ORIGINAL ARTICLE

Disposable Wireless Immuno-Sensing Chips

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Abstract: A disposable immuno-sensor chip which is proposed for use in continuous health monitoring and for early diagnosis of infectious disease. On-chip high-power density wireless power sources and on-chip wireless data transfer technologies are developed to minimize chip production costs.

Keywords: immuno-sensor chip, wireless power feeding and data transfer, disposable sensor chip

Introduction

Medical costs have risen continuously, partly in response to population aging population. Early diagnosis is a crucial element in slowing this rise. However, this entails frequent medical examinations, which can increase inconvenience and expense. Convenient and inexpensive home or workplace-based medical examination systems can be developed using disposable bio-sensing devices. In addition, preventing large-scale infections requires rapid screening for infectious diseases, especially in developing countries. Such systems would also benefit from small and disposable sensors.

Conventional disease inspection methods such as RIA (Radio Immuno Assay) [1] and ELISA (Enzyme Linked Immuno Sorbent Assay) [2, 3] can effectively detect disease markers (proteins or viruses), but require laboratory facilities and trained technician, raising obstacles for use at home or in developing countries.

To address this problem, a disposable bio-sensing chip using CMOS-LSI was developed [4, 5] with four main components: a disease marker detector, a signal processor, a power source and a data transmitter. This paper introduces a novel disposable bio-sensing chip design using on-chip micro power sources and on-chip wireless data transfer devices.

Device structure and inspection principle

Figure 1 shows a schematic of the proposed sensor chip and corresponding health monitoring system. Antibodies are used to detect specific disease markers on an array of CMOS-based hall sensors. A micro power source (e.g., a micro coil or on-chip micro galvanic battery) and a wireless data transfer device (e.g., a micro coil, exposed electrodes or an electrochromic micro display) are fabricated on the chip. The sensor chip starts to work when exposed to the inspection solution. It then wirelessly transfers the inspection result. After usage, the sensor chip is thrown away. In general, CMOS chip fabrication costs are proportional to chip size, which should thus be minimized not only through the chip design but also by using a high density power source and a small data transfer device. The proposed sensor chip proposed is intended for one-time use only, and thus does long term stability is not a concern.

Figure 2 shows the working principle of the sensor chip. We use immune response (i.e., antigen-antibody reaction) to detect disease markers. We use an antibody designed to react only with a specific disease marker (antigen), making the sensor highly sensitive. The antibodies are fixed on a Hall sensor array fabricated in a CMOS chip. Podocalyxin, which is a marker of kidney disease, is the detection candidate [6].

When the sensing chip is introduced in a specimen such as urine and blood, the markers (if they exist) are fixed on the chip using antibody-antigen reaction (Fig. 2 (a)). Micro-magnetic-beads made of ferromagnetic material covered with antibodies which also specifically react with the target marker, are then mixed into the solution. Thus, if the specimen includes the target marker, the micro-magnetic-beads are fixed on the device using the marker (antigen) as a "bonding" material (using the sandwich method [7]) (Fig. 2 (b)). The on-chip battery is then activated through the addition of salts such as NaCl chip has an array of Hall sensors beneath the antigen, which detect the magnetic field orthogonal to the surface. When a magnetic field parallel to the surface is applied, no output signal is generated without the micro-magnetic-beads because the magnetic field is orthogonal to the Hall sensor axis. On the other hand, if micro-magnetic-beads exist on the chip (i.e., the specimen includes the marker), the magnetic field's vertical component is induced, which can be detected by the Hall sensor array (Fig. 2 (d)). The sensing result is then wirelessly transmitted to a data acquisition unit. After inspection, the sensor chip can be thrown away.

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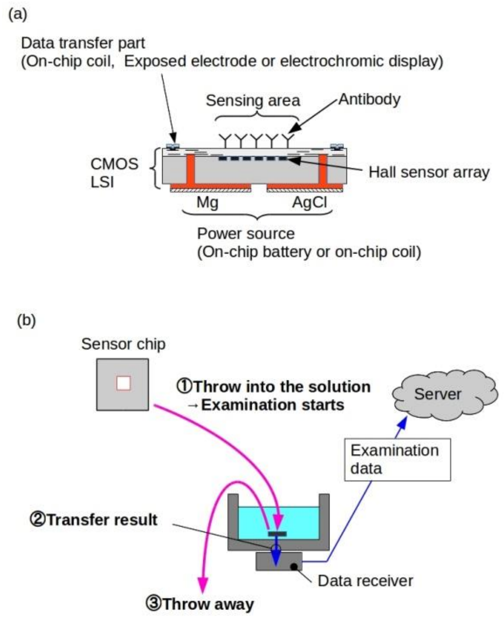

Figure 1. (a) Schematic of a disposal immune-sensor chip and (b) sensing system using the chip.

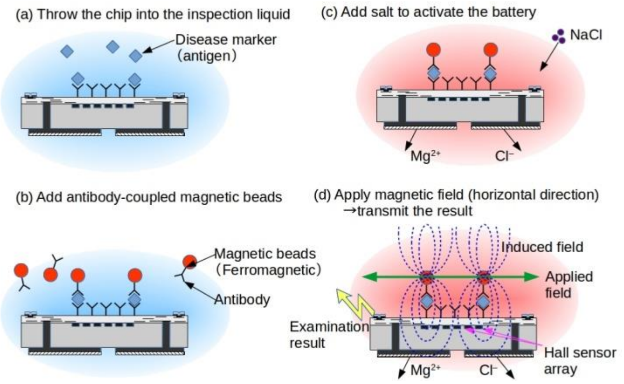

Figure 2. Sensing procedure. (a) The disease marker is trapped on the sensor surface using antigen-antibody reaction. (b) The magnetic beads were fixed in response to the presence of antigens. (c) The sensor chip activates an on-chip battery to add some salt. (d) The magnetic bead can be detected by measuring the induced magnetic field.

Sensor chip components

CMOS LSI for magnetic bead detection

Several previous studies have examined magnetic labeled immunoassays [8, 9], but these were based on complex and expensive technologies, such as superconducting quantum interference device (SQUID) or giant magnetic resistive device (GMR). Aytur proposed a CMOS-based wireless immunosensor [10] fabricated on a 0.25 μm standard CMOS rule with dual Damascene layers. The chip has a 32 by 32 Hall sensor pair array and each output of the pair is fed to a differential amplifier to detect magnetic beads. Figure 3 shows the CMOS chip with the Hall sensor array and signal processor.

In contrast, the proposed chip is designed to address the lower sensitivity and higher noise floor of the Hall sensor. The magnetic field generated by the magnetic bead decays at a cubed rate of the change in distance. To enhance the sensitivity, the sensor area was etched back so to minimize the distance between the magnetic beads and the semiconductor layer. This improves the sensing signal by an estimated factor of 21. To reduce noise, a drain current of the Hall sensor was modulated by RF. This converts the magnetic signal from the bead into much higher frequency regions where the noise floor is lower.

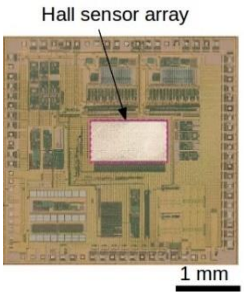

Figure 3. Hall sensor array and signal processor on CMOS chip.

Power source technologies

The sensor chip is made of CMOS-LSI, which requires electrical power. Wireless power feed methods include magnetic induction [11-13], photo voltaic cell [14, 15] and ultrasonic [16] and on-chip power generation methods such as electrochemical cells [17, 18] and bio-fuel cells [19].

The proposed system places a priority on minimizing production costs through the use of high power density and structural simplicity, thus giving advantages to magnetic induction power feeding and electrochemical cells.

Magnetic induction power feed

Magnetic induction power feeding is an approach for sensor chips. Onizuka wirelessly directly fed 2.5 mW directly through the inductive coupling of a CMOS chip at a distance of 20 μm [11]. However, the close proximity of the coil requires precise positioning.

We fabricated a test chip for wireless power feeding in a 0.18 μm standard CMOS process. As shown in Fig. 4, the chip has an 18-turns on-chip coil with a width of 15 μm and a peripheral area of 8.9 sq. mm. For wireless power feeding, a 10-turn transmission coil with a diameter of 8 mm is placed just above the chip, and a low drop rectifier circuit on the chip generates 142 μW output with a load of 2.2 kohm. For practical use, the transmission coil is intentionally misaligned and a 2 mm offset causes a 20% reduction of output power [20].

On-chip micro battery

Using an on-chip micro battery presents another solution. Figure 5 shows an on-chip micro battery which can be fabricated on the sensor chip using a screen printing method [21]. To simplify the system, a single cell battery should provide sufficient voltage and power for a CMOS chip. We respectively used Mg and AgCl as the anode and cathode materials. Chip size, and thus cost, can be minimized by using a micro-battery with a high power density.

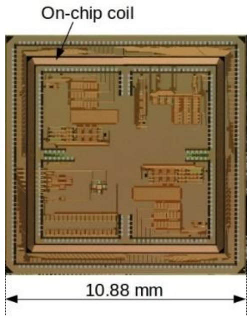

Figure 4. CMOS chip with an on-chip coil.

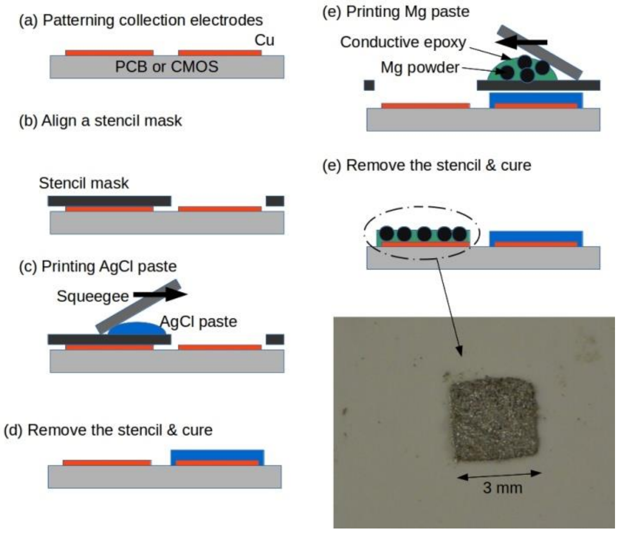

Figure 5. A screen printable on-chip Mg/AgCl battery.

Figure 6 shows the voltage and electric power generated by the on-chip battery [21]. The open circuit voltage and maximum power were respectively 1.6 V and 0.078 mW/mm^2, which are sufficient for a state-of-the-art low power CMOS chip.

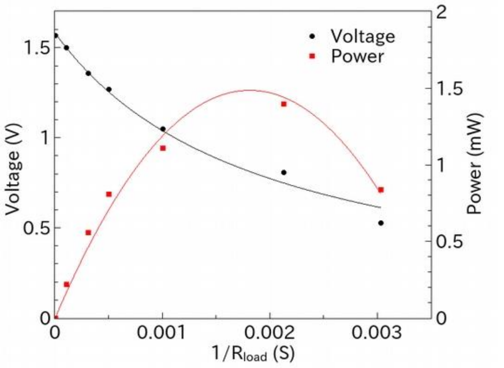

Figure 6. Performance of the on-chip Mg/AgCl battery. 0.14M NaCl solution was used as an electrolyte.

Data transfer technologies

The sensing data should be transferred to the external inspection system. Wireless data transfer is also required to reduce costs. Many wireless data transmission methods have been developed such as electric field coupling [4], magnetic field coupling [5, 22] and light emission [21]. Electro-magnetic waves cannot propagate through the electrolyte and thus cannot be used in this system. This paper introduces three methods for wireless data transfer: magnetic field coupling, electric field (capacitive) coupling and on-chip electrochromic displays.

Magnetic field coupling data transfer

The test chip obtained up to 2 mW of power through wireless coupling under a 25-30 dBm power feed at 80 MHz [10]. The coupling efficiency was approximately 8% at a distance of 1 mm. The chip extracted the clock signal from the wireless coupling, ran measurements, and digitized the output signal to transmit a serial code at 250 kbps. The signal was returned with a 40 MHz carrier and decoded using an I/Q demodulator and successfully digitized using an oscilloscope.

Capacitive coupling data transfer

Figure 7 shows the schematic of data transfer method using capacitive coupling. A voltage according to the transmitting digital data is applied to the exposed electrodes on the sensor chip. Receiver electrodes are capacitively coupled to the sending electrodes, thus the electric signal could be transferred through the electrolyte. Figure 8 shows the sending and as-received signals. The received signal was distorted by the high-pass characteristics of the capacitive coupling. As shown in Fig. 9, a digital signal processing method is used to compensate for the distortion. First, the high-pass filtered signal was numerically integrated. We can compensate for the baseline drift by using “0” levels at the beginning and end of the start condition. After digital processing, the transmitted data was successfully recovered.

Data transfer using on-chip electrochromic display

An electrochromic display fabricated on the sensor chip can show the digital data as a color image which can be easily observed by a CCD/CMOS camera. An electrochromic material such as polyaniline (PANi) changes its color depending on its oxidation state [23]. Energy is only required during the oxidation or reduction processes, thus minimizing power consumption. This provides advantages to other display devices, such as LCDs, through simplifying the structure and fabrication procedures. Figure 10 shows a schematic for the on-chip electrochromic display [24]. Au electrodes were deposited on a mimic CMOS chip made of Si, SIO_2 and Al, and SU-8 was patterned on them to protect the chip. The PANi thin film can be selectively grown on the Au electrodes by electro deposition. When zero voltage (vs Ag/AgCl reference electrode) was applied, the PANi was in a reduced state and the color was yellow. On the other hand, when positive voltage is applied to the electrode, the PANi film oxidized and the color changed to green (Fig. 10 (b)). The array of the PANi display as shown in Fig. 10 (c), showing 1 byte of data on the sensor chip.

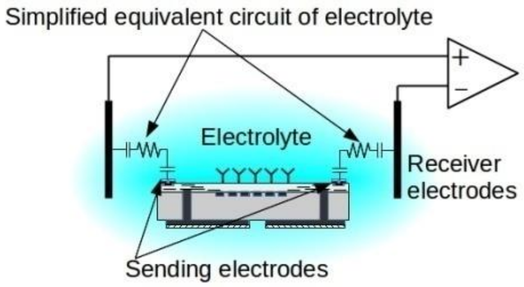

Figure 7. Schematic of a capacitive coupling data transfer method.

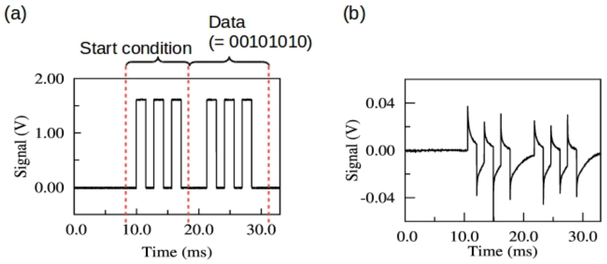

Figure 8. Experimental result of the capacitive coupling data transfer. (a) Sending data and (b) receiving data.

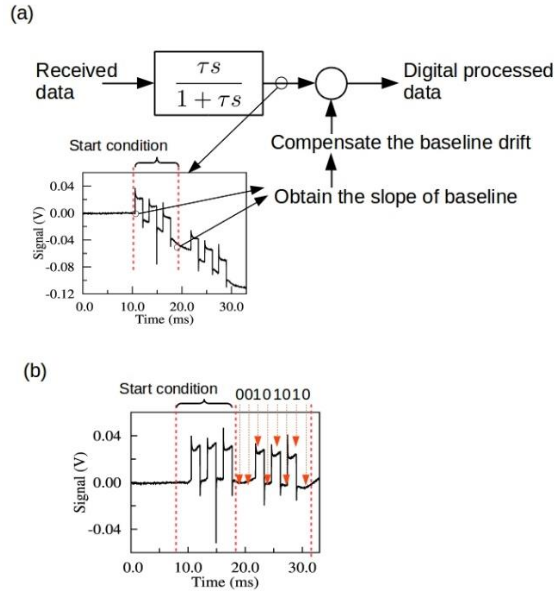

Figure 9. (a) Digital signal processing method and (b) recovered digital data.

Figure 11 shows the operational result of the PANi micro display. The pixel color was yellow under an applied voltage of 0 V vs Ag/AgCl. When the voltage increased to

0.4 V vs Ag/AgCl, color of the corresponding pixel changed to green. The energy consumption of the display was 0.675 µW/pixel. The response time for color change was as low as 100 ms.

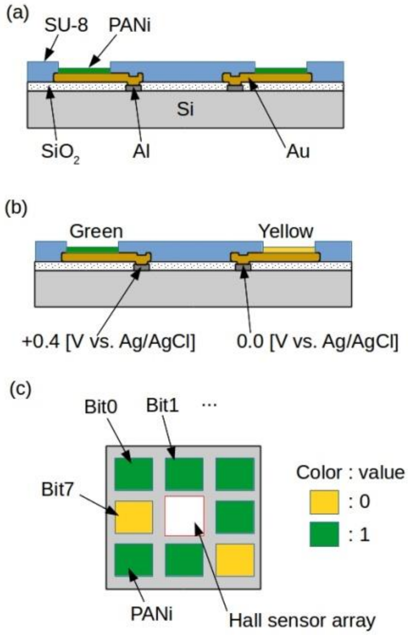

Figure 10. Schematic of an on-chip electrochromic display for optical data transfer.

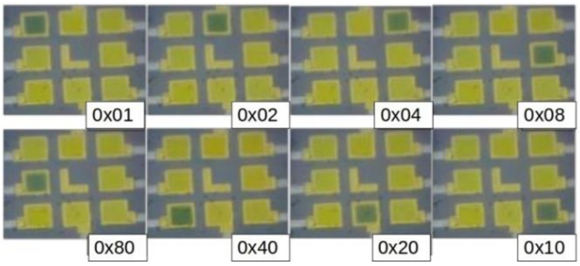

Figure 11. Operational result of the on-chip electrochromic display. The color of each pixel could be successfully controlled.

Summary

We propose an easy-to-use health monitoring system using a disposable bio-sensing chip. To reduce chip manufacturing costs, we integrated various wireless power sources and data transfer methods which can be easily fabricated on a CMOS chip. The use of a magnetic field coupling power feed, which only requires a micro coil, was demonstrated. To future reduce the chip area and cost, a high power density on-chip micro battery was developed for fabricated on the CMOS chip by a standard printing method. Wireless data transfer through the electrolyte was also demonstrated. The micro on-chip coil could successfully transfer data at rates as high as 250 kbps. The electric field coupling method, which does not need a large coil, was also demonstrated. In addition, an on-chip electrochromic display was developed to provide optical data transfer using a CCD/CMOS camera.

Any combination of the proposed power source and data transfer methods can be used for the proposed bio-sensor.

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