].

A thermal biochip to diagnose anemia by detecting the change of red blood cells has been developed. Using this system, the

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